SAN2020
E-BOOK

Welcome

In the context of the COVID19 pandemic, the XXXV Annual Meeting of the Argentinian Society for Neuroscience Research took place under a ***virtual*** *format, opening an opportunity to widely reach the neuroscience community in Argentina and abroad.*

Conserving the classical structure the meeting included ***plenary lectures***, ***symposia***, ***young investigator talks*** *and* ***poster presentations***, *as well as* ***round tables*** *discussing career advancement, work environment topics and a special event dedicated to LATBrain (Latin American Brain Iniciative).*

The meeting was supported, as every year, on the principles of ***scientific excellence*** *and* ***nationwide representation, with a special emphasis in gender equality***.

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Inappropriate behavior can be reported to congresosan2020@gmail.com.

Program

	Oct 7	Oct 8	Oct 9
9:00 - 11:00	**Symposia Wed-S1 to Wed-S4:** Beckwith & de la Fuente, Falzone & Jerusalinsky, Kochen, Rayes.	**Symposia Thu-S5 to Thu-S9:** Amador, Bellini, Bianchi & Kamienkowski, Locatelli & Sumbre, Rossetti.	**Symposia Fri-S10 to Fri-S14:** Espósito & Morgenstern, Goldin, Pigino, Berardino & Sonzogni, Tagliazucchi
11:30 - 12:30	"Eduardo De Robertis" Plenary Lecture **Gustavo Murer: What mechanisms underlie Parkinson's disease symptoms?**	Plenary Lecture: **Zhigang He: From axon regeneration to function recovery after CNS injury**	Plenary Lecture: **Tracy Bale: 50 years since Leloir's Nobel: Maternal stress and energy signals critical to neurodevelopment.**
12:30 - 13:30		Latbrain Initiative	
13:30 - 14:30	Políticas de Ciencia y Técnica en Argentina		IBRO LARC CEPAL: Gender Survey Results
14:30 - 15:30	Young Investigator Talks: Wed-YIT-1 to Wed-YIT-4	Young Investigator Talks: Thu-YIT-5 to Thu-YIT-8	Oral Communications
16:00 - 17:00	Plenary Lecture: **Kay Tye: Neural Representations of Social Homeostasis**	"Hector Maldonado" Plenary Lecture: **Sheena Josselyn: Making memories in mice.**	"Ranwell Caputto" Plenary Lecture: **Juana Pasquini: Cinco décadas de Neurociencias en América Latina: Siguiendo los pasos de Ranwel Caputto**
17:00 - 19:30	E-Poster **Session 1**	E-Poster **Session 2**	E-Poster **Session 3**
19:30 - 21:00	Looking for a postdoc abroad? Tips for international postdoc interviews.	Asamblea SAN	

Plenaries

Wednesday 7th · 11:30 - 12:30

"De Robertis" Lecture:
What mechanisms underlie Parkinson's disease symptoms?

Gustavo Murer

Grupo de Neurociencia de Sistemas, Instituto de Fisiología y Biofísica Bernardo Houssay, Facultad de Medicina, Universidad de Buenos Aires

Parkinson's disease is caused by the loss of nigrostriatal dopaminergic neurons. Chronic dopamine deficiency raises functional and structural changes in the striatum that lead to the appearance of its main symptom: scarcity and slowness of voluntary movement. Given its unsettled etiology, current antiparkinsonian strategies aim at restoring stimulation of striatal dopamine receptors. The gold standard therapy is the administration of L-dopa, a dopamine precursor that alleviates motor symptoms in early stages of the disease. However, motor fluctuations (the return of symptoms before it is time for the next dose of L-dopa) and L-dopa-induced dyskinesia are common in advanced stages of the disease. During the talk I will overview our work with animal models of the disease on the mechanisms underlying Parkinsonism and L-dopa-induced dyskinesia.

Wednesday 7th · 16:00 - 17:00

Plenary Lecture:
Neural Representations of Social Homeostasis

Kay Tye

Salk Institute for Biological Studies

Most social species organize into social dominance hierarchies. These hierarchies decrease aggression, save energy, & maximize survival for the entire group. Individuals must consider their social rank in any social encounter and adjust their behavior accordingly. Despite social and dominance behaviors being critical for successful interactions with other group members and ultimately, our survival, it is not completely clear how the brain encodes social rank. The medial prefrontal cortex (mPFC) has been implicated in social dominance expression in rodents, and in social rank learning in humans. However, exactly how the mPFC encodes social rank and which circuits mediate this computation is not known. We developed a trial-based social competition assay in which mice compete for rewards, as well as a computer vision tool to track multiple identical animals. Together, these novel task and tool facilitated social dominance behavior quantification. We found that the mPFC encodes behavior during the competition using multiple-hidden states that are rank-independent, and mPFC population dynamics encode social rank and competitive success. The population social rank representation translated into differences at the individual cell level in the responses to task-relevant events across ranks. Finally, we identified a circuit of mPFC cells that

Plenaries

project to the lateral hypothalamus that contribute to the social rank encoding and drive dominance behavior during the reward competition.

Thursday 8th · 11:30 - 12:30

Plenary Lecture:
From axon regeneration to function recovery after CNS injury

Zhigang He
Boston Children's Hospital

Spinal cord injury disrupts the axonal connection between the brain and the spinal cord below the lesion, contributing to unrecoverable functional deficits. A long term interest of my lab is to develop novel repair strategies to promote axon regeneration and restore lost function. Towards this, our research are focusing on the following questions: (1). Why injured axons fail to regenerate and how to promote axon regeneration? (2). How to increase the functionality of regenerated or spared axons after injury? I will present our recent results on each of these fronts.

Thursday 8th · 16:00 - 17:00

"Hector Maldonado" Lecture:
Making memories in mice

Sheena Josselyn
Hospital for Sick Children/University of Toronto

Understanding how the brain uses information is a fundamental goal of neuroscience. Several human disorders (ranging from autism spectrum disorder to PTSD to Alzheimer's disease) may stem from disrupted information processing. Therefore, this basic knowledge is not only critical for understanding normal brain function, but also vital for the development of new treatment strategies for these disorders. Memory may be defined as the retention over time of internal representations gained through experience, and the capacity to reconstruct these representations at later times. Long-lasting physical brain changes ('engrams') are thought to encode these internal representations. The concept of a physical memory trace likely originated in ancient Greece, although it wasn't until 1904 that Richard Semon first coined the term 'engram'. Despite its long history, finding a specific engram has been challenging, likely because an engram is encoded at multiple levels (epigenetic, synaptic, cell assembly). My lab is interested in understanding how specific neurons are recruited or allocated to an engram, and how neuronal membership in an engram may change over time or with new experience.

Plenaries

Friday 9th · 11:30 - 12:30

Plenary Lecture: 50 years since Leloir's Nobel: Maternal stress and energy signals critical to neurodevelopment

Tracy Bale

University of Maryland School of Medicine

Profound disparities exist in maternal-child health outcomes between racial and ethnic groups. Africa-American (AA) women in the United States are significantly more likely to experience preterm birth, fetal growth restriction, maternal and infant mortality than white women. For instance, infant mortality rates remain exceptionally high in the U.S., where babies born to AA women die at 2.5X the rate as babies born to white women. The mechanisms through which fetal antecedents contribute to morbidity and mortality involves dynamic interactions between the maternal and fetal environments. Maternal stress, obesity and diabetes are known risk factors for offspring, including significant impacts on neurodevelopment. In several mouse models in our lab, we have identified maternal and transplacental signals important to brain development impacted directly and indirectly by the maternal milieu. For example, we identified the X-linked, stress sensitive, nutrient sensor O-glycosyltransferase (OGT) as a placental biomarker of maternal stress. Genetic placental-specific targeting of OGT produced developmental and metabolic impairments, and lasting impacts on hypothalamic function. Similarly, in our mouse model of maternal diet high in fat and low in soluble fermentable fiber, pregnant mice on a low fiber diet produce offspring with high levels of placental hypoxia, gut and brain inflammation and higher rates of infant mortality due to the highly proinflammatory prenatal environment.

Friday 9th · 16:00 - 17:00

"Ranwel Caputto" Lecture: Five decades of neuroscience in Latin America: following in the footsteps of Ranwel Caputto

Juana María Pasquini

Juana M. Pasquini Depto Química Biológica e IQUIFIB Facultad de Farmacia y Bioquímica UBA- CONICET Buenos Aires Argentina

Latin American neurochemistry was born in different countries between the 1950s and 1960s with different degrees of representation and participation. Right from the start, neurochemistry was very prominent in Venezuela, Argentina, Mexico, Uruguay, Chile and Brazil. As a matter of fact, due to the important development of neuroscience en Argentina ISN organized the second meeting in Buenos Aires, in 2001. After a brief introduction, we will take a look at the development of neurochemistry in Latin America. Argentina was the home of Ranwel Caputto. This Ranwel Caputto Lecture will highlight Caputto's personality and leadership in the neurochemistry of the twentieth century. We will also seize the opportunity to outline you on a tour of the experimental work that my students have done over the years, especially in lines related to iron metabolism in the central nervous system.

Symposia

Wednesday · Oct 7th · 9:00 - 11:00

Open Neuroscience: new approaches for new tools

Chairs: ***Verónica de la fuente.*** *IFIBYNE-UBA-CONICET.* ***Esteban J. Beckwith.*** *Life Sciences Department, Imperial College London*

High-throughput Monitoring of Insect Behaviours, From the Lab to the Field

QUENTIN GEISSMANN
University of British Columbia

Organisms are adapted to environments where conditions are largely periodic (e.g. daily, yearly), and therefore partially predictable. They have evolved mechanisms to modulate their physiology and behaviour through time, using their internal clocks to effectively 'model' the future state of their environment. The study circadian insect behaviours has been limited by our methodological ability to classify and quantify behaviours over long durations, for a large number of individuals. I will present two open-source and high-throughput methods based on raspberry pi cameras that were built to address these limitations. First, the Ethoscope, which is primarily developed to study sleep in the laboratory. Second, the Sticky pi, a smart insect trap that can score when, where and which insects are active. I will use these two tools as examples to highlight the tremendous opportunities that, as a scientific community, we are given to develop, share and adapt both hardware and software. Such collective and distributed ownership of open research tools, I will argue, often leads to very innovative research.

Open source hardware for behavioral neuroscience research

LEX KRAVITZ
Washington University in St Louis

Neuroscientists often invent new devices and methods to further their experiments. Recent developments in prototyping and fabrication such as 3D printing, laser cutting, and production of custom printed circuit boards have lowered the bar to entry for designing novel hardware. This has produced a wave of open-source hardware devices that have enabled new experiments and answers in neuroscience research. The Kravitz Lab has developed several devices for measuring rodent behavior including smart pellet dispensers, embedded video tracking cameras, and home-cage based activity sensors. This talk will review the development and use of these devices, and provide an overview of the motivation behind producing and sharing open-source hardware for neuroscience research.

Symposia

Open-source tools for systems neuroscience

JAKOB VOIGTS
MIT, Open Ephys.

Open-source tools are gaining an increasing foothold in neuroscience. The rising complexity of experiments in systems neuroscience has led to a need for multiple parts of a setup to work together seamlessly, which means that open-source tools that expose more interfaces and can be understood and modified more easily have an advantage and allow scientists to conduct better experiments with less effort than closed tools. Open Ephys is a nonprofit with team members distributed all around the world. Our mission is to advance our understanding of the brain by promoting community ownership of the tools we use to study it. We are making and distributing cutting edge tools that exploit modern technology to bring down the price and complexity of neuroscience experiments. A large component of this is to take tools that were developed in academic labs and helping with documentation, community support, and distribution. More recently, we have been working on establishing standards that make it possible to combine many existing experimental methods, such as miniaturized microscopes, electrode drive implants, or silicon probes seamlessly in one system. In the longer term, our development of new tools, interfaces and our standardization efforts have the goal of making it possible for scientists to easily run complex experiments that span from complex behaviors and tasks, multiple recording modalities, to easy access to data processing pipelines.

Just Another Tool for Online Studies": An open-source tool to conduct cognitive science experiments online.

ELISA FILEVICH
Humboldt-Universität zu Berlin.

Behavioural data collection for cognitive (neuro)science traditionally takes place in a physical laboratory environment: participants come to the lab, receive instructions from an experimenter and complete a computer-based task. This provides high control over stimulus presentation and participants' behaviour, but also comes at a very high cost in time and money. This naturally sets a limit to the number of participants that can be collected, and is one of the factors contributing to the reproducibility crisis in the field. As an alternative, in cases where only behavioural data are collected, experiments can be conducted online, with participants performing cognitive tasks from their homes and submitting result data through the Internet. This dramatically decreases the time and costs required to collect a full dataset, in turn allowing for larger, more diverse —and thus more representative— samples than the common sample of university students. We have developed an open-source web application to assist in setting up a server for online data collection (JATOS, jatos.org). JATOS supports online studies, including longitudinal and group studies. I will detail the requirements to run a study online, and describe the most common tools available to build and and

Symposia

run studies online. I will also give an overview of the advantages and (more importantly), limitations of collecting data online.

Wednesday · Oct 7th · 9:00 - 11:00

Amyloid β Peptide, Tau aProtein, NGF Metabolism. Early Biomarkers and Associated Mechanisms in Alzheimer´s Diseasec

Chairs: ***Diana Jerusalinsky.*** *IBCN, UBA-CONICET.* ***Tomas Falzone.*** *CONICET-UBA*

Amyloid beta oligomers in neural development and degeneration

WILLIAM KLEIN

Departments of Neurobiology and Neurology, Northwestern University

Human amyloid beta (Aβ42) is unusually prone to self-association, and its oligomers manifest a gain-of-function neurotoxicity. Evidence strongly indicates that soluble Aβ oligomers (AβOs), not amyloid plaques, are the pathogenic form of Aβ in Alzheimer's disease (AD). AβOs manifest in an AD-dependent manner in humans and animal models. Experimentally, they induce memory dysfunction and multiple facets of AD neuropathology. Evolutionary retention of the toxin-forming Aβ sequence is surprising but could be explained if, under some circumstances, AβOs were essential to neural function. Supporting this idea, we have discovered that AβOs are transiently expressed in the developing retina of chick (which has an Aβ sequence identical to humans) and are required for proper cell placement. AβOs appear first in the optic nerve layer, spread outward into specific cell bodies and synaptic layers, then down-regulate, with low expression remaining near photoreceptors. AβO expression is like a molecular wave progressing across the retina, virtually disappearing when circuitry has been established. Intravitreal injections of BACE inhibitor or AβO antibody during development cause disrupted nerve cell placement and formation of retina folds as found in various pathological conditions. AβOs thus constitute a new type of peptidergic hormone with a critical short-lived role in CNS development, suggesting AβO presence in AD may be a pathological reprise of a role played in neural development.

Symposia

From balanced axonal transport in health, to impaired dynamics in human models of tauopathies: untangling the road to neurodegeneration

TOMAS FALZONE
CONICET-UBA

The microtubule associated protein Tau undergoes many pos-translational modifications such as a tight developmental regulation of balanced 3R-4R tau isoform expression in the human nervous system. Tau protein dysfunction is a key step in the process leading to neurodegeneration in tauopathies and its imbalance, due to overexpression or either towards 3R or 4R tau isoforms, has been closely associated with disease. While some disease hypotheses are focused on the toxic gain of function of abnormal tau aggregates, others propose that tau loss of function properties are involved in triggering neuronal death. Different studies have unlocked new functional roles for tau in neuronal homeostasis that range from the regulation of axonal transport dynamics to the modulation of neuron electrical properties. However, little is known on how tau isoform balance or tau protein levels exert a regulation over these critical cellular functions. We have modulated tau isoforms or its expression levels in human derived neurons to unravel the molecular pathways in which tau control axonal transport. Our work supports the role of tau in the tight control of intrinsic neuronal phenotypes such as the regulation of molecular motor activity in axonal transport making it relevant for understanding neuronal dysfunction that can lead to disease.

The deregulation of the NGF metabolism is present as from preclinical Alzheimer's disease and it is revealed in body fluids.

A. CLAUDIO CUELLO
Department of Pharmacology and Therapeutics, McGill University; Visiting Professor, Oxford University

Our laboratory (Bruno and Cuello, PNAS, 2006) discovered a novel NGF metabolic pathway demonstrating that proNGF is released in an activity-dependent manner and converted to mature NGF (mNGF) in the extracellular space and that the remaining, receptor-unbound mNGF, is ultimately degraded by metalloproteases. This pathway has been validated pharmacologically and shown to be compromised in Alzheimer's and in Down syndrome. More recently, we have found that the deregulation of the NGF metabolism is already present in DS at AD pre-symptomatic stages (Iulita et al Alz&Dementia 2016) and more recently found deregulated in the brains of non-cognitively impaired bearing asymptomatic AD pathology (Pentz et al, Mol. Psychiatry, 2020). The deregulation of the NGF pathway could reveal "silent" (preclinical) AD pathology. We found that incremental levels of plasma proNGF in DS individuals in transition from DS-AD asymptomatic to DS-AD symptomatic predicted a severe subsequent cognitive deterioration (Iulita et al, Alz&Dementia 2016). A deregulation more faithfully revealed in the cerebrospinal fluid from DS AD asymptomatic and symptomatic (Pentz et al, unpublished). CONCLUSIONS The above observations indicate that

the investigation of levels of key molecules of NGF metabolic pathway in plasma and in cerebrospinal fluids offers an opportunity to reveal the ongoing, silent, preclinical Alzheimer's pathology as well as to facilitate preclinical AD therapeutic interventions.

Cognitive studies and biomarkers in predementia stage of patients with Alzheimer Disease

RICARDO ALLEGRI
Instituto Neurológico Fleni

The main pathophysiological mechanism underlying Alzheimer's disease (AD) involves extracellular amyloid deposits and neurofibrillary degeneration secondary to abnormal tau protein hyperphosphorylation. AD is present many years before symptoms develop. Bateman et al. detected amyloid deposits over 20 years, and neurofibrillary degeneration over 10 years, prior to the onset of clinical symptoms. Prior to the development of the AD biomarker, clinical diagnosis was identified as either possible or probable, and definite diagnosis needed to be confirmed by post-mortem brain tissue histopathology The discovery of AD biomarkers gave rise to a new paradigm in relation to degenerative dementias. The biomarker assay allows in vivo assessment of pathophysiological disease traits. Current biomarkers used in clinic for AD include: Aβ1-42, total tau and phosphorylated tau assay in cerebrospinal fluid (CSF), tructural neuroimaging studies such as brain magnetic resonance imaging (MRI) and hippocampal volume analysis, functional neuroimaging of metabolic activity such as fluorodesoxyglucose (FDG) positron emission tomography (PET) and Protein-identifying neuroimaging using amyloid and tau PET. We like to describe our experience in clinical practice with the use of biomarkers in predementia stages of patients with Alzheimer Disease and the future with the next blood AD biomarkers.

Symposia

Wednesday · Oct 7th · 9:00 - 11:00

New advances in the analysis of neuroimages: their application to the study of functional and morphometric aspects of the human brain.

Chairs: ***Sylvia Kochen.*** *(ENyS), CONICET – Univ. Nacional A. Jauretche (UNAJ) – Hosp. El Cruce "N. Kirchner", F. Varela, Pcia Buenos Aires.*

Voxel-Based Morphometry - From the lab into the clinic

IGNACIO LARRABIDE

Pladema - CONICET/UNICEN

Voxel-based morphometry is a computational statistics approach for neuroanatomy that measures differences in local concentrations of brain tissue, through a voxel-wise comparison of multiple brain images. Its single subject version, which relaxes the statistical hypothesis, compares and studies an individual to a group in search for local tissue density differences. Despite this technique having been known for a while, it has not been largely used or extensively validated to be used in a clinical setup. In this talk, we will present the latest results along this line, its potential use and the clinical value of VBM in the clinical practice.

Application of machine learning techniques to the study of the human brain: methodological approaches, advances and challenges

PATRICIO ANDRES DONNELLY KEHOE

Centro Internacional Franco Argentino de Ciencias de la Información y de Sistemas (CIFASIS-CONICET)

The use of machine learning has become widespread in various areas related to medicine. Its application in MRI neuroimaging is in a state of permanent advance, and multiple initiatives point to a multimodal, multicenter implementation with a mainly translational focus. In this dissertation, we will discuss the main challenges and approaches to face them. We will analyze a framework to generate massive datasets, including the interaction with image acquisition systems (from a manual to an automated approach), the requirements at the clinical record level to develop translational methods, and harmonization to generate knowledge bases with images from different MRI machines. Then, we will present various techniques for the systematic extraction of robust features in a multimodal approach, and the use of classifiers, deepening into multiple classifier systems (MCSs), Random Forest (RF), and Deep Neural Networks (DNN).

Structural DWI characterization of structural connectivity and volumetry MR analysis in Epilepsy Patients.

JUAN PABLO PRINCICH

ENyS - Centro de Estudios en Neurociencias y Sistemas Complejos.

During this talk i will address methodological issues related to MRI performed in epilepsy patients. Will discuss about DWI structural connectivity estimation and topology findings on a population of patients with epilepsy and malformation of cortical development (FCD). In the second part of the presentation i will show performance abilities of automatic segmentation and atlasing softwares implemented on a dataset of hippocampal sclerosis patients with epilepsy. Additionally will debate about potential MRI features that can be evaluated wit more advanced analysis methods. Finally i will address the importance of formulating biological relevant hypothesis to be investigated with modern analysis techniques.

Applying multimodal neuroimaging to study human brain plasticity.

VALERIA DELLA-MAGGIORE

IFIBIO, Facultad de Medicina, Universidad de Buenos Aires

In the past decades, magnetic resonance imaging (MRI) has contributed significantly to our understanding of brain mechanisms and the identification of biomarkers of neurological and psychiatric diseases in humans. However, each MRI sequence on its own has several limitations. For example, a functional sequence (BOLD) allows studying dynamic changes in brain activity induced by learning but not the neuroplasticity associated with these changes. The combination of different types of sequences (functional, structural and diffusion), allows to address more complex questions and identify subtle changes in brain morphology and function, such as those associated with learning. In this presentation, we will discuss this multimodal approach in the context of a study aimed at characterising the role of the hippocampus in the early consolidation of motor memories.

Symposia

Wednesday · Oct 7th · 9:00 - 11:00

Invertebrate models to address fundamental questions in neurobiology

Chair: ***Tomas Diego Rayes.*** *Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB) Departamento de Biología, Bioquimica y Farmacia UNS.*

Polarization vision as a source of visual contrast in arthropods

MARTIN BERÓN DE ASTRADA

Instituto de Biociencias, Biotecnología y Biología Traslacional (IB3); Dpto. de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales; UBA

The polarization of light is a light quality invisible for the human eye. However, the sensitivity to the angle of light polarization to enhance visual contrast has been recognized in a number of animals inhabiting aquatic environments. So far, the visual mechanisms underlying such capabilities remain unknown. In the last couple of years we have studied the mechanisms underlying polarization vision in the crab Neohelice granulata. We have quantified animals' escape response and changes in heart rate as indexes of visual sensitivity. By presenting polarized motion stimuli with only linear polarization contrast (no intensity or spectral contrast) we observed maximum animals' responses when object and background polarizations were aligned with the vertical and horizontal orientations. The addition of polarization contrast to threatening intensity contrast stimuli enhanced significantly a low threshold alert response of the animals but produced no effect on higher threshold defensive behaviors. In line with theoretical models, our results provide experimental evidence that crabs perform a two-channel (vertical/horizontal) computation to achieve polarization contrast vision. We will discuss how such a two channel system maximizes information acquisition in the animals' natural environment together with the limitations that polarization information processing might have.

The Drosophila Ih channel shapes circadian rhythms and sleep through the control of neuronal bursting frequency

NARA MURARO

IBioBA-CONICET-MPSP, Argentina

Circadian rhythms have been extensively studied in Drosophila, however, still little is known about how the electrical properties of clock neurons are specified. We have performed a behavioral genetic screen through the downregulation of candidate ion channels in the lateral ventral neurons (LNvs) and show that the hyperpolarization-activated cation current Ih is important for the behaviors that

the LNvs command: temporal organization of locomotor activity and sleep. Using whole-cell patch clamp electrophysiology we demonstrate that small LNvs are bursting neurons, and that Ih is necessary to achieve the high frequency bursting firing pattern characteristic of both types of LNvs. Since firing in bursts has been associated to neuropeptide release, we hypothesized that Ih would be important for LNvs communication. Indeed, we demonstrate that Ih is fundamental for the recruitment of PDF filled dense core vesicles to the terminals at the dorsal protocerebrum and for their timed release, affecting the temporal coordination of circadian behaviors.

Actuating a memory: how C. elegans remembers a learned behavioral preference

DANIEL COLÓN-RAMOS

Department of Neuroscience, Yale University School of Medicine, CT, USA

How different plasticity mechanisms act together in vivo and at a cellular level to transform sensory information into behavior is not well understood. We show that in Caenorhabditis elegans two plasticity mechanisms-sensory adaptation and presynaptic plasticity-act within a single cell to encode thermosensory information and actuate a temperature preference memory. Sensory adaptation adjusts the temperature range of the sensory neuron (called AFD) to optimize detection of temperature fluctuations associated with migration. Presynaptic plasticity in AFD is regulated by the conserved kinase nPKCε and transforms thermosensory information into a behavioral preference. Bypassing AFD presynaptic plasticity predictably changes learned behavioral preferences without affecting sensory responses. Our findings indicate that two distinct neuroplasticity mechanisms function together through a single-cell logic system to enact thermotactic behavior.

A clock-controlled vitamin A pathway in the brain mediates seasonal photoperiodic responsiveness in the monarch butterfly

CHRISTINE MERLIN

Texas A&M University, USA

Seasonal adaptation to changes in light:dark regimes (i.e., photoperiod) allows organisms living at temperate latitudes to anticipate environmental changes. The circadian system has been implicated in measurement and response to the photoperiod. Yet, the key molecular pathways linking clock genes or the circadian clock to insect photoperiodic responses remain largely unknown. We showed that inactivating the clock in the North American monarch butterfly using loss-of-function mutants

Symposia

for circadian activators and repressor abolishes photoperiodic responses in reproductive output. Transcriptomic approaches in the brain of monarchs raised in long and short photoperiods, summer monarchs, and fall migrants revealed a molecular signature of seasonal-specific rhythmic gene expression that included several genes belonging to the vitamin A pathway. Rhythmic expression of these genes was abolished in clock-deficient mutants, suggesting that the vitamin A pathway operates downstream of the circadian clock. Importantly, a CRISPR/Cas9-mediated loss-of-function mutation in the gene encoding the pathway's rate-limiting enzyme, ninaB1, abolished photoperiod responsiveness independently of visual function in the compound eye and without affecting circadian rhythms. Together, these results provide the first genetic evidence that the clock-controlled vitamin A pathway mediates photoperiod responsiveness in an insect, a function that could be evolutionary conserved in animals.

Thursday · Oct 8th · 9:00 - 11:00

Auditory processing, vocal production and motor control

Chair: ***Ana Amador.*** *Dept. of Physics, University of Buenos Aires and IFIBA, CONICET, ARGENTINA*

Tuning Auditory Circuits for Vocal Communication

SARAH WOOLLEY
Columbia University

Social communication reflects the coordinated development of sensory and motor circuits around signals that convey information. The young brain learning to communicate with hearing and voice builds auditory and vocal motor circuits that are functionally coupled to perceive and produce similar signals. I will describe progress using songbirds to understand how species identity dictates the capacities and limits of vocal learning, how early experience shapes auditory and vocal circuits, and how species and learning combine to map auditory tuning onto vocal acoustics.

Low dimensional models and electrophysiology to study neural dynamics in songbirds

ANA AMADOR
Dept. of Physics, University of Buenos Aires and IFIBA, CONICET, ARGENTINA

Symposia

Birdsong is a complex motor activity that emerges from the interaction between the peripheral system, the central nervous system and the environment. The similarities to human speech, both in production and learning, have positioned songbirds as unique animal models for studying the production and perception of this learned motor skill. In this work, I will present a low dimensional dynamical system as a model of the avian neural network for song production. We developed a neural model in which the variables were the average activities of different neural populations within the nuclei of the song system. We performed electrophysiological experiments to record neural activity from one of these nuclei during song production in canaries (Serinus canaria) and found that the low dimensional model could reproduce the neural dynamics observed. Also, this model could reproduce the respiratory motor patterns used to generate song. We showed that sparse activity in one of the neural nuclei could drive a more complex activity downstream in the network. This interdisciplinary work shows how low dimensional models can be a valuable tool for studying the emergence of complex motor tasks.

Mechanisms for variability and plasticity in vocal motor performance in songbirds

MIMI KAO
Tufts University

Complex motor skills, such as speech or playing a musical instrument, are not innately programmed, but are learned through a process of trial and error. Learning requires motor exploration and performance evaluation. How are these processes implemented in the brain and what happens in disease? Songbirds provide an experimentally tractable model to address these questions. Like humans, they learn to vocalize, first by listening to the sounds of adults during a sensitive period and then by using auditory feedback to practice and modify their vocalizations. In addition, songbirds possess a discrete cortical–basal ganglia circuit specialized for learning and producing song. Variable burst firing in the cortical outflow nucleus of this circuit, LMAN, drives song variability, and manipulations that abolish burst firing in LMAN eliminate song plasticity. Here, I will describe evidence that neurons in this circuit have access to feedback signals, gradually changing their activity in response to feedback perturbation. In addition, I will show that changing the timing and amount of LMAN bursting is sufficient to drive cumulative changes in the acoustic features, timing, and sequence of song. Subsequent inactivation of LMAN did not restore song, indicating that changes in vocal output were encoded in the motor circuit. Together, these findings highlight the importance of temporally precise burst firing in cortical–basal circuits for motor performance, plasticity, and pathology.

From Song to Synapse

RICHARD MOONEY
Department of Neurobiology Duke University

Symposia

Vocalizations are an essential medium for social recognition and sexual signaling in mammals and birds. Whereas many types of vocalizations are innate, including courtship vocalizations of mice, songbirds learn their courtship songs in a process with many parallels to human speech learning. I will discuss recent advances from our lab highlighting the neural mechanisms that enable birdsong learning, including the formation of auditory memories of vocal models, evaluation of song performance, and basal ganglia-dependent vocal exploration and reinforcement. How the learned song is integrated with innate vocalizations will also be considered, with reference to recent studies that genetically map neural circuits for innate vocalizations in mice.

Thursday · Oct 8th · 9:00 - 11:00

Stress, Inflammation and Aging: What`s new on this relationship?

Chair: ***Maria Jose Bellini.*** *Centro de Investigaciones Biomédicas (CINBIO). Universidad de Vigo (España)*

Perinatal stress and brain inflammation

YOLANDA DIZ-CHAVES

Centro de Investigaciones Biomédicas (CINBIO). Universidad de Vigo (España)

Stressing life experiences occurring during perinatal life may result in permanent alterations in the function of the nervous, immune and metabolic systems. Maternal stress increases the inflammatory response in the offspring, altering brain function by the modification of local inflammation, increasing the risk of depression, schizophrenia and autism. Mother restraint stress (MRS), increases IL1β mRNA levels in the hippocampus of both male and female pups. Also, TNFα mRNA levels and immunoreactivity in CA1 are increased in males. The total number and reactivity of Iba1-immunoreactive cells are augmented both in male and females, corresponding to a reactive status. Maternal perinatal food restriction (MPFR) in rats, increases the mRNA expression of proinflammatory mediators and the number of GFAP and Iba1-immunopositive cells in the dentate gyrus of males but not in females rats. Moreover, LPS administration induces a significant increase in proinflammatory indicators and Iba1-immunoreactive cells in the hippocampus of prenatally stressed pups. Perinatal stress-induced generates long-lasting modifications in the inflammatory status of the

hippocampus both in mice and rats. Also, an evident sexual dimorphism in the case of MPFR is observed. Furthermore, MRS alters the immune response of the hippocampus to peripheral inflammation that results in enhanced activation of microglia and astrocytes in response to a proinflammatory insult.

Circadian prenatal programming of the stress axis

MARIANA ASTIZ

Institute of Neurobiology, Center of Brain, Behavior and Metabolism, University of Lübeck, Germany

During pregnancy, maternal endocrine signals such as glucocorticoids (GCs) drive fetal development and program physiology. GCs are produced by the hypothalamic-pituitary-adrenal (HPA) axis every day at the beginning of the active phase and in response to stress. A disruption of maternal GC homeostasis, increases the offspring's risk of developing psychiatric disorders later in life. We show that the time of GC administration, rather than the dose, is a predictor of behavioral phenotypes in mice. Offspring of mothers receiving GCs out-of-phase compared to their own circadian rhythm show elevated anxiety, impaired stress coping and stress axis regulation. On the other hand, if the maternal exposure takes place at the beginning of the active phase, the phenotype of the offspring is comparable to that of control mice. These differences suggest the involvement of the circadian clock "gating" the GC-induced programming effects. When we followed up the underlying mechanism, we found that the fetal clock, specifically the clock protein REVERBα, determines the sensitivity to GC treatment by controlling the daily availability of the GC receptor (GR) in the hypothalamus. Similarly, in a retrospective observational analysis in humans we found that children whose mothers received antenatal GCs out-of-phase compared to their own circadian rhythm tend to show altered stress-related behavior at the age of 5.

Different responses of aging rodents to therapeutic approaches with IGF-1 gene therapy: Does sex matter?

MARIA JOSE BELLINI

Instituto de Investigaciones Bioquímicas de La Plata (INIBIOLP)- Facultad de Ciencias Médicas, Universidad Nacional de La Plata-CONICET-La Plata, Buenos Aires, Argentina

Our research focusses on the possible modulation of neural cells and brain outcomes during aging process employing IGF-1 gene therapy, a molecule known to be essential for synaptic plasticity and neuronal survival. In this work, we explored the effects of gene therapy in two experimental models of natural aging: aged mice (male and female) and senile female rat. First, we quantified frailty through a clinical assessment of aged mice, to explain the heterogeneity in clinical outcomes for older patients. We compared the 31-items Clinical Frailty Index and a set of behavioral tests in mice of 24 months before and after intramuscular IGF-1 gene therapy. We observed a clear effect of therapy in both sexes. Considering that sex is a factor that influences the incidence of all major complex

diseases, our principal outcome is to use different frailty indexes calculations to identify sex differences and therapy efficiency in aging models. We also explore the effects of IGF-1 gene therapy on microglial cells in 28 months old female rats. We found that IGF-1 influences microglial number, phagocytic activity, and transcriptomic expression; suggesting that IGF-1 gene therapy could be an effective treatment to modulate microglial activation and to induce an anti-inflammatory microenvironment favorable to neuronal survival. Our work reinforces the beneficial effects of IGF-1 on aging and could be a useful tool to treat age-related neurodegenerative pathologies in a sex-specific manner.
cinbio.es

Sex differences in brain mitochondria: Differential response and susceptibility to cellular damage?

GEORGE E. BARRETO
Department of Biological Sciences, University of Limerick, Limerick, Ireland

Mitochondria respond differentially to brain damage, and these mechanisms may be important during acute inflammation and for repair during the post-injury period. At basal levels, the expression of cytokines and chemokines are different in men vs women's brain, and so is the production of oxidative stress coupled with the mitochondrial membrane potential and the mitochondrial permeability transition pore. Interestingly, the activity/expression of some mitochondrial complexes of the electron transport chain are more expressed in women, and this raises the hypothesis that endogenous hormones may be playing a role in promoting said mitochondrial activity. By inducing early menopause in animals (ovariectomy and orchidectomy) and cells (siRNA aromatase) there is a shift in lipid metabolism and this is reflected on how mitochondria respond to metabolic damage. A large part of these effects may be related to the expression of neuroglobin, a cytosolic protein, but which, in the face of brain trauma, is transported to mitochondria where it interacts with Complex I and, mostly Complex III, and proteins such as cyc1, ETFDH/Q/ETFA and p32/c1qbp complexes, thus regulating apoptotic mechanisms, oxidative phosphorylation, mitochondrial immunometabolism, and these are all different depending on the sex. In this talk, we will discuss these mitochondrial mechanisms responsible for a response to metabolic damage, emphasizing how the female mitochondria respond differently compared to males.

Symposia

Thursday · Oct 8th · 9:00 - 11:00

Representation of language networks. A talk between the Brain and Artificial Intelligence

Chairs: ***Bruno Bianchi.*** *Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN-UBA, CONICET.* ***Juan Esteban Kamienkowski.*** *Laboratorio de Inteligencia Artificial Aplicada (Instituto de Ciencias de la Computación, FCEyN, UBA - CONICET)*

Understanding naturalistic speech processing using invasive and noninvasive electrophysiology

LIBERTY HAMILTON
The University of Texas at Austin

Understanding natural speech involves parsing complex acoustic cues from multiple sources in order to create meaningful percepts. Our work uses encoding models to understand how the brain extracts phonological and acoustic information from naturalistic speech stimuli, using a combination of intracranial electrophysiology in patients undergoing surgical treatment for epilepsy and scalp EEG in non-patient participants. This talk will describe efforts to extend encoding models to continuous speech from highly dynamic, noisy, audiovisual stimuli.

Computational models of language processing reveal concept representations in the human brain

ALEXANDER HUTH
Departments of Computer Science & Neuroscience, The University of Texas at Austin

Natural language evokes widespread BOLD responses in the human brain, and these responses are mostly selective for particular concepts. Here we use voxelwise encoding models combined with novel computational methods to probe several aspects of concept-specific responses. First, are concept representations grounded in sensory modalities, or are they purely amodal? Using visually-grounded word embedding spaces we find that not only are representations of concrete words (e.g. apple) grounded in visual properties, but so are representations of closely related abstract words (e.g. education). Second, is it sufficient to model how the brain responds to single words, or should we also consider more complete phrases? Using new machine learning techniques we find that phrase-based models are significantly and substantially better for predicting BOLD responses in nearly every area of the brain. We also use these new phrase-based models to try to understand what concepts are represented or processed in each brain area, with some surprising results.

Symposia

Visual words for mental health characterization

DIEGO FERNANDEZ SLEZAK
Lab. de Inteligencia Artificial Aplicada, DC, FCEN, Universidad de Buenos Aires

Discourse analysis has been successfully used to identify mental state alterations caused by mental disorders or use of different types of drugs. Indeed, processing of speech may predict future mental health in a prodrome population. In this talk we will explore how this idea may be extrapolated into visual words, i.e. defining a common language of paintings and drawings which shows the underlying mental state of the authors.

Natural language in real brains and artificial neural networks

LEILA WEHBE
Carnegie Mellon University

This is an exciting time to be studying language in the brain. Newly proposed NLP methods that can represent the meaning of sequences of words allows us to relate representations of the meaning of text to the brain activity acquired when participants read that text. What can this tell us about the brain? What can it tell us about those NLP models? Is there a benefit from combining both into a common model? In this talk I will set up the background behind this approach and discuss recent progress along these three topics.

Thursday · Oct 8th · 9:00 - 11:00

Computations in neural circuits

Chairs: ***Fernando Locatelli.*** *IFIByNE, UBA-CONICET.* ***German Sumbre.*** *Ecole Normale Superieure*

Connectivity and computations of the olfactory bulb

RAINER FRIEDRICH
Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

Symposia

In the olfactory bulb (OB), structurally similar odorants evoke overlapping activity patterns across the input channels, the olfactory glomeruli. Neuronal circuits within in the OB reduce the overlap (correlation) between related activity patterns and normalize their variance. Hence, the OB performs a transformation akin to whitening, a fundamental early step in pattern classification. To analyze the underlying mechanisms we measured odor-evoked activity in the OB of a zebrafish larva and subsequently reconstructed the full wiring diagram by volume electron microscopy. This "functional connectomics" approach revealed an overrepresentation of triplet connectivity motifs that privileges multisynaptic reciprocal inhibition among output neurons (mitral cells) with similar tuning. Tuning-dependent multisynaptic connectivity specifically inhibited mitral cells that contributed strongly to pattern correlations. This connectivity was necessary and sufficient to reproduce whitening in generic network models. Hence, whitening in the OB is achieved by higher-order structure in the wiring diagram that is adapted to natural input patterns. These results provide direct insights into the network mechanism underlying a fundamental neural computation and illustrate the potential of "functional connectomics" approaches to analyze complex structure-function relationships in neuronal circuits.

Multisensory integration in the context of escape, from cell circuits to behavior

VIOLETA MEDÁN
IFIByNE CONICET - FCEN UBA

Different sensory systems provide animals with valuable information that allows them to identify possible threats and react accordingly. In fish, the Mauthner cell receives inputs from the visual and auditory systems and commands the C-start escape response. We combined optic tectum and auditory stimulation with in vivo intracellular recordings to study multisensory integration in the Mauthner cell of goldfish. We found that weak audio-tectal cues produce a sublinear multisensory enhancement of the Mauthner cell response. Paralleling electrophysiological results, behavioral experiments provided a functional role for multisensory integration. We found the strongest multisensory enhancement when multimodal stimuli have minimum intensity while it disappears as salience increases. In addition, spatial alignment and temporal overlap between auditory and visual cues contribute to enhanced multisensory integration.

Timely multimodal interactions underly flexible control of walking in Drosophila

EUGENIA CHIAPPE
Champalimaud Neuroscience Program

All animals exhibit stability and flexibility in their locomotive systems to navigate and respond to highly unpredictable habitats on a moment-by-moment bases. These conserved functional principles are thought to emerge largely from the continuous interaction between internally generated neural signals and sensory feedback. However, it remains unclear how canonical computations are formed from these sensorimotor interactions to sustain stability in a flexible manner. In this talk, I will describe our attempts to answer this question focusing on a visuomotor network in the fly whose function is thought to contribute to gaze and course stability. By performing analysis of behavior in simultaneous with recordings of neural activity, our work shows that this network combines multimodal signals in a timely manner to control the steering movements of the fly continuously but on a moment-by-moment and context-specific bases. This context is set by the instantaneous coordination movement across legs, which in turn is guided by both the behavioral goal of the fly and the current circumstances of the terrain. Because stability and flexibility are hallmarks of locomotion across animals species, even though their bodies and the environment through which they move can be so different, our findings may provide a framework to examine how CNS may be functionally organized for the visual control of walking stability in other species, or even different modes of locomotion, such as flight.

Principles of functional circuit connectivity: Insights from the zebrafish optic tectum

GERMAN SUMBRE

Ecole Normale Superieure

Spontaneous neuronal activity is spatiotemporally structured, influencing brain computations. Nevertheless, the neuronal interactions underlying these spontaneous activity patterns, and their biological relevance, remain elusive. We addressed these questions using two-photon Ca2+ imaging of intact zebrafish larvae to monitor the spontaneous activity fine-structure in the tectum. The spontaneous activity is organized in topographically compact assemblies, grouping functionally similar neurons rather than merely neighboring ones, reflecting the tectal retinotopic map. Assemblies show attractor-like dynamics, improving visual detection in noisy natural environments. These assemblies also emerged in “naive” tecta (tecta of enucleated larvae before the retina connected to the tectum). We thus suggest that the formation of the tectal network circuitry is genetically prone for its functional role. This capability is an advantageous developmental strategy for the prompt execution of vital behaviors, such as escaping predators or catching prey, without requiring prior visual experience. Mutant zebrafish larvae for the mecp2 gene display an abnormal spontaneous tectal activity suggesting disrupted functional connectivity. These mutant fish show no attractor circuits and an exagerated visual response, suggesting that the functional connectivity of the optic tectum acts as a virtual top-down fovea, improving spatial resolution.

Symposia

Thursday · Oct 8th · 9:00 - 11:00

Food for Thought: How diet composition impacts on brain functions in adult rodents and their offspring

Chairs: ***Maria Florencia Rossetti.*** *Institute of Health and Environment of Litoral (ISAL), CONICET-UNL, Department of Clinical Biochemistry. Faculty of Biochemistry and Biological Sciences, National University of Litoral (UNL). Province of Santa Fe. Argentina.*

The impact of a high fat diet on cognition and hippocampal function

ANDREZA DE BEM
Universidade de Brasilia

Worldwide, especially in Western civilizations, most of the staple diets contain high amounts of fats, carbohydrates and comparatively low quantities of protein, leading to the increasing number of overweight and obese individuals. The well recognized association between energy dense diets and metabolic disorders also leads to an increasing investigation of its impact on the brain, behavior and cognition. Ous studies show that mice recognition memory and mood behavior are compromised after a shot time of HFD. Besides these changes are accompanied by increased BBB permeability and by reduction on synaptic plasticity. Hippocampal mitochondrial function is also affected, even after a longer period of HFD consumption, as well as astrogliosis. An early overexpression of proinflammatory cytokines (TNF-a and IL-6) occurs, and when treated with the anti-inflammatory drug, Infliximab, behavioral and BBB alterations were prevented. These results indicate rapid effect of the consumption of HFD leading to cognition and mood disorders, possibly by disrupting BBB homeostasis, a process that contribute to neuroinflammation. These findings have important implications for the contribution HFD intake to the development of neurodegenerative disorders.

Transgenerational effects of maternal high-fat diet: role of the microbiome

SHELLY BUFFINGTON
The University of Texas of Medical Branch

Behavioral phenotypes are determined not only by the host genome, but by the hologenome, the combination of host and microbial genes. Gut microbiota are emerging as key regulators of both normal nervous system physiology and disease states. Working in the maternal high-fat diet model of autism, we recently identified a single bacterial species, Lactobacillus (L.) reuteri, which rescues social dysfunction and related deficits in social reward circuit plasticity. Specifically, we found that MHFD exposure induces long-term, functional changes in the offspring gut microbiome associated with

dysregulation of the oxytocinergic system, deficits in social interaction-induced long-term plasticity in ventral tegmental area dopaminergic neurons, and resulting social impairments. Reconstitution with L. reuteri restored oxytocin levels, interaction-induced VTA plasticity, and social behavior in the offspring. In a follow-up study, we showed that L. reuteri rescues social dysfunction in multiple models of ASD of diverse pathoetiology (i.e., environmental, idiopathic, and genetic models) and that this rescue depends on vagus nerve integrity and oxytocin receptor signaling in dopaminergic neurons. Finally, I will present data from our ongoing investigation into how the MHFD-induced changes in the maternal gut microbiome alter maternal immune function and affect offspring brain development. Our findings identify the gut microbiome as a therapeutic target for neurodevelopmental disorders.

Cafeteria diet induces progressive changes in hypothalamic mechanisms involved in food intake control over time

GISELA PAOLA LAZZARINO

Linköping University

To elucidate progressive hypothalamic changes in the development of obesity, we studied the effects of a highly palatable 'junk-food' cafeteria diet (CAF) intake from weaning on the mRNA levels and DNA methylation state of feeding-related neuropeptides and hormone receptors in individual hypothalamic nuclei at different feeding periods. A short-term of CAF increased energy intake and adiposity, without affecting neuropeptides' expression. In the medium-term, the greater energy intake of CAF led to increased adiposity, hyperleptinemia, and overweight, related to an orexigenic response of lateral hypothalamus, and paraventricular and ventromedial nuclei, given principally by the upregulation of Orexins, Agouti Related Protein, and Neuropeptide Y. The arcuate nucleus displayed an anorexigenic signal with higher Proopiomelanocortin expression, not sufficient to keep the energy intake under regular values. Most of the changes in neuropeptidic mRNA levels induced by CAF were related to epigenetic modifications in their promoter regions. Metabolic and molecular changes were intensified in the long-term. These results showed that the hypothalamic energy homeostatic system is disrupted after a CAF medium-term intake, presumably through epigenetic mechanisms, leading to the development of obesity.The alterations observed in these hypothalamic nuclei could add information about their differential role in food intake control and how their action is disrupted in the development of obesity

Short-term, long-term and transgenerational effects of a highly palatable 'junk-food' diet on the mesolimbic system

MARÍA FLORENCIA ANDREOLI

Instituto de Desarrollo e Investigaciones Pediátricas (IDIP) "Prof Dr Fernando Viteri" Hospital de Niños de la Plata - Min de Salud/Comisión de Investigaciones Científicas CIC-PBA

Symposia

We studied the effects of a palatable 'junk-food' cafeteria diet (CAF) on the expression of key genes of the mesolimbic system, evaluating short-term, long-term and transgenerational effects in female rats. In the short term (30 days) CAF intake deregulated the dopamine (DA) pathway increasing the expression of DA transporter (DAT) in ventral tegmental area (VTA) with decreased methylation status of its promoter and decreasing DA receptor (DRD) 2 expression in accumbens nucleus (NAc). These alterations reflect a reduced DA signalling which could promote excessive intake of palatable foods. However, in the long term (80 days CAF) the changes were reversed. The effects were transmitted to the offspring involving epigenetic mechanisms. At PND10, maternal CAF decreased the transcription of tyrosine hydroxylase (TH), DRD2 and DAT in VTA with changes in the methylation status of their promoters. In NAc, maternal CAF diet reduced DRD1, DRD2 and DAT expression in the offspring, although changes in the methylation patterns were only detected in DAT promoter. A decrease in DA synthesis by TH and reduced actions through its receptors suggest a reduced DA signalling more pronounced than in the dams. These results provide novel insights about how junk-food can affect the reward system through life and in the early postnatal life of the offspring. Particularly important is the expression decline of DRD2 given its physiological implication in obesity and addiction.

Friday · Oct 9th · 9:00 - 11:00

Balancing movement: exploring dichotomies in neural circuits for action

Chairs: ***Maria Soledad Esposito.*** *Centro Atómico Bariloche, Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).* ***Nicolas Andres Morgenstern.*** *Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, Portugal*

Theta oscillations in the dorsal striatum signal reward in a virtual reality navigation task

CAMILA L. ZOLD

Instituto de Fisiología y Biofísica (IFIBIO) Houssay, CONICET - Universidad de Buenos Aires, Buenos Aires, Argentina.

The striatum (STR) is important for aspects of learning like the use of reinforcement information to bias subsequent action selection. In particular, STR oscillations are known to be modulated during learning and space navigation tasks, and they may contribute to information processing between brain areas. However, little is known about the role of STR local field potential (LFP) oscillations in

reward signaling. Using a virtual reality task, we studied if STR oscillations are involved in reward signaling. Thus, we trained head-fixed mice to explore and obtain rewards in a virtual linear track. The track consisted of rewarded areas separated by unrewarded corridors. A sequence of licks was required to obtain a reward upon reaching a rewarded area. Once animals were familiarized with the task, we included 20% omissions. We used an array of four chronically implanted tetrodes to record single unit and LFP activity in the dorsomedial STR of mice performing this task. We found a strong modulation of theta oscillations during the task associated with reward consumption. Interestingly, this increase in theta power was absent if reward is omitted. Also, we found that a high proportion of striatal neurons were phase-locked to the theta rhythm and responded to different events in the task. Using a local STR reference for LFP recordings showed that reward induced theta modulations were still present, suggesting a local origin and a possible role in circuit-level codification of reward.

Contribution of the basal ganglia pathways on the initiation and execution of motor sequences

FATUEL TECUAPETLA

Instituto de Fisiologia Celular, Universidad Nacional Autonoma de Mexico

The performance of an action relies on the initiation and execution of appropriate movement sequences. Two basal ganglia pathways have been classically hypothesized to regulate this process via opposing roles in movement facilitation and suppression. By using a series of state-dependent optogenetic manipulations, we interrogated the contributions of each pathway and found that both the direct striatonigral pathway and the indirect striatopallidal pathway are necessary for smooth initiation and the execution of learned action sequences. In an attempt to identify the contribution of the excitatory inputs to these pathways we also manipulated their thalamic and cortical inputs uncovering specific subcircuits contribution during the initiation, execution, and structuration of motor sequences.

Pyramidal tract neurons drive corticostriatal feed-forward excitation through cholinergic interneurons

NICOLÁS ANDRÉS MORGENSTERN

Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, Portugal

The striatum is composed of medium spiny neurons (MSNs), the only neuronal subtype projecting outside this structure, and small populations of GABA- or acetylcholine-releasing interneurons. These sparse interneurons can broadly modulate MSNs input integration and spiking, controlling striatal output. The main excitatory input to the striatum arises from two corticostriatal populations: intratelencephalic (IT) and pyramidal tract (PT) neurons. However, their specific connectivity to striatal interneurons, as well as the polysynaptic impact that pathway-specific activation has on MSN computations, remains underexplored. Here, using slice electrophysiology, optogenetics and

Symposia

transgenic mice, we found that the activation of PT evokes biphasic signals in MSNs, by eliciting a second excitatory phase impinging immediately after direct corticostriatal excitation. This delayed phase is mediated by striatal cholinergic interneurons that are efficiently recruited by PT, but not by IT inputs. Thus, PT afferents, by selectively activating local microcircuit players, trigger acetylcholine-dependent striatal events, conveying feed-forward excitation to MSNs.

Learning to walk without the brain: Spinal excitatory interneurons define age-dependent locomotor circuit plasticity

AYA TAKEOKA
Neuroelectronics Research Flanders, VIB, KU Leuven

While severe spinal cord injury to a mature nervous system often leads to irreversible paralysis, neonatal rodents receiving a complete injury at thoracic level demonstrate as adults proficient hindlimb locomotion without re-establishment of connection to the brain. However, how the spinal cord achieves such autonomous functionality remains obscure. Using neurotransmitter identity and developmental origin as criteria, we uncover that age of injury impacts excitatory/inhibitory (E/I) circuit balance by affecting survival, connectivity and neurotransmitter phenotype switching of defined excitatory interneuron subpopulations, but not inhibitory cohorts. Concomitant proprioceptive afferent (PA) ablation with neonatal injury leads to paralysis and disrupts E/I circuit balance. While movement-directed augmentation of PA-activity or viral intervention partially restore E/I balance shift, mice receiving injury as adults never regain control of hindlimb movement. Together, our study implicates that both activities of PAs and cell-intrinsic plasticity at the time of injury shape autonomy of spinal circuit to walk without the brain.

Friday · Oct 9th · 9:00 - 11:00

Perspectives on Educational Neuroscience Research

Chair: ***Andrea Paula Goldin.*** *Laboratorio de neurociencia, Universidad Torcuato Di Tella – CONICET*

The key... Knowing who you teach and knowing who teaches you.

CECILIA INÉS CALERO
Área de Educación, Universidad Torcuato Di Tella - CONICET

Symposia

Teaching can be defined as behavior with the intent to facilitate learning in another (Pearson 1989), and is also described as a facilitator of accurate social transmission of knowledge by narrowing the range of inferences that learners make to acquire new cultural concepts (Kline, 2015), if we include a mentalistic and a culture approach to the definition. According to these theoretical frameworks, teaching can be understood as a natural instinct that humans share across cultures, which seems to develop early, probably shaping most of our learning experiences. Therefore, given its significance, understanding how this dynamic bi-directional relation within the teacher-learner dyad works, both inside and outside formal education settings, is essential. In the present talk I will present an exploration of simple tasks and paradigms developed by our group which seek to describe and compare what happens when different types of students and teachers are introduced into this dyad. For example, knowledgeable versus naïve learners, or learning experiences that include teachers and students that are not not familiar with each other. All in all, the main goal of the presentation is to mark the importance of both knowing who teaches you, but also of knowing who you teach, in order to achieve meaningful knowledge transmission.

The UB-EDU1st Chair of Neuroeducation as a research environment

ANNA FORÉS MIRAVALLES
Universidad de Barcelona

With the focus on improving education, the UB-EDU1s Chair of Neuroeducation of the University of Barcelona investigates, from a transdisciplinary perspective, how to apply advances in neuroscience to the educational field. The Chair has set up a network of networks with world leaders in the field, in order to both investigate and disseminate findings in neuroeducation. Through the organization of international congresses, conferences, master's degrees and courses, it offers society in general, and teachers in particular, the latest results from research in the field. With this aim, the Journal of Neuroeducation has been recently launched. In this symposium, we will share the working lines carried out by the Chair and its scientific community.

Impact of poverty and a cognitive stimulation program on executive functioning and its neural correlates in a preschool population

VERÓNICA NIN
Centro de Investigación Básica en Psicología, Universidad de la República, Uruguay

There is evidence of a substantial improvement in various cognitive processes during early childhood, among them, the basic processes that allow for autonomously and self-regulating behaviour in novel and changing scenarios, such as school settings. Altogether, these processes are called Executive Functions (EF) and they allow i) to temporarily maintain, update and manipulate information in consciousness (working memory), ii) to inhibit automatic and dominant responses in favor of subdominant responses that are appropriate to contingencies (inhibitory control), and iii) to adapt

the set of rules that are followed depending on the context (cognitive flexibility). Higher cognitive functions such as reasoning and planning are rooted in the aforementioned basic functions. However, not all developmental scenarios equally promote the maturation of these aspects of cognition. In this work we show that in a population of children attending preschool in Montevideo, Uruguay, poverty has an important impact on performance in tasks that require EF. Also, some neural correlates recorded by EEG are sensitive to the socioeconomic context. In particular, in a task that evaluates inhibitory control the amplitude of the N2 and P3 components elicited by incongruent stimuli are modulated by SES. Finally, we show that a program designed to promote cognitive development through video games promotes improvement in tasks that require inhibitory control and reasoning.

Building a Global Science of Learning for Education: A Role for Neuroscience?

ANDREA A. CHIBA

Professor, Dept. of Cognitive Science and Program in Neuroscience; Co-Director Temporal Dynamics of Learning Center, University of California San Diego; Co-Founder Global Science of Learning for Education Network.

The Science of Learning (SoL) is a multi-disciplinary science that ranges from the very basic cellular and molecular science of how an organism learns, to how children and adolescents use their brains, bodies, and sociality to best learn in cultures and classrooms, to methods for augmenting and restoring the capacity to learn. The trauma of poverty and poor health adds even more complexity, regardless of culture or country. Our growing global population of children exists in disparate cultures and circumstances yet face common challenges requiring coordinated and effective solutions. Great affluence is juxtaposed with extraordinary poverty; education and health care crises persist in many nations. This is an incredible loss of human potential. Many nations focus resources on restoring mental and physical health but lack sufficient understanding of what every child needs to learn, flourish and prevent later developmental problems. Conserving, restoring, nurturing, and optimizing the most basic ability to learn and thrive, especially for those children exposed to the worst of economic and social circumstances, requires concerted action by a global community of scientists, technologists, educators, policy makers, activists, and philanthropists. Neuroscience has the opportunity to play a central role in the science of learning, making a pre-emptive effort to place the brain-body and learning as a motivator to designing learning contexts that vary according to needs.

Symposia

Friday · Oct 9th · 9:00 - 11:00

Molecular Mechanisms Underlying Axonal Degeneration and Synaptic Disconnection in Progressive Neurodegenerative Diseases

Chair: ***Gustavo Pigino.*** *INIMEC-University of Illinois*

Necroaxoptosis: a degenerative mechanism involved in pathologies of the aged nervous system

FELIPE COURT

Center for Integrative Biology, Faculty of Sciences, Universidad Mayor, Chile

Accumulating evidence suggest that degeneration of axons is an early event in several neurodegenerative conditions, including Alzheimer's disease, Amyotrophic lateral sclerosis, and Parkinson's disease. Interestingly, axonal degeneration also takes place as a consequence of healthy aging, and studies in animal models suggest that this degenerative process contributes to the loss of cognitive functions during ageing. Axonal degeneration involves destruction programs that are independent of the survival of the cell soma, and is associated to NAD+ depletion and mitochondrial dysfunction in the axonal compartment. Recently, we have demonstrated that necroptosis, a programmed cell death process, is involved in axonal degeneration after diverse stimuli as well as in models of neurodegenerative conditions, including Parkinson and Alzheimer disease. Importantly, necroptosis activation and axonal degeneration are dependent on several parameters associated to the ageing process, including a decrease in NAD+ levels in the brain, mitochondrial dysfunction and ROS production, inflammation and pathogen ligands. We propose that an age-dependent increase in the susceptibility to activation of the necroptosis machinery in neurons is associated to progressive axonal degeneration during healthy ageing, a process that can be accelerated by diverse stimuli with pathological consequences.

Molecular Mechanisms Underlying Tau Toxicity and Axonal Degeneration in Tauopathies

NICHOLAS KANAAN

Michigan State University

Deposition of pathological tau is implicated in several progressive neurodegenerative disorders characterized by axonal and neuronal degeneration. Although several tau modifications are associated with sporadic disease and tau mutations cause inherited tauopathies, the molecular pathways engaged by tau to cause degeneration are still being defined. Current thinking suggests disease-related tau modifications exert toxicity by disruption of microtubules and/or enhancing

aggregation. However, evidence from our group and others supports an alternative explanation. That is, tau acts to regulate signaling pathways and toxicity is due to aberrations of this function. We discovered an N-terminal motif in tau that becomes exposed in pathogenic forms of tau and causes axonal transport impairment through a protein phosphatase-1 (PP1)-dependent signaling cascade. Our hypothesis is that pathogenic tau, particularly those with abnormal conformations, cause toxicity through aberrations of a PP1-dependent mechanism. Recent work has examined the impact of pathological tau species (e.g. mutant tau and phospho-tau) on the interaction with PP1 isoforms, the activity of PP1 and axonal transport functionality in primary neurons. Our work shows that multiple forms of tau impair transport via this mechanism, by enhancing the interaction with and activity of PP1. Ongoing studies will assess whether additional pathological forms of tau affect this mechanism and other PP1-dependent neuronal processes.

Molecular mechenasim underlying synaptic disconection in Parkinson´s disease.

GUSTAVO PIGINO
INIMEC-University of Illinois

Parkinson's disease (PD) has been associated with a lack of communication between two neuronal populations, the substantia nigra and striatal neurons. The lack of proper communication is associated with a progressive synaptic dysfunction followed by a dying-back pattern of axonal degeneration of the substantia nigra neurons, that project and connect with striatal neurons. We propose that a vital neuronal process, required to support those affected axons known as fast axonal transport (AT) is drastically affected. Even more, we propose that this axonal transport failure triggers a progressive decrement of key biological material important for the normal synaptic and axonal functions that sustain synaptic communication and a myriad of neuronal circuitry. The identification of molecular targets that underly AT alterations promises the development of effective therapeutic strategies to treat PD, as well as other neuropathies caused by defects in axonal transport collectively termed dispheropathies. We evaluated the effect of the Parkinsonian toxin MPP+ on kinesin-1 and cytoplasmic dynein driven AT. Pharmacological and cellular biological experiments revealed increased activity of a specific axonal serine/threonine kinase activity responsible for the inhibition of the anterograde direction of AT and an increased rate of retrograde AT. In summary, alterations in bidirectional AT represent an early event in the development of PD.

Symposia

Friday · Oct 9th · 9:00 - 11:00

The epigenetic basis of behavior

Chairs: ***Bruno G Berardino.*** *Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA - IQUIBICEN (CONICET).* ***Silvina V Sonzogni.*** *Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, UBA - IQUIBICEN (CONICET)*

NRSF in novel epigenetic programs that contribute to hippocampal memory deficits and neuronal stunting after early-life adversity

TALLIE Z. BARAM

Departments of Pediatrics, Anatomy / Neurobiology, Neurology, Developmental and Cell Biology; University of California-Irvine, US

Early-life adversity (ELA) is linked with lifelong risk of cognitive and memory problems dementia, yet the responsible mechanisms remain unclear. We imposed ELA by rearing rat pups in simulated poverty, assessed hippocampus-dependent memory in adulthood and probed related changes in gene expression, the underlying transcriptional processes, and the consequent disrupted hippocampal development. Adult ELA rats had poor hippocampus-dependent spatial memory and stunted hippocampal dendritic trees. RNA-seq identified ~140 differentially expressed genes. Bioinformatics uncovered glucocorticoid receptor and, unexpectedly, the transcription factor neuron-restrictive silencer factor (NRSF/REST) as putative upstream regulators. To examine the role of NRSF in the mechanisms of ELA-induced memory problems, we transiently blocked the binding of NRSF to the chromatin. Blocking NRSF function immediately after the ELA period rescued both spatial memory and the impoverished dendritic structure of hippocampal neurons in ELA rats. Blocking NRSF function in vitro augmented dendritic complexity of developing hippocampal neurons, suggesting that NRSF represses genes involved in neuronal maturation. These findings establish a novel, surprising contribution of NRSF to ELA-induced transcriptional programming which disrupts neuronal maturation. The repression of neuron-specific genes might be adaptive, promoting cell survival by reducing high energetic cost of neuronal differentiation and activity.

Molecular adaptations to early-life adversity: Insight from human postmortem brain studies

GUSTAVO TURECKI

Department of Psychiatry, McGill University, Montreal, Canada

Suicide is a complex behaviour that frequently associates with a history of early-life adversity. Dr. Turecki's talk will discuss how adversity during childhood may differentially regulate molecular processes in the brain and increase lifetime risk of suicide. He will present data from his laboratory suggesting that specific biological pathways are regulated by the early-life environment through

diverse epigenetic processes, which may contribute to suicide risk by differentially adjusting behavioural trait and emotional development, as well as influencing cognitive function. A conceptual framework to understand suicide risk among individuals exposed to early-life adversity will be presented.

Epigenetics Effects of Stress

FRANCES A CHAMPAGNE

Department of Psychology, University of Texas at Austin

Exposure to stress during development can shape a broad range of phenotypic outcomes. In addition to programming response to stressors, these early experiences shape later cognitive and social behaviors. Endocrine, neurobiological and molecular studies suggest that the quality of the early environment – particularly qualities indicative of stress or threat – can have lasting effects on multiple biological systems. Epigenetic changes induced by these environmental exposures may mediate the link between stress and phenotypic outcomes. We have examined the epigenetic, neurobiological and behavioral consequences of early life stressors in rodents with correlational studies also conducted in humans. Prenatal stress is associated with increased stress responsivity, altered neurodevelopmental trajectories and impairments in social/reproductive behaviors. These phenotypic outcomes are predicted by epigenetic variation in the placenta and associated with region-specific changes in gene expression and DNA methylation in the brain. Postnatal exposure to low vs. high stress environments is predictive of reduced maternal behaviour and impaired cognition in later life. Altered DNA methylation of hormone sensitive genes may account for these effects. Future work on the phenotypic outcomes and the molecular mechanisms that shape these outcomes may provide further insights into the within and across-generation emergence of stress-induced behavioral strategies.

Role of TET methylated DNA cytosine dioxygenase in addiction

JIAN FENG

Department of Biological Science, Program in Neuroscience, Florida State University, USA

The role of DNA methylation in drug addiction has been increasingly appreciated. Recently, additional forms of DNA epigenetic modifications have been identified through the oxidation of methylated DNA cytosine via TET dioxygenases (TET1, TET2, TET3). However the functional role of TETs in addiction remains largely unknown. We have found that TET1 in the nucleus accumbens (NAc), a key brain reward region, is implicated in cocaine action. In the NAc, there are two major types of medium spiny neurons (MSN), which are classified based on their distinct projections and gene expressions, including enrichment of dopamine D1 and D2 receptors. Though D1- and D2-MSNs are intermingled with similar morphology, they demonstrate different (and often opposite) roles in drug addiction. To identify TET1's cell type specific functions, we generated the D1- and D2-

MSN specific Tet1 knockout mice and characterized their addiction behaviors by using cocaine conditioned place preference and intravenous self-administration. We found that TET1 not only plays opposite roles in D1- and D2-MSNs in cocaine addiction, its effect is also sex-specific. We have been performing whole genome bisulfite sequencing to illustrate TET1 mediated DNA methylation changes in D1- and D2-MSNs. To gain more insight of the DNA epigenetic basis of addiction, we are continuing to explore the role of TET dioxygenases in other aspects of addiction, such as susceptibility difference.

Friday · Oct 9th · 9:00 - 11:00

Neural correlates of dreaming and dreamlike states

Chair: ***Enzo Tagliazucchi.*** *Physics Department, University of Buenos Aires*

Dream affect: Phenomenology, neural correlates, and continuity across sleep-wake cycle

PILLERIIN SIKKA

Department of Cognitive Neuroscience and Philosophy, University of Skövde (SWE)

We experience affective feelings (i.e., emotions and moods) not only when we are awake but also when we are asleep — during dreaming. Despite considerable research, existing theories and empirical findings disagree about the frequency, nature, and correlates of dream affect. Although there is a large body of research on the neural basis of REM sleep, little is known about the specific neurophysiological markers for dream phenomenology, including dream affect. In this presentation, I will give an overview of recent research on (1) the frequency, valence, and phenomenological content of dream affect and how these are influenced by study methodology, (2) the neural correlates of dream affect, and (3) the continuity of affective feelings across the sleep-wake cycle. These studies show that the results and conclusions regarding dream affect are very different, even contradictory, depending on the methodology used to measure dream emotions. Findings also demonstrate cross-state continuity regarding both the phenomenology and the underlying neural processes of affective feelings. I will discuss the implications these findings have for the study of (the neural correlates of) affective experiences across the sleep-wake cycle.

Symposia

Meditation, hypnagogia and the stability of consciousness

TRISTAN BEKINSCHTEIN
University of Cambridge

It seems limiting that we talk about phenomenology and experiences but then we measure reaction times and errors. Can we study the contents of our mind? I would argue that we are always studying content in cognitive neuroscience but not caring or not willing to engage in the question. I will present two main methods to capture what we think -direct and indirect- that may allow us to formalize the questions about content. I would also like to discuss two methods in cognitive neuroscience to map the underpinnings of the contents: neural decoding and intensity tracking. I will illustrate the results and discussion with EEG and fMRI experiments during pharmacologically-induced states, sleep transitions and meditative techniques.

Mind mapping with words: what computational speech approaches can tell us about our dreams

NATÁLIA MOTA
Brain Institute UFRN and Physic's Department UFPE

Why do we dream? How does a dream reveal our inner reality? Those questions are for centuries in human culture and investigated in different ways, always facing a challenge: how to avoid the external subjectivity to interpret dreams out of the dreamer reality? Computational approaches that automatize semantic and emotional analysis are a possible path to solve this problem. During this talk, we will explore how to study memory reverberation at dreams using semantic analysis in a sleep-lab experiment and during remote access of dream reports during the COVID19 pandemic. We found that visual memory residue persists throughout the transition to sleep, increasing during N1 in proportion to the time spent in this stage. In contrast, the progression of sleep gradually neutralizes the affective memory residue, which decreases in proportion to the time spent in N1 and reaches a minimum during N2. During COVID 19 pandemics we also investigated how Does dreaming change and/or reflect mental suffering related to social isolation and the fear of contamination. For that purpose, we applied natural language processing tools to study 239 dream reports from 67 individuals either before the Covid-19 outbreak or during March-April, 2020, when quarantine was imposed in Brazil following the pandemic announcement by the WHO. Pandemic dreams showed a higher proportion of anger and sadness words and higher average semantic similarities to the terms “contamination” and “cleanness”.

Symposia

The psychedelic state as a waking dream

ENZO TAGLIAZUCCHI
Physics Department, University of Buenos Aires

Ever since the modern rediscovery of psychedelic substances by Western society, several authors have independently proposed that their effects bear a high resemblance to the dreams and dreamlike experiences occurring naturally during the sleep-wake cycle. I will present evidence supporting this hypothesis, both from phenomenological and neurophysiological perspectives. First, I will discuss the results of large-scale semantic analyses comparing dream reports to those given by users of different psychoactive compounds, and demonstrate that the content of psychedelic experiences is the closest match to dream content. Second, I will present the results of EEG experiments conducted under the effects of N,N-dimethyltryptamine (DMT), a potent and short-lasting serotonergic psychedelic capable of inducing immersive and oneiric experiences, drawing parallels with the known electrophysiological changes that take place during the descent from wakefulness into REM sleep.

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YIT-1

Chair: Graciela Mazzone

Aβ promotes amyloidogenic processing of APP through a Go/βγ signaling.

ANAHI BIGNANTE
INIMEC-CONICET-UNC

BACE1 cleavage on amyloid precursor protein (APP), is rate-limiting on Aβ biosynthesis. Some in vitro studies have demonstrated that exogenous Aβ triggers its own production by a mechanism which are unclear. Our previous findings suggest that APP acts as a pathologic receptor of Aβ, able to provoke neurodegeneration through Go/βγ intracellular signaling. In this work, we evaluated the role of APP/Go/βγ signaling, induced by aggregates of Aβ, promoting the encounter and interaction of APP with BACE1. Using quantitative colocalization, we found that fibrillar Aβ (fAβ) provoked an increase in the localization of APP and BACE1 in recycling endosomes (RE). Employing mutant forms of APP, we verified that this event is dependent of the interaction of APP with fAβ and with Go intracellular. Likewise, pharmacological inhibition of βγ with gallein, abrogated the Aβ-dependent convergence of endogenous APP and BACE1 in hippocampal neurons. Using Bimolecular Fluorescence Complementation (BiFC) technique in human neurons derivate from IPSCs, we found that fAβ and oligomeric Aβ (oAβ) were able to increment the APP/BACE1 interaction in RE; effect that was avoided by gallein. Finally, we correlated changes in APP and BACE1 interaction with changes in β-processing of APP by WB. Collectively, these findings uncover a feed-forward mechanism of amyloidogenesis that might contribute to amyloid pathology in early stages of Alzheimer's disease and suggest that gallein might have clinical relevance

Oxidative distress in Alzheimer Disease human organoids

MARIANA HOLUBIEC
Instituto de Biología Celular y Neurociencia "Profesor Eduardo De Robertis" IBCN (UBA-CONICET)

While highly polarized neurons deal with physiological changes in local levels of reactive oxygen species (ROS), it is known that in early stages of Alzheimer disease (AD) imbalances in the management of ROS occur, promoting abnormal macromolecules oxidation. To test the association of increased oxidation and intracellular dynamic defects in the progression of AD we developed human brain organoids from iPSC control and APP Swedish mutation (APPSwe). We characterized organoid cell composition and AD pathological hallmarks, such as amyloid-like deposits stained with antibodies and classical Congo-red. Furthermore, we observed, in APPSwe organoids, an increase in Aβ reactive

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area as well as a decrease in full length APP levels by western blot and immunostaining. In addition, we developed a technique for microinjecting organoids with viral vectors or probes to measure mitochondrial dynamics and morphology, superoxide anion levels and reactive oxygen species. We found a significant increase of superoxide anion levels in live imaging of APPSwe organoids. We also described an increase in Glutaredoxin-2 reactive area and integrated intensity, suggesting changes in thiol-based regulation in AD. Our results highlight the relevance of modeling neurological diseases using complex tissue arrangements, and points to a clear impairment in oxidative stress pathways that, if modulated, could be used as a therapeutic strategy for treatment of abnormal oxidation in AD.

Early life stress and the programing of stress-coping abilities in juvenile rats

MARÍA EUGENIA PALLARÉS

1-"Laboratorio de Programación Perinatal del Neurodesarrollo". Instituto de Biología Celular y Neurociencias "Prof. E. de Robertis" (IBCN)- Facultad de Medicina, Universidad de Buenos Aires; 2-"Laboratorio de Neurobiología del Estrés". Instituto de Investigaciones Biotecnológicas (IIB). UNSAM. CONICET.

Prenatal stress (PS) predisposes individuals to develop emotional disorders in later life, including depression and anxiety, which might be mediated by dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis response. However, to date, little studies have examined the effects of PS on stress coping abilities of younger individuals and it relevance for the early onset of stress-related disorders. In here we assessed the impact of PS on the emergence of anxiety-/depressive- like behaviors and HPA response to an acute stress in juvenile rats. We explored possible underlying molecular bases by changes in candidate stress-related genes and DNA-methylation levels in the hippocampus, a key structure in stress regulation. Also, we tested patterns of maternal behavior within early lactation. Stress during pregnancy enhanced pup-directed behavior of stressed dams. In the offspring, PS rats had enhanced stress-coping abilities than non-prenatally stressed rats. In the hippocampus, PS increased the expression of bdnf-IV and crhr1 although several sex differences changes on glucocorticoids and on BDNF receptors expressions were found. PS changes the hippocampal epigenetic landscape only in male offspring. Our results show that PS and maternal behavior induce dynamic alterations in the offspring that should be adaptive at younger ages, but potentially maladaptive in later life, highlighting the importance of including an ontogenetic approach when assessing the effects of PS.

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YIT-2

Chair: Verónica de la Fuente

Dopamine modulates adaptive forgetting in medial prefrontal cortex

FRANCISCO TOMÁS GALLO

Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencia Cognitiva y Traslacional (CONICET - Fundación INECO - Universidad Favaloro. Laboratorio de Sueño y Memoria, Instituto Tecnológico de Buenos Aires (ITBA).

There are several ideas about the mechanisms of forgetting; some indicate that it is an active process that could be non-specific, but also dependent on the content depending on how it occurs. This study explores an active and selective forgetting mechanism whose function is to optimize the use and evocation of stored information. Anderson (1) developed a procedure in humans that he called "Evocation Practice Paradigm" in which an effect of "Retrieval-Induced Forgetting" is evidenced and it is postulated that it occurs by an executive control mechanism. Activation of the frontal areas during practice may indicate that forgetting of unpracticed items occurs by a mechanism of inhibitory control over medial temporal lobe (MTL) structures, of which there is extensive literature in humans. In our laboratory, a retrieval-induced forgetting paradigm for rodents was successfully developed (2). Using this paradigm, we show results in accordance with the alignments and hypotheses in humans. There is evidence of a dopaminergic role in PFC to solve tasks that require working memory or cognitive flexibility. We examined the effect of D1 receptor (D1R) blockade on mPFC during evocation. We observed that the activity of the ventral tegmental area (VTA) is necessary for the retrieval-induced forgetting but that this effect can be restored with the infusion of D1R agonists in the mPFC. We observed, using agonists and antagonists, a modulating effect of dopamine in the mPFC on retrieval-induce

What we know of stress effects on memory: an integrative view through the behavioral tagging mechanism

PAMELA LOPES DA CUNHA

Instituto de Biología Celular y Neurociencias "Pr. E. De Robertis", CONICET. Facultad de Medicina. Universidad de Buenos Aires. Buenos Aires, Argentina. Centro de Neurociencias Cognitivas. Universidad de San Andres. Buenos Aires, Argentina

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The stress events influence a range of cognitive functions, including memory. However, its precise mechanisms are still unknown. Studying the interaction between acute stress event with different learning tasks, we found that stress can have both beneficial and detrimental effects on the consolidation of hippocampal-dependent memories. Our results support the Behavioral Tagging Hypothesis (BT) as a mechanism underlying the formation of long-term memories (LTM). According to this, some events could influence temporally associated memories by providing plasticity-related proteins (PRPs), necessary for the consolidation of the mnesic trace, or by competing for them. The BT also propose the association of these PRPs with a learning-induced neuronal tag, where proteins can be selectively used to maintain the plasticity that underlies memory. Experiments in rats showed that a weak training, which only induces short term memory, can be stabilized into LTM if an acute stress is experienced within a specific time window before or after learning. This promoting effect depends on protein synthesis induced by stress and the glucocorticoid receptors activation. However, if training is strong enough to generate LTM, a stress event impairs memory and our results support the competition for available proteins. Finally, we wondered if a similar phenomenon occurs in human memory. We also found a narrow time window for the stress modulation and learning-strength dependent effects.

AMPA receptor expression requirement during long-term memory retrieval and its association with mTORC1 signaling

MAGDALENA PEREYRA

1 Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina, 2 CONICET-Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencia "Dr. Eduardo De Robertis" (IBCN), Buenos Aires, Argentina.

Recently we reported that mechanistic/mammalian target of rapamycin complex 1 (mTORC1) activity during memory retrieval is required for long-term memories expression. Here we used inhibitory-avoidance task to evaluate the potential hippocampal mechanisms by which mTORC1 signaling participates in memory retrieval. First, we studied GluAwd-subunit trafficking during memory recall and its relationship with mTORC1 pathway. We found that pretest infusion of GluR23ɣ, a peptide that selectively blocks GluA2- containing AMPA receptor (AMPAR) endocytosis, prevented the amnesia induced by the inhibition of mTORC1 during retrieval. Additionally, we found that GluA1 levels decrease and GluA2 levels increase at the postsynaptic density subcellular fraction of rapamycin-infused animals during memory retrieval. Besides, GluA1 levels decreased at the synaptic plasma membrane fraction. Then, we evaluated the requirement of AMPAR subunit expression during retrieval. Infusion of GluA1 or GluA2 antisense oligonucleotides (ASO) before testing impaired memory retention. Memory impairment induced by GluA2 but not GluA1 ASO was reverted by GluA23ɣ infusion before testing. Our work indicates that de novo GluA1 and GluA2 AMPAR subunits expression is required for memory retrieval and suggests that mTORC1 might

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Chair: Alejandra Pacchioni

regulates AMPAR trafficking during retrieval. Our present results highlight the role of mTORC1 as a key determinant of memory retrieval that impacts the recruitment of different AMPAR subunits.

Chronic exposure to a Glyphosate Based Herbicide alters the expression of key molecules involved in hypothalamic regulation of the rat oestrous cycle.

GUILLERMINA CANESINI

Instituto de Salud y Ambiente del Litoral (ISAL), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral-CONICET, Santa Fe, Argentina.

Glyphosate-based herbicides (GBHs) are extensively used and it has been reported that they may act as endocrine disruptors. Activation of steroid receptors in specific hypothalamic regions like the anteroventral periventricular nucleus (AvPv) and the arcuate nucleus (Arc) is necessary for ovulation and a normal oestrous cycle. This study aimed to describe the effects of chronic exposure to GBH during adult life, at levels close to the reference dose, on the hypothalamic regulation of the oestrous cycle. Adult rats were exposed for 3 months to 2 mg/kg/day of GBH through their diet (GBH Group-GG; Control Group-CG with saline solution). mRNA expression of Kisspeptin (Kiss) was evaluated in brain nuclei isolated by micropunch. GBH rats showed a lower percentage of time in proestrus-oestrous stages when compared to controls. Immunohistochemistry for oestrogen receptor alpha (ERα) and progesterone receptor (PR) showed changes in expression in AvPv, Arc and medial preoptic nuclei (Mpo) in rats exposed to GBH, the same as for REA and SMTR (ERα co-regulators). Kiss mRNA results showed significantly lower expression in the Mpo of the GG. These results suggest that a dose of GBH considered safe alters the rat´s cyclicity and modifies the expression of key brain molecules involved in its regulation. Therefore, these changes may provide new evidence of the possible effects of glyphosate on fertility at hypothalamic level.

The role of ghrelin receptor on the modulation of palatable food intake

MARIA PAULA CORNEJO

IMBICE

Ghrelin is a hormone relevant in the context of eating disorders, as it promotes the consumption of palatable foods. Strikingly, ghrelin receptor, the growth hormone secretagogue receptor (GHSR),

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signals in the presence and in the absence (constitutive activity) of ghrelin. GHSR is expressed in the ventral tegmental area (VTA), a key nucleus of the mesolimbic pathway involved in processing rewarding experiences, such as the consumption of palatable foods. Ghrelin administration to humans activates reward-related brain nuclei, and intra-VTA administration of ghrelin in rodents increases, while GHSR blockage decreases, the intake of and the motivation for palatable foods. To understand the role of GHSR in the mesolimbic pathway and its regulation of high-fat (HF) food intake, we developed a binge-like eating protocol, in which mice are daily and time-limited exposed to a HF diet. We found that wild-type mice escalate HF diet intake over days and display an activation of the mesolimbic circuit, while GHSR-deficient mice eat less HF diet and show no activation of the mesolimbic pathway. We also found that blocking constitutive GHSR activity reduces HF diet intake in the binge-like eating protocol. Recently, we also showed that GHSR expression exclusively in dopamine neurons is sufficient to restore specific appetitive and consummatory behaviors towards HF diet. Thus, our studies show that GHSR in the mesolimbic pathway regulates reward-related behaviors towards HF diet.

Fasting induces remodeling of hypothalamic neuronal circuits controlling food intake and neuroendocrine axis in a growth hormone secretagogue receptor-dependent manner

GIMENA FERNANDEZ

Laboratorio de Neurofisiología. Instituto Multidisciplinario de Biología Celular (IMBICE) [CONICET -CIC-PBA -Universidad Nacional de La Plata (UNLP)], La Plata, Buenos Aires, Argentina.

The morphological and functional remodeling of neuronal circuits have been proposed to play a key role to ensure the control of the body homeostasis. Under energy-deficit states, the arcuate nucleus (ARC) neurons producing Agouti-related peptide (AgRP) and neuropeptide Y (NPY; ARCAgRP/NPY neurons) are activated and help to coordinate neuroendocrine and behavioral responses, including food intake, through projections to the hypothalamic paraventricular nucleus (PVH; ARC→PVH projections). Plasma ghrelin levels increase under energy-deficit states and activate ARCAgRP/NPY neurons by acting on the growth hormone secretagogue receptor (GHSR). Here, we hypothesized that activation of ARCAgRP/NPY neurons in fasted mice would promote morphological remodeling of the ARCAgRP/NPY→PVH projections in a GHSR-dependent manner, and such structural changes mediate the fasting-induced activation of the hypophysiotropic corticotrophin-releasing factor (CRF) producing neurons of the PVH. Using different experimental strategies we show that the connectivity between hypothalamic circuits controlling food intake and neuroendocrine responses can be remodeled in the adult brain, depending on the energy balance conditions, and that GHSR activity is a key regulator of this phenomenon.

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YIT-4

Chairs: Azul Silva, Lorena Rela.

Dynamical modeling and cortical oscillations in Serinus canaria song

SANTIAGO BOARI
IFIBA-CONICET and DF, FCEN, UBA

Sensorimotor integration is a crucial aspect for encoding auditory representations of learned vocal behavior. Songbirds provide an excellent animal model to address this, since they are vocal learners and the neural circuits for song learning, production and perception are well understood. A dynamical model for the population activity in brain regions of this "song system" can reproduce characteristic air sac pressure patterns of canary song. For a cortical sensorimotor nucleus that presents similar activity patterns while singing and while perceiving the bird's own song (BOS), the model predicts synchronized population activity at distinct temporal instances of song syllables. In this talk, I will discuss the neural model and its predictions. Also, I will report evidence of synchronous activity in response to auditory playbacks of the BOS. Extracellular recordings using 32-channel silicon probes allowed to study the local field potentials (LFP), single unit activity, and spatial synchronization. Rhythmic features of the song of canaries (Serinus canaria) allowed us to uncover neural oscillations locked to the behavior, which shows that predictions are compatible with experiments. Grouped data from different subjects share these features, suggesting a general strategy for neural coding. This program illustrates an example of the power that dynamical models provide to neuroscience research, in the form of testable hypotheses that drive -and feedback from- experiments.

Directional neurons selective for horizontal movement in a crab and their role in visually guided steering behaviour

FLORENCIA SCARANO
Center for Mind/Brain Sciences (CIMeC). University of Trento

Many animals rely mainly on vision to guide their behavior, for that they need to get information on the direction of moving objects, such as prey and predators. This can be achieved by direction

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selective neurons. Crabs offer several experimental advantages for studying some fundamental principles of neural processes involved in the directional component of behavioral responses. In these animals, the ability to pursue a moving prey requires fixing and tracking it with a region of the retina, which implies perceiving the directions in which the image deviates from the fixation point (Land & Layne, 1995). The neural mechanisms by which arthropods carry out these behaviors are unknown. Performing intracellular recordings in the lobula complex of the crab Neohelice granulata, we discovered neurons highly sensitive to direction that respond only to horizontal moving objects, thus reflecting an adaptation to the flat environment where they live. They respond with high frequency discharge of action potentials in the preferred direction, and with a sustained hyperpolarization in

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Chairs: Juan Ferrario.

the null direction (Scarano et al, 2020). Furthermore, the collective activity of these neurons as an ensemble is suited to function as a deviator-detector system of targets moving away from the eye lateral pole. Based on this, we propose a role of these neurons for object tracking in crabs. These results provide a clear example of neuronal adaptation to salient features of a natural environment.

Increased activity of D5R-Kv1.3 pathway in cholinergic interneurons contributes to the hypercholinergic state of parkinsonism and dyskinesias

CECILIA TUBERT

Grupo de Neurociencia en Sistemas, IFIBIO Houssay - UBA - CONICET

Balanced actions of dopamine (DA) and acetylcholine (ACh) shape striatal function. Striatal cholinergic interneurons (ChIs) are the main striatal ACh source. In Parkinson´s disease (PD), DAergic nigrostriatal neurons degenerate, leading to a hypercholinergic state. L-dopa treatment can induce dyskinesias (LID). Previously, we found that ChIs are hyperexcitable in a mouse model of PD as result of a reduced Kv1.3 current, and, recently, that ChIs from LID mice are even more hyperexcitable. Our aim is to identify the mechanisms underlying this hyperexcitability, which are potential new

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therapeutic targets for Parkinson's disease and dyskinesias. Because the D5R, which has constitutive (ligand-independent) activity, excites ChIs in physiological conditions, we hypothesize that an alteration of D5R signaling causes ChIs hyperexcitability in PD. With ex-vivo electrophysiological recordings, we found that D5R increases ChIs excitability by reducing a Kv1.3 current through a cAMP dependent signaling cascade. Moreover, in PD and LID mouse models, elevated levels of cAMP contribute to ChIs hyperexcitability. Finally, preliminary results suggest that this pathway is overactive due to an increased constitutive activation of D5R that entails an increased cAMP production followed by a reduction in Kv1.3 current, resulting in ChIs hyperexcitability.

Neuron-class specific responses govern adaptive remodeling of myelination in the neocortex

SUNG MIN YANG
Harvard University

Myelination plasticity plays a critical role in neurological function, including learning and memory. However, it is unknown whether this plasticity is enacted through uniform changes across all neuronal subtypes, or whether myelin dynamics vary between neuronal classes to enable fine-tuning of adaptive circuit responses. We performed in vivo two-photon imaging to investigate the dynamics of myelin sheaths along single axons of both excitatory callosal projection neurons (CPN) and inhibitory parvalbumin+ interneurons (PV-IN) in layer 2/3 of adult mouse visual cortex. We find that both neuron types show dynamic, homeostatic myelin remodeling under normal vision. However, monocular deprivation results in experience-dependent adaptive myelin remodeling only in PV-INs,

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Chairs: Ana María Contin.

but not in CPNs. Monocular deprivation induces an initial increase in elongation events in myelin segments of PV-INs, followed by a contraction phase affecting a separate cohort of segments. Sensory experience does not alter the generation rate of new myelinating oligodendrocytes, but can recruit pre-existing oligodendrocytes to generate new myelin sheaths. PV-INs also show a concomitant increase in axonal branch tip dynamics independent from myelination events. These findings demonstrate that distinct classes of neocortical neurons individualize adaptive remodeling of their myelination profiles to diversify circuit tuning in response to sensory experience.

Modulation of human sleep by the moon cycle

Young Investigator Talks

LEANDRO CASIRAGHI
University of Washington

Environmental changes driven by the moon cycle are widely relevant in nature, but they are often unnoticed by humans. Lab studies have suggested potential effects of the moon cycle on sleep, but the detection of these in natural living conditions is challenged by modern life habits and ubiquitous access to electric light. To overcome this confound, we studied the sleep patterns of three Toba-Qom communities with different levels of access to electric light: a rural community with none, another with very limited access, and an urbanized community. Sleep timing showed a variation throughout the moon cycle, with delayed sleep times on nights preceding the full moon in the three populations. We hypothesized that this represents an adaptation to the hours of evening moonlight in the week before the full moon, which allow for extended evening activity. In fact, moonlight during the evening in the community with no electricity emulated the effects of the access to electric light on sleep that we previously reported in the Toba-Qom. Our results indicate that the availability of moonlight is a strong modulator of sleep and suggest that before access to artificially lit environments moonlight must have been an important driver of early night activity. The persistence of this modulation even in participants with full access to electric light suggests it could be driven by a different environmental cue other than moonlight, for example, changes in the gravitational pull of the moon.

Potential use of the circulating neuronal glycoprotein M6a as a stress biomarker.

MELISA MONTELEONE
Instituto de Investigaciones Biotecnológicas-UNSAM-CONICET

Depression affects hundreds of people. Despite its complex etiology, it is accepted that chronic stress is a key factor in its onset. Since stress main effects occur in the brain, an inaccessible area, we focused in detecting stress molecules in peripheral fluids such as blood or saliva. We showed that the neural glycoprotein M6a can be detected in serum. M6a contributes to neural plasticity promoting neurite and filopodium growth and synaptogenesis (Alfonso 2004, Brocco 2010, Formoso 2016). Next, we showed that M6a is carried in extracellular vesicles (EVs). EVs are liberated by cells in physiological and pathological conditions, can be isolated from almost all fluids and are used in the diagnosis of several diseases. Then, we showed that M6a-carrying EVs, but not EVs without M6a, induced a phenotypical change in COS-7 cells observed as filopodium formation. This indicates that M6a coupled to EVs might participate in cellular communication and contribute to cellular plasticity maintenance. Since M6a has also been related to several neuropsychiatric disorders, we studied serum M6a levels in chronically stressed animals. We found that stress altered M6a levels in blood. Thus, we proposed M6a as a putative stress biomarker (Monteleone, 2017). Now using patient saliva samples, we showed that M6a levels positively correlated with the scores for the perceived stress

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scale in individuals diagnosed with depression. This reinforces the idea of M6a as a stress-responsive protein

Fighting fish: how the social decision making network and sex steroids can explain aggression.

MARÍA FLORENCIA SCAIA
Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires.

The neural substrate of social behavior has been described as a "social decision-making network" (SDMN) in which each brain area is involved in multiple forms of social behavior, including aggression. Interestingly, the neuroendocrine basis of fighting behavior is understudied in females when compared to males. The aim of this study is to compare mechanisms regulating intrasexual aggression in male and female fish. In the first module, we studied the neural substrate of aggression in zebrafish. After performing dyadic encounters, behavioral data is clustered into two groups corresponding to

both sexes. Network analysis shows a higher activation in all brain areas in animals exposed to social interaction, and suggests that patterns of brain activation in the SDMN in female winners differs from female losers and males. This suggests that differences in fighting behavior between males and female are related to differential pattern of brain activation in the SDMN. In the second module we studied the role of sex steroids on aggression in the cichlid Cichlasoma dimerus. Multivariate analysis including hormonal, morphometric and behavioral variables suggests that clustering of males and females into winners and losers is explained by specific agonistic displays, and that estradiol might have a role not only as a positive modulator of aggression, but also as a negative modulator of submission. This study highlights the importance of studying different species to study aggression.

Prefrontal mechanism of resilience after adolescent chronic stress: Implications for dysregulation of fear responses in a model of posttraumatic stress disorder

EVELIN COTELLA
Pharmacology & Systems Physiology , University of Cincinnati

Young Investigator Talks

Developmental stress is usually considered negative, although it is thought that mild to moderate stress during this period can sometimes promote adaptive responses, contributing to adult resilience. We first characterized the effects of chronic variable stress in adolescence (adol CVS) on behaviors related to corticolimbic functionality, to assess possible adult vulnerability and resilience to stress. Sprague Dawley rats were subjected to variable chronic stress in adolescence (adol CVS, 2 weeks, PND45). Adol CVS attenuated the impact of single prolonged stress (SPS), a robust model of PTSD on extinction and reinstatement in a fear conditioning paradigm. The analysis of Fos immunoreactivity pointed to the infralimbic cortex (IL) as a strong candidate for the mechanism behind the effect. We then studied the effect inhibition of IL activity during the experience of SPS by chemogenetics. This intervention enhanced the outcomes in a fear conditioning paradigm, pointing also to a possible involvement of the IL in mechanisms behind risk to PTSD after traumatic experiences. By electrophysiology, we observed that adol CVS is capable of preventing the reduction in excitability of the IL evoked by SPS. Our results indicated involvement of the IL in mediating effects related to resilience after adolescent stress and added new insights into the possible mechanisms behind developmentally driven interindividual differences in the vulnerability to disorders such as PTSD.

When it comes to addiction, it might be better to listen to your gut

SANTIAGO CUESTA

Universidad de Texas Southwestern Medical Center

Substance use disorders (SUDs) affect millions of people worldwide. Yet, no successful evidence-based treatments have been developed. As with other mental health disorders, many factors contribute to SUD risk, including genetics, development, and environment. Recently, the gut-brain axis has emerged as a two-way street in host-microbial interactions. Gut microbiota composition and specific gut microbes modulate different social, stress-related, and cognitive behaviors and an altered gut microbiota has been associated with diverse neurological conditions, including SUDs. However, determining whether these microbiota changes cause, enhance, or are the consequence of psychiatric disease remains unclear. In this talk. I will focus on a) the mechanisms by which specific gut bacteria sense host signals that are altered with psychostimulant use, b) how gut bacteria respond to these host signals to establish themselves within the gut, and c) whether these changes in gut physiology affect the vulnerability to SUDs. Establishing a mechanistic understanding of the gut-brain axis will enable the development of new therapeutic strategies, including the identification of microbial targets that can be non-invasively exploited to reduce SUDs.

Transient Serotonin Inhibition during sensitive periods of development alters anxiety-related behavior and alcohol intake on adolescent mice.

MARÍA CAROLINA FABIO

Instituto de Investigaciones Médicas Mercedes y Martín Ferreyra (INIMEC-CONICET-UNC). Facultad de Psicología UNC.

Young Investigator Talks

Serotonin (5-HT) plays an important role in the organization of the central nervous system and in the development of psychiatric disorders, including anxiety, depression and addiction. Notably, disruption of the 5-HT system during sensitive periods of development exerts long term consequences, including altered anxiety response and problematic use of alcohol. We analyzed, in mice, the effects of transient 5-HT depletion at embryogenesis, infancy or adolescence on subsequent anxiety-like behavior, alcohol-induced anxiolysis and alcohol intake. We found that

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YIT-8

Chairs: Nicolás Unsain.

transient 5-HT inhibition during embryogenesis (gestational days 14-17; 200 mg/kg PCPA) induces compulsive-like behaviors and enhance ethanol-induced anxiolysis. We also injected PCPA at infancy (postnatal days 14-16; PD14-16) or adolescence (PD40-42). And found that female, but not male, mice transiently depleted of 5-HT at adolescence but not those depleted at the perinatal stage exhibited a significant reduction in anxiety response, which was accompanied by a significant reduction on alcohol intake. Transient 5-HT inhibition at prenatal stages may induce compulsive-like behaviors and make adolescents more vulnerable to anxiolytic effects of ethanol, making them more prone to consume higher amounts of alcohol. Nevertheless, when 5-HT system is interrupted during adolescence PCPA may selectively act as a protective factor for subsequent emergence of anxiety disorders and problematic use of alcohol.

La SUMOilación como regulador de proteínas clave involucradas en la respuesta al estrés

MAIA LUDMILA BUDZIÑSKI

Instituto de Biomedicina de Buenos Aires-CONICET- Instituto Partner de la Sociedad Max Planck (IBioBA-CONICET-MPSP)

El eje hipotalámico-pituitario-adrenal (HPA) es fundamental para controlar la respuesta al estrés. Los glucocorticoides (GC), ayudan a orquestar esta respuesta y a restaurar la homeostasis a través de un feedback negativo en varias regiones del cerebro. La hiperactividad del eje y altos niveles de GC en pacientes depresivos se atribuyen a alteraciones en la regulación del feedback, causadas por la función alterada del receptor de glucocorticoides (GR). Los antidepresivos (ADs) disminuyen lostrastornos neurobiológicos de la depresión, incluida la hiperactividad del eje HPA, y alivian los síntomas depresivos, en parte mediante la restauración de las funciones del GR.

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FKBP51 es un inhibidor de la actividad del GR y su expresión aumentada está relacionada con la resistencia del GR, convirtiéndolo en un blanco terapéutico importante. La actividad del GR está regulada por la conjugación de SUMO a FKBP51, la cual es necesaria para la inhibición dependiente de Hsp90 de FKBP51 sobre la actividad del GR. Demostramos que los ADs inhiben la SUMOilación de FKBP51 al reducir la interacción entre la E3 ligasa PIAS4 y FKBP51. Además, que los ADs inhiben la interacción de FKBP51 con Hsp90 y por tanto con el GR, restaurando así la actividad del GR. Estos resultados describen la acción de los ADs como moduladores de la SUMOilación de FKBP51, como un interruptor molecular para restaurar la sensibilidad del GR, proporcionando nuevos potenciales mecanismos de intervención farmacológica.

Sexual dimorphism and cognitive impairment in a transgenic rat model of Alzheimer's-like brain amyloidosis versus normal aging

MARTIN HABIF
Laboratory of Neuroplasticity and Neurotoxins (LAN&N). IBCN "Prof. EDUARDO DE ROBERTIS" Facultad de Medicina-UBA

McGill-R-Thy1-hAPP transgenic rat model (Tg) of Alzheimer´s Disease (AD) harbors the human APP with two familial AD mutations (Sw/Ind), which favor its amyloidogenic processing and Aβ accumulation. We recently reported LTM (previous reports only addressed STM) and social interaction deficits in 4 and 6-month-old (mo) hemizygous Tg males, while 4mo females seemed to learn and remember as wild type littermates (wt). To further characterize cognitive features in Tg rats and discriminate putative age deficits from those likely due to amyloidosis, we evaluated 12mo rats in a set of behavioral tasks. Both wt and Tg males and females equally habituated to the open field (OF). For the step-through inhibitory avoidance (IA) performance, whilst wt and Tg females formed LTM with memory persistence (after 14 days), wt males showed only LTM, and Tg neither of them. Wt rats of both sex showed STM and LTM for the novel object recognition (NOR) task, while Tg animals only showed STM. Unlike wt males, wt females were able to discriminate novel object location (NOL), but neither Tg females nor males could complete the task. Our results highlight sexual dimorphism in learning and the establishment of new associative memories in middle-aged rats. Also support potentially predictive features of the Tg model based on specific cognitive alterations, suggesting that similar changes might be present in preclinical AD phases, though unnoticed due to the neural and cognitive reserve of human beings.

Cholecystokinin (CCK) modulates ventral tegmental area (VTA) GABAergic plasticity

VALENTINA MARTINEZ DAMONTE
Stanford University

Young Investigator Talks

The neural substrate of social behavior has been described as a “social decision-making network” (SDMN) in which each brain area is involved in multiple forms of social behavior, including aggression. Interestingly, the neuroendocrine basis of fighting behavior is understudied in females when compared to males. The aim of this study is to compare mechanisms regulating intrasexual aggression in male and female fish. In the first module, we studied the neural substrate of aggression in zebrafish. After performing dyadic encounters, behavioral data is clustered into two groups corresponding to both sexes. Network analysis shows a higher activation in all brain areas in animals exposed to social interaction, and suggests that patterns of brain activation in the SDMN in female winners differs from female losers and males. This suggests that differences in fighting behavior between males and female are related to differential pattern of brain activation in the SDMN. In the second module we studied the role of sex steroids on aggression in the cichlid Cichlasoma dimerus. Multivariate analysis including hormonal, morphometric and behavioral variables suggests that clustering of males and females into winners and losers is explained by specific agonistic displays, and that estradiol might have a role not only as a positive modulator of aggression, but also as a negative modulator of submission. This study highlights the importance of studying different species to study aggression.

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OC-1

Chair: Patricia Setton

Intramuscular insulin-like growth factor-1 gene therapy modulates reactive microglia after traumatic brain injury

MACARENA LORENA HERRERA

Departamento de Farmacología. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba. Instituto de Farmacología Experimental de Córdoba (IFEC). CONICET

Reactive gliosis is a key feature and an important pathophysiological mechanism underlying chronic neurodegeneration following traumatic brain injury (TBI). In this study, we have explored the effects of intramuscular IGF-1 gene therapy on reactive gliosis and functional outcome after an injury of the cerebral cortex. Young adult male rats were intramuscularly injected with a recombinant adenoviral construct harboring the cDNA of human IGF-1 (RAd-IGF1), with a control vector expressing green fluorescent protein (RAd-GFP) or PBS as control. Three weeks after the intramuscular injections of adenoviral vectors, animals were subjected to a unilateral penetrating brain injury. The data revealed that RAd-IGF1 gene therapy significantly increased serum IGF1 levels and prevent working memory deficits after one week of TBI. At the same time, when we analyzed the effects of therapy on glial scar formation, the treatment with RAd-IGF1 did not modify the number of glial fibrillary acidic protein but we observed a decrease in vimentin immunoreactive astrocytes at 7 days post-lesion in the injured hemisphere, compared to animals treated with RAd-GFP. Moreover, IGF-1 gene therapy reduced the number of Iba1+ cells with reactive phenotype and the number of MHCII+ cells in the injured hemisphere. These results suggest that intramuscular IGF-1 gene therapy may represent a new approach to prevent traumatic brain injury outcomes in rats.

Hypothalamic proopiomelanocortin expression restricted to GABAergic neurons prevents overfeeding and Neuropeptide Y overexpression

MILAGROS TROTTA

Laboratorio de Neuroendocrinología Molecular, Instituto de Fisiología y Biofísica "Bernardo Houssay" (IFIBIO, UBA-CONICET), Universidad de Buenos Aires-CONICET

The arcuate nucleus is a key regulator of energy homeostasis in which different neuronal populations integrate peripheral signals of energy status. In particular, arcuate proopiomelanocortin (POMC) neurons inhibit food intake and promote energy expenditure. Due to the existence of different subpopulations of POMC neurons secreting antagonistic neurotransmitters such as glutamate or GABA, it is proposed that Arc-POMC neurons could have different physiological roles and targets. In the present study, we aimed to elucidate the contribution of the subpopulation of Arc-POMC GABAergic neurons in the control of energy balance by expressing Pomc exclusively in GABAergic-

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POMC neurons. We found that Pomc rescue restricted to GABAergic neurons leads to food intake normalization and body weight enhancement. Surprisingly, these physiological improvements were achieved with the recovery of Pomc expression in only 25% of total hypothalamic POMC neurons. Immunohistochemical analysis showed that GABAergic POMC neurons preferentially project to the dorsomedial hypothalamus (DMH), a nucleus that induces food intake by releasing NPY. In addition, we found that DMH-NPY expression is negatively correlated with Pomc expression in GABAergic-POMC neurons, suggesting that food intake may be regulated by an Arc-GABAergic-POMC→ DMH-NPY pathway.

Motor replays of song during sleep in a suboscine bird

JUAN FRANCISCO DÖPPLER

Laboratorio de Sistemas Dinámicos, Departamento de Física, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; IFIBA-CONICET

Birdsong production requires a precise control of the respiratory system and muscles in the syrinx, the avian vocal organ. Oscine birds use a set of highly developed neural nuclei which produce precise patterns of activity to achieve this. Interestingly, these patterns have been shown to occur spontaneously during sleep. Even more, while the respiratory pathway is blocked during sleep (and thus birds don't sleep-sing), the pathway innervating the syrinx is not, and this activity arrives at the muscles, making the periphery a window into the sleeping brain. In tyrannid suboscine birds (phylogenetically close to oscine birds, usually considered non-learners) such developed neural nuclei haven´t been found, thus making this window a unique tool to study sleep in the non-learning brain. In this work we study the suboscine Pitangus Sulphuratus. We focus on the obliquus ventralis, a muscle involved in the amplitude modulation of sound during song. We show that events of song-like activity occur during sleep, as in the case of oscine birds. This activity is consistent with the rehearsal of the song, or part of it, and has some variability not observed during wake. We also find a set of qualitatively different events, compatible with another vocalization, usually produced during territorial dispute and accompanied by a behavioral display. Using recordings of the sleeping bird we show that the activity is consistently produced during sleep simultaneously with the behavioral display.

Sensory adaptation and the representation of complex odors in the antennal lobe of Apis mellifera.

FEDERICO GASCUE

Laboratorio de Plasticidad Sensorial/IFIByNE/UBA

Sensory systems must be adjusted based on the animal's experience in order to optimize perception of relevant information and ignore stimuli without predictive value. In this context, one of the main phenomena that modulate the olfactory system is adaptation, which is defined as the decrease of the sensitivity or response to an odor after a sustained exposure to it. Adaptation may occur in brief

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intervals of time and depends on the immediate experience of the animal. In this project, we use Apis mellifera to study the representation of binary mixtures of odors in the brain after sensory adaptation to one of the components. We performed calcium imaging experiments to measure odor induced signals in the antennal lobe, the first olfactory neuropil in the insect brain. We determined that, after olfactory adaptation, response patterns encoding the mixture are drastically altered, in a way that favors the representation of the non-adapted component. These changes are relatively brief, lasting about a minute. Additionally, by means of behavioral experiments, we show that adaptation reduces appetitive learning of the adapted component, while it enhances learning of the other component in cases in which it would normally stay occluded. These results suggest that olfactory adaptation is critical to allow detection of minor components present in complex mixtures, emphasizing that sensory adaptation is a fundamental mechanism to improve sensitivity to salient and discrete stimuli.

Nav1.8 relation with chronic inflammatory pain and aging

DIEGO NICOLÁS MESSINA

Laboratorio de Neurobiología del Dolor, Instituto de Histología y Embriología de Cuyo (IHEM - CONICET - UNCuyo)

We aimed to determine the expression pattern of Nav1.8 in primary sensory neurons of the DRG in young adult rats (3-6 months) and aged rats (12-18 months), and correlate this pattern with the behavioral changes observed in a model of chronic inflammatory pain. We quantified the expression of Nav1.8 by ABC/DAB immunohistochemistry in serial sections of L4 and L5 DRGs from Wistar rats aged 3, 6, 12 and 18 months. We induced inflammation with an intradermal injection of Complete Freund's Adjuvant solution (CFA) in 8 3-months-old and 12 14-months-old rats. We evaluated two types of pain during 120 days after CFA: spontaneous pain, using the spontaneous foot lifting test (SFL) and evoked pain, with the von Frey test. Nav1.8 staining intensity in small neurons was lower in 3-month-old than in 6-month-old rats (36.5±0.9% vs 49.9±1.3%, $p<0.0001$), and it was similar between 12 and 18 months. The proportion of Nav1.8 positive neurons (intensity ≥40%) tended to increase with age from 35% at 3 months to 69% at 18 months ($p=0.0368$). Aged rats had a faster reversal of the SFL phenotype than young ones (21 d vs 28 d) although its intensity was higher to begin with. The reversal of mechanical hyperalgesia was slower in aged rats (49 d vs. 21 d). Lower Nav1.8 expression in young rats associated with lower intensity of SFL events and with a faster reversal of mechanical hyperalgesia. A higher expression of Nav1.8 could be related to the persistence and intensity of pain in aged individuals.

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OC-2

Chair: Nicolás Unsain

Neural bases of Predictions during reading

BRUNO BIANCHI
Laboratorio de Inteligencia Artificial Aplicada (DC-FCEN-UBA)

Our brain is constantly performing predictions about upcoming events. By doing this, we can anticipate actions to take and rapidly respond to those probable future events. For example, during visual tasks, such as reading, predictions allow us to plan and perform ocular movements (that are responsible for the inspection and processing of the visual field) and to integrate words with their context more easily. In a series of studies, we analyzed the brain bases of predictions performed while reading natural stimuli, and modeled the Predictability (i.e. the variable that represents how probable is to guess a word before reading it) with computational models: (1) on an eye movement experiment, where participants read short stories, we analyzed how different computational models can mimic Predictability effect on gaze duration; (2) on an EEG experiment, where participants read Memory-Related and Common Sentences in a Serial Visual Presentation paradigm, we analyzed how different sources of predictions impacts on Evoked Potentials, like the N400; (3) finally, in an eye-movements and EEG co-registration study, where participants read Memory-Related and Common Sentences in a natural reading paradigm, we analyzed how Evoked Potentials are modified by natural reading. We conclude that predictions are performed using different sources (semantical, grammatical, syntactical, mnemonic, etc), and that there are different brain mechanisms underlying mnemonic predictions.

A Bayesian model for guidance of eye movements in visual search in natural images

GASTON BUJIA
Laboratorio de Inteligencia Artificial Aplicada (ICC)

From detecting potential threats to search for some desired object like food, visual search is one of the most essential visual abilities for humans. In the last decades, there was a large development of models that accurately predict the most likely fixation locations (saliency maps), although they are not able to follow the sequence of eye movements (scanpaths). Today, one of the biggest challenges in the field is to go beyond saliency maps to predict task-specific scanpaths. Particularly, in visual search tasks in artificial images, Ideal Bayesian observers have been proposed to model the visual search behavior as an active sampling process. In this process, during each fixation, humans incorporate new information and update the probability of finding a target at every location. Here, we propose a combined approach for predicting scanpaths, using state-of-the-art saliency maps to model prior

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image information in a Bayesian searcher framework. We collected eye-movement visual search data (N=57) in natural indoor scenes and compare different variants of the model. First, we compare different state-of-the-art saliency maps with human fixations, reaching similar AUC performances in the first fixations as in other datasets, but AUC strongly drops after that. Second, we compare different search strategies against human's scanpaths. Our model achieves the best agreement between metrics and outperforms other strategies, generating scanpaths almost indistinguishable from humans.

A Computational Theory for the Emergence of Grammatical Categories in Cortical Dynamics

DARIO JESUS DEMATTIES

Centro Científico Tecnológico Conicet Mendoza, Instituto de Ciencias Humanas, Sociales y Ambientales, Mendoza, Argentina

A general agreement in psycholinguistics claims that syntax and meaning are unified precisely and very quickly during online sentence processing. Although several theories have advanced arguments regarding the neurocomputational bases of this phenomenon, we argue that these theories could potentially benefit by including neurophysiological data concerning cortical dynamics. In this work we introduce a computational model inspired in the dynamics of cortical tissue. In our model, proximal afferent dendrites produce stochastic cellular activations, while distal dendritic branches contribute independently to somatic depolarization by means of dendritic spikes, and finally, prediction failures produce massive firing events preventing formation of sparse distributed representations. This model combines semantic and syntactic constraints for each word in a sentence context until grammatically related word function discrimination emerges spontaneously by the sole correlation of lexical information from different sources without applying complex optimization methods. We show that the sparse activation features returned by our approach are well suited to accomplish grammatical function classification of individual words in a sentence. In this way we develop a biologically guided computational explanation for linguistically relevant unification processes in cortex which connects psycholinguistics to neurobiological accounts of language.

Restoration of plasticity in tissues with neuronal ischemia

SABRINA NATALÍ GUISANDE DONADÍO

Grupo de neurociencia computacional / IFLP / UNLP

Cerebrovascular ischemia is an interruption or decrease in blood supply to the brain that reduces the flow of oxygen and nutrients needed to maintain normal cell function. Neuronal cell death in a particular region changes the receptive fields of the neurons surrounding the damaged tissue. Healthy neurons surrounding the injury experience a disinhibition of their receptive fields and expand into the injury. This expansion is determined by the distance from the healthy neuron to the lesion and the extent of the damage. In this work we developed a computational and analytical model

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that considers a lesion in a neuronal population and investigated the effects of the lesion on the surrounding receptive fields. It is found that exists an optimal value of plasticity for which the functional recovery is maximum. At the experimental level, investigating the neuronal signals of the imagined visuomotor tasks is very important to detect possible neuronal damage. Hence, experimental EEG data are analyzed by combining an information theory approach that takes into account signal causality, together with a quantification of centrality levels for the different nodes, to discriminate imagined and performed visuomotor tasks considering different rhythmic oscillations. It was found that the imagined cognitive processes coincide with high levels of centrality in the alpha frequency band for the different nodes, and that it is possible to discriminate the performed and imagined task.

Electrophysiological characterization of a behavioral index that quantifies the degree of loss of consciousness in epileptic seizures

CLAUDIO SEBASTIÁN SIGVARD

Instituto Balseiro

In 2009, the Consciousness Seizure Scale (CSS) was proposed to quantify the degree of loss of consciousness, summarizing the response of a patient to 8 behavioral items performed by a clinical practitioner during or after a seizure. The 8 items quantify the ability to interact with the practitioner, to recognize the seizure as such, and the degree of memory impairment. Here we analyzed the physiological correlates of the CSS by studying the electric potential recorded with intracranial electrodes in patients requiring an exploratory study before epilepsy surgery. We analyzed 26 seizures recorded from 5 patients, each with 5-6 electrodes and each electrode with 9 contacts (1599 signals in total). We found that the items that assessed memory impairment were positively correlated with the total duration of the seizure, with maximal correlation between the electrical anomaly and the behavioral tests approximately 60 seconds after seizure onset. The items assessing the ability to interact with the practitioner, instead, were positively correlated with the propagation velocity throughout the recruited areas, with maximal correlation between electrical and behavioral properties approximately 30 seconds after seizure onset. We conclude that the signals recorded with intracranial electrodes contain information about the different capacities that sustain conscious processing, and that the impairment of different capacities follows discernable temporal profiles.

Characterization of color induction by perceptual distance reveals a simple perceptual law

NICOLÁS VATTUONE

Insituto Balseiro, Centro Atómico Bariloche

The perceived color of a stimulus depends not only on its spectral properties but also on those of its surround. For instance, a patch that looks gray on an achromatic background appears reddish on a green background, and greenish on a red background. Previous studies showed that the effect of the

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surround is repulsive: It enhances the perceptual difference between stimulus and surround. We performed psychophysical experiments to quantify the repulsion. To report the results, a notion of distance in color space was required. We therefore proposed an individually tailored metric in color space that captured the perceptual abilities of each observer. To define the metric, we determined the minimal chromatic difference between a stimulus and its surround required by each subject to detect the stimulus. Next, observers performed discrimination experiments between two spatially localized stimuli presented in a surround of a different chromaticity. The surrounding color affected the discrimination thresholds. Quite remarkably, when these thresholds were expressed in the color coordinates defined before, the change in thresholds followed a simple law that only depended on the distance between the surround and the two compared stimuli. Perceptual coordinates, hence,

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OC-3

Chair: Alejandra Pacchioni

reveal the symmetry of the repulsion effect. This finding was confirmed with a third experiment, in which subjects were asked to match the color of two stimuli presented in two different surrounds.

Specific tyrosine phosphorylation of α7 nicotinic receptor modulates its ionotropic and metabotropic responses

JUAN FACUNDO CHRESTIA

Departamento de Biología Bioquímica y Farmacia U.N.S. / Instituto de Investigaciones Bioquímicas de Bahía Blanca INIBIBB-CONICET

The α7 nicotinic acetylcholine receptor in neurons is associated to neurological and neurodegenerative disorders. α7 is also expressed in glial and immune cells, where it plays a role in neuroprotection and inflammation. Protein phosphorylation is an important regulatory mechanism involved in physiological and pathological processes. We investigated the role of tyrosine phosphorylation of α7 in its dual ionotropic/metabotropic function. In cells expressing α7, single-channel activity appears as brief isolated openings and episodes of few openings in quick succession (bursts). Inhibition of Src family kinases by PP2 as well as co-expression of α7 with an inactive Src kinase increase the duration and frequency of bursts, while inhibition of tyrosine phosphatases decreases open and burst durations without affecting channel amplitude. A mutant α7 lacking

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phosphorylation sites shows longer burst durations and insensitivity to PP2, thus revealing that the two tyrosine residues in the intracellular domain (ICD) are involved in receptor modulation. Cells exposed to a specific α7 agonist show an increase of ERK1/2 phosphorylation, which is detected neither in the presence of Src family kinases inhibitors nor in cells expressing the mutant receptor lacking tyrosines. Thus, phosphorylation negatively modulates ionotropic α7 activity probably by enhancing desensitization whereas the phosphorylated state of α7-ICD is required for the metabotropic receptor responses.

Executive deficits in early use of cocaine: Structural and functional signatures of caudate depend upon route of administration

LAURA ALETHIA DE LA FUENTE
COCUCO/DF-IFIBA/UBA

Despite of evidence suggesting that the route of administration should be taken into account to assess the short and long-term effects of cocaine consumption, to our knowledge no study to date has characterized clinically relevant neuropsychological and physiological variables comparing individuals with histories of smoked cocaine dependence (SCD) and insufflated cocaine hydrochloride dependence (ICD). The present study examined a sample of 25 participants who fulfilled criteria for SCD, 22 for ICD, and 25 healthy controls matched by age, gender, education, and socioeconomic status. An exhaustive NPS battery was used to assess cognitive domains (attention, executive functions, fluid intelligence, memory, language and social cognition). We complemented this NPS assessment with structural (MRI) and functional (fMRI) neuroimaging data. We found that different routes of administration led to equally different profiles of neurocognitive impairment, with the SCD group being specifically associated with deficits in executive-attention functions. Consistent with risk models, executive-attention function deficit is better explained by age and age at the first use of the drug. SCD presented reduced grey matter density relative to ICD and CTR in the bilateral caudate, a key area for executive functions and attention. Specifically, connectivity between left caudate and inferior frontal regions in SCD mediated performance-structure association.

Evaluation of microglial depletion followed by repopulation in chronic CPZ-induced demyelination

ANABELLA AYELEN DI PIETRO
Departamento de Química Biológica, Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires-CONICET

Demyelinated axon degeneration is the major cause of irreversible neurological disability in patients with progressive multiple sclerosis (MS). Cuprizone (CPZ) administration for more than 12 weeks can model progressive MS in triggering chronic demyelination, neurodegeneration, astrogliosis and exacerbated microglia (MG) activation. MG are physiologically dependent on colony-stimulating factor 1 receptor (CSF-1R) signaling and can thus be almost completely eliminated from the brain

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using CSF-1R inhibitors like BLZ945. Our previous results show that continuous BLZ945 treatment attenuates demyelination but exacerbates axonal degeneration, whereas MG depletion followed by repopulation has been shown to normalize MG chronic activation. The present work aimed to compare the effects of continuous and intermittent BLZ945 treatment on chronically CPZ-demyelinated mice. Mice were fed either control or CPZ chow for 12 weeks and orally gavaged vehicle or BLZ every week (continuous) or every other week (intermittent) from the 5nd week. BLZ induced a reduction in the number of MG in all structures evaluated and equally attenuated demyelination in both protocols. Functional evaluation showed no significant differences across groups. In conclusion, the intermittent protocol failed to yield microglial repopulation, and future experiments with sparser BLZ945 treatment may help test our hypothesis. These studies may render therapies to effectively treat patients in progressive stages of MS.

Early neuroprotective effects of Palmitoylethanolamide after perinatal asphyxia.

MARÍA INÉS HERRERA

CONICET - UCA. Centro de Investigaciones en Psicología y Psicopedagogía (CIPP)

Perinatal asphyxia (PA) is an obstetric complication associated with poor gas exchange, which continues to be a morbidity factor in neurodevelopment. Therefore, we aimed to study early neuroprotective effects of the endogenous lipid compound, Palmitoylethanolamide (PEA), in an experimental model that induces PA in the immature rat brain. PA was induced by placing newborn Sprague Dawley rats in a 37 ° C water bath for 19 minutes. PEA treatment (10 mg/kg) was administered subcutaneously during the first hour of life. Examination of neurobehavioral development was performed from postnatal day 1 (P1) to postnatal day 21 (P21). Hippocampal modifications were analyzed with Immunohistochemistry and Western Blot at P21. During the first 3 weeks of life, there was a significant delay in weight gain, as well as in the appearance of negative geotaxis and the sensory eyelid, auditory startle and air righting reflexes, being the forelimb placing and grasp reflexes the most affected. In the CA1 hippocampal region, PA-induced neuronal morphological damage and biochemical changes were evidenced by a decrease in the microtubule associated protein-2 (MAP-2) reactive area and protein expression level at P21. Treatment with PEA attenuated hippocampal damage and several functional alterations observed in neurodevelopment. These results contribute to the future establishment of early intervention strategies for the developing brain.

Bilirubin disrupts calcium homeostasis in neonatal hippocampal neurons: a new pathway of neurotoxicity

ROSSANA RAUTI

International School for Advanced Studies (SISSA), Trieste, Italy

Oral Communications

Severe hyperbilirubinemia leads to bilirubin encephalopathy in neonates, with irreversible neurological sequelae. We investigated the neuronal vulnerability to unconjugated bilirubin (UCB) toxicity. The calcium (Ca2+) homeostasis is crucial for neuron survival. Ca2+ release from endoplasmic reticulum (ER) during ER-stress can lead to apoptosis trough Caspase-12 activation. By live Ca2+ imaging we monitored Ca2+ signals in hippocampal neuroglia cells exposed to UCB doses, showing the ability of UCB to alter intracellular Ca2+ homeostasis. The contribution of intracellular Ca2+ stores and the activation of proteins involved in the apoptotic Ca2+ signaling were also assessed. Thapsigargin, specific inhibitor of Sarco/endoplasmic reticulum ATPase pumps, significantly reduced the duration of Ca2+ oscillation associated with UCB exposure indicating that UCB strongly interfered with the reticulum Ca2+ stores. Contrarily, in pure astrocyte cultures, spontaneous Ca2+ transient duration was not altered by UCB. The protein content of GRP78, AT6, CHOP, Calpain and Caspase-12 treated with UCB was twofold higher compared to controls. Ca2+-dependent Calpain and Caspase-12 induction by UCB were significantly reduced when cells were pretreated with the ER-stress inhibitor 4-PBA. We showed the direct interference of UCB with neuronal intracellular Ca2+ dynamics, suggesting ER Ca2+ stores as a primary target of UCB toxicity with the activation of the apoptotic ER-stress-dependent pathway.

Recent advances in psychedelic drugs reasearch: antidepressant-like effect after a single dose of ibogaine or its metabolite noribogaine in rats

PAOLA RODRIGUEZ CAMAROT

Departamento de Neurofarmacología Experimental. Instituto de Investigaciones Biológicas Clemente Estable

Preclinical research in psychedelics drugs has dramatically increased within the last decade focus on its therapeutic potential in psychiatric disorders. Observational data and animal studies have demonstrated a potent anti-addictive effect of psychedelic alkaloids ibogaine (Ibo), and its metabolite noribogaine (Nor); however, the underlying mechanism remains under study. We hypothesized that the anti-addictive property of both psychedelics can be related to an antidepressant-like effect, since ibogaine and noribogaine inhibit the serotonin transporter, and ibogaine increased the brain-derived neurotrophic factor RNAm levels in the rat prefrontal cortex. We evaluated the behavioral effects (dose- and time-dependence) induced by a single dose of Ibo and Nor administration (20 and 40 mg/kg i.p.) by the rat forced swim test. A correlation between plasma and brain concentrations of Ibo and Nor and the behavioral response was performed. Ibo and Nor induced a dose- and time-dependent antidepressant-like effect without changes of motor activity. A correlation between plasma and brain concentrations and behavior was found. Notably, that behavioral effect was not reproduced by an equivalent dose of the classic selective serotonin reuptake inhibitor fluoxetine (40 mg/kg, i.p., single injection). Our results suggest a polypharmacological mechanism underpinning the antidepressant-like effects of Ibo and Nor, and we propose that this effect can collaborate to its anti-addictive property.

Oral Communications

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OC-4

Chair: Graciela Mazzone

Unveiling neuronal glycoprotein M6a partners by high throughput quantitative mass spectrometry

GABRIELA APARICIO

Instituto de Investigaciones Biotecnológicas IIBio-UNSAM

The molecular mechanisms underlying structural neuronal plasticity are not completely understood. In this regard, neuronal membrane glycoprotein M6a contributes to this process by unknown mechanisms. Alterations in M6a levels are associated with mental disorders like schizophrenia, depression and Alzheimer's disease. Evidence suggests that the extracellular loops of M6a command its neuroplastic function. Therefore, we aimed to identify proteins that associate with M6a's extracellular loops. We generated a chimera protein that only contains the extracellular loops of M6a and performed a co-immunoprecipitation with rat hippocampus samples followed by TMT/MS identification. Data analysis revealed 72 candidate proteins to interact with M6a's extracellular loops. Gene ontology analysis showed that 45 of these proteins are located at the synapses while 22 are in the surface of oligodendrocytes. We characterized the interaction of M6a with piccolo, SV2B, and synapsin 1 in cultured hippocampal neurons. Moreover, we demonstrated the interaction between M6a with proteolipid protein (PLP) in N2a cells. Finally, a disease-associated genes and variants screening by DisGeNET revealed that most of the 72 proteins are involved in "autistic disorder," "epilepsy," and "seizures" increasing the spectrum of disorders in which M6a could play a role. Data are available via ProteomeXchange with identifier PXD017347.

Signs of vascular alteration and inflammation in different brain areas of SHR pups

JOANA ANTONELA ASENSIO

IHEM-CONICET, Mendoza, Argentina

Fetuses suffering intrauterine growth restriction (IUGR) are at high risk of brain injury and motor disabilities. Vascular rarefaction and inflammatory processes have been associated with these

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pathologies. We previously observed a delay in cerebellar layers stratification and neurodevelopmental impairment in spontaneously hypertensive rat pups (SHR), a proposed model of IUGR. In this work, SHR brains were obtained at P7 and P14; age matched normotensive Wistar Kyoto rats served as controls. The morphology and number of medium-caliber vessels was studied with Masson's trichrome. Our results indicate that SHR showed a significant increase in the number of these vessels from both gray and white matter. We also performed double labeling for anti-Caveolin-1 and isolectin B4 to study microvasculature and microglial cells. No changes were found in the amount and ramifications of brain microvessels. A significant increase in the number of ameboid microglia was noticed in the cerebellum of the SHR at P7 and P14. GFAP expression, an important component of astrocytes cytoplasm, was increased in homogenates from motor cortex that included corpus callosum, and its localization in this area was confirmed by GFAP IFI. Insulin-like growth factor gene expression was increased in the cerebellum of SHR; probably related to the significant increase in the number of ameboid microglia. We conclude that SHR brain shows vascular adaptations and glial activation in response to gestational hypoxia.

IMT504 provides analgesia by modulating cell infiltrate and cytokine milieu in rats with hindpaw inflammation

CANDELARIA LEIGUARDA

Instituto de investigaciones en medicina traslacional (IIMT-CONICET-UNIVERSIDAD AUSTRAL)

IMT504 is a non-CPG, non-coding synthetic ODN exerting long-lasting anti-allodynic effects in rats undergoing unilateral hindpaw inflammation. The purpose of the present study is to address cellular and molecular mechanisms at the site of injury potentially underlying the anti-nociceptive role of IMT504. Analysis of pain-like behavior, locomotor activity, histology, cell infiltration by flow-cytometry, secreted proteins by protein microarrays or ELISA (β-endorphins) in the inflamed hindpaws were employed to study the impact of a single subcutaneous administration of IMT504 in male adult rats undergoing complete Freund´s adjuvant-induced hindpaw inflammation. We show that a single subcutaneous dose of IMT504 results in a 6-week-long full reversal of mechanical and cold allodynia, compromising neither acute pain perception nor locomotor activity. The anti-nociceptive effects of systemic IMT504 correlated with reductions in hindpaw dorsoventral thickness, plasma extravasation, decreases in B-cell and macrophage counts, and an increase in CD8+ T-cell counts. Moreover, a profound downregulation in several pro-inflammatory cytokines as well as of β-endorphin, plus mild upregulation of IL-10, were also observed at the site of injury. Altogether, we provide new evidence demonstrating that the anti-nociceptive actions of IMT504 relate to modulation of the peripheral immune system at the site of injury, and support its use as a novel anti-inflammatory drug against chronic pain.

The input shapes the output: commonly used neuronal activation protocols induce different transcriptional responses

JERONIMO LUKIN

Oral Communications

IBioBA - Max Planck Partner Institute

Activity-driven gene expression is necessary to implement synaptic plasticity mechanisms required to encode, store and retrieve long-lasting information. The precise activity-transcription coupling has been extensively studied in neuronal cultures but the underlying mechanisms are not fully clear yet. Multiple studies approached this question using 3 stimulation protocols: KCl, Bicuculline (Bic) and TTX withdrawal (TTXw). KCl drastically changes membrane potential in a sustained manner, Bic induces synaptic bursting and TTXw, elicits a rebound-based neuronal activity response after a long-lasting silencing. Despite these protocols have different mechanisms of action, they have been indistinguishably employed in the field. Thus, we wonder whether they can be considered as truly equivalent protocols. To address this question, we used activity-driven gene expression as a proxy: we stimulated neuronal cultures with KCl, Bic and TTXw and globally examined mRNA expression at different time-points by RNA-seq. PCA analysis showed strong divergencies, with TTXw being clearly different compared to KCl and Bic. Gene set enrichment analysis and clustering approaches indicated that each protocol induced specific modules of genes with particular temporal dynamics and related to different biological processes. These results indicate that KCl, Bic and TTXw are not functionally equivalent what might help explain multiple discrepancies found throughout the extensive literature of the field.

Long term Glyphosate exposure impairs synaptic development and cognitive functions in juvenile rats

SEBASTIAN LUNA
LATOEX, FbioyF UNR

Glyphosate (Glyph)-based formulations are the most widely used herbicides in the world and their consumption has increased dramatically in recent years. The nervous system results highly vulnerable to a wide spectrum of environmental pollutants that may be linked to the development of brain disorders. In this sense, pesticides exposure has been proposed as the main environmental factor associated with deficits in neurobehavioral performance and neurodegenerative pathologies. Therefore, in the present study we aimed to describe the Glyph effect in the regulation of synaptic assembly in the hippocampus, through in vitro and in vivo assays. Our results reveal that Glyph exposure during a critical period of synaptogenesis decreased dendritic spine density as well as synaptic protein expression, such as PSD-95 and Synapsin-I, in mature cultured neurons. In addition, the exposure of juvenile rats to Glyph reduced PSD-95 protein levels and altered postsynaptic organization in the hippocampus. To associate these abnormalities with cognitive dysfunction we evaluated spatial learning and memory and recognition memory by the Morris water maze and the Novel Object Recognition tests, respectively. We found that Glyph treatment induced memory deficits in both tests compared to controls. Together, these findings suggest that Glyph exposure alters neuronal maturation and synaptic organization impairing normal brain connectivity and complex cognitive behaviour.

Oral Communications

A new antagonist of Caenorhabditis elegans glutamate-activated chloride channels with anthelmintic activity

ORNELLA TURANI

Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB) - UNS

Nematode parasitosis causes mortality and morbidity in humans and losses in livestock and domestic animals. The acquisition of resistance to current anthelmintic drugs has prompted the search for new compounds for which the nematode Caenorhabditis elegans has emerged as a valuable platform. We have previously synthetized a library of compounds and determined that dibenzo[b,e]oxepin-11(6H)-one (doxepinone) reduces swimming rate, induces paralysis, and decreases the rate of pharyngeal pumping on C. elegans. To identify the drug targets, we performed a screening of strains carrying

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Chair: Juan Ferrario

mutations in Cys-loop receptors involved in worm locomotion for determining resistance to doxepinone effects. A mutant strain that lacks subunit genes of the glutamate-gated chloride channels (GluCl), which are targets of the antiparasitic ivermectin, is resistant to doxepinone effects. To unravel the molecular mechanism, we measured whole-cell currents from GluClα1/β receptors expressed in mammalian cells. Glutamate elicits macroscopic currents whereas no responses are elicited by doxepinone, indicating that it is not an agonist of GluCls. Preincubation of the cell with doxepinone produces a significant decrease of the decay time constant and net charge of glutamate-elicited currents, indicating that it inhibits GluCls. Thus, we identify doxepinone as an attractive scaffold with promising anthelmintic activity and propose the inhibition of GluCls as a potential anthelmintic mechanism of action.

Long-lasting antiallodynic effects of IMT504 in rats with spared nerve injury relate to strengthened migration of mesenchymal stem cells towards injured nerves

MAILÍN CASADEI

Acute and Chronic Pain Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET

Oral Communications

Peripheral neuropathic pain is caused by injury or dysfunction of peripheral nerves, and is characterized by allodynia and hyperalgesia. Neuropathic pain is complex and difficult to treat, in many cases resistant to currently available pain drugs. We have shown that multiple systemic doses of the oligodeoxynucleotide (ODN) IMT504 result in clear and long-lasting antiallodynic and anti-inflammatory effects in rats with unilateral sciatic nerve crush or hindpaw inflammation. Interestingly, in rats with sciatic nerve crush, virtually identical allodynia-preventing effects were observed after systemic administration of IMT504 or exogenous rat bone marrow mesenchymal stem cells (BMMSC). Here, we address the role of IMT504 in a model of chronic neuropathic pain, and the involvement of BMMSC. Early or late IMT504 administration revert mechanical and cold allodynia in animals undergoing persistent neuropathic pain. The effect exhibits a considerably quick onset and is long-lasting. The ODN also appears to potentiate the mobilization, migration and homing of BMMSCs into injured nerves. If these effects on BMMSCs relate to the antiallodynic actions of IMT504, it remains to be further demonstrated. However, our results support the idea that this ODN could be a promising therapeutic agent in the treatment of chronic neuropathic pain, also in humans.

Alcoholic Wernicke-Korsakoff Syndrome in a young adult

FRANCESCA MARIANI

Department of Neuropsychology, Institute of Neurology, Hospital de Clínicas. University of the Republic

Introduction: Wernicke-Korsakoff (WK) Syndrome is commonly described in patients with a long history of hard alcoholic drinking. Cases of young people allows to suspect a previews brain condition. Objective: to present a case of WK Syndrome in a young patient with all the neuropsychological features. Participants and Methods: 36 years old man, right – handed with primary school education and history of school failure. Premature and low birth weight. Problematic use of alcohol and other substances. Neuropsychological evaluation: Mini-Mental State Examination (MMSE), Trail Making Test (A), phonological and semantic fluency, Rey-Auditory Verbal Learning Test (RAVLT), Visual Anticipation Brixton test (BT); Stroop Visual Color and Word Test; 7/24 Spatial Recall Test, Rey Osterrieth Complex Figure; Kaufman Brief Intelligence test (K-BIT). Results and Conclusions: An amnestic and dysexecutive syndromes both of moderate to severe entity were found preceded by a confusional state and compatible with WK encephalopathy. A compound IC of 75 (low) is further disclosed. CT and MRI are normal. The SPECT shows a bilateral prefrontal, anterior and medial temporal moderate hypoperfusion that involves both thalamus, following the typical pattern described for WK syndrome, contrasting with no structural lesions. Alcoholic WK is infrequently seen in young adults. In this case there is a toxic intake added to a probable developmental cognitive disorder. Both conditions could induce brain risk.

Multidimensional signatures of negatory inhibition are differentially disrupted in frontotemporal dementia and Parkinson's disease

MARIANO NICOLÁS DÍAZ RIVERA

Center of Cognitive Neuroscience. Universidad de San Andrés, Buenos Aires, Argentina

Oral Communications

Processing of linguistic negation distinctively recruits inhibitory mechanisms. Here, we assessed whether such domain can reveal neurocognitive markers of inhibitory disorders. We tested two groups with distinct neurodegenerative patterns along inhibitory circuits (behavioral variant frontotemporal dementia [bvFTD] and Parkinson's disease [PD]), healthy controls (HCs), and patients with preserved inhibitory circuitry (Alzheimer's disease [AD]). Subjects read negative and affirmative sentences and either performed or suppressed a manual response to them. We examined (a) measures of online oscillatory dynamics (via high-density EEG) as well as associations between such signatures and (b) neuroanatomical patterns (via voxel-based morphometry) and (c) fMRI-derived resting-state functional connectivity (FC). Relative to HCs, both bvFTD and PD patients exhibited altered oscillatory correlates of negatory inhibition –viz., disruptions of inhibitory delta modulations for negation only in suppressed-response trials. Such abnormalities correlated with the volume and FC of inhibitory regions in both bvFTD (e.g., superior and orbitofrontal gyri) and PD (e.g., medial and precentral gyri and cerebellum). Conversely, AD patients showed no specific oscillatory patterns across conditions nor correlations with inhibitory regions. Briefly, linguistic negation can tap into the (dys)function of inhibitory mechanisms, paving the way for a potential neurocognitive marker of bvFTD and PD.

Probiotic Bacillus subtilis protects from Parkinson's disease-associated alpha-synuclein aggregation in C. elegans

EUGENIA GOYA

Centre for Discovery Brain Sciences/University of Edinburgh

The accumulation of misfolded alpha-synuclein (α-syn) protein into pathological aggregates plays a central role in the pathogenesis of Parkinson's disease (PD) and other synucleinopathies. Although PD is primarily considered to be a central nervous system disease, recent discoveries have implicated the gut microbiome in the progression and severity of this condition. However, how gut bacteria affect PD remains unclear. C. elegans is an ideal model for studying the effects of gut bacteria on physiological processes at a single species-single gene level. We showed that B. subtilis PXN21, a probiotic strain commercially available for human consumption, both inhibits aggregation and efficiently removes preformed aggregates in a C. elegans model with ectopic expression of human α-syn. This protection is seen in young and ageing animals and is partly mediated by DAF-16 (FOXO). Multiple B. subtilis strains trigger the protective effect via both spores and vegetative cells, partly due to biofilm formation in the gut of the worms and the release of bacterial metabolites. Using comparative transcriptomics analysis, we identified host metabolic pathways that are differentially regulated by the probiotic, including lipid metabolism. Functional validation revealed the sphingolipid metabolism pathway as a key host mechanism that is altered by the bacteria to induce protection. Our findings provide a basis for exploring the disease-modifying potential of B. subtilis as a dietary supplement.

Oral Communications

L-dopa causes oscillatory activity in striatal cholinergic interneurons from parkinsonian mice via dopamine D1/D5 receptors

RODRIGO MANUEL PAZ

Grupo de Neurociencia de Sistemas, Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Universidad de Buenos Aires, CONICET.

Striatal cholinergic interneurons (SCIN) are key modulators of the striatal circuitry controlling voluntary movement and goal-directed behavior. Aberrant striatal cholinergic signalling contributes to the symptoms of Parkinson's disease (PD) and L-dopa induced dyskinesia (LID), a major complication of antiparkinsonian L-dopa therapy. However, the mechanisms causing SCIN dysfunction in PD and LID remain uncertain. Here we used slice electrophysiological approaches to show that SCIN exhibit enhanced Kir and reduced leak currents in a mouse model of LID. These changes cause exacerbated hyperpolarizing responses that coexist with an enhanced excitability, resulting in a burst-pause firing pattern that persists after the dyskinetic effect of an L-dopa dose has worn off. Additionally, we show that a negative slope region of the Kir conductance curve is responsible for the oscillatory behaviour. Stimulation of dopamine D1/D5 receptors mimics the physiological changes induced by L-dopa administration, but D1/D5 receptor blockade does not modify the persistent hyperexcitability and oscillatory activity observed in dyskinetic mice. However, blunting intracellular cAMP signaling restores normal hyperpolarizing responses and dampens oscillatory activity in dyskinetic mice. Our data unravel a mechanism causing aberrant SCIN activity in LID and point at D1/D5 receptor regulation of Kir2 and leak channels as potential targets to restore normal striatal cholinergic function in PD and LID.

Alterations of specific cortical GABAergic circuits underlie abnormal network activity in a mouse model of Down syndrome

JAVIER ZORRILLA DE SAN MARTIN

Institut du Cerveau de Paris (ICM)

Down syndrome (DS) results in various degrees of cognitive deficits. In DS mouse models, recovery of behavioral and neurophysiological deficits using GABAAR antagonists led to hypothesize an excessive activity of inhibitory circuits in this condition. Nonetheless, whether over-inhibition is present in DS and whether this is due to specific alterations of distinct GABAergic circuits is unknown. In the prefrontal cortex of Ts65Dn mice (a well-established DS model), we found that the dendritic synaptic inhibitory loop formed by somatostatin-positive Martinotti cells (MCs) and pyramidal neurons (PNs) was strongly enhanced, with no alteration in their excitability. Conversely, perisomatic inhibition from parvalbumin-positive (PV) interneurons was unaltered, but PV cells of DS mice lost their classical fast-spiking phenotype and exhibited increased excitability. These microcircuit alterations resulted in reduced pyramidal-neuron firing and increased phase locking to cognitive-relevant network oscillations in vivo. These results define important synaptic and circuit mechanisms underlying cognitive dysfunctions in DS.

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OC-6

Chair: Ana María Contin

Hierarchical learning of olfactory discrimination in a visual context

MACARENA AMIGO DURÁN

Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) – CONICET - Partner Institute of the Max Planck Society

The ability to learn that a sensory stimulus signals a reward or punishment is one of the brain functions most critical for adaptation and survival. How animals integrate information about learnt sensory stimuli with spatial context and animal internal state is not completely understood. Here we developed a learning paradigm to evaluate the influence of spatial context on the association of an odor with a reward. Water-restricted mice were trained to perform a GO/NO GO discrimination task in which the animal learns to drink water or not depending on the visual context in which the odor is presented. In head-fixed conditions, animals arrive to different spatial contexts by running in a virtual reality environment. We show that animals reached to criterion within a few sessions. Linking response, locomotion speed and inhalation rate changes throughout the learning process, the last two depending on trial types. Mice learnt to discriminate odors faster than visual contexts, suggesting a difference in stimuli salience. Since appropriate response to odor help animals to adapt changing environments, we also studied how flexible is this behavior. We carried out a reversal learning protocol where the odor rewarded was changed, in the same context as before. Results showed that it took between 2-4 sessions to reverse the behavior. We developed an odor-in-context task suited to probing the neural basis of spatial context modulation of an olfactory-based behavior and its flexibility.

Oral Communications

Disinformation and political polarization: A study of the impact of political beliefs in the ability to detect “fake news”

LAOUEN MAYAL LOUAN BELLOLI

Laboratorio de Inteligencia Artificial Aplicada, Depto. de computación, FCEyN, UBA–CONICET

The use of social media is growing, and the spread of ‘fake news’ with direct impact on political decisions has raised to new levels. Social media (and their non transparent algorithms) are the main organisations to be pointed out as responsibles for this issue, and they started to implement different strategies on their platforms to reduce disinformation. One of the proposed mechanisms is not allowing people to share a news before a certain delay, in order to reinforce inhibitory control, that, in theory, permits a more rational analysis of the news. Polarization is known to affect people’s judgement. Since its origin, Argentina has had a strong political crack, nowadays represented by two of its major political parties: Kirchnerismo and Macrismo. In this work, we studied the impact of Argentinian political polarization on the subjects’ ability to detect disinformation and misinformation, and the use of delay times to improve their performances. For this purpose, we conducted an experiment where 715 subjects classified a set of news as ‘fake’ or ‘real’ with or without a previous delay time. We found (1) a strong confirmation bias when the news disagreed with subjects’ political beliefs, and (2) that adding a delay not only does not help to deal with that bias, but worsens the detection of real news when the news is aligned with the subject’s political beliefs.

Evaluation of the usability of a cognitive training videogaming platform in the elderly.

MARÍA EMILIA CLEMENT

Hospital Privado de Comunidad, Mar del Plata, Argentina

Dementia is today one of the leading causes of disability and dependency in older people around the world; its prevalence is increasing rapidly, and it has no cure. Before its onset, there is a phase of transition called Mild Cognitive Impairment (MCI), which seems a promising period to test treatments to delay dementia. Cognitive training is a therapy currently tested worldwide in people with MCI as prevention and treatment tool. Mate Marote is an Argentine open source software specifically designed to train executive functions. While it was tested in 5-to-8 year olds with excellent results, Mate Marote games were never tested in older adults. In this work we present the first feasibility study, including 11 volunteers between 66 and 84 years old, without dementia. We evaluated the usability of the platform and the performance of the subjects in the adapted games. To implement a randomized clinical trial with this software, some elements must be modified. Still, from this pilot study we conclude that Mate Marote is well adapted for older adults without dementia, and that both frequency and duration of the sessions are suitable for this group of people.

Oral Communications

Unsupervised analysis of animal behavior in a skilled motor learning task

ALVARO TOMAS CONCHA ALVAREZ PRADO
Neurobiology of Movement, Instituto Balseiro, UNCUYO-CNEA

A fundamental assumption in behavioral neuroscience is that animal activity, while performing defined tasks, can be vastly described by a finite set of stereotyped movements. Further so, information about animal behavior can be correlated with simultaneous recordings of neural activity allowing us to study the encoding of different movements in the brain, their underlying neural circuits and their modifications during motor learning. However, classifying different types of movements can be a complex endeavor. As the extension of animal activity recordings may be too large to be manually classified and such classification may not be reproducible between subjects. Even more so, heuristically created categories (e.g., walking, running, jumping) tend to ignore inherent information regarding intra- and inter-animal variability, found in unrestricted behavior. In this work, unsupervised machine learning techniques were used to classify different types of movements, produced by mice performing a learned skilled motor task (accelerating rotarod). In particular, t-SNE maps were used to find intrinsic relationships between high-dimensional feature vectors, describing the frequency spectrum of mouse movements. In this manner, we expected to shed light over the underlying structure of these features, cluster them accordingly and identify these clusters with patterns of movement, improving our understanding of the dynamics and learning process of this motor task.

Searching for Active Forgetting Mechanisms of Aversive Memories

JULIANA DALTO
Laboratorio de Memoria / IBCN / UBA-CONICET

Although it has been demonstrated the existence of active forgetting (AF) mechanisms for several acquired experiences, there is no such evidence of these mechanisms for aversive memories already consolidated. Based on previous work of our group and others we evaluated the participation of different molecular pathways on AF of aversive memories in the ventral tegmental area (VTA) and dorsal hippocampus (HP). We first decided to evaluate if dopamine in the VTA supports AF of aversive memories. However, we found that blocking D1 subtype receptors in the VTA impairs the formation of conditioned place aversion memory and the formation and duration of inhibitory avoidance (IA) memory in a training-dependent manner. Then, we evaluated the role of GABA neurotransmission in the AF of IA memory and found that positive allosteric modulation of GABAA receptors via benzodiazepine systemic administration or infusion in the HP appears not to affect the duration of this memory. Finally, we also recently started to study the role of the GTPase Rac1 in AF of IA memory. Our preliminary results seem to show that the inhibition of this protein in the HP extends the duration of this memory. Until now, we have made an important progress searching for molecular mechanisms that could be mediating AF of consolidated aversive memories. Our results

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seem to indicate that Rac1 could be mediating this process in the HP and thus open a new range of future studies to advance in the understanding of AF.

Behavioral phenotypic outcomes in juvenile rats following infant maltreatment

JAZMÍN GRILLO BALBOA

Laboratorio de Programación Perinatal del Neurodesarrollo/ Instituto de Biología Celular y Neurociencias "Prof. E. De Robertis", Facultad de Medicina/ Universidad de Buenos Aires

Friday · Oct 9th

OC-7

Chair: Marcela Brocco

Early-life stress (ELS) increases the propensity to develop psychopathologies later in life. Much of the evidence regarding the effects of ELS focuses on adults, leaving younger ages unexplored. Because in human scenarios of ELS the mother is present but her behavior is abnormal, an ELS naturalistic rodent model is desirable for translational studies. Here we examine the phenotypic outcomes of juvenile Wistar rats exposed to the scarcity-adversity model (SAM) of low nesting resources, which elicits adverse caregiving conditions (e.g.: maltreatment) toward neonates. SAM was performed from postnatal day (PND) 8-12, a critical period for the development of brain structures related to stress and emotional regulation in pups. Male and female offspring at PND 25-29 were evaluated in the open-field and forced swimming test for anxiety-/depressive-like behaviors. Mothers from the SAM condition showed increased violent conducts toward their pups and a fragmented behavior. SAM offspring revealed greater exploratory behaviors, while a lessened anxious-like behavior was only evident in males. Conversely, depressive-like behaviors were higher in males compared to females. Our results show that exposure to a violent and unpredictable perinatal environment has sex-specific consequences on juvenile offspring's behavior. Further study of the neurobehavioral phenotype of SAM-reared individuals could be key to understanding the early onset of ELS-related psychopathologies.

The role of right hemisphere in language processing. Investigation of communication abilities in temporal lobe epilepsy patients.

ANA CAROLINA LOMLOMDJIAN

Centro de Epilepsia ENYS - Htal El Cruce

Oral Communications

In the last decades the progress of neurosciences extended the neurobiological bases of language. However the role of the right hemisphere (RH) remains controversial. In epilepsy, considered a model of study of cognitive networks, language studies have focused on left hemisphere processing. Communication abilities, in which right hemisphere's processing is required, have remained unexplored. The purpose of this study was to investigate communication abilities in patients with right temporal lobe epilepsy (RTLE) by comparing their performance to that of patients with left TLE (LTLE). We studied 117 pharmacoresistant TLE patients: 52 with RTLE and 65 with LTLE. Subjects underwent a comprehensive battery of language and communication assessment. We analyzed epilepsy clinical and general neuropsychological data. The results showed that patients epilepsy located in RH had significantly lower performance compared to the left group in conversational (X2 28,3 RR 3,7 p<,001) and narrative discourse (X2 20,3 RR 3,5 p<,001), in emotional prosody (X2 15,03 RR 2,2 p<,001) and in pragmatic skills such as interpretation of figurative (X2 19,3 RR 3 p<,001) and indirect language (X2 17,7 RR 2,8 p<,001) and social situations (X2 14,8 RR 5,5 p<,001). Right anterior temporal structures would have a direct role in prosody processing, and a core contribution in discourse and pragmatic processing as a link between semantic, language and social processing to build a coherent meaning.

Training in a cue-guided maze increases adult neurogenesis in specific pallial circuits of zebrafish

LAURA SOLEDAD MAZZITELLI FUENTES

Departamento de Física Médica, Centro Atómico Bariloche -CONICET/CNEA

The teleost brain is under continuous remodeling of its neuronal circuits by adult neurogenesis. Neuronal progenitors proliferate and differentiate into adult-born neurons. During maturation, neurons that don't integrate synaptically are subjected to cell death programs. Thus, network activity is critical to promote synaptogenesis and survival of maturing neurons. We aimed to study if training in a cognitive task promotes adult neurogenesis in the zebrafish pallium. We trained zebrafish in a diamond-shape maze to achieve a relational association of internal cues. After 5 days of training, fish achieve ~80% of correct choices, and we observe an increase in cell proliferation, specifically in the caudal region of the dorsolateral pallium (cDl) and in the rostral dorsomedial pallium (rDm). Furthermore, we studied if learning-related neuronal activity modifies the survival of new neurons. We labeled a cohort of proliferating progenitors and trained fish in two different temporal windows: 0-14 dpi and 12-30 dpi. We found that training increases the number of new-born neurons in rDm and cDl from 0-14 dpi, but only rDm neurons are upregulated when training from 12-30 dpi. We conclude that adult zebrafish succeed to learn a relational task, this cognitive activity promotes neuronal progenitor proliferation and adult neurogenesis in specific regions of the pallial network at different time slots. This is the first report relating adult neurogenesis to a cognitive process in fish.

Oral Communications

Modulation of hippocampal-prefrontal cortex connectivity during contextual guided episodic memory recall in rodents

JUAN FACUNDO MORICI

Laboratorio de cognición molecular. Instituto de Neurociencias cognitivas y traslacionales (CONICET-FAVALORO-INECO). Universidad de Favaloro

Remembering which experiences occur at a particular context is a complex process that requires the interaction between multiple brain areas. The recall of a specific memory can be triggered by contextual information and relies on the interaction between the hippocampus (HIP) and the prefrontal cortex (PFC). It has been shown that the synchronization of HIP-PFC theta oscillations is enhanced during the resolution of contextual/spatial working memory tasks. However, little is known about how the HIP and PFC are coordinated during a contextual-guided recall of an episodic-like memory. To address this, we performed electrophysiological recordings in behaving rats during the retrieval phase of the object-in-context memory task (OIC). We observed an increase in HIP-PFC LFP coherence in the theta range when animals explore contextually mismatched objects. We also analyzed the activity of PFC neurons during the OIC test. Interestingly, 50% of PFC cells showed firing rate modulations during the test with respect to their baseline activity (25% responded to object exploration and 25% to non-object exploration periods). In addition, 25% of PFC neurons were phase-locked to the hippocampal theta rhythm. Altogether, these results suggest that HIP-PFC functional connectivity in the theta band is differentially modulated depending on the contextual congruence of the presented stimuli. In addition, PFC neurons encode different types of information that may be necessary for the OIC resolution.

Online assessments of larger contexts modulation in word Predictability in Short Stories

LENA VALESKA PERONI

Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computacion, FCEyN, UBA-CONICET

When reading, we are continuously predicting upcoming words, allowing us to integrate information and to guide eye movements. These predictions are operationalized as the Predictability and measured as the probability of guessing the next word from the previous context. Predictability reflects high-level processes taking place during reading and is a strong predictor of eye movements and brain activity. It is estimated by asking many participants to complete the most probable word that follows a given context. This task is called cloze-task and is usually collected in-lab, resulting in a time-consuming and expensive experiment.Here, we present an analysis of three corpora of online cloze-task experiments: (C1) a corpus of Common and Memory-Encoded Sentences collected both online and in-lab, (C2) a corpus with similar material, collected in two independent online experiments, and (C3) a corpus of sentences drawn from short stories collected online, both isolated or contextualized.We observed that the online cloze-task replicates the results from the in-lab one

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(C1) and is consistent between independent experiments (C2) Interestingly, these results clearly show that Predictability is highly dependent on large contexts (C3) Thus, online cloze-task makes the collection for larger samples easy and generates robust and more precise measures. Moreover, it allows us to explore the effects of larger contexts (up to 3000 words) in the Predictability, that could be impossible otherwise.

Role of 5-HT2A Receptor in Social Behaviour in Mice

AGOSTINA SACSON

Laboratorio de Memoria y Cognición Molecular, INCyT

The serotonergic system and more precisely the type 2A serotonin receptor (5-HT2AR) is involved in a wide variety of cognitive and emotional functions. Specifically, the social impairments observed in different psychiatric disorders, such as schizophrenia and Asperger's syndrome, have been linked with a hypofunction of 5-HT2AR. However, the mechanisms underlying this phenotype remain unclear. In this study we analyze the role of 5-HT2AR in social preference and dominance using a genetically modified mouse model that presents a constitutive deletion of 5-HT2AR (KO) compared to conspecific wild type (WT). For this purpose, we use the three-chamber social interaction test (SI) and the dominance tube (TD). We also explore the role of this receptor in the prefrontal cortex in social behavior by infusing adult WT animals with a selective 5-HT2AR antagonist (MDL) prior to the social interaction test. Male and female KO mice had lower social preference compared to WT mice, and genotype was a strong predictor of matches won in duels in the TD. Furthermore, the acute administration of MDL in the mPFC of WT mice had no effect on the SI suggesting that the receptor is necessary during development for the animals to demonstrate normal social behavior but is not recruited during the task. Moreover, preliminary SI results from animals that selectively express 5-

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HT2AR in the cortex suggest that the apparent developmental role of the receptor might be mediated by its expression in the cortex.

Stress-induced reconsolidation impairment on a declarative verbal memory

JESSICA SÁNCHEZ BEISEL

Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE UBA-CONICET)

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Understanding how and when acute stressors modulate memory processes continues to be a challenge. We have proposed that a function of reconsolidation is to induce changes in the behavioral expression of memory by the influence of concurrent experiences, instead of its potential to be reactivated. Here, we adapted the widely used in neuropsychological clinic Rey Auditory Verbal Learning Test to evaluate the effect of the cold pressor stress (CPS) during the reconsolidation of this declarative memory. According to previous studies on declarative memories, the working hypothesis of the present study was that CPS administered post-memory reactivation-labilization will improve the long-term memory expression of this declarative memory. A decay in memory performance was found at the time of memory reactivation (Day 6). Contrary to our initial predictions, the CPS administration during reconsolidation impaired the long-term memory expression (Day 7), an effect that is dependent on the presence of a mismatch condition in the Reactivation Session. No differences in recognition tests were found. Results highlight the complex stress-memory relationships.

Developmental impact of SSRI antidepressants on emotional prefrontal circuits in mice

TAMARA SOL ADJIMANN
Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA - CONICET)

Early-life exposure to antidepressant drugs acting as selective serotonin reuptake inhibitors (SSRIs), like fluoxetine, has long-lasting detrimental consequences in prefrontal circuits crucially engaged in stress-coping and mood control. Thus, mice treated with fluoxetine during a postnatal critical period (P2 to P14) show alterations in the connectivity of the prefrontal cortex to dorsal raphe nucleus (PFC-to-DRN) circuit, accompanied by increases in depressive-like and anxiety behaviors in adult life. In this study, we investigated the short-term effects (at P15) of fluoxetine exposure in the critical period on the synaptic connectivity of the developing PFC-to-DRN circuit, and whether this could affect the response of DRN serotonin neurons to stress. Our quantitative analysis using a high-resolution microscopy technique (array tomography) showed a synaptic hyper-innervation of the developing PFC-to-DRN circuit in fluoxetine-exposed mice in comparison to controls. These changes in PFC afferents were detected onto both serotonin and non-serotonin neurons of the DRN. Additionally, early fluoxetine exposure topographically dampened the activation of DRN serotonin neurons in response to an acute stress (forced swim), as revealed by c-Fos immunohistochemistry. These findings indicate that early-life exposure to SSRIs alters the ontogenetic trajectory of the PFC-to-DRN synaptic circuit, likely contributing to adult emotional alterations.

Major Depressive Disorder and Borderline Personality Disorder: Emotional regulation and neuroimaging

VICENTE CAMACHO-TÉLLEZ
Grupo de Investigación en Neurociencias Aplicadas a las Alteraciones de la Conducta. FLENI, Buenos Aires, Argentina.

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Emotional problems figure in many clinical conditions (Sheppes, 2015), such as Major Depressive Disorder (MDD) or Borderline Personality Disorder (BPD) (Vitriol, 2017). Both disorders share clinical and biological characteristics, included the emotion's neural circuit (Goodman, 2010). The objective is to describe the differences in cortical thickness, brain volumetry, cognitive emotional regulation between both disorders and to explore the correlation between emotional regulation and cortical thickness. Materials and methods: 19 MDD patients, 18 BPD and 20 healthy controls were recruited. Cognitive Emotional Regulation Questionnaire (CERQ) was applied. MRI were obtained with a GE 3T scanner and processed with FreeSurfer 6.0 toolset. CERQ's score and volume structures were compared. Pearson's correlation for correlation between CERQ and cortical thickness. Results: CERQ score is higher in MDD patients compared to controls, [X2(1)=10.35] ($p<0.01$). Hippocampal volume is lower in BPD patients compared to controls: $F(2,54)=4.71$; $p<0.05$. Globus pallidus, volume is lower in BPD patients compared to both groups: $F(2,54)=6.89$; $p<0.01$. Cortical thickness is lower in BPD patients compared to controls ($p<0.05$). At higher score in CERQ, lower cortical thickness in left inferiorparietal region in MDD group ($p<0.05$; $r = -0.58$). Conclusions: There are differences in cortical thickness, hippocampal and globus pallidus volume. Cortical thickness is modulated by emotional regulation.

Analysis of Effective Connectivity in micro networks of Single and Multi-Unit Activity and Local Field Potential in Human Mesial Temporal Lobe Epilepsy

SANTIAGO COLLAVINI

Neurosciences and Complex Systems Unit (EnyS), CONICET, Hosp. El Cruce "N. Kirchner", National University A. Jauretche (UNAJ),

Intracranial electroencephalography is the common clinical diagnosis protocol to identify the epileptogenic zone for surgical treatment of drug resistant epilepsy patients. Analyze simultaneous recordings with clinical macro- (cM) and research micro-electrodes (rM) allows us to obtain a better understanding at microscale of how neural network works before and during epileptic seizures. We registered brain activity from cM and rM (AdTech,USA) implanted bilaterally in amygdala and hippocampus of two patients with bilateral mesial-temporal epilepsy, following clinical criteria. Recordings were obtained from 96 microelectrodes located at Seizure-Onset-Zone (SOZ;n=32), ipsilateral but outside of SOZ (n=16) and contralateral to SOZ (n=48). It was noted that the detection and clustering techniques are very sensitive to background noise, which is ten-fold increased during seizures. A way to overcome this drawback is analyze the firing rate (FR) of neurons whose spikes exceeds at least 5 times the amplitude of noise during seizure. We generate different types of micro networks with the SU and MU registered in SOZ and estimate the effective connectivity from autoregressive multivariate models. The preliminary results described 84% of neurons (128/152) showing different types of seizure-related firing patterns. In terms of effective connectivity, we find that the dynamics of the micro networks before and during the seizures present characteristic out-degree patterns.

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KCNQ4 in the reticular activating system (RAS): contribution to the circadian rhythm modulation.

SOFIA STUPNIKI
Laboratorio de Canales Iónicos, INIBIBB-UNS/CONICET

The M-current is a voltage-gated potassium current generated by channels composed by KCNQ2-5 subunits. The pedunculopontine nucleus (PPN) is part of the Reticular Activating System (RAS), associated with sleep regulation. As little is known about the composition, subcellular location and physiological implication of the M-current in PPN, our aim was to demonstrate the presence of KCNQ4 in the PPN, and its contribution to the neuronal function of this nucleus. We used a transgenic mouse lacking KCNQ4 expression (KO) and one with fluorescent-labeled cholinergic neurons (tdTomatoStop+ChAT::Cre). Using qPCR, immunofluorescence and electrophysiology on brain slices, we demonstrated that only a subpopulation of cholinergic neurons (around 27%), located on the external limits of the PPN has KCNQ4-mediated M-current. We also found that KCNQ4 regulates the expression of other KCNQ subunits. In KO mice, the expression profile changed drastically respect with the WT: Kcnq2 expression decreased, Kcnq3 increase and Kcnq5 disappeared. To study the influence of KCNQ4 on circadian rhythm we used behavioral testing. KO mice exhibited alterations in the activity cycles showing a higher sensitivity to changes in the light-darkness cycles. In summary, we found that some PPN cholinergic neurons have KCNQ4-dependent M-current and this subunit contributes to modulate the circadian rhythm. Since the PPN is affected in certain neurological diseases, KCNQ4 might be a potential pharmacological target.

“Thinking out loud”: an open-access EEG-based BCI for inner speech recognition

NICOLAS NIETO
Instituto de investigación en señales, sistemas e inteligencia computacional, sinc(i) - UNL/CONICET

Surface electroencephalography (EEG) is a standard and noninvasive way to measure electrical brain activity. By analyzing those signals it is possible to detect activation patterns that allow interpreting the brain mechanisms related to a particular task. Recently, with the developments in the artificial intelligence (AI) community, great advances have been achieved in the automatic detection of brain patterns, allowing the creation of increasingly faster, more reliable and accessible Brain-Computer Interfaces (BCIs). Although different paradigms can be used to communicate, in the last few years, interest has grown to interpret and characterize the “inner voice”. This paradigm, called inner speech, raises the possibility to execute an order by just thinking about it, allowing a more ‘natural’ way of communication. Unfortunately, since it is a recently explored field, there are no EEG datasets publicly available, limiting the development of new techniques and AI algorithms for inner speech recognition. In this work we construct a dataset with 10 subjects using the inner speech paradigm, in order to i) better understand the brain mechanisms and patterns related to the inner voice and, ii) to provide to

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the scientific community with an open-access multiclass EEG database of inner speech commands seeking at fostering the rapid development of new AI methods for robust inner speech recognition.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Optimization of linear polyethylenimine/ DNA polyplexes transfection into murine neurosphere cultures.

Agustín Jesús Byrne [1], Yamila Azul Molinari [1], Juan Manuel Lázaro Martínez [2], Paula Gabriela Franco [1]

1 Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Química Biológica. Cátedra de Química Biológica Patológica. Instituto de Química y Fisicoquímica Biológicas (IQUIFIB) (UBA-CONICET). Buenos Aires, Argentina.

2 Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Química Orgánica. Cátedra de Química Orgánica 2. Instituto de Química y Metabolismo del Fármaco (IQUIMEFA) (UBA CONICET). Buenos Aires, Argentina.

Presenting author:
***Agustin Jesus Byrne**, agusbyrne08@gmail.com*

Neurospheres (NS) cultures are valuable tools for deciphering the regulation of neural cell differentiation in vitro. However, their study is somehow restricted because NS primary cultures are difficult to transfect using conventional methods. Here, we propose a transfection protocol by using linear polyethylenimine (PEI) nanoparticles in order to develop a low-cost method that has minimal cell toxicity and maximal efficiency in delivery and expression of a reporter plasmid.

We synthetized PEIs of different molecular weights and evaluated their toxicity in NS cultures. The PEI of 22KDa was chosen for subsequent analysis, as it retained cell viability over 70% up to doses of 4ug/ml. A green fluorescent protein (GFP) expression vector was incubated with the selected polymer at different ratios. Analysis of PEI:DNA polyplexes by agarose gel electrophoresis revealed that best combination for complex formation was 0.8:1 ratio.

After NS generation from postnatal mice brains, dissociated cells were seeded at different densities and exposed to PEI:DNA polyplexes for two hours for preliminary evaluation of transfection. After 24 hours, a pulse of propidium iodide was performed to detect cell death. Cultures were fixed, nuclei were stained by Höescht and cells were analyzed for GFP expression. GFP+ cells were detected in all the conditions, although in a low proportion (5%). Optimization of other variables should be performed in order to improve transfection efficiency.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Human 5-HT3 receptors: Structural and functional features.

Albano Mazzarini Dimarco [1,2], Cecilia Bouzat [1,2], Jeremías Corradi [1,2]

1 Instituto de Investigaciones Bioquímicas de Bahía Blanca - INIBIBB
2 Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur

Presenting author:
***Albano Mazzarini Dimarco**, amazzarini@inibibb-conicet.gob.ar*

The 5-HT3 receptor is a ligand-gated ion channel that converts the binding of serotonin (5-HT) into a transient cation current which mediates fast excitatory responses in peripheral and central nervous systems. Five human subunits (A-E) have been identified to date. The A subunit can assemble to form homomeric receptors (5-HT3A), or combine with B-E subunits to form heteromeric receptors (5-HT3AB-E). To determine subunit composition and stoichiometry of heteromeric receptors we constructed a high-conductance A subunit (AHC), which allowed us to detect single-channel events, and expressed the AHC with C, D or E subunits. From macroscopic currents we observed an increase in the 5-HT EC50 values for all subunit combinations with respect to that of 5-HT3AHC. Expression of the AHC to form 5-HT3AHC receptors showed opening events of homogeneous amplitudes. However, when AHC was expressed in combination with one of the C-E subunits, events with different amplitudes were detected, thus confirming the expression of heteromeric receptors. In-silico studies provided insights into the contribution of the different subunits to the binding site conformation. Thus, our results confirm that C-E subunits can combine with the A subunit to form heteromeric receptors, and bring structural and functional details about the different human 5-HT3 receptors that can be expressed.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Neuropilin-2 (NRP2) but not neuropilin-1 (NRP1) regulates sympathetic axon outgrowth inhibition by estrogenized myometrial explants in 3D co-cultures

Analía Richeri, Gaby Martínez, Gabriela Vierci, Ileana Sosa, Mónica Brauer, Alfonso Taboada

Laboratorio de Biología Celular, Departamento de Neurofarmacología Experimental. Instituto de Investigaciones Biológicas Clemente Estable (IIBCE). Avenida Italia 3318. Montevideo, Uruguay.

Presenting author:
***Analía Richeri**, aricheri@iibce.edu.uy*

Uterine neural connections represent a simple neural circuit to study the finest mechanisms of axon remodeling. Neurons innervating the uterus respond to physiological alterations in systemic levels of estrogen (E2) with changes in their terminal axons. Sympathetic axons disconnect when E2 rises and re-connect when E2 is low. The uterus releases diffusible molecules that exert neuronal sub-set-specific effects. Here we investigated if NRP1 and NRP2 signaling could mediate as negative regulators of sympathetic axonal growth. Functional blocking antibodies against NRP1 and NRP2 in three-dimensional co-cultures of sympathetic ganglion/myometrial explants were employed. Female rats of different hormonal conditions (low or high systemic E2) were used as tissue donors. There was no difference in axonal length and direction of outgrowth in sympathetic axons extended from ganglionic explants co-cultured with myometrial control explants (GC vs C-myo; P/D ratio = 1). However, when ganglionic explants were co-cultured with E2-myo explants axons were strongly inhibited and repelled (GE vs E2-myo; P/D ratio < 1). This effect depended on the distance between explants. Axon outgrowth inhibition by E2-myo explants was prevented by NRP2 blockade (Nrp2B GE vs E2-myoP/D ratio=1). In contrast, blocking NRP1 did not avoid the axon outgrowth inhibition exerted by E2-myometrium. Together, our data demonstrate the exclusive requirement of NRP2 in E2-induced impairment of sympathetic axon outgrowth.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Molecular mechanisms governing the maturation of GABAergic inputs onto newborn granule cells in the adult hippocampus

Ayelen I. Groisman, Andrea A. Aguilar, Alejandro F. Schinder, Damiana P. Giacomini

Laboratorio de Plasticidad Neuronal, Fundación Instituto Leloir Av. Patricias Argentinas 435, Buenos Aires, Argentina.

Presenting author:
Ayelen Ivana Groisman, *ayelen.groisman@gmail.com*

In all mammals, the dentate gyrus of the hippocampus (DG) produces new neurons throughout life that are known to be involved in information processing. We elaborated a detailed spatio-temporal map for the integration of adult-born granule cells (GCs) within two main populations of GABAergic interneurons of the preexisting circuit, parvalbumin (PV-INs) and somatostatin (SST-INs). However, the molecular mechanisms that govern the integration of GCs remain unknown. To study the molecular tuning of GABAergic synapses onto GCs, a retrovirus expressing shRNA against Neuroligin-2 (NL2), a molecule involved in the development of inhibitory synapses, was injected in the DG of adult mice. Spontaneous inhibitory postsynaptic currents (sIPSC) were recorded in mature or 6 week-old GCs expressing shNL2 or GFP. Our results show elevated Rinput, reduced sIPSC frequency, and increased rise-time for perisomatic but not distal inhibitory contacts in shNL2-expressing GCs. To get deep insight into the development of inhibitory synaptic contacts onto GCs, we setup a combined expansion microscopy/immunostaining protocol and we were able to track PV-IN boutons onto developing GCs. Electrophysiological recordings are underway. Our preliminary data reveal NL2 as a critical modulator for the formation and maturation of perisomatic inhibition in developing GCs of the adult brain.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Identification and characterization of novel hypothalamic isomiRs related to anxiety-like behavior induced by perinatal protein malnutrition

Octavio Gianatiempo, Bruno G Berardino, Rocío Priegue, Eduardo T Cánepa

Laboratorio de Neuroepigenética y Adversidades Tempranas – Departamento de Química Biológica – Facultad de Ciencias Exactas y Naturales – Universidad de Buenos Aires / Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN) – Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina

Presenting author:
***Bruno Gabriel Berardino**, bberardino@qb.fcen.uba.ar*

Perinatal malnutrition programs stress responses and developmental trajectories leading to cognitive, mood and behavioral impairments later in life. Epigenetic mechanisms, such as microRNAs (miRNAs), have been proposed as the molecular basis for these effects. While miRNAs are widely studied in the literature, less attention has been paid to miRNA sequence variants, i.e. isomiRs. In this study, we aim to identify and characterize novel isomiRs that might be responsible for the anxiety-like behavior observed in malnourished rodents and which is reverted by an enriched environment. For this purpose, we analyzed the hypothalamic miRNAome through Illumina sequencing technology. Hypothalamus was chosen based on previous PET results. We found that isomiRs are prominently expressed in the hypothalamus of young adult male mice and we described their isoform patterns. Furthermore, we identified a set of miRNAs and isomiRs that could be responsible for the phenotypic reversion of anxiety traits. The predicted mRNA targets for this set are in accordance with RNA-seq results for malnourished and control mice. These targets were enriched in cellular pathways that could explain behavioral differences, e.g. axon guidance and neurogenesis. IsomiRs might play an important role in epigenetic regulation in the hypothalamus of young adult male mice accounting alongside canonical miRNAs for differences seen in anxiety-like behavior of malnourished mice exposed to an enriched environment.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

CircTulp4: a circular RNA that regulates working memory, anxiety and reward-related behavior in mice

Camila Pannunzio [1], María Laura Gimeno [1], Sebastián Giusti [1], Natalia Pino [3], Mora Ogando [1], Belén Pardi [1]

1 Biomedicine Research Institute of Buenos Aires - CONICET - Partner Institute of the Max Planck Society
2 Max Planck Institute for Experimental Medicine, Göttingen, Germany
3 Institute of Developmental Genetics, Helmholtz Zentrum München, Germany

Presenting author:
Camila Pannunzio, *camilapannunzio4@gmail.com*

Circular RNAs (circRNAs) are a newly characterized class of noncoding RNAs. These molecules derive from exonic sequences and are the products of an alternative mechanism of splicing known as backsplicing, which yields a single-stranded RNA molecule with covalently joined ends. Using a systematic high throughput identification of numerous circular transcripts in nerve tissue samples, we have selected a circular RNA transcript derived from the Tulp4 (Tubby-like protein 4) gene to perform a functional characterization, based on its high expression level and its synaptic enrichment. We have recently generated a transgenic knock-out mouse line to model circTulp4 loss-of-function in vivo . To do so, we used the CRISPR/Cas9 technique to mutate the splicing acceptor site used in the backsplice reaction. Electrophysiological and proteomic experiments demonstrate that circTulp4 KO mice have alterations in the excitatory neurotransmission and exhibit modified levels of synaptic proteins.

More recently, we performed a microscopic quantitative analysis of brain sections having asparse population of genetically labelled neurons expressing EGFP. The results show that mice lacking circTulp4 have an increased number of dendritic spines. Notably, extensive behavioral phenotyping of circTulp4 KO mice suggests that circTulp4 affects specific aspects of different behaviors including cognition, anxiety and reward.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Histone deacetylase gene expression is regulated by sex chromosome complement in the amygdala of the developing mouse brain

Camila Sosa [1], Carla D Cisternas [1,2,3], Romina Conti [2], María Julia Cambiasso [1,2]

1 Instituto de Investigación Médica Mercedes y Martín Ferreyra
2 Cátedra de Biología Celular, Facultad de Odontología, Universidad Nacional de Córdoba, Córdoba, Argentina.
3 Cátedra de Fisiología Animal, Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Argentina.

Presenting author:
***Camila Sosa**, csosa@immf.uncor.edu*

Sexual differentiation of the rodent brain depends mainly on the action of androgens secreted by the fetal testis during the perinatal "critical period" (E17-P10). Recently, the role of genetic factors derived from sex chromosome complement has been recognized. Both hormonal and genetic factors interact to induce long lasting effects on sexually dimorphic gene expression. Epigenetic histone modifications have emerged as mechanisms of regulation and maintenance of hormonal-dependent effects in the brain and histone deacetylation induced by histone deacetylases (Hdacs) has recently been implicated in brain masculinization. To analyse the contribution of sex chromosome complement on this process, we evaluated the expression of Class I and II Hdacs in E15 amygdala derived from the "Four Core Genotypes" mouse model which comprises XX and XY gonadal males and XX and XY gonadal females. The mRNA expression of Class I Hdac1, 2 and 8 as well as Class II Hdac4 and 6 in amygdalae was analyzed by qPCR. Hdac1, 2 and 8 expression levels were higher in amygdala derived from XX embryos compared to XY, irrespectively of gonadal sex. No differences were observed in Hdac4 and 6. Our results suggest that sex chromosomes may determine a sexually dimorphic gene expression through Class I Hdacs in specific areas of the mouse brain before the in utero exposure to gonadal hormones. Current experiments are evaluating candidate genes regulated by Class I Hdacs relevant to sexual differentiation.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

IMT504 provides analgesia by modulating cell infiltrate and cytokine milieu in rats with hindpaw inflammation

Candelaria Leiguarda [1], Constanza Potilinski [1], Julia Rubione [1], Pablo Tate [1], Marcelo J Villar [1], Alejandro Montaner [2], Veronica Bisagno [3], Luis Constandil [4]

1 Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET, Buenos Aires, Argentina.
2 Instituto de Ciencia y Tecnología "Dr. César Milstein", CONICET, Fundación Pablo Cassará, Buenos Aires, Argentina.
3 Instituto de Investigaciones Farmacológicas – CONICET, Buenos Aires, Argentina
4 Departamento de Biología, Laboratorio de Neurobiología, Facultad de Química y Biología, Universidad de Santiago de Chile, Santiago, Chile.

Presenting author:
***Candelaria Leiguarda**, candelarialeiguarda@gmail.com*

IMT504 is a non-CPG, non-coding synthetic ODN exerting long-lasting anti-allodynic effects in rats undergoing unilateral hindpaw inflammation. The purpose of the present study is to address cellular and molecular mechanisms at the site of injury potentially underlying the anti-nociceptive role of IMT504. Analysis of pain-like behavior, locomotor activity, histology, cell infiltration by flow-cytometry, secreted proteins by protein microarrays or ELISA (β-endorphins) in the inflamed hindpaws were employed to study the impact of a single subcutaneous administration of IMT504 in male adult rats undergoing complete Freund´s adjuvant-induced hindpaw inflammation. We show that a single subcutaneous dose of IMT504 results in a 6-week-long full reversal of mechanical and cold allodynia, compromising neither acute pain perception nor locomotor activity. The anti-nociceptive effects of systemic IMT504 correlated with reductions in hindpaw dorsoventral thickness, plasma extravasation, decreases in B-cell and macrophage counts, and an increase in CD8+ T-cell counts. Moreover, a profound downregulation in several pro-inflammatory cytokines as well as of β-endorphin, plus mild upregulation of IL-10, were also observed at the site of injury. Altogether, we provide new evidence demonstrating that the anti-nociceptive actions of IMT504 relate to modulation of the peripheral immune system at the site of injury, and support its use as a novel anti-inflammatory drug against chronic pain.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Effects of nuclear receptor PPARγ and RXR activation on NPC and OPC primary culture

Débora Rodríguez [1], Laura Gómez Pinto [2], Patricia Mathieu [3], Ana M. Adamo [4]

1 Débora Rodríguez
2 Laura Gómez Pinto
3 Patricia Mathieu
4 Ana M. Adamo

Presenting author:
Debora Vanesa Rodriguez, *rodriguez-debora@hotmail.com*

CNS demyelination is a pathological process by which myelin is lost from around axons, while remyelination is the repair process by which oligodendrocytes (OL) restore myelin to demyelinated axons. Retinoid X (RXRs) are nuclear receptors forming homodimers, or else heterodimers with peroxisome proliferator-activated receptors (PPARs), which regulate OL differentiation and maturation. The aim of the present work is to study the single or joint activation of RXRγ and PPARγ by specific agonists 9 cis retinoic acid (RA) and pioglitazone (PIO), respectively, in primary cultures of neural progenitor cells (NPC) obtained from the SVZ of young adult rats, and oligodendroglial precursor cells (OPC), microglia and astrocytes obtained from the cerebral cortex of newborn rats. Results show that 10 µM RA induced a significant increase in GFAP+ astrocytes at the expense of Nestin+/GFAP+ cells derived from NPC, concomitantly with a significant decrease in the proportion of proliferative Ki67+ cells. Also, 10 µM RA increased the morphological complexity of both PDGFRα+ OPC and MBP+ OL, an effect also observed after 3-day treatment with 1 and 5 µM PIO. Microglia treatment with 5 µM PIO increased the production of NO induced by LPS, and astrocyte treatment with 5 µM PIO and 10 µM RA showed an increase in the number of GFAP+ cells. These results suggest the participation of RXRγ and PPARγ in OPC differentiation and the microglial and astrocyte response, which may be relevant to myelin repair.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Characterization of Photo-induced Oxidative Modifications of α-Synuclein

Ezequiel Giménez [1], Gian Franco Cavazzutti [1], Andrés Martín Toscani [1], Thomas Jovin [2], Henning Urlaub [3], Lisandro Falomir Lockhart [1]

1 Laboratorio de Neuroquímica y Biofísica de Enfermedades Neurodegenerativas, INIBIOLP-CONICET, Facultad de Ciencias Médicas, Universidad Nacional de La Plata, Argentina
2 Laboratory of Cellular Dynamics, Max Planck Institute for Biophysical Chemistry. Göttingen, Germany.
3 Bioanalytical Mass Spectrometry Group, Max Planck Institute for Biophysical Chemistry. Göttingen, Germany.

Presenting author:
***Ezequiel Giménez**, egimenez@med.unlp.edu.ar*

A gain of toxic function of the protein α-Synuclein (aSyn) has been largely linked to the development and progress of Parkinson's disease (PD) and related Synucleinopathies. However, the identity of aSyn toxic species remains elusive. In this way, post-translational modifications (PTMs) are a well-known source of variability of proteins´ structure, function, and localization, and are therefore possible modulators of the physiopathology of aSyn in neurons. Our project aims for a better understanding of the initial molecular events leading to PD and the development of innovative tools for the early diagnosis of Synucleinopathies. For this purpose, we have optimized protocols to modify aSyn employing a photochemical method that uses Rutheniun (II) Tris(bipyridine) as photosensitizer. Particularly, we have generated, characterized, and quantified covalent cross-linked oligomers and nitrated species via fluorescence spectroscopy, and mass spectrometry. Since aSyn is an intrinsically disordered protein, it can adopt multiple conformations, depending on the environment and interacting partners. Therefore, we also applied photo-oxidation protocols to compare the susceptibility of aSyn to be modified when adopting helix-rich or cross β-sheets (fibrillar) structures. This is a first step towards the development of new strategies that could recognize and quantitate specific aSyn PTMs as early potential biomarkers of Synucleinopathies in complex biological samples.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Unveiling neuronal glycoprotein M6a partners by high throughput quantitative mass spectrometry

Gabriela Inés Aparicio [1], Karina Formoso [2], Antonella León [1], Alberto C. Frasch [3], Camila Scorticati [1]

1 Instituto de Investigaciones Biotecnológicas - Universidad Nacional de San Martín (IIBio-UNSAM-CONICET),
2 Instituto de Investigaciones Biomédicas (BIOMED), Facultad de Ciencias Médicas, Pontificia Universidad Católica Argentina (UCA), CONICET
3 Vicerrectorado, Edificio de Gobierno, Universidad Nacional de San Martín (UNSAM)

Presenting author:
***Gabriela Aparicio**, gaparicio@iibintech.com.ar*

The molecular mechanisms underlying structural neuronal plasticity are not completely understood. In this regard, neuronal membrane glycoprotein M6a contributes to this process by unknown mechanisms. Alterations in M6a levels are associated with mental disorders like schizophrenia, depression and Alzheimer's disease. Evidence suggests that the extracellular loops of M6a command its neuroplastic function. Therefore, we aimed to identify proteins that associate with M6a's extracellular loops. We generated a chimera protein that only contains the extracellular loops of M6a and performed a co-immunoprecipitation with rat hippocampus samples followed by TMT/MS identification. Data analysis revealed 72 candidate proteins to interact with M6a's extracellular loops. Gene ontology analysis showed that 45 of these proteins are located at the synapses while 22 are in the surface of oligodendrocytes. We characterized the interaction of M6a with piccolo, SV2B, and synapsin 1 in cultured hippocampal neurons. Moreover, we demonstrated the interaction between M6a with proteolipid protein (PLP) in N2a cells. Finally, a disease-associated genes and variants screening by DisGeNET revealed that most of the 72 proteins are involved in "autistic disorder," "epilepsy," and "seizures" increasing the spectrum of disorders in which M6a could play a role. Data are available via ProteomeXchange with identifier PXD017347.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Stiffness of collagen type I inhibits axon growth of sympathetic neurons: a 3D culture model to study mechanical signals

Gaby Fabiana Martínez [1], Jimena Fagetti [1], Gabriela Vierci [1], Mónica Brauer [1], Nicolás Unsain [2], Analía Richeri [1]

1 Laboratorio de Biología Celular, Departamento de Neurofarmacología Experimental. Instituto de Investigaciones Biológicas Clemente Estable (IIBCE). Avenida Italia 3318. Montevideo, Uruguay.
2 Laboratorio de Neurobiología, Instituto de Investigación Médica Mercedes y Martín Ferreyra, INIMEC-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Universidad Nacional de Córdoba (UNC), Friuli 2434, Córdoba (5016), Argentina.

Presenting author:
***Gaby Fabiana Martínez**, g6bym6r@gmail.com*

Mechanical signals influence axon growth of both CNS and PNS neurons. Type I collagen (Col-I) has been widely used as a substrate to study axon growth, since it emulates an in vivo environment. Here, we evaluated the influence of Col-I stiffness to the extent of sympathetic axon growth in three dimensions (3D). With this aim, superior cervical ganglion explants from neonatal rats were cultured in soft or stiff Col-I 3D matrices. Stiff Col-I 3D matrices were achieved following 4hs of treatment with glycolaldehyde (GA). Sympathetic axon growth was greatly influenced by Col-I stiffness both after 24 and 48hs. The main findings were: (1) explants seeded in soft Col-I matrices, formed radially symmetric halos composed of an intricate meshwork of neurites; (2) in stiff Col-I matrices, the neurites fasciculated, and formed smaller and apparently less dense halos; (3) neurites showed limited growth in stiff Col-I matrices evidenced by reduced length compared to those that grew in soft matrices and (4) a loss of growth cones in axons growing in Col-I stiff matrices was also evidenced. Here we showed that a mechanical property of the microenvironment, such as stiffness, can be less favorable to the growth of sympathetic axons. Together these results provide insights to the understanding of how growing neurons are affected when they interact mechanically with their environment, an issue that should be considered in tissue engineering and organoid research.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Genetic risk factors for Alzheimer's Disease in adults with Down Syndrome in the Argentine population

Giulia Clas, Lucia Pertierra, Nahuel Magrath, Fernanda Tapajóz, Tatiana Itzcovich, Matias Niikado, Micaela Barbieri, Horacio Martinetto, Gustavo Sevlever, Ricardo Allegri, Ezequiel Surace.
FLENI

Presenting author:
***Giulia Solange Clas**, clas.giulia.s@gmail.com*

Alzheimer's disease (AD) is the most common cause of dementia in individuals over the age of 65. Brains of people with AD frequently exhibit features due to abnormal protein deposition. It has been shown that the ε4 allele of the APOE gene and the R47H variant of TREM2 increase the risk of AD. On the other hand, Down Syndrome (DS) is the most frequent genetic form of intellectual disability. Life expectancy of individuals with DS is currently 60 years. Starting at age 40, people with DS have an increased risk of dementia and almost all of them have histopathological features of AD in their brains. Since there is not much information on biomarkers and genetic risk factors of dementia in DS, we proposed to analyze them.

Sixteen participants with DS were recruited Cognitive status was assessed by clinical and neuropsychological evaluations. Also, participants underwent positron emission tomography to evaluate global cerebral metabolism (FDG) and cerebral Aβ (PiB), respectively. AD risk variants in APOE and TREM2 were analyzed by RFLP-PCR.
Ten participants exhibited the 3/3 genotype in APOE, four the 3/4, and two had the 2/3. We found a trend towards a greater presence of the risk allele ε4 in participants with cognitive impairment. In agreement with its low population frequency, we did not observe the R47H risk variant in this group.

Overall, data obtained here set the ground for further investigations on factors modulating dementia onset in adults with DS in our population.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Exploring the AMPK signalling as a potential intermediate in yerba mate-induced neuroprotection

Hernán E. Hauché P., Pedro Ballestero, Tomás Eidelman, Melina P. Bordone, Juan E. Ferrario

Laboratorio de Neurobiología de la Enfermedad de Parkinson. iB3, FBMC, FCEN, UBA-CONICET.

Presenting author:
Hernán Ezequiel Hauché Pedernera, *hernanhauche@gmail.com*

Alzheimer's disease (AD) is the most common cause of dementia in individuals over the age of 65. Brains of people with AD frequently exhibit features due to abnormal protein deposition. It has been shown that the ε4 allele of the APOE gene and the R47H variant of TREM2 increase the risk of AD. On the other hand, Down Syndrome (DS) is the most frequent genetic form of intellectual disability. Life expectancy of individuals with DS is currently 60 years. Starting at age 40, people with DS have an increased risk of dementia and almost all of them have histopathological features of AD in their brains. Since there is not much information on biomarkers and genetic risk factors of dementia in DS, we proposed to analyze them.

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Overall, data obtained here set the ground for further investigations on factors modulating dementia onset in adults with DS in our population.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

The cutting edge of DYRK1A in axonal transport regulation and its implications in neurodegenerative diseases.

Iván Fernandez Bessone, Jordi L Navarro Cnobel, José Emanuel Martínez, Mariana I Holubiec, Trinidad MM Saez, Tomás L Falzone
Instituto de Biología Celular y Neurociencia (IBCN, UBA-CONICET)

Presenting author:
Ivan Fernandez Bessone, *ifernandezbessone@gmail.com*

The complexity of axonal transport regulation has become extremely relevant since it is proposed that transport defects are a necessary step in the progression of neurodegenerative diseases. Recently, DYRK1A, a dual specificity kinase located in chromosome 21 has been associated with abnormal early aging of the nervous system, since it modulate APP and tau protein.

To unravel whether DYRK1A has a role in axonal transport regulation, understand its impact in the molecular pathways that control transport, and identify its role in disease progression, we have inhibited DYRK1A function in human neurons derived from iPSC for 48 hours using harmine 7,5 uM. We performed live-cell imaging to generate high resolution tracking of the APP vesicle within extended and polarized axons. This experiments revealed a significant reduction on the retrograde component of APP transport. To probe the role of DYRK1A, we then induced short term DYRK1A overexpression that resulted in an opposite phenotype. Moreover, we tested whether long term DYRK1A overexpression is linked to different underlying molecular mechanisms. Together, our results highlight the role of DYRK1A in axonal transport by different mechanisms that can be proposed as modulatory of the APP vesicle transport.

Our work stress new functions for DYRK1A in the molecular pathways that control axonal transport, and shed light on putative therapeutic strategies targeting transport dynamics in neurodegenerative diseases.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Signs of vascular alteration and inflammation in different brain areas of SHR pups

Joana Antonela Asensio [1], Rodrigo Damián García [2], Alicia Mabel Seltzer [1]
1 IHEM-CONICET, Mendoza, Argentina
2 IMBECU-CONICET, Mendoza, Argentina

Presenting author:
***Joana Antonela Asensio**, joanaantonelaasensio@gmail.com*

Fetuses suffering intrauterine growth restriction (IUGR) are at high risk of brain injury and motor disabilities. Vascular rarefaction and inflammatory processes have been associated with these pathologies. We previously observed a delay in cerebellar layers stratification and neurodevelopmental impairment in spontaneously hypertensive rat pups (SHR), a proposed model of IUGR. In this work, SHR brains were obtained at P7 and P14; age matched normotensive Wistar Kyoto rats served as controls. The morphology and number of medium-caliber vessels was studied with Masson's trichrome. Our results indicate that SHR showed a significant increase in the number of these vessels from both gray and white matter. We also performed double labeling for anti-Caveolin-1 and isolectin B4 to study microvasculature and microglial cells. No changes were found in the amount and ramifications of brain microvessels. A significant increase in the number of ameboid microglia was noticed in the cerebellum of the SHR at P7 and P14. GFAP expression, an important component of astrocytes cytoplasm, was increased in homogenates from motor cortex that included corpus callosum, and its localization in this area was confirmed by GFAP IFI. Insulin-like growth factor gene expression was increased in the cerebellum of SHR; probably related to the significant increase in the number of ameboid microglia. We conclude that SHR brain shows vascular adaptations and glial activation in response to gestational hypoxia.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Is mGlu3Δ4R, the truncated isoform of metabotropic glutamate mGlu3 receptor, implicated in Alzheimer's pathogenesis?

Juan Turati, Julieta Rudi, Tomás Álvarez Llenás, Lila Carniglia, Carla Caruso, Mercedes Lasaga, Daniela Durand

Instituto de Investigaciones Biomédicas (INBIOME, UBA-CONICET)

Presenting author:
Juan Turati, *juanturati@gmail.com*

mGlu3R exert crucial protective functions in normal and ill brain. It has been shown that human brain also expresses mGlu3Δ4R, a truncated isoform of mGlu3R lacking the exon 4 coding for the transmembrane domain. In heterologous expression systems mGlu3Δ4R was shown to act as a negative dominant of mGlu3R, and a possible association with schizophrenia was reported. However, the function of this isoform in CNS resident cells or in other pathologies has been largely ignored. We described for the first time a possible correlation between Δ4 and AD onset using PDAPP-J20 mice. Now, we are reporting that Δ4 is expressed by normal astrocytes and neurons and that Aβ did not induce GRM3 splicing in these cells; rather, Aβ inhibited both mGlu3R and mGlu3Δ4R protein expression. Thus, we wondered if, inversely, Δ4 may lead to Aβ overproduction, considering that canonical mGlu3R regulates amyloidogenesis in astrocytes. We transfected cultured astrocytes with pCMV-GRM3Δ4 plasmid and observed increased levels of Δ4 mRNA and a disorganization of astrocyte monolayer, accompanied by increased cell death compared to mock cells. Indeed, Δ4 overexpression reduced Scavenger receptor-A mRNA levels, suggesting a failure in Aβ clearance. A possible reduction in mGlu3R protein levels after Δ4 overexpression was also observed in preliminary results. Taken together, our results encourage us to study mGlu3Δ4R as a novel target in AD research field, possibly becoming an early biomarker of AD.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

ERK activation dynamics after learning experience in mice

Julieta Millan [1], Santiago Ojea Ramos [2], Mariano Guillermo Blake [3], Mariana Feld [2], María del Carmen Krawczyk [1], Mariano Martín Boccia [1]

1 Laboratorio de Neurofarmacología de los Procesos de la Memoria, FFyB, UBA
2 Laboratorio de Neurobiología de la Memoria, IFIByNE, UBA-CONICET
3 IFIBIO Houssay, UBA-CONICET

Presenting author:
***Julieta Millan**, julimillan6@gmail.com*

During memory consolidation, extracellular signal-regulated kinases (ERK) regulate the expression of several proteins involved in synaptic plasticity, but they also show other important roles locally at the synapse. There are many studies that explore ERK synaptic activation, most of them focusing on Long Term Potentiation at a specific moment in time. Here, our aim is to describe time-dependent ERK activation in the synaptosomes of mice hippocampus after a learning experience. Using an Inhibitory Avoidance task, we trained different groups of mice: Unshock (Un), Shock (Sh), and Immediate Shock (ShI). We measured ERK activation levels in the cytosolic compartment 45 minutes after training, and in the synaptic content -the soluble protein fraction within the synaptosomes- at 5, 15 and 45 minutes after training. We found that, in the cytosolic fraction, there is a dramatic decrease in phosphorylation levels in most experimental groups compared to naïve animals. In particular, ERK2 showed the greater differences, as it is commonly observed. At the synaptic compartment, however, the differences appeared only in ERK1 in ShI vs Sh, and ShI vs Un at 15 and 45 minutes respectively, but not 5 minutes after training. Thus, our results show that synaptic activation of ERK differs greatly from the general cytosolic activation, suggesting differential kinetics and potential functions.Cellular and Molecular Neurobiology

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

TGFβ in the remyelination process

Laura Ivonne Gómez Pinto, Debora Rodriguez, Ana Adamo, Patricia Mathieu
Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, IQUIFIB-CONICET, Argentina.

Presenting author:
***Laura Ivonne Gómez Pinto**, ivonnegomezpinto@gmail.com*

We have demonstrated the interplay between Notch and TGFβ signaling in adult neural progenitor cell cultures. In these cultures, TGFβ favored the oligodendroglial cell fate and oligodendroglial precursor cell (OPC) proliferation, and induced OPC differentiation and maturation. Considering the possible participation of TGFβ in the remyelination process, the aim of the present work is to study, both in vitro and in vivo, the changes induced by this cytokine on OPC maturation and on the inflammatory process. To analyze TGFβ effects on OPC maturation, in vitro experiments were carried out on OPC primary cultures. After OPC treatment with TGFβ for 3 days, no changes were observed in the percentage of PDGFRα+ and MBP+ populations compared to control. However, the presence of TGFβ induced an increase in the morphological complexity of OPC and mature oligodendrocytes. For in vivo experiments, control and 14-day-cuprizone (CPZ)-treated rats were intraperitoneally injected with TGFβ or its vehicle 3 days before removing the toxin from the diet. Preliminary results obtained 0, 3 and 7 days after CPZ withdrawal showed lesser microgliosis in TGFβ-treated animals. Moreover, TGFβ induced a decrease in phagocytic microglia at 3 days. These anti-inflammatory effects went together with a higher number of MAG+ cells at 0 and 3 days. These results suggest that TGFβ might have positive action in the remyelination process, although more experiments are necessary to confirm these observations.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

ASIC1a channels, IL-6 and activation of the ERK pathway

Libia Catalina Salinas [1], Rodolfo Gatto [2], Osvaldo Daniel Uchitel [1], Carina Weissmann [1]

1 Instituto de fisiología, Biología molecular y Neurociencia IFIBYNE-CONICET, Argentina
2 Department of Bioengineering, University of Illinois at Chicago, Chicago, IL USA

Presenting author:
Libia Catalina Salinas Castellanos, *libia_catalina53@hotmail.com*

ASIC (Acid sensing Ion Channels) are sodium channels activated by tissue acidosis. ASIC1a is the most abundant subunit in the mammalian central nervous system. This subunit permeates not only sodium but, slightly, calcium ions, and so can contribute to neuronal injury in pathological conditions. Changes in regional pH levels in the brain have been observed in a number of neurological and neurodegenerative disorders and could lead to channel activation. In fact, ASIC1a channels have been lately implicated in several neurological diseases: blocking this channel improves models of cerebral ischemia, Parkinson´s disease, Huntington´s disease. Additionally, these diseases share a feature in common: neuroinflammation. IL-6 is the main cytokine in the CNS, increased in these diseases.

It has been previously documented that ASIC1a channel activation trigger ERK phosphorylation, a pathway involved in pain, proliferation and disease.
Our preliminary results show that IL-6 through its receptor induces ERK activation via ASIC1a channels through the MEK pathway in HEK cells and neuron cultures.
We show that both, tozililumab (TCZ) -to block IL-6 receptors-, as well as the ASIC1a inhibitor Pctx-1, abolish ERK increases. As expected, the inhibition of the MEK pathway (blocked by the inhibitor PD98059) is also involved in the ERK increase through IL-6-ASIC1a. Establishing the exact role of ASIC1a, and inflammation in pathologies could lead the way to therapies with specific channel blockers.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Wnt7b induces changes in axonal development through regulation of microtubule behavior.

Lorena P. Neila, Silvana B. Rosso
Laboratorio de Toxicologia Experimental, FBioyF, UNR

Presenting author:
Lorena Paola Neila, *lorepneila@gmail.com*

In the nervous system, a proper microtubule dynamic and organization is crucial for the initiation, extension and maintenance of neurites. Wnts proteins, through different cascades, regulate cytoskeletal network and the activity of effectors to control neuronal polarity, axon and dendrite development. In this work, we focused our attention on the role of Wnt7b on earlier neuronal development, particularly in axonal growth. We previously showed that Wnt7b affects the establishment of neuronal polarity and axonal outgrowth since Wnt7b stimulated neurons evidenced increased axonal length and complexity. Importantly, we recently observed that Wnt7b increases microtubule stability (around 30%) in immature neurons compared to controls. Moreover, Wnt7b induced the formation of looped microtubules at the axonal growth cones. In next studies, we will carefully analyze the organization of microtubules in the growth cone of Wnt7b stimulated neurons. To go further, we found that pharmacological inhibition of JNK mediated pathway (PCP pathway) abolished the Wnt7b effects on axonal morphology. Consistently, we then evidenced that neurons exposed to Wnt7b showed an increase in the activity of JNK. This effect was observed by immunofluoresces and Western blot approaches. In future experiments, we hope to determine whether changes in microtubule dynamics induced by Wnt7b are mediated by alterations on JNK activity.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Quantitative analysis of the neuroprotective effects of FK506 on axotomy-induced axonal degeneration in the Drosophila wing

Luciana Florencia Godoy, Ana Belén Ramos Hryb, Mario Rafael Pagani

Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, Universidad de Buenos Aires, CONICET, Buenos Aires, Argentina

Presenting author:
Luciana Godoy, *lucianafgodoy@gmail.com*

The immunosuppressant FK506 protects the nervous system upon several kinds of injuries both in vivo and in vitro. However, the properties and mechanisms involved in its neuroprotective effect remain obscure. Here we aimed to investigate the effects of FK506 in the neurodegeneration induced by an in vivo axotomy on the L1 nerve of Drosophila adult wing. After a complete transection of the L1 nerve on the right wing, we examined the structural changes in glutamatergic neurons expressing GFP. The left wing was left intact and used as an internal control. To evaluate the injury, we developed a quantification system based on objective continuous variables to replace the discrete categorization commonly used. Four days post-axotomy, injured L1 nerves displayed a 39% width reduction and increased number of small highly-circular particles when compared to intact wings. Immediately after the axotomy, adult flies received either vehicle or FK506 for 4 days. Toxicity studies showed that 0.01 to 1 μM FK506 treatments did not alter the adult fly survival. Neither 0.01 μM nor 0.1 μM FK506 treatments affected the nerve width loss. However, 0.01 μM FK506 reduced the axonal fragmentation and the probability of small highly-circular particles. In conclusion, the quantitative analysis in the wing axotomy paradigm revealed specific properties in the neuroprotective effect of FK506 in vivo. Future studies will examine specific mechanisms involved in such effects of FK506 on axonal fragmentation.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Calcium-dependent regulation of the endoplasmic reticulum stress sensor PERK

Macarena Fernandez, Sebastian Bairo, Mariana Bollo.
Instituto de Investigación Médicas Mercedes y Martín Ferreyra INIMEC-UNC-CONICET

Presenting author:
***Macarena Fernandez**, maquifernandez@immf.uncor.edu*

The endoplasmic reticulum (ER) plays a critical role in a variety of processes, where Ca2+ acts as a key messenger. The accumulation of unfolded proteins into the organelle activates a signal transduction cascade called Unfolded Protein Response (UPR). An immediate response, which attempts to restore homeostasis, is the attenuation of protein synthesis due to the activation of PERK, an ER transmembrane kinase, by auto-phosphorylation. We demonstrated that Calcineurin (CN) interacts directly with PERK increasing its activity. Interesting, in astrocytes, CN has a cytoprotective effect dependent on PERK. In addition, we detected active ER Ca2+ release through the translocon during acute phase of UPR. Although the involvement of Ca2+ signaling in a multitude of cellular functions has been well documented, little is known about its role in restoring homeostasis, once UPR is activated. Here, we evaluated the dependence of Ca2+ on PERK phosphorylation by immunocytochemistry and we analyzed PERK/CN interaction, after induces stress and pharmacologically modify translocon activity. This was further studied by using a cell line deficient in all isoforms of IP3 receptor. Moreover, we demonstrated that, PERK forms a macromolecular complex with translocon pore (Sec61α) and CN by performing a blue native PAGE followed by a second dimensional gels. Overall these data strongly suggest that PERK is activated by Ca2+ signal originated through the translocon during acute phase of UPR.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Assessing the distribution of tanycyte processes and their vascular contacts within the basal hypothalamus of mice

Maia Uriarte [1], Tomás Crespo [1], Mirta Reynaldo [1], Paula Reggiani [2], Rodolfo Goya [2], Mario Perelló [1], Pablo Nicolás De Francesco [1]

1 Laboratorio de Neurofisiología del Instituto Multidisciplinario de Biología Celular (CONICET, UNLP, CIC-PBA), 1900 La Plata, Buenos Aires, Argentina

2 Instituto de Investigaciones Bioquímicas de La Plata (INIBIOLP), Facultad de Ciencias Médicas, UNLP, 1900, La Plata, Argentina

Presenting author:
***Maia Uriarte**, maiauriarte.90@gmail.com*

Hypothalamic tanycytes are specialized ependymal cells that line the floor of the third ventricle and emit processes into the surrounding hypothalamic parenchyma. Given their strategic location, these cells are believed to play several key functions, including energy homeostasis, nutrient sensing, and hormonal transport and regulation. Here, we used an adenoviral vector expressing GFP (Rad-GFP) to label the ependymal walls, including tanycytes and their processes, providing fine structural detail throughout these structures. By imaging a series of consecutive brain slices we obtained a collection of fluorescence z-stacks which we later re-combined into a continuous volume spanning the basal hypothalamus. This was accomplished by applying a global elastic registration procedure guided by local inter-stack landmark pairs, using an image analysis pipeline we developed for the software package Fiji and its plugin TrakEM2. Following this procedure, we were able to map the three-dimensional distribution of tanycytes processes throughout the sampled volume, as well as to describe and quantify several parameters, including the type and percentage of processes that extend to the different hypothalamic nuclei, their overall morphology and orientation, and the distribution of contact classes based on morphological criteria. Altogether, our results provide valuable insights for the further understanding of these intriguing cells and their putative roles in the hypothalamic physiology.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Long-lasting antiallodynic effects of IMT504 in rats with spared nerve injury relate to strengthened migration of mesenchymal stem cells towards injured nerves

Mailín Casadei [1], Esteban Juan Fiore [2], Candelaria Leiguarda [1], Julia Rubione [1], Florencia Coronel [3], Mariana García [2], Guillermo Mazzolini [2], Marcelo Villar [1], Alejandro Montaner [4], Pablo Brumovsky [1]

1 Acute and Chronic Pain Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET, Av. Juan D. Perón 1500, Derqui, Pilar, Buenos Aires, Argentina.
2 Gene Therapy Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET, Av. Juan D. Perón 1500, Derqui, Pilar, Buenos Aires, Argentina.,
3 Pain in Cancer Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET, Av. Juan D. Perón 1500, Derqui, Pilar, Buenos Aires, Argentina., 4 Instituto de Ciencia y Tecnología "Dr. César Milstein", CONICET, Fundación Pablo Cassará, Ciudad Autónoma de Buenos Aires, Argentina.

Presenting author:
***Mailín Casadei**, Mcasadei@austral.edu.ar*

Peripheral neuropathic pain is caused by injury or dysfunction of peripheral nerves, and is characterized by allodynia and hyperalgesia. Neuropathic pain is complex and difficult to treat, in many cases resistant to currently available pain drugs. We have shown that multiple systemic doses of the oligodeoxynucleotide (ODN) IMT504 result in clear and long-lasting antiallodynic and anti-inflammatory effects in rats with unilateral sciatic nerve crush or hindpaw inflammation. Interestingly, in rats with sciatic nerve crush, virtually identical allodynia-preventing effects were observed after systemic administration of IMT504 or exogenous rat bone marrow mesenchymal stem cells (BMMSC). Here, we address the role of IMT504 in a model of chronic neuropathic pain, and the involvement of BMMSC.

Early or late IMT504 administration revert mechanical and cold allodynia in animals undergoing persistent neuropathic pain. The effect exhibits a considerably quick onset and is long-lasting. The ODN also appears to potentiate the mobilization, migration and homing of BMMSCs into injured nerves. If these effects on BMMSCs relate to the antiallodynic actions of IMT504, it remains to be further demonstrated. However, our results support the idea that this ODN could be a promising therapeutic agent in the treatment of chronic neuropathic pain, also in humans.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Simultaneous electrophysiological and transcriptomic study of cell states in dopaminergic neurons

Marcela Lipovsek [1], Lorcan Browne [1], Darren Byrne [1], James Lipscombe [2], Iain Macaulay [2], Jonathan Mill [3], Matthew Grubb [1]

1 Centre for Developmental Neurobiology - King's College London
2 Earlham Institute - Norwich Research Park
3 University of Exeter

Presenting author:
***Marcela Lipovsek**, marcela.lipovsek@kcl.ac.uk*

Dopaminergic (DA) neurons in the olfactory bulb regulate the transmission of information at the earliest stages of sensory processing, and are one of the few neuronal types in the mammalian brain continually generated throughout postnatal life. Here, we ask whether this continuous neuronal production results in a gradient of cell states within the resident population. Birthdating in 4-week old DAT-IRES-Cre/Flox-tdT mice revealed that resident DA neurons span an age range of at least 3 weeks. We next collected individual DA neurons by either manual sorting of tdT positive DA neurons, or aspiration after patch-clamp recordings in acute slices (Patch-seq), and performed deep single-cell RNA sequencing. Clustering analysis identified putative subpopulations of DA neurons, while cell trajectory analysis described a single, unbranched, trajectory that closely matched the clusters. Further analysis revealed differentially expressed genes, significantly enriched for GO terms related to neuronal and synaptic function, indicating that the identified trajectory may reflect a transcriptional maturational gradient. Ongoing analysis of electrophysiological properties along the identified trajectory will reveal whether it describes a gradient of functional states. In summary, we are exploring a hitherto unanticipated gradient of cell states within a specific neuronal subtype that could underpin the functional maturation of DA cells in the postnatal brain.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Impact of Val66Met polymorphism in the brain-derived neurotrophic factor (BDNF) gene in the vulnerability to cocaine addiction induced by chronic stress

M. Julieta Boezio [1], Milena Jandar Paz [2], Daiana Rigoni [1], Liliana M. Cancela [1], Agustín Anastasia [2], Flavia Bollati [1]

1 IFEC- CONICET. Departamento de Farmacología, Fac. De Ciencias Químicas, Universidad Nacional de Córdoba, Argentina.,
2 Instituto Ferreyra (INIMEC-CONICET-Universidad Nacional de Córdoba), Córdoba, Argentina.

Presenting author:
***María Julieta Boezio**, mjulib7@gmail.com*

The main goal of this project is to evaluate the influence of a single-nucleotide polymorphism (SNP) on the brain-derived neurotrophic factor (BDNF) gene leading to a valine (Val) for methionine (Met) substitution (Val66Met) in the BDNF prodomain in a model of cross sensitization between stress and cocaine. This SNP has been associated with mood disorders, stress and drug abuse in the human carriers. However, the underlying circuitry and mechanisms involved remains cryptic. We will use male and female BDNF Val/Val and BDNF Met/Met knock-in mice to assess the impact of this SNP on the vulnerability to develop stress-induced cocaine addiction. First, we will evaluate relevant behavioral differences between genotypes generated in response to chronic restraint stress and cocaine. For these experiments, male and female mice will be restrained daily for 30 min, in acrylic tubes specifically designed for this purpose, during 5 consecutive days, while control animals are kept in their home cages. Two weeks after the last stress (day 19), the animals will be exposed to a challenge of cocaine or saline and behavioral sensitization will be evaluated in an open field. In these experiments, we will analyze the effect of stress on locomotor sensitization and anxiety-like behavior using different doses of cocaine. Then, we will evaluate molecular and structural changes in the two subdivisions of nucleus accumbens (NA), core and shell, in mice from both genotypes under this protocol.Cellular and Molecular Neurobiology

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Changes in alternative splicing of GluN1 NMDAR subunit in a GluN2A KD model

María Laura Gobbini, María Florencia Acutain, María Pilar Canal, Natali Rozic, María Verónica Báez

Instituto de Biología Celular y Neurociencias Prof. Dr. E. de Robertis (IBCN CONICET-UBA)

Presenting author:
María Laura Gobbini, *laugobbini@yahoo.com.ar*

NMDAR receptor (NMDAR) is a heterotetramer composed of two obligatory subunits, GluN1; and two regulatory subunits, GluN2 (A to D) or GluN3 (A and B). Alternative splicing of GluN1 mRNA produces eight splice variants that alternate in, N1 cassette at the N terminal or, concerning the C-terminal, GluN1 variants are due to the presence or absence of C1, C2 and C2' cassettes.

Previous works have described that knock-down (KD) of GluN2A regulatory subunit produces alterations in expression of GluN1. In this work, we analyse if changes in GluN1 expression in GluN2A KD are related to changes in NDMAR subcellular localization and also, if these changes are associated to modifications in NMDAR splicing variants. Preliminary results showed that N1 cassette inclusion does not change due to GluN2A KD, nonetheless, we found changes in the alternative splicing of C-terminus cassettes. Furthermore, we observed changes in GluN1 levels both at soma and dendrites. Although these are preliminary results, they suggest that changes in GluN2A modulates the NMDAR localization and the alternative splicing of GluN1.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Reduction of Malvolio (DMT1) in glial cells alters locomotor behaviour in Drosophila melanogaster.

María Silvina Marcora [1], Mario Rafael Pagani [2], Melina Petrissans [2], Micaela Vicente Biscardi [2], Jorge Correale [3], Juana Maria Pasquini [1]

1 Instituto de Química y Fisicoquímica Biológica (IQUIFIB), Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires-CONICET, Buenos Aires, Argentina.
2 Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO)-Houssay, Facultad de Medicina, Universidad de Buenos Aires-CONICET, Buenos Aires, Argentina.
3 Instituto de Investigaciones Neurológicas Dr. Raúl Carrea, FLENI, Buenos Aires, Argentina.

Presenting author:
***Maria Silvina Marcora**, silvinamarcora@gmail.com*

Iron deficiency in early life affects the development of brain structure, neurotransmitter systems and can lead to hypomyelination. This deficiency is also associated with behavioural and cognitive alterations which are not reversed by postnatal iron intake.
Divalent metal transporter 1 (DMT1) participates in intracellular iron export from endosomal compartments as part of the transferrin-bound iron uptake and mediates non-transferrin-bound iron uptake. The only member of the DMT1 family present in Drosophila melanogaster, Malvolio (Mvl) has shown capacity to transport iron. However, its role in glial cell physiology has not been reported yet.

We found that Mvl mutant flies displayed reduced locomotor activity, including distance travelled, mobile time and mean velocity, and altered habituation in an open-field arena. Using the UAS/GAL4 binary system to downregulate Mvl in a specific cell type, we observed that Mvl downregulation in neurons did not affect behaviour. However, in glial cell analyses, Mvl downregulation in ensheathing cells, but not in astrocytes, reduced locomotor activity and affected habituation. Immunofluorescence assays revealed no changes in the number of glial cells. These results suggest that Mvl might be relevant for ensheathing cell function, which in turn may modulate locomotion and cognition. These and future findings will help unveil Mvl participation in glial iron homeostasis and study its contribution in normal and pathological conditions.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

NO2-OA prevents neovascularization and induces vascular regrowth in Oxygen-Induced Retinopathy

María Victoria Vaglienti [1], Paula Virginia Subirada [1], María Belen Joray [2], María Constanza Paz [1], Pablo Federico Barcelona [1], Gustavo Bonacci [1], María Cecilia Sánchez [1]

1 Departamento de Bioquímica Clínica- CIBICI-CONICET- FCQ, UNC.
2 IRNASUS-CONICET-UCC

Presenting author:
***María Victoria Vaglienti**, vickyvaglienti@gmail.com*

Inflammation, oxidative and nitrosative stress are involved in Neovascular Retinopathies (NR). Nitro-fatty acids are electrophilic signaling mediators with anti-inflammatory and cytoprotective properties. Here, we hypothesized that Nitro-oleic acid (NO2-OA) can be beneficial for retinal cells in NR. For this, we used the Oxygen-Induced Retinopathy model. Briefly, C57BL/6 mice were exposed to 75% O2 from P7 to P12, after that they were brought to room air (RA) for additional five (P17) days. Age-match mice in RA were used as controls. Some OIR mice were i.o. injected at P12 with 5 µM of NO2-OA and i.p. at P14 with 15 mg/Kg of NO2-OA. At P17 mice were sacrificed. Retinas were used for microscopy and Western blot or RT-PCR assays. The NO2-OA biological activity was also assessed at P12 RA. Finally, the NO2-OA effect on neovascularization was evaluated by tube formation assay. GraphPad Prism was used for statistical analysis. The NO2-OA induced vascular regrowth, decrease neovascularization and produced significant changes in GS and GFAP at P17 OIR. RT-PCR revealed a significant increase in VEGF levels in OIR mice respect to RA mice, but not difference between NO2-OA treatment respect to vehicle at P17. Finally, a significant decrease in the total segment length and number of tubular structures was observed after NO2-OA treatment. These findings suggest that NO2-OA could be beneficial or cytoprotective for retinal cells in NR.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

NF-kB as key contributor of the comorbidity between chronic restraint stress and cocaine self-administration

Marianela Sanchez [1], Paula Avalos [1], Daiana Rigoni [1], Andrea Guzman [1], Julieta Boezio [1], Bethania Mongi [1], Bisbal Mariano [2], Bollati Flavia [1]

1 IFEC - CONICET Depto. Farmacologia Facultad Cs. Quimicas -UNC
2 Instituto Ferreyra

Presenting author:
***Marianela Adela Sanchez**, marianela.sanchez@hotmail.com*

Stress is a well-known risk factor in the development of psychostimulant addiction and relapse vulnerability. We showed that a deregulation of glutamate homeostasis, including a decrease of GLT-1 glutamate transporter and postsynaptic changes in Nucleus Accumbens core (NA), underlie cross-sensitization to cocaine following stress. NFkB, an ubiquitous transcription factor, induce the expression of gene targets closely involved in glia maintenance of GLU homeostasis. We propose a central role of NfkB signaling in stress-induced deregulation of GLU homeostasis and facilitation of cocaine self-administration in rats. Firstly we showed that PDTC, an inhibitor of NFkB nuclear translocation, prevents the expression of sensitization to cocaine following chronic stress (2h-restraint x 7 days). Secondly, we designed lentiviral vectors (dn IKK) targeted NF-kB. The lentiviral vectors (bisitronics), express GFP promoter and the dominant negative of the IKK, abrogates the activation of NFkB. The results obtained in culture showed the expression of lentiviral vectors in the host cell. Then, the lentiviral vectors will be administered in NA of rats to be tested in a cross sensitization model between cocaine and chronic stress as well as changes on GLU homeostasis in the NA. Thus, we put forward the advantageous use of genetic manipulation techniques to study in deep the NFkB-dependent neurobiological mechanisms of comorbidity between exposure to stress and cocaine abuse

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Maneb and α-synuclein: friends or foes in neuronal toxicity?

Melisa A. Conde [1], Melania Funk [2], Natalia P. Alza [1], Romina M. Uranga [1], Gabriela A. Salvador [1]

1 INIBIBB-DBByF-UNS,
2 INIBIBB

Presenting author:
***Melisa Ailén Conde**, mconde@inibibb-conicet.gob.ar*

Maneb (Mb) exposure and α-synuclein (α-syn) overexpression are triggering factors of Parkinson's disease. In this work, we studied the response to Mb toxicity in neurons stably expressing the human wild type α-syn gene (WT α-syn).

In control neurons, Mb cytotoxicity involved an increase in reactive oxygen species (ROS), α-syn overxpression and the loss in plasma membrane integrity. Experiments with the antioxidant N-acetylcysteine proved that the increase in α-syn expression induced by the pesticide was redox-dependent. In addition, WT α-syn neurons exposed to Mb showed decreased ROS content and less plasma membrane damage, with no additional changes in α-syn expression. To further characterize the response to Mb exposure, FoxO3a and Nrf2, two transcription factors activated upon cell injury, were evaluated. Mb exposure triggered Akt phosphorylation and the kinase-dependent FoxO3a inhibition in control cells. However, Mb exposure had no differential effect on FoxO3a status in WT α-syn cells. On the other hand, the expression of Nrf2-regulated phase-two antioxidant genes was increased in WT α-syn neurons. These results show that a neuroprotective response can be elicited when α-syn is overexpressed prior to pesticide exposure. Additional studies are necessary to solve the question whether α-syn is friend or foe in pesticide-induced toxicity.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

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1 IFEC - CONICET Depto. Farmacologia Facultad Cs. Quimicas -UNC
2 Instituto Ferreyra

Presenting author:
***Marianela Adela Sanchez**, marianela.sanchez@hotmail.com*

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E-Posters

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1 INIBIBB-DBByF-UNS
2 INIBIBB

Presenting author:
Melisa Ailén Conde, *mconde@inibibb-conicet.gob.ar*

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E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Insights on Alpha Synuclein in Parkinson's Disease: potential role on intracellular trafficking defects

Milagros Ovejero [1], Laura Gastaldi [3], Monica Remedi [3], Vaishali Sharma [2], Mariano Bisbal [1], Thomas M. Jovin [2], Donna J. Arndt-Jovin [2], Alfredo Caceres [1]

1 Instituto Ferreyra (INIMEC-CONICET-Universidad Nacional de Cordoba), Cordoba, Argentina, 2 Laboratory of Cellular Dynamics, Max-Planck-Institute for Biophysical Chemistry, Gottingen, Germany, 3 Instituto Universitario de Ciencias Biomédicas de Córdoba (IUCBC)

Presenting author:
Milagros Ovejero, *movejero@immf.uncor.edu*

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons of the substantia nigra and the intracellular accumulation of α-synuclein (AS) in Lewy bodies. While the pathogenic mechanisms of PD is still debated, many lines of evidence point to a role of intracellular trafficking defects. Increased expression of AS is associated with a higher incidence of PD, but we know little about the molecular mechanisms induced by AS that precede neurodegeneration. We use an innovative exocytic pathway synchronization system which allows coordinated release of transmembrane proteins from the endoplasmic reticulum (ER) using a specific drug. This tool enable us to study whether AS affects the dynamics of vesicular transport between the ER and the Golgi apparatus, and the release of vesicles from the latter towards neural processes. We found that AS expression induces a delay in vesicles release from the Golgi apparatus to neuronal processes in hippocampal neurons. This result suggests a possible mechanism by which AS generates toxicity that may have consequences on neuronal physiology. We are currently working to assess whether the same effect is present in human reprogrammed neurons derived from induced pluripotent stem cells (iPSC).

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Studying the in situ organization of the spectrin cortical skeleton of axons and dendrites in drosophila melanogaster

Nahir G. Gazal [1], E. Axel Gorostiza [3], Nicolás Unsaín [1,2]

1 Instituto de Investigación Médica Mercedes y Martín Ferreyra (INIMEC), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Universidad Nacional de Córdoba, Córdoba, Argentina.
2 Instituto Universitario de Ciencias Biomédicas de Córdoba (IUCBC), Córdoba, Argentina.
3 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE) CONICET - Universidad de Buenos Aires, Buenos Aires, Argentina.

Presenting author:
***Nahir Guadalupe Gazal**, nggazal@immf.uncor.edu*

Actin, spectrin and associated proteins form a periodic scaffold in neuronal axons and dendrites, with a period below the resolution limit of conventional microscopy. This Membrane-associated Periodic Skeleton (MPS) is present in all neurons examined across animals, suggesting it is a conserved and fundamental component of neuronal extensions. Most studies have been performed in cultured neurons. However, it is known that axons and dendrites do not develop and behave the same in culture compared to their natural environments, where are exposed to particular diffusive and fixed cues in 3D. In this recently-started project, we will first describe the normal abundance, distribution and regularity of the MPS in axons and dendrites of neurons in the nervous system of Drosophila melanogaster. We will also study how the MPS responds to physiological changes in the architecture of the neuronal processes. For this purpose, we selected two groups of neurons with well characterized axonal and dendritic structures, that also suffer dendritic remodeling during development (ppk neurons in larvae) and axonal remodeling on a daily fashion (pdf neurons in adult fly). Image acquisition will be performed by super-resolution approaches (Expansion Microscopy and STED). We expect that in tissue, a given neuronal population will share a characteristic arrangement of their MPS across their distinct subdomains and will be consistently remodeled during physiological changes in neuronal architecture.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

A reliable workflow for single-nuclei RNA-seq of hippocampal adult-born granule cells

Natalí Belén Rasetto [1], Ariel Berardino [2], Maria Luz Vercesi [2], Tomás Vega Waichman [2], Luciana Ferella [1], Juliana Brown [3], Paola Arlotta [3], Ariel Chernomoretz [2], Alejandro Schinder [1], Damiana Giacomini [1]

1 Laboratory of Neuronal Plasticity, Leloir Institute-CONICET
2 Laboratory of Integrative Systems Biology, Leloir Institute-CONICET
3 Department of Stem Cell and Regenerative Biology, Harvard University

Presenting author:
Natalí Belén Rasetto, *rasettonatali@gmail.com*

Adult hippocampal neurogenesis plays a critical role in spatial memory, retrieval, context discrimination, and clearance of memory traces. In the mouse dentate gyrus, the maturation of adult-born granule cells (GCs) lasts several weeks and can be divided in 4 phases based on their functional characteristics. Although the distinctive electrophysiological and morphological features of each stage have already been described, the molecular mechanisms that control the progression through the different stages towards a mature phenotype are still unknown. To investigate the molecular mechanisms instructing structural and functional maturation in each developmental stage of adult-born GCs, we set up an efficient protocol for high-throughput single-nuclei RNA sequencing applying Chromium 10X Genomics technology. We used double transgenic mice, Ascl1CreERT2;CAGfloxStopSun1sfGFP to allow conditional expression of Sun-1/sfGFP in the nuclear membrane of adult-born GCs. At specific time points, dentate gyri were microdissected and fluorescent nuclei were isolated and purified using FACS. This approach resulted in the purification and successful RNA-seq of 3000 nuclei obtained from 2-week-old immature GCs. We present a preliminary bioinformatic analysis of these data indicating that the experimental workflow described here is a reliable method to explore the molecular principles of neuronal maturation and integration in the adult brain.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

A new antagonist of Caenorhabditis elegans glutamate-activated chloride channels with anthelmintic activity

Ornella Turani [1], María Julia Castro [2], María Belén Faraoni [2], Darío Gerbino [2], Cecilia Bouzat [1]

1 Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB) - UNS
2 Instituto de Química del Sur (INQUISUR) - UNS

Presenting author:
***Ornella Turani**, ornellaturani@gmail.com*

Nematode parasitosis causes mortality and morbidity in humans and losses in livestock and domestic animals. The acquisition of resistance to current anthelmintic drugs has prompted the search for new compounds for which the nematode Caenorhabditis elegans has emerged as a valuable platform. We have previously synthetized a library of compounds and determined that dibenzo[b,e]oxepin-11(6H)-one (doxepinone) reduces swimming rate, induces paralysis, and decreases the rate of pharyngeal pumping on C. elegans. To identify the drug targets, we performed a screening of strains carrying mutations in Cys-loop receptors involved in worm locomotion for determining resistance to doxepinone effects. A mutant strain that lacks subunit genes of the glutamate-gated chloride channels (GluCl), which are targets of the antiparasitic ivermectin, is resistant to doxepinone effects. To unravel the molecular mechanism, we measured whole-cell currents from GluClα1/β receptors expressed in mammalian cells. Glutamate elicits macroscopic currents whereas no responses are elicited by doxepinone, indicating that it is not an agonist of GluCls. Preincubation of the cell with doxepinone produces a significant decrease of the decay time constant and net charge of glutamate-elicited currents, indicating that it inhibits GluCls. Thus, we identify doxepinone as an attractive scaffold with promising anthelmintic activity and propose the inhibition of GluCls as a potential anthelmintic mechanism of action.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Mesenchymal stem cell-derived Schwann cell exosomes promote neurite outgrowth and axonal protection in vitro.

Paula Andrea Soto [1,2], Rodrigo López Leal [3], Patricia Setton-Avruj [1,2], Felipe Court [3,4,5]

1 Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Química Biológica. Cátedra de Química Biológica Patológica. Buenos Aires, Argentina.
2 CONICET. Universidad de Buenos Aires. Instituto de Química y Fisicoquímica Biológicas (IQUIFIB). Buenos Aires, Argentina
3 Center for Integrative Biology, Faculty of Sciences, Universidad Mayor de Chile, Santiago, Chile, 8580745.
4 FONDAP Center for Geroscience, Brain Health and Metabolism, Santiago, Chile, 8580745., 5 Buck Institute for Research on Ageing, Novato, San Francisco, CA 94945, USA.,

Presenting author:
***Paula Andrea Soto**, paula.asoto02@gmail.com*

Schwann cells (SC) play a crucial role in axonal biology not only providing trophic support but also participating in the regulation of different processes during axonal development, maturation, and regeneration. A recently described form of communication between SC and axons is through extracellular vesicles called exosomes (Ex). It has been established SC-Ex participation in physiological and pathophysiological processes, e.g. during myelination and regenerative conditions. One of the main goals of regenerative medicine is to find new cell sources to be used in cell therapies for the treatment of degenerative diseases. Adipose-derived mesenchymal stem cells (AdSC) provide a promising tool due to their availability through a low-invasive method, their high rate of proliferation, and their ability to differentiate into other cell types, including SC (dSC-AdSC). Thus, the present work evaluates the effect of SC, AdSC and dSC-AdSC derived Ex on neurite outgrowth and axon protection in vitro. To this end, SC, AdSC and dSC-AdSC were cultured and Ex were obtained by ultracentrifugation. Using dorsal root ganglia cultures, Ex effects were evaluated in terms of neurite outgrowth and axonal integrity after treatment with vinblastine or mechanical axotomy, showing significant differences after dCS-AdSC Ex treatment. Our results demonstrate positive effects of dSC-AdSC Ex on neurite outgrowth and axonal protection, bringing about a potential acellular tool for regenerative strategies.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

The neurotrophin receptor p75NTR is involved in choroidal neovascularization

Paula Virginia Subirada [1], Maria Victoria Vaglienti [2], Agustín Fierro [3], Alejandra Jurado [3], O'Brien Paula [3], José Luna Pinto [3], Maria Cecilia Sánchez [2], Agustín Anastasía [1], Pablo Federico Barcelona [2]

1 Instituto Ferreyra, INIMEC-CONICET-UNC.
2 Departamento de Bioquímica Clínica, CIBICI-CONICET, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.
3 Centro Privado de Ojos Romagosa. Fundación VER. Córdoba, Argentina.

Presenting author:
***Paula Virginia Subirada**, psubirada@gmail.com*

Choroidal neovascularization (CNV) is the pathological angiogenesis of the choroidal plexus and it represents a key feature in the wet form of age related macular degeneration (AMD). CNV is triggered by a pro-inflammatory response settled after a damage in the retinal pigmented epithelium (RPE). The growing neovessels invade the retina inducing photoreceptor degeneration. Current treatments are inefficient, therefore a better understanding of the pathophysiology of AMD is necessary to develop novel therapeutic approaches. The p75 neurotrophin receptor (p75NTR) is recognized as one of the main surface proteins involved in the transduction of death signals and recently also vascular changes. Here, we aim to determine if p75NTR participates in the development of neuronal and vascular alterations in a mouse model of laser-induced CNV. Confocal images obtained 7 days after the laser injury showed overexpression of p75NTR in macrophages in the RPE-choroid, and in Muller glial cells around the lesioned area in the retina. When the laser treatment was provided to p75NTR KO mice, we observed a reduction in the area and perimeter of choroidal neovessels as well as a decreased macrophage infiltrate by immunostaining. In accordance, the neuronal dysfunction observed by electrorretinography (ERG) on this CNV model was reduced on p75NTR KO mice, as the amplitude of the a-wave was preserved after the laser. Our outcomes suggest that p75NTR would participate in the development of CNV.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Mitochondrial function in mouse brain cortex synaptosomes during aging. Alterations in motor performance

Paulina Lombardi [1], Analía G Karadayian [1], Juan I. Guerra [1], Rodolfo Cutrera [3], Juanita Bustamante [2]

1 Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Fisicoquímica, Buenos Aires, Argentina. CONICET- Universidad de Buenos Aires, Instituto de Bioquímica y Medicina Molecular (IBIMOL), Buenos Aires, Argentina,
2 Centro de Altos Estudios en Ciencias de la Salud, Universidad Abierta Interamericana, Buenos Aires, Argentina,
3 CONICET - Universidad de Buenos Aires, Instituto de Fisiología y Biofísica Bernardo Houssay, (IFIBIO), Buenos Aires, Argentina

Presenting author:
***Paulina Lombardi**, paulina.lombardi@gmail.com*

The aging process is characterized by a progressive decline of physiological and metabolic functions. Changes in mitochondrial bioenergetics and increased free radical production have been associated with brain aging. With the purpose of analyzing the effect of aging in motor performance and mitochondrial function in nerve terminals, 3-, 10- and 20-month-old mice were used. For evaluation of motor performance, tightrope and footprint tests were carried out. Brain cortex synaptosomes were isolated by a Ficoll gradient procedure. Mitochondrial function, cardiolipin content and reactive oxygen species were determined. Behavioral results showed a decrease in neuromuscular coordination in 10 and 20-month old mice (80-70%) and impairment in gait balance in the oldest mice (increase in step distance and overlap at 70%) as compared with young animals. Likewise, preliminary results show that acetylcholinesterase activity was increased by 35% in the oldest mice. Moreover, changes were observed in enzymatic activity of mitochondrial respiratory complexes with aging. Increased superoxide levels (11 and 21%) were found in 10- and 20-month-old mice as compared with young animals. H2O2 production rates were 43% decreased in the oldest mice. Mitochondrial membrane potential and cardiolipin content were unaffected in aged mice. It seems that respiratory complexes activity and ROS modulation could contribute to preserve mitochondrial integrity and function in synaptic terminals.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Chemical-LTP induce changes in the acetylation state of synaptic protein and PSD95 clustering in cultures of mice hippocampal neurons

Sebastián Rivas [1], María Florencia Acutain [2], Verónica Báez [2], Ramiro Freudenthal [1]

1 Instituto de Biociencias, Biotecnología y Biología traslacional-FCEN-UBA / CONICET
2 Instituto de Biología Celular y Neurociencias-FMed-UBA-CONICET

Presenting author:
***Ricardo Sebastian Rivas**, sebasrivas.2021@gmail.com*

Protein acetylation affects synaptic plasticity and memory, but its effects on synaptic composition are poorly understood. Previous work of our group shows a memory facilitation effect of an inhibitor of the cytoplasmic histone deacetylase 6. The literature reports an increase in the clustering of PSD95 after TSA treatment and also an augmented microtubule spine entry frequency after LTP induction in hippocampal neurons in culture.

We evaluate the changes induced by a high glycine LTP protocol (chLTP) in the PSD95, synapsin and acetylation clusters. The chLTP was applied to 18 DIV mice hippocampal neurons in culture and evaluated before treatment (ctrl), 0, 5, 15 and 45 minutes after it. We found an increase in the fluorescence intensity, area and density of acetylation clusters after chLTP induction as well as an increase in the area and density of PSD95 clusters. Furthermore, the percentage of acetylated particles that colocalized with PSD95 was also increased, pointing that this change occurs in the PSD. In addition, we observed an increase in the proportion of small PSD95 particles 15 and 45 minutes after LTP induction. Finally, the puncta density of synapsin increased immediately after chLTP and puncta intensity diminished 15 minutes after it. This could be related to an LTP induced presynaptic vesicles accumulation and later depletion.

These findings show that learning-and-memory related mechanism as LTP affects protein acetylation state and composition at the PSD.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Study of behavior and the BDNF signaling pathway in hyposerotonergic Pet1-/- mice

Rocío B Foltran [1], Sophie Scotto-Lomassese [2], Catherine Béchade [2], Luc Maroteaux [2], Silvina L Diaz [1]

1 Inst. de Biología Celular y Neurociencias. CONICET-UBA. Buenos Aires, Argentina
2 Institut du Fer à Moulin. Sorbonne University, INSERM U1270. Paris, France

Presenting author:
***Rocío Beatriz Foltran**, rociobfoltran@gmail.com*

Modulation of serotonergic neurotransmission has revealed as an exciting tool to study the process of neurogenesis in the adult hippocampus (HC). In Pet1-/- mice most of serotonergic neurons do not differentiate, leading to a 80 % depletion of serotonin, showing enhanced survival of newborn neurons in the HC. We wondered if the supernumerary neurons in these mice could modulate certain behaviors. Compared to their respective control group, young adult male Pet1-/- mice showed a tendency to an increased compulsive behaviour in the Nestlet® shredding test, but no effect was seen in the Marble Burying test. In the Object Pattern Separation (OPS), hyposerotonergic mice showed a better discrimination index than control mice. As the brain derived neurotrophin factor (BDNF) signaling pathway is linked to neuron survival, BDNF isoforms and their receptors were analyzed in the HC by Western blot and RT-qPCR. We couldn't observe any differences in protein levels, compared to their respective controls. In contrast, when analyzing the expression of the different transcripts of the BDNF gene, we observed a significant increase in the expression of the transcript VI. Our results show that this hyposerotonergic mice model is similar in their behavior to other serotonin-depleted animal animal models described in the bibliography. On the other hand, the BDNF pathway could be involved in the regulation of neurogenesis when serotonin is depleted.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

How does GPCR interaction alter calcium channels modulation?

Santiago Cordisco Gonzalez, Clara Inés McCarthy, Emmanuel Bortolotto, Agustina García Melano, Silvia Susana Rodríguez, Jesica Raingo, Emilio Román Mustafá

1 Electrophysiology Laboratory of the Multidisciplinary Institute of Cell Biology (Argentine Research Council (CONICET)), Scientific Research Commission of the Province of Buenos Aires (CIC-PBA) and National University of La Plata (UNLP)

Presenting author:
Santiago Cordisco Gonzalez, *scgonza0@gmail.com*

Several G protein-coupled receptors (GPCR) are able to form homo or heteromers. Currently, there is an increasing amount of information about dramatic changes in the GPCR activity level and signaling cascades when receptor-receptor interaction occurs. Our laboratory is dedicated to understand the impact of voltage-gated calcium channel (CaV) regulation in neuronal function. We have studied the role of GPCR-mediated modulation of several CaV subtypes. Our current aim is to uncover the dramatic changes in this modulation due to hetero and homomerization of GPCRs. Here, we will present several pieces of evidence suggesting that dopamine receptor type 2 (D2R) and ghrelin receptor (Growth Hormone Secretagogue Receptor, GHSR) heteromers, dopamine receptor type 1 (D1R) and GHSR heteromers, GHSR homodimers and D1R homodimers have a unique effect on CaV activity. Using different experimental approaches, we investigate the effect of GPCR dimerization on their agonist-dependent activity as well as the basal effect due to constitutive activity of the GPCR. In this line we test compounds reported as inverse agonists and GPCR mutants (lacking of constitutive activity) to block or reduce the GPCRs interaction and/or their constitutive activity. GPCRs heteromers have a profound impact on CaV function and this GPCRs interaction could produce novel signaling pathways for the modulation of CaV.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Exogenous ketone bodies ameliorate neurodevelopmental defects associated with daf-18/PTEN mutations

Sebastián Giunti [1,2], Pamela Azcona 1, María José De Rosa [1,2], Diego Rayes [1,2]

1 Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB-CONICET)
2 Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur

Presenting author:
***Sebastián Giunti**, sebagiunti@gmail.com*

The phosphatidylinositol 3-kinase (PI3K) signaling pathway is a conserved signal transduction cascade involved in several processes, including neurodevelopment (ND). The lipid phosphatase PTEN inhibits the PI3K signaling to activate FOXO. PTEN mutations are strongly linked to ND disorders. Ketogenic diets (KGD) was proposed as a nutritional strategy for treating core symptoms of ND disorders. The mechanistic bases of these beneficial effects are not understood. The reduced availability of carbohydrates in KGD leads to ketone bodies production in the liver. The ketone body β-hydroxybutyrate (βHB) was reported to induce FOXO transcription factor in mammals. Taking advantage of its relative simple anatomy, genetics, high degree of conservation and short lifespan, we used the nematode C. elegans to mechanistically analyze the effects of βHB in PTEN (daf-18 in worms) mutants.

In C. elegans, mutants in daf-18/PTEN also exhibit ND defects and fail to translocate DAF-16/FOXO to the nucleus. We found that exogenous βHB induces DAF-16/FOXO translocation in this nematode. Moreover, daf-18/PTEN mutants grown in the presence of βHB show enhanced behavioral responses in comparison with the controls. Taken together, these preliminary results support the hypothesis that the exogenous ketone body βHB could ameliorate ND defects caused by daf-18/PTEN mutations, and may constitute a first step in validating exogenous βHB as a potential novel pharmacological treatment for ND disorders.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Long term Glyphosate exposure impairs synaptic development and cognitive functions in juvenile rats

Sebastian Luna, Silvana Rosso
1 LATOEX, FBioyF, UNR, CONICET

Presenting author:
***Sebastian Luna**, seba_14_8@hotmail.com*

Glyphosate (Glyph)-based formulations are the most widely used herbicides in the world and their consumption has increased dramatically in recent years. The nervous system results highly vulnerable to a wide spectrum of environmental pollutants that may be linked to the development of brain disorders. In this sense, pesticides exposure has been proposed as the main environmental factor associated with deficits in neurobehavioral performance and neurodegenerative pathologies. Therefore, in the present study we aimed to describe the Glyph effect in the regulation of synaptic assembly in the hippocampus, through in vitro and in vivo assays. Our results reveal that Glyph exposure during a critical period of synaptogenesis decreased dendritic spine density as well as synaptic protein expression, such as PSD-95 and Synapsin-I, in mature cultured neurons. In addition, the exposure of juvenile rats to Glyph reduced PSD-95 protein levels and altered postsynaptic organization in the hippocampus. To associate these abnormalities with cognitive dysfunction we evaluated spatial learning and memory and recognition memory by the Morris water maze and the Novel Object Recognition tests, respectively. We found that Glyph treatment induced memory deficits in both tests compared to controls. Together, these findings suggest that Glyph exposure alters neuronal maturation and synaptic organization impairing normal brain connectivity and complex cognitive behaviour.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Unraveling the structural determinants responsible for calcium potentiation of the α9α10 nicotinic cholinergic receptor.

Sofia Gallino [1], Paola Plazas [2], Juan Boffi [1], Ana Belen Elgoyhen [1]
1 INGEBI, CONICET
2 Instituto de Farmacología, Fac Medicina, UBA

Presenting author:
***Sofia Ludmila Gallino**, sofi.gallino@gmail.com*

The α9α10 nicotinic cholinergic receptor (nAChR) is a pentameric cation-permeable ion channel that mediates the inhibitory synapse between efferent fibers and outer hair cells of the cochlea. Each nAChR subunit comprises a large extracellular amino-terminal domain, four transmembrane domains (TM1-TM4) and a long cytoplasmic loop between TM3 and TM4. Expression of rat α9 and α10 nAChR subunits in Xenopus laevis oocytes yields functional α9 and α9α10 receptors, but not α10 homomeric nAChRs. One of the functional differences between α9 and α9α10 nAChRs is the modulation of their ACh-evoked responses by extracellular calcium (Ca2+). While α9 nAChRs responses are blocked by Ca2+, ACh-evoked currents through α9α10 n AChRs are potentiated by Ca2+ in the micromolar range and blocked at millimolar concentrations. In order to identify the structural determinants responsible for Ca2+ potentiation, we generated chimeric and mutant subunits, expressed them in Xenopus oocytes and performed electrophysiological recordings under two electrode voltage clamp. Our results suggest that the TM2-TM3 loop of the α10 subunit contains structural determinants responsible for the potentiation of the α9α10 nAChR by Ca2+. Moreover, we identified α10 E45 and E175 as key residues involved in this potentiation.

E-Posters

CELLULAR AND MOLECULAR NEUROBIOLOGY

Neurosphere approach to understand CNS regeneration

Yamila Molinari [1], Matías Pibuel [2], Agustín Byrne [1], Daniela Poodts [2], Mariangeles Díaz [2], Silvina Lompardía [2], Lucas Silvestroff [1], Paula Franco [1]

1 UBA Facultad de Farmacia y Bioquímica, Departamento de Química Biológica - IQUIFIB CONICET
2 UBA Facultad de Farmacia y Bioquímica, Departamento de Inmunología - IDEHU CONICET

Presenting author:
***Yamila Azul Molinari**, yamila.azul.m@gmail.com*

Neural stem and progenitor cells (NSC/NPC) from the subventricular zone (SVZ) are able to generate all neural cell types and can be cultured as free-floating aggregates called neurospheres (NS). NS cultures are useful tools to model the cellular processes that take place during endogenous repairment that occur in the central nervous system (CNS) in a sequential and orderly manner.

In the present work, we first developed NS cultures to evaluate the effect of the demyelinating agent Cuprizone (CPZ) on NSC/NPC behavior. CPZ treatment of NS cultures revealed its direct effect on NSC/NPCs proliferation and differentiation mechanisms. The finding that cell migration was also affected by CPZ, led us to investigate extracellular matrix (ECM) involvement in the control of cell migration from NS. Hyaluronic acid (HA) is a linear non-sulfated glycosaminoglycan found in the ECM that acts as structural support and exerts regulatory functions in the SVZ over development and regeneration processes. We used the inhibitor of HA synthesis 4-methylumbelliferone (4-MU) to evaluate HA requirement for cell migration in NS cultures. HA depletion affected NSC/NPC proliferation, as it diminished NS size at doses higher than 125µM 4-MU, and also reduced the number of migratory cells detached from adherent NS. These findings reinforce HA requirements for the control of NSC/NPC proliferation and migration and could help to develop new strategies to improve CNS regeneration.

E-Posters

CHRONOBIOLOGY

Drosophila clock neurons as a model to explore the selective vulnerability to huntingtin polyglutamine elongation

Ana Ricciuti, Nara I. Muraro
IBioBA- MPSP

Presenting author:
Ana Ricciuti, *camilatortello@gmail.com*

One of the hallmarks of polyglutamine (polyQ) diseases is the selective vulnerability of different neurons in spite of ubiquitous expression of the pathogenic protein. The reasons behind this specificity underlying neurodegeneration is still an unsolved mystery. It has been reported that the two circadian clusters of lateral ventral neurons (LNv) of Drosophila melanogaster respond differently to the elongation of the polyQ tract of huntingtin (Htt) protein. It has been shown that while HttpolyQ protein functionally ablates the small LNvs (sLNvs) subgroup, the large LNvs (lLNV) remain unaltered. Our goal is to explore this differential response of LNvs to the HttpolyQ.

In order to do this, we are taking two different experimental approaches: overexpressing the human track of huntingtin polyQ protein in LNvs and downregulating the fly endogenous huntingtin protein in these same clusters. In each of these different paradigmes, we are studying morphological phenotypes and the consequences over the behaviors these neurons command.

Here we show preliminary data suggesting that downregulation of the fly endogenous huntingtin with dHttRNAi expression in LNvs impairs circadian rhythmicity and affects sleep behaviour. Also, we will share results that question the lLNvs immunity to HttpolyQ, since we find that lLNvs of aged flies display HttpolyQ protein aggregation, both in their somas and on axonal projections.

E-Posters

CHRONOBIOLOGY

Consequences of one year of Antarctic isolation on sleep, chronotype and social jetlag

Camila Tortello [1], Agustín Folgueira [2], Juan Manuel Cuiuli [2], Juan Manuel Lopez [2], Guido Simonelli [3], Walter Mac Cormack [4], Diego Andrés Golombek [1], Daniel Eduardo Vigo [1], Santiago Andrés Plano [1]

1 (1) Chronobiology Lab, National University of Quilmes (UNQ), (2) Institute for Biomedical Research (BIOMED), Catholic University of Argentina (UCA) and National Scientific and Technical Research Council (CONICET), Argentina.
2 (a) Argentine Joint Antarctic Command, (b) Neurology Department, Central Military Hospital, Argentine Army, Ciudad Autónoma de Buenos Aires, Argentina.
3 University of Montreal, Quebec, Canada.
4 Argentine Antarctic Institute, Argentina.

Presenting author:
Camila Tortello, *camilatortello@gmail.com*

Circadian misalignment has shown deleterious consequences on human health. Light exposure and social cues are two of the most important zeitgebers that guarantee circadian rhythms synchronization. Antarctica offers the possibility to explore and describe circadian rhythms functions during isolation and extreme photoperiod conditions. This research aimed to analyze the impact of one year of Antarctica confinement on sleep duration, naps, chronotype, and social jetlag. During five winter campaigns at Belgrano II Argentinian Antarctic Station each crew was assessed with the Munich Chronotype Questionnaire (MCTQ) throughout a year (March - May July Sep Nov) (N=84).

E-Posters

CHRONOBIOLOGY

Exploring the roles of GABA in the sleep circuit of Drosophila

Florencia Fernandez-Chiappe, Nara I. Muraro
Biomedicine Research Institute of Buenos Aires - CONICET - Partner Institute of the Max Planck Society

Presenting author:
***Florencia Fernandez-Chiappe**, florenciafch@gmail.com*

Sleep is a complex behavior regulated by both homeostatic and circadian mechanisms. The neural circuits involved in sleep homeostasis are not well described yet. However, it has been previously proposed that GABAergic inputs to the large lateral ventral neurons (lLNvs) of Drosophila may be responsible of informing those highly integrative arousal neurons about the sleep homeostat status. On the other hand, the current paradigm proposes that the main circadian pacemaker of the Drosophila brain, the small lateral ventral neurons (sLNvs) have only minor influence in the control of sleep behavior.

Starting from this point, our aim is to describe the mechanisms of GABAergic inhibition in both sLNvs and lLNvs, their influence on sleep behavior and their role on the sleep homeostat. For this, we have performed specific genetic manipulations and quantified sleep behavior under basal and sleep deprivation conditions. Moreover, we have collected preliminary electrophysiological recordings to identify the extent of the role of the neurotransmitter GABA in the neuronal circuit studied, given that our final goal is to describe this network in detail. Our findings confirm that the lLNvs receive information about the sleep homeostat status via the GABA A receptor Rdl through a complex neuronal circuit. They also suggest that the sLNvs are involved not only in the control of the circadian sleep timing, but also can regulate the
quantity and quality of sleep.

E-Posters

CHRONOBIOLOGY

Mating alters the function of circadian clock

Sabrina C. Riva [1], Sofía Polcowñuk [2], Lihuen Soria-Mercier[1], Sebastian Risau Gusman[1], M. Fernanda Ceriani[2], D. Lorena Franco[1]

1 Departamento de Física Médica, Centro Atómico Bariloche, Comisión Nacional de Energía Atómica (CNEA), San Carlos de Bariloche, Río Negro, Argentina
2 Fundación Instituto Leloir, IIBBA, CONICET

Presenting author:
***Sabrina Carla Riva**, sabririva21@gmail.com*

In Drosophila, the most studied circadian behavior is locomotor activity, which is very well described in males. In the last years it has been reported that once mated, females present differences in their diurnal activity compared to males, in particular they lose their rest period during daylight hours. The decreased daytime sleep observed could be due to an interference with the circadian system, or on the contrary, it could be a homeostatic response associated to an increased egg-laying activity. To explore the hypothesis that the signaling generated by mating could alter the normal function of the circadian clock and modify the temporal organization of behavior, we performed a high resolution analysis of locomotor activity using a video tracking method. Comparing the cycles of resting activity in virgin and mated females, as well as in males, we observed that, in contrast to males and virgins, mated females lose the ability to anticipate the night-day transition when motor activity is analyzed in light: dark cycles. Our results show that this post-mating response is mediated by the action of the sex peptide (SP) in pickpocket (PPK) expressing neurons, since the decreased expression of the SP receptor (SPR) in these neurons restores the ability to anticipate the light / dark transition in the females mated. To analyze the postsynaptic target of PPK-SPR + sensory neurons we used the anterograde trans-tango trans-synaptic tracing tool. Our preliminary data show small later

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COGNITION, BEHAVIOR AND MEMORY

Role of 5-HT2A Receptor in Social Behaviour in Mice

Agostina Sacson, Juan Facundo Morici, Pedro Bekinschtein, Noelia Weisstaub

Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencia Cognitiva y Traslacional (CONICET - Universidad Favaloro - Fundación INECO)

Presenting author:
***Agostina Sacson**, agostina.sacson@gmail.com*

The serotonergic system and more precisely the type 2A serotonin receptor (5-HT2AR) is involved in a wide variety of cognitive and emotional functions. Specifically, the social impairments observed in different psychiatric disorders, such as schizophrenia and Asperger's syndrome, have been linked with a hypofunction of 5-HT2AR. However, the mechanisms underlying this phenotype remain unclear. In this study we analyze the role of 5-HT2AR in social preference and dominance using a genetically modified mouse model that presents a constitutive deletion of 5-HT2AR (KO) compared to conspecific wild type (WT). For this purpose, we use the three-chamber social interaction test (SI) and the dominance tube (TD). We also explore the role of this receptor in the prefrontal cortex in social behavior by infusing adult WT animals with a selective 5-HT2AR antagonist (MDL) prior to the social interaction test. Male and female KO mice had lower social preference compared to WT mice, and genotype was a strong predictor of matches won in duels in the TD. Furthermore, the acute administration of MDL in the mPFC of WT mice had no effect on the SI suggesting that the receptor is necessary during development for the animals to demonstrate normal social behavior but is not recruited during the task. Moreover, preliminary SI results from animals that selectively express 5-HT2AR in the cortex suggest that the apparent developmental role of the receptor might be mediated by its expression in the cortex.

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COGNITION, BEHAVIOR AND MEMORY

Sigma-1 antagonism inhibits binge ethanol drinking at adolescence

Leandro Ruiz-Leyva [2], Agustín Salguero [1], Ignacio Morón 3, Enrique Portillo-Salido [4], Cruz Miguel Cendán [2], Rodrigo García Virgolini [1], Ricardo Marcos Pautassi [1]

1 Instituto de Investigación Médica M. y M. Ferreyra (INIMEC–CONICET-Universidad Nacional de Córdoba), Córdoba, C.P. 5000, Argentina,
2 Department of Pharmacology, Faculty of Medicine, University of Granada, Spain
3 Department of Psychobiology and Centre of Investigation of Mind, Brain, and Behaviour (CIMCYC), University of Granada, Spain
4 Drug Discovery and Preclinical Development, Esteve Pharmaceuticals, Parc Científic de Barcelona, Barcelona, Spain

Presenting author:
***Agustín Salguero**, agustinsalguero21@gmail.com*

Background: ethanol use during adolescence is a significant health problem, yet the pharmacological treatments to reduce adolescent binge drinking are scarce. The present study assessed, in male and female adolescent Wistar rats, if the sigma-1 receptor (S1-R) antagonists S1RA or BD-1063 disrupted ethanol drinking. Methods: three times a week, for two weeks, the rats received the S1-R antagonists. Thirty min later they were exposed, for 2 h, to a bottle of 8% or 10 % v/v ethanol. A 24 h, two-bottle, ethanol intake test was conducted after termination of these procedures. Results: the rats given 64 mg/kg S1RA drank, in each binge session, significantly less than vehicle counterparts. Male rats given 4 or 16 mg/kg S1RA drank significantly less than those given 0 mg/kg in session 3 or in session 1 and 2, respectively; whereas female rats given 4 or 16 mg/kg drank significantly less than females given 0 mg/kg in session 2–5 or in sessions 2–6, respectively. Administration of 32 mg/kg, but not of 2 or 8 mg/kg, BD-1063 suppressed, across sessions, ethanol drinking. S1-R antagonism reduced absolute ethanol drinking at the two-bottle choice post-test. Conclusions: the results indicate that S1-R antagonists may be promising targets to prevent increases in ethanol intake at adolescence. The persistent effect of S1-R antagonism in free-choice drinking suggests that modulation of the S1-R is altering plastic effects associated with ethanol exposure.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Anodal tDCS of the primary motor cortex selectively reduces action processing in ecological discourse

Agustina Birba [1], Francesca Vitale [2], Iván Padrón [2], Martín Dottori [1], Manuel de Vega [2], Máximo Zimerman [3], Lucas Sedeño [4], Agustín Ibáñez [1]

1 Universidad de San Andrés, Buenos Aires, Argentina
2 Instituto Universitario de Neurociencia (IUNE), Universidad de La Laguna, Tenerife, Spain
3 Institute of Cognitive and Translational Neuroscience (INCYT), INECO Foundation, Favaloro University, Buenos Aires, Argentina
4 National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

Presenting author:
***Agustina Birba**, abirba@udesa.edu.ar*

Non-invasive stimulation of the primary motor cortex (M1) modulates processing of decontextualized action words and sentences. This suggests that language comprehension hinges on brain circuits mediating the bodily experiences evoked by verbal material. Yet, despite its relevance to constrain mechanistic language models, such findings fail to reveal whether and how relevant circuits operate in the face of everyday texts. Using a novel naturalistic discourse task, we examined whether direct modulation of M1 excitability influences the processing of narrated actions. Following random group assignment, participants received anodal or sham transcranial direct current stimulation over the left M1 or anodal stimulation of the left ventrolateral prefrontal cortex. Immediately afterwards, they listened to action-laden and neutral stories and answered questions on information realized by verbs and circumstances. Anodal stimulation of the left M1 selectively decreased outcomes on action- relative to non-action information –a pattern that discriminated between stimulated and sham participants with 74% accuracy. This result was particular to M1 and held irrespective of the subjects' working memory and vocabulary skills, attesting to its specificity. Our findings suggest that modulation of motor-network excitability might lead to transient unavailability of putative resources needed to evoke actions in naturalistic texts, opening promising avenues for the language embodiment framework.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Multimodal neurocognitive markers of naturalistic narratives distinguish among neurodegenerative diseases

Agustina Birba [1], Sol Fittipaldi [1], Judith C. Cediel Escobar [3], Cecilia Gonzalez Campo [1], Agustina Legaz [2], Mariano Diaz Rivera [4], Miquel Martorell Caro [2], Florencia Alifano [2], Agustín Ibáñez [1], Adolfo García [1]

1 Universidad de San Andrés, Buenos Aires, Argentina.
2 National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina.
3 Instituto de Psicología, Universidad del Valle, Cali, Colombia.
4 National Agency of Scientific and Technological Promotion (ANPCyT), Buenos Aires, Argentina

Presenting author:
***Agustina Birba**, Agustina.birba@gmail.com*

Neurodegeneration has multi-scalar impacts, including cognitive, anatomical, and functional disruptions. Disease-specific convergences among these levels can be traced by targeting higher-order domains. In particular, motor and social impairments in Parkinson's disease (PD) and behavioral variant frontotemporal dementia (bvFTD) are echoed by deficits in action and social verbal meanings, respectively. Yet, no single ecological paradigm can capture those signatures. Here, combining voxel-based morphometry, fMRI, and EEG connectivity with a naturalistic language task, we describe disease-specific signs of PD, bvFTD, and Alzheimer's disease (AD). We assessed comprehension of four stories highlighting action, non-action, social, and non-social events. PD patients presented selective action-text deficits related to the volume of action-observation regions, connectivity across motor-related and multimodal-semantic hubs, and frontal EEG hypo-connectivity. BvFTD patients exhibited selective social-text deficits, associated with atrophy and spatial connectivity patterns along social-network hubs, and right fronto-temporal EEG hypo-connectivity. AD patients showed impairments in all stories, with widespread atrophy and spatial connectivity patterns, and heightened right occipito-temporal EEG connectivity. Briefly, our ecological task captures multimodal double dissociations between PD and bvFTD with no comparable pattern in AD, opening new avenues for their neurocognitive typification.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Brain signatures of statistical information acquisition in the absence of behavioral learning

Ernesto Betman [2], Alejandro Wainselboim [1]
1 INCIHUSA-CONICET,
2 INAHE-CONICET

Presenting author:
***Alejandro Javier Wainselboim**, awainselboim@gmail.com*

Statistical information, i.e. the recurrent co-occurence of events or stimuli, underlies multiple aspects of life, and is a robust source of information for learning. Behavioral results after training in artificial grammars, have shown that infants and adults sense, store and use statistical information to acquire different aspects of the trained grammar. What happens though, when statistical aspects of the training stimuli are not learned? Does this imply that recurrent stimuli information has not been sensed and/or stored by the brain? In the present study, 7 year-old children (N=13) were briefly trained in an artificial grammar task involving learning the designations of several figures. Behavioral responses after training were at chance level, evidencing absence of learning. Electroencephalographic recordings during testing were used to calculate Intersite Phase Clustering, a measure of synchrony between electrode sites. Results showed increased interhemispheric synchronization when testing trials displayed an incongruence between the figure shown and the designation heard. This increase of synchronized activity may facilitate neural integration and information exchange between regions, necessary to solve the incongruence of stimuli shown. More importantly, it is evidence that statistical information was indeed sensed and stored, even in the absence of behavioral learning.

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COGNITION, BEHAVIOR AND MEMORY

Novelty as a modulator of memory retrieval and the divergent creative process

Alejo Ramiro Barbuzza [1], Daniela Ramirez Butavand [2], Pedro Beckenstein [2], Fabricio Ballarini [1]

1 Instituto de Biología Celular y Neurociencias, Facultad de Medicina, UBA-CONICET, Buenos Aires, Argentina
2 Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencias Cognitivas y Traslacionales, Universidad Favaloro-INECO-CONICET
3 Departamentos de Ciencias de la Vida, ITBA

Presenting author:
***Alejo Ramiro Barbuzza**, barbuzza.alejo@gmail.com*

Education is the most transformative tool of the human mind; and, in this sense, learning and memory are two fundamental pillars on which knowledge is based. Previous studies have shown that the presentation of a novelty could improve the memory consolidation process in both rodents and humans. Furthermore, the novelty positively modulates, within a time window, the retrieval of different memories in rodents. Therefore, the objective of this work was to evaluate the effect of novelty on memory retrieval in humans, especially in high-school students. Our results showed that a novel neuroscience class improved the retrieval of declarative memories in high-school students when this novelty occured immediately before the evocation, but not when the separation between them was one hour.

On the other hand, recent studies in neuroimaging have shown that creativity and episodic memory share neural networks, so we studied the effect of novelty on creativity. We found that novelty positively modulates the divergent thinking process, a component of creativity, when the association between the two is immediate. Likewise, a competition effect was found between the evocation of graphic memories and creative processes, which would not be bilateral. Finally, we developed a new paradigm to evaluate episodic memory.

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COGNITION, BEHAVIOR AND MEMORY

Investigating the effects of contextual information in hybrid visual search

Alessandra Barbosa [1], Juan E Kamienkowski [2], Juan E Kamienkowski [3], Matias Ison[1]

1 School of Psychology, University of Nottingham (UK)
2 Laboratory of Applied Artificial Intelligence, Computer Science Institute, School of Exact and Natural Science, University of Buenos Aires – National Council of Science and Technology, Buenos Aires, Argentina
3 Physics Department, School of Exact and Natural Science, University of Buenos Aires, Buenos Aires, Argentina

Presenting author:
***Alessandra Barbosa**, alessandraqhb@hotmail.com*

Visual search is the action of looking for something. While much is known about elements that influence visual search efficacy when one isolated item is searched for, search in real life is more complex, often involving various possible targets kept in memory (hybrid search). While it has long been known that in visual search there is a linear dependence between response times (RT) and visual set sizes (VSS), memory search has been found to increase logarithmically with memory set size (MSS) for sets of up to 100 items. This number, that extend well beyond the limits of working memory, poses a challenge to current theories of visual search. A gap also remains regarding the interplay of inhibitory control, which refers to the ability to effectively subdue thoughts, behaviour, and irrelevant stimuli, in hybrid search strategy and termination. In an online experiment, participants searched for potential targets in images containing different number of stimuli with or without context. Here we show that, in target present trials, regardless of the presence of contextual information and single trial memorisation, the relationship between RT and VSS is linear, while between RT and MSS is logarithmic. In target absent trials, however, we found large differences between context-present and context-absent trials, suggesting a different strategy when the target is absent. In a follow-up experiment, we are currently investigating whether this can be linked to inhibitory control.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Unsupervised analysis of animal behavior in a motor skill learning task

Alvaro Concha [1], Leonardo Molano Ramirez [2], Damian Hernandez [2], Maria Soledad Esposito [2]

1 Instituto Balseiro - Universidad Nacional de Cuyo,
2 CONICET - Departamento de Física Médica, Centro Atómico Bariloche e Instituto Balseiro, Rio Negro, Argentina

Presenting author:
***Alvaro Tomas Concha Alvarez Prado**, alvaro.concha@ib.edu.ar*

A fundamental assumption in behavioral neuroscience is that animal activity while performing defined tasks can be vastly described by a finite set of stereotyped movements. Information about animal behavior can be then correlated with simultaneous recordings of neural activity, allowing us to understand how the brain encodes particular behaviors, what are the underlying neural circuits and how these circuits are modified during motor learning. However, classifying different types of movements can be a complex endeavor. On the one hand, the extent of animal activity recordings may be too large to be manually classified and such a classification may not be reproducible between subjects. On the other, heuristically created categories (e.g., walking, running, jumping) tend to ignore inherent information regarding intra- and inter-animal variability frequently found in unrestrained behavior. In this work, we used unsupervised machine learning techniques to classify different types of movements executed by mice performing a motor skill learning task known as accelerating rotarod. In particular, t-SNE maps were used to find intrinsic relationships between high-dimensional feature vectors within the frequency spectrum of mouse movements. In this way, we expect to elucidate the underlying feature structure, cluster them accordingly and identify these clusters with specific mouse movement patterns, improving our understanding of the dynamics of the learning process of a new motor skill.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Functional connectivity of the retrosplenial cortex in object recognition memory formation

Ana Belén de Landeta [1], Magdalena Pereyra [1], Magdalena Miranda [2], Pedro Bekinschtein [2], Jorge H Medina [1], Cynthia Katche [1]

1 Laboratorio de Memoria, Instituto de Biología Celular y Neurociencia "Prof. E. De Robertis" (IBCN), Facultad de Medicina, CONICET-UBA, Buenos Aires, Argentina

2 Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencia Cognitiva y Traslacional, CONICET-INECO-Universidad Favaloro, Buenos Aires, Argentina

Presenting author:

***Ana Belén de Landeta**, anabdelandeta@gmail.com*

Recently we demonstrated that retrosplenial cortex (RSC) is required for object recognition (OR) memory consolidation. Here, we aimed to study which brain structures interact with the RSC to process OR memory in rats. We selected six brain structures that are connected to the RSC to study their interaction in OR memory formation: perirhinal cortex (PRH), medial prefrontal cortex (mPFC), anteromedial thalamic nuclei (AM), medial entorhinal cortex (MEC), hippocampus (HP) and anterior cingulate cortex (ACC). First, we studied the participation of these structures in OR memory by bilateral infusions of the GABA receptor agonist muscimol. We observed an amnesic effect when inactivating the PRH, mPFC, AM and MEC, but not after HP or ACC inactivation. Then, we studied the functional connections by unilateral inactivation of RSC and each of the six structures in the same (ipsilateral) or the opposite (contralateral) hemisphere. Our results showed an amnesic effect of ipsilateral inactivations of RSC-PRH, RSC-mPFC, RSC-AM, or RSC-MEC. Conversely, contralateral inactivation of RSC-ACC produced memory impairment, while RSC-HP inactivation had no effect on memory. Thus, our ipsilateral inactivation findings reveal that RSC and at least another region involved in OR memory processing are required to form OR memory. In conclusion, our results show that several cortico-cortical and cortico-thalamic pathways appear to be important for OR memory consolidation.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Associations between fiction exposure, reading habits, expository and narrative text comprehension in young adults

Angel J. Tabullo [1], María F. Chiófalo [2]

1 INCIHUSA, CCT Mendoza, CONICET. Pontificia Universidad Católica Argentina, Facultad de Humanidades y Ciencias Económicas

2 Pontificia Universidad Católica Argentina, Facultad de Humanidades y Ciencias Económicas

Presenting author:
***Angel Javier Tabullo**, angeljtabullo@gmail.com*

Print exposure is one of the main predictors of reading comprehension in children and adults. The present study analyzed the association between high quality literary fiction exposure (classics, laureate writers) and popular genre fiction (best sellers), reading habits and comprehension of narrative and expository texts. Our sample consisted of 215 young adults (84% of them female, M = 24,35 ± 7,35 years). Participants completed a reading habits questionnaire, an Author Recognition Test (including high quality literary fiction authors and popular genre authors) and two standard tests of expository and narrative text comprehension. 83 subjects also completed measures of verbal and non-verbal intelligence. Linear regression models showed that the only significant predictors of expository (R2 = 0,193) and narrative (R2 = 0,193) (p's < 0.001) text types were: ART literary fiction (Expository: β = 0,337, Narrative: β = 0,254, p's < 0.025) and maternal education (Expository: β = 0,162, p = 0,024; Narrative: β = 0,219, p = 0,002). These effects remained after controlling for verbal and non-verbal intelligence. The results suggests that reading literary fiction imposes higher cognitive demands, particularly on high order inference making processes, improving comprehension for all text types. The additional effect of maternal education highlights the importance of the mother in the home literacy environment, which is probably mediated through linguistic input and literacy practices.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Acute Hippocampal Neutralization of the Neuronal Glycoprotein M6a Impairs Memory Consolidation in an Inhibitory Avoidance Task in Mice

Antonella León [1], Julieta Millán [2], Gabriela Inés Aparicio [1], María del Carmen Krawczyk [2], Mariano Martin Boccia [2], Camila Scorticati [1]

1 Laboratorio de Neurobiología Molecular y Celular - Instituto de Investigaciones Biotecnológicas (IIBio-UNSAM -CONICET)

2 Laboratorio de Neurofarmacología de los Procesos de Memoria – Facultad de Farmacia y Bioquímica (FFyB, UBA)

Presenting author:
***Antonella León**, aleon@iib.unsam.edu.ar*

Membrane glycoprotein M6a, together with M6b and proteolipid protein (PLP/DM20), belongs to the PLP family. M6a promotes neurite, axon, filopodium/spine and synapse formation in primary hippocampal neurons and cell lines. Altered M6a expression and genetic variants are linked with psychiatric disorders in human and animal models. However, the participation of M6a in physiological processes has not been established yet. Molecular cascades triggered by new experience induce synaptic plasticity and cell-wide alterations, critical for a new memory to consolidate. To study M6a's role in memory processes, we injected the neutralizing M6a-mAb or an IgG isotype (control group) into the hippocampus after training in an inhibitory avoidance task in mice. Memory retention was tested at 3, 6 and 48 hours post-training and animals were sacrificed to evaluate synapse number in the hippocampus. Our results show that M6a-mAb administration immediately after training did not affect short-term memory (3 hours). On the other hand, we evidenced an involvement of M6a in long-term memory consolidation, as M6a-mAb injection significantly reduced task performance when mice were tested at 6 and 48 hours. This was accompanied by a decrease in synapse number in the CA1 region. Altogether, our results suggest that M6a is involved in memory consolidation and might play a key role on synaptic plasticity induced by learning.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Motor-language coupling in bilinguals: Insights from a keyboard writing task in L1 and L2

Boris Kogan [1], Enrique García-Marco [2], Agustina Birba [3], Camila Cortés [4], Margherita Melloni [3], Agustín Ibáñez [3], Adolfo García [3]

1 Universidad Nacional de Mar del Plata
2 Universidad de la Laguna
3 Universidad de San Andrés
4 Universidad Favaloro,

Presenting author:
***Boris Kogan**, bkogan86@gmail.com*

Abundant research shows that the speed of our manual movements can be modulated by simultaneous processing of manual action verbs (MaVs), suggesting that motor circuits are recruited by both effector-specific semantic and action processes. Whereas this is well established for native languages (L1s), ubiquitous since intrauterine life, little is known about its manifestation in late foreign languages (L2s), usually appropriated after age 7. Here we timed keystroke activity while Spanish-English bilinguals typed MaVs, non-manual action verbs, and non-action verbs in their L1 and L2. We measured first-letter lag (the time-lapse between word presentation and first keystroke) and whole-word lag (the time-lapse between first and last keystroke) as motor planning and execution indexes, respectively. Crucially, MaVs facilitated typing performance in L1 but delayed it in L2, even when subjects' typing skills, age of L2 learning, and L2 competence were entered as covariates. No effects were observed on motor planning. These outcomes indicate that motor-language coupling effects manifest even in languages lacking infant exposure, and that they are differentially shaped by age of language appropriation. Tentatively, these interlinguistic discrepancies might reflect the differential taxing of semantic mechanisms by L1s and L2s. By extending language grounding models, our results may shed light on the role of embodied mechanisms throughout life.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Emotional episodic memory formation during Covid-19 quarantine: Preliminary results

Candela Sofía León, Matías Bonilla, Facundo Antonio Urreta Benitez, Cecilia Forcato

Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires.

Presenting author:
***Candela Sofía León**, cleon@itba.edu.ar*

Memory processes are modulated by anxiety. People's mental health has been deteriorated due to the Covid-19 pandemic, showing higher levels of anxiety. Thus, we hypothesize that episodic memory encoding and consolidation were impaired in the pandemic context. To test this, participants watched an aversive or neutral video on day 1 and they were tested immediately and on day 7. Our preliminary results indicate that the encoding and consolidation of aversive content were impaired. Furthermore, memory decay between day 1 and 7 was reduced for the neutral content and the anxiety level negatively correlated with the amount of true details for the aversive memory, on day 1. Moreover, we found a decrease in encoding and consolidation of neutral true information for males. The means of anxiety values did not differ between genders, and, considering that females typically exhibit higher baseline levels of anxiety, this suggests that males would be more affected in the pandemic context. The lower performance for males in the neutral group could be understood when considering this fact, because there is an optimal range of anxiety that facilitates memory processes and at the extremes values the performance is impaired. We consider that aversive information encoding was impaired due to the aversive context of pandemic and its emotional consequences.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Necessity and sufficiency of mushroom bodies' neurons for interval timing in Drosophila

Canela Pedreira González, Lia Frenkel

Laboratorio de Neurociencias del Tiempo- iB3 | Instituto de Biociencias, Biotecnología y Biología traslacional- Facultad de Ciencias Exactas y Naturales- Universidad de Buenos Aires

Presenting author:
***Canela Pedreira González**, canelapedreira@hotmail.com*

The neurobiological basis of time estimation are still an unsolved puzzle. The main hypothesis propose that it encloses cognitive processes such as attention, learning, working memory and decision-making. Under this view, time estimation is a specific type of working memory in which the neuronal network would keep the internal representation of time without an external stimulus, and behaviour would be the result of decisions based on time perception. To understand the ability to estimate time in the range of seconds to few minutes, we make use of the interval timing skill of the fly Drosophila melanogaster. Our lab designed an experimental setup that enables the study of a time-referenced memory in the fly Drosophila melanogaster based on a well-known behavioural response in the fruit fly, the proboscis extension response to a sucrose solution. Briefly, we offer a sucrose solution drop to a thirsty/hungry at a fixed interval and record its behavioural response. We operationally define time-referenced memory when the fly extends its proboscis anticipating the appearance of the drop. Here we present our project to unveil which are the necessary and sufficient neurons from the mushroom bodies to learn this time-referenced memory.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Learning and memory in Drosophila melanogaster during predation exposure, by the spider Menemerus semilimbatus

Christian Carpio Romero [1], Lia Frenkel [2], Ramiro Freudenthal [1]

1 Laboratorio de plasticidad neuronal y memoria, IB3, departamento FBMC, FCEN, UBA, CONICET,
2 Laboratorio de neurociencias del tiempo, IB3, departamento FBMC, FCEN, UBA, CONICET

Presenting author:
Christian Mauricio Carpio Romero, *christianc.romero@gmail.com*

In this work, we established a new paradigm for the study of learning and memory in Drosophila melanogaster. This paradigm highlights the strategies used by flies to evade one of their natural predators, the spider Menemerus semilimbatus, in a controlled environment. The running hypothesis postulates the existence of memory processes involved in the storage of useful strategies to survive a risk of predation.

The main objective was to find the parameters that describe the behavior of flies to keep themselves alive when faced to a predator, interpreted as a learning process. And finally, to study the memory dynamics of Drosophila melanogaster, defining which parameters are descriptors of behaviors in which memory retention can be evaluated.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

6-OHDA-induced dopaminergic neuron degeneration exacerbates anxiety-related behaviors in BDNFMet/Met mice

Constanza Milena Jandar Paz, Agustín Anastasía
Instituto Ferreyra (INIMEC-CONICET-Universidad Nacional de Córdoba), Córdoba, Argentina

Presenting author:
***Constanza Milena Jandar Paz**, cjandarpaz@immf.uncor.edu*

A SNP in the BDNF gene is present in more than 25% of the human population. It results in a Va66Met substitution within the BDNF prodomain (pBDNF) sequence. This SNP is associated with increased susceptibility to develop certain psychiatric and neurodegenerative disorders as anxiety, addictions, and progression and cognitive deficit in Parkinson's disease. As all these disorders include CNS dopaminergic systems malfunction, we hypothesize that the Met variant of pBDNF alters the structure and function of dopaminergic neurons and increase their vulnerability to degenerate. We studied in vivo if the presence of the Met allele increases the susceptibility of dopaminergic neurons to degenerate after the injection of the specific neurotoxin 6-OHDA using behavioral test. We found that BDNFVal/Metand BDNFMet/Metmice injected with 6-OHDA showed motor asymmetries in the cylinder test and an increase in the number of ipsilateral turns in an open field test(OFT), as compared to BDNFVal/Valmice. Interestingly, we observed that only BDNFMet/Met mice with 6-OHDA showed less activity in the center of the arena in the OFT, and only these experimental group showed decreased latency to enter the dark side in the light dark box test (anxiety-related behaviors). These results suggest that CNS dopaminergic systems are more susceptible to degenerate in Met allele carrier mice, which could help to explain the increased incidence of motor and mood disorders associated with the Val66Met SNP in humans

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Categorical discrimination and target detection in visual search: An investigation using concurrent EEG and eye movement recordings

Damian Ariel Care [1], Bruno Bianchi [1], Juan Esteban Kamienkowski [1], Matias J. Ison [2]

1 Laboratorio de Inteligencia Artificial Aplicada (ICC, CONICET-UBA, Argentina)
2 School of Psychology (University of Nottingham, UK)

Presenting author:
***Damian Ariel Care**, damianos.care@gmail.com*

Early access to visual information, like category, plays an important role in visual search. In particular, the N170 ERP component, a hallmark of face processing, emerges in the occipitotemporal cortex around 170 ms after stimulus onset with an increased amplitude to faces. Here, we aimed to study how its sensitivity to category information extents to a free viewing paradigm. We co-registered EEG and eye-tracking to investigate fixation related potentials to pictures of different categories during visual search. Participants were asked to search for one target from an array of faces and objects embedded in random noise. Firstly, we hypothesized that a larger N170 would be elicited by fixations to faces in comparison to objects. Secondly, based on a recently proposed framework [Kamienkowski et al., 2018], we hypothesized that EEG signatures underlying early target detection reflect saccade inhibition, and would, therefore, be activated differently for 'hard' distractors (same category as the target) than 'easy' distractors (different category). In this study, we show a stronger activation for fixations to faces than to objects. Consistent with our second hypothesis, we also found significant differences between components elicited by fixations to easy and hard distractors. These results generalize the characterization of the N170 to a wider range of experiments, and show specific category discrimination components potentially associated with eye movement guidance.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Acute physical exercise improves long-term recognition memory

Daniela Ramirez Butavand [1], Magdalena Miranda [1], Fabricio Ballarini [2], Pedro Bekinschtein [1]

1 Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencias Cognitivas y Traslacionales, Universidad Favaloro-INECO-CONICET
2 Instituto de Biología Celular y Neurociencias, Facultad de Medicina, UBA-CONICET, Buenos Aires, Argentina
3 Departamentos de Ciencias de la Vida, ITBA

Presenting author:
***Daniela Ramirez Butavand**, daniramirezbe@gmail.com*

The computational process for differentiating similar input patterns has been called pattern separation. In rodents, pattern separation depends on Brain-Derived Neurotrophic Factor (BDNF) and adult neurogenesis in the dentate gyrus. It is also known that acute exercise increases BDNF in both rodents and humans. Recently, we have developed an immersive task in which we could test the effect of acute exercise on spatial pattern separation. In this work, we developed a task to evaluate object pattern separation in humans, which allows parametric manipulation of memory similarity. Therefore, we can manipulate the load on pattern separation processes. In addition, we assessed the effect of acute exercise on this task. Our results showed that participants who were tested immediately after training (short-term group) were able to solve the task both in the recognition images and in those in which it was required to separate patterns. Participants who were evaluated 24 hours later (long-term memory, control group), showed a significant decrease in their memory retention. However, participants who cycled for 25 minutes and were tested 24 hours later (long-term memory, acute group), significantly improved their performance compared to the control group in both object recognition and pattern separation, and reached similar rates to those of the short-term group. In summary, we have implemented a simple non-invasive manipulation that generates significant improvements in human cognition.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Molecular Mechanisms involved in pattern separation in perirhinal cortex

Dinka Piromalli Girado, Magdalena Miranda, Pedro Bekinschtein
INCyT (Instituto de Neurociencia Cognitiva y Traslacional)

Presenting author:
Dinka Marina Piromalli Girado, *dinkapiromalligirado@gmail.com*

The ability to separate similar experiences into differentiated representations is proposed to be based on a computational process called pattern separation, and it is one of the key characteristics of episodic memory. Although pattern separation has been mainly studied in the dentate gyrus of the hippocampus, this cognitive function if thought to take place also in other regions of the brain. The perirhinal cortex is important for the acquisition and storage of object memories, and in particular for object memory differentiation. The present study was devoted to investigate the importance of the cellular mechanism of endocytosis for object memory differentiation in the perirhinal cortex and its association with brain-derived neurotrophic factor (BDNF), which was previously shown to be critical for the pattern separation mechanism in this structure. In accordance with the request for international regulations for the existence of gender parity in research, this work used female and male rats for all its experiments and comparatively analyzed its results. In this work, we used a peptide (Tat-P4) to block endocytosis and to showed that is necessary for the pattern separation mechanism in the perirhinal cortex. We also provide evidence from a molecular disconnection experiment that BDNF and endocytosis-related mechanisms interact for memory discrimination in both male and female rats.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Alcoholic Wernicke-Korsakoff Syndrome in a young adult

Francesca Mariani, Laura Bocos, Sergio Dansilio
Department of Neuropsychology, Institute of Neurology, Hospital de Clínicas. University of the Republic.

Presenting author:
Francesca Mariani, *f.marianielola@gmail.com*

Introduction: Wernicke-Korsakoff (WK) Syndrome is commonly described in patients with a long history of hard alcoholic drinking. Cases of young people allows to suspect a previews brain condition. Objective: to present a case of WK Syndrome in a young patient with all the neuropsychological features. Participants and Methods: 36 years old man, right – handed with primary school education and history of school failure. Premature and low birth weight. Problematic use of alcohol and other substances. Neuropsychological evaluation: Mini-Mental State Examination (MMSE), Trail Making Test (A), phonological and semantic fluency, Rey-Auditory Verbal Learning Test (RAVLT), Visual Anticipation Brixton test (BT); Stroop Visual Color and Word Test; 7/24 Spatial Recall Test, Rey Osterrieth Complex Figure; Kaufman Brief Intelligence test (K-BIT). Results and Conclusions: An amnestic and dysexecutive syndromes both of moderate to severe entity were found preceded by a confusional state and compatible with WK encephalopathy. A compound IC of 75 (low) is further disclosed. CT and MRI are normal. The SPECT shows a bilateral prefrontal, anterior and medial temporal moderate hypoperfusion that involves both thalamus, following the typical pattern described for WK syndrome, contrasting with no structural lesions. Alcoholic WK is infrequently seen in young adults. In this case there is a toxic intake added to a probable developmental cognitive disorder. Both conditions could induce brain risk.Cognition, Behavior and Memory

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Spontaneous Ca2+ activity and long-term memory reactivation in a mushroom body-like center of the crab Neohelice granulata

Francisco J. Maza, Francisco J. Urbano, Alejandro Delorenzi

IFIBYNE, UBA-CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina

Presenting author:
***Francisco Javier Maza**, fjmaza@fbmc.fcen.uba.ar*

A wide range of neuronal oscillations has been described in high-order brain centers of bilateral animals. The proposed roles of such rhythmic activities include modulation of input selection and plasticity, linking the activity of different neuronal assemblies, and integration and consolidation of information. Evidence suggests monoamines may control the oscillatory activity that reflects the internal states of the organism. In the high-order memory centers of insects, the mushroom bodies, projections of dopaminergic neurons present slow oscillating activity necessary to memory consolidation. Structural and physiological studies suggest a correspondence between crustacean hemiellipsoid bodies and insect mushroom bodies. In N. granulata, the hemiellipsoid body shows, for instance, aminergic innervation, elevated expression of proteins necessary for memory processes, and plasticity in neuronal activity that reflects context-dependent memory attributes. Preliminary data analysis shows, utilizing in vivo calcium imaging, spontaneous low-frequency activity in both naïve and in animals trained in an aversive memory paradigm 24 h before. In trained animals, the activity evoked upon the presentation of the aversive stimulus differs for naïve crabs. Data provide ground to our next steps exploring the roles of high-order brain center oscillating activity, including changes in animal's internal states, stimuli processing, and memory reactivation/expression processes.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Frequency and Emotional Priming Could Drive Complex Decision Making

Franco Agustín Bernal, Tomas Alves Salgueiro, Axel Brzostowski, Pablo Nícolas Fernandez Larrosa
IFIByNE-CONICET//FCEN, UBA

Presenting author:
Franco Agustín Bernal, *bernalfrancoagustin@gmail.com*

Some decision-making (DM) processes require quick answers, while more complex decisions require greater cognitive engagement. Under the hypothesis that frequent exposure to a stimulus or its association with an emotional valence could drive DM, online cognitive experiments were conducted, involving different tasks on the computer. The experiments consisted of choosing a face (from 4 options) after being presented with different frequencies (1, 6, or 12 times over 20 presentations) or the same frequency (5 times) but associated with positive, negative, neutral, or mixed sentences. Two versions of the experiments were performed: the 1st group was asked to choose a face without any specification (Non-Specified task, NST); while the 2nd group was asked to choose a face for an important task (Important task, IT). Our results showed: 1. The 12th repeated stimulus (12) was significantly more chosen in the NST group [Factorial ANOVA: F(3, 292)=9,6498, p=,00000; post hoc LSD test: p<0.009 respect to other frequencies of NST and IT group]; 2. This priming was observed mainly when response time was fast; 3. The faces with a positive association were significantly more chosen than others, with no group differences [Factorial ANOVA:F(3, 332)=303,11, p=0,000; post hoc LSD test: p<0.000 positive association & other]. These results support our hypothesis, showing that emotional priming is more powerful than frequency one, as the latter depends on the task type and response time.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Behavioral analysis of a 3xTg murine model for Alzheimer´s disease: sex-specific differences age-dependent

Gisela Romina Bustos [1], Maria del Carmen Krawczyk [1], Julieta Millan [1], Mariano G Blake [2], Mariano M Boccia [1]

1 Laboratorio de Neurofarmacología de los Procesos de Memoria, Cátedra de Farmacología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires (UBA), Buenos Aires, Argentina.
2 Instituto de Fisiología y Biofísica (IFIBIO UBA-CONICET), Facultad de Medicina, Universidad de Buenos Aires (UBA), Buenos Aires, Argentina.

Presenting author:
***Gisela Romina Bustos**, minabustos05@gmail.com*

Alzheimer´s disease is a neurodegenerative disorder, characterized by extracellular Amyloid-? peptide neuritic plaques and neurofibrillary tangles, composed of filamentous aggregates of hyperphosphorylated tau protein. In 2003, LaFerla and co-workers developed a triple transgenic (3xTg) mouse model harboring PS1M146V, APPSwe, and tauP301L transgenes. In the present work, we carried on two distinct behavioral tasks at different ages (3 to 6 months) to study 3xTg mice performance in order to assess possible cognitive impairment. In addition, we examined potential sex-specific differences on each behavioral task.

In our modify version of the Inhibitory Avoidance Task, 3xTg male mice had significant differences in their latencies to step-trough compare to wild type mice at four and seven months. When studying 3xTg female mice, differences were observed only at four months old. Interestingly, both wild type and 3xTg mice had increased latencies to step-trough when tested 48h post-training. Notwithstanding, wild type performance was significantly better than 3xTg mice suggesting memory impairment by the latter. When studying behavioral performance in the Holeboard task, only females at 3 months old and males at 5 months old showed significant differences when compare to control groups. Taking these results together, we might conclude there are sex- specific differences between 3xTg and wild type mice depending both on the behavioral task and the age of the subjects.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Slow Wave detection algorithm in non-REM sleep

Giulia Carbonari[1], Eugenia Moris[1], Cecilia Forcato [2], Rodrigo Ramele [3], Ignacio Larrabide [1]

1 PLADEMA, UNICEN-CONICET

2 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires (ITBA), 3 Centro de Inteligencia Computacional, Depto. de Ingeniería Informática, Instituto Tecnológico de Buenos Aires (ITBA)

Presenting author:
***Giulia Carbonari**, gcarbonari@gmail.com*

Sleep is a natural, reversible resting-state and in mammals it is formed by the cyclical occurrence of Rapid Eye Movement (REM) and non-REM sleep. The later one includes slow wave sleep (SWS) and light sleep. SWS is characterized by a generalized bi-stability of cortical membrane potentials, alternating between "up" and "down" states with a periodicity of approximately one second.

Due to the essential roles of SWS in cognition, sleep restoration and memory consolidation, multiple methods have been used to improve slow-wave sleep, one of the least invasive being auditory closed-loop stimulation.

In this work, we developed a labeling tool to perform manual annotations on EEG signals based on python and the popular MNE package. This tool performs a semi-automatic labeling to assist a visual expert in the identification of the signal components.

As we are particularly interested in Slow Oscillations (SO) and its role in memory function, this program was used to tag five naps and extract the sections where SO were identified. Based on this analysis, parameters that characterize each signal component were extracted: slope, frequency of waves with multiple peaks, and amplitudes. Thus, this tool is the initial step to perform an automatic SO detection to develop the auditory closed-loop stimulation mentioned above.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Asymmetric updating of adverse events predictions in healthy population with different levels of trait anxiety

Guillermo Solovey [1], Mariela Sued [1], María Eugenia Szretter Noste [1], Maria Eugenia Pedreira [2], Rodrigo Fernández [2]

1 Instituto de Cálculo (UBA-CONICET)
2 IFIBYNE (UBA-CONICET)

Presenting author:
***Guillermo Solovey**, gsolovey@gmail.com*

How do people change their beliefs when faced with new information? One of the most robust findings is that people weigh evidence according to its valence, i.e. whether a piece of information is better or worse than previously thought. According to many studies, when it comes to self-relevant beliefs, desirable evidence has a larger impact on learning than undesirable evidence. In this work, we aim to understand: (a) the relationship between updating asymmetry and personality traits such as optimism and anxiety; (b) how is arousal (electrodermal activity) signaling the updating process; (c) the impact of learning and memory 3-month after the experiment. We present results of two experiments: a laboratory experiment (N=33) and a follow-up online study (N=340) using both bayesian and frequentist statistical models to assess our research questions.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Behavioral alterations induced by voluntary ethanol intake and noise exposure in male rats

Gustavo Ezequiel Buján [1], Héctor Alejandro Serra [1], Sonia Jazmín Molina [2], Laura Ruth Guelman [2]

1 Universidad de Buenos Aires. Facultad de Medicina. 1ª Cátedra de Farmacología. Buenos Aires, Argentina.
2 Universidad de Buenos Aires. Consejo Nacional de Investigaciones Científicas y Técnicas. Centro de Estudios Farmacológicos y Botánicos (CEFyBO, UBA-CONICET). Buenos Aires, Argentina.

Presenting author:
Gustavo Ezequiel Buján, *gbujan@hotmail.es*

Given that human adolescents usually consume ethanol (EtOH) in the presence of high noise intensities, the use of an animal model could provide relevant data. Therefore, the aim of the present study was to assess whether both agents could produce changes in different behavioral parameters in adolescent rats.

Male Wistar rats in early adolescence (28 days old) were subjected to voluntary EtOH consumption for intermittent 24-hour periods for two weeks, using the two-bottle choice paradigm (5% EtOH/1% sucrose). A subgroup was exposed to noise (2h, 95-97 dB) after the first week. All animals were evaluated on different behavioral tasks, including open field, elevated plus maze and inhibitory avoidance.

Results showed a decrease in associative memory (AM) and an increase in anxiety-like behaviors after noise exposure or EtOH intake, when compared with sham rats. In noise-exposed animals that consumed EtOH, an increase in exploratory behavior was also observed.

This findings suggest that exposure to stressors such as noise or EtOH presented individually might trigger an increase in anxiety-like behaviors that seem to lead to a deficit in AM. A counteraction of anxiety-related behaviors seems to be added when both agents are present together, suggesting a compensation of the stressful effect.

In conclusion, adolescence would represent a period of great vulnerability to physical and chemical agents that may interact to achieve more adaptive behavioral performance.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Understanding a complex task: An exploratory study using a web–based Trail Making Test digital version

Gustavo Ezequiel Juantorena [1], Ignacio Linari [1], Agustín Petroni [1], Juan Esteban Kamienkowski [1,2]

1 Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN (UBA-CONICET)
2 Departamento de Física, FCEyN, UBA.

Presenting author:
***Gustavo Ezequiel Juantorena**, gjuantorena@gmail.com*

The Trail Making Test (TMT) is one of the most popular neuropsychological tasks. It has two parts: A) participants have to connect 20 consecutive numbers and B) both numbers and letters are connected in an alternate order (1-A-2-B, etc). Different measures of the performance on the TMT are standard markers of executive functioning in both clinical and neurotypical populations. In particular, the time completion difference between parts B and A reflects the additional cognitive load present in part B, mostly related to inhibitory control, working memory, and set switching. With a few exceptions, the TMT is administered in the original format, using pencil and paper.

Here, we designed two browser-based versions of the TMT that recorded continuous hand movements. We conducted two experiments. In the first experiment, we used a local browser-based task in the laboratory. In a second experiment, we implemented a digital version of the TMT and collected data online. We present preliminary results on both experiments, showing the well-known patterns on the TMT measures, in particular, the time difference between parts B and A. Moreover, we emphasize the potential of online experiments to access larger and more varied samples, along with other tasks, and describe a simple pipeline using open-access tools.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Modeling the ocular movement in Eye-Tracking

Ana Laura Frapiccini [1], Gustavo Gasaneo [1], Gustavo Gasaneo [2], Jessica A. del Punta [1], Karina V. Rodriguez [1], Karina V. Rodriguez [2]

1 Universidad Nacional del Sur - IFISUR
2 Centro Integral de Neurociencias APlicadas

Presenting author:
***Gustavo Gasaneo**, ggasaneo@criba.edu.ar*

The registration of eye movements can be considered the source of information to what is happening in the brain, where most of the information gathered from the visual field is processed [1]. Eye movements can be registered with an eye tracker, a device that detects the position and movements of the eyes. The eye tracking techniques have been used in various fields, for example, in health studies such as Alzheimer's disease.

In the last few years our group has dedicated to investigate eye movements from a physical point of view. Recently, we introduced a very simple model of the eye movements as the solution of a driven damped harmonic oscillator. In the present work we return to the investigation of saccadic movements as proposed previously, but having in consideration the decomposition of the movement into eyeball and pupil. Starting with a proposal to model horizontal eye movements [6,7], we study the parameters involved in it. We investigate the values that best fit the parameters describing the activation force responsible for horizontal saccades, independently of the task being performed and check the model with reading experimental data.

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

The Trail Making Test: a physical model describing subjects performance

Gustavo Gasaneo [1y2], Adrian A. Jimenez Gandica [1], Jessica A. del Punta [1]
1 Universidad Nacional del Sur - IFISUR
2 Centro Integral de Neurociencias APlicadas

Presenting author:
***Gustavo Gasaneo**, ggasaneo@criba.edu.ar*

In this contribution we explored the possibility of modeling as a dynamical physical process the behavior of subjects performing a neuropsychological test. We address the study by considering subjects performing the Trail Making Test in its part A. To be able to model the subjects behavior we first implement a digital version of the test which allows us to register the eye movements of the subjects during the performance. With the model recently introduced by some of the authors [1,2] we can represent the eye movements with a Langevin equation. This association allows us to transform the subject behavior into a particle moving in a plane. Some of the physical magnitudes involved in the model can be associated then with some neuropsychological constructs like processing speed, visual search speed and mental flexibility. The model introduced can also be related to the Diffusion Model for decision making introduced in Ref. [3].

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

Trail Making Test Revisited: Eye and hand movements during the resolution of a complex task

Ignacio Linari, Gustavo Juantorena, Agustín Petroni, Juan E. Kamienkowski
Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, Fac. de Cs. Exactas y Naturales, Universidad de Buenos Aires - CONICET

Presenting author:
Ignacio Linari, ignaciolinari@gmail.com

The Trail Making Test (TMT) is a widely used neuropsychological test for the diagnosis of executive dysfunctions in a range of clinical conditions. It has two parts, in which participants must connect 20 consecutive numbers (TMT-A) or both numbers and letters in alternating order (TMT-B; 1-A-2-B, etc.). TMT is a complex task and involves several stages supported by different executive functions. It is usually done with paper and pencil and only the total time is quantified, which does not allow a detailed analysis. Here, we designed a digital version where hand and eye positions were measured. This allows us to study with improved precision the components of the task in neurotypical participants. We show that the overall performance is similar to the traditional version, and that it correlates with a general executive functions assessment (IFS). Moreover, eye movements are similar in both parts, but there are fewer fixations in A, which is compatible with a faster resolution. In particular, there are fewer fixations in the initial exploration and planning phases during the task in A. Accordingly, it was observed a longer delay in the outgoing movements of the hand in B, but not in the eye. Finally, the number of items remembered in each step correlates with a better resolution of the task. These results pave the way for a detailed analysis of complex tasks such as TMT, providing a deeper understanding of the processes underlying the resolution of traditional tests.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Deficits in metacognition of emotion recognition in dementia

Indira Garcia Cordero [1], Joaquin Migeot [2], Alexia Aquino [1], Sol Fittipaldi [1], Mariano Díaz Rivera [1], Adolfo Garcia [1], Agustín Ibañez [1]

1 Universidad de San Andrés, Buenos Aires, Argentina

2 Center for Social and Cognitive Neuroscience, School of Psychology, Universidad Adolfo Ibáñez, Santiago de Chile, Chile

Presenting author:

***Indira Ruth Garcia Cordero**, indira.garciacordero@gmail.com*

Metacognition (monitoring) of emotion recognition is fundamental for social interactions. Although dementia patients present deficits in emotion recognition and self-awareness, their metacognition of affective processes remains poorly understood. We recruited 18 patients with behavioral variant frontotemporal dementia (bvFTD), 27 with Alzheimer's disease (AD), and 38 demographically-matched controls. Participants performed the Ekman's facial emotion recognition test and, after each trial, provided a confidence judgment about their performance. A metacognitive index was calculated weighing performance against associated confidence ratings. Whole-brain grey matter (GM) volume was associated with the index via voxel-based morphometry multiple regression analyses. Both patient groups presented impairments in metacognition of negative emotions: disgust was specifically impaired in bvFTD, and sadness in AD. In bvFTD patients, reduced GM volume of limbic and subcortical regions was associated with emotion recognition deficits; while the frontal, insular, and cingulate cortices were linked to metacognitive impairments. In AD, temporal and parietal areas were associated with emotion recognition; whereas parietal and frontal regions were linked to metacognition. Recognition and metacognition of emotions shared several structural substrates. Further research in this direction can illuminate the bases of daily socio-behavioral alterations in these disorders.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Caloric restriction recovered cerebellar motor and cognitive abilities in aged rats

Ivanna Castro Pascual [1], Bruna Pereira Sorroche [2], Florencia Elisa Curzel [3], Fernando Gabriel Altamigano [1], Mariana Lucila Ferramola [4], Maria Gabriela Lacoste [1], Marcela Delgado [4], Mauricio Martin [5], Ana Cecilia Anzulovich [1,4]

1 Laboratorio de Cronobiología, IMIBIO-SL, CONICET-UNSL, San Luis, Argentina
2 Centro de Pesquisa em Oncologia Molecular, Hospital de Câncer de Barretos, São Paulo, Brasil
4 FQByF, UNSL, San Luis, Argentina
5 Laboratorio de Neurobiología, INIMEC, CONICET-UNC, Córdoba, Argentina

Presenting author:
Ivanna Castro Pascual, *ivannacastropascual@gmail.com*

The beneficial effects of caloric restriction would work through epigenetic processes, but this is largely unexplored. Here, we examine the hypothesis that CR recovers learning and motor coordination associated to changes in Bdnf and TrkB DNA methylation, in old rats. For that, male Holtzman rats -young (3-mo-old, n=8), old (22-mo-old, n=9), both fed ad-libitum, and 18-mo-old rats fed a 40% calorie restricted diet for 3 months (n=4)- were kept under 12h-light: 12h-dark, 22-24 °C and water ad-libitum. Performing the Single Reaching Pellet test, we observed that the percentage of the total success rate and the quality of the first attempt during performance are significantly lower in the old compared to the young and old rats with CR ($p < 0.05$). As a control the olfactory sense and mood of the animals, the Buried Food Pellet and Corner Test were performed respectively. Samples (n=6) of cerebellar DNA from the three groups, were examined by bisulfite sequencing at CpG sites in regulatory regions in exons 3 and 9 of Bdnf and exon 1 of TrkB genes, to measure methylation with base-specificity. We observed 89 to 100% methylation at the CpG site in exon 9 of Bdnf gene, with no significant differences between groups. Methylations were not detected at the CpG sites in exon 3 of Bdnf nor exon 1 of TrkB gene, in any of the experimental groups. Our results show there is no association between cognitive CR benefits and CpG methylation of cerebellar Bdnf and TrkB genes in the studied exons.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Conscious processing of narrative stimuli synchronizes heart rate between individuals

Pauline Pérez* [1,2,3], Jens Madsen* [4], Leah Banellis [5,6], Başak Türker [1,2,3], Federico Raimondo [1], Vincent Perlbarg [7], Melanie Valente [1], Marie-Cécile Niérat [12], Louis Puybasset [8,9], Lionel Naccache [1,2,3,10,11], Thomas Similowski [12,13], Damian Cruse [5,6], Lucas C Parra# 4, Jacobo D Sitt# [1,2,3]

1 Institut du Cerveau et de la Moelle épinière, ICM, F-75013, Paris, France.
2 Inserm U 1127, F-75013, Paris, France.
3 CNRS UMR 7225, F-75013, Paris, France
4 Department of Biomedical Engineering, City College of New York, New York, USA
5 School of Psychology, University of Birmingham, Birmingham, B15 2TT, England
6 Centre for Human Brain Health, University of Birmingham, Birmingham, B15 2TT, England
7 Bioinformatics and Biostatistics Core Facility, iCONICS, IHU-A-ICM, Institut du Cerveau et de la Moelle épinière, Paris, France
8 Department of Anesthesia and Intensive Care, Pitié-Salpetrière Hospital, Paris, France
9 Sorbonne Université, CNRS, INSERM, Laboratoire d'Imagerie Biomédicale, LIB, Paris, France
10 Department of Neurophysiology, Hôpital de la Pitié-Salpetrière, AP-HP, F-75013, Paris, France.
11 Faculté de Médecine Pitié-Salpêtrière, Sorbonne Université, 75013, Paris, France.
12 Sorbonne Université, INSERM, UMRS1158 Neurophysiologie Respiratoire Expérimentale et Clinique, F-75005 Paris, France

Presenting author:
Jacobo Sitt, *jdsitt@gmail.com*

Heart rate has natural fluctuations that are typically ascribed to autonomic function. Recent evidence suggests that conscious processing can affect the timing of the heartbeat. We hypothesized that heart rate is modulated by conscious processing and therefore dependent on attentional focus. To test this we leverage the observation that neural processes can be synchronized between subjects by presenting an identical narrative stimulus. As predicted, we find significant inter-subject correlation of the heartbeat (ISC-HR) when subjects are presented with an auditory or audiovisual narrative. Consistent with the conscious processing hypothesis, we find that ISC-HR is reduced when subjects are distracted from the narrative, and that higher heart rate synchronization predicts better recall of the narrative. Finally, patients with disorders of consciousness who are listening to a story have lower ISC, as compared to healthy individuals, and that individual ISC-HR might predict a patients' prognosis. We conclude that heart rate fluctuations are partially driven by conscious processing, depend on attentional state, and may represent a simple metric to assess conscious state in unresponsive patients.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Behavioral phenotypic outcomes in juvenile rats following infant maltreatment

Jazmín Grillo Balboa, Ailén Alba Colapietro, Marta Cristina Antonelli, Verónica Pastor, María Eugenia Pallarés

Laboratorio de Programación Perinatal del Neurodesarrollo. Instituto de Biología Celular y Neurociencias "Prof. E. De Robertis", Facultad de Medicina, Universidad de Buenos Aires. Buenos Aires, Argentina.

Presenting author:
***Jazmín Grillo Balboa**, jazmin.grillo28@gmail.com*

Early-life stress (ELS) increases the propensity to develop psychopathologies later in life. Much of the evidence regarding the effects of ELS focuses on adults, leaving younger ages unexplored. Because in human scenarios of ELS the mother is present but her behavior is abnormal, an ELS naturalistic rodent model is desirable for translational studies. Here we examine the phenotypic outcomes of juvenile Wistar rats exposed to the scarcity-adversity model (SAM) of low nesting resources, which elicits adverse caregiving conditions (e.g.: maltreatment) toward neonates. SAM was performed from postnatal day (PND) 8-12, a critical period for the development of brain structures related to stress and emotional regulation in pups. Male and female offspring at PND 25-29 were evaluated in the open-field and forced swimming test for anxiety-/depressive-like behaviors. Mothers from the SAM condition showed increased violent conducts toward their pups and a fragmented behavior. SAM offspring revealed greater exploratory behaviors, while a lessened anxious-like behavior was only evident in males. Conversely, depressive-like behaviors were higher in males compared to females. Our results show that exposure to a violent and unpredictable perinatal environment has sex-specific consequences on juvenile offspring's behavior. Further study of the neurobehavioral phenotype of SAM-reared individuals could be key to understanding the early onset of ELS-related psychopathologies.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Effect of an intra hypothalamic gene therapy with IGF 1 on behavioral parameters

Jeronimo Pennini [1], Franco Juan Cruz Dolcetti [1], Eugenia Falomir-Lockhart [1], Macarena Herrera [2], María José Bellini [1]

1 Instituto de Investigaciones Bioquímicas de La Plata "Profesor Doctor Rodolfo R. Brenner" (INIBIOLP)
2 Instituto de Farmacología experimental de Córdoba (IFEC)

Presenting author:
Jeronimo Pennini, *JeronimoPennini1@gmail.com*

Aging is characterized by a coordinated organs and tissues functional impairment The hypothalamus, a region known to regulate many basic functions such as growth, development, reproduction and metabolism, is proposed as a regulatory center of aging Evidence demonstrates that the inhibition or activation of microglial or neural transcription factor NF κB of the basal hypothalamus (affects the life expectancy and the " of aging, as well as the release of GnRH There is solid evidence that middle age (rats do not respond to estradiol positive feedback with an appropriate modulation of excitatory and inhibitory hypothalamic neurotransmitter release This imbalance could cause reduced activation of GnRH neurons, reduced GnRH release, and an abnormal LH surge The MA rat brain reduction of factors like IGF 1 could be the reason of the affected modulation on excitatory and inhibitory hypothalamic release These findings provide a link between inflammation, response to stress and systemic and cerebral aging.

It is well known that IGF 1 plays a physiological role in neuroprotection and neuroinflammation. We decided to investigate the effects of intrahypothalamic gene therapy for IGF 1 in MA rats. We propose that transgenic IGF 1 will modulate neuroinflammation and delay reproductive senescence.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Modulation of Hippocampal-prefrontal cortex connectivity during contextual guided episodic memory recall in rodents

Juan Facundo Morici [1,2], Noelia Weisstaub [1], Camila Zold [2]

1 Instituto de Neurociencias cognitivas y traslacionales (CONICET-FAVALORO-INECO). Solis 453, Capital Federal, Argentina.
2 Instituto de Fisiología y Biofísica Bernardo Houssay (UBA-CONICET). Paraguay 2155, Capital Federal, Argentina.

Presenting author:
Juan Facundo Morici, *faq.morici@gmail.com*

Remembering which experiences occur at a particular context is a complex process that requires the interaction between multiple brain areas. The recall of a specific memory can be triggered by contextual information and relies on the interaction between the hippocampus (HIP) and the prefrontal cortex (PFC). It has been shown that the synchronization of HIP-PFC theta oscillations is enhanced during the resolution of contextual/spatial working memory tasks. However, little is known about how the HIP and PFC are coordinated during a contextual-guided recall of an episodic-like memory. To address this, we performed electrophysiological recordings in behaving rats during the retrieval phase of the object-in-context memory task (OIC). We observed an increase in HIP-PFC LFP coherence in the theta range when animals explore contextually mismatched objects. We also analyzed the activity of PFC neurons during the OIC test. Interestingly, 50% of PFC cells showed firing rate modulations during the test with respect to their baseline activity (25% responded to object exploration and 25% to non-object exploration periods). In addition, 25% of PFC neurons were phase-locked to the hippocampal theta rhythm. Altogether, these results suggest that HIP-PFC functional connectivity in the theta band is differentially modulated depending on the contextual congruence of the presented stimuli. In addition, PFC neurons encode different types of information that may be necessary for the OIC resolution.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Validating a behavioral test for studying sociability using fast-scan cyclic voltammetry

Juan Martin Uehara, Juan Emilio Belforte, Estefania Pilar Bello

Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO Houssay), Universidad de Buenos Aires, Facultad de Medicina - CONICET

Presenting author:
Juan Martin Uehara, *ueharajm@gmail.com*

The three-chamber test and the reciprocal social interactions test are the most widely used paradigms to study sociability in rodents. However, they were not initially developed for simultaneous electrochemical recordings. In the former, the apparatus is not well suited for handling moving wires and it only allows the simultaneous presentation of two stimuli as a maximum, while in the latter the aggressive behaviors initiated by the conspecific are not restricted. This work aims to validate a social interaction test compatible with fast-scan cyclic voltammetry and that allows the free circulation of implanted mice and the presentation of multiple stimuli of different novelty, salience and valence. In the interaction phase, subject mice spent more time exploring an age and sex-matched conspecific than an object. In addition, they preferred to investigate a novel demonstrator over a familiar one in the recognition phase. The number of entries to the exploration zones was also significantly different in both phases. Discrimination indexes remained stable in a retest conducted one week later, although differences within each phase were less significant. Other variables such as latency to first visit and length of the first visit were particularly relevant when the affective state of the demonstrators was modified. Validating this test is the first step towards studying the dopaminergic contribution to social interaction and the social phenotype of a murine model of schizophrenia.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

K-Complex detection algorithm in non-REM sleep

Aylin Agatha Vazquez Chenlo [1], Julia Carosi [1], Giulia Carbonari [2], Cecilia Forcato[1], Rodrigo Ramele [3]

1 Departamento de Bioingeniería, Instituto Tecnológico de Buenos Aires (ITBA)
2 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires (ITBA)

Presenting author:
Julia Carosi, *jcarosi@itba.edu.ar*

Sleep is a natural and reversible state of rest. In mammals it is characterized by the cyclical occurrence of Rapid Eye Movement (REM) and non-REM sleep. The latter is characterized by the presence of sleep spindles, K-Complexes (KCs), slow cortical waves and fast hippocampal waves. During sleep there is a spontaneous reactivation of recently acquired information. The slow waves orchestrate the hippocampal-cortical communication by synchronizing their activity with the fast thalamic sleep spindles and the fast hippocampal waves, favouring the transfer of information from the hippocampus to the cortex and its long-term consolidation. KCs are a type of slow wave that can be evoked by different stimuli or occur spontaneously during sleep. Studies indicate that it is possible to induce the reactivation of specific memories through the presentation of cues linked to the learned task resulting in induced KCs and memory enhancement.Different types of slow oscillatory activity (slow and delta waves) are regularly identified by visual inspection or with methods based on the morphological analysis of waveforms. In this work, we propose a method based on Machine Learning techniques, extracting features and using classification algorithms to identify signal segments. On the other hand, we differentiate between induced and spontaneous KCs. Different statistical parameters of accuracy and efficiency of the algorithm are contrasted against visual inspection provided by experts.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Searching for Active Forgetting Mechanisms of Aversive Memories

Juliana Fátima Dalto [1], Fernando Castillo Díaz [1], Magdalena Pereyra [1] Jorge Horacio Medina [1]

1 Instituto de Biología Celular y Neurociencia "Prof. Eduardo de Robertis"
2 Facultad de Medicina,
3 Universidad de Buenos Aires
4 Consejo Nacional de Investigaciones Científicas y Técnicas

Presenting author:
***Juliana Fátima Dalto**, julianadalto@hotmail.com*

Although it has been demonstrated the existence of active forgetting (AF) mechanisms for several acquired experiences, there is no such evidence of these mechanisms for aversive memories already consolidated. Based on previous work of our group and others we evaluated the participation of different molecular pathways on AF of aversive memories in the ventral tegmental area (VTA) and dorsal hippocampus (HP). We first decided to evaluate if dopamine in the VTA supports AF of aversive memories. However, we found that blocking D1 subtype receptors in the VTA impairs the formation of conditioned place aversion memory and the formation and duration of inhibitory avoidance (IA) memory in a training-dependent manner. Then, we evaluated the role of GABA neurotransmission in the AF of IA memory and found that positive allosteric modulation of GABAA receptors via benzodiazepine systemic administration or infusion in the HP appears not to affect the duration of this memory. Finally, we also recently started to study the role of the GTPase Rac1 in AF of IA memory. Our preliminary results seem to show that the inhibition of this protein in the HP extends the duration of this memory. Until now, we have made an important progress searching for molecular mechanisms that could be mediating AF of consolidated aversive memories. Our results seem to indicate that Rac1 could be mediating this process in the HP and thus open a new range of future studies to advance in the understanding of AF.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Spaced learning induces spatial object recognition memory persistence through a Behavioral Tagging process

Julieta Correa [1], Ramiro Tintorelli [1], Pablo Budriesi [1] Haydée Viola [1]

1 Laboratorio de Memoria, Instituto de Biología Celular y Neurociencia "Prof. E. De Robertis" (IBCN), Facultad de Medicina, UBA-CONICET

2 Departamento de Fisiología, Biología Molecular y Celular "Dr. Héctor Maldonado" (FBMC), Facultad de Ciencias Exactas y Naturales, UBA

Presenting author:
***Julieta Correa**, correajulietaa@gmail.com*

Persistence is the main attribute of long-term memory (LTM) and a strategy to improve it is to act on specific mechanisms several hours after learning. Here, we assessed the effects of spaced learning to promote memory persistence. Using a spatial object recognition (SOR) task in rats, we designed a protocol of 2 learning sessions. A weak SOR (wSOR) training session induced short-term but not LTM, whereas a strong SOR (sSOR) training session formed a 24 h-LTM which did not last 7 days. We found that a wSOR-retraining session performed 1 but not 7 days after a sSOR training promotes SOR-LTM persistence. However, this effect was not observed when the wSOR was replaced by a test session. Our results suggest that this promotion depends on the mechanism of sSOR-LTM expression induced during the second training, and that a reconsolidation process has not been involved. Based on the Behavioral Tagging hypothesis, we postulate that retraining will mainly retag the sites initially labeled by the prior training and the memory expression would provide the proteins needed to be used by the learning-tag in order to reinforce or stabilize the memory trace. Also, we studied whether a similar approach could be applied in elementary-school students, with the aim of improving teaching strategies. A first study using a geometrical-figure test showed a LTM enhancement in the group of students that received a second learning session (test or retraining) 2, 7 or 14 days after the first one.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Word learning and semantic integration: memory reactivation as a key mechanism for building the mental lexicon

Julieta Laurino [1], Cecilia Forcato [2], María Eugenia Pedreira [1], Laura Kaczer [1]
1 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE - UBA - CONICET)
2 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires (ITBA)

Presenting author:
***Julieta Laurino**, julilaurino@gmail.com*

Learning the meaning of new words is an important aspect of human language. But after learning, we must be able to recall these meanings and integrate them with other lexical items accordingly. In the present study we hypothesize that reactivating a novel word´s meaning could be a key mechanism for a successful lexical integration. We performed a series of online studies analyzing the contribution of memory reactivation to: lexical integration (Study 1) and updating of a word's meaning (Study 2). Native speakers of Spanish (18-35 years) learned a list of low-frequency Spanish words with their definitions. The following day, Reactivated groups were exposed to a reminder consisting of the list of words but without their definitions. Non Reactivated groups did not receive a reminder. In Study 1 (N=112), memory retention was evaluated 48 h after training with a cued-recall test or a semantic judgment task. In Study 2 (N=81), participants learned new information for each of the words' definitions and memory retention was evaluated 48 h after training using a cued-recall test. Results of Study 1 show a significant enhancement of words' memory and semantic recognition speed in the Reactivated group. Study 2 reveals a significant enhancement of the new information's memory that increases according to the reactivation strength of each word. Taking into account both results, we demonstrated the importance of memory reactivation for constructing and updating our mental dictionary.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Effect of subliminal feedback on metacognition in a visual perception task

Julieta María Zapata [1], Nicolas Alejandro Comay [1], Gabriel Della Bella [1]

1 Departamento de Física UNS - IFISUR, Bahía Blanca - Centro Integral de Neurociencias Aplicadas, Bahía Blanca.
2 Departamento de Física UNS - IFISUR, Bahía Blanca.
3 Laboratorio Especializado en Aprendizaje y Neurociencias, Buenos Aires.

Presenting author:
***Karina Viviana Rodriguez**, kkrodri@gmail.com*

There are not specific regions of the human brain specialized on the reading task, but language and visual regions interact to make possible this fundamental activity for academics just as for daily life. Reading ability is generally achieved between the five and seven years old and, it is generally, a difficult task. There is a percentage of the children population for which reading is even a much more difficult task [1]. In this presentation we want to explore a possible method to identify and quantify the reading difficulty.

Having in mind the idea of evaluating difficulty while reading, we performed a study where neurotypical and dyslexic children eye movements were registered while they were reading, on a monitor, a short text designed for their age. The signal obtained was processed using tools developed under python with the purpose of obtaining physical magnitudes that can be associated then with processing speed and visual search speed. The study of these neuropsychological constructs in the complete text, in every line and finally in each word permitted us to find the aspects which represent the degree of difficulty for each group also for each subject.

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

Combining eye tracking and machine learning techniques to detect dyslexia

Karina Viviana Rodriguez [1], Francisco Iaconis [2], Gustavo Gasaneo [1] Alejandra Mendivelzua [3], Laura García Blanco [3], Manuela Sanchez [3]

1 Departamento de Física UNS - IFISUR, Bahía Blanca - Centro Integral de Neurociencias Aplicadas, Bahía Blanca.
2 Departamento de Física UNS - IFISUR, Bahía Blanca.
3 Laboratorio Especializado en Aprendizaje y Neurociencias, Buenos Aires.

Presenting author:
***Karina Viviana Rodriguez**, krodri@criba.edu.ar*

Recent studies estimate that 10 percent of the children population of Argentina suffers from Specific Learning Disorder. Dyslexia, being one of them, is considered a neurological learning disability [1]. In this presentation we combine machine learning techniques and eye tracking signals to explore the possibility of developing a tool to detect dyslexia in childrens.

The study performed included 25 neurotypical children evaluated at the school and a group of eleven children diagnosed with dyslexia evaluated in the psychopedagogue's office. The task assigned to all of the subjects was to read on a monitor a short text designed for their age. During the reading the eye movements were recorded with an eye tracker mounted on the monitor.

In this work, the signals were processed using tools developed under python with the purpose of obtaining several variables such as mean time per fixation, number of saccades, mean size of saccades and other nine magnitudes. As part of the analysis performed, we applied Principal Component Analysis, Linear Discriminant Analysis and logistic regression to the data. The three techniques implemented were able to identify dyslexic from neurotypical children. We believe that the techniques implemented, combined with other tools, could help mental health professionals to diagnose.

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

Detection of difficulties of children in reading task using processing speed.

Karina Viviana Rodriguez [1], Francisco Iaconis [2], Gustavo Gasaneo [1], , Alejandra Mendivelzua [3], Laura García Blanco [3], Manuela Sanchez [3]

1 Departamento de Física UNS - IFISUR, Bahía Blanca - Centro Integral de Neurociencias Aplicadas, Bahía Blanca.
2 Departamento de Física UNS - IFISUR, Bahía Blanca.
3 Laboratorio Especializado en Aprendizaje y Neurociencias, Buenos Aires.

Presenting author:
***Karina Viviana Rodriguez**, kkrodri@gmail.com*

There are not specific regions of the human brain specialized on the reading task, but language and visual regions interact to make possible this fundamental activity for academics just as for daily life. Reading ability is generally achieved between the five and seven years old and, it is generally, a difficult task. There is a percentage of the children population for which reading is even a much more difficult task [1]. In this presentation we want to explore a possible method to identify and quantify the reading difficulty.

Having in mind the idea of evaluating difficulty while reading, we performed a study where neurotypical and dyslexic children eye movements were registered while they were reading, on a monitor, a short text designed for their age. The signal obtained was processed using tools developed under python with the purpose of obtaining physical magnitudes that can be associated then with processing speed and visual search speed. The study of these neuropsychological constructs in the complete text, in every line and finally in each word permitted us to find the aspects which represent the degree of difficulty for each group also for each subject.

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

Disinformation and political polarization: A study of the impact of political beliefs in the ability to detect "fake news"

Laouen Belloli [1,2], Joaquín Navajas [2,3], Nira Dinerstein [4], Ariel Merpert [4], Laura Zommer [4], Andrea Goldin [2,3]

1 Laboratorio de Inteligencia Artificial Aplicada, Depto. de computación, FCEyN, UBA–CONICET
2 Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ministry of Science, Buenos Aires, Argentina
3 Laboratorio de Neurociencia, Universidad Torcuato Di Tella
4 Chequeado

Presenting author:
Laouen Mayal Louan Belloli, *lbelloli@dc.uba.ar*

The use of social media is growing, and the spread of 'fake news' with direct impact on political decisions has raised to new levels. Social media (and their non transparent algorithms) are the main organisations to be pointed out as responsibles for this issue, and they started to implement different strategies on their platforms to reduce disinformation. One of the proposed mechanisms is not allowing people to share a news before a certain delay, in order to reinforce inhibitory control, that, in theory, permits a more rational analysis of the news.

Polarization is known to affect people's judgement. Since its origin, Argentina has had a strong political crack, nowadays represented by two of its major political parties: Kirchnerismo and Macrismo.

In this work, we studied the impact of Argentinian political polarization on the subjects' ability to detect disinformation and misinformation, and the use of delay times to improve their performances. For this purpose, we conducted an experiment where 715 subjects classified a set of news as 'fake' or 'real' with or without a previous delay time. We found (1) a strong confirmation bias when the news disagreed with subjects' political beliefs, and (2) that adding a delay not only does not help to deal with that bias, but worsens the detection of real news when the news is aligned with the subject's political beliefs.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Online assessments of larger contexts modulation in word Predictability in Short Stories

Lena V Peroni [1], Bruno Bianchi [1], Diego E Shalom [2] Juan E Kamienkowski [1], Juan E Kamienkowski [2]

1 Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN, UBA - CONICET
2 Departamento de Física, FCEyN, UBA

Presenting author:
***Lena Valeska Peroni**, lena.peroni@gmail.com*

When reading, we are continuously predicting upcoming words, allowing us to integrate information and to guide eye movements. These predictions are operationalized as the Predictability and measured as the probability of guessing the next word from the previous context. Predictability reflects high-level processes taking place during reading and is a strong predictor of eye movements and brain activity. It is estimated by asking many participants to complete the most probable word that follows a given context. This task is called cloze-task and is usually collected in-lab, resulting in a time-consuming and expensive experiment.Here, we present an analysis of three corpora of online cloze-task experiments: (C1) a corpus of Common and Memory-Encoded Sentences collected both online and in-lab, (C2) a corpus with similar material, collected in two independent online experiments, and (C3) a corpus of sentences drawn from short stories collected online, both isolated or contextualized.We observed that the online cloze-task replicates the results from the in-lab one (C1) and is consistent between independent experiments (C2) Interestingly, these results clearly show that Predictability is highly dependent on large contexts (C3) Thus, online cloze-task makes the collection for larger samples easy and generates robust and more precise measures. Moreover, it allows us to explore the effects of larger contexts (up to 3000 words) in the Predictability, that could be impossible otherwise.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Sleep hygiene impacts on episodic memories in young and older adults during quarantine by Covid-19: preliminary results

Leonela M Tassone [1], Paula B Martinez [1], Malen D Moyano [1], Solferino [1], Carolina Feldberg [2], Florencia Tartaglini [2], Ignacio Brusco [3], Cecilia Forcato [1]

1 Laboratorio de Sueño y Memoria, Departamento de Ciencias de la vida, Instituto Tecnológico de Buenos Aires (ITBA)

2 Instituto de neurociencias Buenos Aires- INEBA

3 Centro de Neuropsiquiatría y Neurología de la Conducta- CENECON, Facultad de Ciencias Médicas, Universidad de Buenos Aires

Presenting author:
***Leonela Tassone**, LTASSONE@ITBA.EDU.AR*

Sleep benefits off-line memory consolidation. Due to quarantine by Covid-19, sleep routines and sleep quality were affected. Preliminary results from our Lab showed that episodic memory formation is impaired by emotional variables, such as anxiety and depression. We hypothesize that sleep hygiene during quarantine positively impacts memory processes and emotional variables. To test this, we perform a 21-day study. Young and older participants were trained on the episodic memory task (video of neutral content). On day 7 they were tested and half of them began a sleep hygiene program. On day 14, participants were trained in a new episodic task and were tested on day 21. We found that young and older adults that received the sleep hygiene treatment had a positive impact on memory performance. Furthermore, older adults had better performance in memory recognition than young adults independently of the hygiene treatment. Moreover, older adults that received the sleep hygiene treatment showed a positive correlation between the total amount of sleep hygiene activities and the amount of correct recognition as well as a negative correlation with false recognition. We did not found a significant effect on emotional variables. These results demonstrate that sleep hygiene can be an effective tool for young and older adults to improve memory, however one-week treatment is not enough to induce emotional improvements."

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Cross-cultural differences in affective assessment for emotionally-loaded words

Leticia Sarli, Nadia Justel
1 Lab. Interdisciplinario de Neurociencia Cognitiva, CEMSC3, ICIFI, UNSAM,
2 CONICET
3 Universidad de Córdoba

Presenting author:
***Leticia Ileana Sarli**, leti.sarli@gmail.com*

Words loaded with emotional content can be found on advertising, news articles and public speeches, and have been used widely on experimental settings to understand the underlying mechanisms of word recognition and retrieval. Even though word meaning is linked to its cultural environment, little emphasis is given to the potential cultural differences carried by words within the same language. The purpose of this study was to compare the affective ratings of two Spanish-language adaptations of the ANEW word-set, Argentina and Spain. The 1034 words from each dataset were split into three categories, according to their valence: positive, neutral, and negative; and later compared on the dimensions of valence, arousal and dominance. The Argentinean sample showed higher levels of arousal for negative and neutral words compared to the Spanish sample While valence interacted with gender, since the female participants on the Argentinean sample rated neutral and positive words as more pleasant that their Spanish counterparts; and overall, the Argentinean sample rated negative words as more pleasant as well. Moreover, the Argentinean sample showed higher dominance for emotional words than the Spanish sample. These results show that affective assessment varies between regions even when the same language is spoken, addressing the need for culturally-specific stimuli selection on neuroscientific research.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Neurophysiological markers after memory reactivation: the lasting footprints of the reconsolidation process

Libertad Campassi [1,2], Eugenio Rodríguez Balboa [3], Germán Campos-Arteaga [3], Ismael Palacios-García [3], María Eugenia Pedreira [1], Luz Bavassi [1,2]

1 Laboratorio de Neurociencias de la Memoria, IFIBYNE, UBA, CONICET
2 Departamento de Física, Fcen, UBA
3 Pontificia Universidad Católica de Chile, Laboratorio de Neurodinámica Básica y Aplicada, Escuela de Psicología, Santiago, Chile.

Presenting author:
***Libertad Campassi**, libertadcampassi@gmail.com*

The process of reconsolidation is fundamental in daily life, it is responsible for updating both the strength and the content of a consolidated memory. Reconsolidation occurs when original information is reactivated by the presentation of specific reminders that trigger memory labilization followed by a re-stabilization phase. In a previous study, we showed that the retrieval of memories that had gone through the reconsolidation process involved a more extensive and with a higher clustering coefficient neural network than memories that had been re-exposed to the original context. These results raise new questions about how and when these lasting changes are printed in the brain. In this work, with an EEG of 64 channels, we explored to characterize the dynamic changes that occur in the brain network during the strengthening of a declarative memory . In this line, we analyzed the neurophysiological markers at a resting state immediately after the presentation of a reminder that triggers reconsolidation and another that does not. We found differences between both neural correlates. The resting after the presentation of the reminder that triggers reconsolidation had a higher amplitude of low frequencies (less than 4Hz) in the left central-parietal zone and a decreased in the right frontal region. These results might be the lasting footprints that reconsolidation prints in the brain.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

α-MSH modulation of the impairment in contextual fear memory induced by High-fat diet consumption; possible glial changes.

Guadalupe Herrera [1], Mercedes Lasaga [2], Teresa Scimonelli [1]

1 IFEC-CONICET. Depto. Farmacología. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba, Argentina.

2 Instituto de Investigaciones Biomédicas INBIOMED UBA-CONICET, Facultad de Medicina, Buenos Aires, Argentina.

Presenting author:

***Lucia Guadalupe Ximena Herrera**, guadalupe.herrera@mi.unc.edu.ar*

High-fat diet (HFD) consumption is associated with cognitive deficit and neurodegenerative diseases. The HFD effects on the central nervous system could be related to neuroinflammation, and even consumption of HFD for a short time period has been shown to exacerbate the inflammatory response to a mild immune challenge. The hippocampus is one of the most vulnerable brain regions to HFD-induced alterations. α-MSH is a potent anti-inflammatory peptide and previous results of our group indicated that α-MSH could reverse the effect of acute neuroinflammation on memory consolidation and reconsolidation. Here we studied the effect of HFD (60% of calories from fat) consumption on cognitive deficits. HFD impaired contextual fear (hippocampal dependent) memory if it is consumed during a long-term, and also after short-term consumption in rats that received a mild immune challenge (LPS 10µg/Kg). The treatment with α-MSH (0.1ug/0.25ul) in dorsal hippocampus reversed the effect of short-term HFD in contextual fear memory. We also determined possible changes in hippocampal structural plasticity. Preliminary results showed no differences in total spine density in dorsal hippocampus. Besides, we determined that the expression of GFAP was decreased. Our present results indicate that HFD consumption for a short period sensitizes SNC to mild immune challenge and produces impairment in the contextual fear memory that could be reversed by α-MSH and could be related to changes in glial cells.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Hierarchical learning of olfactory discrimination in a visual context

Macarena Amigo Durán, Sebastián A. Romano, Antonia Marin-Burgin, Noel Federman

Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) – CONICET - Partner Institute of the Max Planck Society

Presenting author:
Macarena Amigo Durán, *macky.amigo@gmail.com*

The ability to learn that a sensory stimulus signals a reward or punishment is one of the brain functions most critical for adaptation and survival. How animals integrate information about learnt sensory stimuli with spatial context and animal internal state is not completely understood. Here we developed a learning paradigm to evaluate the influence of spatial context on the association of an odor with a reward. Water-restricted mice were trained to perform a GO/NO GO discrimination task in which the animal learns to drink water or not depending on the visual context in which the odor is presented. In head-fixed conditions, animals arrive to different spatial contexts by running in a virtual reality environment. We show that animals reached to criterion within a few sessions. Linking response, locomotion speed and inhalation rate changes throughout the learning process, the last two depending on trial types. Mice learnt to discriminate odors faster than visual contexts, suggesting a difference in stimuli salience. Since appropriate response to odor help animals to adapt changing environments, we also studied how flexible is this behavior. We carried out a reversal learning protocol where the odor rewarded was changed, in the same context as before. Results showed that it took between 2-4 sessions to reverse the behavior. We developed an odor-in-context task suited to probing the neural basis of spatial context modulation of an olfactory-based behavior and its flexibility.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Relationship between activity in the open field, light-dark box, multivariate concentric square field, sucrose preference test, and ethanol intake in adolescent rats

Macarena Soledad Fernández 1, Ana Ferreyra 1, Ricardo Marcos Pautassi [1,2]

1 Instituto de Investigación Médica M. y M. Ferreyra (INIMEC – CONICET-Universidad Nacional de Córdoba), Córdoba, Argentina.
2 Facultad de Psicología, Universidad Nacional de Córdoba, Córdoba, Argentina.

Presenting author:
***Macarena Soledad Fernández**, macarenasoledadfernandez@gmail.com*

We analyzed factors that discriminate between adolescents at-risk of escalating into excessive alcohol consumption from those that – despite exhibiting similar level of initial alcohol exposure -- will not progress towards excessive or problematic alcohol consumption Adolescent Wistar rats were sequentially evaluated from PD 25 to 28 in anxiety behaviors, exploration of a novel context, risk assessment and shelter and anhedonia in open field tests, throught light-dark box, open field, multivariate concentric square field and sucrose preference test, respectively. Subsequently, the animals were evaluated for alcohol consumption using a double-bottle intake test (alcohol vs. water) of DP 32-47. The aim was to build a predictive model for alcohol consumption at adolescence, as a function of behavioral traits (anxiety and risk assessment behaviors, preference for sweet flavors, and activity level in an open field) that previous studies associated with addictive behaviors in humans. The model significantly explained 11% of the variance of alcohol consumption scores. Anxiety-related variables were those that contributed the most to the explanation of the dependent variable. The model explained free-choice alcohol consumption, but not overall liquid or sucrose consumption. The results shed light on vulnerability factors, specific to the adolescent stage, that promote engagement in problematic trajectories of alcohol use.

Keywords: ethanol consumption, adolescent, anxiety

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Development and testing of a novel Memory Discrimination Task for assessing cognitive deterioration in the elderly

Magdalena Miranda [1], Daniela Ramirez Butavand [1], Agustina Birba [2] Sol Fittipaldi [2], Alejandro Ramos Usaj [1], Adolfo García [2], Agustín Ibañez [2], Pedro Bekinschtein [1]

1 Laboratorio de Memoria y Cognición Molecular, Instituto de Neurociencia Cognitiva y Traslacional, CONICET-INECO-Universidad Favaloro
2 Universidad de San Andrés, Buenos Aires, Argentina

Presenting author:
***Magdalena Miranda**, miranda.magdalena.lb@gmail.com*

Dementia and cognitive impairment can progress silently for years. Recent guidelines highlight the importance of preclinical/preventive intervention for their treatment. However, their gradualness escapes classical neurocognitive evaluations, complicating preclinical diagnosis. Current studies indicate that one of the first regions affected during Alzheimer's disease (AD) is the anterior subhippocampal region. The interest in tasks that specifically recruit these regions is growing as they could prove particularly sensitive to the onset of neurodegeneration. In this line, tasks that require integrating multiple features of an object into a coherent representation in order to differentiate among similar stimuli (e.g., Memory Binding Task or Memory Discrimination Task) are useful for early detection of AD. Since aging is the most important non-genetic risk factor for AD and our research aims to distinguish normal cognitive decline from disease, we began by studying the sensitivity and specificity of memory performance changes to aging. We developed a novel Memory Differentiation Task (MDT) that integrates core features of the Binding and Differentiation Tasks. We found that performance in the similar (but not dissimilar) condition of this task correlates with performance on the Binding Task. Moreover, although memory differentiation is affected by aging, memory generalization is spared, suggesting that the MDT could be specifically sensitive to normal cognitive deterioration.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Declarative memory consolidation dynamics: new time windows and its implications for clinical application

Malen D Moyano [1], Matias Bonilla [1], Marcelo F Blanco [1], Ignacio Brusco [2], Maria Eugenia Pedreira [3], Laura Kaczer [3], Cecilia Forcato [1]

1 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires (ITBA)
2 CENECON, Facultad de Medicina, Universidad de Buenos Aires
3 IFIByNE - CONICET, Universidad de Buenos Aires

Presenting author:
***Malen Moyano**, malenmoyano@gmail.com*

After encoding, memories are in a labile state followed by a stabilization process known as consolidation. Spontaneous reactivation occurs during sleep and wakefulness (without the re-exposure to keys linked to learning). Here, we investigate whether declarative memories in humans suffer spontaneous labilization/stabilization processes after learning or if they only pass through a single time window of lability. Participants learned a list of five pairs of non-sense syllables on day 1. Immediately after, 30 min or 3 hours later they received an interference list that acted as an amnesic agent. They were finally tested on day 3. The two control groups were only trained and tested in one of the tasks. We found that the interference task learned at usual times after learning (immediately and 3 h latter) impaired memory stabilization, however, 30 min after it has no impairing effects. Thus, immediately after learning the memory is labile, it passes through a rapid stabilization 30 min later where it is temporally protected against interference and it becomes labile again around 3 h later. Thus, the dynamics of the declarative memory consolidation seems not to be an all or nothing process. Further studies should be done to test if similar waves of lability exist after cued memory reactivation. Knowing the different time windows susceptible to interferences becomes fundamental for the design of new psychotherapy treatments for anxiety disorders such as phobias.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Conflict-Related Brain Activity after Individualized Cognitive Training in Preschoolers from Poor Homes

Marcos Pietto [1], Federico Giovannetti [1], Maria Soledad Segretin [1] Juan Kamienkowski [2], Sebastián Lipina [1]

1 Unidad de Neurobiología Aplicada (UNA, CEMIC-CONICET)
2 Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN-UBA

Presenting author:
***Marcos Luis Pietto**, marcos.pietto@gmail.com*

Cognitive Control (CC) plays an important role in learning and self-regulatory processes. Socioeconomic status (SES) has been linked to neural activity related to CC processing. Little is known about the influence of cognitive interventions on children's brain functioning, and how the individual differences modulate the impact of those interventions. In the present study, a quasi-experimental design was implemented to evaluate the impact of cognitive training on cognitive performance and neural activity in 85 preschoolers from low-SES homes. Before and after the intervention children were assessed with a mobile EEG device during the performance on a Go/NoGo task. Based on their performance on a Stroop-like task at the pre-intervention stage children were classified into two groups (high- and low-performers) and then assigned to intervention and control groups within each performance level. Each group completed a set of activities during the intervention stage with different difficulty levels based on their basal performance. Results showed that children in the high-performance intervention group benefited the most at the neural level (i.e., conflict-related activity). The low-performance intervention group also verified changes at the behavioral level (i.e., increased RT´s after error/go ratio). Findings contribute to the consideration of individual differences in the design of interventions with adaptive algorithms, and the use of neural technology in ecological contexts.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Musical training affects language in 4- and 5-year-old children

María Angélica Benítez [1], Verónika Diaz Abrahan [2], Favio Shifres [3], Nadia Justel[2]

1 Laboratorio Interdisciplinario de Neurociencia Cognitiva (LINC), Centro de Estudios Multidisciplinario en Sistemas Complejos y Ciencias del Cerebro (CEMSC3), Instituto de Ciencias Físicas (ICIFI), Escuela de Ciencia y Tecnología (ECyT), Universidad de San Martín (UNSAM). Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Universidad Nacional de Córdoba (UNC).

2 Laboratorio Interdisciplinario de Neurociencia Cognitiva (LINC), Centro de Estudios Multidisciplinario en Sistemas Complejos y Ciencias del Cerebro (CEMSC3), Instituto de Ciencias Físicas (ICIFI), Escuela de Ciencia y Tecnología (ECyT), Universidad de San Martín (UNSAM). Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).

3 Laboratorio para el Estudio de la Experiencia Musical (LEEM). Departamento de Música. Facultad de Bellas Artes (FBA). Universidad Nacional de La Plata (UNLP)

Presenting author:
***María Angélica Benítez**, mariabenitez@conicet.gov.ar*

Musical training affects the development of different cognitive functions. This can be receptive (auditory perception of musical stimuli) or active (produce music through musical instruments or their voice). The aim of this study was to evaluate the effect of 12 weeks of receptive or active musical training on language and visuospatial ability for preschool children. They were randomly split into three groups: receptive or active musical training or a control group (without training). Language and visuospatial ability were evaluated through WPPSI-III (Information, Vocabulary, Word Reasoning, Receptive Vocabulary, Block Design, Object Assembly) and ENI (Language Repetition, Stick Construction, Copying a Complex Figure). Visuospatial ability and language-dependent measures were examined using a univariate analysis of variance (ANOVA). Significant differences were found between groups in the performance of the linguistic tasks. Children with musical training obtained better results than those of the control group in the majority of the subtests. In the visuospatial tasks, significant differences were found between the groups in Object Assembly here the musically trained children obtained higher scores than the control group. The results showed that the 12-week musical training could have the ability to improve the performance of the children of 4 and 5 years of age on language tasks and raises questions about its effect on other cognitive functions, such as visuospatial ability.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Serotonin 5-HT2a receptors in the mPFC participate in the mechanism underlying Retrieval Induced Forgetting in rats

María Belén Zanoni, Pedro Bekinschtein, Noelia Weisstaub
Laboratorio de Memoria y Cognición Molecular (INCyT, Favaloro - INECO – CONICET), Buenos Aires, Argentina.

Presenting author:
María Belén Zanoni Saad, *mbzanoni@gmail.com*

Over the past several decades, neurobiological research on memory has been focused on the mechanisms underlying memory storage. Nevertheless, the study of forgetting and, specifically, active forgetting has been increased since Anderson et al. showed in 1994 that the retrieval of certain memories could cause the forgetting of related, but not explicitly evoked information by a mechanism called retrieval-induced forgetting (RIF). The behavioral paradigm used to characterize this phenomenon in humans was then adapted for rats, opening the possibility to perform causal studies. As with humans, in rats, RIF is competition-dependent, cue-independent, and reliant on the prefrontal cortex. This work aims to explore if and how the serotonergic system participates in RIF. Specifically, we first used an antagonist of the serotonin receptor 2A in the medial prefrontal cortex and then specific inhibitors for members of the βarr2 signaling pathway. We found that only the animals exposed to the conditions that promote the retrieval-induced forgetting appear to be susceptible to the effect of the serotonin receptor 2A antagonist and the PI3K inhibitor, which is part of the Barr2 pathway, showing memory for the competing item. RIF could be thought of as a mechanism for optimizing the storage and use of information that can guide behavior, Thus, identifying key components of its neural mechanisms are relevant for the understanding of adaptive memory in rodents and humans.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Evaluation of the usability of a cognitive training videogaming platform in the elderly.

María Emilia Clément [1,2], Melina Vladisauskas [3,4], Martín A Miguel [4,5], Daniela Macario Cabral [3,5], Pablo Ioli 1, Andrea Paula Goldin [3,4]

1 Hospital Privado de Comunidad. Mar del Plata, Argentina.
2 Hospital Bernardo Houssay. Mar del Plata, Argentina
3 Laboratorio de Neurociencia, Universidad Torcuato Di Tella
4 Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ministry of Science, Buenos Aires, Argentina.
5 Laboratorio de Inteligencia Artificial Aplicada, Depto. de computación, FCEyN, UBA–CONICET

Presenting author:
***María Emilia Clement**, maria.emilia.clement@gmail.com*

Dementia is today one of the leading causes of disability and dependency in older people around the world; its prevalence is increasing rapidly, and it has no cure. Before its onset, there is a phase of transition called Mild Cognitive Impairment (MCI), which seems a promising period to test treatments to delay dementia.

Cognitive training is a therapy currently tested worldwide in people with MCI as prevention and treatment tool. Mate Marote is an Argentine open source software specifically designed to train executive functions. While it was tested in 5-to-8 year olds with excellent results, Mate Marote games were never tested in older adults.

In this work we present the first feasibility study, including 11 volunteers between 66 and 84 years old, without dementia. We evaluated the usability of the platform and the performance of the subjects in the adapted games.

To implement a randomized clinical trial with this software, some elements must be modified. Still, from this pilot study we conclude that Mate Marote is well adapted for older adults without dementia, and that both frequency and duration of the sessions are suitable for this group of people.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Review of fear memory in Drosophila melanogaster: similarities and differences between electric shock and a predatory environment.

María Eugenia Samman [1,2], Lia Frenkel [1,3], Ramiro Freudenthal [1,2]

1 iB3 | Instituto de Biociencias, Biotecnología y Biología traslacional- Facultad de Ciencias Exactas y Naturales- Universidad de Buenos Aires
2 Instituto de Fisiología y Biología Molecular y Neurociencias (IFIBYNE)- CONICET
3 Fundación Instituto Leloir- Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA)- CONICET

Presenting author:
***María Eugenia Samman**, mariaeugeniasamman@gmail.com*

Laboratory conditions are the usual approach to unveil the neurobiological basis of memories. The fly Drosophila melanogaster is not an exception and the olfactory memory associated with an electric shock is the paradigmatic example. On the contrary, our laboratory developed a set up to study the process of learning and memory in D. melanogaster under semi natural conditions: the memory of the successful strategies to survive to a natural predator, the spider Menemerus semilimbatus. A simple experimental device enables us to measure whether flies learnt to avoid contact with the spider or not. The focus is to investigate learning and fear memory in Drosophila generated in a predatory environment at the systemic, cellular, synaptic and molecular levels, and to compare it with the characterized olfactory memory associated with electric shock. Here we expose our strategy to evaluate our central hypothesis: learning tasks that requires the integration of multiple sensory modalities in a changing environment will recruit neural and computational processing to resolve the ambiguity that is going to be different from the one that recruits the memory of contingency between the smell and the electric shock. Specifically, we'll compare which neuronal groups are recruited in the formation of fear memory. Then, we'll evaluate which signalling cascade participates in the synaptic plasticity. To finally compare the results obtained with those of aversive memory due to electric shock.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

GluN2A-NMDAR hippocampal KD increases seizure susceptibility without changes in LTM

Maria Florencia Acutain [1], Jordana Luft Gerber [3], Diana Alicia Jerusalinsky [1], Lucas de Oliveira Alvares [3], Maria Veronica Baez [1]

1 Instituto de Biologia Celular y Neurociencia Prof. E de Robertis (IBCN-UBA-CONICET)
2 Facultad de Medicina, Universidad de Buenos Aires (UBA)
3 Instituto de Biociências, Universidad Federal de Rio Grande do Sul (UFRGS)

Presenting author:
***Maria Florencia Acutain**, facutain@yahoo.com*

Epilepsy represents one of the more complex and misunderstanding neurological disorders characterized by recurrent unprovoked seizures which lead to aberrant firing in brain circuits. Furthermore, mutations in NMDA receptor (NMDAR) subunits were related to Epilepsy. In cognitive related brain structures, like hippocampus, GluN2A and GluN2B subunits are the NMDAR most expressed regulatory subunits, and undergoes a tightly regulation. It was shown that the balance in these synaptic GluN2-type subunits is responsible for adequate glutamatergic neurotransmission, which is altered in several neurological disorders. In order to better understand the role of GluN2A in synaptic plasticity and behavior, we induce a knock-down (GluN2A-KD) in the CA1 region of young adult Wistar rats and perform several tasks. We evaluate locomotion, spatial exploration, associative (novel object recognition) and emotional memory (fear conditioning), as well as anxiety like parameters to characterize the KD model. Furthermore, we test seizure induced susceptibility in those rats. Our results showed that LTM was unaltered in GluN2A KD rats. Nevertheless, these animals were more susceptible to reach the stratus epilepticus than controls. These results suggest that GluN2A down regulation, and also, the imbalance in synaptic GluN2-type subunits, could facilitate seizure outcome that is a hallmark in several types of Epilepsy.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Sporadic Alzheimer's Disease: Study of Streptozotocin-Induced neurodegeneration in female rats

Maria Florencia Zappa Villar, Juliette López Hanotte, Facundo Peralta, Sofía Sánchez Caro, Julián Grondona, Paula Cecilia Reggiani

Biochemistry Research Institute of La Plata Professor Dr. Rodolfo R. Brenner (INIBIOLP). School of Medical Sciences, National University of La Plata, Argentina.

Presenting author:
Maria Florencia Zappa Villar, *mfzappa@med.unlp.edu.ar*

Sporadic Alzheimer's disease (SAD) is the most prevalent neurodegenerative disorder and it is characterized by progressive decline in memory and cognitive performance, which left unabated will likely affect 152 million people by 2050. Women represent more than two-thirds of patients with SAD worldwide, facing a higher risk for multimorbidity of brain disorders for which we have no effective therapies.

However, female animal models are usually excluded in preclinic research. Our aim was to evaluate the female brain disorder in a rat SAD model induced by intracerebroventricular injection of streptozotocin (icv-STZ).

We evaluated 4 animal groups: Sham, STZ, OVX and OVX+STZ (N=8). OVX and OVX+STZ groups were ovariectomized and, seven days later, STZ and OVX+STZ groups were injected with 3 mg/kg icv-STZ. Body weight of all rats was registered along the experiment every week. During the last two weeks until the end of the study (day 30 post icv-STZ), we performed several behavioural tests: species-typical behaviour (Marble Burying), object recognition memory (Novel Object Recognition), spatial memory (Barnes Maze), and depression-like behaviour (Forced Swim Test).

Our preliminary results show that STZ affected behavioural performance differently in the SAD model depending on the ovarian status of female rats. This verifies our hypothesis that ovarian steroid levels modify the impact of neurodegenerative effects induced by STZ icv.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Sex always matters: differential facilitation of an aversive memory by exercise in mice.

M. Jimena Santos [1], Soledad Picco [1], María Krawczyk [2], , Julieta Millan [2], Rodrigo Fernández [1], M. Eugenia Pedreira [1], Mariano Boccia [2],

1 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE) UBA-CONICET

2 Laboratorio de Neurofarmacología de los Procesos de Memoria, Cátedra de Farmacología, Fac. Farmacia y Bioquímica, Universidad de Buenos Aires/CONICET. Buenos Aires, Argentina.

Presenting author:
***María Jimena Santos**, jimenasantos23@gmail.com*

In the last years a growing body of research have focused in the study of physical activity on cognitive processes. Studies carried out in humans and rodents have found a correlation between exercise and improved cognition. Thus, exercise appears as a non-pharmacological tool for ameliorate cognitive impairments associated with aging. However, despite some encouraging results, variability in terms of positive effects on memory processes exists throughout the literature. In this sense, biological sex appears as an important variable of such modulation. Here we explored in males and females young mice adults the effect of wheel running in the consolidation and reconsolidation of an aversive memory. Briefly, after a period of adaptation to the wheel, animals were trained in the inhibitory avoidance task. Immediately after one group was allowed to run on the wheel for 20 minutes while another group ran after a reactivation session. Results revealed an improvement in memory when animals ran within the consolidation window but no effect was evident during reconsolidation. Furthermore, memory enhancement was found only in males. In terms of performance on the wheel running, no differences between sexes were found in distance traveled or speed, although preliminary results seem to indicate that females take longer time to get on the wheel. Ongoing research is aimed to deepen in the behavioral and physiological implications of such modulation and the differences between both sexes.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

The morphosyntactic decomposition of Spanish verb-noun compounds: an ERP study

María Mercedes Güemes [1], Joaquín Menéndez [2], Carolina Gattei [3] Alberto Iorio[2], Alejandro Wainselboim [4]

1 Institute of Philology and Hispanic Literature "Dr. Amado Alonso"- University of Buenos Aires,
2 Faculty of Psychology, University of Buenos Aires, Argentina/ Behavioral Biology Laboratory – Institute of Biological and Experimental Medicine,
3 IFIBA - Physics Institute of Buenos Aires, Argentina Neuroscience Laboratory - Torcuato di Tella University, Argentina Pontifical Catholic University of Buenos Aires, Argentina,
4 Human, Social and Environmental Research Institute - CONICET-Mendoza, Ciudad de Mendoza, Argentina

Presenting author:
***María Mercedes Güemes**, mercedesguemes@conicet.gov.ar*

The aim of this study is to investigate if Spanish verb-noun compounds, such as lavaplatos, are processed as unitary lexical units, or combinatorily through their constituents. Previous work has shown the importance of verb argument structure in the processing of these words (Güemes et al. 2019). In the present work, compounds were classified in two groups according to their semantic transparency: transparent or Agentives (AG), in which the referent takes the role of agent, and more opaque or Metaphorical (MET), which involve methaphorical patterns to construct their meaning. A lexical decision task was conducted with EEG recordings; the paradigm included two visual presentation modes: as whole words (Standard presentation), or separated into their constituents (Split presentation). Behavioral results showed that in both conditions AG compounds were responded significantly better and faster than MET words. An N400 effect was found for both AG and MET, but was enhanced for MET words in both presentation modes. This finding supports the view that MET compounds are decomposed into constituents. Therefore, semantic opacity of MET compounds does not seem to lead to differences in decomposition procedures: while in AG compounds the meaning of both constituents can be easily integrated to form compound meaning; in MET words, this procedure must be inhibited, and compound meaning accessed through the metaphoric relation that links both constituents.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Dichotic listening to unveil the processing of temporal information in sensorimotor synchronization

María Paula Caral [1], Ignacio Spiousas [2], Rodrigo Laje [2]

1 Laboratorio de Dinámica Sensomotora, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes.
2 Laboratorio de Dinámica Sensomotora, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes - CONICET.

Presenting author:
***María Paula Caral**, paulacaral@hotmail.com*

Sensorimotor synchronization (SMS) is the almost specifically human ability of synchronizing movements to an external, periodic sequence of stimuli and underlies much of music and dance. SMS belongs to millisecond timing, that is the processing of temporal information in the range of hundreds of milliseconds. Little is known about the brain mechanisms involved in this time range and in SMS in particular--for example, whether time processing takes place at the peripheral level, or at the sensory cortex, or at the motor cortex or it's distributed across many regions. The simplest task to study SMS is paced finger tapping: a participant is presented with an auditory stimuli (a periodic sequence of brief tones at a fixed pitch) and is instructed to tap in synchrony with the sounds. In experiments where auditory feedback is added to the taps, both stimuli and feedback are sent to both ears. In this work we manipulate stimuli and feedback to direct them into either the same or different ears (dichotic listening) in order to determine whether the processing of the time interval between stimuli and feedback, key to the error correction process, is done at the peripheral level or at higher stages. Preliminary results are compatible with the hypothesis that the processing takes place at auditory cortex and/or higher stages. To tell if at least part of the processing could be done at peripheral level when the information is available on the same side we need to test more subjects.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Search of functional and behavioral evidences of olfactory sensory pre-conditioning in honeybees Apis mellifera

María Paula Ospital, Fernando Locatelli

Departamento de Fisiología, Biología Molecular y Celular; FCEN; Instituto de Fisiología, Biología Molecular y Neurociencias; UBA-CONICET, Argentina.

Presenting author:
María Paula Ospital, *ospitalpaula@gmail.com*

Animals must be able to learn which elements of the sensory input belong together and constitute an object. To address the mechanisms related to this ability in honeybees we use an olfactory pre-conditioning protocol, which involves three phases. The first one is the stimulation with a binary odor mixture. Second, one of the components of the mixture is reinforced according to a Pavlovian conditioning protocol. Third, we test if the non-reinforced component of the mixture elicits the learned response. A positive response would serve as evidence that both odors have been associated during the first phase. Results obtained so far indicate a weak effect in the short-term and no long-term memory. In a second experiment we shortly desynchronized the odors during the first phase with the mixture, assuming that this would facilitate the detection of the individual components as constituents of the mixture. Despite of that, no evidence of pre-conditioning was observed. Finally, we performed calcium imaging of the neural activity patterns elicited by pure odors and mixtures. We address whether the patterns of activity elicited by pure odors are more similar to each other after sensory pre-conditioning than before, which it would constitute evidence that stimulation with an odor retrieves the other one. Nevertheless, our results indicate the opposite. So far, all our results indicate that olfactory sensory preconditioning is not a robust phenomenon in honey bees.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Early memory impairment in altered fasting glucose patients?

María Pilar Canal [1], Mariana Gabriela Munner [2], Ornela Azul Caruso [2], María Verónica Baez [1]

1 IBCN (CONICET - UBA)
2 Hospital General de Agudos Jose María Penna

Presenting author:
***María Pilar Canal**, pili.canal31@gmail.com*

Type 2 Diabetes (DBT2) is a metabolic syndrome characterized by an increase in glucose and insulin blood levels (hyperglycemia and hyperinsulinemia respectively). This syndrome is closely related to neurodegeneration and central nervous system damage.

Prediabetes 2 (preDBT) is considered to be a step before DBT2, with glucose levels intermediate between normal and DBT levels. However, it is not well understood if preDBT per se, or the progression to DBT2, could cause cognitive decline. Because of this, we decided to investigate whether this damage can be found in patients with altered fasting glucose (AG), the first clinical demonstration of preDBT. For this reason, AG and control patients were asked to perform the Rey–Osterrieth complex figure test (ROCF), to discard any impairment in graphical performance and procedural memory; the SAGE test, to assess different stages of early memory impairment; and the evocation of a list of words, to evaluate long term memory (LTM). We found that there were no significant differences between AG and control groups in the ROCF test or in LTM. However, AG patients showed a poor performance in the SAGE test, due to an impairment in short term memory (STM), attention, construction of simple forms and associative memories. Furthermore, performances in the SAGE test correlate in a negative form with the increase in glucose levels .

These preliminary results lead us to hypothesize that cognitive impairment could start during AG period.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Involvement of newborn and mature granule cells in contextual memory engrams.

María Sol Ramos , Lucía Rodriguez , Mora Ogando , Macarena Amigo Durán , Sebastian Alejo Romano , Antonia Marin Burgin , Noel Federman

Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) – CONICET - Partner Institute of the Max Planck Society

Presenting author:
***Maria Sol Ramos**, m_sol_ramos@hotmail.com*

Memories are believed to be encoded by memory traces or engrams, represented within subsets of neurons that are synchronously activated during learning. The hippocampus is a brain region required for learning, memory and spatial coding. The input region of the hippocampus, the dentate gyrus (DG), plays a major role in these processes and generates new adult-born granule cells (abGCs) throughout life. However, the participation of these neurons in memory engrams remains unclear. Here we investigated abGCs and mature granule cells (mGCs) contribution to an enriched environment (EE) engram. On day one we injected tamoxifen to express Tomato in abGCs using double transgenic cfostTA; Ascl1CreERT2; CAGFloxStopTom mice. An AAV9-TRE-GFP was then used to label activated neurons in the DG. Temporal control over GFP expression was achieved by administering an on-Dox diet. Mice were taken off-Dox 4 weeks after tamoxifen injection and 48 hs prior to EE exposure. Our preliminary results showed that the proportion of activated abGCs after EE was higher than the proportion of mGCs activation, implying that newborn neurons are strongly activated after contextual encoding. To further evaluate the contribution of abGCs to other hippocampal-dependent behaviors, we are conducting experiments training mice to perform a GO/NO GO discrimination task in a virtual reality environment. These experiments will shed light on the contribution of newborn neurons to contextual memory engrams.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Using pupillometry to study sentence comprehension: cognitive effort and syntactic complexity

Marisol Murujosa [1,2], Carolina Gattei [2,3,4,5], Diego Shalom [2,3,4], Yamila Sevilla [1,2]

1 Universidad de Buenos Aires. Facultad de Filosofía y Letras. Instituto de Lingüística.
2 Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)
3 CONICET – Universidad de Buenos Aires. Facultas de Ciencias Exactas. Instituto de Física de Buenos Aires (IFIBA)
4 Universidad Torcuato Di Tella. Laboratorio de Neurociencia
5 Pontificia Universidad Católica Argentina

Presenting author:
***Marisol Murujosa**, marisolmurujosa@gmail.com*

Task-evoked pupillary responses (TEPR) have been used as a reliable neurophysiological index of cognitive effort in different domains (Beatty, 1982; Beatty & Lucero-Wagoner, 2000). In the sentence comprehension domain, TEPRs have provided a measure of differential processing cost according to the type of structure and its syntactic complexity (e.g, Just and Carpenter, 1993; Scheepers & Crocker, 2004; Sevilla et al. 2014). Sentences with subject-extracted (S) relative clauses (RC), have been consistently reported in psycholinguistic literature to be easier to process than object-extracted (O) RCs (e.g. in Spanish, Betancort et al., 2009; Sánchez et al., 2017). However, there have been no studies evaluating the comprehension of RCs in Spanish using TEPRs. In this study, an auditory sentence comprehension task with SRCs and ORC in Spanish was carried out. Response accuracy, reaction times (RTs) and TEPRs were measured during the task. Pupil diameter was monitored using a desktop-mounted, video-based eye tracker at a sampling rate of 1000 Hz. Linear mixed-effect models were fitted for data analysis. Results show that ORCs were harder to comprehend than SRCs: more prone to errors ($p < .001$), processed more slowly ($p < .001$) and showed higher increase in pupil size ($p = .03$). Our data agrees with previous studies on the comprehension of RCs and confirm the sensibility of TEPRs as a proxy for cognitive effort related to syntactic processes in sentence comprehension.

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E-Posters

COGNITION, BEHAVIOR AND MEMORY

Training Scientific Thinking: Effect of an Intervention on Argentinian Adolescents' Critical Thinking Skills

Martina Boscolo [1], Melina Furman [2,3], Lorena Rela [4], Pedro Bekinschtein [5], Rodrigo Laje [2,6], Andrea P. Goldin [1,2]

1 Laboratorio de Neurociencia, Universidad Torcuato Di Tella.
2 Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ministry of Science, Buenos Aires, Argentina.
3 Escuela de Educación, Universidad de San Andrés.
4 Instituto de Fisiología y Biofísica Bernardo Houssay, Facultad de Medicina, Universidad de Buenos Aires, CONICET.
5 Laboratorio de Neurociencia y Sociedad, Instituto de Neurociencia Cognitiva y Traslacional, CONICET, Fundación INECO, Universidad Favaloro.
6 Laboratorio de Dinámica Sensomotora, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Bernal, Argentina.

Presenting author:
***Martina Boscolo**, martiboscolo@gmail.com*

Scientific or critical thinking is an intentional cognitive process of knowledge application which consists of using evidence to revise an existing theory, and constitutes a very important part of inquiry-based learning. This type of reasoning, associated with executive functions and prefrontal and temporal areas, is considered an essential skill for the 21st century citizen. Evidence suggests that it can be improved through specific training, and that, under certain circumstances, it is possible to transfer its learning to different domains in everyday life. We designed an instrument to test scientific thinking skills and we used it to evaluate 290 argentinian adolescents' responses before and after attending a scientific camp organized by the NGO Expedición Ciencia.

Keywords: scientific thinking, critical reasoning, transfer, training, adolescence

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Mass behavioral assay to measure odor attractiveness and plasticity in Drosophila melanogaster

Matías Alemán [1], Fernando Locatelli [2], Nicolás Pírez [2]

1 Departamento de Fisiología, Biología Molecular y Celular; Facultad de Ciencias Exactas y Naturales; Universidad de Buenos Aires, Argentina.
2 Instituto de Fisiología, Biología Molecular y Neurociencias; UBA-CONICET, Argentina.

Presenting author:
***Matías Alemán**, matialeman@hotmail.com*

Insects rely on olfaction to find food and mate. The olfactory cues that drive different behaviors are expected to have been determined by evolution and thus the neurobiological mechanisms involved in detecting and encoding relevant odors are assumed to depend on hardwired circuits. However, it is well established, that learning and memory have a large impact in tuning olfactory guided behaviors. The fly Drosophila melanogaster is one of the models in which the link between olfactory circuits and behavior is best understood. In order to unveil the neural bases of odor guided behavior, big efforts are made to identify attractive, aversive and neutral odors. Here we started a project aimed at establishing a simple method that would allow us to measure innate and acquired odor attractiveness. The method is based on a differential trap assay. Fifty flies are enclosed in a chamber, which includes two vials with odorant solutions. Once the flies enter the vials, presumably attracted by the odors, they can´t come out. The attractiveness is determined based on the ratio between the numbers of flies trapped in each vial. So far, we found the experimental conditions in which propionic acid shows strong attractiveness, but 2-heptanone and ethyl butyrate do not. Interestingly, these results were obtained in flies that were reared in vials scented with propionic acid. Future experiments will address if the preferences change when flies are reared in a medium with one of the neutral odors.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

False memory formation during Covid-19 quarantine: age, sleep quality and emotional variables. Preliminary results.

Matías Bonilla [1], Facundo Antonio Urretra [1], Candela Sofía León [1], Natalia Lippmann-Mazzaglia [2], Camila Calvo [2], Manuel Garrido [2], Cecilia Forcato [1]

1 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires.
2 Innocence Project Argentina

Presenting author:
***Matías Bonilla**, bonillamatias@gmail.com*

Aging is a crucial factor in the formation of false memories. Older adults are prone to create a higher rate of false memories. Anxiety and depression as well as sleep quality were affected by Covid-19 pandemic situation. Preliminary studies of our Lab showed that codification and consolidation of episodic memories as well as recognition were impaired in young adults. Thus, we hypothesized that facial recognition of perpetrators involved in criminal events had to be impaired. Participants watched a video of a criminal act on day 1. On day 2 they had to recognize the perpetrator on a facial recognition round. Based on age range a significant difference was observed in the proportion of correct recall. Older people recognized the perpetrator significantly less than teens (21.74%, 50% respectively) and they did not differ with young adults (31.25%). There were no significant differences in the self-confidence rate (~68%) between groups, even if the perpetrator was recognized or not. Older adults who slept worse and those who scored higher in anxiety traits had more false recognitions. It is important to highlight that the overall recognition rate was low (35%). We suggest that this deficient performance was due to the actual stressful situation and the consequences in the sleep quality. Thus, it is important to have these results in consideration if a facial recognition round has to be carried out in this context to define someone's life destiny.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Dopaminergic and Noradrenergic systems in memory stabilization: a behavioral tagging approach

Matias Schroeder, Camila Fullio, Diego Moncada

Laboratorio de Biología del Aprendizaje y la Memoria, Instituto de Biología Celular y Neurociencia, CONICET-UBA, Buenos Aires, Argentina

Presenting author:
Matias Nicolas Schroeder, *matias.nicolas.sch@gmail.com*

It is proposed that the consolidation and reconsolidation of memories are based on a behavioral tagging and capture process. That is, the setting of a tag at the appropriate neural substrate during learning, or memory reactivation, ensures the stabilization of the trace upon the capture of newly synthesized proteins (PRPs). Also, dopamine and noradrenaline have been considered neuromodulators in various processes, including memory. Here, we studied whether these neurotransmitters and their main sources (Ventral Tegmental Area -VTA- and Locus coeruleus-LC-) act on memory by regulating the synthesis of PRPs on brain structures where they will be stored.

We show that coupling the activation of the VTA to a training in the spatial object recognition task, or the reactivation of its memory, ensures the stabilization of the memory trace, otherwise impaired by the administration of protein synthesis inhibitors during learning or reconsolidation. This process relies on the function of hippocampal dopaminergic receptors and subsequent protein synthesis. Similar findings are reported for the LC and the β-adrenergic receptors, along with further insights on these neurotransmitter systems functions.

In summary, our results suggest that the VTA and the LC act over the hippocampus via the D1/D5-dopaminergic and the β-adrenergic receptors, thus regulating the synthesis of the PRPs required for memory stabilization; revealing a way in which neuromodulator systems regulate lasting memories.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Synaptic output of dopaminergic neurons only modulate positively contextual memory in Drosophila

Melina Petrissans, Carolina D'Odorico, Micaela Vicente Biscardi, Mario Rafael Pagani

Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, Universidad de Buenos Aires, CONICET, Buenos Aires, Argentina.

Presenting author:
***Melina Petrissans**, melipetrissans@gmail.com*

An emerging model in associative learning and memory in Drosophila, suggests that dopaminergic neurons (DANs) modulate the synaptic output of mushroom body neurons driving the appropriate behavior (approaching or avoidance). However, whether DANs are involved in contextual memory is unclear. Here, we examined the role of dopaminergic neurons in contextual memory in freely behaving flies. We blocked neuronal activity of specifics subset of DANs by using the thermosensitive allele Shits1.

We found that contextual memory is promoted by two kinds of DANs. The first kind corresponds to those DANs that prevented habituation during training in the contextual learning (PPM2), whereas the second kind corresponds to neurons that promoted habituation during training (PAL). Interestingly, there are no DANs preventing contextual memory, as it was found for learning.

Contextual memory required synaptic output from a smaller number of dopaminergic neurons than that required for contextual learning. Of note, DANs involved in contextual memory are not the same neurons implicated in learning as it is reported in associative learning.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Machine Learning algorithms to increase children motivation in cognitive training videogames

Matias Schroeder [1], Camila Fullio [1], Diego Moncada [1]
1 Laboratorio de Neurociencia, Universidad Torcuato di Tella - CONICET
2 Laboratorio de Inteligencia Artificial Aplicada, Depto. de computación, FCEyN, UBA–CONICET

Presenting author:
***Melina Vladisauskas**, m.vladisauskas@gmail.com*

Mate Marote is an open source cognitive-training software aimed at children from 5 to 8 y.o. It consists of a set of computerized games specifically tailored to train executive functions (EF): a class of processes critical for purposeful goal-directed behavior, including working memory, flexibility, and cognitive control.

For the last ten years we have been using this software to measure and train children's EF at their own schools. The interventions involve 4 sequential stages: (1) familiarization, (2) pretest (baseline), (3) training and (4) posttest. At present, all children start playing each training game at the same difficulty level. While the trials' complexity rapidly adjusts to the child's performance, starting in a non-challenging level may cause some children a motivational decrease, which is a known factor that can diminish the positive outcomes of a cognitive training intervention.

In the present study, we used Machine Learning to create an algorithm that classifies children in groups according to their performance in stage 2 in order to personalize stage 3. We trained and tested the algorithm with data from an intervention in which 73 6-year olds participated. This is the first time that we apply these computational models to our data, and preliminary results suggest that the algorithm fits the data neatly and can be applied in future interventions. Further studies will test whether this approach results in better cognitive training.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Inhibition of astrocyte function in the basolateral amygdala complex during the acquisition of contextual fear memory

Melisa Riva Gargiulo [1], Victor Molina [1], Crhistian Luis Bender [1]

Instituto de Farmacología Experimental de Córdoba-CONICET. Facultad de Ciencias Químicas, Departamento de Farmacología, Universidad Nacional de Córdoba, Córdoba, Argentina.

Presenting author:
***Melisa Riva Gargiulo**, melisa.gargiulo.080@mi.unc.edu.ar*

Introduction
In the last decades, the acknowledge of the fundamental contribution of astrocytes to the synaptic functioning and plasticity promoted the study of the role that astrocyte could have on memory. However, little is known about the role of astrocytes from the basolateral amygdala complex (BLA-C) on the contextual fear conditioning (CFC).

Methods
To target astrocyte function during the CFC we used fluorocitrate (FLC) that selectively and temporally inhibits astrocyte metabolism. Adult wistar male rats were bilaterally canulated in BLA-C and leave for recovery for 10 days. Then they were infused with different doses of FLC (0.5 or 1 nmol/0.5 uL) or saline 60 minutes before conditioning. Memory was evaluated 2 and 4 days after conditioning in the same context using freezing time as fear memory index.

Results
The groups of animals that received FLC (with both doses) showed a significant reduction of freezing during memory testing respect to saline treated controls. Thus, functional inhibition of BLA-C astrocytes during CFC disrupted the fear memory.

Conclusions
The results suggest that BLA-C astrocytes play a role in the acquisition/consolidation phases of CFC, suggesting that they are critically involved on the formation of fear memories.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Characterization of age-related differences in impulsivity among adolescent and adult rats

Micaela Betsabe Marini, Cecilia Martinez
Grupo Neurociencias de Sistemas, IFIBIO-Houssay, UBA-CONICET

Presenting author:
***Micaela Betsabe Marini**, micaelamarini@gmail.com*

Adolescence is a developmental period in which many behavioral and physiological changes occur, preparing individuals for their independence. There are age-related increases in social interactions and a also a clear preference for risk-taking/novelty seeking behaviors. Consistently with this, in freely-moving experiments in a self-initiated task we have found a higher amount of premature responses in adolescent rats. Thus, the aim of this project is to fully characterize how adolescents and adults learn an action sequence in order to obtain a reward and also to find which aspects of adolescent behavior could be at the basis of the impulsivity we have previously observed in this task. We will train p30, p 45 and p60 rats of both sexes and evaluate their performance in other paradigms such as the open field and Y-maze. Here we show the results obtained with the first group of adults. In a next stage, after the behavioral analysis is complete, we will assess the involvement of different brain structures with pharmacological inactivation.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Synaptic output of dopaminergic neurons controls contextual learning by promoting antagonistic behaviors in Drosophila

Micaela Vicente Biscardi, Carolina D`Odorico, Melina Petrissans, Mario Rafael Pagani

Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, Universidad de Buenos Aires, CONICET, Buenos Aires, Argentina.

Presenting author:
Micaela Vicente Biscardi, *mikavi98@hotmail.com*

Accumulated evidence supports an emerging model for the neuronal control of behavior in associative learning in Drosophila. In such model, dopaminergic neurons (DANs), which encode the unconditional stimuli, modulate the synaptic output of mushroom body neurons driving the appropriate behavior (approaching or avoidance). However, studies in vertebrates have shown that self-motivated contextual learning and other forms of learning depend on distinct molecular and cellular mechanisms. Here, we examined the role of dopaminergic neurons in contextual learning in freely behaving flies.

We blockade or enhanced neuronal activity of subset of DANs by using the several GAL4 lines to drive the expression of the thermosensitive allele Shits1 or TrpA1. We found that in contextual learning, flies showed habituation of the exploratory activity, which is controlled by DANs. Preliminary studies indicate that, habituation was promoted by two different clusters of DANs. Three neurons from the PAL cluster or one to four PPL2 neurons, or possibly both subsets contributed to promote habituation. Interestingly, habituation also was prevented by two different clusters of DANs. Neurons from the PAM cluster and one to two neurons from the PPM2 cluster were individually sufficient to prevent habituation. Taken together, habituation of a motivated behavior is under positive and negative control of DANs.Cognition, Behavior and Memory

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Cognitive function of hippocampal dentate gyrus during goal-guided spatial behavior

Natalia Soldi [1], Luciana Farella [1], Alejandro F. Schinder [1], , Verónica C. Piatti [1],

1 Laboratorio de Plasticidad Neuronal - Fundación Instituto Leloir - Instituto de Investigaciones Bioquímicas Buenos Aires- CONICET

Presenting author: ***Natalia Soldi***, *natalia.soldi@gmail.com*

The hippocampus is essential for episodic memory and is thought to be involved in binding stimuli to their spatio-temporal context. However, how similar experiences are distinguished remains unknown. The dentate gyrus (DG) of the hippocampus is needed for the discrimination of similar spatial stimuli. Therefore, we think that DG could contribute to the distinction of similar events experienced temporally close in the same context. We set up an everyday spatial memory task in a crossword-like maze with easy or difficult paths to find a reward. Adult mice were co-infected with an AAV-floxed HA-hM4Di plus a CAG-Cre retrovirus in the dorsal DG, which resulted in the expression of the silencing synthetic receptor hM4Di in commissural DG fibers. This strategy allowed the DG perturbation upon application of the synthetic agonist clozapine-N-oxide (CNO) while the animals explored the maze. In a single day we evaluated the animals' learning of two new spatial routes of the same level of challenge with or without CNO. The mice learned easy or difficult journeys to the goal, but CNO-mediated DG perturbation slowed down the acquisition of the second daily route, independently of the complexity of the path. Performance on the difficult but not the easy path was impaired on the everyday memory test under CNO effect. These results suggest that the DG is necessary for learning similar spatial experiences and for daily complex memory retrieval.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Out of the Body Experience during Sleep Paralysis: an altered state of consciousness

Nerea L. Herrero [1], Francisco T. Gallo [1], Pablo Gleiser [3], C Forcato [1]

1 Laboratorio de Sueño y Memoria, Departamento de Ciencias de la vida, Instituto Tecnológico de Buenos Aires (ITBA)
2 COMISION NACIONAL DE ENERGíA ATOMICA
3 Departamento de Fisica Medica, Centro Atomico Bariloche

Presenting author:
Nerea Lucia Herrero, *nerea.herrero73@hotmail.com*

Sleep paralysis is caused by an intrusion of REM sleep in wakefulness. It is characterized by the incapacity to move, the sense of a presence, auditory and visual hallucinations and in some cases, out of body experiences (OBE). OBE is an altered state of consciousness, defined as a subjective sensation of being outside one's own body. It can occur spontaneously or it can be induced.

Here, we conducted an interview with subjects who experienced OBE during sleep paralysis (natural OBEs) and subjects who have learned to initiate it (learned OBEs).
We observed that learned and natural OBEs described the state of consciousness associated with the experience as similar to wakefulness or even increased. This augmented state was related to a subjective perception of increase in information processing.

Learned OBEs significantly identified sounds and body vibrations before the OBE was initiated thus they could be considered as aura sensations for OBE initiation. Importantly, we found that learned OBEs showed significantly more positive emotions associated with the experience (like peace and joy) while natural OBEs showed more negative emotions.
At present, there is no specific treatment for sleep paralysis. Sleep hygiene is recommended and selective serotonin reuptake inhibitors are used but they are not always effective. Thus, we propose that the OBE could be used as a way to overcome sleep paralysis.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Your environment defines you: The effects of environmental stimulation over the brain in an early obesity rat model

Nicolás Fabre [1], Guillermina Canesini [1], Rocio Schumacher [1] Cora Stoker [1], Luisa Gaydou [1], María F. Andreoli [2], Jorge G. Ramos [1], María F. Rossetti [1]

1 Institute of Health and Environment of Litoral, CONICET-UNL, Department of Clinical Biochemistry Faculty of Biochemistry and Biological Sciences, Santa Fe, Argentina

2 Institute of Development and Pediatric Research (IDIP), La Plata Children´s Hospital and Scientific Research Commission, Province of Buenos Aires (CIC-PBA), La Plata, Argentina.

Presenting author:
***Nicolás Fabre**, fabrenicolas04@gmail.com*

Early obesity has been related to changes in the normal structure and function of the brain. Environmental stimulus can intensify or attenuate these changes. We analyzed the effects of an early obesity model, and the later exposure to an enriched environment (EE), over metabolic parameters, mRNA expression of key brain genes, and cognitive performance. For that, litters of Wistar rats were kept unchanged (Normal Litter, NL) or reduced to 3/4 male pups (Small Litter; SL). At postnatal day 21 (PND21), a group of NL and SL rats were sacrificed to evaluate short-term changes. The remaining animals were divided into EE and standard environment (SE) conditions, and at PND90 they were tested in the Episodic-like memory (ELM) and Locomotion activity (LA) tests, and then sacrificed to evaluate medium-term changes. CA1, CA3, and GD areas were isolated from the rat brain by micropunch technique, and gene expression of BDNF and VEGF was evaluated by Rt-qPCR. In PND21, SL showed an increase in adiposity and levels of glucose, cholesterol, and triglycerides ($p < 0.05$). In PND90, the SL-SE group showed lower performance in the ELM test compared to SL-EE, NL-SE, and NL-EE ($p<0.05$). In the LA test, NL-EE showed a higher frequency of rearing compared to NL-SE, SL-SE, and SL-EE ($p<0.05$). Gene expression is still under study. These results show that early obesity could affect metabolic parameters and cognition in the short and medium-term, while EE could attenuate these changes.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Interval timing in Drosophila: an opportunity to reveal the neurobiological basis of time perception

Nicolás Lautaro Tassino, Lia Frenkel

Laboratorio de Neurociencias del Tiempo- iB3 | Instituto de Biociencias, Biotecnología y Biología traslacional- Facultad de Ciencias Exactas y Naturales- Universidad de Buenos Aires

Presenting author:
Nicolás Lautaro Tassino, *nicotassino@gmail.com*

The neurobiological basis of time estimation are still an unsolved puzzle. A sexy hypothesis proposes that it encloses cognitive processes such as attention, learning, working memory and decision-making. Time estimation would be a specific type of working memory and behaviour would be the result of decisions based on time perception. To understand the ability to estimate time we make use of the interval timing skill of the fly Drosophila melanogaster. We designed an experimental setup that enables the study of a time-referenced memory in the fly based on the proboscis extension response to a sucrose solution. Briefly, we offer a sucrose solution drop to a thirsty/ hungry fly at a fixed interval and record its behavioural response. We operationally define time-referenced memory when the fly extends its proboscis anticipating the appearance of the drop. Preliminary results with w1118 strain suggest that flies develop an anticipatory proboscis extension reflex (A-PER) over time. The response gets closer to the interval of the experiment as trials increase. Only 40% of the flies have shown A-PER at the sixth trial while 80% did at the ninth. For an interval of 60 seconds this response gets as close as 55,5s ± 4,6s at the evaluation trial. Here we demonstrate that wild type Canton S stock are able to learn intervals. We conclude that our experimental setup is promising to unveil the mechanisms involved in temporal reference memory and propose a neurogenetic strategy to approach it.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Not so resting state: Signatures of word memory consolidation during resting-state EEG

Nicole Coaker [1], Leonardo Molano Ramírez [2], Laura Kaczer [1] Luz Bavassi [1]
1 Laboratorio de Neurociencias de la Memoria, IFIBYNE, UBA, CONICET,
2 Centro Atómico Bariloche

Presenting author:
Nicole Coaker, *nikicoaker@gmail.com*

Learning new vocabulary can be characterized by a great deal of individual variability. Brain activity patterns at rest are associated with various cognitive abilities, but their implication in the formation of linguistic memories has not been determined so far. In this study we hypothesize that the level of word learning obtained by an individual will differentially modulate the spontaneous activity of the brain after the task. The protocol consists of 4 stages: first, subjects perform a series of neuropsychological tests: digit span, phonological and semantic fluency, in order to have a general measure of their short-term memory and their language abilities. Second, the first EEG recording at rest (eyes-closed) is performed, which serves as a baseline. Afterwards, a word learning task is carried out, where participants have to learn the names and definitions of nine novel words. Finally, the EEG activity is recorded again at rest for 5 min. We carried out a spectral analysis, determining the intensity of the various frequency bands and compared both resting state periods with nonparametric statistical analysis. Our preliminary results show a positive correlation between alpha power (8-12 Hz) and the memory for new definitions. Besides, the obtained topography reveals a right lateralization, in coincidence language processing studies. We plan to study the synchronization for alpha between specific brain areas involved in memory and language.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Electronic reading: Impact of different digital devices on reading comprehension

Pedro Benedetti*[1], Andrés Cotton*[4], Fabricio Ballarini [1,2] Valeria Abusamra**[3,4], Daniela Ramírez Butavand [1,2]**

1 ITBA
2 Instituto de Biología Celular y Neurociencias, UBA, CONICET,
3 CIIPME, CONICET,
4 UBA

Presenting author:
***Pedro Joaquín Benedetti**, pedrojbenedetti@gmail.com*

It is increasingly common to read and study on electronic devices and previous research suggests that technology influences the way we read and process textual information.Therefore, we decided to investigate the impact of the device type (smartphone or computer) on reading comprehension from a psycho and neurolinguistic perspective. A website and a reading comprehension screening were designed and 1619 people were evaluated considering their ages, formal education and reading habits. The score obtained and the efficiency (score/time) were compared in 3 age groups: 15-30 years, 31-50 years and 51-70 years.

Significant differences in efficiency were observed (one-way ANOVA: $F(2.1616)=7.03$, $p=0.0009$) and the post hoc analysis of multiple comparisons showed a significant improvement in the efficiency of the younger age group in comparison with both the 31-50 year-old group ($p=0.0048$) and the 51-70 year-old group (0.0140). No differences were observed in the score obtained by these groups (one-way ANOVA: $F(2.1616)=2.60$, $p=0.0747$).

When comparing the performance between smartphone and computer reading in the different age groups, no statistically significant differences were found in the obtained scores (two-way ANOVA, device factor: $F(1.1598)=0.1818$, $p=0.6699$), nor in the efficiency (two-way ANOVA, device factor: $F(1.1598)=1.842$, $p=0.1749$).

*, ** Equal Contribution.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Behavioral Tagging as a mechanism for aversive-memory formation under acute stress.

Ramiro Tintorelli*, Pamela Lopes da Cunha*, Julieta Correa, Pablo Budriesi, Haydée Viola

Laboratorio de Memoria, Instituto de Biología Celular y Neurociencia "Prof. E. De Robertis" (IBCN), Facultad de Medicina, UBA-CONICET, Buenos Aires, Argentina.

Presenting author: ***Ramiro Tintorelli***, *ramitintorelli@gmail.com*

The Behavioral Tagging hypothesis (BT) postulates that a weak learning experience, that only induces short-term memory, can be benefited from another event that provides the plasticity-related products (PRPs) to establish a lasting memory. According to BT, the weak learning sets a transient neural-tag at specific activated sites; thus, LTM would be formed by the temporal and spatial convergence of this learning-tag and the PRPs. Also, BT proposes that the tags set by different tasks located in a common population of neurons could compete for the available PRPs.

In this work, we focused on studying how an extrinsic stressor affects the formation of an aversive memory, analyzing the results under the BT framework. Rats were subjected to a weak inhibitory-avoidance training (wIA) and we observed that stress (elevated platform) experienced 1 hour before wIA training promoted IA-LTM formation. This effect was dependent on glucocorticoid-receptor activity as well as protein synthesis in the dorsal hippocampus. However, the same stress impaired the LTM induced by a strong IA-training. Since this negative effect was reverted by a novel-OF exploration, a PRP-provider event, a competence for the PPRs utilization could be taking place. Finally, it was demonstrated that stress immediately after IA-training does not prevent the setting of learning-tag, but it also promotes IA-LTM formation. These findings reveal that acute stress could impact on IA-LTM formation through the BT processes.

*Equal contribution.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Nonlinear Heart Rate Variability analysis of a Compassionate Schools Research Initiative

Rocio Martínez Vivot [1], Marcela Matos [2], Isabel Albuquerque [2], Frances Maratos[3], Paul Gilbert [3], Daniel E Vigo [1]

1 BIOMED - UCA - CONICET
2 Center for Research in Neuropsychology and Cognitive Behavioral Intervention - University of Coimbra
3 University of Derby

Presenting author:
***Rocío Martinez Vivot**, rmartinezvivot@gmail.com*

While compassionate-based interventions have shown numerous benefits in diverse populations, our aim is to contribute to the validation of the efficacy of the Compassionate Schools Program (CSP) by addressing the role of the autonomic nervous system in the improvement of well-being indicators.

Nonlinear HRV analysis was conducted in 153 Portuguese teachers enrolled in the CSP Trial (the data corresponds to the Portuguese Compassionate Schools Research Initiative). Preliminary results suggest significant differences between nonlinear HRV indexes (SampEn and alfa1) when comparing the intervention group versus the control group. These results hint at an increase in flexibility (adaptability) in the physiological functioning and "complexity", confirming the CSP may exert part of its effects by influencing autonomic activity.

The importance of this work lies in the validation of the usefulness of this program as an effective psychological intervention to promote physiological well-being in educators that could reduce burnout, depression and other stress symptoms.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Multimodal neurocognitive signatures of naturalistic action language in frontal lobe epilepsy: A combined behavioral, neuroimaging, and machine learning approach

Sebastian Moguilner[1], Agustina Birba[1], Daniel Fino[3] Roberto Isoardi [3],Celeste Huetagoyena [4], Raul Otoya [4], Viviana Tirapu [3], Fabián Cremaschi [2], Adolfo Garcia [1], Agustín Ibáñez [1]

1 UDESA
2 UNCUYO
3 FUESMEN
4 NEUROMED

Presenting author:
***Sebastian Moguilner**, sebagam@gmail.com*

Standard frameworks to diagnose frontal lobe epilepsy prove nosologically unspecific, as they reveal deficits that also occur across other epilepsy types. Moreover, most existing results are undermined by low ecological validity. To face this challenge, we employed a naturalistic discourse paradigm combined with structural and functional brain connectivity measures in an analytical setting that integrates inferential statistics and machine learning. We assessed 19 frontal lobe epilepsy patients, 19 healthy controls, and 20 posterior cortex epilepsy patients, matched for sex, age, education, and neuropsychological variables. An ANCOVA revealed an interaction between group and condition for the action texts [$F(2,110) = 8.14$, $P < .01$, $\eta 2 = .26$)], showing that patients with frontal lobe epilepsy were selectively impaired in grasping verb-related information. Such deficit was selectively and specifically correlated with (a) reduced integrity of the anterior thalamic radiation ($r = 0.869$, FDR-corrected $P = .038$), and (b) hypoconnectivity between the primary motor cortex and the left-parietal/supramarginal regions ($r = 0.707$, FDR-corrected $P = .046$). Machine-learning classifiers based on the above neurocognitive measures yielded 75% accuracy rates in discriminating individual frontal lobe epilepsy patients from both controls and posterior cortex epilepsy patients. Taken together, this multimodal approach opens new venues to complement mainstream cognitive assessments in epilepsy.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

A highly demanding working memory task reduces the reconsolidation of a threat memory and its biases processing towards threat

Soledad Picco [1,2], Rodrigo Fernandez [1,2], Maria E. Pedreira [1,2]

1 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE)- CONICET, Ciudad de Buenos Aires, Argentina.
2 Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Ciudad de Buenos Aires, Argentina.

Presenting author:
***Soledad Picco**, solepicco@gmail.com*

Consolidated memories can be reactivated into a labile state by the presentation of a reminder. The reactivation of the memory trace is followed by a process of re-stabilization known as reconsolidation. In most of reconsolidation studies, a second task, with similar characteristics to those of the target memory, is used as an amnesic agent.

Anxiety manifest as a persistent and generalized defensive system, activated when predicted aversive events are perceived as a threat and uncertain. In laboratory, threat conditioning has been taken as the paradigm for assessing fear memories and anxiety related disorders. In the framework of the reconsolidation the idea that this process would allow to modify this type of maladaptive memories has been proposed.

Here we aim to interfere the re-stabilization of an implicit aversive memory in humans using a high demanding working memory task, which aimed to overload this transient memory system. To reach such goal, we designed a 3 day protocol, and compared a trained threat conditioning group, that 24hs later had or not a reminder, or a fake working memory task; 48hs after, all 3 groups performed an extinction follow by a reinstatement and several tasks targeting cognitive bias towards threat. We revealed that the memory reconsolidation interference is effective for the implicit memory retention but not for the declarative memory. Finally, we showed how the interference reduced biased processing towards threat.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Familiarity and Confidence Could Prime Complex Decision Making With Social Implications

Tomás Alves Salgueiro [1], Franco Agustín Bernal [1], Damián Furman [2] Juan Manuel Pérez [2], Pablo Nicolás Fernández Larrosa [1]

1 IFIByNE - CONICET // FCEN, UBA
2 ICC / DC // FCEN, UBA

Presenting author:
***Tomás Alves Salgueiro**, tomasalvessalgueiro@gmail.com*

Some decision-making processes, like those during presidential elections, are complex and require great cognitive engagement. Under the hypothesis that frequent exposure to candidate image (familiarity) or its confidence (associated to previous information, with emotional content) could drive decision-making, online social surveys were conducted during the 2019 Argentine Presidential Elections, as well as news (scraped from written media published from September 21 to October 27) were analyzed to assess each candidate mention frequency. Familiarity (F), Confidence (C), and Voting probability (VP) were estimated for each candidate from the surveys, as well as the main means used by the participants to inform themselves about the candidates. Through a least-squares analysis, C and F were observed to be the variables that mostly explain the VP variance. Significant differences were observed between candidates for three variables [Kruskal-Wallis test; C: H(5, n=2467)=244,1753;p=0,000; F: H(5, n=2467)=809,8072;p=0,000; VP: H(5, n=2467)=620,8873;p=0,000]. In a cross-analysis between variables and for different candidates, C was found to correlate better (than F) with VP (Spearman Correlation) but both were significant in most analyses. Besides, the average of F, C, and VP for each candidate correlates significantly with the frequency of mentions (for the written media analyzed), advertising costs, and election results.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Do I need to know who is teaching me? Effects of prior knowledge about teachers on learners' performance.

Tomás Delgado*, Julieta Goldstein*, Ariel Haimovici, Cecilia Inés Calero
Laboratorio de Neurociencia, Universidad Torcuato Di Tella

Presenting author:
Tomás Delgado, *tmsdlgd@gmail.com*

Recently, a Bayesian approximation was proposed for understanding pedagogical situations (Shafto et al, 2008)*. In this context, different models have evaluated how a teacher chooses limited examples with the objective of having a learner infer (learn) a concept. But these don't explore the relevance that knowing your teacher may have on learning. Hence, we wondered how prior information about the teacher would affect learners' inferences of new concepts.

Extending the Little Teachers project, we present a new paradigm, in which a teacher helps a learner to find a secret box on the screen using a limited set of cues. First, young adults were placed in the learners' role knowing (or not) that they were receiving cues chosen by 2nd, 4th or 6th graders, and then they were placed in the teachers' role. Our ongoing results indicate that (1) performance increases when playing consecutively with the same teacher and (2) knowing the teachers' age has a complex impact: It improves performance at first, but it seems to overshadow the teachers' particular strategies. In fact, it had a significant negative effect on performance for learners whose teachers were 2nd graders. Interestingly, adults in the teachers' role chose examples highly biased by the strategies used by their teachers, even when they reported those as "bad". These results suggest that prior knowledge about teachers can affect learners' performance and teaching strategies.

* Equal Contribution

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Assessment of autonomic reactivity: Comparison of two heart rate analytical approaches

Verónica Adriana Ramírez, Eliana Ruetti
Unidad de Neurobiología Aplicada (UNA, CEMIC-CONICET); Facultad de Psicología (UBA)

Presenting author:
V***erónica Adriana Ramírez***, *veronica.adriana.ramirez@gmail.com*

Heart rate (HR) has been shown to be a robust autonomic measure of emotional reactivity. However, there are discrepancies in the analytical approaches applied, which leads to difficulties in the comparison of results between studies. Also, the choice of different analytical approaches does not always respond to differences in research questions. At present, two predominant approaches are employed: a synchronous approach (e.g. pre vs. post-intervention) and a longitudinal approach, which analyzes the differences in HR trajectories throughout a task. The objective of this work is to describe and compare the profiles of autonomic reactivity to an emotional modulation task according to the two paradigms of analysis most prevalent in the current psychophysiological literature. To do that, a sample of 44 children aged 5 was constituted and their HR was recorded throughout the viewing of a video with different emotional content. HR was analyzed under the two approaches mentioned above. Under the synchronous approach, no differences were found between HR according to emotional modulation. However, the longitudinal analysis showed statistically significant differences between the conditions. Due to the temporal characteristics of emotional processes, it does not seem sufficient to compare HR between a point before and a point after an emotional induction. The results suggest the importance of considering analytical methodologies according to the complexity of the phenomenon studied.

E-Posters

COGNITION, BEHAVIOR AND MEMORY

Emotional responses to music perception: An electromyography study

Veronika Diaz Abrahan [1], Guzman Alba [2], Nadia Justel [1], Miguel Angel Muñoz [2]

1 Laboratorio Interdisciplinario de Neurociencia Cognitiva (LINC). Centro de Estudios Multidisciplinarios en Sistemas Complejos y Ciencias del Cerebro (CEMSC3). Instituto de Ciencias Físicas (ICIFI). Escuela de Ciencia y Tecnología (ECyT). Universidad Nacional de San Martin. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Argentina.

2 Centro de investigación mente cerebro y comportamiento (CIMCYC). Universidad de Granada. España.

Presenting author:
***Verónika Diaz Abrahan**, abrahanveronika@gmail.com*

Music has an extraordinary ability to evoke powerful emotion. However, the psychophysiological mechanisms underlying the effects of music perception remain poorly understood. The aim of the present study was to evaluate the effect of music perception on the electromyography response (EMG). A total of 23 healthy volunteers participated in the study (mean age = 22.42, SD = 2-9). Facial muscle activity (zygomaticus and corrugator) was recorded while the participants listened to 48 musical excerpts with different emotional valence (pleasant, unpleasant, and neutral), lasting 7—13 seconds each. Electromyography signals were filtered using a bandpass from 100 to 500 Hz and a notch filter at 60 Hz. After recording, the musical excerpts were rated in terms of Valence, Arousal, and Dominance using the computerized version of the Self-Assessment Manikin. The EMG data obtained were analyzed with the Student's t-test, while the subjective assessment was analyzed with repeated measures ANOVA. The subjective assessment showed that the pleasant excerpts presented higher values of valence, arousal, and dominance than the unpleasant and neutral ones ($p < .001$). The results of EMG showed greater corrugator activity for unpleasant excerpts than for pleasant and neutral ones ($p < .001$). The zygomaticus showed greated activity for pleasant than unpleasant and neutral excerpts ($p = .012$). These results show that music induces emotions through physiological changes.

E-Posters

DEVELOPMENT

Birth and birth-mode affect markers of inflammation in the mouse brain

Alexandra Castillo-Ruiz [1], Carla D. Cisternas [2], Nancy G. Forger [1]
1 Neuroscience Institute, Georgia State University, Atlanta, GA, USA
2 Instituto de Investigación Médica M y M Ferreyra, INIMEC-CONICET-UNC, Córdoba, Argentina

Presenting author:
***Alexandra Castillo-Ruiz**, acastilloruiz@gsu.edu*

Birth is an inflammatory event, prompted by inflammation at the fetal/maternal interface. Additionally, as the fetus enters the outside world, it experiences changes that under any other circumstance could elicit an immune response: hypoxia, mechanical pressure, and exposure to microbes. However, whether birth elicits an immune response that extends to the brain and whether this is altered by birth mode is unknown. To study these questions, we manipulated birth mode (vaginal vs Cesarean) in mice and collected blood plasma and hypothalamic samples containing the paraventricular nucleus (PVN, a key region for brain-immune interactions) before and after birth to examine inflammatory cytokines. In the periphery, we found that while the pro-inflammatory cytokines TNFα and IL-6 showed, respectively, high levels perinatally or just before birth, the anti-inflammatory IL-10 tripled within 3h of birth. In contrast, PVN expression of these cytokines peaked post-delivery only: IL-6 at 3h, TNFα and IL-10 within three days. A Cesarean birth slightly altered patterns of TNFα and IL-10 in the periphery, and muted the peak in IL-6 production in the PVN following birth. Preliminary analyses of microglia, the brain immune cells, in the PVN reveal that birth and birth mode affect their numbers and morphology. Taken together, our results indicate that a vaginal birth triggers an immune response in the newborn's body and brain and that some aspects of this response are altered by birth mode.

E-Posters

DEVELOPMENT

Language development in the first years of life: associations with socioeconomic factors, use of electronic devices, home literacy environment and reading comprehension in caregivers

Angel J. Tabullo [1], Lucas J. Gago-Galvano [2]

1 INCIHUSA, CCT Mendoza, CONICET. Pontificia Universidad Católica Argentina, Facultad de Humanidades y Ciencias Económicas

2 Laboratorio de Cognición y Políticas Públicas (CogPub), UBA, CONICET

Presenting author:

***Angel Javier Tabullo**, angeljtabullo@gmail.com*

Home literacy environment studies have observed correlations between book access and shared reading practices with early language development in infants. The objective of the present work was to study early language development in a sample of 12 to 40 month old children, and is association with: home reading habits, attitude towards reading in caregivers, reading comprehension in caregivers and frequency of use of electronic devices (smartphones, pc, TV); while controlling for age and socioeconomic factors. Our study sample consisted of 136 primary caregivers of children (53 girls; M = 26,34 ± 7,55 months). Early linguistic development was evaluated with Mc Arthur-Bates Communicative Development Inventory (CDI), words and sentences form. Multiple linear regression showed that attitude towards reading (B = 0.188) and pc use (B = 0.238) (p's < 0.034) were significant predictors of CDI words score (R2 = 0.431, p < 0.001), while CDI sentences score was specifically associated with attitude towards reading (B = 0.185, p = 0.022) (R2 = 0.383, p = 0.001). Our results suggest that the caregivers' attitude towards reading was the main predictor of early vocabulary and syntax production development. This effect might be mediated by greater adult involvement and engagement on literacy practices, which may provide additional stimulation for these children. Interestingly, Pc use was the only additional predictor of expressive vocabulary.

E-Posters

DEVELOPMENT

Evaluation of executive functioning in a population of Uruguayan children of an early school age belonging to different socioeconomic levels

Carina Aldecosea [1], Melina Vladisauskas [2], Andrea P. Goldin [2] Veronica Nin [1]

1 Centro de Investigación Básica en Psicología, Facultad de Psicología, Uruguay

2 Laboratorio de Neurociencia, Universidad Torcuato Di Tella. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)

Presenting author:

***Carina Aldecosea**, carinaaldecosea@gmail.com*

The development of the cognitive processes that allow the proper regulation of behavior and emotions shows a strong association with the child's socioeconomic status (SES), which in turn influences social and educational outcomes from a very early age. Basic executive functions (EFs) are a set of superior cognitive processes that underlie flexibility in a goal-directed behavior. They encompass working memory, inhibitory control, and cognitive flexibility, functions involved in higher EFs like planning.

Here we continue the line of work carried out by our laboratory on the evaluation of executive functions by assessing a group of children with an expanded age range. We aimed to assess whether growth impacts the performance in EFs tasks in a SES dependent way. We conducted a transversal study with a sample of 278 children from 4 to 7.5 years old that attend public educational centers. We found that for working memory (assessed with Corsi blocks) and planning (assessed with Tower of London), the impact of SES varies with age. In contrast, SES affects inhibitory control abilities (measured with the incongruent block of the flower-heart task) in every age studied. Even more, a global EF measure (the mix block of the flower-heart task) does not show an association either with age nor SES.

These results underscore the importance of understanding how age and SES interact to produce developmental outcomes, and not to assume an homogeneous adverse effect of poverty on development.

E-Posters

DEVELOPMENT

Development and evaluation of a long-term retinal degeneration model in rabbits using oxidant agents. In vitro and in vivo assays. Preliminary studies.

Carolina Del Valle Bessone [1], José Domingo Luna [2], Luciana Cervera [2], Daniel Alberto Allemandi [1], Daniela Alejandra Quinteros [1]

1 Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA), CONICET and Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, 5000-Córdoba, Argentina.

2 Área de Cirugía de Vítreo y Retina, Centro Privado de Ojos Romagosa S.A. and Fundación VER, 5000-Córdoba, Argentina

Presenting author:

***Carolina Del Valle Bessone**, cbessone@unc.edu.ar*

During the development of neurodegenerative ocular diseases, such as glaucoma, macular degeneration, or other retinopathies, oxidative stress is the main cause of cell damage. The increase in reactive oxygen and nitrogen species can overwhelm the cell's natural defense mechanisms, with possible effects including the production of endogenous antioxidants and activation of pathways that lead to cell death such as apoptosis, necrosis, or autophagy. Furthermore, produce damages the structure and function of the axons that compose neuronal cells of the retina. This project describes the development and evaluation of a long-term model of retinal degeneration (RD) in rabbits through the co-administration of oxidant agents as glutamate (GLUT) and L-buthionine-S, R-sulfoximine (BSO) that trigger apoptosis by cytotoxicity and oxidative stress of retinal cells, mainly RGCs. The RD model in rabbits was evaluated by in vivo studies of optical coherence tomography (OCT) in time and histological studies in sections of retina for 18 days. Results showed progressive deterioration of retina in presence of oxidizing agents at 18 days. OCT studies evidenced a remarkable decrease in the thickness of the retina over time respect of the control. Histological studies showed notable disruption of layers of retina together with migration and reduction of cells, mainly RGCs. Results are encouraging for developing a long-term in vivo model of retinal degeneration for future neuroprotective drug testing.

E-Posters

DEVELOPMENT

Validation of a mouse model of double burden of malnutrition and its interaction with social stress: focus on the long-term effects on neuroinflammation and behavior

Claudio Dario Barrios, Amaicha Mara Depino

Presenting author:
Claudio Dario Barrios, *claudiobarrios@outlook.com*

About one in every three persons worldwide suffer malnutrition, comprising two different conditions: undernutrition and overweight/obesity. Recently, changes in dietary patterns and lifestyle have brought about the occurrence of overweight in the same household or person suffering the consequences of undernutrition. This phenomenon is known as the double burden of malnutrition and is growing in developing countries and vulnerable groups. The consequences of this double malnutrition are at the moment unknown, partly due to the lack of animal models where to study them.

This project is aimed to develop a model of double malnutrition, by combining a mouse model of undernutrition (timed separation of the pups from the dam), and a model of obesity (cafeteria diet after weaning). We will study the consequences of this diet on brain development, by studying adult behavior and brain structure. Moreover, as different forms of malnutrition result in neuroinflammation, we will study whether inflammatory cells and molecules are involved in the combined effects of neonatal undernutrition and juvenile overweight on the brain. Finally, we will test in these animals the effects of social stress during a juvenile window of vulnerability in brain development, as some consequences of nutrition are only observed when the animals are challenged. We hope that our project will help identify the consequences of the double malnutrition and develop treatments to reverse its burden.

E-Posters

DEVELOPMENT

BDNF and EphA3 ectodomain stimulate retinal ganglion cell axon growth and guidance

Gonzalo Spelzini [1,2], LUISA RENEE TERUEL [1,2], MARA MEDORI [1,2], LUCIANO FIORE [1,2], GABRIEL SCICOLONE [1,2]

1 CONICET – Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencias "Prof. E. De Robertis" (IBCN).
2 Universidad de Buenos Aires, Facultad de Medicina, Departamento de Biología Celular, Histología, Embriología y Genética

Presenting author:
***Gonzalo Nicolás Spelzini**, gonzalospelzini@hotmail.com*

We demonstrated that tectal EphA3 stimulates axon growth of nasal retinal ganglion cells (RGC) toward the caudal tectum preventing them from branching in the rostral tectum. BDNF stimulates RGC axon growth and branching. However its effect on RGC axon guidance is not clear and there is no evidence about the combinatorial effects of EphA3 ectodomain and BDNF. Our purpose was to study the individual and combinatorial effects of EphA3 and BDNF on RGC axon growth and guidance. We cultured chicken embryo nasal retinal explants and dissociated RGCs on poly-L-lysine/laminin and exposed them to control conditions, to EphA3 ectodomain (aggregated EphA3-Fc), to BDNF or to EphA3-Fc plus BDNF to evaluate their effects on axon growth and guidance. In order to evaluate the participation of gradients of BDNF and EphA3 on the axonal guidance of nasal RGCs, we developed a chemotaxis test using the Dunn's chamber. The results showed that: EphA3-Fc and BDNF increase the length of nasal RGC axons and that nasal RGC axons change their directions of growth toward gradients of EphA3 and BDNF. Besides, EphA3-Fc and BDNF together present the highest effects in comparison to the effects produced by any of them alone. This demonstrates that BDNF and EphA3 not only stimulate RGC axon growth but their gradients also have chemoattractant effects on nasal RGC axons, suggesting that both of them present synergistic effects. Grant: UBACYT 0769.

Key words: axon growth, axon guidance, Eph/ephrin, BDNF, retinal ganglion cells, chick embryo, development.

E-Posters

DEVELOPMENT

Role of brain masculinization in the development of autism-related behaviors in animals prenatally exposed to valproic acid

Macarena Varela [1], Araceli Seiffe [1,2], Amaicha Mara Depino [1,3]

1 CONICET-Universidad de Buenos Aires, Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), Buenos Aires, Argentina.
2 Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Fisiología, Biología Molecular y Celular, C1428EHA, Buenos Aires, Argentina.
3 Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Biodiversidad y Biología Experimental, Buenos Aires, Argentina.

Presenting author:
***Macarena Varela**, varelamacarenar@gmail.com*

Autism Spectrum Disorder(ASD) is characterized by social deficits and fixed or repetitive behaviors. Epidemiological data shows that ASD affects men and women in a proportion of 4:1, which could indicate higher male susceptibility and/or female resilience. Studying the causes of male prevalence of ASD could help determine its etiology as well as identify potential therapeutic targets.

Aiming to understand the biology behind male susceptibility and/or female resilience to ASD, we hypothesize that brain masculinization is necessary for the expression of ASD related behaviors in a prenatal valproic acid(VPA) exposure model. Prenatal VPA exposure results in social deficits, increased fixed or repetitive behaviors and neuroinflammation. Male rodents go through a perinatal brain masculinization process characterized by testosterone aromatization into estradiol which results in adult male sexual behaviors.

This project combines both models(VPA and brain masculinization) via prenatal and postnatal mice treatment. On gestational day 12.5, pregnant dams will be injected with either VPA or saline. On days 2,5 and 8 female offspring will be injected with either estradiol or oil. Behavioral tests will be analyzed to study the effects of female brain masculinization on ASD related behaviors of prenatally exposed VPA mice. Tissue will be obtained for histological and molecular testing to study cellular and molecular alterations mediating VPA and masculinization effects on female behavior.

E-Posters

DEVELOPMENT

uPA promotes retinal progenitors proliferation, neuronal differentiation and retinal ganglion cells axon growth

Mara Medori [1], Manuel Robaldo [1], Gonzalo Spelzini [1], Jonathan Rondon [1], Luciano Fiore [1], Viviana Sanchez [1], Gabriel Scicolone [1]

1 CONICET – Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencias "Prof. E. De Robertis" (IBCN). Ciudad de Buenos Aires, Argentina.

2 Universidad de Buenos Aires, Facultad de Medicina, Departamento de Biología Celular, Histología, Embriología y Genética. Ciudad de Buenos Aires, Argentina.

Presenting author: ***Mara Medori***, *mara_medori@hotmail.com*

Previously we demonstrated that urokinase-type plasminogen activator (uPA) increases neuronal migration and neuritogenesis in chicken tectal neurons. Other reports involved uPA in proliferation processes. The purpose of this work was to evaluate the role of uPA in chicken retinal development.

We observed that uPA receptor (uPAR) expresses in developing retina, including the retinal ganglion cells (RGCs) that establish topographic connections with the tectum.

In order to investigate whether uPA regulates the level of proliferation of retinal progenitors and neuronal differentiation, we cultured dissociated retinal cells obtained from embryos of 5 days of development (E5) and exposed them to control conditions or uPA. The proportion of cells expressing BrdU and presenting neuronal phenotype were evaluated. Results showed that uPA increases the proportion of BrdU+ cells and projecting neurons. Then we studied the effect of uPA on RGC axon growth in retinal explants obtained from E7 exposed to control conditions or uPA. Results showed that uPA increases RGC axon growth. In order to investigate downstream signaling participating in uPA-mediated axon growth, the level of FAK activity was evaluated by immunocytochemistry and Westernblot. Results showed that uPA increases FAK activity. This work shows that uPA promotes proliferation of retinal progenitors and the level of neuronal differentiation, also increases RGC axon growth by increasing the level of FAK activity.

E-Posters

DEVELOPMENT

Beta1 integrin is necessary for retinal ganglion cell axon growth mediated by EphA3

Mara Medori [1], Jonathan Rondon [1], Gonzalo Spelzini [1], Manuel Robaldo [1], Luciano Fiore [1], Gabriel Scicolone [1]

1 CONICET – Universidad de Buenos Aires, Instituto de Biología Celular y Neurociencias "Prof. E. De Robertis" (IBCN). Ciudad de Buenos Aires, Argentina.
2 Universidad de Buenos Aires, Facultad de Medicina, Departamento de Biología Celular, Histología, Embriología y Genética. Ciudad de Buenos Aires, Argentina.

Presenting author:
***Mara Solange Medori**, mara.medori.73@gmail.com*

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.

In order to investigate the signaling mechanisms involved in the EphA3-mediated RGC axon growth, we evaluated the role of beta1 integrin in this process. For this purpose, we cultured chicken embryo nasal retinal explants on poly-L-lysine/laminin and exposed them to control conditions, to EphA3 ectodomain (aggregated EphA3-Fc), to a blocking anti-Beta1 integrin antibody and to EphA3-Fc plus the blocking anti-Beta1 integrin antibody.

Axon density, axon length, growth cone morphologies, interstitial axonal filopodia density and length were evaluated after 3 and 6 hs of treatment at phase contrast microscopy and with immunocytochemistry against acetylated tubulin.
The results showed that EphA3-Fc increases axon density and length, increasing the proportion of extending growth cones and decreasing the density of interstitial filopodia, whereas anti-Beta1 integrin decreases all parameters evaluated. Anti-Beta1 integrin prevents EphA3-mediated axon growth and growth cone extension.
These results show that Beta1 integrin activity is necessary for control and EphA3-mediated RGC axon growth.

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Key words: axon growth, Eph/ephrin, Beta1 integrin, retinal ganglion cells, retinotectal system, chick embryo, development.

E-Posters

DEVELOPMENT

In search of Biomarkers of Maternal Stress: FELICITy Study

Ritika Sharma [1], Camilla Zelgert [2], Peter Zimmermann [2] Gabriela Berg [3], Bibiana Fabre [3], Rory Wilson [1], Melanie Waldenberger [1], James Macdonald [4], Theo Bammler [4], Martin Frasch [5], Silvia Lobmaier [2], Marta Antonelli [2,6]

1 Research Unit of Molecular Epidemiology, Inst. of Epidemiology, Helmholtz Zentrum Munich, Oberschleißheim, Germany
2 Klinikum rechts der Isar-TUM, Dept. of OBGYN, Munich, Germany
3 Facultad de Farmacia y Bioquímica, UBA, Buenos Aires, Argentina
4 University of Washington, Department of Environmental and Occupational Health Sciences, Seattle, WA, United States of America
5 University of Washington, Dept. of OBGYN, Seattle, WA, United States of America
6 Instituto de Biologia Celular y Neurociencia, UBA, Buenos Aires, Argentina

Presenting author:
***Ritika Sharma**, ritika.sharma@helmholtz-muenchen.de*

Children affected by prenatal stress (PS) might show alterations of the fetal ANS and HPA axis. Subjects were recruited from a cohort of pregnant women attending the "Klinikum rechts der Isar" of the Technical University of Munich (TUM). Pregnant women were screened for stress exposure using Cohen Perceived Stress Scale and were classified into stressed group (SG, PSS-10≥19, n= 55) and control group (CG, PSS-10<19, n=55). Fetal electrocardiograms were recorded by taECG. Coupling between mHR and fHR was analyzed resulting in fetal stress index (FSI). Upon delivery, hair strands were collected for cortisol measurements and newborn's cord blood and saliva samples were collected. DNA was extracted from saliva samples (n=114) and DNA methylation was measured using EPIC Bead-Chip array. To identify associations between cortisol/FSI and methylation, linear regression models adjusting for confounders (sex, age, smoking and cell-types) were run. FSI was significantly higher in fetuses of SG when compared to CG. No difference in methylation levels were found in PS newborns. The top hit of the regression analysis is cg15652683 (p = 2.16e-06), a CpG annotated to VIPR2 gene (Chr 7q36.3) coding for Vasoactive Intestinal Peptide Receptor 2. VIP is a small peptide with important neuroendocrine functions. Our work is ongoing and aims to develop an electrophysiological and epigenetic biomarker panel as an early non-invasive measure of the neurodevelopmental outcome of PS-exposed infants.

E-Posters

DEVELOPMENT

Sex-specific hippocampal (HC)-related behavioral and biochemical alterations observed in adolescent rats subjected to voluntary ethanol (EtOH) intake and noise exposure

Sonia Jazmín Molina [1], Gustavo Ezequiel Buján [2], Laura Ruth Guelman [2]

1 Universidad de Buenos Aires. Consejo Nacional de Investigaciones Científicas y Técnicas. Centro de Estudios Farmacológicos y Botánicos (CEFyBO, UBA-CONICET). Buenos Aires, Argentina.

2 Universidad de Buenos Aires. Facultad de Medicina. 1ª Cátedra de Farmacología. Consejo Nacional de Investigaciones Científicas y Técnicas. Centro de Estudios Farmacológicos y Botánicos (CEFyBO, UBA-CONICET). Buenos Aires, Argentina.

Presenting author:
Sonia Jazmín Molina, *sonia.molina@live.com.ar*

EtOH intake in the presence of noise is usual in human adolescence. Animal models studies have shown that both stimuli presented separately might have detrimental effects on the CNS, such as oxidative imbalance and behavioral alterations. Therefore, the aim of this work was to investigate the effects of EtOH intake and noise exposure on HC-related behavioral and biochemical parameters in adolescent rats. Wistar rats (28-days-old) were subjected to 10% EtOH using the two-bottle choice drinking-in-the-dark paradigm, during 4h/d for 4 days. After the last session, rats were exposed to noise (95-97 dB, 2h). Finally, Open field and Y-maze tests were performed to evaluate behavior and HC tissue was dissected to assess reactive oxygen species (ROS) levels and catalase activity (CAT).Results showed a significant decrease in exploration in females and a decrease in contextual memory in males in EtOH, noise and EtOH+Noise groups when compared with controls. In addition, an increase in ROS levels was found after EtOH intake in females and a decrease after noise exposure in males as well as in EtOH+Noise groups in both sexes. Finally, no significant changes in anxiety-like behavior and CAT were found in either group. These findings suggest that EtOH and noise exposure might produce different HC-related behavioral and biochemical changes, some of which are sex-specific. Further investigations are needed to understand the biochemical mechanisms that could underlie the behavioral changes.

E-Posters

DEVELOPMENT

Rol of kinesin-1 on axonal transport of Diacylglicerol Lipase in cortical neurons

Trinidad MM Saez, Iván Fernandez Bessone, Francisco Grenoli, María Sol Sargiotto, Jordi Navarro, Emanuel Martinez, Mariana I Holubiec, Tomás L Falzone

Laboratorio de Transporte Axonal y Enfermedades Neurodegenerativas, Instituto de Biología Celular y Neurociencia (IBCN, UBA-CONICET), Facultad de Medicina, Universidad de Buenos Aires

Presenting author:
***Trinidad M Saez**, tsaez@fmed.uba.ar*

Endocannabinoid (eCB) signaling modulates the brain wiring by regulating axonal growth, guidance and synaptogenesis. The diacylglycerol lipases (DAGL-α and DAGL-β) synthesize 2-arachidonoyl-glycerol (2-AG), an endogenous ligand for the cannabinoid receptors types 1 and 2 (CB1 and CB2). Acquisition of precise neuronal connectivity requires a proper targeting and accurate spatiotemporal localization of both, CB1R and DAGL, on the surface of navigating axons. Previously, we demonstrate that CB1R axonal transport, localization and presentation at the growth cones depend on Kinesin-1 molecular motor. Defects in CB1R axonal transport triggers dysfunctions in eCB-dependent axonal growth. Here, we tested whether kinesin-1 deficiency also affects the intracellular trafficking of DAGL-β. Using high resolution live imaging of fluorescent DAGL -β vesicles we characterized the axonal transport properties of DAGL-β and the dependency on kinesin-1 in the delivery of DAGL-β. Also, we characterized the colocalization of DAGL-β vesicles with Kinesin-1 in cortical neurons. Our preliminary data reveal that DAGL-β vesicles moves at slower speeds than CB1R vesicles and KLC1 deletion could impair DAGL-β average velocity. These results suggest that kinesin-1 could play a role in both, DALG and CB1R intracellular trafficking.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Role of striatal somatostatinergic interneurons in Parkinson's disease motor symptoms and L-dopa-induced dyskinesias

Agostina Stahl, Verónica Risso, Juan Belforte, Lorena Rela, Gustavo Murer
IFIBIO Houssay- UBA, CONICET

Presenting author:
Agostina Mónica Stahl, *agostinastahl@yahoo.com*

Action selection relies on the coordinated activity of striatal direct and indirect pathways, strongly modulated by dopamine (DA) and cholinergic neurons. Loss of mesencephalic DA neurons in Parkinson's disease (PD) is thought to disrupt the balance between these modulators resulting in an alteration of basal ganglia circuits and motor disabilities. Striatal non cholinergic interneurons also play key roles in modulating striatal projection neurons, but their potential contribution to motor symptoms of PD is poorly understood. The goal of this project is to identify the role of striatal somatostatinergic interneurons (iSOM+) in the expression of motor deficits and the development of L-dopa-induced dyskinesias (LID). To this aim, we use Som-Cre mice unilaterally lesioned with 6-OHDA as a model of PD and evaluate behavioral performance while modulating iSOM+ activity using chemogenetic tools. As a first approach, we delivered a viral vector that directs the expression of an inhibitory DREADD in iSOM+, unilaterally into the striatum, and evaluated motor deficits by using three behavioral assays in the presence and absence of its synthetic ligand. Subsequently, mice were treated with increasing doses of L-dopa and we evaluated whether LID expression is altered by iSOM+ inhibition. Preliminary results showed that after L-dopa treatment (6 mg/kg), inhibition of iSOM+ increased LID expression , while no effects were found on basal locomotion nor on the development of motor deficits.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Altered neurovisceral responses to social and cognitive stress in hypertensive disease: a multidimensional approach

Agustina Legaz [1], Adrián Yoris [2], Lucas Sedeño [2] Sofía Abrevaya [2], Miguel Martorell [2], Florencia Alifano [2], Adolfo M. García [1], Agustín Ibañez [1]

1 Cognitive Neuroscience Center (CNC), Universidad de San Andrés, Buenos Aires, Argentina
2 National Scientific and Technical Research Council (CONICET), (C1126AAB), Buenos Aires, Argentina

Presenting author:
***Agustina Legaz**, agustinalegaz@gmail.com*

Hypertensive disease (HTD), one of the most important risk factors for cerebrovascular and cardiovascular disorders, is characterized by high propensity to stress. Since stress is underpinned by both cardiac and neural factors, multidimensional insights are required to understand its disturbance in this disease. Here, we studied cardiodynamic, neurophysiological, and neuroanatomical signatures of stress in HTD patients and healthy controls. Subjects performed the Trier Social Stress Test, a gold-standard task comprising a baseline and a psychosocial stress period. During both stages, we measured a sensitive HRV parameter (the low frequency/high frequency [LF/HF ratio]) and online neurophysiological signatures (the heartbeat-evoked potential [HEP]). Also, we obtained neuroanatomical measures via voxel-based morphometry. Compared to controls, HTD patients exhibited increased LF/HF ratio and greater HEP modulations during baseline, reduced changes between baseline and stress periods, and non-significant stress-related HRV modulations associated with the grey matter volume of putative frontrostriatal regions. Briefly, HTD patients presented signs of stress-related autonomic imbalance, reflected in a potential basal stress overload and a lack of responsiveness to acute stress, accompanied by multimodal neural alterations. These findings extend current models of stress in HTD and inform relevant clinical and theoretical agendas targeting heart-brain interactions.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Neonatal exposure to 17β-benzoate estradiol makes females more similar to males in several autism-relevant behaviors

Araceli Seiffe [1], Mauro Federico Ramirez [1], Claudio Barrios [1], María Milagros Albarrán [1], Amaicha Mara Depino [2]

1 Institute for Physiology, Molecular Biology and Neurosciences (IFiByNe-UBA-CONICET) - Department of Physiology, Molecular and Cellular Biology, Faculty of Exact and Natural Sciences, UBA.
2 Institute for Physiology, Molecular Biology and Neurosciences (IFiByNe-UBA-CONICET) - Department of Biodiversity and Experimental Biology, Faculty of Exact and Natural Sciences, UBA.

Presenting author:
***Araceli Seiffe**, aseiffe@gmail.com*

Autism spectrum disorders (ASD) are characterized by reduced sociability, diminished communicative skills and repetitive behaviors. Notably, the proportion between boys and girls diagnosed with ASD is about 4:1 which suggests a higher susceptibility in boys to develop ASD. A striking difference between males and females in humans and other mammals is that males suffer a process of brain masculinization, due to the early exposure to gonadal hormones which, in turn, affect the organization of the brain. This developmental hallmark is essential for the adult animal to express the appropriate sexual behaviors in presence of a receptive female.

Our aim was to evaluate how the process of masculinization itself influences different behaviors relevant to ASD. To this aim, we studied sex differences and the effects of brain masculinization of female mice on different autism-relevant behaviors. We evaluated postnatal behavior, juvenile play and adult tests that evaluate sociability, repetitive behaviors, anxiety and depression. Finally, we performed the urine marking test and evaluated the oestrus cycle to assess the whether the protocol of neonatal exposure to estradiol resulted in brain masculinization and reproductive organs underdevelopment.
Our results show that the sex differences observed in exploration, repetitive behaviors and depression-related behaviors are largely reduced when females are neonatally treated with estradiol.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Ablation of Nkx2.1 derived striatal interneurons results in Tourette – like phenotypes

Camila Coll, Juan Pablo Beccaria, Bárbara Yael Braz, Analía López Díaz, Juan Emilio Belforte, Mario Gustavo Murer

Instituto de Fiosiología y Biofísica Bernardo Houssay (IFIBIO) UBA-CONICET

Presenting author:
***Camila Coll**, collcami@gmail.com*

Tourette Syndrome (TS) is a neurodevelopmental disorder that usually starts during childhood. Although it is characterized by motor and vocal tics, most patients also present comorbid conditions including OCD and ADHD. Pathophysiology of TS is unknown, however, there are studies showing a reduce number of PV+, nNOS+ and ChAT+ striatal interneurons (SIs) in the brain of TS patients. Previous studies have tried to reproduce TS phenotype in mice by generating an ablation of a specific type of SI, but none have shown spontaneous tics. In order to reproduce more closely the striatal changes reported, we performed a combined ablation of SIs using a Cre/loxP transgenic system to express human diphtheria toxin receptor in Nkx2.1+ cell lineage, combined with intrastriatal diphtheria toxin administration. Immunohistochemistry assays showed that lesion exclusively affected SIs. Lesioned mice not only developed abnormal involuntary movements resembling motor tics (See Beccaria et al. poster) but also behaviors reminiscent of common comorbid conditions, including an increase in stereotypies (grooming), locomotion, and spontaneous repetitive behaviors (rearing and head poking), as well as a reduction in immobility time, compared to their control littermates. These phenotypes suggest perseverative-like behaviors and hyperactivity, compatible with OCD and ADHD comorbidities. In summary, animals with ablated Nkx2.1 derived SIs develop TS-like phenotypes.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Cognitive impairment and reactive gliosis in a rat model of AD-like brain amyloidosis

Caterina Sister [1], Martin Habif [1], Federico Filippin [1], Alicia Rossi [2], Valeria Berkowicz [1], Claudio Cuello [3], Alberto Javier Ramos [2], Diana A. Jerusalinsky [1]

1 Lab. of Neuroplasticity & Neurotoxins (LaNyN), IBCN - UBA/CONICET, School Medicine, University of Buenos Aires, Ciudad de Buenos Aires, Argentina

2 Lab. of Molecular Neuropathology , IBCN - UBA/CONICET, School Medicine, University of Buenos Aires, Ciudad de Buenos Aires, Argentina

3 Dept Pharmacology and Therapeutics, McGill University, McIntire Building, Montreal, Quebec, Canada

Presenting author:
***Caterina Laura Sister**, cate.sister@gmail.com*

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with overproduction of Aβ peptides in the brain that ultimately aggregate into insoluble fibrils forming plaques, inducing a sustained inflammatory response known as “reactive gliosis”. Previous reports using mice AD models pointed out some glial cell alterations.
McGill-Thy1-APP transgenic (Tg) rat model of AD-like brain amyloidosis reliably resembles human neural and cognitive disease development. We have addressed the influence of sexual dimorphism in learning and memory, showing deficits in long-term associative memory (spatial and aversive) in 13 month-old heterozygous males. Hence, we performed an imaging-based quantitative study to gain insight into Aβ deposition and reactive gliosis in those Tg rats and their wild type littermates (wt). Analysis of Tg rat brain slices showed Aβ deposition in plaques, preferentially localized in hippocampus and somatosensory cortex and an increased GFAP+ area. By using morphological descriptors, we analyzed cell size and shape to determine the degree of reactive gliosis in rats of both genotypes. Astrocytes in Tg animals were bigger, extensively branched, likely consistent with an exacerbated inflammatory response, compared with a smaller area and perimeter, more ameboid-shaped/poorly ramified astrocytes in wt rats. These results point to the relevance of searching for an interplay between reactive gliosis and mild cognitive impairment at middle age.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Preventing memory deficit with an AAV vector expressing a single-chain antibody against amyloid β oligomers in animal models of Alzheimers' disease

Daniela Alejandra Salas [1], Magalí Cercato [1], Federico Filippin [1] María Clara Selles [2], Martín Habif [1], Tomás Gonzalez Garello [1], Anna Salvetti [3], Alberto Luis Epstein [4], William Klein* [5], Sergio Ferreira* [2], Diana Alicia Jerusalinsky* [1], Natalia Colettis.

1 IBCN (UBA-CONICET), Argentina,
2 Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil,
3 INSERM, U1052, Cancer Research Center of Lyon (CRCL), Université de Lyon (UCBL1), CNRS UMR_5286, Centre Léon Bérard, Lyon, France
4 UMR INSERM U1179-UVSQ, Université de Versailles Saint Quentin en Yvelines, 78180 Montigny le-Bretonneux, France
5 Department of Neurobiology, Northwestern University, Evanston, USA,

Presenting author:
***Daniela Alejandra Salas**, daniale.salasd@gmail.com*

Amyloid β oligomers (AβO)-induced alterations in synaptic structure and function was proposed to be implicated in early cognitive impairment in Alzheimer's disease (AD), long before evident neurodegeneration took place. Thus, specifically targeting AβO by immunotherapy could be an alternative for AD treatment. McGill-R-Thy1-APP transgenic rats with human APP bearing the Swedish and Indiana mutations (of familial AD) in homozygous (+/+) condition, was reported to show cognitive deficits at 3 months. Meanwhile, heterozygous (+/-) rat showed a more subtle and slower developing phenotype, though with consistent memory impairment in 4 month old males. We aimed to evaluate the efficacy of an anti-AβO single-chain variable fragment antibody (NUsc1) expressed from an adeno-associated (AAV) viral vector, to prevent that memory impairment. Two month-old (+/-) rats received an ICV injection of that AAV-NUsc1, which drives neuronal expression of NUsc1. After 2 months, long-term memory (LTM) performance was assessed in either injected or not Tg females and males, and their wt littermates. Both Tg and wt females showed similar LTM performance. Instead, Tg males showed LTM deficits, while those vector-treated expressed LTM as wt rats, indicating that AAV-NUsc1 was able to prevent such deficits. Using same AAV-NUsc1 in different mouse AD models we had also shown STM improvement. Therefore, this sort of immunotherapy emerges as a novel promising experimental tool for AD treatment.

*Corresponding authors o patent owners o inventors

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

In C. elegans, alterations in neuronal membrane glycoprotein 1 (nmgp-1) impair dauer recovery, egg-laying and chemosensation

Eliana M Fernández, Yamila B Cutraro, Melisa C Monteleone, Marcela A Brocco
Instituto de Investigaciones Biotecnológicas (IIBio-UNSAM-CONICET)

Presenting author:
Eliana Mailén Fernández, *emfernandez@iibintech.com.ar*

Individual welfare depends on maintenance of homeostasis. Long-lasting adverse environments results in stressful conditions that may damage the organism. We have shown in mammal models that chronic stress paradigms -which resemble human depressive states- alter brain GPM6A levels. The GPM6A participates in neuronal differentiation and morphology establishment. There is a gap between the cellular GPM6A functions and its role in systemic stress response. The nematode C. elegans exhibits a GPM6A ortholog, the neuronal membrane glycoprotein 1 (NMGP-1). Due to shared features between nematode and mammals and because of the genetic tools available, we used C. elegans as a simpler model to study NMGP-1 participation in stress response. We have characterized NMGP-1 functions using RNAi knockdown and two non-null, hypomorphic mutant alleles. Analysis of interfered or mutant alleles showed a reduced egg-laying rate and an increased recovering time from the stress-resistant dauer stage. In addition, defects in egg-laying induced egg retention in nmgp-1-deficient worms. In addition, worms lacking NMGP-1 showed a normal response to attractant such as diacetyl, but an altered repulsive response to SDS. Moreover, nmgp-1(RNAi) worms showed morphological alterations on ASJ chemosensory neurons, responsible of dauer exit. Altogether these results shed light in NMGP-1 role in C. elegans. These mutants represent an attractive platform to test drugs modulating stress response.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Analysis of temporal structures using MRI, VBM and their histological correlation in patients with surgical resistant temporal epilepsy.

Ernesto Gonzalez Stivala [1], Hernán Kulsgaard [4], Micaela Sanzo [1] Mariana Bendersky [3], Juan Pablo Princich [2], Lucía Alba Ferrara [3], Ignacio Larrabide [4], Silvia Kochen [3], Fabián Loidl [1], Luciana D'Alessio [1]

1 IBCN-CONICET, Facultad de Medicina, UBA.
2 Hospital El Cruce, Buenos Aires.
3 ENyS-CONICET, Buenos Aires.
4 Universidad Nacional del Centro, Buenos Aires

Presenting author:
***Ernesto Gonzalez Stivala**, egstivala@fmed.uba.ar*

Objective: To determine the neuronal and glial density in the resected temporal pole (TP) cortex of patients with resistant temporal lobe epilepsy (RTLE). These findings were related to brain neuroimaging (MRI) and voxel-based morphometry (VBM).

Methods: Patients with RTLE were included. Surgical piece was fixed to perform morphological analysis and qualitative analysis of the tissue. 3T MRI images and VBM were used to calculate TP volume. The patients were divided in 2 groups based on volume reduction.

Results: 21 patients (10 women) with RTLE were included. According to the MRI, 19 patients had hippocampal sclerosis. Five patients presented focal cortical dysplasia. We found higher neuronal density in layer III in patients with volume reduction. Furthermore, a positive correlation between neuronal density in layer III and volume reduction was found by adding both poles. Dysplasia patients presented a tendence towards a higher neuron/glia ratio. In contrast, a greater amount of glia was found in patients with changes in the pole signal on MRI, although not statistically significant (p=0.012)

Conclusions: In this exploratory study, patients with the greater extension of volume reduction showed a higher neuronal density. An increase in neuronal density has previously been observed in patients with dysplasia.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Corticostriatal connectivity balance in L-DOPA-induced dyskinesia under and after the acute effect of L-DOPA

Ettel Keifman [1], Mariela Verónica Escande [1], Jesica Nahir Unger [1], Juan Emilio Belforte [1], Mario Gustavo Murer [1]

1 Grupo de Neurociencia de Sistemas, IFIBIO Houssay, UBA-CONICET

Presenting author:
***Ettel Keifman**, keifman.ettel@gmail.com*

Striatal medium spiny neurons (MSNs) are key in action selection. A balanced activity of direct pathway MSNs (dMSNs) and indirect pathway MSNs (iMSN) is needed for an appropriate motor performance. Midbrain dopaminergic neurons provide this balance by modulating MSNs' response to cortical inputs. In Parkinson's disease (PD) nigrostriatal dopaminergic neurons degenerate and an imbalance in favor of iMSNs over dMSNs appears. Chronic treatment with L-DOPA, a DA precursor widely used to treat PD symptoms, causes abnormal movements known as L-DOPA-induced dyskinesia (LID) in up to 30% of patients and is thought to emerge from an imbalance in MSN activity. Under the hypothesis that chronic L-DOPA treatment may produce aberrant plasticity phenomena that affect corticostriatal connectivity that underlie LID, we studied functional and structural changes that emerge from PD and from an acute and chronic L-DOPA treatment. We used in vivo juxtacellular recordings on transgenic mice showing MSN type-specific expression of fluorescent proteins, and we assessed MSN responsiveness to motor cortex stimulation before (off) and following (on) an acute L-DOPA challenge. Off L-DOPA, we did not find differences from PD corticostriatal connectivity. However, on L-DOPA dMSN reverted from their previous disconnection from cortical inputs. Therefore, during LID dMSN prevailed over iMSN. Interestingly, iMSN seemed to contribute less to this imbalance after chronic treatment with L-DOPA.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Probiotic Bacillus subtilis protects from Parkinson's disease-associated alpha-synuclein aggregation in C. elegans

Eugenia Goya, Feng Xue, Cristina Sampedro Torres-Quevedo, Lourdes Riquelme-Dominguez, Maria Doitsidou
Centre for Discovery Brain Sciences, University of Edinburgh, United Kingdom

Presenting author:
***Eugenia Goya**, eugenia.goya@ed.ac.uk*

The accumulation of misfolded alpha-synuclein (α-syn) protein into pathological aggregates plays a central role in the pathogenesis of Parkinson's disease (PD) and other synucleinopathies. Although PD is primarily considered to be a central nervous system disease, recent discoveries have implicated the gut microbiome in the progression and severity of this condition. However, how gut bacteria affect PD remains unclear. C. elegans is an ideal model for studying the effects of gut bacteria on physiological processes at a single species-single gene level. We showed that B. subtilis PXN21, a probiotic strain commercially available for human consumption, both inhibits aggregation and efficiently removes preformed aggregates in a C. elegans model with ectopic expression of human α-syn. This protection is seen in young and ageing animals and is partly mediated by DAF-16 (FOXO). Multiple B. subtilis strains trigger the protective effect via both spores and vegetative cells, partly due to biofilm formation in the gut of the worms and the release of bacterial metabolites. Using comparative transcriptomics analysis, we identified host metabolic pathways that are differentially regulated by the probiotic, including lipid metabolism. Functional validation revealed the sphingolipid metabolism pathway as a key host mechanism that is altered by the bacteria to induce protection. Our findings provide a basis for exploring the disease-modifying potential of B. subtilis as a dietary supplement.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Histologic and functional outcome of excitotoxic and traumatic in vivo spinal cord injury models

Graciela L Mazzone [1], Wendy Moncada Herrera [2], Martina Poodts [1] Julieta Roncoroni [1], Samuel Cockey [3], Romina Sierra [1], Esteban J Fiore [4], Guillermo D Mazzolini [4]

1 Developmental Biology & Regenerative Medicine Laboratory, Instituto de Investigaciones en Medicina Traslacional (IIMT), CONICET-Universidad Austral, Derqui-Pilar, Buenos Aires, Argentina
2 Universidad Nacional Pedro Ruiz Gallo, Lambayeque, Perú
3 College of Liberal Arts and Sciences, University of Florida, Gainesville, FL, USA
4 Gene Therapy Laboratory, IIMT, CONICET, Universidad Austral. Argentina

Presenting author:
***Graciela Lujan Mazzone**, graciela.mazzone@gmail.com*

Increase in the knowledge of spinal cord injury (SCI) pathophysiological mechanisms would help developing therapeutic strategies to improve neurological function. In this work, we have established a traumatic (compression, by an aneurism clip) and a chemical (kainic acid -KA) in vivo injury models, at the border of thoracic-lumbar axial level, using BALB/c and GLASTCreERT2;Rosa26Tom double-transgenic mice. The outcome was analysed by histology and locomotor behavioural tests (including the Basso mouse locomotor scale -BMS-). While traumatic SCI resulted in permanent impairment, locomotor deficiencies were partially restored in the KA model at 8 days after injury. In the chemical SCI model, some differences, between left and right sides, were observed in the foot printing and Ladder Rung walking task tests. Histological studies suggested an increase in the prevalence of Tom+ cells within the injury site at 14 days after traumatic injury. Our results might involve the recruitment of bone marrow stromal cells previously found to trigger regenerative mechanisms. Supported by Universidad Austral, CONICET and, ICTP-UNESCO.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Alterations of specific cortical GABAergic circuits underlie abnormal network activity in a mouse model of Down syndrome

Javier Zorrilla de San Martin [1], Cristina Donato [2], Jérémy Peixoto [3], Andrea Aguirre [1], Vikash Choudhary [1], Angela Michela De Stasi [1], Joana Lourenço [1], Marie-Claude Potier [1]

1 nstitut du Cerveau (ICM), CNRS UMR 7225 – Inserm U1127, Sorbonne Université, Paris, France.
2 Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Belvaux, L-4367, Luxembourg.
3 Institut Pasteur, Paris.

Presenting author: ***Javier Zorrilla de San Martin***, *javierzsm@gmail.com*

Down syndrome (DS) results in various degrees of cognitive deficits. In DS mouse models, recovery of behavioral and neurophysiological deficits using GABAAR antagonists led to hypothesize an excessive activity of inhibitory circuits in this condition. Nonetheless, whether over-inhibition is present in DS and whether this is due to specific alterations of distinct GABAergic circuits is unknown. In the prefrontal cortex of Ts65Dn mice (a well-established DS model), we found that the dendritic synaptic inhibitory loop formed by somatostatin-positive Martinotti cells (MCs) and pyramidal neurons (PNs) was strongly enhanced, with no alteration in their excitability. Conversely, perisomatic inhibition from parvalbumin-positive (PV) interneurons was unaltered, but PV cells of DS mice lost their classical fast-spiking phenotype and exhibited increased excitability. These microcircuit alterations resulted in reduced pyramidal-neuron firing and increased phase locking to cognitive-relevant network oscillations in vivo. These results define important synaptic and circuit mechanisms underlying cognitive dysfunctions in DS.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Reliability and validity of a new Mouse Tic Severity Scale

Juan Pablo Beccaria, Camila Coll, Murer Gustavo, Belforte Juan
GNS - IFIBIO Houssay - UBA - CONICET

Presenting author:
Juan Pablo Beccaria, jpbeccaria@gmail.com

Sudden, rapid, recurrent, non-rhythmic motor movements or vocalizations are the main medical sign of Tourette Syndrome (TS). Since their intensity and manifestation is exceedingly variable, tics are challenging to quantify. The Yale Global Tics Severity Scale (YGTSS) is perceived as the gold-standard clinical scale for tic quantification not only for TS but also for any other disorder that may present tics. YGTSS measures tic complexity, frequency, intensity and interference with normal behavior. In addition, since YGTSS is used world-wide, it provides comparable and reproducible data. However, there is no similar method for scoring tics in animal models. The present work aims to validate a mouse tic severity scale (MTSS) based on YGTSS standards. For that, we used a new murine model of TS developed in our lab, in which selective ablation of striatal Nkx2.1+ derived interneurons leads to exacerbated spontaneous repetitive behaviors including tic-like movements (See Coll et al. poster). High temporal resolution videos of lesioned and control mice were thoroughly watched and scored by two treatment-blinded observers. Lesioned mice showed a higher score than their control littermates both globally and in every scale section. Moreover, total punctuation and presence of particular patterns of movements correlated with lesion extent. These results suggest that MTSS might be a valid and reproducible scale to measure tics in mice.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Nigrostriatal and mesolimbic dopaminergic pathways involved in cognitive emotional behavior alterations in a parkinsonism model

Leandro Gabriel Champarini [1], Macarena Lorena Herrera [1], Gastón Diego Calfa [1] Victor Alejandro Molina [1], Claudia Beatriz Hereñú [1]

1 Universidad de San Andrés, Buenos Aires, Argentina
2 Instituto de Psicología, Universidad del Valle, Cali, Colombia
3 National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina
4 Centro Médico Neurólogos de Occidente, Cali, Colombia

Presenting author:
***Mariano Nicolás Díaz Rivera**, marianodiaz-rivera@hotmail.com*

Impairments of action conceptualization (a cognitive domain grounded in motor brain networks) are pervasive in early Parkinson's disease (PD). Yet, treatment options for these deficits are virtually unexamined and no study has tackled them via non-invasive brain stimulation. Here, we recruited 22 PD patients and performed a five-day randomized, blinded, sham-controlled study to assess whether anodal transcranial direct current stimulation (atDCS) over the primary motor cortex, combined with cognitive training, can boost action-concept processing in this population. On day 1, participants completed a picture-word association (PWA) task (involving action-verbs and object-nouns) and a resting-state EEG protocol. They were then randomly assigned to either an atDCS (n = 11, 2 mA for 20 m) or a sham tDCS (n = 11, 2mA for 30 s) group and performed an online PWA practice over three days. On day 5, they repeated the initial protocol. Relative to sham tDCS, the atDCS group exhibited faster reaction times for action (as opposed to object) concepts in the post-stimulation test, along with enhanced EEG connectivity across motor-related electrodes. These results suggest that action-concept deficits in PD are distinctively grounded in motor networks and might be countered by direct neuromodulation of such circuits. Also, they provide new evidence for mechanistic semantic models and inform a thriving agenda in the embodied cognition framework.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

PPARγ pathway, a potential therapeutic target for peripheral nerve injuries

María Fernanda Maag [1], Cecilia Casali [2], Gonzalo Piñero [1], Paula Soto [1], Leandro Parra [2], María del Carmen Fernandez Tome [2], Patricia Setton [1], Vanina Usach [1]

1 Cátedra de Química Biológica, FFyB, UBA. IQUIFIB-CONICET
2 Cátedra de Biología Celular y Molecular, FFyB, UBA. IQUIFIB-CONICET

Presenting author:
***Maria Fernanda Maag**, fer.maag@gmail.com*

Inflammation plays a key role in Wallerian degeneration (WD), as evidenced by an increase in the expression of cytokines and chemokines and arachidonic acid metabolites such as prostaglandins (PG), among others. PGJ2 is the endogenous ligand of PPARγ, a transcription factor which regulates the expression of anti-inflammatory genes. PPARγ activation is also promoted by pharmacological agonists such as rosiglitazone and indomethacin. Our group has previously shown the spontaneous migration of systemically transplanted multipotent bone marrow cells (BMMC) to the injured sciatic nerve to exert a beneficial effect on nerve regeneration through an immunomodulatory mechanism. The aim of the present work is to evaluate whether the PPARγ pathway is involved in BMMC immunomodulatory effects in a WD model promoted by 8-second crush of the sciatic nerve. An increase in PGE2 and PGJ2, as well as in Cox-1 and PPARγ levels were promoted as a consequence of injury, while indomethacin selectively blocked the increase in PGE2. Although BMMC, indomethacin and rosiglitazone promoted an increase in PPARγ and COX-1 levels in naïve nerves, a synergic effect upon that promoted by sciatic nerve crush was not observed. Our results suggest the participation of the PPARγ pathway in the immunomodulatory effect promoted by systemically transplanted BMMC and open a new field for potential therapeutic strategies after peripheral nerve injuries.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Action semantics and the motor system: A neuromodulatory study on Parkinson's disease patients

Mariano N. Díaz-Rivera [1], Diana M.A. Suárez-García [2], Agustina Birba [3], , Máximo Zimerman [1], Jesús A. Diazgranados [4], Agustín Ibáñez [1], Johan S. Grisales [3], Juan F. Cardona [3], Adolfo M. García [1]

1 Universidad de San Andrés, Buenos Aires, Argentina
2 Instituto de Psicología, Universidad del Valle, Cali, Colombia
3 National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina
4 Centro Médico Neurólogos de Occidente, Cali, Colombia

Presenting author: ***Mariano Nicolás Díaz Rivera***, *marianodiaz-rivera@hotmail.com*

Impairments of action conceptualization (a cognitive domain grounded in motor brain networks) are pervasive in early Parkinson's disease (PD). Yet, treatment options for these deficits are virtually unexamined and no study has tackled them via non-invasive brain stimulation. Here, we recruited 22 PD patients and performed a five-day randomized, blinded, sham-controlled study to assess whether anodal transcranial direct current stimulation (atDCS) over the primary motor cortex, combined with cognitive training, can boost action-concept processing in this population. On day 1, participants completed a picture-word association (PWA) task (involving action-verbs and object-nouns) and a resting-state EEG protocol. They were then randomly assigned to either an atDCS (n = 11, 2 mA for 20 m) or a sham tDCS (n = 11, 2mA for 30 s) group and performed an online PWA practice over three days. On day 5, they repeated the initial protocol. Relative to sham tDCS, the atDCS group exhibited faster reaction times for action (as opposed to object) concepts in the post-stimulation test, along with enhanced EEG connectivity across motor-related electrodes. These results suggest that action-concept deficits in PD are distinctively grounded in motor networks and might be countered by direct neuromodulation of such circuits. Also, they provide new evidence for mechanistic semantic models and inform a thriving agenda in the embodied cognition framework.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Multidimensional signatures of negatory inhibition are differentially disrupted in frontotemporal dementia and Parkinson's disease

Mariano N. Díaz-Rivera [1,2], Agustina Birba [1,3], Sol Fittipaldi [1,3], , Cecilia González-Campo [1,3], Agustín Ibáñez [1,3,4,5,6], Adolfo M. García [1,3,4,7]

1 Centro de Neurociencias Cognitivas, Universidad de San Andrés, Buenos Aires, Argentina
2 Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT), Buenos Aires, Argentina
3 National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina
4 Global Brain Health Institute, University of California, San Francisco, United States
5 Center for Social and Cognitive Neuroscience (CSCN), School of Psychology, Universidad Adolfo Ibáñez, Santiago, Chile
6 Universidad Autónoma del Caribe, Barranquilla, Colombia. 7 Faculty of Education, National University of Cuyo (UNCuyo), Mendoza, Argentina

Presenting author:
***Mariano Nicolás Díaz Rivera**, marianonicodr@gmail.com*

Processing of linguistic negation distinctively recruits inhibitory mechanisms. Here, we assessed whether such domain can reveal neurocognitive markers of inhibitory disorders. We tested two groups with distinct neurodegenerative patterns along inhibitory circuits (behavioral variant frontotemporal dementia [bvFTD] and Parkinson's disease [PD]), healthy controls (HCs), and patients with preserved inhibitory circuitry (Alzheimer's disease [AD]). Subjects read negative and affirmative sentences and either performed or suppressed a manual response to them. We examined (a) measures of online oscillatory dynamics (via high-density EEG) as well as associations between such signatures and (b) neuroanatomical patterns (via voxel-based morphometry) and (c) fMRI-derived resting-state functional connectivity (FC). Relative to HCs, both bvFTD and PD patients exhibited altered oscillatory correlates of negatory inhibition –viz., disruptions of inhibitory delta modulations for negation only in suppressed-response trials. Such abnormalities correlated with the volume and FC of inhibitory regions in both bvFTD (e.g., superior and orbitofrontal gyri) and PD (e.g., medial and precentral gyri and cerebellum). Conversely, AD patients showed no specific oscillatory patterns across conditions nor correlations with inhibitory regions. Briefly, linguistic negation can tap into the (dys)function of inhibitory mechanisms, paving the way for a potential neurocognitive marker of bvFTD and PD.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Role of the Piriform cortex on the development of social behaviors.

Mauro Federico Ramírez [1], Mariana Graciarena [2], Amaicha Mara Depino [3]

1 Institute for Physiology, Molecular Biology and Neurosciences (IFiByNe-UBA-CONICET) - Department of Physiology, Molecular and Cellular Biology, Faculty of Exact and Natural Sciences, UBA
2 Institute for Physiology, Molecular Biology and Neurosciences (IFiByNe-UBA-CONICET)
3 Institute for Physiology, Molecular Biology and Neurosciences (IFiByNe-UBA-CONICET) - Department of Biodiversity and Experimental Biology, Faculty of Exact and Natural Sciences, UBA

Presenting author:
Mauro Federico Ramirez, *mauroramirez.ar@gmail.com*

Autism spectrum disorder (ASD) is a group of pathologies characterized by social impairment and restricted and repetitive behaviors. Our lab has validated a pharmacological model where mice prenatally exposed to Valproic Acid (VPA) express ASD related behaviors, along with a higher glucose metabolism, increased cFos activity, and reduced myelinization in the Piriform Cortex (Pir). The aim of this project is to evaluate whether neuronal activity and myelination in the Pir underlie the differences in sociability. First, to test the hypothesis stating that an increase in the activity of the Pir impairs sociability, we will inject Adeno associated virus (AAV) expressing Designer Receptors Exclusively Activated by Designer Drugs (DREADD´s) bilaterally in this structure, and evaluate sociability after clozapine-N-oxide (CNO) administration. We will use AAV-CaMKIIa-hM3D(Gq)-mCherry to increase the neuronal activity of WT mice, and AAV-CaMKIIa-hM4D(Gi)-mCherry to decrease the activity of VPA animals. Next, to evaluate whether Pir hypomyelination contributes to a lower sociability in VPA mice, we will inject Lysophosphatidylcholine 1% (LPC), a demyelinating agent bilaterally in the Pir and evaluate sociability after 7 days (when Pir myelin loss is already detectable) and 21 days (when spontaneous remyelination has occured). With this approach, we aim to better understand the role of the Pir in the modulation of social behavior in mice.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Stereoelectroencefalography (iSEEG) signal during altered consciousness (AOC) in epilepsy

Nuria Campora [1], Brenda Giagante [1], Silvia Oddo [1] Carolina Lomlomjian [1], Alejandro Nasimbera [1], Anilu Daza Restrepo [1], Silvia Kochen [1]

1 ENyS, CONICET
2 Hospital El Cruce Nestor Kirchner

Presenting author:
***Nuria Campora**, nuriacampora@yahoo.com.ar*

The alteration of consciousness (AOC) during seizures is one of the most striking features. The neuronal network that must be altered for the AOC in focal seizures is not well known. We characterized the epileptic discharge in focal seizures with different grades of AOC. The consciousness Scale (CSS) was proposed to quantify the degree of loss of consciousness, summarizing the response of a patient to 8 behavioural items performed by a clinical practitioner during and after a seizure. We analysed the physiological correlates of the CSS by studying the epileptic discharge recorded with intracranial electrodes in patients requiring an exploratory study before epilepsy surgery (12 patients, 53 seizures). In mesial temporal epilepsy (n=14 seizures), profound AOC was associated with hippocampal compromised and longer seizure. There was a trend of greater left compromised. Meanwhile in frontal epilepsy (n=39 seizures), profound AOC was associated with pre-frontal compromised, bigger size of cortical cortex with epileptic activity and longer seizures, without hippocampus compromised. We concluded that iEEG signal characteristics during AOC were different according epilepsy zone. In frontal seizures, the surface affected by epileptic discharge was related to AOC, while it was not seen in temporal seizures. It would be related to the wide neural network that is necessary to maintain consciousness, which can be affected in different ways at different points in it to produce AOC.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

A nanobiotechnological approach to promote sciatic nerve regeneration

Paula Andrea Soto [1], Marianela Vence [1], Gonzalo Miguel Piñero[1], Vanina Usach [1], Marcela B. Fernández van Raap [2], Patricia Setton-Avruj [1]

1 Universidad de Buenos Aires-CONICET. Instituto de Química y Fisicoquímica Biológicas (IQUIFIB). Facultad de Farmacia y Bioquímica. Departamento de Química Biológica. Cátedra de Química Biológica Patológica.
2 Instituto de Física La Plata (IFLP – CONICET), Departamento de Física, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP).

Presenting author:
***Paula Andrea Soto**, paula.asoto02@gmail.com*

Traumatic peripheral nerve injuries constitute a huge concern to public health, as damage leads to a decrease or even loss of sensitivity and mobility of the innervated area. Among cell therapies explored with encouraging outcomes, adult stem cells have advantageous characteristics and are thus promising agents in nerve regeneration. In this work, we propose a strategy for cell therapy enhancement by magnetic targeting in an in vivo Wallerian degeneration model. To this end, adipose-derived mesenchymal stem cells (AdMSC) were loaded with superparamagnetic iron oxide nanoparticles (SPIONs), systemically transplanted and magnetically recruited into the injured sciatic nerve. AdMSC incubation with 100 μgFe/mLDMEM nanoparticles resulted in the incorporation of 5.0 ± 0.2 pgFe/cell without affecting cell viability. Intravenous injection of AdMSC or AdMSC-SPIONs immediately after sciatic nerve compression revealed cell arrival at the lesion site 7 days post-injury. Transmission electronic microscopy results show the presence of SPIONs in the injured nerves. Systemically transplanted, magnetically recruited AdMSC-SPIONs induced a recovery in the number of myelinated axons and myelin basic protein organization, indicative of remyelination, and in nerve conduction, a sign of functional recovery. In sum, our results show magnetically assisted delivery of AdMSC as a promising strategy to promote cell arrival and recruitment and enhance sciatic nerve regeneration after traumatic injury.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Yerba mate (Ilex paraguariensis) in a Drosophila model of Parkinson´s disease: Can it protect synaptic connections?

Pedro Ballestero [1,2], Sebastian Romano [1], Hernan Hauche P. [2] Roy Rivero [3], Irene Taravini [3], Oscar Gershanik [2], Melina Bordone [2], Nara Muraro* [1], Juan Ferrario*.

1 Biomedicine Research Institute of Buenos Aires - CONICET - Partner Institute of the Max Planck Society
2 Instituto de Biociencias, Biotecnología y Biomedicina - FCEyN – UBA
3 Facultad de Bromatología – UNER

Presenting author:
***Pedro Ballestero**, pedroballestero88@gmail.com*

Parkinson's disease (PD) is the second neurodegenerative disorder in prevalence. Its origin is unknown, but its pathophysiological characteristic is the progressive degeneration of dopamine-releasing neurons of the Substantia nigra.A clinical study conducted in Argentina revealed that the consumption of yerba mate (YM) has an inverse association with the risk of developing PD (Gatto, 2015), and we found that YM extract induces a strong neuroprotective effect on dopaminergic neurons in vitro (Bernardi, 2019). Given these results, we hypothesized that the YM extract would also protect neurons from the deleterious effects caused by the expression of human alpha synuclein (aSyn) in a widely used Drosophila melanogaster model of PD. To reach this goal, we have set up the administration of YM to these fly disease model and produced preliminary behavioral and molecular data. Preliminary experiments using GRASP (GFP Reconstitution Across Synaptic Partners) technique, showed an increased GFP signal (a reporter of synaptic connections) between circadian and dopaminergic neurons in aged wild-type flies treated with YM, suggesting more connectivity in treated flies. Unfortunately, these experiments were interrupted by the pandemic when we were going to replicate this study in the aSyn flies. Our preliminary results show that YM administration improves motor coordination in PD flies and could also maintain synapses in wild-type flies; perhaps an indication of healthier neuronal circuits?Disorders of the Nervous System

*Shared corresponding authors

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

L-dopa causes oscillatory activity in striatal cholinergic interneurons from parkinsonian mice via dopamine D1/D5 receptors

Rodrigo Manuel Paz [1], Cecilia Tubert [1], Agostina Stahl [1], , Yimy Amarillo [2], Lorena Rela [1], Mario Gustavo Murer [1]

1 Universidad de Buenos Aires, CONICET, Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, 2155 Paraguay Street, Buenos Aires 1121, Argentina

2 Departamento de Física Médica, Centro Atómico Bariloche and Instituto Balseiro, CONICET, 9500 Ezequiel Bustillo Avenue, San Carlos de Bariloche, Río Negro 8402, Argentina.

Presenting author:
***Rodrigo Manuel Paz**, rodrigomanuelpaz@gmail.com*

Striatal cholinergic interneurons (SCIN) are key modulators of the striatal circuitry controlling voluntary movement and goal-directed behavior. Aberrant striatal cholinergic signalling contributes to the symptoms of Parkinson's disease (PD) and L-dopa induced dyskinesia (LID), a major complication of antiparkinsonian L-dopa therapy. However, the mechanisms causing SCIN dysfunction in PD and LID remain uncertain. Here we used slice electrophysiological approaches to show that SCIN exhibit enhanced Kir and reduced leak currents in a mouse model of LID. These changes cause exacerbated hyperpolarizing responses that coexist with an enhanced excitability, resulting in a burst-pause firing pattern that persists after the dyskinetic effect of an L-dopa dose has worn off. Additionally, we show that a negative slope region of the Kir conductance curve is responsible for the oscillatory behaviour. Stimulation of dopamine D1/D5 receptors mimics the physiological changes induced by L-dopa administration, but D1/D5 receptor blockade does not modify the persistent hyperexcitability and oscillatory activity observed in dyskinetic mice. However, blunting intracellular cAMP signaling restores normal hyperpolarizing responses and dampens oscillatory activity in dyskinetic mice. Our data unravel a mechanism causing aberrant SCIN activity in LID and point at D1/D5 receptor regulation of Kir2 and leak channels as potential targets to restore normal striatal cholinergic function in PD and LID.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Electrical Cortical Stimulation during Stereoelectroencephalography (SEEG) in drug resistant epilepsy. Experience in a High Complexity Public Hospital in Argentina.

Silvia Oddo, Brenda Giagante, Patricia Solis, Santiago Collavini, Juan Pablo Princich, Pablo Seoane, Caroliana Lomlomdjian, Silvia Kochen
Hospital EL Cruce. ENyS. CONICET

Presenting author:
***Silvia Oddo**, silviaoddo4@gmail.com*

aElectrical Cortical Stimulation (ECS) Stereoelectroencephalography (SEEG)-based presurgical evaluation of epilepsies has a double objective: to define the epileptogenic zone (EZ) and to map cortex functionality in relation with the surgical plan.

This study was performed at the Video-EEG unit of the Neurosciences Service of the El Cruce Hospital, since January 2016 to December 2019. We analyzed 36 patients (p) with drug resistant epilepsy, surgery candidates, with indication of depth electrodes implantation (SEEG). ECS is performed between two adjacent contacts. During current injection, cognitive tasks are performed according to the stimulated cortical zone. Clinical response and / or appearance of post-discharge (PD), are recorded.
The epileptogenic zone (EZ) diagnosis was as follows: 14 p (39%) have mesial temporal lobe epilepsy , 9 p (25%) frontal lobe epilepsy, 5 p (14%) lateral temporal lobe epilepsy, 3 p (8%) occipital lobe epilepsy, 2 p (6%) insular epilepsy, 1 p (3%) parietal lobe epilepsy and 2 p (5%) no define EZ diagnosis. In 14 p (39%) ECS triggered provoked seizures similar as theirs usual. In 14 p (39%) ECS triggered functional symptoms related with cortical stimulated area.

EEC has been used to localize function in the human brain. Its clinical value for preserving eloquence, shortening postoperative motor and linguistic deficits, and increasing quality of life is well established and recognized and contribute to define EZ.

E-Posters

DISORDERS OF THE NERVOUS SYSTEM

Effects of late bone marrow mononuclear cell transplantation in rats with sciatic nerve crush. Analysis of a potencial therapeutic window

Vanina Usach [1], Mailin Casadei [2], Gonzalo Piñero [1] Marianella Vence [1], Pablo Brumovsky [2], Patricia Setton-Avruj [1]

1 Cátedra de Química Biológica, FFyB, UBA. IQUIFIB-CONICET

2 Instituto de Investigaciones en Medicina Traslacional (IIMT) CONICET-Austral Facultad de Ciencias Biomédicas, Universidad Austral

Presenting author:
***Vanina Usach**, vaninausach@gmail.com*

When systemically transplanted after lesion, multipotent bone marrow cells (BMMC) migrate spontaneously to the injured sciatic nerve, as observed in a model of reversible sciatic nerve crush. Once at the Ipsilateral nerve, BMMC promote regeneration in terms of morphology, slightly improve the amplitude of compound muscle action potential and fully prevent injury-associated neuropathic pain. To propose systemic BMMC transplant as a potential therapeutic strategy, the aim of the present work is to determine the most adequate moment for BMMC transplant after injury to optimize effects on nerve regeneration. To this aim, adult Wistar rats submitted to 8-second sciatic nerve crush were systemically transplanted with BMMC at different survival times post lesion and sacrificed 7 days after transplant. Cell recruitment was confirmed by confocal microscopy and transplant effects were evaluated only in animals transplanted 7 days post injury. Results show the highest number of BMMC recruited into the ipsilateral nerve when transplanted at the peak of demyelination, 7 days post injury. Partial recovery was observed in terms of myelin and axonal protein organization and levels; with no effects on sciatic functional index detected. However, a remarkable and sustained reduction in mechanical and cold allodynia was promoted by late BMMC transplant. Further experiments are needed to establish the best timing for late BMMC transplant towards improvement of peripheral demyelination processes.

E-Posters

INTEGRATIVE SYSTEMS

Flip & pip? Visual attention modulations on auditory encoding are shaped by audiovisual precision but also unimodal uncertainty

Francisco Cervantes Constantino, Thaiz Sánchez-Costa, Germán A. Cipriani, Alejandra Carboni
Universidad de la República - Uruguay

Presenting author:
***Francisco Cervantes Constantino**, fcervantes@psico.edu.uy*

Our environment propagates audiovisual (AV) signals that we need to attend to oftentimes. Visual and auditory contributions can serve jointly as a basis for selection, but it is unclear what hierarchical effects arise when initial selection criteria are unimodal, or involve uncertainty.

We investigated the effects of visuospatial selection on auditory processing with electroencephalography (EEG). Using temporal response function models (TRF) of the auditory EEG timeseries, we addressed the neural encoding of tone pips probabilistically associated to spatially-attended visual changes ('flips'). AV precision (temporal uncertainty) was manipulated while participants sustained goal-driven, visuospatial selective attention. The roles of unimodal (visuospatial and auditory) uncertainties were further investigated.

TRF estimates showed AV precision determined cross-modal modulations, but also did visuospatial uncertainty by enabling the visual priming of tones when relevant for auditory segregation. Auditory uncertainty, in addition, determined susceptibility of early tone encoding to change by incoming visual update processing.

Sensory uncertainty is one factor considered in computational proposals of attention where precision weighting acts as primary mechanism for selection. The findings provide a hierarchical account of the role of uni- and cross-modal sources of uncertainty on the neural encoding of sound dynamics in a multimodal attention task.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Central Autonomic Network association with cardiac autonomic sleep-wake rhythm in healthy adults.

Agustina E. Wainsztein [1], Vicente Camacho-Téllez [1], Carolina Abulafia [1] Mirta Villarreal [1], Daniel Vigo [1], Ximena Goldberg [2], Carles Soriano-Mas [3], Salvador M. Guinjoan [1], Mariana Castro [1]

1 Grupo INAAC, FLENI-CONICET Neurosciences Institute, Buenos Aires, Argentina
2 Parc Taulí University Hospital, Universitat Autònoma de Barcelona, Spain
3 Bellvitge Biomedical Research Institute-IDIBELL Barcelona, Spain

Presenting author:
***Agustina Wainsztein**, awainsztein@gmail.com*

BACKGROUND: Resting heart rate variability (HRV) has been shown as an index of inhibitory control, adaptability and health. The Central Autonomic Network (CAN) comprises brain regions also involved in behavioral and emotional processes. Evidence on the relationship of cortical thickness of CAN components and HRV sleep-wake cycle is scarce. We investigated neural correlates of HRV chronobiological patterns in healthy individuals. METHODS: Thirteen participants (10 female; mean age: 36 ±12) underwent 24hr-HRV recordings following structural MRI. Cortical and subcortical volumetry were performed (Freesurfer). Sleep-wake HRV measures (i.e, HF and RMSSD) were calculated and correlated with cortical thickness of CAN regions. Self-reported mental health measures were examined. RESULTS: Cortical thickness of right anterior cingulate (ACC) and insula, bilateral precentral and inferior frontal gyrus (IFG) areas, were positively correlated with sleep-HF and RMSSD ($p<.05$). Increased diurnal-HF and RMSSD were associated with greater orbitofrontal, and right ACC and insula respectively ($p<.05$). CONCLUSIONS: Greater cortical thickness of CAN regions may be associated with increased sleep and wake cardiac parasympathetic control in healthy adults. HRV chronobiological patterns could serve as an index of preserved neural architecture and functioning subsequently leading to emotional well-being. Future research should aim to identify early neurophysiological biomarkers of psychopathology.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Chronic and passive alcohol administration induces ΔFosB expression in mesocorticolimbic brain areas in adolescent and adult rats

Aranza Wille-Bille [1], Andrea Godino [1], Ricardo Pautassi [1]

1 Instituto de Investigación Médica Mercedes y Martín Ferreyra (INIMEC-CONICET-UNC), Córdoba, Argentina
2 Facultad de Psicología (Universidad Nacional de Córdoba), Córdoba, Argentina

Presenting author:
***Aranza Wille-Bille**, aranza.wb@gmail.com*

We have shown that adolescent rats consumed less alcohol than adults, when assessed across an intermittent and chronic two-bottle choice test, and exhibited a progressive increase in alcohol intake and preference, whereas adults exhibited a stable pattern. Despite drinking less alcohol, adolescent consumption was associated with greater ΔFosB expression in several areas of mesocorticolimbic pathway. ΔFosB is an early transcription factor, that regulates gene expression and accumulates after chronic exposure to drugs. Here, we assessed if ΔFosB induction is dependent on an escalating pattern of alcohol exposure, rather than in the volume of exposure. Adolescent or adult rats were intermittently administrated vehicle, escalating (0.5- 2.5 g/kg) or high, constant (2.0 g/kg) doses of intragastric alcohol, across 18 sessions. Seventy-two hours after the last administration, ΔFosB was quantified in Prelimbic Cortex, Nucleus Accumbens, Striatum, Basolateral Amygdala and Central Nucleus of Amygdala, by immunohistochemistry. We found that both patterns of alcohol exposure increased ΔFosB levels, equally in adolescent and adult rats. The constant doses exacerbated ΔFosB in all brain areas but in Central Nucleus of Amygdala, whereas the escalating doses induced ΔFosB expression in Prelimbic Cortex and Basolateral Amygdala. The study further confirmed that chronic and passive alcohol exposure induces ΔFosB in brain areas involved in reward processing, in adolescent and adults.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Remapping of hippocampal place cells in an unrewarded contextual memory task

Azul Silva [1], Pedro Bekinschtein [2], Mariano Belluscio [1]
1 GNS, IFIBIO, UBA-CONICET
2 INCYT, CONICET

Presenting author:
***Azul Silva**, azzzulsilva@gmail.com*

In order to retrieve an episodic memory our brain needs to integrate the contextual information available. But usually, the information is incomplete, so which memory is retrieved in a particular situation? Pattern completion allows us to generalize and retrieve memories although information is partial. On the other side, when we need to encode a new memory without interfering with a pre-existing one, pattern separation is involved. The hippocampus has a key role in these memory processes.

Some hippocampal neurons, place cells (PC), are tuned to spatial location and generally change their tuning when sensory inputs change (remapping). But sometimes, although the context changes, PC doesn't remap. Accumulating evidence has suggested that the hippocampal ability of storing and distinguishing between different situations and contexts, can be related with place cell's remapping.

The aim of this project is to understand how the remapping observed in CA1 and CA3, two hippocampal regions, correlates with the evocation of contextual memories. To tackle this question we use a behavioral task that allows us to discriminate if an animal recognizes a context as new (pattern separation), or as one it already knows (pattern completion). We carried out electrophysiological recordings in CA3 and CA1 while the animal was performing the task. Preliminary results shows that there is a correlation between the amount of remapping and the memory that the animal is recalling.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Impulsive responses of adolescent rats in a rewarded task

Cecilia Martinez [1,2], Gustavo Murer [1], Mariano Belluscio [1]

1 Laboratorio de Fisiología de Circuitos Neuronales, IFIBIO-Houssay, UBA-CONICET
2 Dto Fisiología Biología Molecular y Celular, FCEN, UBA.

Presenting author:
***Cecilia Martinez**, ceciliamartinez256@gmail.com*

The striatum controls the execution of precise movements and action sequences. Whether to perform or not an action at the right time is key to survival. We have previously studied the activity of the dorsal striatum of adult rats (>p60) in a self-initiated task that required, after a minimum waiting time, the emission of an 8-licks sequence to obtain a reward. Interestingly, we found a modulation of the neuronal activity previous to the initiation of the learned sequence. This anticipatory activity was related to reward expectancy, reflecting the animals' subjective valuation of timing. As regulatory circuits become mature during adolescence, we trained p30 rats in the same task with the aim of studying their striatal activity. Though adolescents were able to learn the action sequence and showed an improvement in the performance throughout training, they had a strong impulsivity prevalence: they made twice as much the number of premature entries with 8-lick sequences per reward as adults. Besides, they showed differential anticipatory activity between timely and premature trials, which also diverged from the neuronal activity of the adults. Together with the behavioral data, our results show age-related differences in the striatal signaling that could underlie the control of the timely execution of actions.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Nociceptive responses of cortico-striatal neurons of the Anterior Cingulate Cortex in an animal model of chronic pain

Constanza Ilarraz [1], Mario Acuña [2], Thomas Nevian [2] Fernando Kasanetz [1]

1 Grupo de Neurociencias de Sistemas, Instituto de Fisiología y Biofísica (IFIBIO) Houssay, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina

2 Department of Physiology, University of Bern, Switzerland

Presenting author:
***Constanza Ilarraz**, cotydie@gmail.com*

Pain is a sensory and emotional experience mediated by distributed brain networks. Maladaptive functional changes in the so called “pain matrix” may participate in the chronification of pain. In particular, during chronic pain (CP), the representation of noxious stimuli shifts from the typical nociceptive circuits to the limbic system, involved in the affective and motivational assessment of pain.

Cortico-striatal (CS) neurons of the Anterior Cingulate Cortex (ACC) may play a key role in linking nociceptive and limbic systems during CP. The ACC is a main area of the pain matrix and is essential for the affective connotation of pain. Its projections to the medial striatum (MS) converge with other limbic inputs and the midbrain dopamine system. However, it is unknown how this neurons process nociceptive signals and how this is affected during CP.

To address this issue we used a mice model of neuropathic pain and recorded specifically CS-ACC neuronal activity in response to noxious stimuli in freely behaving animals. For that, we imaged neuronal calcium signals through a GRIN lens implanted over the ACC and a miniature microscope mounted on the head.

Our preliminary results show that a set of CS-ACC neurons were activated by nociceptive stimuli and that injured animals exhibited a differential pattern of affective behavioral responses to those stimuli. Further experiments will permit us to better understand the role of CS-ACC neurons on the affective expression of CP.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Analysis of beta bursts activity along the primary motor cortex depth in a rodent model of Parkinson's disease

Daniela Piña Novo, Gustavo Murer, Mariano Belluscio,
Grupo de Neurociencia de sistemas, IFIBIO Houssay-UBA-CONICET

Presenting author:
***Daniela Piña Novo**, danielanovo77@yahoo.com*

The nigrostriatal degeneration developed during Parkinson's disease leads to changes in the oscillatory activity both of the basal ganglia and the motor cortex (MC). In particular, exaggerated beta bursts (15–35 Hz) have been shown to emerge after dopamine depletion. This pathological beta band exacerbation is also correlated with motor symptoms of the disease, such as bradykinesia and rigidity. Thus, along with the symptomatic relief resulting from the administration of L-DOPA, which is the gold standard medication, there is a decrease in the prevalence of beta activity. Our previous characterization of beta bursts in MC of hemiparkinsonian mice disclosed a similar pattern, with an increase in their amplitude, duration and occurrence. Interestingly this pattern reversed during the acute effect of L-DOPA, but reappeared when L-DOPA effects have worn off. Here we evaluated the relationship of beta bursts occurrence and their amplitude with the depth within MC. Additionally, we performed the same analysis but separating in rest and movement periods. We found that in lesioned animals, whether they had not received L-DOPA or were out of its acute effect, the number of beta bursts differed significantly along cortical depth. Particularly, there was an increase around layer 5. Beta burst amplitude profile exhibited a small increment around this depth but it didn't differ significantly.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Visual sensitivity of giant neurons to the size of moving objects in the crab Neohelice granulata

Estela Lanza [1,2], Daniel Tomsic [1,2]

1 Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Fisiología, Biología Molecular y Celular, Buenos Aires, Argentina.
2 CONICET-Universidad de Buenos Aires

Presenting author:
***Estela Manuela Lanza**, estela.m.lanza@gmail.com*

The semiterrestrial crab Neohelice (previously Chasmagnathus) granulata is proven to be a remarkable model to study the neurobiology behind visualy guided behaviors. Crabs allow the possibility of intracellular recording from neurons located in high visual centers of living animals. As this crab is preyed upon by gulls, large objects elicit a scape response. In the past we have extensively recorded giant neurons from the lobula (third optic neuropil), which are sensitive to large moving objects and are involved in the scape behavior. These animals also prey upon smaller crabs. Recent experiments revealed that a small dummy moving at ground level elicits strong chasing responses, whereas the same dummy elevated 10 cm above the ground elicits reliable escape responses. With the aim of characterize the sensitivity of lobula giant (LG) neurons to size and elevation of moving objects we recorded the electrophysiological responses of LG neurons to large, medium and small translational visual stimulus with linear trajectories at the equator of the eye and small objects with linear trajectories above and below the equator.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Assessing connectivity in the adult zebrafish pallium

Julio Castillo [1], Lucas Mongiat [2]
1 Balseiro Institute
2 Medical Physics Department, Centro Atómico Bariloche

Presenting author:
***Julio Roberto Castillo Elias**, vettocastilloe@gmail.com*

The pallium of teleosts is a brain structure implicated in different forms of cognitive learning. Experimental data have shown that learning and memory systems are more conserved throughout evolution than previously thought, with teleost fish relying on homologous neural substrates for learning and memory processes as mammals. For example, molecular and behavioral studies in teleosts suggest that the telencephalic dorsomedial (Dm) region shares homology with the basolateral amygdala of mammals, whereas the dorsolateral (Dl) telencephalic region shares homology with the mammalian hippocampus. Preliminary results from our group indicate that the functionality of pallial sub-structures is not homogeneous along the rostrocaudal axis. Moreover, little is know about the connectivity between different pallial circuits, whereas a few studies demonstrated glutamatergic connections between Dl and Dm in pallial slice preparations at the medial rostrocaudal level. In this work, we combine a whole-brain ex vivo preparation with field electrophysiological recordings and calcium imaging to characterize connectivity between different pallial circuits along the rostrocaudal axis. Our preliminary data, validate the Dl to Dm glutamatergic connectivity at the medial level of the rostrocaudal axis. Furthermore, we have evidence for an undescribed glutamatergic connection between the caudal Dl and rostral Dm.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Local inhibitory interactions shape early olfactory representation in Drosophila melanogaster

Lautaro Duarte [2], Fernando Locatelli [1,2], Nicolás Pírez [1,2]

1 Departamento de Fisiología, Biología Molecular y Celular; Facultad de Ciencias Exactas y Naturales; Universidad de Buenos Aires, Argentina
2 Instituto de Fisiología, Biología Molecular y Neurociencias; UBA-CONICET, Argentina.

Presenting author:
***Lautaro Alejandro Duarte**, duartelautaro5@gmail.com*

Odorants are detected by receptor neurons (ORNs) that project to the antennal lobe (AL), the first olfactory neuropil in the brain. Once in the AL, ORNs make synaptic contacts with: i) projection interneurons (PNs), the first olfactory neurons that send olfactory information to the rest of the brain; and ii) local neurons (LNs) that form a dense network of lateral interactions within the AL. Anatomical and functional studies indicate that this network redistributes sensory information, presumably to enhance encoding of meaningful odors. To study the role of GABAergic interactions in the local processing of odors in Drosophila sp, we performed calcium imaging experiments of pure odorants and their mixtures. The difference between the activity patterns elicited by the mixtures and that expected based on the activity elicited by the components uncovered several asymmetrical lateral inhibitions. By blocking the expression of GABA-A receptors in PNs, we revealed the pattern of activity that the mixture should evoke if the inhibitory interactions were absent. Interestingly, the measured activity patterns fulfill the expected features of a functional code, however the comparison among pure odorants and mixtures uncovers different lateral interactions, presumably based on other inhibitory mechanisms that compensate the lack of GABA-A receptors. These results are consistent with a model in which the local AL network is established by experience and homeostasis dependent plasticity.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Modulatory activity of dopamine neurons in a self-paced behavioral task

Marcos Coletti, Gustavo Murer, Mariano Belluscio
GNS, IFIBIO,UBA-CONICET

Presenting author:
Marcos Antonio Coletti, *coletti.marcos@gmail.com*

Midbrain dopamine neurons (DAn) signalize the occurrence of a reward as a result of an action taken. Several studies analyze the DAn activity during a behavioral task mediated by a cue that predicts the value of the action to be taken. However, little is known about DAn activity during the performance of a behavioral task in which the action to be taken should be self-initiated.

This work aims to characterize the activity of DAn that innervate the striatum in a self-paced instrumental task. The animal has to estimate a minimum waiting time to enter into a port and initiate a licking sequence to obtain a reward. If the waiting time is not reached the probability of obtaining a reward is zero, even if the licking sequence is done.
Neuronal activity in the ventral tegmental area (VTA) and the substantia nigra (SN) was recorded using tetrodes during the performance of the self-initiated behavioral task.
Preliminary results show that there is a modulation of the neuronal activity in VTA that marks the boundaries of the action sequence, while the SN neuronal activity is modulated around the time for the reward. Interestingly though, some DAn responses differentiate a licking sequence initiated on time from sequences initiated prematurely, both before port entry and at the time of reward.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Shifting the exploration/exploitation balance using a virtual reality foraging task

M Alejandra Prost, Gustavo Murer, Camila Zold
IFIBIO-Houssay, UBA-CONICET

Presenting author:
María Alejandra Prost, *alejandraprost@gmail.com*

A correct balance between exploitation of known resources and exploration of new territories is key to animals' survivor in a natural environment. Many environmental clues such as the quality, quantity and stability of available resources can influence this balance. Different structures have been associated with this decision-making process. We focused on the dorsomedial striatum, which is proposed as an integrator of information about the environment and the animal's internal state. To study the role of the dorsomedial striatum in the exploration-exploitation balance, we designed a virtual reality task. Head-fixed mice explore a virtual linear track consisting of short rewarded areas (RA) separated by unrewarded corridors. Upon reaching the RA, animals are required to perform a sequence of licks to obtain a drop of water as reward. Each consecutive reward requires an exponentially increasing number of licks to be obtained. We determined the breaking point as the maximum number of rewards obtained before the animal decides to stop exploiting the current RA and runs to the next one. We used an array of four chronically implanted tetrodes to record single unit and LFP activity during the task. So far, we have been able to shift the animals' exploration/exploitation balance by changing the length of the corridors separating the RA (longer corridors led to greater breaking points). We are currently analysing single unit activity to determine how is this codified in the structure.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

A project to study how reward and punishment modulate visually evoked responses in the primary visual cortex

M. Florencia Santos, Camila L. Zold

Grupo de Neurociencias de Sistemas, Instituto de Fisiología y Biofísica B. Houssay (IFIBIO-Houssay), UBA-CONICET

Presenting author:
***María Florencia Santos**, santos.mflorencia@gmail.com*

The primary visual cortex (V1) neuronal activity encodes basic properties of visual stimuli. Experience dependent plasticity has been observed in V1 as a way to improve visual perception. However, recent studies show that V1 neural plasticity is also related to reinforcement learning. When rodents experience an association between a visual stimulus and a contingent future reward, a proportion of V1 neurons develop reward timing activity. Cholinergic projections from the basal forebrain (BF) have been shown to be necessary and sufficient to induce the reward timing activity in V1. However, little is known about whether this activity evolves simultaneously in the BF and V1 during learning. On the other hand, if V1 encodes the behavioral significance of visual stimuli in a general way, we hope that it may also encode the time interval between visual stimuli and contingent punishments. To unveil this, we implanted C57BL/6 adult male mice with a microelectrode array in V1 and performed electrophysiological recordings in head-fixed mice learning a visually cued rewarded task. Mice were trained to perform a lick sequence in order to receive a water reward in 70% of cases. We trained 4 mice that successfully learned the task and we identified neurons responding to visual stimulus. To continue with the project, we plan to carry out simultaneous recordings on V1 and BF and also analyze V1 activity in animals exposed to Pavlovian stimulus-reward and stimulus-punishment associations.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Mechanisms and predictors of response in treatment- resistant depression

Maria Lucia Fazzito [1,2,3], Juan José González 2, Leticia Fiorentini [1,2,3], Mirta Fabiana Villarreal [1,2,3], Salvador Martín Guinjoan [1,2,3]

1 CONICET
2 Fundación FLENI
3 Universidad de Buenos Aires

Presenting author:
***Maria Lucia Fazzito**, mlfazzito@fleni.org.ar*

Major depressive disorder (MDD) is a common medical problem and a major public health concern. It has high prevalence and is the main source of disability-adjusted life year. Around 10% of the patients show a lack of response or remission after two courses of appropriate antidepressant dosage within an adequate duration of time (treatment-resistant depression; TRD). They show a poor prognosis and can be treated with intravenous ketamine (IK). This is more invasive than pharmacotherapy, imply higher costs, monitoring and the need to regularly attend to receive it. Thus, there is a necessity to develop predictors of response to the treatment, so patients are selected more appropriately and treated timely.

The predictors and mechanisms of treatment response in TRD, continue to be widely unsettled. However, in recent years, research on functional neuroimages has contributed to characterize some brain circuits involved.

We are currently recruiting a sample of patients diagnosed with TRD who are currently treated with IK (n=10). All participants are being studied before and after the treatment with 3T MRI (volumetric T1, resting-state BOLD, and DTI) and neuropsychological testing.

We aim to study the evolution of clinical, cognitive and imaging variables to find mechanisms and predictors of response to treatment. In this poster in particular, we aim to show the changes in brain connectivity before and after the treatment.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Is the modulation of lateral habenula neuronal activity relevant for spatial processing not involving emotional cues? A preliminary study

Marina Luz Ingravidi [1], Azul Silva [1], Franco Chiesa Docampo [1,3], Mariano Belluscio [1], Joaquín Piriz [1,2], Verónica de la Fuente [1,2]

1 Instituto de Fisiología y Biofísica "Bernardo Houssay" (IFIBIO-UBA-CONICET). Grupo de Neurociencia de Sistemas. Facultad de Medicina, Buenos Aires, Argentina
2 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE-UBA-CONICET) Buenos Aires, Argentina.
3 Instituto Tecnológico de Buenos Aires. Buenos Aires, Argentina.

Presenting author:
***Marina Luz Ingravidi**, maru.luz98@hotmail.com*

The lateral habenula (LHb) is a key structure in neural circuits that encodes motivation. It receives inputs from the basal ganglia and limbic structures and projects to regions such as the ventral tegmental area and the rostromedial tegmental nucleus. Furthermore, the LHb is functionally related to the hippocampus, albeit not directly connected. Accordingly, there is some evidence showing that the LHb is necessary for spatial processing. The main goal of our study is to understand the involvement of the LHb in the processing of spatial information and ultimately to assess how it functionally interacts with the hippocampus for the coding and processing of spatial information. We present herein preliminary data obtained using a novel object location memory paradigm and optogenetics to modulate LHb neuronal activity in long-evans rats. Both channelrhodopsin expressing rats and control rats showed no long term memory when blue light was administered to LHb during training. Considering that in control experiments (no light stimulation) both groups learned equally well, we hypothesize that light itself might be exerting an effect per se, which seems possible according to the literature. It is worth mentioning that optogenetic modulation of LHb neurons does not affect locomotion or anxiety levels, and the same manipulation affects contextual fear conditioning memory. Future experiments will be discussed in order to continue the project.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Motor networks and the simultaneous coordination of multiple targets

Martina Radice [2], Graciela Kearney [2], Lidia Szczupak [2]

1 Departamento de Fisiología, Biología Molecular y Celular; Facultad de Ciencias Exactas y Naturales; Universidad de Buenos Aires, Argentina.
2 Instituto de Fisiología, Biología Molecular y Neurociencias; UBA-CONICET, Argentina
.

Presenting author:
***Martina Radice**, radicemarti@gmail.com*

Neuronal circuits that control motor behaviors orchestrate multiple tasks, including the inhibition of self-generated sensory signals. Are these multiple targets under the radial control of the central pattern generator (CPG) responsible for motor control?

In the leech, T mechanosensory neurons respond to light touch on the skin and also to pressure caused by contraction of the body wall. In the isolated nervous system this sensory neuron shows phase-dependent inhibitory postsynaptic potentials (IPSPs) during dopamine-induced fictive crawling. The timing and magnitude of the T-IPSPs are highly correlated with motoneuron activity in the contraction phase. These results indicate that the central network responsible for crawling sends a reafferent inhibitory signal onto the T cells, concomitant with the signal to the motoneurons.

NS neurons are premotor neurons, at the center of a vast recurrent inhibitory network that affects all the motoneurons in the leech. During crawling NS is subjected to IPSPs tuned to the motor pattern.

In the present investigation we explore the temporal coincidence between signals delivered to motor, premotor and the sensory neurons and the underlying network architecture. While motoneuron activity controls motor contraction, recurrent inhibition sets a limit onto motoneuron activity, and reafferent inhibition precludes spurious sensory activation. Are these different functions controlled directly by the CPG or do they depend on the motor output?

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Studying the role of the Lateral Entorhinal Cortex in the modulation of the piriform cortex neuronal activity

Olivia Pedroncini, Noel Federman, Antonia Marin Burginn
IBioBA-CONICET-MPSP

Presenting author:
Olivia Pedroncini, *olipedroncini@gmail.com*

The piriform cortex (PC), main region of the olfactory cortex, receives afferent (bottom-up) sensory inputs from the olfactory bulb (OB) carrying odor information through the lateral olfactory tract (LOT); and extensive (top-down) inputs from higher-order areas such as the lateral entorhinal cortex (LEC). To understand the contribution of LEC to the processing of odors we study its functional connectivity to the posterior PC (pPC). We infected LEC with adeno-associated virus expressing channelrhodopsin under CamKIIa promoter to activate excitatory LEC afferents arriving to pPC. We recorded then, in acute brain slices, postsynaptic currents in different principal neurons of the pPC in response to photostimulation. We found that excitatory long-range projections coming from LEC differentially modulate the response to LOT stimulation along the layers of the pPC. Layer 3 deep pyramidal neurons appear to be more affected by LEC activation than layer 2 pyramidal neurons. On the other hand, we discovered that excitatory inputs from LEC recruit local inhibition, independent of the LOT evoked inhibition. This results in a different inhibitory dynamics only for layer 3 neurons. We did not find direct inhibitory long-range projection from LEC to pPC. To assess the role of LEC in the processing of odors in vivo, we are conducting experiments to photoinactivate it during an associative odor-context-reward task and evaluate the effect of LEC inhibition on this olfactory behavior.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Analysis of Effective Connectivity in micro networks of Single and Multi-Unit Activity and Local Field Potential in Human Mesial Temporal Lobe Epilepsy

Santiago Collavini [1], Ulises Romero [1], Carlos H. Muravchik [2], Silvia Kochen [1]

1 Neurosciences and Complex Systems Unit (EnyS), CONICET, Hosp. El Cruce "N. Kirchner", National University A. Jauretche (UNAJ), Calchaqui 5401, Florencio Varela 1888, Buenos Aires,Argentina

2 Research Institute of Electronics, Control and Signal Processing (LEICI), National University of La Plata-CONICET, Calle 116 s/n, La Plata B1900, Argentina.

3 National Council of Scientific and Technical Research(CONICET), Argentina

4 Scientific Research Commission of the Province of Buenos Aires (CIC-PBA), Argentina

Presenting author:
***Santiago Collavini**, santiagocollavini@gmail.com*

Intracranial electroencephalography is the common clinical diagnosis protocol to identify the epileptogenic zone for surgical treatment of drug resistant epilepsy patients. Analyze simultaneous recordings with clinical macro- (cM) and research micro-electrodes (rM) allows us to obtain a better understanding at microscale of how neural network works before and during epileptic seizures. We registered brain activity from cM and rM (AdTech,USA) implanted bilaterally in amygdala and hippocampus of two patients with bilateral mesial-temporal epilepsy, following clinical criteria. Recordings were obtained from 96 microelectrodes located at Seizure-Onset-Zone (SOZ;n=32), ipsilateral but outside of SOZ (n=16) and contralateral to SOZ (n=48). It was noted that the detection and clustering techniques are very sensitive to background noise, which is ten-fold increased during seizures. A way to overcome this drawback is analyze the firing rate (FR) of neurons whose spikes exceeds at least 5 times the amplitude of noise during seizure. We generate different types of micro networks with the SU and MU registered in SOZ and estimate the effective connectivity from autoregressive multivariate models. The preliminary results described 84% of neurons (128/152) showing different types of seizure-related firing patterns. In terms of effective connectivity, we find that the dynamics of the micro networks before and during the seizures present characteristic out-degree patterns.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

KCNQ4 in the reticular activating system (RAS): contribution to the circadian rhythm modulation.

Sofia Stupniki [1,2], Tsogbadrakh Bayasgalan [3], Adrienn Kovács [3] Andrea Csemer [3], Peter Szentesi [3], Krisztina Pocsai [3], Leonardo Dionisio [1,2], Guillermo Spitzmaul [1,2], Bálazs Pal [3]

1 Laboratorio de Canales Iónicos, INIBIBB-CONICET. Bahía Blanca, Argentina
2 Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur. Bahía Blanca, Argentina.
3 Department of Physiology, Faculty of Medicine, University of Debrecen. Debrecen, Hungría

Presenting author:
***Sofia Stupniki**, sofistupniki@gmail.com*

The M-current is a voltage-gated potassium current generated by channels composed by KCNQ2-5 subunits. The pedunculopontine nucleus (PPN) is part of the Reticular Activating System (RAS), associated with sleep regulation. As little is known about the composition, subcellular location and physiological implication of the M-current in PPN, our aim was to demonstrate the presence of KCNQ4 in the PPN, and its contribution to the neuronal function of this nucleus. We used a transgenic mouse lacking KCNQ4 expression (KO) and one with fluorescent-labeled cholinergic neurons (tdTomatoStop+ChAT::Cre). Using qPCR, immunofluorescence and electrophysiology on brain slices, we demonstrated that only a subpopulation of cholinergic neurons (around 27%), located on the external limits of the PPN has KCNQ4-mediated M-current. We also found that KCNQ4 regulates the expression of other KCNQ subunits. In KO mice, the expression profile changed drastically respect with the WT: Kcnq2 expression decreased, Kcnq3 increase and Kcnq5 disappeared. To study the influence of KCNQ4 on circadian rhythm we used behavioral testing. KO mice exhibited alterations in the activity cycles showing a higher sensitivity to changes in the light-darkness cycles. In summary, we found that some PPN cholinergic neurons have KCNQ4-dependent M-current and this subunit contributes to modulate the circadian rhythm. Since the PPN is affected in certain neurological diseases, KCNQ4 might be a potential pharmacological target.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Developmental impact of SSRI antidepressants on emotional prefrontal circuits in mice

Tamara S. Adjimann, Carla V. Argañaraz, Mariano Soiza-Reilly
Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET)

Presenting author:
Tamara Sol Adjimann, *tamara.adjimann@gmail.com*

Early-life exposure to antidepressant drugs acting as selective serotonin reuptake inhibitors (SSRIs), like fluoxetine, has long-lasting detrimental consequences in prefrontal circuits crucially engaged in stress-coping and mood control. Thus, mice treated with fluoxetine during a postnatal critical period (P2 to P14) show alterations in the connectivity of the prefrontal cortex to dorsal raphe nucleus (PFC-to-DRN) circuit, accompanied by increases in depressive-like and anxiety behaviors in adult life. In this study, we investigated the short-term effects (at P15) of fluoxetine exposure in the critical period on the synaptic connectivity of the developing PFC-to-DRN circuit, and whether this could affect the response of DRN serotonin neurons to stress. Our quantitative analysis using a high-resolution microscopy technique (array tomography) showed a synaptic hyper-innervation of the developing PFC-to-DRN circuit in fluoxetine-exposed mice in comparison to controls. These changes in PFC afferents were detected onto both serotonin and non-serotonin neurons of the DRN. Additionally, early fluoxetine exposure topographically dampened the activation of DRN serotonin neurons in response to an acute stress (forced swim), as revealed by c-Fos immunohistochemistry. These findings indicate that early-life exposure to SSRIs alters the ontogenetic trajectory of the PFC-to-DRN synaptic circuit, likely contributing to adult emotional alterations.

E-Posters

NEURAL CIRCUITS AND SYSTEMS NEUROSCIENCE

Major Depressive Disorder and Borderline Personality Disorder: Emotional regulation and neuroimaging

Vicente Camacho-Telléz [1], Agustina Wainsztein [1], Mariana Castro [1] Mirta Villarreal [2], Salvador Guinjoan [3]

1 Grupo de Investigación en Neurociencias Aplicadas a las Alteraciones de la Conducta. FLENI, Buenos Aires, Argentina.
2 Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET), Argentina.
3 Servicio de Psiquiatría. FLENI, Buenos Aires.

Presenting author:
***Vicente Camacho-Téllez**, vicentct@hotmail.com*

Emotional problems figure in many clinical conditions (Sheppes, 2015), such as Major Depressive Disorder (MDD) or Borderline Personality Disorder (BPD) (Vitriol, 2017). Both disorders share clinical and biological characteristics, included the emotion s neural circuit (Goodman, 2010).

The objective is to describe the differences in cortical thickness, brain volumetry, cognitive emotional regulation between both disorders and to explore the correlation between emotional regulation and cortical thickness. Materials and methods: 19 MDD patients, 18 BPD and 20 healthy controls were recruited. Cognitive Emotional Regulation Questionnaire (CERQ) was applied. MRI were obtained with a GE 3T scanner and processed with FreeSurfer 6.0 toolset. CERQ s score and volume structures were compared. Pearson's.

E-Posters

NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

Structural remodelling of microglia and dendritic spines in the Nucleus Accumbens core underlie chronic restraint stress-induced cocaine sensitization

Bethania Mongi-Bragato*, María Paula Avalos*, Marianela Sánchez, Axel Gorostiza, Daiana Rigoni, Andrea Susana Guzmán, Gastón Diego Calfa, Flavia Bollati

IFEC-CONICET. Departamento de Farmacología, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Argentina

Presenting author:
Bethania Mongi-Bragato, *mongibragato.bethania@gmail.com*

Stress has long been known to increase vulnerability to drug addiction. Studies from our lab showed that stressful experience causes enduring neuroadaptations on glutamate system in the Nucleus Accumbens (NAc) which enables sensitized response to cocaine. Similarly, we evidenced glutamate mechanisms implied in psychostimulant sensitization induced effects at immune level. However, there is no evidence of the role played by microglia in this phenomenon. Here we evaluate the effect of minocycline (MNC), an inhibitor of microglia activation, on stress-induced cocaine sensitization, morphological changes of microglia and postsynaptic structural modifications in the NAc core. Rats were exposed to restraint stress (2 h/day x 7 days) and treated with MNC (30 mg/Kg/12h) or vehicle for 5 days previous cocaine (15 mg/kg) or saline challenge administration (Day 21). On this day, locomotor activity, NA immunofluorescence for iba-1 (microglia marker) and dendritic staining with a lipophilic dye (DiI) were performed. MNC was able to prevent stress-induced cocaine sensitization and stress-induced hyper-ramification of accumbal microglia. In parallel, stress-induced postsynaptic structural remodelling were reversed with MNC by reorganizing the density of each spine type. These results reveal a critical role of microglia in postsynaptic structural adaptations following stress to trigger cocaine sensitization and demonstrates promising evidence of MNC as therapy to prevent this comorbidity.

* Equal Contribution.

E-Posters

NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

An approach to address the effects of microglia depletion on degeneration and regeneration after olfactory nerve damage

Diego M. Topsakalian, Luis E. Acosta, Ana P. Piantanida, Jesica N. Unger, Juan E. Belforte, Lorena Rela
IFIBIO Houssay (CONICET- UBA)

Presenting author:
Diego Martín Topsakalian, *diegotopsa@gmail.com*

Olfactory ensheathing glia is recognized for its ability to promote axonal growth, a property that is normally used to explain the regenerative capacity of the olfactory nerve. However, little attention has been paid to the possibility that immune cells (microglia/macrophages) present in the afferent olfactory pathway participate in its repair, although they show signs of activation after damage. To determine whether microglial cells present in the afferent olfactory pathway mediate damage severity and/or recovery, we propose to analyze the effects of microglia depletion by PLX5622 in a mouse model of damage to the olfactory nerve by the olfactotoxin methimazole. The functional status of the olfactory nerve will be evaluated by a habituation/dishabituation olfactory test at four or fourteen days after damage. In addition, the same day of the behavioral test, we will collect tissue to obtain an anatomical correlate from histological preparations of the bulb and olfactory mucosa, to verify the microglial depletion and to evaluate the sensory neuron integrity. If microglial cells play a role in damage severity and/or resolution, we expect that the animals show partially conserved olfactory function or slower recovery, respectively, with PLX5622 treatment. This approach sets the basis to analyze whether inflammation modulates the neurotrophic properties of olfactory ensheathing cells.

E-Posters

NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

IGF1 gene therapy promotes synaptic remodeling by microglia

Eugenia Falomir-Lockhart [1], Franco Juan Cruz Dolcetti [1], Macarena Lorena Herrera [2], Jeronimo Pennini [1], Ángeles Arévalo-Arévalo [3], Bjorn Spittau [4], Claudia Hereñu [2], María José Bellini [1]

1 Instituto de Investigaciones Bioquímicas de La Plata "Profesor Doctor Rodolfo R. Brenner" (INIBIOLP-UNLP-CONICET), La Plata, Argentina
2 Departamento de Farmacología, Facultad de Ciencias Químicas. UNC. Instituto de Farmacología experimental de Córdoba (IFEC-UNC-CONICET), Córdoba, Argentina
3 Laboratorio de Esteriodes Neuroactivos, Departamento de Neurobiología Funcional y de Sistemas, Instituto Cajal (CSIC), Madrid, España
4 Intitute for Anatomy, University of Medicine of Rostock, Rostock, Germany

Presenting author:
***Eugenia Falomir-Lockhart**, eugefalomir@gmail.com*

Microglia are the resident immune cells of the central nervous system (CNS). These cells play important roles in healthy and diseased brain in order to maintain homeostasis. One of these roles is the maintenance of synapses. Microglia promote synaptogenesis by secreting growth factors and regulate the number of synapses during the process of synaptic pruning. In the adult CNS, microglial ramifications interact with synaptic terminals and synaptic clefts, dendritic spines and astrocytic processes. During aging, microglia go through an age-related degeneration characterized by reduced migratory and phagocytic capacity, low production of neurotrophic factors and are more insensitive to stimuli. Consequently, these alterations lead to an impaired surveillance of the surrounding environment, impaired synaptic regulation and, therefore, loss of brain homeostasis. Thus, it is of great interest to design strategies to keep the microglia working correctly. In this regard, IGF1 has shown to be able to act on aged microglia, promoting their proliferation and their phagocytic capacity. We implemented IGF1 gene therapy in aged rats of 28 months-old and studied how it affected microglial activity. We observed that microglia increased phagocytic activity and synaptic remodeling. Moreover, these animals presented better motor performance. These results suggest that IGF1 gene therapy could be an effective treatment to modulate microglia activation and promote motor improvement.

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NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

Synaptic and cellular plasticity of cortico-striatal neurons of the Anterior Cingulate Cortex associated to neurophatic pain

María Jesús Trujillo, Constanza Ilarraz, Fernando Kasanetz

Grupo de Neurociencias de Sistemas, Instituto de Fisiología y Biofísica (IFIBIO) Houssay, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina.

Presenting author:
***María Jesús Trujillo**, jesutruji@gmail.com*

Chronic neuropathic pain (NP) is a highly prevalent and debilitating neurological condition. On the cellular level, the elevated pain sensitivity is induced by aberrant neuronal plasticity at all stages of the nociceptive pathway. Whereas a lot is known about the mechanisms mediating NP in the peripheral nervous system and in the spinal cord, less is known about these processes in brain areas where pain is eventually perceived.
The Anterior Cingulate Cortex (ACC) is a key area of the nociceptive system, is essential for encoding pain affect and is hyperactive in patients suffering from chronic pain. Also, synaptic and cellular modifications in ACC neurons are necessary for the expression of nociceptive sensitization in animal models of NP.

Recent data suggest that abnormal recruitment of basal ganglia (BG) structures may facilitate the persistence of pain. In this context, we speculate that abnormal nociceptive processing during NP could spread to the BG through aberrant neuronal plasticity in cortico-striatal (CO-ST) neurons of the ACC. However, little is known on how NP affects these neurons.

To gain insight on this, we evaluated the synaptic and cellular modification in CO-ST ACC neurons associated with NP. To do this we combined neuronal identification with fluorescent retrograde tracers and ex-vivo electrophysiological recording (brain slices) in a rodent model of NP. Our preliminary data shows that NP impairs the integration of synaptic inputs into CO-ST ACC neurons.

E-Posters

NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

Corticosterone modulates Acid sensing ion channels type 1a (ASIC-1a) dependent long-term potentiation at the mouse anterior cingulate cortex

María Natalia Gobetto, Carlota González-Inchauspe, Adriana A. Albanese, Osvaldo D. Uchitel

1 Instituto de Fisiología, Biología Molecular y Neurociencias. CONICET - UBA

Presenting author: ***María Natalia Gobetto***, *natygobetto@gmail.com*

Acid-sensing ion channels (ASIC) are involved in synaptic plasticity, activity-dependent long-term potentiation (LTP) is an example. Neurons in the anterior cingulate cortex (ACC) express ASIC-1a. Its postsynaptic activation generates synaptic currents (ASIC1a-SCs) that add to the glutamatergic excitatory postsynaptic currents (EPSCs). Corticosterone (CS) has been shown to modulate ASIC-SCs. In wild type (WT) and ASIC-/- C57BL/6 mice, aged P30-60, we performed whole-cell patch-clamp recordings from pyramidal neurons in layer II/III of the ACC to evoke glutamatergic AMPA receptor-mediated EPSCs. After blocking AMPA, NMDA, GABA and glycine receptors (r), we detected ASIC-SCs sensitive to ASIC-1a inhibitor psalmotoxin-1 (PcTx1). CS added to the aCSF increased ASIC1a-SC amplitude. PcTx1 reduced the amplitude of ASIC1a-SCs treated with CS. Under control conditions, a single theta-burst stimulation (TBS) did not cause LTP of glutamatergic EPSCs. After incubation with CS, one TBS induced significant LTP of EPSC amplitudes in WT. The magnitude of LTP when CS was applied together with an NMDAr inhibitor was not significantly different to that with CS alone. In the presence of CS, LTP was abolished when ASIC-1a was blocked by PcTx1, and impaired in ASIC-/-. Pre-treatment with CS at 35°C showed enhanced EPSCs. We have demonstrated that CS, acting through ASIC-1a, reduces the threshold for LTP induction of glutamatergic ESPCs. The effect of CS is also enhanced by temperature.

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NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

Altered HCN channel function in thalamic ventrobasal neurons of leptin-deficient mice

Paula Perissinotti, Lucila Kargieman, Agustin Rocha, Tomas Grosso, Francisco Urbano
IFIBYNE-UBA-CONICET

Presenting author:
Paula Patricia Perissinotti, *peripali@gmail.com*

The Hyperpolarization-activated Cyclic Nucleotide-gated (HCN) channel is a voltage-gated ion channel that carry the H-current (IH). The expression of HCN1-4 isoforms is abundant in the thalamus. This channel is activated at sub-threshold potentials and works as an intrinsic and slow voltage-clamp that tends to stabilize the resting membrane potential, regulating the neuronal excitability and the synaptic integration. Leptin is a pleiotropic hormone that regulates numerous CNS functions. The dense distribution of leptin receptor mRNA in the thalamus suggests that leptin could act as a neuromodulator of thalamocortical activity. Here, we studied the electrophysiological expression of IH in ventrobasal (VB) neurons in brain slices from wildtype (WT) or the leptin-deficient mouse (ob/ob). IH density was increased by 22% in WT females compared to WT males. However, IH density was altered regardless of the gender in the ob/ob mice. Similarly, IH density decreased by 22% in ob/ob males (WT, n=23; ob/ob, n=22) and 16% in ob/ob females (WT, n=14; ob/ob, n=11). The time constant of deactivation was slower in the ob/ob compared to the WT for either males or females. In order to study whether IH alterations could be reversed, leptin was injected in vivo through a cannula implanted in the VB nucleus of ob/ob mice. We found that 24 hours after injecting leptin, IH density reached values as observed in WT, confirming that alterations of HCN channel function could be reversed by leptin.

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NEURAL EXCITABILITY, SYNAPTIC TRANSMISSION AND NEURON-GLIA INTERACTIONS

Dynamics of vesicular fusion in chromaffin cells – an amperometric view

Samuel Alfonso-Bueno, Luciana I. Gallo, Fernando D. Marengo
Instituto de Fisiología, Biología Molecular y Neurociencias, Universidad de Buenos Aires, Consejo Nacional de Investigaciones Científicas y Técnicas, Buenos Aires, Argentina

Presenting author:
Samuel Alberto Alfonso Bueno, *alfonsosamuel25@gmail.com*

Chromaffin cells release adrenaline to the extracellular space through Ca2+-dependent exocytosis after fusion of secretory vesicles to the plasma membrane. Using amperometry, the dynamics of vesicular fusion can be recorded with sub-millisecond temporal resolution. A carbon fiber microelectrode is placed in close contact to the cell and, by applying an oxidation potential to the electrode, single-vesicle release of adrenaline can be detected as individual current spikes. Kinetic parameters, as amplitude (I), charge (quantal content, Q), half-width time (t1/2) and the decay time constant (τdecay), of the spike can be determined for each amperometric event. In this work, we evaluated the dynamics of vesicular fusion in mouse chromaffin cells by analyzing the amperometric spikes registered during stimulation with K+ 50 mM for 2 min. We analyzed the distribution of events according to Q and found that the Q1/3 distribution was best fit as the sum of three Gaussians after the comparison of one, two and three Gaussians fit with AIC and Fisher statistical tests. These vesicular subpopulations could also be described by the other kinetics parameters of the amperometric events when evaluated in relation to Q. These results strengthen the evidence for the presence of subpopulations of secretory vesicles. This analysis will be useful to determine key proteins regulating the dynamic of fusion of the different subpopulations of secretory vesicles in neurosecretory cells."

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Long term effect of social isolation during adolescence on β-catenin levels as well as on anxiety: role of dopamine neurotransmission

Alejandrina Funes [1,2], Cintia N. Konjuh [1], Silvana B. Rosso [1,2], Alejandra M. Pacchioni [1,2]

1 Facultad de Cs. Bioquímicas y Farmacéuticas, UNR
2 CONICET

Presenting author:
***Alejandrina Funes**, alejandrina.funesp@gmail.com*

Adolescence is a key period of development, where major cognitive and neurobiological changes occur. Results from our lab showed that 5 days of social isolation (SI) in adolescent rats lead to short term molecular changes in the Wnt/Bcatenin pathway and to higher cocaine reinforcing properties during adulthood. In the present study, we assessed if dopamine (DA) is involved in SI impact on Bcatenin changes in specific brain areas. We also investigated a possible SI impact on behavioral responses such as anxiety during adolescence. To carry out our objectives, male and female Wistar rats were isolated (SI) between PND30 to 35, or kept in their home cages (controls). All rats were treated with Sulpiride (100 mg/kg, i.p.) or Vehicle during the SI period. Then, they were sacrificed on PND36 or PND45 and [?]catenin levels were analyzed by Western blot in Prefrontal Cortex (PFC) and in Nucleus Accumbens (NAcc). Also, behavioral studies were carried out to evaluate anxiety levels. Open Field and light/dark transition tests were performed between PND42-44, while only the Open field test was performed in those animals that were sacrificed on PND36. Our findings showed that SI decreased Bcatenin levels in PFC and modified anxiety like behaviors (especially in females) on PND44. We also found that a systemic administration of Sulpiride reverses the impact of SI on Bcatenin levels in PFC as well as the behavioral effects.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Evaluation of microglial depletion followed by repopulation in chronic CPZ-induced demyelination

Anabella Ayelen Di Pietro [1], Victoria Sofia Berenice Wies Mancini [1], Marianela Vence [1], Juana Maria Pasquini [1], Jorge Daniel Correale [2], Laura Andrea Pasquini [1]

1 Departamento de Química Biológica, Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires-CONICET, Buenos Aires, Argentina.
2 Instituto de Investigaciones Neurológicas Dr. Raúl Carrea, FLENI, Buenos Aires, Argentina.

Presenting author:
***Anabella Ayelen Di Pietro**, anabella.a.dipietro@gmail.com*

Demyelinated axon degeneration is the major cause of irreversible neurological disability in patients with progressive multiple sclerosis (MS). Cuprizone (CPZ) administration for more than 12 weeks can model progressive MS in triggering chronic demyelination, neurodegeneration, astrogliosis and exacerbated microglia (MG) activation. MG are physiologically dependent on colony-stimulating factor 1 receptor (CSF-1R) signaling and can thus be almost completely eliminated from the brain using CSF-1R inhibitors like BLZ945. Our previous results show that continuous BLZ945 treatment attenuates demyelination but exacerbates axonal degeneration, whereas MG depletion followed by repopulation has been shown to normalize MG chronic activation. The present work aimed to compare the effects of continuous and intermittent BLZ945 treatment on chronically CPZ-demyelinated mice. Mice were fed either control or CPZ chow for 12 weeks and orally gavaged vehicle or BLZ every week (continuous) or every other week (intermittent) from the 5nd week. BLZ induced a reduction in the number of MG in all structures evaluated and equally attenuated demyelination in both protocols. Functional evaluation showed no significant differences across groups. In conclusion, the intermittent protocol failed to yield microglial repopulation, and future experiments with sparser BLZ945 treatment may help test our hypothesis. These studies may render therapies to effectively treat patients in progressive stages of MS.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Involvement of cannabinoid CB1 receptor in stress-induced enhancement of extracellular glutamate in nucleus accumbens core after extinction of cocaine-conditioned place preference

Andrea Susana Guzman [1], María Paula Avalos, Pia Valentina Euliarte, Marianela Adela Sanchez, Daiana Rigoni, Julieta Boezio, Flavia Andrea Bollati, Miriam Beatriz Virgolini, Liliana Marina Cancela

IFEC-CONICET, Departamento de Farmacología, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.

Presenting author:
***Andrea Susana Guzman**, andrea.guzman@unc.edu.ar*

Previous findings from our lab have demonstrated pharmacologically the role of the cannabinoid CB1 receptors (CB1Rs) within nucleus accumbens core (NAcC) in restraint stress-induced reinstatement of extinguished cocaine-conditioned place preference (CPP). Given the well-established role of glutamatergic transmission within NAcC in reinstatement of cocaine seeking, we evaluated the effects of AM251, a highly selective CB1R antagonist, and ACEA, a highly selective agonist, on stress-induced changes in extracellular glutamate levels within NAcC under reinstatement conditions. In vivo microdialysis experiment in male Wistar rats, combined with HPLC and electrochemical detection was used. Firstly, a reinstating stress session (30 min of restraint), but not a non-reinstating stress session (15 min of restraint), increased the extracellular glutamate levels within NAcC in animals that were re-exposed to the drug-paired compartment after extinction of cocaine-CPP. Interestingly, the microinjection of AM251 directly into NAcC inhibited this stress-induced increase of glutamate, and the microinjection of ACEA potentiated it when combined with the non-reinstating stress. These data suggest that CB1Rs in NAcC modulate the context-specific enhancement of glutamate after restraint stress. These findings may be explained in the framework of a dysregulation of glutamate homeostasis in NAcC and provide neurochemical basis to investigate in vivo mechanisms underpinning stress-induced relapse.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Synthesis and functional evaluation of new analogs of caffeine as modulators of the cholinergic system

Camila Fabiani [1], Brunella Biscussi [2], Juan Pablo Munafó [1], Jeremías Corradi [1], Ana Paula Murray [2], Silvia Antollini [1]

1 INIBIBB, Dpto. Biol. Bioq. Farmacia. Univ. Nac. del Sur – CONICET, Bahía Blanca, Argentina.
2 INQUISUR, Dpto. Qca. Univ. Nac. del Sur – CONICET, Bahía Blanca, Argentina.

Presenting author:
Camila Fabiani, *camilafabiani1@gmail.com*

Cholinergic deficit is regarded as an important factor in Alzheimer's disease. Two molecular targets for its treatment are the acetylcholinesterase (AChE) and the nicotinic receptor (nAChR). We previously demonstrated that caffeine acts on nAChRs as a weak agonist and it is known that it inhibits AChE. Here, we synthetized more potent bifunctional caffeine analogs. A theophylline fragment was connected with a pyrrole fragment through homologation from 3 to 7 carbon atoms to form the compounds C3 to C7 (Cn). We found that all Cn inhibited the AChE, having C7 the strongest effect. To explore if the analogs influence the nAChR conformational state, crystal violet (CrV) and nAChR-rich membranes from T. californica were used. The analogs produced changes in the KD values of CrV, being C5 and C6 the most potent. To understand the molecular mechanism underlying these conformational changes, we recorded single-channel events from muscle nAChR. The compounds activated muscle nAChR at low concentrations and the activation was as isolated openings even at the highest Cn concentrations. Our results demonstrate that the new compounds behave as dual modulators by acting as AChE inhibitors and as nAChR agonists. To gain insight about the molecular interaction of these compounds with nAChR we performed in-silico studies. Our results bring new information about the mechanism of modulation of pharmacologic targets for the design of new therapies for the intervention in neurological diseases.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

β3 Integrin and Focal Adhesion Kinase as a Signaling Pathway for MMP-9 Induction of Transient Synaptic Plasticity in D1 vs D2-MSN in Cocaine Relapse

Constanza Garcia-Keller, Reda Chalhoub, Michael D Scofield, Daniela Neuhofer, Ana Clara Bobadilla, Sade Spencer, Peter W Kalivas

1 Department of Neuroscience, Medical University of South Carolina, Charleston, SC, USA.

Presenting author:
Constanza Garcia-Keller, *cgarciakeller@gmail.com*

BACKGROUND: Cocaine use elicits neuroplasticity within the medium spiny neurons (MSNs) of the nucleus accumbens core (NAcore), chemically coded as selectively expressing D1 or D2 dopamine receptors, that leads to increased vulnerability to relapse, even after protracted abstinence. Matrix metalloproteinases (MMPs) are inducible endopeptidases that degrade extracellular matrix (ECM) proteins and reveal an RGD domain that binds and signals through integrins. Integrins are heterodimeric receptors composed of αβ subunits, and their primary signaling kinases are the focal adhesion kinase (FAK) and integrin linked kinase (ILK). Previous results show that β3 integrin is upregulated after cocaine self-administration and MMP-9 activity is increased during cued-reinstatement of cocaine and promotes transient synaptic plasticity in NAcore MSN (t-SP: increases in spine head diameter (dh) and AMPA/NMDA (A/N)). Besides, recent data challenged the functional dichotomy of D1 and D2-MSN in the direct/indirect pathways hypothesis and their role during extinctions vs drug seeking.

METHODS: Male Sprague Dawley, male and female D1- and D2-Cre Long Evans transgenic rats and C57BL transgenic mice were trained to self-administer cocaine, after which self-administration animals were extinguished or exposed to abstinence, and then reinstated by cocaine-conditioned cues. We used a morpholino antisense strategy to knock down the β1 or β3 integrin subunits or inhibitors to prevent phosphorylation of the

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Essential role for Rac1 in chronic stress-induced sensitization to cocaine in nucleus accumbens.

Daiana Rigoni [1], M. Julieta Boezio [1], M. Paula Avalos [1], Andrea S. Guzmán [1], Marianela A. Sánchez [1], Mariano Bisbal [2], Liliana M. Cancela [1], Flavia Bollati [1]

1 IFEC- CONICET. Departamento de Farmacología, Fac. De Ciencias Químicas, Universidad Nacional de Córdoba, Argentina.

2 Instituto Ferreyra (INIMEC-CONICET-Universidad Nacional de Córdoba), Córdoba, Argentina.

Presenting author:
***Daiana RIgoni**, daiana.rigoni.dr@gmail.com*

Several laboratories have demonstrated that the RhoGTPase Rac1 mediates structural and behavioral plasticity in response to cocaine exposure in nucleus accumbens (NA). Specifically, repeated exposure to cocaine negatively regulates Rac1 activity in NA and is responsible for the expansion of dendritic spines, through a mechanism mediated by Cofilin. Our previous results have shown long-term changes in proteins regulating actin cytoskeleton in the NA during the expression of cross-sensitization between stress and cocaine. We have previously described modifications in levels of Cofilin phosphorylation and enhancement in AMPAR surface expression in NA core. Thus, the main goal of this project is to evaluate the role of Rac1 signaling pathway in the development of cocaine sensitization induced by stress. For this purpose, we have generated a lentivirus overexpressing Rac1 protein or a shRNA to suppress Cofilin expression, that were administered intra-NA core before a challenge with cocaine in pre-stressed rats, when behavioral sensitization was evaluated. Additionally, we have examined changes in the AMPAR surface expression. Our findings reveal that the overexpression of Rac1 is sufficient to prevent stress-induced sensitization to cocaine and impedes the GluR1 surface enhancement in NA core observed in pre-stressed animals. These findings constitute a molecular mechanism influencing actin cytoskeleton remodeling in the NA during cross sensitization between stress and cocaine.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

2'-Hydroxy-4',5'Dimethyl-4Dimethylaminochalcone, a novel fluorescent flavonoid with capacity to detect aluminium in cells and modulate Alzheimer's disease target

Fabiola Kamecki [1], Carolina Marcucci [1], Mariela Ferreira-Gomes [1], , Laureano Sabatier [2], Damijan Knez [3], Marina Rademacher [1], Alejandra Marcos [1], Felicitas de Tezanos Pinto [1], Luciana Gavernet [2], Natalia Colettis [1], Mariel Marder [1]

1 Universidad de Buenos Aires. Consejo Nacional de Investigaciones Científicas y Técnicas. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB), Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina.
2 Universidad Nacional de La Plata, Facultad de Ciencias Exactas, Departamento de Ciencias Biológicas. Laboratorio de Investigación y Desarrollo de Bioactivos (LIDeB), Química Medicinal. La Plata, Buenos Aires, Argentina.
3 University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia.

Presenting author:
***Fabiola Kamecki**, fabiolakamecki@hotmail.com*

Alzheimer's disease (AD) is a progressive multifactorial neurodegenerative disorder with several factors contributing to its aetiology such as abnormal protein aggregation (e.g., β-amyloid peptide), oxidative stress, alterations in neurotransmitter levels (e.g., acetylcholine, monoamines), ion metal accumulation in the brain (e.g., aluminium), among others. Due to the complex nature of this disease, there is a critical need to develop multitarget-directed compounds to address the different pathways involved.

In this context, the aim of this work was to synthesize a simple chalcone derivative with capacity to affect different key targets of AD neurodegeneration. Consequently, we report here a microwave-assisted synthesis of a new chalcone derivative, namely 2'-hydroxy-4',5'-dimethyl-4-dimethylaminochalcone (1).

Compound 1 selectively chelated aluminium, inhibited the aggregation of Aβ1-42 peptide at 10μM (80.5 ± 6.3 %), behaved as a radical scavenger and inhibited acetylcholinesterase in vitro (IC50= 4.7 ± 1.1 μM). An extensive spectral study (UV/visible, fluorescence and MS) of chalcone 1/Al3+ complex as well as a molecular modelling study of its 3D conformation confirmed the structure of the complex (2:1). Additionally, chalcone 1 was capable of interacting with aluminium in cell lines HEK293T and SH-SY5Y.

In conclusion, chalcone 1 is a novel probe for the detection of Al3+ in cells and it can be regarded as a promising multifunctional ligand for AD treatment.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Predicting olfactory perception using deep learning algorithms

Federico Zamberlan, Camila Sanz, Laura Alethia de la Fuente, Enzo Tagliazucchi
Laboratorio de Neurociencia Cognitiva Computacional (COCUCO), DF, UBA

Presenting author:
Federico Zamberlan, *federicozamberlan@hotmail.com*

Unlike vision and hearing, the sense of smell remains poorly understood, difficult to model, and even harder to predict. Despite the vital evolutionary role of olfaction, crucial to identify safe food sources or detect nearby fires, we still lack a reliable and principled method to predict the smell of a molecule from its chemical structure: the only reliable way to determine the odour associated with a certain compound is to smell it. We propose a deep learning architecture to predict the odour of molecules from its representation as a chemical graph. The application of sequential convolutional operations is capable of identifying relevant patterns at multiple scales, allowing us to find important relationships that have eluded previous machine learning strategies based on more macroscopic approaches. We validated this approach using data from FlavorDB, a website with almost 26 thousand molecules associated with their respective tastes and smells. After representing the adjectives used to describe tastes and odors as semantic vectors, we were able to predict the projection values in a reduced latent space by training our models using the chemical graphs of the respective molecules, outpeforming previous machine learning algorithms. The computational prediction of odours has potential to accelerate the design of new molecules to be used as fragrances, as well as to unveil the neurobiological principles associated with information processing in the olfactory system.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Preclinical evidence for the atypical antipsychotic-like profile of Cannabidiol: effect on the extracelullar levels of DA in the prefrontal cortex, and a 5-HT1A-mediated mechanism

Jessika Urbanavicius [1], Neielly S Rodrigues [2], Julieta Pomi [1], Ximena López [1], Francisco S Guimaraes [2], Cecilia Scorza [1]

1 Deparatment of Experimental Neuropharmacology, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay

2 Department of Pharmacology, Medical School of Ribeirao Preto, University of Sao Paulo, Brazil

Presenting author:
***Jessika Urbanavicius**, jessikau@gmail.com*

The phytocannabinoid Cannabidiol (CBD), a non-psychotomimetic constituent of Cannabis sativa, has emerged as a potential atypical antipsychotic, which mechanism of action is currently under study. Among different brain targets, dopamine (DA) neurotransmission and the serotonin 5-HT1A receptors (5-HT1A-R) could be related to CBD antipsychotic actions. In the context of the collaboration among our research groups, we studied the local (0.2, 1 and 5 µM) or systemic (60 mg/kg/i.p.) effect of CBD on DA extracellular levels in the medial prefrontal cortex (mPFC) by the in vivo microdialysis technique in non-anaesthetized male adult rats. DA levels in artificial cerebrospinal fluid (aCSF) were collected (1.5 µl/min/20 min) and analyzed by HPLC-ED. The role of 5-HT1A-R was also evaluated through the systemic administration of WAY100635 (5-HT1A-R antagonist; 0.3 mg/kg/i.p.) before CBD i.p. injection. Results showed that CBD significantly increased DA levels 20 to 60 min after i.p. injection (60 % from baseline), and this effect was significantly prevented in WAY100635 pre-treated animals. Although in a lower and shorter magnitude, local infusion of only 1 µM CBD evoked a significant increase in prefrontal DA extracellular levels (20 to 40 min; 30 % from baseline). Overall, our results demonstrated a 5-HT1A-R-mediated mechanism in DA modulation induced by CBD and suggest the engaging of other brain regions than mPFC. This action could underlie the CBD atypical antipsychotic property.

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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

The BDNF pathway in a model of enhanced neurogenesis via depletion of serotonin

Karen M. Stefani, Rocío B. Foltran, Agustina Resasco, Antonela Bonafina, Silvina L. Diaz

Instituto de Biología Celular y Neurociencia Prof. E. De Robertis, CONICET - Universidad de Buenos Aires, Buenos Aires, Argentina

Presenting author:
***Karen Melany Stefani**, karen.stefani.1995@gmail.com*

Neurotrophic factors are relevant regulators of the neurogenic process at different levels. In particular, the brain-derived neurotrophic factor, BDNF, is highly expressed in the hippocampus (HC) of rodents and participates in the control of neuronal proliferation and survival in the dentate gyrus. Likewise, serotonin (5-HT) is also involved in the regulation of neurogenesis. Indeed, both 5-HT enhancement and depletion increase neuronal survival in the HC of mice. We analyzed the protein expression of the BDNF isoforms by Western Blot, pro-and mature-BDNF, and their respective receptors p75 and TrkB, in the HC of mice chronically treated with para-chloro-phenyl-alanine (PCPA), an inhibitor of 5-HT synthesis. Increased expression of p75 receptor with decreased expression of pro-BDNF was observed after chronic PCPA. Another group of mice received a 5-HT1A receptor agonist for 1 week after 4 weeks of PCPA. This treatment reestablished the expression of pro-BDNF, and induced a higher increased of p75 receptor levels. It has been demonstrated that PCPA-treated mice have a higher number of immature neurons in the HC. Given that immature neurons participate in the pattern separation process, the object pattern separation test was conducted. A better performance of hyposerotonergic mice was not confirmed in this assay. Altogether, our results show that molecules in the BDNF signaling pathway are differentially expressed under diverse configurations of the serotonergic system.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Executive deficits in early use of cocaine: Structural and functional signatures of caudate depend upon route of administration

Alethia de la Fuente [1], Sofía Schurmann Vignaga [2], Pilar Prado [2], Rosario Figueras [2], Lucia Lizaso [2], Facundo Manes [2], Marcelo Cetkovich [2], Enzo Tagliazucchi [1]

1 Buenos Aires Physics Institute (IFIBA) and Physics Department, University of Buenos Aires
2 Institute of Cognitive and Translational Neuroscience (INCYT), INECO Foundation, Favaloro University, Buenos Aires, Argentina.
3 National Scientific and Technical Research Council, Buenos Aires, Argentina

Presenting author:
***Laura Alethia de la Fuente**, lauralethia@gmail.com*

Despite of evidence suggesting that the route of administration should be taken into account to assess the short and long-term effects of cocaine consumption, to our knowledge no study to date has characterized clinically relevant neuropsychological and physiological variables comparing individuals with histories of smoked cocaine dependence (SCD) and insufflated cocaine hydrochloride dependence (ICD). The present study examined a sample of 25 participants who fulfilled criteria for SCD, 22 for ICD, and 25 healthy controls matched by age, gender, education, and socioeconomic status. An exhaustive NPS battery was used to assess cognitive domains (attention, executive functions, fluid intelligence, memory, language and social cognition). We complemented this NPS assessment with structural (MRI) and functional (fMRI) neuroimaging data. We found that different routes of administration led to equally different profiles of neurocognitive impairment, with the SCD group being specifically associated with deficits in executive-attention functions. Consistent with risk models, executive-attention function deficit is better explained by age and age at the first use of the drug. SCD presented reduced grey matter density relative to ICD and CTR in the bilateral caudate, a key area for executive functions and attention. Specifically, connectivity between left caudate and inferior frontal regions in SCD mediated performance-structure association.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

New insights into the range of behaviors induced by the dopamine D1 agonist SKF-38393 in normal and hemiparkinsonian mice

Liliana T. Tribbia [1], Juan E. Belforte [2], Gustavo Murer [2], Oscar S. Gershanik [3], Irene R.E. Taravini [1]

1 Laboratorio de Neurobiología Experimental. LNE-FBRO-UNER, Gualeguaychú, Entre Ríos, Argentina.
2 Grupo Neurociencia de Sistemas, IFIBIO-Houssay, UBA-CONICET, Ciudad de Buenos Aires, Argentina.
3 Consultor Emérito Laboratorio de Neurobiología de la Enfermedad de Parkinson y Laboratorio de Neurobiología Experimental, Universidad de Buenos Aires, Universidad de Nacional de Entre Ríos y CONICET.

Presenting author:
***Liliana Teresita Tribbia**, teresita.tribbia@gmail.com*

Parkinson's disease is the second most prevalent neurodegenerative disease worldwide. The degenerative process primarily affects dopaminergic neurons of the substantia nigra pars compacta, which innervates the striatum through the nigrostriatal pathway. Medium spiny neurons comprise more than 90% of the neurons in the striatum and are organized into two GABAergic projection systems: striatonigral pathway, expressing D1-type dopamine receptors (D1R) and striatopallidal pathway, expressing D2R. The stimulation of D1R by selective agonists (like SKF-38393) participates directly in the development and manifestation of abnormal involuntary movements (AIMs). However, no scoring systems exist to evaluate the multiple components of SKF-38393-induced stereotypy in normal and hemiparkinsonian mice. Therefore, we propose to improve the behavioral measurement parameters related to the stereotypies and movements of these mice in order to better understand the behavioral properties of this dopamine agonist. C57BL/6J mice lesioned by 6-OHDA injection into MFB and control mice were treated with increasing doses of SKF-38393 (0.5-1-2mg/kg/day) or distilled water (VEH) for 15 days. The experimental groups were 6-OHDA/SKF, 6-OHDA/VEH, control/SKF and control/VEH. We have designed a new scoring scale for AIMs based on careful observation of each experimental subject and were able to recognize and rate a broad spectrum of behaviors related to SKF treatment.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Doxycycline modifies tau fibrillization and reduces its toxicity

Luciana Medina [1], María Florencia González Lizárraga [1], Sabrina Sequeira [1], Rita Raisman-Vozari [3], Sergio Benjamín Socías [1], Rosana Nieves Chehín [1]

1 IMMCA Instituto de Investigación en Medicina Molecular y Celular Aplicada (CONICET - UNT – SIPROSA), Tucumán, Argentina
2 INSIBIO Instituto Superior de Investigaciones Biológicas (CONICET-UNT), Tucumán, Argentina
3 ICM - Institut du Cerveau et de la Moelle Epinière - Hôpital Pitié Salpêtrière , Paris, France

Presenting author:
***Luciana Medina**, lumedina000@gmail.com*

Tauopathies are neurodegenerative diseases characterized by the aggregation of the microtubule associated protein tau, without a cure to date. The increasing incidence of these disorders, and the extensive time required for the development and approval of novel drugs, highlight the need for testing and repurposing known safe molecules for new indications. Using biophysical and biochemical techniques we investigated the effect of doxycycline, a member of the tetracycline antibiotic family, on tau amyloid aggregation and neurotoxicity. Doxycycline reduced tau fibrillization in a dose-dependent manner, and increased protease sensitivity of tau fibrils. Also, doxycycline blocked tau seeding and diminished the toxicity of tau aggregates in cell culture. Overall, our results expand the spectrum of action of doxycycline against aggregation-prone proteins, opening novel perspectives for its use as a disease modifying drug for tauopathies.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

BDNF-TrkB signalling in nucleus accumbens shell is implicated in perinatal protein malnutrition-induced anhedonia

María Cecilia Gutiérrez, María Cecilia Perondi, Gabriel Cuadra, Analía Valdomero

Department of Pharmacology, FCQ, UNC - IFEC (CONICET). Córdoba, Argentina.

Presenting author:
María Cecilia Gutiérrez, *cecilia.gutierrez@unc.edu.ar*

Clinical studies have suggested that early malnutrition increases the risk of developing depressive disorders in adulthood. The molecular mechanisms underlying depression have been studied for decades, however many of them remain unknown. Previous results from our lab have shown that perinatal protein undernutrition-induced anhedonia correlates with an increment in the levels of brain derived neurotrophic factor (BDNF) in the nucleus accumbens (NAc). Here, we evaluate the high affinity receptor of BDNF (TrkB) and its phosphorylated form (p-TrkB) levels in the NAc of adult animals submitted to a perinatal protein deprivation schedule (D-rats) and well-nourished animals (C-rats) after sucrose preference test. To confirm whether BDNF-TrkB signaling pathway is involved in the onset of anhedonia, we administered intra-NAc shell ANA 12, a selective antagonist of TrkB. The results showed a significantly higher p-TrkB/TrkB ratio in the NAc of D-rats compared to C-group. Furthermore, D-animals infused with vehicle exhibited a significant reduction of sucrose preference in relation to C-rats. Bilateral infusion of ANA-12 reverses such depression-like behaviour promoting an antidepressant effect. These results suggest a key role of BDNF-TrkB signalling in the NAc shell in the neurobiological mechanism underlying behavioural abnormality demonstrated in undernourished animals.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

The argentine valerian species, Valeriana carnosa, as a MAO-A inhibitor with antidepressant -like effects in mice.

Marina Rademacher [1], Carolina Marcucci [1], Fabiola Kamecki [1], Juan Manuel Anselmi Relats [1], Hernán Gerónimo Bach [3], Marcelo Luis Wagner [2], Rafael Alejandro Ricco [2], Natalia Colettis [1], Mariel Marder [1]

1 Universidad de Buenos Aires. Consejo Nacional de Investigaciones Científicas y Técnicas. Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB). Facultad de Farmacia y Bioquímica. Buenos Aires, Argentina

2 Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Farmacología. Cátedra de Farmacobotánica. Buenos Aires, Argentina

3 Instituto Nacional de Tecnología Agropecuaria (INTA). Instituto de Recursos Biológicos. Buenos Aires, Argentina

Presenting author:
***Marina Rademacher**, marina.radem@gmail.com*

Folkloric preparations of valerian roots have been used as sedatives/anxiolytics and sleep inducers since ancient times. Our country harbors thousands of plant species, which lack scientific information although many of them are used in folk medicine. We have studied hydroalcoholic extracts of an Argentine valerian (underground parts): Valeriana carnosa Sm. from Patagonia Argentina, known as Ñancolahuen in Mapuzungum language. We have already shown that they presented ligands for the benzodiazepine binding site of the GABAA receptor, increased the sleeping time induced by sodium thiopental and showed anxiolytic-like activities in mice. We evaluated in vitro the capacity of V. carnosa extracts to inhibit human and mice MAO-A. As it showed inhibitory capacity over these enzymes (IC50 (95%CI): 285.8 (212.6 to 384.2) µg/mL ethylic extract over hMAO-A; 1 mg/mL, 80% inhibition over MAO-A of mice´s brain homogenate), possible antidepressant effects were evaluated. Mice treated with V. Carnosa extract under acute (100 mg/kg, one i.p., injection) and chronic treatments (100 mg/kg/day, in drinking water, for 28 days) were evaluated in the tail suspension and locomotor activity tests. While the acute administration revealed no significant effect on mice, chronic treatment showed a significant antidepressant-like behaviour. Furthermore, locomotor activity of mice was not affected. V. carnosa could become a novel CNS herbal product for the treatment of depression and related disorders.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Recents advances in psychedelic drugs reasearch antidepressant-like effects after.a single dose of ibogaine or its metabolite noribogaine in rats

Paola Rodríguez [1], Jessika Urbanavicius [1], José Pedro Prieto [1], , Sara Fabius [1], Ana Laura Reyes [3], Valclav Havel [4], Dalibor Sames [4], Cecilia Scorza [1]

1 Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo – Uruguay
2 Laboratorio de Síntesis Orgánica, Departamento de Química Orgánica, Facultad de Química - Universidad de la República, Montevideo – Uruguay
3 Centro Uruguayo de Imageneología Molecular, Montevideo – Uruguay
4 Department of Chemistry, Columbia University, New York – United States

Presenting author:
***Paola Carolina Rodriguez Camarot**, prodriguez@fq.edu.uy*

Preclinical research in psychedelics drugs has dramatically increased within the last decade focus on its therapeutic potential in psychiatric disorders. Observational data and animal studies have demonstrated a potent anti-addictive effect of psychedelic alkaloids ibogaine (Ibo), and its metabolite noribogaine (Nor); however, the underlying mechanism remains under study. We hypothesized that the anti-addictive property of both psychedelics can be related to an antidepressant-like effect, since ibogaine and noribogaine inhibit the serotonin transporter, and ibogaine increased the brain-derived neurotrophic factor RNAm levels in the rat prefrontal cortex. We evaluated the behavioral effects (dose- and time-dependence) induced by a single dose of Ibo and Nor administration (20 and 40 mg/kg i.p.) by the rat forced swim test. A correlation between plasma and brain concentrations of Ibo and Nor and the behavioral response was performed. Ibo and Nor induced a dose- and time-dependent antidepressant-like effect without changes of motor activity. A correlation between plasma and brain concentrations and behavior was found. Notably, that behavioral effect was not reproduced by an equivalent dose of the classic selective serotonin reuptake inhibitor fluoxetine (40 mg/kg, i.p., single injection). Our results suggest a polypharmacological mechanism underpinning the antidepressant-like effects of Ibo and Nor, and we propose that this effect can collaborate to its anti-addictive property.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Lead and Ethanol exposure reduces mitochondrial respiration in neuroblastoma SH-SY5Y cells. Impact on aldehyde dehydrogenase 2 functionality.

Romina Deza-Ponzio [1], Tuany Eichwald [1,2,3,4,5,6], Paula A. Albrecht [1], , Lucía E. Fernandez-Hubeid [1], Liliana M Cancela [1], Fernando J Irazoqui [2], Alexandra Latini [3], Miriam B Virgolini [1]

1 IFEC-CONICET. Departamento de Farmacología. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba, Córdoba, Argentina
2 CIQUIBIC-CONICET. Departamento de Química Biológica. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba, Córdoba, Argentina
3 Departamento de Bioquímica, Centro de Ciencias Biológica, Universidad Federal de Santa Catarina, SC, Brasil.

Presenting author:
***Romina Deza Ponzio**, rdezaponzio@gmail.com*

Clinical and experimental evidence demonstrates that the neurotoxicant lead (Pb) induces neurobehavioral alterations, including an altered response to drugs. We have previously reported that perinatally-Pb-exposed rats showed elevated ethanol (EtOH) intake, which seems to be mediated by brain acetaldehyde (ACD) accumulation. Aldehyde dehydrogenase 2 (ALDH2) is a mitochondrial oxidoreductase that metabolizes ACD to acetate during EtOH metabolism, with NAD+ as the limiting factor of the reaction. Based on a reduced brain ALDH2 activity and expression observed in the Pb-exposed rats, in vitro experiments were performed in SH-SY5Y cells to elucidate the mechanisms that modulate ALDH2 function in the presence of Pb and EtOH. Thus, whole intact neuroblastoma cells were exposed to Pb (10µM), EtOH (200 mM) or Pb plus EtOH (10µM/200mM) for 24 h and thereafter analyzed in an Oxygraph Oroboros 2K for oxygen consumption rates. Initially, basal respiration was assessed followed by mitochondrial chain inhibitors. The results replicated the in vivo data in terms of ALDH2 inhibition after Pb, EtOH, or the combination treatment in SH-SY5Y cells. High-resolution respirometry shows that Pb and EtOH exposure decreased routine and maximal respiratory capacity as well as the respiratory reserve capacity. It can be concluded that Pb and EtOH cause mitochondrial toxicity by altering bioenergetics in SH-SY5Y cells, with possible consequences on NAD+ availability and thereby ALDH2 functionality.

E-Posters

NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Bilirubin disrupts calcium homeostasis in neonatal hippocampal neurons: a new pathway of neurotoxicity

Rossana Rauti [1], Mohammed Qaisiya [4], Claudio Tiribelli [3], Laura Ballerini [1], Cristina Bellarosa [3]

1 International School for Advanced Studies (SISSA), Via Bonomea, 265, 34136 Trieste, Italy
2 Department of Biomedical Engineering, Tel Aviv University, Tel Aviv, Israel
3 Fondazione Italiana Fegato (FIF), Bldg Q-AREA Science Park Basovizza, SS14 Km 163,5, 34149 Trieste, Italy,
4 College of Pharmacy and Medical Sciences, Hebron University, West Bank, Hebron, Palestine,

Presenting author:
***Rossana Rauti**, rossanarauti@mail.tau.ac.il*

Severe hyperbilirubinemia leads to bilirubin encephalopathy in neonates, with irreversible neurological sequelae. We investigated the neuronal vulnerability to unconjugated bilirubin (UCB) toxicity. The calcium (Ca2+) homeostasis is crucial for neuron survival. Ca2+ release from endoplasmic reticulum (ER) during ER-stress can lead to apoptosis trough Caspase-12 activation. By live Ca2+ imaging we monitored Ca2+ signals in hippocampal neuroglia cells exposed to UCB doses, showing the ability of UCB to alter intracellular Ca2+ homeostasis. The contribution of intracellular Ca2+ stores and the activation of proteins involved in the apoptotic Ca2+ signaling were also assessed. Thapsigargin, specific inhibitor of Sarco/endoplasmic reticulum ATPase pumps, significantly reduced the duration of Ca2+ oscillation associated with UCB exposure indicating that UCB strongly interfered with the reticulum Ca2+ stores. Contrarily, in pure astrocyte cultures, spontaneous Ca2+ transient duration was not altered by UCB. The protein content of GRP78, AT6, CHOP, Calpain and Caspase-12 treated with UCB was twofold higher compared to controls. Ca2+-dependent Calpain and Caspase-12 induction by UCB were significantly reduced when cells were pretreated with the ER-stress inhibitor 4-PBA. We showed the direct interference of UCB with neuronal intracellular Ca2+ dynamics, suggesting ER Ca2+ stores as a primary target of UCB toxicity with the activation of the apoptotic ER-stress-dependent pathway.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Analysis of the morphological remodeling of orexigenic AgRP fibers in the brain of fasted mice: A potential regulatory role of the Ghrelin signaling

Daniela Alejandra Cassano, Gimena Fernandez, Pablo Nicolas De Francesco, Guadalupe García Romero, Maria Jose Tolosa, Mirta Reynaldo, Mario Perello
Laboratorio de Neurofisiología - Instituto Multidisciplinario de Biología Celular (IMBICE)

Presenting author:
***Daniela Alejandra Cassano**, danicassano@hotmail.com*

Agouti-related peptide-producing neurons of the arcuate nucleus (ARC-AgRP neurons), which innervate several appetite-related brain regions, are activated in fasting states. Recently, we found that the ARC-AgRP projections to the hypothalamic paraventricular nucleus are remodeled in fasting states in a growth hormone secretagogue receptor (GHSR)-dependent manner. Here, we tested if the fasting-induced activation of ARC-AgRP neurons promotes morphological remodeling of other hypothalamic (lateral hypothalamic area, LHA) and extra-hypothalamic (paraventricular thalamus, PVT, and central amygdala, CeA) ARC-AgRP projections and its dependence on GHSR. We performed fluorescent immunostaining against AgRP in brains of ad libitum fed or fasted mice with pharmacological or genetic blockage of the GHSR signaling and estimated the density and strength of ARC-AgRP fibers. We found that: 1) the density and strength of ARC-AgRP fibers increase in the LHA of fasted mice, whereas no differences were detected in the PVT and CeA. 2) Fasting-induced increase of the marker of neuronal activation c-Fos in the LHA was abrogated in ARC-ablated mice. 3) Fasting-induced remodeling of ARC-AgRP→LHA projections was not affected in mice with pharmacological or genetic blockage of GHSR signaling. This evidence shows that the remodeling of the ARC-AgRP fibers in fasting state occurs in a brain region-dependent manner and that the GHSR activity does not regulate this phenomenon in the LHA.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Mapping the location of the growth hormone secretagogue receptor in the mouse brain using a novel fluorescent ligand

Franco Barrile [1], Nicolás De Francesco [1], Paula Cornejo [1], Maria José Tolosa [1], Agustina Cabral [1], Guadalupe García Romero [1], Mirta Reynaldo [2], Mario Perelló [1]

1 Comisión Nacional de Investigaciones Científicas y Técnicas (CONICET)
2 Comisión de Investigaciones Científicas de la Provincia de Buenos Aires (CIC-PBA)

Presenting author:
***Franco Barrile**, francobarrile@gmail.com*

The growth hormone secretagogue receptor (GHSR) is a G-protein coupled receptor highly expressed in the brain that modulates a variety of metabolic, endocrine, autonomic and behavioural functions. GHSR is activated by ghrelin and blocked by a liver-derived hormone named Liver-expressed antimicrobial peptide 2 (LEAP2). Here, we developed a novel fluorescent GHSR ligand based on the N-terminal sequence of LEAP2, hereafter called FLEAP2, and assessed its capability to label GHSR in the mouse brain. We found that FLEAP2 impaired ghrelin-induced food intake in the same fashion that native LEAP2 when administrated intracerebroventricularly (ICV) in mice. Furthermore, in mice ICV-injected with FLEAP2, we found that brain regions with the highest fluorescent signal were the CA3 region of the hippocampus and the arcuate nucleus of the hypothalamus. In order to test the specificity of FLEAP2 towards GHSR labelling, we ICV injected mice with FLEAP2 after ICV pre-treatment with vehicle, native LEAP2 or ghrelin. We analysed the level of fluorescent signal in the arcuate nucleus of these mice, as it is the brain region with highest GHSR expression, and mice pretreated with native LEAP2 or ghrelin had lower fluorescent signal than vehicle pretreated mice. Thus, current data indicate that FLEAP2 specifically binds to GHSR and is an appropriate tool to study LEAP2 binding and function in the mouse brain.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Bone marrow cell transplant plays an immunomodulatory role in a reversible model of Wallerian degeneration in mice.

Gonzalo Piñero [1,2], Marianela Vence [2], Marcos L. Aranda [3], Magalí C. Cercato [2], Paula A. Soto [1,2], Vanina Usach [1,2], Patricia Setton-Avruj [1,2]

1 Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Química Biológica, Cátedra de Química Biológica Patológica. Buenos Aires, Argentina.
2 CONICET - Universidad de Buenos Aires, Instituto de Química y Fisicoquímica Biológicas (IQUIFIB). Buenos Aires, Argentina.
3 CONICET - Universidad de Buenos Aires, Centro de Estudios Farmacológicos y Botánicos (CEFyBO). Buenos Aires, Argentina.

Presenting author:
***Gonzalo Miguel Piñero**, gonzalopiniero@gmail.com*

Initiated upon nervous system damage, Wallerian degeneration (WD) is a process characterized by axonal degeneration, demyelination and a strong inflammatory response. Working on a model of acute sciatic nerve lesion in rats, our group has shown the beneficial effects of systemic bone marrow mononuclear cell transplant on morphological and functional parameters, as well as the prevention of neuropathic pain. The current work thus seeks to further validate the experimental model in mice and aims to dig deeper into the mechanisms involved in bone marrow cell therapy.

Adult C57BL/6J mice were subjected to 8-sec sciatic nerve crush and immediately intravenously transplanted with bone marrow cells. The evolution of the degeneration-regeneration process was evaluated at different survival times. Gene and protein expression of the main cytokines involved in WD, as well as lesion-associated macrophage phenotypes, were also analyzed.

Initial findings corroborated the experimental model in mice but, most important, proved bone marrow cell efficiency in reducing the expression of some proinflammatory cytokines and increasing that of antiinflammatory IL-10. In addition, transplanted cells induced a decrease in iNOS+ macrophages at the expense of an increment in CD206+ cells and an anticipated rise in Arg-1+ macrophages. Taken together, our results endorse bone marrow cell therapy as an alternative approach to accelerate nerve recovery and postulate these cells as potential immunomodulator.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Intramuscular insulin-like growth factor-1 gene therapy modulates reactive microglia after traumatic brain injury

Macarena Lorena Herrera [1], Leandro Gabriel Champarini [1], Eugenia Falomir Lockhart [2], Franco Juan Cruz Dolcetti [2], Jerónimo Pennini [2], Claudia Beatriz Hereñú [1], María José Bellini [2]

1 .Universidad Nacional de Córdoba, Facultad de Ciencias Químicas. Departamento de Farmacología. Córdoba, Argentina. Instituto de Farmacología Experimental de Córdoba (IFEC-CONICET), Córdoba, Argentina
2 Universidad Nacional de La Plata, Facultad de Ciencias Médicas. Buenos Aires, Argentina. Instituto de Investigaciones Bioquímicas de La Plata (INIBIOLP-CONICET), La Plata, Argentina.

Presenting author:
***Macarena Lorena Herrera**, macarena.herrera@unc.edu.ar*

Reactive gliosis is a key feature and an important pathophysiological mechanism underlying chronic neurodegeneration following traumatic brain injury (TBI). In this study, we have explored the effects of intramuscular IGF-1 gene therapy on reactive gliosis and functional outcome after an injury of the cerebral cortex. Young adult male rats were intramuscularly injected with a recombinant adenoviral construct harboring the cDNA of human IGF-1 (RAd-IGF1), with a control vector expressing green fluorescent protein (RAd-GFP) or PBS as control. Three weeks after the intramuscular injections of adenoviral vectors, animals were subjected to a unilateral penetrating brain injury. The data revealed that RAd-IGF1 gene therapy significantly increased serum IGF1 levels and prevent working memory deficits after one week of TBI. At the same time, when we analyzed the effects of therapy on glial scar formation, the treatment with RAd-IGF1 did not modify the number of glial fibrillary acidic protein but we observed a decrease in vimentin immunoreactive astrocytes at 7 days post-lesion in the injured hemisphere, compared to animals treated with RAd-GFP. Moreover, IGF-1 gene therapy reduced the number of Iba1+ cells with reactive phenotype and the number of MHCII+ cells in the injured hemisphere. These results suggest that intramuscular IGF-1 gene therapy may represent a new approach to prevent traumatic brain injury outcomes in rats.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Orcokinin neuropeptides inhibit courtship and are involved in the regulation of other innate behaviors in the fruit fly Drosophila melanogaster

Mariano Volonté [1], Valeria Silva Moeller [2], Angelina Palacios Muñoz [2], Lía Frenkel [3], John Ewer [2], Sheila Ons [1]

1 CREG - UNLP
2 CINV - UV
3 IB3 - UBA

Presenting author:
***Mariano Volonté**, volontemariano@hotmail.com*

In animals, neuropeptidergic signaling is essential for the regulation of survival and reproductive-related processes. Among arthropod neuropeptide systems, Orcokinins are poorly studied, in despite of its high level of conservation in different Orders. There are currently no reports on the role of Orcokinins in the experimental insect model Drosophila melanogaster. In the present work, we exploited genetic tools available in this species in order to elucidate functional roles of Orcokinins in the regulation of different innate behaviors; ecdysis, sleep, circadian activity and courtship. We found that a reduction in Orcokinin gene expression provoked a slight shortening in pre-ecdysis, a reduction in daytime locomotor activity and an increased duration of total daytime sleep, occurring in a smaller number of sleep episodes that were of greater average duration. The strongest effect was observed in courtship behavior, where OKs RNAi-mediated gene silencing provoked a marked disinhibition in male courtship, both toward a female and a male target. Orcokinin is emerging as an important neuropeptide family in the regulation of vital processes in insects, such as reproduction and post-embryonic development. In the case of the fruit fly, our results suggest an important role in courtship inhibition.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Hypothalamic proopiomelanocortin expression restricted to GABAergic neurons prevents overfeeding and Neuropeptide Y overexpression

Milagros Trotta [1], Estefania Pilar Bello [1], Ramiro Alsina [1], José Luis Ferrán [4], Marcelo Rubinstein [3], Viviana Florencia Bumaschny [1,2]

1 Grupo de Neurociencias de Sistemas, Instituto de Fisiología y Biofísica Bernardo Houssay (IFIBIO, UBA-CONICET)
2 Departamento de Fisiología, Facultad de Medicina, Universidad de Buenos Aires.
3 Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres". INGEBI (CONICET)
4 Departamento de Anatomía Humana y Psicobiología, Facultad de Medicina, Universidad de Murcia, España

Presenting author:
***Milagros Trotta**, mili.trotta@gmail.com*

The arcuate nucleus is a key regulator of energy homeostasis in which different neuronal populations integrate peripheral signals of energy status. In particular, arcuate proopiomelanocortin (POMC) neurons inhibit food intake and promote energy expenditure. Due to the existence of different subpopulations of POMC neurons secreting antagonistic neurotransmitters such as glutamate or GABA, it is proposed that Arc-POMC neurons could have different physiological roles and targets. In the present study, we aimed to elucidate the contribution of the subpopulation of Arc-POMC GABAergic neurons in the control of energy balance by expressing Pomc exclusively in GABAergic-POMC neurons. We found that Pomc rescue restricted to GABAergic neurons leads to food intake normalization and body weight enhancement. Surprisingly, these physiological improvements were achieved with the recovery of Pomc expression in only 25% of total hypothalamic POMC neurons. Immunohistochemical analysis showed that GABAergic POMC neurons preferentially project to the dorsomedial hypothalamus (DMH), a nucleus that induces food intake by releasing NPY. In addition, we found that DMH-NPY expression is negatively correlated with Pomc expression in GABAergic-POMC neurons, suggesting that food intake may be regulated by an Arc-GABAergic-POMC→ DMH-NPY pathway.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

The neuropeptide RhoprCCHamide2 inhibits serotonin-stimulated transcellular Na+ transport in Rhodnius prolixus.

Natalia Capriotti [1], Juan Ianowski [2], Sheila Ons [1]

1 Laboratorio de Neurobiología de Insectos, Centro Regional de Estudios Genómicos. Facultad de Ciencias Exactas, Universidad Nacional de La Plata, Bvd 120 y 62 (1900), 1900 La Plata, Buenos Aires, Argentina.

2 Department of Anatomy, Physiology, and Pharmacology; University of Saskatchewan, Saskatoon, SK, Canada S7N 5E5.

Presenting author:
***Natalia Capriotti**, nataliacapriotti@gmail.com*

Rhodnius prolixus is a blood-feeding insect vector of Chagas' disease. During each blood meal the animals ingest large volumes of blood, that may be up to 12 times the unfed body mass. These large blood meals impose a significant osmotic stress for the animals due to the hyposmotic condition of the ingested blood compared to the insect's haemolymph. We investigated the ion transport machinery triggered by stimulation with the diuretic factor serotonin and the effect of the neuropetide modulator RhoprCCHamide2. Ussing chamber assays revealed that serotonin-stimulated transepithelial short circuit current (Isc) was blocked by treatment with the Na+ channel blocker amiloride or the Na+/K+-ATPase inhibitor ouabain. Incubation in Na+-free, but not Cl--free saline, blocked the effect of serotonin on Isc. Moreover, treatment with NKCC and NCC blockers had no effect on Isc or fluid secretion. Treatment with neuropeptide RhoprCCHamide2 diminished serotonin-stimulated Isc across the crop. The results suggest that Na+ undergoes active transport via an apical amiloride-sensitive Na+ channels and a basolateral ouabain-sensitive Na+/K+-ATPase while Cl- is transported through passive paracellular pathway. RhoprCCHamide2 reduces transport by inhibiting transcellular Na+ transport.

E-Posters

NEUROENDOCRINOLOGY AND NEUROIMMUNOLOGY

Alterations generated by neonatal overfeeding on homeostatic control of food intake at weaning are restored in adulthood.

Rocio Schumacher [1], Maria F. Rossetti [1], Gisela P. Lazarino [3], Guillermina Canecini [1], Nicolas Fabre [1], Cora Stoker [1], Maria F. Andreoli [4], Jorge G. Ramos [1]

1 Instituto de Salud y Ambiente del Litoral (ISAL), UNL-CONICET, Santa Fe, Argentina.
2 Departamento de Bioquímica Clínica, FBCB-UNL, Santa Fe, Argentina.
3 Center for Social and Affective Neuroscience, Department of Clinical and Experimental Medicine, Linköping University, 58x xx Linköping, Sweden.
4 Instituto de Desarrollo e Investigaciones Pediátricas (IDIP) Hospital de Niños de la Plata - CIC-PBA, La Plata, Argentina.

Presenting author:
***Rocio Schumacher**, rociosch09@gmail.com*

Nutrition during the perinatal period is critical to determine health in life. We analyzed the effects of neonatal overfeeding on the brain control of food intake in rats at postnatal day (PND) 21 and at PND90. Male Wistar rats were raised in small litters (4 pups/dam, n=14, SL) or normal litters (10 pups/dam, n=14, NL). Half of these animals were sacrificed at PND21. The rest were fed with standard chow diet, the body weight and food intake were controlled weekly until PND90 when they were sacrificed. The brain was frozen and cut with the cryostat, the arcuate nucleus (ARC) was isolated of slice by micropunch technique. RNAm and DNA were isolated and analyzed by RT-qPCR and methylation-sensitive restriction enzymes, respectively. At PND21, SL rats showed greater body weight and characteristic features of metabolic syndrome. The ARC showed increased gene expression of the neuropeptides Pro-opiomelanocortin (POMC), Cocaine and amphetamine regulated transcript and Neuropeptide Y, Leptin and Ghrelin receptors and hypomethylation state of the POMC promoter. At PND90, SL rats restored the main alterations in body weight, neuropeptides and hormone receptors expression in ARC. Neonatal overfeeding causes early alterations in the brain circuits that control food intake, but these alterations can be restored in adulthood. This work shows the importance of developmental plasticity to restore the early changes in the central pathways involved in metabolic mal-programming.

E-Posters

SENSORY AND MOTOR SYSTEMS

Innate and acquired bases of discrimination and generalization between odors

Agustin Lara [1], Emiliano Marachlian [2], Fernando Locatelli [1]

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

2 Institut de Biologie de l'Ecole Normale Supérieure (IBENS), Ecole NormaleSupérieure, CNRS, INSERM, PSL Université Paris, Paris, France.

Presenting author:
***Agustin Lara**, agustin.e.lara@hotmail.com*

Odorants are primarily sensed by olfactory receptor neurons that send their axons to the antennal lobe, the first olfactory neuropil in the central brain of insects. There, each odorant or odorant mixture is encoded by a unique combination of co-activated neurons that represents its primary neural representation. In previous studies we showed that appetitive experience with an odorant changes the internal representation of a mixture containing that odorant. The pattern of activity elicited by the mixture becomes more similar to the representation of the rewarded odorant. This change was interpreted as a mechanism that improves the perception of the rewarded component, which otherwise might get occluded by the perception of the mixture. In the present study we used honey bees Apis mellifera as a model to analyze to what extent the degree of discrimination or generalization between two odors can be predicted based on the similarity between their respective neuronal representations in the antennal lobe. We evaluated whether the changes induced by learning at the level of the representation of mixtures in the antennal lobe, does indeed correlate with the ability of animals to detect the rewarded component immersed in the mixture. Here we confirm that the shift in the representation of the mixture toward the rewarded odor correlate with an increased ability to recognize that component and with a reduced perception of the novel odorant presented in the same mixture.

E-Posters

SENSORY AND MOTOR SYSTEMS

Identification of the gustatory processing center in a blood-sucking insect

Agustina Cano [1], Martín Berón de Astrada [1], Sebastián Minoli [2], Romina Barrozo[2]

1 Instituto de Biociencias, Biotecnología y Biología Traslacional (IB3); Departamento FBMC, FCEyN; Universidad de Buenos Aires

2 Laboratorio de Fisiología de Insectos, Instituto de Biodiversidad y Biología Experimental y Aplicada (IBBEA-CONICET), DBBE - Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina

Presenting author:
***Agustina Cano**, agustinacanopl@gmail.com*

The gustatory sense provides animals with reliable information about the quality of a food source, contributing to discriminate nutritious from harmful food. Rhodnius prolixus is a vector of Chagas disease in Latin America. They use the gustatory sense to evaluate the quality of a potential food source or vertebrate host in order to make a feeding decision: to eat or not. Thus, when the insect takes a gorge of blood, gustatory receptor neurons (GRNs), housed inside pharyngeal structures or sensilla, provide the brain with gustatory information about the feeding source. If the ingested blood fulfills the insects' requirements the animal will start feeding. If not, the insect will abandon the host looking for another one. To study the regions of the brain where the GRNs of the pharynx arborise, we traced their axonal projections by means of back-fills with a fluorescent dye. Our results showed that all pharyngeal GRNs arrive to the brain through the labral nerves and arborise in the suboesophageal ganglion (SOG) and that some continue to the posterior ganglion (PG). Two sort of neurons were identified: 1- a thick GRN which innervates the contralateral region of the SOG, named as H neuron; 2- a cluster of GRNs, ca. 5, that innervates the ipsilateral region of the SOG and then continues to the PG. This is the first study that shows peripheral projections to the central nervous system in R. prolixus, revealing the SOG as the primary gustatory processing center.

E-Posters

SENSORY AND MOTOR SYSTEMS

Molecular mechanisms of cell death in a mouse model of progressive hearing loss

Camila Carignano [1,2], Marcela Vera [1,2], Leonardo Dionisio [1,2], Eugenio Aztiria [1,2], Ezequiel Rías [1,2], Guillermo Spitzmaul [1,2]

1 Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB-UNS/CONICET))
2 Departamento de Biología, Bioquímica y Farmacia (DBByF), Universidad Nacional del Sur (UNS)

Presenting author:
***Camila Carignano**, ccarignano@inibibb-conicet.gob.ar*

KCNQ4 is a voltage-gated K+ channel whose dysfunction in the inner ear is the main cause of the progressive hearing loss (HL) DFNA2. It develops in 2 phases: first, a mild HL (40-60 dB) and later, it progresses to a profound HL (> 90 dB). Previously, using a knock-out mouse model of the human DFNA2 (Kcnq4-/-), we reported that outer hair cell (OHC) degeneration may explain the first phase of HL and inner hair cell (IHC) and spiral ganglion neuron (SGN) degeneration occur in the second phase of HL. Now, we performed a functional hearing test, correlating these results with the molecular events leading to cell death and ultrastructural changes in the Organ of Corti's surface in both phases. We observed a profound HL starting at middle-aged (40-week-old (W)) Kcnq4-/- mice, as revealed by Preyer´s reflex test. By immunofluorescence, we found caspase 3-mediated apoptosis (Cas-3) in SGNs and OHCs of Kcnq4-/- mice at different time points: in SGNs it was found late, at 54W and 68W, which correlates with our functional studies elucidating the profound HL of the last phase. On the other hand, OHCs showed a Cas-3 positive signal in 4W and 10W Kcnq4-/- mice, which could explain the mild HL of the first phase of DFNA2. IHCs did not show Cas-3 signal but they exhibited remarkable stereocilia defects by scanning microscopy, such as fusion and giant stereocilia in old mice. Collectively, these results are useful to understand the mechanisms involved in the human DFNA2.

E-Posters

SENSORY AND MOTOR SYSTEMS

Grouped single-unit activity in a cortical avian nucleus supports a population model of birdsong production in Serinus canaria

Cecilia T. Herbert [1], Santiago Boari [1], Gabriel B. Mindlin [1], Ana Amador [1], Cecilia T. Herbert [2], Santiago Boari [2], Gabriel B. Mindlin [2], Ana Amador [2]

1 Dpto. de Física, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires, Argentina.
2 Instituto de Física de Buenos Aires, IFIBA-CONICET, Buenos Aires, Argentina.

Presenting author:
Cecilia Thomsett Herbert, *herbertceci@gmail.com*

Birdsong requires fine coordination of the muscles in the vocal organ and respiratory system. The song system, which is the neural architecture dedicated to song production in oscine birds, poses a beautiful opportunity to model the activity of a circuit of interconnected neural nuclei for the production of complex behaviour.
Such a model has been developed previously by our laboratory. Our model makes specific predictions about the timing of population neural activity in different nuclei needed to produce song and can reproduce respiratory patterns observed in canary song phrases of different types.

In this work, the model was used to generate respiratory patterns that correspond to two types of phrases of canary song, given a proposed sparse activity in nucleus HVC (proper name), one of the nuclei involved. This telencephalic nucleus plays a key role in the production of motor commands, but the neural code it uses is still under debate.

We put our model to the test by recording extracellularly from nucleus HVC in singing canaries, isolating single-units that fire during particular phrase types and analyzing at which song instances these neurons fire.

We found that grouped activity across animals is in good correspondence to the population activity that can produce realistic respiratory patterns in our model for the two types of phrases studied. Furthermore, the experimental data show activity in additional song instances that will enrich further iterations of the model.

E-Posters

SENSORY AND MOTOR SYSTEMS

Sensory adaptation and the representation of complex odors in the antennal lobe of Apis mellifera

Federico Gascue, Nicolás Pírez, Fernando Locatelli
Instituto de Fisiología, Biología Molecular y Neurociencias (IFIByNE); UBA-CONICET, Argentina.

Presenting author:
***Federico Andrés Gascue**, fgascue@gmail.com*

Sensory systems must be adjusted based on the animal's experience in order to optimize perception of relevant information and ignore stimuli without predictive value. In this context, one of the main phenomena that modulate the olfactory system is adaptation, which is defined as the decrease of the sensitivity or response to an odor after a sustained exposure to it. Adaptation may occur in brief intervals of time and depends on the immediate experience of the animal. In this project, we use Apis mellifera to study the representation of binary mixtures of odors in the brain after sensory adaptation to one of the components. We performed calcium imaging experiments to measure odor induced signals in the antennal lobe, the first olfactory neuropil in the insect brain. We determined that, after olfactory adaptation, response patterns encoding the mixture are drastically altered, in a way that favors the representation of the non-adapted component. These changes are relatively brief, lasting about a minute. Additionally, by means of behavioral experiments, we show that adaptation reduces appetitive learning of the adapted component, while it enhances learning of the other component in cases in which it would normally stay occluded. These results suggest that olfactory adaptation is critical to allow detection of minor components present in complex mixtures, emphasizing that sensory adaptation is a fundamental mechanism to improve sensitivity to salient and discrete stimuli.

E-Posters

SENSORY AND MOTOR SYSTEMS

Testing neural models with the appropriate species

Javier N. Lassa Ortiz, Cecilia T. Herbert, Santiago Boari, Gabriel B. Mindlin, Ana Amador

Physics Department, Faculty of Natural and Exact Sciences, University of Buenos Aires and IFIBA, CONICET

Presenting author:
***Javier Nahuel Lassa Ortiz**, jlassa@df.uba.ar*

The nervous system representation of a motor program is an open problem for most behaviors. In birdsong production, it has been proposed that some special temporal instances, linked to significant aspects of the motor gestures used to generate the song, are preferentially represented in the cortex. In this work, we compute these temporal instances for two species, and report which of them is better suited to test the proposed coding (as well as alternative models) against data. Moreover, we present a neural additive model that shows that this sparse representation in the cortex is enough to generate a complex motor output.

E-Posters

SENSORY AND MOTOR SYSTEMS

Parallel processing channels for binaural cues in the Lateral Superior Olive

Jimena Ballestero [1], Andrew Brughera [2,3], Jason Mikiel-Hunter [3], David McAlpine [3],

1 Instituto de Fisiología y Biofísica (IFIBIO) Bernardo Houssay, Grupo de Neurociencia de Sistemas, Universidad de Buenos Aires, CONICET, Buenos Aires, Argentina.
2 Boston University Dept. of Biomedical Engineering, U.S.A.
3 Macquarie University Hearing and Dept. of Linguistics, Australia

Presenting author:
***Jimena Ballestero**, jimena.ballestero@gmail.com*

The lateral superior olive (LSO) and medial superior olive (MSO) are the first nuclei in the ascending auditory pathway that encode binaural information. MSO principal neurons extract information concerning the temporal fine structure of sounds underpinning sensitivity to interaural time differences (ITDs). LSO neurons extract interaural level differences (ILDs) and ITDs conveyed in the envelope of high frequency sounds (envelope-ITDs). LSO neurons are heterogeneous both in their intrinsic properties as well as in their synaptic inputs. How this heterogeneity impacts the coding properties of LSO neurons has been source of debate. In a previous work we have proposed to characterize the responses of LSO and MSO neurons in terms of their filtering properties in response to fast variation of electrical inputs (ZAP stimulus). Here, by using the ZAP stimulus, we assessed the filtering properties of a large population of LSO neurons. We have identified two neural populations: low-pass neurons characterized by a low frequency cut-off frequency (< 100Hz) and resonant neurons characterized by a high cut-off frequency (> 100 Hz) sometimes accompanied by a peak in the impedance profile. The filtering profile could be modulated both by blocking Kv1.1/2 channels and by changing the cell membrane potential. Both types of neurons were present along the tonotopic axis of the LSO. We suggest these two populations constitute parallel channels of processing for high frequency sound in the LSO.

E-Posters

SENSORY AND MOTOR SYSTEMS

Motor replays of song during sleep in a suboscine bird

Juan F. Döppler [1], Ana Amador [1], Franz Goller [2], Gabriel B. Mindlin [1]

1 Departamento de Física, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires; IFIBA-CONICET
2 Institute of Zoophysiology, University of Münster; School of Biological Sciences, University of Utah, Salt Lake City

Presenting author:
***Juan Francisco Döppler**, dopplerjuan@gmail.com*

Birdsong production requires a precise control of the respiratory system and muscles in the syrinx, the avian vocal organ. Oscine birds use a set of highly developed neural nuclei which produce precise patterns of activity to achieve this. Interestingly, these patterns have been shown to occur spontaneously during sleep. Even more, while the respiratory pathway is blocked during sleep (and thus birds don't sleep-sing), the pathway innervating the syrinx is not, and this activity arrives at the muscles, making the periphery a window into the sleeping brain.

In tyrannid suboscine birds (phylogenetically close to oscine birds, usually considered non-learners) such developed neural nuclei haven´t been found, thus making this window a unique tool to study sleep in the non-learning brain.

In this work we study the suboscine Pitangus Sulphuratus. We focus on the obliquus ventralis, a muscle involved in the amplitude modulation of sound during song. We show that events of song-like activity occur during sleep, as in the case of oscine birds. This activity is consistent with the rehearsal of the song, or part of it, and has some variability not observed during wake. We also find a set of qualitatively different events, compatible with another vocalization, usually produced during territorial dispute and accompanied by a behavioral display. Using recordings of the sleeping bird we show that the activity is consistently produced during sleep simultaneously with the behavioral display.

E-Posters

SENSORY AND MOTOR SYSTEMS

Evidence for activity-dependent axonal arbor growth and maturation in developing zebrafish lateral line afferent neurons

Lucia Salatino [1], Ana Belen Elgoyhen [2], Paola Plazas [1]
1 Instituto de Farmacología, Facultad de Medicina, UBA
2 INGEBI-CONICET

Presenting author:
***Lucia Salatino**, lu.salatin@gmail.com*

Spontaneous electrical activity (SEA) expressed by developing sensory systems is required for the correct assembly and function of neuronal circuits. In order to decipher which mechanisms are involved in this process, we used the Zebrafish (Danio rerio) lateral line system (LL). The LL allows fishes and amphibians to detect water motion and pressure changes and consists of clusters of mechanosensory hair cells and non-sensory supporting cells. LL hair cells are innervated by afferent and efferent neurons, and share structural, functional and molecular similarities with hair cells in the vertebrate inner ear. Zebrafish LL afferent neurons (AffN) exhibit SEA between 5 and 7 days post-fertilization (dpf), however is unknown if it plays any role in the assembly of the LL system. We silenced SEA in single LL AffN by stochastic over-expression of inward rectifier K+ channels and analyzed the phenotype and the dynamics of axonal arbor growth. Suppression of SEA in single LL AffN led to a decrease in axonal arbor length and innervation area in the hindbrain. Moreover, silenced neurites display higher motility as well as higher formation and elimination rates than WT ones, which are features of immature neurons. Our results provide an in vivo demonstration that SEA regulates axonal arbor maturation, growth and territory in the hindbrain, in developing LL AffN.

E-Posters

SENSORY AND MOTOR SYSTEMS

Noise exposure triggers changes of synaptic function in mammalian hair cells

Luis E. Boero [1,2], Shelby Payne [3], María Eugenia Gómez-Casati [2], Mark A. Rutherford [3], Juan D. Goutman [1]

1 Instituto de Investigaciones en Ingenieria Genética y Biología Molecular Dr. Héctor Torres (INGEBI-CONICET)
2 Instituto de Farmacología - Facultad de Medicina - UBA
3 Washington University School of Medicine - Department of Otolaryngology

Presenting author:
Luis Ezequiel Boero, *le.boero@gmail.com*

Noise-induced hearing loss has gained relevance as one of the most important sources of hearing loss. Acoustic trauma (AT) can alter auditory function and reduce the number of synapses between inner hair cells (IHCs) and afferent neurons but less is known about its impact in the ability of IHCs to signal auditory information. Here we intend to address if the capacity of IHCs to release neurotransmitter is altered after AT.

Auditory function tests and confocal imaging confirmed that one day after exposure to a 120 dB noise for 1 hour, mice displayed elevated hearing thresholds and a reduction in the number of synapses per IHC. We measured changes in membrane capacitance (ΔCm) triggered by step depolarizations as a proxy of IHC exocytosis. IHCs from noise-exposed mice displayed larger ΔCm jumps compared to unexposed IHCs. Using depolarizations of increasing duration, we found larger [?]Cm for pulses longer than 100 ms. No differences in calcium entry were observed for any of the applied depolarizations. To determine if this potentiated release was triggered by glutamate released during AT and acting retrogradely, we made use of the vesicular transporter vGluT3 knock-out (KO) mouse. Exposed KO showed reduced ΔCm compared to controls, in contrast to what has been observed in WT mice. These results suggest that AT enhances vesicle release in IHC, possibly by accelerating vesicle recruitment, and this would be dependent upon the intense glutamate release.

E-Posters

SENSORY AND MOTOR SYSTEMS

Graph Theory tools for characterize Motor/ Imaginary Movements in EEG

Román Baravalle [1], Natalí Guisande [1], Monserrat Pallares [1], Federico Miceli [1], Mauro Granado [1], Fernando Montani [1]

1 IFLP, CONICET & Universidad Nacional de La Plata (UNLP), La Plata, Argentina

2 Departamento de Física, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), La Plata, Argentina.

Presenting author:
***Román Baravalle**, romanbaravalle@gmail.com*

Measures of the relative contribution of EEG oscillations are particularly useful to investigate the emergent properties of the rhythmic activities of the brain. The different rhythms of the brain activity are of functional importance to understand how information is processed in the mammalian brain. We used the Bandt-Pompe (BP) permutation methodology for the evaluation of the probability distribution function (PDF) associated with the EEG time series considering the different rhythmic oscillations bands. Based on the quantification of the ordinal "structures" present in the EEG signals and their local influence on the associated probability distribution, we incorporate the time series' own temporal causality through an algorithm of easy implementation and computation.

In our current study, we quantify the network connectivity strength across electrodes using a symbolic formalism for assessing the PDF. We estimate the causal BP PDF associated to the different electrodes, and for the different frequency bands, to measure the interconnectivity across electrodes using the Jensen-Shannon Divergence between them. In this way obtain a representation of the brain networks when executing different visuo-motor tasks. We evaluate the most relevant interconnectivity for frequency bands during different motor/imagery activities. Interestingly the node centrality provides us a measure that could discriminate between imaginary and realized movements.

E-Posters

SENSORY AND MOTOR SYSTEMS

Optogenetic activation of olivocochlear efferent fibers fibers: in the quest for the source of GABA.

Tais Castagnola, Ana Belén Elgoyhen, Juan Diego Goutman, Carolina Wedemeyer

Instituto de Investigaciones en Ingeniería Genética y Biología Molecular - INGEBI (CONICET)

Presenting author:
Tais Castagnola, *chiscastagnola@gmail.com*

During development, inner hair cells (IHCs) in the mammalian cochlea are unresponsive to acoustic stimuli but instead present intrinsic electrical activity, crucial for the normal development of the auditory pathway. During this same period, neurons originating from the medial olivocochlear complex (MOC) transiently innervate IHCs. This innervation is mediated by acetylcholine (ACh), activating nicotinic receptors assembled by α9 and α10 subunits and is responsible for controlling IHC excitability during this period. Even though this is a cholinergic synapse, previous evidence indicates the presence of abundant GABA and presynaptic GABAB receptors. Moreover, the application of GABAB receptors agonists can reduce ACh release. To determine the source of GABA in the MOC – IHC synapse, transgenic mice expressing channelrodhopsin (ChR2) in GABAergic and cholinergic fibers were used. We show here for the first time, that MOC fibers can be optogenetically activated in ChAT-Cre/ChR2 mice (n=3).

In addition, immunohistochemistry techniques were used to characterize expression in these transgenic mice. On the other hand, to further understand the mechanisms of GABA modulation we used calcium imaging techniques that allowed us to estimate activity at a single synapse level. Altogether these results suggest that ACh might be released from fibers that have a GABAergic identity.

E-Posters

SENSORY AND MOTOR SYSTEMS

The medial efferent system during development of the auditory pathway

Valeria Carolina Castagna [1], Luis Ezequiel Boero [1], Mariano Di Guilmi [2], Ana Belén Elgoyhen [2], Maria Eugenia Gomez Casati [1]

1 Instituto de Farmacología, Facultad de Medicina, UBA
2 Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, Dr. Héctor N. Torres(INGEBI)

Presenting author:
***Valeria Castagna**, valeriacarolinacastagna@gmail.com*

The auditory system of many mammals develops after birth. It is known that before the onset of hearing inner hair cells (IHCs) of the cochlea are innervated by neurons of the afferent system and transiently by neurons of the medial olivocochlear (MOC) system. During this period, IHCs exhibit spontaneous periodic depolarization patterns, that produce the release of the neurotransmitter, glutamate. These events induce stereotyped bursts of action potentials that are transmitted to the auditory circuits in the brain and promote physiological maturation and the proper establishment of the tonotopic map. The transient efferent innervation to IHCs of the cochlea has been proposed as a modulator of this activity. In this work, we sought to understand the function of this transient synapse during the beginning of hearing. We used a previously reported genetically modified mice carrying an α9 cholinergic receptor subunit point mutation that leads to enhanced responses to MOC activity. First, we analyze the onset of hearing and we found that these knock-in gain of function animals start to hear a day before than wild types, which means that the MOC system might be involved in cochlear development. Second, we observed that the maturation of the auditory system is a process that occurs from the periphery towards the higher nuclei. Finally, we evidenced that afferent synapse formation begins as a multiple innervation and then, a 'prune' and refinement of these synapses occurs.

E-Posters

SENSORY AND MOTOR SYSTEMS

Functional evidence of the crustacean lobula plate as optic flow processing center

Yair Barnatan [1], Daniel Tomsic [2], Julieta Sztarker [2]

1 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE) CONICET, Universidad de Buenos Aires
2 Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE) CONICET, Universidad de Buenos Aires & Departamento de Fisiología, Biología Molecular y Celular Dr. Héctor Maldonado, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires

Presenting author:
***Yair Barnatan**, ybbarnatan@gmail.com*

When an animal rotates it produces wide field image motion over its retina, termed optic flow (OF). OF blurs the image compromising the ability to see. Image shifts are stabilized by compensatory behaviors collectively termed optomotor response (OR). In most vertebrates and decapod crustaceans such reflex behavior involves mainly eye movements that consists in a slow tracking phase of the wide field image motion followed by a fast-resetting phase. We used the mud crab Neohelice granulata to tackle a major question in crustacean's visual processing: which region of the brain is the neural substrate for processing OF? It has long been known that dipteran lobula plate (3rd optic neuropil) is the center involved in processing OF information. Recently, a crustacean lobula plate was characterized by neuroanatomical techniques, sharing many canonical features with the dipteran neuropil. In this work we present a functional evaluation of the role of crab's lobula plate on the compensatory eye movements to rotational OF by performing electrolytic lesion experiments. We show that lesioning the lobula plate greatly impairs OR while keeping intact other visually guided behaviors, such as avoidance response upon an approaching stimulus. Even when OR is present in some lobula plate lesioned animals, these show reduced speed of eye tracking. Altogether, these results present strong evidence about an evolutionary conserved site for processing optic flow shared by crustacean and insects.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Deep neural network-based Language Models for estimating word-Predictability

Alfredo Raul Umfurer [1], Juan E. Kamienkowski [1], Juan E. Kamienkowski [2], Bruno Bianchi [1]

1 Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN, UBA - CONICET
2 Departamento de Física, FCEyN, UBA

Presenting author:
***Alfredo Raul Umfurer**, alfredoumfurer@gmail.com*

When we read printed text, we are continuously predicting upcoming words to integrate information and guide future eye movements. Thus, the Predictability of a given word (i.e. the probability of guessing it from its previous context) has become one of the most important variables when explaining human behavior and information processing during reading. In parallel, the Natural Language Processing (NLP) field evolved by developing a wide variety of applications.

In a previous study [Bianchi et al. 2020] we showed that using different word embeddings techniques (like Latent Semantic Analysis and FastText) and N-gram-based language models we are able to partially captured aspects of human-Predictability in long Spanish texts and to better understand the behavior of eye movements during reading.

In the present study, we aim to estimate a new computer-based Predictability using more complex and recent models. In particular, we used a deep neural network-based Language Model (AWD-LSTM), that can address more long-term dependencies on the text. We found that this model can also partially capture other aspects of the effect of human-Predictability on eye movements, and when added to the previously tested models, it can enhance their performance.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Intrinsic membrane properties modulate the GABAB mediated synchronization entrainment of Thalamocortical neurons

Angela Isabel Tissone [1,2,3], Germán Mato [1,3], Yimy Amarillo [1,3]

1 CONICET. CCT Patagonia Norte
2 Universidad Nacional del Comahue. CRUB
3 Gerencia de Área Investigación y Aplicaciones no Nucleares. Gerencia de Física. Departamento de Física Médica. CNEA. Centro Atómico Bariloche

Presenting author:
***Angela Isabel Tissone**, anyisone@gmail.com*

Oscillations of the Thalamocortical (TC) circuit are related to the generation and maintenance of global rhythms that appear in the electroencephalogram (EEG) and that characterize functional states of the brain. The ability of the TC circuit to generate these oscillations lies in the combination of the intrinsic properties of the neurons that form the circuit and their recurrent synaptic connections. It has been shown in genetically modified animal models that the lack of the low threshold calcium channel T decreases the delta wave component present in the EEG during N-REM sleep and produces alterations of the sleep cycle. In addition, the overexpression of IT in animal models produces an absence epileptic phenotype that includes the presence of Spike-Wave Discharges (SWDs): the EEG hallmark of the disease. The input of reticulothalamic neurons (nRT) onto TC neurons has a synchronizing effect through the activation of GABAB receptors. It has been proposed that this effect is involved in the hypersynchronization that characterizes SWDs. We develop a 3-compartment model that represents the morphology of TC neurons and added the relevant postsynaptic inputs to study how they interact with the intrinsic cellular physiology. In particular we studied how different temporal statistical distributions of synaptic nRT to TC neurons inputs affect entrainment, and how this is modulated by the physiological properties of the intrinsic ion conductances of TC neurons.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Neural bases of Predictions during reading

Bruno Bianchi [1], Diego E. Shalom [2], Juan E. Kamienkowski [1], Juan E. Kamienkowski [2],

1 Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, FCEyN, UBA - CONICET
2 Departamento de Física, FCEyN, UBA

Presenting author:
***Bruno Bianchi**, brunobian@gmail.com*

Our brain is constantly performing predictions about upcoming events. By doing this, we can anticipate actions to take and rapidly respond to those probable future events. For example, during visual tasks, such as reading, predictions allow us to plan and perform ocular movements (that are responsible for the inspection and processing of the visual field) and to integrate words with their context more easily. In a series of studies, we analyzed the brain bases of predictions performed while reading natural stimuli, and modeled the Predictability (i.e. the variable that represents how probable is to guess a word before reading it) with computational models: (1) on an eye movement experiment, where participants read short stories, we analyzed how different computational models can mimic Predictability effect on gaze duration; (2) on an EEG experiment, where participants read Memory-Related and Common Sentences in a Serial Visual Presentation paradigm, we analyzed how different sources of predictions impacts on Evoked Potentials, like the N400; (3) finally, in an eye-movements and EEG co-registration study, where participants read Memory-Related and Common Sentences in a natural reading paradigm, we analyzed how Evoked Potentials are modified by natural reading. We conclude that predictions are performed using different sources (semantical, grammatical, syntactical, mnemonic, etc), and that there are different brain mechanisms underlying mnemonic predictions.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Electrophysiological characterization of a behavioral index that quantifies the degree of loss of consciousness in epileptic seizures

Claudio Sebastián Sigvard [1,2], Melisa Maidana Capitán [1,2], Nuria Cámpora [3], Silvia Kochen [3], Inés Samengo [1,2]

1 Instituto Balseiro
2 Departamento de Física Médica
3 Neurosciences and Complex Systems Unit (ENyS), Consejo Nacional de Investigaciones Científicas y Técnicas, Hospital El Cruce "Néstor Kirchner" y Universidad Nacional Arturo Jauretche.

Presenting author:
***Claudio Sebastián Sigvard**, sebastiansigvard@gmail.com*

In 2009, the Consciousness Seizure Scale (CSS) was proposed to quantify the degree of loss of consciousness, summarizing the response of a patient to 8 behavioral items performed by a clinical practitioner during or after a seizure. The 8 items quantify the ability to interact with the practitioner, to recognize the seizure as such, and the degree of memory impairment. Here we analyzed the physiological correlates of the CSS by studying the electric potential recorded with intracranial electrodes in patients requiring an exploratory study before epilepsy surgery. We analyzed 26 seizures recorded from 5 patients, each with 5-6 electrodes and each electrode with 9 contacts (1599 signals in total). We found that the items that assessed memory impairment were positively correlated with the total duration of the seizure, with maximal correlation between the electrical anomaly and the behavioral tests approximately 60 seconds after seizure onset. The items assessing the ability to interact with the practitioner, instead, were positively correlated with the propagation velocity throughout the recruited areas, with maximal correlation between electrical and behavioral properties approximately 30 seconds after seizure onset. We conclude that the signals recorded with intracranial electrodes contain information about the different capacities that sustain conscious processing, and that the impairment of different capacities follows discernable temporal profiles.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

A Computational Theory for the Emergence of Grammatical Categories in Cortical Dynamics

Darío Dematties [1], Silvio Rizzi [2], George K. Thiruvathukal [2], Mauricio David Pérez [3], Alejandro Wainselboim [1], B. Silvano Zanutto [4]

1 Centro Científico Tecnológico Conicet Mendoza, Instituto de Ciencias Humanas, Sociales y Ambientales, Mendoza, Argentina
2 Argonne National Laboratory, Lemont, IL, United States
3 Microwaves in Medical Engineering Group, Division of Solid-State Electronics, Department of Electrical Engineering, Uppsala University, Uppsala, Sweden
4 Instituto de Biología y Medicina Experimental-CONICET, Buenos Aires, Argentina

Presenting author:
Dario Jesus Dematties, *ddematties@mendoza-conicet.gob.ar*

A general agreement in psycholinguistics claims that syntax and meaning are unified precisely and very quickly during online sentence processing.
Although several theories have advanced arguments regarding the neurocomputational bases of this phenomenon, we argue that these theories could potentially benefit by including neurophysiological data concerning cortical dynamics.
In this work we introduce a computational model inspired in the dynamics of cortical tissue.

In our model, proximal afferent dendrites produce stochastic cellular activations, while distal dendritic branches contribute independently to somatic depolarization by means of dendritic spikes, and finally, prediction failures produce massive firing events preventing formation of sparse distributed representations.

This model combines semantic and syntactic constraints for each word in a sentence context until grammatically related word function discrimination emerges spontaneously by the sole correlation of lexical information from different sources without applying complex optimization methods.

We show that the sparse activation features returned by our approach are well suited to accomplish grammatical function classification of individual words in a sentence. In this way we develop a biologically guided computational explanation for linguistically relevant unification processes in cortex which connects psycholinguistics to neurobiological accounts of language.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Wavelets for sleep scoring: A machine learning approach

Eugenia Moris [1], Cecilia Forcato [2], Ignacio Larrabide [1]
1 PLADEMA, UNICEN-CONICET
2 Laboratorio de Sueño y Memoria, Depto. de Ciencias de la Vida, Instituto Tecnológico de Buenos Aires (ITBA)

Presenting author:
***Eugenia Moris**, euge.moris@gmail.com*

Motivation: Sleep scoring it a common method used by experts to monitor the quantity and quality of sleep in people. But it is a time-consuming and labour-intense task. Because of this, automatic sleep scoring has been recently studied using machine learning techniques.

Materials and Methods: We present a Random Forest algorithm that uses discrete Wavelets [2] to extract features from each epoch and perform a classification into different Sleep Stages (S1, S2 and S3). Wavelets provide information about time as well as frequency domain. Only one channel (Fpz-Cz) was used, from the public data-set Sleep-EDF [1].

Results: After assessing the results with different alternatives of discrete wavelets, the discrete Mayer wavelet was chosen because it provided the best results. The classification produced an accuracy of 82% and a F-score of 60% over the test data.
Conclusion: We observed that wavelets are a good choice when identifying different sleep stages. The class that had the worst performance during classification was Stage 1. This might be due to the lower number of samples. A proper data balance might improve the previous results.

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E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Describing attention test with eye tracking in an entropy-complexity plane

Francisco Ramiro Iaconis [1], Jessica Adriana Del Punta [2], Adrian Jimenez Gandica[1], Claudio Delrieux [3], Gustavo Gasaneo [4]

1 Departamento de Física, Universidad Nacional del Sur - IFISUR, Bahía Blanca.
2 Departamento de Matemática, Universidad Nacional del Sur, Bahía Blanca.
3 Departamento de Ing. Eléctrica y Computadoras, Universidad Nacional del Sur- CONICET
4 Centro Integral de Neurociencias Aplicadas, Bahía Blanca.

Presenting author:
***Francisco Iaconis**, franciscoiaconis@gmail.com*

To assess attention, psychologists use different tests. Two of them are the Trail Making Test (TMT parts A and B) and the Perception of Differences Test (PDT). The results are usually based on time employed and right answers. Eye-tracking technology may significantly improve these assessments gathering indirect latent information about the subjects' performance. However, raw eye-tracking data interpretation still poses challenges, since most of the underlying processes are not well understood.

In this work we propose a novel analysis, based on statistical complexity measures, for time series obtained from an eye-tracking version of these tests. A total of 86 participants performed the PDT, and 65 performed the TMT. From each time series we calculated two probability distributions: position, related to where the subject is looking, and directional patterns [1], related to the directions followed by the gaze. For each distribution we calculated the Jensen-Shannon entropy and the statistical complexity [2]. The results were placed in an entropy-complexity plane, which displays typical specific features associated with different complex dynamics, showing that PDT behaves similar to the Logistic Equation (chaotic antipersistent behavior) while TMT behaves similar to fractional Brownian motion (chaotic persistent behavior).

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E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

A Bayesian model for guidance of eye movements in visual search in natural images

Gaston Bujia [1], Melanie Sclar [1], Sebastián Vita [1], Guillermo Solovey [2], Juan Kamienkowski [1]

1 Laboratorio de Inteligencia Artificial Aplicada (ICC-UBA)
2 Instituto de Cálculo (UBA)

Presenting author:
***Gaston Bujia**, gastonbujia@gmail.com*

From detecting potential threats to search for some desired object like food, visual search is one of the most essential visual abilities for humans. In the last decades, there was a large development of models that accurately predict the most likely fixation locations (saliency maps), although they are not able to follow the sequence of eye movements (scanpaths). Today, one of the biggest challenges in the field is to go beyond saliency maps to predict task-specific scanpaths. Particularly, in visual search tasks in artificial images, Ideal Bayesian observers have been proposed to model the visual search behavior as an active sampling process. In this process, during each fixation, humans incorporate new information and update the probability of finding a target at every location.

Here, we propose a combined approach for predicting scanpaths, using state-of-the-art saliency maps to model prior image information in a Bayesian searcher framework. We collected eye-movement visual search data (N=57) in natural indoor scenes and compare different variants of the model. First, we compare different state-of-the-art saliency maps with human fixations, reaching similar AUC performances in the first fixations as in other datasets, but AUC strongly drops after that. Second, we compare different search strategies against human's scanpaths. Our model achieves the best agreement between metrics and outperforms other strategies, generating scanpaths almost indistinguishable from humans.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Single Subject Voxel Based Morphometry for atrophy detection in temporal epilepsy with hippocampal sclerosis

Hernán Külsgaard [1], Juan Pablo Princich [2], Ignacio Larrabide [1]

1 Pladema Institute - UNICEN/CONICET, Tandil, Buenos Aires

2 Estudios en Neurociencias y Sistemas Complejos (ENyS), UNAJ/CONICET, Florencio Varela, Buenos Aires

Presenting author:

***Hernán Claudio Külsgaard**, hkulsgaard@plademe.exa.unicen.edu.ar*

Single Subject Voxel Based Morphometry (SSVBM) is a technique used for cortical atrophy detection for individuals. However, is rarely used for Hippocampal Sclerosis (HS) detection. Our goal was to analyze the SSVBM performance on patients with unilateral HS.

We performed modulated SSVBM for the whole brain on MRI T1 images of 36 patients with HS on the left hemisphere, 22 on the right side and 59 healthy subjects. We used a statistical threshold of $p<0.001$ (uncorrected) and for those without detections on the hippocampus, we did another test at $p<0.005$. Additionally, we compared the patients with and without detections using group VBM ($p<0.05$ FDR corrected) and analyzed their normalized hippocampal volumes.

The sensitivity for hippocampal atrophy detection using $p<0.001$ was 72% and 86% for the left and right hemisphere respectively, with 86% specificity. For the test at $p<0.005$ only on those without detections at previous threshold (10 lefts and 3 rights), sensitivity was 70% and 30% respectively, with specificity of 71%. The group analysis showed significant greater hippocampus volumes for HS patients without detections at $p<0.001$, whereas their normalized hippocampal volumes were inside the range of healthy subjects.

SSVBM is sensitive and specific for atrophy identification in patients with HS. Although, there were limitations for those patients with partial hippocampal volume preservation. Using a threshold of $p<0.005$ increases sensitivity in detriment of specificity.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Modeling of global brain activity performs spectral content transitions as seen in fMRI data of human sleep-wake cycle

Ignacio Martin Perez Ipiña [1], Yonatan Sanz Perl [2], Gustavo Deco [3], Enzo Tagliazucchi [4,5], Helmut Laufs [6]

1 Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires
2 Instituto de Neurologia Cognitiva
3 University Pompeu Fabra - Center for Brain and Cognition - ICREA5
4 Instituto de Física de Buenos Aires, Facultad de Ciencias Exactas y Naturales CONICET- Universidad de BuenosAires
5 Departamento de Física, Facultad de Ciencias Físicas, Matemáticas y Naturales - Universidad Nacional de San Luis
6 Departamento de Neurología, Universidad de Kiel

Presenting author:
***Ignacio Martin Perez Ipiña**, iperezipina@gmail.com*

The human brain is a complex system comprising 10^11 functional units (neurons) and 10^15 connections between them (synapses). Considering the extremely high number of associated degrees of freedom, it is surprising that the human brain routinely self-organizes into temporally stable and qualitatively distinct modes of information processing (alternatively, modes of consciousness), such as the different stages of the wake-sleep cycle.(1) Given the technical difficulties and insurmountable ethical obstacles to the detailed causal manipulation of brain activity in humans, mechanistic explanations accounting for the wide repertoire of these modes of consciousness is scarce.

With the objective of advancing such mechanistic explanations for the loss of consciousness during deep sleep, we implemented semi-empirical generative models of large-scale brain activity recorded with functional magnetic resonance imaging (fMRI) in a cohort of healthy adults. Besides the fMRI data, the semi-empirical nature of the models is given by realistic estimates of the network that couples interacting non-linear equations characterized by a Takens-Bogdanov bifurcation.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Noise-driven multistability versus deterministic chaos in phenomenological semi-empirical models of whole-brain activity

Juan Piccinini, Yonatan Sanz Pearl, Enzo Tagliazucchi
Buenos Aires Physics Institute and Physics Department, University of Buenos Aires, Buenos Aires, Argentina

Presenting author:
Juan Ignacio Piccinini, *piccijuan@gmail.com*

An outstanding open problem in neuroscience is to understand how neural systems are capable of producing and sustaining complex spatiotemporal dynamics. Computational models that combine local dynamics with in vivo measurements of anatomical and functional connectivity can be used to test potential mechanisms underlying this complexity. We compared two conceptually different mechanisms: noise-driven switching between equilibrium solutions (modeled by coupled Stuart-Landau oscillators) and deterministic chaos (modeled by coupled Rossler oscillators). We found that both models struggled to simultaneously reproduce multiple observables computed from the empirical data. This issue was especially manifest in the case of noise-driven dynamics close to a bifurcation, which imposed overly strong constraints on the optimal model parameters. In contrast, the chaotic model could produce complex behavior over an ampler range of parameters, thus being capable of capturing multiple observables at the same time with good performance. Our observations support the view of the brain as a non-equilibrium system able to produce endogenous variability. We presented a simple model capable of jointly reproducing functional connectivity computed at different temporal scales. Besides adding to our conceptual understanding of brain complexity, our results inform and constraint the future development of biophysically realistic large-scale models.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Study of states of consciousness under the effects of anesthetics through the use of information quantifiers.

Nicolás Fuentes[1], Alexis García [1], Ana Carolina Maldonado [1,2], Diego Mateos [2,3,4]

1 Facultad de Ciencias Exactas Físicas y Naturales. Universidad Nacional de Córdoba
2 Consejo Nacional de Investigaciones Científicas y Técnicas de Argentina (CONICET)
3 Facultad de Ciencia y Tecnología. Universidad Autónoma de Entre Ríos (UADER)
4 Instituto de Matemática Aplicada del Litoral (IMAL-CONICET-UNC)

Presenting author:
***Marcos Nicolás Fuentes**, nicolasfuentes11@gmail.com*

In the surgical practice it is of critical importance to know the state of consciousness that the patient has. Generally, this work is done by anaesthesiologists using visual inspection. To deal with this problem for some time, indices have been developed that allow to quantify the patient's state of consciousness. However, these measures often have a great computational cost or needed expensive equipment. This generates the demand to develop new indexes, based on fast algorithms and open source. In this work we analyse electrocorticogram monkeys records under different anaesthesia using information quantifiers. The results showed that the use of these measures allows to detect the different states of consciousness of the monkeys. In addition, it could be seen that the effect of anaesthesia on brain dynamics varies depending on the anaesthetic used. These results show that these metrics could be used as indices of consciousness in patients under anesthesia.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Hierarchical decomposition of a large-scale database of cognitive neuroimaging activation maps using graph-theoretical tools.

Matías Palmucci [1], Enzo Tagliazucchi [1]

1 Computational Cognitive Neuroscience Lab (COCUCO), Departamento de Física, FCEyN, UBA
2 Escuela de Ciencia y Tecnología, Universidad Nacional de San Martín (UNSAM), Buenos Aires
3 Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)

Presenting author:
***Matías Palmucci**, matiaspalmucci@gmail.com*

Since the seminal work by Biswal et al. (Biswal et al., 1995) - later expanded using multivariate methods by Beckmann and colleagues (Beckmann et al., 2005) - it is known that spontaneous brain activity recorded using fMRI presents a spatio-temporal organization consistent with well-defined neural systems. This correspondence was revealed for the first time by Smith and colleagues (Smith et al., 2009), who compared the independent components obtained from a database of fMRI task activation maps (http://www.brainmap.org/) with those obtained from resting state fMRI data. The striking correspondence between both sets of components suggested that spontaneous brain activity recapitulates spatio-temporal patterns that might be required for the rapid reaction to environmental demands. A total of 3072 association test maps of activation meta-analysis were downloaded from (www.neurosynth.org) of which we classified 400 maps corresponding to different terms associated with cognitive processes. Combining graph-theoretical tools with modularization optimization algorithms, we performed a hierarchical clustering of these maps and observed task-positive and negative clusters at a coarse-level, which were then subdivided into maps associated with well-defined functions. In contrast with the work by Smith et al., the correspondence between task-derived maps and resting state networks was only manifest at an intermediate resolution.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Phase and amplitude coupling of high-frequency oscillations in seizure records

Mauro Granado [1], Román Baravalle [1], Federico Miceli [1], Fernando Fabián Montani [1]

1 IFLP, CONICET & Universidad Nacional de La Plata (UNLP), La Plata, Argentina.
2 Departamento de Física, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), La Plata, Argentina

Presenting author:
***Mauro Granado**, granadomauro@gmail.com*

Epilepsy is a chronic neurological disease that affects 1 in 200 people. In 30% of those affected there is a negative response to pharmacological treatment, where this type is called refractory epilepsy. In this case, a surgical intervention is indicated as treatment, where success consists in finding the cortical area responsible for the generation of seizures, called the epileptogenic zone.

In this work, electrical recordings of this area were studied in patients with refractory epilepsy in order to discern the underlying oscillatory mechanisms during the epileptic process. For this, neuronal activity was studied for basal (far from the seizure) and preictal (immediately before the seizure) periods through recordings of intracerebral electrodes implanted in patients to achieve a greater resolution of the local field potential. Then, the intrinsic dynamics of the two types of records was discerned by using a time windows analysis and studying the amplitude and phase couplings for each signal. The causality of these records was also quantified through information theory tools and the Bandt-Pompe permutation methodology, which showed an increases in the carry of information of brain oscillations in the range of high frequencies.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Computational models with STDP characteristics based on Skinner´s Behavioral Theory

Monserrat Pallares Di Nunzio [1], Fernando Montani [2]
1 Instituto de Física La Plata, CONICET, UNLP
2 Instituto de Física La Plata, CONICET, UNLP

Presenting author:
***Monserrat Pallares Di Nunzio**, monsepallaresdinunzio@gmail.com*

Memories are represented by highly interconnected neural circuits in the brain and the spike-timing-dependent plasticity (STDP) is one of the most important neurochemical foundations of learning and memory. In this work, we diagram the behavior of a network in the cerebral cortex, where excitatory neurons have plasticity in the form of STDP, in its two varieties: long-term depression and long-term potentiation. These forms of plasticity trigger rewards or punishments, according to Skinner's behavioral theory on which the network was based. We simulate a neural network with 1000 neurons, with axon conduction delay and following the rule of STDP plasticity. We found an explanation of the enigma of the distal reward, associated with a characteristic dopaminergic frequency whose value is around 25 Hz. For the analysis of the results, several tools of graph theory and information theory were implemented. We studied the dependence of the order parameter Fisher's Information with the number of excitatory and inhibitory neurons. We found that the Closeness Centrality takes higher values for excitatory neurons, which is congruent with the generation of long-term plasticity. Finally, we observe how Fisher's information decreases as the system evolves, which would be compatible with a phase transition. This system fulfills with a process of learning that combines the reward with the STDP, which reaches a maximum value of the estimator complexity in its temporal evolution compatible with a chaotic state.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Characterization of color induction by perceptual distance reveals a simple perceptual law

Nicolás Vattuone [1], Thomas Wachtler [3], Inés Samengo [1]

1 Insituto Balseiro, Centro Atómico Bariloche
2 Department of Medical Physics, Centro Atómico Bariloche
3 Department of Biology II, Ludwig-Maximilians-Universität München, Martinsried, Germany
4 Bernstein Center for Computational Neuroscience, Munich, Germany

Presenting author:
***Nicolás Vattuone**, nicolas.vattuone@gmail.com*

The perceived color of a stimulus depends not only on its spectral properties but also on those of its surround. For instance, a patch that looks gray on an achromatic background appears reddish on a green background, and greenish on a red background. Previous studies showed that the effect of the surround is repulsive: It enhances the perceptual difference between stimulus and surround. We performed psychophysical experiments to quantify the repulsion. To report the results, a notion of distance in color space was required. We therefore proposed an individually tailored metric in color space that captured the perceptual abilities of each observer. To define the metric, we determined the minimal chromatic difference between a stimulus and its surround required by each subject to detect the stimulus. Next, observers performed discrimination experiments between two spatially localized stimuli presented in a surround of a different chromaticity. The surrounding color affected the discrimination thresholds. Quite remarkably, when these thresholds were expressed in the color coordinates defined before, the change in thresholds followed a simple law that only depended on the distance between the surround and the two compared stimuli. Perceptual coordinates, hence, reveal the symmetry of the repulsion effect. This finding was confirmed with a third experiment, in which subjects were asked to match the color of two stimuli presented in two different surrounds.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Development of an automated tool based on medical images and graph convolutional neural networks to aid in the diagnosis of autism spectrum disorder

Rodrigo Echeveste [1], Inés Samengo [2], Enzo Ferrante [3], Diego Milone [3]

1 Research Institute for Signals, Systems and Computational Intelligence sinc(i), FICH–UNL/CONICET, Santa Fe, Argentina

2 Instituto Balseiro and Departamento de Física Médica, Centro Atómico Bariloche, San Carlos de Bariloche, Río Negro, Argentina

3 Research Institute for Signals, Systems and Computational Intelligence sinc(i), FICH–UNL/CONICET, Santa Fe, Argentina; equal contributions

Presenting author:
***Rodrigo Echeveste**, recheveste@sinc.unl.edu.ar*

The current lack of trustworthy biomarkers for autism spectrum disorder (ASD), constrains the range of viable diagnostic strategies to the observation of a set of behavioural characteristics defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) V of the American Psychiatric Association: persistent deficits in social interaction and communication, repetitive or restrictive patterns of behaviour, among others. These characteristics are usually revealed by the Autism Diagnostic Interview-Revised (ADI-R), and the Autism Diagnostic Observation Schedule (ADOS).

Convolutional neural networks make it possible to find patterns in high dimensional data with a complex structure. In this work, we apply these capabilities to resting state functional magnetic resonance (R-fMRI) obtained from an international multisite database (ABIDE I), containing ASD individuals as well as controls. By training a particular type of networks termed graph convolutional neural networks (hence adapted to the domain at hand), we reach the state of the art in terms of performance for this dataset. An additional virtue of these models is that, once trained, one can use them to investigate which aspects of the image determine the model's predictions. This method hence provides a new route to find ASD markers based on neuroimages to, not only assist in the diagnosis of this disorder, but also to better understand it.

E-Posters

THEORETICAL AND COMPUTATIONAL NEUROSCIENCE

Restoration of plasticity in tissues with neuronal ischemia

Natalí Guisande, Roman Baravalle, Federico Miceli, Fernando Montani
Instituto de Física de La Plata (IFLP), Universidad Nacional de La Plata, CONICET CCT-La Plata (1900) La Plata, Argentina

Presenting author:
***Sabrina Natalí Guisande Donadío**, guisandenatali@gmail.com*

Cerebrovascular ischemia is an interruption or decrease in blood supply to the brain that reduces the flow of oxygen and nutrients needed to maintain normal cell function. Neuronal cell death in a particular region changes the receptive fields of the neurons surrounding the damaged tissue. Healthy neurons surrounding the injury experience a disinhibition of their receptive fields and expand into the injury. This expansion is determined by the distance from the healthy neuron to the lesion and the extent of the damage. In this work we developed a computational and analytical model that considers a lesion in a neuronal population and investigated the effects of the lesion on the surrounding receptive fields. It is found that exists an optimal value of plasticity for which the functional recovery is maximum. At the experimental level, investigating the neuronal signals of the imagined visuomotor tasks is very important to detect possible neuronal damage. Hence, experimental EEG data are analyzed by combining an information theory approach that takes into account signal causality, together with a quantification of centrality levels for the different nodes, to discriminate imagined and performed visuomotor tasks considering different rhythmic oscillations. It was found that the imagined cognitive processes coincide with high levels of centrality in the alpha frequency band for the different nodes, and that it is possible to discriminate the performed and imagined task.

E-Posters

TOOLS DEVELOPMENT AND OPEN SOURCE NEUROSCIENCE

Cholesterol measurement by HPLC with UV detection

Alejandro Omar Sodero, María Alejandra Paulazo
Instituto de Investigaciones Biomédicas (BIOMED), UCA-CONICET

Presenting author:
Alejandro Omar Sodero, *alejsodero@gmail.com*

We present a sensitive high performance liquid chromatography (HPLC)-based method for the determination of free cholesterol in brain tissue and cell cultures. The method does not require the derivatization of the analyte and uses separation and quantification by reversed-phase HPLC coupled to UV detection. Lipids are methanol/chloroform extracted following the method of Bligh and Dyer, and separated using isopropanol/acetonitrile/water (60/30/10, v/v/v) as mobile phase. Lineal detection is observed in a wide range of concentrations, from 62.5 to 2000 ng/µL. The complete method was validated measuring a significant cholesterol increase in the brains of C57BL6 mice between postnatal days 2 and 10, and a significant cholesterol decrease in glial cells in culture treated with an inhibitor of the protein deacetylase SIRT-1. We consider this analytical method a useful tool to assess free cholesterol levels in brain samples and cell cultures.

E-Posters

TOOLS DEVELOPMENT AND OPEN SOURCE NEUROSCIENCE

A Bayesian probabilistic graphical model to reveal the statistics of neuroanatomical properties in small samples

Bautista Arenaza [1], Mariana Vallejo [2], Sergio Lindenbaum [3], Juan Pablo Princich [2], Silvia Kochen [2], Mariana Bendersky [2], Paula Gonzalez [2], Inés Samengo [1]

1 Centro Atómico Bariloche and Instituto Balseiro. San Carlos de Bariloche, Río Negro.
2 Estudios en Neurociencias y Sistemas Complejos (ENyS) - Hospital El Cruce. Universidad Nacional Arturo Jauretche (UNAJ). Fcio. Varela, Buenos Aires.
3 Instituto de Tecnologías Nucleares para la Salud. San Carlos de Bariloche, Río Negro.

Presenting author:
***Bautista Arenaza**, bautista.arenaza@gmail.com*

The statistical dependencies between the anatomical properties of brain structures, both in health and disease, is typically inferred in the severe undersampled regime. MRI scans are often segmented into hundreds of measures of localized brain areas, while the number of scanned volunteers often remains woefully below. Since naive estimation methods tend to overestimate the correlations between the measured properties, a drastic reduction in dimensionality is required. To that end, we developed a Bayesian inference method based on a probabilistic graphical model that detects collections of measures that co-vary tightly, and therefore, need not be described independently. We applied the method to T1 images segmented into 300 anatomical measures by the freely available software FreeSurfer, obtained from 207 subjects aged 18-60 of both sexes, with no known neurological disorders, from Buenos Aires and Bariloche. The inferred correlation matrix was structured into almost independent blocks. Some blocks contained only the thicknesses of the analyzed cortical areas, while others mixed cortical surfaces and volumes. Hence, thicknesses tend to vary independently from volumes and surfaces. Many of the blocks contained bilateral structures, yet, a few asymmetric cases were found, as for example, around the Broca area. The segmentation for Bariloche was almost identical to the one for Buenos Aires. Regional differences, hence, are not significant when defining the quasi-independent sets.

E-Posters

TOOLS DEVELOPMENT AND OPEN SOURCE NEUROSCIENCE

Sparse labelling with AAV-PHP.eB, a noninvasive gene delivery method: Optimization of a protocol for morphological and anatomical connectivity analyses

Carlos A. Pretell Annan [1], L. Teresita Tribbia [2], Germán La Iacona [3], Irene R.E. Taravini [2], Diego E. Pafundo [1], Juan E. Belforte [1]

1 Grupo Neurociencia de Sistemas, IFIBIO-Houssay, UBA-CONICET, Ciudad de Buenos Aires, Argentina.
2 Laboratorio de Neurobiología Experimental. LNE-FBRO-UNER, Gualeguaychú, Entre Ríos, Argentina.
3 Servicio de Microscopía del IFIBIO-Houssay, UBA-CONICET, Ciudad de Buenos Aires, Argentina.

Presenting author:
Carlos Alfredo Pretell Annan, *carlos.a.pretell@gmail.com*

Since its inception, neuroscience has been captivated by the morphological understanding of neural elements and their intertwining into complex circuits. Studies concerning structure-function relationships at the single cell level and those aimed at delineating anatomical connectivity at neural network level are fundamental for the elucidation of both physiological and pathophysiological processes of the central nervous system (CNS). Although various methods exist for studying neuronal morphology, drawbacks can be encountered in certain settings: e.g., heavy metal staining can hamper simultaneous neurochemical analyses, and genetically-directed labelling can result in insufficient sparseness for adequate reconstruction of complex arborizations. If a detailed study of neuroanatomical projections with conventional or viral tracers is to be combined with a morphological analysis of the cellular elements receiving these inputs, a sparse labelling allowing visualization of axonal processes and performance of immunofluorescence (IF) would be favored. Hence, we optimized a protocol for sparse neuronal labelling taking advantage of a commercially available adeno-associated virus (AAV) variant developed for efficient noninvasive CNS gene delivery: AAV-PHP.eB. We present data supporting its use for 3D neuronal reconstruction, spine density analysis, and the complementation with AAV tracers and IF to analyze local and distal afferents to individual neurons in prefrontal cortex of mice.

E-Posters

TOOLS DEVELOPMENT AND OPEN SOURCE NEUROSCIENCE

A visualization technique to support exploratory analysis of eye movements' variables in reading

Leandro Luque [1], María Luján Ganuza [1], Silvia Mabel Castro [1], Osvaldo Agamennoni [2]

1 Grupo de Visualización y Computación Gráfica, ICIC (UNS-CONICET), Universidad Nacional del Sur (UNS), San Andrés 800, Altos del Palihue, 8000 Bahía Blanca, Buenos Aires, Argentina
2 Laboratorio de Neurociencias Cognitivas (LDNC). UNS-CIC, DIEC. Comision de Investigaciones Científicas (CIC).

Presenting author:
***María Luján Ganuza**, mlg@cs.uns.edu.ar*

Reading is a feedback process that requires the integration of different cognitive systems and is an ideal field for exploring the relationships between eye movements with top-down processes. Eye-Tracking (ET) is a non-invasive technology that allows the capture of eye movements with high temporal precision. During the reading process, different characteristics of words, phrases, and the complete story being read influence these movements. Several mathematical models study eye movements during reading short sentences, however, the extension of these findings to natural reading has not been yet studied in depth. The characteristics of the text and the number and variety of the variables involved difficult this modeling task.

Our technique provides a visual representation of the parameters of interest identified in the eye movements data for a typical reading experiment (dwell time, pupil diameter, among others), integrating all of them in a single view.

We focus on short stories, short-length texts that condense a large amount of information. The technique makes it possible to perform the analysis in the context of natural reading and without an a priori formal mathematical model, representing a valuable tool in the first steps of model development to help understanding variables relationships. It allows the analysis of not only short stories reading, but also encourages the generation of new hypotheses to address research activities related to eye movements in reading.

E-Posters

TOOLS DEVELOPMENT AND OPEN SOURCE NEUROSCIENCE

"Thinking out loud": an open-access EEG-based BCI for inner speech recognition

Nicolás Nieto [1], Victoria Peterson [2], Juan Kamienkowski [3], Hugo Leonardo Rufiner [1]

1 Instituto de Investigación en Señales Sistemas e Inteligencia Computacional, sinc(i) - UNL/CONICET
2 Instituto de Matemática Aplicada del Litoral, IMAL - CONICET
3 Laboratorio de Inteligencia Artificial Aplicada, LIAA - UBA/CONICET

Presenting author:
***Nicolas Nieto**, nnieto@sinc.unl.edu.ar*

Surface electroencephalography (EEG) is a standard and noninvasive way to measure electrical brain activity. By analyzing those signals it is possible to detect activation patterns that allow interpreting the brain mechanisms related to a particular task. Recently, with the developments in the artificial intelligence (AI) community, great advances have been achieved in the automatic detection of brain patterns, allowing the creation of increasingly faster, more reliable and accessible Brain-Computer Interfaces (BCIs).

Although different paradigms can be used to communicate, in the last few years, interest has grown to interpret and characterize the 'inner voice'. This paradigm, called inner speech, raises the possibility to execute an order by just thinking about it, allowing a more 'natural' way of communication. Unfortunately, since it is a recently explored field, there are no EEG datasets publicly available, limiting the development of new techniques and AI algorithms for inner speech recognition. In this work we construct a dataset with 10 subjects using the inner speech paradigm, in order to i) better understand the brain mechanisms and patterns related to the inner voice and, ii) to provide to the scientific community with an open-access multiclass EEG database of inner speech commands seeking at fostering the rapid development of new AI methods for robust inner speech recognition.