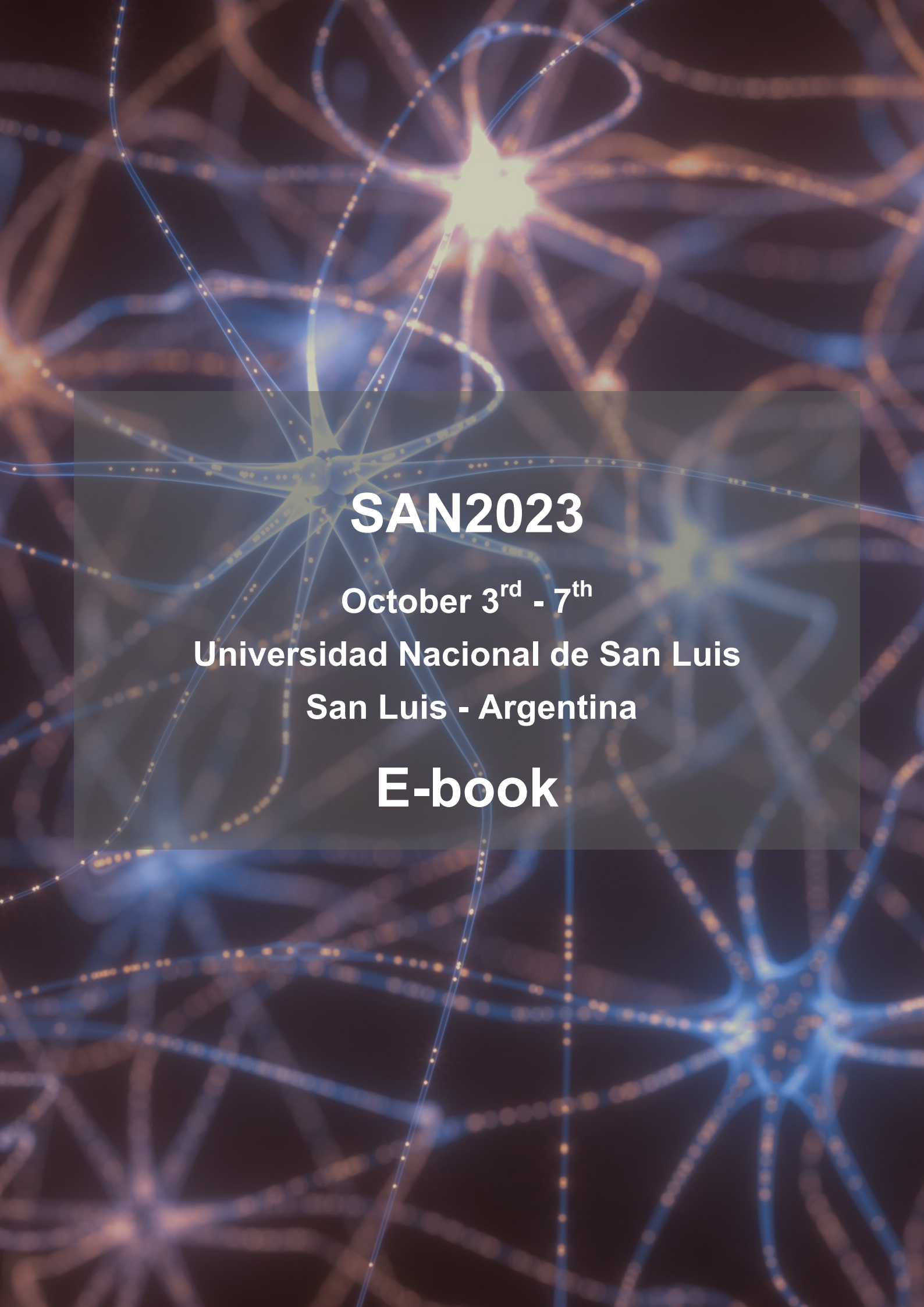

SAN2023

October 3rd - 7th

Universidad Nacional de San Luis

San Luis - Argentina

E-book

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SPONSORS & VENUE

VENUE

The XXXVIII Annual Meeting of the SAN will be held at the Auditorium of the National University of San Luis, San Luis, Argentina, from October 2nd to 7th, 2023. The meeting will be held mainly in face-to-face format.

CODE OF CONDUCT

All attendees are required to agree with the following code of conduct. Organizers will enforce this code throughout the event. We expect cooperation from everyone to help ensure a safe environment for everybody.

No unauthorized recording

It is not allowed for attendees to record or take photos of scientific material unless explicit prior consent is given by the presenter. This restriction applies to all the scheduled events in the conference. If you become aware of someone making unauthorized recordings, please contact congreso.anual.san@gmail.com immediately. Any person or organization recording without authorization may be subject to legal actions by the affected presenter, the organizations they are affiliated with, or by SAN.

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Unacceptable behavior

Harrasment, intimidation or discrimination in any form is not tolerated at the event. This includes any improper and unwelcome verbal or physical behavior that might reasonably be expected to cause offense or humiliation to another person.

Inappropriate behavior can be reported to congreso.anual.san@gmail.com the SAN2023 Organizing Committee or SAN Council members. The event organizers reserve the right to take any action to prevent violations of this Code of Conduct.

PROGRAM

OCTOBER, Monday 2nd

11-20 hrs Pre meeting Courses

OCTOBER, Tuesday 3rd

11-17:30 hrs Pre meeting Courses

16:00-19:00 hrs Registration

OCTOBER, Wednesday 4th

08:30-09:00 hrs Registration

09:00-09:30 hrs **AUDITORIUM - Opening Words: Marta Antonelli**

09:30-10:30 hrs **Opening Lecture "Dra Amanda Pellegrino": Alyson Fournier -** Molecular Mechanisms regulating axonal neuroprotection and repair

Chairs: Nicolás Unsain & Marta Antonelli

10:30-12:30 hrs **MICROCINE – S1.- Neurotour**

Maria Florencia Rossetti (virtual): Offspring brain and placental programming in a rodent model of maternal cafeteria diet

Fernando Altamirano: Chronobiological and epigenetic basis of cognitive functions in a model of aging subjected to caloric restriction.

Soledad Espósito: Brainstem circuits for motor control

Chairs: Gabriela Salvador y Fernando Altamirano

AUDITORIUM – S2.- Symposium olfactory processing

Kevin Franks: Sequence decoding with millisecond precision in the olfactory cortex

Cindy Poo: Neural basis of odor-guided navigation

Antonia M Burgin: Learning embeds multidimensional encoding of experience in olfactory cortex

F. Albeanu: Sensorimotor prediction errors in the mouse olfactory cortex

Chairs: Antonia Burgin, Noel Federman y Romano

12:30-14:00 hrs Lunch

14:00-16:00 hrs	**MICROCINE – S3.- On the role of the vagus nerve and cholinergic signaling in multi-scale metabolic optimization and activeinference** Harold Schulz: Physiological foundations of the vagal efferent and afferent circuitry Franceso Cerritelli (virtual): The role of touch in the neurobiological development of the mother-newborn dyad Anjali Bhat: False inference in the brain and the immune system: Autoimmunity, allergies, hallucinations Martin Frasch: Multi-scale organization of cholinergic signaling in immunometabolism: is there evidence of immunoceptive inference? **Chair:** Martin Frasch **AUDITORIUM – S4.- Circuit maladaptations in neuropsychiatric disorders** Jacques Barik: "Nicotine disrupts Top-Down Habenular control over Cholinergic Signals to Gate Motivation" Natalia De Marco: "The Emergence of Network Activity Patterns-An Early Window to Autism Spectrum Disorder" Francois Georges: "Emotion in Action: Anatomical and Functional characterization of Amygdala-Striatal circuits" Marisela Morales: "Ventral tegmental area neuronal diversity, connectivity, unanticipated types of neurotransmission and behavior" **Chairs:** Mariano Soiza & Sebastian Fernandez
16:00-16:30 hrs	Coffee Break
16:30-17:30 hrs	**ORAL COMMUNICATION** **MICROCINE** 1.-Nahir Guadalupe Gazal 2.-Natali Rasetto 3.-Ivana Maria Gomez 4.-Juliette López Hanotte 5.-Christell Tatiana Becerra Flores

	AUDITORIUM 6.-Juan Ignacio Ispizua 7.-Luciano Cavallino 8.-Catalina María Galván 9.-Facundo Fainstein 10.-Ana Paula Toselli
17:30-18:30 hrs	**MICROCINE - Grant writing Workshop:** Guntram Bauer, Human Frontiers Science Program **Chair:** Lidia Szczupak
18:30-20:00 hrs	Social Organized by: Comisión de Política Científica - Claudia Capurro
20 hrs	Social Organized by Red de Estudiantes

OCTOBER, Thursday 5th

09:00-11:00 hrs	**MICROCINE – S6.- Dynamics and computations in large neuronal populations** Ines Samengo: The emergence of a metric in the representation of space from neuronal population activity Ivan Davidovich (Virtual): Uncovering functional connectivity in continuous attractor networks Emilio Kropf: Unique potential of immature adult-born neurons for the remodeling of CA3 spatial maps Soledad G. Cogno (Virtual): Minute-scale periodic sequences in the medial entorhinal cortex **Chair:** Soledad G. Cogno **AUDITORIUM – S5.- What do we know, and don't know, about sleep?** Daniela Noain: Could modulation of brain slow oscillatory activity become a new treatment alternative for Parkinson's disease? Lessons learnt from animal studies. María J. Leone: School start times, chronotype, sleep and academic success in Argentinian adolescents G. Gliestro: Divergent evolution of sleep homeostasis open new

perspectives on the function of sleep
Luis de Lecea: Sleep and wake control across lifespan

Chairs: Nara Muraro & Esteban Beckwith

11:00-11:30 hrs Coffee Break

11:30-12:30 hrs **AUDITORIUM - Plenary Lecture: "De Robertis" – Analia Bortolozzi**
Emotional brain circuit mapping in Parkinson's disease

Chairs: Juan Ferrario & Diana Jerusalinsky

12:30-14:00 hrs Lunch

14:00-16:00 hrs **YOUNG INVESTIGATOR SYMPOSIUM**
MICROCINE
1.-Rodrigo Echeveste
2.-Jose A. Fernandez-Leon
3.- withdrawn
4.-Ana Fabiola Macchione
5.-Victoria Peterson

Chairs: Mariana Ferramola & Tomas Dámelio

AUDITORIUM
6.-Alejandro Cámera
7.-Ivanna Castro-Pascual
8.-Emiliano Marachlian
9.-Paula Subirada
10.-Paula M Wagner

Chairs: Diego Moncada & Sol Ramos

16:00-19:00 hrs **Poster Session 1 (odd numbers) & coffee**

19:00-20:00 hrs **Assembly SAN**

OCTOBER, Friday 6th

09:00-11:00 hrs

MICROCINE – S7.- Neurodevelopment in the womb and after birth: on stressors and resilience

Gerlinde Metz: Impacts of Prenatal and Transgenerational Stress on Brain Development

William Fifer: Adverse exposures affect maternal, fetal and infant sleep and subsequent neurobehavioral development

Jose A. Fernandez Guasti: Prenatal stress and endocrine milieu as factors influencing sexual preference

Bea Van den Bergh: Maternal–fetal stress and DNA methylation signatures in neonatal saliva

Chair: Marta Antonelli

AUDITORIUM – S8.- Acetylcholine signaling: from receptors to human disease

Francisco Barrantes: Structure and function meet at the nicotinic receptor-lipid interface

Patricio Iturriaga: From zebrafish to rats: the role of nicotinic receptors in behaviours

Cecelia Bouzat: Insights from the molecular functional level to understand why implementing the alpha7 nicotinic receptor as a therapeutic drug target is so challenging

Marina Picciotto: Acetylcholine signaling relevant to anxiety and depression

Chair: Marina Picciotto

11:00-11:30 hrs

Coffee Break

11:30-12:30 hrs

Plenary Lecture "Hector Maldonado" – Angela Casini:
Supramolecular theranostics to reach out the brain

Chairs: Marta Antonelli & María E. Pedreira

12:30-14:00 hrs

Lunch

14:00-16:00 hrs	**AUDITORIUM – S9.- Time Waits For No One – Not Even Neuroscience** Victoria Acosta Rodriguez: Circadian Rhythms in Aging and Longevity Diego Fernandez: Environmental light influences behavior through distinct retina-brain circuits Ivana Bussi: Fear keeps my mice awake during the day Esteban Beckwith: Social interactions impact sleep and the clock **Chairs:** Leandro Casiraghi & Diego Golombek
16:00-18:30 hrs	**Poster Session 2 (even numbers posters)& Coffee**
18:30-19:30 hrs	**UNSL Honoris Causa Ceremony Prof. Edvard Moser**
19:30-20:.00 hrs	**Social organized by: Comisión de Género y Diversidad**

OCTOBER, Saturday 7th

09:00-11:00 hrs	**MICROCINE S10.- Sexual and maternal behaviors in challenging contexts: disentangling the affiliative world of female rats** Daniela Agrati: Development of sexual motivation in the female rat throughout adolescence Alonso Fernandez Guasti: Alterations in the sexual behavior of diabetic female rats Mariana Pereira: How mothers mother? Neurobiology of Maternal Sensitivity Natalia Uriarte: Flexibility in behavioral strategies of mother rats raising pups of different ages **Chairs:** Daniela Agrati & Natalia Uriarte **AUDITORIUM S11.- Plasticity of cortical circuits in development and adulthood** Guillermina Lopez Bendito: Development and Plasticity of Sensory Circuits Daniel Schulz: Probing tactile feature encoding, sensori-motor integration and neuronal plasticity in mice through a cortical closed-loop brain-machine interface

	Alejandro Schinder: Activity-dependent integration of developing neurons of the adult hippocampus **Chair:** Alejandro Schinder
11:00-11:30 hrs	Coffee Break
11:30-12:00 hrs	**AUDITORIUM - Closing Plenary Lecture "Ranwel Caputo":** **Edvard Moser** – Neural network dynamics in entorhinal cortex : Space and time **Chairs:** Marta Antonelli & Mario Guido
13:00-13:30 hrs	Farewll Lunch

PRE-MEETING COURSES

C1.- Data Analysis of Calcium Imaging Signals in Neural Circuits:

Organizers: Germán Sumbre (Institut de Biologie de l´École Normale Superieure, CNRS, INSERM) and Violeta Medan (IFIBYNE-UBA/CONICET y FCEN-UBA).

Instructors: Sebastián Romano (Instituto de Investigación en Biomedicina de Buenos Aires, IBIOBA-MPSP, CONICET) and Emiliano Marachlian (Institut de Biologie de l´École Normale Superieure, CNRS, INSERM).

Teaching Assistants: Nicolás Martorell (IFIBYNE-CONICET/UBA) and Verónica Pérez Schuster (iB3-FBMC y DF-FCEN, UBA).

Audience: Undergraduate and graduate students in the fields of biology, physics, engineering, computer science, and related disciplines. Basic programming knowledge, especially in MATLAB and/or Python, is desirable.

Overview: The main aspects of calcium imaging data analysis will be covered, from neuron detection to population-level analysis of calcium signals. The activities will be organized into classes that introduce theoretical concepts during the mornings and practical sessions with pre-collected datasets (provided by the instructors or contributed by the students) in the afternoons, to practice different analysis techniques.

Course objectives:

By the end of the course, students are expected to:
Understand the basic concepts of in vivo calcium signal acquisition, advantages, and limitations of different acquisition techniques.
Learn techniques for handling and preprocessing imaging data, with a focus on managing large datasets. Software, toolboxes, and analysis strategies.
Become familiar with typical pipelines for analyzing fluorescence time series.
Grasp the basic concepts of large dataset analysis techniques: topography, dimensionality reduction and clustering, linear regression, and deconvolution.

DOWNLOAD THE PROGRAM: Análisis de Datos de señales de Imaging de Calcio de circuitos neuronales

C2.- Spatial filtering techniques for electroencephalography signals

Organizer:

Victoria Peterson (Instituto de Matemática Aplicada del Litoral, IMAL, UNL-CONICET Santa Fe, Argentina; Facultad de Ingeniería Química, FIQ-UNL, Santa Fe, Argentina).
Instructors: Catalina María Gálvan (Instituto de Matemática Aplicada del Litoral, IMAL, UNL-CONICET Santa Fe, Argentina; Facultad de Ingeniería Química, FIQ-UNL, Santa Fe, Argentina) and Bruno Zorzet (Instituto de Investigación en Señales, Sistemas e Inteligencia Computacional, sinc(i), UNL-CONICET, Santa Fe, Argentina).

Audience: Undergraduate and graduate students in the fields of biology, physics, engineering, computer science, and related disciplines.
Requirements: Basic understanding of linear algebra, optimization and programming (preferably in Python).
Overview: Brain activity recorded through surface electroencephalography (EEG) can be thought of as the result of a linear mixture of different statistical sources. These sources can originate from the group of neurons underlying the EEG sensor location, as well as neighboring groups of neurons. Additionally, other non-brain sources may be present in the EEG recordings, which ultimately will be defined as signal artifacts.

Statistical generative models assume that brain signals arise from the activity of uncorrelated sources, and these sources appear distorted in the recorded signal as a consequence of the linear mixing process.
In the context of spatial filtering, the objective is to transform the signal that exists in the “sensor” space to the “source” space. Spatial filtering methods can be used to improve the signal-to-noise ratio, identify the most correlated source to a specific event, find independent sources, etc. Thus, the application of spatial filters to the EEG signal could be performed for: (i) reducing the dimensionality of the input signal, (ii) feature extraction, (iii) elimination of noise sources. Throughout this course, the main spatial filtering algorithms used in EEG signal processing to enhance the signal-to-noise ratio, extract features, and remove artifacts will be reviewed.
Course objectives:
By the end of the course, students are expected to:
– Understand the basic neurophysiological concepts underlying electroencephalography signals
–Learn basic methods of spatial filtering of time series.
–Understand basic concepts of statistical signal processing.
–Acquire basic implementation skills in MNE-Python of specific spatial filtering methods.

DOWNLOAD THE PROGRAM: Programa__EEG

PLENARY LECTURES

Dr. Edvard Moser

Nobel Prize in Physiology or Medicine 2014
Supported by Human Frontier Science

Neural network dynamics in entorhinal cortex: Space and time

I will discuss recent advances in our understanding of the brain´s mechanisms for tracking space and time, brain functions that are generated not merely by integration of sensory inputs but rather by internal dynamics of the cortex. In mammals, space is mapped by complex neural networks in the hippocampus and medial entorhinal cortex. These brain areas contain specialized position-coding cell types, including the grid cells of the medial entorhinal cortex – cells that are active when animals are at specific locations that tile environments in a periodic hexagonal pattern. I will show how recent technological developments allow the dynamics of thousands of neurons to be monitored during behavior. Based on experiments with these new technologies, I will show how the dynamics of grid cells arises in interactions among large neural populations and how the joint activity of grid cells operates on a low-dimensional manifold with the topology of a torus, in agreement with continuous attractor network models of grid cells. I will show that this topology is present in rat pups before spatial experience, before eye opening and opening of ear canals, consistent with an innate or maturational origin of the manifold structure. I will finally show how time – in the form of codes for duration and order - is encoded across seconds to hours in the population state space of entorhinal neural networks and how specialized dynamics of the lateral part of entorhinal cell populations provides the brain with a neural code that uniquely expresses the passage of cumulative experience correlated with (but not identical to) time.

International Human Frontier Science Program Organization

Dr. Analía Bortolozzi - Laboratorio de Neurofarmacología de Sistemas. Departamento de Neurociencias y Terapéutica Experimental. Instituto de Investigaciones Biomédicas de Barcelona. CSIC. Barcelona. Spain.

Emotional brain circuit mapping in Parkinson's disease

Depression and anxiety are common in people with Parkinson's disease (PD), affecting women more than men. Addressing these non-motor symptoms has not been the focus of PD research, although psychiatric symptoms can be as distressing to patients and families as the motor aspects of the disease. Pathologically, PD is characterised by the loss of dopamine (DA) neurons in the substantia nigra pars compacta and the presence of intracellular inclusions called Lewy bodies and Lewy neurites, composed mainly of α-synuclein (α-Syn). Abundant Lewy pathology is also found in other brain regions, including the raphe nuclei of the midbrain, which may contribute to non-motor symptoms. Indeed, dysfunction of the serotonergic (5-HT) system, which regulates mood and emotional pathways, occurs during the premotor phase of PD. However, little is known about the functional consequences of α-Syn inclusions in this neuronal population, apart from DA neurons. In this talk, I will discuss the role of α-Syn in the regulation of 5-HT function in health and disease. Understanding the relative contributions to α-Syn-related changes in the 5-HT system may provide a basis for identifying Parkinson's patients at risk of developing depression and may lead to a more targeted therapeutic approach.

Dr. Angela Casini - Medicinal and Bioinorganic Chemistry. Technical University of Munich (TUM). Department of Chemistry. Garching b. München. Germany.

Supramolecular theranostics to reach out the brain

Dr. Alyson Fournier - McGill University, Montreal, Canada

Molecular Mechanisms regulating axonal europrotection and repair

SYMPOSIA

S1.- Federal Neuroscience Symposium

Title: NeuroTour 2023: A Federal Outlook of Neuroscience in Argentina

Chairs: On behalf of Federalization Commission of the SAN
Gabriela Salvador – INIBIBB-UNS-CONICET, salvador@criba.edu.ar
Fernando Gabriel Altamirano – Universidad Nacional de San Luis, fergabalt@gmail.com

Specific Goal of the NeuroTour Symposium

According to the information surveyed by the SAN in 2021, three districts in Argentina concentrate 90% of researchers in the area of Neuroscience: 61% are based in the city of Buenos Aires and 15% and 14% in the provinces of Córdoba and Buenos Aires, respectively. In this context, and within the framework of the recently created Federalization Commission of the SAN, a series of activities were carried out during 2022, including the organization of a pilot experience: the Federal

NeuroTour Symposium at the Annual Meeting.

In this first edition we gathered five researchers from outside the main research nodes representing the provinces of Tucumán, Chaco, Santa Fe, Entre Ríos, and Mendoza. Emphasis was made on inviting non-affiliated speakers and the inclusion of young investigators. We believe that fostering a federal community requires continual work over several years and even decades. For this reason, we present a second edition of the NeuroTour hoping to make this event a tradition within the SAN annual meeting.

As previously mentioned, the main goal of the Federal NeuroTour 2023 is to broaden the neuroscience network along our country. Consequently, the spirit of this symposium was to include several lines of investigation carried out in locations outside the main nodes of SAN. For this reason, in this symposium there is no specific research topic but rather a landscape of neuroscience done out of the most represented areas in SAN. Speakers that will participate in this symposium have their labs in Santa Fe, San Luis, Rio Negro and Tucumán.

Speakers

Maria Florencia Rossetti - Instituto de Salud y Ambiente del Litoral, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral-CONICET- Santa Fe.
Title: Offspring brain and placental programming in a rodent model of maternal cafeteria diet.
Abstract: One of the objectives of her research project is to explore the importance of maternal nutritional environments during prenatal and early postnatal life on brain functions and to provide novel mechanisms through which such early experiences may lead to the onset of metabolic syndromes, neurodevelopmental disorders and other brain disorders later in life.

María Florencia Rossetti received her master's degree in Biotechnology at the University of Litoral (UNL), Santa Fe. She obtained a Ph.D in Biological Sciences at the UNL. Currently, she works at the Instituto de Salud y Ambiente del Litoral, UNL-CONICET and Departamento de Bioquímica Clínica y Cuantitativa, Facultad de Bioquímica y Ciencias Biológicas, UNL in Santa Fe, Argentina.

Fernando Gabriel Altamirano - Facultad de Química, Bioquímica y Farmacia, Universidad Nacional de San Luis
Title: Chronobiological and epigenetic basis of cognitive functions in an aging model under caloric restriction"

Abstract: Caloric restriction (CR) positively influences aging processes affecting, among others, the cognitive capacities of the hippocampus. Rhythmic variations in memory and associative learning processes throughout the day suggest the participation of the circadian clock in regulating these functions. Despite growing evidence, the molecular basis of CR efficacy has not yet been fully elucidated, nor has the influence of this metabolic context on the temporal and circadian expression of factors related to cognition, antioxidant defense systems and epigenetic regulation remains unexplored.

Fernando Gabriel Altamirano received his master's degree in Biological Sciences at the Universidad Nacional de San Luis, and he has obtained a Ph.D in Neuroscience (Universidad Nacional de Córdoba). Currently, he is a postdoctoral student at the Instituto de Investigación Médica Martín y Mercedes Ferreyra, working on the role of chromosome imbalance in energetic metabolism and cellular senescence.

María Soledad Espósito - Departamento de Física Médica – Centro Atómico Bariloche, CNEA, San Carlos de Bariloche, Rio Negro
Title: Brainstem circuits for motor control in health and disease

Abstract: Movement is a defining property of the animal kingdom. However, how the nervous system produces diverse and precise actions based on animals' need continues to be the subject of deep research. This is because execution of diverse movements involves neuronal networks distributed throughout the nervous system. Brainstem motor centers are key components of these networks that have only recently begun to be unraveled establishing that specific brainstem subpopulations embedded into particular upstream and downstream circuits are dedicated to the execution of specific motor programs. The general goal of the lab is to contribute to the understanding of how precise brainstem circuits participate in the generation of particular motor behaviors in health and disease. We are currently focusing on two lines of research. On the one hand, we address the contribution of brainstem circuits to the acquisition of new motor skills. We postulate that motor learning takes place within a multi-level system in which distributed circuit elements, including brainstem circuits, contribute to the formation of a motor memory. Our results support our hypothesis demonstrating that midbrain glutamatergic neurons are necessary for the consolidation of a new motor skill. On the other hand, we are evaluating how particular brainstem circuit dysfunction underlies specific symptoms of Parkinson's disease. To this end, we have developed a novel model of synucleinopathy which offers new opportunities to study the contribution of individual network elements to disease pathomechanisms.

Maria Soledad Esposito received her master's degree in Biological Sciences at the University of Buenos Aires (UBA) and she obtained her Ph.D at the Leloir Institute Foundation focused on adult hippocampal neurogenesis. After graduating, she completed a postdoc at the Friedrich Miescher Institute for Biomedical Research in Switzerland. During her postdoc, she worked to characterize the connectivity between the brain and the spinal cord. Currently, she works at the Medical Physics Department at the Centro Atómico Bariloche, Rio Negro, Argentina.

Diego Ploper - Instituto de Investigaciones en Medicina Molecular y Celular Aplicada del Bicentenario, Tucumán.
Title: A Transgenic Cellular Model to Probe α-Synuclein Aggregation and Seeding for Parkinson's Disease

Abstract: The amyloid aggregation of α-synuclein (α-Syn) within dopaminergic neurons constitutes a pivotal hallmark of Parkinson's disease (PD). The deleterious accumulation of this protein within dopaminergic neurons is believed to be a key contributor to the

disease's pathogenesis, with intercellular transfer of these aggregates posited as the primary mechanism for disease progression. Here we introduce an enhanced transgenic model designed to investigate α-Syn aggregation and seeding in cultured cells. By utilizing SHSY5Y cells stably overexpressing α-Syn-tagRFP, our study demonstrates that the application of exogenous recombinant human α-Syn preformed fibrils (α-Syn-PFF) elicits an elevation in the count of endogenous α-Syn-tagRFP puncta. Notably, these puncta exhibit positive signals for Thioflavin S (ThS), an amyloid-specific probe, as well as phospho-α-Syn (S129), a hallmark associated with toxic α-Syn species in PD. This observation suggests that exogenous fibrils can serve as seeds to catalyze aggregation of the endogenous protein. Additionally, exogenous α-Syn-PFF induced lysosomal biogenesis, revealing lysosomal stress. Importantly, these effects are confined to α-Syn amyloid fibrils, as exposure to amyloid fibrils originating from other proteins did not influence these parameters. Lastly, as a proof of concept, we illustrate the model's utility in identifying novel compounds that inhibit α-Syn protein aggregation, phosphorylation, seeding, and uptake.

Diego Ploper received his master's degree in chemistry at the University of Tucuman. He obtained his Ph.D in Biological Chemistry at the University of California, Los Angeles (2015) focused on Signaling Crosstalk between the Wnt, BMP and Endolysosomal Pathways in Development and Disease under the supervision of Prof. Edward De Robertis. Currently, he is working at Instituto de Investigaciones en Medicina Molecular y Celular Aplicada del Bicentenario, Tucumán.

S2.- Symposium olfactory processing

Chairs:
Antonia Marin Burgin, Noel Federman & Sebastian Romano

Symposium summary

For most organisms, odorant cues guide behaviors critical for survival. However, olfactory processes are less understood than those of other sensory modalities. This symposium will cover recent work on how olfactory neuronal circuits of mammals transduce odorants into experience-dependent odor percepts. The symposium will have three talks addressing different aspects of odor processing highlighting new concepts in sensory processing related to the finding of multidimensional information in primary sensory areas.

Speakers

Kevin Franks - Duke University, USA
Title: Sequence decoding with millisecond precision in the olfactory cortex
Abstract: Neural sequences lasting tens to hundreds of milliseconds are thought to mediate essential cognitive processes, including navigation, memory encoding and retrieval, and sensory discrimination. However, the extent to which downstream cortical circuits can resolve the precise temporal structure of these sequences remains relatively unexplored. If so, the neural circuit operations that afford these circuits their exquisite temporal sensitivity are unclear.

In the olfactory system, odors activate different combinations of olfactory bulb (OB) glomeruli that respond with odor-specific onset latencies that tile the sniff cycle. Recent studies indicate that the precise timing of glomerular responses is critical for odor identification. However, the relative importance of glomerular identity versus glomerulus onset latencies in recruiting distinct ensembles of piriform cortex (PCx) neurons is unknown. As these factors are difficult to dissociate using odors, we used patterned optogenetic OB stimulation as fictive odor inputs while recording from large populations of mouse PCx neurons. Stimulating either non-overlapping glomeruli or stimulating the same glomeruli but shuffling their sequence order evoked equivalently distinct PCx responses. Remarkably, simply introducing small amounts of jitter in stimulus onset times (mean ISI ± st. dev: 5.2 ± 4.7 ms) when activating the same glomeruli in the same order evoked distinct PCx activity patterns.

We hypothesized that cortical inhibition would be critical for ensuring the temporal selectivity of PCx responses. However, surprisingly, dampening local inhibition actually improved response discriminability by slightly increasing the gain of PCx responses.

Instead, we propose that the precise temporal selectivity we observe in PCx responses emerges through a delay-line architecture established by the combination of diffuse and distributed projections from OB to PCx and long-range recurrent connectivity between PCx neurons.

Our findings therefore provide insights into the general computational principles and mechanisms that underlie the encoding and decoding of precise neural sequences in cortical circuits.

Bio: Kevin Franks first learned about the plasticity of ocular dominance columns as an undergraduate studying Biomedical Science and Philosophy and has been fascinated about how experience shapes perception ever since. His Ph.D. work, with Terry Sejnowski at UCSD, involved modeling synaptic transmission and postsynaptic calcium dynamics. As a postdoc, first with Jeffry Isaacson at UCSD and then with Richard Axel and Steve Siegelbaum at Columbia, Kevin functionally and anatomically characterized piriform cortex circuitry. His lab is currently investigating different aspects of olfactory processing.

Cindy Poo - Allen Institute, USA
Title: Neural basis of odor-guided navigation

Abstract: Odors are a fundamental part of the sensory environment used by animals for ethological behaviors. In this talk, I will discuss our recent efforts towards understanding the neural basis of flexible behavior by investigating olfacto-hippocampal dynamics during navigation and foraging. Primary olfactory (piriform) cortex is thought to be dedicated to encoding odor identity. Using neural ensemble recordings in freely moving rats performing a novel odor-cued spatial choice task, we show that posterior piriform cortex neurons also carry a robust spatial map of the environment. Piriform spatial maps were stable across behavioral contexts independent of olfactory drive or reward availability, and the accuracy of spatial information carried by individual neurons depended on the strength of their functional coupling to the hippocampal theta rhythm. Ensembles of piriform neurons concurrently represented odor identity as well as spatial locations of animals, forming an “olfactory-place map”. Our results reveal a previously unknown function for piriform cortex in spatial cognition and suggest that it is well-suited to form odor-place associations and guide olfactory navigation. Finally, I will describe our current efforts in developing an odor patch foraging paradigm to study inter-regional dynamics during flexible decision making.

Bio: Cindy Poo received her undergraduate degree in neuroscience from Brown University. She completed her doctoral training in the laboratory of Dr. Jeffry Isaacson at the University of California, San Diego, where she used in vitro and in vivo patch-clamp

recordings to understand synaptic mechanisms contributing to odor-evoked activity in olfactory cortex. Cindy was a postdoctoral researcher at the Champalimaud Research in Lisbon, Portugal, in the lab of Dr. Zachary Mainen. She was supported by postdoctoral fellowships from the Helen Hay Whitney Foundation and Human Frontiers Science Programme. She started recently he group at the Allen Institute. Her current research uses freely-moving and head-fixed rodent behavioral paradigms combined with contemporary electrophysiological recording, perturbation, and data analysis methods to further understand the olfactory system in the context of spatial navigation. Cindy's long-term research goal is to understand the neural dynamics and mechanisms for olfactory perception, cognition, and behavior in distributed circuits across the brain.

Florin Albeanu - CSHL, USA.
Title: Sensorimotor prediction errors in the mouse olfactory cortex

Abstract: During behavior, sensation and action operate in closed-loop. Movements shape sensory input, and sensory inputs guide motor commands. Through experience, the brain may learn the reciprocal relationship between sensory inputs and movements to build internal models that accurately predict the sensory consequences of upcoming actions (sensorimotor predictions). This exchange of sensory inputs and egocentric expectations is at the core of active perception. In vertebrates, olfaction is intrinsically linked to motor action through sniffing and, just as for other sensory modalities, via head and body movements. However, due to technical challenges, most studies to date have probed olfactory processing during passive odor sampling. Even when studying odor-guided navigation, the effect of movements on olfactory representations has been rarely analyzed.

We hypothesized that, in closed-loop olfaction, mice predict the sensory consequences of their actions (next most probable odor input). Movement related predictions of expected odor input get compared with current odor input within olfactory cortex to represent olfacto-motor prediction errors. To test these hypotheses, we developed a closed-loop behavioral task (Smellocator) where head-fixed mice are trained to steer the left-right location of an odor source by controlling a light-weight lever with their forepaws. In this manner, 1) we link a precise motor action to well-defined sensory expectations (odor location) and 2) subsequently violate the learned expectations via an array of online sensorimotor feedback perturbations in expert animals.

Strikingly, expert mice readily counter brief sensorimotor perturbations, by making precise corrective movements that provide us a read-out of their individually learned sensorimotor predictions. Importantly, odor-driven responses in cortical (anterior olfactory nucleus and piriform) neurons are strongly re-shaped by olfacto-motor expectations. Transient and longer term (block-style) perturbations often trigger neural

responses that are stronger than those evoked by any other task variable. Our results suggest that the olfactory cortex computes sensorimotor prediction errors by integrating sensory information with movement-related predictions, presumably relayed via top-down feedback. Using cell-type analysis and flexible activity manipulations, we are currently identifying the circuit elements that facilitate the comparison of olfactory inputs with olfacto-motor predictions.

Bio:Florin Albeanu studied Biochemistry and Neuroscience at the University of Bucharest and at MIT. During his PhD at Harvard with Venki Murthy and Markus Meister, he investigated the logic of odor maps in the olfactory bulb. As a Fellow at Cold Spring Harbor Laboratory (CSHL), using patterned-illumination optogenetic methods, Florin analyzed input-output transformations in olfactory neural circuits. He is currently a Professor at CSHL and focuses on understanding the algorithms underlying sensorimotor transformations in the brain.

Antonia Marin Burgin - IBioBA-CONICET-Max Planck partner Institute, Argentina
Title: Learning embeds multidimensional encoding of experience in olfactory cortex
Abstract: Precise adaptation of behaviors relies on the capacity of animals to associate different types of information, such as multimodal sensory, internal state and motor signals, but it remains unclear where and how in the brain this integration occurs. We study whether individual neurons at the earliest stages of cortical odor processing can gather diverse aspects of behavior during learning. We developed a task in which mice explored a virtual corridor to learn that a particular odor is rewarded only when presented at a specific visual context, and performed piriform neuronal recordings in their first training session and when they became experts. Odor identity could be decoded from ensemble activity in both training stages. After learning, individual piriform neurons also carry information about a variety of olfactory, non-olfactory sensory, motor and cognitive task parameters. Expert animals show associative neuronal responses selective to individual visual context-odor combinations, and neurons that signal choice in anticipation of the animal's response, revealing traces of cross-modal associations in a primary sensory cortex. Learning enhanced a multidimensional encoding scheme organized around odor-encoding neurons that integrate spatial context-dependent modulation and reward-related signals at a single-neuron level. Our findings suggest that learning entails computational mechanisms by which task-relevant information is embedded into olfactory processing in the piriform cortex, allowing sensory representations to be adjusted according to behavioral requirements.

Bio: Antonia Marin Burgin studied Biology at the University of Buenos Aires and obtained a PhD in Biological Sciences, University of Buenos Aires working on neuromodulatory circuits in the leech. She did a research internship at the Institute of Physiology,

University of Wuerzburg, Germany where she worked on pain nociceptors during her PhD. Antonia was then a Postdoctoral Fellow at the University of California San Diego, USA where she worked with Bill Kristan in the development of sensory-motor circuit in the leech, and then with Massimo Scanziani working in interactions among excitatory and inhibitory circuits of the rodent hippocampus. She is currently a Principal Investigator at IBioBA-CONICET-Max Planck partner Institute in Buenos Aires. Her lab focuses in how experience shapes processing in both the hippocampus and the piriform cortex.

S3.- On the role of the vagus nerve and cholinergic signaling in multi-scale metabolic optimization and active inference.

Chair: Martin G. Frasch Department of Obstetrics and Gynecology, Center on Human Development and Disability, University of Washington, Seattle, WA, USA

Symposium summary

The brain as a predictive system that constantly defines itself versus the world around it, that is a concept that has been gaining traction in neuroscience, from cell to integrative scales of organization, expanding to immunology and drawing on the general notions of non-equilibrium thermodynamics and active inference. What is driving brain's or immune system's predictive computing in health and disease? There is some evidence that metabolic constraints play an important role. Across different scales of organization, from cell to the system level, there has been evidence for the role of cholinergic signaling and the vagus nerve, respectively, as the physiological substrates representing this concept. Here, we bring together experts from the respective fields of neuroscience and clinical medicine to share their insights in this fascinating field and generate fruitful conversations to fuel new ideas.

Speakers:

Harold Schulz (Confirmed) Department of Physiology and Biophysics, University of Nebraska College of Medicine, Omaha.
Title: Physiological foundations of the vagal efferent and afferent circuitry.

Abstract: It is now well accepted that alterations in sympathetic and vagal outflow far beyond the norm can both initiate disease and contribute to the progress and severity of many disorders. The complexity of the autonomic nervous system can be appreciated as one considers the central and peripheral interactions between neurons, glia, and other components of this system. It is important to appreciate this complexity when thinking about brain-body communication.

Francesco Cerritelli (virtual) Department of Neuroscience, Imaging and Clinical Sciences | University "G. d'Annunzio" – Chieti. Italy

Title: The role of touch in the neurobiological development of the mother-newborn dyad
Abstract: Touch is the most basic mammalian maternal behavior. As soon as an infant is born, mammalian mothers begin to engage in the species-typical repertoire of maternal behavior, and these postpartum behaviors consist primarily of close physical proximity and the provision of maternal touch. Being such a widespread mammalian

behavior, early maternal touch must carry important implications for survival and adaptation and contribute to the growth and development of the young.

Anjalí Bhat Wellcome Centre for Human Neuroimaging, Queen Square Institute of Neurology, London, UK.
Title: False inference in the brain and the immune system: Autoimmunity, allergies, hallucinations

Abstract: A fundamental question remains open: why are psychiatric disorders and immune responses intertwined? Answers may lie in the active inference paradigm. Is there an immunological analogue of sensory attenuation? Is there a common generative model that the brain and immune system jointly optimise? Can the immune response and psychiatric illness both be explained in terms of self-organising systems responding to threatening stimuli in their external environment, whether those stimuli happen to be pathogens, predators, or people?

Martin Frasch - Department of Obstetrics and Gynecology, Center on Human Development and Disability, University of Washington, Seattle, WA, USA
https://depts.washington.edu/chdd/iddrc/res_aff/frasch.html
Title: Multi-scale organization of cholinergic signaling in immunometabolism: is there evidence of immunoceptive inference?

Abstract: There is strong evidence that immune and metabolic responses on cellular and systems scales are two sides of the same coin. The study of immunometabolism has yielded many insights into the joint nature of these physiological patterns. Cholinergic signaling and the vagus nerve appear in the center of these patterns, on the cellular scale – exemplified by the behavior of microglia; on the systems' scale – exemplified by the responses to inflammation.

S4.- Circuit maladaptations in neuropsychiatric disorders

Chairs:

Mariano Soiza-Reilly – Instituto de Fisiología, Biología Molecular y Neurociencias (CONICET-UBA), C.A.B.A. Argentina.

Sebastian P Fernandez – Institute Pharmacology Moléculaire Et Cellulaire (CNRS), Valbonne, France.

Symposium summary

Neuropsychiatric disorders represent a major global burden for health care systems and one of the most prevalent disabling conditions for individual's life. The complexity of psychopathologies such as autism spectrum disorders, anxiety, depression and drug abuse, among others, have challenged our view about the structure and function of neural circuits, indicating that specific dysregulations in neurodevelopmental and/or adult molecular, cellular and connectivity events can have a direct impact on brain's functional homeostasis and behavioral outputs. Recently developed techniques, genetic tools and analytical methods have contributed enormously to increase our knowledge in this regard. This symposium seeks to shed some light on recently uncovered maladaptive brain mechanisms underlying different aspects of neuropsychiatric disorders, and how these findings could help to develop novel prospective therapeutical treatments.

Speakers

Jacques Barik, PhD – Institute Pharmacology Moléculaire Et Cellulaire (CNRS), Valbonne, France.

Title: "Nicotine disrupts Top-Down Habenular control over Cholinergic Signals to Gate Motivation"

Abstract: Smoking is a major contributor to disease burden worldwide, driven by dependence to nicotine, the primary reinforcing and addictive component of tobacco. Nicotine addiction is a chronic relapsing disorder associated with multiple psychiatric comorbidities, and few effective interventions currently exist to curb addiction to nicotine. The neurocircuitry underlying nicotine dependence is broad, complex and depends on the stages of the disease process. It is well-acknowledged that nicotine impacts the reward system with prominent alterations of the firing properties of VTA dopamine (DA) neurons consequently biasing the responses to natural and addictive rewards. Yet the underlying mechanisms responsible of VTA DA alterations remain elusive. Here, we exposed mice to chronic nicotine in their drinking water to mimic the

prolonged and intermittent nicotine absorption of nicotine in humans. Combining viral tracers and optogenetic approaches, we aim to investigate the effects of long-term nicotine intake on inputs to the reward system, establishing a parallel between circuit-based electrophysiological analyses and behavioral assessments in an operant conditioning task. We will present data showing that chronic nicotine consumption induces cellular alterations within inputs to the reward system that relate to changes in motivational state for natural rewards.

These changes may influence the incentive attribution process induced by drugs of abuse in the addiction process.

Natalia De Marco Garcia, PhD – Weill Cornell Medical College, NY, USA.
Title: "The Emergence of Network Activity Patterns-An Early Window to Autism Spectrum Disorder"

Abstract: During neonatal development, sensory cortices generate spontaneous activity patterns shaped byboth sensory experience and intrinsic influences. How these patterns contribute to the assembly of neuronal circuits is not clearly understood. Using in vivo calcium imaging in young mouse pups, we show that spatially segregated assemblies of interneuron and pyramidal cells are already evident at neonatal stages. In this talk, I will cover recent work from my lab indicating that GABAergic inputs shape cortical network patterns that balance the number of interneurons integrating into maturing cortical networks during a critical window of development. In addition, I will discuss how imaging approaches including longitudinal 2-photon and widefield calcium imaging can be used to study the link between genetic predispositions for neurodevelopmental disorders and their impact on early network dynamics, and functional connectivity.

Francois Georges, PhD – Institut des Maladies Neurodégénératives (CNRS), Bordeaux, France.
Titlte: "Emotion in Action: Anatomical and Functional characterization of Amygdala-Striatal circuits"

Abstract: In humans and animals, changes in emotional states are known to modify posture, fine motor control, and/or coordination, inducing either beneficial or detrimental effects on motor performance. This suggests an overlap between neural circuits underlying emotions (limbic system) and motor control (basal ganglia). We thus performed an extensive review of the anatomical limbicto-basal ganglia direct connections and chose to focus on the amygdala to caudate-putamen (CPu) projections in mice. The CPu is the gate of entry of the basal ganglia and is involved in action selection and movement. The amygdala is a key limbic structure involved in emotional processing.

We hypothesize that amygdala-CPu neurons can trigger emotional modulation of movement. Using anatomical tracing tools, combined with in vivo and ex-vivo electrophysiology and fiber photometry, we show that the basolateral amygdala (BLA) complex is the main amygdala input to the CPu. These excitatory projections preferentially target medium-spiny neurons and parvalbumin interneurons. To define this neuronal sub-population, we mapped the inputs and outputs of the BLA-CPu neurons and determined the sources of their neuromodulators. Calcium imaging in vivo further confirms the functional connectivity of the main inputs to BLA-CPu neurons and shows that they respond to different sensory challenges.

Marisela Morales, PhD - National Institutes of Drug Abuse-NIH, Baltimore, USA.
Title: "Ventral tegmental area neuronal diversity, connectivity, unanticipated types ofneurotransmission and behavior"

Abstract: The ventral tegmental area (VTA) participates in different aspects of motivated behavior, and our research has been conducted towards testing the hypothesis that the different roles ascribed to VTA are mediated by distinct subsets of neurons that through specific circuitry integrate information from specific neurons from different brain areas. At the cellular level, studies of VTA information processing have, for a long time, been focused on resident dopamine neurons, and more recently on local inhibitory GABA neurons. However, for more than 10 years, we have been providing evidence for the existence of glutamate neurons in the VTA, glutamate neurons that project in parallel to some of the same brain structures as the dopamine neurons and begun to determine their role in behavior. By combination of classical and emerging anatomical techniques, we have found that VTA glutamate neurons establish both local and long-range connections. By optogenetic behavioral studies, we have found that VTA glutamate neurons throughout selective synapses play roles in reward, aversion, or social behavior. In the process, we have identified different subclasses of VTA glutamatergic neurons, some of them co-release dopamine and others co-release GABA. As part of this talk, I'll present some our findings on co- release of neurotransmitters and proposed models for co-release of glutamate and dopamine, as well as co-release of glutamate and GABA.

S5.- What do we know, and don't know, about sleep?

Chairs:
Nara I. Muraro – Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA)-CONICET-MPSP
Esteban J. Beckwith – Instituto de Fisiología Biología Molecular y Neurociencias (IFIByNE)-UBA-CONICET

Speakers:

Daniela Noain - Department of Neurology, University Hospital Zurich Switzerland

Could modulation of brain slow oscillatory activity become a new treatment alternative for Parkinson's disease? Lessons learnt from animal studies.

Intro: Parkinson's disease (PD) is characterized by damaging intracellular α-synuclein (αSyn) deposition that propagates extracellularly contributing to disease spread. Intracellular αSyn is sensitive to degradation, whereas extracellular αSyn may be eliminated by glymphatic clearance, a process shown in rodents to be increased during slow-waves sleep (SWS). Also, SWS appears to be closely linked with the velocity of motor symptoms progression and pharmacologically enhancing SWS results in objectively and subjectively improved sleep scores in PD patients. Here, we explored whether long-term slow-wave modulation in murine models of PD presenting αSyn aggregation alters pathological protein burden and, thus, might constitute a valuable therapeutic target.

Approach: We exerted slow-waves enhancement in VMAT2-deficient and A53T mouse models of PD by twice daily administration of sodium oxybate (200mg/kg, p.o.) 5 days/week for 4 months.

Slow-waves deprivation in VMAT2-deficient mice consisted of 16h/day sleep deprivation using the platform-over-water method. We then performed a variety of histopathological, immunofluorescence, biochemical, and molecular assessments over brain samples from sleep-modulated healthy and PD mice to assess αSyn protein load and the potential mechanisms associated to its alteration upon sleep modulation. Results: Sleep-modulating treatments showed that enhancing slow waves in both VMAT2-deficient and A53T mouse models of PD reduced pathological αSyn accumulation compared to control animals. Non-pharmacological sleep deprivation had the opposite effect in VMAT2-deficient mice, severely increasing the pathological burden. Regarding potentially involved mechanisms, we found that SWS enhancement via sodium oxybate was associated with increased recruitment of aquaporin-4 to perivascular sites, suggesting a possible increase of glymphatic function. Furthermore, mass spectrometry

data revealed differential and specific upregulation of functional protein clusters linked to proteostasis upon slow-wave-enhancing interventions. Take-home message: Overall, the beneficial effect of pharmacological SWS enhancement on neuropathological outcome in murine synucleinopathy models mirrors findings in models of Alzheimer and encourage further preclinical and clinical studies unravelling the potential of sleep-based interventions as therapeutic strategy in PD. Outlook: We are currently implementing at preclinical and clinical level non-pharmacological SWS-enhancing approaches with increased specificity and scalability. Our efforts intend to help pave the way to novel therapeutic implementations for neurodegenerative diseases characterized by protein accumulation in the mid-term.

María Juliana Leone - Universidad Torcuato Di Tella Argentina

School start times, chronotype, sleep and academic success in Argentinian adolescents Human physiology, behavior and performance show daily fluctuations. Light, social cues, culture and age modulate the properties of circadian rhythms. Even though humans are active during the day and rest at night, the phase of entrainment under light-dark conditions (i.e. chronotype) differs between individuals and it also changes with age. Importantly, chronotype is delayed during adolescence, but school start times continue starting very early in the morning. This 'perfect storm' becomes a 'perfect hurricane' in Argentina, where the cultural habits are later than in many other countries. In the last years, we have been studying the impact of school schedules on chronotype, sleep and academic success of adolescents of different ages who were randomly assigned to one of three school timings (starting at 07:45, 12:40 or 17:20) at the beginning of their secondary school. In this talk, I will present results from our previous and current cross-sectional and longitudinal studies, where we evaluated how chronotype and sleep change along adolescence, and how the interplay between chronotype and school schedules affect sleep and school success on Argentinian adolescents.

Giorgio Gilestro - Department of Life Sciences, Imperial College London United Kingdom

Divergent evolution of sleep homeostasis open new perspectives on the function of sleep.

Sleep is a highly conserved behaviour among the animal kingdom, appearing in species as distant as jellyfishes and elephants. Understanding what drives this evolution and which traits are universal implies understanding what sleep really is and what it does. This is the ultimate question in the field.

It is generally believed that sleep serves a crucially important yet mysterious "core function" that is shared among all animals and that drives its evolution, but the evidence behind this hypothesis is lacking. In my talk, I will challenge this idea by telling the

surprising story of how sleep evolved in seven different species of the Drosophila subgenus. We show that those aspects of sleep that are believed to be universal – such as its homeostatic regulation – are in fact only present in D. melanogaster and not in the other six Drosophila species we tested. We show that the difference in sleep homeostasis between melanogaster and the other species can be explained by a different underpinning cell-biology regulating synaptic strength upon prolonged wakefulness, at the same time providing a possible evolutionary mechanism and reinforcing the connection between sleep homeostasis and synaptic strength.

Luis de Lecea - Stanford University United States

Sleep and wake control across lifespan

The arousal construct underlies a spectrum of behaviors that include sleep, exploration, feeding, sexual activity and adaptive stress. Pathological arousal conditions include stress, anxiety disorders, and addiction. In the past few years we have used optogenetics to interrogate neuronal circuits underlying transitions between arousal states. Here I will present causal evidence of a critical period during adolescence in which disruption of sleep/wake cycles associated with increased dopaminergic tone results in deficits in social interactions in adult mice. I will also present a new mechanism underlying sleep fragmentation during aging. Hypocretin (hcrt) neurons are hyperexcitable in aged mice. We identified a potassium conductance known as the M-current, as a critical player in maintaining excitability of Hcrt neurons. Genetic disruption of KCNQ channels in Hcrt neurons of young animals results in sleep fragmentation. In contrast, treatment of aged animals with a KCNQ channel opener restores sleep/wake architecture. Finally, I will talk about our recent work demonstrating that focused ultrasound differentially affects excitatory vs inhibitory neurons in deep brain structures, paving the way to non-invasive neuromodulation of subcortical circuits in humans.

S6.- Dynamics and computations in large neuronal populations

Chair:

Soledad Gonzalo Cogno – Kavli Institute for Systems Neuroscience and Centre for Algorithms in the Cortex, NTNU, Trondheim, Norway.

Symposium summary

During the second half of the 20th century, discoveries like orientation selectivity in the visual cortex and spatial selectivity in the entorhinal-hippocampal circuit were major breakthroughs that greatly advanced our understanding of how individual neurons encode features of the external world in their spiking activity. Yet, a long history of theoretical work suggests that brain function emerges from the collective activity of large neuronal populations. Most of these theories, however, have remained untestable due to the lack of technologies to probe neural circuits, and therefore the mechanisms underlying neuronal computation at the circuit level remain elusive. This landscape of uncertainty is now coming to an end, since technological advances from the last decade are making it possible to record from hundreds to thousands of cells simultaneously, and to perturb neural networks with single-cell resolution. These unprecedented advances are calling for an integrative approach where experimental and theoretical neuroscience are combined to understand how large neuronal populations compute. The main goal of this symposium is to take a step in that direction and present four complementary examples of how we can probe the inner mechanisms of neural circuits to understand emerging computations.

Speakers

With this symposium we bring together scientists from diverse areas of Neuroscience who share the common goal of elucidating the mechanisms that underlie brain function through the lens of interdisciplinary research and with a focus on neuronal circuits computation. Ranging from fully theory to a combination of modelling and experimental work, the speakers were carefully selected to guarantee gender balance (50% of the speakers and male and 50% are female) and a balance in seniority levels.

Inés Samengo– Department of Medical Physics and Instituto Balseiro of Centro Atómico Bariloche, CONICET, Argentina
Title: The emergence of a metric in the representation of space from neuronal population activity

Abstract: The firing probability of sensory neurons changes with the value of the stimulus they are sensitive to. Moreover, continuous modifications of the stimulus typically produce continuous distortions of the population activity probability distribution. Mathematically, this selectivity induces a metric in the space of stimuli that reflects their discriminability in terms of the population activity they evoke. This talk discusses how a metric of physical space emerges from the population activity of both place and grid cells. The properties of the metric depend on the number of cells in the population, on their intrinsic dynamics, and on the way they tile the space of stimuli. We conclude that the subjective metric is only Euclidean if the relative phases of the grid cells of a given module obey a mathematical relation dictated by the shape of the single-cell firing distribution. Deviations from this pattern give rise to representations in which physical space is not Euclidean.

Iván Davidovich – Edmond and Lily Safra Center for Brain Sciences and Racah Institute of Physics, The Hebrew University of Jerusalem, Israel (Virtual)
Title: Uncovering functional connectivity in continuous attractor networks

Abstract: Recent technologies enable large scale recordings, offering a unique opportunity to elucidate network connectivity from spiking activity. This task is challenging in general, because correlations between the neurons might arise which are not due to direct connections. In particular, continuous attractor network models (CANs), which have been used to model a wide range of brain functions, suffer from this issue and it has been argued that reliably estimating connectivity for them is not possible. We explore different approaches to connectivity inference in a simulated system of this kind and show that accounting for the patterns of global covariation encoded in the low-dimensional attractor manifold can reveal features of the true connectivity. We also highlight the importance of evaluating the credibility of our inference process, particularly in systems with rigid correlation structures. Our inference methods could be generalized to other systems operating on low-dimensional manifolds.

Emilio Kropff – Leloir Institute – IIBBA/CONICET, Argentina
Title: Unique potential of immature adult-born neurons for the remodeling of CA3 spatial maps

Abstract: Mammalian hippocampal circuits undergo extensive remodeling through adult neurogenesis. While this process has been widely studied, the specific contribution of adult-born granule cells (aGCs) to spatial operations in the hippocampus remains unknown. Here we show that optogenetic activation of 4-week-old (young) aGCs in free-foraging mice produces a non-reversible reconfiguration of spatial maps in proximal CA3, while rarely evoking neural activity. Stimulation of the same neuronal cohort on

subsequent days recruits CA3 neurons with increased efficacy but fails to induce further remapping. In contrast, stimulation of 8-week-old (mature) aGCs can reliably activate CA3 cells but produce no alterations in spatial maps. Our results reveal a unique role of young aGCs in remodeling CA3 representations, a potential that can be depleted and is lost with maturation. This ability could contribute to generate orthogonalized downstream codes supporting pattern separation.

Soledad Gonzalo Cogno – Kavli Institute for Systems Neuroscience and Centre for Algorithms in the Cortex, NTNU, Trondheim, Norway. (Virtual)
Title: Minute-scale periodic sequences in the medial entorhinal cortex
Abstract: The medial entorhinal cortex (MEC) hosts many of the brain's circuit elements for spatial navigation and episodic memory, operations that require neural activity to be organized across long durations of experience. While location is known to be encoded by a plethora of spatially tuned cell types in this brain region, little is known about how the activity of entorhinal cells is tied together over time. In MEC, theta and gamma oscillations provide temporal structure to the neural population activity at subsecond time scales. It remains an open question, however, whether similarly powerful coordination occurs in MEC at behavioural time scales, in the second-to-minute regime. Here we show that MEC activity can be organized into a minute-scale oscillation that entrains nearly the entire cell population, with periods ranging from 10 to 100 seconds. The oscillation sometimes advanced uninterruptedly for tens of minutes, transcending epochs of locomotion and immobility. Throughout this ultraslow oscillation, neural activity progresses in periodic and stereotyped sequences. By combining the experimental data with training of recurrent neural networks we probe the mechanisms underlying the stereotyped sequences and the conditions under which the ultraslow oscillation is robust in presence of perturbations. We further show that the MEC sequences may have the potential to serve as a scaffold for processes that unfold at behavioural time scales.

S7.- Neurodevelopment in the womb and after birth: on stressors and resilience

IBRO Symposium

Organizer:

Marta C. Antonelli. Instituto de Biología Celular y Neurociencia "Prof. Dr. Eduardo De Robertis". Facultad de Medicina. UBA. Argentina

Symposium summary:

Pregnancy is a significant time in women´s life but it can also be very challenging. During the gestational period, women like any other subject can be exposed to endogenous and exogenous challenges that may be perceived as unpleasant, aversive or threatening in such a way that the homeostasis, wellbeing and overall health is threatened. If stress persists during the nursing period, it will lead to deficient parenting interfering with the mother-infant attachment. This implies that during critical periods of brain development, i.e., pregnancy and nursing periods, the baby is subjected to environmental negative influences known to shape developmental trajectories, including neuronal connections. This apparently healthy baby, if exposed to a repeated stressful situation later in life, may show impairments in the functional development of affective and reward circuits, cognition, and response inhibition. We understand that the relevance of this symposium is that it will bring together five neuroscientists geographically distant with long lasting background on the stress and resilience field to discuss the effects of perinatal insults on neurodevelopmental and neuroendocrinological programming.

Speakers:

Gerlinde A.S. Metz, Canadian Centre for Behavioural Neuroscience. Department of Neuroscience. University of Lethbridge. Lethbridge, Alberta, Canada. Department of Obstetrics & Gynecology, University of Alberta, Edmonton, Alberta, CANADA.
Title: "Impacts of Prenatal and Transgenerational Stress on Brain Development"

William P. Fifer, Department of Pediatrics, Columbia University Medical Center, New York, New York.USA.
Title: "Adverse exposures affect maternal, fetal and infant sleep and subsequent neurobehavioral development"

José Alonso Fernández-Guasti, Departamento de Farmacobiología, Centro de Investigación y Estudios Avanzados del Instituto Politécnico Nacional, MEXICO.
Title: "Prenatal stress and endocrine milieu as factors influencing sexual preference"

Bea R.H. Van den Bergh. Health Psychology Research Group, University of Leuven (KU Leuven), Leuven. Belgium.
Title: "Prenatal exposure to maternal anxiety is associated with white matter microstructure and cognition in 28-year old offspring"

Silvia M. Lobmaier .Virtual. Department of Obstetrics and Gynecology, Klinikum Rechts Der Isar, Technical University of Munich, Munich, GERMANY.
Title: "Fetal heart rate variability responsiveness to maternal stress"

S8.- Acetylcholine signaling: from receptors to human disease

Supported by Human Frontier Science Program

Chair:
Guntram Bauer, Human Frontier Science Program
Marina Picciotto, Yale University, USA

Cecilia Bouzat, INIBIBB, Bahía Blanca, Buenos Aires, Argentina
Insights from the molecular functional level to understand why implementing the alpha7 nicotinic receptor as a therapeutic drug target is so challenging

Patricio Iturriaga-Vásquez, Universidad de la Frontera, Chile
From zebrafish to rats: the role of nicotinic receptors in behaviours

Francisco Barrantes, CONICET, Argentina
Structure and function meet at the nicotinic receptor-lipid interface

Marina Picciotto, Yale University, USA & International Human Frontier Science Program Organization
Acetylcholine signaling relevant to anxiety and depression

S9.- Time waits for no one - Not even Neuroscience

Chairs:
Leandro Casiraghi, UdeSA, UNQ, CONICET
Diego Golombek, UdeSA, UNQ, CONICET

Abstract:

Very often the temporal variable is ignored or only slightly considered in experimental science. In particular, neuroscience focuses on “where” phenomena occur, their duration and intensity (“how much”), and, eventually, on their underlying mechanisms (“how”), while the “when” is often diluted in the experimental design or statistics. However, time can offer an irrefutable source of independent variation on our data, in all fields of research of the brain and of behavior. In consequence, considering the time of the day, lighting patterns, seasonality, or the sleep/wake status of the study subjects or experimental preparations is fundamental for the understanding of our research object.

In this symposium, we invite the SAN community to consider “time” in their experiments and research in their experimental designs, the environmental conditions, and the analysis and interpretation of their results. Temporal variation, in its different dimensions (from milliseconds to seasons) is fundamental for neuroscience. To illustrate this, examples will be presented representing different fields within the study of the nervous system and behavior, going from the neural basis of rhythms in metabolism and feeding, the regulation of fear-related circuits, photic and non-photic pathways mediating behavior, and the consideration of sleep as a fundamental factor modulating virtually all neurophysiologic variables.

Speakers:

Victoria Acosta-Rodríguez. UT Southwestern Medical Center Department of Neuroscience, Peter O’Donnell Jr. Brain Institute, victoria.acosta@utsouthwestern.edu. PhD, Universidad Nacional de Córdoba.

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Program:

Acosta-Rodriguez, V. Circadian Rhythms in Aging and Longevity

Caloric restriction (CR) without malnutrition promotes health and longevity in mammals, yet the mechanisms are poorly understood. We previously reported that classic CR protocols not only reduce the total intake, but also induce chronic cycles of 2-hour feeding and 22-hour fasting in mice. Thus, it was unclear whether calories, fasting or feeding time could independently contribute to longevity. To disentangle this, we tested a control group fed ad libitum (AL) vs five 30% CR protocols varying how often and when mice had access to food. We included classic CR protocols in which mice consumed their allotment as a single meal in less than 2h at the beginning of the day or night (CR-day and CR-night), or smaller meals distributed over 12h (CR-day-12h and CR-night-12h), or evenly spread out throughout 24h (CR-spread) to avoid nocturnal-biased feeding pattern adopted by nocturnal rodents. We found that CR alone, without fasting, extends lifespan by 10%. However, longevity benefits are boosted to 20% if any fasting period is present and to 35% when feeding/fasting cycles match their natural clock-driven activity. Transcriptomic analysis in the liver under AL show that with aging, inflammation and metabolic pathways are up and downregulated, respectively. In the longest-lived group, night-feeding reduces such aging- related alterations, maintains robust 24h oscillations in gene expression at older ages, and improves glucose and hormonal homeostasis. We

also identified genes sensitive to caloric intake, fasting, and feeding time. Our results demonstrate that circadian interventions promote longevity and provide a novel perspective to further explore mechanisms of aging.

Diego C. Fernandez. Environmental light influences behavior through distinct retina-brain circuits

Animal physiology is profoundly modulated by daily changes in light. In mammals, light is detected by the retina and routed to brain areas. Among them, visual centers drive image-forming functions, whereas a wide range of retino-recipient brain targets process light signals to control innate processes, including sleep/wake cycles, metabolism, and affective behavior. In the lab we apply a curiosity-driven approach to address some of the following questions: What are the mechanisms and the neuronal circuits that allow us to extract time information from changes in light? Are these mechanisms similar to those that generate an internal representation of the visual scene? Can lighting conditions affect the way the brain communicates with other systems? What are the processes that govern the development and maturation of circuits processing environmental signals? The information obtained from this basic approach becomes particularly relevant for investigating the neural basis of disorders linked to deleterious environmental factors, such as light pollution and circadian disruption. Therefore, elucidating the pathways by which irregular light exposure impacts brain homeostasis would expand the opportunities to develop innovative therapeutics strategies, including non-pharmacological interventions. In a broader view, understanding how artificial lighting sources affect our physiology is critical in the design of better lighting conditions for improving human health and the environmental impact.

Ivana L. Bussi. Fear keeps my mice awake during the day.

Circadian rhythms are behavioral and physiological rhythms with a period close to 24hs. They can be synchronized by stimuli of different nature, being the light-dark cycle the most powerful synchronizer in mammals. Fearful stimuli, such as the threat of predation, are likely to appear with a 24h periodicity. We hypothesized that cycling fearful stimuli presented during the active phase of the mice could lead to a shift in the temporal distribution of behavior.

To mimic more natural conditions in the lab, we built a set up consisting of a nesting area separated from a foraging area from which animals need to seek all their food and water. The foraging area can be rendered dangerous by applying an aversive stimulus, mild electric foot shocks. Throughout different experiments, we timed foot shocks to match the active phase or the resting phase in mice subjected to different light conditions. We showed that when random foot shocks are delivered in a 12-h window

during the active phase, mice switch the phase of their foraging and home-cage activity to the opposite “safe” phase. Upon release into constant conditions mice continue foraging and feeding with the same phase as when the fearful stimulus was present. Taken together these results suggest that cyclic fear not only acts as a synchronizer of circadian rhythms in mice but also leaves a time stamp on a circadian oscillator, resetting the phase of foraging and home-cage activity behavior. This concept is particularly important for memory and learning research as it incorporates a new variable to be considered at the time of performing fear conditioning tasks in mice.

Esteban Beckwith. Social interactions impact sleep and the clock

A large number of species have a social organization, where the interaction with other conspecifics is crucial for the individual and the specie. Social interactions perceived as positive are associated with improved health. Conversely, social isolation has been shown to negatively affect behaviour and health. In particular, increased aggression, anxiety, food consumption, changes in activity levels, and deficits in learning and memory are all consequences of a socially impoverished environment. In humans, the perception of being excluded from social interaction is sufficient for an increase in neural activity and leads to poor sleep quality, which in turn leads to a large number of physiological and behavioural deficits. Like in humans, the negative consequences of social isolation are observed in other social species.

Drosophila melanogaster has become essential for exploring the neurobiological bases of behaviour. Recent work has established that this fly is a social animal. Drosophila flies form non-stochastic interaction networks, which depend on chemical cues, both gustatory and olfactory, use social information to modulate decision making, are capable of training their circadian clock using social cues, and establish hierarchies among males. All this has shown that the social context imposes relevant changes in physiology and behaviour, and enables the use of this model to explore behavioural and social strategies that are adaptive for the species, as well as their genetic and molecular bases.

In this presentation, I will discuss results from the laboratory where we show that the social context modulates locomotion, sleep and can set the pace of the circadian clock.

S11.- Sexual and maternal behaviors in challenging contexts: disentangling the affiliative world of female rats

Chairs:
Daniella Agrati – dagrati@fcien.edu.uy Sección Fisiología, Facultad de Ciencias. Universidad de la República. Uruguay.
Natalia Uriarte – natiuria@fcien.edu.uy Laboratorio de Neurociencias, Facultad de Ciencias. Universidad de la República. Uruguay.

Symposium summary

Sexual and maternal behaviors are highly conserved among mammals. These affiliative behaviors are characterized by proximity seeking between individuals, which reflects their strong motivational basis. The neuroendocrine basis of these reproductive behaviors have been extensively studied in the laboratory rat as a reference model, however much remains yet to be understood about the complexity of their regulation.

The objective of this symposium is to look at sexual and maternal behaviors, beyond the standard conditions of study, in more challenging reproductive contexts and models, to deepen our analysis of their complexity. To this aim, the symposium will bring together neuroscientists from different geographic regions focused on the study of sexual and maternal behaviors in the female rat in non-classical reproductive periods, such as adolescence and litter overlapping, and models of pathologies, such as diabetes and depression. We expect that this conjunction of experimental approaches will promote discussion and critical analysis of current and future research directions, as well as regional collaborations.

Speakers:

Daniella Agrati. Sección Fisiología, Facultad de Ciencias, Universidad de la República. Uruguay.
Title: “Development of sexual motivation in the female rat throughout adolescence”.
Abstract: In-person presentation: This talk will describe the maturation of female rat sexual motivation and behavior throughout adolescence employing different behavioral models. It will also delve into the possible role of sex steroids – their levels and receptor expression in the sexual neural circuitry- in this developmental process.

Alonso Fernández-Guasti. Departamento de Farmacobiología, Centro de Investigación y Estudios Avanzados del Instituto Politécnico Nacional, México.
Titlte: “Alterations in the sexual behavior of diabetic female rats”

Abstract: In-person presentation: This talk will focus on the alterations in the expression of sexual behavior and motivation of female rats in a streptozotocin-induced model of diabetes mellitus type 1 and type 2. It will also deepen into the effect of insulin treatment on these behavioral deficits and the changes in the activation of the sexual neural circuit that may underlie them.

Mariana Pereira. Department of Psychological and Brain Sciences, University of Massachusetts, Amherst, Estados Unidos.
Tiltle: “How mothers mother? Neurobiology of Maternal Sensitivity”.
Abstract: In-person presentation: This talk will focus on the neurobiological mechanisms that allow mothers to dynamically coordinate caregiving decisions to resolve the constantly changing needs of their offspring, as well as to provide mechanistic insight into how maternal sensitivity is compromised by postpartum depression.

Natalia Uriarte. Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República. Uruguay.
Title: “Flexibility in behavioral strategies of mother rats raising pups of different ages”.
Abstract: In-person presentation: This talk will focus on the behavioral and cognitive adaptations that mothers exhibit while caring for their offspring in challenging reproductive contexts such as the overlapping litter model in the rat. Emphasis will be placed on the neural basis underlying this behavioral flexibility.

S12.- Plasticity of cortical circuits in development and adulthood

Organizer

Alejandro Schinder – Fundación Instituto Leloir Buenos Aires, Argentina E-mail: aschinder@leloir.org.ar

Symposium summary

Brain function relies on the establishment of proper circuits occurring during development, followed by the subsequent ability to refine and rewire specific neuronal connections according to environmental and physiological requirements. Multiple regions of the cortex maintain the capacity for remodeling, expressing mechanisms that are already present in the developing brain, such as activity-dependent synaptic modification. This symposium will present three distinct examples of cortical remodeling that illustrate the dynamic capacity for activity-dependent modification. Guillermina Lopez-Bendito will tell us about the refinement of thalamic projections reaching the barrel cortex that occurs during perinatal development. Dan Shulz will share his latest discoveries on the plasticity in the adult somatosensory cortex using a brain-machine interphase (BMI) approach where barrel cortex maps become rewired over time to control a mechanical arm. Alejandro Schinder will talk about remodeling of hippocampal networks through the integration of adult-born neurons, a process that is largely modulated by the activity of local circuits.

Speakers

Guillermina López-Bendito Institute of Neuroscience (IN), Developmental Neurobiology Unit, Alicante, Spain
Title: Development and Plasticity of Sensory Circuits
Abstract Our research team runs several related projects studying the cellular and molecular mechanisms involved in the development of axonal connections in the brain. In particular, our aim is to uncover the principles underlying thalamocortical axonal wiring, maintenance and ultimately the rewiring of connections, through an integrated and innovative experimental programme. The development of the thalamocortical wiring requires a precise topographical sorting of its connections. Each thalamic nucleus receives specific sensory information from the environment and projects topographically to its corresponding cortical. A second level of organization is achieved within each area, where thalamocortical connections display an intra-areal topographical organization, allowing the generation of accurate spatial representations within each cortical area.

Therefore, the level of organization and specificity of the thalamocortical projections ismuch more complex than other projection systems in the CNS. The central hypothesis of our laboratory is that thalamocortical wiring influences and maintains the functional architecture of the brain. We also believe that rewiring and plasticity events can be triggered by activity-dependent mechanisms in the thalamus. In this talk, I will present our recent data on the activity-dependent mechanisms involved in sensory circuits development and how these circuits acquire sensory-modality specificity. I will also present data on the role of thalamic spontaneous activity in promoting neuroplastic cortical changes following sensory deprivation. Within these projects we are using several experimental programs, these include optical imaging, manipulation of gene expression in vivo, cell and molecular biology, biochemistry, cell culture, sensory deprivation paradigms and electrophysiology.

Daniel E. Shulz Paris-Saclay Institute of Neuroscience, CNRS, Université Paris-Saclay, France
Title: Probing tactile feature encoding, sensori-motor integration and neuronal plasticity in mice through a cortical closed-loop brain-machine interface

Abstract: Tactile information is acquired and processed in the brain through concerted interactions between movement and sensation. We study neuronal processes responsible for the coding of sensorimotor information by using a comprehensive approach including electrophysiological, imaging, optogenetic and behavioral strategies in rodents. We use this knowledge to implement sensory feedback injected to the brain for improving the motor control of a brain machine interface.

Alejandro Schinder Fundación Instituto Leloir, Buenos Aires, Argentina
Activity-dependent integration of developing neurons of the adult hippocampus

Abstract: Learning and memory involve a delicate balance between networks capable of persistent information storage and circuits that rewire to adapt to environmental demands or learn new behavioral traits. The hippocampus undergoes extensive rewiring due to its capacity to generate new neurons that will contribute with thousands of new connections, integrate within preexisting structures, and provide alternative paths for information processing. Neuronal growth in the adult hippocampus recapitulates aspects of perinatal development although at slower pace, demanding >8 weeks in the mouse dentate gyrus. Over this time, molecular identity, morphology, electrical properties and synaptic connections evolve dynamically towards a mature granule cell

phenotype. This process results in developing neurons expressing distinct functional properties as they move towards maturation. In my talk I will discuss how different forms of activity influence neuronal maturation and function, present recent data on the molecular principles responsible for bringing neural stem cells through the pathway to granule cells, and share evidence on the role of developing neurons and their enhanced plasticity in spatial encoding in the hippocampus.

YOUNG INVESTIGATORS TALKS

01 | Neural control of escape speed during and after a visually threating stimuli

Alejandro Cámera (1), Mariano Belluscio, Daniel Tomsic
(1) University of Western Australia, Australia

Escape responses to danger stimuli have been studied across many groups of animals. One of these animals is the crab Neohelice granulata. On this model the MLG2 neuron has been shown to be involved in the running speed of the crab during the escape response execution. The neural response of the MLG2 to looming stimuli of various dynamics match the running speed of the crabs to those same stimuli. Via mathematical modeling a hypothesis was proposed that MLG2 performs the visuo-motor transformation that controls the animals' escape velocity (1). However, this was achieved using a combination of behavioral experiments made with a tracking ball device and intracellular recordings obtained from immobile animals on an electrophysiology setup, i.e., the behavioral and neuronal responses were obtained from different animals. In the last few years, we began to perform extracellular recordings while the crab is running on a treadmill device to record both neural and behavioral data simultaneously. Supporting our initial hypothesis, we found that both the initial response of the MLG2 and its' spontaneous firing rate are enough to anticipate the running speed and the time of escape of the animal. But we also show that after the stimuli stops moving the MLG2 activity is modulated by the animals running speed. This suggests that the MLG2 does not only rely on visual stimuli to control the animal's velocity but can integrate proprioceptive information as well.

(1) Oliva & Tomsic, JEB (2016).

02 | Aging disrupts clock and epigenetic factors circadian rhythms and makes rhythmic the clock-controlled expression of DNA repair enzymes. Effects of a caloric restricted diet.

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Disruption of circadian rhythms and alterations in the DNA repair systems, constitute part of the biological and molecular basis of motor and cognitive aging (Lacoste et al., 2017; Langie et al., 2017). Azis Sancar et al. (2015) reported that the DNA nucleotide excision repair is regulated by the cellular

clock. Given cerebellum is very susceptible to oxidative stress and DNA damage, we analyzed the aging consequences on the circadian regulation of the DNA base excision repair (BER) system and the daily profiles of BER-related epigenetic factors, in the cerebellum. We also evaluated the effect of caloric restriction (CR) and investigated the mechanism of Ogg1 and Ape1 circadian regulation. Three- and 22-mo-old rats treated or not with a 40% CR diet and maintained under constant darkness, were used in this study. We observed that BMAL1 protein, as well as Sirt1 and Dnmt1 expression display circadian rhythms($p<0.05$) in the cerebellum. Of note, Ogg1 and Ape1 expression is arrhythmic in this tissue. Aging disrupts clock and epigenetic factors circadian rhythms and makes rhythmic the BER enzymes expression. CR partially restored the temporal patterns. Transient transfection experiments showed that Ogg1 and Ape1 expression is regulated by the BMAL1:CLOCK transcription factor. We expect our results contribute to the understanding of the circadian regulation of the DNA BER system and how nonpharmacological strategies could improve aging- related circadian decline in the cerebellum.

03 | Noradrenergic Mediated Brain State Switch.

EMILIANO MARACHLIAN

The environment is complex and continuously changing whereby brains need to be able to adapt and quickly shift between resting, working or arousal states in order to allow adaptative behaviors. These global state shifts are intimately linked to the brain-wide release of the neuromodulators. Although the neurons that release neuromodulators generally have projections throughout the whole brain, there are only studies showing neuromodulators effects in specific functions and/or specific brain areas and still remains unclear what is the effect in the whole brain dynamics and how neuromodulators affect the information flow and computations in the entire brain.

In order to disentangle the specific circuit involved in the brain dynamic changes associated with noradrenaline release We used zebrafish larva as experimental model in combination with light-sheet microscopy. Whole-brain dynamics with single-neuron resolution was monitored while simultaneously recording free tail movement as a behavioral output. In addition optogenetic manipulation and cell type identification were performed.

Results show a noradrenergic neurons mediated switch in the brain state when animals perform a strong scape behavior. The switch is characterized by the shutting down of a vast majority of active neurons at the same time that the inactive neurons start up. The activation of neurons located in the Locus Coeruleus (LC) seem to trigger the switch. In addition we found that, when the switch is spontaneous, before the LC activation there is a ramping activity in a neuronal subpopulation located in another noradrinergic area, the NE-MO. I will present a characterization of the brain dynamic before and after the shift (by using spontaneous, stimuli and optogenetically triggered events) together with a components, role and dynamics description of the noradrenergic neuronal circuit involved in the brain state and behavior switch..

04 | Retinal alterations induced by choroidal neovascularization are reduced in p75NTR KO mice.

Subirada, PV1; Tovo, A2; Vaglienti, MV2; Vicentin D3; Ribotta NA3; Luna Pinto, JD3; Sánchez, MC2; Anastasía, A1; Barcelona, PF2.

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

Purpose: Age related macular degeneration (AMD) is one of the leading causes of blindness in adults over 60 years. In wet AMD, abnormal vascular tufts (termed choroidal neovascularization, CNV) invade the retina inducing photoreceptor degeneration. The p75 neurotrophin receptor (p75NTR) is involved in the transduction of neuronal death signals and it also participates in vascular changes. Here, we aim to determine the p75NTR role during retinal neurodegeneration in a mouse model of CNV.

Methods: 2-months old WT and p75NTR KO mice were injured in the retina using a photocoagulation laser. Mice with sham procedure were used as controls. 7 days after laser, mice were sacrificed. Retinas and retinal pigmented epithelium (RPE)-Choroid were processed separately.

Results: Western blot of neural retinas showed increased expression of p75NTR after the laser in CNV mice respect to control. Confocal images evidenced expression of p75NTR in Muller glial cells but not in pericytes, neurons nor in choroidal vessels. p75NTR KO mice with CNV showed decreased GFAP protein levels, reduced number of pycnotic nuclei, decreased TNFα mRNA, lower percentage of mononuclear phagocytic cells (MPCs) infiltrated and partial preservation of the retinal functionality, respect to WT CNV mice. The neovascular area was reduced in p75NTR KO CNV mice, although no changes in VEGF levels were detected.

Conclusions: Our results suggest that p75NTR is involved in retinal and vascular alterations in the CNV mice.

05 | Pharmacological modulation of the circadian clock as a novel strategy to treat glioblastoma.

WAGNER Paula M1,2, GUIDO Mario E1,2

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The circadian timekeeping regulates diverse cellular processes in organs, tissues, and even in individual cells, including tumor cells. Nowadays, it is known that the cellular clock is composed of the transcripcional machine and the metabolic/cytosolic oscillator which work together to maintain the cellular homeostasis. However, habits of the modern life have severely altered the cellular temporal organization and can cause an increased risk of cancer. In particular, glioblastoma (GBM) is the most common and aggressive type of brain tumor of the central nervous system. Due to its great resistance to conventional therapies, it is necessary new chemotherapeutic approaches considering the impact of the circadian clock on tumor biology (review in Wagner et al 2021). Previous results evidenced a strong interaction between the metabolic oscillator and the transcriptional machinery in T98G cells (Wagner et al 2018). Here, we investigate how the metabolic/cytosolic oscillator modulation can be used as a novel strategy for GBM treatment using a selective pharmacological inhibitor of glycogen synthase kinase 3β (CHIR99021). The results showed a cytotoxic effect, a delayed wound closure, alterations on lipid droplets oscillations and redox state in CHIR-treated cells compared to control cells. Understanding and delving into tumor regulation from a chronobiological viewpoint will further help to design new treatments that maximize therapeutic benefits.

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J. Mol. Sci. 2021, Vol. 22, Page 8289 22, 8289

06 | Machine Learning for modeling of cortical visual processing

Dr. Rodrigo Echeveste

Abstract: Employing tools from machine learning for modeling in computational neuroscience is an area of great expansion in recent years, and has become mutually beneficial for both fields. One of the central ideas behind this approach is that by optimizing artificial neural networks under biological constraints for tasks which are relevant for the brain, it is possible to find models that imitate different aspects of visual cortical processing. Deep convolutional neural networks (DNNs) were originally inspired by visual sensory processing, and are currently the best predictors of mean responses in multiple areas of the cortex. However, these models are not designed to faithfully represent the uncertainty of their predictions, which is central in the context of perception, where the information we receive from our senses is always noisy and incomplete. Moreover, these models lack dynamics, and do not capture the huge variability in cortical responses both over time and trials.

In this talk I'll first give a short overview of the state of the art in ML methods based on DNNs as models of cortical visual processing, to then focus on models which incorporate recurrent connections to go beyond mean responses and capture stereotypical features of cortical dynamics, such as transients and oscillations. Finally I'll show an example of how these types of models can be used to bridge current knowledge between physiology and perception in disorders such as autism.

07 | Error minimization for path integration through place-grid cells dynamic coupling

Jose A. Fernandez-Leon1,2,3,*, Ahmet K. Uysal1, Daoyun Ji1

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Keywords: place cells; grid cells; continuous attractor model; path integration; dynamics

Abstract: Grid cells (GCs) in the medial entorhinal cortex (MEC) use speed and direction to map the environment during spatial navigation. Hippocampal place cells (PCs) encode place and seem to minimize the accumulated error of GCs for path integration. However, the dynamic relationship between both cell types and the involved mechanism for error minimization is yet to be understood. Recent theoretical studies have also suggested the possibility of a network of loops between the Hippocampus and MEC. The dynamical coupling between these cell types could coordinate the integration of velocity input to the GCs network and update the network's estimated position using PC network signals. A realistic toroidal topology model of GCs was implemented based on path integration to address this issue. Place cell-like neurons were modeled by defining their PFs through visual flow detection and proximity information during the animal's exploration of a squared arena. PFs appeared mostly during early exploration, helping to decrease the path integration error of GCs. Relatively slow-emergent PCs enabled anchoring signals for a precise GCs path integration. Consistent with experimental observations that place cells can retrieve spatial information from grid-like cells to create a more accurate spatial representation, the dynamic coupling between PCs and GCs may be one of the key components of the brain's navigational system.

Reference: https://www.nature.com/articles/s41598-022-25863-2

08 | Withdrawn

09 | Breathing alteration against hypoxia as a function of early ethanol exposure.

Macchione, AF 1-2

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Maternal ethanol (EtOH) intake during pregnancy and lactation is a highly frequent “social” behavior in Argentine, exposing fetus or neonates to moderate EtOH intoxication through the amniotic fluid and placenta. Early EtOH exposure triggers a spectrum of neurobehavioral dysfunctions affecting, also, the breathing response. In an animal model equivalent to the 3 rd trimester of the human gestation we explore the early ethanol exposure effects on the ventilatory responses in normoxic and hypoxic-air conditions. We also study central areas involved in breathing modulation as the solitary tract nucleus and the medullary raphe system. Our results show that a brief and early ethanol exposure alters both basal and hypoxia-induced breathing frequencies and apneas through modifications in the activation patterns of central areas of study. Actually, early ethanol exposure induces a basal breathing depression in normoxic conditions but, against a hypoxic challenge, ethanol triggers two consecutive altered events: first a lower hyperventilation rate during the hypoxic event itself and then, during the post-hypoxic period, ethanol elicit the emergency of an adaptive phenomenon, the ventilatory long-term facilitation. Alterations in the activation patterns in the NTS and raphe obscurus, and an increase in the 5HT levels in the medullary raphe nuclei (magnus, obscurus y pallidus) were observed as a function of different ways of early ethanol exposure.

Funding by MINCyT-Cba; FONCyT and SECyT-UNC.

10 | Towards Co-adaptive Learning for Motor Imagery Brain-Computer Interfaces.

Victoria Peterson – Instituto de Matemática Aplicada del Litoral, IMAL, FIQ-UNL, CONICET, Santa Fe, Argentina

Brain-computer interfaces (BCIs) can be thought of as co-adaptive systems, in which the user learns to control the computer while the computer learns to decode the user's brain activity. When used across multiple days, such as in motor imagery (MI) BCIs for rehabilitation, the recorded brain activity exhibits high variability. To enable adaptive and supportive machine learning systems for decoding the brain activity, we proposed an adaptation algorithm named BOTDA [1] that can avoid recalibration of the whole system across BCI sessions. Although the method showed promising results in offline experiments with real MI-BCI datasets, it remains to be determined whether its success depends on the subject's ability to perform the MI task or on the model's adaptive capabilities. Thus, we hypothesize that the adaptation based on BOTDA is successful only when: H1) the patterns provided by the user correspond to the mental task to be performed and H2) the calibration data used to train the decoding model is discriminative enough from the decoding system's viewpoint. Results from realistic simulations suggest that BOTDA could be a valuable tool for developing co-adaptive MI-BCI systems.

Reference

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ORAL COMMUNICATIONS

CO-1-Microcine | Staurosporine treatment in hiPSC-derived motor neurons produce gaps in the spectrin lattice of axons.

Cellular and Molecular Neurobiology

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The membrane-associated periodic skeleton (MPS) is a protein structure of actin “rings” located transversely to the axon and separated every 190 nm by “spacers” of α/β-spectrin tetramers. In mature neurons, the MPS is organized along almost the entire axonal shaft that correlates with βII-spectrin’s homogenous distribution. During the maturation of human induced Pluripotent Stem Cells (hiPSCs) in culture, we observed an intriguing interruption in the otherwise uniform distribution of βII-spectrin along axons, referred to as βII-spectrin gaps (βIIs-gaps). These appear as stretches devoid of βII-spectrin. To determine if βIIs-gaps are associated with axonal constriction or loss, phase contrast and co-immunofluorescence analysis against various cytoskeletal and membrane proteins demonstrated that the lack of βII-spectrin is specific and that the axon shows no changes in those areas. Consequently, we subjected 2-week-old cultures to acute stress using sub-lethal doses of staurosporine, arsenite and L-glutamate. Remarkably, a significant increase in the occurrence of axons with βIIs-gaps under staurosporine treatment was observed. STED microscopy of βII-spectrin showed that the MPS is unaffected outside of the βIIs-gaps. Staurosporine was also found to induce βIIs-gaps in dorsal root ganglion neurons, but not in hippocampal neurons, derived from mouse embryos. We believe the study of βIIs-gaps will provide valuable insights into the formation and dynamics of the MPS in axons.

CO-2-Microcine | Characterizing multiple states of neuronal development in the adult hippocampus using single-nuclei RNA-seq

Cellular and Molecular Neurobiology

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Adult hippocampal neurogenesis plays a critical role in spatial memory formation, context discrimination, and clearance of memory traces. In the mouse dentate gyrus, the maturation of adult-born granule cells lasts several weeks and can be divided in 4 phases based on electrophysiological and morphological features. However, the molecular mechanisms underlying the progression through those discrete phases are still unknown. We have proposed that maturation is driven by sequential changes in the gene expression program, and should be revealed by transcriptome analysis. We thus set up an approach for high-throughput single-nuclei RNA sequencing applying Chromium 10X Genomics technology to interrogate the transcriptomic profile of new granule cells at different ages. We used Ascl1CreERT2;CAGfloxStopSun1sfGFP mice to allow conditional expression of Sun-1/sfGFP in the nuclear membrane of developing granule cells at identified ages and isolate fluorescent nuclei using FACS. Clusterization of two separate datasets identified multiple partitions that define a pathway from radial glia-like cells to mature neurons. Several clusters represent intermediate stages of maturation that were previously unknown. The emergence of novel transcriptional markers for the intermediate states was validated by in situ hybridization using RNAscope. These results are beginning to reveal key players involved in neuronal maturation and function with high temporal resolution.

CO-3-Microcine | Study of ghrelin transport in hypothalamic tanycytes and their possible involvement in ghrelin CSF clearance

Neuroendocrinology and Neuroimmunology

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Hypothalamic tanycytes are polarized ependymoglial cells that line the ventral part of the third ventricle (V3) and emit processes through the hypothalamic parenchyma and median eminence contacting blood vessels, neurons and other glial cells. We recently described that tanycytes internalize the orexigenic hormone ghrelin trough clathrin-mediated endocytosis. Here, we study its uptake and transport direction in these cells with a fluorescent ghrelin tracer (Fr-ghr) using in vivo, ex vivo and in vitro strategies.

First, we centrally injected mice with Fr-ghr and observed a fluorescent signal in tanycytes 15 min post-injection that was reduced by 87% at 30 min and returned to control values at 60 min. We then studied mouse hypothalamic explants incubated with Fr-ghrelin on their outer side (contacting terminals) or within the V3 (contacting soma), and observed fluorescence within tanycytes only in the second condition. Finally, we used primary cultures of rat hypothalamic tanycytes incubated with a 5-min pulse of Fr-ghr to quantify the intracellular redistribution of fluorescent signal over time. We observed that the signal was mostly found in somas after the 5 min pulse, and significantly increased in processes and terminals after 10 min. After 30 min, fluorescence decreased in the whole cell.

This evidence shows that tanycytes internalize ghrelin in their CSF-contacting soma and transport it to their terminals, possibly playing a role in CSF ghrelin clearance.

CO-4-Microcine | Streptozotocin induces behavioral changes and reactive astrocytes in a sex-dependent manner

Cognition, Behavior, and Memory

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Male rodents have been the default model organism in neuroscience research, including for the intracerebroventricular (icv) streptozotocin (STZ)-induced Alzheimer's disease (AD) model. Our objective was to compare the effect of icv-STZ injection in male and female rats with and without ovaries. Male rats were separated into control and STZ groups. Fourteen days before STZ injection, half of female rats were ovariectomized (OVX), or left with intact ovaries (Female group), and then separated into control or STZ groups on the same day as male rats. Two weeks later, behavioral tests were conducted for spatial memory (Barnes Maze) and depressive-like behavior (Forced swimming test). Immunofluorescence analyses were performed in the hippocampus. STZ affected spatial memory and increased depressive behavior in male, but not in female rats. We assessed GFAP expression and JAK2/STAT3 signaling activation, and we found sex differences on astrocyte reaction to STZ, with astrocyte reactivity evidence only in male rats. Also, STZ induced synapse loss in male rats, although it did not affect the expression of astrocyte proteins relevant for synapses, independent of the sex. We conclude that STZ affected differentially male and female rats, and OVX did not render the rats more vulnerable to STZ. Therefore, experimental design changes should be considered in order to set up a female sporadic AD model, and sex differences in the icv-STZ model should be addressed and further studied.

CO-5-Microcine | Postnatal GABA shift in the piriform cortex may support the ability of home-nest odor discrimination in infant rats

Development

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Background: In rat pups, home odor preference is present at postnatal day (P) 5; however, the ability to discriminate home nest odors from other nests appears on P10. The developmental shift in GABA signaling in the piriform cortex (PCX) could be a possible explanation at the neuronal level for why P10 pups discriminate their nest odor from other similar nests but not younger pups.

Methods: To test this hypothesis, we used a computational model of the PCx for rat pups constructed with our experimental data, including data from P5 and P10 PCx GABA synaptic input profile, then simulated the home-odor processing discrimination. During both periods, we also studied the expression of the KCC2 chloride extruder in the PCX using RT-qPCR and Western blotting.

Results: The results show that the number of active neurons and evoked spikes in response to two highly similar odors were higher than for the other nest in the P10 circuit, but this comparison was identical in the P5 circuit, suggesting discrimination odor ability in the P10 circuit but not in P5. Moreover, gene and protein expression of KCC2 was significantly upregulated in P10 compared to P5, suggesting a shift of GABAergic transmission from depolarizing to hyperpolarizing.

Conclusions: Our results support the idea that the ability to discriminate between closely associated nest odors in P10 rat pups may be attributed to the developmental shift in GABAergic signaling in the PCx between P5 and P10.

CO-6-Auditorio | Beyond Neurons: Glial Contribution to Circadian Structural Plasticity in D. Melanogaster

Chronobiology

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The small lateral ventral neurons (s-LNvs) are a core pacemaker in the D. melanogaster circadian network. They rhythmically release the neuropeptide Pigment Dispersing Factor (PDF), acting as a synchronizer for the rest of the clock. In phase with the rhythm of PDF levels, s-LNvs dorsal termini adopt different structures during the day. This property, named circadian structural plasticity, relies on a functional glial clock; but the nature of this reliance is unknown. In this work, we delve into this interaction .

Using GFP reconstitution assays, we found that s-LNvs termini contact two glial subtypes in a circadian manner: astrocytes and ensheathing glia (EG). Then, we found that short-term adult-specific blockage of gliotransmission in either cell type dampens structural remodelling without affecting PDF neuropeptide levels: even a 12 hours silencing of the astrocytes compromises neuronal remodeling .

Lastly, knocking down maverick (a ligand of the BMP pathway that may act as gliotransmitter) in astrocytes has a similar effect on the remodelling as blocking vesicle release; on the other hand, MAV KD has no effect when downregulated in the EG.

Our results suggest that glial subtypes contribute to shape neuronal terminals differently: while communication from both astrocytes and EG is important for structural remodeling, different gliotransmitters may be recruited to mediate this effect.

CO-7-Auditorio | REMEMBERING THE OPPONENT: NEURONAL ACTIVATION ASSOCIATED WITH SOCIAL MEMORY IN ZEBRAFISH

Cognition, Behavior, and Memory

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In male zebrafish, Danio rerio, we observed that there is a memory of an agonistic encounter against a particular opponent, which generates a behavioral modulation in successive encounters. This effect is prevented by treatment with an amnesic agent (MK-801) after the first encounter. Evaluating the neuronal activation through C-fos protein quantification in thelencephalic nuclei, significant differences were found between the fish with social interaction and the control group (isolated fish without interaction), showing greater neuronal activation in the ventral nucleus of the ventral telencephalic region (Vv) when the individuals had social interaction. The same trend was observed in the dorsal nucleus of the ventral region (Vd) and in the medial nucleus of the dorsal region (Dm). In the lateral nucleus of the dorsal telencephalic area (Dl), a greater activation was observed in fish previously exposed to MK-801 (they interact against an opponent of which they would have no memory) than in fish treated with water (they interact with an opponent of which they would have memory). We also found differences in the correlation between nuclei (Vv,Vd,Dm,Dl) for each treatment (water, MK-801 and control group), evaluating not only the activation of each nucleus but also the interaction between them. Finally, we did not observe a clear relationship between the levels of aggressiveness shown by individuals and neuronal activation.

CO-8-Auditorio | Self-supervised learning approach for inter-subject transfer learning in motor imagery brain-computer interfaces

Theoretical and Computational Neuroscience

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Reducing calibration time is crucial for enhancing the usability of brain-computer interfaces based on motor imagery. Due to the high inter-user variability of electroencephalography (EEG) signals, a user traditionally has to endure long and tedious calibration sessions to collect enough personalized training data before using the system. This need has become even more evident with the advent of deep learning decoding models, whose performance strongly depends on the volume of data available for training. Inter-user transfer learning, where other users' data is used to train the model, reduces the required amount of personalized training data. In this context, self-supervised learning strategies can be used to pretrain the first stages of the model on a pretext task and then adapt it to the task of interest through fine-tuning with a few data from the target user.

Here, we propose a self-supervised learning approach based on a fully convolutional encoder-decoder network. The reconstruction of EEG segments of a channel is used as the pretext task. Then an ensemble of the pre-trained encoders per EEG channel, followed by a classification block, conforms the final decoding model. This model is fine-tuned with a small dataset of the target user in the final MI-classification task.

CO-9-Auditorio | Replay of respiratory song patterns during adult canaries night sleep

Sensory and Motor Systems

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Activation of circuits in the forebrain during sleep has been linked to the consolidation of memories, including motor memories. However, the specific motor patterns reproduced during sleep remain largely elusive in any system. Single-cell measurements in these brain areas in songbirds have not allowed the detection of specific song patterns and a precise study of variants not observed during daytime performance. It has recently been discovered that in zebra finches this activity can be detected in the muscles of the vocal organ. Interestingly, this activity was not simultaneous with song-like respiratory events, which were thought to be inhibited. In this work we show that domestic canaries (Serinus canaria) exhibit spontaneous song-like activity in respiratory muscles and in air sac pressure fluctuations. These events are frequent predominantly towards the end of the night, shorter than daytime vocalizations but with similar rhythmic patterns. We find that the syllable sequences observed during the night deviate from the most probable sequences during daytime vocalizations. More generally, this result contributes to a program aimed at quantitatively studying dreamt complex motor patterns.

CO-10-Auditorio | Chronic variable stress reduces the availability of neural precursors in the rat hippocampal dentate gyrus

Neuroendocrinology and Neuroimmunology

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Exposure to adverse life events can contribute to the development of depression. The dentate gyrus (DG) of the hippocampus, known for its remarkable plasticity through neurogenesis, is one of the regions sensitive to such alterations. Hypotheses like match/mismatch attempt to elucidate how the relationship between early-life experiences and later adulthood plays a crucial role in stress coping strategies. In this study, we aimed to investigate the impact of early maternal separation (SMT) and chronic variable stress (CVS), both individually and combined, on the neural precursor population. Male rats underwent 4.5 hours of SMT between postnatal days 1 to 21. Subsequently, between postnatal days 50 to 74, the rats were exposed to a CVS protocol and concurrently treated with either the antidepressant Tianeptine (TIA) at 10 mg/kg or vehicle. The number of neural precursors in the subgranular zone of the DG was quantified using immunohistochemistry targeting SOX2 and confocal microscopy. Our findings revealed that only CVS exposure led to a significant 46% reduction in the neural precursor cell population. Furthermore, this impact was morphologically distinct, with the supra-pyramidal zone being the most affected. Interestingly, TIA was effective in restoring the number of neural precursors to control levels only in the infrapyramidal zone. Collectively, our results cannot be explained by the match/mismatch hypothesis, suggesting that alternative hypotheses must be considered.

POSTER SESSION 1 - Odd numbers

001 | Reduced expression of GluN2A induces a delay in neuron maturation in primary neuronal cultures

Cellular and Molecular Neurobiology

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NMDA receptors (NMDARs) play an important role in synaptic plasticity both in physiological and pathological conditions. GluN2A and GluN2B are the most expressed NMDAR regulatory subunits, in the hippocampus and other cognitive-related brain structures. GluN2B is characteristic of immature structures and GluN2A of mature ones. Changes in GluN2A expression were associated with complex phenotypes that led to complex neurodevelopmental disorders, including the occurrence of seizures. However, little is known about the role of GluN2A in these phenotypes. In this work, we reduced GluN2A expression in mature neuronal cultures and observed an altered GluN2A/GluN2B ratio. Furthermore, those neurons exhibit an increase in immature dendritic spines and dendritic branching, as well as increased response to glutamate stimulus. This phenotype (considering GluN2A/GluN2B ratio, index branching and glutamate response) resembles those observed at immature neuronal stages in vitro. This immature phenotype led to a higher response to glutamate stimulus which, in vivo, would be the basis of reduced threshold for seizure-onset in GluN2A-pathological conditions.

003 | THE INFLUENCE OF VAL66MET POLYMORPHISM IN THE BDNF GENE ON THE ANXIOLYTIC EFFECTS OF PHYSICAL EXERCISE

Cellular and Molecular Neurobiology

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Numerous studies have underlined the favorable impact of physical exercise (PE) on mental well-being, particularly its association with increased neurogenesis in the hippocampus. One major proposed mechanism involves elevation of brain-derived neurotrophic factor (BDNF). There is substantial divergence in individual responses to EF associated with genetic variations. Within the BDNF gene, a single nucleotide polymorphism, present in approximately one quarter of the world's population, results in the substitution of a valine for a methionine at position 66 (Val66Met) in the BDNF prodomain. People harboring this SNP exhibit increased susceptibility to psychiatric conditions. Our study sought to assess the impact of PE on anxiety-related behaviors in knock-in mice harboring the human Val66Met SNP. These mice reflect the phenotypic attributes of humans with this polymorphism. The experiment encompassed six experimental groups: wild-type BDNFVal/Val homozygotes, BDNFVal/Met heterozygotes, and BDNFVal/Met homozygotes, with each genotype subjected to exercise or sedentary conditions. The exercised groups participated in a treadmill at a speed of 15 m/min for 30 minutes per day, five days per week for three weeks. Preliminary findings indicate that in mice carrying at least one Met allele, PE does not mitigate certain anxiety-related phenotypes. This research aims to refine our understanding of PE as an anxiolytic agent in individuals carrying Met alleles.

005 | Sexually Dimorphic Behavioral Responses and Synaptic Plasticity Elicited by Amphetamine Administration

Cellular and Molecular Neurobiology

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Drug addiction is a chronic brain disorder triggered by repeated exposure to drugs. There is increasing evidence for sex differences in many aspects of drug addiction including vulnerability, withdrawal and treatment outcome. Behavioral sensitization, characterized by a progressive and persistent increase of specific behaviors following repetitive drug exposure, has garnered attention. Also, neuroadaptive responses underlying drug abuse would involve synaptic plasticity, a mechanism regulated by sex steroids. Given this, we aimed to study sex differences in behavioral sensitization and neuronal plasticity associated with Amphetamine (Amph) exposure.To address this, male and female thy-1 eGFP mice of 21 and 33 days (PN) were treated with Amph or vehicle and the locomotion was recorded. After 1 day of withdrawal, subjects were challenged with the same administration protocol to evaluate sensitization. Brain samples were collected four hours after the last Amph exposure to analyze dendritic spines of hippocampal pyramidal neurons. We observed that acute Amph induced greater hyperlocomotion in females than in males at PN21. Behavioral sensitization was observed in females at PN23 and in males at PN35, highlighting differences across sexes at both ages studied. Also, acute exposure to Amph increased the number of stubby spines in males at PN23. These results provide insight into the sexual dimorphism in behavioral responses and synaptic plasticity associated with Amph exposure.

007 | Variant Y39E of alpha-synuclein: Structural insights and aggregation properties

Cellular and Molecular Neurobiology

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Altered protein aggregation and accumulation is associated with different neurodegenerative diseases such as Creutzfeldt-Jakob's, Alzheimer or Parkinson disease (PD). The latter is classified as synucleinopathy, which is characterized by the abnormal aggregation and accumulation of α-synuclein (αSyn), forming oligomers and fibrils. Less is known about the toxic species of αSyn aggregates. However, with regards to its aggregation it has been discovered that next to the central non-amyloid β-component region (NAC) of αSyn further N-terminal regions are crucial. One of these regions expands over residues 36-42, whose elimination prevents protein aggregation. Y39 is located within this region and was found to be phosphorylated in advanced stages of PD. The mutation Y39E imitates this phosphorylation and allows to study its impact on protein aggregation and toxicity. Using biophysical methods such as NMR and circular dichroism amongst others we found that the Y39E αSyn variant has a different aggregation profile compared to the wild-type species. NMR studies revealed that that the structural features of Y39E αSyn, at a monomeric level, does not differ significantly from WT αSyn, thus changes in aggregation from the transition of monomers into oligomers and/or fibrils are likely due the loss of function of Tyr at position 39 of the protein. Results focused on membrane binding and toxicity in cell and animal models for αSyn aggregation validate the measurements performed in vitro.

009 | EXTRACELLULAR VESICLE DELIVERY TO RELIEVE THE EFFECTS OF CHRONIC STRESS

Cellular and Molecular Neurobiology

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Mental disorders affect one billion people worldwide. One of their causal agents is chronic stress, which produces a glucocorticoid hypersecretion that can cause mood changes. The serum of stressed individuals contains proteins related to mental diseases, several of them transported by extracellular vesicles (EVs). Among them, M6a, a stress-sensitive neuronal protein whose expression is reduced in the hippocampus of stressed animals. Our aim was to study whether modulating M6a levels in EVs and their administration can alleviate some of the stressed-induced deleterious effects. Since large amounts of EVs are required, to obtain them without using large animal cohorts, we isolated EVs from the hippocampal cell line HT22. To modulate M6a levels we used two strategies: culture treatment with the synthetic glucocorticoid dexamethasone (DEX) or EVs loaded with a plasmid encoding M6a (M6a-EVs). Both treatments increased the M6a cellular levels with respect to the control. Also, after 24 h of intranasal M6a-EVs administration in naive (non-stressed) mice improved their performance in the forced swimming test. Since animals exposed to chronic stress exhibit changes similar to those reported in human depressed patients, we will evaluate whether administration of VEs-M6a to animals exposed to chronic stress can alleviate some of the consequences of stress. Thus, in vitro obtained EVs loaded with molecules of interest could be used as a novel treatment for stress-induced disorders.

011 | Cellular and Molecular underpinnings of Sleep Homeostasis: DNA damage as sleep inductor in Drosophila

Cellular and Molecular Neurobiology

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Sleep is a conserved behavior across the animal kingdom; however, the biological purpose of sleep remains a mystery. The molecular and cellular mechanisms underlying the need for sleep are still poorly characterized. With the present project we will test the general hypothesis that DNA damage accumulates during wakefulness, and is preferentially repaired during sleep. This novel hypothesis arises from recently published work in zebrafish. We propose to study the potential universality of this striking mechanism, establishing whether these causal relationships also occur in insects. Using the experimental advantages offered by Drosophila melanogaster, we have developed a thermogenetic assay that demonstrates that neuronal activation promotes the need for sleep in flies, and is accompanied by DNA damage. At the molecular level, in fish it has been reported that the protein Parp1, which binds to DNA damage sites and participates in their repair, is necessary to promote sleep. Since the molecular components of the DNA damage response show high evolutionary conservation, we will test whether proteins involved in DNA repair mechanisms in Drosophila are also molecular components that regulate sleep homeostasis. Our experiments will shed light on the relationship of DNA repair and sleep homeostasis throughout evolution, and may lead to new interventions to treat sleep disorders, improve sleep efficiency and brain function.

013 | Synaptotagmin -7 overexpression modifies the dynamics of single exocytotic events in mice adrenal chromaffin cells

Cellular and Molecular Neurobiology

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Synaptotagmins are major Ca2+ sensors that trigger vesicle-to-plasma-membrane fusion. Different synaptotagmin isoforms exert characteristic effects on the rate and extent of exocytosis, and modulates the content release through their effects on fusion dynamics. Although there are at least 17 Syt isoforms, chromaffin cells express only two: synaptotagmin-1 (Syt-1) and synaptotagmin-7 (Syt-7) (Proc Natl Acad Sci USA 105, 3998–4003, 2008). In this work, we analyzed the effect of Syt-1 and Syt-7 overexpression on the dynamics of dense core vesicle fusion, measured by carbon fiber amperometry, in primary cultures of mice chromaffin cells. We found that the overexpression of any of these isoforms does not affect the frequency of exocytotic events, the relative frequencies of pre-spike or stand-alone-feet, or the amount of catecholamines released from a single vesicle. However, Syt-7 does affect some parameters associated to fusion kinetics. In particular, the overexpression of Syt-7 decreased significantly the amplitude of amperometric spikes; and in addition we observed an increase tendency in the half-width, (t1/2), that reflects the duration of the individual exocytotic events, and in the spike rising time. Finally, Syt-7 reduced the duration of pre-spike and stand-alone feet, but did not affect their amplitudes. These results suggest that Syt-7 destabilizes the initial fusion pore and slows down the final fusion pore expansion.

015 | Role of Rho GTPase RhoD in neuronal development

Cellular and Molecular Neurobiology

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Rho GTPases are small signaling proteins of the RAS superfamily. One of the less studied members of this family is RhoD, the only Rho GTPase to be expressed exclusively in mammals. RhoD has the particularity of having increased intrinsic GDP/GTP exchange activity. Available data suggest RhoD plays an important role in the organization and regulation of actin cytoskeleton dynamics and Golgi apparatus homeostasis. Although information about the activity, regulation and function of this protein in neuronal cell biology is limited, results of our lab propose an important role of RhoD at least in neuronal differentiation. Based on the above, the aim of this study is to obtain new data of RhoD activity and function in neuronal polarity and development. In order to study spatio-temporal activation patterns of RhoD activity, we develop and characterize a FRET-based biosensor that will be used in our neuronal systems. Furthermore, the down-regulation of endogenous RhoD by an shRNAi generated in our lab, alters neuritic outgrowth and development in cultured 2 and 10 d.i.v. hippocampal neurons. As well, RhoD negative mutant expressions decreased neuronal complexity. Moreover, using plasma membrane protein engineered with reversible aggregation domains, we observe that expression of RhoD negative mutant delays the anterograde trafficking of post-Golgi plasma membrane protein carriers. These data suggest RhoD plays an important role during neuronal differentiation and neuritic outgrowth.

017 | Molecular transitions that control functional development during adult neurogenesis

Cellular and Molecular Neurobiology

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The dentate gyrus (DG) of the hippocampus generates adult-born granule cells (abGCs) throughout life, which are then integrated into pre-established neural circuits, adding plasticity to the network. abGCs require over 8 weeks to reach a mature phenotype and the process can be divided in 4 phases, according to morphological and electrophysiological features. Although developing abGC properties are highly described, the molecular mechanisms underlying the process are still unknown. We proposed that adult neurogenesis is controlled by specific transcriptional regulators and effectors that guide the transitions between stages. To unravel these molecular bases, we studied the transcriptomic profile developing abGCs (see poster by Rasetto et al). Based on a preliminary database containing 2-week-old GCs, we selected effector molecules expressed in immature GCs and evaluated their role during GCs development by functional knock out. We are currently analyzing how different candidate molecules downregulated by CRISPR/Cas9 or shRNAs in vivo affect growth and functional integration of developing abGCs. This approach will allow us to study the role of upstream master genes that regulate adult neurogenesis maturation.

019 | MOLECULAR AND STRUCTURAL MODULATORS OF ALPHA-SYNUCLEIN AGGREGATION AND MEMBRANE INTERACTIONS

Cellular and Molecular Neurobiology

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Aberrant fibrillar aggregation of the protein α-synuclein (αS) is associated with Parkinson's disease. Recently, studies have shown that molecular events related to the physiological and pathological roles of αS might be regulated by specific sequence motifs or even by a single residue. In this work, we have investigated structural details of the role of the Y39 residue in the context of aggregation and lipid binding properties by studying the wild-type protein (wt αS) and its site-directed mutants Y39F, Y39L, and Y39A. We found that the Y39F mutant exhibited a similar aggregation profile compared with wt αS, whereas the species containing the Y39L and Y39A mutations showed a significant decrease in the rate and amount of aggregated protein. H4 cellular model and animal model of C. elegans for αS aggregation validated the measurements performed in vitro. Furthermore, using NMR and circular dichroism, clear structural differences were observed between the vesicle-bound forms of the αS variants at the aggregation-prone hydrophobic domain (NAC). In light of our results, we conclude that the removal of aromatic residues at position 39 impairs the amyloid fibril formation of αS and the aromaticity at position 39 determines the membrane-bound conformation of αS by modulating lipid interactions involving the central hydrophobic NAC domain. Overall, our results shed light on the mechanistic basis behind aggregation, membrane damage, and cellular toxicity in amyloid diseases.

021 | Early response of immune myeloid cells after olfactory nerve damage

Cellular and Molecular Neurobiology

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The olfactory nerve regenerates efficiently. After damage to sensory neurons, increased proliferation of stem cells is observed in the olfactory epithelium, which restores the neuronal population in about two months. Besides neuronal axons, the olfactory nerve is populated by immune myeloid cells, which proliferate and get reactive after damage to the nerve, and olfactory ensheathing cells, which are recognized for their neurotrophic properties. We propose that the mechanisms involved in the reparative capacity of the olfactory nerve involve an early response of immune cells that interact with olfactory ensheathing cells. In this study, we began to evaluate the morphological changes of immune myeloid cells at early stages of the nerve repair process after damage, following administration of an olfatototoxin (methimazole). Preliminary results after Sholl analysis of cells immunostained for Iba1 (Ionized calcium-binding adaptor molecule 1) in the olfactory bulb of methimazole-treated mice show reduced cell complexity in this group, particularly on days 2 and 3 post-injury, which is compatible with a reactive microglia phenotype early after damage. Together with measures of cell reactivity markers and a pharmacological approach to selectively eliminate immune myeloid cells, these experiments will contribute to determining whether these cells trigger responses in olfactory ensheathing cells and/or modulate the repair process.

023 + CO-1-Microcine | Staurosporine treatment in hiPSC-derived motor neurons produce gaps in the spectrin lattice of axons

Cellular and Molecular Neurobiology

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The membrane-associated periodic skeleton (MPS) is a protein structure of actin "rings" located transversely to the axon and separated every 190 nm by "spacers" of α/β-spectrin tetramers. In mature neurons, the MPS is organized along almost the entire axonal shaft that correlates with βII-spectrin's homogenous distribution. During the maturation of human induced Pluripotent Stem Cells (hiPSCs) in culture, we observed an intriguing interruption in the otherwise uniform distribution of βII-spectrin along axons, referred to as βII-spectrin gaps (βIIs-gaps). These appear as stretches devoid of βII-spectrin. To determine if βIIs-gaps are associated with axonal constriction or loss, phase contrast and co-immunofluorescence analysis against various cytoskeletal and membrane proteins demonstrated that the lack of βII-spectrin is specific and that the axon shows no changes in those areas. Consequently, we subjected 2-week-old cultures to acute stress using sub-lethal doses of staurosporine, arsenite and L-glutamate. Remarkably, a significant increase in the occurrence of axons with βIIs-gaps under staurosporine treatment was observed. STED microscopy of βII-spectrin showed that the MPS is unaffected outside of the βIIs-gaps. Staurosporine was also found to induce βIIs-gaps in dorsal root ganglion neurons, but not in hippocampal neurons, derived from mouse embryos. We believe the study of βIIs-gaps will provide valuable insights into the formation and dynamics of the MPS in axons.

025 | Understanding pathological remodeling of reactive astrocytes: Epigenetically-controled downregulation of homeostatic genes

Cellular and Molecular Neurobiology

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Astrocytes support neurons metabolically via nutrients, ionic balance, water regulation, neurotransmitter recycling, antioxidants, and the blood-brain barrier. After brain damage, some reactive astrocytes become pro-neurodegenerative, showing inflammation, and dropping their normal roles. We studied epigenetic impacts on homeostatic genes in these reactive astrocytes. Astrocytic cultures were exposed to LPS (25 ng/ml) or HMGB1 (500 ng/ml) for 18 hours, followed by recovery periods of 24, 72 hours, and 7 days. This exposure prompted reactive astrogliosis, evident through GFAP staining, morphological changes, and heightened IL-1B and IL-6 expression via qPCR. Remarkably, acute exposure resulted in enduring astroglial DNA hypermethylation and reduced expression of homeostatic genes (LDHA, glutamine synthase, Kcnj10, Slc16a1, Aqp4). Notably, the key DNA methylation regulator, MAFG-1, along with DNMT1 and DNMT3a, were also upregulated. Reduced homeostatic gene expression correlated with heightened promoter CG island methylation, observed through methylation-sensitive PCR 72 hours after LPS or HMGB1 exposure. Treating cells exposed to LPS or HMGB1 with decitabine, an FDA-approved DNMT1 inhibitor, halted gene downregulation. In summary, our findings reveal that reactive astrocyte pathological remodeling leads to lasting suppression of homeostatic gene expression through critical CG island methylation in promoters. Notably, DNMT inhibitors like decitabine can mitigate this process.

027 | The glycoprotein GPM6a and the adhesion molecule ICAM5 enhance neuronal plasticity

Cellular and Molecular Neurobiology

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The molecular mechanisms of neuronal structural plasticity are not fully understood. In this regards, neuronal membrane glycoprotein M6a promotes neuronal plasticity through unclear mechanisms. Since the extracellular loops of GPM6a (ECs) command its function, previous results from our laboratory determined that the intercellular cellular adhesion molecule 5, ICAM5, co-immunoprecipitated with the ECs of GPM6a. Here, we aimed to study the possible functional association of GPM6a and ICAM5 in hippocampal culture neurons and cell lines. We found that ICAM5 colocalized in cis with GPM6a in neurons at 5 DIV and N2a cells. Moreover, hippocampal neurons and N2a cells co-expressing GPM6a/ICAM5 showed significantly higher filopodia number and neurite extension compared to neurons and N2a cells overexpressing GPM6a or ICAM5 alone. Moreover, ICAM5 rescued GPM6a-ECs mutant´s phenotype when both protein were coexpressed in neurons and N2a cells. Cell aggregation assays were performed in order to validate extracellular domains interaction between ICAM5-ectodomain and GPM6a-ECs in HEK293 cells. We found at 20 minutes a significant increase in double aggregates of GPM6a cells with ICAM5 cells compared to the control groups and GPM6a mutant. Taken together, we validate the association between GPM6a and ICAM5 probably through their extracellular domains. Furthermore, both proteins induce neuronal structural plasticity synergistically.

029 | Gamma audiovisual stimulation promotes integration of granule cells born in the aging hippocampus

Cellular and Molecular Neurobiology

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Non-invasive gamma audiovisual stimulation at 40 Hz can reduce levels of amyloid beta peptide and improve memory performance in several mouse models of Alzheimer's disease. However, the mechanisms that transduce light and sound stimulation ("flickering") into cellular and circuit changes remain elusive. Because neurogenesis in the aging hippocampus is particularly sensitive to behavioral stimuli, the effects of gamma flickering might be revealed by analyzing its impact on developing new neurons. Using light and sound pulses, we studied the impact of 40 Hz stimuli on the development of neurons born in the hippocampus of 8-month-old mice. Gamma flickering enhanced the 40 Hz component in dentate gyrus oscillations and boosted circuit remodeling as shown by the accelerated growth of the dendrites and mature electrophysiological features of newly generated neurons. These results reveal that audiovisual stimuli awaken mechanisms that promote neuronal plasticity not only under pathological conditions, but also in the healthy aging brain.

031 | Neuronal Glycoprotein GPM6a Promotes Neurite Outgrowth in Dorsal Root Ganglion (DRG) Neurons

Cellular and Molecular Neurobiology

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The peripheral nervous system (PNS) has a unique capacity for functional recovery and self-repair after an injury. Both the intrinsic capacity of PNS neurons to re-initiate axon growth and the reprogramming features of PNS glial cells contribute to nerve regeneration. However, the complete molecular mechanism underlying PNS regeneration have not been elucidated yet. The membrane neuronal glycoprotein GPM6A is involved in neuronal development and structural plasticity in the CNS, and recent evidence suggests that GPM6a interacts with molecules from the PNS and could be expressed in DRG neurons. Here, we characterized the localization of the GPM6a protein using embryonic and adult DRG neuron cultures and immunohistochemistry of DRG explants. Our results show that GPM6a is localized in the surface of DRG neurons throughout development but not in Schwann cells. Furthermore, blocking GPM6a using a structural monoclonal anti-GPM6a antibody significantly decreased neurite outgrowth in dissociated DRG neuron cultures. Altogether, our results show for the first time that GPM6a is expressed in the PNS and participates in neurite extension. These new evidence suggests that GPM6a could contribute to axon regeneration in the PNS.

033 | Characterization of reactive astrocytes and peri-plaque astrocytes in an Alzheimer's Disease (AD) rat model

Cellular and Molecular Neurobiology

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Astrocytes are essential for the maintenance of the brain homeostasis. In AD it has been proposed that astrocytes may suffer an atrophy that reduces their ability to sustain neuronal metabolism and synaptic function. We here analyzed in detail the astroglial morphology, the expression of essential astroglial proteins glutamine synthase (GS) and aquaporin-4 (AQP4), the rate of neuronal survival and the presence of Aβ plaques in the brain cortex. Employing the McGill-R-Thy1-APP transgenic rat (Tg) model of AD at 7, 13, and 20 months of age, we compared heterozygous, homozygous and wild-type animals. We observed that plaques are present in homozygous animals at 13 and 20 months and GFAP+ reactive astrocytes are morphologically different at different distances of the plaque by Sholl analysis. Reactive astrogliosis was already observed in 7 months-old Tg animals, at the pre-plaque stage. At 13 months, a reduction in GS expression was evident in peri-plaque astrocytes, while distal astrocytes remained unaffected. The typical end-feet AQP4 expression was lost in peri-plaque astrocytes. The abundance of cortical neurons declines from 7 to 20 months in both wild type and Tg rats.

Our findings indicate that reactive astrogliosis precedes plaque formation and occurs in absence of significant neuronal loss. In addition, astrocytic homeostatic ability declines in the proximity to the plaques presenting atypical morphologies compared with distal astrocytes.

035 | INTERACTIONS BETWEEN ALUMINUM(III) IONS, αSyn AND A NEW N-ACYLHYDRAZONIC METALLOPHORE: IMPLICATIONS FOR THE TREATMENT OF ALUMINUM-ASSOCIATED PARKINSONISM

Cellular and Molecular Neurobiology

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α-synuclein (αSyn) is an intrinsically disordered protein that can interact with physiological metal ions, a process which contributes to the pathological mechanism underlying Parkinson's disease (PD). Exogenous metals have also been linked to PD through their action on protein aggregation and oxidative stress. Aluminum(III), in particular, constitutes a known neurotoxic agent. In addition to increase the production of reactive oxygen and nitrogen species, exposure to Al3+ also causes iron dyshomeostasis through amplified Fe3+/Fe2+ redox activity. In this context, the development of new drugs to preclude the accumulation of such metal ions is crucial to slowing down the progression of PD. In this work, we evaluated the interactions of αSyn and the ligand 2-hydroxy-3-methyl-benzaldehyde 3,4,5-trimethoxybenzoyl hydrazone (MTMP) with Al3+. Both binary and the ternary system were considered. The nature and affinity features of αSyn-metal complexation were described at a residue specific level of resolution, combined with studies focused on the metal sequestering potential of MTMP. Aggregation kinetics experiments correlated well with the αSyn-Al3+ interaction profile. Cell-based assays are currently underway to validate our findings in a cellular context and extend our studies to other experimental models of aluminum-related parkinsonism.

037 | Analysis of the activation of the unfolded protein response pathways in cellular models of TDP-43 proteinopathies

Cellular and Molecular Neurobiology

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The abnormal aggregation of TDP-43 into cytoplasmic inclusions in affected neurons is a pathological hallmark of a group of neurodegenerative diseases called TDP-43 proteinopathies, which include amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Recent evidence suggests that endoplasmic reticulum (ER) stress and the unfolded protein response (UPR) are important players in ALS/FTD aetiology. The accumulation of unfolded proteins in the ER induces three signaling cascades initiated by the transmembrane proteins IRE1, ATF6 and PERK. To study the role of the UPR in TDP-43-mediated pathogenesis we used HEK293 cells overexpressing wild-type, nuclear TDP-43 or a cytoplasmic form of TDP-43 which recapitulate key ALS/FTD features. Biochemical analysis of endogenous UPR components were performed to study the effects of TDP-43 dysregulation on UPR activity. Our Western Blot results using the ER stressor tunicamycin (Tn) show the activation of the UPR branches IRE1/xBP1 and PERK/ATF4. However, expression of TDP-43 variants does not significantly alter the activation of these UPR pathways under basal and Tn-induced conditions. We are currently performing immunocytochemistry experiments to analyze UPR activation combined with TDP-43 overexpression on a cell-by-cell fashion. Lastly, we also want to pursue these studies in neuroblastoma Neuro2a cells, which show neuronal-like features. These experiments will contribute to understand the role of UPR activation in ALS/FTD.

039 | Interplay Between Cytoskeletal Dynamics and Intracellular Trafficking Under the Effects of Alpha Synuclein

Cellular and Molecular Neurobiology

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Defects in intracellular trafficking have been described as a common mechanism in neurodegenerative diseases. One of the most studied proteins in relation to nervous system diseases is Alpha Synuclein (AS) protein. While it is known to be related to Parkinson's disease and synucleinopathies, the mechanisms by which this protein induces neurodegeneration remain unknown. In this study, we investigated the effects of the AS protein on intracellular trafficking. For this purpose, we used primary cultures of rat hippocampal neurons and a synchronization system of the exocytic pathway. Here, we demonstrate that the AS protein induces selectively defects in intracellular trafficking. We used two models to study the exocytic pathway, the p75NTR receptor, and the Transferrin receptor (TfR). Our results indicate that only the trafficking of the p75NTR receptor was altered, while that of TfR remained unchanged. Apparently, the mechanism by which AS affects intracellular trafficking is through the modification of the actin cytoskeleton, altering the fission from the Golgi of p75NTR vesicles, whose fission machinery requires Dynamin anchoring to actin filaments. Surprisingly, we managed to rescue the observed effect on intracellular trafficking using CofilinS3A. It is worth noting that this mutant Cofilin also managed to reverse the effects of AS on neuronal cytoarchitecture. The findings described here help to understand the mechanisms by which AS may be inducing neurodegeneration.

041 | Age-dependent and modality-specific changes in the phenotypic markers Nav1.8, ASIC3, P2X3 and TRPM8 in male rat primary sensory neurons during healthy aging

Cellular and Molecular Neurobiology

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Nav1.8, ASIC3, P2X3 and TRPM8 are phenotypic markers typically associated with nociception that are involved in chronic and pathological pain. Despite this, their impact on normal somatosensory perception in aged rats remains unexplored. We hypothesized that aging changes the expression and functions of these proteins in subpopulations of primary sensory neurons in the dorsal root ganglion (DRG). To test this, we combined immunohistochemistry, quantitative image analysis, Western blotting and IB4 and trkA to examine the expression levels and localization of the four nociceptive markers in different neuronal subpopulations of the DRG and cutaneous nerve terminals at ages ranging from 3 to 24 months in healthy male Wistar rats. We then used behavioral testing and in vivo pharmacological intervention to explore (a) responses to mechanical and cold stimuli and (b) whether antagonism of these proteins affects these behaviors at different ages. Geriatric rats had significantly decreased sensitivity to mechanical and cold stimuli than younger rats. In parallel, we observed differing changes in the expression of Nav1.8, ASIC3, P2X3 and TRPM8 in the DRG at different ages. Interestingly, we found that ASIC3 and P2X3 can alter normal mechanosensation and Nav1.8 and ASIC3 contribute to cold sensitivity. This is the first report detailing the changes in the expression pattern and function of Nav1.8, ASIC3, P2X3, and TRPM8 throughout aging in healthy male Wistar rats.

043-CO-2-Microcine | Characterizing multiple states of neuronal development in the adult hippocampus using single-nuclei RNA-seq

Cellular and Molecular Neurobiology

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Adult hippocampal neurogenesis plays a critical role in spatial memory formation, context discrimination, and clearance of memory traces. In the mouse dentate gyrus, the maturation of adult-born granule cells lasts several weeks and can be divided in 4 phases based on electrophysiological and morphological features. However, the molecular mechanisms underlying the progression through those discrete phases are still unknown. We have proposed that maturation is driven by sequential changes in the gene expression program, and should be revealed by transcriptome analysis. We thus set up an approach for high-throughput single-nuclei RNA sequencing applying Chromium 10X Genomics technology to interrogate the transcriptomic profile of new granule cells at different ages. We used Ascl1CreERT2;CAGfloxStopSun1sfGFP mice to allow conditional expression of Sun-1/sfGFP in the nuclear membrane of developing granule cells at identified ages and isolate fluorescent nuclei using FACS. Clusterization of two separate datasets identified multiple partitions that define a pathway from radial glia-like cells to mature neurons. Several clusters represent intermediate stages of maturation that were previously unknown. The emergence of novel transcriptional markers for the intermediate states was validated by in situ hybridization using RNAscope. These results are beginning to reveal key players involved in neuronal maturation and function with high temporal resolution.

045 | Etv5 is involved in the maturation of adult dentate gyrus newborn neurons.

Cellular and Molecular Neurobiology

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Generation of new neurons in adult mammals is restricted to discrete regions of the central nervous system, the subventricular zone (SVZ) of the lateral ventricles, and the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG). Adult neural stem cell population, known as radial glia cell like (RGLs), have self-renewal capacity which is highly controlled by different factors. These cells can generate intermediate progenitors that pass through several well characterized developmental stages before they become mature granular cells (GCs). Functional integration of these new neurons into the preexisting circuits requires dendrite and axonal growth, and synapse formation. Here, we show that the Pea3 transcription factor, Etv5, is expressed in the postmitotic cells, committed to the neuronal linage during hippocampal adult neurogenesis. We observed that ablation of Etv5 in adult-neuronal precursors results in a delay in GCs maturation, impairs the dendritic morphological development and spine dendrite maturation of adult-born neurons in vivo. In summary, our data, indicates that Etv5 plays a key role in the development and the plasticity of newly generated neurons.

047 | Harmful effects of Cadmium on the Substantia nigra

Cellular and Molecular Neurobiology

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Several studies have investigated the association between heavy metals, such as Cadmium (Cd), and neurological diseases, including Parkinson's disease. Cadmium is known to induce oxidative stress, neuronal apoptosis and damage to the neural pathways. We studied its toxic effects in the Substantia nigra. Two groups of Wistar rats were used; the control group received regular water, and the other group consumed drinking water with 15ppm of Cd for 60 days. Cryostat midbrain sections (15 µm thick) were stained with Nissl and Hoescht 33342 using standard histological procedures. The histological examination of the brain sections showed changes in the normal structure in the Cd-intoxicated rats. We observed an increase in apoptotic cells with irregular shapes and darkly stained and condensed nuclei. Cadmium may be recognized as an environmental factor involved in the etiopathogenesis of neurodegenerative diseases, however further studies are necessary to elucidate the specific mechanisms of Cd-induced neurotoxicity.

049 | Functional evidence of immature neurons in the adult human hippocampus

Cellular and Molecular Neurobiology

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The generation of new granule cells (GCs) in the hippocampus is a remarkable form of plasticity that occurs in most mammals. The existence of this process in the human hippocampus has been investigated combining different techniques such as DNA labeling with thymidine analogs or 14C incorporation and, more recently, high-quality immunofluorescence and single-nucleus RNA sequencing that provided evidence for the presence of immature GCs. Approaching adult human neurogenesis from several standpoints is key to fully understand this extraordinary form of structural plasticity. In order to uncover functional evidence of developing GCs, we have set up a protocol for ex vivo electrophysiology in hippocampal slices from patients suffering intractable refractory epilepsy that result in the resection of this structure. Whole cell recordings from GCs belonging to 5 young adult patients showed that most neurons in the granule cell layer exhibit mature features. However, bioinformatic analysis revealed a small cluster of neurons with depolarized membrane potential, high input resistance, and decreased number of spikes elicited by current injection. GCs that belonged to this cluster also displayed a low frequency of excitatory postsynaptic currents, suggesting poor connectivity with entorhinal cortex afferents. Further histological analysis of these samples will unveil whether these immature functional properties correlate with the presence of immature neuronal markers.

051 | Unraveling Circadian Control: How Food and Light Interactions Shapes Motivation Behavior in Female and Male Mice

Chronobiology

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Most living organisms possess a circadian timing system that has evolved to finely tune their daily interaction with the environment. In mammals, the main circadian clock is synchronized by the light-dark (LD) cycle. Nutrition also strongly influences circadian rhythms. Specifically, when food intake is limited to a few hours each day, it can become a strong synchronizer that triggers food anticipatory rhythms.
We have shown that motivation for food reward is regulated in a circadian manner in mice, peaking at night. This study aims to characterize how the rhythm in motivation is affected by misaligned food and light schedules. We exposed male and female C57Bl/6j mice to 4-hour time-restricted feeding during the light (TRF-D) or dark (TRF-N) phase of the LD cycle. Then, motivation was assessed using the Progressive Ratio task at three different time points. Nucleus Accumbens tissue was collected for mRNA analysis through bulk RNA-seq and single nuclei RNA-seq approaches.
In female and male TRF-N groups, where light and food schedules are aligned, the motivational state increased with fasting hours. Misaligned schedules triggered sex-specific responses. Male TRF-D mice exhibited a greater self-imposed caloric restriction, leading to increased motivational levels at all time points. Females displayed a unique 'double peak' motivational response. These findings advance understanding of circadian impact on motivation, aiming to aid psychiatric and substance abuse treatment.

053 | Is there a link between youth screen media use late at night, sleep-wake circadian rhythm changes in puberty and academic performance?

Chronobiology

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The increase in portable electronic devices and screen media habits late at night, used by young adolescents, is concerning the education community about the delaying sleep on set, the sleep deprivation and poor academic performance. This scientific article aims to analyze the sleep-wake circadian rhythm in teenagers and its relationship with emotional, cognitive, and overall health development. The article studies the changes in sleep-wake circadian rhythm during adolescence, the delay in sleep phase, the use of screens at night, and their association with academic performance and morning school schedule. The approach of chronobiology and chronopsychology is employed to understand how biological and social rhythms affects teenagers daily life. The importance of chronotypes and genetic variability in synchronizing rhythms with the light-dark cycle is emphasized. Additionally, the effects of “Social Jet Lag” in adolescents are discussed, and the relationship between puberty and changes in sleep-wake rhythm is explored. It becomes necessary to start promoting at school, sleep health habits looking for psychoeducate teenagers as a way to reduce sleep deprivation during the week, and all the risk in mental health associated, enhancing the academic performance.

Key Words: chronopsychology- adolescents- sleep deprivation – school schedule

055 | Central daily regulation of splenic macrophage clock: Role of norepinephrine

Chronobiology

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The suprachiasmatic nucleus (SCN) functions as the central clock in mammals, synchronizing endogenous cellular clocks with the day/night alternation. Splenic macrophages (MΦ) play pivotal roles in fundamental immune responses. However, a comprehensive understanding of the central circadian regulation of these cells remains elusive. The SCN and spleen communicate through the sympathetic nervous system (SNS), that release norepinephrine (NE) in regions housing MΦ. To elucidate NE's influence on the molecular clock regulation of spleen MΦ, a rat model of localized sympathetic denervation was developed using guanethidine. Rats received saline or guanethidine injections and were euthanized at 6 zeitgeber times (ZT) across a 24-hour cycle (ZT2, 6, 10, 14, 18, 22). Spleens were isolated for ex vivo cultures. BMAL1 and ACTIN protein levels were assessed in splenic adherent cells. Control rats' splenic MΦ displayed daily oscillations of BMAL1, with a peak occurring at the midpoint of the light period. Remarkably, ex vivo splenic MΦ from the guanethidine-treated animals showed a loss of the 24-hour BMAL1 oscillation and significantly lower levels, compared to controls. Both control and sympathectomized rats displayed daily Rev-Erbα expression rhythms. However, guanethidine administration induced a phase delay and increased expression of Rev-Erbα. These findings underscore the SCN-mediated regulation of the molecular clock in splenic adherent cells through the NE sympathetic pathway.

057 | EFFECT OF AN I.C.V. INJECTION OF AGREGATED BETA-AMYLOID (1-42) ON THE TEMPORAL ORGANIZATION OF THE AMYLOIDOGENIC PATHWAY IN RAT HIPPOCAMPUS

Chronobiology

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Alzheimer's disease(AD) is a neurodegenerative disorder causes dementia in the elderly. The accumulation of Aβ in the brain plays a key role in the pathogenesis of AD. In the amyloidogenic pathway, Aβ generation is mediated by amyloid precursor protein processing that is subsequently proteolysis by β/γ-secretases. Elevated levels of Aβ causes an increase in oxidative damage Besides cognitive deficits, AD patients show alterations in their circadian rhythms. Previously, we found that an intracerebroventricular (i.c.v) injection of Aβ(1-42) modified the daily patterns of Tbars and protein carbonyl in the rat hippocampus. Taking into account those observations, our objective was to investigate the effects of an i.c.v injection of Aβ(1-42) on daily rhythms of β/γ-secretases, BMAL protein levels, and chlorotyrosine and nitrotyrosine levels in the rat hippocampus. Four-month-old males Holtzman rats were divided into two groups defined as: control and Aβ-injected. Daily rhythms of β/γ-secretases expression were analyzed by RT-PCR, chlorotyrosine and nitrotyrosine levels were determined by ELISA and BMAL levels by Western blots. We found that an i.c.v. injection of Aβ(1-42) modified variation of β/γ–secretases, BMAL1,chlorotyrosine and nitrotyrosine. Thus, elevated Aβ peptide levels alter temporal patterns of nitrosative stress-related parameters and, consequently, would negatively affect cellular clock activity and the transcription of their target genes.

059 | Motivation for a reward is affected by gut microbiota depletion and the loss of the circadian clock protein per2 in mice

Chronobiology

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The circadian system regulates several physiological, metabolic, and behavioural rhythms with a period close to 24 h. The molecular basis of this clock consists of a series of negative feedback mechanisms between specific genetic components, such as Per, Cry, Clock and Bmal1 genes. When the availability of food is restricted to an interval of the day (time restricted feeding, TRF), the animals adapt to this condition by feeding only during this interval and develop a food anticipatory activity (FAA) driven by a food-entrainable oscillator (FEO). One of the peripheral circadian oscillators is the gut microbiota, which regulates the synthesis and release of neuromodulators through the microbiota-gut-brain axis.

In this work, we present evidence that motivation for food reward – assayed through the progressive ratio schedule – is affected by microbiota depletion and the loss of the circadian gene Per2. In this sense, our results indicate that microbiota depletion with antibiotic treatment affected FAA and motivation under a TRF protocol, demonstrating a role for the gut microbiota in regulating brain reward functions. Moreover, motivation was significantly diminished in the Per2-/- mice, confirming a role of Per2 in motivation processes.

Together, these findings contribute to gain knowledge in potential mechanisms of circadian modulation of motivational states in order to improve treatment related to psychiatric disorders or drugs of abuse and mental disorders.

061 | The circadian system modulates tumor progression: role of immune response and tumor microenvironment

Chronobiology

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Most physiological and behavioral functions exhibit daily rhythms synchronized with the environmental light-dark (LD) cycle. Shift work and night work desynchronize biological rhythms, including those of the immune system, promoting the development of cancer. Previously, we reported in a non-metastatic murine melanoma model that circadian desynchronization (CJL, 6-hour advance of the LD cycle every 2 days) increases tumor growth rate and disrupts the daily patterns of M1 (anti-tumoral) and M2 (pro-tumoral) macrophages. Here, we observed that CJL induces an increase in the percentage of animals with lung metastases, as well as in the number of metastatic foci. In addition, we found a daily pattern in lung macrophage levels under LD: M1 macrophages exhibited higher levels at the end of the night and the beginning of the day, while M2 macrophages showed elevated levels at the beginning of the night. Additionally, CJL abolishes these patterns. On the other hand, we assessed the role of the tumor microenvironment: conditioned media obtained from tumors extracted at different time points induce tumor cell proliferation and migration, as well as differentiation of M0 macrophages into M1/M2, in a time-dependent way based on the tumor extraction time. These findings demonstrate that circadian desynchronization promotes metastasis formation. Moreover, this fact could depend on immune response dysregulation, which in turn could be modulated by the tumor microenvironment.

063 | Effects of Sleep Deprivation on Political Polarization

Chronobiology

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Sleep deprivation in humans results in a series of motor, sensory, emotional, and cognitive effects that appear to increase with the reduction of the hours of nighttime sleep. Sleep deficiency also leads to a general decline in mood followed by an increase in irritability and emotional volatility. Self-regulation and monitoring are also significantly affected, leading to emotional disinhibition and an increase in the intensity of responses to negative stimuli, as well as reductions in confidence, empathy, and humor. These cognitive effects of sleep deprivation suggest the hypothesis that it would also impact our opinions and emotions regarding political and moral issues.
The current research aims to evaluate whether sleep deprivation can intensify ideological and affective political polarization. To do this, we conducted a pilot study with a within-subjects design (N=44) to estimate the effects of a night of “short sleep” (4-5 hours) compared to a night of “normal sleep” (6-9 hours) on political and affective polarization. We found a trend toward increased polarization after nights of limited sleep, which we will attempt to confirm in a future study. In another ongoing pilot study, we are currently evaluating the effects of total sleep deprivation over a full night on these measures of polarization. The preliminary results indicate that when people are sleep deprived, they express more negative sentiments towards individuals identified with the opposing political party.

065 | Design and validation of a method to study sleep behavior based on smartphone use

Chronobiology

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The problem of assessing how and when a certain large population sleeps is of great interest to researchers in sleep health. Current methods of tracking sleep are either very precise but costly (i.e. actigraphy through wearables), or easily scalable but of very low precision (i.e. subjective sleep reports). A recently proposed alternative relies on collecting big volumes of longitudinal data from mobile applications and social networks activity that can be analyzed to estimate sleep periods. These sources of information enable researchers to readily access a significant volume of data obtained under natural conditions, and recent studies suggest that, due to their extensive nature, these data facilitate the study of sleep phenomena on a large scale with reasonable reliability. In this pilot study, we propose a model that estimates the sleep events from data of interactions with Android smartphones obtained by their users through Google Takeout, and present preliminary data from a validation study. We also present a set of tools to organize, share and process the estimated sleep parameters using the R language.

067 | Differences in metabolic pathways are associated with time-dependent severity in septic mice

Chronobiology

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Sepsis is a syndrome caused by a dysregulated host response to pathogens, representing the leading cause of death from infection. In murine models, mortality rates largely depend on the circadian system. Mice intraperitoneally inoculated with high doses of lipopolysaccharide (LPS; 20 mg/kg) at the end of the day exhibit a higher mortality rate (~80%) than those inoculated at the middle of the night (~30%), along with a worse inflammatory response and hypothermia. To study the mechanisms involved in this daily variation, we conducted a proteomic analysis on serum samples collected 2 hours after LPS inoculation at both time of the day. We observed that proteins increased at the middle of the night are related to glucose metabolism, energy utilization, and lipid metabolism. On the other hand, differentially expressed proteins at the end of the day are involved in the inflammatory response, oxidative stress, and cellular communication, migration, and adhesion. Additionally, we evaluated glycemia after stimulation at both time points and found that animals exhibit pronounced hyperglycemia in response to LPS within 2 hours after the stimulus, only in mice stimulated at the end of the day. In conclusion, LPS triggers different metabolic responses based on timing of the stimulus. Moreover, the increase in blood glucose levels in response to LPS at the end of the day may signal centrally and/or promote the activation of the inflammatory response, leading to increased severity.

069 | Study of dopaminergic tone in context memory and generalization of contextual learning.

Cognition, Behavior, and Memory

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Dopamine is essential in several processes, such as motivation, arousal, sleep, learning and memory in vertebrates and invertebrates. Preliminary studies in our laboratory indicate that certain groups of dopaminergic neurons (DANs) promote memory to context. Our working hypothesis considers that dopaminergic tone regulates generalization. This is a cognitive capacity that allows the application of knowledge acquired in a given situation to similar situations in the future. To study the role of dopaminergic neurons in memory and memory generalization we conducted a contextual learning trial designed as follows: The animal is trained in one context and then tested in the same or a similar or a different context. Through this test it is possible to detect memory to the original context, normal generalization and overgeneralization. Through this assay we will be able to measure generalization in a series of genotypes in which we manipulate the excitability of DANs. Manipulation of dopaminergic neurons was carried out by ion channels targeting specific groups of dopaminergic neurons using the GAL4/UAS expression system.Our preliminary results suggest that at least two groups of DANs differentially modulate context habituation and context recognition memory.

071 | Cholinergic Facilitation of Contextual Discrimination Learning in Mice

Cognition, Behavior, and Memory

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Acetylcholine (ACh) functions as a neuromodulator, playing a crucial role in hippocampal-associated cognitive processes such as learning and memory. Previous work in the laboratory has shown that endogenous ACh release into the dentate gyrus of the hippocampus produces a reconfiguration of inhibitory circuits, which results in a net disinhibition of excitatory neurons, favoring plasticity of incoming inputs. As a next step we decided to test the hypothesis that an endogenous release of acetylcholine can promote learning. For this we: 1) developed a behavioral task to study contextual discrimination in a head fix mice using virtual reality.; 2) study how increasing endogenous ACh release affects learning the task. We used a chemogenetic approach to endogenously release ACh during learning by using Chat-HM3DQ mice injected with CNO. Water restricted animals were trained to perform a GO/NO GO visual discrimination task, in which the animal learns to drink water or not depending on the virtual visual context. We designed four increasingly difficult visual discrimination contexts to evaluate cholinergic modulation of learning. Preliminary results show that animals with increased cholinergic activity learn the task faster than control animals. In conclusion, we developed a behavioral paradigm suited to probing the neural basis of learning spatial context and its flexibility with neuromodulators.

073 | Involvement of basolateral amygdala astrocytes in contextual fear memory

Cognition, Behavior, and Memory

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Little is known about the role of astrocytes from the basolateral amygdala complex (BLA-C) on the contextual fear conditioning (CFC), a relevant paradigm to understand fear related disorders. Previous experiments in our lab showed that administration of fluorocitrate (FLC, an astrocyte inhibitor) in the BLA-C before CFC, impeded the acquisition of fear memory. To gain insights into mechanisms, we tested if FLC-induced memory deficits could be reversed by the co-administration of putative gliotransmitters: glutamate and d-serine, known to be release by astrocyte and to be involved in learning induced plasticity. We also evaluated if FLC administration during the consolidation memory phase could disrupt the memory formation and explored if astrocyte plasticity is observed during this time window.
Adult Wistar male rats were infused intra-BLA-C with FLC and a mixture of glutamate and d-serine before CFC. Memory was evaluated 2 days later analyzing percentage of time of defensive behaviors. Another group of animals were conditioned and administered intra-BLA-C 5 minutes after CFC, to target the consolidation phase. In another set of experiments, rats were sacrificed 1 hour after CFC for immunofluorescence staining of GFAP to evaluate morphological and/or expression changes in astrocytes during the consolidation phase. All together, the data suggest that BLA-C astrocytes play a role in early phases of the consolidation window.

075 | Social isolation changes Drosophila sleep amount in a memory dependent manner

Cognition, Behavior, and Memory

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Social interactions influence behavior in numerous species, including humans. Changes in food intake, sleep patterns, mood, and aggressiveness are prominent examples of such behavioral shifts. In the fruit fly Drosophila melanogaster, a pivotal model for probing the genetic underpinnings of behavior, sleep reduction coincide with increase feeding and heightened aggression during isolation. Our hypothesis posits that alterations in locomotion intensity arising from social isolation are sustained by long-term memory mechanisms triggered by the experience of solitude.
To test this, we stablished a socialization/isolation paradigm using a video-tracking system that measures movement patterns and evaluates sleep, mirroring prior observations. Following this, we administered a cold-shock protocol to impair the acquisition of this specific form of memory. Additionally, we examined the impact of solitude on two mutant fly strains with essential roles in memory acquisition and consolidation, namely rutabaga (rut) and dunce (dnc). Our findings pointed to a role for rut in this process. Employing a genetic strategy to selectively suppress rut expression in the mushroom bodies – the memory acquisition hub in flies – we demonstrated the suppression of behavioral alterations prompted by isolation. Subsequent experiments will involve the restoration of rut expression solely in this neuropil to further prove the implication of the memory systems in the bahvioral changes induced by isolation

077 | Calcium imaging in CA3 in object recognition task

Cognition, Behavior, and Memory

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The hippocampus plays an important role in memory and spatial orientation. In particular, it has been shown that DG avoids interference between similar memories but the mechanism is unknown. Here, we hypothesize that the information encoding is modulated by the demand for pattern separation in the DG-CA3 circuit. To explore this possibility, we performed calcium imaging recordings in CA3 with the miniscope in a behavioral task that required pattern separation and object recognition. Our preliminary results hint to a decrease in neuronal correlation in close objects than in far ones.

079 | Learned together or apart: the effect of acquisition conditions on the strengthening by indirect memory reconsolidation

Cognition, Behavior, and Memory

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Memory reconsolidation is the mechanism by which consolidated memories are updated in strength and/or content. An underlying hypothesis to these findings suggests that reconsolidation would be “reactivation specific”, implying that only the reactivated elements would be susceptible to modifications. Our main goal was to study the extent of the strengthening due to reconsolidation, that is, to see whether it affects not reactivated elements. To test this hypothesis, we conducted a 3-day study. On day-1, subjects learned face-name pairs (target memory) along with the interleaved presentation of common use objects (peripheric elements). Subjects were instructed to learn the face-name pairs (target memory) and between these presentations they were asked to make a judgment call on a certain aspect of the object shown. On day-2 two types of reminders of the target memory were used. The group called RI received a reminder with prediction error that leads to reconsolidation, and the other group, RC, received a reminder without prediction error that doesn’t involve reconsolidation. On day-3 both the target and peripheric elements of the memory were evaluated. In accordance with previous experiments, the memory for target elements was strengthened in group RI, but not in RC. Here we found that the RI group also showed better recognition of the new objects (peripheric memory) than the RX group and also showed greater sensitivity at discriminating between conditions.

081 | Role of a previous nap on facial recognitions. Preliminary results.

Cognition, Behavior, and Memory

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Approximately, 70% of erroneous convictions in the USA are attributed to flawed facial identifications. Recently, it has been observed that a period of sleep before facial recognition reduces the misidentification of innocent individuals when the perpetrator is absent from the lineup. However, a similar study did not show distinctions between sleeping and non-sleeping groups. Notably, neither of these studies objectively measured sleep. Slow Wave Sleep (SWS) plays a fundamental role in maintaining the synaptic homeostasis in the brain. SWS prevents the oversaturation of synaptic strength that occurs during wakefulness, enabling the encoding of new information upon waking. Hence, this study aimed to examine the role of sleep in memory discrimination during a lineup. Participants watched a video depicting a criminal act on day 1 and were immediately tested for free recall of the event. On day 2, half of the participants slept for 40 min while undergoing polysomnography, while the other half remained awake. Subsequently, they underwent facial recognition in a lineup and were evaluated for their recall of the event. Preliminary data suggests a trend indicating that a short nap before the lineup can increase correct recognitions in the lineup when the perpetrator is present. This study has the potential to revolutionize the judicial process by utilizing our understanding of sleep's role in memory to enhance the accuracy of facial recognition within the legal system.

083 | Metacognition of computational processes underlying eye movement guidance in visual search

Cognition, Behavior, and Memory

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Visual search, a fundamental human activity, entails a series of eye movements that integrate both bottom-up and top-down information to make goal-driven decisions. This process engages executive functions such as attention, memory, and decision-making. Using computational models and a behavioral experiment, we address a key open question: to what degree are individuals conscious of their own computational processes? In this study, a total of 50 participants completed a visual search task within natural scenes, providing both objective responses (clicking on the target location) and subjective responses (encircling the perceived target area). We assessed the predictive capability of the Entropy-Limit Minimization model in terms of both gaze path prediction and human responses. Preliminary findings demonstrate the model's proficiency in anticipating human behavior; however, certain limitations persist in fully capturing the underlying human actions.

085 | Environmental enrichment rescues pattern separation deficit in a rat transgenic model of Alzheimer's-like brain amyloidosis

Cognition, Behavior, and Memory

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Adult hipocampal neurogenesis (AHN) is impaired in animal models of Alzheimer's disease (AD) and in post-mortem AD brains. AHN promotes pattern separation (PS), a cognitive process by which similar stimuli are discriminated in hippocampus-dependent tasks. Moreover, PS is affected in individual with high genetic risk for AD and in patients diagnosed with AD. Here, we evaluated if the exposure to an enriched environment (EE) was able to rescue PS deficit in the McGill-R-Thy1-APP transgenic (Tg) rat model of AD, in which deficits in AHN have been previously described. To this end, 6-month-old Tg and wild-type (WT) rats were assigned to EE, or continued living in standard cages, until 9-month-old, when they were submitted to the spontaneous location recognition (SLR) task to assess PS. Using two configurations of the SLR task, the similarity of the to-be-remembered locations were parametrically manipulated by altering the spatial positions of objects-dissimilar or -similar to vary the load on pattern separation. Results showed that in the objects-dissimilar configuration all groups were able to solve the task. In contrast, in the objects-similar configuration Tg rats not exposed to EE were unable to solve the task while Tg rats exposed to EE did. These results provide evidence of a specific cognitive deficit in this Tg rat model that has not been previously studied and that is sensitive to environmental stimulation.

087 | Daily intake of omega-3 polyunsaturated fatty acids reduces risk of cognitive decline

Cognition, Behavior, and Memory

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Aging is the accumulation of cellular and molecular damage during life, with the brain suffering some loss-of-function. In addition, a chronic inflammatory state that is attributed to reactive microglia characterizes the aging process.
Omega-3 (w-3) polyunsaturated fatty acids (PUFAs) are involved in many cellular functions affecting membrane fluidity and integrity, and they are the main precursors for the biosynthesis of eicosanoids. It has been observed that the intake of w-3 PUFAs has beneficial effects in patients with cardiovascular and age-related diseases. Moreover, administration of w-3 PUFAs after brain injury in mice promoted the formation of immature neurons, micro vessels, and oligodendrocytes. However, their anti-inflammatory and antioxidant effects are controversial.
This study set out to explore the effects of 6-months of dietary supplementation with w-3 PUFAs on cognitive behaviour and inflammatory and oxidative status in aged rats. For this purpose, 18-month-old female Sprague Dawley (SD) rats received fish oil supplementation daily. With the aim of evaluating different behaviours the rats performed cognitive and motor tests.
Our data showed that treatment reduced cognitive deterioration compared with the control group. Interestingly, we observed that the rats receiving w3 supplementation showed similar performance to naïve SD rats of 6 and 12 months.
The results of this study suggest that a daily intake of w-3 PUFAs delays age-related cognitive decline.

089 | Peripheral plasticity leads to memories of varying strength based on past experiences

Cognition, Behavior, and Memory

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During foraging, honey bees Apis mellifera are capable of assessing food quality. Flowers encountered in nature can differ in several aspecst being sucrose concentration and nectar quantity the most significant for bees. Choosing the optimal food sources requires assessing and comparing these traits.
Recent studies conducted in our laboratory have demonstrated that bees can stabilize stronger associative memories when the unconditioned stimulus exceeds the expectations. Accordingly, honey bees whose expectations of reward are frustrated show weaker memory retention than those who receive the same reward that they expected. Our current objective is to elucidate the mechanism responsible for this modulation in memory strength.
Here, we observed that bees form short-term memory faster when their expectation of the unconditioned stimulus is exceeded. On the other hand, the group whose expectation was frustrated learned slower. These results reveal that without a memory consolidation process, there is differential learning performance among the different groups. This could be attributed to the differential sensitivity of receptors, leading to the formation of distinct short-term memories in the different groups. Therefore, we are conducting eleactroantennogram recordings to test how peripheral plasticity contributes to memory capacities.

091 | Role of the Lateral Entorhinal Cortex in the destabilization/reconsolidation of Fear Memories

Cognition, Behavior, and Memory

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The destabilization and subsequent reconsolidation of fear memories is a complex process through which a previously consolidated memory becomes susceptible to modifications and interferences. In this sense, it has become a potential therapeutic target for the treatment of disorders associated with abnormal memory expression such as the post-traumatic stress disorder (PTSD) and phobias.
Our previous studies have shown a critical interaction between two key structures for this process: the basolateral complex of the amygdala (BLA) and the dorsal hippocampus (DH), regardless of the scarce direct connections between them. In the present work we explore the involvement of the Lateral Region of the Entorhinal Cortex (L-Cent) in the reconsolidation of fear memories as a functional mediator between BLA and DH. Using the GABAergic agonist Muscimol (MUS) we have been able to disable L-CEnt and evaluate changes both in the fear conditioning task and in structural plasticity of the DH.

093 | Successive Negative Contrast in humans: non-monetary incentives and their control over behavior

Cognition, Behavior, and Memory

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Successive Negative Contrast (SNC) is a paradoxical reinforcement effect (PRE) observed when a reinforcer is devalued before cues associated with a higher reinforcement magnitude. This phenomenon is believed to be inherent to mammals, who, apart from extinction (an allocentric learning mechanism), may also show egocentric learning related to their own emotions. While animal models typically use primary reinforcers, human studies often rely on monetary incentives. In this study, three distinct computerized behavioral tasks of instrumental SNC were examined, using points redeemable for gifts as reinforcer. Participants' reaction times (RT) were measured expecting differences in the devaluation condition (80-10 points) as compared to a control group, consistently reinforced with 10 points. Although the RTs revealed promising trends, an ANOVA revealed statistically significant differences only in the trials factor, whereas the interaction effect of Group x Trials did not show any significant differences. Two of the tasks are suitable for a future study, but the lack of differences between conditions (i.e., neither SNC nor inverted SNC) implies that points might not be controlling behavior. In a new pilot study, we measure pupil dilation, EEG and electrodermal activity. Preliminary results show arousal increments linked to reward devaluation. The efficacy of non-monetary incentives in human subjects is discussed.

095 | Mental representation of fractions and its demographic dependencies, a Massive Online Experiment.

Cognition, Behavior, and Memory

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This study explored how the performance on different mathematical tasks, among them 'fractions estimation', 'mental rotation' and 'complex calculations' relate to one another in a large sample of individuals (n= 22,221). We designed a Massive Online Experiment with a set of 23 questions extracted from tests used to identify difficulties in mathematical performance, which was distributed via social media. To evaluate the similarities and differences among distinct groups of cognitions, we analyzed the educational attainment, age, and gender dependencies of participants' performance on each task. Our online data shows reliable patterns that are in line with previous literature, while making a novel contribution suggesting that mental rotation and fractions estimation tasks may rely on common processes with a common developmental pathway. This aligns with the theory of double-representation of fractions, which posits that ratio magnitudes are doubly represented in the brain, either as analog holistic quantities or as exact numerical values. Our data suggests that when the exact calculation of a fraction is unfavorable or impossible, an analog holistic representation of fractions might emerge. These findings demonstrate the utility of the approach we propose, using large samples collected through the internet to evaluate the similarities and differences among distinct groups of cognitions.

097 | Examining the influence of the Cdk5/p35 Complex on Working Memory and the Effects of Methylphenidate Treatment in an ADHD Mouse Model

Cognition, Behavior, and Memory

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Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental condition characterized by symptoms of hyperactivity, impulsivity, and memory deficits. The treatment of ADHD includes the use of psycho-stimulants, such as methylphenidate (MTPH). One of the crucial symptoms of ADHD is working memory (WM) impairment that is defined as a short-term memory used for the planning and execution of cognitive functions. Transgenic mice lacking p35 (p35KO), the activating subunit of Cdk5 present key hallmarks of ADHD animal models..Cdk5/p35 complex regulates neuronal survival, dopaminergic neurotransmission and synaptic plasticity among others. Given that, we aimed to study the contribution of the Cdk5/p35 complex to WM and explore the impact of MTPH treatment, taking into account potential sex differences. We used transgenic mice deficient p35KO and wild type (WT) control of 21-25 postnatal days. We assessed WM using the Y-maze task and neuronal activity in brain related areas using c-FOS immunostaining. Data was analyzed using ANOVA. The p35KO mice of both sexes exhibited impaired WM compared with WT mice. Also, the performance of p35KO males treated with MTPH was similar to WT male control group, which suggests an improvement of WM induced by MTPH. In conclusion, our study emphasizes the importance of the Cdk5/p35 complex in WM processes. Moreover, it demonstrates the potential of MTPH to rescue WM impairments caused by disrupted Cdk5 activation in males.

099 | A matter of time: Temporal Order Recognition Memory and ERK1/2 Activation in Mice

Cognition, Behavior, and Memory

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Recognition memory in mice depends on the identification and judgment of prior and near events, involving brain regions such as the medial prefrontal cortex (PFC) and the hippocampus. It can be assessed through simple object exploration tasks. This study delves into Temporal Order Recognition Memory (TORM), induced by a two-session protocol. We observed no significant differences in temporal discrimination between sexes at 2 months of age, but reduced object exploration and better long-term (24-hour) discrimination index in males at 3 months of age. Furthermore, we studied the temporal relation between recognised objects by developing a Temporal Novel Object Recognition (TeNOR) protocol. TeNOR revealed mice's preference for novel objects over recently familiar ones, but not over old familiar ones.
We also studied Extracellular-signal Regulated Kinase 1/2 (ERK1/2) activation, known for its involvement in learning and memory processes, and observed an increase in ERK2 activation kinetics specifically in the PFC one hour after a single training session (TR). Interestingly, a second TR inhibited this increase, resetting the pathway kinetics and leading to a subsequent rise in activation one hour later.
For data analysis we used glm-models, accounting for the nested structure of each mouse and its housing box. These results lay the foundations for pharmacological intervention studies of ERK1/2 pathway in order to further understand its contribution to temporal memory formation.

101 | EXPLORING NEOHELICE GRANULATA BEHAVIOR TO ELEVATED STIMULI ON INCLINED SUBSTRATES

Cognition, Behavior, and Memory

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Violinist crabs use a simple rule to categorize visual stimuli: dangerous if perceived in the dorsal region of the retina; harmless if perceived at or below the equator. The Neohelice crab also reacts to elevated moving stimuli; however, unlike the violinist crabs, it exhibits predatory behavior towards smaller crabs. Thus, depending on the elevation of movement, the same object can evoke two completely opposing behaviors, escape or pursuit. It might be assumed that, as proposed for violinist crabs, Neohelice decides how to respond to moving objects based on the retinal region with which they are detected. However, the habitats occupied by Neohelice often feature significant inclinations, causing the crab, when positioned downhill from a small object moving on the ground, to see it above itself. Consequently, according to the hypothesis of categorization by retinal position, the crab should respond by escaping and never pursuing. To test this hypothesis, we conducted experiments in a laboratory arena using a small object moved on an inclined plane. The results show that crabs can pursue and capture the object even when it moves above their eyes. Therefore, the hypothesis of the simple rule for identifying stimuli as prey or predator based on retinal position is incorrect. Crabs incorporate knowledge of substrate inclination to decide the object's significance.

103 | Is metacognition associated with autistic traits? No link found between visual metacognition and AQ scores.

Cognition, Behavior, and Memory

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Metacognition, the human capacity to recognize accurate decision-making, represents a pivotal cognitive process intertwined with learning and personal development. Recent investigations have delved into the intricate association between metacognition and autism spectrum disorders (ASD). However, the body of evidence remains inconclusive. While some studies suggest diminished levels of metacognitive sensitivity in individuals with ASD, others do not substantiate this claim. Capitalizing on the presence of autistic traits within the broader population, our research explores the interplay between visual metacognition and autistic traits across a cohort of 360 neurotypical participants. Our assessment of metacognition hinged on the alignment between individuals' confidence and the accuracy of their choices within a visual two-alternative forced-choice task. Concurrently, we gauged autistic traits using the Autism-spectrum Quotient (AQ) score. Through a regression analysis, our findings revealed no statistically significant correlation between autistic traits and metacognition or the level of confidence in the task. Furthermore, an examination of AQ sub-scales also yielded no discernible link with metacognition. In sum, our research does not substantiate the hypothesis asserting an association between autistic traits and metacognition in the broader population.

105 | Effects of different types of Environmental Enrichment in behavior and adult hippocampal neurogenesis

Cognition, Behavior, and Memory

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Environmental enrichment (EE) is defined as the ensemble of elements or features added to the housing to stimulate the animals and facilitate the performance of natural motivated behaviors. It's widely accepted that complex EE induces increases in adult hippocampal neurogenesis as well as performance in memory tests in rodents, besides improving animal welfare. Although simple EE is often used and recommended in animal facilities around the world, not much is known about how it could affect behavioral and neurogenic parameters in these animals. To study this, Swiss mice of both sexes were allocated into 4 housing situations: standard, complex EE and two simple EE (tube or board house) for 8 weeks. Observations in the home cage were performed to assess the occurrence of maladaptive stereotyped behaviors, and the Splash, Novelty Suppressed Feeding and Urine Sniffing tests were performed to analyze affective states. The Object Pattern Separation task was used to study spatial memory related to newborn neurons in the hippocampus. Finally, 4-week-old newborn neurons were quantified to analyze changes in adult neurogenesis. Our results show that the complex EE induces changes in all these parameters as expected, but both simple EE housings have different effects along the tests performed, which are not as robust as the ones for the complex EE. This would allow the inclusion of these kind of EE in animal facilities to better welfare without interfering with experimental variables.

107 | Exploring the neural correlates of naturalistic hybrid search tasks: Concurrent magnetoencephalography and eye-tracking recordings

Cognition, Behavior, and Memory

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In hybrid visual and memory search (HS) tasks, observers are asked to search for any item of a previously memorized set of items. One of the main signatures of HS is a robust linear relationship between response time and visual set size and a logarithmic relationship between RT and memory set size. However, little is known about the underlying neural mechanisms in HS. One reason is that eye movements produce artifacts in M-EEG signals, which are much larger than the signals of interest. Here, we aim to start uncovering the neurophysiological mechanisms underlying HS. To that end, we combined MEG and eye tracking recordings while participants performed a “new mapping” naturalistic search task, where the memory set changes in each trial, as in most real life scenarios, where the search targets rarely repeat. After identifying and characterizing robust markers of neural and saccadic spike artifacts in the signal, we implemented a deconvolution analysis approach and found a P300m component in the fixation-related fields from targets when compared to distractors. Moreover, we found significant task effects in low-frequency oscillations, such as parieto-occipital Alpha activity suppression during memorization of the items. Altogether, our approach provides a way to study the role of specific neurophysiological signals in complex scenarios that include eye movements, such as HS, to get a deeper understanding of the brain mechanisms of memory encoding and search in natural tasks.

109 | Early-life stress due to infant maltreatment reshapes stress-response behavior in adult rats

Cognition, Behavior, and Memory

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Early parental care is crucial for the proper development of the cortico-limbic circuits regulating the stress response and emotional well-being. Thus, infant maltreatment may lead to mood-related disorders, impairing individuals' capacity to deal with stress. Here, we employed the "Scarcity-adversity model" (SAM) in rats limiting the nesting resources during postnatal days (PND) 8-12– and studied its impact on maternal and adult offspring's behavior. While the SAM did not affect dam weight gain or fecal corticosterone metabolites, we did find a heightened maternal anxiety-like phenotype in the Elevated plus maze (EPM), shown by a reduced tendency to explore the open arms. Adult offspring underwent a series of anxiogenic tests to assess their reactivity to stress. SAM males showed a decreased locomotor activity in the Open field test; and an earlier, more prolonged time in immobility in the Forced swim test. SAM rats of both sexes exhibited an increased open-arm latency, lower closed-arm latency, and a tendency to decrease their risk-assessment behaviors in the EPM. These results suggest that the SAM protocol induces lasting alterations in the risk-taking behavior, reactivity to novelty and to acute stressors in rodents, with males being more vulnerable than females. Our findings underpin the crucial role of a nurturing early-life environment in fostering both mental and physical well-being later in life, thereby reducing the risk of psychopathology.

111 | NEUROPHYSIOLOGICAL CORRELATES OF A SLEEP PARALYSIS EPISODE

Cognition, Behavior, and Memory

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Introduction. Sleep paralysis is a REM sleep parasomnia characterized by the inability to perform voluntary movements while the person feels awake and conscious of the surrounding environment. Recently, it has been demonstrated that it is possible to determine the exact onset of a sleep paralysis episode by instructing the dreamer in advance to perform a pre-agreed eye movement, which can be observed in a polysomnography recording. In this study, we present the results obtained from the analysis of the signal obtained during a sleep paralysis episode. Materials and Methods. The participant was instructed to move their eyes from left to right three times when experiencing a sleep paralysis episode. A standard polysomnography was conducted, and the obtained signal was subjected to bandpass filters from 0.16 to 65Hz, a 50Hz Notch filter, and ICA filters. Spectral power density was analyzed in frequency bands of interest during sleep paralysis episodes, normal REM sleep, wakefulness, and NREM stage 1 sleep. Results. During the episode, there was an increase in power density in the alpha (8-13Hz), beta (15-30Hz), and gamma (45-65Hz) frequency bands compared to normal REM sleep. On the other hand, power density during the episode was similar to NREM stage 1 sleep in the theta (4-9Hz), alpha (8-13Hz), and beta (15-30Hz) frequency bands. In comparison to wakefulness, power density during the episode was lower in the alpha (8-13Hz), beta (15-30Hz), and gamma (45-65Hz) frequency band

113 | Exploring the role of dCA1 Serotonin 2A Receptors during Retrieval of Recognition Memory in Rats

Cognition, Behavior, and Memory

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Episodic memory can be defined as the memory for unique events. The serotonergic system, one of the main neuromodulatory systems in the brain, appears to play a role in it. Despite a clear involvement of hippocampus (HPC) in episodic memory, information regarding the mechanisms and neurotransmitter systems involved are not completed understood. Although the serotonergic system has been linked to HPC functionality and modulation, its role in memory processing is scarce. Recognition memory can be defined as the ability to recognize if a particular event or item was previously encountered and is thus considered, a form of episodic memory. The rodent HPC, and the dorsal CA1 (dCA1) region in particular contributes to object recognition memory. Serotonin 5-HT2a receptors (5-HT2aR) are distributed extensively in the brain, including the HPC. To analyze the role of dCA1-5-HT2aR in recognition memory we combined stereotaxic infusion of a selective antagonist with behavioral tasks in rats. We found that blockade of dCA1-5-HT2aR before the retrieval phase affects the resolution of recognition tasks that involves spatial information but it does not affect the recognition of the objects per se. These results suggest that HPC 5-HT2aR are involved in recognition memory when contextual information is an important feature of the task.

115 | Unraveling the object recognition memory system, flexibility, compensation and adaptation.

Cognition, Behavior, and Memory

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The retrosplenial cortex (RSC) is involved in navigation and contextual memory, functions that are essential for an individual's life. Our findings in rodents showed that the RSC is required for object recognition memory (ORM) consolidation and retrieval only when it is intact during acquisition. If this does not happen a RSC-independent memory is formed. However, cerebral activity patterns exhibited an increase in RSC activity during retrieval (test session) when the RSC was inactive during acquisition (training session) compared to a non-inactivated group. We suggest that this increase could be due to the flexibility of the ORM system. We observed that when RSC is inactive during memory acquisition (training session) but active during memory retrieval (test session), the RSC is integrated in the memory system, and thus is required for memory updating (after the test session) and retrieval (during re-test). Nevertheless, if RSC is inactive during both memory acquisition and retrieval, the RSC is not integrated into the ORM system. In conclusion, our results showed that the ORM is flexible. We propose that there are several memory circuits, but there is one preferred circuit that is the most efficient to store and retrieve memory. Still, it is possible that the ORM system adapts according to the physiological environment of the brain structures that form the different circuits and modify the main memory circuit when it is damaged to store the information.

117 | Acute intrahippocampal administration of melanin-concentrating hormone (MCH) impairs memory consolidation and decreases the expression of MCHR-1 and TrkB receptors

Cognition, Behavior, and Memory

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Melanin-concentrating hormone (MCH) is a hypothalamic neuropeptide with a role in memory processes. Our study seeks to provide new evidences about its participation in memory consolidation and its relation with glutamatergic and BDNF/TrkB system. MCH (25, 50, 200, and 500 ng) was acutely administered in both hippocampi of male rats immediately after finishing the sample trial of two hippocampal-dependent behavioral tasks: the Novel Object Recognition Test (NORT) and the modified Elevated Plus Maze test. Results indicated that MCH (200 and 500 ng) impaired memory consolidation in both tasks compared with vehicle-treated rats. A second group of experiments were performed with MCH 200 ng, administered alone or co-administered with a MCHR-1 antagonist (ATC-0175) at the end of the sample trial in the NORT. After that, the hippocampi were dissected out to study the expression of MCHR-1, BDNF, TrkB and NMDA subunits. The co-administration of MCH (200 ng) with ATC-0175 reverted the MCH-dependent detrimental effect on memory. Moreover, MCH induced a significant decrease in MCHR-1 and TrkB expression but did not modify BDNF and NMDA receptor subunits NR1, NR2A, and NR2B expression. These results suggest that MCH in vivo elicits pro-amnesic effects in the rat hippocampus by decreasing the availability of its receptors and TrkB receptors, thus linking both endogenous systems to memory processes. Further experiments will be performed in order to explore such interesting connection.

119 | The Role of Context in Semantic Ambiguity Processing: Insights From Behavioral and Pupillometry Measures

Cognition, Behavior, and Memory

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Semantic ambiguity, the phenomenon of words having multiple meanings, represents a potential challenge for human language performance. It has been proposed that the frequency of each meaning and the immediate sentence context provide primary disambiguating cues. However, little is known about the effect of the context seconds to minutes before an ambiguous word appears (such as the conversation topic). Moreover, it is not yet clear whether integrating information from the context optimizes the disambiguation process by reducing the associated neurocognitive demands. First, we evaluated whether it is possible to bias the interpretation of an ambiguous word by previously presenting a context related to one of its meanings (n=47). We further adapted this protocol to register pupil dilation while performing the behavioural task as a measure of neurocognitive demand (n = 16). Results showed that ambiguous words were processed faster ($p<0.0001$), more accurately ($p=0.036$) and with reduced neurocognitive demands (i.e., smaller pupil dilation) ($p=0.037$) when preceded by a context related to one of their meanings. Taken together, the results of this study suggest that adults' lexical-semantic representations can be updated based on their most recent experiences. Importantly, semantic context seems to guide neurocognitive resources and thus optimizes the disambiguating process, as revealed by pupillometric data.

121 | Emotional Induction Through Music. A comparison between European and Latin American music

Cognition, Behavior, and Memory

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Music can induce different emotional states on listener, a phenomenon termed Emotional Induction through Music (EIM). It has been mainly explained by intrinsic musical features, which lead to a classification of songs in two categories: arousing and relaxing. However, other aspects as contemporaneity and cultural proximity with music might influence EIM. This study aims to assess the EIM comparing music from different contexts and periods (European vs Latin American). Self-report measures (valence, arousal) and physiological parameters (heart rate variability [HRV] and skin conductance level [SCL]) were evaluated on an Argentinian sample (28 healthy volunteers, M = 27.45; SD = 1.31). After a three-minute physiological baseline, participants listened to musical fragments (arousing Latin American vs relaxing Latin American vs arousing European vs relaxing European) for three minutes each one. After each excerpt, participants rated their valence and arousal. Results showed that arousing Latin American music was rated as more positive and arousing than European music, and both were more positive and arousing than relaxing music. Physiologically, both arousing music elicited higher SCL than relaxing music. Moreover, arousing Latin American music presented an increase in low frequency component (HRV indexes) compared whit baseline and European arousing music. Thus, contemporaneity and cultural proximity could generate a differential effect and enhance EIM.

123 + CO-4-Microcine | Streptozotocin induces behavioral changes and reactive astrocytes in a sex-dependent manner

Cognition, Behavior, and Memory

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Male rodents have been the default model organism in neuroscience research, including for the intracerebroventricular (icv) streptozotocin (STZ)-induced Alzheimer's disease (AD) model. Our objective was to compare the effect of icv-STZ injection in male and female rats with and without ovaries. Male rats were separated into control and STZ groups. Fourteen days before STZ injection, half of female rats were ovariectomized (OVX), or left with intact ovaries (Female group), and then separated into control or STZ groups on the same day as male rats. Two weeks later, behavioral tests were conducted for spatial memory (Barnes Maze) and depressive-like behavior (Forced swimming test). Immunofluorescence analyses were performed in the hippocampus. STZ affected spatial memory and increased depressive behavior in male, but not in female rats. We assessed GFAP expression and JAK2/STAT3 signaling activation, and we found sex differences on astrocyte reaction to STZ, with astrocyte reactivity evidence only in male rats. Also, STZ induced synapse loss in male rats, although it did not affect the expression of astrocyte proteins relevant for synapses, independent of the sex. We conclude that STZ affected differentially male and female rats, and OVX did not render the rats more vulnerable to STZ. Therefore, experimental design changes should be considered in order to set up a female sporadic AD model, and sex differences in the icv-STZ model should be addressed and further studied.

125 | Characterization of impulsivity differences between adolescent and adult rats in a self-initiated rewarded task

Cognition, Behavior, and Memory

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Mammals undergo multiple physiological and behavioral changes associated with the transition between youth and adulthood which help them acquire the skills necessary for their independence. In general, adolescents exhibit characteristic behaviors, such as increases in social interactions, a preference for novelty, and risk-taking activities. In previous work from our lab, we found age-related differences in the performance of male Long Evans rats in a self-paced rewarded task. Since developmental divergences between sexes might affect learning, here we studied the performance of both male and female adolescents and adults. In this task, after a minimum waiting interval of 2.5 s, the animals must enter a nose poke and emit an eight-lick sequence onto a sipper tube to obtain a reward.

Consistently with our former electrophysiology results, we found a higher prevalence of impulsive trial-starting in adolescents. We also analyzed other behavioral markers that could account for the premature response in adolescents such as locomotor activity, memory formation, and decision-making in the spontaneous exploration of a multiple-regions arena.

Our results show that adolescent rats display more premature responses in the rewarded task. Still, this impulsivity is not related to increases in their locomotor activity, deficits in memory formation, or risk-taking behaviors, suggesting impulsivity of action could be an individual trait.

127 | Fear and reward BLA-mPFC network dynamics during memory reconsolidation and extinction

Cognition, Behavior, and Memory

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The basolateral nucleus of the amygdala (BLA) and the medial prefrontal cortex (mPFC) have been implicated in fear-related responses and reward-seeking behaviours. In the BLA, different positive and negative valence neuronal subpopulations are known to be activated during fear memory acquisition, reconsolidation or extinction. At the same time, these subpopulations are differentially connected to mPFC prelimbic (PL) and infralimbic (IL) subdivisions. Here, we record local field potentials (LFP) and neuronal activity simultaneously in the BLA and mPFC of rats during appetitive or aversive memory acquisition, reconsolidation and extinction. Since the LFP is a proxy for population-based neural activity and given that there is evidence that the retrieval of positive or negative memories differs in the coupling and power of the theta (4-10 Hz) and gamma (40-120 Hz) oscillations in both the BLA and the mPFC, we explore the dynamics of theta and gamma oscillations synchronization between the PL or IL subdivisions of the mPFC and the BLA. In particular, we studied how the transition between memory reconsolidation and extinction occurs, in terms of BLA-mPFC network dynamics when successive conditioned stimuli are presented in the absence of the unconditioned stimulus.

129 | Memory retention characteristics of a novel 'learning under predation' task in Drosophila melanogaster

Cognition, Behavior, and Memory

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Drosophila under predation express a variety of defensive behaviors. Predation has been proposed to promote rapid learning; thus, it is valuable to utilize a natural predator as a source of unconditioned stimulus to study behavior responses, in comparison to more rigid ones such as electric shocks. Here we study the interaction between the spider Menemerus semilimbatus, a Salticid specialized predator of Diptera, and Drosophila. This spider stalks and prays flies in a direct attack to which Drosophila displays a range of defensive behaviors. Here we define and explore the long-term memory revealed as the retention of the Drosophila freezing response, its context specificity that suggest that this type of memory is associative, and the possible molecular pathways involved in processing and retaining memories.

131 | The Psychedelic Gaze: Unveiling Eye Movements During Free Exploration of Artworks Under Psilocybin

Cognition, Behavior, and Memory

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Classical psychedelics are renowned for their capacity to induce profound shifts in consciousness, affecting perception, emotional states, cognition, and self-awareness. This double-blind placebo-controlled study explores psilocybin's effect on visual perception and ocular dynamics. Framed within the context of the entropic brain theory, we hypothesized that visual spatial exploration would manifest as less concentrated and more uniform, yielding an increase in the entropy of the fixation probability distribution. A cognitively undemanding task that presented participants with pleasurable stimuli was selected, fostering a naturalistic milieu conducive to sustained attention. Using an eye tracker, gaze fixations were recorded as participants freely explored artworks on a screen under the effects of psilocybin. Participants also provided self-assessments of emotional and aesthetic aspects for each artwork, while a post-task questionnaire covered various aspects of the aesthetic experience (AEQ). Results reveal higher emotional and flow scores of the AEQ under psilocybin. Eye tracker data revealed that psilocybin induces a shorter and more focused visual exploration, and thus a less entropic fixation distribution.These outcomes challenge the foundations of the entropic brain hypothesis, instead suggesting an inverse narrative: participants attribute exaggerated interest values to specific areas or scenes within the visual stimuli.

133 | Beyond Phosphorylation: ERK2 dimerization influence on memory and plasticity.

Cognition, Behavior, and Memory

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While extensive research has focused on ERK1/2 phosphorylation and its relevance to memory and plasticity, the impact of its dimerization remains largely unexplored. Here, we study the role of ERK2 dimerization on systems with different levels of complexity using native gel electrophoresis, behavioral and pharmacological approach. We assess the ERK2 dimerization level during glycine-induced chemical long-term potentiation (cLTP) in mature rat cortex primary cultures, as well as in mice hippocampus following inhibitory avoidance (IA) memory reactivation. Additionally, we assess the influence of DEL-22379 (DEL), an ERK dimerization inhibitor that doesn't affect phosphorylation, on IA memory reconsolidation and cLTP.

Our findings reveal that ERK2 dimerization is prompted by cLTP, and this process is suppressed by DEL. We also found that, in this model, DEL is capable of inhibiting both ERK dimerization as well as phosphorylation. Furthermore, reactivating a weak IA memory led to decreased ERK2 dimerization in IA-trained mice, while no changes were found after a strong IA memory reactivation. We also report that when ERK2 dimerization is inhibited after strong IA memory reactivation using DEL, mice behave similar to weak IA-trained mice.

This study is the first to document ERK dimerization in neural tissues and to explore the impact of DEL on memory and plasticity processes. These initial insights underscore the potential role of ERK dimerization in plasticity and memory.

135 | Temporal variation in maternal care of rats induced by limited bedding and nesting paradigm and influence on infant developmental milestones and behavioral profile

Cognition, Behavior, and Memory

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The alteration of maternal care during the first week of altricial species' postnatal life impacts the pups' early developmental milestones. However, whether these neurobehavioral maturational processes are susceptible to alterations of maternal care in specific time windows is unknown. We explored here a temporal variation of maternal care in rats through exposition to the limited bedding and nesting (LBN) paradigm in four temporal windows during postpartum days: 2-4, 5-6, 7-9, and 2-9 and recorded maternal behavior. Likewise, we assessed the developmental milestones of pups on postnatal days 13-14. We found that LBN occurring during the first five days of postpartum induces a significant variation in maternal care. Furthermore, dams with higher maternal care variation in early postpartum have pups with reduced body weight gain but no alteration in the eye-opening day or odor-guided behaviors. The most prolonged LBN protocol was the only one that altered the home-nest odor preference and nipple attachment behavior of pups from both sexes. These results suggest that maternal care is mainly susceptible to alteration in early postpartum days by LBN and impacts somatic pups' development milestones but not odor-guided behaviors, which are altered by a more prolonged LBN protocol. These results also open a discussion about exploring sensitive periods of development for maternal care influence through the LBN paradigm.

137 | Involvement of retrosplenial cortical α7 nicotinic acetylcholine receptors in aversive memory processing

Cognition, Behavior, and Memory

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In the retrosplenial cortex (RSC), the role of cholinergic modulation via α7 nicotinic receptors (nAChRs) and their involvement in memory is unknown. In recent years, the RSC has been shown to deteriorate in the early stages of Alzheimer's disease (AD). Likewise, the cholinergic system has been postulated as one of those responsible for cognitive impairment in patients with AD. Great interest has arisen in the study of α7 nAChRs as more specific targets for the treatment of this disease. For this reason, we aim to study the role of α7 receptors of the RSC in memory processing. We infused a selective α7 nAChRs antagonist into RSC to assess its role in different phases of aversive memory processing using an inhibitory avoidance task. We found that α7 nAChRs are required for memory expression in the RSC. These results identify these receptors as key players in the expression of an aversive memory and highlight their significant potential as therapeutic targets for Alzheimer's disease.

139 | Exploring Spatial Memory Through Virtual Reality: Re-Design of RULIT memory task

Cognition, Behavior, and Memory

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The target of the presented research is to improve the understanding of visuospatial learning and memory. Based on a previous investigation, where the development of a gamified Ruff-Light task (G-RULIT) was created to comprehend the way people store information, it was decided to take this method to a more immersive experience with the use of Virtual Reality (VR) technology.

The G-RULIT is a weblike 2D puzzle in which the participants were asked to discover a secret unique path leading to the solution. However, this tool does not allow the investigator to establish the same condition of testing in every participant, thus significant conclusions could not be made if external stimulation was not considered. Nevertheless, with VR equipment the environment where the experiment takes place can be manipulated. Furthermore, it enhances the way the participants are exposed to a task by letting them live the experience in first person. Therefore, using the Unity 3D game engine, a 3D version of G-RULIT was developed, where the participant is now immersed in a maze-like scene instead of just seeing it on a screen. Taking both, the 2D version and the VR version, into consideration, results obtained through experimentation will be compared to analyze which tool is more adept to understand visuospatial memory. Subsequently, same tests will be performed with modified stimulus, such as the addition of physical activity before testing to observe how it affects the subject's performance.

141 | Remembering how to run: exercise effects on aversive memory consolidation.

Cognition, Behavior, and Memory

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Physical exercise is known to have beneficial effects on general health and wellbeing in humans and it is also related to neuronal plasticity, increasing neurogenesis and consequently leading to improvements in processes such as learning and memory. In this sense, wheel running performance in mice appears as an extensively used behavioral approach for neurobiological studies. On the other hand, knowledge of sex-related running profiles of laboratory mice is certainly useful for biomedical research looking at the effect of physical exercise on specific physiological aspects that are assessed in each particular experiment. With this in mind, we looked into the effects of exercise in the consolidation of an aversive memory in female and male CF-1 mice. Animals trained in the Inhibitory Avoidance task received one of two different footshock intensities (0.3 or 0.4 mA) and immediately after were allowed to run in a plastic mouse running wheel. Running effects on memory consolidation were evaluated 48 h after the training session. Preliminary results show that exposure to the wheel after a training session of an aversive memory can negatively modulate mice's long-term performance, depending on the amount of running time. Nevertheless, no changes in memory performances were observed if animals were placed in the wheel-cages 3h post training, suggesting that engaging in wheel-running has no nonspecific impact on the memory consolidation of an IA task in mice.

143 | Analysis of phosphodiesterase 4, DUNCE, in contextual memory and memory generalization

Cognition, Behavior, and Memory

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Intellectual disability affects 1.5 to 3 percent of the global population, impacting directly on an individual's development and quality of life. Memory generalization is a cognitive function that allows the individual to apply certain acquired information or skill in a similar situation in the future. Generalization is impaired in individuals with intellectual disability. This work is part of a larger investigation that aims to understand the molecular and neural mechanisms implicated in generalization. Preliminary results showed that a reduced expression of dunce promotes overgeneralization. In the work presented here, we enhanced the expression of the dunce gene in all neurons. Assuming then an increase in the dunce protein, a decrease in cAMP and PKA activation was expected, which we propose to be associated with a reduction in generalization and thus a more specific memory formation. In order to test this hypothesis, double transgenic flies and parental controls were exposed to a context and then tested in the same, a similar or a different context. Memory recall was assessed measuring the distance traveled in these contexts, understanding normal behavior as recognition memory in the same context, generalization in the similar context, and no recalling in the different context. Contrary to expectations, preliminary results show that the overexpression of dunce gene has no effect on either recognition memory or generalization compared to its parental controls.

145 | Modulating factors on inhibitory control in preschoolers

Cognition, Behavior, and Memory

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Introduction. Several studies have raised the importance of analyzing emotional and cognitive processing comprehensively, which involves studying these processes and including various levels of organization. For example, socio-environmental household conditions and autonomic reactivity are predictors of cognitive performance. However, few studies include different organization levels, especially with girls and boys. Objective. Predict the performance of 5-year-old children in a Stroop-type task from socio-environmental (i.e., household living conditions) and individual factors (gender, heart rate, HR), and task characteristics (reaction time, RT, block). Methodology. A pictorial Stroop task was performed on 73 children aged 5 (51% girls) from different socio-environmental conditions (30% favorable). They were randomly assigned to the Neutral Condition or Positive Condition (59%). HR, performance, and RT were recorded in each task trial. Results. All variables, except gender, were predictors of performance. The probability of responding incorrectly to trials and responding to the most difficult block increased when evaluated under the Positive Condition and unfavorable socio-environmental conditions. HR and RT were positive predictors. Discussion. Comprehensive analyses allow a more comprehensive understanding of complex emotional and cognitive processes. Cognitive performance can be predicted from various individual and socio-environmental factors during development.

147 | FORMATION, EXPRESSION AND RECONSOLIDATION OF AVERSIVE MEMORY: THE ROLE OF ASTROCYTIC GLUTAMATE UPTAKE IN THE CONTEXTUAL FEAR CONDITIONING TASK

Cognition, Behavior, and Memory

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One of the functions of astrocytes is to control the permanence of glutamate in the synaptic space, exerted by specific transporters expressed throughout the brain. Here we studied the role of the glutamate transporter GLT-1, specifically located in astrocytes, in the consolidation, expression and reconsolidation of Contextual Fear Conditioning (CFC) memory. Dihydrokainic acid (DHK), a selective GLT-1 inhibitor, was infused into the rat hippocampus in order to affect different stages of memory. We observed that DHK administration around conditioning did not affect long term memory (LTM) consolidation induced by a strong training session. However, short-term memory (STM) or LTM expression was impaired when DHK was administered 15 min before test sessions. Also, if applied 15 minutes after a reactivation session, DHK impaired memory reconsolidation. In contrast, after a weak training session, which only induced STM, hippocampal inhibition of GLT-1 showed a promotion of LTM formation. In conclusion, we found that GLT-1 blockade close to training time helps to consolidate CFC memory induced by weak training but not by strong training. However, the blockade of this transporter also interferes with memory expression and reconsolidation. We describe the complete dynamics of an aversive memory under the hippocampal effects of astroglial glutamate reuptake blockade, being a site of action for the development of new post-traumatic stress and cognitive impairment treatments.

149 | Influence of stress in de dynamic of GluA2 subunit during fear memory destabilization/reconsolidation process

Cognition, Behavior, and Memory

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When a consolidated memory is retrieved, it can enter a labile state followed by a new process of stabilization dependent on protein synthesis defined as destabilization/reconsolidation. It is known that the internalization of the glutamate receptor subunit GluA2 in the hippocampus of rodents accompanied this process and plays a key role in the plasticity of such process. However, at an experimental level, it has been observed that the exposure to emotional stress prior to contextual fear conditioning, generates resistance to the destabilization/reconsolidation process. In the present study, we assessed if a stressful event influences the dynamics of expression of the GluA2 subunit during destabilization/reconsolidation process. For this, we use previously stressed and conditioned mice C57BL/6 which were reactivated one day later in the same conditioning context. The animals were sacrificed before or after retrieval, CA1 and Dentate Girus (DG) DH were obtained for WB analysis. The preliminary findings could assure that the dynamic expression of GluA2 subunit in the hippocampus is stifled because of the stress exposure.

151 | Exploring the interaction between memory expression and internal states through image analysis in Neohelice

Cognition, Behavior, and Memory

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Predicting whether a particular stressor strengthens or disrupts a specific memory phase is intricate. Unlike theories focused on modulating memory strength, our hypothesis posits that the behavioral expression of reactivated memories is determined, at least in part, by the interplay between internal states (emotions) and mnemonic traces when memories are labile. There, changes in concurrent internal states form emotional traces that will unfold during memory reactivation, modulating expression in evaluation sessions.
In this study, within the aversive memory paradigm of Neohelice, we analyzed behavioral changes during the acquisition and retrieval of this memory (changes in the escape response triggered by a visual danger stimulus – VDS) and variations due to different internal states (water deprivation stress, fluoxetine). The parameter of "crab's silhouette shift" in the training arena induced by the VDS (obtained through ImageJ routines) significantly correlated with manually measured distance traveled (Kinovea software), faithfully reflecting the escape response and the learning curve. Likewise, from position heatmaps during VDS stimulation, the one-dimensional parameter "stationary area" was obtained. The interaction between these 2 variables is considered as an adjunct parameter to jointly assess displacement along with location. These image analysis could constitute tools for studying behavioral changes induced by emotional states in this aversive memory paradigm.

153 | Role of 5-HT2AR in prefrontal cortex activity and plasticity in social behavior

Cognition, Behavior, and Memory

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Serotonergic signalling has shown to be a key player in the modulation of social behavior. Specifically, serotonin type 2A receptors (5-HT2AR), known to be involved in a variety of behaviors, have also been linked to social cognition through the pathophysiology of different psychiatric and neurodevelopmental disorders, and its role in the mechanism of action of so-called “prosocial” drugs. Our lab found that 5-HT2AR knockout (htr2a-/-) had reduced discrimination indexes in the three-chambers social interaction test (SI) compared to wild types (htr2a+/+) mice. By genetically restoring the expression of 5-HT2AR in the forebrain, mice reached discrimination indexes similar to htr2a+/+. To further analyse the role of cortical 5-HT2AR in social behaviors, we used c-fos immunohistochemistry to indirectly gauge SI neural activity. Considering the potential developmental role of 5-HT2AR, we analysed the impact of the lack of 5-HT2AR’s expression on prefrontal cortex structural plasticity by studying dendritic spines. Preliminary data showed lower spine density in htr2a-/- mice’s infralimbic prefrontal cortex, suggesting distinct structural plasticity. These findings suggest a possible role of 5-HT2AR in social behavior in adult mice that might be potentially tied to prefrontal cortex plasticity differences.

155 | Is PKA needed for original memory but not for generalization memory?

Cognition, Behavior, and Memory

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The generalization of learning is a cognitive function that allows us to apply the knowledge acquired in one situation to similar situations. It is a fundamental phenomenon in responding to new stimuli, which have rarely occurred in the same way in the past. Although it is a well documented phenomenon, its molecular and cellular basis are not clear. Previous studies in our laboratory showed that the genetic manipulation of the phosphodiesterase 4, Dunce, controls the level of generalization in contextual memory and olfactory conditioning. These data suggested that PKA signaling might be involved in learning generalization. Although the role of PKA in learning and memory has been determined, its role in generalization is unclear.
In order to determine the role of PKA in generalization we suppress PKA activity by a PKAC1 RNAi in neurons in Drosophila and examine memory and generalization. To assess memory, we used the contextual learning paradigm, where memory is tested in three different contexts, the original context, a similar or a different one.
Preliminary results suggested that the suppression of PKA impaired memory retrieval induced by the original context, without affecting the memory retrieved by a similar context. These results suggest that PKA function is not necessary for the generalization process and other molecular mechanisms might be involved.

157 | Role of dopaminergic signaling in behavioral tagging and memory reconsolidation

Cognition, Behavior, and Memory

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The behavioral tagging (BT) hypothesis states that memory stabilization requires the setting of tags at experience-specific neural substrates, and the capture of newly synthesized plasticity related proteins (PRPs) at said substrates. We have previously described this mechanism in both memory consolidation and reconsolidation. Here, we study the role of the ventral tegmental area (VTA) and the D1/D5 dopaminergic receptors in the BT process underlying memory reconsolidation. Infusion of D1/D5 dopaminergic receptors antagonist SCH23390 15 minutes before reactivation of spatial object location (SOR) memory impaired its reconsolidation. This amnesic effect could be prevented if a novel open field (OF) was explored 60 minutes before or after memory reactivation, but not 3 hours before or after. This rescuing effect was protein synthesis dependent. Furthermore, the inactivation of the VTA also prevented memory reconsolidation, effect which was once again countered by the exploration of an OF. We also saw the amnesic effect of protein synthesis inhibitor emetine (eme) could be prevented with the electrical stimulation of the VTA, provided dopaminergic receptors were functional. Finally, we analyzed molecular correlates associated with the stabilization process of a memory reactivated in the presence of SCH23390, and how the exploration of an OF affected these parameters. Thus, our results suggest dopaminergic signaling regulated PRPs synthesis required for memory reconsolidation.

159 | A hiperexcited state of the basolateral amygdala complex influences the changes in hippocampal structural plasticity associated with the fear memory destabilization/reconsolidation process.

Cognition, Behavior, and Memory

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The occurrence of the destabilization/reconsolidation process of a fear memory plays a pivotal role in the appearance of some symptoms of PTSD and other anxiety disorders.
It is known that the basolateral complex of the amygdala (BLA) is a key area modulating such clinical manifestations. Interestingly, a hiperexcitability of this area was observed concomitantly with the stress exposure and with changes in the dynamisms of hippocampal structural plasticity.

In this work we seek to observe and reverse the impairment of the structural plasticity of dorsal hippocampus due to a pharmacological hyperexcited state in the BLA that emulates the behavioral and structural manifestations of the stress prior to conditioning fear memory. Subsequently, intraperitoneal d-cycloserine (partial NMDA receptor agonist) was used prior to memory recall to reverse the behavioral and synaptic impairment.

161 | Reading comprehension and cognitive skills in primary school children from different socioeducative contexts

Cognition, Behavior, and Memory

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Plenty of evidence suggests that socioeconomic factors (such as mother education or unsatisfied basic needs) have an impact on children's neurocognitive development, leading to differences in cognitive abilities, language outcomes and reading achievement. However, the specific effects of socioeducational context (SE) have been less studied. The following study aimed to compare the cognitive skills of primary school children from different SE, and to examine their contribution to reading comprehension. Our study sample consisted on 358 children (53.4% girls, Mean age: 9.24 ± 1.20 years) from the 2nd to the 5th grade. According to the Educational Opportunities scale, 43% of them belonged to a "low" SE, and the rest to a "medium" context. The children completed a series of computerized tests: selective attention ("Registered Behavior Tool"), shifting ("TMTB"), fluid intelligence (Raven) and reading comprehension ("LEE test"). Cognitive skills improved with grade and SE, while reading comprehension increased with grade and was better among medium (vs low) SE third graders. A path analysis model showed that selective attention and fluid intelligence significantly predicted comprehension and partially mediated the effects of grade and SE. Our findings indicate that: 1) SE predicts cognitive development and reading achievement in primary school, 2) this last effect is partially mediated by SE-related individual differences in selective attention and fluid intelligence.

163 | A short nap enhances memory acquisition in a high school setting

Cognition, Behavior, and Memory

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Sleep deprivation and poor sleep quality are prevalent among high school students, negatively impacting academic performance. Both factors hinder various memory processes, primarily their acquisition. This could be related to a decrease in synaptic downscaling, a process that occurs during slow-wave sleep and allows the encoding of new information upon waking. Here, we assessed if sleeping a short nap in the classroom could enhance acquisition of a Biology lesson.
We conducted a 1-day experiment with 78 students aged 15-17 years. The Nap group slept for 20 min in the library while their brain electrical activity was recorded. Meanwhile, the Control group remained in the classroom engaging in quiet activities. Subsequently, both groups received a Biology lesson from their teacher and took a multiple-choice exam.

The Nap group showed significantly better performance in the exam compared to the Control group, suggesting that a short nap can enhance subsequent learning. Contrary to expectations, this may be explained by the percentage of time spent in S1 sleep. Additionally, it was observed that higher percentages of S2 sleep were associated with lower performance. This might be attributed to sleep inertia, as learning occurred within the 20 min following awakening.

Our findings suggest that short naps in the classroom can promote subsequent learning, and to avoid sleep inertia, it is recommended to wait at least 30 minutes after a 20 min nap before acquiring new information.

165 | Measuring Executive Functions with a computerized software: results for unsupervised interventions

Cognition, Behavior, and Memory

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Mate Marote is an open source cognitive-training software aimed at children between 4 and 8 years old. It consists of a set of computerized games specifically tailored to train and evaluate executive functions (EF): a class of processes critical for purposeful, goal-directed behavior, including working memory, planning, flexibility, and cognitive control. During the last ten years several studies were performed using this software to measure and train children EF at their own schools in supervised interventions. Aiming to scale our interventions, since 2015, we have started to conduct unsupervised, but controlled, studies with children's own teachers' help. In this poster we show that children's EF performance obtained from a battery of standardized tests resulted from unsupervised interventions is comparable to the results reported in the literature. Divided into "time constraint tasks" and "unconstrained" tasks, we were able to replicate expected difficulty effects and an age effect with most of the analyzed variables. We also found important discrepancies between the expected and the observed response time effects, specifically for the time constraint tasks. We implemented a modification for the latter and hereby discuss the benefits and setbacks of this new possible strategy for unsupervised setting testings.

Our results indicate that our battery can be used to measure this EFs in unsupervised settings in the future, allowing us to scale the software use in schools.

167 | Effects of undernutrition and obesity on neurodevelopment and metabolism.

Development

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Malnutrition includes undernutrition and overweight/obesity, and various animal models have been established to explore their effects on health. A recent malnutrition type, double burden of malnutrition (DBM) emerges in vulnerable groups, where undernutrition and overweight coexist creating unknown public health issues. No animal model yet replicates DBM complexities, metabolic outcomes, and neurodevelopmental impacts. Our goal is to establish an animal model of DBM, to study its implications on health. For this, we developed two models:one of undernutrition (long maternal separation, LMS) and one of obesity (cafeteria diet, CAF). In LMS, we separated half the litter 8hrs/day between postnatal days (PD) 5-21.This protocol resulted in reduced weight in male and female mice. In addition, LMS males exhibited reduced social behavior, while LMS females showed heightened depressive-like behavior. For CAF, animals were maintained on a 14-week cafeteria diet starting at PD21. CAF animals showed increased body weight, glucose and cholesterol levels, all associated with metabolic syndrome. CAF animals exhibited a decrease in locomotion across various behavioral tests, but increased swimming time in the forced swim test. Combining LMS and CAF models for DBM, we'll explore distinct behavior and metabolic effects.This integrated approach aims to unveil health challenges and mechanisms in this malnutrition type, shedding light on nutrition, neurodevelopment, and metabolism interterplay

169 | Infant maltreatment stress alters adrenal gland histology in a rat model

Development

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Infant maltreatment is a public health problem that affects a large part of the world population. In Argentina, 7 out of 10 children are subjected to violent discipline methods, including physical and psychological aggression. Early stress generates dysregulation of the stress response system; however, little is known about the impact of infant maltreatment stress on the adrenal glands, end effectors of the hormonal cascade that synthesize glucocorticoids. In this work, we used the scarcity-adversity model (SAM) in rats during postnatal days (PND) 8-12 to induce maternal maltreatment and evaluate histological parameters in the adrenal glands and serum corticosterone levels of Control and SAM offspring of PND 13 and PND 28. The analysis of the adrenocortical zones showed that, compared to the control rats, SAM pups had a greater thickness in the undifferentiated zone at both ages and a lower thickness of the zona fasciculata at PND 13. The cells of the zona fasciculata, which synthesize glucocorticoids, had a smaller cytoplasmic radius and the sinusoids in that zone were thicker in the SAM offspring compared to the Control ones at both ages. PND 13 SAM pups showed higher basal levels of corticosterone compared to controls. These results indicate a histological alteration in the adrenal glands of lactating SAM offspring that persists postweaning up to PND 28. This condition can affect the response of individuals to subsequent stress, compromising their health later in life.

171 | Transcriptional analysis of the splicing factor RBFOX1 and the transcription factor NPAS3 and their role in human brain evolution

Development

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Morphological and functional evolution may result from changes in regulatory elements. We suggest studying differences in these regions tied to core genes in the developing brain to understand the human brain’s genetic basis for morphological and cognitive differences. Key developmental genes, RBFOX1 and NPAS3, experienced accelerated non-coding evolution in humans, accumulating numerous Human Accelerated Regions (HARs), many acting as transcriptional enhancers in transgenic tests. However, these enhancers are just a portion of potential gene-regulating non-coding regions. To explore 7400 potential enhancers in NPAS3 and RBFOX1 loci marked by ENCODE, we’ll employ a massive parallel reporter assay (MPRA) on human neural stem cells for enhancer scoring. This technique helps compare genetic variations between humans and other lineages and assess variant effects in regulatory regions. MPRA results will be validated by creating transgenic zebrafish lines expressing eGFP for selected elements. Genetically engineered mice will also test RBFOX1-HARs, evaluating effects on RBFOX1 expression, brain development, epilepsy, and neurodevelopmental disorders.

173 | Differential Contribution of Cerebrovascular Disease and Its Association with cognition and Sociodemographic Factors in Patients with Alzheimer's Disease and Frontotemporal Dementia in Latin America

Disorders of the Nervous System

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Latin America and the Caribbean (LAC) are experiencing a growing prevalence of dementia, surpassing rates observed in other Western regions. The etiology of these dementias is complex, influenced by cultural, socioeconomic, and genetic factors. However, our understanding primarily derives from North American and European populations, leaving gaps in knowledge regarding the neural and behavioral dimensions of dementias in LAC.

Notably, LAC populations exhibit a heightened prevalence of cerebrovascular disease (CVD), a significant marker of dementia. In this context, our study aims to elucidate the distinct contribution of CVD to two prevalent neurodegenerative diseases, Alzheimer's Disease (AD) and the behavioral variant of frontotemporal dementia (bvFTD), within the LAC region.

We will investigate classic CVD indicators, such as white matter hyperintensities (WMH) and lacunar infarcts through magnetic resonance imaging (MRI), while examining their relationship with clinical diagnosis, demographic factors (age, sex), socioeconomic status (years of education), and cognitive profiles (Mini Mental State Examination) across six Latin American countries. To establish regional specificity and identify shared patterns, we will compare our findings with a non-Latin American cohort (USA). This research deepens our understanding of dementia's complexities in LAC.

175 | Automated speech analysis for the detection of mild cognitive impairment: A multidimensional neurocognitive approach

Disorders of the Nervous System

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Detecting early markers of neurocognitive decline is vital in brain aging research. Recent works show that automated analysis of timing and word property patterns in verbal fluency tasks can reveal robust markers of Alzheimer's disease. Here we examine whether these approaches can boost the detection of mild cognitive impairment (MCI). Fifty-two MCI patients and 54 healthy controls performed phonemic and semantic fluency tasks. Automated tools were used to extract timing (e.g., articulation rate) and word property (e.g., frequency, granularity) features from participants' responses. These features were analyzed via a generalized linear model (GLM) and machine learning tools, compared with standard cognitive measures, and used for brain atrophy prediction. A GLM showed that word frequency, granularity, phonemic length, and imageability were significantly altered in MCI subjects, with no significant differences for timing measures. Machine learning analysis yielded robust classification (AUC = 0.77 ± 0.05), outperforming classification based on standard cognitive tasks. MCI participants showed atrophy of the left temporal pole, and their frequency and granularity patterns correlated with the volume of frontal and temporal regions, respectively. These results suggest that automated word property analysis in verbal fluency tasks can reveal robust markers of MCI, highlighting the utility of fine-grained language screenings to better characterize brain (dys)function in the elderly.

177 | A dual approach to ablate Nkx2.1+ striatal interneurons: Implications in understanding Tourette syndrome

Disorders of the Nervous System

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Tourette Syndrome (TS) is a disorder marked by motor and vocal tics, impulsivity and repetitive behaviors. Postmortem studies reveal reduced PV+, NOS+ and ChAT+ striatal interneurons (SI) in TS patients. Notably, all the SI subtypes affected in TS derive from a cell precursor expressing Nkx2.1. To reproduce the striatal changes reported, we performed a combined ablation of SI using two different approaches. First, a specific Nkx2.1+ SI ablation was produced by administrating intrastriatally diphtheria toxin (DT) in adult mice that express human diphtheria toxin receptor (hDTR) in the Nkx2.1+ cell lineage. With this approach, we obtained ablations of all SI that ever-expressed Nkx2.1. Ablated mice developed abnormal involuntary movements akin to motor tics and repetitive behaviors.

Next, we injected Nkx2.1-Cre adult mice intrastriatally with a virus that expresses hDTR in a Cre-dependent manner. After three weeks of expression we administrated DT intraperitoneally to produce a specific ablation of SI that at time of infection were expressing Nkx2.1. Lesioned mice showed exacerbated hyperlocomotion but did not develop tic-like movements.

Although preliminary, our findings suggest that tics are only induced after targeting the Nkx2.1 cell lineage early during development. Also, that alterations of the Nkx2.1 cell lineage at different postnatal moments may result in diverse behavioral syndromes relevant to understanding basal ganglia related neuropsychiatric disorders.

179 | Effects of gonadal hormones absence since weaning on social behavior in adult female mice

Disorders of the Nervous System

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Autism Spectrum Disorder (ASD) is characterized by decreased sociability and increased repetitive behaviors, with a significant sex bias: over 80% of ASD diagnoses are in males. This implicates sex-related factors in ASD development. Previous experiments from our group demonstrated that male mice prenatally exposed to VPA at GD12.5 exhibit reduced sociability at weaning and in adulthood. In contrast, VPA-exposed females display reduced juvenile play at postnatal day (PD) 21, but sociability remains unaffected in adulthood.

To explore non-reproductive ASD-related behaviors influenced by gonadal hormones, we investigated adult female CF1 mice ovariectomized (OVX) or subjected to sham (SHAM) surgery at PD21. We then ran a battery of behavioral tests in adulthood, to evaluate ASD-relevant behaviors. Our analysis revealed comparable sociability levels between SHAM and OVX adult females. However, when we evaluated the habituation to a social stimulus, OVX mice exhibited increased sniffing of the stimulus in initial presentations, suggesting altered social novelty assessment. Our ongoing research aims to assess adult sociability in VPA-exposed females following ovariectomy at PD21, to evaluate the role of gonadal hormones on female resilience to VPA effects on sociability.

181 | Engineered Tau microRNAs modulate neuronal physiology and rescue tauopathy phenotypes in a preclinical model

Disorders of the Nervous System

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Abnormal protein tau accumulation is the hallmark of several neurodegenerative diseases, named tauopathies. Strategies directed to reduce tau in the brain are promising for therapeutic intervention, yet, development of long-term treatments needs optimization, and better understating of the functional pathways potentially affected by tau reduction. Here we developed artificial microRNAs targeting the human MAPT mRNA to dwindle tau protein synthesis. In human differentiated neurons in culture, microRNAs-directed tau reduction decreased neuronal firing but did not affect neuronal morphology nor impaired axonal transport. In turn, in the htau mouse model of tauopathy, microRNA expression into the medial prefrontal cortex prevented pathological tau accumulation, modulated firing activity of putative pyramidal neurons, and improved glucose uptake in PET scans. Moreover, local tau knockdown prevented cognitive decline in aged htau mice. Our results demonstrate target engagement of designed tau-microRNAs and provide proof of concept for their therapeutic benefit to rescue tauopathy-related phenotypes.

183 | Neuronal cyto-specific lentivectors: A new tool for the analysis of selective vulnerability in tauopathies

Disorders of the Nervous System

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Tauopathies are neurodegenerative diseases associated with the abnormal metabolism of Tau protein, which leads to neuronal dysfunction and dementia symptoms. While Tau downregulation is a promising therapeutic strategy, global tau reduction might lead to undesired effects. Hence, developing more precise tools for Tau reduction only in affected neurons will enhance therapy efficiency and safety.
Two fundamental characteristics of Tauopathies are “selective neuronal vulnerability” and “selective regional vulnerability”, which indicate that the pathology affects specific neuronal types, and progressively impacts certain brain regions in a stereotyped and predictable manner.

The general aim of this project is focused on understanding the mechanisms underlying selective vulnerability due to the post-transcriptional regulation of Tau. We aim to express effective Tau-reducing microRNAs (Facal et al., 2023), but in a cyto- site specific manner.

We constructed lentiviral vectors (LVs) to achieve expression restricted to glutamatergic vs. GABAergic neurons, using engineered promoters for glutamatergic (CamKII) or GABAergic neurons (GAD67/h56D). LVs carrying reporter genes were stereotactically injected into the mouse prefrontal cortex to analyze the expression in the injected areas. Further studies will involve specific expression of anti-Tau miRNAs in cultured human neurons and in a mouse model of tauopathy, to determine the outcomes of locally restricted tau downregulation.

185 | Glyphosate based formulations affect synapse formation and cognitive function in developing rats.

Disorders of the Nervous System

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The widespread use of pesticides around the world increases the risk of environmental contamination by different formulations which can be potentially noxious for non-target organisms including human beings. Many reports have indicated toxic effects of Glyphosate based herbicides (GBH) on nervous system development and functioning. Evidence suggest that GBH toxicity could be associated with neurodegenerative disorders, such as Parkinson´s and Alzheimer´s disease. Our previous studies demonstrated that the active ingredient of GBF (Glyph) alters cognitive function in developing rats and decreased neuronal maturation and synapse. In the present work, we analysed how adjuvants present in the formulations may influence the Glyph neurotoxicity. Rats were exposed to GBF (70 or 100 mg Glyph/kg b.w.) from PND 7 to 27 and behavioural tests were carried out to evaluate motor activity and cognitive function. To study the mechanism underlighting the Glyph toxicity we examined the contribution of the Wnt signalling pathways. Particularly, we analysed the effectors of Wnt cascades such as B-catenin and CaMKII. In addition, we studied the GBH effect on neuronal maturation and synapse on 21 DIV neurons. Results indicated that the presence of adjuvants in formulations markedly exacerbated the glyphosate neurotoxicity by affecting behaviour and dendritic maturation in hippocampal neurons. Preliminary results also indicate a downregulation of Wnt/B-catenin pathway after GBH treatments.

187 | Sleep disturbances in patients with psychogenic non-epileptic seizures

Disorders of the Nervous System

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Introduction: Psychogenic non-epileptic seizures (PNES) account for 20% of patients referred to epilepsy referral centers. An association between alterations in sleep-wake patterns and PNES has been described. The aim of this study is to assess sleep disturbances and associated parameters in a cohort of PNES patients compared to epilepsy controls.

Methods: All consecutively admitted patients to the VEEG unit diagnosed with PNES between 2017 and 2020 were included. Controls with epilepsy were selected, matched for age and sex. Patients were evaluated using the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, a MEQ questionnaire and a sleep diary. Chi-squared test, paired t-test, and Pearson's test were used for statistical analysis. Results: A total of 26 patients in the PNES group and 26 in the control group (CG) were included in the study. Significantly worse sleep quality (P = 0.003) and increased daytime sleepiness (P = 0.04) were observed in the PNES group. No differences in chronotype were observed among patients. The presence of nocturnal events was not associated with poorer sleep quality.

Conclusions: Patients with PNES exhibit alterations in sleep quality and increased daytime sleepiness, which were not related to nocturnal events, sleep duration, or the hypnotic effects of medications. Correcting sleep disorders could prove useful in improving the quality of life for these patients.

189 | Effects of the Val66Met polymorphism in the BDNF gene on intracellular trafficking: implications in neuropsychiatric disorders

Disorders of the Nervous System

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A polymorphism in Brain Derived Neurotrophic Factor (BDNF) gene at ≈25% frequency leads to the substitution of Valine with Metionine at position 66 (Val66Met) in the sequence of the prodomain of BDNF (pBDNF) and is associated with cognitive deficits. Although little is known about the mechanisms through which this variant affects human behaviour, it has been demonstrated that pBDNF Met induces growth cone retraction and morphological changes in dendrites and dendritic spines, both in vitro and in vivo in neurons of the CNS. We propose that pBDNF Met induces structural alterations in CNS circuits by perturbing intracellular protein trafficking. To test this, pBDNF Val and pBDNF Met expression vectors were cloned into neurons. Initial optimization of plasmid transfections was conducted in both Hek293 cell cultures and 7 DIV neurons. Preliminary analysis has demonstrated that pBDNF induces cell death. Characterization involved quantifications of pyknotic nuclei, along with biochemical and immunofluorescence analysis of active caspase 3 and c-Jun N-terminal kinases (JNK). Ongoing experiments seek optimal timing for studying the impact of pBDNF on intracellular trafficking prior to the cell death. Once determined, a synchronization system of the secretory pathway in cultured neurons will be employed to study protein trafficking within the endomembrane system. These experiments will enhance understanding the mechanisms behind vulnerability to CNS disorders in pBDNF Met carriers.

191 | BEHAVIORAL CHARACTERIZATION OF KINDLING PENTHYLENETETRAZOLE MODEL IN SPRAGUE-DAWLEY RAT OF BOTH SEXES

Disorders of the Nervous System

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BACKGROUND: Pentylenetetrazol (PTZ) epilepsy model in rodents has been used for more than 40 years to test new anticonvulsant drugs using the behavioral Racine scale as a reference. However, due to phenotypical differences, this scale is not universally applicable to all rodents and strains. In the present study, we characterized the behavioral evolution of epileptic symptoms in a rat PTZ kindling model in both sexes. METHOD: PTZ saline solution was administered at 70mg/kg i.p. the first day and then 35 mg/kg every other day for 5 weeks to 1-month-old Sprague-Dawley rats of both sexes. The activity was videorecorded for 30 minutes and the behavior test was evaluated. For the histological study, animals were perfused 1, 2, and 3 months after the last PTZ administration and brains were collected. RESULTS: Ten behaviors were described: catalepsy, facial jerk, neck jerk (agitation or assent), forelimb jerk, clonic seizures or tonic seizures (sitting or lying on belly), and tonic-clonic seizure (wild jumping). While latency and frequency of facial and neck jerks reduce over the experiment, catalepsy parameters tend to increase. First clonic or tonic seizures appears in male and female animals after 2.2 ± 2.0 and 2.3 ± 0.21 PTZ injections, respectively, while tonic-clonic seizures (wild jumping) require 15.3±1.3 and 14.7±0.7 injections. Immunofluorescence exploration revealed a significant increase in GFAP (+) cells in the hippocampus of kindled rats compared to controls.

193 | Study of melanin-concentrating hormone (MCH) and glutamatergic systems in the streptozotocin (STZ)-induced Alzheimer's disease (AD) model in male rats.

Disorders of the Nervous System

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MCH is a hypothalamic neuropeptide that regulates memory, although with contradictory effects. In agreement, it has been postulated to be involved in AD neuropathological mechanisms. In this work, we study behavioral and molecular changes in the MCHegic system in the STZ-induced AD model. Considering the impact of AD on the glutamatergic system, we evaluated markers in our model that are poorly studied. Cognitive performance were evaluated in intracerebroventricularly STZ or vehicle administered male rats in the Novel Object Recognition (NOR) at 15, 30, 60, 90 or 120 days post-administration. After that, we evaluated MCH levels in cerebrospinal fluid (CSF) by ELISA and MCH receptor 1 expression (immunofluorescence or western blot) in hippocampus or hypothalamus. Regarding the glutamatergic system, we measured NMDA 2A and 2B receptor subunit in hippocampus. We found that cognitive deficits appeared later, T90 and T120. MCH CSF levels were similar at all the stages studied and MCHR-1 expression at primary cilia of hippocampal neurons or protein levels did not shown differences between STZ and control group. However, in the hypothalamus we found increased MCHR-1 expression at T30, 90 and 120. In terms of the glutamatergic system, 2A subunit were significantly increased at T15 and T60. Meanwhile, 2B levels decreased at the later T120 time point. Our results suggest that in this AD model, MCHergic system is modified at hypothalamus whereas the glutamatergic system at hippocamppus

195 | Molecular characterization of tau pathology in Argentinean patients with primary tauopathies

Disorders of the Nervous System

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Tauopathies, as Alzheimer's disease, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD), are neurodegenerative diseases characterized by the abnormal metabolism of Tau, which accumulates as insoluble hyperphosphorylated neuronal deposits. In each type of tauopathy, this process starts in certain brain nuclei and repeats a defined progression pattern, which gives rise to different clinical signs and symptoms, but some tauopathies present mixed phenotypes which makes the clinical diagnosis process complicated. Current diagnosis criteria do not absolutely differentiate among tauopathies from each other and from other neurodegenerative diseases. Thus, post-mortem analysis and its correlation with previously observed clinical signs is an utmost need to understand the molecular bases of each type of tauopathy and refine diagnosis.
In this project we address this issue through the analysis of post-mortem brain samples from patients diagnosed with primary tauopathies (PSP/CBD) in Argentina. We analyze the presence of pathological Tau and changes in Tau isoforms contents in different regions of the brain. In further studies, we will determine MAPT mutations and local variants of candidate genes putatively affecting tau processing and their transcriptomic profile. We show here that one patient initially diagnosed with PSP presents an increase in Tau3R isoforms in basal ganglia and prefrontal cortex, suggesting a 3R tauopathy.

197 | Development of a preclinical algorithm for the selection of potentially effective drugs for Glioblastoma treatment and in vitro validation

Disorders of the Nervous System

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Glioblastoma (GBM) is the most frequent primary malignant brain tumor in adults. Although the survival of these patients is ~12 months, their treatment, i.e. surgery, chemotherapy with temozolomide and radiation, has not changed since 2005. We developed an in silico model for the selection of potentially effective drugs that are used in the clinic. We used gene expression and drug sensitivity data (IC50) of cancer cell lines from the Genomics of Drug Sensitivity in Cancer (GDSC) database and applied this algorithm to predict IC50 values for GBM samples deposited in The Cancer Genome Atlas (TCGA). Following validation steps, we selected chemotherapeutic drugs that met parameters such as high predicted sensitivity for GBM, ability to cross the blood-brain barrier, overexpression of the target in GBM vs. normal tissue, and correlation with worse prognosis.
We initiated the in vitro evaluation of Etoposide, an inhibitor of topoisomerase II (TOP2). We assessed the effect of Etoposide on the viability of the GBM cell lines with high (U-87) and low (U251) TOP2 expression. We found that GBM cells were much more sensitive to Etoposide than to temozolomide, and their sensitivity was dependent on TOP2 expression levels (higher TOP2 levels led to higher IC50 values). Etoposide did not exert toxicity in primary mouse astrocytes at the therapeutically effective concentrations. Our findings suggest that this algorithm could help to rationally select drugs for preclinical evaluation.

199 | Acetylcholine dynamics in depression

Disorders of the Nervous System

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Stressful life events are primary risk factors favoring depression. In mice, chronic social defeat (CSD) induces susceptibility and resilience to stress. Both phenotypes are causally linked to distinct cellular and synaptic adaptations of Ventral Tegmental Area (VTA). However, the underlying homeostatic mechanisms are far from solved. The cholinergic (ACh) transmission is key to modulate VTA homeostasis. CSD causes a marked hyperactivity of laterodorsal tegmemtum (LDTg) cholinergic cells projecting to the VTA, which is a prerequisite for the subsequent maladaptations in VTA dopamine neurons, and the appearance of a depressive-like symptoms. Resilient mice exhibit a diminished sensitivity of VTA nicotinic acetylcholine receptors (nAChRs) when exposed to the exogenous agonist nicotine, suggesting a key role of ACh transmission/sensitivity of nicotinic systems in delineating susceptibility and resilience to depression. Here, we address the temporal dynamics of ACh transmission in vivo using fiber photometry measures of endogenous ACh release and calcium transients to unravel pre- and post-synaptic VTA adaptations during CSD. We also investigate how ACh transmission impacts VTA subnetworks considering the cellular heterogeneity of VTA neurons and the sensitivity of nAChRs using ex vivo electrophysiology and pharmacological approaches. This project will give new precedent to understand the neurobiological mechanisms in vivo underlying the susceptibility and resilience to stress.

201 | Comorbidity between chronic restraint stress and cocaine self-administration. Participation of Nuclear Factor Kappa B (NF-kB) in Nucleus Accumbens core.

Disorders of the Nervous System

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Stress is a well-known risk factor in the development of addiction and relapse vulnerability. Studies from our lab, showed that stress can elicit a sensitized response to the psychomotor and stimulant effects of cocaine, as well as a facilitation of cocaine self-administration behavior. Consistently, stress induced alterations in glutamate mechanisms in the nucleus accumbens core (NAcc) have been linked with behavioral findings. Several lines of evidence reported a close linkage between glutamate and the activation of the Nuclear Factor-Kappa B (NF-kB). We propose a central role of Nf-kB signaling in stress -enhanced vulnerability to cocaine self-administration. Thus we designed lentiviral vectors DnIKK, that expresses the dominant negative of the IKK activity to nullify the transcription factor activity. Animals were exposed to stress 2 hs daily for a week. One week after the last stress session, all animals were treated whit lentivirus DnIKK. On day 21, animals were assigned to behavioral studies and biochemical test. Ours results demonstrated that the genetic inhibition of NF-kB, was sufficient to prevent stress-induced cross sensitization to cocaine and the facilitation of cocaine self-administration.These result suggest a central role of NF-kB on the long-term neurobiological mechanism induced in the NAcc by stress, promoting the expression of cross-sensitization to cocaine and facilitation of cocaine self-administration behavior.

203 | IMPACT OF ORAL EXPOSURE TO LOW DOSES OF THE HERBICIDE 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D) ON THE MOTOR RESPONSE TO COCAINE IN RATS

Disorders of the Nervous System

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4° Laboratorio de Toxicología Experimental, Área Toxicología, Departamento de Ciencias de los Alimentos y el Medioambiente, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario, Santa Fe, ARGENTINA.2,4-D is currently the second most widely used herbicide in the world. Previous evidence from our laboratory indicates that it produces neurotoxic effects in animal models and may contribute to cognitive and psychiatric disorders related to dopaminergic alterations. These changes could also modify the vulnerability to psychoactive substances. Our goal is to determine whether oral exposure to low doses of 2,4-D for a period of 20 days induces changes in the cocaine stimulant effects and whether these changes depend on sex. For this purpose, PND30 rats of both sexes were fed for 20 days with either regular or 2,4-D contaminated food (25 mg/kg/day). Thereafter, in PND50 the rats were individually placed in motor activity boxes. After an hour of habituation, they received a cocaine (5 mg/kg i.p.) or saline injection, and motor response was evaluated for another 2 hours.Although our results are preliminary, they would indicate that female rats experience a significant increase in exploratory response in a novel environment when exposed to 2,4-D. Also, the motor response to cocaine in 2,4-D-treated animals would be different from saline in female rats. In contrast, male rats appeared to show similar results regardless of prior exposure. Even though these results are preliminary, we are confident that they will provide insight into the potential impact of exposure to environmental contaminants on vulnerability to cocaine.

205 | Structural connectivity alterations and Contributions to prediction biomarkers in drug-resistance Epilepsy

Disorders of the Nervous System

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Epilepsy is a chronic and frequent disease. One-third of the patients have drug-resistance, most commonly in the form of Temporal Lobe Epilepsy with Hippocampal Sclerosis (TLE-HS) or Focal Cortical Dysplasia (FCD). Previous studies reported network alterations, but few have compared both types. This study aimed to characterise the global network topology and structural connectivity in TLE-HS, FCD and healthy controls (HC) using diffusion-weighted images (DTI). 115 adults of both sexes (FCD= 20, TLE-HS= 48 and HC= 47) were scanned on a 3T MRI scanner. Weighted connectivity matrices were obtained in DSIstudio. The epilepsy effect on network topology was assessed by general linear models. Sex, age, lateralisation and duration of disease were included as covariates. Results revealed clustering and small-wordness coefficient, transitivity and global efficiency decrease in FCD. The predictive models demonstrated loss of fractional anisotropy in patients, using linear discriminant analysis in NBS predict. Connectivity decrease in right TLE-HS was associated with the duration of epilepsy, particularly in subcortical edges. The model of left TLE-HS revealed significant performance as a classifier, using edges linking temporal and orbitofrontal regions in the ipsilateral hemisphere. FCD model suggested a tendency for connectivity loss. Overall a distinct connectivity reorganization related to the type of epilepsy. The predictive models could be clinically relevant as classifiers.

207 | Multidimensional Evaluation of Surgery for Epilepsy: Longitudinal Study in a Public Hospital

Disorders of the Nervous System

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In the cohort of 111 evaluated patients, the current mean age was 38 years (SD: 10), with 53% being female. The mean age at the time of surgery was 33 years (SD: 10), with a median of 10 seizures per month (mean of 21 with SD of 28). The average duration of epilepsy was 21 years (SD: 12), and the average age of onset was 13 years (SD: 9). Patients had an average of 3 previous antiepileptic medications before surgery (SD: 1). Perinatal antecedents were observed in 5%, while febrile seizures affected 21%, meningitis 9%, and family history of epilepsy or febrile seizures 6%. Regarding the types of surgery, 80% corresponded to anterior temporal lobectomies + amygdalohippocampectomy (ATL + AH), 5% to ATL + AH + extratemporal surgery, and 14% to extratemporal procedures. Left lateralization was present in 59% of patients. Magnetic resonance imaging (MRI) was performed in all patients, with 93% of cases showing lesions. Additionally, 100% of patients underwent Video-EEG, 17% underwent positron emission tomography (PET) (of which 14% were pathological), 23% underwent Stereoelectroencephalography (SEEG), and 8% underwent functional MRI. Pathological anatomies revealed that 68% corresponded to hippocampal sclerosis (HS), 16% to Focal Cortical Dysplasia (FCD) (ILAE type 1 or 2), 5% to cavernomas, 3% to gliomas, 1% to Dysembryoplastic Neuroepithelial Tumor (DNET), and 6% to uncharacteristic findings. The analysis was conducted at an average of 4.29 years post-surgery.

209 | Early-life stress shapes developing prefrontal to dorsal raphe circuit

Neural Circuits and Systems Neuroscience

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Early-life experience can influence neural circuit development. Although this can help an individual to adapt to environmental conditions, it can also lead to maladaptive circuit alterations that could increase the adult vulnerability to develop psychiatric disorders. The stress of maternal separation (MS) in mice during a critical period of ages (between postnatal days (P) 2 to 14) represents a well-established model of how early-life stress alters the adult emotional control with the appearance of anxiety and depressive-like symptoms. We propose that this critical period is a crucial neurodevelopmental window for the maturation of emotional circuits such as the one connecting the prefrontal cortex (PFC) to the dorsal raphe nucleus (DRN). We found that MS increases the PFC synaptic innervation of the DRN, a nucleus known for harboring most of the serotonin (5-HT)-producing neurons, a neurotransmitter key in stress-coping and mood regulation. MS-exposed mice concomitantly show an early enhancement of 5-HT neuron activity in response to stress, suggesting functional changes in the PFC-DRN circuit. Preliminary results indicate that the early activity of PFC glutamate projection neurons engaged in the PFC-DRN circuit could be selectively affected by early-life stress. Our study contributes to the understanding on how early-life adversity impacts on neurodevelopment of mood and emotional brain circuits.

211 | Acquisition of non-olfactory encoding improves odor discrimination in olfactory cortex

Neural Circuits and Systems Neuroscience

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Olfaction is influenced by contextual factors, past experiences, and the animal's internal state. Whether these information is integrated at the initial stages of cortical odour processing is not known, nor how these signals may influence odour encoding. Here we revealed multiple and diverse non-olfactory responses in the primary olfactory (piriform) cortex (PCx), which dynamically enhance PCx odour discrimination according to behavioural demands. We performed recordings of PCx neurons from mice trained in a virtual reality to associate odours with visual contexts to obtain a reward. We found that learning shifts PCx activity from encoding solely odours to a regime in which positional, contextual, and associative responses emerge on odour-responsive neurons that become mixed-selective. The modulation of PCx activity by these non-olfactory signals was dynamic, improving odour decoding during task engagement and in rewarded contexts. This improvement relied on the acquired mixed-selectivity, demonstrating how integrating extra-sensory inputs in sensory cortices can enhance sensory processing while encoding the behavioural relevance of stimuli.

213 | Instrumental role of cortico-striatal neurons of the Anterior Cingulate Cortex in the manifestation of pain-related unpleasantness

Neural Circuits and Systems Neuroscience

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The perception of pain is a multidimensional experience arising from distributed brain activity. However, how the brain encodes this experience remains elusive. Particularly, little is known about the neuronal mechanisms associated with the unpleasantness that characterizes pain.

A key structure for the affective processing of pain is the Anterior Cingulate Cortex (ACC). The dense excitatory connections between the ACC and the dorso-medial striatum may serve as a path for nociceptive information to the mesolimbic system, critical for the motivational modulation of behavior. Here we addressed the instrumental role of ACC cortico-striatal (ACC-CS) neurons in pain-related behaviors using a chemogenetic approach with inhibitory dreadds to interfere with their activity. We characterized in mice reflexive responses to noxious stimuli and more complex behaviors that reflect the subject's motivation to alleviate aversive sensations. Preliminary results indicate that the inhibition of ACC-CS neurons impaired the processing of pain-associated aversion. Thus, dreadd-treated mice showed a defective performance in a real-time conditioned place avoidance test, where control animals avoided spending time in a compartment paired with a noxious stimulus. Finally, additional to extensive behavioral analysis, we are monitoring the activity of ACC-CS neurons through in vivo neuronal calcium imaging using a miniature microscope to discern their role in the encoding of pain-related behaviors.

215 | Activity-dependent synaptogenesis in mossy fiber terminals from adult-born granule cells

Neural Circuits and Systems Neuroscience

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Neurogenesis occurs in the dentate gyrus (DG) of the adult mammalian hippocampus and is involved in spatial encoding and learning. Cohorts of adult-born granule cells (aGCs) are continually added into the DG in a highly regulated process. Projections of aGCs contact interneurons in the hilus as well as pyramidal cells in CA3. Electron microscopy studies have shown that boutons of young aGCs establish new connections on dendritic spines of pyramidal cells already occupied by mossy fiber terminals of mature GCs, leading to postsynaptic spines in contact with multiple boutons. In mature aGCs, the majority of synapses are formed by single boutons. It has been proposed that the more active synapses are more likely to remain connected, suggesting an activity-dependent competition among presynaptic terminals. To test this hypothesis, we aimed to compare the structure of presynaptic terminals in cohorts of aGCs growing under chronic conditions of enhanced activity or electrical silencing in vivo. Preliminary data suggests that aGCs developing in conditions of high activation tend do display more complex presynaptic boutons compared to those that grow under electrical silencing. Moreover, terminals of mature aCGs located in close proximity of active young aGCs show smaller terminals, which hints in favor of synaptic competition. Current experiments are underway to determine whether aGCs at different developmental stages display distinct sensitivity to activity-dependent competition.

217 | Presynaptic voltage gated calcium channels are inhibited by glucagon like peptide 1 receptor (GLP-1R) and ghrelin receptor (GHSR) activity

Neural Circuits and Systems Neuroscience

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Anti-obesity therapies have the potential to improve quality of life of diabetic patients. In this context, the glucagon-like peptide-1 (GLP-1) is a multifaceted gastrointestinal hormone with a large therapeutic potential. GLP-1 receptor (GLP-1R) agonists, like Liraglutide, are commercially available drugs to treat both diabetes and obesity. Another gastrointestinal hormone implicated in food intake is ghrelin, which acts on its specific receptor (GHSR). GLP-1R and GHSR are both G protein coupled receptors (GPCR). We previously demonstrated that GHSR controls neuronal voltage gated calcium channels that control neurotransmitter release and that may contribute to its orexigenic effects. On the other hand, the molecular mechanism by which GLP-1 reduces food intake remains unclear. Here we found that increasing GLP-1R expression reduces CaV2.2 current in a heterologous expression system (GLP1-R plasmid added versus calcium current density linear regression R=0.07514 Slope=70.25 n=120) and that acute Liraglutide 0.2 µM application further reduces the current (current inhibition: 49.47±12,14 % n=4). Notably we observed co localization of GHSR and GLP1-R in brain areas that control food intake such as Lateral Parabrachial Nucleus: T thus we plan to study a putative crosstalk between the effect of these two relevant GPCRs at central level. This work is supported by a collaborative grant with Qatar University (NPRP13S-0209-200315)

219 | A chemogenetic approach to understand the role of the piriform cortex in an olfactory-contextual associative learning task

Neural Circuits and Systems Neuroscience

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In the last ten years, new findings changed the way we think about sensory representations in the cerebral cortex, showing that their nature is plastic and can be modified by experience. In particular, a unique feature of olfactory processing is its high dependence on past experience, context, and the animal's internal state.

To deepen the understanding of the modulation of sensory learning, we developed an olfactory-contextual conditioning paradigm in a virtual reality environment in which mice learn to associate an odor with a water reward when presented in a specific visual context.

Here we studied the piriform cortex (PCx), the largest region of the olfactory cortex, by performing in-vivo electrophysiological recordings while animals behave in the task, and started to address the importance of this brain region by bilaterally silencing its excitatory neurons using chemogenetics.

Interestingly, preliminary results show that silencing PCx impaired the animal's performance. What is more, the ability to distinguish odors was more affected than the one to discriminate visual contexts. These results suggest that the piriform cortex plays an important role in the studied task and that it may be linked to both olfactory and associative functions.

221 | Misinformation and Consolidation Processes in the Performance of Eyewitnesses. Preliminary Results.

Neural Circuits and Systems Neuroscience

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The dynamic nature of memory constitutes a fundamental aspect to consider in the field of eyewitness testimony. The malleability of memories varies as time progresses, determining periods of greater or lesser vulnerability to external influences. In practice, these influences can be related to misinformation suggested intentionally or accidentally by interrogators during the testimonial process.

In this study, we employed an online paradigm to replicate a testimony and recognition process related to a fictional crime. Participants watched a video and were subsequently questioned about it using suggestive questions. The waiting period between viewing the video and the suggestive interrogation varies among different groups, aiming to expose the impact of suggested disinformation during moments when memory could be potentially labile or consolidated. Finally, a second non-suggestive interrogation is conducted, accompanied by recognition lineups.

Preliminary data reveal a susceptibility to misinformation among those participants who responded to the suggestive questionnaire shortly after acquisition, resulting in errors both in recognition and responses to directed questions.

223 | Synchronized oscillations in circadian neurons in Drosophila

Neural Circuits and Systems Neuroscience

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Sleep is an essential behavior in most animals, highly conserved across the animal kingdom. Its timing is regulated by the circadian clock, which in Drosophila comprises around 150 neurons. This work focuses on a cluster of circadian neurons termed LNvs, which play an as-of-yet not fully described role in the regulation of the sleep/wake behavior. LNvs can be further subdivided into large and small LNvs (lLNvs and sLNvs). We performed patch clamp experiments that show sustained oscillations of the membrane potential with frequencies in the order of 0.5Hz, consistently so across individuals. We found that the oscillations disappear upon the exposure to the acetylcholine blocker mecamylamine, and a phase response curve suggests they are exogenously supported. By performing simultaneous patch clamp recordings we found that pairs of similar neurons are highly synchronized, and that the sLNv oscillations lag behind the lLNv oscillations by about a tenth of a cycle. Furthermore, neurons in other regions of the brain were also found to oscillate, and do so at the same frequency than the LNvs, with different degrees of lag, always within a few tenths of a cycle duration. The apparent ubiquity of the oscillations in the fly brain may provide an added layer of complexity to neural information processing, a phenomenon we will study in the future.

225 | AAV-mediated sparse labeling of striatal medium spiny neurons for analysis of dendritic spine density in a mouse model of Parkinson's disease

Neural excitability, synaptic transmission and neuron-glia interactions

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The striatum is involved in action selection/initiation. It loses dopaminergic innervation in Parkinson's disease as a result from mesencephalic dopaminergic neuron degeneration. Animal models show that dopaminergic denervation produces dendritic spine loss in striatal medium spiny neurons (MSNs) of both the direct (D1) and indirect (D2) pathways. In other disorders, dendritic spine loss has been linked to the dysfunction of microglia, immune cells with phagocytic capacity.

We hypothesize that reactive microglia in experimental parkinsonism participate in the pruning of striatal synaptic structures.

Here we characterized the time course of dopaminergic denervation of the striatum in a mouse model of experimental parkinsonism. We observed maximal dopaminergic denervation of the striatum 1 week post-lesion. To label MSNs, we administered a viral vector (AAV PHP.eB-pAAV-CAG-GFP) to reporter mice for D1 neurons (D1 Tom) with or without denervation that received doxycycline (a microglia inhibitor) or vehicle from 1 to 6 weeks post-lesion. We present an exploration of analysis parameters of micrographs acquired under structured illumination microscopy to determine dendritic spine density in MSNs in these groups to ultimately analyze correlation between spine density and behavior.
If the results support our hypothesis, it will contribute to position microglia-mediated processes as potential therapeutic targets to treat the disease.

227 | Optogenetic activation of inner hair cells in the mammalian cochlea

Neural excitability, synaptic transmission and neuron-glia interactions

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Inner hair cells (IHCs) in the mammalian cochlea are considered the true phonoreceptors as they are responsible for both the detection of environmental sounds and the signaling of acoustic information to the brain. IHCs present synapses with spiral ganglion neurons (SGNs) that are characterized by the presence of a specialized presynaptic organelle called ribbon. Due to the critical role that these synapses play, multiple studies have concentrated in investigating the physiological basis of its function. However, due to the fragility of the tissue and small size of these cells, purely electrophysiological approaches have been challenging. Here, we investigated the possibility of expressing the light-activated conductance, channelrhodopsin2 (ChR2), in IHCs to circumvent the need for a patch-clamp electrode controlling these cells. Mice carrying a floxed ChR2 cassette were crossed with others expressing Cre under the control of the vesicular glutamate transporter type 3 promotor. The specific expression of ChR2, fused to YFP, was visualized in IHCs, whereas the photo-currents were elicited by illumination with a 470 nm LED at various intensities and recorded by the patch-clamp technique. The relationship between the amplitude of these light responses and the LED power was drawn, finding a maximum photo-current of 520 ± 77 pA with a narrow dynamic range, since minimal to maximal activation was achieved within ~12.5 % of the total LED potency.

229 | Striatal somatostatinergic interneurons physiology in control and parkinsonian mice

Neural excitability, synaptic transmission and neuron-glia interactions

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Parkinson's disease (PD) is a neurodegenerative disease whose symptoms are caused by loss of nigrostriatal dopaminergic neurons and subsequent changes in striatal circuitry function. Chronic administration of L-dopa remains the gold standard treatment, but patients often develop involuntary movements known as L-dopa-induced dyskinesia (LID). Altered function of striatal interneurons regulating the balance of the striatal projection pathways may be linked to the emergence of PD symptoms and LID. Here, we focus on GABAergic striatal interneurons that also release somatostatin (iSOM). We have seen that LID in PD mice relates to an enhanced expression of the cell activity marker c-Fos in iSOM. Using ex vivo patch-clamp recordings, we are studying iSOM physiology in control, PD and dyskinetic mice. Under control conditions, 64% of iSOM are spontaneously active even after GABAergic and glutamatergic synaptic blockade and exhibit a variety of firing frequencies (from 2 to 20 Hz) and activity patterns (from regular to bursty). Whole-cell recordings show transitions between regular pacemaker-like firing and a burst-pause pattern in individual iSOM. Moreover, some iSOM show very depolarized membrane potentials leading to depolarization block of firing. We are performing cell-attached recordings to assess the effects of dopaminergic denervation and chronic L-dopa treatment on the spontaneous activity of iSOM.

231 | Towards a comprehension of dopaminergic modulation of pain: physiological, morphological and neurochemical characterization of dopamine-sensitive neurons of the Anterior Insular Cortex.

Neural excitability, synaptic transmission and neuron-glia interactions

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Pain is a sensory and emotional experience that arises from distributed brain activity. The anterior insular cortex (AIC) is a key brain region for pain perception, integrating sensory, emotional, motivational, and cognitive functions. The mesolimbic dopaminergic system, known for responding to motivational events, modulates pain perception and is disrupted in pathological pain conditions. Dopamine release in the AIC affects nociception, particularly inducing pain relief through D1 receptors (D1R). Despite this, it is not clear how dopamine controls AIC microcircuits activity.
In order to characterize the dopaminergic system of the AIC in mice, we first identified dopamine-sensitive neurons within the AIC. Our findings revealed that D1R-bearing neurons located in the superficial layers of the AIC are primarily inhibitory interneurons, while D1R-positive cells in deeper layers comprise both pyramidal cells and interneurons. Through a combination of immunohistochemistry, electrophysiology, and morphological reconstructions, we thoroughly characterized the interneurons expressing D1R in the AIC. Furthermore, we assessed the impact of D1R agonists on the excitability of these neurons.
Together, this data will aid in comprehending how dopamine influences information integration in AIC microcircuits. In the near future we will address the role of AIC dopamine-sensitive neurons on pain related behaviors using neuronal calcium imaging in vivo and chemogenetic manipulations.

233 | Differential effects of dopamine agonism in the nucleus accumbens between conditioned taste aversion and latent inhibition depend on the degree of familiarity with sugar.

Neurochemistry and Neuropharmacology

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The reward system integrates the sweet taste with positive post-ingestion consequences. This system, activated by dopamine, becomes more active when sweet foods are repeatedly excessively consumed beyond homeostatic needs. The nucleus accumbens shell (NACsh) is a key part of this circuit and acts as a sensor, promoting hedonic feeding. However, the role of dopaminergic activity in the NACsh during the formation and extinction of aversive taste memories needs further detailed study. Accordingly, this research aimed to evaluate the effects of bilateral infusion of the dopaminergic agonist apomorphine in the NACsh before the acquisition of conditioned taste aversion (CTA) and latent inhibition (LI). Groups of Wistar rats were exposed to varying levels of sugar familiarity before CTA acquisition: Novel, familiar, and high-familiar. Each group was divided into two treatment subgroups: control (Dimethyl sulfoxide at 10% in physiological saline; 0.05 ul/0.5 ul) or apomorphine (9 ul/0.5 ul). Our results demonstrate that during the acquisition and retrieval of aversive memory, apomorphine treatment did not affect novelty, familiarity, and high familiarity groups compared to controls. Furthermore, the apomorphine treatment in the novelty group did not enhance CTA extinction. In the familiarity group, it did not increase LI, but it did in the high-familiar group. These outcomes collectively suggest the varying activity of dopamine receptors based on the level of sugar familiarity.

235 | Phthalocyanines as Molecular Scaffolds to Block Disease-Associated Protein Amyloid Aggregation: The case of α-Synuclein

Neurochemistry and Neuropharmacology

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Parkinson´s disease (PD) is the second most common age-related neurodegenerative disorder, affecting millions of people worldwide. α-Synuclein (αSyn) is a highly soluble, intrinsically disordered protein that is abundantly expressed in the brain and predominantly localizes to presynaptic terminals, in close proximity to synaptic vesicles. Since misfolding and amyloid aggregation of αSyn is thought to play a critical role in PD, the aggregation pathway of the protein represents then an obvious target for therapeutic intervention in this disorder. Therefore, understanding the molecular events behind αSyn amyloid assembly and its inhibition is of high clinical importance. In this context, the discovery of small molecules targeting disease-associated protein aggregation is considered one of the most active therapeutic approaches. From the screening of large libraries of small molecules, potential candidates with different chemical structures were found to modulate the aggregation of distinct amyloid proteins. Notably, poly-aromatic scaffolds belonging to polyphenols and porphyrinoids were predominantly identified by these screenings. Particularly, phthalocyanines were shown to exhibit anti-scrapie activity and inhibition of αS, tau, and Aβ amyloid assembly. In this work, we report at a residue specific level of resolution the structural and molecular basis for the inhibitory mechanism of a phthalocyanine molecule on αs fibril amyloid assembly.

237 | Folate modulates the effects of third-trimester gestation-equivalent ethanol exposure

Neurochemistry and Neuropharmacology

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Prenatal exposure to ethanol (PEE) results in various neurobehavioral deficits in the developing fetus. In rats, the period spanning postnatal days (PDs) 4-9 corresponds to the human third trimester of gestation and is characterized by rapid synaptogenesis, myelination, and maturation of crucial brain structures and transmitter systems. Seeking potential remedies to counteract the harmful impacts of PEE, researchers have turned their attention to nutritional supplements like folate, a member of the vitamin B family that plays a vital role in DNA synthesis, amino acid metabolism, and strengthening antioxidant defenses. We assessed anxiety responses, open field activity and ethanol intake in male and female rats that, on PDs 4-9, had been administered ethanol (0.0 or 5 g/kg/day) preceded by folate (0.0 or 20 mg/kg). Neonatal exposure to ethanol did not modify anxiety responses nor exploratory activity but led to reduced body weight during infancy and reduced ethanol intake at adolescence. The latter effect, which likely reflects conditioned aversion derived from the pairing of ethanol's sensory and pharmacological effects, was countered by folate administration. Folate also ameliorated ethanol-induced reductions in body weight. These findings suggest that folate, a treatment with minimal adverse effects, holds the potential to modulate neurobehavioral consequences of prenatal ethanol exposure.

239 | Role of Wnt canonical pathway on the impact of Social Isolation during adolescence over cocaine effects in rats: sex-specific differences.

Neurochemistry and Neuropharmacology

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Adolescence is a developmental period associated with high stress sensitivity. Likewise, some evidence supports the relationship between stress exposure and drugs use. Our team is focused on understanding the role of Social Isolation (SI) as well as age and sex in vulnerability to cocaine in rats. Furthermore, we are evaluating the role of the Wnt canonical pathway by measuring b-catenin levels in brain areas. Recently, we showed that 5 days of SI from postnatal days (PND) 30 to 35 decreases b-catenin levels in Prefrontal Cortex (PFC); and increases cocaine response in adult male rats. Here, we examine if 5 days of SI (PND30-35) would induce cocaine sensitization on PND45 as well as changes on b-catenin levels in PFC, in female and male rats. Our results showed that SI induced cocaine (5mg/kg i.p.) sensitization only in male rats ($p<0,05$). Also, isolated males displayed lower exploratory ($p<0,05$) and higher anxiety ($p<0,05$) responses than controls. In contrast, female rats showed similar cocaine responses regardless previous SI exposure. In addition, b-catenin levels in PFC would decrease after cocaine injection in control as well as in isolated male rats ($p<0,01$). Moreover, the role of PFC's b-catenin in SI-induced cocaine sensitization will be confirmed by intraPFC pathway inhibitor infusions. Overall, these results contribute to understand the behavioural and neurobiological differences associate to stress impact during adolescence, over cocaine effects on both sexes.

241 | Pharmacological blockage of the growth hormone receptor reduces ad libitum and ghrelin-induced food intake in mice

Neuroendocrinology and Neuroimmunology

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The neuroendocrine mechanisms that regulate food intake are only partially known, despite such behaviour is essential for survival. Ghrelin and growth hormone (GH) are two orexigenic hormones that act via growth hormone secretagogue receptor (GHSR) and GH receptor (GHR) respectively. In mice, both hormones increase food intake by acting on the AgRP/NPY neurons of the hypothalamic arcuate nucleus (ARH) and their actions seems to crosstalk. Recently, we reported that mice with genetic ablation of GHR specifically in neurons fail to increase food intake in response to ghrelin. Since the genetic ablation of GHR also affects neural circuit connectivity, we take advantage of the well-characterize GHR antagonist pegvisomant to test if the acute pharmacological blockage of GHR affects ghrelin-induced food intake in mice. We found that pegvisomant (4 mg/Kg, ip) decreases acute food intake in wild-type, but not in GHR-knock out, mice as well as NPY gene expression in the ARH. Also, we found that pegvisomant treatment abrogates the orexigenic effects of systemically injected ghrelin (0.2 mg/kg) but does affect the ghrelin-induced increase of c-Fos in the ARH. Thus, pharmacological blockage of GHR signalling in mice reduces ad libitum and ghrelin-induced food intake via a mechanism that may involve NPY expression in the ARH.

243 | Agouti-related protein-expressing neurons mediate enhanced saccharine intake in calorie restricted male mice

Neuroendocrinology and Neuroimmunology

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Animals under calorie restriction (CR) display enhanced reward-related behaviors towards palatable stimuli, and the molecular basis underlying such adaptations remain uncertain. Agouti-related protein (AgRP)-expressing neurons, located in the arcuate nucleus (ARH), are able to sense circulating factors. AgRP neurons are activated under energy deficit condition, such as CR, and the connection between AgRP neurons and reward-related behaviours is established. We studied if AgRP neurons orchestrate the enhancement of reward-related behaviours observed in mice under CR. Male mice were fed with the 40% of their daily food intake for 5 days and were also exposed to a non-caloric sweetener solution, saccharine, for 4 hours before each meal. Wildtype mice under CR showed an increase of saccharine intake. Using an ARH ablated mouse model, we found that the ARH integrity was required for CR-induced enhancement of saccharine intake. The use of Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to selectively inhibit AgRP neurons led to a reduction of CR-induced enhancement of saccharine intake. Conversely, excitatory DREADDs selectively in AgRP neurons showed that activation of AgRP neurons alone was sufficient to induce saccharine intake in ad libitum fed mice. In conclusion, AgRP neurons activation is required for enhanced saccharine intake in CR, and sufficient to induce saccharine intake in fed mice.

245 | Exploring the Relationship Between Sleep and Immunity

Neuroendocrinology and Neuroimmunology

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There is evidence that sleep has a supportive role in the immune response. The present study focuses on the concept of sickness behavior, which includes a whole series of behavioral changes that arise in response to immune system activation. Previous results demonstrate that changes in sleep and activity are some of the most common behavioral manifestations of infection, seen in vertebrates and invertebrates. However, we still lack a complete understanding of the mechanisms underlying the interactions between both systems. To investigate this, we used the fly Drosophila melanogaster as an experimental model. Its experimental adaptability, coupled with our knowledge of its sleep and innate immunity mechanisms shared with mammals make it an ideal candidate.

Evaluation of behavioral outcomes to infection were done manually via thoracic injections with a precision microinjector. Monitoring of activity patterns was achieved by real-time tracking and analysis through a behavioral profiling platform. Specifically, we injected Staphylococcus aureus and Enterococcus faecalis, Gram positive lethal bacteria that induce the Toll pathways, one of the insect immune arms. We analyzed lifespan and several activity and sleep parameters. We manage to recapitulate the behavioral responses characterized by an increasing activity and a subsequent reduction to sleep. We also tested different concentrations of bacteria, searching for a sublethal dose that induce the behavioral change.

247 + CO-3-Microcine | Study of ghrelin transport in hypothalamic tanycytes and their possible involvement in ghrelin CSF clearance

Neuroendocrinology and Neuroimmunology

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Hypothalamic tanycytes are polarized ependymoglial cells that line the ventral part of the third ventricle (V3) and emit processes through the hypothalamic parenchyma and median eminence contacting blood vessels, neurons and other glial cells. We recently described that tanycytes internalize the orexigenic hormone ghrelin trough clathrin-mediated endocytosis. Here, we study its uptake and transport direction in these cells with a fluorescent ghrelin tracer (Fr-ghr) using in vivo, ex vivo and in vitro strategies. First, we centrally injected mice with Fr-ghr and observed a fluorescent signal in tanycytes 15 min post-injection that was reduced by 87% at 30 min and returned to control values at 60 min. We then studied mouse hypothalamic explants incubated with Fr-ghrelin on their outer side (contacting terminals) or within the V3 (contacting soma), and observed fluorescence within tanycytes only in the second condition. Finally, we used primary cultures of rat hypothalamic tanycytes incubated with a 5-min pulse of Fr-ghr to quantify the intracellular redistribution of fluorescent signal over time. We observed that the signal was mostly found in somas after the 5 min pulse, and significantly increased in processes and terminals after 10 min. After 30 min, fluorescence decreased in the whole cell.
This evidence shows that tanycytes internalize ghrelin in their CSF-contacting soma and transport it to their terminals, possibly playing a role in CSF ghrelin clearance.

249 | Previous reproductive experience increases the ratio of dopaminergic D1:D2 receptors in the striatum and the effect of a D1 antagonist in postpartum estrous rats

Neuroendocrinology and Neuroimmunology

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Postpartum estrous (PPE) rats, which are maternally and sexually motivated, prefer the pups over a male; however this preference is stronger in females with a previous reproductive experience than in primiparous rats. As mesocorticolimbic dopaminergic system and dopamine in the medial preoptic area have been implicated in the control of maternal motivation, this study aimed to determine if this system differs between primiparous (PRIM) and multiparous (MULT) PPE females. To board this question we employed two strategies: 1) compared the expression of the dopaminergic receptors D1 and D2 in nucleus accumbens(NAcc), medial prefrontal cortex, medial preoptic area, and dorsal striatum(DS) between these mothers, and 2) compared the effect of the D1 antagonist SCH-23390 on maternal behavior and locomotor activity of PRIM and MULT rats. MULT females exhibited a greater binding to the D1 antagonist [H3]-SCH-23390 than PRIM dams in NAcc and DS, but no differences were detected in other areas. MULT females presented a reduced binding to the D2 antagonist [H3]-nemonapride only in the NAcc shell. Moreover, while 0.025 and 0.05 mg/kg sc of SCH-23390 increased the latency to reunite the litter in the nest and decreased locomotor activity of the dams, the effects of the lower dose were greater in MULT females. These results reveal a possible mechanism that can partially underlay the motivational differences between PRIM and MULT PPE rats.

251 | Automated clustering of larval zebrafish motor behavior reveals two different modes of fast escapes

Sensory and Motor Systems

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Detecting threats and triggering adequate evasive behaviors when warranted is one of the most critical behaviors animals perform. However, not all stimuli trigger the same evasive behaviors and we still have a rudimentary understanding of how the brain processes sensory information to select the correct motor behavior.

Zebrafish show a diversity of evasive behaviors some of which have a known neural basis, but how stimulus salience affects the selection of specific motor behavior is not known.

To bridge this gap, we filmed behavior of larval zebrafish while presenting a set of threatening visual and auditory stimuli, which triggered diverse evasive responses. Since manual labeling of hundreds of individual responses is extremely time consuming and prone to biases, we developed an automated pipeline to identify fast evasive behaviors.

We first extracted animal trajectories using DeepLabCut. Next, we developed an algorithm that segments the trajectory and recognizes rapid motor events, including evasive responses. Employing methods for dimensionality reduction (t-SNE, UMAP, autoencoders) and clustering (K-means, Random Forest), we categorized the events into three consistent groups: 1) slow escapes to visual stimuli, 2) fast escapes to auditory and multisensory stimuli, 3) non-evasive fast reactions. Our findings strongly support the hypothesis of two discrete modes of escape: fast and slow with no intermediate motor patterns.

253 | Intensity and polarization cue summation enhances object discrimination

Sensory and Motor Systems

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The usage of polarized light to enhance object or motion detection, termed object-based polarization vision, has been recognized in a number of animals inhabiting intertidal and aquatic environments. However, the visual computations and neural mechanisms underlying such capabilities remain unknown.

In the last couple of years we have been studying the polarization contrast sensitivity in the grapsid crab Neohelice granulata. We quantified the escape response and the changes in heart rate of animals evoked by a looming disk with an 82° polarization difference between the object and the background. More than 90% of the animals responded by freezing or escaping. We co-rotated the e-vector of light from object and background and found that the escape response varied periodically with a 90º period. Maximum responses were obtained for object and background e-vectors near the vertical and horizontal orientations. The cardiac response matched these results. In line with theoretical models, our results provide experimental evidence that crabs perform a two-channel (vertical/horizontal) computation to achieve object-based polarization vision maximizing sensitivity in its natural environment (Basnak et al., 2018). To study how polarization contrast (PC) is combined with intensity contrast (IC) information we modified a 3D monitor to modulate differentially the intensity of vertical and horizontal polarized light. We confronted animals with edge motion stimuli translating laterally.

255 | Central auditory synapse alterations in mice with enhanced and suppressed medial olivocochlear efferent activity.

Sensory and Motor Systems

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Spontaneous activity in the immature inner ear plays a critical role in the development of precise connectivity in the central auditory system. This is modulated by the medial olivocochlear system (MOC). In mice with enhanced MOC activity (KI), synaptic dysfunctions were observed in the medial nucleus of the trapezoid body (MNTB) (Di Guilmi et al., 2019). In the present work, we performed electrophysiological recordings and morphological 3D reconstructions of the calyx of Held (CH)-MNTB synapse at P12-14 in three mouse models: WT, KI and KO (which lacks MOC activity). Short term synaptic plasticity (STP) experiments displayed a significant higher rate of depression in the KI than WT and KO (10Hz; τWT=2.99±0.21s, τKI=1.96±0.24s, τKO=3.42±0.56s, n=16, ANOVA, p=0,001; 100Hz; τWT=4.89±2.42s, τKI=2.32±0.98s, τKO=7.09±1.58s, n=16, ANOVA, p=0.013). Morphological analysis of CHs in WT and KI mice by volumetric reconstructions from serial electron microscopy images at P25 showed that the KI has a lower proportion of complex CHs compared to WT (69% vs. 83%). Considering that the CH morphology determines the STP, the larger depression rate in the KI aligns with the observation that principal MNTB neurons receive innervation from CHs with simple morphologies (Grande & Wang, 2011). The present results suggest that the transient cochlear efferent innervation to IHCs during the critical period is involved in setting the correct synaptic transmission at central auditory nuclei.

257 + CO-9-Auditorio | Replay of respiratory song patterns during adult canaries night sleep

Sensory and Motor Systems

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Activation of circuits in the forebrain during sleep has been linked to the consolidation of memories, including motor memories. However, the specific motor patterns reproduced during sleep remain largely elusive in any system. Single-cell measurements in these brain areas in songbirds have not allowed the detection of specific song patterns and a precise study of variants not observed during daytime performance. It has recently been discovered that in zebra finches this activity can be detected in the muscles of the vocal organ. Interestingly, this activity was not simultaneous with song-like respiratory events, which were thought to be inhibited. In this work we show that domestic canaries (Serinus canaria) exhibit spontaneous song-like activity in respiratory muscles and in air sac pressure fluctuations. These events are frequent predominantly towards the end of the night, shorter than daytime vocalizations but with similar rhythmic patterns. We find that the syllable sequences observed during the night deviate from the most probable sequences during daytime vocalizations. More generally, this result contributes to a program aimed at quantitatively studying dreamt complex motor patterns.

259 | Speech-induced suppression during natural unsubscripted dialogues

Sensory and Motor Systems

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When engaged in a conversation, one receives auditory information from the other's speech but also from the own speech. However, this information is processed differently by an effect called Speech-Induced Suppression (SIS). Here, we studied brain representation of acoustic properties of speech in natural unscripted dialogues, using concurrent electroencephalography (EEG) and high-quality speech recordings from both speakers. Firstly, we reproduced a broad range of previous findings on listening to another's speech using encoding techniques from different speech features (spectrogram, envelope, phonemes, etc). Moreover, we achieved better performance when predicting the EEG signal even in a complex scenario such as natural dialogues, in particular in the theta band. Secondly, we found no response when listening to oneself on different frequency bands, evidencing a strong effect of SIS. The present work shows that this mechanism is present, and even stronger, during natural dialogues. Furthermore, the methodology presented here opens the possibility of a deeper understanding of the related mechanisms in a wider range of contexts and an increasing complexity in speech features.

261 | Neural oscillations are synchronized to birdsong rhythms

Sensory and Motor Systems

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The generation of complex behaviors, like vocalizations, requires precise interactions among the nervous system, peripheral systems, and the environment. A well-established model is the song of oscine birds, whose production involves precise control of the respiratory system and vocal organs, receiving neural input from the “neural song system.” Specifically, the telencephalic nucleus HVC (proper name) is involved in perception, learning, and plays a crucial role in generating motor commands, yet the neural coding is still under research.
We analyzed extracellular electrophysiological recordings of 4 adult male canaries (Serinus canaria) during song production, recorded in different stereotaxic coordinates of HVC over several days. We investigated the relationship between neural activity peaks and song rhythm, aiming to determine if they are correlated. We compared the multiunit activity profile with the sound envelope. Our findings unveil synchronized neuronal firing with the ongoing song, with distinct phase-locking patterns dependent on the repertoire of phrases sung by the individual and the spatial coordinates of the neuronal recordings. We categorized these behaviors, quantifying their properties.
These findings deepen the understanding of the neural coding in the HVC at a broader analytical level. By analyzing the general profiles of sound envelopes and multiunit activity, we employed a perspective that provides additional information complementing single-unit data.

263 | ROLE OF THE BRAINSTEM IN MOTOR LEARNING

Sensory and Motor Systems

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Mammals have the ability to generate an infinite variety of motor behaviors, from simple actions such as walking to highly complex movements like object manipulation or speech. Some motor patterns are present at birth while new motor skills can be acquired through training and experience. Communication among numerous brain areas is needed to ensure accurate acquisition and execution of motor programs. However, the classical model for motor learning proposes that only a subset of structures along the motor command pathway within forebrain and cerebellum are subjected to activity-dependent adjustments and become reorganized during acquisition of a new skill. In contrast, downstream motor regions located in the brainstem are considered to be simple executive centers for stereotyped motor behaviors. In this study, we challenged this model by testing the role of a midbrain region classically described as a locomotor center in learning the accelerating rotarod task. In this task, mice learn new motor strategies to stay in a rod that is rotating at increasing speed. By using a combination of strategies ranging from local drug administration, molecular biology, cutting-edge viral and mouse genetic tools, and unsupervised machine learning techniques to classify animal's behavior, we have found that the midbrain locomotor center is necessary to consolidate this new skill.

265 | Temporal context influences the error correction mechanism in a paced finger tapping task

Sensory and Motor Systems

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Sensorimotor synchronization (SMS) is the mainly specifically human ability to move in sync with a periodic external stimulus, as in keeping pace with music. The most common experimental paradigm to study its largely unknown underlying mechanisms is the paced finger tapping task, where a subject taps to a periodic sequence of brief tones. Contrary to reaction time, this task involves temporal prediction because the subject needs to trigger the motor action in advance in order for the tap and the next stimulus to occur simultaneously, and an error correction mechanism takes the past performance as input to adjust the following prediction. In a different temporal task, it has been shown that exposure to a distribution of temporal intervals creates a “temporal context” that can bias the estimation/production of a single target interval. As temporal estimation and production are also involved in SMS, we asked whether a paced finger tapping task would show any temporal context effect. In this work we show that temporal context can indeed be generated in a paced finger tapping task via period perturbations, and that the shape and size of the resynchronization curve (synchrony error as a function of stimulus number) depends on the temporal context. We conclude that the underlying error correction mechanism in SMS depends on the temporal context in much the same way as in other, simpler temporal tasks.

267 | Neural Patterns in the Hybrid Search Task on Natural Scenes: Concurrent EEG and Eye-tracking Study

Theoretical and Computational Neuroscience

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In everyday behaviors, often arises the need to locate a single instance from a range of possible targets in a display containing distractor items. For instance, imagine we are inspecting a supermarket aisle to find a specific cookie from a list of our preferred ones. The cognitive constrains and the concurrent memory load may play crucial roles in elucidating how ecologically relevant parameters collectively impact neural activity. Through a concurrent EEG and eye-tracking experiment, we investigated the influences of task-related variables on fixation-related potentials (FRPs) during a hybrid search paradigm, where participants sought any of multiple memorized targets, with varying memory set sizes (MSS). We explored the contributions of different task components on the fixation evoked-responses, including task progression, target presence, and the MSS, using linear model-based analysis. This approach effectively handled the temporal overlap inherent in natural viewing responses. Additionally, we implemented a specialized tool for conducting this type of analysis in Python, enabling us to explore solvers other than ordinary least squares (OLS) that are more aligned with the characteristics of actual data. Altogether, we showed how combining empirical and analytical approaches allows us to distinguish interacting neural processes while preserving the genuine traits found in real-world tasks.

269 | Unmasking visual perception: neural-like representations emerge in artificial neural networks optimized for Bayesian probabilistic inference.

Theoretical and Computational Neuroscience

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The Bayesian theory of visual perception assumes that, given a stimulus, the brain performs probabilistic inference to estimate probabilistic distributions over unobservable variables. This process involves combining sensory information with previous expectations captured by a prior distribution. To understand how this process might occur in the cortex, we train artificial neural networks for a perceptual task: performing Bayesian inference in the context of natural images. In this case, we train Variational Autoencoders, which simultaneously learn a generative model of image patches alongside the corresponding inference model. We show that, under the requirement of optimal inference and using sparse activations, representations similar to those observed in the visual cortex emerge within the network. Notably, when an explicit contrast variable is included in the model, the network is able to not only correctly represent mean estimates about these unobservable variables but also the level of remaining uncertainty after the observation.

271 | Flexible Attractors in Entorhinal Networks

Theoretical and Computational Neuroscience

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Entorhinal grid cells use a hexagonal pattern to encode spatial information based on an animal's location. Maps within a grid cell module share spacing and orientation, differing only in relative two-dimensional spatial phases. Feed-forward networks model grid pattern formation, with entorhinal cells assimilating spatial inputs through Hebbian plasticity. Alignment can be achieved if a two-dimensional continuous attractor recurrent connectivity is imposed. Yet, this architecture has the drawbacks of being complex to construct and rigid, allowing no deviations from the hexagonal pattern such as the ones experimentally observed.

Our study proposes a simpler approach: a one-dimensional attractor for grid alignment. Employing topological data analysis, population activity constitutes a torus-like sample, retaining essential architectural features. Contrary to convention, in our model, architecture and attractor representation aren't topological identical entities, challenging prior assumptions of brain-wide attractor networks.

We also explore the possibility that one-dimensional attractors could enable path integration computations by harmonizing feed-forward and recurrent inputs along a 1D track. We discuss how extending these ideas to an open field exploration would suggest that entorhinal networks are not specifically tuned to perform 2D path integration but rather benefit from a simpler connectivity scheme which enables them to perform more flexible computations.

273 + CO-8-Auditorio | Self-supervised learning approach for inter-subject transfer learning in motor imagery brain-computer interfaces

Theoretical and Computational Neuroscience

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Reducing calibration time is crucial for enhancing the usability of brain-computer interfaces based on motor imagery. Due to the high inter-user variability of electroencephalography (EEG) signals, a user traditionally has to endure long and tedious calibration sessions to collect enough personalized training data before using the system. This need has become even more evident with the advent of deep learning decoding models, whose performance strongly depends on the volume of data available for training. Inter-user transfer learning, where other users' data is used to train the model, reduces the required amount of personalized training data. In this context, self-supervised learning strategies can be used to pretrain the first stages of the model on a pretext task and then adapt it to the task of interest through fine-tuning with a few data from the target user.

Here, we propose a self-supervised learning approach based on a fully convolutional encoder-decoder network. The reconstruction of EEG segments of a channel is used as the pretext task. Then an ensemble of the pre-trained encoders per EEG channel, followed by a classification block, conforms the final decoding model. This model is fine-tuned with a small dataset of the target user in the final MI-classification task.

275 | Quantifying Cerebral Dynamics in Parkinson's: Deep Brain Stimulation Effects Explored

Theoretical and Computational Neuroscience

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Parkinson's disease stands out as a prominent neurodegenerative disorder with profound impacts on both movement and muscular control, affecting a global community of over 6 million individuals. Among the array of available treatments, Deep Brain Stimulation (DBS), characterized by the implantation of cerebral electrodes, has emerged as a highly effective intervention. By delivering electrical pulses, DBS alleviates motor symptoms such as tremors and rigidity, thereby enhancing patients' overall quality of life. However, beneath its impressive efficacy, a pivotal question lingers: What precisely unfolds within the cerebral dynamics of a person with Parkinson's, and how does DBS modulate these dynamics?

To unravel this intricate inquiry, our investigation delved into a meticulous analysis of high-density EEG records sourced from Parkinson's patients experiencing both active and inactive DBS, juxtaposed against a control group. Employing classical metrics like power spectrum and drawing from information theory, encompassing entropy and complexity, we aimed to uncover nuanced shifts in neural patterns and responses induced by DBS.

Our results reveal significant differences in the power spectrum and information quantifiers between control subjects and those with Parkinson's when DBS is turned off. However, these differences noticeably diminish when DBS is turned on. This suggests that brain dynamics are indeed impacted by Parkinson's disease, yet the implementation of DBS tends

277 | Meaningful feedback: user-centered coadaptive brain-computer interfaces

Theoretical and Computational Neuroscience

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Brain Computer Interfaces (BCIs) are systems that measure the brain activity and convert it into artificial control outputs. For motor neurorehabilitation, these technologies can be used to transform movement attempt/imagination into visual and/or somatosensory feedback. Experimental evidence shows that up to 50% of people are not able to command a BCI in the first session. Of these, about 20% are unable to gain control of the BCI throughout session of usage. In this work we design a user-centered stimulation protocol which provides feedback based on operant conditioning, taking into account optimal levels of attention and motivation.

The protocol is designed as a videogame, considering contributions from cognitive-behavioral psychology. The Neurofeedback is based on the outputs of an algorithmic solution that can adapt to the user's brain changes. The user needs to focus on the imagination of the grasping movement to reach a bag full of money. The feedback is designed so as to be adjusted as the user's performance improves, aiming to achieve the greatest possible autonomy from the algorithm. The reinforcers will gradually decrease depending on the subject's performance. The level of fatigue will be monitored to stop or/and pause the game when necessary. A diary of progress will also be delivered to the user by the end of each BCI session. We expect that by means of this percentage of inefficiency in BCI users disminish.

279 | Contribution of image statistics and semantics in local vs. distributed decoding of EEG rapid serial visual presentation

Theoretical and Computational Neuroscience

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Spatio-temporal patterns of evoked brain activity contain information that can be used to decode and categorize the semantic content of visual stimuli. This procedure can be biased by statistical regularities which can be independent from the concepts that are represented in the stimuli, prompting the need to dissociate between the contributions of image statistics and semantics to decoding accuracy. We trained machine learning models to distinguish between concepts included in the THINGS-EEG dataset using electroencephalography (EEG) data acquired during a rapid serial visual presentation protocol. After systematic univariate feature selection in the temporal and spatial domains, we constructed simple models based on local signals which superseded the accuracy of more complex classifiers based on distributed patterns of information. Simpler models were characterized by their sensitivity to biases in the statistics of visual stimuli, with some of them preserving their accuracy after random replacement of the training dataset while maintaining the overall statistics of the images. We conclude that model complexity impacts on the sensitivity to confounding factors regardless of performance; therefore, the choice of EEG features for semantic decoding should ideally be informed by the underlying neurobiological mechanisms.

281 | Reintroduction of an extinct song into a population of wild birds

Tools Development and Open Source Neuroscience

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Bird songs are a stellar model in Neuroethology and Neuroscience since they allow us to study, among other things, the process of learning a song by juveniles. In this work, we generate synthetic songs using a mathematical dynamical system derived from an avian production model. Then, we continuously played these synthetic songs through an autonomous and robust ad-hoc electronic system designed to record and play audio files. In this way, we build an artificial vocal tutor for wild juveniles. We use this vocal tutor in the reintroduction of an extinct song into a population of wild juveniles of Rufous-collared sparrows (Zonotrichia capensis). The success of our strategy allows us to study if the synthetic song is preserved and passed to subsequent generations.

283 | Two ‘lab-made’ devices employed as electronic Von Frey test, for animal behavioral neurology experiments.

Tools Development and Open Source Neuroscience

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Our group is dedicated to the study of multipotent adult stem cells and its effects on peripheral neuropathies induced by compression and trauma, analyzing morphological, functional, and behavioral aspects. The devices available to evaluate motor and sensitive responses after a sciatic nerve injury are very expensive. In this context, the aim of this work is to present two devices, built with commercial components. One for electronic Von Frey test and the other for Von Frey test and electrophysiological experiments. The first prototype consists of a simple Arduino with a HX711 module, attached to a single beam load cell. This equipment, considering its simplicity, has the advantage of both being robust and precise. The second device consists of a STM32 attached to an ADS1256 which can be set to achieve two different functionalities. When attached to a load cell with the proper configuration it converts to an electronic Von Frey that can be set to multiple sample rates, in our case, to 1000 samples per second (sps). On the other hand, the equipment set to its maximum sps (30000), can be employed for preliminary electrophysiological studies. Both prototypes were calibrated to up to 60 ±0.1g (a threshold for our normal vs. injured parameters) and their functionality was tested in the rat model of Wallerian degeneration studied in our group. Overall, this lab-made equipment is a good substitute in our country for the otherwise imported and expensive versions currently available.

285 | Study of MPS in transgenic Drosophila melanogaster line using nanobodies for his detection

Tools Development and Open Source Neuroscience

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Axons and dendrites possess a particular arrangement of their cortical skeleton, referred to as the Membrane-associated actin/spectrin Periodic Skeleton (MPS). The MPS is a periodic protein structure consisting of actin “rings” located transversely to the axon and separated every 190 nm by α/β-spectrin tetramer “spacers”, making the MPS only visible using super-resolution microscopy approaches. Most studies have described the MPS in cell culture and the dynamics of the spectrin “spacers” within each period have not been investigated in detail. Our project will shed light into these aspects in the nervous system of Drosophila melanogaster. Since β-spectrin is expressed in all fly cells, it is necessary to “tag” β-spectrin in a cell specific manner. For this, we are using CRISPR/Cas9-mediated editing to produce a transgenic fly, in which the endogenous β-spectrin gene can be recombined in a cell-type and time-specific manner to include C-terminus tags that can then be detected by nanobodies. Thus, a specific neuronal population will recombine to include a C-terminus “ALFA-tag” and that subpopulation can then suffer a second recombination to replace “ALFA-tag” by “BC2-tag”. We are going to show advances in the molecular cloning steps towards CRISPR/Cas9-mediated editing as well as the production of the nanobodies for the detection of the tags. This transgenic fly will allow the examination of dynamical properties of the MPS in nerve tissue.

289 | Comisión Especial SAN de Divulgación y Comunicación

Comisión Especial SAN de Divulgación y Comunicación

Carla Argañaraz ((IFIBYNE, FCEN, UBA), Maria José Bellini (INIBIOLP, La Plata), Maria Mercedes Benedetto (INIMEC, Córdoba), Camila Coll (IFIBIO, Fmed-UBA), Lautaro Duarte. (IFIBYNE, FCEN, UBA), Juan Ferrario. (ININFA,UBA, CONICET, CABA), Nicolas Martorell.(IFIBYNE, FCEN-UBA), Sonia Jazmín Molina.(CEFYBO, UBA-CONICET), Agostina Stahl. (IFIBIO, Fmed-UBA), Lidia Szczupak (IFIBYNE, FCEN, UBA)

Durante el 2023 la comisión se abocó a tres tareas principales:

i)Generación de podcasts en los que se entrevista a miembros de la SAN que trabajan en diversos temas de investigación con el fin de acercarle a la sociedad no solo los contenidos de la investigación sino también las formas en que ésta se realiza y las vivencias de las/los investigadores. Estos podcasts se difunden via Spotify

(https://open.spotify.com/show/6LdyBg9iilTrQ7g9tdAiFX),

ii)Generación de breves artículos científicos que relatan en un lenguaje coloquial los resultados alcanzados por miembros de la SAN y que fueron publicados en revistas internacionales

(https://saneurociencias.org.ar/categoria/articulo-de-divulgacion/) y

iii)Información para socias/os es difundida por Instagram (https://www.instagram.com/saneurociencias/) y por X

(https://twitter.com/SAN_neuroAr).

POSTERS SESSION 2 - Even posters

002 | Neuroanatomical analysis of the mouse brain areas where the actions of growth hormone secretagogue receptor and Glucagon-like Peptide-1 Receptor converge

Cellular and Molecular Neurobiology

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Ghrelin is a stomach-derived hormone that acts in centrally expressed growth hormone secretagogue receptor (GHSR) and increases food intake as well as glycemia. The Glucagon-like peptide-1 (GLP-1) is a gastrointestinal-derived hormone that acts via the GLP-1 receptor (GLP-1R) in order to reduce food intake and glycemia. Interestingly, GHSR and GLP-1R expression has been observed within many similar brain nuclei suggesting they may act on common neuronal sets to mediate its neurobiological effects. Here, we explored the extent of this putative direct GHSR and GLP-1R interaction in the brain. We mapped the distribution of the GHSR in the mouse brain and examined the localization of this receptor using two complementary approaches: 1) binding of a fluorescent-labeled ghrelin (Fr-ghrelin) in wild-type mice, or 2) visualizing the endogenous fluorescence in GHSR-eGFP mice. In both cases, the presence of GLP-1R was visualized by immunohistochemistry using a validated anti-GLP1R antibody. We found that cells containing both GHSR and GLP-1R are mainly located in the lateral parabrachial nucleus. In contrast, simultaneous presence of GHSR and GLP-1R was much less extensive elsewhere in the brain (e.g. hippocampus, hypothalamus). We also found several areas, such as lateral septal nucleus, medial and basolateral amygdaloid nucleus, rich in GLP-1R fibers that seem to contact GHSR+ neurons. Thus, we conclude that GHSR and GLP-1R largely act on distinct but functionally related cells.

004 | Cannabidiol (CBD) is able to release abnormal cholesterol accumulation in aged astrocytes.

Cellular and Molecular Neurobiology

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The brain stands out as the body's most cholesterol-abundant organ, accounting for approximately 25% of the total cholesterol present in the body. Within neurons, cholesterol's significance is underscored by its pivotal role in facilitating neurite growth, synaptogenesis, and the optimal functioning of both pre and post-synaptic compartments. As a result, precise regulation of cholesterol homeostasis within the brain is imperative to avoid potential imbalances that could significantly impair brain performance.
Prior findings from our research group have strongly suggested a connection between the decline in neuronal cholesterol levels during the aging process and the emergence of cognitive impairments. Given the impermeability of the blood-brain barrier to cholesterol, the maintenance of brain cholesterol equilibrium relies heavily on de novo synthesis, primarily orchestrated by glial cells.

In the scope of this study, we present evidence indicating that the aging process triggers an increase in miR33 levels. This, in turn, instigates a Niemann-Pick phenotype in aging astrocytes, leading to the accumulation of cholesterol within lysosomal compartments. Moreover, utilizing astrocyte-neuron cocultures, we have ascertained that the transfer of cholesterol from astrocytes to neurons becomes compromised in vitro-aged astrocytes and could be improved by cannabinoids.

006 | SIGNALING MECHANISMS INVOLVED IN NEURITE OUTGROWTH INDUCED BY ANG II AT2 RECEPTORS

Cellular and Molecular Neurobiology

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We explored neurite outgrowth induced by Ang II AT2 receptors and the participation of different signaling pathways. Previously, we demonstrated that AT2 receptors induced neurite outgrowth in neuroblastoma cell lines, Neuro2A and SH-SY5Y. We used specific inhibitors to enlighten the role of different signaling in neurite outgrowth. SH-SY5Y cells were pretreated with the inhibitors, stimulated with CGP42112 and allowed to differentiate (3 days). Cells exhibiting at least one neurite longer that a cell body showed a 2-fold increase when stimulated with Ang II or CGP42112. Similar results were observed in cells with 2 or more neurites. Our results suggest that PI3K is not important in AT2R-induced neurite outgrowth. On the contrary, inhibition of MEK/ERK, SphK1 and c-Src pathways prevented neurite outgrowth induced by CGP42112. CGP42112 stimulated a rapid and transient (30 sec) phosphorylation of c-Src at residue Y416 (indicative of activation), following by a Src deactivation as indicated by phosphorylation of Y527. In summary, we demonstrated that AT2R-stimulated neurite outgrowth in SH-SY5Y cells involves participation of MEK, SphK and c-Src and suggests a possible transactivation of TrkA. AT2 signaling pathway is a key player in neuronal differentiation and might be a potential target for therapeutic treatments.

008 | Role of oligodeoxynucleotide IMT504 on neural progenitor cells after a demyelination process.

Cellular and Molecular Neurobiology

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Many central nervous system (CNS) diseases, such as multiple sclerosis, occur in the context of demyelination, a pathological process in which the myelin sheaths that surround axons are lost. Remyelination is a complex process where oligodendroglial precursor cells (OPC) proliferate, migrate and mature into oligodendrocytes to restore the myelin sheath in the CNS. Adult neural progenitor cells (NPC) from the subventricular zone (SVZ) can differentiate into OPC and contribute to the remyelination process. IMT504 is a non-CpG oligodeoxynucleotide consisting of 24 nucleotides and characterized by 2 specific PyNTTTTGT sequences. IMT504 has shown immunomodulatory effects and regenerative properties. In this context, our goal is to study the effect of IMT504 on NPC from the SVZ in a rat cuprizone (CPZ) demyelination model. Demyelinated rats were intracranially injected with IMT504 in the lateral ventricle after CPZ withdrawal. Seven days later we analyzed the contribution of NPC to remyelination by analyzing the different cell populations in the SVZ and the surrounding corpus callosum (CC) through immunohistochemistry. Our results showed an increase in OPC (PDGFRα+) and microglial (Iba1+CD68+) cell populations in the SVZ and CC. Altogether, these results show a potentially beneficial impact of IMT504 on NPC cell fate decisions toward a remyelinating lineage and microglial activation.

010 | Study of the role of Protein 4.1/Coracle in the cortical cytoskeleton of Drosophila melanogaster neurons

Cellular and Molecular Neurobiology

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Actin, spectrin, and associated proteins form a periodic membrane-associated skeleton (MPS) that is ubiquitously present in axons and dendrites of all neuronal types. The protein 4.1 stabilizes the spectrin-actin interaction and their connection to the plasma membrane. The protein Coracle (D4.1) in Drosophila melanogaster is the sole ortholog of mammalian protein 4.1. Due to limited knowledge about Coracle in Dm neurons and the fact that protein 4.1 has not been described as part of the neuronal MPS, we will first determine the structure, function, and evolution of Coracle by integrating information from its primary sequence, secondary structure, and protein-protein interactions. To assess whether different Coracle mutants affect the turnover dynamics of spectrin in the MPS, we will evaluate the β-spectrin-GFP fly using FRAP and FCS techniques. Furthermore, super-resolution microscopy techniques ExM and STED will be employed to determine the localization and potential function of D4.1 in the MPS of axons and dendrites in different neuronal populations. Additionally, we will study whether the loss or gain of Coracle function in these specific neuronal populations of larvae and adults modifies the development and/or maintenance of the MPS. We believe that this work, besides establishing the groundwork for understanding Coracle in neurons, will enable subsequent studies associated with other Coracle functions related to MPS dynamics.

012 | PARKINSON'S DISEASE-LINKED V15A ALPHA SYNUCLEIN VARIANT

Cellular and Molecular Neurobiology

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Parkinson's disease can manifest either as a sporadic form, which is common or as an inherited autosomal dominant trait resulting from missense mutations. Nine potentially pathogenic variants of α-synuclein (αSyn) associated with familial PD have been identified to date. This includes the well-studied A30P, E46K and A53T variants, as well as A30G, H50Q, G51D, A53E, and A53V. Recently, the novel α-synuclein variant V15A was identified in two Caucasian and two Japanese families with Parkinson's disease. Using a combination of NMR spectroscopy, membrane binding assays, and aggregation assays we show that the V15A mutation does not strongly perturb the conformational ensemble of monomeric α-synuclein in solution, but weakens its affinity for membranes. Attenuated membrane binding raises the concentration of the aggregation-prone disordered α-synuclein in solution, allowing only the V15A variant but not wild-type α-synuclein to form amyloid fibrils in the presence of liposomes. These findings, together with earlier research on other missense mutations of α-synuclein, suggest that maintaining a balance between membrane-bound and free aggregation-competent α-synuclein is critical in α-synucleinopathies.

014 | Cholesterol hydroxylation in astrocytes under an inflammatory context: A Susceptibility Factor for Alzheimer's Disease?

Cellular and Molecular Neurobiology

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Cholesterol 24-hydroxylase (CYP46) catalyzes cholesterol hydroxylation to 24(S)HOC, crucial for brain cholesterol elimination. While CYP46 is mainly associated with neurons, brain damage like traumatic brain injury or Alzheimer's escalates its expression in astrocytes. Yet, CYP46's role in astrocytes during pathologies remains uncertain. Our findings reveal elevated CYP46 levels in reactive astrocytes exposed to lipopolysaccharide (LPS) or IL-6, a proinflammatory cytokine. Furthermore, IL-6 induces APP synthesis in rat primary reactive astrocytes via CYP46 mediation; blocking CYP46 impairs this IL-6-induced process. Our results establish a connection between CYP46 and APP, indicating heightened APP levels in 24(S)HOC-treated reactive cortical astrocytes compared to controls. Notably, this increase in APP protein arises transcriptionally, as Actinomycin D treatment fails to elevate APP mRNA levels. Our initial data suggests that 24(S)HOC may operate through histone 3 remodeling and acetylation-associated epigenetic mechanisms.
Considering Aβ's antimicrobial potential, we propose that under brain proinflammatory states, prompted by microbial infections, 24(S)HOC might mediate APP production and processing in astrocytes as a defense. Conversely, this process could predispose individuals to Alzheimer's disease. To explore this, we've established an in vivo brain infection model utilizing C. albicans.

016 | DOWNREGULATION OF REDOX-SENSITIVE TRANSCRIPTION FACTORS AND NEURONAL FERROPTOSIS AS UNDERLYING MECHANISMS OF MANEB-INDUCED TOXICITY

Cellular and Molecular Neurobiology

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Epidemiological studies provide evidence of a strong association between the use of dithiocarbamate pesticides, such as Maneb (MB), and the risk of Parkinson's disease. Here, we tested the hypothesis that MB increases α-synuclein expression and downregulates several redox-sensitive transcription factors, thus promoting neuronal death. For this purpose, we challenged neuronal and primary glial cultures, and mice with MB. When exposed to MB, neurons showed α-synuclein upregulation accompanied by markers of oxidative stress. This was associated with diminished glutamate-cysteine ligase catalytic subunit and heme oxygenase-1 mRNA expression and upregulation of the NRF2 repressor, BACH1. MB treatment also downregulated glutathione peroxidase 4 mRNA levels in neurons, which was coincident with increased content of reactive oxygen species, lipid peroxidation, and mitochondrial alterations. These deleterious effects were prevented by treating MB-exposed neurons with ferrostatin-1, an inhibitor of ferroptosis. In glial cell cultures, MB triggered microglial and astrocyte activation. In mice, MB-induced neurodegeneration provoked motor impairment associated with enhanced α-synuclein expression in midbrain. Our results show that MB-induced neurotoxicity downregulates NRF2 pathway and elicits neuronal death probably triggering mechanisms associated with ferroptosis.

018 | Unveiling the function of a synaptically enriched circular RNA

Cellular and Molecular Neurobiology

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Circular RNAs (circRNAs) are a novel category of noncoding transcripts, originated from exonic regions and produced by backsplicing, process that generates a covalently linked single-stranded RNA molecule. Despite their recent discovery, circRNAs remain largely unexplored.
In a recent study, we performed a screening in which we identified numerous circRNAs in nerve tissue samples. Among these, we selected a transcript originating from the Dtnb (Dystrobrevin Beta) gene for in-depth functional analysis.

Expression levels in different mouse tissues revealed a pronounced enrichment of circDtnb in the brain, where this circular isoform of the transcripts outweighs the linear one. Further analysis in primary neuronal cultures revealed an increase in circDtnb expression during neuronal maturation, a distinct enrichment in neurons over astrocytes, and a preferential localization within synaptic compartments, with a greater circular-to-linear ratio.

Functional analysis of circDtnb involved loss-of-function experiments in primary neurons transfected with circDtnb-specific shRNA constructs. Downregulated cells showed a trend of increased mEPSP frequency in whole cell patch clamp recordings, and a consistent increase in dendritic spine count.

To study the role of circDtnb in vivo, we generated a novel loss-of-function transgenic mouse line. Our next objectives center on validating and characterizing this mouse model, aiming to provide valuable insights into circDtnb's biological r

020 | Developing a Neuro-Specific Tool for RNAi silencing: from nice ideas to real challenges

Cellular and Molecular Neurobiology

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The use of RNAi technology to control gene expression holds great promise as a potential therapeutic strategy.RNA-based medicines have gained clinical approval, and others are in various stages of research(Zhu et al 2022).We've developed a RNAi targeting Fyn tyrosine kinase's mRNA, which combined with lentiviral particles delivered into the striatum, reduced dyskinesia in a pre-clinical mice model of Parkinson's disease (Bordone et al 2021).Although viral transduction is restricted to the infected areas, Fyn expression is ubiquitous throughout the different striatal cells, mediating different roles.Thus our plan involves enhancing the accuracy of gene knock-down within specific neuronal subgroups.Our aim is to design a molecular scalpel to provide a fine therapeutic option that shall direct therapeutic effect and reduce side effects.To reach this goal we've designed a strategy using a modified Cre-LoxP system to restrict expression of RNA molecules into dopamine D1R-expressing neurons.We've cloned the synapsin promoter inverted between lox71/lox66 sequences upstream a EGFP reporter that should only express in the presence of the recombinase Cre.We cloned and tested this construct in the N2A cell line and in this poster we will discuss our strategy, present in vitro experiments results and discuss this and other strategies towards reaching our goal.The next step is to go forward with the already validated miRNA against Fyn and test its efficacy in a mouse model of LID.

022 | Tetraspanin 8 as a regulator of hippocampal dendrite development and connectivity

Cellular and Molecular Neurobiology

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During nervous system development, the formation of neuronal connectivity requires the precise control of dendrite growth, branching and synapse formation. Tetraspanins (TSPANs) represent a large family of proteins that participate in the control of neuronal development. Despite the progress obtained in recent years, little is known about the role of TSPAN8 in the control of hippocampal dendrite development and synaptic connectivity. Here, we observed that TSPAN8 is expressed in the rat hippocampus during the first two weeks of postnatal development and into adulthood. Immunofluorescence assays show that TSPAN8 is localized in the CA1-CA3 regions and dentate gyrus of the developing mouse hippocampus. By using subcellular fractionation, we also observed that TSPAN8 is present in hippocampal synaptic fractions, including the postsynaptic density. Taking advantage of the postnatal expression of TSPAN8 by hippocampal developing neurons, we used loss of function assays to examine how altered TSPAN8 expression impacts dendrite morphology and dendritic spine formation and maturation of these neurons. Our findings demonstrate that TSPAN8 regulates dendrite growth, branching and complexity of hippocampal neurons. Loss-of-function assays also show that reduced TSPAN8 levels cause a significant increase in the density of hippocampal dendritic spines, thus suggesting that TSPAN8 might regulate the formation of excitatory synaptic contacts of developing hippocampal neurons.

024 | Effects of maternal malnutrition on stress related gene expression and epigenetic mechanisms in dams and female offspring mice

Cellular and Molecular Neurobiology

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Maternal malnutrition impacts brain development and long-term mental health, elevating the risk to suffer of anxiety and depression disorders. DNA methylation is a key neuronal mechanism for adapting to environmental changes. In this study, female mice exposed to normal-protein (NP) or low-protein (LP) diets during gestation and lactation were assessed for behavior and gene/protein expression in mothers and female offspring. We observedthat a LP diet in pregnancy and lactation led to anxiety-like behavior and anhedonia in mothers and offspring. Reduced GR expression occurred in both hippocampus (HP) and amygdala (AMY) of mothers and LP offspring. we noted an increase in plasma corticosterone levels in offspring. Malnourished offspring displayed lower Bdnf exon VI and an increase in the expression of Dnmt3b and Gadd45b in HP. AMY showed a trend towards reduced Dnmt3b. A 5mC dot blot in HP of mothers and offspring revealed no found differences between NP al LP animals on global 5mC levels. These findings indicate HPA axis dysregulation in offspring, potentially increasing anxiety-like behaviors in adult LP offspring.

026 | miR-191-5p is a positive regulator of neuronal complexity in the mammalian brain cortex

Cellular and Molecular Neurobiology

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Emerging evidence suggests that microRNAs, critical post-transcriptional regulators of mRNA translation and stability, plays a crucial role in dendritic and synaptic development.
Here, we investigated the role of miR-191, a microRNA implicated in neurodegenerative diseases that is expressed in the murine brain cortex starting from peak cortical neurogenesis.
To elucidate the role of miR-191-5p function, we generated a novel approach using the CRISPR/Cas9 system delivered via intra-ventricular injections of the pan-neuronal PHP.eB adeno-associated virus (AAV), to deplete miR-191-5p in the early postnatal mice brain by editing the dicer processing bulge site.

Using Golgi-Cox staining coupled with confocal microscopy to assess the morphology of cortical interneurons by Sholl analysis, we found that depletion of miR-191-5p significantly shortened the average length of neuronal processes and reduced the total surface area of the dendritic tree. Additionally, cortical neurons exhibited decreased overall complexity under miR-191-5p depletion, which is consistent with a role for miR-191-5p in dendritic development. Tracing the processes of in vitro miR-191-5p depleted vs control N2A cells showed similar results.

Overall, this data suggests that miR-191-5p act as a positive regulator of neuronal branching during brain development. Further experimentation could unravel the regulatory mechanisms governing the observed phenotypes in vivo.

028 | ilex Paraguariensis (Yerba mate) and Chlorogenic acid increase AMPK phosphorylation and modulate downstream pathway in the neuroblastoma cell line SH-SY5Y

Cellular and Molecular Neurobiology

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Neuroprotection is one of the key challenges in neurodegenerative disorders, therefore, understanding their mechanisms may help develop strategies to delay the process. The identification of neuroprotective compounds enormously helps to reach this goal. Previously we have demonstrated that Yerba Mate (YM) enhances the survival of dopaminergic neurons in primary mesencephalic cultures, similar to green tea and coffee. These beverages have been negatively linked with the development of Parkinson's disease (PD). They share several active compounds, remarkably polyphenols, such as chlorogenic acid (CGA). To investigate whether YM regulates intracellular mechanisms related to the growth and survival of dopaminergic neurons, we focused on AMPK, a key signaling molecule involved in cell metabolism, strongly linked with neuroprotection, and potentially activated by CGA. Using the simplified model of the SH-SY5Y cell line, we tested the phosphorylation status of AMPK at different concentrations with an extract of YM and CGA. We have found that YM and CGA regulate AMPK phosphorylation. In addition, we will discuss additional preliminary results including the regulation of other regulatory molecules by RT-qPCR and WB. Further work is still necessary to fulfill our hypothesis, but current results settle down the first steps towards understanding how Yerba mate and CGA may modulate neuronal health potentially impacting the progression of neurodegenerative pathologies such as PD.

030 | Mitochondrial vulnerability to oxidation in human brain organoids modelling Alzheimer's Disease.

Cellular and Molecular Neurobiology

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Reactive Oxygen Species (ROS) and mitochondrial dysfunction are implicated in Alzheimer's disease (AD). However, the exact mechanism involved remain unclear. Damage to mitochondrial membrane and inhibition of mitochondrial respiration are thought to contribute to the progression of the disease. However, the lack of suitable human models that replicate pathological features, together with impaired cellular pathways, constitutes a major challenge in AD studies. We induced pluripotency in patient-derived skin fibroblasts carrying the Swedish mutation in App (APPswe), to generate human brain organoids that model AD, and studied redox regulation and mitochondrial homeostasis. We found AD-related pathological hallmarks in APPswe organoids, including elevated Aβ levels, increased extracellular amyloid deposits, and enhanced tau phosphorylation. Using live-imaging spinning-disk confocal microscopy, we found an increase in mitochondrial fragmentation and a significant loss of mitochondrial membrane potential in APPswe brain organoids subjected to oxidative conditions. Ratiometric dyes revealed a selective increase in mitochondrial superoxide anion and hydrogen peroxide levels in APPswe organoids, coupled to impairments in cytosolic and mitochondrial redoxin expression. This suggests a selective increase in mitochondrial vulnerability to oxidative conditions in APPswe organoids, indicating that the abnormal metabolism of APP leads to specific changes in mitochondrial homeostasis.

032 | COMPARATIVE AND FUNCTIONAL ANALYSIS OF MAMMALIAN NON-CODING ACCELERATED REGIONS IN THE NPAS3 GENE

Cellular and Molecular Neurobiology

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NPAS3 (Neuronal PAS Domain Protein 3) is a transcription factor largely expressed in the developing brain, and its deficiency in mammals has been correlated with neurophysiological pathology such as epilepsy. To understand the evolution of its transcriptional regulation and expression patterns across history, our team previously designed biocomputational algorithms to detect accelerated genomic regions in mammals: regions that exhibit prolonged conservation in the phylogenetic tree yet in certain branches accumulate nucleotide changes faster than the neutral evolution rate. Among 24,007 mammalian accelerated regions (MARs) we found, 3,476 are non-coding (ncMARs) potentially involved in vertebrate phenotypic innovation. Notably, NPAS3 possesses up to 30 ncMARs, suggesting its relevance in mammalian brain evolution. In this study we will aim to characterise NPAS3-ncMARs as enhancers via transgenic zebrafish assays, shedding light on their transcriptional role. To discern mammalian-specific functional shifts, we will contrast enhancer activity between mammalian and non-mammalian sequences. Upon identifying expression differences in NPAS3-ncMARs, we'll generate genetically modified mouse models, unveiling evolution's impact on NPAS3 expression in vivo. Comparing NPAS3 expression in diverse vertebrates will confirm how regulatory region changes have influenced its expression, contributing to novel morphological traits.

034 | Resolving intracellular signalling behind Müller glial intrinsic photosensitivity

Cellular and Molecular Neurobiology

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The retina captures light for image and non-image forming functions through two sets of specialized photoreceptors cells. Remarkably, Müller glia (MC), derived from neuronal precursors and the most abundant retinal glial cell type, have been shown to express blue- and UV-sensitive opsins (Opn3, RGR and Opn5) and to respond to blue light (BL) via G-protein signaling towards calcium release from internal stores. We aimed to further characterize the intrinsic photoreceptor capacity of the inner retina focusing on MC. MC primary cultures obtained from chicken embryos (E8) stimulated with BL (480 nm), were monitored for cAMP cellular responses by RIA and fixed for ICC detection of transcriptional factors activated by BL.

We present our recent results showing intrinsic cellular responses in primary cultures of avian MC elicited by BL. MC in culture displayed marked increases in their intracellular cAMP levels 5-10 min after BL stimulation (1min), which returned to basal levels 30 min after stimulation. This response showed dependence on opsin activation concomitant with p-CREB nuclear translocation beginning 30 min after BL stimulus. Overall, our results indicate mixed intracellular responses in MC in culture induced by BL, implying both calcium and cAMP signaling. The complex output in MC intrinsic photosensitivity, remains to be elucidated; considering their multiple described functions our results suggest a higher level of complexity for light detection within the retina.

036 | Exposure to β-amyloid oligomers promotes spatiotemporal patterns of activation in Rho GTPas; Rac1, Cdc42 and RhoA.

Cellular and Molecular Neurobiology

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Synaptic loss is a key factor in cognitive dysfunction associated with Alzheimer's disease (AD). Oligomers of β-amyloid (Aβ) are implicated in dendritic spine alteration and synaptic plasticity, but the molecular mechanisms remain incompletely understood. In this context, Rho GTPases, functioning as molecular switches, are crucial for actin dynamics and dendritic spine structure. In most studies examining their activation in AD, biochemical extraction assays, constitutively active or negative dominant mutants are used, which fail to resolve spatio-temporal activation dynamics. Recently, Förster resonance energy transfer (FRET) sensors have been developed and refined, enabling highly precise spatial and temporal radiometric measurements. Using these tools, we aimed to gather new and detailed evidence on the activation dynamics of Rho GTPases—RhoA, Rac1, and Cdc42—during early and late exposure to pathogenic forms of β-amyloid 1-42 in cell lines and neuronal cultures. Early exposure to Aβ1-42 oligomers led to increased Rac1 activity and reduced RhoA at 30 minutes, which reversed after an hour, with RhoA increasing and Cdc42 decreasing. After 24 hours of exposure, Rac1 and Cdc42 activity declined, while RhoA remained unchanged. These findings suggest that changes in Rho GTPase activity, linked to AD, are more complex than previously thought, underscoring the need for further investigation into signaling pathways governing the onset of dendritic spine loss.

038 | Endocytic trafficking of Gpm6a is altered by mutation of the key residue E258 critical for its function in filopodia formation

Cellular and Molecular Neurobiology

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Gpm6a is a neuronal membrane glycoprotein that functions in the processes of neuronal development and its overexpression leads to the extensive formation of filopodia. Previously, we showed that Gpm6a lacking C- but not N-terminal cytoplasmic tail fails to induce filopodium formation and we identified K250, K255, and E258 within the C-terminus as the key functional residues in this process. We observed that Gpm6a lacking C-terminus and the point mutation E258A, display high accumulation in the cytosol suggesting that cell surface trafficking is affected. Since different types of membrane outgrowth, filopodia formation including, require polarized membrane transport we hypothesized that the incapacity of the mutant Gpm6a to induce filopodium formation could be linked to the disrupted trafficking of mutant Gpm6a. Here, we show using confocal microscopy that the mutant forms of Gpm6a that fail to induce filopodia formation display preferential localization to the Lamp1-positive structures.

Our colocalization assays show that the wt Gpm6a and all studied mutant proteins clearly progress from the plasma membrane to Lamp1-containing late endosomal/ lysosomal structures but the Gpm6a ΔC-EGFP and E258-EGFP mutations result in increased accumulation of Gpm6a in these compartments. At the same time, the overexpression of E258-EGFP leads to decreased neuronal arborization as assessed by Sholl analysis and differences in the colocalization of Gpm6a with Rab 11.

040 | The role of a brain-enriched circular RNA on the dopaminergic pathway

Cellular and Molecular Neurobiology

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Among the extensive array of non-coding RNAs, a relatively young subclass known as circular RNAs (circRNAs) has been identified. These transcripts are the products of an alternative mechanism of splicing known as backsplicing. Due to its high expression in the brain and synaptic-enrichment, we have selected a circular transcript derived from the Tulp4 gene (circTulp4) for functional characterization. To do so, we have generated a transgenic mouse line to model circTulp4 loss-of-function in vivo. More recently, we have performed an extensive behavioral characterization of our circTulp4-deficient (CD) mouse line where we have demonstrated that the CD mice present an increase in locomotor activity. Moreover, we observed that CD male mice show an alteration in the reward-related behavior revealed by an increase in the overall sucrose preference index. These results prompted us to explore a potential alteration of the dopaminergic pathway in CD mice. To achieve this, we have conducted new tests to evaluate impulsivity and reward behaviors. In order to examine if there exists a sex difference, we decided to complete the battery of tests also in female mice. Additionally, we have also performed electrophysiological analysis in the medial prefrontal cortex, an area enriched with dopaminergic innervations.

The experimental pipeline presented here will allow us to assess whether an alteration of the dopaminergic pathway contributes to the phenotype of circTulp4-deficient mice.

042 | The GTPase Rab21 is required for neuronal development and migration in the cerebral cortex

Cellular and Molecular Neurobiology

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The development of the complex structure of the mammalian neocortex requires the proper migration of developing neurons from the ventricular zone containing neural progenitors to the cortical plate. The precise coordination of different cellular processes such as cytoskeleton dynamics, membrane trafficking and cell adhesion during migration is achieved by a variety of signaling pathways. GTPases play a central role in all these processes. The small GTPase Rab21 regulates migration and neurite growth in developing neurons. Moreover, regulators and effectors of Rab21 have been implicated in brain pathologies with cortical malformations, suggesting a key function for the Rab21 signaling pathway in cortical development. Mechanistically, it has been posited that Rab21 influences cell migration by controlling the trafficking of endocytic vesicles containing adhesion molecules. However, direct evidence of the participation of Rab21 or its mechanism of action in the regulation of cortical migration is still incomplete. In this study, we demonstrate that Rab21 plays a critical role in the differentiation and migration of pyramidal neurons by regulating the levels of the amyloid precursor protein on the neuronal cell surface. Rab21 loss of function increased the levels of membrane-exposed APP, resulting in impaired cortical neuronal differentiation and migration.

044 | Exploring MOC System Influence on OHC Degeneration in DFNA2-Related Deafness

Cellular and Molecular Neurobiology

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DFNA2, a form of progressive deafness linked to mutations within the voltage-gated potassium channel KCNQ4, exhibit chronic depolarization of outer hair cells (OHC) culminating in hearing loss. The efferent cholinergic neurons of the Medial Olivocochlear (MOC) system regulate OHC excitability by activating additional potassium channels (BK and SK2). This action aids KCNQ4 in restoring the cell's membrane potential. To determine whether the efferent system can mitigate the tissue degeneration observed in a DFNA2 mouse model, a genetic approach was employed to enhance MOC potency. We merge this model with one exhibiting increased efferent tone Kcnq4-/-//Chrnα9L9´T/L9´T (KO-KI). Cochleae from both KO-KI and their respective WT-WT controls, aged 4 weeks, were dissected for immunostaining to elucidate tissue characteristics. We found a marked ~46% reduction in OHC count along the cochlear length in KO-KI mice compared to WT-WT, with no variation in inner hair cell numbers. By confocal imaging, we studied the location of MOC terminals in OHC for both genotypes: KO-KI displayed a ~14% mislocalization, an anomaly absence in WT-WT mice. Furthermore the number of synaptic terminals per OHC was ~30% lower in KO-KI mice, accompanied by a ~24% reduction in their volume.
These findings suggest that increasing MOC system activity might not reduce OHC loss in DFNA2-related deafness. This could be due to excessive calcium influx, potentially increasing the OHC stress.

046 | Oligodeoxynucleotide IMT504: Role in oligodendrocyte progenitor cell proliferation and maturation and microglia cell proliferation, activation and phagocytic capacity.

Cellular and Molecular Neurobiology

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Demyelination consists in myelin loss from around axons, while remyelination restores myelin and resolves functional deficits. Multiple sclerosis is a high-incidence inflammatory demyelinating disease in which remyelination frequently fails. IMT504 (IMT) is a non-CpG oligodeoxynucleotide consisting of 24 nucleotides and characterized by 2 specific PyNTTTTGT sequences. Given the regenerative and immunomodulatory properties of IMT504, our work aims to study its role in microglial and oligodendrocyte (OL) progenitor cell (OPC) contribution to remyelination. Primary cultures of OPCs and microglia were obtained from cerebral cortical tissue of 1- to 2-day-old rats. OPCs were treated with or without IMT, cultured for 24h and fixed for immunocytochemistry (ICC) assays on proliferation. Also, OPCs were treated once or twice every 48h and fixed for ICC assays to evaluate PDGFRα+ OPCs and mature MBP+ OLs. Microglia were treated with or without IMT for 24h, subsequently incubated for 1h with fluorescent latex beads for phagocytosis assays, or cultured for 24h to assess proliferation. Results showed IMT-induced morphological changes compatible with microglia activation and an increase in their phagocytic capacity. Furthermore, IMT reduced microglia proliferation. IMT also reduced OPC proliferation and induced an increase in their differentiation into mature OL. These findings support potentially beneficial properties of IMT which may aid therapy development for demyelinating diseases.

048 | Novel viral-based cell-type specific Parkinson's disease model

Cellular and Molecular Neurobiology

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Parkinson's disease (PD) is the second-most common neurodegenerative disorder and is characterized by a progressive multi-neuronal dysfunction originating a plethora of debilitating motor and non-motor symptoms. Two cardinal features characterized the disease: the presence of intracellular protein aggregates enriched in alpha-synuclein and the selective vulnerability to neurodegeneration of particular subsets of neuronal subtypes in specific brain regions whereas other apparently similar cells are resistant. To assess the patho-mechanism underlying selective vulnerability we developed a cell-type specific viral vector that conditionally overexpresses a mutant variant of alpha-synuclein that allows to induce synucleopathy within individual circuit elements in vivo. When delivered to dopaminergic neurons of the substantia nigra pars compacta, our approach recapitulates the main hallmarks of the disease, namely Lewy-body-like aggregation, progressive dopaminergic neuronal death and nigrostriatal projections loss. The circuit-specificity of our approach not only allow us to unveil central pathomechanisms of the disease, but also to disentangle the circuit elements underlying less studied motor and non-motor PD symptoms.

050 | Rac1 Activity Biosensor in a Stress-Induced Sensitization to Cocaine Model

Cellular and Molecular Neurobiology

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Recent studies suggest an important role for RhoGTPase Rac1 signaling in models of cocaine addiction. In our laboratory, we have demonstrated that the modulation of cofilin activity, a regulatory protein involved in actin cytoskeleton dynamics, is crucial to the structural and functional neuroadaptations within the Nucleus Accumbens core (NAc) triggered by chronic stress exposure. These adaptations contribute to an increased vulnerability to cocaine abuse. The activity of cofilin is regulated by Rac1. Our hypothesis proposes that a decrease in Rac1 activity leads to increased cofilin activity in the dendritic spines of the NAc during stress-induced cocaine sensitization. Thus, the objective of this project is to characterize the activity of Rac1 in the NAc using lentiviral particles that express an activity biosensor based on fluorescence resonance energy transfer (FRET). To design the lentiviral vector, we cloned the Rac1bios2G biosensor from the original pTriEx plasmid into the pLV-eGFP plasmid, incorporating a CMV promoter to optimize its expression. Subsequently, we generated lentiviral particles containing pLV-Rac1bios2G in HEK cell lines.

In our stress-induced cocaine sensitization model, we will administer lentiviral particles into the NAc of male Wistar rats one week after chronic stress exposure (day 14). On day 21, a cocaine challenge injection will be administered, and we will analyze the Rac1 activation pattern at 5, 15, 30, and 45 minutes post-injection.

052 | Development and circadian characterization of the transgenic strain DG11 of Caenorhabditis elegans

Chronobiology

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Circadian rhythms are based on endogenous clocks that allow organisms to regulate their daily behavior,physiology and metabolism. Such rhythms are modulated by external signals and can be synchronized bylight and temperature cycles.The biological clock in C. elegans has not been completely characterized at the molecular level. However,some proteins have been described in the nematode as putative homologs to the mammalian/fly core clock genes.In this work, we generated a transgenic line of C.elegans(DG11 strain) with the luciferase reporter psur-5::luc::gfp (to record luminescence in vivo) and permeable to neuronal RNAi treatment. We did not find any significant differences in either period or synchronization in the DG 11 strain compared to the control strainunder the cold-warm(CW) cycle(89.4 vs. 92.3% of synchronized populations, respectively).Both strains retained circadian rhythms of ~25 h under constant conditions.RNAi is extensively used to study C. Elegans gene functions;in this sense, the DG11 strain will allow us to carry out RNAi feeding experiments to study the role of genes homologous to the central clock of flies and mammals(such as lin-42, aha-1 and kin-20) through the inhibition of their expression in neurons.The development of this strain will allow us to advance the studies of the molecular bases involved in the central pacemaker of the C. elegans'clock, turning it into a novel model organism for the study of diseases due to alterations of the circadian cycle.

054 | Exploring the role of the chloride channel ClC-a in Drosophila sleep circuits

Chronobiology

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The circadian oscillator of Drosophila is composed of approximately 150 clock neurons that express a set of molecular components, called clock genes, which through negative feedback loops coordinate the oscillation of transcription and translation of certain genes and proteins. A subgroup of clock neurons, called ventral lateral neurons (LNvs) is characterized by the expression of the neuropeptide Pigment Dispersing Factor (PDF) and play a fundamental role in the control of alertness. LNvs are essential for the regulation of sleep/wake behavior via a yet not fully understood neuronal circuit. Previous work from our laboratory has identified ClC-a, a voltage-dependent chloride channel, as a potential key element in the physiology of the LNvs. This channel has not been explored in Drosophila adult neurons before. Therefore, the main objective of this project is to characterize the role of neuronal ClC-a and its mechanism of action. Our initial findings indicate that downregulation of ClC-a in LNvs increases sleep in female flies. Consistently, downregulation of ClC-a in LNvs and glial cells reduces latency to siesta sleep in both females and males. In addition, our experiments suggest that ClC-a may be involved in the detection of sensory information, such as light and mechanical stimuli. Future work will explore how ClC-a affects LNvs physiology using patch-clamp electrophysiological approaches.

056 | Glycinergic inhibition shapes circadian oscillation in membrane potential of Drosophila clock neurons

Chronobiology

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In Drosophila, the central circadian clock comprises 150 neurons distributed in different clusters, which receive inputs from the environment, process the information and organize the animal pattern of daily activity. The interaction among these clusters through neuropeptides has extensively been studied. However, only recently the impact of communication through classical neurotransmitters and their role in the temporal organization of daily activities has been uncovered. Thus, the impact of glycinergic neurotransmission in the adult fly brain are not entirely clear.
We had previously shown that LNvs are glycinergic and that downregulation of glycine receptor subunits in putative sLNv targets impairs rhythmicity. Employing a technique for anterograde transsynaptic circuit tracing, we now found evidence of connectivity among the sLNvs Interestingly, sLNvs express the glycine receptor subunit GRD, whose knock down triggered behavioral phenotypes reminiscent of GlyT knock down (period lengthening under DD). GRD localization to the sLNvs was further confirmed by immunohistochemistry. Finally, employing a genetic encoded sensor, we uncovered a role of glycine in setting the sLNv membrane potential, which appears to change between day and night. Thus, we propose that in addition to a direct clock-control, the sLNvs recruit non cell-autonomous extrinsic signals (i.e., glycine) to shape their own excitability and hence coherence within the central pacemaker.

058 | Olfactory signaling and social entrainment of circadian rhythms

Chronobiology

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The olfactory system plays a crucial role in the capacity of social cues to synchronize the circadian clock. The goal of this project is to dissect the mechanisms that underlie locomotor activity entrainment by social interactions employing Drosophila melanogaster. We performed experiments using two fly lines entrained at different light schedules: a white-eye mutant entrained to a light schedule that is advanced 6 hours relative to a wild type (WT) strain. After a week of social interactions in darkness between the two groups in a ratio 70:30, the activity of the flies was individually recorded for 4 days. We observed that the majoritarian population was able to entrain the minoritarian one, regardless the genotype of the group in greater proportion. To test if this entrainment was through olfactory cues, we used a cannula to connect the interacting populations, only allowing the passive passage of volatile molecules. We found that flies in the minoritarian group were entrained to the phase of the majoritarian group, in spite of which group (advanced or delayed) was the majority. We also performed social interactions between WT and an anosmic mutant population that do not resynchronize their phase.

Combining genetics and immunocitochemistry strategies, as well as available connectome datasets, we are investigating how the olfactory system output neurons connects to the circadian relevant circuits.

060 | Aging alters biochemical and molecular basis of memory, in the rat temporal cortex.

Chronobiology

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Aging is a progressive, accumulative and deleterious process occurring in most living species. The temporal cortex (TC) is one of the neocortical association areas that underlies the long-term storage of declarative memory and it is particularly affected by aging. Here, we studied how aging affects the biochemical and molecular basis of memory, in the TC of male Holtzman rats. For this purpose, we analyzed BMAL1 and RORa protein levels, Bdnf, Rc3 and Nrf2 mRNA levels, CAT and GPx expression and enzymatic activity, and lipid peroxidation levels, in the TC of 3- and 22-mo-old rats. An IBM SPSS Box-Plot analysis showed no variation in BMAL1 and RORa protein levels nor CAT antioxidant activity, decreased GPx expression and activity ($p<0.01$ and $p<0.01$, respectively) and Nrf2 mRNA levels ($p<0.05$), and increased MDA levels ($p<0.05$), in the TC of aged animals. However, unexpectedly, Bdnf and Rc3 mRNA levels increase significantly, with the aging process ($p<0.0001$ and $p<0.01$). Previously, we observed that aging abolishes circadian rhythms of clock transcription factors, BMAL1 and RORa, in the TC. This may produce an internal desynchronization between metabolism and antioxidant defenses, increasing the oxidative stress. Thus, the resulting oxidative redox environment would alter the endogenous clock activity and clock-controlled genes expression such as Cat, Gpx, Bdnf and Rc3. Increased expression of Bdnf and Rc3 would be important to maintain cortical functions in the aged animals.

062 | Molecular clock in the nematode C. elegans: role of the proteins LIN-42, KIN-20 and AHA-1

Chronobiology

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Circadian rhythms are endogenous oscillations, which allows organisms to adapt to the cyclical changes present in nature. They are regulated by a set of genes, called “clock genes”, which make up the central clock. This central clock is entrained by Zeitgebers, such as light and temperature cycles. Circadian clocks are pervasive throughout nature, yet they remain unexplored and uncharacterized in the nematode C. elegans. Here, we analyze the effect of LIN-42, KIN-20 and AHA-1 proteins on the regulation of nematode circadian rhythms using a reporter system based on bioluminescence. We find that the absence of the LIN-42, KIN-20 and AHA-1 proteins produce a lengthening of the endogenous period. We also show that LIN-42 and KIN-20 are expressed in the same tissues and KIN-20 regulates LIN-42 levels. In addition, thanks to the application of the auxin-indicated degradation (AID) technique, we were able to observe that the LIN-42 and KIN-20 proteins regulate circadian rhythms specifically in neurons. These findings further our understanding of the mechanisms by which these conserved clock proteins interact to regulate rhythmic processes in the adult nematode C. elegans.

064 | ELECTROPHYSIOLOGICAL CORRELATES OF DREAM EXPERIENCE IN NON-REM SLEEP FOLLOWING DREAM INCUBATION: PRELIMINARY RESULTS

Chronobiology

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Sleep promotes the consolidation and strengthening of recently acquired memories. This enhancement is driven by the reactivation, transfer, redistribution, and integration of information. Such information processing gives rise to what we recognize as dream content. Dreaming does not solely depend on the global state of oscillatory activity of the cortex; instead, it relies on localized oscillatory activity. Some theories suggest that dreaming correlates with a decrease in the power of low-frequency oscillatory activity and an increase in the power of high-frequency activity, as measured by electroencephalography (EEG), compared to periods without dream content. On the other hand, dream content can be incubated during the wakefulness preceding sleep or during hypnagogia. During hypnagogia, the frequency of dream-like reports is notably high (around 80-90%), encompassing vivid experiences. Additionally, prior research has demonstrated that incubating dream-like content during hypnagogia results in approximately 67% of dream content being related to the incubation instructions.
In this study, we will discuss preliminary results concerning the electrophysiological correlates of dreaming in a dream incubation paradigm during the hypnagogic period, as well as its impact on dream content in Non-REM Stage 2 sleep.

066 | Exploring the contribution of circadian structural plasticity to seasonal adaptation

Chronobiology

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Daily rhythms in animal physiology are typically coordinated by central pacemakers located within the brain, which involve a dozen of so-called clock genes. In Drosophila melanogaster, clock genes are expressed in 150 neurons that are clustered in functional groups according to their anatomical location and transcriptional profiling. Under constant conditions, circadian activity largely depends on the activity of the small lateral ventral neurons (sLNvs), which undergo circadian remodeling of their axonal projections. The morphology of their processes change throughout the day, displaying a highly elaborated arbor in the subjective morning and a less branched structure in the early subjective night. Thus, structural plasticity could modify the way in which the network is wired, but how these changes contribute to network response to environmental challenges and which are the molecular mechanisms underlying this process is less clear. If structural plasticity were recruited to mediate the adjustment to a changing photoperiod, a phase-locked relationship between the molecular clock and this cellular output would be anticipated. To explore the relationship between photoperiodic adaptation and structural remodeling we analyzed the profile of wild type flies at the molecular, cellular and behavioral levels. This approach uncovered an unexpected connection between light and structural plasticity that was further dissected under different light and temperature paradigms.

068 | It's a wild worm: Circadian characterization of wild Caenorhabditis elegans isolates

Chronobiology

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Circadian rhythms are an adaptative feature found throughout nature which enables living beings to anticipate daily variations in their environment. The nematode C. elegans is currently used as a novel model for circadian research given the array of powerful genetic and neuro-behavioral tools at disposal. The strain of C. elegans widely used in the laboratory is the N2, which is considered domesticated. Various studies show that recent isolates of C. elegans are highly divergent at a genomic level with respect to the N2 strain, due to the accumulation of numerous mutations in the latter. In this work, we use a locomotor activity recording system to circadian screen wild C. elegans isolates. Our results show that the both the N2 strain and the wild isolates were synchronized to a cold-warm (CW) cycle. MY23, JU1172, JU830 and DL238 tended to be truly entrained to the zeitgeber, while the other worm strains (especially the control N2 strain) showed varying degrees of masking. Indeed, ~30% of the N2 populations were entrained to CW cycles, increasing to 73%, 66%, 60% and 53% in the MY23, JU1172, JU830 and DL238 strains, respectively. All assayed strains retained circadian rhythms of ~24 h under constant conditions, except for JU1652 which had a period of ~23 h. Circadian characterization of wild C. elegans isolates, together with genomic data, would enable the possibility of identifying genomic regions (or even genes) involved in synchronization.

070 | How the media might be contributing to candidate choice and political polarisation: perspectives on the 2019 presidential elections in Argentina.

Cognition, Behavior, and Memory

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Political polarization is the extreme stances of groups viewing politics and society as a division between “us” and “them”. It is induced by shared political/ideological representations and emotional elements. Previous research has shown that repetition or association with positive content can induce the choice of certain faces. In the 2019 Argentinean elections, we observed a significant correlation between the frequency of candidates’ mention in the media and their familiarity. Trust in them also correlated significantly with the positive perception of them in news headlines. Both familiarity and trust were explanatory variables for the voting probability. The present study assesses whether familiarity and trust can be predictors of the vote, as well as analyzes voting communities in a cluster analysis associated with ideological self-perception or the media outlets they consume to inform themselves. Our results show that both familiarity and trust predict the candidate chosen, being social variables of political interest to be manipulated. We found key links between political ideology, media consumption, and elected candidates in voter population characterization. The media’s significant impact on promoting candidates and influencing their election has been demonstrated in past elections, including the 2023 PASO. These mechanisms’ continued existence only serves to erode people’s freedoms, harming relationships between different groups and the overall democratic system.

072 | Differential modulation of attentional ERPs in smoked and insufflated cocaine-dependent associated with neuropsychological performance

Cognition, Behavior, and Memory

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Cocaine consumption is linked to reduced attentional ERPs -P3a and P3b, indicating bottom-up and top-down deficits respectively. At cognitive level, faster routes of administration (e.g., smoked cocaine [SC]) show larger impairments than slower routes (e.g., insufflated cocaine [IC]). We assess these ERPs based on the route of cocaine administration. We expected SC dependent (SCD) to exhibit reduced P3a modulation, and both SCD and IC dependent (ICD) to show reduced P3b modulation. We studied 25 SCD, 22 ICD matched by poly-consumption profiles, and 25 controls matched by demography. We combined EEG data from the Global-Local task with attentional cognitive tasks. At the behavioral level, SCD displayed attentional deficits in both bottom-up and top-down processes, while ICD only showed a tendency for top-down deficits. Modulation of P3a and P3b was lower in consumers. We observed subtle route-based differences, with larger differences in the P3a for SCD and in the P3b for ICD. Neurophysiological and behavioral data converged. Different routes of administration lead to distinct modulations of attentional neurocognitive profiles. Specifically, SCD showed greater attentional impairment, mainly at bottom-up/P3a, while ICD at top-down/P3b deficits. These findings emphasize the crucial role of considering the route of administration in both clinical and research settings and support the use of attentional ERPs as valid measures for assessing attentional deficits in substance abuse.

074 | EEG CORRELATES OF ARTISTIC CREATIVITY IN POST-INCUBATION HYPNAGOGIA: A LINK BETWEEN NEUROSCIENCE AND PHILOSOPHY

Cognition, Behavior, and Memory

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This study delves into the philosophy and neuroscience of dream incubation and artistic creativity. The relationship between dreams and creativity is notable. Around 8% of our dreams stimulate creativity. Dreams are linked to the expression of new relationships between concepts, barely hinted at during wakefulness: thus, an idea may finally emerge into consciousness as a retained dream. In this sense, dreams are thoughts in a different biochemical state. Our goal is to propose a philosophical framework for operationalizing instances of creativity through electroencephalographic (EEG) patterns during hypnagogia.

We delve into the potential impact of dream incubation during hypnagogia on enhancing artistic creativity a dimension previously explored with Dormio, a project from MIT Media Lab oriented toward reducing inhibitory processes that restrict divergent thinking. This exploratory investigation aims to uncover the EEG correlates associated with post-incubation hypnagogia involving artists as experimental subjects, which may elucidate the surge in creativity upon awakening.

Consequently, our study aims to analyze EEG patterns during hypnagogia, shedding light on their potential role for artistic creativity. With meticulous focus on experimental design and a laboratory-based philosophy, this work seeks a comprehensive understanding of the neural substrates underpinning the relationship between dream incubation and artistic creations.

076 | EFFECT OF SELENIUM SUPPLEMENTED DIET ON MEMORY PROCESSES DURING ADOLESCENCE AND ADULTHOOD IN HEALTHY RATS

Cognition, Behavior, and Memory

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Selenium (Se) deficiency has been associated with several brain disorders, including neurodegenerative diseases. In addition, the rapidly developing brain is particularly sensitive to Se levels. Based on these findings, our aim was to evaluate the effects of a Se supplemented diet on memory processes in adolescence and adulthood in healthy rats. To test this, male pups were randomly divided into 2 groups at 21 days (post-weaning): Se-Adequate (SeA) (n=12) and Se-Supplemented (SeS) (n=12). At adolescence (D40) and adulthood (D70), novel object recognition and object location tests were performed. In the object recognition test, the group exposed to the SeS diet during adolescence showed greater long-term memory retention compared to the adolescent SeA group. In the object location test, the adult SeS group showed an increase in long-term memory retention compared to the adolescent SeS group. These results, showing that a Se supplemented diet initiated early in development and maintained until adulthood can improve different types of memory at different stages of life in healthy rats, suggest a protective role of Se not only against neurodegenerative diseases but also in the prevention of these diseases.

078 | Understanding Fear Generalization through Pavlovian Fear Conditioning in mice

Cognition, Behavior, and Memory

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Fear is characterized by the perception of risk, serving as a valuable adaptive mechanism for survival. However, when it becomes dysregulated, it can lead to the development of anxiety disorders, phobias, etc. where individuals exhibit an exaggerated and generalized fear response that goes beyond the initial traumatic event. Understanding the mechanisms that underlie fear generalization holds substantial implications for therapeutic interventions. In order to study fear generalization in rodents, Pavlovian Fear Conditioning (FC) is commonly employed. This involves associating a conditioned stimulus (CS), like a tone, with an aversive unconditioned stimulus (US), typically an electric foot-shock. To assess fear generalization, a safe context is introduced alongside the aversive conditioning context to evaluate whether mice exhibit fear responses towards a context which lacks an aversive component. Also, a distinct tone (CS-) is included to further investigate cued fear generalization. By presenting a different conditioned stimulus that is not paired with the aversive US, we can determine whether fear extends to stimuli sharing similarities with the CS but lacking the aversive associations. Our results show no evidence of contextual fear generalization, suggesting successful discrimination between the conditioning context and the safe context. However, the mice exhibited a pronounced fear response to the CS-, displaying increased freezing behavior compared to baseline levels.

080 | Evaluating the semantic representation contextualization of polysemic words

Cognition, Behavior, and Memory

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Polysemy (words with the same spelling and different, but related, meaning) is a feature present in many languages. For example, in English it is estimated that 80% of words are polysemic. This generates that, when we come across a word, either visually or aurally, our brain must quickly interpret what meaning is being referred to, based on the context in which it appeared. The mechanisms that operate to carry out this processing are not precisely known.

Meanwhile, state-of-the-art computational Language Models have achieved a level of language comprehension that allows them to recognize the correct meaning that is being assigned to polysemic words when used in context.

In the present work we present a preliminary comparative analysis between behavioral responses of humans and the mechanisms that operate in Language Models against the interpretation of neutral sentences (which do not allow defining the meaning of the polysemic words present) contextualized with biasing paragraphs. This work is a first step towards a better understanding of the brain mechanisms underlying this process.

082 | From On-Task to Off-Task: EEG Low Frequency Markers for Discriminating Intentional and Unintentional Mind-Wandering

Cognition, Behavior, and Memory

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Mind-wandering, the phenomenon where attention strays from the present task, is often intentional or unintentional. The intentionality aspect of this mind-wandering has been identified as a crucial predictor of different outcomes, both beneficial and harmful. Intentional and unintentional task-unrelated thoughts (TUTs) have various connections to neural responses, behavior, clinical findings, and functional correlations. In our study, we aimed to explore the electrophysiological landscape of intentional and unintentional TUT by examining the individual and collective distinguishing power of 52 predefined EEG markers. They were extracted from EEG recordings while participants engaged in a Sustained-Attention-to-Response Task (SART). Our findings revealed unique electrophysiological signatures in the low-frequency range, notably in theta and alpha frequencies. Specifically, increased theta features were the most discerning between on-task and off-task states, while alpha band characteristics were indicative of intentional TUT in contrast to unintentional TUT. These findings are well-aligned with modern theories that see alpha activity as an indicator of inward-focused attention and as a mechanism to protect internal processes from outside distractions. Our research confirms the validity of the intentionality dimension in mind-wandering and represents progress towards the real-time recognition and handling of maladaptive mind-wandering.

084 | Binge-like ethanol exposure and possible amelioration of Omega-3 (ω-3) Fatty Acid on anxiety-like behavior and long-term spatial memory in adolescent rats.

Cognition, Behavior, and Memory

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The Panamerican Health Organization reports to Argentina among Latin American countries with the highest alcohol drinking per capita. Adolescents are among the most vulnerable to negative alcohol effects. Ethanol (EtOH) exposure may cause behavioral disorders related to anxiety and memory impairments. Besides, ω-3 mitigates EtOH-induced effects on anxiety-like behaviors and spatial memory in neonate or adult rats. Yet, no literature was found about these effects in adolescence.
In this study, we analyze the behavioral effects of EtOH exposure and the possible mitigation of ω-3 or DHA (one of its main components) in adolescent Wistar rats. We administered 2 or 0g/kg of EtOH (ig) at postnatal days-PDs 28, 30 and 32. 15 min after, one set of animals received ω-3 (720mg/kg, ig) or its equivalent volume of corn oil and were evaluated in an elevated plus maze (PD36) to measure anxiety-like behavior. Other animal groups received DHA (1mg/kg, ip) or an equivalent volume of albumin and were evaluated in a Barnes maze to measure short- (PD36) and long-term (PD41) spatial memory.
EtOH treated animals spend less time in open arms, but this time increases significantly in EtOH+ω-3 animals. Besides, EtOH animals traveled more distance prior to escape hole at PD41, but this variable decreases in EtOH+DHA animals. These results suggest that, while EtOH elicits anxiety-like behavior and impairs long-term spatial memory, ω-3 or DHA seem to mitigate both negative EtOH effects in adolecents.

086 | Psychedelic microdosing: Results from a double-blind placebo-controlled study

Cognition, Behavior, and Memory

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The use of low sub-perceptual doses of psychedelics, known as 'microdosing,' has gained popularity recently. While anecdotal reports suggest various benefits, the lack of placebo-controlled studies limits our understanding of microdosing and its effects. Traditional lab research may also miss the motivation of microdosers, potentially underestimating positive impacts on creativity and cognition. We recruited 34 participants beginning psilocybin mushroom (Psilocybe cubensis) microdosing. In a double-blind placebo-controlled study, we examined the acute and short-term effects of 0.5g of dried mushrooms on subjective experience, behavior, creativity, perception, cognition, and brain activity. Acute effects were significantly stronger for the active dose, but only when participants correctly identified their condition. These changes coincided with reduced theta band EEG power and consistent Lempel-Ziv signal complexity. Other measurements showed minimal effects, with slight cognitive impairment. Low psilocybin doses yield noticeable effects and altered EEG patterns but lack evidence for improved well-being, creativity, or cognition. Our findings suggest that expectations may contribute to anecdotal microdosing benefits.

088 | EFFECT OF INTRACISTERNAL RAD-IGF1 IN ANXIETY-LIKE BEHAVIOR IN A RAT MODEL OF NEUROTOXICITY

Cognition, Behavior, and Memory

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Parkinson's disease is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons, resulting in a range of motor and non-motor symptoms. Although motor deficits are the main criteria for diagnosis, there is growing evidence that non-motor symptoms may also play an important role in the disease progression. We aimed to investigate the possible effect of IGF-1 in the progression of emotional-like behavior deficits in a rat model of neurotoxicity inducedby 6-OHDA infusion into the dorsolateral striatum. We assessed the behavioral changes in male Wistar rats after 1, 2 and 3 weeks post-lesion using the elevated plus maze, light-dark box, and forced swimming tests. After 6-OHDA infusion, immunohistochemical analysis revealed a decrease in tyrosine hydroxylase immunoreactivity in the substantia nigra, ventral tegmental area, and striatum, indicating partial lesion of the nigrostriatal dopaminergic system. Furthermore, we found an increase in mRNA levels of proinflammatory cytokines IL-1 in the striatum. Our results showed anxiety-like behavior at 2 and 3 weeks post-lesion, beforethe onset of motor impairment. And IGF-1 was able to prevent such behavior at week 3.

090 | Bedtime procrastination and sleep outcomes in adolescents and young adults

Cognition, Behavior, and Memory

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Bedtime Procrastination (BP) is defined as the unnecessary and voluntary delay of bedtime, without a valid reason to explain this delay, along with the awareness that this action will have negative consequences for oneself. Previous studies have observed that this behavior is linked to negative sleep outcomes and is more prevalent in individuals with low self-control and later chronotypes (i.e. “late owls”). While the majority of research has focused on adults, BP might be particularly challenging in adolescents and young adults, as they often exhibit later chronotypes and the adolescents are still developing their self-control capacity. This study aims to examine the influence of BP on sleep and its relationship with psychological variables and chronotypes in highschool students and young adults. In a pilot study, 28 young adults completed an online questionnaire featuring validated scales for BP, general procrastination, sleep quality, chronotype, self-control and psychological distress. Participants tended to be nocturnal (45.8% were moderately owls) and displayed a moderately high level of BP (25.6±6 on a 9-45 points scale) which had a significant correlation with subjective sleep quality and sleep duration. Sleep quality also correlated with psychological distress. Besides that, general procrastination correlated with self-control values. Our preliminary results confirm that adequate solutions for better sleep are needed that address BP specifically in these populations.

092 | Emotional memory alterations in mice after the interruption of chronic ethanol drinking plus a single intraperitoneal administration.

Cognition, Behavior, and Memory

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Excessive ethanol consumption is capable of inducing neuroinflammatory processes, resulting in limbic structures changes which, in turn, can impact on memory and learning processes. In this sense, the protocol for ethanol administration used in the present work becomes relevant. It was designed for the study of the above mentioned phenomena but until now, it lacks of studies about its impact on emotional-like memories potentially associated with the neuroinflammatory changes. To do that, adult male C57BL/6N mice were exposed to a chronic consumption of ethanol in a liquid diet (5% v/v) with a final administration of 3 g/kg (i.p.) ethanol. On day 5 of withdrawal, animals were trained with high or low intensity Pavlovian fear conditioning. In the first case and after the extinction process, a subthreshold reminder of the fear memory induced a greater expression of it in a subsequent retention test in withdrawn animals. On the other hand, these animals expressed a greater fear response than control group, as well as a trend for an increased fear response induced by exposure to a new context after mild training. Taken altogether, these alterations in the discrimination of contextual cues and in the reacquisition of fear memories as well as the observed emotional sensitization could be linked to the aforementioned neurochemical changes and concurrently represent the first characterization of the effect of this alcohol consumption protocol in terms of emotional memory profile.

094 | IS RUTABAGA, A MEMORY GEN, INVOLVED IN TIME ESTIMATION?

Cognition, Behavior, and Memory

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The neurobiological basis of time estimation has not been clearly established yet. One possibility is that It encloses cognitive processes such as attention and/or working memory. We hypothesise that time estimation could be a type of immediate/short-term memory in which time itself is the stimulus that launches a behaviour. We developed an automatized interval-timing experimental setup for Drosophila melanogaster in which an isolated fly is presented at a fixed interval with a sucrose drop that is only available for 10s. We analysed the animal proboscis extension response (PER) over time and previous results showed that training increases the time until PER, anticipating the occurrence of the drop. Here we investigate if rutabaga, a well known gen involved in short-term memory mechanisms, is also engaged in time estimation. Firstly, we downregulated rutabaga in the mushroom bodies, neuropiles involved in learning and memory. Surprisingly, we found both morphologic and functional phenotypes in the eyes of experimental flies. We thus adopted an auxin-inducible gene expression system that enables rutabaga downregulation without all the undesirable phenotypes. Later, we check on the arousal state of these flies and their controls. Finally, we are evaluating the necessity of rutabaga in the mushroom bodies for the ability to estimate time or, at least, to demonstrate a time-reference memory.

096 | Impact of limited bedding and nesting paradigm on maternal behavior of rat. A networks analysis approach

Cognition, Behavior, and Memory

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Home-cage disruption of maternal care by limiting the bedding and nesting material (LBN) in rats during the early postpartum period impacts the neurobehavioral development of offspring. Mother rats exposed to LBN are reported to exhibit fragmented maternal care resulting from more frequent and shorter bouts of maternal behavior and unpredictability resulting from higher transitions from one type of maternal behavior to another. Fragmentation and unpredictability profiles could be inferred from a daily video recordings analysis of maternal behavior; however, it is challenging to infer from direct and continuous observations. In this work, we propose a method to analyze maternal behavior and determine fragmentation and unpredictability profiles from direct and continuous observations using network analysis. We recorded the maternal behavior of rats exposed to the LBN paradigm from postpartum days 2 to 9 and analyzed it using inferential statistics. Using NetLogo software, behaviors were also visualized as a network, with each behavioral repertoire as nodes and their links. Network analysis was able to visualize and quantitatively analyze the fragmentation and unpredictability of maternal behavior in LBN dams, characterized by a more connected and less segregated network with decreased measures of centrality at various nodes compared to the control dams' network, characterized by a less connected and more segregated network, with a higher measure of centrality in few nodes.

098 | Bridging Affective Computing and Neuroscience: A Predictive Analysis of Emotional Arousal and Valence Dynamics.

Cognition, Behavior, and Memory

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In the field of affective computing, traditional methods have relied on predictive models that use summary annotations to interpret emotions. Such an approach often overlooks the continuous and evolving nature of emotional states. This work presents a novel exploration of the temporal progression of emotions using the Continuously Annotated Signals of Emotion (CASE) dataset. We present the first performance standard for predictive models that leverage continuous annotations on this dataset, achieving better results than baseline models in certain scenarios. Our work includes the creation and evaluation of predictive models across affective dimensions, showing that models focusing on arousal are more effective than those targeting valence, a conclusion consistent with established affective neuroscience research. Furthermore, our study illustrates that predictions enriched with past data features provide more insight than predictions relying on future data, suggesting a primacy of physiological activity in shaping affective experience and subsequent annotation. These findings provide a deeper understanding of emotional temporal dynamics and have significant implications for both affective computing and the broader field of affective neuroscience, underscoring the promise of this cross-disciplinary methodology.

100 | Generalization of maladaptive memories during reconsolidation

Cognition, Behavior, and Memory

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Remembering can trigger a process called reconsolidation that destabilizes memories and turn them into a reactive state until their restabilization. Interfering with this process can disrupt consolidated memories. Thus, it was proposed to design treatment therapies for traumatic memories, phobias, and addictions by acting in this phase. However, reconsolidation is also a mechanism that allows memory updating. This could enable innocuous events, associated with a reminder of aversive or fear-related experiences, to become incorporated into the trace, resulting in a maladaptive generalization of the memories sought to attenuate. Here we begin to study this possibility. To do this, we trained animals in a contextual fear conditioning task and evaluated the possibility of transferring the fear memory to the spatial context to a non-contextual cue (tone), innocuous to the animals, during its reconsolidation. Conversely, we studied whether the reactivation of a tone fear conditioning memory can generalize into an aversive memory towards a novel context during the reconsolidation phase. Our results show that if the reminders that retrieve these memories incorporate cues not contained during learning, the aversion to the conditioned stimulus generalizes toward these cues. This first approximation suggests that information added to a trace while aversive memories reconsolidate can originate and generalize maladaptive memories.

102 | Testing the effect of Ork1 potassium leak channel in Drosophila sleep neurons

Cognition, Behavior, and Memory

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The circadian oscillator of Drosophila is composed of around 150 clock neurons expressing molecular components, called clock genes, which coordinate the oscillation of gene expression and physiological parameters with a period close to 24 hours. A subgroup of clock neurons, called ventral lateral neurons (LNvs), is characterized by the expression of the neuropeptide Pigment Dispersing Factor (PDF) and plays a fundamental role in controling alertness. The LNvs are essential for the regulation of sleep/wake behavior via a neuronal circuit still under study. Previous work from our lab identified Ork1, a potassium open rectifier channel, as a potential element in the physiology of the LNvs. We observed that downregulation of this channel exclusively in LNvs causes a significant lengthening of the free running period and a reduction of overall rhythmicity under constant conditions. Due to its properties as a leak potassium conductance, Ork1 overexpression has been extensively used as a genetic tool for neuronal silencing. However, little has been studied regarding its canonical function in the tissues where it is naturally expressed. Therefore, the aim of this project is to characterize the endogenous role of neuronal Ork1 and its effects on circadian rhythms and sleep control. As a first approach we began to explore the effect of Ork1 downregulation in determining behavioral outputs. Future work will study Ork1 effects on LNvs physiology using patch-clamp electrophysiology.

104 | Longitudinal characterization of morphological and behavioral alterations in the streptozotocin (STZ)-induced sporadic Alzheimer's disease (AD) model

Cognition, Behavior, and Memory

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In this work, we performed a longitudinal characterization of morphological and behavioral alterations in the STZ-induced AD model. To this end, male rats were administered intracerebroventricularly with STZ, or vehicle, and 15, 30, 60, 90 and 120 days post-administration were subjected to the Novel Object Recognition (NOR) test and to the modified Elevated Plus Maze (mEPM) test, followed by immunohistochemistry studies. Glycemia was not altered at any time point. At 15 days, STZ-treated rats showed a significant decrease number in NeuN-positive neurons and an increased density of GFAP-positive astrocytes in parietal cortex and hippocampus. Also, the number of ChAT-positive neurons was decreased in cortex while cholinergic fiber density was decreased in hippocampus. These morphological modifications persisted across all the time points studied. Regarding behavioral performance, STZ-rats showed cognitive deficits in the NOR at 90 and 120 days post-STZ administration while no alterations were observed in the mEPM test at any time point. Based on these results, we could define, in this AD model, two phases: an early one (15, 30 and 60 days post-STZ administration) characterized by morphological alterations and a late one (90 and 120 days post-STZ administration) when cognitive deficits appear. This temporal pattern recapitulates what has been observed in AD, where pathophysiological changes begin years before cognitive deficits are manifested.

106 | Attenuation of robust aversive memory through control of fear generalization during recall: effect of propranolol.

Cognition, Behavior, and Memory

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Reconsolidation, a retrieval-dependent process, has been considered an opportunity for attenuating the negative features of traumatic memories. Memory weakened in this way suggests an effective therapeutic strategy to provide long-term relief. However, very aversive memories are often resistant to this process. Here, after the induction of a robust fear memory in mice using strong fear conditioning, we examined whether it is possible to render it susceptible to pharmacological disruption according to the degree of generalized fear (GF). For this, based on the perceptual similarity between the associated context (CA) and non-associated contexts (CB, CC, and CD) to the aversive event, we established an ordered gradient of GF. We observed that as the exposure context became less similar to CA, the fear response decreased (CA-CB vs CC-CD). Next, in conditioned mice, we injected propranolol (PROP) after exposure to the different contexts. In males, PROP treatment resulted in a reduced fear response following exposure to CA or CB, but not CC or CD, compared to the control group. In females, the decrease in fear response due to PROP was observed after exposure to CC, but not to the other contexts, compared to the control group. From a clinical viewpoint, this would be of considerable relevance since, following this strategy, the treatment of psychiatric disorders associated with traumatic memory formation would be more effective and less stressful.

108 | Medial prefrontal cortex altered encoding of contextual information in a schizophrenia mouse model

Cognition, Behavior, and Memory

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The medial prefrontal cortex (mPFC) forms adaptable complex contextual representations that include spatial and emotional elements to guide goal-directed behaviors. Altered mPFC activity has been associated with the cognitive deficits observed in schizophrenia (SZ). However, it is still unclear how mPFC neurons encode contextual information and how these representations are affected in SZ. Here we recorded mPFC neurons in a validated SZ-mouse model (NMDA receptors ablated in corticolimbic GABAergic interneurons, KO) and control mice during exploratory tasks with varying emotional and cognitive loads: a social-object discrimination task (SO) and Y-maze spontaneous alternation test (YM). In the SO task, nearly half of the recorded neurons exhibited discriminating responses either to the location of the social stimulus, the object or both. Also, in YM we found 26% neurons encoding the center of the maze just before the turning decision point suggesting they are involved in the decision making process. Notably, KO mice maintained response quality of encoding neurons in both tasks, but we detected a significant reduction in the percentage of responding neurons at the population level. These results suggest an underrepresentation and altered recruitment pattern of cortical units during heightened cognitive demands in KO mice. Our findings provide insights into mPFC's cognitive resource allocation during exploratory behaviors and its relevance to SZ-related cognitive disorders.

110 | Effect of internal states on verbal memory expression: exploring modulation through images

Cognition, Behavior, and Memory

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Predicting whether a specific stressor facilitates, strengthens, or interrupts a particular phase of memory is not a simple task. Unlike theories centered around positively or negatively modulating memory strength during different phases of the process, our working hypothesis postulates that the interplay between internal states (emotions) and mnemonic traces when memories are labile plays a crucial role in the behavioral expression of reactivated memories. During consolidation and reconsolidation, changes in concurrent internal states create emotional traces that will also unfold during memory reactivation and thus modulate its expression in testing sessions. Recent findings have already provided evidence for this hypothesis (Maza et al., 2023; Sánchez Beisel et al., 2022); for instance, a mild stressor (cold pressor stress, CPS) administered specifically during reconsolidation a) increased arousal during the testing session and b) jointly impaired the long-term expression of a verbal declarative memory (RAVLT), a list of 15 neutral nouns. In this study, we present the results of a paradigm designed to assess whether inducing a high-arousal emotional state (using IAPS images) is a sufficient condition to negatively modulate the expression of this neutral verbal memory.

112 | Exploring the effects of enriched environments on Neohelice granulata crab memory.

Cognition, Behavior, and Memory

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This study explores the impact of environmental enrichment (EE) on short- and long-term memory in Neohelice granulata crabs using a Pavlovian contextual conditioning model. While the cognitive effects of inhabiting enriched surroundings have been extensively studied in mammals, little is known about their influence on crustaceans. We examined memory performance in crabs housed in enriched and standard environments.

Brain-Derived Neurotrophic Factor (BDNF) is a neurotrophin present in vertebrates and is linked to memory enhancement. Previous studies have shown how BDNF expression increases in mice exposed to EE. We conducted a western blot analysis using BDNF antibodies on brain extracts from mice, flies, and crabs to compare the presence of neurotrophins in these models. An adsorption experiment was conducted to assess antibody specificity. Additionally, we performed an in silico comparative analysis of neurotrophins from humans, mice, flies, and the crab species Eriocheir sinensis. This comparison revealed similarities in neurotrophins across species, highlighting the conservation of these neurotrophic factors.

Our study provides novel insights into the effects of EE on memory in crabs, thereby expanding our understanding of cognitive responses to environmental stimuli in non-traditional model organisms. This research paves the way for further exploration of neuroplasticity in crustaceans and contributes to the broader understanding of memory mechanisms.

114 | Digital Neuropsychology: Remote anti-saccade task using webcam-based eye tracking

Cognition, Behavior, and Memory

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Recently, there has been growing interest in the development of remote webcam-based eye tracking (ET) prototypes for conducting web-based experiments. These prototypes seek to explore broader and more challenging demographics, with potential applications in telemedicine. However, lower camera quality and the presence of ambient noise have posed new hurdles. To address these challenges, an improved webcam-based remote ET prototype is presented. In particular, enhancements have been introduced to optimize its usability for cognitive and clinical tasks by eliminating the need for constant mouse interaction. The spatio-temporal resolution and reliability of the prototype are evaluated, and its performance is assessed using the anti-saccade task, a well-established cognitive experiment that measures inhibitory control by analyzing eye movement behavior. The results of this experiment closely parallel those obtained with high-quality laboratory ETs, highlighting increased error rates during anti-saccade trials and accelerated response times for incorrect answers. Finally, the prototype demonstrates consistent calibration over time, an important metric for reliability of results.

116 | Neural representation and perception of conflicting olfactory information

Cognition, Behavior, and Memory

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In nature, animals must be able to respond to situations that combine aversive and appetitive information. Furthermore, the stimuli predicting negative or positive consequences may change depending on experience or can be innate. In this study, we investigated how honey bees process and respond to conflicting information contained in complex odor stimuli. To do this, we trained honey bees to associate an odor with an appetitive reward. Subsequently, we tested the bees using a mixture that contained the learned odor along with a neutral one. In this case, honey bees responded positively, demonstrating their ability to detect the presence of the learned odor even within a novel mixture. However, when bees were tested with a mixture combining the appetitive learned odor with a negative pheromonal odor, the appetitive response was inhibited. This result prompted us to investigate whether this suppression occurs at the level of the first center of odor processing, the antennal lobe (AL). By using calcium imaging to study how mixtures and components are encoded in the AL, we identified that plasticity at this early stage of odor processing enables animals to respond accordingly to the hierarchical status of the odor. Our study sheds light on the underlying mechanisms of odor perception and provides a better understanding of how behavior emerges in complex situations.

118 | Separate neural tracts encode appetitive and aversive olfactory information in honey bees

Cognition, Behavior, and Memory

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A salient feature of insects and vertebrate olfactory circuits is the existence of multiple neural tracts that form parallel pathways between periphery and higher brain centers. This aspect has sparked the interest of functional and computational approaches that ask whether the different tracts convey redundant or different information. We investigate the role of the two main olfactory tracts described in the honey bee brain and called the lateral and the medial tracts. In previous studies we measured odor representation in the lateral tract and found that appetitive but not aversive learning increases the representation of the conditioned odor. Also, we found that bees can recognize the presence of appetitive and aversive learned odors when both are in a mixture, which suggests that these odors are processed in parallel and without getting mixed. These lead as to postulate that information about aversive and appetitive odors might be split in the antennal lobe. To address this, we performed experiments based on appetitive and aversive learning, and found that lesions of the medial tract do not impair the conditioned response elicited by appetitive learned odors while lesions of the lateral tract do. On the contrary, lesions of the lateral tract do not impair conditioned response elicited by aversive learned odors while lesions the medial tract do. Next, we will perform calcium imaging to evaluate whether appetitive and aversive odors are differentially encoded by both tracts.

120 | GABAERGIC MODULATION IN THE FORMATION OF DECLARATIVE MEMORY AND FACE RECOGNITION

Cognition, Behavior, and Memory

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Benzodiazepines are the most commonly used drugs to treat anxiety in eyewitnesses of crimes. They increase GABA inhibitory effect, which negatively affects encoding and consolidation of aversive memories. Eyewitness memory is essential in judicial decisions. However, memory is malleable leading to the formation of false memories. Here, we studied whether a low dose of Clonazepam (CLZ) impairs encoding as well as consolidation of faces and verbal narrative. To assess this, we performed two experiments using a double-blind design. On day 1, subjects watched a crime video and received CLZ 0.25 mg or placebo before (Exp. 1) or after the video (Exp. 2) to assess the effect on encoding and consolidation, respectively. One week later (day 8), the memory was assessed using a culprit present/absent lineup and asking for a verbal narrative. Regarding encoding, we found that the CLZ group recalled significantly less number of details on day 8, while central details did not differ between groups. Regarding consolidation, in the absent lineup, we observed a trend indicating that CLZ negatively impacted on correct rejections, leading to more innocents being chosen. These results suggest that a low dose of Benzodiazepine could modulate memory encoding and consolidation impacting both testimony as well as lineup choice. These results are relevant in the judicial field to assess the reliability of the eyewitness elections.

122 | Reactivation of emotional memories

Cognition, Behavior, and Memory

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Emotional memory is defined as the mental representation of events with an affective load, which are stronger and less susceptible to forgetting than neutral ones. After a cue-reminder presentation, consolidated memories can be reactivated and strengthened or updated by reconsolidation. Some studies compare the effectiveness of presenting all the original material (complete reminder) or a part of it (incomplete reminder) to reactivate memories. The present study aims to hone a paradigm to reactivate emotional memories and to assess such effect on memory persistence. We evaluated complete and incomplete reminders to reactivate visual and verbal emotional memories, using a three-day protocol. On Day 1, participants learned a list of emotional and neutral pictures (Experiment 1, N = 43) or words (Experiment 2, N = 59), and were assessed through a free recall task. On Day 2 (24 hours later), reactivated groups were exposed to a complete or incomplete reminder, and non-reactivated groups were not. On Day 3 (15 days later), memory persistence was evaluated through free recall and recognition tasks. Both reactivated groups recalled more items than non-reactivated ones on Day 3. Moreover, emotional content was better remembered than neutral only in free recall. In recognition task, neutral words were better recognized than emotional ones. This effect was absent for pictures. These findings suggest that complete and incomplete reminders can reactivate and strength emotional memories.

124 | Using the observational fear learning paradigm to study neural circuits underlying social memories in mice

Cognition, Behavior, and Memory

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Social learning refers to situations in which individuals learn from other members of their social group. Both humans and non-human animals can acquire fears by witnessing their conspecifics being subjected to adverse events. In rodents, different paradigms exist to study social learning, such as observational fear learning (OFL). Although several studies have advanced the understanding of the circuits involved in social learning, mechanistic understanding at the circuit level remains limited. The overall goal of our long-term project is to comprehend the neural circuits involved in social learning. Specifically, we are interested in understanding whether oxytocin, crucial for processing social information, is involved in the formation of memories acquired through observation. Here, we present the development of the OFL paradigm using mice, in which a subject observes a conspecific being trained in a fear conditioning task. The demonstrator learns directly by experiencing tones (conditioned stimulus) and electric shocks (unconditioned stimulus), while the observer associates the tones with the distress of its conspecific. Additionally, we showcase experiments designed to investigate the role of oxytocin in OFL. Observational memories provide a useful model for studying the neural mechanisms of vicarious learning, and their investigation is crucial for gaining a better understanding of disorders that exhibit alterations in the social transmission of information, such as autism.

126 | Delving into the claustrum: uncovering its function in learning and memory

Cognition, Behavior, and Memory

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The claustrum is a brain structure that remains shrouded in mystery due to the limited understanding of its cellular structure, neural pathways, functionality and physiological aspects. Significant research has unveiled connections spanning from the claustrum to the entire cortex as well as subcortical areas. This widespread connectivity has led to speculations of its role in integrating information from different brain regions, possibly contributing to processes such as attention, consciousness, learning and memory. Our working hypothesis posits that claustrum neural activity contributes to the formation, stabilization and updating of long-term memories in mice. Initial findings indicate that intra-claustral administration of Lidocaine immediately after a training session or memory recall leads to a decline in behavioral performance in an inhibitory avoidance task. Nevertheless, this does not seem to be the case for the acquisition or retrieval of this type of memory. Moreover, inhibition of the claustrum's synaptic activity appears to impair stabilization but not the acquisition or retrieval of an unconditioned memory formed in a hole-board task. Looking ahead, this project aims to delve into the influence of the cholinergic system on these memory processes within the claustrum, investigating both the modulating effects of acetylcholine input and the cholinergic output projecting to other relevant subcortical regions.

128 | Behavioral testing to study resilience and vulnerability to stress in a mouse model of gestational restraint

Cognition, Behavior, and Memory

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The gestational stress affects the trajectory of brain development, resulting in the modification of cognitive and socio-emotional functions. However, not all individuals deal on the same way to stress. In order to analyze the mechanisms of resilience to stress, we are setting up a mice model of gestational restraint in which, pregnant CF1 adult females were subjected to movement restriction for 45 min, three times per day, from GD10 to GD19. GD0 was set on the day of vaginal plug observed. Weight of dams and pups were controlled. In order to separate between resilient and susceptible mice, all pups were subjected to Splash test at 5 weeks of age. In both cases, the evaluation consisted on one first splash followed by 45 min of restraint and then other 5 min splash test. Grooming time, frequency and latency to groom was evaluated in each test. Using a PCA test we separated animals in resilient, susceptible and control animals. This analysis show us that the best variable to separate animals is the latency to groom in the second splash. Other behaviors related with anxiety and depression were analyzed in the three different groups: control, resilient and susceptible mice in order to study which consequence are observed due to gestational restriction on dams.

130 | ROLE OF SLEEP IN DECLARATIVE MEMORY FORMATION: HOW TO ENHANCE THE PERSISTENCE? PRELIMINARY RESULTS

Cognition, Behavior, and Memory

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Memories become labile after encoding and stabilize through consolidation. They can re-enter this labile state after a reminder, followed by re-stabilization (reconsolidation). Sleep plays a crucial role in memory formation, while Non-Rapid Eye Movement sleep (Non-REM) favors memory consolidation, it has been proposed that REM sleep promotes memory generalization and integration. To test this, we conducted a two-day experiment: participants were trained on day 1 using a sound-word paradigm, followed by a nap of 40 min or 90 min or staying awake, and were evaluated one week later (day 8). Positive correlations emerged between Non-REM sleep time, slow wave activity, spindle count, and day 8 performance for both nap duration groups. However, no significant differences were observed in performance between groups. Notably, REM sleep correlated negatively with day 8 performance and positively with confusion errors. In order to enhance memory, reminders were administered six days after initial learning, leading to improved memory performance for those who napped after the learning. The correlations between sleep and memory performance remain inconclusive. Initial findings suggest that REM sleep's role lies in integration and generalization shown by growing confusion errors over time. Conversely, Non-REM sleep appears to support the consolidation of specific items and memory persistence, highlighting the role of reconsolidation in maintaining updated memories for long-term effects.

132 | Behavioral and neural differences between recent and remote autobiographical memories recollection

Cognition, Behavior, and Memory

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Autobiographical memory (AM) refers to an individual's personal experience, therefore, the way we recall this type of memories is susceptible to changes over time. It has been well documented that, over time, people tend to remember things with more general (semantic) details than vivid or subjective (episodic) details. To study the differences between recent and remote AMs recollection, we have developed an experimental design that aims to minimize laboratory intervention in the recall process. This allows recollection to be as free from the context of the experiment as possible, making it a more ecological approach to AM studies. In our protocol, people were requested to bring to mind specific personal events which were more likely to be recent or remote, and once in mind, to silently elaborate them during a period of time. We implemented different behavioral measures, such as the amount of time a person needs to recall a specific memory (access time), the emotionality and importance of the recalled event as well as the degree of details the individual remembers, along with electroencephalographic (EEG) recordings during the task and several psychological tests. As a control task, participants had to guess animal riddles and mentally elaborate the features and context of these animals. Our general hypothesis is that the age of the autobiographical memory (AM) and the degree of subjective measures have a direct effect on both the access time and the neural markers involved.

134 | Histone Methyltransferases Plays a Fundamental role on Nicotine Preference in Zebrafish

Cognition, Behavior, and Memory

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Psychostimulants regulate behavioral responses in zebrafish via epigenetic mechanisms. We have previously shown that DNA methylation and histone acetylation inhibition abolish nicotine-induced conditioned place preference (CPP) but little is known about the role of histone methylation in addictive-like behaviors. To assess the influence of histone methylation on nicotine-CPP, zebrafish were treated with a histone 3 (H3) lysine-9 (K9) dimethyltransferase G9a/GLP inhibitor, BIX-01294 (BIX), which was administered before conditioning sessions. We observed a dual effect of the inhibitor BIX: at high doses inhibited while at low doses potentiated nicotine reward. Transcriptional expression of α6 and α7subunits of the nicotinic acetylcholine receptor and of G9a, DNA methyl transferase-3, and HDAC-1 were upregulated in zebrafish with positive scores for nicotine-CPP. BIX treatment per sé did not affect transcriptional levels of epigenetic enzymes that regulate trimethylation or demethylation of H3. BIX reduced H3K9me2 protein levels in a dose-dependent manner in key structures of the reward pathway. Our data demonstrate that H3 methylation catalyzed by G9a/GLP is involved in nicotine-CPP induction. Dimethylation of K9 at H3 is an important epigenetic modification that should be considered as a potential therapeutic target to treat nicotine reward and perhaps other drug addictions.

136 | OSKM gene therapy to improve neurogenesis and age-associated cognitive decline in middle-aged rats.

Cognition, Behavior, and Memory

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Changes in the central nervous system (CNS) over time are associated with a progressive deterioration in neurogenesis and synaptic connections, which generate loss of spatial memory, object recognition memory, lethargy, among other effects. of the aging of the CNS. These functional alterations correlate with morphological and molecular changes throughout the CNS. In this work we will focus on studying the hippocampus, a region of active neurogenesis, as a potential therapeutic target. We characterize aging at the level of spatial memory evaluated by the Barnes maze test and the object recognition test.

It is known that when the expression of four genes encoding four transcription factors, Oct4-Sox2-Klf4-c-Myc, is induced for a short period of time, cell identity can be maintained and, at the same time, reversal of marks. epigenetic characteristics associated with age (Horvat reference), observing a phenotype with less cognitive deterioration.

It was injected bilaterally into the subgranular zone of the dentate gyrus region of the hippocampus of 6 12-month-old rats. After performing the Barnes maze test and the SLR, it was found that the rats treated with the OSKM genes for cognitive impairment showed a better learning capacity compared to the untreated ones. Regarding object recognition, an improvement was also found in the treated rats.

138 | IMPLEMENTATION OF THE AUTOMATIZED INTERVAL-TIMING EXPERIMENTAL SETUP AND EXPLORATION OF MUSHROOM BODIES INVOLVEMENT IN TIME-REFERENCE MEMORY

Cognition, Behavior, and Memory

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The neurobiological basis of time estimation has not been clearly established yet. One possibility is that It encloses cognitive processes such as attention and/or working memory. We hypothesise that time estimation could be a type of immediate/short-term memory in which time itself is the stimulus that launches a behaviour. We first developed a manual setup for the study of a time-referenced memory in flies based on the proboscis extension response (PER) to a sucrose solution. When analysing the last PER for each interval, we found that a 9-trials fixed-interval training significantly increases the time until last-PER (from 32.53±3.29s to 50,83±1.49s), which results in almost a 10s anticipation of sucrose appearance. Here we show the development of an automatized interval-timing experimental setup for Drosophila melanogaster in which the isolated fly is presented at a fixed or variable interval with a sucrose drop that is only available for 10s. Moreover, we show the implementation of DeepLabCut software to track proboscis position over time and automatically analyse it. In addition, we study the necessity of mushroom bodies (MB) processing for this time-reference memory. We introduce some experiments where we can reversibly deplete synaptic vesicles specifically in the MB by keeping the flies at high temperature. We also rule out whether differences among groups could be due to alterations in general responsiveness.

140 | Targeted therapeutic strategy: Astrocyte-selective AAV-mediated IGF1 overexpression in the hippocampus to address sporadic Alzheimer's Disease in a rat model

Cognition, Behavior, and Memory

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Sporadic Alzheimer's disease (sAD) is the most prevalent neurodegenerative disease. The cerebral histopathological study shows that the hippocampus (Hc) is severely damaged and presents marked reactive astrogliosis affecting neuronal function. We propose to use an astrocyte-targeted therapy mediated by bicistronic serotype 9 adeno-associated viruses (AAVs) driven by the gfaABC1D promoter (astrocyte-specific) overexpressing IGF1 using a sAD rat model mediated by the intracerebroventricular (icv) injection of streptozotocin (STZ). Methodology, young male rats were divided into 3 groups: SHAM, GFP and IGF1. On Experimental Day (ED) -28, animals received bilateral injections of artificial cerebrospinal fluid (aCSF)(SHAM), AAV-GFP (GFP), or AAV-IGF1 (IGF1), in Hc. On ED 0, animals received icv-aCSF (SHAM) or STZ (GFP/IGF1) (3mg/kg) bilaterally. Among ED +14/+25 behavioural tests were performed. Transgenes overexpression was confirmed by RT-qPCR and immunohistochemistry. GFP group showed significant impairment in exploratory and species-typical behaviour, recognition memory, spatial learning and memory, and a decrease in astrocyte complexity. IGF1 overexpression prevented STZ-induced changes in exploratory behaviour, learning and memory, and astrocyte complexity impairment ($p<0.05$). We explored a specific therapy that prevents the detrimental actions given by decreased astrocyte complexity, enhances their neuroprotection, and restores their modulatory properties in our sAD model.

142 | Testing chronic odorant exposure and its role on attractiveness in Drosophila melanogaster

Cognition, Behavior, and Memory

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Insects rely on the olfactory system, among other things to find food and mate. The olfactory cues that drive different behaviors are expected to have been determined by evolution and thus their neurobiological mechanisms 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. The main goal of this project is to unveil the effect that exposure to olfactory stimuli during the larval development has on the olfactory preference in adulthood. Flies were reared in either aversive or appetitive odors and 5 to 7 days after hatching we evaluated their preference for each odorant. We used a method that allows us to measure innate and acquired odor attractiveness. Changes in the innate valence of the odors were analyzed by comparing treated flies with the corresponding controls. Our results show that the environment where the animals are reared modulates the behavioral response during adulthood. These results provide a novel paradigm to study olfactory memories that resist metamorphosis.

144 | NRLP3 INFLAMMASOME INVOLVEMENT IN COGNITIVE DEFICIT INDUCED BY HIGH-FAT DIET AND/OR CHRONIC STRESS

Cognition, Behavior, and Memory

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Previously, we showed that chronic stress (CS) and/or high-fat diets (HFD) promote cognitive impairment. We compared the effect of HFD and/or CS in C57Bl/6J (WT) and TLR4 KO male mice to analyze the role of NLRP3 inflammasome in cognitive impairment. For 12 weeks, starting at 4 weeks of age, mice were fed a standard diet (SD) or HFD. Then, they were exposed (or not) to CS for 8 weeks. We conducted the Object location test (OLT) and Barnes Maze (BM) to assess cognitive performance. Our results showed that HFD or CS decreased the discrimination index (DI) in OLT, while in KO only CS altered it. In WT, CS and HFD decreased the time in the target quadrant (TTQ) in BM. Regardless of the treatment, KO mice showed higher DI in OLT, spent more TTQ, and made fewer reference and working errors in BM, showing better spatial learning and memory than WT. Hippocampal mRNA expression levels of NLRP3 inflammasome components were assessed by qPCR. In WT mice, HFD or CS upregulated NLRP3 and PYCARD mRNA expression, suggesting an inflammatory process in the hippocampus of these animals. In contrast, KO mice showed lower expression of PYCARD, IL18 and caspase-1 possibly implying decreased NLRP3 inflammasome activity. These results suggest the involvement of TLR4 in the development of cognitive deficits in WT mice in response to HFD and/or CS. Further analysis of protein expression will be necessary for a better understanding of the role of TLR4 in this animal model.

146 | Hippocampal encoding of odor-spatial associative memory

Cognition, Behavior, and Memory

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The ability to store new information through a process of learning and retrieve it over time is an essential property of the brain. While navigating an environment, animals form an internal representation of space through the integration of diverse internal and external cues. This process depends on a specific brain region: the hippocampus. Information reaches the hippocampus via the dentate gyrus (DG) as the initial stage of the trysinaptic circuit and then propagates through CA3 and CA1. In our research, we are conducting experiments training mice in a virtual reality environment to perform a discrimination task. Under head-fixed conditions, water restricted mice learn to drink water or not, depending on distinct cues presented in a virtual corridor. Employing in-vivo electrophysiology recordings, we compared the response of DG and CA3 neurons in expert and naïve animals. Our aim is to decipher how these neurons encode and adjust their response to various task variables throughout the learning process. Furthermore, we want to understand the involvement of distinct DG neural populations in this task. We used c-fos GFP and Ascl1 mice to label engram neurons and adult-generated granule cells. Focusing in expert animals, we analyzed neural activation using confocal microscopy. Finally, we performed ex-vivo electrophysiology to record miniature postsynaptic currents. This allowed us to study potential differences in synaptic connectivity between engram and non-engram cells.

148 | Beyond neurons: involvement of Arc and BDNF on spatial memory stages affected by astroglial glutamate uptake blockage

Cognition, Behavior, and Memory

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This study aimed to investigate the role of glutamate transporter GLT–1, located in astrocytes, in spatial memory consolidation, expression, and reconsolidation, along with exploring the cellular mechanisms that occur under GLT-1 blockage. We used the spatial object recognition (SOR) task in rats, and administered dihydrokainic acid (DHK), a selective GLT-1 inhibitor, in the dorsal hippocampus. While a strong training session induced long-term memory (LTM) formation, a weak training session induced short-term memory. Inhibiting GLT-1 around a weak SOR training session promoted SOR-LTM formation. This effect was prevented by the administration of a protein-synthesis inhibitor. Moreover, SOR-LTM promotion by DHK was dependent on hippocampal activity-related cytoskeletal protein (Arc) translation and on brain-derived neurotrophic factor (BDNF) action, plasticity related proteins necessary for memory consolidation. Alternatively, DHK administration before a test session impaired SOR-LTM expression. This effect was prevented if Arc translation was pharmacologically blocked, but not by inhibiting BDNF action. Furthermore, if applied before a reactivation session, DHK impaired reconsolidation and this effect was not reversed by Arc translation inhibition. These findings reveal that hippocampal Arc and BDNF play a pivotal role in spatial memory processes, shedding light on the intricate molecular mechanisms of memory processes, governed by the activity of both neurons and glia.

150 | Enhancing long-term memory consolidation: HDAC6 inhibition and synaptic protein acetylation

Cognition, Behavior, and Memory

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Histone deacetylases (HDAC) are enzymes that, as a target of inhibition, have been associated with improving memory formation. HDACs' inhibitors generally used are isotype unspecific. Tubastatin A (TubA) is a specific inhibitor of HDAC6, a mainly cytoplasmic isotype. Here we investigated the effect of TubA on long-term memory consolidation of Inhibitory Avoidance (IA) task in mice and the changes in acetylation levels induced by TubA and by IA training on tubulin acetylation. We found, firstly, an increase in acetylation levels in hippocampal synaptic proteins in extracts made 45 minutes after TubA injection in naive animals. Acetylation was studied by western blot on a ~50 kDa band using an antibody that recognizes acetylated lysines (pan-acetylation) and another that recognizes acetylated lysine 40 from alpha tubulin (K40); both bands overlap. Secondly, that administration of TubA injected intrahippocampal immediately after training facilitates long-term memory consolidation (tested 2 and 8 days post-training). Finally, we found that AI training induces an increase in the pan-acetylation band in hippocampal synaptic proteins but not in K40. These results show that HDAC6 inhibition facilitates long-term memory consolidation and indicate a regulation of synaptic protein acetylation levels during this process. Also suggest that the tubulin acetylation that occurs at the synapse is different from K40.

152 | The presence of co specifics during nicotine exposure alters drug preference in a dose dependent manner in zebrafish (Danio Rerio).

Cognition, Behavior, and Memory

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In this study we aimed to evaluate whether grouped exposure to nicotine elicits different responses to those of individuals exposed in isolation and whether these responses varied with the concentration of nicotine used.

By exposing fish to either a grouped or an isolated CPP Protocol we observed that grouped Nicotine exposure elicits a stronger, more robust CPP. When Nicotine concentration is risen to 50mg/L, however, the animals exposed as a group show negative CPP scores as opposed to the isolated exposure that continue to elicit higher values of CPP score in both 15mg/L and 50mg/L conditions. These results may indicate that being exposed as a group enhanced the effects of nicotine to a point that higher concentrations resulted in an exacerbation of its negative, anxiogenic effects, outweighing its rewarding, anxiolytic properties. Fish tested in isolation regardless of being conditioned as a group or not showed no difference in mean speed, time spent in the upper half of the tank and other behavioural parameters commonly associated with anxiety. Interestingly, fish conditioned in isolation to 15mg/L displayed a higher distance swum when in the drug-paired side of the tank in comparison with grouped exposure that yielded similar CPP values. This behaviour could be associated with a higher seeking component in fish that underwent an isolated conditioning as opposed to fish being conditioned as a group regardless of the CPP score obtained by both conditions.

154 | Binge-like ethanol intake at adolescence exacerbates limited access ethanol consumption at adulthood, in a S1RA sensitive manner

Cognition, Behavior, and Memory

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The antagonism of the Sigma-1 receptor (S1-R) seems to modulate the motivational effects of ethanol and ethanol intake. It is still unknown if this antagonism would protect from the promoting effect that a history of adolescent ethanol exposure exerts on ethanol intake at adulthood. We examined, in adults rats exposed (BINGE group) or not (CTRL group) to binge-like ethanol intake throughout adolescence (8-10% , PDs 30-47; nine 2-hrs sessions), ethanol intake in limited access ethanol sessions (PDs 111-119; five 2 hours sessions) after the administration of the sigma antagonist S1RA (0, 4 or 16 mg/kg). We found that BINGE rats drank significantly more alcohol than CTRL animals at adulthood, and that the administration of 16 mg/kg S1RA significantly decreased adult ethanol intake in both groups. Rats given 0 mg/kg S1RA were exposed to an additional 1hour limited access session, and subsequently sacrificed for determination of blood ethanol levels (BELs). BINGE rats drank significantly more ethanol than CTRL in this sessions and achieved a BEL of 40 mg/dL, which significantly correlated with their absolute ethanol intake scores. These results indicate that S1-R antagonists may be promising targets to prevent ethanol intake at adulthood, even after a history of chronic and substantial adolescent ethanol exposure.

156 | Visual emotional context at encoding influences item memory for L2 speakers

Cognition, Behavior, and Memory

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Previous research found word processing differences between first (L1) and second (L2) languages that are modulated by language of presentation, modality, and emotionality. In life, however, words are embedded in different contexts that impact perception and memory. This study aimed to assess how visual emotional contexts influence emotional word memory. Fourteen bilingual volunteers completed an encoding-retrieval task in their L1 and L2. At encoding, 126 emotional words were paired with emotional pictures. Emotional categories were positive, neutral and negative. At retrieval, participants performed a recognition task in which the 126 target words were presented in isolation, combined with 126 novel words. Results showed language differences for item memory. For L1, negative words were better recognized when paired with neutral pictures. For L2, positive words encoded in negative and neutral contexts and negative words in negative contexts were recognized better. L1-L2 differences in emotional processing extend beyond perception and can be modulated by contextual information. For L1, word and context emotionality might compete for attentional resources and affect encoding; hence, the least emotionally demanding context (neutral) might boost memory performance. For L2, less word-context competition might be allowing for valence-related sensibilities to appear. Thus, emotional congruency did not affect positive words, but it did affect negative L2 items.

158 | Cerebellar and Cellular alterations induced by chronic self-administration of opioids in male Wistar rats

Cognition, Behavior, and Memory

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“Introduction: The cerebellum is currently considered as an integrating system that supports cognitive and emotional functions. In opioid use disorder, it activates the μ receptor in the cerebellum. So how does chronic opioid use affect the cerebellum? Our hypothesis is that there will be changes in the volume of the cerebellum, and there will be a decrease in neurons and astrocytes.

Material and Methods: Eleven male Wistar rats at P35 were used, they underwent jugular vein cannulation (6 control and 5 consumption) for self-administration in automated cages (Med-Associates model ENV-018V). Modeling was performed in FR1 for a phase from PR9-4 to a maintenance phase with morphine (0.01 or 0.1 mg/kg/infusion) or saline (0.9%) for the control group During FR1 . A 3D FLASH structural MRI sequence was performed before starting FR1 (P57), during FR1 (P70), and at the end of PR9-4 (P105) with the following parameters: TR = 30.76 ms, TE = 5 ms , angle of rotation = 10°, slice thickness = 25.6 mm, FOV = 28.2 x 19 x 25.6 mm, isometric voxel = 160 μm. Histology was performed in the regions that mark cerebellar volume changes for the cell count of neurons and astrocytes.

Results: The results of the magnetic resonance revealed structural changes of local volume such as the decrease of the cerebellar fissure and the increase of the superior cerebellar peduncle and the ventral spinocerebellar tract, as well as changes in the cell count of these areas.”

160 | The ketogenic diet as an epigenetic modulator

Cognition, Behavior, and Memory

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The ketogenic diet (KD) is high in fat and very low in carbohydrates, leading to ketone bodies synthesis. They serve not only as an alternative energy source but also as epigenetic modulators. We administered the KD to B6 mice from P21 to P80, alongside a control group that was fed a regular diet. Behavioral tests were conducted to evaluate the effects of KD on sociability, recognition memory, and anxiety-like behavior. We obtained mRNA from hippocampus to evaluate gene expression related to neuronal excitability regulation (Kcnq2), oxidative stress (Foxo3, Sod2, Sod1) and memory processing (Chrna7). KD mice exhibited increased sociability. They showed a lower exploratory ratio during the NOR test, indicating a short-term recognition memory impairment. In the open field, KD mice displayed increased thigmotaxis, suggesting elevated anxiety-like behavior. In KD mice, Sod1 and Sod2 expression significantly increased, while and Kcnq2 and Chrna7 decreased. Our results suggest that altered Chrna7 expression due to KD may play a role in the observed impairment in the short-term recognition memory. The upregulation of Sod1 and Sod2 highlight KD´s potential role modulating oxidative stress pathways. Changes in Kcnq2 expression could modulate neuronal excitability. Coupled with increased antioxidant enzyme expression, this could contribute to the diet's neuroprotective effects and possibly underlie its therapeutic potential in ASD and epilepsy.

162 | Effects of postnatal NMDA receptor ablation in cortical interneurons on social behavior

Cognition, Behavior, and Memory

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Schizophrenia is a chronic neurodevelopmental disorder that includes social withdrawal, blunted affect, and altered discrimination of social stimuli with emotional valence. To date, several attempts have been made to mimic these deficits in animal models, with mixed results. We have previously developed a mutant mouse in which the NR1 subunit of the NMDA receptor is postnatally ablated in GABAergic interneurons of the cortex and hippocampus (InterKO). This mutant has shown preliminary signs of social dysfunction, including mating, nest building, and social memory deficits. The aim of this work was to further characterize the social phenotype of this model related to schizophrenia. To this end, we developed a new behavioral paradigm to determine whether interKO mice can discriminate conspecifics based on their affective states as control mice do. We also devised a second paradigm based on prolonged social interaction to establish whether InterKO mice exhibit a biased preference towards solitary living. Additionally, we conducted resident-intruder and tube tests to study aggression and dominance in mutants. Finally, other tests ruled out possible effects of anxiety and working memory on social behavior. Determining the face validity of the postnatal NR1 knockout mouse is useful for studying the pathophysiology of schizophrenia and for developing new treatments for refractory symptoms.

164 | Systemic Thymulin gene therapy reverses memory and behavioral impairments and reduces neuroinflammation in a rat model of sporadic Alzheimer's disease

Cognition, Behavior, and Memory

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To investigate Sporadic Alzheimer's disease (sAD) therapies, we used an sAD model in rats based on a single intracerebroventricular (icv) streptozotocin (STZ) injection, resulting in increased hippocampal microglia and astrocytes 3 months after icv-STZ administration. Thymulin (FTS), a thymic peptide, has demonstrated anti-inflammatory effects. We employed an adenoviral vector (RAd-FTS) for systemic overexpression of FTS through intramuscular (IM) injections. Rats were divided into 3 groups: SHAM, STZ, and FTS. Animals received bilateral icv injections of artificial cerebrospinal fluid (SHAM) or STZ (STZ and FTS groups) (3mg/kg). At weeks 1 and 6 post STZ, FTS animals received IM injections of RAd-FTS. Before sacrifices (13 week), we are performed behavioral tests to evaluate species-typical, exploratory, anxiety and depressive-like behaviors, and recognition memory. Through immunohistochemistry experiments, we assessed immature neurons and microglia in the hippocampus. STZ-treated animals exhibited impaired exploratory activity, and recognition memory. However, FTS group showed no significant differences compared to the SHAM group in all evaluated behaviors. Although FTS did not recover immature neurons affected by STZ, it did have a central anti-inflammatory effect by reducing microglial reactivity. Therefore, systemic thymulin overexpression effectively reversed altered behavioral changes caused by STZ, and had an anti-inflammatory impact in the sAD rat model.

166 | Serotonin 2A receptor activity in the rat mPFC promotes Retrieval-Induced Forgetting in rats by modulating dCA1

Cognition, Behavior, and Memory

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Forgetting is a ubiquitous phenomenon that is actively promoted in many species. The act of remembering some experiences can cause forgetting of others, in both humans and rats. We previously found that when rats need to retrieve a memory to guide exploration, it reduces later retention of other competing memories encoded in that environment. As with humans, this retrieval-induced forgetting (RIF) relies on prefrontal control processes, is competition-dependent, and is cue-independent. RIF is thought to be driven by inhibitory control signals from the prefrontal cortex that target areas where the memories are stored. This work aims to explore if and how the serotonergic system participates in RIF and, in particular, if the βarr2 signaling pathway is recruited when competition between memories is taking place. Additionally, we studied if the mPFC-Nucleus Reuniens (RE) – Dorsal CA1 (dCA1) circuit is supporting this phenomenon. We modified the spontaneous object recognition procedure and used a pharmacological approach to manipulate the serotonin receptor 2A (5-HT2AR) activity and signaling in the medial Prefrontal Cortex (mPFC) of rats and also to inhibit downstream structures. We found that RIF in rats requires prefrontal serotonin signaling through 5-HT2AR and the βarr2 signaling pathway is at least one of the pathways recruited. Importantly, RIF depends not only on the activity of dCA1 and RE separately but also on the signaling between the mPFC 5-HT2AR and the dCA1.

168 + CO-5-Microcine | Postnatal GABA shift in the piriform cortex may support the ability of home-nest odor discrimination in infant rats

Development

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Background: In rat pups, home odor preference is present at postnatal day (P) 5; however, the ability to discriminate home nest odors from other nests appears on P10. The developmental shift in GABA signaling in the piriform cortex (PCX) could be a possible explanation at the neuronal level for why P10 pups discriminate their nest odor from other similar nests but not younger pups.

Methods: To test this hypothesis, we used a computational model of the PCx for rat pups constructed with our experimental data, including data from P5 and P10 PCx GABA synaptic input profile, then simulated the home-odor processing discrimination. During both periods, we also studied the expression of the KCC2 chloride extruder in the PCX using RT-qPCR and Western blotting.

Results: The results show that the number of active neurons and evoked spikes in response to two highly similar odors were higher than for the other nest in the P10 circuit, but this comparison was identical in the P5 circuit, suggesting discrimination odor ability in the P10 circuit but not in P5. Moreover, gene and protein expression of KCC2 was significantly upregulated in P10 compared to P5, suggesting a shift of GABAergic transmission from depolarizing to hyperpolarizing.

Conclusions: Our results support the idea that the ability to discriminate between closely associated nest odors in P10 rat pups may be attributed to the developmental shift in GABAergic signaling in the PCx between P5 and P10.

170 | Transcriptional regulation and molecular evolution of the delta-like 1 gene

Development

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Delta-like 1 (Dll1) is the gene encoding for DELTA1 protein, the canonical ligand of Notch receptor and a key player in the notch signaling pathway. Dll1 is involved in neurogenesis during embryo development and defines the properties of the adult nervous system. Understanding Dll1 transcriptional regulation during development and its variations across evolution is key to unravel the genetic basis of the extant brain diversity among species, particularly in our evolutionary lineage.

In order to do this, we study different non coding genetic elements with high conservation among vertebrates. To assess the ability of these elements to act as transcriptional enhancers, we generated transgenic mice carrying reporter proteins under the control of these elements and determined their expression pattern both spatially and temporally. At the same time, we evaluated the in vivo function by generating knock-out mice harboring deletions of these enhancers. Using qPCR we found that several of these deletions produce a reduced Dll1 expression. RNAseq showed that many genes potentially controlled by this pathway were either up or down regulated.

172 | The impact of early fluoxetine exposure on serotonin content and neuronal activity after memory tasks in adult mice.

Development

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Perinatal exposure to antidepressants (ADs) may have long term consequences in affective behaviors during childhood. This have been also well characterized in adult mice after postnatal exposition to ADs. Nevertheless, the impact of this kind of exposition on memory tasks, adult neurogenesis as well as brain 5-HT levels has been less explored. Therefore, we orally treated male and female C57BL/6 mice, from postnatal day 2 (P2) to P14 with the AD fluoxetine (10 mg/kg) or vehicle. Survival of newborn neurons in the hippocampus (HC) of adult mice was analyzed through EdU and BrdU labeling, showing a significant decrease of neurons in mice that have received fluoxetine. Whereas 5-HT levels were significantly lower in the HC of Flx-treated mice at P15, brain levels were similar to controls in adult mice. In addition, mice that received Flx assayed in the memory object recognition test and the object pattern separation had a significantly worse performance than control animals. Expression of the immediate early gene c-fos in the dorsal HC was increased by the AD treatment. All in all, our results show that early exposition to Flx in mice affects the development of newborn neurons in the HC with lasting consequences on memory abilities as well as in dorsal hippocampal expression of c-fos after memory tasks.

174 | Yerba mate (Ilex paraguariensis) as a neuroprotective agent in Parkinson's disease models

Disorders of the Nervous System

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder and its hallmark is the gradual deterioration of dopamine-releasing neurons in the Substantia nigra. A study conducted in Argentina uncovered a link between the consumption of yerba mate (YM) and a reduced risk of PD development (Gatto, 2015). Our own investigations have revealed that YM extract exhibits a robust ability to safeguard dopaminergic neurons in vitro (Bernardi, 2019). These findings encourage us to explore whether YM extract could also protect neurons from the detrimental consequences associated with the expression of human alpha synuclein (aSyn) in a Drosophila m. model of PD. We settled down the conditions to feed flies with YM and evaluated both behavioral and molecular parameters. Although we have not observed behavioral changes in YM-treated flies, Western blot analysis exhibited a reduction in the levels of aSyn in flies treated with YM. Moreover, employing the GRASP method, we detected an elevated GFP signal—an indicator of synaptic connections—between a population of dopaminergic and the Ventral Lateral neurons in aging flies feeded with YM, suggesting a potential preservation of synaptic connectivity. Finally, we explored regulation of gene expression for aSyn, AMPK and downstream expression markers of autophagy from fly heads by q-RT-PCR. Our preliminary data shows that YM treatment modulates these genes giving cues about the cellular mechanisms potentially involved.

176 | Downregulation of the Fyn kinase in an experimental model of tauopathy: functional consequences and therapeutic perspectives

Disorders of the Nervous System

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Tauopathies are neurodegenerative diseases, showing accumulation of hyperphosphorylated Tau. Tau is a microtubule-associated protein, predominantly expressed in neurons, involved in many neuronal processes. In many tauopathies, Tau becomes abnormally hyperphosphorylated at specific sites, reducing its affinity for axonal microtubules and promoting its accumulation in the somatodendritic compartment. The src-Fyn kinase has been characterized as a crucial mediator of Tau-dependent neurodegeneration, and it is hypothesized that Tau-Fyn interaction is required for Tau toxicity. This interaction is enhanced in pathologic conditions, favoring the overstimulation of glutamatergic receptors, which generates what is known as “excitotoxicity”. Here we analyzed the interaction between Tau and Fyn, in the development of Tau pathology in the hTau mouse model of tauopathy, which primarily accumulates phospho-Tau in the prefrontal cortex (PFC) and develop cognitive impairments from 6 months-old. We performed specific downregulation of Fyn in the PFC of 3-months-old hTau mice, by stereotaxic injections of lentiviral vectors carrying microRNAs to target Fyn mRNA. Six months after treatment, mice were analyzed using a battery of behavioral tests, in vivo electrophysiological recordings of PFC neurons and molecular-post mortem analyses. We determined whether Fyn downregulation has a beneficial impact on neuronal physiology and phenotypic impairments in aged hTau mice.

178 | Validating new strategies to treat behavioral deficits associated to neurofibromatosis type 1

Disorders of the Nervous System

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Rasopathies are a family of genetic conditions characterized by aberrant amplification of the Ras/mitogen activated protein kinase (MAPK) signaling cascade. Neurofibromatosis type 1 (NF1) is an autosomal dominant Rasopathy caused by haploinsufiency of the NF1 gene, which codes for neurofibromin – a negative regulator of activated Ras. Symptoms of NF1 include increased risk for benign or malignant tumorigenesis, musculoskeletal and skin abnormalities, pain hypersensitivity and cognitive deficits. Cognitive symptoms of NF1 include impaired executive functioning, autistic features, speech and language delays, attention deficits, hyperactivity, and impulsivity. Our lab has focused on identifying behavioral abnormalities in a mouse model of NF1 with the ultimate goal of designing viral vectors that can be administered systemically to reverse these effects. Using new adeno-associated viral vectors (AAVs) that can target populations of interest in the central and peripheral nervous system after intravenous injection, we screened AAV-encodable transgenes capable of therapeutically modulating Ras-MAPK signaling in NF1 haploinsufficient cells in vitro and in vivo, to correct behavioral and cellular phenotypes in NF1 model mice. This work will provide important initial preclinical evidence for the utility of AAV-based gene therapies in the treatment of NF1 in non-oncological related symptoms.

180 | Electrophysiological alterations during action semantic processing in Parkinson's disease

Disorders of the Nervous System

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Assessments of action semantics consistently reveal markers of Parkinson's disease (PD). However, neurophysiological signatures of the domain remain under-examined in this population, especially in conditions that allow patients to process stimuli without stringent time constraints. To bridge this gap, we assessed event-related potentials and time-frequency modulations in healthy individuals (HPs) and PD patients during a delayed-response semantic judgment task involving related and unrelated action-picture pairs. Both groups had slower response times for unrelated trials compared to related ones, but they exhibited discrepant electrophysiological patterns. HPs presented significantly greater N400 amplitudes as well as theta enhancement and mu desynchronization for unrelated relative to related trials. Conversely, N400 and theta modulations were abolished in the patients, who further exhibited a contralateralized cluster in the mu range. None of these patterns were associated with the participants' cognitive status. Taken together, our results suggest that PD involves multidimensional neurophysiological disruptions during action-concept processing, even under task conditions that elicit canonical behavioral effects. New constraints thus emerge for translational neurocognitive models in this population.

182 | Preclinical study of therapeutic potential of cannabidiol on cocaine and caffeine-induced sensitization and neuroinflammation in mice

Disorders of the Nervous System

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Cannabidiol (CBD), a non-psychotomimetic cannabinoid from the plant Cannabis sativa, has been proposed as a potential candidate for the treatment of cocaine use disorders; however contradictory data exist. Our previous studies, have shown that street-seized smoked cocaine samples were frequently adulterated with caffeine. We demonstrated that caffeine accelerates and enhances the cocaine-induced locomotor sensitization in rodents. Pretreatment of CBD attenuated this effect, supporting its therapeutic potential. It is well-known that the expression of psychostimulant-induced locomotor sensitization is associated with neuroinflammatory processes, involving the microglial reactivity. Regarding the CBD anti-inflammatory property, we hypothesized that CBD prevents the cocaine and caffeine-induced neuroinflammatory process and helps to attenuate the sensitization. Male adult mice were treated with CBD (20 mg/kg/i.p.) and CocCaf (5:2.5 mg/kg) or its respective vehicles for 5 days. Locomotor activity was recorded in an open field by the video-tracking software EthoVision XT 17.0. Microglial reactivity in the nucleus accumbens (NAc) was evaluated by anti-Iba1 immunofluorescence (microglial marker). As expected, CocCaf-induced locomotor sensitization was accompanied by an increase in Iba-1 immunoreactivity in the NAc. However, CBD did not attenuate the behavioral effects. It remains to be tested whether CBD attenuates the neuroinflammation associated with behavioral sensitization.

184 | The role of serotonin regulation on locomotive behavior

Disorders of the Nervous System

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Anxiety disorders are a group of conditions that negatively affect quality of life. They can manifest in different ways and intensities and are characterized by a variety of neuroendocrine and neurotransmitter abnormalities. Recent studies have reported that inhibition of the serotonergic pathway in the fruit fly causes anxiety-like phenotypes, similar to what occurs in mammalian models. Serotonin controls diverse biological functions in animals, such as sleep, eating habits, and locomotion, among others. Previous research has reported a link between the Drosophila serotonin receptor 5HT1B and anxiety-like phenotypes, observed as changes in the locomotion pattern during an open-field test. This work opens doors for Drosophila as a model for the study of the pathways related to anxiety disorders and the physiological consequences derived from their misregulation, from a genetic and cellular point of view. In this work, we will genetically manipulate the serotonergic pathway in order to model an anxious phenotype, and we will evaluate the locomotive impact in both control and stress conditions.

186 | TGF-β Gene Therapy Attenuates Behavioral Impairments and Manifestations of Dopaminergic Neurodegeneration induced by 6-hydroxydopamine in rats

Disorders of the Nervous System

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Parkinson's disease is a neurodegenerative disorder associated with neuroinflammation and characterized by the progressive loss of nigro-striatal dopaminergic neurons. Our study focuses on the striatum area (CPu), where these neurons establish their synapses, and on non-motor symptoms that usually precede the motor deficits that occur in late stages of the disease. We have shown that 3 weeks after bilateral intrastriatal administration of selective neurotoxin 6-hydroxydopamine (6-OHDA) in Wistar male rats, the animals showed cognitive deficits and anxiety-like behavior that preceded motor disabilities. TGF-β3 is a cytokine that regulates cell proliferation, neurite outgrowth, and anti-inflammatory effects in the central nervous system. We aimed to generate overexpression of TGF-β3 with therapeutic goals in neuronal and glial cells. The introduction of the rat TGF-β3 coding sequence carried in a recombinant adenoviral vector (rAD-TGFβ3) into the cerebrospinal fluid 14 days after 6-OHDA administration, reduced cognitive impairment and anxiety-like behavior evaluated through behavioral tests. Through qRT-PCR and Western blot analysis of CPu samples we studied the expression of inflammatory cytokines and the content of presynaptic proteins. We conclude that rAD-TGFβ3 could be a possible therapeutic approach to restore and modulate the mentioned changes in the 6-OHDA Parkinson animal model.

188 | Can daily event narratives distinguish Alzheimer's from frontotemporal dementia? A natural language processing study

Disorders of the Nervous System

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Dementia can disrupt how persons experience daily scenarios, affecting the representation of events and their own participation in them. In particular, Alzheimer's disease (AD) seems to impact the recall and understanding of people and objects involved, while behavioral variant frontotemporal dementia (bvFTD) seems to influence the perspective adopted by the subjects, often leading to a depersonalized viewpoint. As entities are manifested by nouns and perspective through the chosen grammatical person, AD and bvFTD might exhibit distinctive irregularities in their linguistic construal of daily events. However, no study has examined if such linguistic hallmarks differentiate these dementia types, let alone combining natural language processing tools with inferential and machine learning analyses. Here, persons with AD, bvFTD, and healthy controls (HCs), narrated their typical day. We used feature-extraction tools to quantify the nouns, verbs, first-person markers, and third-person markers. Our findings exhibited a specific impairment in noun retrieval for the AD population compared to HCs, while individuals with bvFTD tended to employ third-person references, emphasizing an exocentric perspective. Collective analysis of these features offered a reliable classification of patients within each group. Taken together, we underscore the potential of utilizing specific anomalies in daily narratives as a diagnostic clinical tool for distinguishing between AD and bvFTD.

190 | Preprocessing of snRNAseq data from striata in the 6-OHDA mouse model of Parkinson's disease and levodopa induced dyskinesia: From raw data to annotated clusters.

Disorders of the Nervous System

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The striatum is a complex brain region essential for motor function and implicated in levodopa (L-DOPA)-induced dyskinesia (LID), the main side effect of Parkinson's disease (PD) treatment. The aim was to perform single nuclei RNAsequencing (snRNAseq) from striata of intact and hemiparkinsonian mice with or without LID to obtain cell-type specific transcriptional profiles. For this, hemiparkinsonism was induced with an unilateral injection of 6-OHDA in the mid forebrain bundle and 3 weeks later, dyskinesia was induced by L-DOPA for one week. Twenty hours after the last injection, striata were immediately dissected for nuclei isolation. cDNA libraries were prepared and sequenced from 8500 FACS-sorted nuclei from 4 samples/group using a droplet-based RNA sequencing technology (10X Genomics). Data were first preprocessed to generate high quality expression matrices from each sample and then integrated into a single one containing 46973 nuclei that were clustered and annotated based on the expression of unique and well-established mRNA markers. This approach allowed us to identify dSPN, iSPN, eSPN interneurons, microglia, astrocytes, mature oligodendrocytes, oligodendrocyte precursor cells and pericytes, and most of them were equally represented among treatments. This is the first transcriptomic study that has been done on LID at the single cell level. In the future, we will address the transcriptional changes undergoing the different striatal population upon PD and LID.

192 | CHIA OIL PREVENTIVE THERAPY ADMINISTERED BY ORAL ROUTE TO A PARKINSONIAN RAT MODEL

Disorders of the Nervous System

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Parkinson's disease (PD) is a neurodegenerative disease characterized by the progressive loss of dopaminergic neurons causing motor and non-motor symptoms. Chia oil (CO) contains α-linolenic acid (ALA) with antioxidant and anti-inflammatory effects. The aim of this work was to investigate the effect of CO on the PD 6-OHDA neurodegeneration rat model, by assessing behavioral alterations, clinical and histological parameters. CO composition was analyzed by CG-MS showing a 63% of ALA content. 2-month-old male Wistar rats were injected with 6-OHDA or vehicle through stereotaxic surgery (week 0). CO (1g/kg/day) was orally administered for 1 week prior to the 6-OHDA administration (week -1) and for 4 weeks after. Behavioral tests analysis showed that CO does not modify anxiety parameters but improves cognitive ones. The animal weights and their water/food intake decreased the day after surgery and increased normally afterwards. Physiological parameters were measured in feces, urine, cerebrospinal fluid and serum without significant changes in urine volume, osmolarity and protein content. No toxicological effect was found in liver parameters. Liver, aorta, brain, kidney and small intestine did not show any morphological changes by histological analysis. We conclude that CO treatment did not affect physiological parameters and is a great source of ALA that prevents or decreases neurodegenerative processes and cognitive impairment induced by 6OHDA in the parkinsonian model.

194 | Single chain antibody against Abeta- oligomers improves performance for some memory tasks in elderly rats

Disorders of the Nervous System

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In early stages of Alzheimer's disease (AD) beta-amyloid oligomers (AβO) cause synaptic impairment and memory decline as shown in animal models. NUsc1, a single chain variable-fragment antibody (scFv) that binds a subpopulation of soluble AβOs prevented AβO-induced short-term memory (STM) deficit in mice. We developed an Adeno-Associated virus-derived vector to express NUsc1 (V) in neurons. The transgenic McGill-R-Thy1-APP rat (Tg) model of AD suffers a progressive amyloid pathology, with cognitive deterioration affecting long-term memory (LTM) of object recognition (NOR) and persistence of foot-shock avoidance (IA) memory. Treatment of 5 months-old Tg rats with V restored LTM expression of NOR (Colettis et al., SAN 2023). V-treatment of elderly Tg and wild type (wt) 15 months-old rats by i.c.v. infusion was assessed in exploratory behavior (OF), NOR and IA task performance two months later. Tg animals showed NOR-STM recovery without significant changes in any of the other tasks/memories. However, V-treated wt female rats improved their performance for STM and a tendency to rescue LTM in the NOR task, being able to also express persistence in the IA task.

Our results suggest that, although V failed to rescue LTM deficits typical of this Tg AD model at an advanced age and development of the pathology, it was successful to recover capacities in young Tg and in elderly wt females. This represents a significant advance in experimental gene therapy at early AD and in aging.

196 | Extensive and Detailed Analysis of Sleep and Locomotion Patterns of Parkinsonian Genotypes in Drosophila melanogaster

Disorders of the Nervous System

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Parkinson's disease (PD) ranks as the second most common neurodegenerative syndrome, significantly affecting motor function, quality of life, and life expectancy of patients. Motor symptoms associated with PD are attributed to the loss of dopaminergic neurons in the region of the Substantia Nigra Compacta (DA-SNc) in the brain. Moreover, it is increasingly evident that PD patients experience a range of non-motor symptoms, including sleep disorders. Of particular interest is REM sleep behavior disorder (RBD), as recent studies highlight that a considerable percentage of patients diagnosed with RBD eventually develop PD. In this research project, the aim is to delve into the behavioral repercussions of mutations related to PD and RBD in Drosophila melanogaster. The investigation encompasses the study of anomalies in locomotion patterns, sleep architecture, and sudden movements during sleep. Flies at different life stages – young, adult, and old – were analyzed to assess the progression of these symptoms. The goal was to correlate behavioral defects related to both PD and RBD, with PD molecular mechanisms (such as mutations in alpha-synuclein genes and loss of Gba expression) restricted to neuronal groups responsible for sleep and locomotion control. The insights gained from this study will provide a deeper understanding of the affected neuronal groups in PD and RBD, in addition to further establishing RBD symptoms as an early indicator of PD.

198 | Role of the Mesencephalic Locomotor Region in gait disorders associated with Parkinson's disease

Disorders of the Nervous System

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Locomotion is a fundamental behavior for animals, allowing them to move and interact with their environment. It requires the correct functioning of local circuits in the spinal cord and supraspinal structures responsible for the selection of motor programs, among which the mesencephalic locomotor region (MLR) stands out. The detailed study of these structures and the circuits in which they are embedded is essential to comprehend the etiology of certain neurodegenerative syndromes that impair motor capacity. For example, Parkinson's disease (PD) is characterized by a plethora of highly debilitating motor and non-motor symptoms, and while some of them are relieved by the administration of dopamine derivatives, others, such as Freezing of Gait (FoG), are not. FoG is defined by the inability to perform a movement despite the intention to do so, causing falls and negatively affecting patients' quality of life. Here, by globally silencing MLR's activity and manipulating the activity of its glutamatergic neurons, we study the link between its malfunction and the development of FoG, using a novel behavioral test that provides information on the latency of the onset of locomotion. Our results expand the possibilities for PD symptoms' study, highlight the importance of the MLR in the control of locomotor behavior and, at the same time, point out the need to delve into the implication of the loss of functionally distinct neuronal subpopulations in this region.

200 | Structural connectivity as a predictor of therapeutic response in resistant depression treated with ECT: Preliminary results

Disorders of the Nervous System

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Major Depressive Disorder (MDD) is a serious public health problem, due to its high prevalence and the severe disability that it can entail. In 30-40% of patients there is an incomplete response after two therapeutic attempts with an adequate dose and duration. In this group, considered to suffer from treatment-resistant MDD (TRMDD), the most effective therapeutic option is electroconvulsive therapy (ECT). There are no standardized and reproducible biomarkers to predict response to ECT in TRMDD. We are carrying out a study aimed at characterizing structural connectivity as a predictor of response to ECT treatment. To this end, we are measuring diffusion-weighted magnetic resonance neuroimaging and clinical, including cognitive, evaluations, are being explored in a group of 26 patients with TRMDD in the Service of Psychiatry of Fleni Foundation.

202 | Unraveling the role of brain masculinization in gender bias within autism spectrum disorders

Disorders of the Nervous System

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Autism spectrum disorders (ASD) are characterized by reduced sociability and repetitive behaviors. Notably, this disorder is approximately 4 times more prevalent in boys than girls. To investigate this bias, we used a mouse model: valproic acid (VPA). This model is particularly interesting because it mirrors the gender bias seen in humans. Our hypothesis posits that the process of brain masculinization is necessary for VPA to impact autism-related behaviors. To test this, in the VPA model, we injected pups with 5 µg 17β-estradiol benzoate (E2) on postnatal days 2, 5, and 8, replicating the testosterone surge males experience during early development.

When we analyzed juvenile behavior, we observed that VPA-exposed females displayed altered social behavior, with the phenotype rescued by estradiol exposure. Conversely, in adulthood we observed that VPA-E2 females did not habituate to social stimuli in both the social interaction test and the social habituation and novelty recognition task. By assessing different parameters including ovaries development, sexually dimorphic brain nuclei and hormone concentrations in plasma, we were able to validate the successful implementation of the masculinization protocol. Other areas relevant to the model—such as the cerebellum, CA2 region of the hippocampus, and piriform cortex—showed no differences between the groups.

In summary, we can affirm that gonadal hormones drive ASD sex bias, impacting perinatal and juvenile stages.

204 | Behavioral and cellular analysis of the cognitive and emotional consequences of persistent neuropathic pain in mice.

Disorders of the Nervous System

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Chronic neuropathic pain (NP) is a severe neurological condition with significant clinical relevance. Beyond sensory discomfort, it leads to cognitive impairments and emotional disorders, lowering patients' quality of life. Although this comorbidity is clinically recognized, the cellular pathophysiological mechanisms bridging persistent pain and cognitive/emotional issues remain uncertain.

The spared nerve injury of the sciatic nerve (SNI), a well-established model that is useful to study the long-term consequences of NP in rodents, has been shown to lead to cognitive and emotional impairments concomitant with neural changes in various brain regions. However, research often focuses on time-periods close to the lesion. To understand in detail the long-term behavioral impact of SNI intervention animals were subjected to several behavioral tests at one, two, three and four months post-lesion. Spatial working memory, sociability as well as locomotion and exploratory behaviors showed no differences between groups. Additional analysis conducted al 4 months post-surgery showed preserved performance related to anxiety and repetitive behaviors. These results indicate that SNI in young adult mice is not sufficient to induce robust cognitive and emotional symptoms associated to persistent NP. To further evaluate the impact of NP we plan to analyze the expression of neurodegeneratives markers in brain areas associated to affective encoding.

206 | Assessment of acute and chronic treatment with the potassium channel blocker 4-AP on behavioral deficits displayed by a TDP-43 transgenic model of ALS/FTD

Disorders of the Nervous System

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TDP-43 is the main component of the pathological cytoplasmic inclusions found in two incurable neurodegenerative diseases, amyotrophic lateral sclerosis and frontotemporal dementia. This nuclear protein is involved in RNA metabolism, among other functions. Our transgenic mice with inducible cytoplasmic expression of TDP-43 in forebrain neurons recapitulate behavioral phenotypes, neurodegeneration and gene expression changes that occur in both diseases. We recently described in these animals a reduction in cellular and global brain activity. In order to investigate a potential causal link between this decrease and the profound behavioral phenotypes observed in this model, we evaluated the effect of acute and chronic systemic injection of the FDA-approved neuronal activity enhancer drug 4-Aminopyridine (4-AP). In the acute protocol, animals were tested in the different tasks 3 hs after 4-AP injection at 1-month post transgene induction, while in the chronic protocol the injection occurred daily during 30 days before testing. Transgenic animals subjected to the acute protocol showed similar deficits in spatial and working memory (Y-maze), locomotion and exploratory behavior (Open Field) and spasticity (clasping) as those injected with vehicle. Preliminary experiments using the chronic protocol suggest a partial recovery of some these deficits. These results indicate that a persistent activity-inducing treatment might be useful as a potential therapy for these pathologies.

208 | Auditory threshold discrimination based on EEG and eye tracking data

Integrative Systems

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We propose novel visual-auditory multisensory signal analysis techniques to explore how auditory and visual stimuli processing interact, and how one modality is managed when attention is captured by the other. We conducted an experiment that modified traditional speech audiometry by introducing visual stimuli, where images were integrated into conventional setup. This experiment combines eye-tracking and brain EEG signals, with the aim to discriminate different auditory thresholds from brain activity and eye movement.

Six participants followed two experimental phases. Initially, disyllabic words were presented in auditory form at an intensity loud enough for allowing accurate discrimination. At the same time two images were presented on a computer screen. The subjects were instructed to choose the image corresponding to the heard word. In the second part, a similar sequence was repeated with a lower auditory level (only fifty percent of words could be recognized).

Pupil size and gaze paths were tracked synchronically with the EEG signal during the experiments. Novel statistical-complexity-based evaluation methods were applied to these fused signals. The evaluated parameters were used as feature vectors to represent these signals, with which a classification model was trained. We used three different classification models (Decision Trees, Random Forest, K-Nearest Neighbors). The best model achieved a 79% accuracy in threshold determination.

210 | Lateral hypothalamic glutamatergic inputs to VTA glutamatergic neurons mediate prioritization of innate defensive behavior over feeding

Neural Circuits and Systems Neuroscience

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The lateral hypothalamus (LH) has long been implicated in feeding behavior and defense responses by its interactions with distinct brain structures, including the Ventral Tegmental Area (VTA). Emerging evidence indicates that LH-glutamatergic neurons infrequently synapse on VTA-dopamine neurons, but establish multiple synapses on VTA-glutamatergic neurons, mediating innate defensive behavior. Here, we investigate whether LH-glutamatergic inputs to VTA-glutamatergic neurons play a more extensive role in different types of innate behavior. We found that activation of LH-glutamatergic neurons innervating the VTA promoted active avoidance, long-term aversion, and escape attempts. In addition, activation of this LH-glutamatergic pathway to VTA decreased feeding behavior in both sated and food restricted mice. By testing feeding behavior in the presence of a predator, we observed that ongoing feeding behavior was interrupted in food restricted mice, and that this predator-induced decrease in feeding behavior was abolished by VTA photoinhibition of glutamate release from LH-glutamatergic fibers. By VTA specific neuronal genetic ablation, we established that predator-induced decreases in feeding behavior were mediated by VTA-glutamatergic neurons but not by neighboring dopamine or GABA neurons. We uncovered an unanticipated neuronal circuit between LH-glutamatergic inputs to VTA-glutamatergic neurons that plays a role in prioritizing escape instead of fighting, freezing, or feeding.

212 | Early ethanol exposure elicits ventilatory alterations by a serotonergic phenotype in neonate of rats

Neural Circuits and Systems Neuroscience

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Alcohol consumption is highly frequent during pregnancy and lactation. Early ethanol exposure (EEE) affects the development, triggering different neurobehavioral dysfunctions and also affecting respiratory regulation. The serotonergic system modulates the respiratory frequency through efferents towards areas of the brainstem responsible for the generation of the respiratory rhythm.The mains goals of this study are to: i) analyze serotonin-5HT levels in areas of the medullary raphe according to acute or chronic EEE, or also the combination of both, and ii) correlates 5HT levels and plethysmographic recordings against an hypoxic challenge.The results indicate that breathing frequencies depress under any form of EEE. But, first acute ethanol intoxication elicits major breathing depression while the prior ethanol exposure induces ventilatory plasticity phenomena to recover and elevate them. Besides, any form of EEE is associated with an increase in 5HT levels in the medullary raphe nuclei analyzed. In turn, we find a significant association between 5HT levels in the raphe magnus and the ventilatory rates during hypoxia. Actually, higher respiratory frequencies are found in pups with lower 5HT levels in this nucleus. These results allow us to think about how the EEE with a moderate dose (2.0g/kg) induces a serotonergic phenotype that may be affecting the respiratory processes of metaplasticity observed in an hypoxic event. Financial support by FONCyT, CONICET and UNC.

214 | Decoding the Role of Homologous Metabotropic Glutamate Receptors MGL-1 and MGL-2 in Nutritional Perception of C. elegans

Neural Circuits and Systems Neuroscience

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Unraveling the intricate neural circuits governing an animal's perception of its nutritional state is paramount. Here, we utilize C. elegans to shed light on these mechanisms. We concentrate on two neuronal G protein-coupled receptors (GPCRs), MGL-1 and MGL-2. These GPCRs have piqued our attention due to the high levels of autophagy exhibited by double mutants, a phenomenon characteristic of hungry animals, even in well-fed ones.

Similar to other species, hunger triggers heightened feeding rates in C. elegans upon encountering food. We found that well-fed mgl-1; mgl-2 double mutants display elevated feeding rates, evident in increased pharyngeal pumping velocity and augmented gut food volume. Additionally, these well-fed animals exhibit reduced locomotion upon encountering food, a behavior akin to genuinely starved worms. This observation implies that these receptors perceive signals pertaining to the animal's nutritional status.

In addition, we unveil reduced feeding rates in mgl-1 mutants, in contrast to heightened rates in mgl-2 mutants. This disparity underscores the opposing effects of these receptors.

We are now focused on the neuronal circuits involved in nutritional sensing, while also elucidating the signals that activate these GPCRs.

The conservation of behavioral plasticity linked to nutritional states across the animal kingdom, underscores the potential universal relevance of our findings.

216 | Neuronal firing during seizures in epilepsy surgery candidates

Neural Circuits and Systems Neuroscience

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INTRODUCTION

Patients with drug-resistant epilepsy could benefit from surgery if the epileptogenic zone(EZ) is identified. Intracranial electroencephalography with macro-microelectrodes records single neuron (SN) activity during seizures. Our goal is to evaluate SN behavior during seizures.

MATERIALS AND METHODS

Macro-microelectrodes were implanted in patients with drug-resistant epilepsy, recording signals via the Cervello system at 30 kHz. Firing rates (FR) of SN activity were analyzed in 15-second intervals before and after ictal onset. Electrodes covered ictal onset zone (IOZ), close propagation zone (CPZ), and distal propagation zone (DPZ). For comparisons, repeated measures ANOVA was employed. Signal processing was done in MATLAB using WAVE_CLUS and FieldTrip.

RESULTS

A total of 80 epileptic seizures from 11 different patients were analyzed; 1932 groups of neurons were identified, 257 in the EZ, 607 in the CPZ, and 1033 in the DPZ. A statistically significant difference was found in the firing rates before and after the ictal onset. In patients with temporal lobe epilepsy, there was a significant difference between firing rates of neurons ipsilateral to the EZ and those in contralateral regions.

CONCLUSIONS

The analysis of the behavior of the SN contributes to our comprehension of neural network dynamics during seizures, with particular significance for temporal lobe epilepsy cases where it may aid in lateralization determination.

218 | Rhythmic Motor Control and Premotor Modulation

Neural Circuits and Systems Neuroscience

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The execution of rhythmic motor behaviors requires multiple control mechanisms to adjust the behavioral output, narrowing down the degrees of freedom of a system with multiple units.

Leeches crawl on solid surfaces through a succession of elongation and contraction body waves. Each segmental ganglion contains the neurons required to produce this rhythmic motor pattern, and dopamine evokes fictive crawling in isolated midbody ganglia. The pair of premotor NS (nonspiking) neurons are connected to motoneurons through a central network that provides recurrent inhibitory signals onto the motoneurons. We aim at understanding the role of NS in the context of crawling. During fictive crawling NS neurons receive inhibitory signals, tuned to the contraction phase of crawling, monitored through the DE-3 motoneuron. The results suggest that the inhibitory signals in NS are delivered by the rhythmogenic circuit that controls the motoneuron output. Thus, excitatory signals to DE-3 are correlated to inhibitions in NS that, in turn, can restrict the motoneuron activity.

Extracellular recordings and spike sorting analysis revealed that removing NS from the circuit enhances the firing frequency and duty cycle of DE-3 and motoneurons that fire in-phase with it. Moreover, the firing frequency of motoneurons that are active out of phase from DE-3 is not modified by this.

To this point the data indicates that the premotor NS neuron acts as an homeostatic element, restricting the motor output.

220 | Neural correlates of cognitive impairment phenotypes following a COVID-19 infection

Neural Circuits and Systems Neuroscience

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Subjective complaints on cognitive function impairment following a COVID-19 infection is a recently studied phenomenon that can last for over a year. 42 patients (32 females, 10 males, mean age 56) have approached the clinic with such symptoms and have performed below average on neurocognitive clinical evaluations, mainly in attention, executive control, memory, and language. In this study, we analyze the topology of their functional networks based on connectivity matrices built from resting state functional magnetic resonance imaging protocols carried out on these patients, and compare them to a matched control group (45 patients; 27 females, 18 males, mean age 58) with no prior cognitive impairments at the time of study. Our analysis shows a seizable difference between groups in the average clustering coefficient computed on a range of thresholds (percentage of maximum number of connections in a given network), mostly in the salience network, but also in the dorsal attention and frontoparietal networks. These results support the hypothesis of a difference in neuroanatomical substrate between the two groups and, furthermore, that the COVID-19 infection would be responsible for it.

222 | Inhibition of striatal cholinergic interneurons by chemogenetic manipulation induce compulsive and perseverative behaviors in mice.

Neural Circuits and Systems Neuroscience

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A reduced number of striatal cholinergic interneurons (SCIN) could be implicated in neuropsychiatric conditions like obsessive-compulsive disorder and Tourette syndrome. Previous research showed altered social interactions and increased repetitive behaviors after selective SCIN ablation. However, whether these alterations are related to SCIN signaling impairment or to plastic changes emerging after SCIN lesion, remain uncertain. To explore acute SCIN inhibition effects, ChatCre heterozygous mice were injected with a viral vector (pAAV-hSyn-DIO-hM4DGi-mCherry) to selectively express an inhibitory DREADD in SCIN. Comprehensive behavioral tests, including open field, hole board, marble burying, nesting, grooming, and social interaction assessment, were conducted using CNO or vehicle. Although locomotion in CNO treated mice remained normal, SCIN inhibition notably increased head dippings during the hole board test. Furthermore, SCIN inhibition led to more buried marbles, frayed cotton for nest assembly, and grooming events, but had no effect on social interactions. Immunofluorescence (anti-mCherry and anti-Chat) confirmed DREADD expression specificity in SCIN. Ex-vivo validation demonstrated significant reduction in SCIN spontaneous firing frequency upon CNO application. In summary, acute SCIN inhibition exacerbated ritualistic behaviors in mice, supporting the notion that SCIN may play a role in suppressing compulsive and perseverative behaviors seen in psychiatric disorders.

224 | Effect of leptin on mechanical sensitivity in Ob/Ob and WT mice.

Neural excitability, synaptic transmission and neuron-glia interactions

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Leptin performs numerous actions in the brain. We reported that leptin has effects on somatosensory thalamic networks by decreasing GABAergic release from the thalamic reticular nucleus and the firing frequency of neurons in the Ventrobasal nucleus (VB). Electrophysiological recordings in the obese Ob/Ob mice supported that the development of the thalamocortical system in the absence of endogenous leptin decreases the functional expression of the HCN channel (H current) in the VB. This channel influences membrane properties and synaptic integration within a neuron circuit. In Ob/Ob mice, although they lack circulating leptin, the receptor remains functional. It is for this reason that by applying exogenous leptin, we expected to see a modification in the neuronal signals that relay somatosensory information (mechanical sensitivity, pain, itch) to the cortex. In this work, we cannulated the VB and injected leptin (1ug) in one hemisphere and vehicle in the other. Twenty-four hours later, we either performed patch clamp experiments or a behavioral study (Von Frey test) to assess the mechanical sensitivity of the animals. We found that leptin application increased the H-current density recorded in thalamocortical slices, thus restoring its dysregulation observed in the ob/ob mice (WT, n=9; Ob/Ob, n=7, ANOVA, $p<0.05$). The application of Leptin induced mechanical allodynia (2-way RMANOVA: genotype and treatment, WT: n=6, Ob/Ob: n=7, $p=0.03$ for treatment).

226 | Probing AMPA receptors at ribbon synapses in the mammalian cochlea by glutamate-uncaging

Neural excitability, synaptic transmission and neuron-glia interactions

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AMPA receptors in the mammalian brain mediate fast neurotransmission and are typically found in specific regions of the synapse called postsynaptic densities (PSDs). Across synapses a great variability of PSDs sizes and number of AMPA receptors has been described. This morphological heterogeneity is determinant of a variability of functional responses in the postsynaptic neuron. In the mammalian inner ear, glutamatergic synapses are also formed between inner hair cells (IHCs) and spiral ganglion neurons (SGNs). At these synapses all aspects of sound information are encoded and transmitted to the brain for further processing. A key aspect of the presynapse (IHCs) is the presence of a 'synaptic body' or 'ribbon' that concentrates large amounts of synaptic vesicles ensuring high rates of exocytotic events. Postsynaptic terminals of SGNs are characterized by large PSDs, 5 to 10 times bigger than those found in the brain. We speculate that PSDs are not saturated during normal neurotransmission and are able to accommodate large amounts of glutamate released by IHCs. To investigate this, we implemented a glutamate photolysis method by which a laser pulse is flashed upon the synapse previously bathed with a caged-glutamate compound, producing fast transients in glutamate concentration. Responses to glutamate uncaging were recorded by patch-clamp directly on SGNs terminals. Both the intensity and the duration of laser pulses could be modulated to generate transients of different sizes.

228 | ATP-dependent P2X7R activation controls presynaptic homeostatic plasticity

Neural excitability, synaptic transmission and neuron-glia interactions

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Homeostatic synaptic plasticity (HSP) regulates synaptic strength to stabilize the activity of a neuron or a neuronal circuit. HSP mechanisms can operate on pre and postsynaptic terminals. An increased number of reports indicate that neurotransmission and Hebbian plasticity are modulated by ATP and its P2X and P2Y purinergic receptors. However, very little is known about how ATP modulates synaptic strength in HSP. We have previously reported that ATP and P2X7 receptors (P2X7Rs) modulate the homeostatic adjustment of synaptic efficiency. Here we investigate the functional changes occurring in the presynaptic terminal by this purinergic signalling pathway. To carry out this work, we use hippocampal dissociated cultures and functional imaging techniques to estimate changes in presynaptic function. Our results show that blocking neuronal activity triggers an increase in extracellular ATP levels and suggest that P2X7Rs activation is necessary to the compensatory increase in presynaptic Ca2+ and vesicular release upon chronic inactivity. The results obtained show the importance of purinergic signalling in the homeostatic adjustment of activity-dependent presynaptic function.

Key words: homeostatic synaptic plasticity, ATP, P2X7

230 | GABA and ACh are co-transmitted from olivocochlear efferent terminals during development

Neural excitability, synaptic transmission and neuron-glia interactions

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During development, inner hair cells (IHCs) in the mammalian cochlea are unresponsive to acoustic stimuli but fire sensory-independent action potentials, crucial for the normal development of the auditory pathway. During this period, neurons from the medial olivocochlear complex (MOC) transiently innervate IHCs. This innervation is mediated by acetylcholine (ACh), activating nicotinic receptors α9α10 and is responsible for controlling IHC excitability during this period. Even though this is a cholinergic synapse, GABA through presynaptic GABAB receptors reduces the amount of ACh released. While we described the GABA-mediated mechanisms, the source of GABA and the role of GABAergic modulation are poorly understood. Using mice expressing channelrodhopsin (ChR2) under the control of either GAD or ChAT promoters we show that optogenetically activated fibers in GAD-cre/ChR2 mice produced postsynaptic responses that were blocked with cholinergic antagonists. Finally, calcium imaging experiments were performed with stimulation of MOC fibers, allowing us to resolve the activation of single synaptic sites. Altogether these results strongly suggest that ACh is being co-transmitted with GABA from MOC fibers. Whereas ACh acts postsynaptically activating α9α10 receptors, the role of GABA is presynaptic, as a negative feedback signal to locally regulate cholinergic inhibition of IHCs. Calcium imaging experiments suggest that GABA modulation operates differently at each synaptic site.

232 | Screening of positive allosteric modulators for the alpha9-alpha10 nicotinic cholinergic receptor.

Neurochemistry and Neuropharmacology

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Hearing loss affects 360 million people (5% of the world's population and 42% of the population over 75 years of age). While half of hearing loss is genetic in origin, the other 50% is due to environmental conditions. Among them, prolonged exposure to loud noise is the main cause of hearing loss. One of the main challenges in the field of hearing is to find a pharmacotherapeutic strategy to prevent the damage produced by noisy environments, when these cannot be avoided. Recent studies have postulated the α9α10 nicotinic cholinergic receptor present in the sensory hair cells of the cochlea as a therapeutic target for the development of drugs that increase the activity of the olivocochlear efferent system, in order to prevent acoustic trauma. The aim of this work is to test possible positive allosteric modulators (PAMs) of α9α10 and their potential to prevent hearing loss due to the exposure to loud noise. To this end, we tested several candidates for PAMs or agonists of certain receptors that are closely or distantly related to α9α10 such as α7, α4β2 or α4β4 and serotonin receptors in recombinant α9α10 receptors expressed in Xenopus laevis oocytes. Up to this point, Chlorophenyl biguanide, a selective serotonin receptor agonist, has been evaluated; also Ivermectin and TQS, PAMs of α7 nAChRs; NS-9283, an α4β2 nAChR PAM; and LY–2087101 PAM of α7, α4β2 and α4β4 nAChRs which did not positively modulate the α9α10 receptor.

234 | Memory Recovery through Aβ-Oligomers Selective Gene-Immuno-Therapy in an Alzheimer's Disease Rat Model at an Early Stage

Neurochemistry and Neuropharmacology

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β-Amyloid oligomers (AβOs) were reported as early contributing to synaptic impairment and memory deficits in animal models of Alzheimer's Disease (AD). A single-chain antibody fragment NUsc1, selectively target a subpopulation of AβOs and rescued short-term memory (STM) in mice models. To neutralize AβOs and enhance therapeutic efficacy, we developed an Adeno-Associated virus-derived vector for expressing NUsc1 (V) in the brain.

The McGill-R-Thy1-hAPP heterozygous transgenic (Tg+/−) rat model of AD displays progressive amyloid pathology, impairing the formation/recall of novel object recognition (NOR) long-term memory (LTM).

We evaluated if early V treatment could rescue NOR LTM in (Tg+/−) rats. Both Tg and wild-type (wt) male rats 10-12 weeks old, were i.c.v. infused with V or saline (control). After two months, exploration to an open field (OF), new object discrimination and recognition (NOR) and LTM were assessed. Both V-treated and control, wt and Tg+/− rats showed similar exploratory behavior and habituation to the OF. Tg+/− rats failed to express LTM for NOR, whereas prior V treatment restored this capacity Current AD therapies underutilize genetic tools. Unlike the already approved ADUCANUMAB and LECANEMAB, expensive antibodies targeting higher-order of Aβ aggregates, V offers a viable, accessible advancement in vector-mediated immunotherapy, enabling sustained scFv NUsc1 neuronal expression to neutralize toxic AβOs.

236 | Evaluating the Neuroprotective Potential of a New Tetracycline in a Novel Cell Model of Parkinson's Disease

Neurochemistry and Neuropharmacology

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Parkinson's disease (PD) is a chronic neurodegenerative disorder that affects millions worldwide. It involves the progressive loss of dopaminergic neurons in the substantia nigra pars compacta, and is thought to be triggered by the presence of toxic amyloid aggregates of α-Synuclein (αS), predominantly phosphorylated at Serine 129 (S129). Currently, no drug is able to stop, nor slow down, neuronal death in PD. Several tetracyclines (TCs) (Minocycline, Doxycycline, Chlortetracycline and Demeclocycline) have shown neuroprotective effects in preclinical models, but their antibacterial activity limits their use. Therefore, modified TCs without antibiotic action were designed and screened for their ability to inhibit αS aggregation. Here we further evaluate one of the best inhibitors, ChloRed2 (CR2), derived from Chlortetracycline. In SH-SY5Y cells, a PD cellular model, CR2 showed no toxicity and conserved important antioxidant properties present in TCs. In addition, in transgenic SH-SY5Y-αS-RFP cells, CR2 inhibited the ability of pre-formed αS fibrils (αS-PFF) to seed endogenous αS. Surprisingly, CR2 also inhibited the phosphorylation of αS at S129 and lysosomal stress induced by αS-PFF. These results poise CR2 as an attractive drug candidate for further in vivo tests and uncover hidden properties of TCs that could be harnessed for further drug development.

238 | Behavioral effects induced by intranasal administration of melanin-concentrating hormone in rats: relevance of its role in mood disorders

Neurochemistry and Neuropharmacology

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The hypothalamic neuropeptide melanin-concentrating hormone (MCH) has been involved in the regulation of mood disorders, like depression, a high prevalent psychiatric disorder worldwide; however, its role remains under study. We demonstrated an interaction between MCHergic and monoaminergic systems, since MCH acute and locally administered into the dorsal and median raphe, and the Locus Coeruleus, induced a prodepressive response in the rat forced swim test. An anhedonic response was also demonstrated after its acute and intranasal (i.n.) systemic administration in the sucrose preference test. Given the well-known comorbidity between depression and anxiety disorders, we hypothesized that the MCH-induced anhedonic response is accompanied by an anxiogenic response and an increase in corticosterone levels (a stress hormone resulting after the activation of the hypothalamus-pituitary-adrenal axis). To explore this hypothesis, we evaluated the anxiety-related behaviors following i.n. administration of MCH (15 µg/30 µL) in male adult rats using the open field (OF) and elevated plus maze (EPM) tests. Our results showed that MCH did not induce significant changes in anxiety-related responses, neither in the OF nor in the EPM test, at 30 or 60 min after administration. Ongoing experiments are being carried out to measure the plasmatic corticosterone levels, to elucidate its role in anxiety. Our findings collaborate to the understanding of the role of MCHergic system in mood disorders.

240 | Potential neuroprotective effect of DDox in Parkinson's disease models: A novel non-antibiotic doxycycline derivative with alpha-Synuclein anti-aggregating properties

Neurochemistry and Neuropharmacology

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Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by the loss of dopaminergic neurons due to misfolding and aggregation of a-synuclein (aS) protein. These toxic aggregates disrupt normal cellular processes, leading to neuronal dysfunction and death. Although previous reports indicate that doxycycline (DOX) has the potential to interfere with aS aggregation, its antibiotic activity confers a limitation for long-term treatments. Here, we synthesized and tested a novel reduced form of DOX (DDox), with diminished antibacterial activity. DDox exhibited an enhanced and dose-dependent anti-aggregating effect against aS. Additionally, DDox showed no toxicity in SH-SY5Y cell lines. Moreover, in transgenic SH-SY5Y-aS-RFP cells where endogenous aS aggregates were induced by treatment with exogenous pre-formed aS fibrils (aS PFF), co-treatment with DDox reduced αS seeding. However, the same effect was not observed when DDox was used as a pre-treatment, suggesting a direct effect on aS PFF. Remarkably, DDox inhibited fluorescentlly-labeled aS PFF uptake and aS PFF-triggered lysosomal stress, which represent novel properties for tetracyclines in PD models. Our results suggest that DDox is a non-toxic molecule with non-antibiotic activity and neuroprotective properties, which make it attractive for in vivo preclinical PD studies.

242 | Role of neonatal sex differences in DNA demethylation in the organizational effects of testosterone

Neuroendocrinology and Neuroimmunology

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Sex differences in neurochemical cell phenotype may have broad consequences and underlie differences in neural function, morphology, connectivity, and neurotransmitter production in males and females. Recent studies have shown that the expression of enzymes that place or remove DNA methylation marks is greatest in the first week of life, overlaps with the perinatal critical period of sexual differentiation and a neonatal inhibition of DNA methylation or demethylation abolishes sex differences in cell phenotype. Here, we explored how early sex differences in gene expression of TET 1-2-3, GADD45a-b and TDG (involved in the removal of 5-methylcytosine) may correlate with gene expression of oxytocin (OXT) and the oxytocin (OT) receptor (R) in specific regions of the mouse brain. mRNA expression was evaluated by qPCR in brain punches of prefrontal cortex (PFC), preoptic area (POA) and the paraventricular nucleus of the hypothalamus (PVN) at postnatal day (P) 7 and 18-19. In PFC, we found sex differences (males>females) in TET1-2-3, TDG and Gadd45a-b expressions and a higher OTR-expression in males at P7($p<0.05$). We also evaluated OT expression by immunohistochemistry at P18-19 in the POA, PVN and the supraoptic nucleus of the hypothalamus and found higher expression in female POA. Overall, these results suggest that a sex-specific pattern of active DNA demethylation machinery during neonatal life could underline the organizational effects of hormones on neurochemical phenotype.

244 | Neonatal overfeeding in male rats alters eating behaviour and hedonic control of food intake in adulthood

Neuroendocrinology and Neuroimmunology

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We analysed the impact of neonatal overfeeding and the exposure in adulthood to a cafeteria diet (CAF) on eating behaviour and on the expression of key genes of the reward dopaminergic pathway of the brain. Male Wistar rats were raised in small (4 pups/dam, SL) or normal litters (10 pups/dam, NL). From weaning to postnatal day 90 (PND90), they were fed with control diet (CON). From PND90 and for 11 weeks the animals received CON (3 kcal/g) or cafeteria diet (CAF) (4,85 kcal/g) (NL-CON, NL-CAF, SL-CON, SL-CAF; 10-14 rats/group). Body weight and food intake were recorded weekly. Elevated Plus Maze (EPM) and Specific Sensory Satiety test (SSS) were performed. Brains, blood and fat pads were obtained. Ventral Tegmental Area (VTA), was isolated by micropunching technique. For mRNA analysis, qPCR was performed. CAF consumption increased body weight, energy intake and adiposity ($p<0,001$). CAF groups preferred sweet food ($p<0,0001$). Eating behaviour in SSS test was altered in SL-CON, NL-CAF y SL-CAF ($p<0,05$). EPM test results showed anxiety-related behaviour in SL-CAF ($p=0,0012$). In VTA, SL-CAF enhanced the expression of Tyrosine Hydroxylase (TH) and Dopamine Receptor D2 (DRD2), without altering Dopamine Receptor D1 (DRD1) and Dopamine Active Transporter (DAT) ($p<0,05$). We are currently studying other nuclei involved in the reward system. This work provides the first evidences that neonatal overfeeding alters eating behaviour in adult life by modifications in the hedonic system.

246 | LEAP2 has greater accessibility and longer lasting effects than ghrelin in the mouse brain

Neuroendocrinology and Neuroimmunology

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Liver-expressed antimicrobial peptide 2 (LEAP2) is a newly discovered hormone that acts via the growth hormone secretagogue receptor (GHSR) and impairs the actions of ghrelin, a stomach-derived orexigenic hormone. Here, we used mice to study the extent to which LEAP2 reaches the hypothalamus and the neuronal circuits engaged by LEAP2 to antagonize ghrelin's orexigenic effect. First, we confirmed that centrally-injected LEAP2 decreases overnight food intake and body weight as well the orexigenic effect of simultaneously-injected ghrelin. Then, we studied the kinetics of the inhibitory effect of LEAP2 on ghrelin-induced food intake, and found that centrally-injected LEAP2 blocks the orexigenic effect of ghrelin injected 1-, 3- or 8-h later but not the effect of ghrelin injected 24-h later. Also, we assessed the ability of a centrally-injected fluorescent variant of LEAP2 (F-LEAP2) to label the brain at different time points, and found that F-LEAP2 labeled neurons, which were mainly localized in the arcuate nucleus, even 3-h after injection. We also incubated the external side of hypothalamic explants with F-LEAP2 or fluorescent ghrelin, and found that F-LEAP2 showed greater diffusion into the tissue than fluorescent ghrelin. Altogether, our results suggest that 1) LEAP2 induces a long-term inhibitory effect on the orexigenic effects of ghrelin, presumably because it remains bound to GHSR, and 2) LEAP2 displays a greater accessibility to the brain than ghrelin.

248 | Investigating the Impact of Prepubertal 17β-Estradiol Exposure on Behavioral Traits Relevant to Psychiatric Conditions

Neuroendocrinology and Neuroimmunology

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Psychiatric disorders exhibit sex-related differences in their prevalence. Conditions like autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are more prevalent in men, and anxiety and depression more prevalent in women. However, the mechanisms underlying this bias remain poorly understood.

During mammalian perinatal development, gonadal sexual hormones play a key role in organizing neural circuits, leading to sexual dimorphisms in the brain and sex-specific behaviors in adulthood. While these hormonal effects have traditionally been considered exclusive to the organizational period, emerging evidence suggests that the prepuberty may also be involved in the organization of neural circuits. In fact, on this critical window, from postnatal day 21 to 35, the hormonal profiles significantly differ between sexes. This period is particularly relevant, as we have previously shown that different environmental interventions during this phase have enduring effects on behaviors relevant to psychiatric disorders.

We examine the effects on adult behavior of male and female mice of daily administration of 17β-estradiol during the period we suggested as critical. Particularly, we assess anxiety, depression, and sociability-related behaviors, aiming to uncover biological mechanisms in distinct psychiatric disorders prevalence. This research promises insights into sex-specific influences on such disorders, potentially leading to targeted interventions.

250 + CO-10-Auditorio | Chronic variable stress reduces the availability of neural precursors in the rat hippocampal dentate gyrus

Neuroendocrinology and Neuroimmunology

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Exposure to adverse life events can contribute to the development of depression. The dentate gyrus (DG) of the hippocampus, known for its remarkable plasticity through neurogenesis, is one of the regions sensitive to such alterations. Hypotheses like match/mismatch attempt to elucidate how the relationship between early-life experiences and later adulthood plays a crucial role in stress coping strategies. In this study, we aimed to investigate the impact of early maternal separation (SMT) and chronic variable stress (CVS), both individually and combined, on the neural precursor population. Male rats underwent 4.5 hours of SMT between postnatal days 1 to 21. Subsequently, between postnatal days 50 to 74, the rats were exposed to a CVS protocol and concurrently treated with either the antidepressant Tianeptine (TIA) at 10 mg/kg or vehicle. The number of neural precursors in the subgranular zone of the DG was quantified using immunohistochemistry targeting SOX2 and confocal microscopy. Our findings revealed that only CVS exposure led to a significant 46% reduction in the neural precursor cell population. Furthermore, this impact was morphologically distinct, with the supra-pyramidal zone being the most affected. Interestingly, TIA was effective in restoring the number of neural precursors to control levels only in the infrapyramidal zone. Collectively, our results cannot be explained by the match/mismatch hypothesis, suggesting that alternative hypotheses must be considered.

252 | The antisocial network: Larval zebrafish raised in social isolation show lower response thresholds for threat detection but reduced multisensory integration.

Sensory and Motor Systems

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Early postnatal social interaction is critical for establishing proper behavioral patterns while social isolation during early development is a risk factor for various psychopathologies such as depression, anxiety and autistic-type disorders. Zebrafish (ZF) are social vertebrates that aggregate in groups both in nature and in the laboratory and are susceptible to social isolation. In this work, we asked whether early social isolation affects risk assessment and multisensory integration of danger stimuli. Taking advantage that ZF do not require parental care, we kept ZF in groups of 50 individuals or in individual opaque containers since egg fertilization and tested their behavior 10-30 days post fertilization. We evaluated ZF escape behavior in response to visual, acoustic or multisensory stimuli. Isolated ZF showed lower escape thresholds than control ZF. However, while the combination of an auditory and a visual (multisensory) stimulus increases the probability of escape in control ZF, isolated ZF did not show significant multisensory integration. Multisensory integration is proportionally lower when the salience of the unisensory stimuli is high. We speculate that the hyper reactivity triggered by social isolation produces a deficit in decision making: isolated ZF will escape in response to irrelevant stimuli while being unable to correctly integrate complementary sources of information.

254 | Acoustic trauma during the critical period of development alters the correct maturation of the auditory system.

Sensory and Motor Systems

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The auditory system of many mammals develops after birth. Before the onset of hearing, inner hair cells (IHC) are innervated by auditory nerve fibers and transiently by neurons of the medial olivocochlear (MOC) system. During this period, IHCs exhibit periodic depolarization patterns inducing stereotyped bursts of action potentials that are transmitted to the auditory circuits in the brain and promote neuronal survival, physiological maturation, and the proper establishment of the tonotopic map. It has been proposed that the MOC system may be a modulator of this activity. In addition, it has an important role in the protection from noise-induced hearing loss in adult rodents. Here, we evaluated the function of this transient synapse and the consequences of an early acoustic exposure during this critical period by comparing the performance of two different mouse models: an α9 nicotinic receptor subunit knock-out (KO; Chrna9 KO), which lacks cholinergic transmission between efferent neurons and hair cells; and a gain-of-function knock-in (KI; Chrna9L9'T KI) carrying an α9 point mutation that leads to enhanced cholinergic activity. Exposure to loud noise at this early stage, in wild-type produced cochlear threshold shifts and a decrease in neural response amplitudes, together with the loss of ribbon synapses, which is indicative of cochlear synaptopathy. In contrast, the Chrna9L9'T KI was completely resistant to the same acoustic exposure protocol.

256 | Odor mixture detection in Drosophila melanogaster

Sensory and Motor Systems

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Odorants are detected by olfactory receptor neurons (ORNs) that project to the antennal lobe (AL), the first olfactory neuropil in the insect brain. In the AL, ORNs make synaptic contacts with: i) projection neurons (PNs) that send olfactory information to other brain areas; and ii) local interneurons (LNs) that form a dense network of lateral interactions within the AL.

Functional studies indicate that this network reshapes sensory information, presumably to enhance perception of meaningful odors. In this project we investigate the role of GABAergic interactions in relation to learning dependent neural plasticity in the AL. Our previous work showed that the representation of a mixture in the AL changes after aversive conditioning, making the learned component more salient. Now we are performing aversive olfactory conditioning using a T-maze. We train flies to associate an electric shock with an odor that they have to avoid during the test session. To study how animals perceive mixtures, we evaluate the ability of the animals to detect the presence of the learned odor immersed in a binary mixture. To do that, we test the flies with two stimuli: a novel odor versus a mixture that contains the associated odor. Future experiments are directed to evaluate whether blocking the LNs activity impairs learning dependent changes and the ability to detect learned component.

258 | Olfactory sensory adaptation: role and mechanisms

Sensory and Motor Systems

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The olfactory system is exposed to a diversity of chemical stimuli, needing continuous adjustment based on the animal's experience. Sensory adaptation, an important mechanism of modulation, is defined as the reduced sensitivity or response to persistent stimuli. Our study investigates olfactory sensory adaptation using honeybees, focusing on mechanisms, temporal aspects, and behavioral effects. Olfactory receptor neurons (ORN) activity was measured via electroantennograms. Adaptation's induction, duration, and recovery were characterized, alongside with odor identity. Furthermore, to study the behavioral implications of adaptation for the animal, we conducted classical conditioning experiments using odorant mixtures. These experiments showed that adaptation reduces appetitive learning of adapted stimuli, while it enhanced learning of minor mixture's components that normally would stay occluded. We also conducted calcium imaging experiments of antennal lobe projection neurons (PN), which allowed us to observe adaptation-induced neural representation changes. Lastly, a computational model mirrored experimental outcomes, suggesting that reduced ORN and PN responses are sufficient for adaptation, without the need of central plasticity. Overall, our results emphasize that sensory adaptation is critical in maintaining the olfactory system unsaturated and ready to detect changes in the olfactory context.

260 | Exploring the neural encoding of the biomechanics of songbird vocal production: perspective from a biophysical-inspired model

Sensory and Motor Systems

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How vocal communication signals are represented in the cortex is a major challenge for behavioral neuroscience. We used a biophysical model based on the biomechanics of vocal production in songbirds. This mathematical model has as an output synthetic songs that are built to be a copy of the recorded songs uttered by songbirds. This model strongly links vocal production and the biomechanics of the bird's vocal apparatus, allowing us to modify parameters representing the size of the bird's neck and head. We generated a variety of synthetic songs representing birds of different sizes. We presented auditory stimuli while recording neuronal activity in the sensori-motor neural nucleus HVC (proper name) in sleeping Zebra finches (Taeniopygia guttata). This species has the characteristic that HVC nucleus shows neuronal selectivity towards its own song when they are asleep. We found an increase in neuronal activity in response to some of the synthetic but only basal activity when the synthetic songs corresponded to "monstrous" combinations of parameters, where the relationship between "head size" and "neck length" did not follow natural scaling laws. These findings suggest that HVC could be encoding complex biomechanical information about its own song and that scaling laws are naturally encoded in this telencephalic nucleus. Furthermore, these results highlight the value of having biomechanics-inspired modeling tools to conduct experiments that would otherwise not be possible.

262 | Representation of Multisensory Stimuli in the Zebrafish Optic Tectum

Sensory and Motor Systems

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The optic tectum is a structure of the zebrafish brain directly involved in visual processing. Although previous studies suggest that this region also receives auditory inputs, the precise role of that input in information processing remains an open question. We used genetically encoded calcium sensors (elav3:GCaMP6f) and confocal microscopy to record neural activity in the optic tectum of larval zebrafish in response to auditory, visual, and multisensory stimuli. We found that the optic tectum is not only responsive to auditory cues but that auditory input can be integrated with visual cues resulting in enhanced neural responses. Additionally, we show that neural representations in the optic tectum correlate with activity in premotor areas involved in evasive behaviors. We next asked if the neural representations evoked by each type of stimuli was unique. Dimensionality reduction analysis reveals that, notably, the neural representation of multisensory stimuli aligns closely with either the auditory or visual modality, suggesting the absence of an additional unique representation for multisensory stimuli. These results are consistent with behavioral results from our lab indicating that motor evasive responses to multisensory stimuli also cluster in either a 'visual' or an 'auditory' escape mode.

264 | Evaluation of the therapeutic potential D5 receptors ablation in striatal cholinergic interneurons in a mouse model of Parkinson's disease.

Sensory and Motor Systems

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Striatal cholinergic interneurons (SCIN) are the main source of striatal ACh. In Parkinson´s disease (PD), dopaminergic neurons that innervate the striatum degenerate, leading an increase of cholinergic function that contributes to PD symptoms. The gold standard therapy for PD is L-dopa administration, but prolonged treatment may result in dyskinesia.

Recent studies showed that selective modulation of SCINs activity reduces motor deficits have renewed the interest in understanding the mechanisms that alter SCIN function. SCIN become hyperexcitable in parkinsonian and dyskinetic mice due to an increased ligand-independent activity of D5 receptors(D5R). Reducing D5R ligand-independent activity with D1/D5 inverse agonists restores SCIN's normal physiology. Our aim is to clarify the role of D5R in SCINs activity and evidence the potential therapeutic value of reducing the expression of the D5R in these interneurons. For this, we will use two strategies to remove the D5R in SCIN: ChAT-Cre; D5flox/flox mice, to induce D5R ablation from all cholinergic neurons during development, and, D5flox/flox mice injected with a ChAT-Cre viral vector in the striatum, which would allow a selective ablation from SCIN in adulthood. Both groups will be lesioned with 6-OHDA to induce parkinsonism, and treated with L-dopa to induce dyskinesia. We will perform behavioral evaluations for symptoms of parkinsonism and dyskinesias, electrophysiological validations, and immunohistochemical analyses.

266 | Hypergraphs for detection and characterization of sleep states in rats.

Theoretical and Computational Neuroscience

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In the analysis of relationships in systems, graph theory represents connections, but limited to pairs. In reality, the relationships are more complex and the graphs representation loses information. Thus, hypergraphs emerge as a natural extension, proposed by Claude Berge in 1960, to capture these complex relationships. A hypergraph is a pair H(V,E) with vertices and hyperedges covering V. We propose a model based on relationships of graphs with similar vertices but different connections. For example, friendships in social networks, routes between cities or brain connections in different frequencies. Taking m graphs Gi=(W,Ei), i= 1,..,m with cardinality W=k, we create a hypergraph with p=k(k-1)/k vertices and m hyperedges. Laplacian analysis and centrality quantify the hypergraph, revealing its structure and properties. We applied this to real data, analyzing brain connectivity in rats with iEEG in different sleep states. Vertices (k=6 iEEG channels) and graphs Gi (delta, theta, alpha, beta, gamma) form state-specific hypergraphs, allowing comparison.

268 | The dynamics of sensorimotor integration

Theoretical and Computational Neuroscience

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Sensorimotor integration refers to how the sensory feedback originating from motor actions influences the generation of motor patterns. From a dynamic perspective, this can be understood as the impact of a term in the equations governing motor behavior, which is dependent on the variables of the problem in previous instances. An important motor pattern is the generation of periodic behavior, and in this work, we will discuss the impact of delayed feedback in a system capable of displaying these patterns. This question has been addressed when the appearance of periodic motor patterns is due to a Hopf bifurcation. Here we review those results, and then move to explore the rich emergent dynamics arising in delayed systems near a saddle-node in limit cycle bifurcation. Our results reveal a complex subharmonic structure consistent with known activity patterns in multiple fields. We also explore potential applications of this dynamic phenomenon.

270 | Predictive Brain Connectivity Analysis for Treatment Response in Major Depressive Disorder using Resting-State fMRI and Machine Learning

Theoretical and Computational Neuroscience

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Major depression and other mood disorders often require pharmacological interventions, and the responses to these interventions can vary significantly among patients. This variability can lead to costly, prolonged treatments that can be burdensome for patients. Therefore, there is a desire to develop methods that can predict the effectiveness of medications before they are administered. In this study, a predictive modeling approach is proposed to assess the effectiveness of pharmacological treatments in patients with major depression. Machine learning algorithms were applied to resting-state functional magnetic resonance imaging (fMRI) brain images obtained under baseline conditions. The study highlights the utility of non-invasive measurements of brain activity in predicting treatment outcomes, indicating that specific functional connections support accurate prediction of treatment response. The method's ability to forecast outcomes with different treatments in independent patient groups was evaluated. The results demonstrated that baseline brain connections, with feature preselection based on resting-state networks, exhibited a high capacity to predict treatment response. This suggests the feasibility of an automated system based on neurobiological data to enhance treatment decisions in psychiatry.

The need for future research to explore the widespread applicability of these algorithms and their utility in daily clinical practice is emphasized.

272 | Modeling Compact Electronic Neurons: Exploring Neural Dynamics

Theoretical and Computational Neuroscience

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The comprehension of neural networks emerges as a significant scientific endeavor, encompassing a diverse range of methodological approaches across various disciplines. At the heart of these networks lies a multitude of neuron models, reflecting the field's inherent diversity.

In line with this pursuit, a recent significant advancement involves the creation of a novel ultra-compact electronic circuit that emulates the leaky integrate-and-fire dynamics. This novel development aligns harmoniously with the broader objective of understanding neural networks. By employing mathematical modeling to replicate experimental setups, we establish a structured pathway to comprehensively analyze and dissect the intricate system dynamics. This analytical framework not only reveals subtle insights beyond empirical observations but also provides a deeper grasp of the underlying principles at play.

Our mathematical model, rooted in the Morris-Lecar framework, adeptly reproduces experimental outcomes in a qualitative manner. Furthermore, it unfolds a diverse spectrum of dynamic behaviors, encompassing phenomena like bursting, single spiking, and periodic spiking. Beyond capturing the essence of neural behavior, this electronic neuron model emerges as a versatile tool for further exploration and enriched understanding, bridging the gap between theoretical insights and practical application.

274 | High-frequency oscillations biomarkers given by maximum entropy information in epileptic signals

Theoretical and Computational Neuroscience

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Intracranial electroencephalography can directly record local field potentials from a large set of neurons in the vicinity of the electrode. To search for possible epileptic biomarkers and to determine the epileptogenic zone leading to seizures, we investigated the dynamics of the basal and preictal signals. For this purpose, we explored the dynamics of the time series recorded for different frequency bands considering high-frequency oscillations up to 240 Hz. We applied a Hilbert transformation to study the amplitude and phase of the signals, and characterized the dynamics of the different frequency bands in the time entropy-complexity plane, HxC, by comparing the dynamical evolution of the basal and preictal time series.

Our results show that as the system evolves temporally in the preictal state, the signal amplitudes of the HFO bands between 220-230 Hz and 230-240 Hz get closer and closer to the maximum entropy and minimum complexity. We can interpret this as the nature of the system evolving temporally in the preictal state in such a way that the consumption of resources by the system is minimal for the amplitude in the frequencies between 220-230 and 230-240 Hz. In this case the maximum entropy is equivalent to the principle of minimum resource consumption of the system. This corresponds to the minimization of the Gibbs free energy since randomness and low complexity seem to be a constraint for the signal dynamics in the preictal state for the frequency bands between.

276 | Transfer information entropy in records of refractory epilepsy

Theoretical and Computational Neuroscience

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To characterize the nonlinear dynamics of a neural network connecting two stochastic systems, it is necessary to know the flow of information connecting them. A statistical tool commonly used in these studies is the mutual information between the systems. If a time shift is added to this measure, transition probabilities can be studied to discern the dynamical properties of the network. In particular, this method marginalizes the directional information exchanged between the systems by not filtering the information coming from inputs common to the set or shared by both. However, using a Markov process, an asymmetric quantity can be defined between ensembles of neurons through the transfer entropy, which focuses on quantifying the flow of information that circulates only in a given direction between the two systems.

In this work, information transfer was quantified in intracranial recordings from patients with drug-naïve refractory epilepsy. These calculations were performed in those electrodes involved in the area responsible for the generation of epileptic seizures, called the epileptogenic zone. Since transfer entropy is able to detect the directed exchange of information between two systems, in our case, the channels involved according to electrophysiological reports showed an increase in the rate of information transfer in the moments before the epileptic seizure, with respect to a basal temporal recording far before the seizure. Thus, this tool of information theory

278 | DMT Pharmacokinetics and Brain Dynamics: Insights from Whole Brain Modeling

Theoretical and Computational Neuroscience

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DMT, a powerful psychedelic, holds promise for therapeutic applications ranging from addressing mental health conditions to understanding consciousness itself. However, uncovering the precise mechanisms underlying DMT's effects on the human brain remains a complex challenge. In this context, the utilization of Whole Brain models emerges as a valuable tool for dissecting the intricate mechanics of the brain. Whole Brain models provide a comprehensive framework that allows us to simulate and study the collective behavior of brain regions, enabling a bottom-up understanding of brain dynamics.

Using computational models that combine local dynamics with in vivo measurements of anatomical and dynamical functional connectivity of subjects under DMT and Placebo we were able to replicate the effects of the pharmacokinetics of the drug on the dynamic regime of the brain, showing that the onset of the drug results in a shift towards an increasingly unstable state, with oscillations exhibiting a complex envelope, followed by a gradual recovery of the baseline state as the effects of the drug wear off.

Furthermore, by introducing perturbations to different brain areas and observing ensuing effects under the influence of DMT and placebo, we characterize this transient unstable state in terms of its susceptibility to external stimuli, with implications to the understanding of large-scale information transfer during the psychedelic state.

280 | Algorithmic Fairness in Brain-Computer Interfaces for Motor Imagery Detection

Theoretical and Computational Neuroscience

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Brain-Computer Interfaces (BCIs) can transmit information between individuals and computers by monitoring their electrical brain activity using electroencephalogram (EEG) in real-time. The interpretation of these signals using artificial intelligence (AI) algorithms enables the categorization of mental states. However, addressing potential biases that may result from such algorithms, which can favor certain population groups over others, is an important case of study in algorithmic fairness that has not received much attention in the field of BCI.

In this study, we present experiments that help to understand the potential presence of bias with respect to sex on EEG signal decoding for motor imagery detection in BCI. We evaluated multiple databases and AI models. Our findings suggest the possibility that these disparities in performance are linked to the detection of sex-related information in EEG signals by AI models. This discovery exposes the urgency to mitigate biases in AI-based BCIs before deployment, to ensure equity in performance as well as to prevent the amplification of inequalities.

282 | Identification of dialects and individuals of globally threatened Yellow Cardinals using neural networks

Tools Development and Open Source Neuroscience

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Birdsong patterns are complex emergent behaviors that serve roles in communication, mate attraction, and territory defense among avian species. In recent years, machine learning techniques applied to audio field recordings of birdsongs have yielded successful results in studying population distributions and identification of individuals for their monitoring in a variety of bird species, offering promising possibilities in the study of biodiversity and conservation strategies for birds. In this work, we employed deep learning models on sonograms of audio field recordings to explore vocalization statistics in the endangered Yellow Cardinal, a novel application for this species. Our results indicate the presence of vocal signatures that reflect similarities in songs of individuals that inhabit the same region, determining dialects, but which also show differences between individuals that can be exploited by a deep learning classifier to discriminate the bird identities through their songs. Our approach reinforces existing research while automating the characterization of cultural units within the species. When combined with genetic data, this method could enhance management unit delineation, supporting reintroduction initiatives for the Yellow Cardinal. The innovation of neural network-based individual classification, despite limited data availability, holds promise for non-invasive acoustic monitoring, with substantial conservation implications.

284 | 2D recordings of odor-based navigation in vinegar flies and honey bees

Tools Development and Open Source Neuroscience

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The study of the neurobiology of olfaction is strongly influenced by experiments in a wide variety of animal models, as the physiological and computational mechanisms underlying the detection and encoding of odors are highly conserved. This has driven research in insects that exhibit clear odor-guided behaviors and offer advantages for experimental manipulation and the recording of olfactory circuits. The study of olfactory neurobiology requires methodologies that allow for the measurement and manipulation of elements within the olfactory circuit, as well as the ability to make reliable and quantitative measurements of odor-guided behaviors. In this project, our aim is to design a device that enables the recording of navigation trajectories guided by odors with attractive, neutral, or aversive value in two insects that serve as canonical models for the study of olfactory neurobiology: the vinegar fly Drosophila melanogaster and the honeybee Apis mellifera. To achieve this, we have developed a device based on a compensatory sphere, upon which the animal simulates two-dimensional navigation without actual physical displacements. Two devices were constructed, one adjusted to the size and speed of flies and another for bees. The quantitative analysis of speed and direction of movement has been calibrated based on the positive phototaxis of both species. Currently, we are working on adapting the recording and analysis for olfactory stimuli.

286 | Comisión Especial SAN de Género y Diversidades

Comisión Especial SAN de Género y Diversidades

Verónica de la Fuente (IFIBYNE, FCEN, UBA), Nahir Guadalupe Gazal. (Instituto de Investigación Médica Mercedes y Martín Ferreyra (INIMEC-CONICET-UNC), Mariana Inés Holubiec. (IBCN, Fmed-UBA), Verónica Murta. (IFIByNE-CONICET, FCEN-UBA)Leticia Ileana Sarli (Laboratorio Interdisciplinario de Neurociencia Cognitiva (LINC). CEMSC3, ICIFI, Universidad Nacional de San Martin), Mauricio Galiano (Universidad Nacional de Córdoba), Cecilia Martinez (IFIBIO, CABA), Leticia Sarli (Centro de Investigación en Neurociencias y Neuropsicologia, Univ. Palermo, CABA), María Jesús Trujillo (IFIBIO, CABA)

Contribuyó nuevamente en la divulgación en redes de perfiles científicos de socias de SAN con relación al 8M. A fines de 2022 la comisión de Género y Diversidad lanzó, en nuestra comunidad, una Encuesta sobre Salud Mental y Violencias, cuyos resultados fueron analizados durante el transcurso de 2023. Los mismos se expondrán y discutirán durante la actividad Social organizada por la comisión, que tendrá lugar durante el Congreso SAN 2023. Por otro lado, recibió la aceptación del informe correspondiente al subsidio IBRO Diversity (asignado en 2022), así como el segundo pago del mismo. Este dinero permitió a la comisión de Género y Diversidad aportar material a la comisión de Divulgación, con el fin de articular nuevas tareas conjuntas enfocadas en la visibilización de distintas problemáticas. A su vez, participamos activamente en la solicitud del subsidio de Agencia de C y T de la Nación para Ayuda económica para cuidado de personas a cargo de asistentes al Congreso SAN 2023.

288 | Comisión Especial SAN de Federalización

Comisión Especial SAN de Federalización

Fernando Altamirano. (Facultad de Química, Bioquímica y Farmacia, UNSL- IMIBIO-SL, CONICET-UNSL, San Luis), Soledad Picco (IFIBYNE, FCEN, UBA), Lorena Franco (CNEA, Bariloche), María Angélica Benítez (Laboratorio Interdisciplinario de Neurociencia Cognitiva (LINC) CEMSC3 ICIFI UNSAM CONICET), Rodrigo Echeveste (Instituto de investigación en Señales, Sistemas e Inteligencia Computacional, sinc(i), CONICET-UNL, Santa Fe), Rocío Beatriz Foltrán. (Instituto de Investigación en Neurociencias Prof. E. De Robertis, Fmed-UBA), Maria Florencia Rossetti. (Instituto de Salud y Ambiente del Litoral (ISAL), CONICET-UNL, Santa Fe), Gabriela Salvador (Instituto de Investigaciones Bioquímicas de Bahía Blanca), María Ximena Silveyra (Instituto de Investigaciones Biológicas, Mar del Plata), Marta Antonelli (Facultad de Medicina, UBA, CABA)

La comisión ha llevado adelante durante estos dos años acciones tendientes por un lado a incluir en la SAN y a vincular a quienes realizan investigación en neurociencia fuera de los nodos centrales, y por el otro a visibilizar su tarea frente a nuestra comunidad toda. A tal fin, se impulsó la campaña “Sumate a la SAN” en redes y mediante contacto por mail, para promover la afiliación de nuevos miembros. Además se generó un simposio recurrente en la reunión anual denominado “NeuroTour Federal”, que funciona como un muestrario de la investigación realizada en las regiones habitualmente menos representadas. En el mismo sentido y para sumar actividades con mayor periodicidad, se gestionó junto con la Comisión de Conferencias, la inclusión de Conferencias Federales Virtuales, ofreciendo una valiosa vidriera y oportunidad de intercambio para estos grupos. Estas actividades también fueron aprovechadas para acercar a la SAN a investigadores que suelen concurrir a otras conferencias de temáticas afines. Actualmente, se está trabajando junto con la Comisión de Educación, a complementar la oferta de cursos para estudiantes doctorales en provincias en las que existen todavía fuertes vacancias.

290 | Comisión Especial SAN de Historia

Comisión Especial SAN de Historia

Daniel Calvo (IFIBYNE-UBA-CONICET, Fcen- UBA, CABA), Marta Antonelli (Facultad de Medicina, UBA, CABA), Osvaldo Uchitel (IFIBYNE, UBA, CONICET, CABA), Leandro Champarini (IFEC, Córdoba), Agustín Mauro (IDH, Córdoba), Ana Adamo (IQUIFIB, CABA)

Las actividades de la comisión estuvieron enfocadas en indagar la huella dejada por una serie de científicos europeos que llegaron a nuestro país, a fines del siglo XIX y principios del XX, y representan las primeras intervenciones del desarrollo de las neurociencias en Argentina. Para ello, se ha contado con un subsidio de la FENS (2022). En este trabajo inicial se abordó la figura de Cristofredo Jakob (1866-1956), neuropatólogo alemán que desarrolló sus actividades en el Hospicio de las Mercedes UBA (actual Htal Moyano) y en la UNLP entre 1899 y 1956. Como resultado de nuestra primera actividad se confeccionó un poster, que fuera presentado en el congreso internacional de aquella sociedad por Macarena Herrero. Más recientemente, la SAN organizó una visita a los Hospitales Borda y Moyano con la inestimable colaboración de los Dres. Roberto Cacuri y Fabián Loidl que actuaron de enlace, para conocer de cerca y documentar los vestigios de los laboratorios que fundara Jakob, hoy convertidos en un informal museo al cuidado de los hospitales, pero que evidentemente necesita de una profunda restauración. En la citada expedición hemos también tenido la oportunidad de tomar contacto con la documentalista cordobesa Alejandra Molina que se encuentra produciendo un cortometraje sobre la figura del científico alemán y además de departir con el nieto de Jakob que vive en nuestro país y afortunadamente acudió a la reunión.