

XLI SAN
ANNUAL MEETING

OCTOBER 2-4
CIUDAD UNIVERSITARIA
UNIVERSIDAD DE BUENOS AIRES

e-book

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Instituto de Fisiología, Biología Molecular y Neurociencias

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. SAN adheres to the copyright laws guiding the appropriate sharing of scientific research material, including data.

Conference Best Practices

All communication must be carried out in a professional and respectful manner. Live sessions will be moderated and disrespectful messages will not be tolerated. SAN encourages open intellectual discussion in a welcoming and inclusive environment. Inappropriate behavior, harassment or offensive acts towards any member of the community is strictly prohibited and will result in removal from the conference and a report to the host institution of the removed attendee will be issued. Be friendly, welcoming and respectful. When discussing with colleagues, disagreement is an unavoidable occurrence and it is important that all discussions are carried out in good faith and seen as an opportunity to improve others and our own work. Be mindful of the tone and words you choose to communicate with others.

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 SAN 2026 Organizing Committee or SAN Council members. The event organizers reserve the right to take any action to prevent violations of this Code of Conduct.



Programme at a Glance

Wednesday 30 September to Sunday 04 October

Programme at a Glance

30 SEP
WEDNESDAY

09:00 – 09:30
Registration

09:30 – 18:30
Pre-meeting Schools

01 OCT
THURSDAY

09:00 – 09:30
Registration

09:30 – 18:00
Pre-meeting Schools

18:00 – 18:30
Registration

02 OCT
FRIDAY

08:30 – 09:00
Registration

09:00 – 10:00
Plenary Lecture 1
Solla

10:00 – 10:30
Break

10:30 – 12:30
S1 · Aula Magna Pab 2
From Synapses to Cognition: Neural Communication and Brain Dynamics in Health and Disease
S2 · Auditorio IFIBYNE
Neural Perspectives on Behaviour

12:30 – 13:30
Lunch

13:30 – 15:00
Red Argentina de Estudiantes en Neurociencias IFIBYNE

15:00 – 17:30
Poster Session 1 IFIBYNE

17:30 – 18:00
Break

18:00 – 19:00
Plenary Lecture 2
Mameli

19:00 – 21:00
Asamblea SAN IFIBYNE

03 OCT
SATURDAY

09:00 – 10:00
Plenary Lecture 3
Salvador

10:00 – 10:30
Break

10:30 – 12:30
S3 · Aula Magna Pab 2
From Circuits to Models: Emerging Translational Approaches to Alzheimer's Disease Across Species and Scales
S4 · Aula 5
Under Pressure: Neural Mechanisms of Conflict and Action Selection
S5 · Aula 6
Afferent and Efferent Circuits in the Cochlea: From Ribbon Synapses to Central Control

12:30 – 13:30
Lunch

13:30 – 15:00
Simposio Comisión Federalización Aula Magna

15:00 – 17:30
Poster Session 2 IFIBYNE

17:30 – 18:00
Break

18:00 – 20:30
Young Investigator Talks

20:30 – 22:00
Mesa Redonda 2 / Género IFIBYNE

22:00 – 23:00
Party IFIBYNE (22:00 - Following the gender activity)

04 OCT
SUNDAY

10:00 – 10:30
Break

10:30 – 12:30
S6 · Aula Magna Pab 2
Neuronal circuit mechanisms for auditory cognition: from learning to communication
S7 · Aula 5
Neurobiological Signatures of Stress: Sex-Specific Trajectories from Gestation to Adulthood In Rodents and Humans
S8 · Aula 6
Data-Driven Approaches to Understanding Mechanisms of Brain Function

12:30 – 13:30
Lunch

13:30 – 15:00
Mesa Redonda / Taller de Subsidios Internacionales

15:00 – 17:30
Poster Session 3 IFIBYNE

17:30 – 18:00
Break

18:00 – 19:00
Plenary Lecture 4
Hassan



Courses and Small Conference

One course and one ISN Small Conference

Courses and Small Conference

CURSO

Diseño y ejecución de experimentos conductuales

Docentes

Juan Esteban Kamienkowski
Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, Universidad de Buenos Aires, CONICET

Juan Octavio Castro
Laboratorio de Inteligencia Artificial Aplicada, Instituto de Ciencias de la Computación, Universidad de Buenos Aires, CONICET

Ambos PsychoPy Ambassadors, reconocidos oficialmente por la comunidad internacional de PsychoPy. El curso contará con el apoyo del equipo de PsychoPy.

Propuesta

El objetivo principal de este curso es introducir a lxs asistentes al diseño y ejecución de experimentos conductuales y neurocientíficos utilizando una de las herramientas más versátiles y abiertas como es PsychoPy. A lo largo de dos jornadas, se abordarán tanto los fundamentos conceptuales del diseño experimental y los detalles técnicos relacionados a su implementación en computadoras, como las herramientas prácticas necesarias para crear, ejecutar y compartir experimentos.

El curso combina exposición teórica, demostraciones prácticas y ejercicios guiados.

Lxs participantes diseñarán su propio experimento conductual (por ejemplo, tareas de tiempo de reacción o discriminación perceptual), y aprenderán llevarlo a migrarlo a JavaScript para publicarlo en plataformas online como Datapruebas o Pavlovia, la plataforma online asociada a PsychoPy, para su ejecución y recolección de datos vía web.

Durante el segundo día, lxs asistentes podrán probar los experimentos creados por sus propios compañerxs y recibir asesoramiento para diagramar el setup de sus propios proyectos experimentales, sincronizando con otros equipos y perifericos.

Requisitos

No se requieren conocimientos previos de programación, aunque es conveniente tener nociones básicas de Python si luego desean profundizar en otras aplicaciones. También es recomendable, aunque no necesario, tener nociones básicas de psicología experimental o neurociencias cognitivas.

Es deseable que cada participante cuente con una computadora con acceso a internet (o una cada dos personas).

Antes del comienzo del curso, se pondrá a disposición material digital introductorio que permitan tener referencias para la instalación de PsychoPy y tutoriales básicos.

Día 1

TEORÍA

- ¿Qué es PsychoPy? Filosofía, ventajas y aplicaciones.
- Interfaz Builder vs. Interfaz Coder: distintos niveles de control.
- Introducción al diseño experimental en PsychoPy: estímulos, condiciones, rutinas y bucles.
- Conceptos clave: tiempos de presentación, precisión, aleatorización y registro de respuestas.

PRÁCTICA

- Creación paso a paso de un experimento simple (p. ej., tarea de tiempos de reacción o Stroop).
- Uso del Builder para diseñar estímulos visuales y auditivos.
- Introducción al manejo de condiciones desde archivos CSV.
- Subida y prueba del experimento en Pavlovia.

Día 2

TEORÍA

- Buenas prácticas en el diseño y validación de experimentos computarizados.
- Consideraciones sobre sincronización, hardware y entornos de ejecución.
- Cómo extender PsychoPy con código Python.

PRÁCTICA

- Ejecución cruzada de los experimentos entre participantes.
- Revisión de resultados y archivos de datos.
- Introducción a la lectura y análisis de datos de salida.
- Asesoramiento personalizado: diseño de setups para proyectos propios (comportamentales o EEG/fMRI).

ISN SMALL CONFERENCE

Computational approaches to understand brain function: from biochemistry to circuits

Contenido

Se propone una introducción teórico-práctica al modelado computacional de la actividad neuronal, orientada a estudiantes de posgrado e investigadores interesados en comprender cómo se construyen y utilizan modelos biológicos de neuronas y circuitos para estudiar la dinámica del sistema nervioso.

Se abordará el modelado de neuronas a distintos niveles de complejidad, desde la descripción biofísica del potencial de acción en el modelo de Hodgkin-Huxley[1,2] hasta modelos simplificados como LIF o GIF[2], que capturan ciertas características del potencial de acción. Se discutirán las ventajas y desventajas de utilizar modelos simplificados. Luego se profundizará en el modelado de conexiones sinápticas, eléctricas y químicas, explorando qué aspectos pueden ser modelados y que costo computacional lleva asociado.

En la segunda parte, se extenderán estos conceptos al estudio de redes neuronales biológicamente inspiradas, explorando cómo las interacciones sinápticas y los circuitos excitatorios-inhibitorios dan lugar a propiedades emergentes, como circuitos de feedback o feedforward que generan oscilaciones, control de ganancia, acoples temporales o competencias en el encoding, hasta el circuito de ring atractor que permite la navegación espacial. Se introducirá también el uso de herramientas computacionales actuales en Python (principalmente Brian2[4]), que permiten simular de forma accesible y reproducible el comportamiento de neuronas y redes.

Se combinarán exposiciones teóricas con actividades prácticas guiadas en Jupyter notebooks, donde los participantes construirán y analizarán sus propios modelos.[3]

Objetivos

- Introducir los principios básicos del modelado computacional en neurociencia.
- Comprender la formulación matemática de los principales modelos neuronales (HyH, modelos de Izhikevich, LIF, GIF)
- Explorar el comportamiento de redes neuronales, específicamente en los circuitos de feedback, feedforward y atractor ring.
- Familiarizar a los participantes con las principales librerías y entornos de simulación en Python, adquiriendo herramientas prácticas para iniciar sus propias simulaciones.

Requisitos

Tener conocimientos básicos de programación va a ayudar con el entendimiento de las etapas prácticas.

Docentes responsables

- Dr. Claudio Mirasso
- Dr. Emiliano Marachlian
- Dra. Luz Bavassi
- Valentin Agullo
- Facundo Emina
- Agustin Lara

- Macarena Amigo Duran

Día 1

MAÑANA

09:00 – 10:30 **Teoría 1 – Introducción al modelado neuronal**

- Historia breve: de Cajal y Hebb a Hodgkin–Huxley y redes neuronales
- Modelos a distintos niveles: LIF, GIF, Izhikevich, Hodgkin–Huxley.
- Concepto de trade-off entre simpleza y biología.

10:30 – 11:00 *Receso*

11:00 – 12:00 **Teoría 2 – Charla + Notebook práctico – El modelo de Hodgkin–Huxley**

- Canales iónicos y ecuaciones diferenciales.
- Qué reproduce bien y qué simplifica. Ir mostrando como se ve un modelo de una neurona en el notebook y plots con un potencial de acción de HyH.

12:00 – 13:30 *Almuerzo*

TARDE

13:30 – 15:30 **Notebooks prácticos – Ejemplo de neurona HH**

- Charla aplicada: “Qué aprendimos del modelo de HH y cómo se usa hoy”.
- Notebook Python: simulación de un potencial de acción con HH.
- Discusión interactiva con cambios de parámetros.

15:30 – 16:00 *Receso*

16:00 – 18:30 **Notebooks prácticos – Modelos simplificados y sinapsis**

- Introducción al LIF y GIF con notebooks.
- Ejercicios: cambiar parámetros y observar dinámica.
- Modelado de sinapsis simples (AMPA/GABA) en notebooks.
- Mini-ejercicio final del día: comparar curvas FR–I de LIF vs. HH.

Día 2

MAÑANA

09:00 – 12:30 **Teoría 3 – Redes y circuitos (Receso en el medio 10:30 – 11:00)**

- Circuitos de feedback y feedforward para lograr oscilaciones
- Circuito del ring atractor que permite la navegación

12:00 – 13:30 *Almuerzo*

TARDE

13:30 – 17:30 **Práctica intensiva en circuitos (con receso intermedio 15:30–16:00)**

Simulación “desde cero” (2 h)

- Construcción de un circuito excitatorio–inhibitorio pequeño sin librerías.
- Visualización de actividad en tiempo real (spikes, oscilaciones).
- Reflexión: cuánto tiempo lleva y qué limitaciones aparecen.

Uso de librerías (Brian2) (2 h)

- Reproducir el mismo circuito en Brian2.
- Comparar velocidad, escalabilidad y legibilidad del código.

17:30 – 18:30 **Charla de cierre – Análisis conceptual**

Referencias

1. HODGKIN AL, HUXLEY AF. A quantitative description of membrane current and its application to conduction and excitation in nerve. J Physiol. 1952 Aug;117(4):500-44.
2. Ganguly, C., Bezugam, S.S., Abs, E. et al. Spike frequency adaptation: bridging neural models and neuromorphic applications. Commun Eng 3, 22 (2024).
3. Tutorials de Neuromatch Academy (W1D1, W2D3).
4. Stimberg M, Brette R, Goodman DFM (2019), Brian 2, an intuitive and efficient neural simulator, eLife 8:e47314.



Plenary Lectures

Four lectures · Friday 02 to Sunday 04 October

Plenary Lectures

PLENARY LECTURE 1 · FRIDAY 02 · 09:00 – 10:00

Sara A. Solla

Department of Neuroscience, Northwestern University

Low Dimensional Neural Manifolds for the Control of Movement

The ability to simultaneously record the activity from tens to hundreds to thousands of neurons has allowed us to analyze the computational role of population activity as opposed to single neuron activity. Recent work on a variety of cortical areas suggests that neural function may be built on the activation of population-wide activity patterns, the neural modes, rather than on the independent modulation of individual neural activity. These neural modes, the dominant covariation patterns within the neural population, define a low dimensional neural manifold that captures most of the variance in the recorded neural activity. We refer to the time-dependent activation of the neural modes as their latent dynamics and argue that latent cortical dynamics within the manifold are the fundamental and stable building blocks of neural population activity. A focus on motor cortex provides a model for neural control of movement in which "neural modes" are the generators of motor behaviors. We review existing evidence in support of neural manifolds, and present novel results on the relation between latent dynamics, muscle activity, and limb control. A method to align the latent dynamics associated with a simple task allows us to track manifold activity across time and across primates.

PLENARY LECTURE 2 · FRIDAY 02 · 18:00 – 19:00

Manuel Mameli

The University of Lausanne

Neural Circuit Mechanisms for Aversion Processing

Appropriate behavioral strategies when facing aversive experience are necessary for the individual survival. I will present latest results describing lateral habenula’s role in shaping approach and avoidance behaviors. I will highlight how synaptic strength, circuit assembly, and neuronal dynamics contribute to adaptive behavioral responses following environmental threats. Using electrophysiological and imaging approaches I will provide evidence that lateral habenula neurons excitation is a requirement during encoding of threats of different nature spanning from predator attack to newborn vocalisation. I will provide a framework whereby habenular activity represents a switchboard determinant in the transition to physiological threat encoding and pathological negative affect. Altogether this will provide the audience with a general understanding of the neural circuit underlying decision-making and emotional states in health and pathology.

PLENARY LECTURE 3 · SATURDAY 03 · 09:00 – 10:00

Gabriela Salvador

INIBIBB Bahía Blanca

Molecular Mechanisms Underlying Neuron-Glia Metabolic Interactions in Neurodegeneration

Neurodegenerative processes are increasingly understood as metabolic disorders in which neuron–glia interactions critically regulate lipid homeostasis and redox status. Our work has focused on identifying the molecular mechanisms underlying neurotoxicity triggered by oxidative stress, proteotoxicity, iron dyshomeostasis, and pesticide exposure. Early studies from our lab demonstrated that α-synuclein modulates SREBP-dependent transcription, leading to alterations in fatty acid and cholesterol metabolism, thereby reshaping cellular responses to oxidative stress. Building on these findings, we subsequently identified the involvement of molecular components of lipid-dependent resolution pathways. These mechanisms were shown to modulate neuroinflammatory and oxidative processes, highlighting their role in controlling lipid peroxidation and promoting adaptive responses in neurons. More recently, studies using in vivo models of iron overload and pesticide exposure have revealed profound alterations in neutral lipid metabolism, including cholesterol accumulation and increased triacylglycerol hydrolysis. These changes are accompanied by dopaminergic neurodegeneration and motor impairments. Importantly, these alterations are tightly associated with ferroptosis and depend on intercellular metabolic interactions, in which glial cells actively contribute to neuronal lipid remodeling. Collectively, our findings support the concept that neurodegenerative processes can be understood as lipidopathies driven by dysregulated neuron–glia metabolic interactions. Targeting the molecular pathways that govern lipid homeostasis and resolution responses may provide novel therapeutic strategies for neurodegenerative diseases.

PLENARY LECTURE 4 · SUNDAY 04 · 18:00 – 19:00

Bassem Hassan

Paris Brain Institute and Yale School of Medicine

Developmental Emergence of Brain Individuality

The Nature versus Nurture debate has generally been considered from the lens of genome versus experience dichotomy and has dominated our thinking about behavioral individuality and personality traits. In contrast, the role of nonheritable noise during brain development in behavioral variation is understudied. Using the Drosophila melanogaster visual system, I will discuss our efforts to dissect how individuality in circuit wiring emerges during development, and how that helps generate individual behavioral variation.



Symposia

Eight symposia · Friday 02 to Sunday 04 October

Symposia

SYMPOSIUM S1 · FRIDAY 02ND - AULA MAGNA - PAB 2

From Synapses to Cognition: Neural Communication and Brain Dynamics in Health and Disease

CHAIR

María Victoria Oberholzer
Instituto de Neurociencia Cognitiva y Traslacional Fundación Favaloro (INECO-CONICET)

Understanding how the brain coordinates activity across distributed networks is key to explaining cognition in both health and disease. This symposium brings together complementary approaches—from systems neuroscience to clinical research and neurotechnology—to examine how neural communication dynamically supports behavior across multiple levels of organization. Jean-Christophe Comte will present evidence from freely moving rats showing that synaptic strength across hippocampal pathways fluctuates with the sleep–wake cycle, highlighting the roleof brain states in memory processes. Bridging to human cognition, Juan Kamienkowski will explore how neural dynamics support visual search in naturalistic environments, revealing how attention and memory are integrated over time. Lucia Alba Ferrara will address how distributed brain networks support social communication and reorganize under pathological conditions. Finally, Victoria Peterson will discuss how understanding brain dynamics can inform the development of brain–computer interfaces for motor rehabilitation. Together, these contributions illustrate how neural communication operates across scales, linking synaptic mechanisms with cognition and clinical applications.

SPEAKERS

Jean-Christophe Comte

Université Claude Bernard Lyon 1, Francia

Modulation of Brain States Duration Encode Synaptic Strength Dynamics.

Interactions among brain areas are essential for most cognitive functions. Neuronal interactions between these areas depend on the modulation of synaptic strength; however, this modulation remains poorly understood. We recorded evoked responses in four hippocampal pathways in freely moving male rats over a 24-hour period. We show that synaptic strength in these pathways oscillates with a very slow periodicity and correlates with the duration of vigilance states. A model based on hypnogram data and synaptic strength in one pathway was able to predict the evolution of synaptic strength in most pathways, except for one. These results suggest that the temporal succession of vigilance states may contribute to memory processes through rapid modulation of synaptic strength across several pathways during the sleep–wake cycle. This further suggests that memory processes depend not only on sleep duration but also on sleep architecture, as well as on cardiac and respiratory rhythms.

Juan Kamienkowski

Laboratorio de Inteligencia Artificial Aplicada, Instituto de Cs de la Computación, UBA - CONICET

Parsing Brain's Algorithms During Resolution of Visual Search Tasks

Understanding how the human brain orchestrates visual search in naturalistic environments requires moving beyond highly constrained laboratory settings. This talk presents a comprehensive research programme investigating the neural dynamics of active visual exploration by co-registering eye movements with electroencephalography (EEG) and magnetoencephalography (MEG). We will first discuss earlier work demonstrating that target detection during free-viewing elicits reliable fixation-related potentials, including early sensory markers and a robust P3 component akin to classical fixed-gaze paradigms. Expanding on this, we explore how the brain parses a mental programme of visual routines, showing that low-frequency oscillatory activity and baseline shifts track the integration of evidence and task progression across multiple fixations. Furthermore, we address the transition towards more ecologically valid hybrid search tasks, where attention and

memory continuously interact. By applying advanced deconvolution models to disentangle overlapping neural responses, we reveal how memory load modulates early visual processing and frontoparietal beta-band activity. Ultimately, this line of research bridges the gap between active vision and cognitive electrophysiology, offering a spatiotemporal map of the brain's algorithms during naturalistic search.

Victoria Peterson
IMAL-CONICET-UNL, Argentina

The neurophysiology behind the development of brain-computer interfaces for rehabilitation

Brain-computer interfaces (BCI) allow the control of external devices through real-time brain signal decoding. When aiming to use these devices as tools for motor rehabilitation, the development of machine learning algorithms for decoding movement intention or imagination requires a suitable and accurate framework based on the underlying neurophysiology of the mental task to be decoded. In this talk, we will seek to understand the neurophysiology in electroencephalography signals that must be captured to promote effective neurofunctional motor rehabilitation. Challenges in the construction of such algorithms as well as in the certification of proper signal generation from the BCI users will also be discussed.

Lucía Alba Ferrara
ENyS - CONICET

Understanding Brain Communication Through Social Cognition: Evidence from Clinical Neuroscience

Understanding how the brain supports social communication requires integrating evidence from affective and pragmatic language processing as well as clinical models of neural reorganization. Thistalk will present converging findings from functional neuroimaging studies on emotional prosody, idiomatic expressions, and sarcasm comprehension. Results show that while basic affective processing relies on temporal and lateral frontal regions, more complex socio-cognitive demands—such as mental state attribution—engage medial prefrontal and fronto-parietal networks. Similarly, pragmatic language processing recruits bilateral fronto-temporal systems, with contributions from both hemispheres depending on semantic complexity and contextual integration. Evidence from patients with temporal lobe epilepsy further demonstrates that these networks are dynamic and capable of functional reorganization, recruiting alternative regions to preserve social communicative abilities. Altogether, these findings support a model of brain communication as a distributed, flexible system shaped by both cognitive demands and neural plasticity, highlighting theclose interaction between social cognition and language in health and disease.

SYMPOSIUM S2 · FRIDAY 02ND - IFIBYNE

Neural Perspectives on Behaviour

CHAIR
Martin Klappenbach
IFIBYNE-UBA-CONICET

CO-CHAIR
Esteban J. Beckwith
IBioBA-MPSP - CONICET

We propose an engaging symposium that delves into the intricate realm of neuronal processing in animal behavior. This symposium aims to showcase cutting-edge research and foster interdisciplinary discussions among esteemed researchers dedicated to exploring the mysteries of neuronal processing in animal behavior. The symposium will feature four distinguished researchers who have made remarkable strides in the field of animal neuroscience. Through their expertise and dedication, they will present their latest findings, providing valuable insights into various aspects of neuronal processing in animal behavior. Topics covered will include decision-making processes, individuality, circadian rhythms, social behaviours, and the genetic basis of behavior. By encompassing a diverse range of subjects, this symposium will offer attendees a comprehensive understanding of the latest advancements in the field. Moreover, by incorporating a variety of animal models, the symposium will highlight how different species reveal distinct evolutionary strategies that shape behaviour. This symposium holds relevance not only for neuroethologists and neurobiologists but also for researchers interested in broader neuroscience themes. Attendees will engage in stimulating discussions, exchange ideas, and potentially foster collaborations that bridge different areas of neuroscience. We firmly believe that this symposium will make a significant contribution to the annual meeting of the Sociedad Argentina de Neurociencias, providing a platform to gain profound insights into neuronal processing in animal behavior and unravel the intricate complexities of their neural networks.

SPEAKERS

Silke Sachse
University of Würzburg

From brain to behavior: the neural basis of insect olfaction

Most animals rely on their sense of smell to guide behaviors that are essential for survival and reproduction. However, the vast array of odor stimuli presents a significant challenge to neural coding. Using genetically tractable models such as Drosophila melanogaster and the migratory locust (Locusta migratoria), we investigate how insect olfactory circuits encode, process, and assign behavioral value to odors. Using genetic tools, neurophysiological imaging, and behavioral analyses, we dissect the functional organization of olfactory circuits and their contribution to odor coding and odor-guided behavior. Our work demonstrates that olfactory glomeruli - the anatomical units of the first olfactory center, the antennal lobe - have a unique neuronal composition linked to their functional relevance. We also show that higher brain centers decode the behavioral value of an odor and that spatial activity patterns, such as the ring-shaped chemotopic map in the locust antennal lobe, encode ecologically meaningful information. Ongoing studies address circuit plasticity, state-dependent modulation as well as multimodal integration and learning. The talk will summarize our recent insights into the coding strategies and plastic components of the olfactory circuitry of insects

Angeles Salles
University of Illinois, Chicago

Neuroethology of Social Behavior and Acoustic Communication in Bats

Bats are highly social animals with complex vocal communication systems supporting navigation and social interactions. My research investigates the neural and behavioral mechanisms underlying social cohesion, auditory perception, and communication in bats. From a neuroethological perspective, integrating behavioral ecology with neural systems approaches, my lab explores fundamental questions such as how bats recognize roost mates and how this may influence roost fidelity, how hierarchical social structures form, and how context shapes auditory perception of communication sounds. To explore these questions, we employ a

multidisciplinary approach, combining behavioral assays, electrophysiological recordings, neuroanatomical mapping, and computational modeling, spanning both controlled laboratory settings and field environments. In this talk, I will provide an overview of our recent advances and strategies to answer these questions and discuss how our work provides key insights into the neural mechanisms of auditory communication in mammals.

John Ewer
Universidad de Valparaíso

Control of Drosophila behavior by neuropeptides and the circadian clock

We use the fruit fly, Drosophila melanogaster, to study how neuropeptides and the circadian clock regulate animal behavior. Our main focus is ecdysis, the vital behavior used by arthropods to shed their old cuticle at the end of the molt. Ecdysis is controlled by a number of neuropeptides and hormones, which regulate the precise order and timing of the different ecdysial behavioral subroutines. This system provides a useful model to understand how peptide hormones control complex responses, such as satiation, pair bond formation, etc. In addition, the last ecdysis (adult emergence, or eclosion) is regulated by the circadian clock, which restricts emergence to a specific window of time. The circadian control of emergence depends on the activity of two coupled circadian clocks: the central circadian pacemaker in the brain and a peripheral clock located in the prothoracic gland (PG), an endocrine gland whose only known function is the production of the molting hormone, ecdysone. This system provides an opportunity to study how circadian clocks are coupled and how they impose a daily periodicity to a behavior.

Romina B. Barrozo
Laboratorio Neuroetología de Insectos, IBBEA, UBA-CONICET. DBBE - FCEN - UBA

Decoding feeding decisions in a blood-sucking insect

How do blood-sucking insects decide whether to feed? For hematophagous insects, such as kissing bugs and mosquitoes, the decision to bite and ingest blood is a critical behavioral step that determines both feeding success and pathogen transmission. This process emerges from the integration of multiple sensory cues that signal whether a potential food source is suitable or potentially harmful. Appetitive signals promote feeding acceptance, whereas aversive cues discourage contact, biting, or ingestion. Understanding how these opposing signals are detected and integrated is therefore central to understanding the neurobiology of hematophagy. Our work investigates the dynamic interactions between appetitive and aversive peripheral pathways that ultimately lead to acceptance or avoidance of feeding. In particular, we study the sensory mechanisms involved in the detection of phagostimulatory and deterrent cues, identifying pathways associated with feeding promotion and others linked to irritation and evaluation of the meal quality. By characterizing these peripheral pathways across behavioral, sensory, and physiological levels, we provide a mechanistic framework for understanding how blood-sucking insects evaluate feeding opportunities and translate sensory information into behavioral decisions. Decoding these sensory mechanisms may reveal novel targets for strategies that interfere with vector feeding and reduce disease transmission.

SYMPOSIUM S3 · SATURDAY, 3RD - AULA MAGNA PAB 2

From Circuits to Models: Emerging Translational Approaches to Alzheimer's Disease Across Species and Scales

CHAIR

Emilio Kropff
Leloir Institute Foundation - IIBBA/CONICET

Alzheimer's disease (AD) is a multiscale disorder in which genetic susceptibility, vascular dysfunction, neural circuit abnormalities, and cognitive decline interact across time. Understanding these links requires experimental approaches that bridge molecular mechanisms, systems neuroscience, and translational animal models. This symposium brings together four complementary perspectives to examine how AD-related dysfunction emerges across species and levels of organization. The session will begin with a discussion of major AD risk factors, including APOE4, MAPT, PICALM, and APP, focusing on how their interaction contributes to blood-brain barrier dysfunction, neurodegeneration, tauopathy, and amyloidosis, and on therapeutic strategies aimed at restoring neurovascular integrity. The second talk will then address circuit-level abnormalities, presenting evidence that abnormal high-frequency oscillations constitute an early signature of network hyperexcitability in AD, with converging findings from mouse models and human studies. The third talk will establish a physiological baseline in the South American rodent Octodon degus by characterizing hippocampal spatial coding, oscillatory dynamics, and sharp-wave ripple activity in young healthy animals. The final talk will expand this perspective by presenting Octodon degus as a natural model of brain aging and Alzheimer-like pathology, highlighting its potential for studying the links between aging, lipid metabolism, and neurodegeneration. Together, these talks offer an integrated view of Alzheimer's disease from genes and neurovascular mechanisms to neural dynamics and behavior, while also emphasizing the importance of innovative and complementary animal models. The symposium will highlight emerging translational opportunities for identifying early biomarkers, refining disease models, and advancing mechanistically informed therapeutic strategies.

SPEAKERS

Marcelo Coba
Keck School of Medicine, University of Southern California

Alzheimer's genetic risk factors, neurovascular dysfunction and neurodegeneration: Therapeutical approaches

Alzheimer's disease (AD) is a complex brain disorder, with more than 100 risk loci being identified. The interaction between factors is difficult to model, not only because of the interpretation of the mutations in the individual gene function, but also because these mutations are likely to impact different cell types at different stages of the disease. We will focus on the role of the main susceptibility gene for Alzheimer's disease, Apolipoprotein E4 (APOE4) and the risk factors Microtubule Associated Protein Tau (MAPT), the Phosphatidylinositol Binding Clathrin Assembly Protein (PICALM), and the Amyloid-beta precursor protein (APP). We will show their synergic interaction dysregulating blood brain barrier (BBB) function and increasing neurodegeneration. We will discuss tentative therapeutical approaches directed to restore BBB function and their impact on neurodegeneration, tauopathy and amyloidosis.

Christos Lisgaras
Department of Psychiatry, NYU Grossman School of Medicine

Brain Oscillations in Alzheimer's Disease: Converging Evidence from Humans and Mouse Models

Neuronal oscillations are fundamental for coordinating brain activity across spatial and temporal scales, and disruptions in these rhythms emerge early in the Alzheimer's disease continuum. In this talk, I will present translational findings from animal models and human studies demonstrating that abnormal high-frequency oscillations (HFOs; 250-500 Hz) represent an early signature of network hyperexcitability in Alzheimer's

disease. Using wideband electrophysiological recordings in mouse models, we identified HFOs as a previously unknown abnormality that arises before overt neuropathology and cognitive decline, with hippocampal circuits playing a central role in their generation. Extending these findings to humans, fast HFOs (>250 Hz) can be detected noninvasively during sleep in adults with Down syndrome, a population at ultra-high risk for Alzheimer's disease. These results suggest that HFOs may serve as promising translational biomarkers of early circuit dysfunction in Alzheimer's disease dementia.

Emilio Kropff
Leloir Institute Foundation - IIBBA/CONICET

Spatial coding in the hippocampus of young, healthy Octodon degus: a new avenue to investigate brain function during sporadic Alzheimer's disease

Octodon degus is a South American rodent that has attracted increasing interest as a model of aging and sporadic late-onset Alzheimer's disease (AD). Spatial memory deficits have been reported in this species in association with advanced AD-like pathology or hippocampal lesions, underscoring its potential for investigating how hippocampal network function relates to behavioral performance across disease stages. Despite this promise, little is currently known about neural coding mechanisms in the degu brain. Here, we characterize neuronal activity and local field potential dynamics in young, healthy animals during (a) spatial navigation in open-field environments and (b) a novel object location task. We show that CA1 place cells exhibit properties comparable to those described in rats and mice, albeit with overall lower levels of spatial information. Although we did not identify object cells—known to be rare in the rat hippocampus—the introduction of an object elicited novelty-driven exploration accompanied by increased CA1 neuronal activity. We also characterize local field potential oscillations across multiple frequency bands, as well as sharp-wave ripple complexes. Together, these findings point to a shared organizational framework of hippocampal function and establish a foundation for future studies of age- and disease-related hippocampal dysfunction in this species.

Patricia Cogram
Institute of Ecology and Biodiversity (IEB), Faculty of Science, University of Chile,

Unconventional Animal Models of Alzheimer's Disease: Insights from the Natural Aging Model Octodon degus

Understanding the mechanisms that link aging to Alzheimer's disease (AD) remains one of the central challenges in neuroscience. While most experimental systems rely on genetically engineered models, a number of species naturally develop age-associated neuropathological and cognitive changes relevant to human neurodegeneration. The South American rodent Octodon degus has emerged as one of the most compelling natural models of brain aging and Alzheimer-like pathology. As they age, degus exhibit progressive cognitive decline together with key molecular features associated with AD, including amyloid deposition, tau alterations, neuroinflammation, and metabolic dysregulation. In this talk, I will present recent work characterizing Octodon degus as a translational model for studying the relationship between aging, lipid metabolism, and neurodegeneration. I will discuss comparative genomic insights, including variation in APOE and other genes involved in lipid transport and brain homeostasis, and how these findings may inform our understanding of Alzheimer's disease susceptibility across species. These studies illustrate how unconventional animal models can complement traditional transgenic systems and provide new perspectives on the biological mechanisms underlying neurodegenerative disease.

SYMPOSIUM S4 · SATURDAY, 3RD - AULA 5

Under Pressure: Neural Mechanisms of Conflict and Action Selection

CHAIR
Camila Zold
Universidad de Buenos Aires, CONICET, Instituto de Fisiología y Biofísica Bernardo Houssay, Grupo de Neurociencia de Sistemas, Buenos Aires, Argentina.

CO-CHAIR
Salvatore Lecca
University of Lausanne, Department of Fundamental Neurosciences, Lausanne, Switzerland

Adaptive behavior requires organisms to resolve conflicts between competing drives and to translate decisions into appropriate, goal-directed actions. Understanding how the brain integrates emotional evaluation, decision-making strategies and motor circuit function is a fundamental challenge in neuroscience, with implications for fields ranging from learning and motivation to neuropsychiatric disorders and rehabilitation. This symposium brings together four internationally recognized groups to provide complementary, state-of-the-art perspectives on these questions, using techniques that monitor and manipulate neural activity during behaviorally relevant paradigms. The first talk (Salvatore Lecca) examines how the lateral habenula integrates emotional and motivational signals during parental behavior under threat, in situations requiring the prioritization of caregiving over competing defensive responses. The second (Camila Zold) investigates how striatal circuits encode exploration–exploitation decision policies in foraging tasks, where animals continuously arbitrate between alternative behavioral strategies. The third (Nicolas Tritsch) characterizes how dopaminergic dynamics constrain the timing and vigor of actions, shaping how ongoing behavior is adjusted when multiple action demands compete. The fourth (Soledad Esposito) demonstrates how brainstem circuits contribute to the stabilization and consolidation of learned motor behaviors, biasing the retention of selected motor programs over competing alternatives. Together, these studies illustrate how affective evaluation, decision-making strategies, neuromodulatory control, and motor circuits interact to generate adaptive behavior. By bringing together these complementary approaches, the symposium provides a multi-level conceptual framework linking decision-making under conflict with the selection, modulation, and stabilization of adaptive actions. Featuring internationally recognized researchers from Europe, North America, and South America, this session fosters cross-disciplinary exchange, promotes the integration of complementary methodologies, and strengthens collaborations across research communities. It will be of interest to a wide audience of the Argentine neuroscience community, including researchers studying motivation, learning, decision-making, motor control, neuromodulation and neural plasticity, providing opportunities for dialogue and collaboration across experimental systems and conceptual approaches.

SPEAKERS

Salvatore Lecca
University of Lausanne, Department of Fundamental Neurosciences, Lausanne, Switzerland

Lateral habenula neuronal dynamics during parental decision

Parental care requires animals to prioritize offspring needs over competing environmental demands, including potential threats. How the brain supports this rapid decision-making between self-preservation and caregiving remains largely unknown. The lateral habenula (LHb), a key hub in negative affect processing, has recently been implicated in parental behavior. Previous work shows that LHb neurons respond both to aversive stimuli and to pup distress signals that trigger retrieval, suggesting a convergence of threat and caregiving signals within the same neuronal population. Here, we investigate whether LHb activity also supports caregiving decisions under threat. Using a conflict-based behavioral paradigm in mother–father mouse dyads combined with LHb calcium imaging, we examine how aversive stimuli influence parental actions and how LHb neural dynamics reflect the balance between threat processing and infant care.

Camila Zold
Universidad de Buenos Aires, CONICET, Instituto de Fisiología y Biofísica Bernardo Houssay, Grupo de Neurociencia de Sistemas, Buenos Aires, Argentina.

Striatal circuits in exploration–exploitation decisions

In natural environments, animals must constantly balance the tradeoff between exploiting known resources and exploring novel options. How the brain integrates these factors to guide adaptive behavior remains largely unknown. Here, we trained mice in a virtual foraging task in which effort and reward contingencies can be systematically varied. As travel costs increased, animals shifted toward exploitation, exhibiting greater persistence and reduced exploration. At the neural level, single neurons in the dorsomedial striatum encoded multiple task-relevant events, including reward delivery, reward omission, and spatial transitions. Together, these findings suggest that striatal circuits represent key variables underlying adaptive behavior and provide a framework to investigate how other striatal regions contribute to decision-making under more complex conditions.

Nicolas Tritsch
McGill University

Defining the timescales of neuromodulation by dopamine

Dopamine is critical for motor control and reinforcement learning, but the precise molecular mechanisms and timescales of neuromodulation are less clear. In this presentation, I will describe our attempts at better understanding how dopamine contributes to behavior through the study of release patterns and optogenetic manipulations. I will first describe published work highlighting the dynamics of dopamine release in the striatum of mice and their relationship to concurrent fluctuations in another important striatal modulator acetylcholine. I will then share unpublished work taking a critical look at the widely-held view that phasic fluctuations in extracellular dopamine control the vigor of ongoing movements. Our findings help restrain the kinds of mechanisms and timescales that dopamine likely acts on to modify behavior.

María Soledad Espósito
Laboratorio de Neurobiología del Movimiento, Centro Atómico Bariloche, CNEA-CONICET

Brainstem circuits gate motor memory consolidation

Motor memory consolidation is traditionally assigned to cortical and subcortical circuits, with the brainstem viewed as a passive executor of motor behaviors. Here, we identify glutamatergic neurons in the mesencephalic locomotor region (MLR) as essential for motor memory consolidation, as their inhibition selectively impairs retention in rotarod and skilled reaching tasks. These findings establish the MLR as a brainstem hub that gates the stabilization of learned motor skills.

SYMPOSIUM S5 · SATURDAY, 3RD - AULA 6

Afferent and Efferent Circuits in the Cochlea: From Ribbon Synapses to Central Control

CHAIR
Juan Goutman
INGEBI - CONICET

CO-CHAIR
M. Eugenia Gomez-Casati
Instituto de Farmacología, Facultad de Medicina - UBA

This symposium brings together leading experts in auditory neuroscience to present recent advances in our understanding of the afferent and efferent circuits that shape cochlear function. Talks will cover key aspects of ribbon synapses in sensory hair cells, including their morphological and functional diversity and their role in encoding sound information. In parallel, the symposium will explore the modulation of cochlear activity by the medial (MOC) and lateral (LOC) olivocochlear efferent systems, emphasizing their roles in development, synaptic plasticity, and auditory protection. Presentations will integrate a range of approaches from electrophysiology and neuroanatomy to single-cell RNA sequencing, offering a comprehensive view of the molecular identity, functional specialization, and connectivity of these auditory circuits. The goal of this symposium is to offer an integrated perspective on how afferent and efferent pathways shape auditory signaling from the cochlea to the brain, and how these circuits adapt, or become disrupted, under pathological conditions.

SPEAKERS

Carolina Wedemeyer, Ph. D.
Investigadora CONICET. Laboratorio de Fisiología y Genética de Audición, INGEBI-CONICET

Medial Olivocochlear Neurons Co-release GABA and Acetylcholine to Modulate Cochlear Efferent Inhibition

During development, inner hair cells (IHCs) in the mammalian cochlea are unresponsive to acoustic stimuli but instead exhibit spontaneous activity. During this same period, neurons originating from the medial olivocochlear (MOC) complex transiently innervate IHCs, regulating their firing pattern which is crucial for the correct development of the auditory pathway. Although the MOC-IHC is a cholinergic synapse, previous evidence indicates the widespread presence of GABA signaling markers, including presynaptic GABAB receptors (GABABR). In this study, we explore the source of GABA by optogenetically activating either cholinergic or GABAergic fibers. The optogenetic stimulation of MOC terminals from GAD;ChR2-eYFP and ChAT;ChR2-eYFP mice evoked synaptic currents in IHCs, which were blocked by α-bungarotoxin. This suggests that GABAergic fibers release acetylcholine (ACh) and activate α9α10 nicotinic acetylcholine receptors (nAChRs). Additionally, MOC cholinergic fibers release not only ACh but also GABA, as the effect of GABA on ACh response amplitude was prevented by applying a GABABR blocker. In conclusion, we provide evidence indicating that GABA and ACh are co-released from at least a subset of MOC terminals. In this circuit, GABA functions as a negative feedback mechanism, locally regulating the extent of cholinergic inhibition at certain efferent→IHC synapses during an immature stage.

Catherine Weisz, Ph.D.
Senior Investigator, Chief - Section on Neuronal Circuitry, NIH, National Institute on Deafness and Other Communication Disorders

Complex synaptic circuitry of auditory efferent neurons

The exceptional sensitivity and frequency selectivity of hearing is enabled by specialized electromotile outer hair cells (OHC), which are implicated in cochlear amplification. In addition, the auditory system can detect sounds over many orders of magnitude of intensity, but not concurrently. Instead, mechanisms are necessary to shift the gain of the auditory system between detection of softer and louder sounds, and to allow detection of salient sounds above background noise. The medial olivocochlear (MOC) efferent neurons, which are a component of the final stage of the descending auditory system, are implicated as one of the gain control mechanisms of the auditory system. They function by inhibiting OHCs, reducing overall cochlear sensitivity. The MOC system is

commonly referred to as a ‘reflex’, but recent work indicates that the function of both the synaptic inputs and outputs of these neurons are more complex than previously detailed. I'm mouse models, we have identified inhibitory synaptic inputs from the medial nucleus of the trapezoid body (MNTB) that are hypothesized to delay MOC responses and ensure that the MOC system only suppresses sustained sound responses. In addition, we have detailed modulatory inputs that may influence MOC activity over slower time scales, including both serotonergic and cholinergic systems. The convergence of this diverse circuitry indicates that the MOC system is not a simple reflex, but instead is poised to dynamically modulate our auditory system under changing hearing conditions.

Mark Rutherford
Associate Professor of Otolaryngology—Head & Neck Surgery, Washington University School of Medicine, St. Louis, MO, USA.

Calcium-permeable AMPA receptors in the cochlea: role in noise-induced synapse loss and sex-specific synaptopathy in the absence of synapse loss

Unlike typical glutamatergic synapses, the ribbon synapses in the cochlea have a high proportion of GluA2-lacking, calcium-permeable AMPA type glutamate receptors (CP-AMPARs) alongside the regular calcium-impermeable ones. These CP-AMPARs have a greater sodium conductance, in addition to calcium permeability, which is probably important for rapid and efficient action potential generation in response to rapidly changing acoustic inputs to the inner hair cell receptor potential. This powerful ribbon synapse, estimated to contain thousands of receptors, comes with a vulnerability to excitotoxicity. We discovered that blocking the CP-AMPARs is sufficient to prevent noise-induced synapse loss and concomitant reduction of cochlear output, while at the same time allowing hearing function to persist with transmission via the calcium-impermeable receptors. Mice lacking the GluA3 pore-forming subunit or the auxiliary subunit TARP-gamma-2 (Stargazin) have altered expression of the remaining subunits, which leads to progressive hearing loss specifically in female mice. Potential reasons for this, including a shift toward greater calcium permeability, will be discussed.

Amanda Lauer Ph. D.
Vice Director for Faculty Affairs Otolaryngology - HNS Johns Hopkins University School of Medicine

Role of the auditory brainstem-to-ear feedback system in hearing across the lifespan

The role of the medial olivocochlear system in hearing has been debated for many years due to conflicting and variable results in human and animal studies. Emerging evidence shows that this system is plastic and changes with acoustic experience and age. We have implemented a variety of behavioral assays, non-invasive physiological tests, and quantitative anatomical analyses to investigate how genetic manipulations of the olivocochlear system, acoustic experience, and natural aging interact to affect hearing across the lifespan in mouse models. Diminished olivocochlear function appears to be most detrimental to hearing in very young and aged auditory systems. However, plasticity in this system reveals a remarkable capacity to adapt to different acoustic environments. I will also highlight our recent findings in wild and wild-derived bat species that may confer protection against a lifetime of exposure to loud sounds.

SYMPOSIUM S6 · SUNDAY, 4TH - AULA MAGNA PAB 2

Neuronal circuit mechanisms for auditory cognition: from learning to communication

CHAIR

Belen Pardi
IPNP, Inserm, Francia

This symposium highlights how the brain actively interprets sound, integrating sensory inputs with prior experience to support learning, memory, and context-dependent behavior. Speakers will showcase cutting-edge research on auditory circuits—from thalamo-cortical pathways shaping perception and memory, to premotor and mirroring neurons in songbirds encoding self-generated vocalizations—revealing how auditory processing underlies communication, emotion, and adaptive behavior. Together, these talks illuminate the neural mechanisms that link hearing to cognition and the ways they can go awry in neurological and psychiatric disorders.

SPEAKERS

Jan Gründermann
German Center for Neurodegenerative Diseases, Germany

Fear Loops: Thalamo-cortico-limbic dynamics of aversive learning

Growing evidence supports the view that first- and higher-order sensory thalamus is an active participant in adaptive behavior rather than a solely passive sensory relay. The auditory thalamus (medial geniculate body, MGB) is necessary for auditory fear conditioning and we have identified state-dependent plastic MGB neurons whose responses are selectively reshaped during high fear states and fear extinction. This plasticity is mediated by cholinergic control. In addition to classical auditory fear conditioning, which results in passive freezing behavior, MGB activity patterns are furthermore changed during learned escape and active avoidance. These dynamic changes in MGB activity are accompanied by changes in inhibitory regulation from the thalamic reticular nucleus, suggesting circuit-level control of thalamic plasticity across behavioral states.

Andrea Santi
Johns Hopkins University, United States of America

Revealing hidden knowledge in amnestic mice

Alzheimer’s disease (AD) is a form of dementia in which memory and cognitive decline is thought to arise from underlying neurodegeneration. These cognitive impairments, however, are transient when they first appear and can fluctuate across disease progression. Here, we investigate the neural mechanisms underlying fluctuations of performance in amnestic mice. We trained APP/PS1+ mice on a cortically dependent auditory go/no-go task that dissociated learning of task contingencies (knowledge) from its more variable expression under reinforcement (performance). APP/PS1+ exhibited significant performance deficits compared to control mice that were accompanied by aberrant cortical responsivity, stimulus selectivity, and higher-order encoding of reward prediction. Strikingly, behavioral deficits immediately reversed on probe (non-reinforced) trials, when APP/PS1+ mice showed improved stimulus selectivity and recovery of normal reward prediction signaling. Our results suggest that the amnestic phenotype is transient, contextual, and endogenously reversible, and provide neural evidence that stimulus-action knowledge remained intact despite variable ongoing performance. Thus, memory deficits commonly observed in amnestic mouse models, and potentially at early stages of dementia in humans, may relate more to contextual drivers of performance than degeneration of the underlying memory traces. Now, we are exploring these cognitive fluctuations in a more complex and naturalistic setup, to assess continual multi-task learning, memory interference, and retrieval through aging, using our new, fully automated home-cage platform, the Mouse Playground.

Ana Amador
Universidad de Buenos Aires, Departamento de Física, Argentina

Neural coding of complex auditory stimuli in songbirds

Ana Amador will talk about how songbirds process and encode complex auditory signals, focusing on how hearing is essential both for learning and maintaining their songs. She will describe how brain circuits in

songbirds—particularly the premotor nucleus HVC, which receives input from auditory cortex—contain neurons that respond selectively to the bird's own song and show "mirroring" activity during both singing and listening. Her recent work highlights how neural activity in HVC synchronizes with the rhythm of song, providing insight into how complex sounds are represented in the brain.

Belén Pardi
IPNP, Inserm, France

Auditory thalamocortical interactions for adaptive perception

Perception is an active process by which the brain makes sense of the surrounding world, continuously integrating sensory signals with internal priors. This process is profoundly affected in major psychiatric disorders, yet the circuit mechanisms that support it—and how they are disrupted in psychosis—remain poorly understood. Recent studies have highlighted the contribution of higher-order sensory thalamo-cortical circuits in processing internal signals. In this talk, I will present our work investigating the role of auditory circuits in memory-related processing and discuss our recent efforts to uncover how their dysfunction may contribute to the pathophysiology of schizophrenia.

SYMPOSIUM S7 · SUNDAY, 4TH - AULA 5

Neurobiological Signatures of Stress: Sex-Specific Trajectories from Gestation to Adulthood In Rodents and Humans

CHAIR
Mariela Chertoff
Department of biological chemistry, Faculty of Science, University of Buenos Aires, Argentina

CO-CHAIR
Lydia Kogler
Department for Psychiatry and Psychotherapy, Medical Faculty, University of Tübingen, Germany.

This symposium addressed the complex interplay between early environmental factors, sex differences, molecular mechanisms and neurobiological outcomes across developmental and hormonal stages. We will discuss the transgenerational, neurobehavioral effects of stress and maternal behavior on the offspring in a sex-dependent manner. In addition, we will address behavioral changes and molecular links between adverse factors early in life and resilience to affective disorders in adults. Complementary evidence will be presented showing that specific oxytocin receptor gene polymorphisms increase susceptibility to stress and depressive symptoms during pregnancy, suggesting a gene-environment interaction for perinatal mental health risk. Last but not least we will discuss functional neuroimaging data showing that stressor type modulates prefrontal cortex–amygdala connectivity in a sex-specific way. Taken together, these studies highlight the importance of integrating environmental, hormonal, genetic, epigenetic, and neural dimensions to better understand the mechanisms behind neurodevelopmental and sex-dependent origins of affective disorders.

SPEAKERS

Maria Angelica Rivarola
Faculty of Exact, Physical and Natural Sciences, Universidad Nacional de Córdoba, Argentina.

From womb to adolescence: Gestational environmental enrichment shapes maternal care and sex-specific adolescent outcomes after early-life stress

Gestational environmental enrichment (EE) has emerged as a promising non pharmacological strategy to buffer the impact of perinatal stress across generations. Using two established postpartum depression/anxiety models: maternal separation (MS) and intruder male (IM), we evaluated how gestational EE modulates maternal behavior and long term offspring outcomes. EE improved maternal care and reduced anxiety like behaviors in dams exposed to MS or IM, effects associated with increased ΔFosB activity in the medial preoptic area and nucleus accumbens shell, and reduced activation in dorsal hippocampal subregions. In adolescent offspring from the same litters, anxiety like and social behaviors were assessed through elevated plus maze, open field, and social preference tests, integrating outcomes via a composite Z anxiety score. Gestational EE attenuated early life stress effects in a sex dependent manner.

Mariela Chertoff
Laboratorio de Neuroepigenética y adversidades tempranas, Department of biological chemistry, Faculty of Science, University of Buenos Aires, Argentina

Prenatal stress and resilience: Behavioral changes and molecular correlates on a mice model

Stress is a primary risk factor for neuropsychiatric disorders like depression and anxiety. While some individuals are susceptible to these conditions, others exhibit resilience, an adaptive process for coping with adversity. Understanding the biological basis of resilience is vital for developing therapies that mimic natural adaptation. In this study, adolescent offspring of mothers subjected to gestational restraint were classified as resilient (RES) or susceptible (SUS) via the sucrose splash test. After assessing behavioral phenotypes across control, RES, and SUS groups, we performed molecular evaluations of the prefrontal cortex (PFC) in both sexes. Our findings reveal sex-specific differences in stress-coping strategies and neurobiological mechanisms, providing deeper insight into the molecular correlates of resilience in male and female mice.

Daniel Olazabal
Unidad Académica de Fisiología, Unidad Académica de Genética, Facultad de Medicina, Udelar, Asociación de Psicopatología y Psiquiatría de la Infancia y la Adolescencia, Hospital de Clínicas Manuel Quintela, Montevideo, Uruguay

Oxytocin System Polymorphism Variants increase the risk of depression and stress in pregnant women

Prenatal depression and stress are associated with early adversity, pregnancy complications, and long-term effects on child neurodevelopment. The oxytocin (OXT) system is affected by early adverse experiences and has been associated with emotional dysregulation. In the current study, we investigated risk factors for prenatal depression and stress, mainly the effects of early childhood and adolescence trauma, in combination with the presence of certain variants of polymorphism of oxytocin (OXT) and OXT receptor (OXTR) gene. We hypothesized that early trauma had higher negative effects in carriers of genetic variants of the OXTR system, increasing their risk for depression and stress. Early in pregnancy (8–14 weeks), 141 pregnant women from a Uruguayan population were asked to provide DNA samples and complete questionnaires that assessed their experience of child abuse, antecedents of psychiatric conditions, depression symptoms, perceived stress and other variables that included demographic information. Carriers of the variant allele CC of rs2740210 (OXT) or AA of rs237887 (OXTR) had significantly higher risk of experiencing depressive symptoms in abuse women, while the variant AA of the rs53576 (OXTR) had significantly higher scores of perceived stress in abused or non-abused women. Lower income and previous antecedents of depression were also correlated with higher risk of depression and perceived stress. We conclude that early detection and closer follow-up of women with child abuse and OXT/OXTR genetic variants, among other risk factors, could reduce the long-term impact of prenatal depression and stress.

Lydia Kogler
Department for Psychiatry and Psychotherapy, Medical Faculty, University of Tübingen, Germany

Social Stress and the Human Brain: A Sex-Specific Perspective on Limbic Structure and Functional Connectivity

Neural stress regulation is strongly depending on limbic regions such as the amygdala and hippocampus. How the interplay of sex and social stress is associated with structure and connectivity of these regions remains unclear. Analyzing structural brain data and self-reported chronic social stress in 83 healthy, young humans (40 females) show a reduction in hippocampus gray matter volume (GMV) in males, but not females, with higher levels of socially tense interactions. Investigating the resting-state functional connectivity of the amygdala and frontal regions in 77 healthy, young humans (40 females) also reveal sex differences in association with social stress. Females show a higher coupling of the amygdala with the ventral anterior cingulate cortex and the medial prefrontal cortex for social than for achievement stress, and compared to males. Our findings point to a complex interaction between social stress and sex and their impact on neural organization.

SYMPOSIUM S8 · SUNDAY, 4TH - AULA 6

Data-Driven Approaches to Understanding Mechanisms of Brain Function

CHAIR
Emiliano Marachlian
Departamento de Física, FCEyN, UBA - IFIByNE, UBA-CONICET

CO-CHAIR
Mariana Luz Bavassi
IFIByNE, UBA-CONICET - Departamento de Física, FCEyN, UBA

Access to increasingly large and high-quality datasets is rapidly transforming neuroscience. Modern techniques for manipulating and measuring gene expression, imaging, optogenetics, electrophysiology, as well as the application of artificial intelligence to data analysis, are providing unprecedented opportunities to study how the brain works and to address questions that were previously inaccessible. However, the growth in both the quantity and quality of available information also demands that scientists develop new theoretical frameworks and technical tools capable of integrating and interpreting these data, redirecting questions and experiments, and allowing us to fully exploit their potential. In this symposium we will present four different perspectives, ranging from modeling, optogenetics, and machine learning to the analysis of behavioral experiments. Together, these contributions aim to provide a broad overview of the strategies and ideas that are shaping modern neuroscience. We hope this discussion will also help open a broader reflection on what the role of Argentine neuroscience can and should be in this ongoing scientific transformation.

SPEAKERS

Fernanda Selingardi Matias
Universidade Federal de Alagoas, Brazil

Quantifying Cortical Dynamics Using a Symbolic Information Approach: Comparing Experimental Data and Population Models

The increasing availability of high-quality neural recordings provides new opportunities to investigate how collective brain dynamics emerge from interactions among their components. In this talk, I will present a data-driven approach based on information-theoretic measures to quantify the entropy and complexity of neural activity and to establish connections between experimental observations and theoretical models. I will focus on the analysis of entropy and statistical complexity in neural time series, using the Bandt–Pompe symbolization technique to characterize different cortical states. I will first discuss results showing that statistical complexity is maximized close to criticality in spiking data from urethane-anesthetized rats, as well as in a probabilistic cellular automaton network model with a well-defined critical point. I will then discuss the application of these measures to human intracranial recordings during different sleep stages and their comparison with a whole-brain model, illustrating how quantitative descriptors extracted from experimental data can be related to the dynamical regimes generated by the model.

Claudio Mirasso
Institute for Cross-Disciplinary Physics and Complex Systems (IFISC -UIB-CSIC), Palma de Mallorca, España.

Data-Driven Biorealistic Models of Mouse Visual Cortex Dynamics

I'll present a biologically realistic model of the mouse visual cortex comprising both primary visual cortex (V1) and the Lateromedial (LM) visual areas. The model combines datasets on cell-type composition, intrinsic electrophysiology, and connectomics, and uses deep learning to optimize synaptic weights so as to reproduce in vivo Neuropixels recordings. This provides a data-driven, biologically grounded description of circuit dynamics. We will use it to investigate the emergent properties of the coupled V1–LM system and quantify the functional impact of feedback from LM to V1. By comparing isolated V1 models with the full V1–LM circuit, we will highlight differences in receptive field size, time to first spike, and pattern recognition performance. These findings shed light on how top-down feedback shapes early sensory processing and supports computation in biologically realistic cortical networks.

Cecilia Martinez
Laboratorio de Fisiología y Algoritmos del Cerebro, Fundación Instituto Leloir, IBBA-CONICET

Machine Learning Approaches for Studying Learning and Memory

Understanding how animals learn and remember requires a precise account of how their actions change over time. However, behavior has historically been treated as a "black box," measured through coarse, aggregate metrics like trial duration or time spent in a zone. These simplified snapshots often mask the complex, sub-second behavioral dynamics that characterize the actual process of learning. Recent advances in machine learning are revolutionizing behavioral quantification by allowing us to treat movement as a continuous, high-dimensional data stream. In this talk, I will discuss how markerless pose estimation (e.g., DeepLabCut) and unsupervised behavioral segmentation can be used to "deconstruct" complex tasks. By extracting precise body postures and identifying hidden behavioral states, we can observe the fine-grained evolution of strategies during spatial exploration and object-based recognition. These ML-driven approaches reveal that learning is not just a change in an outcome metric, but a fundamental reorganization of behavioral architecture.

Joao Barbosa
Neuromodulation Institute and Neurospin, París, Francia.

Region-specific transformations enable distributed computations of flexible decisions.

Cognitive flexibility is thought to rely on the prefrontal cortex controlling other regions. However, recent evidence shows that information required to compute flexible decisions is distributed across multiple regions (“everything is everywhere”, 2025; International Brain Laboratory, 2025). This shift raises some questions: is ’everything is everywhere’ compatible with different task variables being first computed within specific regions and then broadcasted? If so, how to identify which information is communicated across specific regions to ultimately enable flexible decisions? Here, we tackle these questions by analyzing the dynamics within and between six brain regions of the monkey brain engaged in a context-dependent decision-making task (Mante & Susillo et al., 2013). Decoding from this dataset has previously found task-relevant information across all the recorded regions (Siegel et al., 2015). Using population analyses and data-constrained recurrent neural networks (RNNs) we found significant differences in within-region dynamics not captured by classical decoding analyses. Inspecting communication subspaces (Semedo et al., 2019) inferred with low-rank RNNs, we found that the dimensionality of within regional dynamics was higher than what is communicated downstream in sensory regions (e.g. V4 and MT), replicating previous results in early visual cortex (Semedo et al., 2019). In contrast, within- and across-regional dimensionality did not differ in frontal regions (i.e. LIP, FEF and PFC). Additionally, we found that overall encoding dimensionality reduced with hierarchical position, suggesting progressively more abstract transformations as information propagated downstream. Finally, in-silico perturbations revealed how choice computation abruptly emerged with stronger cross-regional interactions, in contrast to stimuli encoding which remained stable. Perturbing inputs to sensory regions confirmed a bottom-up flow of task-stimuli into the frontal regions. Altogether, using population analyses that go beyond decoding and data-constrained RNN we show that despite task-variables being broadly encoded, each region performs different computations during flexible decision making.



Young Investigator Talks

Twenty talks in Aula Magna, Room 5 and Room 6

Young Investigator Talks

Saturday 03 October · 18:00 – 20:30

Aula Magna

Dynamic computational markers of the sense of agency across the schizotypy spectrum

María da Fonseca · CITECCA, Universidad Nacional de Río Negro · *In English*

Schizotypy, spanning nonclinical psychotic-like experiences to clinical psychosis, has been linked to disturbances of the self, particularly in the sense of agency (SoA). However, it remains unclear whether schizotypy reflects a bias toward self-attribution, reduced sensitivity to sensorimotor evidence, or both, and whether momentary SoA covaries with psychotic-like experiences. We conducted a longitudinal Experience Sampling Method study in which 54 participants completed 34 online sessions. At each session, they reported their current psychological state, including SoA, and performed a validated agency attribution task involving parametrically distorted versions of drawings they had previously produced. We previously validated this task using behavioral modeling and EEG, showing that it captures retrospective SoA and its neural signatures. A hierarchical drift-diffusion model estimated self-attribution bias, sensitivity to sensory evidence, and sensitivity to performance feedback. Higher schizotypy was associated with increased self-attribution bias and reduced sensitivity to sensory evidence. Transient reductions in SoA also coincided with decreased sensitivity to sensory evidence. Paranoia and positive schizotypy were additionally associated with altered self-serving bias and sensory evidence sensitivity. These findings reveal a dynamic relationship between schizotypy, momentary self-experience, and computational mechanisms supporting self-other distinction.

Following the Flow: Studying the Temporal Dynamics of Conscious Experience

Laura Alethia de la Fuente · COCUCO/INCyT, INFINA/UBA · *In English*

Conscious experience unfolds continuously across multiple temporal scales. My research seeks to understand how brain dynamics generate this ongoing flow and how external temporal structures shape it, combining computational neuroscience, naturalistic paradigms, and multimodal neuroimaging.

I first present our work showing that temporal irreversibility of neural activity is a robust signature of consciousness, suggesting that conscious brain activity is intrinsically asymmetric in time. Building on this framework, I investigate how music structures experience. Using EEG, inter-subject correlation, and complexity measures during music listening under different states of consciousness, I examine how neural dynamics synchronize with the temporal organization of naturalistic stimuli and how this process is modulated by psilocybin.

Finally, I show how these principles motivate two emerging research directions: understanding how structured movement practices (5Rhythms®) organize emotional experience across longer timescales, and translating these concepts into multimodal biomarkers (EEG, fMRI, PET and physiology) for detecting residual consciousness in patients with disorders of consciousness. Together, these studies aim to establish a unified framework for understanding consciousness as a dynamic interaction between brain, body, and environment

Xenobiotics and natural agents effects during neural development in Xenopus laevis

Maria Belen Favarolo · Laboratorio de Embriología Molecular/Instituto de Biología Celular y Neurociencias/Facultad de Medicina, Universidad de Buenos Aires · *In English*

The amphibian Xenopus laevis is an established model organism for investigating vertebrate development. In contrast to commonly used amniote models, its external embryogenesis provides a unique opportunity to monitor developmental processes and their disruption or modulation by chemical, environmental or natural agents from the earliest stages. Prior studies in this model have demonstrated that Bisphenol A (BPA) induces

malformations in tadpoles and inhibits γ-secretase activity. Nevertheless, the consequences of BPA exposure during early embryogenesis on neural development remain unexplored. We hypothesize that BPA exposure interferes with the formation of neural precursors, neural plate, neural border, and embryonic midline. Additionally, BPA disrupts critical processes required for proper cephalic development. Furthermore, naturally occurring compounds such as cannabinoids may also play a role in regulating critical developmental processes. Transcriptomic analyses in Xenopus laevis have revealed early expression of both cannabinoid receptors, with CB2 expressed at higher levels than CB1 before and during organogenesis. Both receptors peak during gastrulation and remain expressed throughout primary neurogenesis, key stages of early neural development. We hypothesize that cannabinoid signaling may contribute to the regulation of neural induction and primary neurogenesis in Xenopus.

Lateral Posterior Neurons couple the circadian clock to female reproductive output in Drosophila

Sabrina C. Riva · Departamento de Física y Biología Aplicada a la Salud, Centro Atómico Bariloche, CNEA-CONICET, San Carlos de Bariloche, Argentina. · *In English*

Circadian clocks coordinate physiology and behavior with the daily light-dark cycle through dedicated neuronal outputs. In Drosophila, egg-laying is a reproductive behavior regulated by both mating status and the circadian clock. The lateral posterior neurons (LPNs) constitute a small subset of circadian clock neurons in Drosophila. Using the Drosophila hemibrain connectome, we recently identified reciprocal synaptic connections between LPNs and inhibitory oviposition neurons (oviINs), suggesting that LPNs may provide circadian input to the reproductive circuitry. Here, we investigated the contribution of LPNs to the circadian and reproductive regulation of egg-laying. We found that disruption of the molecular clock specifically in LPNs does not affect the daily rhythm of oviposition, indicating that these neurons are dispensable for circadian timing of egg-laying. In contrast, manipulating LPN neuronal activity markedly alters female fecundity, demonstrating that LPNs selectively regulate reproductive output rather than its temporal organization. These results suggest that LPNs contribute to the neural control of female reproductive output independently of the mechanisms regulating the daily timing of egg-laying.

Room 5

Early postnatal stress disrupts maturation of prefrontal–raphe circuits controlling serotonergic function and emotional behavior.

Carla Veronica Argañaraz · Laboratorio de Neurobiología de Circuitos y Trastornos Psiquiátricos / IFIBYNE / CONICET-UBA

Vulnerability to stress-related disorders is considered to arise from disturbances during early neurodevelopment. Accumulating evidence highlights prefrontal cortex (PFC) circuits as key to the developmental origins of mood disorders. Among these, the projection from the PFC to the dorsal raphe nucleus (DRN)—the main source of forebrain serotonin (5-HT)—plays a central role in emotional regulation and stress responses. There is a mouse critical period for brain development, between postnatal days (P) 2 to 14, when environmental challenges can shape neural circuitry. Maternal separation (MS) is an early-life stress paradigm that induces emotional alterations in adulthood. We examined how MS affects the development and refinement of the PFC–DRN circuit during this critical period. We analyzed changes in PFC–DRN synaptic anatomy using high-resolution microscopy (Array Tomography), and assessed stress-induced activation of serotonergic DRN neurons. We also performed ex vivo patch-clamp recordings from 5-HT and GABAergic DRN neurons in MS mice across postnatal development. Our findings reveal that MS during the first two postnatal weeks disrupts the normal maturation of PFC inputs to the DRN and alters stress-dependent activation of 5-HT neurons. These results identify a key developmental window for PFC–DRN circuit formation, when early-life stress may induce maladaptive changes that could represent a neural substrate underlying increased vulnerability to psychiatric disorders.

Synaptic density in early stages of psychosis and clinical high risk: An association with negative symptoms

Maira Belén Blasco · McGill University · *In English*

Importance: Synaptic dysfunction has been implicated in schizophrenia. However, whether synaptic density is reduced during the earliest stages of psychosis, including clinical high-risk (CHR) states and first-episode psychosis (FEP) was unclear.

Objective: To investigate synaptic density in FEP and CHR, examine the impact of cannabis use, and assess associations with negative symptoms and gray matter microstructure.

Methods: In this cross-sectional study, antipsychotic-free or minimally exposed FEP participants, CHR individuals, and healthy controls underwent 90-minute [18F]SynVesT-1 PET imaging to quantify synaptic vesicle glycoprotein 2A (SV2A) binding. Gray matter microstructure was assessed using diffusion MRI, and cannabis use was confirmed by urine drug screening.

Results: Forty-nine participants were included (16 FEP, 17 CHR, 16 controls). Synaptic density differed significantly across groups, with lower SV2A binding in FEP and CHR than in controls. Cannabis users also showed lower synaptic density. Across groups, reduced SV2A binding was associated with greater negative symptom severity and lower neurite density.

Conclusions: Lower synaptic density is detectable during early stages of psychosis, including CHR, and are associated with negative symptoms and altered gray matter microstructure. These findings support synaptic dysfunction as an early feature of psychosis and highlight the need for longitudinal studies investigating the effects of cannabis.

Prefrontal ERK Dynamics in Temporal Memory and Synaptic Plasticity

Santiago D'hers · Laboratorio de Neurobiología de la Memoria, Instituto de Fisiología, Biología Molecular y Neurociencias, Universidad de Buenos Aires · *In English*

Temporal order memory (TOM) enables organisms to discriminate the relative recency of events. Using a two-session training protocol in mice, we identified a window in which a second exploration session one hour after initial object presentation significantly impaired the stability of the first recognition memory. Extracellular signal-regulated kinase 1/2 (ERK1/2) phosphorylation was dynamically regulated during TOM formation, whereas total MKP3, its cognate phosphatase, increased under inhibitory conditions. In vivo pharmacological interventions using PD (MEK inhibitor) and BCI (MKP3 inhibitor) demonstrated that TOM stability depends on ERK1/2 signaling within the prefrontal cortex (PFC). Intra-PFC inhibition of ERK1/2 mimicked the behavioral interference

effect, whereas MKP3 inhibition protected the initial memory trace. To investigate the cellular and synaptic mechanisms underlying these findings, we performed whole-cell patch-clamp recordings from layer V pyramidal neurons in mouse PFC slices. Slices were pre-incubated with phosphorylation and dimerization modulators, previously shown to impair memory, to determine the effect of ERK1/2 activity regulation on intrinsic neuronal excitability and long-term potentiation (LTP). By integrating behavioral phenotyping, molecular analyses, and electrophysiology, this multi-scale approach seeks to establish mechanistic links between ERK signaling, prefrontal synaptic plasticity, and the temporal organization of episodic memory.

Self-Organization of the Brain's Navigation System: The Emergence of Prospective Coding and Path Integration

Facundo Emina · Physiology and Algorithms of the Brain Lab / Leloir Institute Foundation / University of Buenos Aires · *In English*

Navigating without landmarks relies on path integration (PI), a computation thought to be performed by grid cells in the entorhinal cortex (EC). Classical models either assume fixed connectivity or fail to account for PI. To address this gap, we introduce a self-organizing continuous attractor neural network (CANN) model where PI and predictive coding emerge naturally through learned dynamics. Guided by local Hebbian plasticity, spike-frequency adaptation, and global inhibition, the network develops a continuous spatial code from structured input. Notably, this feedforward learning spontaneously generates prospective coding, anticipating future inputs. This emergent predictive shift strongly aligns with recent experimental findings in the superficial layers of the EC [1]. Furthermore, stacking multiple feedforward layers amplifies this predictive effect, forming a functional predictive hierarchy. When recurrent synapses are introduced, they self-organize under the same biological rules to support continuous PI, allowing the network to update its activity without external input. By bridging established frameworks [2,3], this model reveals how vital navigation and prediction capabilities can spontaneously emerge from basic principles of self-organization. [1] Ouchi, A., & Fujisawa, S. (2024). Science, 385, 776-784. [2] Kropff, E., & Treves, A. (2008). Hippocampus, 18, 1256-1269. [3] Mi, Y., et al. (2014). NeurIPS, 27.

Speech biomarkers for Alzheimer's disease and frontotemporal dementia across Latin American diversity

Franco Javier Ferrante · Cognitive Neuroscience Center, Department of Life and Behavioral Sciences, University of San Andrés · *In Spanish*

Neurodegenerative diseases such as Alzheimer's disease (AD) and frontotemporal dementia (FTD) affect cognition, behavior, and daily functioning. Early diagnosis is critical to reduce their personal, clinical, and social consequences, yet diagnosis and follow-up often rely on costly, time-consuming assessments. Automated speech and language analysis (ASLA) offers a practical window into these disorders, providing fast, objective, and low-cost markers. Previous work from our team has shown that ASLA can distinguish AD, FTD, and related syndromes; support cognitive phenotyping; and reveal language-based alterations linked to specific cognitive domains and neurophysiological markers. Together, these studies suggest that digital language markers capture clinically meaningful signals. However, further validation across sociodemographic heterogeneity is needed. Differences in age, gender, education, dialect, multilingualism, and social determinants of health modulate both language production and dementia presentation. Standard group matching reduces average differences between groups but may miss individual variability, while machine-learning splits can reintroduce imbalance. Our work in 1689 Latin American participants with AD and FTD models this influence using residualization, while differentiating groups and predicting cognitive domains. This approach tests whether ASLA biomarkers remain robust, fair, and clinically informative across heterogeneous populations.

Sex-specific epigenetic and molecular imprints in the prefrontal cortex following early-life stress

Jazmín Grillo Balboa · Laboratorio de Neuroepigenética y Adversidades Tempranas, Departamento de Química Biológica; Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), CONICET-UBA, Argentina. · *In Spanish*

Infant maltreatment is a major risk factor for the development of affective disorders. Using the Scarcity-Adversity Model (SAM), which limits nesting resources (PND 8–12), we previously showed that SAM-exposed dams display violent caregiving. In adulthood, male SAM offspring exhibit passive stress-coping and a blunted corticosterone response, while females show a more resilient phenotype. In this study, we explored the

molecular underpinnings of these differences in the Prefrontal Cortex (PFC) and Amygdala (Amy). In male SAM adults, we observed a significant downregulation of Crh and Ppid, coupled with an upregulation of Nr3c1 in the PFC. Conversely, SAM females showed a specific increase in Bag1 expression, suggesting a potential compensatory mechanism. The most striking differences emerged in epigenetic regulators: male SAM rats showed decreased expression of Dnmt3a, Dnmt3b, and Tet1, while SAM females exhibited a coordinated upregulation of these three markers. Finally, functional connectivity analysis (c−Fos correlations) showed a strong negative correlation between the PFC and Amy in Control females that was lost in SAM females, potentially underlying the behavioral disinhibition observed in the Light-Dark Box. Together, our results suggest that infant maltreatment triggers divergent, sex-specific molecular programs, where females recruit epigenetic pathways that may confer resilience against early life adversity.

Out-Of-Body Experiences During Sleep Show Altered-Self Phenomenology Without A Distinct Clinical Profile

Nerea Herrero · Laboratorio de Sueño y Memoria - Instituto Tecnológico de Buenos Aires (ITBA) · *In Spanish*

Out-of-body experiences (OBEs) during sleep involve a transient disruption of bodily self-consciousness, in which the self or center of awareness is experienced as displaced from the physical body. Although OBEs have been reported in neurological, psychiatric, and dissociative contexts, they also occur in non-clinical populations, raising the question of whether their altered-self phenomenology reflects a broader clinical or dispositional profile. We examined whether sleep-related OBEs are distinguished by a specific episode-level alteration of bodily selfhood, and whether this profile is accompanied by differences in psychological symptoms, depersonalization/derealization, sleep quality, or personality. Adults recruited online reported a vivid or meaningful sleep-related experience, which was classified as an OBE, sleep paralysis, lucid dream, or ordinary remembered dream. Participants completed measures of altered-state phenomenology, mystical-type experience, ego dissolution, personality, subjective sleep quality, psychological symptoms, and depersonalization/derealization. OBEs showed a selective elevation in Disembodiment relative to ordinary dreams, lucid dreams, and sleep paralysis. OBEs also showed higher altered-state intensity, stronger ego dissolution than ordinary dreams and sleep paralysis, and the highest proportion of complete mystical-type experiences. By contrast, sleep paralysis showed an aversive profile characterized by anxiety and impaired control, wh

Age-Related Differences in Pattern Separation Performance: Associations with Neuropsychological Measures

Dinka Marina Piromalli Girado · Instituto de Neurociencia Cognitiva y Traslacional (INCYT) · *In Spanish*

Pattern separation, a hippocampal-dependent process that enables discrimination between highly similar memories, is known to decline with aging. This study investigated age-related differences in a pattern separation task performance and its relationship with neuropsychological measures. Fifty-nine cognitively healthy adults were divided into a younger group (18–55 years, n = 33) and an older group (>55 years, n = 26). Participants completed a the pattern separation task together with a neuropsychological battery including the Addenbrooke's Cognitive Examination III (ACE-III), the INECO Frontal Screening (IFS), the Rey-Osterrieth Complex Figure, and the Digit Symbol-Coding (WAIS). Older adults showed significantly lower pattern separation performance, characterized by a reduced Pattern Separation Index, fewer correct rejections, and more false alarms. Pattern separation performance was significantly associated with executive functioning (IFS), delayed visual memory (Rey-Osterrieth Complex Figure), and a composite working memory index derived from visual and auditory IFS subtests. Ongoing analyses are evaluating the pattern separation task's sensitivity and discriminative ability for differentiating age groups. These findings support the sensitivity of the Pattern Separation Task to age-related memory changes and provide evidence of its convergent validity with established neuropsychological measures of memory and executive functioning used daily in clinical field.

Room 6

Central canal neurons project to respiratory modulatory centers in the mouse brainstem

Joselina Berti · Fundación Instituto Leloir · *In English*

The nervous system uses specialized circuits to maintain homeostasis, yet how the brain senses internal states to regulate autonomic processes remains elusive. CerebroSpinal Fluid-contacting Neurons (CSF-cNs) are a distinct medullospinal population around the central canal, poised as internal sensors. In zebrafish, they detect spinal curvature and CSF changes, but their role in tetrapod circuitry remains unclear. Here, we elucidate CSF-cN connectivity in the mouse brainstem. Using Pkd2l1Cre:Tomato mice to label CSF-cN cell bodies and axons, we identified they project to the caudal medial brainstem, wrapping the hypoglossal nucleus. We found CSF-cNs form profuse GABAergic synapses onto dorsal neurons of the Roller and the Intermedius nucleus of the Medulla (InM). Optogenetic stimulation of CSF-cNs evoked inhibitory postsynaptic currents in Roller and InM neurons, confirming functional synapsis. Molecular and transcriptomic analysis revealed target cells are a heterogeneous population of GABAergic Dbx1-derived neurons that express the transcription factor Otp and Ebf2. Here, we identified the connectivity map of CSF-cNs in the mammalian brainstem and a novel circuit regulating autonomic functions. We propose that CSF-cNs modulate breathing activity through Roller and InM in response to CSF homeostasis, tuning motor hypoglossal activity.

Glucocorticoids induce structural remodeling of hypothalamic tanycytes and alter permeability of the median eminence

Ivana María Gómez · Neurophysiology Laboratory/ Multidisciplinary Institute of Cell Biology (IMBICE), La Plata, Argentina. · *In Spanish*

Hypothalamic tanycytes are polarized ependymoglial cells lining the base of the third ventricle and extending processes toward the median eminence (ME), where they contact fenestrated capillaries, forming a key blood–brain communication interface. We investigated whether glucocorticoids (GCs) induce structural remodeling of tanycytes and how this affects local blood–brain exchange. Wild-type mice received dexamethasone (Dex, 1 mg/kg i.p.) or vehicle for five days. Dex increased the accessibility of plasma-derived molecules to the ME, assessed by Evans blue extravasation. This effect was accompanied by a reduction in the tanycyte–vascular interface and by glucocorticoid receptor (GR) nuclear translocation in tanycytes in vivo. In primary rat tanycyte cultures, Dex induced terminal retraction and shortening of cellular processes, as revealed by live-cell imaging recordings and morphometric analysis of fixed cells. These effects were reversible and prevented by the GR antagonist RU-486. Furthermore, Dex promoted early transcriptional activation and increased vimentin expression in cultured tanycytes, as determined by c-Fos and vimentin immunofluorescence quantification, respectively. Together, these findings identify tanycytes as dynamic regulators of blood-to-brain communication in the hypothalamus and demonstrate that GCs remodel their vascular interface through a GR-dependent mechanism, increasing the accessibility of circulating molecules to the ME.

Evaluating the Saturation Level of AMPA receptors at the Inner Hair Cell Afferent Synapse with Glutamate Uncaging

Walen Gribaudo · Laboratorio de transmisión sináptica del sistema auditivo/INGEBI-CONICET · *In English*

All aspects of sound information are encoded and transmitted to the brain through synapses between inner hair cells (IHCs) and spiral ganglion neurons (SGNs) in the inner ear. Each IHC is connected to 10-20 SGNs through single synaptic contacts. IHCs release glutamate upon stimulation, activating AMPA receptors that are present in postsynaptic densities (PSDs) of SGNs. EPSCs at these synapses are ~20 times larger than mEPSCs in the brain, whereas PSDs are 5-10 times larger than brain PSDs. We hypothesize that these large PSDs enable large synaptic responses with low receptors saturation. To test this, we implemented a “glutamate uncaging” method, where glutamate can be released on individual PSDs with high temporal and spatial control. EPSCs activated on SGNs were recorded with the patch clamp technique. Stimulating with high laser power, saturating AMPA responses were obtained, with 5 times larger amplitude than mean EPSCs. This implies that during synaptic transmission AMPA receptors operate in low saturation. Analyzing rise times of uncaging responses, we observed faster kinetics with larger responses. In contrast, EPSCs presented fast rise times with amplitudes that varied 10-fold. This suggests that EPSCs are produced by a short glutamate transient. Low saturation and fast glutamate clearance allows for high frequency signaling at this synapse.

A metabotropic glutamate receptor is key for nutritional perception in C. elegans

Ailin Lacour · Instituto de Investigaciones Bioquímicas de Bahía Blanca · *In Spanish*

Satiety perception is critical for maintaining energy homeostasis, yet the precise neuroendocrine circuits encoding nutritional state remain elusive. Caenorhabditis elegans allows the determination of neural circuits with a resolution difficult to achieve in other models. Previous work from our laboratory delineated the circuits mediating elevated food intake after fasting, establishing that serotonin and tyramine—the invertebrate counterpart of adrenaline—are crucial for this behavior; however, how the nervous system senses nutritional status remains unknown.

We mapped robust expression of mgl-2, an ortholog of mammalian metabotropic glutamate receptors, to core neurons of the feeding circuit. Here, we demonstrate that mgl-2 mutants are insensitive to satiety, establishing a novel genetic model of hyperphagia. These animals exhibit an increased food intake that closely mimics post-starvation responses. As a consequence, they show enhanced lipid accumulation. Notably, serotonin depletion abolishes this increased food intake in mgl-2 mutants, showing a strict requirement for serotonergic signaling in this response.

We are currently interrogating the activity of key serotonergic and tyraminergic nodes to determine how MGL-2 modulates these pathways. Collectively, our findings reveal that MGL-2 acts as a key receptor for sensing satiety, positioning this receptor as a critical node in the serotonergic network governing feeding behavior.

Parallel antennal lobe subsystems differentially process odor valence in honey bee

Agustin Eleazar Lara · Laboratorio de fisiología y plasticidad sensorial, IFIByNE, UBA-CONICET · *In English*

A salient feature of animal olfactory systems is the presence of multiple tracts that relay information from early sensory stages to higher-order centers, raising the possibility that parallel pathways process information differentially. In Apis mellifera, there are two output projection neuron tracts, connecting the primary olfactory center with higher processing centers; this offers a system to test whether odor information is differentially routed across pathways. Building on evidence that bees recognize appetitive- and aversive-associated odorants in complex mixtures, we asked whether odor information with different hedonic values is segregated across these pathways. To address this, we combined classical conditioning with behavioral readouts, pathway-specific lesions, in vivo calcium imaging, and computational models. Our behavioral data reveal asymmetric processing of learned odorant within mixtures under different hedonic context. Moreover, severing the lateral tract impairs appetitive memory expression, whereas medial tract lesions affect aversive memory expression. Last experiments are testing how inhibitory networks shape the coding in both subsystems, in addition, with computational models to link hypotheses about circuit organization with behavioral and physiological results. Together, these findings support a functional separation between parallel olfactory pathways, with distinct contributions to the processing of odorants with different hedonic values.

Balancing opposing memories: Circuit mechanisms of flexibility in Drosophila

Ana Ricciuti · Felsenberg Lab - Friedrich Miescher Institute for Biomedical Research (FMI) - University of Basel · *In English*

Animals store experiences as memories to guide future behavior, but in dynamic environments new experiences often conflict with prior information, requiring the brain to update its internal representations. When faced with such conflict, the brain must either form a new memory with opposing valence or update the original trace, yet the circuit mechanisms governing this choice remain elusive.

Using a counterconditioning paradigm in Drosophila melanogaster, where cue valence is reversed, we show that conflicting information generates a parallel memory that competes with the original trace to drive behavior. We find that internal states, such as hunger, together with contextual cues, gate the expression of these opposing memories. Strikingly, in vivo calcium imaging revealed that memories of opposite valence are encoded within the same neural population in the Mushroom Bodies, rather than in separate circuits, suggesting a bistable, context-dependent switch.

Combining these functional results with connectome analysis, we identified circuit motifs capable of maintaining flexible representations of cues with opposing valence. These findings suggest a mechanism by which the insect nervous system encodes dynamic environmental change and shifting expectations, offering insight into

the evolutionary basis of behavioral flexibility and the mechanisms potentially disrupted in pathological conditions.

Incompatible dynamical systems underlying sensorimotor synchronization

Ariel Dario Silva · Laboratorio de Dinámica Sensomotora / Departamento de Ciencia y Tecnología / Universidad Nacional de Quilmes · *In Spanish*

In paced finger-tapping tasks employing different types of period perturbations, a “perturbation context” is evident during resynchronization, biasing the error-correction mechanism. In this work, we show, both experimentally and theoretically, that responses to different perturbation types are dynamically incompatible when they are presented in separate experiments with different contexts. In other words, they cannot be described by the same underlying dynamical system. This finding may explain numerous seemingly contradictory results reported in previous studies, as well as the difficulty of reproducing responses to both perturbation types using a single mathematical model. On the other hand, when both perturbation types are presented randomly within the same experiment, the resulting responses are compatible and can be interpreted as produced by a single underlying nonlinear mechanism. We conclude that a single dynamical system can account for responses to perturbations of all types, signs, and magnitudes, which is nonetheless recalibrated according to the perturbation context.

The Non-CpG Oligodeoxynucleotide IMT504 Drives Microglial Immunomodulation and Oligodendroglial Differentiation to Promote Remyelination

Alexis Eduardo Silva Silva · Departamento de Química Biológica. Facultad de Farmacia y Bioquímica. IQUIFIB. UBA-CONICET · *In Spanish*

Multiple sclerosis is characterized by chronic neuroinflammation and impaired remyelination, highlighting the need for therapies that simultaneously modulate immune responses and promote myelin repair (Franklin & Simons, 2022). Our group recently provided the first evidence that the non-CpG immunomodulatory oligodeoxynucleotide IMT504 promotes remyelination in vivo (Mathieu et al., 2024), although the underlying cellular mechanisms remained unknown. We demostrated that IMT504 was internalized by microglia and oligodendroglial lineage cells. In microglia, IMT504 promoted activation, proliferation and phagocytic activity, induced a balanced inflammatory program characterized by increased IL-1β, TNFα, IFNβ and IL-10 expression, reduced IFNγ levels, and activated ERK1/2, p38, JNK and NF-κB signaling. In oligodendrocyte precursor cells, IMT504 reduced proliferation while accelerating differentiation into morphologically complex mature oligodendrocytes through MAPK activation. Together, these findings identify IMT504 as the first non-CpG oligodeoxynucleotide shown to directly coordinate microglial immunomodulation and oligodendroglial differentiation, providing a strong mechanistic rationale for its application as a remyelination-promoting therapy for multiple sclerosis and other demyelinating disorders.

Simposio Federal

SIMPOSIO FEDERAL SAN 2026

Emerging Mechanisms and Therapeutic Strategies in Parkinson’s Disease

The Comisión de Federalización organized this symposium to promote and showcase neuroscience research from across the country. In this context, we bring together two researchers who are exploring new approaches to Parkinson's disease, emphasizing the importance of basic science in driving translational research and advancing the development of novel therapies.

From Neurodegeneration to Regeneration: The Promise of Stem Cell-Derived Exosomes

Dra. Claudia Banchio
Instituto de Biología Molecular Rosario (IBR-CONICET) - Universidad Nacional de Rosario

Parkinson’s disease (PD) is a progressive neurodegenerative disorder caused by the loss of dopaminergic neurons in the substantia nigra. Current treatments provide symptomatic relief but do not prevent neurodegeneration or modify disease progression. Although dopaminergic neuron transplantation has shown promise as a regenerative strategy, challenges related to cell survival, integration, safety, and scalability limit its widespread application. Therefore, there is growing interest in cell- free approaches that retain the therapeutic benefits of stem cells. In addition, the blood- brain barrier (BBB) remains a major obstacle for effective drug delivery to the brain. Extracellular vesicles (EVs) have emerged as promising therapeutic candidates due to their ability to mediate intercellular communication and deliver bioactive cargo across biological barriers. Here, we investigated the therapeutic potential of neural stem cell-derived small extracellular vesicles (NSC-EVs) in in vitro and in vivo models of PD. NSC-EVs isolated from primary murine neural stem cell cultures significantly enhanced dopaminergic neuron survival, reduced apoptosis, and protected against neurotoxin- induced damage. Notably, these EVs are naturally enriched in Catalase, a potent antioxidant enzyme that may contribute to their neuroprotective effects by reducing oxidative stress. Importantly, NSC-EV administration also promoted neuroprotection in experimental models of PD. These findings support NSC-EVs as a promising cell-free therapeutic strategy with neuroprotective and regenerative potential for Parkinson’s disease.

Effects of L-Dopa on Microtubule Dynamics and Synaptic Stability

Dr. Gaston Bisig
Centro de Investigaciones en Química Biológica de Córdoba-CONICET
Departamento de Química Biológica Ranwel Caputto-Facultad de Ciencias Químicas
Universidad Nacional de Córdoba

L-Dopa remains the most effective treatment for alleviating the motor symptoms of Parkinson’s disease and has been the gold-standard therapy for more than five decades. Despite its clinical success, relatively little is known about how prolonged exposure to this therapy may influence neuronal structure and function. I will present recent findings demonstrating that L-Dopa can directly affect the neuronal cytoskeleton, leading to alterations in microtubule dynamics and synaptic stability. Using cultured neurons, we found that L-Dopa promotes the formation of modified microtubules with altered dynamic behavior,

impairing their ability to support the maintenance of dendritic spines and excitatory synapses. These effects result in increased synaptic vulnerability and structural remodeling of neuronal connections. Our results uncover a previously unrecognized interaction between L-Dopa and the molecular machinery that regulates neuronal plasticity. These findings provide a new framework for understanding how chronic exposure to this therapy can influence microtubule function, synaptic architecture, and ultimately neuronal connectivity in Parkinson’s disease.



Posters

368 posters · 12 topics

V Friday 02 October · Poster Session 1
S Saturday 03 October · Poster Session 2
D Sunday 04 October · Poster Session 3

Cellular and Molecular Neurobiology

V-001

Selective detection of amyloid-β oligomers using an ELISA based on conformation-specific antibodies in a transgenic rat model of Alzheimer's disease

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Soluble amyloid-β oligomers (AβOs) are conformational species associated with early synaptic dysfunction and neuronal damage. Experimental models without detectable plaque accumulation allow investigation of their role in early amyloid pathology. However, their heterogeneity and low abundance make their specific detection in biological samples challenging, requiring sensitive and selective detection strategies. Hippocampal and cortical homogenates and cerebrospinal fluid (CSF) samples from 6-month-old male and female Tg+/− McGill-R-Thy1-APP rats and WT controls were analyzed using a sandwich ELISA based on AβO-specific antibodies. In this ELISA, a conventional mAb NU1 was used as a capture antibody and the recombinant M13 bacteriophage displaying the AβO-specific single-chain variable fragment (scFv) NUsc1 on its surface was used for detection. The results showed higher AβO levels in hippocampal and cortical homogenates from Tg animals compared to WT controls. AβO levels were also increased in CSF from Tg animals in relation to WT controls, with statistically significant differences in all three comparisons. This approach enabled the detection of AβOs in brain tissue and CSF at an early stage of amyloid pathology, supporting its use for the molecular characterization of experimental AD models and the study of early oligomeric species. These findings emphasize the significance of evaluating AβOs as potential biomarkers for the identification of early disease stages.

Cellular and Molecular Neurobiology

S-001

Functional implications of disrupting GPM6a–NPTN cis and trans interactions using a synthetic peptide targeting the extracellular domains of GPM6a

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Neuronal architecture is shaped by the formation of diverse protein complexes, including those involving neuronal glycoprotein M6a (GPM6a) and neuroplastin (NPTN). GPM6a and NPTN individually contribute to neuronal morphogenesis, promoting neurite and filopodia outgrowth and synapse formation. We previously demonstrated that co-expression of GPM6a and NPTN decreases neurite outgrowth in N2a cells, although the molecular mechanism underlying this effect remains unknown. Here, we investigated the role of GPM6a extracellular loops in this interaction using a recombinant peptide targeting both GPM6a extracellular domains, previously generated in our laboratory (GPM6a-loops). In N2a cells, treatment with GPM6a-loops restored neurite outgrowth that was abolished by GPM6a–NPTN co-expression for both NPTN isoforms (NPTN65 and NPTN55). Furthermore, cell aggregation assays in HEK293 cells showed that GPM6a-loops prevented aggregate formation between GPM6a- and NP65-overexpressing cells, suggesting interference with their trans interaction. Together, these results suggest that the extracellular loops of GPM6a participate in both cis and trans interactions with NPTN and underscore the essential contribution of these regions to its biological function. These results provide new insight into the molecular mechanisms regulating neurite development and identify the GPM6a–NPTN interaction as a potential target for modulating neuronal morphogenesis.

Cellular and Molecular Neurobiology

D-001

Sex and Region-Specific Impact of a Low-Protein Diet and Environmental Enrichment on Microglial IBA1 Expression in the Hippocampus of Mouse Offspring

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Maternal protein malnutrition has lasting effects that negatively impact brain development and offspring behavior, increasing the risk of anxiety and depression. It has been described that malnutrition increases the risk of a dysregulated immune response leading to neuroinflammation, but little is known about the role of glial cells in response to early-life adversities nor the effect of environmental enrichment on the glial response. In this study, we examined the IBA1+ area in the hippocampus of female and male mouse offspring exposed to a low-protein (8% casein, LP) or normal-protein diet (20% casein, NP) during gestation and lactation until P21. We performed IHC for IBA1 in free-floating sections and analyzed the mean intensity and area of the staining in the hilus and molecular layer of the hippocampus. Results in male offspring at P21 showed a smaller IBA1+ area and higher IBA1 intensity in the LP-group compared to the NP group in both analyzed regions. No significant differences in IBA1 expression were observed in either region in female offspring, nor in maternal IBA1 expression. We extended the analysis to P56 offspring, where a subset of the LP-group was exposed to an enriched environment (LP-EE) to assess whether EE could reverse the effects of perinatal malnutrition. Since EE reversed anxiety-like behavior in previous behavioral assays, we aim to determine whether these restorative effects are also reflected in hippocampal microglia.

Cellular and Molecular Neurobiology

D-013

C3aR expression in microglial cells after brain injury in mice

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Complement 3 alpha receptor (C3aR) is expressed in microglia during embryonic development with a role in pruning and debris clearance. We observed increased complement 3 (C3) immunoreactivity in mouse injured brain after cold injury, likely from blood origin. Recent findings suggest a role of C3-C3aR in brain damage progression, making it a promising target. We aimed to study C3aR expression using qPCR and fluorescence microscopy (epifluorescence and confocal) in a cold injury model in young adult female and male mice (C57/4-5 months). We observed increased C3aR mRNA expression in the injured hemisphere in both males and females. Co-labeling of C3aR with astrocyte marker GFAP (glial fibrillary acidic protein) or microglia marker IBA1 (Ionized calcium-binding adaptor molecule 1) strongly suggests microglial (but not astroglial) receptor expression at 1, 3 and 7 days post lesion. In vitro, using primary cultures of astrocytes and microglia, we observed C3aR expression in microglial cells but not astrocytes under control conditions. After LPS (Lipopolysaccharide) stimulation, microglia showed increased C3aR immunoreactivity, while astrocytes remained C3aR-negative, suggesting strong repression in these cells. Co-treatment with histone deacetylase inhibitor, trichostatin A, did not promote C3aR expression in astrocytes. Given that C3 is known to modulates gliosis, our results position microglia as a first responder and a potential target for C3aR pharmacological inhibition.

Cellular and Molecular Neurobiology

S-002

Applying multinomial Bayesian modeling to vesicle trafficking

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Huntington's disease (HD) is a hereditary neurodegenerative disorder caused by an expanded poly-glutamine stretch in the Huntingtin protein (Htt). Both HD patients and animal models show alterations in the regulated-secretory pathway, evidenced by altered neuropeptide functions and decreased dense-core vesicles (DCV) secretion, respectively. However, Htt´s role in this pathway, and how it becomes affected in HD, remain unclear. We used confocal imaging and bioimage analysis to characterize DCV motility in chromaffin cells. We applied Bayesian statistics to model the probability of each motion type as a function of the experimental conditions and cell regions, using a multinomial logistic regression and fitting different spatial distribution patterns. Under resting conditions, WT-Htt increased DCV motility in the periphery, whereas mHtt induced the same effect but in the central region of the cell. During K+ stimulation, Control cells revealed an increased DCV number near the periphery, with increased DCV motility toward the plasma membrane throughout the cell. The expression of mHtt impaired this last response, reducing the general motility of DCV, and particularly in the direction toward the plasma membrane, an effect absent in WT-Htt-expressing cells. This data contributes to our understanding of Htt biology, showing the importance of Htt activity along the DCV trafficking pathway.

Cellular and Molecular Neurobiology

D-002

Single-cell transcriptomics reveals a pallial GABAergic neurogenic lineage in the pallium of adult zebrafish

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The adult zebrafish pallium is a highly active neurogenic niche, yet adult pallial neuro-genesis has been assumed to generate predominantly glutamatergic neurons. Previous in vivo EdU labeling revealed that ~3% of adult-born pallial neurons adopt a GABAergic phenotype, a proportion that increases approximately fourfold after cognitive training. To test whether pallial neural stem cells (NSCs) generate GABAergic lineages, we analyzed a published scRNA-seq dataset of the adult zebrafish telencephalon. After quality filtering and clustering, we identified 16,321 cells across 15 groups, including 11,130 neuronal-lineage cells. Integrated annotation revealed GABAergic immature neu-rons with pallial identity, co-expressing GABAergic genes (dlx1a, dlx2a, dlx5a, gad1a/b, gad2) and pallial markers (cbln1, nr2f2, sox4a, emx2/3). Their molecular signature ena-bled detection of GABAergic-like pallial neuroblasts (~4% of pallial neuroblasts) and NSCs with GABAergic features (~5% of NSCs). These NSCs expressed pallial markers (emx2/3, wnt3a) alongside GABAergic determinants (nkx2.1, lhx5, zfhx3/4) and were tran-scriptionally distinct from pallial glutamatergic and subpallial GABAergic NSCs. Together, our results support a local GABAergic neurogenic trajectory in the adult zebrafish pallium and reveal previously underappreciated flexibility in adult NSC fate output.

Cellular and Molecular Neurobiology

V-003

Acute effects of continuous caffeine exposure on cell regeneration in the zebrafish retina

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The use of the zebrafish model is crucial to understand central nervous system regeneration, including the retina. Unlike mammals, in which retinal injuries and disease cause blindness, zebrafish repair their retinas through the reprogramming of Müller glia (MG). Investigating the molecular and genetic mechanisms that trigger self-repair enables the design of pharmacological and gene therapies applicable to ophthalmology, aimed at halting vision loss. We aimed to evaluate the effects of caffeine (non-selective adenosine receptor antagonist) on MG reprogramming and proliferation in the zebrafish retina. Retinas were injured via intravitreal injection of CoCl2 (1.3 mM). Zebrafish were exposed to caffeine (5 mg/L) in the tank water for 96h. Immunofluorescence for PCNA, GFAP, and microglia (IB4-positive) were detected in retinal cryosections and whole-mounts. Quantitative RT-PCR was used to determine the expression of GFAP, TNFα, adenosine receptors (A2aa, A1b, A2b), and proneural pluripotency factors (Ascl1a and Lin28). Caffeine decreased Ascl1a expression and increased Lin28a expression in injured retinas. Microglial cells and the transcriptional expression of A2aaR were reduced in caffeine-treated injured retinas. Caffeine treatment reduced MG gliosis in injured retinas. Our findings indicated that caffeine exerts neuroprotective effects in the retinal injury paradigm in zebrafish by modulating the inflammatory response that triggers the induction of retinal progenitors.

Cellular and Molecular Neurobiology

S-003

Dysregulation of the SARA-Smurf2 axis in Temporal Lobe Epilepsy and its modulation by Losartan

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Temporal lobe epilepsy (TLE) is a focal epilepsy characterized by recurrent seizures and frequent pharmacoresistance. Increasing evidence suggests that dysregulation of transforming growth factor β (TGFβ) signaling contributes to epileptogenesis and neuroinflammation. SARA (Smad Anchor for Receptor Activation) is an adaptor protein that facilitates Smad2/3 phosphorylation and TGFβ signaling, whereas Smurf2, an E3 ubiquitin ligase, contributes to the degradation of SARA and TGFβ receptors. However, the role of the SARA-Smurf2 axis in regulating TGFβ signaling during TLE has not been described, and whether this pathway can be therapeutically targeted remains unknown. Using a pilocarpine-induced status epilepticus (SE) model and astrocytes derived from patients with refractory TLE, we identified disruption of the SARA-Smurf2 axis in both systems. SARA and GFAP levels were increased, whereas Smurf2 showed an inadequate increase in SE and was reduced in TLE astrocytes. Treatment of SE and TLE models with Losartan, an angiotensin II type 1 receptor antagonist, shifted SARA and Smurf2 levels toward control values and reduced seizure frequency and duration in SE model. Together, these findings identify dysregulation of the SARA-Smurf2 axis as a molecular feature of TLE and support SARA as a potential therapeutic target. Finally, our results provide experimental evidence supporting the repurposing of Losartan as a potential treatment strategy for drug-resistant epilepsy.

Cellular and Molecular Neurobiology

D-003

SSRI-1 Reduces Mutant Huntingtin Accumulation via SUMOylation Inhibition and Induction of Autophagic Flux

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Huntington's disease (HD) is a rare neurodegenerative disorder caused by mutant huntingtin (mHtt), whose accumulation and aggregation drive progressive neuronal dysfunction and death. Currently there is no cure. SUMOylation has been implicated in mHtt aggregation, suggesting this pathway as a therapeutic target. We previously showed that SSRI-1 acts as a global SUMOylation inhibitor. Here, we investigated whether SSRI-1 reduces mHtt accumulation through modulation of SUMOylation. SUMO1/SUMO2 overexpression alone in HEK293T cells expressing HttQ74-mCherry increased mHtt aggregate formation (Western blot, WB). Both SSRI-1 and ML792, an irreversible SUMOylation inhibitor, decreased SUMOylation and mHtt aggregate formation (WB, immunofluorescence). Under saturating SUMO1/SUMO2 overexpression, this effect was lost, indicating dependence on limiting free SUMO availability. Nickel-agarose pull-down confirmed reduced mHtt SUMOylation after SSRI-1 or ML792 treatment. Both inhibitors also induced autophagic flux, suggesting an additional clearance mechanism. Consistently, SSRI-1 and ML792 decreased endogenous Htt in HD patient fibroblasts, an effect abolished by autophagy inhibition, confirming autophagy-mediated clearance. These findings identify SUMOylation as a druggable pathway regulating mHtt via aggregation and autophagy, supporting SSRI-1 repurposing as a disease-modifying strategy for HD.

Cellular and Molecular Neurobiology

V-004

Transcription factor dynamics underlying adult hippocampal neurogenesis

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Throughout life, the dentate gyrus generates new granule cells (abGCs) that integrate into adult circuits. Using single-nuclei RNAseq of distinct abGCs cohorts, combined with differential gene expression, pseudotime and transcription factors (TFs) regulon analysis, we identified four cellular states: quiescent radial glia-like neural stem cells, proliferative progenitors, immature and mature abGCs. We propose that transitions between states are governed by stage-specific transcriptional regulators. To probe this, we manipulated key TFs to unravel mechanisms underlying abGCs differentiation and integration. Foxo1, Hlf and Tef are expressed in quiescent stem cells, downregulated during development, and switched back on in mature abGCs. This dynamic suggests they act as transcriptional brakes, where initial repression allows growth while reactivation stabilizes a mature homeostatic phenotype. We overexpressed (oe) each TF in abGCs using retrovirus and assessed morphology by confocal microscopy. OeFoxo1-abGCs exhibited an initial transient reduction in dendritic complexity, restored upon maturation. In contrast, oeHlf-abGCs and oeTef-abGCs displayed impaired dendritic growth, preventing neurons from achieving normal morphological complexity. These structural changes may underlie integration dynamics, currently under study. Therefore, we propose that Foxo1, Hlf and Tef tightly control dendritic arborization, acting as homeostatic brakes to stabilize mature neuronal structure.

Cellular and Molecular Neurobiology

S-004

A novel strategy for peripheral nerve regeneration through a bionanotechnological “Hybrid platform”.

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Our group focuses on the development of nanobiotechnological strategies to promote nerve regeneration after a lesion in the peripheral nervous system. To this end, a rat model of Wallerian degeneration induced by a 30 second sciatic nerve crush is employed. In this model, we analyze the analgesic and/or neuroregenerative effects of the systemic transplant of a “hybrid platform” composed of poly(lactic-co-glycolic acid) nanocapsules (NC) loaded with magnetic nanoparticles (MNP) and functionalized with polyethyleneimine (PEI) for the transfection and magneto targeting of bone marrow mononuclear cells (BMMC) to the injury site. Both PLGA-NC and MNP were thoroughly characterized by DLS, TEM, VSM, TG. Experiments with the “hybrid platform” (NC:PEI:DNA) using a mock plasmid loaded with MNPs and labeled with a fluorochrome to detect its recruitment in the ipsilateral nerve demonstrated that the “hybrid platform” does not hinder the effects of native BMMCs and is also optimized by magneto targeting. In the present work we analyzed the effect of the “hybrid platform” NC:PEI:ARNm of native BDNF or NGF on behavioral and functional experiments, such as Von Frey and acetone tests as well as gait analysis. The results obtained show a clear difference between BDNF and NGF analgesic effects. Some promising results encourage us to further explore this approach as a potential therapeutic strategy and a tool to better understand the mechanism involved in nerve regeneration.

Cellular and Molecular Neurobiology

D-004

Stage- and Neuron Type Dependent Roles of the COP9 Signalosome in the Brain

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The COP9 signalosome (CSN) is a nine-subunit protein complex that regulates protein degradation through deneddylation of cullin-based E3 ubiquitin ligases, with CSN5 acting as its catalytic subunit. Despite the importance of the ubiquitin-proteasome system in neuronal development and function, the contribution of CSN to brain development remains poorly understood. In this study, we investigated the consequences of CSN loss-of-function at distinct stages of neuronal development in mice. Using the Cre-loxP system, we conditionally deleted the CSN5 subunit in different neuronal populations. CSN5 ablation in proliferating neuroblasts using Nestin-Cre caused embryonic lethality, likely reflecting impaired cell division. Deletion in early postmitotic excitatory neurons using Nex-Cre resulted in lethality at postnatal day (PD) 1. In contrast, CSN5 deletion in inhibitory neurons using Dlx-Cre led to lethality between PD17 and PD21. Notably, CSN5 loss in mature excitatory neurons of the forebrain had no detectable effect on lifespan or gross brain morphology. Together, these findings reveal stage- and neuron type-dependent requirements for CSN during brain development, highlighting the distinct and context-specific functions of CSN functions in the developing brain.

Cellular and Molecular Neurobiology

V-005

High environmental levels of thyroxine altered Müller glia-derived progenitor cell proliferation, cell death, pluripotency gene expression and neurogenesis in the retina of zebrafish

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The zebrafish is a useful model organism in biomedical research. Its remarkable capacity to regenerate neurons makes this species ideal for studying mechanisms that can pave the way for inducing regeneration in the adult mammalian nervous system. The zebrafish retina regenerates via reprogramming of multipotent Müller glia (MMG). Thyroid hormones (TH) are crucial in the nervous system development and retinogenesis. We aimed to investigate whether excess TH signaling affected MMG proliferation, cell death and neurogenesis. Retinal lesions were induced via intravitreal injections of ouabain or CoCl2. Zebrafish were treated with 300 µg/L thyroxine (T4) or vehicle in the aquarium water for 2, 8, 25, and 60 days. T4 treatment initially inhibited and subsequently increased MMG-derived progenitor cell proliferation. Short-term excess T4 signaling inhibited microglia activation. High levels of T4 caused significant increases in the expression of reprogramming genes. Prolonged excess T4 signaling modified the transcriptional expression of markers for bipolar, MG, rod, cone, ganglion, and horizontal cells. Chronic TH excess increased apoptosis, which counteracted progenitor proliferation and prevented regeneration. Excess TH promoted red-cone genesis and intensified gliosis. Injured retinas treated chronically with TH emulate changes observed in human hyperthyroidism-induced retinopathies. Excess T4 induced regeneration in undamaged retinas, overpacing metabolic damage.

Cellular and Molecular Neurobiology

S-005

An Alzheimer-associated neuronal model to study APP processing and mitochondrial homeostasis

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Abnormal amyloid precursor protein (APP) metabolism and mitochondrial dysfunction are implicated in Alzheimer's disease (AD) pathogenesis. The Swedish mutation (APPSwe), which causes early-onset familial AD, enhances β-secretase cleavage, shifting APP processing toward the amyloidogenic pathway. Previous results in APPSwe patient-derived brain organoids show selective mitochondrial vulnerability under oxidative conditions, suggesting a direct link between APP and mitochondrial homeostasis. We developed glutamatergic neurons (i3N) from wild type (WT) and APPSwe patient-derived iPSCs as a model to study the molecular mechanisms underlying mitochondrial homeostasis alterations in AD. APP distribution was assessed by immunofluorescence with N- and C-terminal APP antibodies revealing an increase in the N-/C-terminal ratio in APPSwe i3N. Neuronal polarization evaluated by quantifying neurite length and morphological progression showed an increased neurites number with longer projections in APPSwe i3N compared with WT i3N. Mitochondrial morphology was characterized by analyzing length and width (MitoTracker-Green) and membrane depolarization was analyzed by TMRE intensity. These findings suggest that APPSwe alters APP metabolism and early neuronal morphological development, providing a useful system to study their relationship with mitochondrial homeostasis and oxidative vulnerability in AD.

Cellular and Molecular Neurobiology

D-005

Role of Serotonin in the Adaptive Response to Acute Stress in Drosophila melanogaster

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Vital physiological functions are sustained through the interaction of specialized structures coordinated by tightly regulated signaling pathways. This homeostasis can be disrupted by internal or external stressors, triggering the release of neurotransmitters essential for systemic adaptation. Among these, serotonin (5-HT) plays a critical yet poorly characterized role in adaptive stress responses. Here, we used Drosophila melanogaster, a model lacking endogenous thermoregulatory mechanisms, to investigate the cellular processes underlying serotonergic involvement in the locomotor response to thermal stress. Control flies exposed to elevated temperatures exhibited a characteristic increase in locomotor activity. To map the specific components of this pathway, we subjected flies deficient in tryptophan hydroxylase, the serotonin transporter (SerT), and individual receptors (5-HT1A, 5-HT1B, 5-HT2A, 5-HT2B, and 5-HT7) to an acute thermal stress protocol and monitored their locomotor patterns. These preliminary results demonstrate a functional role for serotonin signaling in orchestrating the behavioral and physiological response to thermal stress.

Cellular and Molecular Neurobiology

V-006

MAPT Mutations Differentially impairs neuronal physiology in Patient-Derived Glutamatergic Neurons

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Tauopathies are neurodegenerative diseases caused by abnormal tau metabolism, leading to neuronal dysfunction and cell death. Many MAPT mutations have been linked to pathological tau aggregation, microtubule instability, trafficking defects and synaptic dysfunction but physiological impairments caused by each variant are not fully understood. Notably, glutamatergic neurons are proposed to be particularly vulnerable in tauopathies. Here, we generated patient-derived iPSC glutamatergic neurons (I3N) using a genetic induction protocol to investigate phenotypes associated with V337M and R406W tau mutations. Analysis of fluorescent lysosome axonal transport in I3N showed that V337M,but not R406W, increased the retrograde proportion and reduced static lysosomes, without affecting anterograde proportion. However, V337M increased both the anterograde and retrograde segmental velocities, while R406W decreased the retrograde and increased anterograde segmental velocities. In addition, the axon initial segment location was impaired in V337M and R406W neurons. Finally, V337M showed reduced amplitude and frequency of calcium signals whereas R406W showed no differences, suggesting mutation-associated electrophysiological impairments. Overall, these findings reveal that V337M and R406W mutations differentially disrupt axonal transport, AIS location, and calcium signaling. These results provide a valuable platform to study and develop therapy strategies that target specific neuronal subtype.

Cellular and Molecular Neurobiology

S-006

EphA3 Domains Differentially Regulate Axonal Transport, Neuronal Outgrowth, and Differentiation

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The precise establishment of neural circuits in the CNS depends on environmental stimuli exerted by guidance molecules, integrating topographic cues for accurate axon connectivity. Eph receptors and ephrin ligands play essential roles in axon attraction and repulsion; however, how specific Eph motifs contribute to axonal growth and neuronal development remains unknown. Here, we evaluated the intracellular dynamics of the EphA3 receptor using full-length wild-type (WT) and truncated ligand-binding domain- (Δ-LBD) constructs. Data from N2a cells and primary hippocampal neurons expressing Δ-LBD showed increased morphological outgrowth parameters compared to WT suggesting that LBD is involved in subcellular protein localization and differentiation. While both constructs displayed a mobile vesicular phenotype, Δ-LBD showed a significant increase in dynamic transport properties in primary and human iPSC-derived neurons. Surprisingly, we found that EphA3-WT and not Δ-LBD is transferred from transfected distal axons to crossing neighboring axons, suggesting a novel local axonal mechanism of cellular membrane transfer. We propose that this axo-axonal transfer is mediated by Eph receptor interaction with its ligands. Future work will focus on elucidating the underlying pathways using specific inhibitors. To date, no report describes this transfer phenomenon between distal axons, marking a unique event in molecular signaling.

Cellular and Molecular Neurobiology

D-006

Signaling Mechanisms Underlying GPM6a–NPTN-Mediated Neurite Inhibition

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Neuronal morphogenesis requires coordinated regulation of neurite development and cell-surface signaling. Glycoprotein M6a (GPM6a) and Neuroplastin (NPTN) are neuronal membrane glycoproteins that independently promote neurite outgrowth through Src/MAPK and MAPK/p38 signaling, respectively. Increased p38 and/ or MAPK activity induces the dual-specificity phosphatase 1 (MKP-1), a negative regulator of MAPK signaling. Although GPM6a and NPTN have been implicated in the inhibition of neurite outgrowth, the underlying mechanisms remain unclear. Here, we investigated the extracellular and intracellular mechanisms underlying this effect. Disruption of the GPM6a–NPTN interaction with a peptide targeting the NPTN65-specific Ig1 domain, but not the Ig2–3 domains, restored neurite outgrowth, identifying Ig1 as a critical determinant of the inhibitory phenotype. Pharmacological inhibition of Src, p38 MAPK, or MKP-1 also rescued neurite outgrowth in GPM6a–NPTN-expressing cells, indicating that these pathways contribute to the inhibitory effect. Together, our findings show that the GPM6a–NPTN complex inhibits neurite outgrowth through an extracellular interaction coupled to Src-, p38 MAPK-, and MKP-1-dependent signaling, revealing a mechanism by which neuronal membrane proteins integrate extracellular interactions with intracellular signaling to regulate neuronal morphogenesis.

Cellular and Molecular Neurobiology

V-007

In Vitro Characterization of Streptozotocin-Induced Microglial Responses: Implications for Alzheimer's Disease Modeling

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Streptozotocin (STZ) administered intracerebroventricularly is widely used to model sporadic Alzheimer's disease (AD) in vivo, an approach established in the 1990s. In this context, understanding the response of microglia is particularly relevant, given their key role in maintaining brain homeostasis and mediating neuroinflammatory responses. Considering the central role of microglia in brain homeostasis and neuroinflammatory responses, this study aims to characterize the effects of STZ on BV-2 microglial cells in vitro. Cells will be exposed to increasing STZ concentrations to evaluate changes in cell viability, cell death and morphology. The study will further explore oxidative stress and lipid peroxidation, as well as potential changes in microglial status through the analysis of cellular markers and inflammatory mediators. Acridine Orange/Propidium Iodide staining will be used to characterize changes in viable and non-viable cell populations. Preliminary MTT results indicate that STZ exposure affects BV-2 cell viability in a concentration-dependent manner. Ongoing experiments will further characterize the cellular responses induced by STZ and determine whether different concentrations differentially affect microglial survival, oxidative status and cellular phenotype. This approach may provide new insights into the direct effects of STZ on microglia and contribute to a better understanding of its use as an experimental model of sporadic AD. *Facundo Peralta & Camila Juan have equal contribution

Cellular and Molecular Neurobiology

S-007

Altered grin1 splicing variants after GluN2A reduced expression in vivo

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Hippocampal GluN2A knockdown after the developmental switch has been shown to induce a phenotype in rats that resembles that observed in some patients carrying grin2a mutations (the gene that codifies for GluN2A). GluN2A is one of the regulatory subunits of NMDA receptors (NMDARs), key glutamatergic receptors composed of four subunits: two obligatory GluN1 and two regulatory subunits. In the brain, GluN2A predominates in mature circuits, whereas GluN2B is more abundant in immature structures. The grin1 gene, which encodes the GluN1 subunit, generates four splicing variants in the C-terminal region, depending on the combination of three exons. These sequences are involved in membrane trafficking, retention in the endoplasmic reticulum, and interaction with different proteins. In our model, grin1 total expression remained unchanged, although total and synaptic GluN1 protein levels were reduced. However, synaptic GluN2A-containing NMDARs remained unchanged. Based on these results, we aimed to assess grin1 splice variant expression and ribosomal distribution. We found that GluN2A-kd induces a reduction in isoform 1 expression with a concomitant increase in isoform 4 levels, compatible with enhanced trafficking toward synapses. Additionally, ribosomal profiling revealed a shift toward lighter polysomes, suggesting increased translation velocity. Altogether, these findings strongly indicate that GluN2A knockdown triggers compensatory mechanisms to maintain synaptic functionality.

Cellular and Molecular Neurobiology

D-007

The prefrontal 5-HT7 receptor as a therapeutic target in psychiatric disorders including anxiety and depression

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Maternal separation (MS) during the early postnatal period (P2–14) is a well-established model of early-life stress that induces persistent alterations in prefrontal cortical circuits and increases susceptibility to anxiety and depressive-like behaviors in adulthood. Previous studies from our laboratory identified the serotonin 5-HT7 receptor as a key mediator of these long-term effects. We hypothesize that 5-HT7 receptors expressed by glutamatergic neurons in the prefrontal cortex critically contribute to the maladaptive development of the prefrontal cortex–dorsal raphe nucleus (PFC–DRN) circuit following early-life stress. As a first step, we are validating an AAV-mediated short hairpin RNA (shRNA) targeting the last exon shared by all 5-HT7 receptor transcript variants in primary cultures of mouse cortical neurons. The ultimate goal is to design a miRNA targeting this receptor mRNA delivered selectively to glutamatergic neurons. We will assess PFC–DRN synaptic connectivity using high-resolution microscopy and evaluate anxiety and depressive-like behaviors in adulthood. This approach will determine whether selective early reduction of 5-HT7 expression in prefrontal glutamatergic neurons is sufficient to prevent the long-term neural and behavioral consequences of early-life stress.

Cellular and Molecular Neurobiology

V-008

Pathological astroglial remodeling during epileptogenesis: the protective effect of losartan from cell culture to in vivo models

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Pathological astroglial remodeling is a central event during epileptogenesis, contributing to the loss of glial homeostatic functions and neuronal hyperexcitability. In an in vitro astrocyte-enriched culture model, exposure to epileptogenic HMGB1 induced a reactive phenotype characterized by increased NFkB activation, DNA hypermethylation, reduced glutamine synthetase expression (GS), increased levels of the neurotoxic factor MAFG and proinflammatory cytokines. Losartan treatment (1-10 μM) consistently reversed these changes, restoring homeostatic genes GS, Kir4.1, GLT-1 and reducing MAFG and proinflammatory markers (IL-1β, IL-6). To validate these findings in vivo, the effect of losartan was evaluated in two animal models of epileptogenesis. In the hyperthermia seizure model (HS), losartan treatment (30 mg/kg/day) significantly reduced the GFAP+ immunoreactive area in both the hippocampal CA1 and the piriform cortex compared to the vehicle group. In the adult lithium-pilocarpine model of epilepsy, a significant decrease in GFAP+ area was also observed in both regions, and the expression of GS increased, suggesting a reduced reactive gliosis and restoration of the homeostatic astroglial phenotype. Taken together, these results show that epileptogenic astroglial remodeling in vitro and in vivo can be modulated by losartan, establishing itself as a promising therapeutic candidate to prevent epileptogenesis. Supported by grants: PICT 2021-0760, UBACYT, PIP CONICET

Cellular and Molecular Neurobiology

S-008

Reactive astrogliosis induced by neuronal GluN2A knockdown

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Alterations in the expression or localization of NMDA receptors (NMDARs) are associated with multiple neuropathologies. NMDARs are tetramers composed of two GluN1 subunits and two regulatory subunits. In the mature brain, the predominant regulatory subunit is GluN2A. However, mutations in the GRIN2A gene lead to decreased GluN2A expression, resulting in complex phenotypes ranging from neurodevelopmental disorders and intellectual disability to schizophrenia. In our laboratory, we developed a GluN2A knockdown (GluN2A-kd) model in adult rats to investigate the consequences of reduced GluN2A expression. In this model, we found that GluN2A-kd neurons exhibit a more excitable phenotype both in vitro and in vivo. As increased neuronal excitability is often associated with enhanced astrocyte reactivity, we examined astrocyte morphology and reactivity. In this work, we found that GluN2A-kd induced increased astrocyte reactivity in vitro, as evidenced by an increase in astrocytic area. Additionally, we observed altered levels of reactive oxygen species (ROS). These results led us to hypothesize that reduced GluN2A expression induces astrogliosis, which could be an initial cellular response contributing to the hyperexcitability observed in vitro and in vivo in our GluN2A-kd model.

Cellular and Molecular Neurobiology

D-008

Sex-dependent differences and age-dependent regulation of the ASIC1a–ERK pathway in a mouse model of Fabry disease

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Fabry disease (FD) is characterized by early pain manifestations and well-recognized sex differences in clinical presentation, yet the molecular basis underlying these differences remains poorly understood. We previously demonstrated increased ASIC1a expression and ERK activation in pain-related structures of GlaKO mice at 4 and 8 months of age. Here, we extended these studies to determine how ASIC1a–ERK signaling changes across early and adult stages and whether these changes differ between males and females. ASIC1a and phosphorylated ERK (pERK) expression were evaluated in male and female GlaKO mice at 2, 4, and 8 months of age. ASIC1a and pERK levels in dorsal root ganglia (DRG) and spinal cord, representing peripheral and central nervous system tissues, respectively, remained largely unchanged between 2 and 4 months but increased at 8 months in both sexes. Across ages, females consistently exhibited higher ASIC1a and pERK levels than males, already evident at 2 months, before sexual maturation. Similar sex-dependent differences were observed in the cerebral cortex, where female GlaKO mice showed higher ASIC1a and pERK expression than males across the ages examined. Together, these results provide new insight into the temporal and sex-dependent regulation of ASIC1a–ERK signaling in FD and support further investigation of this pathway as a potential contributor to sex-related differences in Fabry-associated pain.

Cellular and Molecular Neurobiology

V-009

Microexon alternative splicing and feeding behavior in C. elegans

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Microexons are short alternative exons up to 51 nucleotides long that are highly enriched in neuronal genes. Their dysregulation has been linked to human neurodevelopmental disorders, including autism spectrum disorders. In the nematode Caenorhabditis elegans, global regulation of microexons is also critical for proper development. Here we show that microexon alternative splicing (AS) changes between C. elegans larval and adult stages and that microexon inclusion is differentially regulated among distinct neuronal types. Consistently with previous evidence that C. elegans splicing is regulated in response to environmental stimuli, we found here that specific microexons are modulated upon food availability. Both the inclusion levels of these microexons and the feeding behavior seem to depend on the DNA topology, which may affect transcription dynamics, as revealed by the effects of the topoisomerase I (TOP1) inhibitor, camptothecin (CPT). CPT treatment alters responses related to food availability such as speed reduction and exploration. Furthermore, animals carrying a mutation in the global regulator of microexon splicing prp-40 exhibit altered food preference, independently demonstrating that disruption of microexon AS has important consequences on animal behavior.

Cellular and Molecular Neurobiology

S-009

E258 residue modulates Gpm6a intracellular sorting and its role in neuronal morphogenesis

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Functional membrane trafficking is critical for neuronal growth and differentiation. In this context, the neuronal membrane glycoprotein M6a (Gpm6a), a four-transmembrane-domain protein of the PLP/DM20 family, plays a major role in neuronal development. Gpm6a overexpression promotes filopodia formation, and its endocytic/recycling pathway regulates synapse formation and maintenance. However, the mechanisms targeting Gpm6a for recycling or degradation are still unknown. Here, we demonstrate that overexpressing the Gpm6a mutant E258A reduces filopodia formation and arborization complexity in rat hippocampal neurons, while compromising neurite outgrowth during N2a differentiation. By live-cell imaging of N2a cells, we show that the E258A mutation increases Gpm6a vesicle dynamics and their colocalization with Rab7 and Lamp1 positive compartments, while it does not alter Gpm6a association with Rab5 or Rab11 positive endosomes, indicating that this mutation redirects intracellular trafficking of Gpm6a towards late endosomal/lysosomal compartments. When LysoTracker labeling was used to confirm compartment identity, we observed that E258A accumulates within the lysosomes. Moreover, an increased association between E258A and GalNAc-T (a TGN marker) was observed. We conclude that E258A leads to enhanced Gpm6a sorting to the degradative pathway and propose the E258 residue as a critical switch regulating Gpm6a targeting for degradation, thereby influencing neuronal morphogenesis.

Cellular and Molecular Neurobiology

D-009

APOE4/4 is associated with reduced mGlu3R in the amyloid plaque microenvironment in Alzheimer's disease

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AD involves β-amyloid (Aβ) accumulation and impaired clearance. Astrocytes contribute to Aβ removal via mGlu3R. Our laboratory previously showed that mGlu3R activation promotes non-amyloidogenic APP processing and increases astrocytic Aβ uptake. We asked whether mGlu3R is associated with APOE4-related risk. Human brain transcriptomic data from AD patients and controls were stratified by APOE3/3, APOE3/4 and APOE4/4, and GRM3 expression was analyzed in plaque, near-plaque and far-plaque. APOE4/4 showed reduced GRM3 vs controls ($pADJ=2.58\times10^{-2}$), driven by the plaque region ($pADJ=2.20\times10^{-2}$). No significant differences were found in other regions or in APOE3/3 and APOE3/4. We next investigated the ApoE–mGlu3R relationship. In primary rat astrocytes, LY379268 increased ApoE expression by 25%, although this was not significant. In PDAPP-J20 mice, previously shown by our laboratory to have reduced hippocampal mGlu3R, ApoE mRNA was significantly reduced in hippocampus vs NTg controls ($p=0.049$), but not in cortex. In primary mouse astrocytes, 30μM NAAG did not alter ApoE or LRP1 mRNA levels. Finally, Aβ uptake was assessed across an NAAG dose-response curve; analysis is ongoing. Together, these findings identify a specific association between APOE4/4 and reduced GRM3 at amyloid plaques. Reduced hippocampal ApoE in J20 mice, together with the role of mGlu3R in astrocytic Aβ clearance, supports a potential link between APOE4-related vulnerability and mGlu3R-dependent glial responses.

Cellular and Molecular Neurobiology

V-010

CBD AS A TISSUE- AND TIME-DEPENDENT MODULATOR OF AUTOPHAGY IN DROSOPHILA MELANOGASTER MODEL OF TAU NEUROTOXICITY

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Tauopathies feature neurotoxic tau accumulation and altered autophagy; CBD reportedly induces autophagy in cell models. In N2a cells and Drosophila, we assessed cannabinoid effects on autophagy and tau neurodegeneration. Screening four cannabinoids identified CBD as the most consistent inducer, the others inhibitory or inactive; CBD was selected. In larval fat body (mCherry-Atg8a; starvation control; inert ethanol vehicle), acute CBD had no effect, whereas chronic treatment significantly increased Atg8a foci without changing Ref(2)P, indicating induced flux, confirmed with tandem GFP-mCherry-Atg8a. In a validated GMR>hTau rough-eye model, chronic CBD did not rescue photoreceptor disorganization; higher doses are under test for dose-limiting effects, and the assay may miss mild effects, warranting complementary approaches. Reanalysing public brain RNA-seq/proteomics (TauWT vs TauR406W across aging), only TauR406W significantly dysregulated autophagy genes and proteins, mainly post-transcriptionally and independently of the age-related decline across genotypes; the null TauWT result may reflect timing, as WT tau phenotypes emerge later. Since CBD boosts flux in vivo, it may counteract tau-driven pathway dysfunction; we are testing this: western blot of total and phospho-tau (pS214, pS396) in adult brains is validated, imaging under way. Together, CBD is a tissue- and time-dependent autophagy modulator, providing new in vivo tools to dissect its role in tau neurodegeneration.

Cellular and Molecular Neurobiology

S-010

Involvement of the α2M/LRP-1 System in Glial Stress and Antioxidant Dysregulation in the Retina of Metabolic Syndrome mice

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Metabolic syndrome (MS)-induced retinopathy involves vascular, glial, and neuronal damage driven by dyslipidemia and hyperglycemia. Having previously shown α2-macroglobulin (α2M) and LRP-1 levels in Müller glia (MGCs) alongside elevated retinal α2M in MS mice, we evaluated the α2M/LRP-1 system in glial stress and antioxidant responses in MIO-M1 cells and a MS mouse model. MIO-M1 cells were treated with high glucose (HG, 30 mM) and aggregated LDL (LDLagg, 100 µg/mL) for 24 h to analyze GFAP, HO-1, α2M, and LRP-1 by western blot. Two-month-old WT and ApoE KO mice fed a fructose (FD, 10% in drinking water) or normal diet (ND) for 3 months received two intravitreal injections of anti-α2M antibody (0.5 µg/µL, 1 µL) or PBS during the final month. Retinas were evaluated for HO-1 immunofluorescence (ANOVA, Bonferroni, $p \leq 0.05$). In MIO-M1 cells, HG + LDLagg upregulated GFAP ($p=0.04$) while decreasing HO-1 ($p=0.04$) and LRP-1 ($p<0.0001$). In mice, treatment-diet ($p=0.007$) and genotype-diet ($p=0.0005$) interactions were significant. Retinal HO-1 increased in ApoE ND PBS vs. WT ND PBS ($p=0.02$) and was reversed by Ab-α2M treatment in ApoE ND ($p=0.0005$) and ApoE FD ($p=0.01$) mice. Metabolic stressors induce glial reactivity and impair antioxidant response in MIO-M1 cells, correlating with retinal α2M accumulation that alters antioxidant defenses in MS mice. Coupled with LRP-1 downregulation in MIO-M1 culture, these findings position the α2M/LRP-1 system as a target in MS-induced retinopathy.

Cellular and Molecular Neurobiology

D-010

"Development of a Viral Vector-Based Therapy Targeting Astrocytes in Alzheimer's Disease"

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Current therapeutic strategies for Alzheimer's Disease (AD) mainly target β-amyloid (Aβ) plaque reduction at advanced pathological stages. However, glial dysfunction appears before plaque formation, offering a window for an alternative therapy. Astrocytes express the metabotropic glutamate receptor mGlu3R, whose activation is neuroprotective: it promotes non-amyloidogenic APP cleavage, Aβ clearance, and neurotrophic factor release. We previously found that mGlu3R levels progressively decline in the hippocampus during pathological aging in AD mice (PDAPP-J20). Hence, restoring mGlu3R could recover these neuroprotective functions. We designed an adenoviral vector (AdV) expressing GRM3 (encoding mGlu3R) under the astrocyte-specific GFAP promoter, with GFP as reporter, and evaluated its cell selectivity, transduction efficiency, and safety. In vitro, astrocyte and microglia cultures/cell lines were transduced with AdV-0 (empty vector). Transduction rates for AdV-0 were 22% in primary astrocytes, 23.5% in U251 cells, and 0% in BV2 microglia. In vivo, C57BL6 mice received intrahippocampal injections of AdV-GRM3 or AdV-0. Over one month, no significant weight changes (p=0.81) or toxicity signs were observed. GFP expression confirmed vector localization within the hippocampus, without spreading to surrounding areas. These preliminary results show that AdV-GRM3 selectively and efficiently transduces astrocytes without evident toxicity, supporting future therapeutic evaluation.

Cellular and Molecular Neurobiology

V-011

Impact of dengue virus infection in neurodegenerative processes associated with tauopathies

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Dengue is an endemic disease in Argentina caused by DENV, whose impact on the central nervous system has gained relevance due to the increasing number of cases with neurological manifestations after infection. Tauopathies are neurodegenerative diseases associated with alterations in Tau protein, including mutations, changes in alternative splicing and post-translational modifications. DENV has been shown to alter alternative splicing in many transcripts. Therefore we hypothesize that DENV infection may affect Tau 3R/4R isoforms balance and promote pathological Tau accumulation. In this project we investigate the association between DENV infection and abnormal Tau metabolism. To this end, primary neurons derived from the htau mouse model were infected with DENV at DIV10. At 10, 20 and 30 days post infection Tau expression was evaluated by RT-qPCR and Western blot. So far, results suggest that DENV infection reduces Tau levels compared to non-infected neurons. Further analyses are ongoing to determine the time course of these changes. In parallel, we analyzed total Tau and p-Tau in cerebrospinal fluid (CSF) samples from individuals with past DENV infection by Western blot, to determine the conditions for this quantification. Together, this ongoing project explores the consequences of acute DENV infection in Tau metabolism, providing an initial framework to investigate the long-term impact of dengue exposure on Tau dynamics in human CSF.

Cellular and Molecular Neurobiology

S-011

Patient-derived fibroblasts as a model for Progressive Supranuclear Palsy: Recapitulating disease associated alteration in autophagy, tau, and mitochondrial function

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Progressive supranuclear palsy (PSP) is a primary tauopathy within a group of neurodegenerative disorders, characterized by pathological tau aggregation in the brain. SQSTM1/P62, a key autophagy marker, delivers ubiquitinated proteins to the autophagosome, regulating tau degradation. Here, we studied skin-derived fibroblasts from a PSP patient carrying a genetic SQSTM1/P62 p.Pro392Leu variant to determine whether autophagic flux and tau metabolism are altered. Tau, p-tau, SQSTM1/P62, and LC3 levels were analyzed by Western blot in fibroblasts from the patient and two control subjects to assess autophagy alterations and potential defects in tau degradation. Patient-derived fibroblasts showed altered autophagic flux, with increased LC3II and p62 after starvation treatment together with increased tau and phospho-tau levels. Mitochondrial morphology (MitoTracker) and membrane potential (TMRE) confocal analysis revealed increased mitochondrial fragmentation and membrane depolarization, indicating disrupted mitochondrial homeostasis. Interestingly, mitochondria-lysosome association assessed by confocal microscopy and colocalization analysis revealed altered mitophagy in patient-derived fibroblasts. Together, these results indicate that both autophagy and mitophagy are specifically impaired in fibroblasts carrying P62 Pro392Leu variant, and that tau is abnormally processed in this cellular model, suggesting that autophagy impairments may contribute to disease pathogenesis.

Cellular and Molecular Neurobiology

D-011

Loss of circTulp4 increases behavioral inhibition in conflict contexts

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Circular RNAs (circRNAs) are non-coding RNAs that have attracted increasing attention due to their diversity and high abundance across tissues, yet their biological functions remain largely unclear, partly because generating precise loss-of-function models is technically challenging. Our lab previously identified numerous circRNAs in human and mouse brain, observing that many are more abundant than their linear counterparts in neural tissue. We focused on circTulp4, a highly expressed circRNA enriched in brain and synaptic fractions, and used CRISPR/Cas9 to generate the first circRNA-deficient (CD) mouse model for a brain circRNA, disrupting circTulp4 biogenesis while preserving linear mRNA and protein expression. Tulp4CD mice show impaired excitatory neurotransmission despite normal neuronal morphology, and altered coping with stress-related challenges. Tulp4CD mice show a categorical, all-or-none failure to initiate approach under motivational-threat conflict (passive avoidance, novelty-suppressed feeding), while fear learning, active avoidance, and unconditioned anxiety-like behavior remain intact, ruling out enhanced aversive memory, impaired active responding, or trait anxiety. This points to a discrete endophenotype of dysregulated approach-avoidance resolution, reminiscent of situational phobia. New data implicates infralimbic PFC-to-amygdala circuits; we are combining RNA pull-down and optogenetic approaches to identify the molecular and circuit mechanisms involved.

Cellular and Molecular Neurobiology

V-012

mGlu3R and GCPII Alterations Across Alzheimer's and Huntington's Disease Models

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Metabotropic glutamate receptor 3 (mGlu3R) is involved in neuroprotective mechanisms and is activated by NAAG, whose availability is regulated by the enzyme GCPII. We aimed to evaluate whether alterations in this system constitute a shared pathophysiological mechanism among neurodegenerative diseases of different origins and to assess the influence of the APOE4 genotype on the expression of its components. mGlu3R and GCPII expression was analyzed in mouse models of Alzheimer's disease (PDAPP-J20) and Huntington's disease (zQ175), as well as GCPII in human samples and CSF data obtained from AD Workbench. In zQ175 mice, mGlu3R showed a trend toward decreased levels in transgenic animals compared with controls ($p=0.073$), consistent with previously published results in PDAPP-J20. For GCPII, Western blots from both models showed bands at molecular weights different from those expected and no significant differences between WT and Tg animals. No clear diagnosis-associated pattern was observed in human samples. Protein abundance data obtained using SOMAmers, expressed as RFU, were analyzed by one-way ANOVA. In CSF samples from patients with Alzheimer's disease, GCPII levels showed no significant differences among individuals with no APOE4 allele, one copy, or two copies of the allele ($F=0.524$; $p=0.593$). The reduction in mGlu3R levels may represent shared pathophysiological mechanism between AD and HD, whereas variations in GCPII do not appear to be associated with these pathologies.

Cellular and Molecular Neurobiology

S-012

Electric activity changes in human glutamatergic derived neurons with tau isoform imbalances.

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Tauopathies are a heterogeneous group of neurodegenerative diseases characterized by abnormal metabolism of tau protein, driving alterations in synaptic, ion channel activity, neuronal dysfunction and death. A key feature of the tau gene (MAPT) is generation of two isoform groups differing in microtubule-binding repeats: three repeats (3R) or four repeats (4R), expressed at a 1:1 ratio in the adult human brain. A hallmark of several tauopathies is a shift in this ratio, seen in progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD), with predominance of 4R tau, or in Pick's disease, with increased 3R tau. Our group previously showed that changes in the 3R/4R ratio regulate axonal transport of APP vesicles, which may affect other cargoes that impair channel distribution and synaptic function. To gain insight into the physiological role of these isoform-specific regulations, we shifted neurons towards 3R or 4R tau and performed calcium imaging using Fluo-3 AM dye in iPSC-derived glutamatergic neurons at day in vitro 25 (DIV25). A customized imaging pipeline was developed to extract frequency, duration, and amplitude of calcium transients. Preliminary results suggest increased 3R/4R ratio raises the frequency of calcium events. In conclusion, these results indicate tau isoform composition plays a key role in regulating neuronal electrical activity and maturation, suggesting disease-associated isoform imbalances may disrupt neuronal network function in the brain

Cellular and Molecular Neurobiology

D-012

Neonatal clonazepam exposure reprograms hippocampal molecular pathways and impairs episodic-like memory in adult rats

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Benzodiazepines are frequently prescribed during early life, yet little is known about their long-term effects on hippocampal maturation and memory-related neural circuits. Here, we examined whether neonatal clonazepam (CLZ) exposure leads to persistent alterations in hippocampal molecular markers associated with neurosteroidogenesis and glutamatergic signaling, and whether these changes are accompanied by deficits in episodic-like memory (ELM). Male rats received CLZ (1 mg/kg/day) or vehicle from postnatal day (PND) 7 to 11 and were evaluated in adulthood. Neonatal CLZ exposure selectively impaired the temporal component of ELM without affecting spatial discrimination. In addition, CLZ animals displayed reduced expression of 5α-reductase type 1, and 3α-hydroxysteroid dehydrogenase in the dentate gyrus and/or CA1, consistent with a long-lasting reduction in the hippocampal neurosteroidogenic pathway. Some of these changes were associated with altered DNA methylation profiles. Moreover, CLZ exposure produced region-specific changes in NMDA receptor subunit expression, characterized by increased GluN1 mRNA levels in CA3 together with decreased GluN2A, GluN2B, and GluN3A expression in CA1. These results show that pharmacological modulation during critical periods of brain development can produce persistent alterations in hippocampal function, potentially through interactions between neurosteroid synthesis, epigenetic regulation, and glutamatergic neurotransmission.

Cellular and Molecular Neurobiology

V-013

Back to the culture: first steps to understand the neuroprotective effect of Yerba Mate on primary dopaminergic cultures.

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons. Neuroprotective strategies that promote survival and preserve the function of these neurons represent a key challenge. Chronic intake of Yerba Mate (YM) has been associated with a reduced risk of PD, and our lab has shown that YM prevents dopaminergic loss in primary cultures. In addition, unpublished results show that YM and its main active compound chlorogenic acid (CGA) activate AMPK and autophagy in SH-SY5Y cells. Since AMPK is a key regulator of cellular energy homeostasis with neuroprotective roles, this CGA-AMPK link points to AMPK as a candidate mediator of YM neuroprotection. To test this pathway, we returned to primary dopaminergic cultures that were treated with YM extract, alone or combined with the AMPK inhibitor dorsomorphin. Dopaminergic neurons were immunostained for tyrosine hydroxylase (TH) to determine survival (by cell counting), total neurite length and soma area. Our in-course results show that dorsomorphin treatment caused a marked loss of neurite outgrowth, which was fully prevented by co-administration of YM extract (restoring neurite outgrowth to control values), while YM alone increased neurite outgrowth above control. These preliminary results reproduce the protective effect of YM on dopaminergic neurons and reveal a robust, YM-sensitive effect of dorsomorphin on neurite development, which will be further characterized.

Cellular and Molecular Neurobiology

S-013

Dense core-vesicle mobility is regulated by Rab11a

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Neurosecretion is a fundamental and tightly regulated process, occurring in specialized cells, like neurons and neuroendocrine cells,which is affected in neurodegenerative diseases. Understanding its regulation can help find new targets to fight these diseases. Rab11a is a small GTPase classically involved in constitutive recycling pathways. However, its role in the secretory pathway of neuroendocrine cells remains unclear. Our previous data showed that Rab11a regulates neurosecretion in chromaffin cells, a well known cellular model for neurosecretion. Here, we followed secretory vesicle trafficking using fluorescently-tagged neuropeptide Y, a natural cargo of these vesicles, transfected to chromaffin cells. Co-transfection of Rab11a, either WT or its mutant forms with impaired GTP/GDP cycle, induced a reduction in the amount of peripheral NPY. Moreover, during unstimulated conditions, Rab11a inactive mutant decreased secretory vesicle mobility compared to Rab11a-WT overexpressing cells, while Rab11a active mutant increased speed and total distance traveled. In K+-stimulated chromaffin cells, both inactive and active mutants decreased secretory vesicle mobility, showing vesicle trajectories with reduced speed compared to Rab11a-WT overexpressing cells. We propose that Rab11a activity plays a fundamental role in neurosecretion by modulating the availability of secretory vesicles at the plasma membrane through the regulation of the vesicular trafficking in chromaffin cells.

Cellular and Molecular Neurobiology

V-002

Glial response to brain cold injury in mice, an animal model of edema

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Glial cells including astrocytes and microglia coordinately respond to brain injuries and are promising targets to modulate damage propagation. Using an edema model by cold injury in young adult female and male mice (C57/4-5 months), we aimed to describe astrocyte and microglia responses at 1-, 3- and 7-days post lesion (DPL). We used qPCR to address mRNA levels of specific genes and immunofluorescent colabeling followed by epifluorescence and confocal microscopy to study immunoreactivity for different glial and neuronal markers. We observed a progressive increase in GFAP (glial fibrillary acidic protein) immunoreactivity and a transient increase in AQP4 (aquaporin 4) immunoreactivity at 1DPL. IBA1 (Ionized calcium-binding adaptor molecule 1) immunoreactivity progressively increased at 1, 3 and 7DPL while NeuN (neuronal nuclear protein) radically decreased around the injury core. Interestingly we observed an increase in C3 (complement 3) immunoreactivity which did not colocalize with any of the markers mentioned. C3 strongly colocalized with mouse IgG, probably suggesting an entrance from peripheral blood. We conclude that this model of brain edema promotes a progressive astroglial response concomitantly with neuronal stress, being suitable for addressing molecular (epigenetic) changes in reactive glial cells at different time points of reactive astrogliosis. Recent preliminary results from our group showed changes in mRNA expression of microglial genes and C3 receptor alpha.

Cellular and Molecular Neurobiology

V-014

Extracellular vesicle-mediated delivery of M6a partially reverses chronic stress-induced behavioral and molecular alterations

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Chronic stress is a major risk factor for neuropsychiatric disorders such as depression. Current treatments are limited by incomplete efficacy and adverse effects. We propose an alternative strategy based on extracellular vesicles (EVs), which are promising vehicles for biomolecule delivery to the brain. Our study focuses on the neuronal glycoprotein M6a, a key regulator of neuronal connectivity whose expression is reduced following chronic stress. EVs were isolated from HT22 cells by differential centrifugation and characterized by TEM and NTA. EVs were loaded with an M6a-GFP or GFP control plasmid using an exogenous loading protocol. Successful delivery was confirmed by plasmid detection and in vitro assays, where recipient cells expressed M6a-GFP and exhibited morphological changes associated with M6a overexpression. The therapeutic potential of M6a-loaded EVs was evaluated in a mouse model of chronic restraint stress. Treatment prevented weight loss. Behavioral analyses using BORIS software showed that mice receiving M6a-loaded EVs spent less time immobile in the Forced Swim Test (FST), suggesting an improved stress-coping behavior. Ongoing studies will evaluate performance in the Splash Test (ST) and quantify M6a levels in serum by ELISA and hippocampus by Western blot. Overall, these findings provide proof of concept that extracellular vesicles can serve as an effective delivery platform for M6a to mitigate the effects of chronic stress.

Cellular and Molecular Neurobiology

S-014

FRESHWATER PRAWN MACROBRACHIUM BORELLII: A NON-CONVENTIONAL PROTEIN SOURCE WITH POTENTIAL BENEFITS FOR BRAIN HEALTH IN METABOLIC SYNDROME

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Metabolic Syndrome (MetS) is associated with cognitive decline and a higher risk of neurodegenerative diseases. Therefore, finding nutritional strategies to protect brain health in this setting is highly important. We examined the potential neuroprotective effects of a protein extract, rich in functional amino acids and derived from the freshwater prawn Macrobrachium borellii, in a rat model of MetS. Male Wistar rats were fed for 90 days with a standard rodent diet, a high-sucrose diet (HSD), or a HSD in which 50% of the protein source was replaced with the prawn protein extract (HSD+CrP). Cognitive performance was evaluated using the Novel Object Recognition and T-maze tests, while anxiety-like behavior was assessed with the open field test. Moreover, oxidative/nitrosative and inflammatory biomarkers, along with acetylcholinesterase (AChE) activity, were analyzed in the cerebral cortex. Compared with HSD-fed rats, HSD+CrP-fed rats showed: (a) improved cognitive performance in both memory tasks; (b) increased percentage of distance traveled in the center zone of the open field; (c) a decreasing trend in ROS and TBARS levels, together with increased catalase activity; (d) reduced chlorotyrosine, nitrotyrosine, and myeloperoxidase levels, while iNOS levels remained elevated; and (e) reduced AChE activity. The results suggest that M. borellii protein extract may be a valuable natural resource for preserving brain health and attenuating cognitive decline associated with MetS.

Cellular and Molecular Neurobiology

D-014

STUDY OF LRP1 LIGANDS AS MODULATORS OF MICROGLIA-MACROPHAGE CROSSTALK UNDER INFLAMMATORY CONDITIONS

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Age-related Macular Degeneration (AMD) is a retinal disease responsible for blindness in adults over 65 years. In its neovascular stage (nAMD), mononuclear phagocytes (MPs) accumulate and induce an inflammatory environment that drives pathological choroidal neovascularization (CNV). LRP1, a receptor expressed in MPs, acts as an anti-inflammatory receptor in various pathologies when activated by ligands like activated alpha-2-Macroglobulin (α2M*) and SP16. Our aim was to evaluate the effect of LRP1 ligands on MPs under inflammatory conditions. BV2 microglia and bone marrow-derived macrophages (BMDMs) were pretreated with LRP1 ligands for 30 min before LPS stimulation. Western blot analysis revealed reduced TNFα expression, wound healing assays showed reduced migration areas, and flow cytometry in BMDMs, attenuated the reduction in the LRP1high subpopulation produced under LPS stimulation (microglia do not present two LRP1 subpopulations). Additionally, BV2 supernatant collected after 2h of LRP1 ligand treatment was used as conditioned medium on BMDMs for 30 min before LPS stimulation. We observed reduced TNFα levels, and a decrease in CD86+ BMDMs, with LRP1high subpopulation restore. In conclusion, these results suggest that LRP1 ligands on microglia and macrophages have an anti-inflammatory effect. Also, LRP1 ligands on microglia promotes the release of soluble mediators that exert similar effects on macrophages. Further studies are needed to understand involved mechanisms.

Cellular and Molecular Neurobiology

V-015

Chronic audiovisual gamma stimulation restores circuit plasticity in the aging hippocampus

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Non-invasive audiovisual stimulation at 40 Hz (AuViS) promotes structural and functional plasticity in the aging hippocampus, but whether these effects persist with prolonged stimulation and advanced aging remains unknown. Chronic stimulation is critical to determine long-term cellular and molecular responses to the clinically ongoing paradigms. We investigated the effects of chronic AuViS on proliferation dynamics and adult hippocampal neurogenesis across aging. Repeated AuViS promoted the differentiation of neural stem cells towards a neuronal fate at the expense of astrogenesis, and enhanced dendritic growth and maturation of adult-born granule cells (aGCs). Responsiveness to AuViS persisted at more advanced ages, indicating that this chronic treatment can preserve neurogenic plasticity despite further aging. Unexpectedly, chronic stimulation reduced the fraction of actively cycling progenitors, raising the possibility that AuViS affects neural stem cell dynamics over time. Whether the stem cell pool changes or becomes depleted and exhausted remains to be determined in ongoing experiments. Together, these findings establish chronic AuViS as a sustained modulator of hippocampal neurogenesis and provide a framework to determine how prolonged stimulation shapes cellular plasticity during aging.

Cellular and Molecular Neurobiology

S-015

Serotonin-mediated Epigenetic Regulation in the Mouse Prefrontal Cortex during Early Postnatal Life

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Psychiatric disorders, including anxiety and depression, may have neurodevelopmental origins, yet the molecular mechanisms underlying vulnerability remain poorly understood. The serotonin (5-HT) system is essential for proper neuronal circuit development during early brain development. Serotonylation, a novel post-translational modification in which 5-HT is attached to protein glutamine residues, may link serotonin signaling to gene regulation. In histone H3, serotonylation occurs at glutamine 5 within H3K4me3-marked nucleosomes (H3K4me3Q5ser) and promotes transcription. We study whether this mechanism contributes to the developmental programming of prefrontal cortical circuits underlying emotional vulnerability. Our analyses show that serotonylation is present in the embryonic forebrain and associated with promoters of genes involved in neurodevelopmental processes. In a mouse model of early-life emotional vulnerability with reduced 5-HT in prefrontal neurons, decreased serotonylation is associated with altered expression of gene networks related to axon development and synaptic maturation. ChIP-qPCR experiments corroborate these findings in our model. Further, RNA-seq analyses reveal differential expression in multiple pathways involved in neuronal circuit development. These findings support a role for serotonylation in prefrontal developmental programs that may contribute to adult emotional vulnerability.

Chronobiology

D-015

Does the lunar cycle affect our sleep? An analysis of the circa-lunar periodicity in sleep's architecture in Buenos Aires, Argentina

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Recent studies have examined the relationship between the lunar cycle and human sleep using self-report, actigraphy, and polysomnography data. In this study, we extend this research by analyzing objective sleep parameters, measured with polysomnography, in people with suspected or diagnosed sleep disorders in Buenos Aires, Argentina. The sample included 955 participants (421 women and 534 men; mean age = 51.5 ± 15.8 years; range 18-89). REM percentage was significantly higher during new moon (NM) than full moon (FM) (17.8% NM vs. 16.2% FM, $p<0.05$), whereas nREM (82.2% NM vs. 83.9% FM, $p<0.05$) and N1 (2.4% NM vs. 3.3% FM, $p < 0.05$) percentages were lower. Men showed a higher percentage of stage N2 sleep than women in NM (61.7% vs 56.3%, $p<0.01$), whereas women showed higher N3 than men during both FM (22.4% vs 18.6%, $p<0.01$) and NM (23.7% vs 18.0%, $p<0.001$). We also compared sleep metrics among women under and over 50 years of age across lunar phases. Women over 50 showed a lower REM percentage (≈4% less, $p< 0.01$) and higher nREM percentage (≈4% more, $p<0.01$) during FM, while women under 50 had higher sleep efficiency than women over 50, although efficiency decreased by 4% during FM ($p<0.05$). These preliminary findings suggest that sex and age may be relevant factors when examining associations between lunar phase and sleep architecture in individuals with suspected or diagnosed sleep disorders.

Chronobiology

V-016

Characterizing resting periods in Neohelice granulata to identify sleep-like behavior in an intertidal animal

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Sleep is a fundamental biological process conserved across animals and known to be regulated by homeostatic and circadian mechanisms. Although sleep has been extensively studied in several animal models, including invertebrates, it remains unexplored in intertidal animals, whose activity is potentially shaped by tidal cycles. We recently reported that the semiterrestrial crab Neohelice granulata exhibits a prolonged period of low activity from morning through early afternoon, characterized by a “resting” posture (low cephalothorax, tucked in claws) guided by an endogenous rhythm, suggesting the possibility of sleep-like behavior. Using DeepLabCut for automated behavioral analysis, we are testing whether sleep deprivation induces a compensatory increase in resting behavior, as predicted by sleep homeostasis. We are also assessing whether the arousal threshold to mechanical stimulation differs between active and resting crabs. We aim to identify specific postural patterns associated with immobility and reduced responsiveness, and to determine whether these postures increase following sleep deprivation. Together, these behavioral criteria will allow us to evaluate whether N. granulata exhibits sleep and provide the first characterization of sleep-like behavior in an intertidal animal.

Chronobiology

S-016

Single Astrocyte Labeling Approaches to Uncover Circadian Structural Plasticity

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The earth's rotation around the sun creates cycles of light and darkness, prompting organisms to develop adaptations known as circadian rhythms. Drosophila melanogaster has about 240 clock neurons responsible for regulating these rhythms through the expression of clock proteins that constitute the molecular clockwork. The axonal terminals of a key group of clock neurons, the small lateral ventral neurons (sLNvs), undergo rhythmic circadian remodeling. They are more complex and highly branched at the start of the day, before daily activity begins, and less complex at night during the rest. This process is known as circadian structural plasticity. Astrocytes, a specific type of glial cell that also harbor a molecular clock, make contacts with clock neurons. Our preliminary results show that cell-to-cell contact between astrocytes and sLNvs changes throughout the day, with a maximum early in the day, when neuronal terminals are more highly branched. These findings raise the possibility that astrocytes themselves may undergo circadian structural remodeling. Recently, using Astro-TRACT, we identify the conditions to express mCD8-GFP in single astrocytes engaged in synaptic interactions with clock neurons. The sparse labeling of isolated astrocytes provides an ideal platform for examining changes in morphology throughout the day. These findings will pave the way for future research.

Chronobiology

D-016

Role of the ClC-a channel in Drosophila behavior and physiology

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The circadian oscillator of Drosophila is comprised of approximately 250 clock neurons that express a set of molecular signatures, including clock genes, which through negative feedback loops coordinate oscillation of transcription and translation of other 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). LNvs play a fundamental role in the control of alertness and 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 physiological regulation of LNvs. This channel has not been explored in the Drosophila adult neurons. Therefore, the main objective of this project is to characterize the roles of neuronal CIC-a and its mechanism of action. Our findings indicate that downregulation of ClC-a in LNvs disrupts neuropeptide trafficking and impairs clock output. Additional behavioral analyses suggest that ClC-a may be involved in detection of sensory stimuli, such as light and mechanical stimuli. To further investigate the physiological basis of these behavioral effects, we are currently performing whole-cell patch clamp recordings in LNvs.

Chronobiology

V-017

Busy as a toad: Movement patterns and daily activity in the terrestrial amphibian Rhinella arenarum

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Animals exert daily rhythms where they switch between active behavior, such as foraging, mating or exploration, and periods of quiet rest. This activity balance is regulated by both circadian factors, such as the daily photoperiod, and behavioral and physiological needs that drive the search for food, water or social interaction. In this pilot study we aimed to determine the main activity patterns in the terrestrial toad, Rhinella arenarum. Our hypothesis, based on a previous field study, is that R. arenarum displays crepuscular/nocturnal activity and that its movement out of the shelter is mainly governed by ambient humidity and water availability. We captured adult male and female toads (n=7) and habituated them to lab conditions. We recorded each toad's activity for a week using a designed home-cage with two available shelters, a wet and a dry zone and an IR camera on top. Animals were tracked using machine-learning-based tools and customized software to extract home occupancy, movement patterns and distance travelled. According to our field findings, toads spent a considerable amount of time in their preferred shelter, especially during the light phase. During nighttime, toads significantly increased their movement and distance travelled. The results are being compared with other amphibian species studied in a similar setup. Our longer-term aim is to use this activity information to study sleep/wake habits and extract neurophysiological activity in these amphibians.

Chronobiology

S-017

Nocturnal time restricted feeding increases motivation for food reward and improve mood related behaviors under environmental enrichment

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Food is a strong non-photic synchronizer of circadian rhythms. In nocturnal animals, time restricted feeding during the night (nTRF), as compared to ad libitum (AL) access to food, improves several behavioral and cognitive processes. In addition, enrichment of the housing cage can also prompt well-being and improve mood related behaviors. The reward system shows a prominent rhythm in the activity of dopaminergic efferents from the nucleus accumbens to the ventral tegmental area. We previously demonstrated that motivation behavior for food reward shows a circadian rhythm, which is disrupted under constant light and chronic jet lag conditions. In this work, we ask whether motivation levels under an enriched environment (EE, vs. unenriched, UE) interact with a nocturnal time restricted feeding protocol (nTRF), taking the hypothesis that the reward system can be entrained by nTRF. Motivation levels were increased both by EE and nTRF. In addition, depressive-like behavior measured by sucrose preference and tail suspension tests was modulated by this interaction, being higher under UE-AL conditions. These results suggest that nTRF is a modulatory circadian input for the reward system and can be proposed as a chronotherapy for treating mood related disorders.

Chronobiology

D-017

Dietary restriction, circadian fitness, and ageing: insights from Drosophila

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Circadian clocks orchestrate the daily timing of numerous physiological processes, and their synchronization is essential for organismal health. Growing evidence links disruptions in circadian timing to ageing. Separately, dietary restriction is a robust intervention for extending lifespan and healthspan, and emerging studies suggest the circadian system may mediate these effects. Yet how dietary restriction, ageing, and the brain's circadian clock interact remains unclear. We argue that Drosophila melanogaster is an ideal model to dissect this relationship, given its short life cycle, well-characterized clock machinery, and extensive genetic tools. We tracked locomotor activity in individual flies across their lifespan, exposing them to diets varying in yeast content, the main protein source in laboratory food. Lowering yeast intake extended lifespan and enhanced circadian and sleep fitness in young and early-aged flies, but not in flies older than 5 weeks. These results support the value of Drosophila as a platform for investigating the crosstalk between circadian health and ageing.

Chronobiology

V-018

A study of focus control and photobleaching in a light-sheet microscope designed for long-term in vivo imaging of neuronal processes in Drosophila

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In animals, daily activity rhythms are regulated by an endogenous circadian clock. To understand the underlying mechanisms, we study the fruit fly Drosophila melanogaster. In these flies, a specific group of neurons known as small ventral lateral neurons (s-LNvs) play a key role in generating the circadian rhythm [1]. The ultimate goal of this project is to use fluorescence microscopy to monitor processes occurring in s-LNv neurons throughout the day in live adult flies. Our laboratory has built a light-sheet microscope designed to image the s-LNv neurons in vivo in adult flies[2]. However, long-term acquisition is limited by focus drift, which degrades the image quality, and photobleaching, whereby the emission of fluorophores is lost due to prolonged light excitation. We present two strategies for controlling drift: a control loop that corrects the relative distance between the objectives that constitute the remote refocusing system and a sample drift correction based on phase cross-correlation [3]. We also systematically quantified photobleaching in live flies, through metrics that defined image quality over time. These improvements enabled imaging of the s-LNvs for five hours in a live fly, allowing observation of neuronal remodelling and intracellular mitochondrial movement. [1] MP Fernandez et al., PLoS Biol 6 (2008) e69. [2] F Tassara et al., bioRxiv (2024) 2024.11.06.622263. [3] M Guizar-Sicairos et al., Opt. Lett. 33 (2008) 156.

Chronobiology

S-018

Chronotype: Validity and reliability of the MEQ

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The chronotype is the behavioral manifestation of the endogenous circadian rhythm, reflecting an individual's tendency toward greater activity during a particular period of the day and toward earlier or later sleep schedules as a result of internal circadian cycles. Its most widely known and used self-report measure is the Morningness-Eveningness Questionnaire (MEQ). Although the MEQ has undergone numerous psychometric adaptations worldwide, relatively few studies have examined its psychometric properties, particularly its temporal stability. In Spanish-speaking Latin America, and particularly in Argentina, although many studies use the questionnaire, no study has reported its psychometric properties. The aim of this study is to provide evidence of the MEQ's factorial validity and reliability. 49 participants took part in the study, of whom 35 completed the test-retest assessment. Based on the scores of the 49 participants from the first assessment, parallel analysis suggested one principal component and one factor; a factor analysis with a one-factor model and the MINRES extraction method showed adequate model fit. Total score at the first and second assessments had a high correlation (r = .88), and agreement between first and second chronotype category was 88.6%, with a weighted kappa of κ = .78. Overall, this study is the first to provide evidence of the factorial validity and reliability of the MEQ in Spanish-speaking Latin America.

Chronobiology

V-036

Daytime and Nighttime Disturbances Trigger Sex-Dependent Shifts in Sleep-Homeostatic Pathways, Neuromodulators, and Feeding Performance in Zebrafish (Danio rerio).

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Introduction: Sleep and arousal are regulated by neurochemical networks, and disrupting these processes can affect downstream behaviors such as feeding. We evaluated daytime and nighttime mechanical disturbances on activity, sleep-homeostatic markers, regulatory pathways, and feeding in zebrafish. Methods: Adult males and females were subjected to 6-h mechanical vibrations (13:00–19:00 h or 21:00–03:00 h) over two days. Day and nighttime locomotor activity was recorded, and ratios were calculated relative to baseline. Food intake behavior was evaluated, and brains dissected for RT-qPCR analysis of purinergic sleep-homeostatic (ada, adora1, adora2), cholinergic (chat), catecholaminergic (th), and neuronal activation (cfos) markers. Results: Nighttime disturbances increased nocturnal activity in males and downregulated ada, while in females they only upregulated adora1 without altering activity. Daytime disturbances altered male activity transiently and reduced chat, whereas females showed delayed nocturnal hyperreactivity, increased ada and adora1, downregulated th and cfos, and a significantly slower food intake speed. Male feeding remained unaffected. Conclusion: Mechanical disturbances trigger sex-dependent responses in zebrafish. Males show immediate vulnerability affecting purinergic and cholinergic pathways, whereas females display a delayed impact after daytime disturbances, where shifts in sleep-homeostatic markers and regulatory pathways impair feeding performance.

Chronobiology

V-019

Endogenous circadian control of chromatophore pigment dispersion in the intertidal crab Neohelice granulata

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Circadian (near 24 h) and circatidal (near 12.4 h) rhythms allow organisms to anticipate daily environmental cycles and optimize physiological responses. In the intertidal crab Neohelice granulata, chromatophore pigment dispersion follows a circadian pattern, with pigments dispersing during the day to darken the animal for UV protection and aggregating at night, causing a lighter phenotype. To investigate the endogenous control of this phenomenon, individual crabs were maintained in continuous darkness (DD) and constant water level for 24–113 h and photographed under IR light every 30 min to quantify carapace color changes. Carapace pigmentation exhibited a robust circadian rhythm in DD, though signal amplitude decreased after the first 24 h—reflecting a transition from initial light-cycle inertia (hourglass effect) to a true free-running rhythm. To account for this amplitude decay, non-linear regression modeling (dampened sine fit) was applied to estimate period (τ). Including the first 24 h of recording yielded estimated values clustered around 24 h. Conversely, excluding the first 24 h increased parameter dispersion, with free-running periods shifting toward longer values ranging from 24 h up to 28.9 h (with several individuals clustering around 27 h). These results confirm an endogenous circadian but not circatidal rhythm of pigment dispersion in N. granulata paving the way for future studies on the dynamics of endogenous clocks properties in decapods.

Chronobiology

S-019

Out of Sync: Sleep–Wake Disruption and Abnormal Brain Rhythms in a Dopamine D2 Receptor Mouse Model of Schizophrenia

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Schizophrenia is a severe psychiatric disorder characterized by disrupted sleep–wake regulation and abnormal brain oscillations. Clinical findings remain inconsistent because of disease heterogeneity and treatment effects. Genetically engineered mouse models provide a controlled approach to investigate the mechanisms underlying these alterations and identify potential biomarkers. We studied mutant mice lacking dopamine D2 receptors in parvalbumin interneurons using continuous 24-h wireless recordings of electrocorticogram, electromyogram, locomotor activity, and video monitoring in a low-intervention home-cage environment. A low-stress sleep deprivation protocol assessed responses to acute sleep loss. Mutant mice (n=17, mixed sex) reproduced key schizophrenia-related features. Both sexes showed shorter non-rapid eye movement (NREM) sleep episodes and increased wakefulness throughout the circadian cycle. After sleep deprivation, mutants displayed impaired nest-building behavior, reduced sleep spindle activity, and abnormal gamma oscillations and coherence, electrophysiological signatures linked to psychosis. These findings demonstrate that selective D2 receptor deletion in parvalbumin interneurons disrupts sleep, behavior, and cortical network activity, supporting this model for studying schizophrenia-related sleep dysfunction.

Chronobiology

D-019

From DNA Damage to Sleep: Unraveling the Sleep Homeostat in Drosophila

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While sleep is an evolutionarily conserved behavior, and different hypotheses have been proposed to explain its homeostatic function, establishing a universal hypothesis remains an active field of research. A recent hypothesis suggests sleep is essential to repair neuronal DNA damage accumulated during wakefulness. This is critical, since post-mitotic neurons require lifetime genome maintenance and produce high levels of reactive oxygen species. We investigate this mechanism using Drosophila melanogaster. First, we observed that sleep deprivation (SD) causes DNA damage accumulation—evidenced by increased gamma-H2Av nuclear foci in confocal imaging—which is reversible upon recovery. Additionally, we conducted a regional analysis of the brain to assess the vulnerability of specific areas to SD-induced damage. To test causality, we utilized the TrpA1 thermogenetic channel to experimentally induce DNA damage in targeted neuronal subpopulations. By evaluating behavioral dynamics over varying activation times, we demonstrated this manipulation significantly increases sleep pressure, measured via DAMs and Ethoscopes. Furthermore, we assessed motor health using climbing assays to rule out generalized motor impairment. As ongoing work, we are standardizing flow cytometry validations and implementing an inducible CRISPR system to trigger acute DNA damage in adults. Our ultimate goal is to determine if DNA damage and its subsequent repair are integral components of the sleep homeostat.

Chronobiology

V-020

Scrolling Into Sleep: Smartphone Use and Sleep Architecture in Young Adults

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Smartphone use has increased exponentially over the past two decades and has become widely integrated into daily life, including before sleep. Growing evidence suggests nighttime smartphone use is associated with delayed sleep onset, reduced sleep duration, and poorer sleep quality in young adults. However, most evidence relies on subjective measures, and objective sleep recordings remain limited. The present study addressed this limitation by objectively assessing nighttime smartphone use and sleep, using polysomnography to characterize sleep architecture and actigraphy to assess sleep-wake patterns. Healthy participants aged 18–25 years (n = 10) were assigned to two groups based on smartphone use before bedtime (use allowed vs. use not allowed, n = 5 each). Preliminary results showed no significant group differences in total sleep time or overall stage durations. However, the smartphone-use group showed a significantly shorter first sleep cycle than controls (88.9 ± 7.2 vs 161.4 ± 44.6 min, $p = 0.021$) and fewer sleep spindles during this cycle (33.9 ± 27.6 vs 110.7 ± 51, $p < 0.05$). These preliminary findings suggest that differences in smartphone use before bedtime, even over a single night, may be associated with measurable differences in the earliest sleep cycle, rather than with overall sleep architecture. Additional analyses are needed to confirm the robustness of these associations and their relevance for healthier digital and sleep habits in young adults.

Chronobiology

S-020

Rest and Repair: How dPARP and DNA Damage Influence Sleep

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What are the evolutionary advantages of sleep? Although it is well established that sleep is a highly conserved behavior throughout the animal kingdom, its precise biological purpose is still unclear. Several theories have been put forward to explain its role. For instance, sleep has been linked to processes such as memory consolidation, synaptic remodeling, and the clearance of neurotoxic by-products that accumulate in the extracellular space during periods of wakefulness. More recently, a novel hypothesis has emerged suggesting that the repair of DNA damage accumulated while awake constitutes a core function of sleep in zebrafish. Could this mechanism be conserved across other animals? Might DNA repair proteins serve as critical molecular sensors in the regulation of sleep? We propose that DNA repair proteins contribute to the molecular machinery of the sleep homeostat in Drosophila. We are evaluating whether dPARP, a protein identified as a key detector of DNA double-strand breaks and mediator of sleep induction in fish, also fulfills this role in insects.

Chronobiology

D-020

Exploring the link between neuronal mitochondrial DNA damage and sleep

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Sleep is a highly conserved biological process whose function remains under intense investigation. Recent evidence suggests that the repair of DNA damage accumulated during wakefulness is a key component of sleep regulation. While nuclear DNA damage has been linked to sleep homeostasis, the role of mitochondrial DNA (mtDNA), particularly vulnerable to oxidative stress, remains largely unexplored. This project aims to determine whether neuronal mtDNA damage acts as a cellular stress signal capable of modifying sleep regulation in Drosophila melanogaster. By addressing whether mtDNA integrity contributes to sleep homeostasis, this study will provide novel insights into the link between genomic stability and physiological regulation of sleep. The findings may help clarify how mitochondrial dysfunction contributes to neuronal vulnerability and sleep-related pathologies.

Chronobiology

V-021

Studying visually-triggered behaviors and the excitability of underlying neurons during diurnal periods with high/low spontaneous activity in crabs

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Daily fluctuations in behavioral activity enable organisms to optimize their interactions with the environment. In the semiterrestrial crab Neohelice granulata, visual processing is essential for predator/prey detection, navigation, etc. Studying spontaneous locomotor rhythms under natural light conditions we described a prolonged rest phase during midday/afternoon and high activity during crepuscular hours/night. Hence, during light hours we can find both periods of high activity and rest. It is not known if factors regulating the activity may also modulate visual pathways and if so, at what level. To test this, two visually-guided behaviors were examined: optomotor responses to different contrasts stimuli and escape responses elicited by a visual danger stimulus. We compared animals tested during periods of high (07:00–10:00 h) vs low (14:00–17:00 h) spontaneous activity under comparable daylight conditions, thereby dissociating activity state from visual responses to changes in illumination. In parallel, intracellular recordings from identified visual neurons belonging to the different optic neuropils taken during both time windows were analyzed considering neuronal excitability and evoked responses. This work provides new insights into the mechanisms by which the nervous system adjusts sensory processing to the physiological and ecological demands of the organism, bridging the activity of identified visual neurons with visually-guided behavior in the intact animal.

Chronobiology

S-021

Seasonal changes in activity/rest rhythms evaluated in LD and DD conditions in the estuarine crab Neohelice granulata

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The estuarine crab Neohelice granulata is an excellent model for chronobiology due to its natural exposure to dual environmental synchronizers (zeitgebers): the solar and tidal cycles. Here, we show changes in the activity/rest rhythms and resting architecture of N. granulata between reproductive (spring/summer) and non-reproductive (autumn/winter) periods of the year and evaluate the role of endogenous control. Activity was recorded under natural light-dark (LD) and constant darkness (DD) conditions. Under LD, activity showed a bimodal pattern with higher nocturnal locomotion. While total daily resting time was conserved across seasons, rest architecture exhibited marked seasonal plasticity. Autumn rest was consolidated into a few long events, whereas spring rest was highly fragmented. Under free-running conditions (DD), crabs showed robust endogenous circadian rhythms with similar periods between sexes. Some animals showed endogenous circatidal rhythms despite constant laboratory water levels. Although some seasonal differences in endogenous rhythmicity were observed, these changes were less pronounced than the striking behavioral plasticity seen under LD conditions. Additionally, non-reproductive crabs displayed crepuscular activity peaks in LD that were absent under DD. These findings demonstrate that N. granulata rhythms are driven by internal clocks and dynamically modulated by seasonal factors to meet shifting ecological demands.

Cognition, Behavior, and Memory

D-021

The cerebellum in social cognition

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Traditionally associated with motor control, the cerebellum is increasingly recognized as an important contributor to social cognition, yet evidence remains dispersed across methodologies, domains and clinical populations. We aimed to systematically review the empirical literature on the role of the cerebellum in social cognition, focusing on Theory of Mind and emotion recognition. Following PRISMA guidelines, searches were performed in PubMed, PsycINFO, Redalyc and SciELO for publications between January 1998 and March 2026. A total of 127 original empirical studies were included, employing functional and structural neuroimaging, lesion models and non-invasive neurostimulation, in both healthy and clinical populations. Findings converge in supporting an active involvement of the cerebellum in social cognition, with a differentiated topographical organization involving Crus I, Crus II and the vermis depending on the domain and type of processing. Deficits associated with cerebellar damage are documented transdiagnostically in ataxias, autism spectrum disorder, schizophrenia, frontotemporal dementia and traumatic brain injury. Results are interpreted within the framework of the cerebellar predictive system, with implications for clinical assessment and for the development of therapeutic interventions in populations with cerebellar damage.

Cognition, Behavior, and Memory

V-022

EEG alpha rhythm modulation using sham neurofeedback during attentional control in a virtual reality environment: a Registered Report

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Neurofeedback provides real-time information about brain activity to induce targeted modulation of neural rhythms. A central assumption of neurofeedback is that the motivational or penalizing valence of feedback acts as a contingent signal capable of modulating brain activity. However, robust neurophysiological evidence supporting this mechanism remains limited. To address this gap, we developed a Virtual Reality (VR) sham neurofeedback system enabling controlled manipulation of feedback valence and evaluation of its effects on EEG alpha rhythm modulation during an attentional task. This study protocol was pre-registered and evaluated before data collection as a Registered report. In a within-subject design, 36 healthy adults, balanced by sex and stratified by age completed positive and negative valence sham neurofeedback conditions and a no-feedback control condition. Continuous EEG was recorded to derive relative alpha power (αrel) over temporo-parietal regions, a marker of increased neural resource allocation. Effects of condition on αrel were assessed using a linear mixed-effects model. Our results showed that αrel decreased significantly during both positive and negative sham neurofeedback compared with the no-feedback control, with no significant difference between positive and negative sham neurofeedback conditions. These findings indicate that feedback valence alone, independent of closed-loop contingency, is sufficient to induce temporo-parietal alpha modulation.

Cognition, Behavior, and Memory

S-022

Distinctive neuromodulator mechanisms to explore a new environment and recognize it a few minutes later.

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Neuromodulators play important roles in complex behaviors, including the balance between exploration and exploitation and the regulation of learning and memory. Although learning generalization is a critical process, its mechanisms remain poorly understood. We established a paradigm to investigate three distinct processes: exploration of a novel context, habituation memory, and recognition memory. Here, we used optogenetic tools to activate (ReaChR) or inhibit (GtACR2) neurons in freely behaving flies. We evaluated dopaminergic, serotonergic, and octopaminergic signaling, as well as brain structures, including the mushroom bodies (MBs) our results show that dopamine bidirectionally modulates habituation: activation reduces habituation, whereas inhibition facilitates it.These effects were not associated with motoneuron neuromodulation. In contrast, inhibition of serotonergic neurons impaired habituation and recognition memory, with reduced and highly variable responses. Manipulation of octopaminergic neurons did not significantly affect these processes. Silencing MBs produced similar variability and memory impairment, suggesting distinct roles for dopamine, serotonin, and MBs in this learning scenario. Finally, optogenetic activation of adenylate cyclase in MBs reduced recognition memory, supporting a role for cAMP signaling in recognition memory, while habituation may involve additional mechanisms. Further experiments are needed to clarify these mechanisms.

Cognition, Behavior, and Memory

D-022

Role of Rac1 and Medial Temporal Lobe Structures in Retrieval-Induced Forgetting

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Retrieval-induced forgetting (RIF) is a form of adaptive forgetting in which selective retrieval of a memory leads to the forgetting of related, competing memories. Our laboratory developed a rodent model of RIF based on object recognition that reproduces key features of the phenomenon observed in humans. Previous work showed that RIF depends on medial prefrontal cortex (mPFC) activity and dopamine D1 receptor activation in this region, and that hippocampal (HP) activity decreases during retrieval practice. However, whether HP and perirhinal cortex (PrC) are causally involved in RIF, and the molecular mechanisms sustaining this form of forgetting over time, remain unknown. This project investigates neuronal activity in the mPFC, HP, and PrC during selective retrieval, and evaluates whether Rac1, a protein involved in synaptic plasticity and memory persistence, mediates RIF by locally inhibiting its activity in HP and PrC during and after retrieval practice. Preliminary results show that local infusion of the Rac1 inhibitor 1A-116 into dorsal CA1 promoted the persistence of object recognition memory for at least 72 hours, suggesting that Rac1 blockade through this route may be a suitable approach to study RIF.

Cognition, Behavior, and Memory

V-023

The Shift Towards Automaticity: How Time Pressure and Stress Influence Complex Decisions

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Grounded in Dual Process Theories, decision-making involves automatic (System 1) and reflective (System 2) processes. While our prior work showed that framing choices as important makes complex decisions less automatic, this study explores conditions that reverse this. We hypothesise that cognitively demanding contexts shift decisions toward automaticity, increasing susceptibility to Repetition Priming (RP). In a two-stage task, participants view four faces repeating 12, 6, 1, and 1 times, then select one face. To modulate cognition, subjects are randomly assigned to an Unspecified Task (UST: “Who do you choose?”) or Important Task (IT: “Who do you choose for an important task?”) group. We evaluate choices and response times under Temporal Limitation (countdown) and Stress (adapted Montreal Imaging Stress Task), alongside BIS-11 impulsivity assessments. Results show time pressure disrupts reflective processing, making the IT group more susceptible to RP. Although impulsivity correlated with RP susceptibility, time constraints increased susceptibility even in low-impulsivity subjects. We anticipate similar outcomes in ongoing stress experiments. These findings suggest external pressures interrupt deliberate evaluation, forcing reliance on implicit biases during complex choices.

Cognition, Behavior, and Memory

S-023

Food-Related Attentional Biases and Eating Disorder Risk Behaviors in Argentine Women

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Eating disorder risk behaviors (EDRBs) constitute a significant vulnerability factor for the development of eating disorders, particularly among young women. Neuroimaging studies have identified structural alterations in brain regions involved in selective attention, cognitive inhibition, and emotional processing in patients with acute underweight. Functional changes may also emerge during subclinical stages, although few studies have examined them in Argentina. The present study explored the relationship between EDRBs and attentional biases toward food-related stimuli in a non-clinical Argentine population. This exploratory, cross-sectional, quasi-experimental study included 123 Argentine women aged 18 or older who were assessed using the EAT-26. Participants were classified into high-risk (≥20; n = 52) and low-risk (n = 71) groups. Of these, 20 participants completed an online Food Stroop task. Reaction times and accuracy rates were analyzed under congruent and incongruent conditions involving high- and low-calorie food stimuli. To date, preliminary findings from 4 participants indicate that the high-risk group exhibited stronger interference in incongruent conditions involving high-calorie foods (RT = 1.308 s vs. 0.791 s in the low-risk group), along with greater performance variability. These findings suggest a possible attentional bias toward food-related and caloric stimuli, supporting the relevance of further research on early detection strategies.

Cognition, Behavior, and Memory

D-023

Neuroendocrine Correlates of Occupational Burnout and Chronic Stress in Secondary School Teachers: An Integrated Biomarker and Psychometric Study in Rancagua, Chile

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Background: Chronic occupational stress reflects allostatic overload, dysregulating the HPA axis. Teacher burnout is usually assessed via self-report, overlooking biological correlates and subjective nuance. We used a mixed-methods design that integrated nail cortisol—a retrospective biomarker of chronic stress—with qualitative narratives. Methods: We conducted a convergent mixed study on secondary school teachers in Rancagua, Chile. We gathered nail cortisol and surveys (n=68; regression models adjusted for sex, hours, and climate) alongside 26 in-depth qualitative interviews coded across eight structural dimensions. Results: Contractual instability was the primary risk factor: teachers with ≤33h had higher clinical stress (75.0%) vs. full-time. Women showed greater stress than men (60.6% vs. 26.7%, p=0.012). Nail cortisol declined under chronic overload (β=−0.85), suggesting hypocortisolism. Qualitatively, distress emerged as an embodied phenomenon: affective-somatic symptoms, parental conflict, and classroom precarity act as triggers, with vocation sustaining work while driving overexertion. Conclusion: Chronic stress in teachers combines neuroendocrine dysregulation with an embodied, systemic toll tied to job insecurity.

Cognition, Behavior, and Memory

V-024

Digital adaptation of the Argentine Spanish version of the Hayling Sentence Completion Test

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Introduction. The Hayling Test measures initiation and inhibitory control. Digital adaptation can reduce costs of neuropsychological assessment, improving accessibility. Still, it requires validation, as digitization may alter psychometric properties. Objective. To adapt a digital version of the Hayling Test in Argentine Spanish. Method. 100 Argentine adults (74% women; mean age 32.6, range 18-65) completed digital versions of the Hayling Test and the Adult Executive Functioning Inventory (ADEXI), both administered through PsychoPy. We examined internal consistency of Part B, reaction times across both parts, Part B reaction time versus total score, and convergent validity with ADEXI Inhibition score. Results. Mean reaction times were 2.01s (SD=0.78) for Part A and 3.17s (SD=2.18) for Part B, with a mean score of 4.47 on Part B (SD=5.20, range 0-22). Internal consistency of Part B was acceptable (Cronbach's alpha=.75; McDonald's omega=.77). Reaction times across parts correlated significantly (rho=.33, p<.001). Part B total score did not correlate with Part B reaction time (rho=.07, p=.47), nor with ADEXI Inhibition (rho=-.09, p=.40). Conclusions. These findings support the internal consistency of the digital Hayling Test. No evidence of convergent validity was found, which may be consistent with the complementary nature of performance-based and rating-scale measures. These results represent an initial step towards a digital assessment tool of executive functions.

Cognition, Behavior, and Memory

S-024

Screen Time versus Problematic Technology Use: Divergent Associations with Adolescent Mental Health and Cognition

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Excessive screen exposure has been proposed as a risk factor for mental health, yet evidence suggests that how screens are used may matter more than how much. We examined this in 3,261 secondary students (grades 1 and 4) from 100 Buenos Aires City schools, collecting gender, socioeconomic status, and school type, plus device-tracked screen time, self-report instruments, and cognitive tests of attention, divergent thinking, and executive functions. 31.3% of students exceeded the anxiety cutoff, 38.1% depression, 37.1% daytime sleepiness, and 24.6% problematic smartphone use. Screen time was 6.16 h/day. Screen time alone showed no independent association with mental health outcomes in multilevel models (random intercept by school); problematic smartphone and technology use remained independently associated with worse outcomes, with technology misuse showing the strongest effect on depression. Exploratory comparisons between at-risk and non-risk groups on attention and fluency tasks showed small but significant differences: lower attention in students at risk for anxiety, depression, and problematic smartphone use, and fewer correct fluency responses among those at risk for depression and anxiety. Sleepiness showed no cognitive differences. These findings suggest that how adolescents use technology, rather than screen time itself, is more strongly associated with mental health and cognition.

Cognition, Behavior, and Memory

D-024

Sex Differences in Spatial Learning Strategies and Neural Activation in Amphibians

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Diverse animal species use spatial learning to navigate their environment and reach survival-relevant goals. To achieve this, they employ different responses, such as egocentric turn and guidance strategies. In mammals, the hippocampus plays a central role in this type of learning, while in amphibians, the medial pallium has been proposed as a homologous structure. Historically, studies on spatial learning have been conducted predominantly in males, limiting our understanding of potential sex differences. In this study, male and female Rhinella arenarum terrestrial toads were trained in spatial learning tasks requiring use of turn or guidance strategies. We then analyzed neural activity in five selected brain structures (including the medial pallium) to identify differences in their activation. Results from the turn strategy experiment revealed sex differences in task learning, with males learning the task in fewer days than females, as well as greater medial pallium activation in the experimental groups compared to the control groups. In contrast, preliminary results from the guidance strategy experiment show a tendency for females to acquire the task in fewer days.

Cognition, Behavior, and Memory

V-025

Development of an Audiovisual Go/No-Go Learning Paradigm for Head-Fixed Mice in Virtual Reality

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Associating sensory cues with reward is a core cognitive function driving adaptive survival. To investigate how animals learn associations between auditory and visual stimuli, we developed an audiovisual Go/No-Go learning paradigm for head-fixed mice in virtual reality (VR). The setup features two monitors positioned at a 100° angle displaying a VR environment, controlled via Bonsai software, which orchestrates task logic and real-time event control. Locomotion is recorded via a rotary encoder attached to a 3D-printed running wheel. Licking responses are detected using an infrared (IR) beam sensor, which triggers a valve to deliver a calibrated water reward upon correct Go performance. Valve actuation is driven by a custom lab-built circuit board, while a National Instruments DAQ board synchronizes all inputs and outputs with millisecond-precision timestamps. Two articulated arms and custom 3D-printed components, including the running wheel and reward port, allow ergonomic adjustment across individual animals. Following validation of the behavioral paradigm, extracellular recordings will be incorporated to investigate the neural basis of learning.

Cognition, Behavior, and Memory

S-025

Human TDP-43 drives behavioral and neuronal alterations in a Drosophila model of ALS/FTD

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Alterations of the nuclear protein TDP-43 are hallmark features of the neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). TDP-43 is an evolutionary conserved protein with multiple cellular functions, most notably related to RNA metabolism. However, its role in the regulation of neuronal activity is less known. In this study, we use a Drosophila melanogaster model express hTDP-43-WT to evaluate a) behavioural phenotypes in flies expressing hTDP-43 in the mushroom bodies (MBs) and b) evoked neuronal activity through PKA and ERK Separation of Phases-based Activity Reporters of Kinase (SPARK) experiments in the antennal lobe olfactory receptor neurons (ORNs). Using a custom-made behavioural tracking software, we assessed locomotor activity (open field test) in Control and MB-expressing hTDP-43 flies. In young hTDP-43 female flies (10-12 days old), we observed decreased distance travelled compered to controls. In addition, we demonstrated that hTDP-43 expression induces PKA and ERK phosphorylation in MB and ORNs, indicating activation of two signaling pathways critical for neuronal function and plasticity. Our results from transgenic flies underscore the utility of using multiple, phylogenetically distant organisms to model complex human neurological diseases, including ALS/FTD.

Cognition, Behavior, and Memory

D-025

Automated Discourse Analysis Reveals Thematic Change After Traumatic Brain Injury in Jorge Luis Borges

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Traumatic brain injury (TBI) can, in rare cases, modify artistic expression. In 1938, Jorge Luis Borges suffered a TBI requiring surgery, with transient aphasia the following months. Soon after, his writing shifted from criollista poetry/essay toward fantastic fiction. This study analyzed his original texts written before and after the injury using automated discourse analysis, asking whether the resulting changes fit mechanisms such as disinhibition, plasticity, or right-hemisphere recruitment. Semi-automated spaCy pipelines generated hypallage and double-negation candidates, manually validated before computing frequencies; shifts were assessed via keyness, semantic fields, topic modeling, and a logistic classifier. The only robust change was thematic: the criollo-suburban universe gave way to the fantastic-metaphysical, confirmed by all four methods ($p < .001$; 82.5% classification accuracy vs. 52.4% baseline). Markers suggesting right-hemisphere recruitment (hypallage density, associative distance, syntactic dedifferentiation) remained stable. Further markers are under study (other rhetorical figures, metaphor density over time, syntactic evolution) as Spanish-language computational literary resources remain scarce. Analysis thus corroborates a clear thematic shift but finds no right-hemisphere signature so far, an expected limit for edited texts vs. speech.

Cognition, Behavior, and Memory

V-026

Contextual Novelty and Visuospatial Memory: A Data-Driven Multivariate EEG Approach

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Contextual novelty can enhance access to stored information, a process relevant both to memory and to the flexible recombination of representations required for divergent thinking. We examined whether novelty influences visuospatial memory and creativity, and whether multivariate EEG dynamics predict memory performance. Twenty-four adults were assigned to a Novelty group, encountering the EEG room for the first time during testing, or a Habituation group with prior room exposure. Participants completed the Rey–Osterrieth Complex Figure (ROCF) and Alternate Uses Task (AUT) with high-density EEG. The Novelty group showed significantly better ROCF performance, whereas AUT performance did not differ between groups. Across resting baseline, ROCF recall, and AUT, we extracted band-specific measures of spectral and aperiodic activity, phase and symbolic connectivity, entropy, complexity, and directional information flow across five brain regions. PCA summarized the standardized features. An Elastic Net model predicted ROCF performance from baseline component scores, task-related changes (Δrecall–baseline and ΔAUT–baseline), group, and Group×component interactions, using leave-one-out validation with internal hyperparameter selection. The model achieved R^2=0.624, r=0.812, and RMSE=0.069. These findings suggest that novelty-related memory enhancement is associated with multivariate EEG configurations shaped by baseline brain state, task-induced changes, and experimental context.

Cognition, Behavior, and Memory

S-026

Digital adaptation of the Trail Making Test (TMT) in Argentine adults: preliminary results

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Introduction. The TMT (Trail Making Test) is a widely used measure of processing speed (Part A) and executive function (Part B). Digital adaptation allows for more standardized and accessible administration than the paper version. This study presents an initial approach to a digital adaptation of the TMT for Argentine adults, which has not yet been validated. Objective. To evaluate performance on a computer-administered TMT in Argentine adults and its association with age and self-reported measures of executive function (ADEXI) and cognitive flexibility (CSF). Method. 126 community adults (73.8% women; mean age 33.5, range 17-65) completed a digital TMT(PsychoPy), the ADEXI, and the CSF. Results. Mean completion times were 21.0s (SD=4.44) for TMT-A and 37.9s (SD=9.11) for TMT-B. TMT-A and TMT-B scores were significantly correlated (ρ =.481, p<.001). Age was correlated with both TMT-A (ρ =.545, p<.001) and TMT-B (ρ =.175, p=.050). When the sample was randomly split into two halves, both parts showed consistent performance across subgroups (p=.327and p=.980). TMT scores were unrelated to ADEXI and CSF (p>.2). Conclusions. The digital TMT-A/B showed association between its parts and stability across random subsamples, along with the expected age-related slowing, though no association with self-reported measures of executive function or cognitive flexibility (ADEXI, CSF), as a first step toward validation in Argentine adults

Cognition, Behavior, and Memory

D-026

Testing-induced strengthening of semantically related episodic elements of a memory following partial reactivation.

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The testing effect is characterized by a direct benefit on memory retention of reactivated and practiced items compared to their restudy. A scarcely explored phenomenon in consolidated episodic memory is how the direct retrieval of an item by retrieval practice can indirectly strengthen non-reactivated items associated by their semantic context. To study the indirect benefits of retrieval practice we designed a 3-day protocol. On Day 1 subjects learned paired-associates belonging to one of 4 semantic categories on a specific context semantically related to the pair. On Day 2, a certain proportion of the pairs from each category were either tested or restudied by a certain percentage (0%, 25%, 50% and 100%). On Day 3 we tested memory retention of every paired-associate. When analyzing accuracy, we found that increasing the proportion of reactivated pairs benefited testing and restudy to a similar degree, with no testing-related advantage in memory accuracy. However, when comparing reaction times, testing significantly reduced response times. Notably, even pairs from the non-reactivated semantic category showed shorter response times than pairs from any restudied category, suggesting an indirect strengthening through shared temporal acquisition context.

Cognition, Behavior, and Memory

V-027

Altered interval timing in patients with mild cognitive impairment

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Interval timing (IT) refers to temporal processing within the seconds-to-minutes range and is closely linked to attention, memory, and executive control. Although alterations in IT accuracy and precision have been reported in Alzheimer's, Parkinson's, and Huntington's diseases, findings in mild cognitive impairment (MCI) remain limited and inconclusive. We evaluated IT accuracy and precision in older adults with MCI and cognitively normal controls using a visual interval reproduction task. Sixty-three adults aged ≥60 years were recruited: 30 with MCI, diagnosed according to Winblad criteria, and 33 cognitively normal controls (normal neuropsychological performance). Participants completed a visual interval reproduction task involving stimulus durations of 3, 6, and 9 seconds. Performance parameters, including peak location, peak height (amplitude), peak width, S1 and S2 rate indexes, and coefficient of variation, were derived from Gaussian model fits. Participants also completed a sustained attention task and the Hospital Anxiety and Depression Scale. Significant group differences were observed in precision and accuracy, with both measures showing lower performance in the MCI group compared with the control group. Reaction time was significantly longer in participants with MCI than in controls. These findings support the potential value of IT as a sensitive tool for detecting early cognitive changes and informing interventions during these initial stages.

Cognition, Behavior, and Memory

S-114

Neurocognitive factors affecting eyewitness memory: analysis of a judicial case

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Eyewitness memory is vulnerable to distortions arising both from encoding conditions and from information received after the event. This study analyzes an Argentine judicial case from the perspective of cognitive neuroscience and memory psychology, examining factors that may have compromised the accuracy of eyewitness identifications. Initial and subsequent statements, the characteristics of the identification lineups, and the conditions of exposure to both the event and post-event information were considered. The following factors were identified: a marked increase in confidence between the initial statements and later identifications; potential biases in lineup composition and administration; the presence of a weapon and high levels of stress; possible co-witness contamination; repeated media exposure to the suspects; and potentially suggestive information provided by authority figures. These factors have been associated with alterations in encoding, familiarity, source monitoring, facial recognition, and retrospective confidence. The case illustrates how multiple mechanisms of memory distortion can converge on the same memory representation and increase the risk of erroneous identifications, highlighting the importance of incorporating evidence from memory science into judicial procedures.

Cognition, Behavior, and Memory

S-027

Learning variability and training order: preliminary results of a cognitive intervention on executive functions in children

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Executive functions (EF) are cognitive functions that allow us to control actions and thoughts and adapt to changing environments, and can be improved through cognitive training. For more than fifteen years, our team has implemented Mate Marote, a free access gaming software to train and assess EF in children. Brief and spaced interventions take place within the classroom with successful results. There are open questions about the best way to train EF, particularly regarding training order: should basic EF be trained first and then more complex ones, or vice versa? Does this intervention differentially affect children? We present preliminary results from 83 children from grades 1 to 3 from different countries and contexts. Interventions ranged from 8 to 13 weekly sessions, 15 minutes each. Cognitive outcomes were assessed before and after training. The experimental groups varied in the order of training tasks. A model was calculated with composite score as outcome, and experimental group, intervention site, and school grade as predictors. We found that grade 1 children benefited less than those from grade 2. No differences were found between grade 2 and 3 or grade 1 and 3. Overall, we did not find an effect of training order. Results are discussed in relation to the importance of learning contexts and variability, as well as limitations and possible modulators (i.e. contextual variables, development, and sample size).

Cognition, Behavior, and Memory

D-027

A Scale of Modifiable Factors Associated with Brain Health (FMASC): Evidence of Validity and Internal Consistency

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Introduction and objectives Several scales assess individually the factors that influence brain health, but no brief instrument integrates multiple domains. This study aimed to develop and evaluate a self-administered scale measuring five factors known to influence brain health. Methods The Scale of Modifiable Factors Associated with Brain Health (FMASC) was developed by selecting representative items from validated instruments (IPAQ, González et al. self-test, ISI, Duke-UNC-11 and SWLS) and refined through a 14-expert panel review. It assesses physical activity, diet, sleep, social support and life satisfaction. It was administered alongside the full original scales in a sample of 2,432 adults. Internal consistency and convergent validity were assessed. Results Convergent validity was statistically significant for all five factors (all $p < 0.001$), with Spearman correlations of moderate to high magnitude. Internal consistency, estimated with Cronbach's alpha, ranged from 0.64 to 0.92 across factors. Conclusion The FMASC showed initial evidence of convergent validity against reference instruments and acceptable internal consistency in most of its domains. Clinical relevance and contribution A brief, multidimensional instrument to assess modifiable brain health factors would facilitate their measurement in clinical and research settings with limited resources.

Cognition, Behavior, and Memory

V-028

Description of Modifiable Factors Associated with Brain Health in Argentine Adults

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Introduction and objectives Several modifiable factors influence brain health, yet data on them in the Argentine population remain scarce. This study aimed to describe these factors in a sample of Argentine adults. Materials and methods A descriptive study was conducted in 2,840 Argentine adults, assessed with a digital battery measuring physical activity (IPAQ), dietary habits (González et al. self-test), sleep quality (ISI), social support (Duke-UNC-11) and life satisfaction (SWLS). Mean age was 47.75 years (SD = 14.8; range 18-98), with a predominance of women (85.6%). Participants were drawn from all 24 jurisdictions of the country, with a higher concentration in Buenos Aires, Córdoba and Santa Fe, and representation of every region. Results 25% did not engage in sufficient physical activity, 14% reported unhealthy dietary habits, 11.9% presented clinical insomnia symptoms, 24% were dissatisfied with their life, and 23% perceived low social support. Conclusion A substantial proportion of participants presented modifiable risk factors, highlighting the need to strengthen brain health promotion strategies at the population level. Clinical relevance and contribution The findings identify priority areas for the promotion of protective brain health factors and provide a national baseline for brain health promotion in Argentina.

Cognition, Behavior, and Memory

S-028

pS6 immunohistochemistry as a tool to study brain activity in cichlid fish

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Individuals in social hierarchies engage in agonistic encounters through aggressive behaviour, driving experience-dependent shifts in social status. Although aggression has historically been studied mainly in males, it is also an important component of female social interactions. The brain network known as the Social Decision-Making Network (SDMN) regulates various social behaviours and provides a suitable framework for studying the neural mechanisms underlying aggression. The cichlid fish Cichlasoma dimerus, presents high levels of aggression in both sexes. In females the aggressive behavior is linked to high circulating estradiol concentrations. To investigate the neural mechanisms underlying female aggression, we aimed to establish a pS6 immunohistochemistry protocol as a proxy for neuronal activity in brain regions of the SDMN. Female brains were sampled to assess pS6 immunoreactivity in different telencephalic areas (dorsal and ventral) and the preoptic area. We successfully established a pS6 immunohistochemistry protocol that allowed the detection and quantification of neuronal activity in these brain regions. Results show a clear cytoplasmic immunostaining in neurons. This methodological approach provides a valuable tool for investigating the neural mechanisms underlying female aggression and, in future experiments, for assessing the role of estradiol by manipulating aromatase activity with fadrozole.

Cognition, Behavior, and Memory

D-028

Repeated noise exposure disrupts hippocampal-dependent behavior in adolescent male and female rats: Can environmental enrichment protect?

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Adolescence is a critical period for brain maturation, during which the hippocampus (HC) may be particularly vulnerable to environmental factors. Noise exposure has been associated with HC-related cognitive and behavioral alterations, but the effects of repeated exposure during adolescence, particularly in females, remain poorly understood. Environmental enrichment (EE) has shown protective effects against noise. This study evaluated repeated noise exposure effects on HC-related behaviors and the protective role of EE in adolescent rats of both sexes. At postnatal day (PND) 21, Wistar rats were housed in standard cages or EE. From PND28, a subgroup was exposed to white noise (95–97 dB, 2 h/day) for five days. Inhibitory avoidance, elevated plus maze, and open field tests were performed. Noise impaired contextual associative memory, increased grooming and exploration, and reduced risk assessment in both sexes, as well as anxiety-like behaviors in females. EE prevented grooming and risk assessment changes, while reducing anxiety-like behaviors and increasing exploration in both sexes. Noise exposure in EE-housed rats produced additional behavioral changes. Overall, repeated noise exposure affected several HC-related memory and behavioral responses in both sexes, while EE exerted modulatory effects with limited preventive efficacy. These findings suggest that repeated noise exposure may produce substantial behavioral alterations that could limit the protective effects of EE.

Cognition, Behavior, and Memory

V-029

Development of a robust and automated reward-delivery system for interval timing experiments in Drosophila

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Interval timing allows animals to predict events based on temporal regularities. To investigate this ability in Drosophila melanogaster, we use a behavioral paradigm in which food-deprived flies receive repeated sucrose rewards at defined time intervals. Reliable reward delivery is essential for accurately characterizing the flies' temporal responses. The current setup automates reward presentation using a motorized syringe, while a top-view camera records behavior. However, mechanical variability in syringe positioning, together with a suction system employed to remove the droplet, can lead to misalignment between the needle and the fly, inconsistent droplet formation, and failures during trials. These issues can compromise an entire experimental run and require manual intervention. We are therefore developing a more robust and automated reward-delivery platform. The syringe support is being redesigned to ensure reproducible alignment and prevent displacement during plunger movement. We are also developing an image-based method to estimate droplet volume from live camera recordings, aiming to use volume as a control variable for motor displacement. Ultimately, the platform will automate reward presentation while requiring only syringe loading and initial positioning, providing a reproducible setup for studying temporal learning in Drosophila. In the long term, this setup will allow to switch among either classical or operant conditioning protocols.

Cognition, Behavior, and Memory

S-029

Thirty-Two Days of Fear: Long-Term Memory Retention and Neural Activation in Amphibians

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Long-term memory retention is essential for adaptive behavior, yet its persistence and neural correlates remain poorly understood in amphibians. We investigated the temporal stability of aversive memories and associated neural activation in Rhinella arenarum. Toads underwent six days of classical conditioning, in which a 300 mM NaCl solution (CS) was paired with an aversive 800 mM NaCl solution (US). Heart rate was recorded through implanted dermal electrodes as a physiological measure of the conditioned response. Independent groups were tested for memory retention 1, 4, 8, 16, 32, or 64 days after acquisition. Conditioned animals showed a significant anticipatory cardiac response to the CS compared with controls at 1, 4, 8, 16, and 32 days, whereas this difference was no longer observed at 64 days. Neural activity assessed through AgNOR staining showed a similar temporal pattern, with increased activation in the amygdala associated with aversive learning up to 32 days, but not at the 64-day retention test. These findings reveal long-lasting but temporally limited aversive memory in amphibians and provide evidence of neural changes associated to its persistence.

Cognition, Behavior, and Memory

D-029

The role of Acetylcholine in Targeted Memory Reactivation in the long-term

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Acetylcholine (ACh) is high during wakefulness and REM sleep but reaches a minimum during slow-wave sleep (SWS). Low ACh during SWS is proposed to shift hippocampal networks from an encoding mode toward a consolidation mode, facilitating memory reactivation and hippocampus-to-neocortex information transfer. Accordingly, pharmacologically increasing ACh during SWS impairs declarative memory consolidation. Memory reactivation can be externally manipulated using Targeted Memory Reactivation (TMR), by re-presenting learning-associated cues. Surprisingly, increasing ACh during TMR does not abolish short-term memory benefits after ~40 min of sleep. Our previous work showed that both complete and incomplete reminders stabilize memories after ~40 min of sleep, whereas only incomplete reminders produce long-term stabilization after ~8 h. Here, we tested whether low cholinergic tone is required for the long-term effects of TMR. Participants learned sound-word associations and received either physostigmine or placebo while half of the associations were reactivated using incomplete reminders. Memory was tested after ~8 h of sleep. Preliminary results showed a TMR benefit in the placebo group, while no comparable benefit was observed under physostigmine. However, the TMR × treatment interaction did not reach statistical significance. These findings raise the possibility that low cholinergic tone may contribute to the long-term effects of targeted memory reactivation.

Cognition, Behavior, and Memory

V-030

Autobiographical Memories and Emotional Characteristics in Response to Musical and Non-Musical Sounds

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Several studies show that music evokes more positive and detailed autobiographical memories than other stimuli (e.g., environmental sounds). However, systematic evaluation of comparison stimuli as experimental controls has been limited. This study evaluated the autobiographical memories evoked in response to musical and non-musical excerpts, analyzing emotional responses, liking, familiarity, and subjective sensations. A within-subject design was used (n = 138). Subjects listened to eight excerpts: two environmental sounds (cafeteria and walking), three noises (white: 20 Hz–20 kHz; pink and brown, with a predominance of low frequencies), two musical pieces (arousing and relaxing), and a voice recording. After each excerpt, subjects reported memories and sensations and rated familiarity, liking, valence, and arousal (1–9 scale). The arousing piece and the walking sound evoked memories with more spatio-temporal references and references to actions, thoughts, and emotions than the voice and the relaxing piece did. The musical pieces received the highest, while white noise had the lowest scores for valence and liking. Environmental sounds were perceived as the most familiar. In conclusion, non-musical sounds can evoke more detailed autobiographical memories than non-self-selected music, highlighting the importance of characterizing the evocative and affective properties of different auditory stimuli to optimize studies on music-evoked autobiographical memories.

Cognition, Behavior, and Memory

S-030

Early-life social and material deprivation drives sex-dependent alterations in social behavior across the lifespan and neuroinflammatory transcriptomic signatures in the prefrontal cortex

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Early-life adversities are a major risk factor for later mental health disorders, but the underlying neurobiological mechanisms remain poorly understood. To address this gap, we established a murine model of social and material deprivation (SMD)—combining reduced nesting, maternal separation, early weaning, and social stress—to better reproduce the complexity of human socioeconomic disadvantage. Offspring exposed to SMD displayed delayed growth alongside heightened anxiety- and depression-like behaviors. These functional changes were accompanied by structural alterations, including reductions in hippocampal area and an enlargement of the prefrontal cortex (PFC). Crucially, SMD altered social interactions and dominance patterns in an age- and sex-specific manner. While alterations in juvenile social play were observed exclusively in females, differences in adult sociability were restricted to males. Additionally, adult social memory was altered in both sexes. Beyond sociability, SMD drove a dominant phenotype in both sexes during the tube test, and increased aggressive behavior in males. Seeking molecular correlates within the PFC, we detected altered Pdgfa expression and sex-specific transcriptomic signatures indicative of neuroinflammation, which we are currently evaluating through microglial immunohistochemistry. Altogether, our findings demonstrate that SMD affects neurodevelopment and social behavior through complex, sex-dependent molecular mechanisms.

Cognition, Behavior, and Memory

D-030

Neurovisceral correlates of food priming and inhibitory control

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Consuming a small amount of palatable food can increase motivation to continue eating, a phenomenon known as food priming. Thus, people restricting their intake may face greater inhibitory-control demands after tasting highly palatable food. Fasted university students (18–35 years; ≥3 h fast) who enjoy potato chips are randomly assigned to a priming condition, in which they consume one chip, or to a no-priming control. Participants watch four 8-minute slow film segments with an open package of chips within reach. During the first two segments, they are instructed not to eat and report craving. After the second segment, they may serve themselves 0–10 chips and must anticipate how many they will choose. The task yields two craving ratings and two prospective consumption measures. Electrocardiogram and skin conductance are recorded continuously. To assess neurovisceral effort, we measure parasympathetic regulation through heart rate variability (RMSSD) and sympathetic arousal through electrodermal activity (EDA). We hypothesize that priming will increase craving and anticipated consumption, with autonomic changes reflecting greater regulatory demand—specifically, decreased RMSSD and heightened EDA. Data collection is ongoing; no group-level conclusions can yet be drawn. This non-invasive paradigm may help characterize neural-autonomic mechanisms of craving, inhibitory control, and relapse-like eating.

Cognition, Behavior, and Memory

V-031

Gestational environmental enrichment in preclinical models of postpartum depression and anxiety: effects in mothers and offspring

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The peripartum constitutes a critical window for the development of postpartum depression (PPD) and postpartum anxiety (PPA), disorders with consequences for maternal and offspring health. Gestational environmental enrichment (GEE) may represent a non-pharmacological preventive strategy. This study evaluated its effects on maternal behavior, emotionality, and neuronal activity in mothers, as well as offspring development, using two PPD/PPA preclinical models: maternal separation (MS) and intruder male (IM). Female Wistar rats were housed under standard conditions or GEE throughout gestation. On postpartum day 1 (PD1), the mothers and their offspring were assigned to one of the treatments: control, MS, or IM. Maternal behavior was assessed in the pup retrieval test (PD3), and anxiety-like behavior in the elevated plus maze (PD22). Neuronal activity was quantified by immunohistochemistry for ΔFosB. Offspring developmental milestones (PD3–21) and body weight were also evaluated. GEE improved maternal behavior and reduced anxiety in response to both stress models, accompanied by changes in ΔFosB in medial preoptic area, nucleus accumbens, amygdala and hippocampus. Offspring exhibited differences in body weight and developmental reflexes. Overall, GEE induces long-lasting modulation of maternal behavior and neuronal activity across key circuits, and influences early offspring development, supporting its potential as a non-pharmacological strategy against peripartum mood disorders.

Cognition, Behavior, and Memory

S-031

Decoding selective auditory attention from continuous speech: A TRF-based approach to dichotic listening paradigms

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Selective auditory attention allows us to focus on a single conversation in a crowded room. Traditional dichotic listening paradigms for brain activity studies rely on probe tones embedded in audio to elicit event-related potentials (ERPs). In this setup, participants attend to speech in one ear while ignoring the other, using the ERP difference across ears as an index of selective attention. While effective, this approach requires artificial stimulus manipulation, constraining experimental design and ecological validity. Here we compare ERP and Temporal Response Function (TRF) analyses. We show that TRFs fitted to the continuous speech signal recover the better attentional modulation captured by probe-tone ERPs, without relying on artificial stimuli. TRFs make it possible to characterize, with fine temporal resolution and channel-level specificity, how the auditory system differentially encodes attended versus unattended speech, all while preserving naturalistic listening conditions. Moreover, it allows us to discriminate between speech attributes that could differentially separate those conditions. We discuss the advantages of this approach for studying selective attention in more ecologically valid settings. We present a new Python library (TRFlearn) that covers the whole M/EEG analysis pipeline in a wide range of naturalistic settings. Our results suggest that TRFs offer a powerful, flexible alternative to ERP-based methods in dichotic listening research.

Cognition, Behavior, and Memory

D-031

Neural correlates of aversive memory extinction: A time-frequency EEG study of post-retrieval processes

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Although fear conditioning is widely used to study anxiety, some aspects of its neural correlates remain unexplored. Reactivating consolidated memories can trigger different modifications depending on the cues presented during reactivation. We employed a three-day threat conditioning protocol in which an angry face (CS+) was paired with an aversive sound (US). Our main objective was to identify neural markers of post-retrieval processes, particularly extinction, triggered by presenting the CS+ six times without the US, 24 hours after acquisition. At the behavioral level, extinction reduced declarative US expectancy and eliminated the cognitive bias in perceived aversiveness. We analyzed 90 seconds of resting-state electroencephalographic activity before and after each reminder cue. A cluster-based permutation test revealed differences between the first and last reminder presentations, with higher beta activity (23–30 Hz) during the last presentation. This is consistent with a previous finding in which lower beta activity was associated with memory reactivation, whereas higher activity was associated with a cue without prior information. Thus, after extinction, brain activity became more similar to that elicited by a non-informative stimulus. Our findings highlight the importance of evaluating neural correlates of post-retrieval processes and suggest that beta activity may relate to implicit memory reactivation and extinction.

Cognition, Behavior, and Memory

V-032

Effects of AI Assistance on Cognitive Tasks

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Artificial intelligence (AI) is increasingly integrated into everyday activities, yet its impact on cognitive performance remains poorly understood. This study investigated the effects of AI-assisted learning on reading comprehension, immediate and delayed recall, recognition memory, and metacognitive calibration. Forty adults from Buenos Aires (Argentina) were randomly assigned to an AI or control group. Participants read a text and produced a summary either with or without AI assistance, according to their assigned condition, before delivering an oral presentation. Immediate recall and reading comprehension were then assessed. After a 20-minute interval, participants completed a delayed recall task, a recognition memory task, and confidence ratings for each response. Familiarity with AI and cognitive ability were also assessed. Participants in the AI group endorsed significantly more lure items than those in the control group, whereas no significant differences were observed in the remaining cognitive measures. These findings suggest that AI-assisted learning may increase susceptibility to accepting plausible but inaccurate information, suggesting that AI-assisted learning may increase susceptibility to false recognition without a corresponding change in confidence, potentially indicating a mismatch between accuracy and metacognitive awareness.

Cognition, Behavior, and Memory

S-032

Dopaminergic Contributions to Socio-Affective Cognition

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Social cognition enables individuals to infer the emotional states of others and adapt behavior accordingly. The ability to detect and respond to the affective states of conspecifics guides adaptive social interactions and is disrupted in neuropsychiatric disorders such as schizophrenia and autism spectrum disorder, where deficits in affective recognition persist despite treatment. Yet the neural mechanisms underlying this capacity remain poorly understood. Dopamine is a compelling candidate neuromodulator, given its established role in motivation, reward, and the processing of emotionally salient stimuli, as well as the alterations in dopaminergic signaling observed across psychiatric conditions associated with social deficits. Beyond its well-characterized contribution to motivation, midbrain dopaminergic systems may also participate in evaluating and discriminating affective signals from others Here, we explore this possibility, considering how dopaminergic signaling relates to distinct dimensions of social behavior. This work contributes to a broader understanding of socio-affective cognition and points to dopaminergic signaling as a potential substrate underlying social dysfunction in neuropsychiatric disorders.

Cognition, Behavior, and Memory

D-032

Sleep, alertness, and fatigue in self-regulated brain-computer interface performance: a preliminary study based on self-reported measures

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While several factors may affect motor imagery-based brain-computer interface (MI-BCI) performance, little attention has been given to the role of sleep, alertness, and fatigue. This study examines the association of these factors with MI-BCI performance, assessed in terms of users' control capability and system accuracy, at the interindividual and intraindividual levels. Two datasets are analyzed. The first, from a self-developed experimental protocol, comprises 12 healthy users who completed 5 MI-BCI sessions, each consisting of 5 blocks of 20 trials of motor imagery versus rest. The second, the Dreyer et al. (2023) dataset, includes 87 users assessed in 1 session comprising 240 trials of right versus left motor imagery. In both datasets, the variables of interest are assessed through self-report questionnaires administered before and after BCI use. At the interindividual level, assessments of attentional difficulties and habitual sleep patterns are analyzed. At the intraindividual level, previous-night sleep duration, pre-session alertness, and post-session fatigue are analyzed. Preliminary results show no clear trend between previous-night sleep duration and BCI performance, but in one dataset, results suggest lower performance among participants reporting higher pre-session sleepiness and higher post-session fatigue. Studying the effect of these variables may provide relevant information for developing BCIs more closely tailored to individual user characteristics.

Cognition, Behavior, and Memory

V-033

Effect of previous social condition on memory formation in crabs Neohelice granulata.

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Social interaction in animals affects nervous system development and behaviors such as aggressiveness and sleep, among others. In the crab Neohelice granulata, long-term memory is impaired in males isolated from conspecifics for at least 6 days. However, this manipulation has not been tested in females, and potential sex differences regarding interaction between social condition and cognitive performance remain unknown. Memory in Neohelice granulata has typically been studied in males by recording their escape response to a visual danger stimulus. Repeated spaced presentation of this stimulus elicits a decrease in the escape response in trained animals relative to controls, a reduction that persists for several days, indicating long-term memory retention. In the present study, we assessed spontaneous activity, initial escape response, learning rate and long-term memory (24 h) in both male and female crabs, maintained under isolated or social (N = 20 crabs, same sex) conditions for 7 days before training. Because wild N. granulata live at high densities, social interaction may represent a natural condition. However, animals can spend variable periods confined to their burrows depending on the season. Studying isolation effects may link social condition to previously reported circannual changes in cognitive performance.

Cognition, Behavior, and Memory

S-033

Sex differences in alcohol consumption and behavioral responses after the interruption of chronic ethanol drinking plus a single intraperitoneal administration

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Alcohol exposure can differentially affect males and females, with sex-related differences in alcohol consumption and behavioral responses. We investigated alcohol consumption and behavioral responses in a model of chronic ethanol consumption plus a single ethanol injection in both sexes. Adult C57BL/6 mice received a liquid diet containing ethanol (5% v/v) for 10 days, followed by ethanol injection (2.5 g/kg, i.p.) on day 11. Alcohol consumption was calculated per cage and expressed as g/kg body weight. Behavioral responses were evaluated using the Open Field Test (OFT) after 24 h of withdrawal and contextual fear conditioning on day 4 of withdrawal. Females showed higher alcohol consumption than males during the last three days of the diet protocol. In the OFT, females showed greater total locomotor activity than males under both control and ethanol-exposed conditions, with a strong tendency toward a sex difference in time spent in the central zone under control conditions. Ethanol-exposed males showed reduced time spent in the central zone and total locomotor activity. In fear conditioning, males showed a trend toward higher freezing than females under control conditions, whereas this difference was significant after ethanol exposure. Ethanol exposure increased freezing in both sexes. Overall, these findings reveal sex-related differences in alcohol consumption and behavioral responses following chronic ethanol exposure and an acute ethanol challenge, highlighting the im

Cognition, Behavior, and Memory

D-033

Adolescent alcohol intake and its influence on decision-making: A systematic review of behavioral and neurobiological evidence.

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Adolescence is a period of vulnerability to risk behaviors, including alcohol use, given the ongoing reorganization of brain circuits involved in behavioral control and reward processing. This study aimed to review evidence on the association between adolescent alcohol intake and alterations in decision-making assessed through behavioral tasks, and to identify the associated neurobiological correlates. A systematic review was conducted in PubMed (May 2026) following PRISMA guidelines, including English-language studies from the last 10 years involving human and animal models that evaluated alcohol exposure during adolescence, decision-making, and neurobiological or neurophysiological measures. Of 144 results, 8 met the inclusion criteria. Some studies identified impairments in cognitive flexibility, risky choice, and reward processing, while others found no behavioral differences associated with alcohol intake. Alterations were observed in striatal, prefrontal, insular, and limbic circuits linked to reward processing, inhibitory control, and behavioral regulation. Additionally, some findings suggest that impulsivity may precede alcohol use. Overall, results indicate that alcohol intake during adolescence may be associated with modifications in neural systems involved in decision-making, even without evident behavioral alterations. Given the limited evidence, further studies, particularly longitudinal ones, are needed to clarify this relationship.

Cognition, Behavior, and Memory

V-034

Traffic and white noise exposure: Differential effects on memory and hippocampus-dependent behaviors in adolescent rats and environmental enrichment as a neuroprotective strategy

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Noise can adversely affect health during development, with the hippocampus (HC) particularly vulnerable to its effects, which may vary by source. White noise effects on the HC are better studied than traffic noise effects, but which is more detrimental remains unclear. Enriched environment (EE) may protect against HC damage. We compared white and traffic noise effects on HC-related behavior in adolescent rats and evaluated EE protection. Adolescent Wistar rats of both sexes were housed in standard or EE cages and exposed to traffic or white noise (2 h/day, 5 days). Open Field, Inhibitory Avoidance, and Elevated Plus Maze were performed. Both types of noise impaired associative memory and increased grooming in both sexes. Traffic noise increased habituation memory (HM) in males and impaired it in females. White noise increased exploration and reduced defensive behaviors (DB) in both sexes, and increased anxiety-like behaviors (ALB) in females. EE prevented some DB and HM alterations depending on sex, while reducing ALB and increasing exploration in both sexes. In summary, white noise produced greater behavioral alterations than traffic noise, suggesting greater effects. Traffic noise had sex-dependent cognitive effects, whereas white noise effects were more consistent across sexes. EE had partial protective effects and induced behavioral changes independently. These findings highlight noise type as a determinant of HC effects, while EE protection depends on noise type and sex.

Cognition, Behavior, and Memory

S-034

5-HT2a receptor modulation of cognitive flexibility

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The ability to modify the behavioral response due to change of contingencies in the environment is defined as cognitive flexibility and it is a core component of the executive functions, those which relies heavily on the prefrontal cortex. Importantly impairment in cognitive flexibility has been reported in several neurodegenerative and neuropsychiatric disorders, including Alzheimer's disease and schizophrenia. The serotoninergic system (5-HT) plays a crucial role modulating prefrontal cortical functions. Among the most densely expressed serotonergic receptors is the 5-HT2a receptor (5-HT2aR), which has been implicated in executive functions like goal-directed behaviors , impulse control and behavioral adaptation. Previous pharmacological evidence suggests that the 5-HT2AR contributes to cognitive flexibility. However, the precise contribution of this receptor, particularly the consequences of constitutive loss of 5-HT2AR signaling, remains to be analyzed. The aim of this project is to analyze the role of 5-HT2aR in cognitive flexibility. For this we use a genetically modified mouse model backcrossed into the C57B/6 strain that has knocked out the 5-HT2aR. We first characterized this animal model through a battery of behavioral tests that includes the Open Field Test, the Light/Dark Box Test and the Forced Swim Test. Subsequently, by using the T-Maze for a reversal learning task we assessed and compared the wild type and the knockout animals.

Cognition, Behavior, and Memory

D-034

Multidimensional Behavioral Analysis Reveals Sex-Specific Vulnerability to a mouse PTSD Model

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Post-traumatic stress disorder (PTSD) shows individual variability and sex differences that may be obscured by group analyses. We characterized sex-specific responses to single prolonged stress (SPS) and tested whether multidimensional analyses could identify vulnerability/resilience profiles. Males and females underwent SPS or control treatment. Behavior was assessed using fear conditioning/extinction, recovery, reinstatement, Y-maze, light–dark box, open field, elevated plus-maze, and tail suspension. ANOVA was complemented by control-referenced z-scores integrating risk assessment, avoidance, cognition, and active/passive coping, followed by sex-specific clustering. SPS increased freezing during extinction session 2 in males only ($p<0.05$). Females showed no fear-conditioning changes but displayed perseveration and longer Y-maze alternation latencies ($p<0.05$). SPS increased passive coping in both sexes ($p<0.05$). Multidimensional analyses revealed sex-dependent patterns: SPS increased males in a high-freezing extinction cluster (χ^2 $p=0.04$), but not vulnerable/resilient clusters, whereas SPS females were more often classified in a vulnerable profile (χ^2 $p=0.0039$) characterized by avoidance, negative cognition, and passive coping. These findings show SPS produces heterogeneous, sex-specific phenotypes and support individual-level multidimensional analyses for detecting vulnerability. Such approaches may better capture human heterogeneity and strengthen translational relevance.

Cognition, Behavior, and Memory

V-035

Influence of sex and time of day on learning and memory in the crab Neohelice granulata.

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Fundamental processes for survival, like learning and memory, can be modulated by diverse factors including sex and circadian rhythm. Understanding how these factors shape cognitive processes, and whether their effects are conserved across taxa, represents an important area of research in comparative neuroscience. The crab Neohelice granulata is an established model for unveiling the mechanisms involved in cognitive processes. So far, studies have focused only on males, except for a preliminary study suggesting that females express long-term memory (LTM) but may not retain short-term memory (STM). Recently, we described circadian activity/rest rhythms in this species, showing high locomotor spontaneous activity during night and crepuscular hours, and a prolonged resting phase at midday/afternoon. This project aims to integrate the effect of circadian rhythmicity and sex on learning and memory in N. granulata. Using a well-established Contextual Pavlovian Conditioning protocol, involving repeated spaced presentations of a visual danger stimulus, we studied learning and memory in male and female crabs trained at either active (early morning) or resting (early afternoon) phases of the day. Our analysis includes comparisons between groups regarding exploratory activity, initial stimulus response, acquisition rate, and either STM (4 h) or LTM (24 h) retention. This approach contributes to identifying sources of variation in learning and memory processes in N. granulata.

Cognition, Behavior, and Memory

S-035

Brain states during driving hazard perception: A concurrent magnetoencephalography and eye movement study

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Hazard perception while driving requires us to quickly identify relevant information in a complex and changing environment. In this study, we investigated the brain and eye-movement dynamics involved in hazard perception using concurrent magnetoencephalography (MEG) and eye tracking recordings. Participants watched 33 naturalistic driving videos similar to those used in UK driving tests and were instructed to press a button whenever they detected a potential hazard. To characterize the fast-changing brain dynamics during the task, we used Dynamic Network Modes (DyNeMo), a data-driven model that identifies recurring patterns of brain activity and tracks how they evolve over time. We found an early visual brain response around 100 ms after fixation onset, followed by later differences in brain activity related to hazard processing. We also identified robust patterns of brain activity associated with visual processing, attention, and motor responses. In ongoing analyses, we track hazard-related objects throughout the videos and combine this information with participants' gaze and button responses. This allows us to study the temporal dynamics from the moment a relevant object first appears, through its transition into a hazard, until the participant responds. Overall, this approach provides a detailed view of how the brain, eye movements, and behavior work together during naturalistic hazard perception.

Cognition, Behavior, and Memory

D-035

Cerebellar Vermis Lesions Increase Impulsive-Like Behaviors in Mice

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The cerebellum contributes to motor and non-motor functions, and its interactions with basal ganglia and cortical circuits may influence impulsive and compulsive behaviors. Building on previous studies from our group, we investigated whether specific regions of the cerebellar cortex contribute to impulsive- and compulsive-like behaviors. Excitotoxic lesions were induced with kainic acid at different levels of the cerebellar vermis in male and female mice. Impulsivity was assessed using the plus-maze, cliff, emergence, and Y-maze tests, while compulsive-like behaviors were evaluated using marble-burying, nesting, and hole-board tests. Motor function was assessed by grip strength, balance, gait, and rotarod tests. Vermis lesions increased impulsive-like responses in both sexes in the plus-maze, cliff, and emergence tests, without inducing compulsive-like behaviors. Motor effects were limited to balance deficits. These findings indicate that the cerebellar vermis contributes to the modulation of impulsive-like, but not compulsive-like, behaviors. Although no compulsive phenotype was detected, further studies targeting the cerebellar hemispheres may reveal distinct impulsive and compulsive phenotypes, potentially resembling the behavioral alterations associated with cerebellar dysfunction in humans. This approach may help identify specific cerebellar regions involved in the regulation of complex behaviors.

Cognition, Behavior, and Memory

D-018

Age-Dependent Regulation of Neurogenesis and Memory by Dbc1

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The protein Dbc1 participates in multiple cellular processes, including transcriptional regulation, DNA damage repair, metabolic modulation, and cell cycle regulation. These functions are mediated through its physical interaction with target proteins, thereby regulating their biological activity. Using constitutive whole body Dbc1 knockout adult mice, we observed impaired neurogenesis in the dentate gyrus (DG), accompanied by specific behavioral alterations. However, it remains unclear whether these effects are due to a direct role of Dbc1 in regulating DG neurogenesis or to indirect consequences of its absence in other regions of the nervous system. In this study, we investigated the specific role of Dbc1 in regulating the cell cycle of neuronal precursors in the DG and its potential impact on cognitive functions. We employed a conditional Dbc1fl/fl mouse model under the control of a nestin promoter and inducible by tamoxifen, allowing the selective deletion of Dbc1 in DG neuronal precursors. DG neuroblasts were quantified using a marker of immature neurons, while neural progenitor status and the degree of neuronal differentiation were assessed based on relative mRNA expression. Cognitive performance was additionally evaluated using different behavioral tests. Our results demonstrate that the effects of Dbc1 deletion are age dependent. As expected, Dbc1 deletion was associated with reduced neurogenesis in 6–8-week-old animals, an effect that was lost in 10–12-week-old mice.

Cognition, Behavior, and Memory

S-036

Studying spatial directional memory in larval zebrafish

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Spatial navigation relies on short and long-term memory, requiring animals to continuously process positional and directional cues. Larval zebrafish are ideal for studying spatial cognition, combining well-characterized behavior with whole-brain imaging and reported head direction and place cells. We design and adapt an experimental arena to study directional memory in head-embedded, tail-free zebrafish larvae. Taking advantage of optomotor responses, our setup combines optic flow visual stimulation via moving oriented bars with direction-specific water jets acting as aversive stimulus. First, we determine the bar rotation angle required to induce directional swimming turns, measured as asymmetric tail bouts. Next, we characterize behavioral and heart rhythms responses to lateral water jets . Finally, we test the larvae's capacity to learn and discriminate associations between optic flow orientation and the location of the aversive stimulus. Tail kinematics are tracked using DeepLabCut. In parallel, we monitor heart rate as a complementary physiological readout, providing a more sensitive measure of state changes that may reveal subtle signatures of associative memory. The system is compatible with light-sheet microscopy for whole-brain imaging, providing a simple and robust framework for studying directional spatial memory. We will present early preliminary results and invite discussion with the community on the ideas, goals, and future directions of this new project.

Cognition, Behavior, and Memory

D-036

The Branching Layers of Memory Updating

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Memory is built through recurrent learning and updating events. Reconsolidation, triggered by mismatches between retrieved memories and current circumstances, destabilizes stored traces and induces gene expression required for restabilization. During this labile state, memories can incorporate new information or lose content if restabilization fails. Since memories can undergo multiple reconsolidation events, tracking the effect of impairing restabilization across successive reactivations allows studying the architecture of updated memories. Implementing this strategy with two reactivation sessions in the spatial object recognition task, in rats, we observed that each reconsolidation event added new information without merging it into a single trace, but by building a scaffold of partially overlapping information layers: disrupting an updated layer spared basal ones, whereas impairing the learning layer also affected subsequent one. Adding a third reactivation session confirmed these phenomena and showed that impairing the learning layer extends amnesia to the two following layers. Yet, the layer scaffolding does not always follow a simple temporal sequence. If the remainder associates with the learning and its first update, the new update links to the original learning information rather than to its update. Thus, memory organizes in layers but depending on the reminder, these layers seem to branch from different memory representations, rather than a linear stack over time

Cognition, Behavior, and Memory

V-037

Sex- and Context-Dependent Modulation of Striatal Cholinergic Interneuron Activity During Novelty Exposure.

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Obsessive-compulsive disorder (OCD) involves dysfunction of cortico-striato-thalamo-cortical circuits, with striatal cholinergic interneurons (SCI) regulating output and salience. SCI ablation induces compulsive and repetitive behaviors without affecting balance or coordination in male mice, but sex differences in SCI activity during behaviors remain unknown. C57BL/6 male and female mice were exposed to home-cage (HC), open-field (OF), or hole-board (HB) contexts for 30 min. Thirty minutes later, mice were perfused, brains were collected and sectioned to quantify phosphorylated S6 ribosomal protein (pS6rp), an activity marker, in ChAT+ striatal neurons by double immunohistochemistry. Behavioral analysis showed that males exhibited greater immobility in the OF than females ($p=0.043$). Immunohistochemical analysis revealed that, in males, pS6rp intensity increased in the OF ($p=0.0017$) and decreased in the HB ($p<0.0001$) compared with the HC context, whereas females showed no significant differences across contexts. Sex differences were observed in the OF ($p<0.0001$) and HC ($p=0.027$), but not in the HB. In the OF, SCI activity correlated negatively with distance traveled ($R^2=0.91$) and center entries ($R^2=0.86$), and positively with immobility ($R^2=0.96$); no significant correlations were observed in the HB. SCI activity depends on sex and context, with stronger changes in males, highlighting sex as a key factor in OCD-related striatal circuit regulation.

Cognition, Behavior, and Memory

S-037

Adolescents' use of cannabis, cognitive deficits and frustration response

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Cannabis use in adolescence represents a critical public health challenge, given that this stage constitutes a window of vulnerability for the development of the central nervous system. In this study, the effect of oromucosal exposure to THC-enriched Cannabis sativa oil administered during adolescence was evaluated in adult rats. The objective was to evaluate how this intervention alters the behavioral response to frustration, using the Successive Negative Contrast (SNC) paradigm. First, the administration method and dosage schedule were validated using a battery of standardized behavioral tests. It was found that: (1) adult rats treated with cannabis moved significantly more than those treated with vehicle in the Open Field test; (2) they spent less time interacting with the novel object in the Novel Object Recognition test; and (3) they spent less time in the dark in the Dark/Light Room test. Finally, in the CNS test, they exhibited a lower frustration response (measured as less suppression of the instrumental response). These results demonstrated that this treatment promotes cognitive memory deficits, as measured by the NOR, as well as differences in the Open Field test, the Dark/Light Room test, and the CNS test. Thus, it can be established as a novel model for studying the effects of cannabis use in adolescence on frustration behavior.

Cognition, Behavior, and Memory

D-037

Socioculturally generalizable speech biomarkers of Alzheimer's and frontotemporal dementia in Latinos

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Neurodegenerative diseases such as Alzheimer's disease (AD) and frontotemporal dementia (FTD) affect cognition, behavior, and daily functioning. Early diagnosis is critical to reduce their personal, clinical, and social consequences, yet diagnosis and follow-up often rely on costly, time-consuming assessments. Automated speech and language analysis (ASLA) offers a practical window into these disorders, providing fast, objective, and low-cost markers. Previous work from our team has shown that ASLA can distinguish AD, FTD, and related syndromes; support cognitive phenotyping; and reveal language-based alterations linked to specific cognitive domains and neurophysiological markers. Together, these studies suggest that digital language markers capture clinically meaningful signals. However, further validation across sociodemographic heterogeneity is needed. Differences in age, gender, education, dialect, multilingualism, and social determinants of health modulate both language production and dementia presentation. Standard group matching reduces average differences between groups but may miss individual variability, while machine-learning splits can reintroduce imbalance. Our work in 1689 Latin American participants with AD and FTD models this influence using residualization, while differentiating groups and predicting cognitive domains. This approach tests whether ASLA biomarkers remain robust, fair, and clinically informative across heterogeneous population

Cognition, Behavior, and Memory

V-038

Prediction error, retrieval practice, and instruction–action congruence during memory reactivation.

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The ability to adapt depends on updating predictions based on the discrepancy between expected and actual outcomes, known as Prediction Error (PE). Through reconsolidation, a PE-inducing reminder reactivates consolidated memories into an unstable state, allowing them to be restabilized and updated. We investigated which type of PE during reactivation—associated with task instructions, specific task cues, or their interaction—best enhances retention. Healthy adults (N = 102) learned 32 face–name pairs on Day 1. On Day 2, participants were assigned to a no-reactivation Control group or one of four reactivation conditions combining Instruction (Explicit vs. Non-explicit instruction) and Reminder type (Complete vs. Incomplete cue). Retention was evaluated on Day 3 via uncued recall and analyzed using generalized linear mixed models. All reactivation conditions significantly improved Day 3 retention relative to the non-reactivated Control group ($p < .0001$). Crucially, the condition combining two sources of prediction error, achieved the highest memory strengthening ($p = .002$). This advantage was most prominent at immediate testing ($p < .001$), before feedback-based relearning compressed group differences. These findings demonstrate that memory strengthening scales with the degree of PE induced during reactivation, providing direct support for a graded prediction-error account of memory reconsolidation.

Cognition, Behavior, and Memory

S-038

Z-score analysis of depressive-like and anxiety phenotypes in mice after early-life stress and serotonin depletion

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Early-life stress is one of the major risk factors for the development of anxiety and depression, and at the same time, serotonin (5-HT) deficits have been linked to the origin of these mental disorders. To study the role of 5-HT in early-life stress effects, we sought to investigate the interaction between 5-HT depletion and maternal separation (MS) in mice. C57BL/6 pups were subjected to the MS protocol (3h/day) during a postnatal critical period (P2-P14) while receiving daily injections of a tryptophan hydroxylase inhibitor (PCPA, 100mg/kg/day s.c.). We then evaluated emotional responses to stress in a battery of behavioral paradigms at adulthood (from P80). Responses in these tasks were analyzed by the Z-score method and the results of the tests were integrated into an Anxiety and a Depressive-like score. Our study showed that male mice were more susceptible to the MS exposure, resulting in long-lasting higher levels of anxiety and depressive-like behaviors which couldn't be reversed with the 5-HT depletion. Interestingly, in the anxiety score, females showed no response to MS alone but did have an increased score when 5-HT was depleted in addition to the stress. Notably, both MS and PCPA treatments increased the proportion of vulnerable vs resilient animals in both scores. Our results emphasize the emotional alterations caused by early-life stress and the interaction with the 5-HT transmission, in the search for understanding the development of psychiatric disorders.

Cognition, Behavior, and Memory

D-038

A Protocol to Modulate Arousal During Retrieval: Increased Arousal and Short-Term Verbal Memory Modulation Expression

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Predicting a stressor's effect during a specific memory phase remains challenging. A mild stressor during memory reconsolidation unexpectedly impaired, rather than enhanced (Coccoz et al., 2013), the long-term expression of a neutral verbal declarative memory (two-trial Rey Auditory Verbal Learning Test (RAVLT; lists of words; Sánchez Beisel et al., 2022)), an effect correlated with increased arousal at retrieval. Are these internal states reinstated during retrieval sessions a key substrate of stress-induced memory impairment? We tested whether this retrieval-induced internal state contributes to stress-related memory impairment by inducing neutral, positive, or negative states before RAVLT retrieval using images from the International Affective Picture System (IAPS) and music. Internal state was assessed with the Self-Assessment Manikin (SAM) after retrieval; memory was measured through free recall, serial position effects, and recognition. Results showed that, effectively, there was an increase in arousal in the negative group (mean difference = −1.57; 95% bootstrap CI: −2.53 to −0.36). However, no significant differences in memory performance were observed across conditions. These findings suggest that the protocol successfully modulated participants' internal states, although this effect did not translate into detectable differences in short-term memory performance.

Cognition, Behavior, and Memory

V-039

Implementation of a Semi-Automatized Interval-Timing Analysis in Time-Reference Memory to Assess the Necessity of Fixed-Interval Repetition.

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The neurobiological basis of time estimation remains poorly understood. One hypothesis proposes that temporal estimation recruits cognitive processes such as attention and/or working memory. We propose an alternative view: time estimation could constitute a form of immediate/short-term memory in which time itself acts as the stimulus that triggers a behavioral response. To test this, we developed an automated interval-timing paradigm for Drosophila melanogaster in which isolated, head-fixed flies are offered nine sucrose drops, each available for 10 s and accessible only through a Proboscis Extension Response (PER). Behavior is recorded with an overhead camera, and DeepLabCut is used to track proboscis length and drop position over time. Here we present the initial implementation of a semi-automated analysis pipeline aimed at determining whether repeated exposure to a fixed inter-drop interval is sufficient to induce interval timing. From normalized temporal series, we compute dynamic kinematic features, including instantaneous velocity, acceleration, movement direction, and distance to the stimulus, for each PER event. These features will be used to characterize the temporal structure of proboscis extension across trials and to test whether responses come to anticipate drop onset/offset as training progresses, a signature expected if flies learn the fixed interval rather than merely responding to the stimulus itself.

Cognition, Behavior, and Memory

S-039

Preliminary analysis on the association between neural activity on an auditory selective attention task and the perceived socioeconomic level on young adults from Buenos Aires, Argentina

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Selective attention is a cognitive process that prioritizes relevant information while inhibiting distractions. Previous evidence in children with low socioeconomic status (SES), shows similar neural activity related to relevant and irrelevant information, possibly reflecting an adaptive response to the specific characteristics of their environments. However, whether this pattern is present in the young adults is unclear. We implemented an auditory selective attention paradigm in which a group of young adults from Buenos Aires simultaneously listened to two short stories (one in each ear) while attending to only one of them. Participants also completed a sociodemographic questionnaire. Neural activity was recorded using an EEG. We expected participants from low SES backgrounds to show a smaller amplitude difference between target and non-target conditions in specific ERP components. Preliminary results (N=33) suggest an association between perceived SES (MacArthur scale) and the N2, but not the P2 component. The observed trend goes in line with developmental literature suggesting that participants reporting lower SES might show a specific sensitivity to distractors, reflected in smaller differences in neural activity between target and non-target. More participants are required to further confirm our results. In addition, other relevant variables such as unpredictability and chaos were collected and might help to clarify the specific mechanisms underlying this association.

Cognition, Behavior, and Memory

D-039

When Attention Meets Distraction in Online Comprehension

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Comprehension requires attending to relevant information while ignoring irrelevant information and distractions. The relation between comprehension and attention is well known but the mechanisms underlying that relationship are a question of research. Attention during online research can be assessed with attention checks or self-reported distractions. This study examined whether, during comprehension, objective attention checks and self-reported distractions are related, and their role in comprehension performance. Participants were 237 psychology students who completed the tasks remotely and unsupervised. While they read text or watched videos, they were interrupted five times, when they had to report their mental state related to mind wandering, and complete attention checks (answering about literal content). Mental state responses included task related thoughts, task unrelated thoughts, external distraction, and mind blanking; distraction was computed by combining the latter three. Attention checks were negatively associated with distraction ($\beta=-.24, p<.001$) and positively with comprehension ($\beta=.28, p<.001$), whereas distraction was negatively associated with comprehension ($\beta=-.20$, $p=.002$). Mediation analysis showed that distraction partially mediated the association between attention checks and comprehension (indirect effect =.048, $p=.003$;14.6% mediated). These findings highlight the role of attentional fluctuations in online learning and the usefulness of attention checks.

Cognition, Behavior, and Memory

V-040

Stereospecific 5-HT6 receptor antagonism by PUC-10 enhances cognitive performance: Neurobehavioral and Translational Insights

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Cognitive dysfunction is a core feature of several neuropsychiatric disorders, including schizophrenia, major depressive disorder and obsessive-compulsive disorder. The 5-HT6 receptor (5-HT6R), a Gs-coupled serotonin receptor enriched in cortico-striatal circuits, is a promising target for modulating cognitive function. Here we examined the neurobehavioral and translational potential of PUC-10, a potent and selective 5-HT6R antagonist of the N-arylsulfonylindole class, which exists as R- and S-enantiomers. Binding and functional assays identified the eutomer, showing higher affinity and potency at 5-HT6R than its antipode (Ki = 2.76 nM; Kb = 15 nM). We evaluated (E)-PUC-10 and racemic PUC-10 in rats after acute and repeated administration, assessing locomotor activity and cognitive performance in the novel object recognition test. Repeated dosing of the racemate was well tolerated, producing only a transient increase in locomotor activity. Notably, (E)-PUC-10 significantly improved novel object recognition in both male and female rats compared with vehicle-treated controls. Moreover, (E)-PUC-10 at 5 mg/kg increased hippocampal expression of the lipidated autophagy marker LC3-II in male rats, consistent with the involvement of autophagy-related processes in the procognitive effects of 5-HT6R blockade. Together, these findings identify the PUC-10 eutomer and support its potential as a therapeutic candidate for cognitive impairment associated with neuropsychiatric conditions.

Cognition, Behavior, and Memory

S-040

Sleep Maintains Innate Immune Competence

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Sleep is a highly conserved behaviour that is essential for organismal health. Although evidence links sleep loss to increased susceptibility to disease, the mechanisms by which sleep regulates innate immunity remain poorly understood. Innate immunity is the evolutionarily conserved branch of the immune system shared by insects and vertebrates, making Drosophila melanogaster an ideal model to investigate these interactions. We study how chronic sleep restriction affects the ability of the host to respond to systemic bacterial infections. To this end, we employ an automated sleep monitoring and restriction system that selectively disrupts sleep while allowing flies to undergo chronic sleep restriction for up to 10 days without compromising survival. Following sleep restriction, flies are challenged with systemic bacterial infections, and host survival, bacterial load, and molecular markers of the innate immune response are assessed to determine how sleep influences immune resistance and disease tolerance. Future work will combine genetic tools with gene expression analyses to identify immune pathways and physiological processes that depend on sleep. By uncovering the mechanisms through which sleep modulates innate immunity, this project aims to establish conserved principles linking behaviour to host defence and provide a mechanistic framework for understanding how chronic sleep loss impairs immune competence across animal species.

Cognition, Behavior, and Memory

D-040

Maternal Depression by Distress (DMD): Behavioral Validation of a Gestational Mouse Model

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Antenatal depression is a prevalent neuropsychiatric condition, yet its mechanisms remain difficult to investigate. We developed and validated the Maternal Depression by Distress (DMD) mouse model to test whether chronic peripubertal stress produces behavioral alterations persisting into pregnancy. Female C57BL/6 mice were socially isolated from weaning and subjected to 15 restraint sessions (2 h/day, 5 days ON / 2 days OFF). Behavioral profiling was conducted at pre-gestational baseline and gestational day 16 using the Sucrose Preference Test (SPT), Splash Test, Forced Swim Test (FST), and Elevated Plus Maze (EPM). Prior to mating, DMD females showed anhedonia ($t(18) = 2.40$, $p<0.05$, $d = -1.08$) and reduced self-care in the Splash Test ($t(9) = 3.58$, $p<0.01$, $d = -2.25$), with no differences in body weight, FST immobility, or EPM exploration. At late gestation, DMD dams exhibited anxiety-like behavior, spending more time in the EPM central platform ($t(10) = -3.03$ $p<0.01$, $d = 1.75$) and increasing closed-arm entries ($t(10) = -2.31$, $p<0.05$, $d = 1.33$). They also showed diminished self-care in the Splash Test ($t(8) = -2.90$, $p<0.05$) and lower sucrose preference ($t(12) = -2.29$, $p<0.05$). In conclusion, the DMD protocol establishes a face-valid preclinical model of gestational distress, providing a robust platform to investigate postpartum trajectories and maternal–fetal neurobiological mechanisms.

Cognition, Behavior, and Memory

V-041

Experimental platform to study associative learning in zebrafish larvae under the microscope.

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Associative learning requires linking sensory cues with biologically relevant outcomes. Zebrafish larvae are a powerful model: optically transparent, small and genetically tractable, ideal for whole-brain imaging, with a well-characterized behavioral repertoire. However, combining behavioral readouts with neural imaging requires paradigms that can be performed while the animal is head-fixed, and most existing protocols either probe non-associative memory or are too complex to implement under a microscope. We developed an experimental platform to study associative learning in zebrafish larvae. Velocity changes in optomotor response assays are paired with aversive stimuli. The larva is restrained with its tail free, allowing motor responses. Moving visual gratings generate optic flow, while brief water jets provide an aversive stimulus. The proposed paradigm is highly naturalistic and closely aligned with the animal's biological experience. The system is designed to enable all training steps to be performed under the imaging microscope, allowing simultaneous recording of behavior and brain activity and providing a novel framework to investigate the neural mechanisms underlying associative learning. We will present a proof of concept demonstrating the functionality and versatility of the system. We will also characterize the range of expected responses to the stimuli across variations in stimulation parameters and discuss preliminary results from associative learning curves.

Cognition, Behavior, and Memory

S-041

α7 nicotinic acetylcholine receptors in the retrosplenial cortex modulate neuronal activity in the retrosplenial cortex and hippocampus during aversive memory acquisition

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α7 nicotinic acetylcholine receptors (α7 nAChRs) in the retrosplenial cortex (RSC), located predominantly on GABAergic interneurons in superficial cortical layers, modulate the acquisition of aversive memory. To investigate the RSC–dorsal hippocampal circuit, this study analyzed the expression profile of the immediate early gene c-Fos in the RSC and hippocampal regions 90 minutes after pharmacological blockade of RSC α7 nAChRs with methyllycaconitine (MLA) during acquisition of an inhibitory avoidance (IA) task. Blocking α7 nAChRs produced a significant increase in c-Fos expression in the anterior RSC (aRSC), particularly in layers 2 and 2/3, as well as in CA1 and CA3. These findings indicate that RSC α7 nAChRs modulate neuronal activity across the RSC–hippocampal circuit during aversive learning. Given the predominant localization of RSC a7nAChRs on GABAergic interneurons, their blockade may alter local excitation–inhibition dynamics and consequently affect the integration of contextual information within the aRSC.

Cognition, Behavior, and Memory

D-041

Effects of the Immunomodulatory Oligonucleotide IMT504 on Learning and Memory in an Alzheimer's Disease Rat Model

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Neuroinflammation and immune dysfunction are increasingly recognized as major contributors to Alzheimer's disease (AD), suggesting that restoration of immune homeostasis may represent a promising therapeutic approach. IMT504 is an immunomodulatory oligonucleotide that promotes protective and reparative responses in experimental models involving chronic inflammation and tissue damage. We therefore investigated whether IMT504 could ameliorate cognitive alterations in the McGill-R-Thy1-APP rat (TG), a model that expresses human amyloid precursor protein with the Swedish and Indiana mutations and develops progressive amyloid pathology and memory impairment. Twelve-month-old TG rats received either physiological saline or IMT504 (20 mg/kg, s.c.) once daily for five consecutive days. Seventy-two hours later, animals were evaluated using open-field, novel object recognition, novel object location, and inhibitory avoidance tasks. Treatment with IMT504 enhanced novel object recognition performance and improved associative memory in the inhibitory avoidance task. In the latter, treatment response differed according to sex: females exhibiting a more marked improvement in performance than males. Overall, these results show that a short systemic treatment with IMT504 benefits specific cognitive domains in TG rats and highlight sex as a relevant biological variable when assessing its therapeutic potential for AD.

Cognition, Behavior, and Memory

V-042

A polyphenol-enriched red wine powder affects recognition memory in mice

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Red wine polyphenols have shown beneficial effects in animal models of metabolic syndrome, inflammatory and neurological diseases, and even in aged flies, worms and mice. To test the brain effects of polyphenols we produced a red wine powder (WP) by freeze-drying encapsulation in a maltodextrin/arabic gum matrix. Then, we tested the WP effects on habituation and recognition memory in C57/BL6 mice, performing open field (OF)/novel object recognition (NOR) behavioral analysis. We observed that 34 days after oral administration of 3% WP the habituation memory evaluated in the OF remained unaffected. Unexpectedly, we detected an impairment in the NOR performance after 24 hours of 3% WP treatment, evidenced as significant reductions in the discrimination and recognition indexes. On the other hand, the chemical analysis of the WP showed good antioxidant capacity in vitro and high levels of polyphenols, demonstrating the concentration capacity of the WP production process. The observed memory effects cannot be attributed solely to polyphenols, the hypothesized bioactive fraction. The wine dry matter is a complex matrix containing glycerol, organic acids and other non-phenolic compounds that may independently influence cognition. Therefore, additional experiments are essential before drawing any definitive conclusions.

Cognition, Behavior, and Memory

S-042

Benefits of a Nap for the Consolidation of Newly Learned Words

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A large body of evidence indicates that non-rapid eye movement (NREM) sleep contributes to the stabilization of newly acquired memories, whereas REM sleep has been proposed to support the integration of new information into pre-existing memory networks. Here, we examined memory consolidation and semantic integration within the same experimental paradigm. Fifty-two participants (M_age = 24.69 years, SD = 4.60, range = 18–37; Wake: n = 25; Sleep: n = 27) learned rare Spanish words paired with images and definitions and then either took a 90-min nap monitored with polysomnography or remained awake. Memory was assessed after training (TR2) and again following the retention interval (TS). Word recall did not differ between groups at training. Across the retention interval, word memory significantly decreased in the Wake group, whereas no significant decline was observed in the Sleep group. Accordingly, memory change differed significantly between groups, with greater forgetting in Wake. In contrast, change in definition memory did not differ between groups. No group differences were observed in semantic integration. Correlational analyses were subsequently performed to examine whether NREM slow-wave and spindle activity, as well as REM theta power, were associated with memory consolidation and semantic integration. These findings will be interpreted in the context of current models of sleep-dependent memory processing, particularly the active systems consolidation framework.

Cognition, Behavior, and Memory

D-042

Critical contribution of young adult-born granule cells to spatial pattern separation

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The dentate gyrus (DG) of the hippocampus is one of the few brain regions where new neurons continue to be generated throughout adulthood. Adult-born granule cells (ABGCs) have been implicated in pattern separation, the process by which similar experiences are transformed into distinct memory representations. However, the specific contribution of young ABGCs to spatial discrimination remains incompletely understood. Here, a modified spontaneous object location recognition task (SOLR) was used to investigate the role of young ABGCs in spatial pattern separation. Reversible silencing of young ABGCs during SOLR allowed us to assess spatial discrimination across configurations with different levels of similarity. Under low pattern-separation demand, animals preferentially explored the more distant object, whereas under high-demand conditions, exploration of the two objects was more similar. Remarkably, silencing a small cohort of young ABGCs produced a behavioral effect comparable to that observed following silencing of the entire DG. These findings suggest that a relatively small population of young ABGCs can exert a substantial influence on spatial discrimination when animals encounter similar spatial configurations. Together, these results support a critical role for young ABGCs in hippocampal pattern separation and highlight their contribution to spatial discrimination during a critical stage of neuronal maturation.

Cognition, Behavior, and Memory

V-043

Can instructed slow breathing persist across sleep onset? Preliminary respiratory and EEG findings

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Slow-paced breathing may provide a way to study whether an instructed bodily pattern can persist during sleep onset. In a randomized within-subject crossover study, 12 participants completed spontaneous-breathing control and paced-breathing (2.5 breaths/min) sessions while lying supine with eyes closed. EEG and respiration were recorded continuously, sleep stages were scored, and 11D-ASC and BMIS were administered. Paced breathing reduced respiratory rate to 2.49 breaths/min compared with 10.69 during control (p=.0078) and participants remained awake for longer (79.7% vs 42.3%, Holm p=.0117). Three participants entered N1 sleep while still maintaining the instructed breathing rate of about 2.5 breaths/min. Alpha activity decreased during control but was relatively preserved during paced breathing (+2.15 dB, Holm p=.0148). When only wakefulness periods were analyzed, this difference was smaller and no longer significant (+1.15 dB, p=.070). No FDR-corrected 11D-ASC effects or BMIS differences were found. In an exploratory analysis, greater alpha preservation was associated with increased Blissful State (ρ=.83, p=.008, FDR=.091). These results show that an instructed slow-breathing pattern can persist into early sleep, raising new questions about how instructions established during wakefulness may continue to guide behavior as consciousness changes across sleep onset.

Cognition, Behavior, and Memory

S-043

Semantic Similarity or Predictability? Quantifying Contextual Influences on Word Processing

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Previous studies have shown that prior context facilitates the processing of thematically congruent words (Laurino & Kaczer, 2025), but the properties underlying that influence remain unclear. This study examines how the semantic content of a written context shapes the later processing of an auditorily presented word, and which properties best account for that influence. Twenty-three participants read short texts and then made an auditory semantic relatedness judgment on a word pair, congruent or incongruent with the preceding context. Eye movements, EEG and responses were recorded. We propose two quantifiable properties: semantic similarity (meaning overlap between context and target) and language-model predictability (how expected a word is given its context). Semantic similarity is quantified with WordNet and FastText; predictability is estimated with open-source language models. We will test whether these continuous measures account for more variability in neurophysiological (e.g., time-frequency representations) and behavioral (e.g., response times) responses than categorical congruence, characterizing how contextual information is represented and used. Additionally, we will test whether the individual measures of context reading (i.e., total fixation times) influence target-word processing. To do so, we will fit trial-level linear mixed-effects models including total fixation times and compare them with models without this predictor.

Cognition, Behavior, and Memory

D-043

Exploring the role of the medial prefrontal cortex in the retrieval of episodic memory

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Episodic memory can be defined as the memory for unique events. In most situations, reality is ambiguous, and the cues that trigger retrieval are often associated with more than one particular memory. The medial prefrontal cortex (mPFC) controls the retrieval of memory traces, inhibiting the less relevant one, in situations where the cues presented could trigger the expression of more than one and cause interference. We have identified that the mPFC, the ventral hippocampus (vHPC), the dorsal hippocampus (dHPC), as well as the perirhinal cortex (PRH), are involved in the retrieval of context guided recognition memories. But it is still not known the type of information they store and the interaction among them. We have previously shown that the different subregions of the mPFC, prelimbic (PL) and infralimbic (IL), are necessary for the control of interference during a contextual version of the object recognition task. However, it is not clear if both subregions process the same type of information. In order to test if information arising from vHPC is processed by the subregions during retrieval control we performed a series of experiments combining behavioral and chemogenetic tools. Our findings show that vHPC-IL projections but no vHPC-PL are required for the retrieval of an contextually guided object memory. These results suggest that vHPC-IL information might be required for the resolution of interference during retrieval.

Cognition, Behavior, and Memory

V-044

Exploring the role of dCA1 Serotonin 2A Receptors in a contextually guided of Recognition Memory task in Rats

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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. 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 during different phases of the recognition memory we combined stereotaxic infusion of a selective antagonist with behavioral tasks in rats. We found that dCA1-5-HT2aR are required for the consolidation and retrieval of a contextually guided object memory task. These results suggest that HPC 5-HT2aR are involved in recognition memory when contextual information is an important feature of the task.

Cognition, Behavior, and Memory

S-044

Hippocampal Microglia is critical for Spatial, but not Aversive, Memory establishment

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In the healthy adult brain, microglia physically interact with a subset of synapses and contribute to the development, maturation, and remodeling of neural circuits, ultimately influencing behavioral outcomes. We examined how the depletion of hippocampal microglia affects spatial and aversive memories processing. To this end, we administered clodronate into the rat hippocampus, and immunofluorescence analyses were performed to determine the time window and specificity of this microglial-depleting agent. Three days after clodronate infusion, we detected a transient reduction in microglial cell number, while the percentage of area occupied by astrocytes and neurons remained unchanged. At this time point, rats were trained in a spatial object recognition (SOR) task, demonstrating successful acquisition and short-term memory (STM) expression; however, they failed to consolidate the memory. Moreover, microglial depletion before the SOR test did not affect long-term memory (LTM) expression but prevented its reconsolidation. In contrast, when rats were trained in an aversive inhibitory avoidance (IA) task under hippocampal microglial depletion, no impairment was observed in either the acquisition or expression of STM or its subsequent consolidation. Nevertheless, microglial depletion before the IA test did not affect either LTM expression or the extinction process. Thus, our results highlight a differential role for hippocampal microglia in the dynamic processes underlying memory.

Cognition, Behavior, and Memory

D-044

Directed Forgetting Utilizing Abstract Visual Stimuli: A Paradigm for Studying Explicit Memory Control

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Voluntary control over memory allows individuals to prioritize relevant information while reducing the influence of information that is no longer useful. Impairments in these mechanisms have been associated with psychiatric disorders including anxiety, PTSD and OCD. Directed forgetting provides a useful paradigm for studying explicit memory control, although most studies have relied on verbal or easily identifiable visual stimuli. Here, we developed a pilot item-method directed forgetting task using abstract geometric shapes to provide a controlled stimulus set suitable for future electrophysiological and aversive-learning studies. Participants encode abstract shapes followed by auditory cues instructing them to remember or forget each item. Memory is subsequently assessed using an old/new recognition task with novel foils and confidence ratings. We expect greater recognition sensitivity for remember-cued than forget-cued stimuli, supporting the use of abstract visual material for studying intentional memory regulation. By combining explicit memory-control instructions with easily reproducible, low-semantic stimuli, this paradigm aims to provide a flexible framework for investigating directed forgetting and the mechanisms underlying voluntary memory control.

Cognition, Behavior, and Memory

V-045

Innate and Learned Valence in Honey Bee Odour Mixture Processing

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Apis mellifera encounter odours as mixtures and must integrate components with different biological relevance. This project investigates how pheromones and learning modify the representation of binary odour mixtures in the antennal lobe and their behavioural expression. Preliminary behavioural results show that, 24 hours after appetitive conditioning, bees respond positively to the learned odour presented alone and when mixed with a neutral odour. However, presenting the learned odour together with a negatively valenced pheromonal component interferes with the expression of appetitive memory. To investigate the underlying neural mechanisms, we performed calcium imaging of antennal-lobe projection neurons during stimulation with aversive pheromones and unlearned odours, presented both alone and in mixtures. The results indicate that, in mixtures with neutral odours, pheromonal components contribute more strongly to the neural representation of the mixture. This suggests that pheromones may dominate or modify the early sensory coding of otherwise neutral environmental odours. Calcium-imaging experiments using learned odours are currently underway. These experiments will determine whether learning modifies this weighting and shifts the representation of the mixture towards the odour associated with reward. Overall, these findings contribute to our understanding of how combinatorial coding, innate valence and experience interact during odour-mixture processing in the honey bee.

Cognition, Behavior, and Memory

S-045

Electrophysiological dynamics of Social Concept Processing: Preliminary Results from a Semantic Priming Paradigm

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Emerging evidence suggests that social language processing (e.g., isolated words such as “greet”) recruits socioemotional circuits, including the right insula and anterior temporal lobe. Such recruitment can be assessed through event-related potentials (ERPs), particularly the N400, and oscillatory analyses. This study examined, using a semantic priming paradigm, whether implicit interactions between social and action verbs are reflected in semantic integration indices, measured through cluster-based spatiotemporal ERP analysis. Exploratory analyses also assessed oscillations in the mu (8–14 Hz) and beta (12–30 Hz) bands, considered indices of motor simulation and sociocognitive processing, respectively. Results revealed a cluster around 400 ms for both social and action verbs, characterized by larger negative deflections for incongruent pairs in both conditions, with a stronger effect for social pairs. Complementarily, time-frequency analysis showed an early (~200 ms) desynchronization in the mu band for action pairs and in the beta band for social pairs. Overall, these findings suggest general semantic integration mechanisms shared across both conditions, alongside modality-specific oscillatory modulations for each semantic domain.

Cognition, Behavior, and Memory

D-045

Astrocyte-neuron interactions in long-term memory persistence

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Memory persistence is an important property of long-term memory. Recent studies have highlighted the contribution of astrocytes to memory processing, yet how astrocyte-neuron interactions support memory persistence remains unclear. Here, we investigated astrocytic mechanisms associated with long-term memory maintenance, including structural interactions between astrocytes and neurons. Manipulation of astrocytic Ank2 impaired remote memory without affecting recent memory and was accompanied by reduced astrocyte-neuron contacts and altered astrocyte morphology. Together, these findings suggest that astrocytic structural regulation contributes to long-term memory persistence.

Cognition, Behavior, and Memory

V-046

Long-term changes in recognition memory after juvenile or adult exposure to stevia

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We previously showed that unlimited access to sugar-sweetened beverages during youth induces long-lasting recognition memory deficits. Here, we examined whether stevia consumption during the juvenile period or adulthood produces similar effects. Male Sprague–Dawley rats, starting at postnatal day (PD) 25 or PD75, received ad libitum access to water (control), 10% sucrose (SUC), or a 4% aqueous Stevia rebaudiana Bertoni decoction for 25 days, followed by 25 days of water only. Recognition memory was then assessed using the novel object recognition test at 2 h (T2), 24 h (T3), and 7 days (T4). Juvenile sucrose-exposed rats failed to discriminate between familiar and novel objects at all retention intervals, confirming persistent memory impairment. In contrast, stevia effects depended on age of exposure and retention interval: adult-exposed rats showed impaired short-term memory (T2, p=0.0003), whereas juvenile-exposed rats showed impaired long-term memory (T3, p=0.0002). Neither stevia-exposed group showed deficits in consolidated memory (T4). These findings indicate that unlimited stevia consumption can produce age- and retention interval-dependent effects on recognition memory that differ from those induced by sucrose.

Cognition, Behavior, and Memory

S-046

Beyond Freezing: New Behavioral Insights into Observational Fear Learning

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Animals can acquire information not only through direct experience, but also through the experience of others, a process known as social learning, which carries important adaptive value by allowing individuals to avoid exposure to potentially dangerous stimuli. In rodents, one of the paradigms most widely used to study the neurobiological mechanisms underlying social learning is the observational fear learning paradigm, in which an individual witnesses an aversive experience -a fear conditioning session- received by a conspecific. This type of paradigm is commonly used not only to study the formation of long-term observational memories, but also, given its aversive nature, to study empathy-like behaviors, particularly during the acquisition phase, when the learning process itself takes place. However, the behavioral variable most commonly analyzed in both cases is freezing behavior, widely used in rodents to assess fear-related responses. In this work, we explore additional behavioral variables that allow for a more detailed characterization of animal behavior, based on pose estimation tools.

Cognition, Behavior, and Memory

D-046

Effect of Garcinol as a Histone Acetyltransferase Inhibitor on Memory Persistence in Mice

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Epigenetic mechanisms have emerged as critical modulators necessary for synaptic plasticity and memory. In particular, histone acetylation has been consistently implicated in memory formation. Garcinol is a naturally occurring compound that functions as a HAT inhibitor. We investigated the effect of post-training systemic administration of Garcinol on memory persistence and histone acetylation levels in the hippocampus of mice. When evaluating NOR memory under a strong training protocol, the results demonstrated that the i.p injection of Garcinol generates a significant memory deficit when animals are tested at 7 days. Conversely, this treatment did not affect long-term memory formation evaluated at 24 hours, suggesting that the amnesic effect is specific to persistence. To elucidate the molecular correlate, acetylation levels in the hippocampus were evaluated one hour after NOR training and Garcinol injection using the Western Blot technique. No significant differences were observed between groups in the acetylation levels of histone H3 or in global acetylation levels. These results indicate that Garcinol selectively affects the persistence, but not the formation of object recognition memory. However, this effect was not accompanied by detectable changes in hippocampal acetylation levels at one hour post-training, raising questions about the temporal window, substrate specificity, or subregional localization of the underlying molecular correlate.

Cognition, Behavior, and Memory

V-047

Sex- and time-dependent effects of alcohol hangover on inhibitory avoidance memory in mice

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Alcohol hangover begins as blood alcohol concentration approaches zero and can cause cognitive disturbances for several hours. However, how the timing of learning during hangover and biological sex shape memory remains unclear. We examined the effects of ethanol administered at different intervals before training on inhibitory avoidance memory in male and female mice. Adult CF-1 mice received vehicle or ethanol (1.9 g/kg, i.p.) 9 or 12 h before training. Based on the female response profiles at these time points, an additional female cohort was trained 10.5 h after treatment. Previously presented 12-h experiments also included 3.8 g/kg ethanol. Mice received a 0.3-mA footshock upon entering the dark compartment. Entry latency was recorded during training (TR) and a retention test (TS) 48 h later. At 12 h, the analysis revealed a significant group-by-session interaction in males: animals treated with 1.9 g/kg ethanol showed significantly lower TS latencies than vehicle-treated mice, consistent with impaired retention. In contrast, no significant interaction was detected in females in either the initial or replication experiments. At 9 h, ethanol did not significantly alter retention in females or males. Likewise, the 10.5-h female cohort showed no significant group-by-session interaction. Training latencies were comparable between groups in the experiment showing impairment. The 3.8 g/kg dose produced substantial mortality, especially in males, limiting its interpretation.

Cognition, Behavior, and Memory

S-047

When Stress Gets Under the Skin: Maternal Perinatal Stress and Early Socioemotional Development

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Maternal perinatal stress (MPS) is a prevalent public health concern that may shape early socioemotional development, yet evidence from Latin America remains scarce. This prospective cohort study examined associations between maternal psychosocial stress across pregnancy and early postpartum and infant socioemotional development at 3 months, considering trimester-specific and cumulative exposure. Maternal depression, anxiety, and contextual stressors were assessed across the perinatal period. Principal component analyses were used to derive stress indices, and hierarchical regressions adjusted for sociodemographic covariates tested their associations with infant outcomes. Higher MPS was significantly associated with less optimal socioemotional development. Depressive symptoms showed the strongest and most consistent associations across models. Both trimester-specific and cumulative stress indices explained developmental variability, suggesting sensitive windows and additive effects. Associations remained robust after covariate adjustment. These findings support early socioemotional programming within the Developmental Origins of Health and Disease (DOHaD) framework and identify maternal depressive symptoms as a salient marker of infant vulnerability. They underscore the need for early detection and prevention strategies targeting maternal mental health, particularly in underrepresented global contexts.

Cognition, Behavior, and Memory

D-047

Evaluation of the therapeutic potential of gallein in a novel APP knock-in mouse model of Alzheimer's disease

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Alzheimer's disease (AD) is characterized by β-amyloid (Aβ) accumulation, neuroinflammation, and cognitive and neuropsychiatric alterations. In vitro studies showed that Aβ amplifies its own production through a pathway in which APP acts as a noncanonical receptor coupled to Go/Gβγ. Since gallein, a Gβγ inhibitor, prevented this mechanism, we evaluated its therapeutic potential in vivo. Homozygous App^NL-F;Psen1^P117L knock-in (APP KI) and wild-type C57BL/6 (WT) mice of both sexes were evaluated at 3 and 6 months using the open-field test, elevated plus maze, novel object recognition test, and Y-maze. Between assessments, mice received gallein or vehicle for eight weeks. Locomotor activity, emotional and exploratory behaviors, risk assessment, and episodic, working, and spatial memory were analyzed. APP KI mice displayed early emotional and exploratory alterations consistent with changes in risk assessment, increased novelty-seeking/impulsivity, and reduced sustained exploration before evident cognitive deficits emerged. Gallein reduced exacerbated exploratory activity and partially normalized these responses without clearly improving cognitive performance. These findings indicate that Gβγ inhibition with gallein attenuates early neurobehavioral alterations, suggesting an early therapeutic window and supporting Gβγ as a target for disease-modifying strategies in AD.

Cognition, Behavior, and Memory

V-048

Intersexual aggression in Cichlasoma dimerus: the importance of female reproductive status

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Historically aggression has been studied in intrasexual encounters specially focusing on males, while aggression between opposite sexes remains understudied. In cichlid fish, reduced intersexual aggression is associated with pair formation, and escalated aggression can impact courtship and the reproductive success. Cichlasoma dimerus is a Neotropical cichlid showing monogamous and biparental behaviour. In our laboratory we study intersexual aggression assessing its relationship with reproductive status and neuronal activation across telencephalic and hypothalamic areas from the Social Decision-Making Network. The main goal of this study is to determine whether intersexual aggression in C. dimerus is related to the gonadal state of females. We performed dyadic encounters between dominant males and females for one hour. Animals were then euthanized and gonads were fixed in Bouin's solution. For ovarian histology different protocols were compared, either using xylene or butyl during dehydration before paraffin inclusion. After topographical coloration, our results suggest that the protocol using butyl better preserves the ovarian follicles and allows an appropriate quantification of different stages of oogenesis and vitellogenesis. These first results of this undergraduate thesis lay the foundations to characterize ovarian histology of females participating in intersexual encounters and to determine how overall levels of aggression can be related to their gonadal status.

Cognition, Behavior, and Memory

S-048

Socioeconomic status as a predictor of neurocognitive performance in adults aged 50 and older

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Argentina is undergoing a profound economic and social crisis that hinders optimal conditions for healthy aging. Socioeconomic context is a psychosocial risk factor that plays an important role in neurocognitive performance and in the response to its deterioration. Thus, the decline of cognitive functions in old age constitutes an issue of growing relevance worldwide, given that its progression can lead to dementia. This study aimed to examine whether socioeconomic status predicts neurocognitive performance in adults over 50 years. Using a cross-sectional design 136 volunteers from the general population (M age 65.9, 68.4% women) were assessed with a socioeconomic index that gathered information on income, education, and occupational attainment, along with a neurocognitive battery composed of the Trail Making Test, fluency tasks, and the Auditory Verbal Screening for Cognitive Alterations. Regression analyses were performed between socioeconomic status and the different tasks. In line with the study's hypothesis, the regression model explained 30% of the variance. Socioeconomic status carried the greatest predictive weight, followed by education. Furthermore, adult socioeconomic status (education, income, and occupation) showed greater predictive weight for neurocognitive performance than childhood socioeconomic status (parents' education and occupation). In conclusion, socioeconomic context influences neurocognitive performance, highlighting education as a protective factor.

Cognition, Behavior, and Memory

D-048

Effect of stimulus and feedback sensory modalities in paced finger tapping

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The interaction between brain and body displays rich temporal and spatial dynamics. The temporal aspects of this interaction, unlike the spatial ones, are not yet very well understood, particularly with regard to how the brain processes temporal information at intermediate timescales, such as during synchronization with a periodic stimulus (i.e., sensorimotor synchronization, or SMS). Our experimental paradigm is the paced finger tapping task, where a participant is instructed to synchronize their finger's movement with a periodic sequence of stimuli by tapping on a surface. Despite its apparent simplicity, this task involves numerous neural processes, such as temporal prediction (as the participant has to predict the next stimulus in order to achieve synchronization), temporal comparison/estimation (as the participant monitors their past performance in order to make corrections), and temporal production (as the participant must produce time intervals). SMS is a spontaneous phenomenon in humans and is quantified by the synchronization error, or asynchrony (that is, the time difference between each response and its corresponding stimulus in the sequence). There exist several conceptual models in the literature (e.g., Fraisse-Paillard and SAM) that attempt to explain the observed dependence of the mean asynchrony on the stimulus and feedback sensory modalities. In this work, we analyze the results of an experiment that casts doubt on these models' predictions.

Cognition, Behavior, and Memory

V-049

Semaglutide modulates consolidation and updating of inhibitory avoidance memory

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Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist widely prescribed for metabolic disease, also acts on central neural circuits. However, its effects on the formation and long-term stabilization of emotional memories remain poorly understood. We tested whether systemic semaglutide modulates different aversive memory processes. Adult CF-1 mice underwent one-trial step-through inhibitory avoidance training and received a single subcutaneous injection of semaglutide (0.1 mg/kg) or vehicle immediately after training, before testing, or after memory reactivation. Memory was assessed up to seven days later. Post-training semaglutide increased step-through latencies at both 48 hours and 7 days, and this enhancement persisted at a second test 24 hours later. The effect was time-dependent: semaglutide given 3 hours after training was ineffective. Pre-test administration did not alter memory expression, indicating that the effect was not due to an acute modulation of retrieval. Semaglutide given immediately after memory reactivation also strengthened subsequent retention. These findings indicate that a single systemic dose of semaglutide strengthens the consolidation and post-retrieval updating of inhibitory avoidance memory without detectable effects on memory retrieval. They identify GLP-1 signaling as a modulator of long-term aversive memory and raise important translational questions about the cognitive effects of this widely used medication.

Cognition, Behavior, and Memory

S-049

Words, Webs, and Time: A Quantitative Analysis of Autobiographical Memory Transformation

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The quantification of memory processes is an ever-evolving area in neuroscience. Memories are reconstructive, with the passage of time and the act of recall taking part in their transformation. Emotionality modulates this trajectory, altering a memory's internal organization and its susceptibility to structural reorganization over time. This modulatory role is particularly relevant for autobiographical memories, the ability to recall personal experiences. Yet, because these memories are inherently variable and subjective, they have long posed a challenge to systematic, quantitative analysis. This study aimed to understand the role of the passage of time and recall in autobiographical memory, and whether their effect differs with the emotional profile of the recalled event. To achieve this, we compared autobiographical narratives of contrasting emotional valence, Argentina's loss to Saudi Arabia and its championship win at the 2022 World Cup, each narrated by the same participant at two temporal instances. Interviews were characterized through NLP (POS tagging, sentiment analysis, semantic embeddings) and graph theory metrics. Using this feature set, a support vector machine model was trained to distinguish narratives from the first temporal instance from those of the second. Through the resulting feature importance, we characterized how autobiographical memories are transformed over the passage of time, and whether this transformation differs with emotionality.

Cognition, Behavior, and Memory

D-049

Neuropsychological assessment in Adult Drug-Resistant Focal Epilepsy patients with Adjunctive Cannabidiol treatment.

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Introduction: Drug-resistant focal epilepsy frequently affects memory, attention, language, and executive functions. While cannabidiol (CBD) is a known therapy, its cognitive impact remains understudied. Cognitive impairment in drug-resistant epilepsy involves static factors (lesions) and dynamic factors (seizures, discharges, medication effects, comorbidities, onset age, duration). Objective: To evaluate the cognitive status of adult patients with drug-resistant focal epilepsy before and after adjunctive CBD treatment. Methods: Prospective, open-label, before-and-after cohort study in patients aged 18–60 at a public hospital in Buenos Aires (6–9 months follow-up). Assessments covered verbal/nonverbal episodic memory, language, executive functions, and attention. Results: Among 44 patients, 38 were responders, 5 non-responders, and 1 worsened. Responders showed statistically significant improvements in verbal/visual memory, language, sustained attention, and shifting attention. Non-responders and worsened groups improved in verbal and visual memory. Depressive symptoms did not significantly impact performance. Conclusions: Unlike conventional therapies, CBD shows no negative cognitive impact in drug-resistant focal epilepsy. Improvements in memory, language, and attention occurred regardless of seizure response.

Cognition, Behavior, and Memory

V-050

Flexibility and robustness of contextual modulation of associative learning

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Perception is strongly influenced by experience and, by associating different stimuli with specific outcomes, animals can predict consequences and generate anticipatory behavioral responses. To study how learning reshapes behavior, we use different associative tasks in which animals have to discriminate among visual or olfactory cues to obtain a water reward. Mice have to learn to lick only for one type of trial. Previous results show that learning induced modulation of behavioral variables, including licking rate, inhalation and speed. To examine the robustness and flexibility of contextual modulation in associative learning, we performed two experiments. First, we assessed the persistence of learned odor and contextual associations by testing expert mice after 7 days without training. Providing an estimate of memory robustness Second, we investigated the flexibility of learned contextual associations using a double-reversal learning task. Mice were first trained to discriminate between two highly similar contexts until they reached expert performance. We then switched the rewarded context to the opposite one and, once mice learned the reversed contingency, switched the rewarded context back to the original one. This paradigm allowed us to assess the ability of mice to update previously acquired associations in response to changes in contextual contingencies. This behavioral characterization will allow us to design future experiments to explore the neural basis of memory.

Cognition, Behavior, and Memory

S-050

From threat perception to PTSD phenotypes: behavioral repertoire of mice in threat memories

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Post-Traumatic Stress Disorder (PTSD) is characterized by exacerbated threat responses related and unrelated to a traumatic experience. Contextual threat conditioning (CTC) is a well-established animal model based on the association of a neutral stimulus with an aversive one, leading to a threat memory. In PTSD, these memories exhibit pathological features —hypermnesia, overgeneralization and deficits in extinction and extinction retention— that differentiate them from non-pathological ones. Predatory Imminence Continuum (PIC) hypothesis proposes that animals display a behavioral repertoire considering a low, medium and high threat perception state. Considering this, CTC was conducted in male and female mice with different electroshock intensities —a “high threat” 0.60 mA and a “low threat” 0.10 mA—. Behaviorally, we assessed the acquisition, recall, generalization and extinction of the threat memory. By quantifying freezing, rearing, jumping, grooming, tail rattling and locomotion, minute per minute, a comprehensive individual behavioral profile across the entire experiment was described. Taking into account the PIC framework, group effects during each test were analyzed and individual responses were traced to delineate profiles of resilience and vulnerability, thereby enhancing the translational relevance of the model.

Cognition, Behavior, and Memory

D-050

Social isolation can bias judgement of ambiguous cues in adult zebrafish

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Cognitive bias in decision-making under ambiguity occurs in animals and humans, with individuals interpreting ambiguous stimuli positively (“optimistic”) and others negatively (“pessimists”). Here, we investigated whether social isolation affects judgement of ambiguous stimuli in adult zebrafish (Danio rerio, 6-8 months). We implemented a Go/No-Go task in a color-coordinated half-radial maze where fish learned to discriminate between positive (P) and negative (N) arms, and were tested in an ambiguous arm sharing elements of P and N arms. During habituation and training, distances traveled and latencies were measured to characterize locomotor and exploratory behaviour. Over testing, discrimination learning was assessed by the latencies to enter these arms, from which later a Judgment Bias Score was calculated to classify fish on a pessimistic/optimistic axis. Control social fish showed individual variability and two behavioral phenotypes: active animals that explored the maze extensively and more static animals that froze or made brief excursions. A week of social isolation increases the proportion of pessimistic vs. optimistic animals, shifting judgment of the ambiguous stimulus toward negative valence. Isolated fish also showed increased locomotor activity and longer latencies to explore unfamiliar maze areas. These results indicate that cognitive bias is individual and plastic, hence recent social interactions can rapidly alter the valence assigned to ambiguous stimuli.

Cognition, Behavior, and Memory

V-051

A computerized card-sorting task based on the Wisconsin paradigm: development and preliminary validation in Spanish-speaking Argentine adults

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Introduction. The Wisconsin Card Sorting Test (WCST) is a widely used measure of cognitive flexibility and executive function. Digital administration improves standardization and access but requires validation; no validated digital WCST-128 exists in Argentina. Objective. To develop and psychometrically evaluate a digital, Spanish-Argentine adaptation of the 128-card WCST. Method. The sample comprised 127 community adults (74.0% women; mean age 34.3, range 18-78) who completed a digital WCST-128 (PsychoPy). We examined descriptive statistics, interrelations among indices, reliability (KR-20 and Spearman-Brown split-half), sociodemographic effects, and performance across the task. Results. Internal consistency was adequate (KR-20=.79; split-half=.89). Error and category indices were strongly interrelated, whereas failure-to-maintain-set was relatively independent. Older age predicted poorer performance (more total and perseverative errors), as expected; no sex differences emerged. Response times were longer for errors than for correct responses. Accuracy increased from the first to the second half of the task (79.3% vs 82.5%; p<.001), indicating learning rather than fatigue. Conclusions. The digital WCST-128 showed adequate reliability and reproduced the expected worsening of performance with age, supporting its use as a scalable measure of cognitive flexibility.

Cognition, Behavior, and Memory

S-051

Same Performance, Different Neural Cost: Effects of Chronic Stress on Brain Oscillations During Selective Attention

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Chronic stress is a maladaptive response to persistent noxious stimuli that induces neurobiological alterations affecting cognitive processes. Behavioural performance often remains stable in such states, yet the neurophysiological mechanisms of selective attention require more precise characterisation. This study assessed the impact of perceived chronic stress on brain oscillations by analysing spectral density during an auditory selective attention task. Participants were classified into Low Perceived Stress (LPS) and High Perceived Stress (HPS) groups using the Perceived Stress Scale (PSS-14). Brain electrical activity was recorded with a 32-channel EEG system during a digits-in-noise (DiN) test, and signals were processed with MNE-Python. Time-frequency analysis used a complex Morlet wavelet (2–45 Hz) to estimate spectral power across groups. Behavioural performance showed no significant differences: both groups achieved a comparable number of correct responses. Electrophysiological analysis, however, revealed significantly higher spectral density in Beta and Gamma oscillations in the HPS group during correct trials, in both frontal and parietal regions. Individuals with high chronic stress therefore sustain performance equivalent to non-stressed individuals at a higher neural cost, since compensatory recruitment of high-frequency activity indicates that additional neural resources are needed to execute selective attention tasks.

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Inter and intra-individual variability of Information-theoretic and spectral EEG measures during autobiographical memory reconstruction

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Characterizing neural dynamics during autobiographical memory (AM) reconstruction is key to understanding how personal experiences are retrieved from distributed representations. We first identified an alpha-beta (9–21 Hz) spectral marker associated with AM reconstruction and then investigated whether this signature reflects stable individual characteristics or trial-specific neural dynamics by comparing it with information-theoretic measures. We recorded EEG activity from 33 participants during AM reconstruction. Using an intraclass correlation coefficient (ICC) framework with subject-level bootstrapping, we quantified the relative contribution of between- and within-subject variance for alpha-beta power, Shannon entropy (H) and Statistical Complexity (C). Preliminary analyses indicate that alpha-beta power is predominantly characterized by within-subject variance, suggesting that this signature of AM reconstruction is dependent on the specific episode being reconstructed. In contrast, H and C show higher between-subject ICC, indicating greater stability across episodes and stronger individual-level signatures. Building on this distinction, we will examine whether inter-individual differences in H and C relate to cognitive and affective profiles (working memory, processing speed, executive control and mood), while testing whether trial-level fluctuations in alpha-beta power relate to episodic phenomenology, including access latency, retrieval difficulty and amount of details

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Sex-Specific Effects of Gestational Environmental Enrichment and Postnatal Stress on Social Behavior and Lateral Septum Gene Expression in Adolescent Rats

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Gestational environmental enrichment (EE) has beneficial effects on neurodevelopment, whereas postnatal stress (PS) is a key factor in epigenetic programming that can shape later behavior. Both experiences can alter the expression of genes involved in the stress response and neuronal plasticity through changes in DNA methylation and other epigenetic marks. This study evaluated whether gestational EE buffers the effects of PS (maternal separation or male intruder exposure [MI]) on social behavior and spatial memory, and on the expression of Bdnf, Nr3c1, Dnmt3a, Tet1, and Tet2 in the lateral septum and hippocampus of adolescent male and female rats. At postnatal day 45, the three-chamber test showed an EE × PS interaction on sociability, with EE attenuating the effect of MI. EE and PS also had main effects on social novelty, with MI reducing and EE increasing the social novelty index. All groups improved spatial memory across trials, with no treatment differences. In the lateral septum, PS and EE × sex affected Bdnf expression, with higher levels in EE males exposed to MI. Nr3c1 and Dnmt3a showed an EE × PS × sex interaction, whereas Tet1 and Tet2 were unaffected. No significant effects were detected in the hippocampus. These results indicate that gestational EE and early-life stress interact to shape adolescent social behavior, with sex- and region-specific effects on gene expression.

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Theta Synchronization During the Resolution of Competing Memories: Exploring the Role of Prefrontal 5-HT2A Receptors

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Successful memory retrieval relies on the ability of hippocampal–prefrontal networks to select relevant information when competing memories are simultaneously activated. In the Object-in-Context (OIC) task, contextual information guides this selection between competing object–context associations. The medial prefrontal cortex (mPFC) is critically involved in this process, and serotonergic signaling through 5-HT2A receptors contributes to interference resolution. To investigate how these receptors influence hippocampal–prefrontal interactions, Wistar rats were implanted with electrodes in the ventral hippocampus (vHPC) and with tetrodes and infusion cannulas in the mPFC, allowing simultaneous local field potential recordings and local pharmacological manipulation. Previous findings showed that vHPC–mPFC theta coherence selectively increases during exploration of the contextually incongruent object, particularly at the beginning of exploratory bouts, supporting a role for theta synchronization in interference resolution. We are currently investigating whether prefrontal 5-HT2A receptor blockade alters this coordinated activity and its relationship with behavioral performance.

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Updating Full-Body Sport Motor Memory Through Sensorimotor Prediction Error and Reconsolidation

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Repetitive correction alone often fails to destabilize established engrams, producing proactive interference from the original habit during high-pressure performance. While human motor reconsolidation has been shown in simple laboratory tasks, its generalization to full-body sport skills remains unknown. This study tests whether a single prediction-error (PE) event can gate reconsolidation to update a consolidated suboptimal motor habit. We propose a three-day protocol in soccer players with an asymmetrical kicking pattern. Day 1: 3D motion capture (100 Hz, 39 markers) records bilateral kicking kinematics to identify a kinematic deviation in the non-dominant leg relative to the dominant-leg pattern. Day 2: after warm-up and baseline recalibration, players perform a single surprise kick with a disguised ultra-light ball generating sensorimotor PE, immediately followed by guided corrective practice with a standard ball. A control group performs equivalent correction without prior PE. Day 3 (24 h later): kinematic retest assesses whether the corrected pattern persists. We hypothesize that only the PE group will show stable kinematic correction at delayed retest, as the mismatch destabilizes the consolidated engram, allowing corrective kinematics to update the habit trace via reconsolidation, whereas controls will exhibit habit recurrence.

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Interaction between 5-HT2A and D1/D5 receptors signalling in the retrosplenial cortex during recognition memory consolidation

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The retrosplenial cortex (RSC) is particularly sensitive to changes that occur in mild cognitive impairment and Alzheimer's disease, making it crucial to understand the neuromodulatory systems that support its function. The RSC has been widely related to spatial and contextual memory, and also integrates sensory information into recognition memories, and previous work from our lab showed that both dopaminergic and serotonergic signalling in the RSC are required for object recognition (OR) memory consolidation. D1/D5 receptor activation reverses the amnesia induced by the ventral tegmental area inactivation, and 5-HT2A receptors (5-HT2AR) critically modulate OR memory processing. In this study, our aim was to analyze how these two systems interact in the RSC during memory processing. Thus, we used the Y-OR task combined with localized bilateral co-infusion into the RSC of SKF38393, a selective D1/D5 receptor agonist, and MDL, a selective 5-HT2AR antagonist, immediately after training and tested 24 h after. This co-infusion reversed the memory deficit induced by 5-HT2AR blockade. Conversely, 5-HT2AR agonist TCB-2 reversed the deficit induced by D1/D5 blockade with SCH23390, showing that activation of either system compensates for inhibition of the other. Together, these results show that dopaminergic and serotonergic signalling interact functionally in the RSC during recognition memory consolidation, supporting a model of crosstalk between these two neuromodulatory systems.

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Nicotine-induced conditioned place preference involves dynamic changes in DNA methylation and hydroxymethylation in the zebrafish brain

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DNA modifications are fundamental for synaptic remodelling in memory-related processes. Cytosine methylation and demethylation marks regulate gene expression and play key roles in addiction-like behaviours. DNA methyltransferases (DNMTs) catalyse methylation of DNA-cytosines (5mC), while TETs enzymes catalyse DNA demethylation to 5-hydroxymethylcytosine (5hmC) and further oxidations. 5hmC is stable and abundant in neurons and regulates gene expression. We examined whether conditioned place preference (CPP) to nicotine regulates 5mC and 5hmC levels in the zebrafish brain. Levels of TET1 mRNA were upregulated while levels of TET2, GADD45, DNMT, and MeCP2 mRNAs were downregulated in the zebrafish brain trained in the nicotine-CPP task. Specific nuclei of the reward circuit showed increases in the 5hmC mark in neuronal subpopulations induced by nicotine-CPP. Other reward structures, showed decreased numbers of cell nuclei containing high levels of 5mC with no changes in the number of cell nuclei showing high levels of 5hmC. Nicotine-CPP increased 5hmC levels and decreased 5mC levels in the whole brain of zebrafish. Here, we demonstrate that the establishment of nicotine-CPP in the zebrafish brain is associated with changes in DNA methylation marks in neurons of the reward circuit, including the upregulation and downregulation of the 5mC mark, along with a net increase in the 5hmC mark. The specific changes in the methylation mark profile depend on the reward structure examined.

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Ultrasonic Vocalizations and Memory Dynamics

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Many vertebrates use species-specific vocalizations to communicate information regarding identity, social status or mood, likely future behavior, environmental conditions, and to facilitate social interactions and spatial perception. It is intriguing to consider whether the emission of different types of information could reflect cognitive processing. However, little is known about the role of vocalizations in the dynamics of memory. Long-Evans rats have long been used as an animal model for studying spatial memory in laboratory mazes. They are social animals, and vocal communication is a regular feature of their social interactions and emotional states. They can emit audible sounds, but they mainly communicate in the ultrasonic frequency range. However, few studies have characterized rat ultrasonic vocalizations (USVs) in individual rats performing a behavioral task. One study reported USVs between 30 and 80 kHz associated with rat speed (Laplagne D. A. and Costa M. E., 2016), while another group found 50-kHz calls during spontaneous spatial exploration (Costa G. et al., 2021). Therefore, we began characterizing USVs in an X-maze while the rat learns and memorize the location of a reward. Preliminary results show an increase in the number and diversity of calls during spatial learning, particularly after reward consumption. We believe that this study could contribute to the field of neuroscience by introducing vocalizations as a potential form of memory externalization.

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Evaluation of Bayesian confidence markers in reinforcement learning

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Confidence in decision-making is a metacognitive process estimating the probability of correct choices and regulating the exploration-exploitation balance. The Bayesian Confidence Hypothesis (BCH) posits this follows probabilistic rules with three signatures: (1) calibration between certainty and accuracy, (2) differential confidence modulation based on discriminability (higher in correct responses, lower in errors), and (3) intermediate confidence under neutral evidence. Its validity in reinforcement learning remains scarcely explored. This pre-registered study evaluated these signatures in a two-armed bandit task (30 adults, 600 trials/subject). Participants chose options with Beta reward distributions, reported confidence (1–4 scale) before feedback, and earned 0–100 points. Analyses utilized mixed logistic regression, ANOVAs, and t-tests. Signature 1 was confirmed: confidence predicted performance (Odds Ratio=3.87, $t(29)=9.98$, $p<.001$). Signature 2 was partially confirmed: confidence increased in correct trials ($\eta^2G=0.311$) but didn't decrease in errors ($\eta^2G=0.034$), revealing overconfidence and valence biases. Signature 3 was unconfirmed: participants showed underconfidence lacking information ($M=0.39$ vs. 0.5, $p=.045$), suggesting adaptive early exploration. Confidence acts as a dynamic metacognitive marker in reinforcement learning, with systematic deviations from normative models.

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Early-life experiences modulate exploratory behavior and reward consumption in adolescent C57BL/6 mice.

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Early-life experiences during rearing are key modulators of behavioral development. We aimed to examine whether sex and rearing conditions modulate exploratory behaviors and hedonic sucrose consumption in adolescent C57BL/6 mice. A factorial ANOVA 2 (Sex) × 5 (Rearing Condition: single mother [SM], biparental [BP], SM with environmental enrichment [SM-Ea], BP with environmental enrichment [BP-Ea] and communal rearing [CC]) factorial design was used to examine behaviors in the Concentric Square Field (CSF) and sucrose consumption in a preference test. Preliminary analyses indicated that CC adolescents showed greater sucrose consumption than all other groups. In addition, SM-Ea and BP-Ea adolescents showed higher sucrose intake than their respective non-enriched peers. In the CSF, a main effect of Ea was observed: SM-Ea and BP-Ea adolescents displayed higher frequencies of entries into transitions and open-field zones. Regarding sex effects, females showed a higher frequency of entries into the light and bridge zones, and a greater sucrose preference than males. Overall, these preliminary findings suggest that greater social complexity and enriched environment are associated with increased preference for natural rewards and enhanced exploratory behaviors in novels contexts. These distinct behavioral profiles suggest that early-life experiences may differentially shape these behavioral domains. Further analyses are ongoing to confirm and extend these findings.

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V-055

Dynamic Difficulty Adjustment in Child Cognitive Training: Converging Evidence Across Two Countries

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For the past 15 years, we have used the web-based cognitive assessment and training platform Mate Marote with children aged 4 to 8. An initial school-based study in Navarra, Spain, showed that a dynamic difficulty progression model effectively enhanced attention. A second study, conducted again in the same school, evaluated a revised version of this progression designed to overcome its limitations. In the present work, we compare both models. Both approaches adapt to the player's initial level; however, the original model slows progression after reaching a balance point, whereas the revised model continuously adjusts task difficulty. We hypothesized improvements in executive functions from pretest to posttest, with greater gains under the revised model. Results showed attentional improvements in both groups, while only the revised model produced additional gains in logical reasoning, cognitive flexibility, and working memory. These findings were replicated with a local school sample in Tandil, Buenos Aires, Argentina.

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NAT10 Inhibition as a Potential Modulator of Long-Term Memory Consolidation in Drosophila melanogaster

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Long-term memory (LTM) consolidation depends on protein synthesis and cytoskeletal remodeling. The acetyltransferase NAT10 may contribute to these processes via acetylation of microtubules and mRNA. Inhibition of NAT10 (iNAT10) with Remodelin has been shown to prevent neurodegeneration in tauopathy models, yet its role in learning and memory remains unexplored. Here, we ask whether iNAT10 facilitates LTM consolidation in Drosophila, using an under-predation training paradigm with the jumping spider Menemerus semilimbatus. We first established a weak-training protocol by exposing w1118 flies to the predator for 1 h and assessing memory retention 24 h later. Unlike the established strong-training protocol (2 h), weak training failed to induce LTM. Preliminary results indicate that post-training administration of Remodelin can facilitate memory consolidation following weak training, as assessed by kymographic analysis of population motor activity. To further characterize the effects of iNAT10 on memory consolidation, we will assess an additional defensive strategy elicited by spider predation: place preference. Specifically, 24 h after training, flies will be tested for their preference between a compartment previously associated with the predator and one inaccessible to it. These findings establish a behavioral framework for investigating the role of NAT10 in LTM consolidation, and whether this mechanism can be harnessed to rescue or enhance memory in pathological models.

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Movement-Onset Theta Modulation in Sparse Scalp EEG Tracks Spatial Prediction Error during Memory-Guided Virtual Navigation

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Spatial navigation deficits emerge early in Alzheimer's disease (AD), driving the search for non-invasive electrophysiological markers of cognitive mapping. While intracranial hippocampal recordings link low- and high-theta activity to movement initiation in spatial virtual navigation, whether non-invasive scalp electrophysiology (EEG) reflects related markers linked to spatial accuracy remains unclear. We recorded 8-channel scalp EEG from 20 healthy adults (20–65 years) who performed a virtual navigation task using remembered locations without visual cues. Participants showed varied prediction accuracy. Low-frequency activity was expressed predominantly over posterior regions. Critically, right-parietal P4 exhibited accuracy-dependent low-theta (2–5 Hz) dynamics: participants with low-error prediction were associated with increased power at movement onset relative to subsequent movements, whereas high-error participants showed a decline. Higher theta (6–9 Hz) showed weaker differentiation. Trial-level analyses (~400 trials) confirmed that movement-onset low-theta modulation predicts navigation accuracy. These findings suggest that movement-onset low-theta dynamics can be detected via sparse scalp EEG to track spatial accuracy, offering a candidate marker for studying age-related cognitive decline in early-stage AD. Corresponding author: Jose A. Fernandez-Leon (jafernandez@intia.exa.unicen.edu.ar) Funding: IBRO Rising Stars Award granted to JAFL (RS-4691970824).

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Neural Dynamics of Prefrontal Cortex during Spatial Navigation in a Virtual Reality Environment

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The medial prefrontal cortex (mPFC) is a key regulator of behavioral adaptation. Its subregions, the prelimbic (PL) and infralimbic (IL), are known to play distinct roles in the expression and extinction of memories. To study these dynamics, we optimized a Virtual Reality (VR) platform integrated with in vivo electrophysiology to record mPFC activity during goal-directed behavior. Male and female C57BL/6 mice (3-4 months old) underwent a dual training protocol. For appetitive training, mice were head-fixed on a rotating cylinder within a VR environment, simulating an infinite corridor where a distinct tone signaled a 15µl water reward in specific zones. Following habituation and training, acute recordings were performed, targeting the PL and IL subregions. Initial implementation of this setup allowed for the simultaneous collection of behavioral and electrophysiological data. We report the acquisition of neural signals from the PL and IL while mice navigated the virtual environment. Preliminary analysis indicates the presence of both spiking and oscillatory activity synchronized with the animal's movement and task transitions. These results confirm the feasibility of the experimental design for recording mPFC dynamics in head-fixed mice. This platform will be used to further investigate the neural representations of memory processes and the interaction between these prefrontal subregions.

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Hippocampal astrocytic GAT-3 blockade impairs aversive memory dynamics

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Astrocyte–neuron communication is essential for synaptic function and behavior. Astrocytes express neurotransmitter transporters that regulate extracellular neurotransmitter levels. GAT-3 mediates GABA uptake and contributes to inhibitory tone, thereby regulating hippocampal neuronal excitability. Here, we investigated the role of hippocampal GAT-3 in aversive inhibitory avoidance (IA) memory. To assess its role in memory consolidation, SNAP-5114, a GAT-3 inhibitor, was administered into the rat hippocampus at different time points around training. SNAP administered 15 min before or 30 min after training impaired long-term memory (LTM) in female rats, whereas more distant administration times had no effect. Administration 15 min before training in males confirmed the findings observed in females. We next examined whether GAT-3 activity was required for LTM expression. SNAP administered 15 min before the IA test, 24 h after training, impaired LTM expression in both sexes. Finally, SNAP administered 15 min before the short-term memory (STM) test, 2 h after training, impaired STM expression in males but, as expected, did not affect subsequent LTM. Together, these findings indicate that astrocytic GAT-3 contributes to the consolidation and expression of aversive memory in both sexes, supporting a role for astrocytic neurotransmitter transporters in memory dynamics and motivating further investigation of their contribution to memory persistence and modification.

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D-056

Long-Term Effects of Prenatal Ethanol Exposure on the Hippocampal-Dependent Memories: A Systematic Review

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Prenatal alcohol exposure (PAE) has detrimental effects on the hippocampus (HC), a structure involved in learning, memory, and spatial navigation processes. Given that PAE may induce damage that persists in the long term, the aim of this review was to examine the effects of PAE on the HC and HC-associated memories in later stages of life. A literature search was conducted in PubMed in May 2026 using terms related to ethanol, prenatal exposure, hippocampus, neurodevelopment, and memory. Data extraction and risk-of-bias assessment followed PRISMA guidelines. The included studies comprised research conducted in animal models that assessed HC-dependent memories using various neuropsychological and behavioral tests, along with their neurobiological correlates. Results showed that PAE negatively affects HC-dependent memories, with effects varying by dose, drinking pattern, frequency, duration, and timing of exposure. Greater alterations were associated with higher ethanol doses and binge-drinking-like exposure, whereas lower doses showed absent or partial effects. Significant behavioral, structural, and molecular differences were found between males and females. These findings highlight the relevance of HC damage as a potential contributor to the cognitive impairment associated with PAE and underscore the need for further research to elucidate how these alterations contribute to cognitive deficits and to improve early detection, diagnosis, and prevention strategies.

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V-057

CHRONIC Baccharis grisebachii DECOCTION REDUCES ANXIETY-LIKE BEHAVIOR IN FEMALE MICE

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Baccharis grisebachii Hieron (Asteraceae) is a South American medicinal plant whose effects on the central nervous system remain largely unexplored. UHPLC–PDA–OT-MS/MS tentatively identified several compounds: 12 flavonoids, 11 cinnamic acid derivatives, one coumarin, one stilbene, and two other phenolics. We evaluated the effects of chronic B. grisebachii decoction (DecBg) consumption on anxiety-like behavior in female C57BL/6J mice. From postnatal day 21, mice received water (CON) or DecBg (10% w/v) for 50 days. Anxiety-like behavior was assessed by the open field test (OFT) and elevated plus maze (EPM) at the same estrous cycle stage. Total distance traveled did not differ between groups in either test (OFT, p=0.2578; EPM, p=0.1507), indicating no major changes in locomotor activity. In the OFT, DecBg mice traveled a greater distance (65.26%; p=0.0255) and entered more frequently (51.45%; p=0.0457) into the central zone, spent more time in the intermediate zone (55.84%; p=0.0499) and central+intermediate zones (60.44%; p=0.0133), and less time in the peripheral zone (-12.71%; p=0.0133) than CON mice. In the EPM, DecBg mice spent more time in the open arms (101.32%; p=0.0489), less time in the closed arms (-11.55%; p=0.0141), and showed increased edge exploration (p=0.0356). These findings indicate that chronic consumption of B. grisebachii decoction produces an anxiolytic-like behavioral profile without altering overall locomotor activity (PIP-0390/23; PIC-UNSJ 1576/26-R).

Cognition, Behavior, and Memory

S-056

Quitting together: Effects of group extinction on nicotine reinstatement.

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Zebrafish exhibit social behaviours, such as shoaling, making them an attractive model for investigating how social interactions influence behaviour. Here, we assessed the rewarding effects of nicotine on zebrafish shoaling behaviour, examined whether the shoal influences the rewarding properties of nicotine. In this study, we have developed a nicotine extinction and reinstatement protocol to later assess how the presence of conspecifics can alter the way nicotine reinstatement takes place. We found that visual interaction with conspecifics during the extinction phase of a reinstatement paradigm does not disrupt the drug-environment association, whereas conspecific presence during the reinstatement challenge abolishes nicotine seeking behaviour. According to these results, nicotine appears to be strong enough to elicit sustained preference despite the presence of conspecifics during extinction but not so strong as to circumvent the distracting factor that arises when conspecifics are present during the reinstatement challenge. Interestingly, when animals undergo grouped extinction in the same tank, implying direct interaction and not only visual social stimuli, nicotine reinstatement is abolished. Our results appear to indicate that the mere view of conspecifics is not enough to counterbalance an appetitive memory of a drug of abuse such as nicotine and that being part of a group is much more disruptive to said memory in a gregarious animal such as the zebrafish.

Cognition, Behavior, and Memory

D-057

Temporal dynamics of frustration: Prefrontal oscillations and licking behavior during unexpected reward loss

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Consummatory Successive Negative Contrast (cSNC) is characterized by reduced consumption following an unexpected reward loss. The resulting aversive emotional state is known as frustration. Although corticolimbic circuits are involved, it remains unclear whether their participation is immediate or emerges later. Examining the temporal dynamics of frustration may improve our understanding of mechanisms involved in its expression and recovery. In two experiments, rats performed a cSNC task with 5-min access to sucrose solution. In Exp. 1, licking was recorded with an automated system. In Exp. 2, LFP (Local Field Potential) were recorded from the anterior cingulate (ACC) and infralimbic (IL) cortices. Alpha (7–12Hz), beta (13–30Hz), and gamma (30–100Hz) activity were analyzed during the first postshift session. Our results show that downshifted rats significantly reduced licking relative to the unshifted group from the second minute onward. Furthermore, downshifted rats increased alpha and decreased beta and gamma activity from the first minutes in ACC and IL. Together, the parallel temporal evolution of licking behavior and prefrontal (PFC) oscillatory activity suggests that frustration emerges early after reward devaluation and that the ACC and IL may be involved in this response. Future studies should examine additional postshift days to characterize the neural dynamics of recovery and employ cell-specific manipulations in the PFC and amygdala to determine their causal roles.

Cognition, Behavior, and Memory

V-058

Adolescent binge-like ethanol intake increases voluntary ethanol consumption in adulthood regardless of subsequent ethanol exposure

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Adolescent binge drinking is associated with later alcohol-related problems. It is, however, still unknown whether it holds a causal role with the emergence of problematic drinking or how it interacts with alcohol exposure in early adulthood. We assessed whether binge-like ethanol self-administration during adolescence, coupled or not with an intensive ethanol exposure in early adulthood, increases voluntary ethanol consumption in later adulthood. Thirty-seven male Wistar rats were exposed or not to nine 2-h binge-like ethanol self-administration sessions (8-10%; postnatal day 27-45, PD27-45). At PD61-65, they received intragastric ethanol (0.0 or 1.5 g/kg, three times daily). Ethanol intake was subsequently measured across six 24-h two-bottle choice tests (8% ethanol vs. water; PD75-87). Adolescent binge exposure increased adult ethanol intake (4.5-6.5 vs. ~2 g/kg/day in controls; $F_{1,32}=32.77$, $p<.001$, $\eta^2=.51$) and ethanol preference ($F_{1,32}=31.16$, $p<.001$, $\eta^2=.49$). Adult ethanol exposure enhanced intake across sessions (adult exposure × session: $F_{5,160}=2.88$, $p<.05$, $\eta^2=.08$), but did not significantly interact with adolescent binge exposure. These results indicate that binge-like ethanol drinking during adolescence produces a robust increase in voluntary ethanol consumption in adulthood that is independent of intensive ethanol exposure in early adulthood.

Cognition, Behavior, and Memory

S-057

Social Modulation of Intersexual Aggression in Cichlasoma dimerus

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Aggressive behavior plays a key role in territory establishment and social organization across vertebrates. Cichlasoma dimerus is a Neotropical cichlid with a marked social hierarchy, in which dominant individuals display aggressive behaviors toward subordinates. While intrasexual agonistic interactions have been extensively described, intersexual aggression remains poorly characterized. Here, we characterized sex differences during intersexual agonistic encounters between dominant males and females. Dyadic encounters lasted 1h, during which aggressive and submissive behaviors were quantified. Males displayed higher aggression ($p = 0.02$) and won all encounters, whereas females exhibited more submissive behaviors ($p = 0.03$). We further investigate whether these interactions are modulated by an audience. As a first step, to test whether virtual stimuli can function as social audiences, we quantified the number of aggressive displays and preference index. Focal individuals were exposed to social and non-social visual stimuli, displaying distinct behavioral responses and characteristic social behaviors toward social and aggressive stimuli. This supports the use of virtual audiences to investigate how social exposure modulates intersexual aggression. We are now comparing behavioral responses and brain activation following dyadic intersexual encounters performed with or without an audience, providing insight into the neural mechanisms underlying the social modulation of aggression.

Cognition, Behavior, and Memory

D-058

Characterization of learning-induced changes in plasticity-related gene expression in the retrosplenial cortex following a novel object recognition task

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Several studies have demonstrated that the retrosplenial cortex (RSC) is strongly implicated in navigation and contextual memory. Previously, we found that the RSC is also required for the processing of an object-recognition memory (ORM) through local pharmacological inhibition of transcription and translation within the RSC. Moreover, our findings in rodents showed that the RSC is required for ORM consolidation and retrieval only when it is intact during acquisition. Taking these results into account, we aimed to assess changes in plasticity-related gene expression and understand their role in the consolidation of the ORM. For this purpose, animals were trained in a novel object recognition task using a Y-maze, and the RSC was dissected and homogenized for Western blot analysis of plasticity-related gene expression.

Cognition, Behavior, and Memory

V-059

Longitudinal Effects of Gestational Restraint Stress on Maternal Behavior and Offspring Social Phenotypes: Uncovering Stress Resilience and Susceptibility

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Gestational stress alters the trajectory of brain development, leading to changes in cognitive and socioemotional functions. However, individual responses to stress vary, with some offspring exhibiting resilience while others display heightened vulnerability. To investigate the mechanisms underlying stress resilience, we employed a gestational restraint stress model in which pregnant CF1 females were subjected to a movement restriction protocol from gestational day 10 to 19. Maternal body weight gain was tracked throughout pregnancy, revealing significant weight variation between stressed and non-stressed dams. Following delivery, early maternal care behaviors, including pup-directed care, self-grooming, and time out of the nest, were evaluated during the first five postpartum days. Once offspring reached adulthood, they underwent several behavioral tests. Immediately following an acute restraint of 45 minutes, the splash test was used to classify animals into resilient and susceptible phenotypes. Additionally, social interaction was evaluated using the three-chamber test to determine social preference over a novel object, differentiating resilient from susceptible individuals. Subsequently, social memory was assessed by exposing subjects to a familiar versus a novel mouse in the three-chamber paradigm to evaluate whether social recognition performance differed according to stress resilience phenotype.

Cognition, Behavior, and Memory

S-058

Childhood Invalidating Environments Are Associated With Dissociative Symptoms and Resting-State EEG Power in Argentine Adults: A Pilot Study

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Adverse childhood experiences are robustly linked to mental health difficulties, with perceived emotional invalidation emerging as a key mechanism linking diverse forms of early adversity. Prior research has reported resting-state EEG alterations in this population with emotional invalidation. In the current pilot study, 10 general-population participants completed the ICES (Invalidating Childhood Environment Scale) and the DES-M (Dissociative Experiences Scale), followed by a 5-minute resting-state EEG recording, including both eyes-open and eyes-closed conditions. Relative power in alpha and beta bands was analyzed. Results indicated a strong association between dissociative symptoms and mother-related perceived invalidation, absorption- dissociative traits and depersonalization. Total scores for maternal invalidation correlated with increased beta during eyes-closed, suggesting persistent hyperactivation and atypical alpha-beta desynchronization. Maternal invalidation also correlated with increased beta during eyes-open, reflecting heightened alertness. Increased alpha during eyes-open correlated with higher dissociation and absorption, suggesting attentional disconnection and regulatory difficulties consistent with previous reports. These preliminary findings indicate that invalidation and dissociation exhibit differentiated resting-state EEG profiles, with beta increases possibly marking hypervigilance and alpha increases indexing dissociative absorption

Cognition, Behavior, and Memory

D-059

AUDITORY MODULATION OF BRAIN OSCILLATIONS AND CONSCIOUS EXPERIENCE DURING WAKEFULNESS

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Altered states of consciousness (ASCs) involve transient changes in perception, cognition, emotion, and the sense of self. Although low-frequency activity is commonly associated with reduced consciousness, recent evidence indicates that conscious experience can persist across markedly different oscillatory regimes, including states with prominent delta activity, suggesting that spectral dynamics should be considered together with measures of neural complexity. This study investigated whether binaural-guided audios from the Monroe Institute's Gateway Experience modulate brain activity during wakefulness and whether these changes are associated with subjective alterations in consciousness. Twenty healthy adults aged 20–30 years completed training with selected audios and subsequently underwent an approximately one-hour, 32-channel EEG recording. Signals were preprocessed using notch, band-pass and low-pass filters and independent component analysis for artifact removal. Power spectral density, Lempel–Ziv complexity, and Shannon spectral entropy were calculated to characterize frequency-specific activity, signal diversity, and spectral organization. Subjective experience was assessed using the 11D-ASC. Results will be interpreted in light of current models proposing that oscillatory activity and neural complexity provide complementary information for characterizing conscious brain states.

Cognition, Behavior, and Memory

V-060

Identification of pharmacological treatments for behavioral defects in Drosophila models of RASopathy

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RASopathies are a group of genetic disorders caused by mutations in genes that primarily affect the RAS/MAPK signaling pathway. These disorders are characterized by clinical features such as cutaneous and skeletal manifestations, short stature, a high incidence of leukemias and intellectual disability. Aiming to identify pharmacological therapies for cognitive impairments, we evaluated the impact of different mutations (cswA72S, SOSA552G, and Rasv12) on behavioral variables using Drosophila as a model, and subsequently, assessed the effect of a pharmacological treatment. Using a contextual paradigm, we analyzed two cognitive processes: context habituation (defined as the progressive decrease in response to repeated exposure to a novel environment) and recognition memory (the ability to discriminate novel stimuli from familiar ones). These processes were quantified using behavioral indices and locomotor activity tracking. Our results revealed differences in the behavioral phenotypes of cswA72S, SOSA552G, and RasV12 compared with control genotypes. Also, the dose-response curve using rosuvastatin (a pharmacological strategy to negatively modulate RAS/MAPK signaling) demonstrated concentration-dependent effects. These preliminary results allow us to conclude that the fly models of RASopathies are sensitive enough to detect behavioral phenotypes and effects in the pharmacological assays.

Cognition, Behavior, and Memory

S-059

BOOSTING THE AGING BRAIN: COMBINED EFFECTS OF INTRAMUSCULAR IGF-1 AND OMEGA-3 FATTY ACIDS ON COGNITION AND ANXIETY

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Insulin-like growth factor 1 (IGF-1) is a pleiotropic hormone essential for neuroprotection, synaptic plasticity, and metabolic homeostasis; its age-related decline is linked to cognitive decline and mood disturbances. Omega-3 fatty acids (EPA and DHA) also exert neuroprotective effects via lipid mediators regulating immune and inflammatory responses. Despite their individual benefits, the potential synergy of IGF-1 gene therapy with dietary Omega-3 remains unexplored, particularly regarding sex differences in middle age. Twelve-month-old male and female Sprague Dawley rats received intramuscular injections of an adenoviral vector encoding IGF-1 cDNA (RAd-IGF1) or vehicle, with or without daily oral Omega-3 for 6 months. We assessed treatment interplay across behavioral and molecular domains using marble burying, novel object recognition, Barnes maze, and forced swim tests, and collected brain tissue to study microglial reactivity as a mechanism. IGF-1 treatment modulated recognition memory and spatial learning, reduced anxiety-like behaviors, and mitigated behavioral despair, with distinct patterns between sexes. We are analyzing whether Omega-3 co-administration potentiates these effects via the neuroinflammatory environment, correlating behavioral gains with microglial phenotype shifts. These findings highlight sex-dependent benefits of peripheral IGF-1 gene delivery and support combined nutritional strategies against age-related cognitive and affective impairments.

Cognition, Behavior, and Memory

D-060

Long-lasting enhancement of aversive memory by acute high-dose ethanol: involvement of VTA α7nAChRs and mPFC D1R signaling

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Acute ethanol intoxication is mainly associated with memory impairments, yet the circuit and receptor mechanisms through which it modulates aversive memory formation remain poorly understood. Here we report that a single high dose ethanol exposure (2.5 g/kg) produces a robust, long-lasting enhancement of aversive memory formation in rats, persisting for at least 21 days in an inhibitory avoidance task. We found that this enhancement depends on α7 nicotinic acetylcholine receptors (α7nAChRs) in the ventral tegmental area (VTA), as local blockade with methyllycaconitine (MLA, 5 ug/ul) abolished the effect. We further show that pharmacological activation of dopamine D1 receptors (D1R) in the medial prefrontal cortex (mPFC) with SKF-38393 (6.25 ug/ul) restored ethanol-induced memory enhancement following intra-VTA α7nAChR antagonism, suggesting the involvement of mPFC D1R signaling in this pathway. Together, these results provide a mechanistic framework for understanding how acute intoxicating ethanol exposure can produce aversive memory enhancement. Acknowledgements: University of Buenos Aires (UBACyT grant to VP), International Society for Neurochemistry (CDG grant to VP).

Cognition, Behavior, and Memory

V-061

NREM Sleep Duration, Fast Spindles, and Face Recognition Memory

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Non-rapid eye movement (NREM) supports episodic memory consolidation, but its contribution to face recognition tasks remains unclear. We examined whether a short nap and its electrophysiological characteristics influenced lineup performance. Thirty-five participants encoded ten unfamiliar faces and then completed either a 40-minute nap followed by 30 minutes of quiet wakefulness (n = 14) or 70 minutes of quiet wakefulness (n = 21). They subsequently performed ten target-present lineups. Recognition accuracy, false identifications, and incorrect rejections did not differ between groups. Within the sleep group, greater total NREM (N2+N3) sleep duration was associated with fewer correct identifications, an effect that remained significant after correction for multiple comparisons. Conversely, greater fast spindle power during N3 was associated with more correct identifications, although this relationship did not survive correction. No other sleep stage or oscillatory measure was significantly related to performance. These findings suggest that a short nap does not generally improve face recognition, but that the duration of individual sleep stages and specific aspects of sleep microstructure may have distinct and potentially opposing associations with performance. The negative association with NREM duration may reflect sleep inertia, whereas fast spindle activity could contribute to the consolidation of facial representations.

Cognition, Behavior, and Memory

S-060

Predator–Prey Categorization Beyond Retinal Position

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The crab Neohelice is both prey to larger animals (e.g., seagulls) and a predator of smaller conspecifics. Experiments conducted on a horizontal substrate showed that, in response to the same moving dummy, crabs may either flee from or pursue it, depending on whether the dummy moves at ground level or above the substrate. Based on these observations, it was hypothesized that the crab uses a simple rule to categorize visual stimuli: stimuli perceived in the dorsal region of the retina are categorized as dangerous, whereas those perceived in the ventral region are categorized as prey. However, the natural habitats of Neohelice often have considerable slopes. Consequently, when a crab is positioned downslope, it may view a small object moving along the ground with the dorsal part of its retina. Conversely, when positioned upslope, it may view an object moving slightly above the ground with the ventral part of its retina. These conditions challenge the hypothesis that predator–prey categorization relies solely on the retinal position of the stimulus. To test this, we moved a dummy over an inclined substrate. Our results show that crabs can pursue the dummy even when it moves above the level of their eyes, and flee from it even when it moves below them. These finding challenge the simple hypothesis that predator–prey categorization is determined solely by retinal position and indicate that additional visual or contextual cues contribute to the categorization of moving objects.

Cognition, Behavior, and Memory

D-061

Effects of maternal peripartum stress on anxiety-like, depressive-like, social and cognitive behaviour in the offspring

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Peripartum depression (PPD), a major depressive disorder subtype affecting 10–20% of women worldwide, compromises maternal well-being and offspring neurodevelopment. Despite its high relevance, the mechanisms by which this condition impacts the fetus and the newborn are unclear. To assess how PPD affects the offspring, we used a murine PPD model that combines chronic mild unpredictable stress and maternal separation during pregnancy and postpartum. At 8 weeks old, male and female offspring born to PPD or control dams underwent a battery of tests to evaluate depressive-like, anxiety-like, social, and cognitive behaviour. Our preliminary findings revealed that males showed more anxious-like behaviours in the open field and novelty suppressed feeding, while in females only a trend was observed. No statistically significant differences emerged in the other behavioral domains, although treatment and sex-specific trends were observed in depressive-like behaviours and cognitive tests: PPD females, but not males, showed reduced immobility time compared to controls in the tail suspension and forced swim tests, possibly reflecting higher resilience to behavioral despair, whereas PPD males showed a trend toward working memory impairment. Together, these findings suggest that PPD affects offspring behavior in a sex-specific manner. Future experiments will focus on exploring the underlying mechanisms of these differences.

Cognition, Behavior, and Memory

V-062

Slow waves during 20-minute naps and the consolidation of declarative memory

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Sleep supports declarative memory consolidation, a benefit largely attributed to slow-wave sleep (SWS). Short 20-min naps contain little SWS and are dominated by stage N2, yet their effect on long-term retention is poorly characterised. Thirty-one healthy adults learned five nonsense syllable pairs embedded in a multimodal context (10 training trials with feedback). Sixteen took a polysomnographically recording of a 20-min afternoon nap; fifteen stayed awake for an equivalent interval performing a distracting task. Memory was tested on Day 1 and Day 7. The nap group showed less memory decay than the wake group (Welch t-test, p=0.044, d=0.77). Only four nappers reached stage N3. None of 14 prespecified sleep predictors, spanning spectral power, slow-wave morphology, spindle density and slow-wave-spindle coupling, was associated with memory change. Therefore, a brief nap predominantly characterized by N2, was associated with reduced forgetting across seven days, without identifiable oscillatory correlates

Cognition, Behavior, and Memory

S-061

Neuromodulatory bases of behavioral specialization in honey bee dance followers (Apis mellifera)

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In the honey bee (Apis mellifera), the waggle dance coordinates colony foraging by recruiting followers that specialize in distinct resources (nectar vs. pollen). While the neurobiology of dancers has been extensively investigated, the neuromodulatory mechanisms underlying behavioral biases in dance followers remain largely unexplored. Here, we investigated how individual differences in dance following relate to gustatory responsiveness and neuropeptidergic signaling across the nervous system. We assessed sugar sensitivity in situ using proboscis extension response (PER) assays during dance following in observation hives. Nectar followers exhibited the highest sugar sensitivity (lowest response thresholds), non-followers displayed intermediate sensitivity, and pollen followers showed the lowest sensitivity (highest thresholds). To elucidate the molecular correlates of these differences, we quantified the expression of neuropeptides and receptors linked to appetitive motivation (NPF, sNPF, sNPFR, TK, and TKR) in antennae, antennal lobes, and protocerebrum via RT-qPCR. Transcript levels varied significantly according to follower profile in a tissue-dependent manner, evidencing coordinated regulation between the sensory periphery and central brain areas. Together, these findings suggest that dance following involves neuromodulatory adjustments across the nervous system, where neuropeptide pathways may play a role in modulating sensory thresholds relevant to foraging tasks.

Cognition, Behavior, and Memory

D-062

A SHORT NAP IMPROVES MEMORY ACQUISITION BUT NOT CONSOLIDATION IN A SCHOOL SETTING

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Sleep deprivation is prevalent among high school students and negatively affects academic performance. During sleep, recently acquired memories are reactivated and consolidated, while slow-wave sleep also promotes synaptic downscaling, restoring the capacity for new encoding. Here, we assessed whether a short nap in the school setting improves both memory consolidation and subsequent memory acquisition. Students were randomly assigned to a Nap or a Wakefulness group. Participants first learned the content of a class, then either napped or remained awake, and afterwards learned the content of a second class. Consolidation of the first class was evaluated before and after the nap/wakefulness period, and acquisition of the second class was assessed immediately after learning it. Results showed that the nap did not improve consolidation of information acquired before the nap, but it did enhance acquisition of information learned afterwards. These findings suggest that, in a school setting, a short nap may not be sufficient to promote memory consolidation, but can still benefit the encoding of new information, highlighting a dissociation between its effects on different memory processes.

Cognition, Behavior, and Memory

V-063

A DAYTIME NAP FACILITATES DECLARATIVE MEMORY ENCODING: EVIDENCE FROM A PAIRED-ASSOCIATE TASK

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Sleep contributes to memory processing, and growing evidence suggests that even brief naps can benefit memory encoding. During wakefulness, the continuous encoding of information leads to a progressive increase in synaptic strength, which is thought to constrain further learning. According to the synaptic homeostasis hypothesis, sleep —particularly slow-wave sleep— promotes a global downscaling of synaptic strength, restoring the capacity for subsequent encoding. Here, we investigated whether a short nap enhances memory acquisition in a laboratory setting. Healthy adults were randomly assigned to a Nap or a Wakefulness group and performed a word-sound paired-associate learning task. Participants in the Nap group showed significantly higher performance in the learning task than those in the Wakefulness group, indicating that a short nap facilitates memory acquisition. These findings support the idea that brief naps may constitute an effective strategy to enhance learning capacity, with promising implications for educational and everyday-life settings.

Cognition, Behavior, and Memory

S-062

Regional glial alterations associated with systemic PCPV2 exposure in adult rats

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PCPV2 is a toxic protein from the perivitelline fluid of the invasive freshwater snail Pomacea canaliculata. Although neurological effects have been reported following systemic administration of purified PcPV2, its effects on the mammalian brain remain poorly understood. Our previous behavioral analyses showed that a single intraperitoneal administration of PcPV2 (250 µg/kg) induced a decrease in body weight and acute and persistent alterations in exploratoryand species-typical behaviors, motor performance, and cognitive function, without detectable changes in cortical oxidative stress markers. To investigate potential cellular mechanisms underlying these effects, we evaluated hippocampal immature neurons, hilus volume, and region-specific glial changes. Iba1 and GFAP immunoreactivity were assessed to evaluate microglial and astrocytic changes, respectively, in hippocampal CA1, CA3 and dentate gyrus and perirhinal cortex. PcPV2 exposure did not alter the number of DCX+ immature neurons or hilus volume. However, Iba1+ microglia showed morphological changes in CA3, with decreased circularity and solidity, suggesting a region-specific alteration in microglial phenotype. Further characterization of microglial and astrocytic responses is ongoing. This approach may help determine whether PcPV2 exposure is associated with region-specific glial changes and identify potential biological substrates underlying the behavioral alterations.

Cognition, Behavior, and Memory

D-063

Supporting research on social semantic deficits: A psycholinguistic database for Spanish-speaking populations and socialness-related variance in lexical performance

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Behavioral-variant frontotemporal dementia (bvFTD) and other socio-affective disorders are associated with deficits in processing social concepts (units denoting interpersonal traits, events, and circumstances). This pattern contributes to diagnosis and the prediction of specific neural alterations. However, social concepts lack normative datasets for underrepresented languages, hindering the strategic selection of stimuli for research in disadvantaged populations. To tackle this gap, we created a normative psycholinguistic database of social and non-social concepts for Spanish-speaking Latinos. Healthy adults rated 600 Spanish words (nouns, verbs, adjectives) for social relevance online. Subsets of 100 high- and low-sociality words (e.g., “friendship” and “button” respectively) were randomly presented and rated on a Likert scale (1 = no sociality, 7 = high sociality). Socialness ratings averaged 5.76 (SD=0.56) for social words and 1.69 (SD=0.62) for non-social words, with consistent bimodal patterns across grammatical categories. Preliminary lexical-task results suggest that social content influences reaction times and accuracy. These data show a clear distinction between social and non-social categories, and the resulting database provides a valuable resource for data collection in underrepresented populations, contributing a Latin American perspective to research on brain dysfunction.

Cognition, Behavior, and Memory

V-064

The Crash Analog Risk Task: A Pilot Paradigm for Studying Interoception and Risk-Taking

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Interoception, the perception of internal bodily signals, has been proposed to influence decision-making through somatic markers that integrate physiological states into cognitive processes. Previous studies associate greater cardiac interoceptive accuracy with less risky decision-making. However, its influence on risk-taking under time pressure remains unclear. This study introduces the Crash Analog Risk Task (CART), a novel paradigm modeled after online Crash gambling games, to examine this relationship. Unlike established tasks such as the Balloon Analogue Risk Task (BART), CART incorporates intrinsic time pressure through a continuously increasing reward multiplier that may crash at an uncertain point. We hypothesize that inducing attention to cardiac signals will increase risk aversion, leading to more conservative decisions in CART. In a randomized between-subjects design, university students were assigned to either an interoceptive Heartbeat Counting Task (HCT) or an exteroceptive control condition. Both groups subsequently completed the CART. A pilot study (N = 20) supported CART's feasibility and showed descriptive differences in the predicted direction: the interoceptive group had lower average cashout multipliers, lower crash rates, and lower mean risk scores than the exteroceptive group, suggesting a possible link between interoceptive attention and more conservative risk-taking. However, larger studies with stronger time-pressure manipulation are needed.

Development

S-063

Developmental fluoride exposure alters social novelty response and repetitive-like behavior in male rat offspring

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Fluoride (F) is naturally present in groundwater worldwide, including Argentina. Because F crosses the placenta and is present in maternal milk, developmental exposure may interfere with brain development. However, the mechanisms underlying its developmental neurotoxicity remain unclear. This study evaluated the effects of developmental F exposure on social and repetitive-like behaviors in male rat offspring. Pregnant Wistar rats received 10 mg/L F in drinking water throughout gestation and lactation. Male offspring were assessed on postnatal day 45 using the Three-Chamber Social Test and Marble Burying Test. In the Three-Chamber Social Test, both control and F-exposed males showed significant sociability, spending more time interacting with an unfamiliar conspecific than with the empty chamber. During the social novelty phase, F-exposed males spent significantly more time interacting with the familiar than with the novel conspecific, suggesting an altered response to social novelty. F-exposed males also buried significantly more marbles than controls, indicating increased repetitive-like behavior. These findings indicate that developmental F exposure alters social novelty response and increases repetitive-like behavior in male rat offspring, supporting specific neurobehavioral effects of early-life F exposure. Further studies are needed to elucidate the underlying neural mechanisms.

Development

D-064

Temporal dynamics of progenitor proliferation and differentiation in the developing neocortex of the plains vizcacha, Lagostomus maximus

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During neocortical development, cortical expansion and gyrencephaly rely on the precise spatial and temporal regulation of neural progenitor proliferation and lineage specification. The aim of this study was to characterize progenitor cell proliferation and differentiation of the developing neocortex in Lagostomus maximus, a gyrencephalic hystricomorph with a gestation of ~155 days. Embryos of 36–134 days (e.d.) and neonates of 2 days were used. Brains (n=60) were analyzed by immunohistochemistry for Ki-67, PCNA, GFAP, Sox2 and β-III tubulin. At 35–40 e.d., PCNA+ and Ki-67+ cells were widespread throughout the neuroepithelium while between 40–60 e.d., both markers were identified in the ventricular, inner and outer subventricular zones. From 65 to 85 e.d., PCNA+ cells remained broadly distributed, whereas from 90–135 e.d. they were restricted to the cingulate cortex, with a distribution similar to GFAP. Between 43–58 e.d., Sox2+ cells predominated in the ventricular and inner subventricular zones, with few isolated cells in the outer subventricular zone; whereas from 69 e.d. to birth, they were mainly restricted to a thin ventricular layer, with scattered cells throughout the cortex. β-III tubulin+ cells were observed in the preplate at 40–45 e.d., and across cortical compartments at 45-50 e.d. These findings suggest a progressive temporal reorganization of progenitor cells, with a reduction in ventricular proliferation and subsequent neuronal and glial differentiation.

Development

V-065

Larval competition with invasive Aquarana catesbeiana induces differential effects on brain morphometry of Rhinella arenarum metamorphs

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Anuran larvae show remarkable sensitivity to environmental stressors, displaying phenotypic plasticity in developmental rates, body morphology, and neural organization. In Rhinella arenarum, larval competition with the invasive American bullfrog (Aquarana catesbeiana) delays larval development and reduces body size at metamorphosis. Here, we tested whether competition with A. catesbeiana tadpoles of different size classes induces differential effects on R. arenarum brain morphometry, specifically analyzing the telencephalon, diencephalon, optic tectum, and rhombencephalon. While competition with small bullfrog larvae did not alter the relative size of any brain region, exposure to large A. catesbeiana larvae significantly modified brain proportions at metamorphosis, leading to a relative enlargement of the diencephalon ($p = 0.0034$) and a reduction of the optic tectum ($p = 0.012$). These results demonstrate that interspecific competition with A. catesbeiana does not merely constrain somatic growth, but triggers a size-dependent developmental response in the central nervous system of the native species. Future studies should determine whether these altered proportions affect specific neuronal populations or post-metamorphic behaviors, highlighting how pressure from invasive competitors shapes neural plasticity during early development.

Development

S-064

uPA accelerates elongation and directs pathfinding of retinal ganglion cells axons.

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Axon growth and guidance are main cellular mechanisms for establishing functional neural circuits. The retinotectal system is the main model for studying the development of neural connections. The urokinase-type plasminogen activator (uPA) -in association with its receptor (uPAR)-triggers extracellular matrix proteolysis during cell motility. We have previously demonstrated that uPA promotes neuritogenesis by a combined proteolytic and non-proteolytic mechanism in the chick optic tectum. However, it is not known whether uPA participates in the axon growth and guidance of retinal ganglion cells (RGC) during the formation of retinotectal connections. The objectives of this work were to investigate whether uPA participates in axon growth and guidance of RGC. For this purpose, we performed immunohistochemistry against uPAR in retinotectal sections and studied the effects of uPA on: a) RGC axon growth in retinal explants and b) axon guidance in dissociated RGCs cultured and exposed to gradients of uPA produced in the Dunn’s chemotaxis chamber using time-lapse imaging. Results showed that uPAR is expressed in RGC axons, uPA exhibits a chemoattractant effect on RGC axons and increases the axon growth velocity by enhancing both maximum velocity and growth-phase velocity. Furthermore, we investigated the uPA-mediated signaling using immunocytochemistry and Western blot, demonstrating that uPA increases FAK activity in RGC axons. UBACYT 20020220100197BA

Development

D-065

Neurotoxicity of ammonium glufosinate and its formulations during development: in vivo and in vitro evidence.

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The increasing use of ammonium glufosinate (GLA), following the emergence of weeds resistant to other herbicides, has heightened the scientific community's interest in its toxic effects on non-target organisms. The nervous system is of particular interest due to its strong structural similarity to glutamate, an excitatory neurotransmitter. Moreover, GLA is an irreversible inhibitor of glutamine synthetase; which could therefore cause structural and functional neurotoxicity. Thus, our study aims to evaluate the neurotoxicity induced by GLA on the CNS through in vivo and in vitro approaches. Wistar rats were exposed to a commercial formulation of GLA at doses of 20 and 40 mg/kg bw from postnatal day 7 to 27. Several behavioral tests were conducted to assess motor activity and cognitive functioning such as: the Open Field Test, Object Recognition Memory Test, and Rotarod Test. Results showed delayed growth in those exposed to the highest doses of the herbicide as well as decreased learning, and memory alterations. Additionally, hippocampal neurons, exposed to pure GLA and a commercial formulation for 48 hr, revealed marked effects on dendrite development since a reduced complexity of dendritic tree was observed by confocal microscopy. Preliminary analyses also showed a decrease in the level of proteins associated with synaptic function. Additionally, GLA treatment induced a downregulation of CaMKII/JNK pathways, which are involved in neuronal development and plasticity process.

Development

V-066

Double hit model of prenatal alcohol exposure and adolescent intermittent alcohol exposure modulates transcriptional plasticity and perineuronal-net organization in the male rat brain

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Prenatal alcohol exposure (PAE) and adolescent alcohol intermittent exposure (AIE) may interact to produce brain changes in areas involved in reward and emotion. Evidence for these interactive effects remains, however, preliminary. This preclinical study examined independent and combined effects of PAE and AIE on ΔFosB immunoreactivity and perineuronal nets (PNNs) in male Wistar rats, in mesocorticolimbic areas. Pregnant dams received ethanol (2,0 g/kg) or water on gestational days 17–20. Male adolescent offspring were given AIE (4,0 g/kg/day) or water across eight sessions (postnatal days 25–38). On postnatal day 42, ΔFosB immunoreactivity was quantified in the prelimbic cortex (PrL), nucleus accumbens core and shell, dorsomedial (DMS) and dorsolateral striatum, basolateral amygdala (BLA), and capsular central amygdala (CeC). PNNs were assessed by Wisteria floribunda agglutinin (WFA) staining in the BLA and PrL. AIE increased ΔFosB immunoreactivity in the DMS, BLA, and CeC ($p<.05$). In the BLA, analysis of ΔFosB expression revealed a significant PAE×AIE interaction ($p<.005$). PAE significantly increased the number of BLA cells surrounded by PNNs. The PAE×AIE interaction for heightened BLA PNN+ cells did not reach significance ($p=.08$, $n2p=.24$). The findings indicate that AIE produces regionally selective ΔFosB induction and that PAE amplifies this effect at BLA. Developmental ethanol may alter transcriptional plasticity and PNN organization within amygdalostriatal areas.

Development

S-065

Dual targets of Hugin in the modulation of a motor program in Drosophila

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Innate behaviors comprise genetically hardwired motor programs frequently coupled to morphogenetic remodeling. By studying pupariation, an innate behavior that reshapes the Drosophila larval body in preparation for metamorphosis, we provide insight into the neural circuits and modulators that generate complex motor patterns and the mechanisms that coordinate them with morphological changes. We have identified the epidermis-derived protein Dilp8 as a signal required for the initiation of the pupariation motor program. Through a targeted genetic screen, we uncover three downstream neuropeptides: Mip, Capa and Hugin. We find that Hugin modulates the pupariation motor program via two parallel, receptor-specific pathways. Peripherally, Hugin signals through epidermal PK2R2 receptor, to stimulate Dilp8 release and modulate the temporal progression and contractions involved in the last stage of motor program. Concurrently, Hugin acts in the central nervous system through an alternative receptor, PK2R1, to differentially modulate the dynamics of the same motor program stage. These data identify a two-level peptidergic node and suggest the existences of a feedback loop between Dilp8 and Hugin.

Development

D-066

Effects of bisphenol A (BPA) during neural development using Xenopus laevis as a model

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Bisphenol A (BPA) is widely used in industry to produce polycarbonate plastics associated with everyday consumption. It has been suggested that it acts as an endocrine disruptor and is associated with developmental disorders. The amphibian Xenopus laevis is a widely used model for studying vertebrate development. Unlike the most used amniote models, its external development facilitates the study of vertebrate embryogenesis and its alterations by chemical and environmental agents from the outset. Studies conducted in this model showed that BPA causes malformations in tadpoles and is capable of inhibiting γ-secretase. However, there are no previous studies investigating BPA exposure during the early stages of development. We previously found that the treatment with 20 µM BPA of X. laevis embryos from the onset of gastrulation to the onset of neurulation delays neural plate folding and increases the density of differentiated neurons at neurula stage. Now, we performed a new treatment window: from the beginning of development to mid-blastula transition. We found that BPA impairs the specification of neural precursors (sox2 expression), neural plate, neural border and embryonic midline (hes 4). Also, our results indicate that BPA disrupts early steps, critical for cephalic development.

Development

V-067

Social Support Promotes Alternative Molecular and Dendritic Adaptations Following Prenatal Stress

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Prenatal maternal stress (PMS) induces alterations in offspring neurodevelopment and behavior. We previously showed that social support to PMS-exposed dams improved offspring memory and social interaction. We investigated mechanisms underlying behavioral recovery. Pregnant mice were exposed to stressors and housed either with a familiar non-pregnant female (ESA) or alone (ES). Controls were non-stressed, socially housed dams (CTA). ES dams showed higher fecal corticosterone levels than ESA and CTA dams at delivery and PD7. RNA-seq of offspring prefrontal cortex identified 625 differentially expressed transcripts in ESvsESA, including protein-coding genes and lncRNA. Gene Ontology analysis highlighted synaptic transmission and neuronal connectivity. ESvsCTA & ESAvsCTA yielded 417 and 1,507 nominally significant genes. Of 73 shared genes, 93% changed in the same direction, with greater effects in ESAvsCTA, suggesting an alternative transcriptional program associated with recovery rather than restoration of the CTA state. Golgi-Cox/Sholl analysis revealed sex-dependent dendritic effects. In females, PMS reduced distal dendritic complexity (CTAvsES 80–150µm $p<0.001$), whereas social support attenuated this reduction (ESvsESA 40–130µm $p<0.001$). In males, PMS altered the radial pattern of dendritic complexity (ES.Radius $p=0.032$) without significant pairwise differences. Social support during pregnancy promotes molecular and structural adaptations linked to behavioral recovery.

Development

S-066

Shared identity, divergent states: comparative expression analysis of the lateral eye and pineal complex in lizards

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One of the reasons behind vertebrate evolutionary success, since their origin over 540 million years ago, is the presence of several photoreceptive organs that allow them a rich perception of the environment. These structures later diverged into the eyes and the pineal complex, comprising the pineal gland and accessory structures like the parapineal organ in lampreys and fishes, the frontal organ in anuran amphibians, and the parietal eye in lizards. According to this hypothesis, the eyes and the pineal complex might be serial homologous structures, since they share a common origin as photoreceptor organs. Within the Character Identity Network (ChIN) framework, the developmental identity of homologous structures is specified by a network of transcription factors, while effector genes confer distinct character states. To study the degree of identity network conservation between vertebrate photoreceptor structures, we are analysing the gene expression pattern in the eye and pineal complex of the lizards Liolaemus darwinii and Tropidurus torquatus, using immunofluorescence and RNA-seq, aiming to map the extent of the shared ChIN and character state genes. Our results indicate a high degree of resemblance between eyes and pineal complex in relation to the expression of developmental genes, like transcription factors, while some genes involved in character states, like light-sensitive opsins, are expressed differentially.

Development

D-067

Distinct embryonic precursors generate gray and white matter astrocytes in the mouse spinal cord

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Astrocytes display two canonical morphologies—protoplasmic in the gray matter (GM) and fibrous in the white matter (WM)—yet recent transcriptomic studies indicate that their heterogeneity is far more extensive. In the developing mouse spinal cord, discrete dorsoventral progenitor domains generate astrocytes that populate both GM and WM. We hypothesized that heterogeneous, fate-restricted ventricular precursors generate either GM or WM astrocytes, explaining their distinct identities despite a shared origin. To test that, we performed in vivo lineage tracing using two complementary approaches: tamoxifen-inducible expression of fluorescent reporters in Glast CreER mice, and the Mosaic Analysis with Double Markers (MADM) system, a Cre-loxP–based strategy inducing intrachromosomal recombination to reconstitute chimeric fluorescent proteins (Tomato and GFP). Sparce fate mapping revealed that astrocyte clones are frequently composed of two daughter cells of the same subtype (either GM or WM), sharing morphology, molecular marker expression, and spatial position. These pairs appear to originate from symmetric divisions occurring after migration near-final settling location. Our study reveals that, in addition to dorsoventral patterning, astrocyte diversity is established by distinct embryonic precursors within each progenitor domain that selectively generate GM or WM astrocytes. These results shed light on the differentiation programs underlying astrocyte heterogeneity.

Development

V-068

Myelination of brainstem axons during the critical period

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The influence of sensory activity on myelination has been extensively studied. Particularly the auditory system is equipped with molecular and anatomical features supporting speed and precision to optimally encode the temporal features of sound where myelination plays a critical role in this process. In altricial mammals, cochlear inner hair cells display spontaneous electrical activity before hearing onset. The pattern and firing rate of these cells are crucial for the correct maturation of the central auditory pathway. The activity of medial olivocochlear system (MOC) leads to an accurate development of precise central connectivity by modulating spontaneous activity in the immature inner ear. While the relationship between sound stimuli and myelination in mature animals was studied, having shown that synaptic activity promotes myelin thickening, the impact of spontaneous activity on myelination during the critical period was not explored. In this study, an ultrastructural study was performed using serial block-face electron microscopy in a wild type (WT) mouse and a mouse model with reduced spontaneous activity (α9KI). Analysis of morphological parameters shows that both the number of myelin sheaths as well as myelin thickness are reduced in the α9KIadult mice. These data suggest that spontaneous activity is involved in brainstem myelination, thereby influencing auditory physiology.

Disorders of the Nervous System

S-067

Reduced GluN2A expression recapitulates schizophrenia relevant behavioral and synaptic features

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NMDA receptors (NMDAR) play a crucial role in synaptic plasticity during development and adulthood. Alterations in the expression of one of the regulatory subunits, GluN2A, have been linked to phenotypes that contribute to neurodevelopmental disorders or to schizophrenia (SCZ). GluN2A expression rise during postnatal development both in human and rodents. As SCZ was proposed to present NMDAR hypofunction, GluN2A downregulation emerges as a possible mechanism involved in disease onset. However, the role of altered GluN2A remains poorly understood. For this reason, we established a GluN2A knockdown (GluN2A-KD) model in young adult rats. Behavioral analyses revealed impairments in spatial map formation, reduced cognitive flexibility, and altered exploration patterns, while general cognition remained intact. To better understand the molecular mechanisms behind these phenomena, we characterize the GluN2A-KD in neuronal cultures. Despite reduced GluN2A expression, synaptic GluN2A levels remain similar to controls. Moreover, we observed an increase in dendritic branching and immature dendritic spines, associated with an increase in glutamate responsiveness. These findings suggest that GluN2A-kd promotes immature neuronal morphology and excitatory imbalance, consistent with the glutamate hypothesis of SCZ. More experiments are required to clarify the molecular mechanisms underlying glutamate sensitivity, as well as the molecular dysregulation consequence of GluN2A-kd.

Disorders of the Nervous System

D-068

Dysregulation of mitochondrial dynamics in cortical neurons derived from familial Alzheimer's disease hiPSCs

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Mitochondrial dynamics are essential in Alzheimer's disease (AD). We differentiated hiPSCs from familial AD patients with PSEN1 variants (p.T119I, p.A246E, p.M146L) and controls into cortical i3-neurons using doxycycline-inducible NGN2, validated by pan-neuronal (TUJ1, MAP2, NeuN) and cortical (TBR1, CTIP2) markers. RT-qPCR of mitochondrial dynamics genes showed high baseline variability among controls. Nonetheless, fAD neurons showed convergent OPA1 downregulation alongside line-specific changes in DLP1, FIS1, and PINK1. Protein levels showed consistently reduced OPA1, whereas DLP1 increased in p.T119I and p.M146L, demonstrating a transcriptional-translational dissociation. Flow cytometry (TMRE and CellROX) confirmed consistent mitochondrial function in controls. Conversely, fAD neurons showed mutation-dependent functional divergence: p.T119I displayed marked mitochondrial membrane potential (ΔΨ_m) depolarization, whereas p.A246E and p.M146L exhibited elevated baseline ROS and decreased ΔΨ_m. Paraquat exposure (50 µM) revealed blunted mitochondrial adaptability and impaired redox response in mutants. Our findings demonstrate a transcriptional-translational dissociation in fusion/fission regulation, indicating that distinct PSEN1 variants affecting different domains generate divergent mitochondrial phenotypes and impairment in i3-neurons.

Disorders of the Nervous System

V-069

Why Some Neurons Die First: Uncovering the Regulatory Programs of Selective Neuronal Vulnerability

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Synucleinopathies are a group of disorders, including Parkinson's disease, characterized by the formation of α-synuclein (αSyn) aggregates and neurodegeneration in specific brain regions. However, the molecular mechanisms underlying the differential neuronal susceptibility, known as selective vulnerability, remain poorly understood. To investigate these mechanisms, we used a mouse model of synucleinopathy that drives pathogenic αSyn overexpression in neuronal populations of the substantia nigra and locus coeruleus, two regions that exhibit distinct temporal patterns of vulnerability. Single-nucleus RNA sequencing, combined with a gene regulatory network reconstructed from public datasets, recovered associations between neuronal vulnerability and gene expression regulators with established roles in neurodegeneration, as well as newly identified candidates not previously linked to this process. In particular, we uncovered a set of 26 regulators that displayed changes in activity in both dopaminergic and noradrenergic neurons that closely paralleled their distinct neurodegeneration kinetics. Neurodegeneration-associated changes in the activity of this set of regulators were further validated using data from human cells and Parkinson's disease patients. Finally, we show evidence suggesting that intrinsic differences in the basal expression of neuroprotective regulatory genes may contribute to the differential responses of these neuronal populations to αSyn pathology.

Disorders of the Nervous System

S-068

Long-Lasting Astroglial Remodeling Following Hyperthermic Seizures During the Latency Period

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Temporal Lobe Epilepsy (TLE) is the most common form of epilepsy in adulthood, and a significant proportion of patients report have suffered complex febrile seizures (cFS), during childhood. The period between cFS and TLE, known as the latency period is thought to involve epileptogenesis. Using a model of hyperthermic seizures (HS), we previously showed that at 15 days post-HS (DPHS), both sexes exhibited moderate reactive gliosis, while males showed an atypical astroglial distribution in the piriform cortex (PC), increased Iba1+ cells, and a more pronounced proinflammatory phenotype. Both sexes also showed decreased AQP4 and Kir4.1 mRNA expression, with AQP4 redistribution in the PC of males. Males further exhibited a lower seizure threshold following pilocarpine exposure at 39DPHS. Given these more pronounced alterations in males, we now asked whether they persist over time. For that purpose, male rat pups were exposed to elevated core temperatures (39–42°C) to induce seizures. Brain tissue was collected at 35DPHS for immunohistochemistry. We found mild persistent reactive astrogliosis in the PC, with a normalized astrocyte distribution, together with an increased number of S100B+ cells. A mild alteration in AQP4 expression was also observed, without significative alterations in neuronal survival as shown by the NeuN+ cell area. These findings suggest that HS induces long-lasting astroglial alterations that may contribute to epileptogenesis. Grants: UBACYT, PIP CONICET

Disorders of the Nervous System

D-069

Characterization of Murine Models of Calcium Dysregulation and Metabolic Dysfunction: Implications for Cognition and Neuroinflammation

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Neurodegenerative diseases such as Alzheimer's disease (AD) are multifactorial conditions in which alterations in different cellular and systemic processes may converge to impair neuronal function and cognition. In this work, we sought to explore the contribution of distinct mechanisms associated with neuronal dysfunction, focusing on intracellular calcium signaling, metabolic dysfunction, and neuroinflammation as distinct but potentially convergent mechanisms associated with cognitive impairment. Three murine models were studied: Ob/Ob mice (leptin mutation) and SAKO and SDKO mice (RyR2 mutations). Cognitive function was assessed using the Barnes Maze, while hippocampal neurogenesis and neuroinflammation were evaluated by immunoassays and RT-qPCR. It was observed that SAKO and Ob/Ob mice showed significant cognitive deficits ($p=0.0234$; $p=0.0034$) and reduced neurogenesis ($p=0.0007$; $p=0.0109$). A non-significant trend toward increased expression of the pro-inflammatory mediators IL-6 and Tyrobp was also observed ($p=0.2858$; $p=0.1905$). These findings indicate that alterations in distinct biological processes, including intracellular calcium signaling and metabolic dysfunction, are associated with convergent changes in cognition, and hippocampal neurogenesis. Together, our results support the relevance of investigating multiple interacting cellular and systemic mechanisms to better understand the multifactorial nature of neurodegenerative diseases such as AD.

Disorders of the Nervous System

V-070

Nothobranchius furzeri: an emerging aging model to study alpha-synucleinopathy in the gut-brain axis.

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Enteroendocrine cells (EECs) are key components of microbiota-gut-brain axis. EECs sense changes in the intestinal microenvironment and transmit signals to the central nervous system (CNS) through paracrine and neuronal pathways. EECs express synaptic proteins and possess axon-like basal processes that form synaptic contacts with vagal afferents. Given these neuronal features, EECs have been proposed as potential sites susceptible to neuronal-like abnormalities, including α-synucleinopathy. Here, we investigated whether physiological aging is accompanied by perturbations in EECs homeostasis and abnormal α-synuclein expression. We used the short-lived vertebrate Nothobranchius furzeri (Nf) to assess age-related changes in EECs. Aging was associated with loss of EECs homeostasis characterized by EECs hyperplasia and increased 5-hydroxytryptamine production. These alterations were accompanied by increased α-synuclein-expressing EECs and accummulation of α-synuclein in the myenteric plexus and the brain. These indicate that EECs are particularly susceptible to age-related changes that may alter intestinal physiology and gut-brain communication. The findings provide a foundation for exploring whether elevated α-synuclein in EECs may initiate peripheral proteinopathy with potential implications for the CNS. Furthermore, this work presents Nf as a valuable model for investigating the link between intestinal aging and neurodegenerative diseases.

Disorders of the Nervous System

S-069

Glutamate Signaling in Guillain-Barré Syndrome: A Potential Biomarker of Neuropathic Pain

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Guillain-Barré syndrome (GBS) is an acute immune-mediated peripheral neuropathy characterized by weakness and paralysis. Although primarily considered a motor neuropathy, pain is a frequent symptom that impacts patients' quality of life. However, it remains underestimated and lacks specific biomarkers. Neuropathic pain is associated with increased glutamate (Glu) release in the spinal cord, activating ionotropic (NMDA and AMPA) and metabotropic receptors. Given its role in nociception, Glu represents a potential biomarker for pain in GBS. This study aimed to determine Glu levels in the cerebrospinal fluid (CSF) of patients with GBS and assess effects on extracellular Ca^{2+} influx in the nociceptive DRG-derived cell line 50B11 and primary DRG neuron cultures. Glu levels were determined in CSF from patients with GBS (CSF-GBS) and controls with non-demyelinating diseases (CSF-C) using an fluorimetric enzymatic assay. In addition, Ca^{2+} influx was assessed in differentiated 50B11 cells and primary DRG neuron cultures loaded with a calcium-sensitive fluorescent dye and imaged using an InCell Analyzer. Cells were exposed to Glu, CSF-C, or CSF-GBS with or without NMDA and AMPA receptor antagonists. Glu levels were significantly higher in CSF-GBS than in CSF-C. Additionally, CSF-GBS induced sustained Ca^{2+} influx in 50B11 cells and primary DRG neuron cultures. These findings support Glu as a potential biomarker of neuropathic pain in GBS and suggest a potential therapeutic target.

Disorders of the Nervous System

D-070

Exploring the involvement of the neurodegenerative disease-related protein TDP-43 in CNS vs other cancers

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TDP-43 is an RNA-binding protein (RBP) that, amongst other functions, participates in mRNA metabolism. It is a key player in neurodegenerative diseases like frontotemporal dementia and amyotrophic lateral sclerosis. Although recent evidence suggests a potential role in other pathogenic processes, the involvement of this protein in cancer is still unclear. In this work, we aimed to 1) investigate the genes/proteins and pathways associated with differential expression of TDP-43 in the CNS cancers and whether they are conserved in other non-CNS cancers, 2) explore correlations with clinicopathological factors, and 3) analyze mutations in the TARDBP gene. For this purpose, we interrogated the CPTAC datasets using cBioportal to stratify samples according to the 25% and 75% quartiles or median TDP-43 expression. RNA splicing and DNA repair were the top pathways present in groups with high TDP-43 expression, consistent with the role of TDP-43 in these processes. Moreover, high TDP-43 expression positively associated with aggressive breast and pediatric cancer types. Lastly, we found low mutational frequency in TARDBP across all studied cancers (generally <1%). Our data is in line with the notion that abnormal RBP expression or function amplify the effects of cancer driver genes, accelerate tumor progression, and promote aggressiveness. Here, we provide evidence for a potential role of TDP-43 in cancer that deserves further investigation.

Disorders of the Nervous System

V-071

Digital Speech Biomarkers for Cognitive and Brain Health Across the Alzheimer's Disease Continuum

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Assessing the Alzheimer's disease continuum (ADC) relies on resource-intensive neuropsychological testing and neuroimaging. Digital speech biomarkers (DSBs) provide a scalable approach, but their ability to predict cognitive and brain health across the ADC is unexplored in Latino populations. We collected speech, cognitive, and neuroimaging data from 150 participants (17 healthy controls, 55 with subjective cognitive decline, 57 with mild cognitive impairment, 21 with Alzheimer's disease dementia [ADD]). DSB features came from brief TELL-app fluency tasks, cognitive features from standardized-test scores (ACE-III, IFS), and brain features from dementia-related MRI regional volumes. Separate machine-learning models used DSB or brain features to predict ACE-III/IFS scores, and DSB or cognitive features to predict hippocampal and ADD-atrophy mask volumes. Performance was assessed with age-adjusted partial Pearson correlations. DSB-gray matter volume associations were tested with multiple regression. DSBs outperformed brain features for ACE-III (r=.67 vs .23) and IFS (r=.55 vs .31), and cognitive features for ADD-atrophy mask volume (r=.38 vs .27), but not hippocampal volume (r=.42 vs .37). Higher word frequency was associated with lower prefrontal cortex volume. DSBs captured cognitive status and structural brain health across the ADC via a fully automated multivariate pipeline, supporting DSBs as a low-cost, scalable alternative for dementia screening and monitoring.

Disorders of the Nervous System

S-070

Oligodeoxynucleotide IMT504: Effects on remyelination in the corpus callosum and cerebral cortex after experimental demyelination

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Demyelination is a pathological process characterized by myelin loss around axons, whereas remyelination restores myelin and function. Multiple sclerosis is an inflammatory demyelinating disease in which remyelination frequently fails. IMT504 (IMT) is a 24-nucleotide non-CpG oligodeoxynucleotide containing two PyNTTTTGT motifs with immunomodulatory and regenerative effects. Based on previous findings in a cuprizone (CPZ)-induced demyelination model, in which IMT was administered for five days before CPZ withdrawal and improved neuroinflammation and remyelination in the corpus callosum (CC), we evaluated a second treatment scheme in which IMT was administered subcutaneously for five days after CPZ withdrawal. Rats were sacrificed at 0 (T0), 5 (T5), and 10 (T10) days after CPZ withdrawal. Oligodendroglial and microglial populations were evaluated in the CC and cerebral cortex (Ctx) by immunohistochemistry. At T5, CPZ-treated rats showed an increase of PDGFRα+ oligodendrocyte (OL) precursor cells (OPCs) and a decrease of mature MAG+ OL in the CC. Phagocytic Iba1/CD68+ microglia increased following demyelination, whereas IMT reduced this response. In the Ctx, IMT did not modify OPC or mature OL populations but increased MAG+ fluorescence intensity compared with saline-treated animals. IMT also induced significant changes in microglial morphological complexity. These findings suggest that IMT modulates the microglial response and may promote remyelination following demyelination.

Disorders of the Nervous System

D-071

The 6-OHDA Model as a Framework to Study Behavioral and Cellular Biomarkers of Prodromal Parkinson's Disease

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Parkinson's disease (PD) is preceded by a prodromal phase, lasting years before motor symptoms appear, marked by non-motor alterations such as neuropsychiatric manifestations, including anxiety disorders. Although the 6-hydroxydopamine (6-OHDA) model has classically been used to study nigrostriatal degeneration, it remains underexploited as a framework to dissect these early, non-motor stages of PD in different dopaminergic areas outside the nigrostriatal pathway. Our research group has progressively built this framework. We previously showed that bilateral intrastriatal 6-OHDA induces anxiety-like behavior in male rats, detectable as early as 1 week post-lesion and persisting through week 3, alongside dopaminergic neurodegeneration in the ventral tegmental area. Notably, IGF-1 gene therapy attenuated the anxiety-like phenotype without preventing neuronal loss. Identifying the mechanisms through which IGF-1 mediates its behavioral effects represents an important aim of our study. We are now developing a mouse model that combines 6-OHDA lesioning with assessments of BBB integrity and anxiety-like behavior, to test whether BBB disruption underlies the prodromal anxiety phenotype. We propose that integrating peripheral (BBB) and behavioral readouts within the 6-OHDA model offers a translational framework to identify early biomarkers of PD, before dopaminergic degeneration is complete, with implications for early diagnosis and intervention.

Disorders of the Nervous System

V-072

Synaptic and physiological impairments associated with tauopathies in the htau mouse model

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Tauopathies are neurodegenerative disorders characterized by pathological accumulation of hyperphosphorylated Tau, a microtubule-associated protein expressed mainly in neurons. Its aberrant hyperphosphorylation reduces affinity for axonal microtubules, promoting accumulation in the somatodendritic compartment. This disrupts synaptic transmission and physiology, promoting neuronal death and neurodegeneration. Glutamatergic neurons appear particularly vulnerable to this Tau-driven dysfunction. We propose analyzing the temporal course of synaptic pathology in the hTau mouse model, performing molecular, histological and electrophysiological analyses. We initially investigated the prefrontal cortex (PFC), which primarily accumulates phospho-Tau leading to cognitive impairments from 6 months of age. Patch-clamp recordings showed decreased firing rate in PFC pyramidal neurons of hTau mice versus wild-type from 3 months of age. Glutamatergic neurons were discriminated using specific reporters to assess progressive Tau accumulation at synaptic terminals via high-resolution immunofluorescence microscopy (Array Tomography). Western blots analyses were used to determine changes in AMPA receptor and phospho-Tau contents in aging hTau PFC synaptosomes. These studies will set the grounds to further evaluate therapeutic strategies preventing synaptic loss in tauopathies. Finally, we will perform cell-type-specific Tau knockdown in the hTau PFC to evaluate its impact on pathology progression.

Disorders of the Nervous System

S-071

Ketogenic diet exposure and glial cells: Exposure to beta-hydroxybutyrate induces morphological changes in astrocytes in vitro.

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Ketogenic diet (KD) is an effective epilepsy treatment whose mechanisms remain unknown. We aimed to assess the effects of ketogenic diet on astrocytes. For that purpose, in silico analyses were performed on public databases showing that the transcriptomic signature of reactive astrocytes in vivo was deeply altered by KD. Specifically, inflammatory genes which as IL1a, C3, and Lcn2 expression were reduced by KD. In vitro, KD was mimicked by beta-Hydroxybutyrate (BHB) treatment (2.5 and 5.0 mM) on rat primary astrocytes exposed to a pro-inflammatory challenge. Cultures were obtained from 2-day-old postnatal rats and divided into 10 groups: Control, LPS, and BHB were added in a pretreatment/posttreatment scheme. Glucose in the culture medium was adjusted to 5.5 mM accordingly. Cells were stained with MitoSOX or GFAP to perform morphological studies. BHB treatment induced a dose-dependent increase in GFAP expression. Pretreatment with BHB (2.5 mM) significantly attenuated the LPS-induced increase in covered area, while posttreatment not only failed to restore astroglial morphology but increased it relative to LPS alone. MitoSox analysis showed that ROS levels were increased in BHB-treated astrocytes. These preliminary findings suggest that BHB exposure increases astrocytic reactivity and ROS, with dose-dependent effects on GFAP expression. Further studies are necessary to completely elucidate the profile of BHB effects on astrocytes and neurons.
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Disorders of the Nervous System

D-072

Effects of yerba mate administration on autophagy in Drosophila melanogaster

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Previous studies showed that yerba mate (YM) extracts and some of its bioactive compounds, such as chlorogenic acid, exert a neuroprotective effect on cultured dopaminergic neurons. Likewise, results in SH-SY5Y cells show that YM treatment induces AMPK activation and an increase in LC3-positive puncta, suggesting that autophagy is involved in its mechanism of action. To support these observations and provide a basis for understanding the link between yerba mate-derived compounds and autophagy regulation, we evaluated the ability of YM to induce autophagy in vivo in the Drosophila melanogaster larval fat body. Drosophila larvae were fed increasing concentrations of YM and, after 48 h, autophagy induction levels were determined using the Atg8-Ch-GFP reporter. Through the acquisition and analysis of confocal microscopy images of the tissue, we established that the most effective concentration for inducing the autophagic process is 10 mg/ml. Upon treating larvae with this concentration, we evaluated additional autophagy markers, which showed a distribution consistent with induction of this process. Characterization of the cellular and molecular mechanisms induced by yerba mate will lay the groundwork for future research aimed at evaluating the neuroprotective potential of these compounds in the context of neurodegenerative diseases, such as Parkinson's disease.

Disorders of the Nervous System

V-073

Glyphosate-based herbicides disrupt neuronal and synaptic function: potential involvement of WNT signaling

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Glyphosate-based herbicides (GBH) are among the most widely used herbicides globally. Although glyphosate (Glyph) is considered a low-toxicity compound, commercial formulations may exert stronger biological effects than the active ingredient alone. We compared the neurotoxic effects of pure Glyph and GBH on neuronal development and synaptic organization. In mature hippocampal neurons (21 DIV), GBH (0.05–0.1 mM) significantly reduced dendritic complexity, spine density and altered spine morphology, while decreasing synaptic clusters along dendrites. Biochemical analysis further revealed a marked decrease in Synapsin I and PSD-95 in GBH-exposed neurons, whereas equivalent Glyph concentrations produced minimal effects. In vivo studies revealed that neonates exposed to GBH exhibited motor and cognitive dysfunction at PND 30. Analysis of the hippocampus showed downregulation of JNK- and CaMKII-mediated non-canonical Wnt signaling. Consistently, bioinformatic and molecular docking analyses revealed favorable predicted interactions of Glyph with Wnt7b effectors, including the Frizzled-7 receptor (FZD7) and the downstream protein Dishevelled-2 (DVL2), supporting a potential direct interaction with key components of this pathway. Together, these findings demonstrate that GBH exert greater neurotoxic effects than pure Glyph, affecting Wnt signaling and disrupting neuronal architecture and synaptic integrity

Disorders of the Nervous System

S-072

Neuroprotective effect of metformin on brain aging and microglial senescence

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Aging is the major risk factor for cognitive decline and neurodegenerative diseases, and is associated with progressive alterations in microglial function, among other hallmarks. Microglial senescence, characterized by loss of homeostatic functions and a chronic proinflammatory state, may contribute to age-related brain dysfunction. The antidiabetic drug Metformin (MET) has emerged as a potential repurposing strategy for neurological disorders. Here, we investigated the effects of MET on brain aging and microglial senescence using in vivo and in vitro models. Adult (9-month-old) and aged (17-month-old) male C57BL/6J mice received MET (250 mg/kg, i.p.; 10 doses during the last month) or vehicle. MET did not affect body weight or fasting glycemia. In aged mice, MET reversed anxiety-like behavior assessed by the open field test. In the Barnes Maze, MET improved spatial learning independently of age and enhanced spatial memory in aged animals. Hippocampal Iba1 immunofluorescence showed reduced microglial reactivity following MET treatment. In vitro, FAC-induced senescence in BV2 microglial cells increased nuclear area and p21/p14 expression, while MET attenuated these changes. Overall, MET improved age-associated behavioral alterations and modulated microglial responses in the aging brain, while attenuating senescence-associated phenotype in microglial cells. These findings support microglia as a target of MET and provide a basis for investigating its neuroprotective mechanisms

Disorders of the Nervous System

D-073

Non-linear, sex-modulated trajectories of Aβ-driven cognitive decline across aging in the McGill-R-Thy1-APP Rat Model of Alzheimer's-Like Brain Amyloidosis

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Alzheimer's disease (AD) progression is influenced by aging and sexual dimorphism, but their interaction with early amyloid accumulation remains unclear. This study longitudinally evaluated cognitive performance—across Open Field (OF), Inhibitory Avoidance (IA), Novel Object Recognition (NOR), and Novel Object Location (NOL) tasks—and amyloid burden in male and female McGill-R-Thy1-hAPP (Tg+/-) and wild-type rats at 4 and 12 months. Intraneuronal human Aβ (hAβ) distribution and hippocampal soluble Aβ40/Aβ42 levels were measured. To map relative cognitive metrics against hippocampal Aβ42 concentrations, NOR was selected over alternative tasks (OF, NOL, IA) because it permits concurrent isolation of short- and long-term memory kinetics within the same cohort and sensory modality. hAβ immunoreactivity was exclusive to Tg+/- rats (cortex and hippocampus). Soluble Aβ40/Aβ42 levels showed sex-dependent dynamics: males had higher concentrations at 4 months, whereas females exhibited a larger increase at 12 months. However, despite higher late-stage amyloid burden, females preserved lower functional sensitivity to Aβ42 accumulation. In contrast, males showed more pronounced cognitive decline with smaller Aβ42 increases, displaying steeper sensitivity slopes. These results demonstrate that Aβ-driven cognitive decline is non-linear and sex-modulated. Integrating sexual dimorphism into preclinical AD detection is essential for precision medicine strategies.

Disorders of the Nervous System

V-074

Amyloid-β-Associated Alterations in Excitatory/Inhibitory Balance in Caenorhabditis elegans

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Alzheimer's disease (AD) is characterized by abnormal amyloid-β (Aβ) aggregation and neuronal loss. Disruption of the balance between excitatory and inhibitory (E/I) neurotransmission may contribute to disease progression. Here, we investigated E/I imbalance in transgenic C. elegans AD models expressing neuronal Aβ. The neuromuscular junction provides a well-characterized system for assessing E/I balance. In young animals (YA), Aβ expression did not alter E/I balance. However, aged animals exhibited increased cholinergic sensitivity (24% and 84% of AD models paralyzed vs 6% and 65% in wild-type (WT), after 30 and 90 min of levamisole exposure, respectively). These findings suggest age-dependent impairment of E/I signaling. Consistently, GABA-dependent escape-response assays revealed functional deficits in aged AD animals (51 ± 6% vs 69 ± 17% in WT). To determine whether Aβ promotes neurodegeneration before functional decline, we assessed GABAergic neuron morphology. Interestingly, despite absence of detectable E/I alterations, 55% of YA AD model animals already exhibited morphological defects, including truncated or misguided neuronal processes. Overall, this study contributes to understanding how Aβ-associated structural damage and E/I signaling alterations emerge during aging, highlighting the progressive dysfunction in AD pathophysiology.

Disorders of the Nervous System

S-073

In vivo mitochondrial oxidative state in animals treated with PQ and the antioxidant EchA

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Classical models of dopaminergic neurodegeneration often utilize paraquat (PQ), which exerts toxicity through oxidative stress and mitochondrial dysfunction that play a key role in progressive dopaminergic neuron death. We evaluated the effect of PQ on in vivo mitochondrial oxidation using the genetic reporter MitoTimer, a protein that photoconverts from green to red upon oxidation. To determine whether the oxidative impact is cell-type specific, MitoTimer was selectively expressed in dopaminergic neurons (TH-GAL4), pan-neuronal (elav-GAL4), or in glia (Repo-GAL4). We assessed the potential neuroprotective effect of Echinochrome A (EchA), a naturally occurring spinochrome present in the roe of the Patagonian sea urchin Arbacia dufresnii. EchA has protective effects in vitro; however, its action on the in vivo mitochondrial redox state in the nervous system is unclear. Locomotor performance and cognitive response were evaluated by placing individual flies in a novel context and quantifying distance traveled and habituation. EchA was administered orally as part of a roe-derived formulation with a known and standardized EchA concentration, currently used to produce an approved and commercialized dietary supplement for human consumption. Brain tissues were examined using fluorescence microscopy to quantify the red/green fluorescence ratio as a direct readout of mitochondrial oxidation. This approach will provide insight into the potential mitoprotective effects of EchA.

Disorders of the Nervous System

D-074

Yerba mate extract stimulates autophagy and modulates AMPK pathway in SH-SY5Y cells: Insights into its neuroprotective potential in Parkinson’s disease.

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Current treatments for Parkinson's disease (PD) are symptomatic and unable to stop neuronal death, highlighting the need for complementary strategies which may delay neurodegeneration such as dietary interventions. Yerba mate (Ilex paraguariensis, YM) has been inversely associated with the development of PD. Previously, our group demonstrated that YM enhances the survival of dopaminergic neurons in primary mesencephalic cultures. Like coffee, mate contains high amounts of Chlorogenic acid (CGA), which may modulate energy metabolism and promote neuronal survival, likely activating AMPK, a pathway involved in energy homeostasis and autophagy, a crucial process in PD pathophysiology that may clear protein aggregates associated with neurodegeneration. However, the mechanisms behind YM extract and CGAs neuroprotective effects are underexplored. Thus, in this study, we use human SH-SY5Y neuroblastoma cells to assess YM and CGAs effect on autophagy. To assess autophagic flux, we evaluated autophagy markers LC3-II levels by immunofluorescence and Western blot, and p62 levels by Western blot. Results show that YM extract increases LC3-II levels and slightly decreases p62/SQSTM1 levels, reflecting an increase in autophagic flux. Therefore, this study outlines enhanced autophagy as a potential neuroprotective mechanism that may position YM as a natural dietary candidate to counteract neurodegeneration.

Disorders of the Nervous System

V-075

Astrocyte and Microglia: temporal changes in relation to β-amyloid plaques in an Alzheimer's disease rat model

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In Alzheimer's disease (AD), glial and neuronal alterations have been described. Using an AD rat model (McGill-R-Thy1-APP), we investigated astroglial and microglial changes across different stages of Aβ plaque development. In the cerebral cortex of homozygous transgenic animals (Tg++) without Aβ plaques (3m old), we observed subtle, dimorphic astrocytic morphological changes without evidence of a massive glial response. In Tg++ animals with incipient plaques (7m old), a gradient of astrocytic reactivity was observed in proximity to plaques, but reactivity was significant even in astrocytes distant from plaques when compared to WT animals. Microglial reactivity was also observed in Tg++ animals, suggesting a global alteration in the glial response at this age. Significant neuronal alterations were not observed at this age. In Tg++ animals with extensive extracellular Aβ deposits (13m old), astrocytic alterations were accompanied by a reduction in homeostatic gene expression (AQP4, GS) without evidence of pathological conversion to neurotoxic astrocytes (MAFG), alongside decreased neuronal survival. These findings indicate subtle early glial alterations before significant plaque deposition, followed by extensive reactive gliosis, but neuronal loss is a late event accompanied by impaired homeostatic capacity in astrocytes. This suggests that astroglial dysfunction is a final stage in AD, probably related to an exhausted astroglial phenotype. Grants: PUE, UBACYT, PIP-CONICET

Disorders of the Nervous System

S-074

Transcriptional signatures of Striatal Spiny Projection Neuron Subtypes in Experimental Parkinsonism and Levodopa-Induced Dyskinesia

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Parkinson's disease (PD) causes major transcriptional and functional alterations in striatal circuitry following the loss of dopaminergic neurons in the substantia nigra pars compacta. Although levodopa (L-DOPA) is essential for managing motor symptoms, chronic treatment frequently leads to L-DOPA-induced dyskinesia (LID), a disabling motor complication. Most transcriptomic studies have focused on peak-dose dyskinesia, particularly in direct pathway spiny projection neurons (dSPNs), while the molecular landscape during the off-L-DOPA phase, when drug effects subside and motor symptoms re-emerge, remains poorly characterized.

In a previous single-nucleus RNA sequencing (snRNA-seq) study using the 6-hydroxydopamine (6-OHDA) mouse model of PD, we identified the major striatal neuronal and non-neuronal populations and their responses to denervation and chronic L-DOPA during the off-state. Here, we performed a higher-resolution analysis of SPN subtypes using RNA markers of striatal compartmentalization and spatial distribution. This approach identified pathway, subtype, and compartment-specific transcriptional adaptations associated with dopaminergic loss and chronic L-DOPA exposure. Our findings provide a framework for understanding striatal circuit imbalance beyond peak-dose dyskinesia and highlight the off-L-DOPA phase as a critical, underexplored aspect of PD and LID pathophysiology.

Disorders of the Nervous System

D-075

TDP-43 cytoplasmic accumulation in clock neurons disrupts circadian rhythms without affecting sleep in a novel Drosophila melanogaster model of proteinopathy

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Sleep and circadian alterations are frequently observed in neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Although aggregation and cytoplasmic mislocalization of TDP-43 constitute central pathological hallmarks of ALS/FTD, their contribution to circadian dysfunction remains poorly understood. To investigate its role in rhythmicity and sleep, we generated novel Drosophila melanogaster models expressing different TDP-43 variants. In young adult males, overexpression of wild-type human TDP-43 (WT) in circadian neurons did not significantly alter circadian period (Tau) compared to controls, although a trend toward reduced Tau power was observed. However, these flies exhibited reduced both total and daytime sleep duration. In contrast, expression of a nuclear localization-deficient TDP-43 variant (ΔNLS), produced a profound disruption of circadian rhythmicity, with almost no flies showing identifiable period. Remarkably, this phenotype was not accompanied by detectable sleep abnormalities. To assess the role of endogenous TBPH (TDP-43 homologue), we downregulated its levels specifically in the neurons of the circadian circuit. We found two types of phenotypes: either period lengthening or arrhythmicity. Together, these results suggest that cytoplasmic mislocalization of hTDP-43 disrupts circadian behavioral output and may contribute to circadian dysfunction associated with the ALS/FTD spectrum.

Disorders of the Nervous System

V-076

Cerebellar Neuroinflammation Modulates Social Behavior in Mice

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Sociability is a complex behavior involving distributed neural circuits, including the cerebellum. Increasing evidence suggests that cerebellar dysfunction may contribute to the behavioral alterations observed in autism spectrum disorder (ASD), although the underlying mechanisms remain poorly understood. Here, we investigated whether cerebellar neuroinflammation contributes to alterations in social behavior. Using the prenatal valproic acid (VPA) mouse model of ASD, we found reduced sociability in male offspring, accompanied by transient alterations in Purkinje cell density during postnatal development that were not maintained into adulthood. To directly assess the contribution of inflammation, we induced neuroinflammation in lobules VI/VII of the cerebellum in adult male mice. This manipulation produced a marked reduction in sociability, without alterations in Purkinje cell density. Systemic treatment with dexamethasone completely prevented the behavioral deficit, whereas ibuprofen produced a partial effect. Dexamethasone treatment was also associated with reduced microglial activation. Together, these findings support a role for cerebellar neuroinflammation in the regulation of social behavior and suggest that microglial activation may contribute to inflammation-induced sociability deficits.

Disorders of the Nervous System

S-075

CRISPR/Cas9-Corrected Isogenic iPSC Lines for Functional Characterization of Two Novel UBQLN2 Variants Identified in an FTD Patient

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Pathogenic UBQLN2 variants have been implicated in neurodegenerative proteinopathies, including frontotemporal dementia (FTD). We previously identified altered protein homeostasis, oxidative stress, mitochondrial polarization, and antioxidant pathways in neural stem cells (NSCs) derived from a patient carrying two novel UBQLN2 variants. Here, we tested whether these variants drive the disease-associated phenotypes by generating CRISPR/Cas9-corrected isogenic iPSC lines and differentiating them into NSCs CRISPR/Cas9 editing generated independent isogenic iPSC clones carrying the corrected UBQLN2 sequence. Two clones were selected and characterized for pluripotency, karyotype, and STR profiling to confirm their identity and parental origin, and subsequently differentiated into NSCs. NSC identity was confirmed by established neural stem cell markers. Protein abundance, mitochondrial membrane potential, and ROS levels were assessed by immunoblotting, immunofluorescence, and flow cytometry. Compared with the parental patient-derived cells, the isogenic NSCs showed reduced UBQLN2 protein aggregation, restored mitochondrial membrane potential, and reduced ROS levels These findings provide functional evidence supporting a causal contribution of the UBQLN2 variants to the observed cellular phenotypes and establish patient-derived and CRISPR/Cas9-corrected isogenic iPSC models for investigating the cellular and molecular mechanisms underlying UBQLN2-associated neurodegeneration.

Disorders of the Nervous System

D-076

Octodon degus as a naturally polymorphic model to study ApoE-associated lipid dysregulation in Alzheimer's Disease

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Classic rodent models for Alzheimer's Disease (AD) mainly rely on transgenic mice overexpressing mutant human genes to mimic rare familial AD, but often fail to reproduce the diversity of its signs and symptoms, raising construct and face validity concerns. Octodon degus instead develop AD-like pathology spontaneously with age, combining a long lifespan, diurnal habits, and naturally occurring ApoE variants (Tan et al., 2022; Hurley et al., 2018; Mugnaini et al., 2022), the strongest genetic risk factor for AD in humans, where isoform-specific effects otherwise require artificially humanized mouse models. We examined whether ApoE variation at position 213 affects cellular lipid homeostasis, comparing two prevalent variants, E and K, representing wild-type-like and risk-associated states. In primary fibroblasts from genotyped animals, ApoE213K cells showed increased lipid droplet number and size versus ApoE213E cells, mirroring APOE4-linked lipid droplet dysfunction in human AD. In human astrocytes engineered to express the degu ApoE213 variants, untargeted proteomic and lipidomic profiling revealed widespread dysregulation of lipid-related proteins and lipids, converging on increased lipid biosynthesis and reduced lipid export, a "lipid trap" phenotype that may underlie the fibroblast lipid droplet phenotype. These findings contribute to establishing Octodon degus as a powerful natural model linking ApoE variation, lipid biology, and Alzheimer's disease risk.

Disorders of the Nervous System

V-077

Repeated cannabinoids injection increases cocaine-induced behavioral response in adolescent rats in a sex dependent manner.

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The use of cannabis oil has grown significantly across all age groups. It is usually a mixture of Cannabidiol (CBD) and Tetrahydrocannabinol (THC). THC, which has psychostimulant effects, may enhance the response to first cocaine exposure, potentially increasing the risk of developing addiction. Adolescents are especially vulnerable to the effects of psychoactive substances. However, there is limited evidence on how low repeated doses of CBD and/or THC affect adolescent response to cocaine. We administered 10 injections of CBD (9 mg/kg, i.p.) and/or THC (3 mg/kg, i.p.) or vehicle to male and female rats starting on postnatal days 30-33. Two or 10 days after finishing the treatment, we assessed their basal behaviors (i.e., anxiety-like behaviors, ALB) and their locomotor response to cocaine (5 mg/kg, i.p.). We found significant sex differences in ALB: CBD increased it in males, whereas THC decreased it in females. Females also showed greater susceptibility to cocaine. Interestingly, CBD enhanced cocaine responses in females 2 days post-treatment, THC reduced it, and CBD+THC appeared to balance these effects. On the other hand, a cocaine injection after 10 days of THC treatment significantly increased locomotor activity compared to controls. Our results suggest that low-dose cannabinoid treatments during adolescence influence anxiety-like behaviors and cocaine responses differently based on sex. Ongoing experiments will assess CBD and CBD+THC after 10 days.

Disorders of the Nervous System

S-076

NMDA receptor hypofunction on GABAergic interneurons results in input-specific Excitatory/Inhibitory imbalance in pyramidal neurons of medial prefrontal cortex

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Excitation/inhibition (E/I) balance is often considered a global property of cortical circuits, although pyramidal neurons (PNs) integrate inputs from distinct afferent pathways. In a mouse model with early postnatal NMDA receptor (NMDAR) ablation in corticolimbic GABAergic interneurons, we tested whether interneuron NMDAR hypofunction disrupts mPFC E/I balance globally or in a pathway-specific manner. Combining anatomical labeling, optogenetic circuit mapping, paired recordings, and synaptic integration analysis, we found that structural and functional E/I imbalance emerged selectively at ventral hippocampal (vHPC) inputs to mPFC PNs, while callosal inputs were unaffected. Structurally, the imbalance was restricted to vHPC synapses on apical dendrites. Functionally, mutants showed an excitation-shifted E/I ratio in vHPC-driven responses due to impaired feedforward inhibition via fast-spiking interneurons, whose preferential excitatory drive from vHPC inputs was selectively lost. Short-term synaptic plasticity was unchanged, excluding altered presynaptic release dynamics as the underlying mechanism. Consistently, GABA-A receptor blockade failed to prolong vHPC-evoked EPSPs in mutant PNs, indicating loss of inhibitory control over hippocampal, but not callosal, input integration. These findings reveal a pathway-specific E/I imbalance caused by interneuron NMDAR hypofunction, suggesting selective disruption of vHPC-mPFC processing rather than global cortical dysfunction.

Disorders of the Nervous System

D-077

Longitudinal Progression of White Matter Hyperintensities and Disease Severity in bvFTD

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Behavioral variant frontotemporal dementia (bvFTD) is associated with increased white matter hyperintensity (WMH) burden, which relates to disease severity and cognition. Yet longitudinal WMH progression in bvFTD remains understudied in Latin America. We included 28 participants from the Instituto Peruano de Neurociencias (20 healthy controls [HC], 8 bvFTD) with MMSE, CDR, T-ADLQ, and MRI assessments at baseline and follow-up (mean interval 2.6±1.0 years). Linear mixed-effects models tested group-by-time effects on clinical and WMH measures. Partial Spearman correlations tested associations between annual WMH-volume change and annual change in MMSE, CDR sum-of-boxes, and T-ADLQ. Analyses adjusted for baseline age, education, sex, and total intracranial volume, and were FDR-corrected. Compared with HC, bvFTD showed steeper annual MMSE decline (β=−2.83; qFDR<.001) and greater annual increases in CDR sum-of-boxes (β=1.50; qFDR<.001), T-ADLQ (β=1.07; qFDR=.041), WMH volume (β=1.07; qFDR<.001), and WMH count (β=2.93; qFDR<.001). Greater WMH-volume increase was linked to faster CDR worsening (p=.013; qFDR=.039) and nominally associated with MMSE decline (p=.046; qFDR=.069). bvFTD patients showed greater longitudinal WMH accumulation alongside faster cognitive and functional decline than HC. Greater WMH progression was linked to worsening disease severity, supporting its potential as a clinically relevant marker of bvFTD progression in this understudied cohort.

Disorders of the Nervous System

V-078

CDK5 deficiency does not impair the differentiation of human induced pluripotent stem cells into dopaminergic neurons

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CDK5, a kinase essential for neuronal development and function, becomes hyperactivated under neurotoxic and stress conditions, contributing to neurodegeneration. However, whether CDK5 is required for acquisition of a dopaminergic phenotype remains unclear. This work aimed to evaluate if CDK5 loss affects the differentiation of human induced pluripotent stem cells (hiPSCs) into dopaminergic neurons. We applied a 60-day differentiation protocol, based on the sequential addition of specific induction and maturation factors, to CDK5 wild-type (WT) and knockout (KO) hiPSCs (FN2.1 cell line). Samples were collected at days 15, 24 and 59 to monitor differentiation and characterize the resulting neuronal phenotype. Dopaminergic differentiation was assessed by RT-qPCR analysis of tyrosine hydroxylase (TH) and dopamine transporter (DAT), together with the ventral midbrain markers PITX3 and FOXA2. We also performed immunofluorescence detection of TH and PITX3. Both WT and CDK5 KO lines showed progressive increases in TH and PITX3 transcript expression throughout differentiation, accompanied by the generation of TH- and PITX3-positive neurons, indicating that CDK5 deficiency does not prevent the acquisition of a dopaminergic phenotype. These findings establish that FN2.1 CDK5 KO hiPSCs can be differentiated into dopaminergic neurons and provide a cellular model for further investigation of CDK5-dependent mechanisms in PD, including mitochondrial function and calcium homeostasis.

Disorders of the Nervous System

S-077

Establishment of a Mouse Model of Stress–Cocaine Cross-Sensitization to Investigate Rac1 Signaling

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Repeated stress exposure potentiates behavioral responses to cocaine through neuroadaptations in the Nucleus Accumbens (NAc). In our laboratory, we previously characterized a cross-sensitization paradigm between repeated restraint stress and cocaine in rats. Here, we aimed to establish and optimize this experimental approach in mice to investigate the molecular and cellular mechanisms underlying this phenomenon. We implemented a protocol involving five days of repeated restraint stress followed by cocaine administration and evaluated locomotor activity as a measure of cocaine sensitization. Following optimization of the experimental conditions, we successfully reproduced cross-sensitization in male mice, whereas this effect was not observed in females. This mouse model expands the experimental approaches available to investigate the mechanisms linking stress to cocaine-induced behavioral sensitization and provides a foundation for further studying the Rho GTPase Rac1 signaling in this context. Previous findings from our laboratory showed that chronic stress induces structural and functional neuroadaptations in the NAc and alters cofilin activity. Given the role of Rac1 in cofilin regulation and actin cytoskeleton dynamics, we hypothesize that stress-induced alterations in Rac1 signaling contribute to NAc dendritic spine remodeling associated with increased vulnerability to cocaine.

Disorders of the Nervous System

D-078

Long-term behavioral profiling of spared nerve injury chronic neuropathic pain mouse model

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Chronic neuropathic pain (NP) is a severe neurological condition with significant clinical relevance. Beyond sensory discomfort, it leads to cognitive and emotional disorders, lowering patients' quality of life. Although this comorbidity is clinically recognized, the mechanisms linking persistent pain and cognitive/emotional issues remain uncertain. The spared nerve injury of the sciatic nerve (SNI) is a model used to study long-term consequences of NP in rodents. Research often focuses on time-periods close to peripheral nerve injury. To understand better the long-term behavioral impact of SNI intervention we evaluated animal behavior from one to four months post-lesion (PL), confirming robust and sustained mechanical allodynia throughout. Working memory and sociability showed no significant differences between groups at any time point. Locomotion in the open field test was reduced at one and two months PL but normalized by month three PL, when reduced relative center exploration emerged. At four months, anxiety-like and repetitive behaviors were normal, except for a selective reduction in induced grooming duration. Our previous work showed no neurodegeneration in cortical and hippocampal regions, while expression of the RNA-binding protein TDP-43, critical for neuronal function, appeared altered in select areas. These results indicate that SNI induces subtle, time-specific behavioral and molecular changes, without overt neurodegeneration or generalized impairment.

Disorders of the Nervous System

V-079

miRNA-seq identifies shared regulatory changes in PSEN1-associated familial Alzheimer's disease

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Pathogenic variants in PSEN1 are the leading cause of familial early-onset Alzheimer's disease (fAD); however, their impact on miRNA-mediated regulatory networks in human neurons remains poorly defined. We performed small RNA sequencing in human iPSC-derived cortical neurons at day 70 of differentiation from six lines: three carrying distinct PSEN1 variants (M146L, A246E, and T119I, a novel variant identified in an Argentinian fAD pedigree) and three wild-type controls. Differential expression analysis (edgeR, FDR < 0.05, $|\log_2 FC| \geq 1.5$) identified 154 dysregulated miRNAs in fAD versus controls (70 up, 84 down). Among the shared changes, miR-4707-3p showed the strongest increase ($\log_2 FC$ +6.3 across variants), while miR-219a-2-3p and members of the miR-34 family were consistently downregulated. miR-219a-2-3p has been implicated in tau regulation, whereas the miR-34 family is linked to p53 signaling and neuronal stress responses. miR-100-5p was also reduced, potentially affecting mTOR-related regulation of autophagy and proteostasis. Target enrichment highlighted neuronal apoptosis, PI3K-AKT/FoxO signaling, and senescence as major affected processes. Together, these findings reveal coordinated miRNA dysregulation across distinct PSEN1 variants, converging on pathways relevant to neuronal survival, stress responses, and proteostasis in fAD.

Disorders of the Nervous System

S-078

Evaluation of the neuroprotective potential of violacein in ex vivo and in vivo models of Parkinson's disease

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Introduction: Parkinson’s disease (PD) is a progressive neurodegenerative disorder lacking disease-modifying therapies. Violacein (Vio), a natural compound from Chromobacterium violaceum, has antioxidant, anti-inflammatory, and neuroprotective properties. This study evaluated its effects in ex vivo and in vivo PD models. Methods: Striatal and hippocampal slices from Wistar rats were exposed to 6-hydroxydopamine (6-OHDA) with or without Vio. Cell viability, SUMO-2/3 conjugation, and SENP3 levels were analyzed. In vivo, rats received bilateral intrastriatal 6-OHDA (10 or 20 µg) and Vio (300 nmol/kg, i.p.), followed by behavioral and oxidative stress analyses. Results: Vio prevented 6-OHDA-induced toxicity ex vivo. SUMO-2/3 conjugation decreased in the hippocampus, while SENP3 levels were reduced in both regions. In vivo, Vio partially improved memory, anxiety- and depressive-like behaviors, mainly at the lower 6-OHDA dose. It also increased GSH and reduced MDA and ROS, especially in the prefrontal cortex and hippocampus. Conclusion: Vio showed neuroprotective effects in PD models, mainly by reducing oxidative stress rather than modulating SUMOylation. These findings support its potential as a disease-modifying therapy, particularly in early or moderate PD onset. Funding: Studentships from CAPES (L.Y.Q. and M.S.P.); CNPq (B.J.C.; productivity in research to L.M.S. and H.I.C.; grants 445750/2023-5 and 403204/2024-0); FAPESC (R.S.V.; C.H.W.; grant 2024TR1733.

Neural Circuits and Systems Neuroscience

D-079

Does social isolation delay inhibition in the habenula of larval zebrafish?

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The lateral habenula (LHb) is a key regulator of dopaminergic and serotonergic pathways involved in motivational and motor functions. It also plays a role in negative reward processing, and changes in LHb function have been linked to depression. During early development, the brain is highly sensitive to environmental inputs, and social interaction is important for normal development. Early-life social isolation can cause long-lasting behavioral changes and has been linked to neuropsychiatric disorders. We aim to study how social isolation during early development affects habenular function in zebrafish. Using in vivo calcium imaging in transgenic zebrafish expressing GCaMP6f, we analyzed habenular neuronal responses to audiovisual stimuli in socially raised and isolated zebrafish between 12 and 17 days old.We and others previously showed that during development habenular responses sharpen and their duration is reduced.This has been linked to a delay in projection of inhibitory vs excitatory inputs. Our results show differences in response duration between age-matched socially raised and isolated animals, with isolated animals showing a tendency toward longer-lasting responses. We are testing the hypothesis that this prolonged activity is similar to the response pattern observed in younger social animals.This could indicate that early social isolation delays the normal development of habenular function and may help explain how early social experience influences later behavior

Neural Circuits and Systems Neuroscience

V-080

Cholinergic gating of entorhinal inputs promotes associative LTP and discrimination learning

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The dentate gyrus (DG) plays a crucial role in hippocampal learning and memory by forming distinct representations. While neuromodulators adapt circuits to enable plasticity, the underlying mechanisms remain unclear. Previous work in the lab has shown that acetylcholine (ACh) release in the DG reconfigures inhibitory circuits, driving excitatory disinhibition and synaptic plasticity. In hippocampal slices, we explored how ACh modulates DG microcircuit plasticity by assessing spike timing-dependent plasticity (STDP) and associative long-term potentiation (LTP). Because lateral and medial entorhinal cortex inputs convey content-specific versus contextual information, we examined their convergence in the DG, finding that ACh selectively modulates both pathways and facilitates associative LTP induction by weakening inhibitory currents. Complementarily, an AdEx-based spiking computational model of the DG tested this disinhibitory mechanism and its impact on information processing. Building on these circuit-level insights, we hypothesized that ACh release boosts learning and memory. Using a head-fixed virtual reality Go/No-Go task in mice, chemogenetically enhancing endogenous ACh release (Chat-HM3DQ) produced a trend toward faster contextual discrimination learning. These results contribute to understanding how ACh-mediated neuromodulation supports cognitive flexibility and memory formation.

Neural Circuits and Systems Neuroscience

S-079

Early postnatal stress disrupts maturation of prefrontal–raphe circuits controlling serotonergic function and emotional behavior.

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Vulnerability to stress-related disorders is considered to arise from disturbances during early neurodevelopment. Accumulating evidence highlights prefrontal cortex (PFC) circuits as key to the developmental origins of mood disorders. Among these, the projection from the PFC to the dorsal raphe nucleus (DRN)—the main source of forebrain serotonin (5-HT)—plays a central role in emotional regulation and stress responses. There is a mouse critical period for brain development, between postnatal days (P) 2 to 14, when environmental challenges can shape neural circuitry. Maternal separation (MS) is an early-life stress paradigm that induces emotional alterations in adulthood. We examined how MS affects the development and refinement of the PFC–DRN circuit during this critical period. We analyzed changes in PFC–DRN synaptic anatomy using high-resolution microscopy (Array Tomography), and assessed stress-induced activation of serotonergic DRN neurons. We also performed ex vivo patch-clamp recordings from 5-HT and GABAergic DRN neurons in MS mice across postnatal development. Our findings reveal that MS during the first two postnatal weeks disrupts the normal maturation of PFC inputs to the DRN and alters stress-dependent activation of 5-HT neurons. These results identify a key developmental window for PFC–DRN circuit formation, when early-life stress may induce maladaptive changes that could represent a neural substrate underlying increased vulnerability to psychiatric disorders.

Neural Circuits and Systems Neuroscience

D-080

Acoustic Startle Reflex in Chinchilla: Standardized Baseline and Intensity–Frequency Effects for Preclinical Auditory Research

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The chinchilla (Chinchilla lanigera) is a valuable model given its human-like hearing range and high sensitivity between 1–8 kHz; however, a species-specific ASR baseline is not yet available. We present a study that standardizes ASR in chinchilla and reports the effects of intensity and frequency as groundwork for implementing, in future phases, gap-prepulse inhibition paradigms (GPIAS). Amplitude and latency were recorded with the Startle Reflex Response system (©MazeEngineers) using 20-ms pulses, intensities between 90 and 115 dB SPL, and four frequencies (1000, 2000, 4000, and 8000 Hz), with randomized presentations and controlled repetitions. Results indicate a consistent increase in startle amplitude with increasing intensity across the tested range, delineating a robust intensity–response function. Response latency remained constant across conditions, suggesting motor gain changes without detectable temporal variations in the reflex pathway. In the frequency analysis, at equivalent intensities, no significant differences were observed in amplitude or latency. These findings provide operational parameters and calibration criteria, define reproducible working windows, and allow estimation of auditory thresholds without timing bias. By establishing this baseline, the study enables the adaptation and validation of GPIAS in chinchilla for the preclinical detection of tinnitus-like behavior and for translational investigations of temporal auditory processing.

Neural Circuits and Systems Neuroscience

V-081

Beyond dopaminergic neurons: neuronal contributions to sleep and motor dysfunction in a Drosophila model of Parkinson's disease

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Parkinson's disease (PD) causes motor dysfunction and non-motor symptoms, including sleep disturbances. The strong association between REM sleep behavior disorder (RBD) and subsequent PD suggests a link between sleep and motor circuits. However, how distinct neuronal populations contribute to these manifestations remains poorly understood. Here, we asked whether α-synuclein–induced dysfunction across neuronal populations affects sleep and locomotion in Drosophila melanogaster. We expressed the PD-associated mutant α-synuclein A53T (α-SynA53T) pan-neuronally or in selected populations and analyzed sleep and locomotor coordination during aging. Pan-neuronal expression altered both sleep and locomotor coordination. Restricting α-SynA53T expression to dopaminergic neurons reproduced both phenotypes, with a stronger progression during aging. In contrast expression in the PPL1 and PPM3 dopaminergic clusters impaired motor coordination without affecting sleep. Expression in LPN neurons, a circadian sleep-promoting population, produced both sleep and locomotor alterations that persisted with age. Together, these findings show that PD-like motor and non-motor phenotypes depend on the neuronal population affected rather than uniformly arising from α-SynA53T expression in dopaminergic neurons. These results support a circuit-level contribution to PD symptoms and motivate ongoing studies to determine whether the distinct phenotypes are associated with differential neurodegeneration.

Neural Circuits and Systems Neuroscience

S-080

Same Performance, Different Brains: Biomarkers of Motor Effectiveness from Resting-State EEG in Tennis Players vs. Non-Athletes

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Research in sports neuroscience has explored whether resting-state brain activity can predict motor performance. This study investigated whether the pre-task aperiodic 1/f exponent (β) is associated with success in a progressive decision-making task. 12 university-level tennis players (TEN) and 14 non-athlete controls (CON), all right-handed, underwent 64-channel resting-state EEG before and after a motor task involving tennis-ball catching under varying visual cue conditions (simple, choice-reaction, and no-go trials). Success rates were calculated for each task. Both groups performed similarly, with no significant differences in success rates. However, TEN showed a significant pre-to-post decrease in 1/f β over right frontal and left parietal regions, consistent with a shift toward a more activated cortical state, whereas CON showed no changes. A significant pre-post interaction in the right frontal region was driven by greater changes in TEN. Only TEN showed a negative correlation between pre-task 1/f β over the left sensorimotor cortex and success rate, indicating that a lower 1/f β (higher excitability) predicted better performance. These findings suggest that resting-state EEG 1/f may be a candidate biomarker of motor effectiveness in trained athletes, despite no overt performance differences between groups. The left sensorimotor cortex may reflect readiness for action, while the right frontal region may differentiate participants at the neural level.

Neural Circuits and Systems Neuroscience

D-081

Closed-loop acoustic stimulation enhances the initiation and persistence of slow oscillation trains during sleep in elderly adults

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Slow oscillations (SOs) during non-rapid eye movement (NREM) sleep are critical for multiple brain functions. Aging is associated with reduced SO amplitude and density, as well as disrupted temporal organization, characterized by more isolated events and shorter rhythmic SO trains. Here, we investigated whether closed-loop acoustic stimulation (CLAS) could restore rhythmic SO activity in elderly adults. Subjects underwent an adaptation and an experimental night and were assigned to a control or stimulation group. We analysed SO temporal organization using metrics previously introduced by our group (Capurro et al., 2026), including the proportions of isolated, consecutive, and train-start SOs and SO train length. Analyses were performed locally around stimulation periods and globally across NREM sleep. CLAS reorganized local SO dynamics by reducing isolated SOs and increasing consecutive SOs, train initiation, and train persistence. Global analyses showed weaker but consistent effects, mainly characterized by longer SO trains. Importantly, these changes occurred without increasing overall SO density, suggesting that CLAS promoted sustained rhythmic SO activity rather than simply increasing SO occurrence. These findings suggest that CLAS may mitigate age-related alterations in SO dynamics and highlight temporal organization metrics as a complementary framework for assessing stimulation efficacy, particularly in systems affected by stimulation latency and jitter.

Neural Circuits and Systems Neuroscience

V-082

Lateral entorhinal cortex contribution to context-dependent odor processing in the piriform cortex

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Sensory representations in the cortex are shaped not only by stimulus features but also by contextual and behavioral signals. In the piriform cortex (PC), neurons initially tuned to odors become modulated by non-olfactory variables such as visual context, but it remains unclear which associative inputs drive this modulation. A candidate source is the lateral entorhinal cortex (LEC), a region involved in context encoding and memory that is monosynaptically connected to PC. We hypothesize that LEC projections to PC provide contextual information and that their inhibition will alter both PC coding and behavioural performance. We developed a dual-virus system to express inhibitory DREADDs specifically in LEC projection neurons to PC. Unexpectedly, DREADD expression also appeared within PC itself, rather than being restricted to LEC, revealing extensive reciprocal connectivity between the two regions and suggesting that a subset of neurons within the recurrent PC circuitry projects back to LEC. In parallel, acute Neuropixels recordings were established with the goal of targeting multiple regions at once. We began with hippocampal recordings to optimize the approach, and used dummy-probes to confirm we can accurately reach both LEC and PC, enabling future simultaneous recordings. Ongoing experiments will assess how the pathway inhibition alters neural representations and task performance, and lays groundwork to test how contextual signals are integrated into olfactory circuits.

Neural Circuits and Systems Neuroscience

S-081

Research Project: Low-Intensity Focused Ultrasound Neuromodulation for Depressive Behavioral Persistence and Prefrontal Plasticity

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Major Depressive Disorder is a leading cause of disability, with ~30% of patients experiencing treatment-resistant depression, often marked by repetitive negative thinking and cognitive rigidity. This project evaluates Low-Intensity Focused Ultrasound (LIFU) as a non-invasive potential approach to modulate prefrontal-striatal circuits underlying behavioral persistence. The study comprises three specific objectives. First, we target the corpus callosum with in vivo LIFU, combined with ex vivo optogenetics and patch-clamp recordings, to evaluate changes in synaptic strength and feedforward inhibition in the medial prefrontal cortex. Second, we assess the behavioral effects of repeated bilateral LIFU targeted to the murine equivalent of the anterior limb of the internal capsule. Third, using a striatal cholinergic interneuron ablation mouse model of compulsive behavioral rigidity, we analyze whether rigid coping strategies facilitate stress chronification following acute social stress. Pilot experiments show that a 5-minute LIFU protocol is sufficient to induce cortical c-Fos expression. Furthermore, preliminary ex vivo patch-clamp recordings on EYFP-positive axonal fields confirm our ability to functionally target and modulate synaptic transmission in prefrontal pathways. This research aims to elucidate the neurobiological mechanisms of LIFU-mediated plasticity, advancing its translation for non-invasive clinical therapies.

Neural Circuits and Systems Neuroscience

D-082

Spatial navigation, working memory and sensory sensitivity: Insights from virtual reality

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To navigate through space, animals must integrate information from the environment. However, what they perceive depends on how they move through it. For example, depending on the direction of movement, they may experience different gradients in the intensity of a stimulus. This puts both their sensitivity to changes in the stimulus and their working memory to the test. To investigate this interaction, we examine how zebrafish larvae adapt their navigation strategies to variations in light intensity across controlled temporal and spatial scales. Taking advantage of their well-characterized phototactic behavior, we develop a spatial navigation paradigm in a virtual reality environment. This requires implementing customized artificial intelligence algorithms to determine the larva's virtual trajectory in real time, while presenting light stimuli according to the virtual testing arena. Ultimately, this approach will allow us to perform the same experiments under a light-sheet microscope to investigate the neural mechanisms underlying the task. We will present preliminary results with the aim of discussing the proposed experiments and their possible interpretations with the community.

Neural Circuits and Systems Neuroscience

V-083

From Internal State to Behavior: A Synchronized Optical System for Multi-Organ Imaging in Zebrafish Larvae

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Animals must combine external and internal information to produce adaptive behaviors: the smell of food, for example, does not trigger the same response in a hungry versus a satiated animal. This integration is constant and bidirectional, yet the underlying mechanisms remain poorly understood. Addressing this topic in a holistic manner is challenging because physiological signals arise from different anatomical regions and they express themselves at different temporal scales. In this context, Zebrafish larvae are an ideal model to address it: fast, ex-utero development, a rich behavioral repertoire, optical transparency granting non-invasive access to internal organs and the nervous system, and genetic tools. We designed and built a low-cost, low-complexity, novel optical system that allows simultaneous multi-organ acquisition in the same individual, capturing lateral and ventral views of the whole larva on a single sensor. Combined with a custom analysis pipeline, this allows extraction of cardiac and intestinal activity together with behavioral segmentation. The system is designed for integration with light-sheet calcium imaging across the whole brain, providing an unprecedented platform to study brain-body axes. We will present preliminary results on the temporal relationship between heart and gut rhythms related with the start of an escape behavior, until now considered spontaneous.

Neural Circuits and Systems Neuroscience

S-082

Beyond immediate effects: aperiodic EEG markers of delayed cortical reorganization after physical exercise

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Acute exercise induces immediate and delayed neurophysiological changes, which may influence subsequent cognitive and behavioral performance, an aspect often overlooked. The aperiodic component of the EEG spectrum, reflecting excitatory/inhibitory balance, offers a complementary window beyond classical oscillatory activity. This study analyzed resting-state, eyes-closed EEG (30 channels) from two healthy participants who performed a HIIT protocol (10x40"/20" at 90% maximal load). We extracted aperiodic components (offset and exponent) at three time points: pre-exercise (PRE), immediately post (POS1), and 5-min post (POS2). Kruskal-Wallis tests assessed changes across moments. Both participants exhibited consistent temporal trends yet with opposing directions: Participant 1 showed a decrease of the magnitude in both components at POS1 and POS2 relative to PRE, whereas Participant 2 displayed an increase. Notably, despite divergent baselines, both showed a significant increase in dispersion of both components at POS2 compared to PRE and POS1. This increased variability suggests the delayed post-exercise period may represent a phase of differential cortical reorganization. These preliminary trends highlight the potential of aperiodic markers to capture individual neurophysiological responses to acute exercise, and underscore the need to consider delayed effects when timing post-exercise cognitive ad behavioral assessments, warranting further investigation with larger cohorts.

Neural Circuits and Systems Neuroscience

D-083

Odor Discrimination and Sequence Learning in Honeybees

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Animals process information from the environment through different sensory systems, including olfaction. In honeybees, olfaction plays a key role in resource detection and behavior. Bees must discriminate complex stimuli in their components and also be able to process their temporal order. Here we study olfactory discrimination in honeybees by using differential conditioning protocols. First, we evaluated the effectiveness of different unconditioned stimuli (US) that maximize odor separation. Using the proboscis extension response (PER), bees were conditioned by pairing odor A (CS+) with sucrose and odor B (CS-) with either quinine or a neutral tactile control stimulus. Next, using the optimal USs combination, we investigated whether honeybees can learn and discriminate odor sequences according to their temporal order, by training them with AB (appetitive) and BA (aversive), and testing them with sequences AB, BA, A and B. Both experiments were analyzed using DLC to track the precise kinematics of the antennae and proboscis response. In the first experiment, we obtained clearer behavioral evidence of aversive learning and discrimination learning, when quinine was used as aversive US rather than the tactile stimulus. These results provide a behavioral framework for investigating olfactory discrimination and temporal sequence processing in honeybees.

Neural Circuits and Systems Neuroscience

V-084

Searching for Neural Signatures of Escape Decisions in Running Crabs Using Tetrode Recordings

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Escape responses to imminent threats are essential for survival, yet the same stimulus does not invariably elicit escape, suggesting that escape expression involves a decision-making process. Previous intracellular and anatomical studies in the crab Neohelice granulata identified several classes of Lobula Giant (LG) neurons involved in visually evoked escape. Here, we investigated the relationship between LG activity and escape behavior using tetrode recordings from crabs running on an air-supported ball. We presented looming stimuli with different temporal dynamics to generate variable behavioral responses. Behavioral analyses revealed substantial variability not only across stimuli and individuals but also across trials within individuals. Thus, the same crab may display a vigorous run, a weak run, or fail to run in response to the same stimulus. We exploit this variability to identify neuronal activity associated with different escape outcomes. Preliminary analyses revealed distinct groups of units that were excited or inhibited by looming stimuli. We are using guided automation to classify neuronal responses and relate them to behavioral outcomes. Our ongoing analyses indicate that both the decision to run or not to run and the velocity of the escape response can be predicted from LG neuronal activity, providing potential neural signatures of escape decisions.

Neural Circuits and Systems Neuroscience

S-083

Sensing satiety: The metabotropic glutamate receptor MGL-2 regulates nutritional state and feeding behavior in C. elegans

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Satiety perception is critical for maintaining energy homeostasis, yet the precise neuroendocrine circuits encoding nutritional state remain elusive. Caenorhabditis elegans allows the determination of neural circuits with a resolution difficult to achieve in other models. Previous work from our laboratory delineated the circuits mediating elevated food intake after fasting, establishing that serotonin and tyramine—the invertebrate counterpart of adrenaline—are crucial for this behavior; however, how the nervous system senses nutritional status remains unknown. We mapped robust expression of mgl-2, an ortholog of mammalian metabotropic glutamate receptors, to core neurons of the feeding circuit. Here, we demonstrate that mgl-2 mutants are insensitive to satiety, establishing a novel genetic model of hyperphagia. These animals exhibit an increased food intake that closely mimics post-starvation responses. As a consequence, they show enhanced lipid accumulation. Notably, serotonin depletion abolishes this increased food intake in mgl-2 mutants, showing a strict requirement for serotonergic signaling in this response. We are currently interrogating the activity of key serotonergic and tyraminergic nodes to determine how MGL-2 modulates these pathways. Collectively, our findings reveal that MGL-2 acts as a key receptor for sensing satiety, positioning this receptor as a critical node in the serotonergic network governing feeding behavior.

Neural Circuits and Systems Neuroscience

D-084

Young adult-born granule cells and CA1 population coding during spatial pattern separation

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The hippocampal formation transforms experiences into distributed neural representations that support the discrimination of similar events. Within this circuit, adult-born granule cells (ABGCs) in the dentate gyrus (DG) have been proposed to contribute to pattern separation, yet their influence on downstream population coding remains largely unresolved. To address this question, a spontaneous object location recognition task (SOLR) was combined with high-throughput calcium imaging in CA1. Neuronal activity was recorded while mice experienced different spatial object configurations in the SOLR, varying in their demands for pattern separation. CA1 population activity was then characterized across these different spatial configurations. In addition, CA1 activity was examined following reversible silencing of young ABGCs to assess whether their contribution is reflected in downstream spatial representations. By combining population calcium imaging across SOLR conditions with selective manipulation of young ABGCs, this approach provides a means to investigate how adult-born neurons in the DG may influence the organization of spatial representations in CA1 during pattern separation.

Neural Circuits and Systems Neuroscience

V-085

Circuit remodeling by adult neurogenesis: Activity-dependent synaptic competition

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Cohorts of adult-born granule cells (aGCs) integrate continuously into the adult hippocampal circuits, generating new connections onto their target cells, which include CA3 pyramidal cells and interneurons. Recent studies from our lab have shown that activation of young (4-week-old) aGCs induces persistent place cell remapping and increased pyramidal cell recruitment in the CA3 region. Together with previous electron microscopy studies, these results suggest that aGCs establish their target connections onto pyramidal cells through activity-dependent competition against preexisting synapses. To test this hypothesis, we studied the structural characteristics of neighboring axonal mossy fiber boutons (MFBs) from young and mature aGCs (“young MFBs” and “mature MFBs”) under conditions of persistent activation of the young cohort. Chronic in vivo optogenetic stimulation of young aGCs induced a substantial reduction in the size of neighboring mature MFBs. However, MFB size was unchanged in boutons farther from active terminals. Electrophysiological recordings to test whether these structural changes are accompanied by the corresponding functional changes in synaptic strength are currently ongoing. These findings support a role for activity-dependent competition in the integration of aGCs, highlighting adult hippocampal neurogenesis as a mechanism that perturbs CA3 network homeostasis by providing a continuous drive for remodeling that favors dynamic encoding.

Neural Circuits and Systems Neuroscience

S-084

Impact of social recognition training on dCA2 synaptic plasticity: preliminary results and analysis considerations

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Social recognition memory (SRM) is the ability to identify and remember conspecifics, an essential feature of social animals. Despite the significant efforts invested in understanding its neurobiological mechanisms, our knowledge at the molecular and circuit levels remains incomplete. Over the last decades, the neuropeptide oxytocin has been shown to be relevant for SRM formation, but the mechanisms at the circuit level are not widely understood. Our aim is to expand the knowledge on the neural circuits through which OXT modulates SRM. Specifically, we want to understand how OXT modulates SRM-associated synaptic plasticity in dorsal CA2 (CA2d). To this end, we used ex-vivo electrophysiology to characterize the neuronal plasticity triggered by peer interaction. We compare different off-line analysis tools for quantifying field postsynaptic potentials (fPSPs) in CA2d, using data from animals that underwent SRT training and from naive animals. Our preliminary results show that in brain slices from adult male mice that underwent a SRT training session, potentiation in dorsal dCA2 was blunted when compared to naive mice. We discuss the constraints of the analyses used, and propose a plan for future analyses.

Neural Circuits and Systems Neuroscience

D-085

Concentration-dependent dynamics of olfactory sensory adaptation in honey bees

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Sensory systems continuously adjust their processing of environmental stimuli based on animal's most recent sensory experience, allowing it to optimize the detection and perception of changes in behaviorally relevant information over stimuli that carry little or no predictive value. One of the main phenomena that rapidly adjusts the system is sensory adaptation, which is defined as a decrease in sensitivity or response to a stimulus after sustained exposure to it. In this study, we investigated whether and how olfactory sensory adaptation in honey bees depends on stimulus concentration. Using electroantennograms (EAG), we measured peripheral olfactory receptor neuron (ORN) activity across different concentrations of acetophenone and 1-hexanol. Our findings reveal a strong concentration dependency in adaptation dynamics: both the initial control pulse amplitudes and the adapted-to-control pulse ratios vary significantly by concentration. Furthermore, response temporal dynamics are altered; the width of the adapted pulse, measured as the time the signal remains at 50% of maximum amplitude, increases significantly post-adaptation compared to control pulses, particularly at higher stimulus concentrations. These findings suggest that peripheral sensory responses are dynamically adjusted according to stimulus intensity, which may help maintain effective odor detection in complex and fluctuating olfactory environments.

Neural Circuits and Systems Neuroscience

V-086

Neuronal dynamics underlying depressive-like states

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Chronic stress induces neurobiological adaptations that can lead to depressive-like states, yet their temporal dynamics remain poorly understood. The lateral habenula (LHb) –a key node for aversion– shows stress-induced hyperactivity, but when these adaptations emerge and become behaviorally relevant is unclear. Here, we identify a temporally-defined onset of stress consequences in mice across behavioral, functional, and molecular levels using chronic corticosterone (CORT) administration. Using spatial transcriptomics, we generated an LHb molecular atlas that revealed topographically and temporally organized gene expression remodeling during CORT. Longitudinal two-photon calcium imaging revealed progressively enhanced LHb neuronal responses to aversive stimuli, with stable excitatory or inhibitory clusters alongside dynamic populations that increased their responses over CORT exposure, with distinct spatial patterns. These changes paralleled behavioral alterations, including reduced active coping and increased apathy-like behaviors. Ketamine reversed LHb remodeling and behavioral alterations when given at remodeling onset, and chemogenetic inhibition of LHb hyperactivity during this window normalized depression-related behaviors. Together, these findings identify shared spatiotemporal signatures across LHb neuronal ensembles, molecular landscape, and behavioral states, revealing a critical time window when antidepressant interventions can reverse stress-induced adaptations.

Neural Circuits and Systems Neuroscience

S-085

The olfactory cortex can learn to encode the subject's spatial location as accurately as the hippocampus

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The hippocampal-entorhinal network has an essential role in spatial cognition. Surprisingly, other brain regions not involved in this canonical spatial encoding network have been recently shown to modulate their neuronal activity according to the subject's spatial location. This includes the remarkable discovery of spatial information encoded in the primary piriform olfactory cortex (PCx) of both rats and mice. Indeed, in a previous study and in work from our lab, rodents were trained in a task to associate olfactory and spatial cues to obtain a reward, and machine learning classifiers were applied to PCx activity to successfully classify the spatial context of each trial. This has been interpreted as spatial maps encoded in the olfactory cortex. However, can the animal's spatial location across time be precisely decoded from PCx activity? Here, we study PCx and hippocampal neuronal activity of mice in different learning stages of this olfactory-spatial association task, and perform a series of spatial location decoding analyses. Our results indicate that the spatial location of the animal is encoded in the PCx once animals learn the task, but not before. Moreover the spatial encoding precision increases around behaviorally relevant locations, and decoding performances in the PCx and the hippocampus are comparable. We discuss how these results could contribute to our understanding of the role of the olfactory cortex in olfactory-cued spatial learning.

Neural Circuits and Systems Neuroscience

D-086

Neuronal assembly dynamics and behavior in the zebrafish habenula.

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Neural activity is not random but displays sparse, organized spatiotemporal patterns, even in the absence of structured external stimulation. Neuronal assemblies, defined as populations of co-activated neurons, have been proposed as fundamental units of neural computation underlying processes such as perception, memory, and behavior. However, their biological relevance and functional significance remain poorly understood. We use calcium imaging to record spontaneous activity in the habenula and identified neuronal assemblies using a PCA based pipeline. In larval zebrafish, we observed repeated, temporally structured patterns of network activity and began investigating how these assemblies change across early developmental stages and whether they are shaped by experience-dependent factors such as social isolation. We also explore their involvement in the response to auditory and visual stimuli. More recently, we developed an approach to simultaneously monitor behavior during calcium imaging, allowing us to directly relate neural assembly dynamics to ongoing behavior. By comparing freely moving larvae with agarose-embedded animals imaged under the microscope, we aim to determine how social isolation influences spontaneous and stimulus-evoked network activity at both the behavioural and neuronal level simultaneously.

Neural Circuits and Systems Neuroscience

V-087

Spiking dynamics in lateral habenula and raphe nuclei revealed by high-density recordings

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The Lateral Habenula (LHb) and the Raphe Nuclei – comprising the Dorsal (DRN) and Median Raphe (MRN) – are critical nodes in the neural circuitry governing emotional valence, stress adaptation, and decision-making. While the LHb is well-established as a center for encoding negative affect, the Raphe nuclei are pivotal in modulating mood and behavioral coping strategies via widespread serotonergic projections. Although anatomical studies have delineated robust glutamatergic inputs from the LHb to the Raphe, the real-time neuronal dynamics of such a projection remain poorly understood. Existing evidence relies on bulk activation of LHb inputs onto the Raphe to establish both functional and behavioral causalities. This method, while powerful, imposes artificial synchrony and masks the naturalistic temporal structure of inter-regional communication. To bridge this gap, we employed in-vivo electrophysiological recordings of neuronal activity using dual Neuropixels 2.0 probes, in adult C57Bl6j male mice under isoflurane anesthesia. To capture naturalistic, spontaneous interaction between these neuronal networks we utilized simultaneous dual-probe recordings. Preliminary analysis identified a subset of units in the Raphe nuclei whose firing dynamics can be modeled based on preceding LHb activity. Ultimately, this work aims to dissect the precise temporal codes the LHb uses to modulate Raphe output providing a granular view of this essential neural circuit of affect.

Neural Circuits and Systems Neuroscience

S-086

Perineuronal nets define two functionally distinct Parvalbumin Interneuron subpopulations in the medial prefrontal cortex

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Perineuronal nets (PNNs) are a fundamental component of cortical synapses regulating synaptic plasticity and circuit function. PNNs form during postnatal development and their alteration is linked to neurodevelopmental disorders. Although PNNs surround multiple cortical neurons, parvalbumin-positive interneurons (PVI) are the cell type most associated with them. PVI provide the main inhibitory drive to pyramidal neurons, supporting E/I balance and gamma oscillations, and PNNs shape their plasticity. Unlike sensory cortices, the mPFC shows fewer PVI with well-developed PNNs, suggesting high- and low-PNN subpopulations with distinct properties. We asked whether PNN status defines functionally distinct PVI subpopulations in adult mouse mPFC, acting as low-plasticity gain-control or high-plasticity dynamic units. WFA labeling revealed three PNN-intensity populations (174 PVI, 7 mice), split at the median into high- and low-PNN groups. Whole-cell recordings showed low-PNN PVI had greater excitability, higher input resistance, longer time constant, lower rheobase, larger AHP, and higher maximal firing rate than high-PNN PVI. Theta-burst stimulation induced long-term potentiation of EPSPs selectively in low-PNN, not high-PNN, PVI. These results show PNN density delineates PVI subpopulations with distinct intrinsic and plasticity properties in the mPFC, potentially forming segregated subcircuits. Ongoing work extends this to an NMDA receptor ablation model relevant to schizophrenia.

Neural Circuits and Systems Neuroscience

D-087

Targeted memory reactivation during sleep promotes more consistent neural dynamics

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Targeted Memory Reactivation (TMR) during non-rapid eye movement (NREM) sleep is widely used to investigate memory reactivation and consolidation. Previous studies have identified electrophysiological signatures of TMR, including cue-evoked oscillatory responses and the reinstatement of learning-related neural representations. However, little is known about how memory reactivation influences the large-scale dynamical organization of brain activity during sleep. Here, we analyzed high-density EEG recordings from a previously published TMR study in which auditory cues associated with prior learning and acoustically matched control cues were presented during NREM sleep. Neural complexity was quantified using Sample Entropy (SampEn) across the full EEG spectrum and canonical frequency bands. We examined both mean entropy and entropy dispersion across cue presentations. Memory-associated cues produced a robust reduction in entropy dispersion, measured using both standard deviation and interquartile range, across all frequency bands. This effect was highly consistent across participants and remained evident at the individual level. In contrast, mean entropy did not differ between memory and control conditions. Likewise, relative spectral power analyses revealed no significant differences between conditions in any frequency band. These findings indicate that memory reactivation during sleep is associated with more consistent neural dynamics without altering overall neural complexity

Neural Circuits and Systems Neuroscience

V-088

Experience dependent changes in neural representations in the dentate gyrus and CA3

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The hippocampus is essential for memory and spatial representation. However, how neurons encode distinct aspects of experience and how this coding changes with learning remain unclear. We recorded neural activity in the dentate gyrus (DG) and CA3 during a virtual reality task in which mice learned associations between odors, visual contexts, and reward outcomes. Using a Poisson generalized linear model, we quantified the contribution of sensory, motor, and cognitive variables to neuronal activity. In expert animals, CA3 neurons encoded more task variables than DG neurons. Moreover, the interaction between the odors and the rewarded context made a larger contribution to neural activity in CA3 than in DG. Context was decoded from both regions, more accurately in CA3 within the context and at earlier corridor positions, whereas odor and reward were decoded similarly. Contextual information emerged with learning in both regions. Reward information was evident from the first session, but odor information was decodable before learning only in DG. Learning increased the contribution of speed, position, and reward in DG, and of position and the odor–context association in CA3. Finally, LSTM-based decoding showed that position and speed could be decoded from CA3 before learning, but from DG only after learning. These results reveal that learning differentially reorganizes neural coding, with CA3 showing greater multiplexing and stronger associative coding than DG.

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Social Isolation of Larval Zebrafish Alters Baseline Locomotion and Behavioral Plasticity in a Passive Coping Assay

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Animals respond to aversive or stressful experiences by selecting actions to escape or avoid them. However, when escape fails to counteract the aversive event, animals suppress it as an adaptive strategy to reduce energy expenditure and minimize harm. Repeated failure to escape can reduce the perceived value of escape. This discounting becomes maladaptive when expressed as hopelessness. Early-life social isolation can alter the evaluation of negative events and contribute to depression. We aimed to determine whether hopelessness is affected by early-life social isolation in zebrafish (Danio rerio). We tested whether one week of social isolation altered their response to sustained inescapable aversive stimulation. We implemented a passive coping assay (PAS) in which 100 larvae (17–23 days old), raised socially or in isolation, were exposed to mild inescapable shock to study the transition from active coping, characterized by escape attempts, to passive coping, characterized by reduced mobility. We found that social isolation increased baseline locomotor activity, reflected in higher mean and instantaneous swimming velocity during acclimation, and reduced wall-hugging behavior. During the PAS, social animals shifted from active to passive coping, reducing swimming velocity during shock, whereas isolated animals failed to adjust and maintained high velocity. Thus, social isolation increases baseline activity and reduces behavioral plasticity during sustained stress.

Neural Circuits and Systems Neuroscience

D-088

Stress-induced dorsal raphe serotonin activation immediately after maternal separation stress in mice

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Early-life stress produces cognitive and emotional symptoms contributing to the etiology of psychiatric disorders, like anxiety and depression. In rodents, many of these symptoms are replicated in a model of early-life stress when pups are subjected to a repeated maternal separation protocol [3hs/day from postnatal day (p) 2 to 14]. Maladaptive changes in this model impact brain circuit development and maturation. While it is thought that serotonin could play a role in this mechanism, very little is known about its potential role. We investigate in this model, if early-life stress through serotonin can modify the capacity of serotoninergic neurons to respond to a mild stress immediately after the end of stress exposure (at p15). To this purpose, we exposed C57BL/6 mice to maternal separation while administering a specific inhibitor of the serotonin synthesis enzyme, Tryptophan hydroxylase, or saline, during the postnatal critical period (p2-14). On the next day, after treatment cessation (p15), mice were subjected to the forced swim test to study dorsal raphe serotonin neuron activation using cFos immunofluorescence and confocal microscopy. Our preliminary results suggest that serotonin could have a crucial role in mediating the effects of early-life stress on the raphe network engaged in stress-coping behavioral strategies.

Neural Circuits and Systems Neuroscience

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Effects of Threat on Decision-Making and Activity Profiles of Neuronal Subpopulations in the Tail of the Striatum

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Animals must balance exploitation of available resources with exploration of alternatives while accounting for travel costs and environmental threats. The tail of the striatum (TS) may integrate salient sensory information with action selection, but how its principal subpopulations contribute to this trade-off remains unclear. D1- and Adora2a-expressing TS neuronal subpopulations have been implicated in distinct responses to threatening stimuli and are hypothesized to differentially bias exploitation and threat-driven exploration. Here, we use a linear virtual reality foraging task to study exploration/exploitation decisions in head-fixed, water-restricted mice. The task comprises rewarded zones separated by non-rewarded corridors. We analyze the activity of these subpopulations using fiber photometry during task performance and present preliminary behavioral and fiber photometry results from two independent comparisons: short versus long corridors, and short corridors with or without threatening bird-call stimuli. Behaviorally, animals adopted more exploitative strategies when corridors were long rather than short; within short corridors, exposure to threatening bird calls shifted behavior toward exploration relative to threat-free corridors. Fiber photometry results indicate that D1- and Adora2a-expressing TS neuronal subpopulations exhibit distinct activity profiles across different phases of the task.

Neural Circuits and Systems Neuroscience

S-088

Piriform cortex multiplexes odor and spatial cues as odor-place associations are learned

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Olfactory processing is shaped by experience, context, and internal state. To understand how learning reshapes responses within olfactory circuits, we trained mice on an associative task in a virtual-reality environment, where animals discriminated among four odor-context combinations for reward. We previously found that after training, odor-responsive neurons in piriform cortex (PCx) acquire mixed selectivity, jointly encoding contextual and associative information, but the process underlying this transition remained unknown. To address this, we recorded PCx activity across learning and applied behavioral and encoding/decoding models to track how representations evolve. Mice acquired the task sequentially: they first learned to discriminate odors (intermediate session) and only later learned to discriminate contexts (expert session). PCx activity followed the same trajectory: intermediate animals encoded mostly olfactory information, whereas expert animals encoded both odor and context, a result confirmed by population decoding. Expert neurons also showed greater multiplexing than those from earlier stages. We also showed that contextual enhancement of odor discrimination depends on an associative learning process, suggesting that the acquired PCx encoding arises specifically from linking odor cues to spatial information during correct task performance. We are now investigating the neural mechanisms underlying this association within PCx.

Neural Circuits and Systems Neuroscience

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Structural Connectivity Associated with Clinical Response Following Ketamine Treatment in Patients with Treatment-Resistant Depression

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Ketamine is a therapeutic option for treatment-resistant depression (TRD) due to its rapid antidepressant effects. We aimed to identify corticolimbic structural connectivity (nSC) patterns before and after ketamine treatment and their association with clinical response. Sixteen patients with TRD underwent diffusion-weighted MRI before and after treatment. nSC was estimated by probabilistic tractography between eight bilateral regions. Clinical response was assessed by percentage change in the Hamilton Depression Rating Scale and correlated with nSC using Spearman correlations. At baseline, connectivity between the left posterior cingulate cortex (PCC) and right ventrolateral prefrontal cortex (vlPFC) was positively associated with response. Post-treatment nSC revealed four connections positively and five negatively associated with response. The positive subnetwork comprised the right orbitofrontal cortex with both thalami and the interhemispheric PCC connection. The negative subnetwork included connections involving both vlPFCs, the left vlPFC with the right dorsolateral prefrontal cortex (dlPFC), the right dlPFC with the left PCC, and the right anterior insula with the left amygdala and left subgenual cingulate cortex. Overall, post-treatment nSC showed more extensive associations with response than baseline nSC, revealing differential corticolimbic circuits consistent with Menon's Tripartite Model.

Neural Circuits and Systems Neuroscience

V-090

Cortico-Cochlear Oscillatory Dynamics in Chronic Tinnitus under the Residual Inhibition Paradigm

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Introduction: Chronic tinnitus affects 14% of adults. We used the residual inhibition (RI) paradigm (temporary acoustic suppression) to study its neurophysiological persistence mechanisms, integrating cortical and cochlear levels for treatment response markers. Methods: We conducted a case-control study on 25 chronic tinnitus patients with normal hearing. Subjects were grouped as Responders or Non-Responders based on noise-induced alleviation. We analyzed EEG and DPOAEs during rest, pre- and post-stimulation, comparing PSD and aperiodic (1/f) components. Results: In Responders, delta activity correlated with tinnitus intensity. PSD lacked group differences, indicating a stable trait. However, Non-Responders showed a steeper spectral slope in the right temporal region (T8) and flattened frontal 1/f slope (Fz). Peripherally, Non-Responders had increased Theta and Gamma in DPOAEs, while Responders showed greater modulation in left temporal 1/f knee frequency (T7). Conclusions: RI resistance is driven by cortical aperiodic structure and efferent control, not just oscillatory power. 1/f dynamics and cochlear rhythms are potential biomarkers for tailored tinnitus therapies.

Neural Circuits and Systems Neuroscience

S-089

Spatial disorientation in pilots: Towards intelligence assistance for angular orientation during flight.

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In aviation, spatial orientation requires integrating body-based and external cues during movement and rotation in three-dimensional space. During flight, aircraft orientation and direction of travel may be dissociated, potentially challenging path integration, particularly when reliable external references are unavailable. Using immersive virtual reality and high-density mobile electroencephalography, human neuronal activity has been shown to realign with sensory cues. Theta phase resetting in the retrosplenial complex upon landmark presentation supports the recalibration of path integration errors during naturalistic human navigation. Therefore, characterizing the non-invasive neural correlates of angular spatial orientation during simulated flights may provide a basis for intelligent systems supporting navigation under sensory uncertainty. Rather than replacing human decision-making, this framework seeks to explore how artificial and biological systems can be integrated to enhance human navigation in challenging flight environments. Keywords: path integration; angular navigation; grid-like representations; theta oscillations; artificial intelligence;

Neural Circuits and Systems Neuroscience

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Deciphering top-down encoding in sensory thalamocortical pathways: implications for schizophrenia

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Perception is a process by which the brain integrates bottom-up sensory information with top-down signals shaped by learned associations, expectations, and task demands. Imbalances between these processes may contribute to perceptual alterations in schizophrenia, yet the circuits implementing top-down information remain unclear. Previous work showed that higher-order auditory thalamic (HOAT) projections convey learned aversive-value signals to secondary auditory cortex (A2). We hypothesized that these pathways shape sensory representations according to learned associations and task demands. Using an auditory-cued Go/No-Go task, we found that selective silencing of HOAT output impaired task acquisition, showing a role in associative learning. Longitudinal two-photon calcium imaging of HOAT axonal boutons in auditory cortex revealed learning-related changes and distinct functional populations, indicating plasticity and encoding beyond stimulus acoustics. We next hypothesized that Go/No-Go learning is altered in a mouse model with schizophrenia-like phenotypes, reflecting impaired updating of internal models. Preliminary data show reduced task acquisition and altered perceptual thresholds in SCZ mice compared with controls. Together, these findings support a role for HOAT circuits in shaping sensory processing according to learned and internally generated information, suggesting that their disruption may contribute to altered perception in schizophrenia-like states.

Neural Circuits and Systems Neuroscience

V-091

Chronic effects of non-invasive audiovisual gamma stimulation on network activity in the aging hippocampus

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Brain oscillations are crucial for cognition. In Alzheimer's disease (AD), disruptions in gamma rhythms have been linked to memory deficits and cognitive decline. Recently, it has been shown that non-invasive audiovisual (AuViS) stimulation at 40 Hz improves pathological symptoms in AD models. Furthermore, it promotes structural plasticity through its positive effects on adult neurogenesis in the aging hippocampus. However, the specific mechanisms by which AuViS induces plastic changes within the circuit and how these modifications can lead to positive behavioral effects remain poorly understood. To assess the impact of AuViS on hippocampal network activity, we performed simultaneous in vivo single-unit and local field potential (LFP) recordings in the CA1 and dentate gyrus subregions of 8-month-old wild type mice exposed to chronic 40 Hz AuViS. We characterized oscillatory power during acute AuViS and free exploration of familiar and novel environments, both before and after six weeks of daily treatment. Preliminary results reveal an enhanced response to the acute stimulation after the treatment, together with lower decay in the endogenous gamma band recorded during spatial exploration. This could be related to similar preliminary observations in human AD patients, describing that AuViS rescues a shift toward lower gamma band, related to disease progression. Finally, we characterized single unit activity during acute stimulation and free exploration.

Neural Circuits and Systems Neuroscience

S-090

Fetal Sulcal Maturation Asymmetry: A Sulcus-Specific Analysis of First Appearance Using a Graded MRI Scale

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INTRODUCTION Cortical development gives rise to hemispheric asymmetries already observable in utero, exemplified by the early appearance and greater depth of the right superior temporal sulcus (STS). Normative trajectories of sulcal laterality remain poorly defined. PURPOSE To compare, sulcus by sulcus, the gestational age at first appearance of cortical sulci between hemispheres, and to test whether lateralization is sulcus-specific rather than uniformly directional. METHODS Public CRL-2025 fetal MRI data: 149 typically developing fetuses, 20.1-38.0 weeks, one scan each. Fifteen sulci were graded per hemisphere on a four-point scale (Grades I-IV; 0 = absent) adapted from van der Knaap et al. Hemispheres were compared per fetus (Wilcoxon signed-rank, Benjamini- Hochberg); the gestational age at 50% presence was estimated per hemisphere by logistic regression. RESULTS Both STS segments were rightward (posterior 50.3% of fetuses asymmetric, 70/75 rightward; anterior 51.7%, 75/77; $q<0.0001$) and appeared earlier on the right (2.16 and 1.48 weeks, respectively; $q=0.0033$). The lateral sulcus was leftward ($q=0.021$). Precentral, postcentral, cingulate, insular and occipitotemporal sulci were asymmetric in 11-19% of fetuses with no consistent side. CONCLUSION Pace and laterality are sulcus-specific: rightward and early for the STS, leftward for the lateral sulcus, fluctuating in five further sulci. Uniform directional asymmetry does not describe the fetal cortex.

Neural Circuits and Systems Neuroscience

D-091

The Role of the Oxytocinergic System in the Pathophysiology of Peripartum Depression: Insights from a Murine Model

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Peripartum depression (PPD) is a severe and often underdiagnosed mood disorder that affects approximately 10–20% of women globally and has profound consequences for both mothers and their offspring. Beyond maternal suffering, PPD disrupts mother–infant bonding, alters the early-life social environment, and increases the risk of neurodevelopmental disorders in children. Only two medications are currently approved specifically for PPD, but their accessibility and effectiveness remain limited. Progress in treatment development is stalled by the scarce knowledge of the neurobiological mechanisms underlying PPD. Given the critical role of oxytocin (OXT) during labour, lactation, maternal care and social bonding, our aim is to evaluate the role of OXT in PPD pathophysiology using a mouse model of PPD. To address this question, we implemented a stress-based model of PPD, combining chronic mild unpredictable stress and maternal separation during pregnancy and postpartum in order to induce a depressive-like phenotype. Our findings show that this model induces depressive-like behaviors, together with deficits in sociability and maternal care. Using cFOS immunostaining as a proxy of neuronal activation, we observed a lower percentage of active OXT+ cells in the paraventricular nucleus of the hypothalamus in the PPD group compared to control dams. These findings suggest that altered OXT activity may contribute to PPD pathophysiology and highlight a potential target for future research.

Neural Circuits and Systems Neuroscience

V-092

A D1 Receptor-Dependent Dopamine Circuit Targeting VIP Interneurons in the Anterior Insular Cortex

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Pain is a subjective, emotional experience arising from distributed brain activity integrating sensory and affective components. The anterior insular cortex (AIC) is central to this process, and dopaminergic signaling via D1 receptors (D1R) in the AIC has been linked to pain modulation. However, the cellular identity and functional properties of D1R-expressing neurons within AIC microcircuits remain poorly characterized. Here, we used anatomical, electrophysiological, and behavioral approaches to characterize D1R-expressing neurons in the mouse AIC. In D1R-Tomato mice, D1R- positive neurons showed a layer-dependent distribution, with superficial layers enriched in inhibitory interneurons and deeper layers containing pyramidal neurons and interneurons. Immunohistochemistry showed that most superficial D1R-expressing interneurons co-express VIP, lacking parvalbumin or somatostatin markers. Consistently, morphological reconstructions revealed bipolar and multipolar architectures typical of VIP interneurons. Ex vivo recordings showed that D1 receptor activation enhances the excitability of D1R-positive neurons, indicating a direct dopaminergic influence on this population. Finally, using c-fos as a marker, we assessed the activation of AIC D1R-expressing neurons during acute visceral pain. Together, these results provide an integrated characterization of D1R-expressing neurons in the AIC and link their recruitment to cortical processing during acute pain.

Neural Circuits and Systems Neuroscience

S-091

Embodied neurocomputation in crab polarimetric vision: a deep learning approach

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The semi-terrestrial crab Neohelice granulata inhabits mudflats where much of the reflected light is polarized. Previous work from our group showed that its photoreceptors process this signal through two orthogonal channels, aligned horizontally and vertically (0° and 90°, respectively). Using a deep learning approach, we trained convolutional autoencoders on a denoising task with natural scenes from the crab's habitat, comparing the biological channel (0°/90°) against a rotated control (45°/135°). The biological channel preserved the scenes' Degree of Linear Polarization (DoLP) with higher fidelity. Using Partial Information Decomposition (PID), we found that decoding the rotated channel requires 70% more synergistic processing, meaning the nervous system would need to integrate both signals jointly rather than reading them independently. Biologically, this added synergy would translate into greater processing resources and, thus, higher metabolic costs. Thus, aligning the biological channels with the 0°/90° axes would increase the efficiency of primary processing of polarimetric information.

Neural Circuits and Systems Neuroscience

D-092

Functional Brain Network Reorganization in Temporal Lobe Epilepsy with Hippocampal Sclerosis

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INTRODUCTION: Temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) involves functional abnormalities extending beyond the temporal lobe. We characterized functional network connectivity (FNC) in unilateral TLE-HS using a normative network template. METHODS: Eighty-eight adults with TLE-HS and 68 healthy controls underwent resting-state fMRI (3T Philips Achieva; TR=3 s; 209 volumes). After DPABI preprocessing, spatially constrained ICA was performed using 105 NeuroMark 2.2 networks. FNC was estimated by Pearson correlation with Fisher z transformation. Group differences across 5,460 network pairs were tested using independent-samples t-tests with FDR correction ($p<0.05$); effect sizes were assessed with Cohen's d. RESULTS: TLE-HS showed altered FNC in 183 network pairs (3.35%; $|d|=0.73–0.88$), with increased connectivity between cerebellar-visual, prefrontal-default mode, and parietal-limbic/sensorimotor networks, and decreased connectivity between sensorimotor-cognitive temporal, visual, and cerebellar-prefrontal networks. CONCLUSION: TLE-HS is characterized by distributed functional network reorganization, with concurrent hyper- and hypoconnectivity extending beyond mesial temporal structures.

V-093

Mechanisms governing the development of synaptic transmission in the lateral habenula

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The lateral habenula (LHb) is a key brain region involved in processing negative stimuli and adaptive responses to aversive situations. While LHb function in adulthood is well characterized, how its synaptic properties evolve during development remains unclear. Perineuronal nets (PNNs), extracellular matrix structures known to regulate synaptic maturation in other brain regions, progressively accumulate in the LHb during development and are altered by negative experiences, suggesting their potential role in LHb synaptic function regulation. Using in vitro electrophysiology in acute brain slices, we show that excitatory synaptic transmission in the LHb differs between young and adult mice. Young mice display lower AMPA/NMDA ratios, slower NMDA receptor kinetics although similar subunit composition. Additionally, they show reduced spontaneous activity, and weaker burst firing. Importantly, degrading PNNs in adulthood recapitulates the AMPA/NMDA synaptic feature of LHb in young individuals. Behaviorally, PNN degradation in the LHb did not alter active avoidance or escape behaviors but modified behavioral strategies in an anxiety-related task. Together, these findings identify developmental changes in LHb excitatory transmission and support a role for PNNs in stabilizing synaptic function and regulating negative affect-related behaviors.

S-092

Validation of an early interferon signaling response in the dopamine-denervated striatum in a mouse model of Parkinson’s disease

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Parkinson's disease is characterized by the progressive loss of striatal dopaminergic innervation and widespread neuroinflammation. Although levodopa (L-DOPA) is the gold standard symptomatic therapy, chronic use generates adverse effects known as L-DOPA-induced dyskinesias (LID). Understanding the cellular adaptations of the striatal network during dopamine depletion and LID, is therefore critical for translational medicine. Using single-nucleus RNA sequencing of striata from intact and hemiparkinsonian mice, we characterized cell-type-specific transcriptional profiles at 5 and 28 days after 6-OHDA-induced dopaminergic denervation. We identified an early inflammatory response characterized by increased expression of interferon (IFN)-related genes across most striatal cell types, including a subset of IFN-responsive microglia. The aims of the project will be to validate the presence of the inflammatory microenvironment in an independent cohort by combining RT-qPCR and confocal immunofluorescence targeting the IFN/JAK/STAT pathway. We will then pharmacologically inhibit this pathway using an FDA-approved drug and assess its effect on neuroinflammation, dopaminergic cell loss and motor function. Finally, we will investigate whether IFN-mediated response contributes to maladaptive circuit changes and susceptibility to LID. Identifying these mechanisms may reveal therapeutic targets to protect striatal circuits and reduce dyskinesias while preserving the motor benefits of L-DOPA

D-093

Synaptic properties of GABA co-releasing synapses in the lateral habenula

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The lateral habenula (LHb) is a key epithalamic structure involved in the regulation of mood, motivation, and reward processing. Acting as a hub between forebrain regions and midbrain monoaminergic centers, its dysfunction has been linked to disorders such as depression and addiction. Understanding the synaptic architecture and neurotransmitter dynamics within the LHb is therefore essential for elucidating its role in brain function and pathology. In this study, we characterized the synaptic properties of GABA co-releasing synapses within the LHb. Whole-cell voltage-clamp recordings were performed in transgenic mice expressing channelrhodopsin-2 (ChR2) in glutamatergic neurons. Optogenetic stimulation allowed selective activation of these inputs while pharmacologically isolating GABAergic currents. We examined the contribution of presynaptic calcium channels to GABA co-release by pharmacologically blocking P/Q-type and N-type calcium channels. Our findings indicate that both channel types support GABA co-release in the LHb, with P/Q-type channels playing a predominant role. The differential contribution of calcium channels to GABA co-release may influence the excitatory-inhibitory balance of habenular output, thereby modulating downstream monoaminergic systems implicated in mood and reward. Understanding these mechanisms could provide new insights into the synaptic basis of neuropsychiatric disorders and highlight potential therapeutic targets for neuropsychiatric disorders.

Neural excitability, synaptic transmission and neuron-glia interactions

V-094

Astroglial Perisynaptic Plasticity and Glutamate Uptake in a Contextual Fear Conditioning Paradigm

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Post-traumatic stress disorder (PTSD) is one of the most prevalent psychiatric disorders worldwide and is characterized by exaggerated threat responses to both trauma-related and trauma-unrelated cues. Morphological and functional alterations in astrocytes contribute to the pathophysiology of PTSD, including changes in the perisynaptic proximity of GLT-1. The expression profiles of GLT-1, GFAP, and Ezrin were analyzed in brain regions critically involved in anxiety and fear processing, including the amygdalar nuclei (BLA and CeA), the bed nucleus of the stria terminalis (BNST), and the dorsal hippocampus (HPC), using a classical contextual fear-conditioning (CFC) paradigm to model alterations relevant to PTSD. CFC is a well-established animal model for studying associative threat memory. In PTSD, threat memories display pathological features—including hypermnesia, overgeneralization, and deficits in extinction and extinction retention—that distinguish them from non-pathological memories. CFC was performed in male and female mice using footshock intensities of 0.10 mA and 0.60 mA, operationalized to model low- and high-threat conditions, respectively. The perisynaptic plasticity induced by the CFC protocol may alter glutamate concentrations within the synaptic cleft, thereby contributing to the molecular and cellular processes underlying the behavioral alterations characteristic of PTSD.

Neurochemistry and Neuropharmacology

S-093

Purinergic Modulation of Acetylcholine Release at the Efferent-Inner Hair Cell Synapse in the Developing Inner Ear

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Before the onset of hearing (postnatal day 12 in mice), inner hair cells (IHCs) are transiently innervated by medial olivocochlear (MOC) efferent fibers and fire spontaneous sensory-independent action potentials essential for normal auditory pathway development. Several studies suggest that this activity is driven and/or modulated by ATP released from cochlear supporting cells. We investigated the role of ATP in modulating MOC-IHC synapses using pharmacology and electrophysiology. IHCs from BALB/C mice at P8-11 were patch-clamped, MOC fibers extracellularly stimulated, and quantal content (m) estimated. ATP reversibly decreased m in a concentration-dependent manner. Suramin, a non-specific P2 antagonist, abolished this effect, while TNP-ATP, a specific P2X antagonist, did not. The P2X agonist α,β-MeATP also had no effect on m. Both ATPγS, a non-hydrolyzable ATP analog, and the P2Y agonist 2-MeSADP mimicked ATP. To identify the P2Y subunit involved, we used specific pharmacology based on RNAseq studies indicating P2Y1 expression in supporting cells and P2Y12 and P2Y14 in MOC neurons. MRS2500, a P2Y1 antagonist, did not prevent ATP-induced inhibition. MRS2690, a P2Y14 agonist, produced no inhibition of ACh release. However, PSB-0739, a P2Y12 antagonist, blocked ATP inhibition, indicating that P2Y12 receptors mediate ATP-dependent reduction in quantal content from MOC fibers.

Neurochemistry and Neuropharmacology

D-094

Deciphering the antidepressant mechanism of action and neuroplastic effects of psilocybin in mice

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Depression is a leading global psychiatric disorder. Conventional antidepressants require chronic administration and frequently fail in treatment-resistant depression. While psilocybin shows promising therapeutic potential, its underlying neurobiological mechanisms remain unclear. Psilocin, its active metabolite, mediates hallucinogenic effects via 5-HT2A receptors but displays higher affinity for other subtypes, including 5-HT2B and 5-HT7. Importantly, 5-HT2B signaling is required for the neurogenic and behavioral effects of classical antidepressants like fluoxetine. In this project, we will investigate the 5-HT2B receptor as a primary candidate mediating psilocybin's antidepressant action. We will evaluate behavioral responses following acute psilocybin administration at a clinically relevant dose and a non-hallucinogenic microdose to characterize its anti-anhedonic profile. The functional contribution of 5-HT2B receptors will be determined using selective pharmacological antagonists and knockout mouse models. In parallel, we will assess psilocybin and psilocin pharmacokinetics to correlate plasma levels with behavioral outcomes. Finally, we will examine long-term neuroplasticity by measuring hippocampal neurogenesis, neuronal survival, and neurotrophin expression in wild-type and transgenic mice. Unraveling these 5-HT2B-dependent mechanisms will bridge basic and clinical findings, paving the way for targeted therapeutics with enhanced efficacy and reduced adverse effects.

Neurochemistry and Neuropharmacology

V-095

Nucleus Accumbens Alterations Linked to Stress-Induced Vulnerability to Cocaine Addiction in Preclinical Models: A Scoping Review

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Exposure to stress is known to modulate vulnerability to cocaine use; however, the preclinical evidence in this field remains heterogeneous and lacks a systematic synthesis. We conducted a scoping review to map the neurobiological changes in the nucleus accumbens (NAc) associated with this vulnerability. We searched PubMed combining terms for stress, NAc, and cocaine, obtaining 294 results that, after a three-stage screening process, were narrowed down to 35 studies in adult rodents (1991-2025), which assessed behavioral sensitization, conditioned place preference, or self-administration. The effects of stress depended on its duration, predictability, and controllability: moderate stressors enhanced reactivity to cocaine, whereas chronic and uncontrollable stress produced opposite effects, consistent with an anhedonic-like phenotype. The NAc emerged as a convergence node where dopaminergic, glutamatergic, and serotonergic systems are reconfigured by stress. The mechanisms with the strongest causal support were: glial neuroinflammation-driven suppression of GLT-1 and cofilin-mediated actin cytoskeleton reorganization in the NAc core, loss of inhibitory control of VTA dopaminergic neurons projecting to the NAc, and activation of dynorphin/KOR signaling in the NAc medial shell. However the underrepresentation of females (4/35 studies) and methodological heterogeneity limit the generalizability of these findings.

Neurochemistry and Neuropharmacology

S-094

Naringin modulates hippocampal CA3 ΔFosB expression and osteocalcin levels in fructose-induced metabolic dysfunction under chronic stress: preliminary evidence for a bone–brain connection.

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Metabolic dysfunction and chronic stress can affect both skeletal and brain homeostasis. Osteocalcin (OCN), a bone-derived hormone, has emerged as a potential mediator of bone–brain communication. Naringin (NAR), a citrus-derived flavonoid with antioxidant and osteoprotective properties, may modulate these responses. We investigated whether NAR affects circulating OCN and hippocampal ΔFosB expression in male Wistar rats with fructose-induced metabolic dysfunction (FRD) exposed to chronic stress (CS). Plasma OCN was measured by immunoassay, and ΔFosB-positive cells were quantified in hippocampal subregions by immunohistochemistry. CS increased OCN levels and selectively increased ΔFosB-positive cells in CA3, but not CA1, CA2, or the dentate gyrus. NAR further increased OCN levels and enhanced ΔFosB expression in CA3 under both stressed and non-stressed conditions. The concomitant modulation of a circulating bone-derived signal and a hippocampal activity-related marker suggests that NAR may influence bone–brain communication. Given the region-specific expression of the OCN receptor GPR158 in CA3, these preliminary findings raise the possibility that OCN signaling contributes to NAR-induced hippocampal responses. Further studies are required to establish whether this association reflects a functional bone–brain pathway.

Neurochemistry and Neuropharmacology

D-095

Optogenetic and Morphological Assessment of Paraquat-Induced Dopaminergic Damage in Caenorhabditis elegans

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Paraquat (PQ) is a herbicide that disrupts the glutathione redox cycle, induces mitochondrial dysfunction, and damages dopaminergic neurons, leading to a Parkinsonian phenotype. The antioxidant N-acetylcysteine (NAC) has been proposed to mitigate PQ-induced toxicity. In this study, we evaluated dopaminergic function using an optogenetic approach and dopaminergic neuronal morphology in Caenorhabditis elegans exposed to sublethal PQ concentrations. Synchronized ZX909 (pdat-1::ChR2(H134R)::mCherry) L4 worms expressing Channelrhodopsin-2 in dopaminergic neurons were exposed to 5 mM PQ and/or 0.5 mM NAC for 24 h. Under blue-light stimulation, PQ significantly reduced locomotor activity, in terms of distance and speed. Dopaminergic integrity was analyzed in the UA44 strain (Pdat-1::α-syn, Pdat-1::GFP) by confocal microscopy in young adults and aged worms. Control and NAC-only animals of both ages displayed normal neuronal morphology. Only ~15% of young adults exposed to PQ or PQ+NAC showed low-severity degeneration of dopaminergic projections, whereas ~50% of aged worms exhibited medium-severity damage. Overall, PQ induced dopaminergic dysfunction and neurodegeneration, while NAC provided little protection in these endpoints. The greater neuronal damage observed in PQ-exposed-aged worms highlights aging as a critical factor that enhances susceptibility to dopaminergic degeneration, providing further insight into the environmental basis of neurodegenerative diseases.

Neurochemistry and Neuropharmacology

V-096

Inhibition of NF-κB by Pyrrolidine Dithiocarbamate Prevents Stress-Induced Cross-Sensitization to Cocaine and Neuroimmune–Glutamatergic Alterations in the Nucleus Accumbens Core

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Stress is a major risk factor for substance use disorders, increasing vulnerability to cocaine-related behaviors through persistent neuroimmune and glutamatergic dysregulation in the nucleus accumbens core (NAcore). Nuclear factor kappa B (NF-κB) is a central transcriptional regulator of stress-induced glial activation, proinflammatory signaling, and glutamate transporter (GLT-1) downregulation. We investigated whether local NF-κB inhibition by pyrrolidine dithiocarbamate (PDTC) in the NAcore reverses stress-induced cocaine cross-sensitization and associated molecular alterations. Rats underwent chronic restraint stress (2 h/day, 7 days). Fourteen days later, bilateral cannulae were implanted into the NAcore. On day 21, stressed and non-stressed rats received intra-NAcore PDTC (5–20 μM) or vehicle before saline or cocaine challenge (15 mg/kg, i.p.). Locomotor activity assessed cross-sensitization. NF-κB signaling and mRNA expression of TNF-α, GLT-1, and IL-10 were analyzed. PDTC dose-dependently abolished behavioral sensitization, suppressed p65 nuclear translocation and IKK phosphorylation, reversed TNF-α upregulation, and restored GLT-1 expression, but did not prevent IL-10 induction. These findings provide pharmacological evidence for a central role of NF-κB activation in the NAcore in stress-induced cocaine sensitization and associated immune–glutamatergic adaptations. Inhibiting this pathway may reduce stress-related vulnerability to substance use disorders.

Neurochemistry and Neuropharmacology

S-095

Stress- induced changes in endocannabinoid system: gender differences and interaction with opioid receptors

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Chronic stress induces persistent maladaptive changes in the nucleus accumbens (NAc) that increase vulnerability to substance use disorders. The endogenous opioid (EOS) and endocannabinoid (eCB) systems converge in the NAc to regulate stress responses and neurotransmission. Our previous work showed that CB1R signaling participates in stress-induced reinstatement of cocaine-seeking behavior. Likewise, alterations in the EOS have been implicated in stress- and drug-induced adaptations. However, the effects of chronic stress on the eCB system in the NAc and the contribution of opioid receptor signaling to these changes in a sex-dependent manner remain poorly understood. Thus, we investigated this interaction using naloxone. Male and female mice underwent chronic stress (6 days, 2 h/day), followed by naloxone (1 mg/kg/day, i.p.) for 5 days. On day 21, NAc levels of μ-opioid receptor, proenkephalin (Penk), CB1R, and eCB machinery components were evaluated. Chronic stress increased Penk and CB1R levels in both sexes, with naloxone preventing the stress-induced increase in CB1R but not Penk upregulation. Stress also altered eCB machinery in a sex-dependent manner. These findings suggest that opioid receptor signaling contributes to stress-induced remodeling of the eCB system in the NAc core, supporting functional opioid–endocannabinoid interactions and highlighting opioid signaling as a potential target for stress-related neuropsychiatric conditions.

Neurochemistry and Neuropharmacology

D-096

Can Cannabis sativa attenuate L-dopa-induced dyskinesias? Preliminary findings in a mouse model of Parkinson's disease

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L-DOPA-induced dyskinesias (LIDs) are a frequent and disabling complication of pharmacological treatment for Parkinson's disease (PD), significantly affecting patients' quality of life. The endocannabinoid system, particularly cannabidiol (CBD), has emerged as a promising therapeutic target due to its neuroprotective, anti-inflammatory, and modulatory effects on dopaminergic neurotransmission. This study aimed to evaluate the therapeutic effects of Cannabis sativa (CS) extract on LID development in an animal model of PD. First, HPLC was used to assess the presence of cannabinoids in plasma from C57BL/6 mice following acute oral administration of CS extract (60, 120, or 240 mg/kg). In an independent experiment, mice with severe nigrostriatal lesions induced by 6-OHDA received CS extract (60, 120, or 180 mg/kg, p.o.) or vehicle daily, 1 h before L-DOPA (12 mg/kg; dyskinesiogenic dose) or vehicle (i.p.) for 15 days. During treatment, LID severity was assessed using a previously validated scale. HPLC analysis detected cannabinoids in plasma following oral administration of CS extract. Preliminary results further suggest a reduction in LID severity in CS-treated animals compared with controls, with a similar trend across all three doses. Further studies are needed to confirm whether CS administration reduces LID severity and to determine whether this effect is associated with modulation of striatal synaptic microstructure.

Neurochemistry and Neuropharmacology

V-097

Serotonergic regulation of gut physiology and homeostasis in Drosophila

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Serotonin (5-HT) is a key neurotransmitter regulating mood, appetite, and sleep. Although 5-HT is synthesized within the central nervous system, the majority is produced by enterochromaffin cells in the intestinal epithelium, underscoring its central role in gastrointestinal physiology. While altered serotonergic signaling is linked to disorders such as Irritable Bowel Syndrome and Crohn's disease, the underlying cellular and molecular mechanisms remain poorly defined. Preliminary findings from our laboratory demonstrate that the Drosophila gut is innervated by serotonergic neurons and that altering 5-HT levels impacts both food intake and defecation frequency. Here, we mapped the expression of serotonin receptors across fly gut epithelial cells and evaluated their role in gastrointestinal homeostasis. We found that 5-HT7r loss of function flies exhibit increased food intake and defecation frequency, indicating that this receptor mediates the serotonergic regulation of gut function and establishing 5-HT as a critical modulator of intestinal homeostasis.

Neurochemistry and Neuropharmacology

S-096

Astrocytic GAT-3 inhibition disrupts memory formation by impairing protein synthesis and reducing Arc levels

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Astrocytes regulate synaptic function through bidirectional communication with neurons. They respond to neurotransmitters, mediate uptake, and release gliotransmitters. GABA, the main inhibitory neurotransmitter in the CNS, controls neuronal excitability. Astrocytes primarily express GABA transporter 3 (GAT-3), which helps terminate GABAergic signaling and maintain neuronal homeostasis. We investigated the role of hippocampal GAT-3 in spatial memory consolidation and expression. Rats were trained in a spatial object recognition (SOR) task that induces long-term memory, and SNAP-5114 (SNAP), a selective GAT-3 inhibitor, was infused into the dorsal hippocampus around either training or test. SNAP impaired both memory consolidation and expression, whereas exposure to a novel open field (OF) rescued these deficits. Additionally, SNAP significantly reduced protein synthesis to levels comparable to emetine, a general protein synthesis inhibitor, as shown by the SUnSET assay. SNAP also decreased activity-regulated cytoskeleton-associated protein (Arc), a plasticity-related protein required for memory formation. Conversely, novel OF exploration increased Arc levels, suggesting that the rescue of SNAP-induced memory impairment involves protein synthesis-dependent mechanisms. These findings reveal a specific role for hippocampal GAT-3 in spatial memory and support astrocyte-dependent GABAergic regulation as a key mechanism in memory, with relevance to neurological disorders.

Neurochemistry and Neuropharmacology

D-097

Behavioral Effects of Chronic Administration of Cannabinoid-Enriched Medicinal Cannabis Oils in Mice

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In recent years, interest in therapeutic alternatives for anxiety and depression has increased due to the limitations and adverse effects associated with conventional pharmacological treatments. Among these alternatives are medicinal cannabis oils, whose main studied component, cannabidiol (CBD), has shown beneficial effects on anxiety- and depression-related behaviors in animal models and humans. Given that Cannabis sativa produces more than 100 phytocannabinoids, we aimed to evaluate the therapeutic potential of cannabidiolic acid (CBDA), cannabigerol (CBG), and cannabidivarin (CBDV). Male and female C57BL/6 mice (7–9 week old) received daily oral administration of cannabis oils enriched in CBD, CBDA, CBG, CBDV (100 mg/kg for each of the 4 compounds) or vehicle (sesame oil) for 35 days. Anxiety-related behaviors were assessed using the Elevated Plus Maze and Novelty Suppressed Feeding Test; anhedonia-related behaviors using the Urine Sniffing and Splash Tests; and memory abilities using the Novel Object Recognition test. None of the oils tested produced significant differences compared with the control group in all of the behavioral tests performed. We hypothesize that the lack of behavioral responses may be due to a stable affective state and positive welfare in these animals. Therefore, we propose to re-evaluate these assays in a chronic-induced stress model, to determine whether therapeutic effects emerge under an altered affective state.

Neurochemistry and Neuropharmacology

V-098

Effects of postnatal exposure to fluoxetine: behavioral and neurogenesis in juvenile and adult mice.

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Perinatal exposure to antidepressants may have long term consequences in affective behaviors during childhood. These impairments have been also well characterized in adult mice after postnatal exposition to selective serotonin reuptake inhibitor (SSRI) antidepressants. Nevertheless, the impact of this kind of exposition on memory tasks as well as on the process of adult neurogenesis has been less explored so far. We orally treated C57BL/6 male and female mice from Postnatal day 2 (P2) to P14 with the SSRI fluoxetine (10 mg/kg) or vehicle. Proliferation and survival of hippocampal newborn neurons was analyzed in P90 mice by means of Ki67 and BrdU labeling, respectively. In addition, 3-weeks-old and 3-month-old mice treated with SSRI were assayed in the memory object recognition test and performed significantly worse than control animals. Similarly, in the object pattern separation test, fluoxetine-treated adult mice were less able to pattern separate, an ability linked to the role of immature neurons. Anxiety-like behaviors were evaluated by novelty suppressed feeding test and elevated plus maze, and were more pronounced in antidepressant-treated animals. Furthermore, weight gain was measured with marked reductions in treated mice at juvenile and adult age. All in all, our results show that early exposition to SSRI antidepressants in mice affects the development of newborn neurons in the hippocampus with lasting consequences on memory abilities and anxious behaviors.

Neurochemistry and Neuropharmacology

S-097

Network Pharmacology-Guided Discovery of Fungal Autophagy Modulators for Tauopathies: Structural and Proteomic Evidence

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Impaired autophagic clearance of hyperphosphorylated tau in tauopathies drives progressive accumulation of toxic tau species. This study examined fungal metabolites from Lion's Mane (Hericium erinaceus), Magic Mushrooms (Psilocybe spp.), and Ergot fungi (Claviceps spp.) as an untapped source of neuroactive compounds, using a computational workflow assessing structural diversity, blood-brain barrier permeability, and toxicity, combined with network pharmacology and protein-protein interaction analysis to identify autophagy-related targets. PPARG, GSK3B, and CSNK2A1 emerged as top candidates due to their complementary links between autophagy and tau pathology. Docking, MM/GBSA, molecular dynamics, and QSAR modelling confirmed stable, target-specific binding for Corallocin A and Erinacerin M (PPARG), Chaetopyranin and Ergocryptine (GSK3B), and Hericioic Acid D and Isohericerin (CSNK2A1), alongside Emodin, a reference compound active on all three targets; QSAR was informative only for PPARG candidates. Reanalysis of an independent hippocampal proteomic dataset from Alzheimer's patients showed significantly altered CSNK2A1 in the CA3 subfield, offering correlative support, while PPARG and GSK3B showed no significant changes, not precluding functional involvement. Overall, these findings identify fungal metabolites as promising multi-target autophagy modulators and provide a systematic strategy for prioritising candidates for experimental validation in tauopathies.

Neurochemistry and Neuropharmacology

D-098

Adolescent social isolation induces sex- and region-dependent changes in corticolimbic neurotransmitter profiles

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Adolescence is a critical period of corticolimbic maturation during which social experiences shape neurochemical systems involved in emotional regulation. Social isolation during this stage may therefore produce sex- and region-dependent alterations in neurotransmitter profiles. We examined the effects of isolated rearing (IR) on monoamines and their metabolites, glutamate (Glu), and GABA in male and female Wistar rats (n=35). Animals were socially reared (SR) or isolated from postnatal day 21 (PND21) and gonadectomised at PND45, after pubertal hormone exposure. At PND55, the medial prefrontal cortex (mPFC), lateral septum (LS), nucleus accumbens (NAc), dorsal hippocampus (dHIP), and amygdala were micropunched and analysed by HPLC. IR reduced DOPAC/DA and Glu in the mPFC but increased DOPAC/DA in the dHIP. In the LS, IR reduced DA and altered DOPAC/DA in a sex-dependent manner, with higher turnover in isolated males. The amygdala was the most broadly affected region: IR reduced DOPAC, 5-HIAA, and GABA levels, while dopaminergic and serotonergic alterations were sex-dependent. Neurochemical measures that were higher in SR females were attenuated under IR. In contrast, the NAc showed only a sex effect on DOPAC/DA. These findings demonstrate that adolescent social isolation does not produce a uniform neurochemical response but induces region- and sex-dependent alterations across corticolimbic systems, with particularly pronounced effects in the amygdala.

Neurochemistry and Neuropharmacology

V-099

Evaluation of a Structural Restoration Strategy to Enhance Antidepressant Response in Major Depression: Effects of GM1 Oligosaccharide (osGM1) Combined with Desipramine in a Murine Model

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Major depression is a leading global health concern and cause of disability. A considerable proportion of patients exhibit limited responsiveness to conventional antidepressants, suggesting incomplete recovery of synaptic plasticity and structural connectivity in fronto-hippocampal circuits. We hypothesize that combining the ganglioside GM1 oligosaccharide (osGM1) with desipramine (DMI), a tricyclic antidepressant, will enhance therapeutic efficacy through BDNF-TrkB-dependent structural restoration. In a murine model of chronic distress induced by social isolation and repeated restraint stress, osGM1+DMI dosing will be optimized to evaluate behavioral and endocrine endpoints. Parallel analyses in Thy1-GFP mice will quantify dendritic spine density and morphology, neuronal arbor complexity, hippocampal neurogenesis, TrkB-ERK/AKT-CREB signaling, and synaptic protein expression across fronto-hippocampal regions. We will test TrkB involvement using the antagonist ANA-12. We will then evaluate the optimized treatment in BDNF Val66Met knock-in mice, a model of reduced BDNF secretion and antidepressant responsiveness. Finally, maternal treatment during gestational distress will be evaluated for its capacity to prevent behavioral, endocrine, and epigenetic alterations in adult offspring, providing insight into the intergenerational mechanisms of antidepressant efficacy.

Neuroendocrinology and Neuroimmunology

S-098

Heat stress induces physiological, behavioral, and hypothalamic alterations in female mice

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Extreme variations of environmental factors can affect physiology and behavior. The aim was to examine the impact of heat stress on general physiology and reproductive neuroendocrinology. Adult female mice were exposed to a heat wave of 8 hours of heat/day, with 33°C maximum and 28°C minimum, for one week (HS group). Control animals (CTL) were maintained at room temperature (21±1°C). At the end of the protocol, animals were classified according to their estrous cycle as Estrus or Diestrus (N=5/group). Significant changes ($p<0.05$) were observed in physiological parameters of HS vs. CTL, including decreased food and increased water intake, and increased body temperature from day 4 of heat exposure onward. In addition, HS showed difficults in nest-building behavior compared to CTL. Differences in the estrous cycling were not observed between HS and CTL. In the arcuate nucleus (ARC) of the hypothalamus, a significant reduction in the number of blood vessels was observed in HS regardless of estrous cycle. Finally, gonadotropin-releasing hormone (GnRH) immunoreactive neurons were detected in the ARC of CTL Estrus animals, with a significant reduction ($p<0.05$) in HS Estrus group, whereas GnRH neurons were not detected in Diestrus animals. The physiological and behavioral alterations, together with hypothalamic changes, indicate that the exposure to a heat wave may induce both physiological adaptive mechanisms and modifications in hypothalamic circuits associated with reproduction.

Neuroendocrinology and Neuroimmunology

D-099

Ghrelin and Glucocorticoids Independently Promote Feeding and Arcuate Nucleus Activation

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Ghrelin (Ghr) is a stomach-derived hormone that exerts potent central effects, including stimulation of food intake and activation of stress mechanisms, resulting in increased circulating glucocorticoids (GC). GC can also stimulate feeding; however, whether the orexigenic effects of Ghr are mediated, at least in part, by GC remains unknown. We hypothesized that Ghr-induced GC release contributes to its orexigenic effects. Here, we used male WT mice to test if the GC receptor antagonist mifepristone (RU486) or the GC receptor agonist dexamethasone (Dex) modulate Ghr-induced food intake o Ghr-induced increment of c-Fos, a marker of neuronal activation, in the hypothalamic arcuate nucleus (ARH), a key region mediating the orexigenic actions of ghrelin. We found that RU486 did not alter the long-lasting orexigenic effect of Ghr. Also, Ghr and Dex both independently increased food intake, while their combined administration produced a further increase in feeding. Consistently, both Ghr and Dex increased the number of c-Fos cells in the ARH, and combined treatment produced an additive effect on the number of c-Fos cells. These preliminary findings indicate that Ghr and GC appear to independently engage orexigenic mechanisms, producing additive effects on food intake and neuronal activation in the ARH. This suggests that the endogenous GC response elicited by ghrelin is not a mediator of its orexigenic action but may contribute to the overall metabolic response to Ghr.

Neuroendocrinology and Neuroimmunology

V-100

Modulation of Autophagic Flux by Tibolone in Models of Neuroinflammation

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Tibolone, a synthetic steroid, has shown neuroprotective effects in the experimental autoimmune encephalomyelitis (EAE) mouse model of multiple sclerosis (MS). In this study, we investigated the impact of tibolone on microglial activation and autophagy using in vitro and in vivo models relevant to MS. In vitro, BV-2 microglia cells were pre-treated with tibolone and stimulated with lipopolysaccharide (LPS), with or without lysosomal inhibitors to block autophagic flux. In vivo, the expression of autophagic markers was evaluated in the spinal cord of EAE mice treated with tibolone. LPS stimulation significantly elevated IL-1β and NLRP3 expression, whereas tibolone pre-treatment effectively prevented these increases. Furthermore, tibolone attenuated NF-κB nuclear translocation and mitochondrial ROS production. Notably, these anti-inflammatory and antioxidant effects were autophagy-dependent, as they were lost upon co-treatment with lysosomal inhibitors. While the autophagosome marker LC3 increased in microglia exposed to LPS, tibolone normalized LC3 levels without blocking autophagic flux. In EAE mice, tibolone administration successfully restored disease-associated alterations of Beclin-1 and p62 in the spinal cord. Collectively, these findings indicate that tibolone exerts pleiotropic anti-inflammatory and antioxidant effects in microglia while normalizing compensatory autophagy, supporting its therapeutic potential for MS treatment.

Neuroendocrinology and Neuroimmunology

S-099

Neonatal testosterone shapes sexually dimorphic expression of the oxytocinergic system and the DNA demethylation machinery in the mouse brain

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Sex differences in the brain arise from interactions between sex chromosomes and the organizational effects of gonadal hormones during the critical period of sexual differentiation. In rodents, males -but not females- undergo perinatal testosterone surges that establish morphological and functional sex differences. Epigenetic mechanisms, including DNA methylation and demethylation, are potential mediators of these processes. Our laboratory previously showed that sex differences in the oxytocin system emerge early in development: higher oxytocin receptor (Oxtr) expression in the prefrontal cortex at postnatal day (P) 7, and lower oxytocin (OXT) expression in the preoptic area (POA) and periventricular hypothalamic nucleus (Pe) at P18 in males. Early sex differences in the DNA demethylation machinery (Tet1-3, Gadd45a/b, Tdg) are also found in the prefrontal cortex during the critical period. To assess the role of gonadal hormones in these differences, female mice were treated with vehicle or testosterone propionate (100 µg) at P0-P1. Treatment significantly affected Oxtr mRNA at P7 and OXT immunoreactive cells at P18 (both $p<0.05$). Moreover, Tet1-2-3 expression in testosterone-treated females trended toward male-like levels at P7. These findings suggest that early sex differences in active DNA demethylation machinery may mediate testosterone's effects on sexual differentiation of the oxytocinergic system.

Neuroendocrinology and Neuroimmunology

D-100

Optimization of a limited bedding and nesting protocol to model sex-specific effects of early-life stress in mice

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Early-life stress (ELS) may constitute a risk factor for negative, physical and mental health problems. Notably, these effects are influenced by sex, with marked sex differences reported on behavior, physiology and molecular processes. Among the animal models to study ELS, the limited bedding and nesting (LBN) is a robust, reproducible, and translationally relevant protocol that disrupts maternal care and induces pup stress. As an initial stage of this work, we are currently optimizing the LBN protocol in mice. The goal is to study the interaction of ELS with the critical period of sexual differentiation of the brain, to be able to study sex-specific risk factors associated with developmental exposure to stress. During this process, different intervals of LBN exposure were tested, with the window between postnatal days 2 and 9 identified as optimal for protocol reproducibility. In addition, the enrichment parameters of the protocol were adjusted. Preliminary results on developmental landmarks showed a significant effect of ELS on weight and anogenital distance (AGD), with ELS-exposed pups exhibiting lower body weight ($p < 0,0001$) and greater AGD ($p < 0,001$). This model will allow us to evaluate the effects of ELS on the oxytocinergic system, which regulates social behavior and is susceptible to ELS-induced alterations, as well as its effects on the DNA methylation and demethylation machinery regulating the expression of its components.

Neuroendocrinology and Neuroimmunology

V-101

Effect of prepubertal administration of 17β-estradiol on autism-related behaviors in male mice prenatally exposed to valproic acid

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Autism spectrum disorder (ASD) is more frequently diagnosed in males than females, suggesting the existence of biological mechanisms conferring resilience in females. Among known environmental risk factors, prenatal exposure to valproic acid (VPA) is strongly associated with the development of ASD-related behaviors, both in humans and animal models. Our group has shown that VPA-exposed male mice display social deficits and stereotyped behaviors, whereas females do not, indicating potential protective effects mediated by gonadal hormones. Additionally, results from our group indicate that diverse environmental factors and stimuli during the pre-pubertal period can modulate the effect of prenatally administered VPA on adult sociability. Here, we administered 17β-estradiol (E2) between postnatal days (PD) 21 and 35, to evaluate whether gonadal hormones in this sensitive period can reverse ASD-like behavioral alterations in VPA-exposed males. Using a validated murine model and a previously tested oral E2 administration protocol, we assessed adult sociability, repetitive and stereotyped behaviors, anxiety-, and depression-related behaviors. We found that VPA mice not exposed to E2 did not exhibit the expected impairments in sociability. This unexpected result may be attributable to the manipulation inherent to the prepubertal treatment procedure, further supporting the possibility that handling during this critical period can rescue social impairments in VPA-exposed animals.

Neuroendocrinology and Neuroimmunology

S-100

Convergent neuroprotective effects of omega-3 fatty acids and psilocybin in preclinical models of stress and alcohol exposure: A scoping review

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Chronic stress and alcohol exposure can impair neuroplasticity through neurotrophic, inflammatory, and stress-axis dysregulation. Omega-3 fatty acids (ω-3) and psilocybin have emerged as potential neuroprotective interventions, but their convergent and divergent effects in preclinical models remain unclear. We conducted a scoping review following PRISMA-ScR and PECO guidelines to map evidence from rodent studies examining chronic stress or alcohol exposure, and the effects of ω-3 supplement and/or psilocybin on brain outcomes. Six PubMed search strategies identified 16,505 records; following the AI-assisted screening and selection process (Claude, Anthropic) 90 studies were assessed in full text and 60 met eligibility criteria. The hippocampus was most frequently studied (n=42). 16 studies assessed BDNF or TrkB, with consistent positive effects of ω-3 on BDNF, whereas responses to psilocybin varied across stress paradigms. Both interventions converged on shared intracellular signaling and structural plasticity, although their temporal profiles differed: psilocybin produced rapid effects after single administration, while ω-3 required sustained exposure. Notably, none of the 19 studies combining ω-3 or psilocybin in alcohol exposure models assessed BDNF or TrkB, revealing an evidence gap. Overall, the literature supports partially overlapping neuroprotective mechanisms but direct evidence of their combined effects is currently lacking.

Neuroendocrinology and Neuroimmunology

D-101

Diverse roles of hypothalamic proopiomelanocortin (POMC) neuronal subpopulations in energy homeostasis: investigating the cholinergic's functions and projection.

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Obesity and diabetes are major public health challenges driven by disruptions in metabolic homeostasis. The hypothalamic arcuate nucleus (Arc) is a critical integrative center for the regulation of energy and glucose homeostasis. Arcuate proopiomelanocortin (POMC) neurons are canonically recognized for suppressing food intake and promoting energy expenditure when activated. However, their role in glucose regulation remains controversial, with divergent effects reported depending on hormonal signalling pathways engaged and autonomic efferences recruited. This heterogeneity may partly stem from the fact that Arc-POMC neurons are not a uniform population but comprise distinct subpopulations according to their neurotransmitter profiles and projection targets. In particular, the roles of other Arc-POMC subpopulations are still poorly understood; one of these co-releases acetylcholine (ChAT-POMC), yet whether they contribute to the regulation of energy and glucose homeostasis remains unknown. In this study, we investigated the functional role of ChAT-POMC neurons: our preliminary findings suggest that these may play a selective role in glucose regulation. Characterizing the physiological functions of distinct Arc-POMC subpopulations may reveal novel neural pathways linking central circuits to peripheral metabolism and ultimately help develop new targeted therapeutic treatments for obesity and diabetes.

Neuroendocrinology and Neuroimmunology

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Sex differences in behavioral, brain and adrenal outcomes in social isolated adolescent rats: role of pubertal gonadal hormone exposure

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Adolescence is a critical period for neurobiological development during which social interaction contributes to emotional regulation. Pubertal gonadal hormones exert organizational effects that may contribute to sex differences in stress responses. This study evaluated whether the pubertal surge modulates behavioral outcomes, locus coeruleus (LC) cell number, and adrenal morphology in socially isolated adolescent rats. Male and female Wistar rats were reared under social or isolated conditions and gonadectomized before (PND23; PrePub) or after puberty (PND45; PostPub). Behavioral tests were performed on PND50–54, and brains and adrenal glands were collected on PND55. Pubertal hormone increased exploratory behaviors (rearings and head-dippings), even under isolated conditions. Females showed more interrupted grooming sequences and fewer head-shakes than males. LC analysis showed higher cell number in females and sex-dependent effects of pubertal hormone exposure, with a decrease in PostPub males and an increase in PostPub females. Adrenal weight was reduced in males by pubertal hormone exposure, while isolation increased adrenal width in females. These findings suggest that social isolation alters behavioral, neural, and adrenal responses during adolescence, with effects modulated by sex and pubertal gonadal hormone exposure.

Neuroendocrinology and Neuroimmunology

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INFLUENCE OF CLIMATE FACTORS ON THE REPRODUCTIVE NEUROENDOCRINOLOGY OF THE PLAINS VIZCACHA (Lagostomus maximus)

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Climate change negatively impacts the physiology and reproduction of wild animals. This study investigated the influence of environmental temperature and humidity on the reproductive neuroendocrine axis of the South American plains vizcacha (Lagostomus maximus), a hystricomorph rodent native to Argentina. A retrospective analysis was conducted using plasma and brain samples collected in March from 2008 to 2025. The Temperature-Humidity Index (THI) was calculated for each year, defining High THI (N=22) and Low THI (N=12) groups. Plasma levels of estradiol, cortisol, and ACTH were measured by ELISA, and hypothalamic expression of gonadotropin-releasing hormone (GnRH), kisspeptin, and glucocorticoid receptor (GR) was assessed by immunohistochemistry. ACTH levels were significantly higher in the High THI group ($p<0.005$), whereas cortisol levels and hypothalamic GR-positive neuron number did not differ between groups. In contrast, estradiol levels were significantly lower ($p<0.001$), accompanied by a reduction in GnRH and kisspeptin-positive neurons in the preoptic area of the hypothalamus ($p<0.002$). These findings identify temperature and humidity as key environmental factors influencing the reproductive axis of the plains vizcacha and suggest that climate-related changes may affect the species long-term population dynamics.

Neuroendocrinology and Neuroimmunology

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Effects of heat stress on hippocampal GABAergic and glutamatergic neurochemical balance and its relationship to anxiety-like behavior

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Climate change may contribute to anxiety disorders. Heat stress impacts the hippocampal formation, altering the balance between excitatory and inhibitory neurotransmission. Our previous studies showed that heat induces anxiety-like behaviors in mice. The aim was to examine GABAergic and glutamatergic components in the hippocampal formation underlying heat-induced anxiety-like behavior. Adult female mice were exposed to a heat wave (8 h heat/day, 33°C maximum and 28°C minimum) for one week (HS group). Controls (CTL) were maintained at 21±1°C. On the last day, mice were also classified as Estrus or Diestrus (N=4/group). GABA-A, Parvalbumin, Calretinin, NMDAR1, and AMPA expression were analyzed by IHC, and optical density (OD) was quantified. GABA-A and Calretinin OD significantly increased ($p<0.05$) in CTL Estrus vs. the other groups, while heat exposure suppressed estrous cycle-dependent fluctuations. Parvalbumin interneuron number significantly decreased ($p<0.05$) during estrus regardless of treatment. NMDAR1 OD increased significantly ($p<0.05$) in CTL Diestrus vs. the other groups, while heat exposure prevented estrous cycle-dependent fluctuations. AMPA OD significantly ($p<0.05$) decreased in the stratum pyramidale and lacunosum-moleculare at Diestrus compared to Estrus. These findings suggest that heat stress disrupts the neurochemical balance of the hippocampal formation in a reproductive hormone-dependent manner, potentially contributing to heat-induced anxiety-like behavior.

Neuroendocrinology and Neuroimmunology

V-103

Neuroprotective potential of spinochromes in a mouse model of olfactory nerve degeneration

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Methimazole (MMZ) is an antithyroid drug with olfactotoxicity as an adverse effect. MMZ-induced olfatotoxicity is mediated by the generation of reactive species following MMZ metabolism in the olfactory epithelium (OE). MMZ rapidly damages sustentacular cells and Bowman's glands, leading to OE disorganization and detachment, inflammation and neuronal dysfunction and loss, features also observed in OE damage induced by viral infection. Here, we propose to test whether a formulation of Echinochrome A (EchA), a naturally occurring spinochrome present in the roe of the Patagonian sea urchin Arbacia Dufresnii, confers neuroprotection against MMZ-induced olfactory degeneration. EchA is an antioxidant with an anti-inflammatory effect in the airways of a mouse model of asthma. We will evaluate measures of OE and nerve integrity, neuronal survival and myeloid cell infiltration and reactivity in mice treated with MMZ (25 mg/kg, intraperitoneally) or vehicle (saline solution). In this study, EchA will be administered orally as part of a roe-derived formulation with a known and standardized EchA concentration, currently used to produce an approved and commercialized dietary supplement for human consumption. Mice will receive EchA (10 mg/kg, orally, once daily) starting 7 days before MMZ administration and continuing until evaluation 3 days after the lesion, or vehicle (saline solution). We expect to determine the potential of EchA as a neuroprotectective agent against olfactory damage.

Sensory and Motor Systems

S-102

Sensory modalities involved in food detection in tadpoles of Rhinella arenarum

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During larval development, anuran amphibians must exploit environmental resources to maximize growth. Although the olfactory and visual systems develop early during ontogeny, little is known about their relative contribution to food detection. We conducted behavioral experiments to determine the sensory modality used by Rhinella arenarum tadpoles to detect food. In a two-choice arena with food enclosed in either a glass cylinder (visual stimulus only) or a mesh cylinder (chemical stimulus only), tadpoles approached the chemical stimulus faster and spent significantly more time displaying foraging behavior around it. In contrast, no oriented responses were directed toward the visual-only stimulus. Complementary experiments assessing food localization ability under light and dark conditions showed that animals tested in total darkness exhibited higher latency to locate the food source compared to those tested in light; however, this was accompanied by a reduction in overall exploratory activity. Together, these results indicate that olfaction would be the primary sensory modality driving food detection in R. arenarum larvae, while visual input might enhance overall exploratory behavior. However, whether vision acts as a direct cue for food localization or purely as a contextual modulator of activity would require further investigation.

Sensory and Motor Systems

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Spectro-Temporal Receptive Fields of the Primary Auditory Cortex in the Rat

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Studying central perceptual representations remains a challenge due to the multidimensional and non-linear nature of auditory perception. The spectro-temporal receptive field (STRF) serves as a linear model representing the optimal stimulus for an auditory neuron. Despite the rat (Rattus norvegicus) being a key biomedical model, STRF properties in its primary auditory cortex (A1) remain not fully described. This study characterized A1 spectro-temporal properties in the rat, extracting functional parameters to describe neuronal response dynamics: characteristic frequency, latency, bandwidth, sparseness index, and signal-to-noise ratio. Acute extracellular neurophysiological recordings were performed in anesthetized adult male rats using A1 microelectrodes. Responses were evoked with TORC (Temporally Orthogonal Ripple Combinations) stimuli, and STRFs were estimated via reverse correlation. Analysis revealed tuned neuronal units with short latencies and a preference for high and low frequencies. Furthermore, the spatial response distribution across A1 functionally corroborated its characteristic tonotopic gradient. In conclusion, estimating STRFs under anesthesia establishes a methodological and functional baseline for rat cortical responses. Strategically, this provides comparative support for future studies contrasting this basal activity with awake animal recordings, enabling the evaluation of cognitive and behavioral influences on auditory processing.

Sensory and Motor Systems

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Decoding Spanish Vowels from Surface Electromyography Using Dimensionality Reduction

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Silent Speech Interfaces aim to decode speech from pre-acoustic physiological signals, providing an alternative to conventional acoustic-based speech recognition. A fundamental question is whether discrete phonetic identities can be recovered from the continuous muscular dynamics underlying speech production. Here, we investigated the feasibility of classifying the five Spanish vowels using surface electromyography (sEMG). We designed and implemented a custom system to synchronously record the activity of three articulatory muscles (Orbicularis Oris, Depressor Anguli Oris, and Mylohyoid) in a native Rioplatense Spanish speaker. Using an incremental analysis approach (thresholding, PCA, and supervised UMAP), we evaluated the separability of the phonetic space. Results showed that the system isolates topological phonetic macro-groups (A, E-I, and O-U). Specifically, extreme motor gestures (A, I, U) were classified with high predictive accuracies (82–100%) under non-linear dimensionality reduction, an algorithmic separation aligning with the phonetic extremes of the traditional vowel triangle. However, intermediate vowels (E, O) showed persistent overlap, suggesting that additional muscular information may be required to fully resolve the vowel space. Overall, these preliminary results support the feasibility of extracting discrete phonetic identities from continuous muscular dynamics.

Sensory and Motor Systems

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Transcriptomic Profiling of the Inner Ear Epithelium: Unraveling the Role of the Efferent System

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Noise-induced hearing loss (NIHL) is becoming a leading type of non-congenital hearing loss, presenting a major societal hazard that begins early in life. Recent studies showed that the medial olivocochlear system (MOC) can mitigate acoustic trauma effects in rodents. We investigated the role of the MOC in NIHL using two mouse models: an α9 nicotinic receptor subunit (nAChR) knock-out (carrying an9 point mutation that leads to enhanced cholinergic activity KO), which lacks cholinergic transmission between MOC neurons and hair cells; and an alpha9 knocking (α9KI) carrying an9 point mutation that leads to enhanced cholinergic activity. Results showed a positive correlation between the degree of hearing loss prevention and the level of cholinergic activity. This study aimed to analyze transcriptomic changes in specific cell types within the organ of Corti following acoustic trauma, to understand the function of the MOC feedback. WT, α9KI, and α9KO mice at 3 weeks of age were exposed to loud sounds (1-16 kHz, 100 dB SPL, 1hr). One week later, we dissected and flash-froze the organ of Corti. We generated single-nuclei sequencing libraries (Evercode WT, Parse Biosciences) from these tissues. Our initial findings show more than 35,000 sequenced nuclei, among which we identified the cell types of interest: inner hair cells (IHCs), outer hair cells (OHCs), supporting cells (SCs), and spiral ganglion neurons (SGNs).

Sensory and Motor Systems

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Modulation of auditory peripersonal space by approaching and receding sound sources

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The peripersonal space (PPS) is defined as the region surrounding the body where we can interact with other objects using our limbs. The representation of objects within PPS depends not only on their physical position but also on other factors, including speed and direction of movement. It has been shown that approaching auditory stimuli can increase PPS extension by making the source appear closer than it actually is, suggesting a possible role for PPS as a warning mechanism that anticipates the time of arrival. We investigated the representation of moving auditory objects within peripersonal space. Stimuli consisted of short white-noise bursts presented in front of the subject (azimuth = 0°) that followed one of three trajectories: looming, receding, or stationary. Sources moved in discrete steps—that is, they were presented at a fixed position for a short period of time, followed by a brief silence, after which they were presented at the next position, repeating this sequence until a set number of steps was reached. After the source finished moving, subjects reported whether they perceived the sound source to be within arm's reach. Reachability judgments were compared across different trajectories that ended at the same position. Perceived reachability changed depending on the trajectory. We discuss the implications of these results for our understanding of PPS.

Sensory and Motor Systems

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Role of the calcium-binding protein Sorcin in the auditory system

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Intracellular Ca2+ compartmentalization is essential for cochlear outer hair cell (OHC) function, which relies on precise Ca2+ homeostasis. Ca2+ participates in mechanotransduction, synaptic signaling and excitotoxicity associated with noise-induced hearing loss. Transcriptomic studies identified oncomodulin and sorcin among the most highly expressed genes involved in Ca2+ homeostasis in OHCs. While oncomodulin is a well-characterized Ca2+ buffer, the role of sorcin in the cochlea remains unknown. To investigate its contribution to auditory physiology, we used sorcin knockout (KO) mice. Immunohistochemistry confirmed sorcin expression in the cytoplasm of wild-type (WT) OHCs but not in KO mice. Under basal conditions, WT and KO animals showed similar ABR and DPOAE thresholds and amplitudes, indicating that sorcin is not essential for normal auditory function. Preliminary analyses of unexposed cochleae suggest altered presynaptic ribbon organization in KO OHCs. Following noise exposure, both genotypes exhibited comparable hearing loss 1 day post-exposure (dpe). However, WT mice recovered within one week, whereas KO mice showed impaired recovery, maintaining elevated thresholds and reduced amplitudes even 45 dpe. Histological analyses revealed similar afferent synapse loss per inner hair cell in both genotypes, but greater OHC loss in KO mice. Together, these findings suggest that sorcin is not essential for basal hearing but plays a protective role during acoustic stress.

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High-fat diet consumption induces apoptosis and increases proinflammatory markers in the cochlea of C57BL/6J mice.

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Obesity affects the auditory system, altering its functionality and processing, but the underlying mechanisms are unclear. The NLRP3 inflammasome has been associated with age-related hearing loss and may play a role in sensorineural hearing loss during obesity, contributing to apoptosis of cochlear hair cells, impairing auditory function. We evaluated the effect of obesity induced by high-fat diet (HFD) consumption on NLRP3 inflammasome expression and survival of cochlear hair cells. Here, 6-7 week-old male C57BL/6J mice (n=24) were fed a control diet (CD, 10% fat, 20% protein, 70% carbohydrates) or a HFD (60% fat, 20% protein, 20% carbohydrates), for 16 weeks. General parameters (body and adipose tissue weight), hearing function (distortion product otoacoustic emissions (DPOAEs)), NLRP3 inflammasome components expression (NLRP3, ASC, Caspase-1, IL-1β, IL-18, IF/qPCR) and apoptosis (TUNEL, caspase-3, Bax, Bcl-2, IF/qPCR) were measured. HFD fed animals presented higher body (83%) and adipose tissue weight, and higher auditory thresholds. Moreover, the HFD group presented a lower number of cochlear hair cells compared to CD, along with higher apoptosis markers (TUNEL (by 47%, p=0.028) and caspase-3 staining). Cochlear levels of NLRP3, ASC, IL-1β, and IL-18 were also increased. These data suggest a role for NLRP3 inflammasome and oxidative stress in hearing impairment induced by metabolic dysfunction, after chronic consumption of a high-fat diet in C57BL/6J mice.

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Sensory and Motor Systems

S-104

From gene to behavior: uncovering TRPA1 function in chemical avoidance in an insect

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Blood-feeding insects rely on chemical cues to avoid harmful compounds, yet the mechanisms underlying deterrent detection remain poorly understood in Chagas disease vectors. We investigated how Rhodnius prolixus detects two electrophilic deterrents: allyl isothiocyanate (AITC) and N-ethylmaleimide (NEM), both known TRPA1 activators. In dual-choice behavioral assays, R. prolixus displayed significant contact avoidance to both compounds. Covering the antennae abolished NEM avoidance, while AITC avoidance persisted even with covered antennae or tarsi, suggesting that both or alternative sensory structures are involved. At the molecular level, RNAi-mediated knockdown of TRPA1 selectively abolished AITC avoidance, confirming its role in this sensory pathway. We conducted an in silico sequence and structural analysis and identified conserved reactive residues in R. prolixus (C714 and C758) corresponding to functional sites in fruitfly and mammals. AlphaFold 3D modeling of TRPA1 homotetramer showed a pore architecture similar to D. melanogaster Cryo-EM structures and revealed the spatial arrangement of these cysteines. Our findings show that electrophilic deterrents engage distinct sensory organs in R. prolixus, with TRPA1 required specifically for AITC avoidance. Persistence of NEM avoidance post-knockdown indicates additional detection mechanisms for harmful electrophiles. We provide new insights into the molecular basis of chemical nociception in blood-feeding insects.

Sensory and Motor Systems

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Ontogenetic changes in eye morphology and sensitivity are associated with wing development in kissing bugs

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Kissing bugs are the vectors of Chagas disease, one of the major endemic diseases in the Americas, now spreading to other continents. We used Rhodnius prolixus as a model species to characterize compound eye growth throughout the post-embryonic development of this hemimetabolous insect. We found that the adult eye is larger than expected from ontogeny. Moreover, while the eye grows symmetrically across nymphal instars, adults show greater ventral growth, resulting in a dorsoventrally asymmetrical eye. By studying a bright pseudopupil in natural mutant animals, we observed no major differences in sampling resolution between the last nymphal instar and the adult stage. However, the adult eye possesses significantly larger ommatidia, particularly in the ventral region, shifting the area of highest sensitivity from the equatorial region in nymphs to the ventral region in adults. A similar growth pattern was observed in Triatoma infestans and Panstrongylus megistus. Analysis of photographic records from 39 species across 10 genera indicates that an asymmetrical eye is the predominant pattern in adult kissing bugs. Notable exceptions in species in which adults are wingless reveal a tight association between a large asymmetrical eye and the presence of wings, suggesting that vision may support dispersal and host-seeking flights.

Sensory and Motor Systems

V-106

Cortical Excitability and Autonomic Regulation during Time-Based Motor Learning

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Motor learning enables progressive performance improvement on repetitive tasks through adaptation and optimization of motor responses, allowing anticipation and accurate execution. This process can induce changes in cortical activity and autonomic regulation. We aimed to analyze how central and autonomic nervous system changes associate with time-based learning of a visuomotor decision-making task. Twenty-three participants (22.4±3 y, 10 male) completed 8 blocks of 40 trials, consisting of hitting a device target at a precise moment guided by a visual cue. The participants received performance feedback after each block to promote learning. Performance was evaluated across blocks to quantify motor learning. Resting-state EEG and ECG were recorded pre- and post-task to assess training-induced neurophysiological changes. Aperiodic brain activity was characterized by the 1/f exponent (assumed to reflect cortical excitability/inhibition balance), while autonomic activity was assessed through heart rate variability (HRV) as an index of parasympathetic modulation. Motor learning was positively associated with increased cortical excitability in frontal and left parietal regions, whereas increased HRV –reflecting parasympathetic predominance– correlated with increased cortical excitability in sensorimotor areas. These findings suggest that motor learning induces region-specific neurophysiological changes, with autonomic regulation selectively linked to sensorimotor cortical dynamics.

Sensory and Motor Systems

S-105

Neural Basis of Mosquito Host-Seeking

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A single mosquito bite can be deadly. By biting humans, mosquitoes transmit pathogens responsible for malaria, yellow fever, Zika, and dengue, which together claim more than half a million lives each year. Only females bite, requiring a blood-meal for egg maturation, and rely on integrating sensory cues to locate hosts. Among these cues, carbon dioxide (CO2) from human breath plays a fundamental role. CO2 triggers activation, transforming behavior from undirected flight to sustained targeted upwind navigation, while simultaneously initiating sensitization, in which other modalities become primed to respond to cues such as body odor, heat, and visual contrast. Activation and sensitization initiate the host-seeking program that culminates in biting. The neural circuits driving host-seeking remain uncharacterized, as the tools to study mosquito central brain circuits have not existed until now. I developed a pipeline integrating whole-cell patch-clamp electrophysiology in a novel ex vivo Aedes aegypti brain explant with dye filling and connectome registration, linking the physiology of each recorded neuron to its synaptic connectivity. I identified distinct projection neuron and interneuron classes matching connectome-defined categories, and used two-photon photoactivation to identify CO2-dedicated projection neurons. This work lays the groundwork for understanding how the mosquito olfactory circuit generates the robust, sustained host-seeking that drives disease transmission.

Sensory and Motor Systems

D-106

From attraction to avoidance: exploring the role of Painless in thermal sensing in a blood-feeding insect

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Heat is a key sensory cue for blood-feeding insects, playing a central role in host-seeking and blood-feeding while allowing the avoidance of potentially harmful conditions. The kissing bug Rhodnius prolixus is highly sensitive to thermal stimuli and can detect both heat and infrared radiation (IR) associated with warm-blooded hosts. However, the molecular mechanisms underlying these responses remain poorly understood. This thesis investigates the role of the gene Painless, a TRPA-type receptor, in thermal stimulus detection in R. prolixus. We hypothesize that Painless mediates thermosensory transduction, across different thermal contexts including aversive heat, IR and host-like temperatures. To test this, we combine RNAi with complementary behavioral paradigms evaluating orientation toward heat and IR, proboscis extension responses (PER) elicited by host-range temperatures, and responses to aversive heat. Three experimental groups will be compared: intact insects, insects injected with control dsRNA, and insects in which Painless expression is reduced by RNA interference (RNAi). Comparing responses among groups will allow us to determine whether Painless participates broadly in thermal sensing or whether its contribution depends on temperature range and behavioral context. By integrating behavioral and molecular data, this project aims to clarify Painless' role in thermal sensing and how it shapes attractive, appetitive, or aversive responses in this blood-feeding insect.

Sensory and Motor Systems

V-107

Role of the Medial Olivocochlear System in Sound Hypersensitivity

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Noise-induced auditory disorders represent a significant global health concern, with hyperacusis —an intolerance to everyday sound levels—constituting a particularly challenging condition. Hyperacusis is thought to result from maladaptive plasticity within the central auditory system, whereby a compensatory increase in neural gain exaggerates sound-evoked responses, often following peripheral auditory damage. The mammalian auditory system possesses an endogenous protective mechanism known as the medial olivocochlear (MOC) reflex. In the organ of Corti, the neurosensory epithelium of the auditory system, inner hair cells (IHCs) transduce auditory signals, whereas outer hair cells (OHCs) mechanically amplify sound-induced vibrations. The MOC efferent system projects directly to OHCs and, when activated by sound, inhibits their amplifying activity. This reflex is considered an important mechanism for protecting the cochlea from acoustic trauma. The aim of this project was to investigate the role of the MOC system in hyperacusis. Using the auditory startle response as a behavioral assay, we evaluated sound sensitivity in wild-type mice and in genetically modified mouse lines that either lack MOC efferent activity (α9 KO) or exhibit enhanced MOC efferent activity (α9 KI).

Sensory and Motor Systems

S-106

Neural-vocal phase coupling reveals structured timing in birdsong production

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Understanding how neural activity encodes motor behavior during vocal production is an unresolved challenge in neuroscience. Songbirds provide an ideal model due to their song dedicated neural networks. Here, we analyze songs from adult canaries (Serinus canaria) by comparing multiunit neural activity recorded in the telencephalic nucleus HVC (MUA) with the acoustic envelope of the produced song (ENV), aiming to identify temporal delays reflecting neural–vocal coupling. We introduce an approach based on cross-correlation functions in short sliding windows, using surrogate data for statistical validation. The resulting delays (τ) are grouped into populations using kernel density estimation, where local maxima and valleys define objective boundaries. While canary song is known to be stereotyped and rhythmic, we find that neural activity also displays a rhythmic organization, temporally aligned with vocal behavior. We identify regimes across birds, including synchronization near $\tau = 0$, positive and negative delays, under correlation and anticorrelation conditions. These regimes reveal multiple structured temporal relationships between neural activity and vocal output, consistent with the known sensorimotor role of HVC, where neural dynamics span distinct phases relative to behavior and may reflect different contributions to vocal production.

Sensory and Motor Systems

D-107

Navigating chemical landscapes: Using microfluidic devices to create complex plumes.

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Although the ability to use environmental chemical cues for navigation is crucial and evolutionarily conserved across all species, we still poorly understand which features animals use to find odor sources. This is primarily because chemical stimuli occur in highly diverse regimes, such as stationary gradients, laminar, or turbulent flow, while tools to control and measure their spatiotemporal dynamics remain limited. We propose to address this gap by combining zebrafish larvae with microfluidics. Zebrafish larvae emerged as a powerful model for behavior and systems neuroscience, thanks to its rich behavioral repertoire, genetic tools availability, optical transparency and small enough for their nares to sit at the chip outlet. We will present the characterization of a PDMS-based microfluidic chip controlled by an electromechanical pressure and flow-control system, enabling olfactory stimuli with precise temporal and concentration control. We demonstrate its ability to reproduce plume-like concentration fluctuations at different spatial locations relative to the odor source and as well as the transition speed between distant points. The system can be integrated with virtual reality and whole-brain imaging, enabling altered feedback experiments to identify which components of plume dynamics are required for navigation toward an odor source. We hope to discuss the goals and strategies of this early stage project with the community.

Sensory and Motor Systems

V-108

Assessment of Acoustic Parameters for DPOAE Detection in Rats: An Initial Step Toward Protocol Development

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Distortion product otoacoustic emissions (DPOAEs) are an objective and non-invasive tool for assessing cochlear function and outer hair cell activity. The aim of this study was to evaluate different combinations of acoustic parameters for DPOAE detection in rats, identifying an initial configuration to establish the basis for an efficient and reproducible protocol. Clinically healthy rats were evaluated using a DPOAE recording system with custom-developed stimulus generation and detection software based on Python. Stimuli varied in duration, intensity, and f2/f1 ratio over a 1–20 kHz frequency range, determined by the recording system components. All recordings were performed under dexmedetomidine sedation. For each frequency, distortion product (DP) amplitudes, baseline noise, and signal-to-noise ratios (SNRs) were determined. DPOAEs were considered detectable when the SNR was ≥6 dB. Protocol selection was based on SNR amplitudes compatible with an expected physiological response and on the highest proportion of frequencies with SNR ≥6 dB SPL. The best-performing configuration used an f2/f1 ratio of 1.22, L1=65 and L2=55 dB SPL, and a duration of 1050 ms. These results represent an initial step toward establishing an efficient and reproducible DPOAE detection protocol in rats and provide a basis for its future application as an objective tool for assessing cochlear function in veterinary medicine.

Sensory and Motor Systems

S-107

Preliminary study on the implementation of a sensorimotor synchronization assessment protocol for adults.

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This study a preliminary administration of an SMS assessment protocol an sensorimotor synchronization (SMS) in adults. The study utilized rhythmic finger-tapping tasks synchronized with isochronous auditory stimuli and tempo/period perturbations (both abrupt and gradual). Video recordings of the tapping sessions were processed using MediaPipe Hand Landmarker for motion tracking (combined with audio event detection) to automatically extract spatial and temporal synchronization metrics, providing complementary quantitative measures alongside clinical observation. The detected stimulus and tapping events were represented as paired time series and compared on a trial-by-trial basis to quantify stimulus–response asynchrony and temporal variability. Preliminary results from individual participants were consistent with synchronization patterns reported in the literature, including negative mean asynchrony (a tendency toward anticipation) and millisecond-scale temporal variability. Distinct behavioral patterns were observed among participants, ranging from stable delays with higher precision at faster tempos to pronounced anticipation, as well as varying levels of stability and variability across conditions. These findings demonstrate the tool's potential for characterizing individual differences in sensorimotor synchronization performance, both for research and for the clinical monitoring of music therapy users.

Sensory and Motor Systems

D-108

Compound-eye optical diversity across South American butterflies

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According to their ecological niche, butterfly compound eyes show regional variation in optical sampling and spectral sensitivity. We examined how optical architecture varies both across homologous eye regions and among six South American butterfly species selected to represent contrasting activity periods (diurnal and crepuscular) and feeding habits (flower- and fruit-feeding). By studying eyeshine reflections at multiple positions along the vertical and anteroposterior axes of the eye, we characterised pseudopupil shape and quantified its area, facet size and interommatidial angles. The pseudopupil was large and vertically elongated in the frontal region, indicating high resolving power and differences between vertical and horizontal sampling resolution. It became smaller and rounder towards the back and in dorsal and ventral regions. Facets were also largest and interommatidial angles were smallest frontally, consistent with greater light-gathering capacity and finer spatial sampling, respectively. Notably, Opsiphanes invirae, a crepuscular fruit-feeding butterfly, showed the largest facet diameter among the species examined, providing a larger optical aperture and thereby increasing the amount of light captured by each ommatidium under dim-light conditions. Current results provide the first examples of how ecological factors shape the visual systems of South American butterflies, whose eye diversity remains largely unexplored.

Sensory and Motor Systems

V-109

Contact chemical information guides mosquito behavioural decisions

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Mosquitoes rely on chemical cues detected by sensory systems to guide behavioural decisions essential for survival and reproduction. While volatile olfactory cues are well studied, how non-volatile chemicals are detected and influence behaviour remains poorly understood. Here, we investigated the neuroethological effects of piperine, a plant-derived alkaloid from black pepper (Piper nigrum), and black pepper extract (BPE) in Aedes aegypti. Our results showed that piperine reduced blood feeding in a dose-dependent manner on artificial membrane feeders and significantly decreased biting on human skin. Similar effects were observed with BPE. Restricting contact with the feeder revealed that piperine deterred feeding only when females could contact it with their tarsi, supporting a role for tarsal contact chemoreception in the decision to feed. Piperine and BPE also deterred oviposition, indicating that the same chemical stimulus modulates distinct behavioural decisions in different stages of the life cycle. In larvae, exposure to piperine induced early motor disturbances and strongly reduced activity, followed by complete mortality within 24 h, while BPE produced stronger effects. Together, these results show that a plant-derived stimulus can influence distinct behavioural outputs across mosquito life stages, from sensory-guided decisions in adults to motor function in larvae, highlighting the importance of chemical information in shaping mosquito behaviour.

Sensory and Motor Systems

S-108

Cell-type-specific molecular plasticity in the Mesencephalic Locomotor Region is necessary for motor memory consolidation.

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It is classically thought that motor memories are formed through neuronal plasticity in higher motor centres, such as the motor cortex, cerebellum, and basal ganglia, while downstream motor regions primarily execute learned motor commands. However, we hypothesize that the formation of new motor skills also requires plastic changes in brainstem centres, such as the Mesencephalic Locomotor Region (MLR), to adapt motor commands to new task demands. The MLR comprises the pedunculopontine (PPN) and cuneiform (CnF) nuclei, containing glutamatergic (Glu-MLR), GABAergic and cholinergic (ChAT-MLR) populations. Using mice, different motor training tasks and cell-type specific pharmacogenetic approaches, we found that de novo protein synthesis in Glu-MLR neurons is necessary for the consolidation of newly learned motor tasks. Moreover, in situ analysis of the MLR in mice that successfully learned these tasks revealed increased expression of proteins involved in signalling pathways classically associated with learning and memory in higher motor centres and with different types of memory, suggesting that these molecular mechanisms are highly conserved. We are now addressing the in vivo electrophysiological correlates of these molecular changes and whether ChAT-MLR neurons also contribute to motor memory consolidation. Our findings challenge the classic view of downstream motor regions, demonstrating that Glu-MLR neurons undergo molecular plasticity required for motor memory consolidation.

Sensory and Motor Systems

D-109

Determination of functional connectivity between the frontal and auditory cortices in rats during the performance of visual and auditory tasks

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To process sensory information and guide behavior in dynamic environments, the brain relies on precise cortical connectivity, with selective attention playing a key role. While top-down control is well-characterized in the visual cortex, its operation in the auditory cortex (AC) remains unclear. This study evaluates functional connectivity between the medial prefrontal cortex (mPFC) and AC in rats during selective attention tasks. Animals were trained in two-alternative forced-choice (2-AFC) tasks under visual and auditory modalities, with simultaneous Local Field Potential (LFP) recordings in the mPFC and AC. Behaviorally, subjects learned both tasks successfully, showing significant modality-dependent performance differences. LFP spectral analysis revealed oscillatory modulations dependent on learning stage and sensory modality. Granger Causality analysis was implemented to determine interaction directionality. The main finding revealed significant differences in top-down information flow between tasks: during the visual modality, a marked, statistically significant increase in top-down beta-band flow occurred during target stimulus presentation. This signature evidences strong directional communication from mPFC to AC during the visual task, suggesting an mPFC-driven inhibitory control mechanism to suppress auditory processing. Overall, these preliminary results provide initial evidence that the mPFC exerts a direct, context-dependent functional modulation on the AC.

Sensory and Motor Systems

V-110

Role of Medial Olivocochlear Activity in the Maturation of Type II Cochlear Afferent Synapses

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In the organ of Corti, inner hair cells (IHCs) transduce auditory signals, whereas outer hair cells (OHCs) amplify sound-induced vibrations. Cochlear afferent innervation includes type I neurons, which contact IHCs and form most of the auditory nerve, and type II neurons, which contact OHCs and whose function remains unclear. The cochlea also receives descending input from the brainstem through the medial olivocochlear (MOC) system, which targets OHCs, and the lateral olivocochlear (LOC) system, which contacts type I afferent terminals. During early development, MOC fibers transiently contact IHCs and modulate their spontaneous activity, thereby influencing the maturation of the auditory system. Previous work from our laboratory has shown that the level of efferent activity affects the developmental time course of auditory function and cochlear synaptic organization. In this study, we investigate how efferent activity influences the development of type II afferent synapses onto OHCs. Using immunofluorescence, we will examine the development of type II afferent synapses from postnatal day 6 to 75 in wild-type mice and in genetically modified mouse lines that either lack (α9 KO) or exhibit enhanced (α9 KI) MOC efferent activity.

Sensory and Motor Systems

S-109

Reinforcement Learning of Bird Vocalizations Using a Discrete Motor Space

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Vocal learning in songbirds provides a model for studying the acquisition of complex motor behaviors. In particular, the zebra finch is one of the best-characterized models, acquiring its song during development through comparison of its vocalizations with those of a tutor. We propose a reinforcement learning algorithm, inspired by Doya and Sejnowski, to reconstruct experimentally recorded respiratory pressure syllables associated with song production. The algorithm explores a discrete motor space in which each syllable is represented as a temporal combination of excitable base gestures activated at discrete times. These gestures are interpreted as motor manifestations of transient events in the bird's neural dynamics. The model successfully reconstructs the analyzed syllables using a reduced number of gestures. Moreover, the learned gestures reveal the spontaneous emergence of a small set of functional primitives shared across individuals, without imposing such a repertoire during learning. These results suggest that vocal production can be represented through combinations of reusable motor primitives, providing a low-dimensional description of the motor structure underlying vocal learning. Thus, learning can be understood not as the optimization of arbitrary continuous trajectories, but as the selection and combination of a finite repertoire of motor primitives.

Sensory and Motor Systems

D-110

KCNQ4 Deficiency Induces Apoptotic Activation and Innervation Changes in Deiters' Cells

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The organ of Corti is a specialized sensory epithelium where interactions between hair cells (HCs) and supporting cells (SCs) are critical for cochlear function. Although KCNQ4 potassium channel deficiency causes progressive outer hair cell degeneration and hearing loss (HL), the involvement of SCs, particularly Deiters' cells (DCs), remains poorly understood. We analyzed DC survival, apoptotic activity, and innervation changes in a Kcnq4 knockout (KO) mouse model. DC distribution was quantified at 4 and 10 weeks using cytocochleograms and three-dimensional confocal reconstructions of phalloidin-labeled whole-mount cochleae. Apoptotic signaling was evaluated by immunodetection of cleaved caspase-3 (cCas3), whereas synaptophysin (SYN) labeling was used to assess presynaptic structures. Despite extensive OHC degeneration, DC numbers remained preserved throughout the cochlea at both ages. However, cCas3 immunoreactivity increased in the DC region, particularly in basal segments, and became more pronounced with age. In addition, the DC region showed a higher density of SYN-positive puncta, suggesting changes in local neural inputs. These findings show that OHC loss in Kcnq4 KO mice is accompanied by apoptotic signaling and altered innervation within the DC region. The preservation of DCs despite increased cellular stress suggests that these SCs may engage adaptive responses to disrupted K+ homeostasis, highlighting a potential compensatory role of DCs during KCNQ4-associated.

Sensory and Motor Systems

V-111

Neuroinflammatory response and KCNQ channels remodeling in the cochlear nucleus of a mouse model of progressive deafness

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First- and second-order sensory neurons of the ascending auditory pathway, located in the spiral ganglion and the cochlear nucleus (CN), respectively, participate in the olivocochlear reflex, which protects hair cells from acoustic overstimulation. The KCNQ4 channel is expressed in the organ of Corti and in the CN. In KCNQ4-knock-out (KO) mice, sensory cells and spiral ganglion neurons degenerate with age, while the impact of KCNQ4 deletion on the CN remains unknown. Therefore, we analyzed the CN structural integrity at middle age in KO animals. We examined the expression of the neuronal KCNQ channel subunits in the CN by qPCR. KCNQ3 expression was significantly increased ($p=0.0418$) in KO mice compared to WT animals at young age, suggesting changes in the CN neurons excitability. In addition, we assessed microglial status in the CN of middle-aged KO mice by brain cryosectioning and immunohistochemical analysis of the microglial marker Iba1. Confocal microscopy revealed a notable increase in the fluorescence intensity ($p<0.0001$) and the number of microglial cells from 0.29 to 0.86 cells/mm2 ($p<0.0001$) within the CN of KO mice compared to WT. Moreover, a slight increase in arborization of Iba1+ cells was observed in KO mice, although it did not reach statistical significance. This finding suggests alterations in neuronal excitability and enhanced microglial reactivity, potentially associated with neuroinflammatory processes that may contribute to neuronal loss in aged animals.

Sensory and Motor Systems

S-110

Temporal modulation of male sensitivity to female acoustic signals in Aedes aegypti

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Mate recognition in mosquitoes relies strongly on acoustic cues generated by wingbeat sounds. In Aedes aegypti, males detect the characteristic flight sounds of females during mate localization and courtship. However, whether male sensitivity to female acoustic signals changes throughout the day remains poorly understood. Here, we investigated whether male behavioural response to female wingbeat sound is modulated by time of day. Responses were evaluated in a uniport behavioral assay across three photophase time windows (ZT0–2, ZT4–6, and ZT9–11) . Males were exposed to playback of female wingbeat sound, male wingbeat sound, or no sound as a control. Males showed a specific behavioral response to female sound, whereas male sound and silence elicited little or no response. Contrary to our initial prediction, males consistently responded to female sound at all three time windows. Moreover, neither response latency nor the number of mating attempts differed across the photophase. These results indicate that Ae. aegypti males discriminate female from male acoustic cues and sustain responsiveness throughout the light period. rather than being restricted to a specific daily window. Our findings provide new insight into the temporal organization of sensory mechanisms underlying mate recognition in Ae. aegypti and contribute to understanding the behavioral processes that regulate reproductive encounters in this mosquito.

Sensory and Motor Systems

D-111

Remodeling of Cochlear Efferent Innervation Following Noise Exposure

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Noise-induced hearing loss is one of the leading causes of sensory disability worldwide. Exposure to intense sounds damages cochlear sensory hair cells and their synaptic contacts with the auditory nerve. The activity of these cells is modulated by the olivocochlear efferent system, which originates in the brainstem. Numerous studies suggest that this system contributes to protecting the cochlea from acoustic trauma. The efferent system has been shown to undergo alterations in animal models of hearing loss caused by aging or genetic mutations that impair mechanotransduction. These alterations include changes in synaptic targets and ion channel expression, suggesting a reversion to an early developmental state. Whether these changes are a consequence of cochlear damage or represent a protective response remains an open question. Here, we investigated whether noise exposure similarly induces efferent plasticity in C57BL/6J mice, a strain highly susceptible to noise-induced damage. Mice were exposed to intense noise, and auditory brainstem responses were recorded one day before, one day after, and one week after acoustic trauma to monitor auditory function. One week after acoustic trauma, cochlear tissue was collected and processed for immunohistochemistry. Efferent innervation and ion channel expression were examined to characterize noise-induced changes in the olivocochlear system.

Sensory and Motor Systems

V-112

Evaluation of the analgesic effects of resveratrol in a chronic acidic saline induced muscle pain model

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Fibromyalgia (FM) is a chronic pain disorder of multifactorial origin, in which central sensitization, neuroimmune alterations, and gut-brain interactions have been proposed to contribute to symptom development. In this context, resveratrol (RESV) emerges as a potential therapeutic agent with neuromodulatory properties. In the present study, we employed a mouse model of chronic muscular hyperalgesia that mimics key features of FM to investigate the analgesic effects of RESV (50 mg/kg). To induce FM-like syndrome two acidic saline (pH 4.0) injections were administrated four days apart into the left gastrocnemius muscle of female BALB/c mice. Von Frey and Choi tests revealed increased mechanical and thermal sensitivity, indicating reduced pain thresholds and enhanced cold responses, which were partially attenuated by RESV. Locomotor parameters, including distance travelled and immobility time, were unaffected. Molecular analyses included RT-PCR assessment of spinal cord P2X4, P2X7, S1PR1 and S1PR3 expression. Spinal cord connexin 36 immunoreactivity, associated with trigeminal mechanical and cold allodynia, remained unchanged. These findings suggest that RESV may exert antinociceptive effects in a mouse model of FM-like pain and may represent a promising adjunct strategy for the management of chronic pain conditions. Supported by Universidad Austral, CONICET and FONCYT.

Theoretical and Computational Neuroscience

S-111

Identification of fMRI anomalies in epileptic patients: a signal analysis perspective

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Epilepsy is a neurological disorder characterized by recurrent seizures caused by abnormal and hypersynchronous neuronal activity. Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is a common form of epilepsy associated with alterations in brain networks involved in episodic memory. We investigated resting-state fMRI abnormalities in MTLE-HS from a signal-analysis perspective. The study included healthy controls (n=68), patients with right- (n=39) and left-lateralized (n=51) MTLE-HS, and patients with focal cortical dysplasia (n=29). BOLD signals were characterized using temporal, spectral, and correlation-based measures, including variance, power spectral density, AR(1), and the full width at half maximum of the autocorrelation function. Functional interactions were assessed through zero-lag and lagged correlations between brain regions. MTLE-HS patients showed reduced variance in the left pericalcarine and right rostral anterior cingulate cortices, together with slower dynamics in several regions. Regardless of the affected hemisphere, anomalous connections involving left temporal regions and both ipsilateral and contralateral areas were identified. These findings suggest that MTLE-HS is associated with widespread alterations in brain dynamics and functional connectivity extending beyond the site of hippocampal sclerosis.

Theoretical and Computational Neuroscience

D-112

Time–space signatures of hybrid search resolution using EEG and eye movements concurrent recordings

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Studying visual and memory processes during hybrid searchi requires disentangling overlapping neural signals arising from the interaction between attention and memory. Conventional event-related methods fail in these ecologically valid settings. We employed a deconvolution-based approach to coregistered EEG and eye-tracking data during a hybrid visual and memory search task with unrestricted eye movements. This methodology successfully isolated fine-grained activation patterns in temporal response functions (TRFs) associated with both task-related main effects and their interactions. Starting with hypothesis-driven models, we replicated established neural components for visual processing and target detection. By extending to hierarchically larger data-driven models, we explored interactions between effects typically studied in isolation. Our results show that TRF estimates remain stable as model complexity increases, supported by improved Pearson's correlation coefficients and controlled variance inflation factors (VIF). We identified a late activation consistent with the P300 component for target detection and found that missed targets elicited similar but weaker responses, suggesting a nuanced neural role beyond binary detection. These findings demonstrate that deconvolution methods, paired with robust performance measures, can uncover the dynamic interplay of attention and memory underlying free-viewing behavior.

Theoretical and Computational Neuroscience

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Subsyllabic motor gestures across species reveal principles of birdsong production

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Birdsong exhibits a high degree of diversity across species, raising the question of how species-specific vocal repertoires emerge from the mechanisms underlying vocal production, and whether general principles of motor organization can be identified across species. We propose that a useful level at which to address this question lies below the syllable, in the organization of subsyllabic motor gestures. Using simultaneous abdominal EMG and air sac pressure recordings, we develop a physiologically grounded computational method to infer these gestures as building blocks for syllables. Across canary and zebra finch songs, the resulting gestures form structured clusters, revealing regularities at what we propose to be a fundamental level of vocal motor organization.

Theoretical and Computational Neuroscience

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Temporal dynamics and deep learning in a recurrent neural network with time delays

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Besides their computational applications like classification and prediction, recurrent neural networks (RNNs) are themselves a model for many phenomena in neuroscience, social dynamics, and other areas, and the diversity of architectural variants and learning algorithms has grown very rapidly in the last 20 years. In many ways, however, the spatially-recurrent architecture —where every node in the network can be simultaneously connected to many others— is considered the most challenging of all, specifically due to the presence of excitatory loops. If the excitatory connections are sufficiently strong, chaotic neural activity patterns arise and the network becomes exponentially sensitive to small changes in initial conditions, causing most training algorithms to fail. If we also consider that the recurrent network model can have time delays, the richness and complexity of possible solutions grows further, as well as the difficulties for numeric simulation, training, and analysis of solutions. In this work we take a deep learning algorithm that can handle the chaotic regime (InnateTraining or Dynamical Attractor) and apply it to the training of chaotic RNNs that also have time delays in the connections between neurons. We show that the algorithm can successfully train a network despite the existence of delays of appreciable size compared to the characteristic time of each neuron.

Theoretical and Computational Neuroscience

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Emergent Navigational Computations in a Self-Organizing Attractor Model

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While continuous attractor neural networks (CANNs) model spatial representations and prospective coding in navigational circuits, joining biologically plausible learning with diverse navigational phenomena remains challenging. We developed a self-organizing firing rate model where a neuronal layer, exhibiting competitive dynamics via adaptation and global inhibition, spontaneously learns to represent space through local Hebbian plasticity. Crucially, this framework captures three complex findings. First, population activity naturally anticipates stimulus positions, matching entorhinal predictive coding. Second, preliminary results suggest recurrent plasticity offers a mechanistic explanation for dynamic speed recalibration in path integration, reflecting rapid hippocampal gain adjustments to cue conflicts. Finally, it addresses novel 3D navigation data : on inclined surfaces, entorhinal grid maps undergo a small, stationary upward shift along the slope axis, preserving overall symmetry. By increasing the synaptic contribution of downhill-oriented conjunctive cells, our network accurately reproduces this shift in omnidirectional cells. Thus, a single framework of adaptation, competition, and synaptic plasticity is sufficient to self-organize circuitry for predictive coding and terrain-dependent mapping, while providing analytical tractability to explore dynamic speed recalibration.

Theoretical and Computational Neuroscience

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From Geometry to Dynamics: Constructing equations from Phase-Space Structure

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Electronic neurons provide physical implementations of neuron-like dynamics, allowing excitable behavior to be studied in controllable and directly measurable systems. Among these implementations, memristive neurons are particularly attractive because nonlinear switching can generate spiking using remarkably simple circuits. Here, we present a continuous two-dimensional model of a previously developed memristive spiking neuron, constructed directly from its experimental voltage-current trajectory. Inspired by a geometrical approach to dynamics [1], the model reproduces the slow evolution along conductive branches and the rapid transitions associated with spike generation. By varying its parameters, it also captures the dependence of firing on input current and the experimentally observed shift of the switching threshold with gate resistance. This framework provides a compact bridge between experimentally accessible memristive hardware and the dynamical-systems description of neuronal excitability. [1] Deng, B. Int. J. Bifurcat. Chaos 4, 823–841 (1994). doi:10.1142/S0218127494000599 [2] Fernandez, L. E. et al. Chaos Solitons Fractals 180, 114555 (2024). doi:10.1016/j.chaos.2024.114555 [3] Wu, J. & Rozenberg, M. In Memristors—The Fourth Fundamental Circuit Element (IntechOpen, 2024). doi:10.5772/intechopen.1004909

Theoretical and Computational Neuroscience

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Evaluating a Trial-Wise Motor Imagery Modulation Quality Metric in a Cross-Subject Adaptation Scenario

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Despite their potential for rehabilitation therapies based on brain-computer interfaces (BCIs), motor imagery (MI) tasks are inherently challenging to evoke. Meaningful feedback should follow each MI trial to promote modulation strategies refinement in a closed loop way. In a previous work, we showed that the cost of aligning a trial to match the training session distribution in a within-subject scenario provides a real-time measure of MI modulation quality. Real-time experiments confirmed that using such a metric for feedback delivery can enhance MI modulation. While promising results, this setup requires a full calibration session. More recently, we extended such adaptation framework to a cross-subject transfer learning scenario, showing that it enables accurate MI decoding without subject-specific calibration. In this work, we investigate if the adaptation cost derived from a model trained on a cross-subject cross-dataset setting can also provide an effective MI modulation quality metric. Specifically, we assess if it reflects MI modulation quality and study its relationship with the intra-subject analogous metric. By demonstrating that a cross-subject adaptation cost metric provides informative trial-wise feedback, we could guide users to control the MI-BCI system from the first day, without requiring a subject-specific calibration. This approach is particularly relevant in rehabilitation contexts, where minimizing setup time directly translates to higher usability.

Theoretical and Computational Neuroscience

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A Shared Entropic Axis Spans States of Consciousness Across Pharmacological and Clinical Conditions

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A general account of how diverse states of consciousness arise from brain activity requires a generalisable quantitative framework. The Entropic Brain Theory proposes that states of consciousness can be ordered along a single dimension defined by spontaneous neural entropy, but this prediction has not been tested across pharmacological and clinical perturbations within a common analytical pipeline. Here we quantify the temporal irregularity of time-resolved small-world topology using sample entropy, applying the same pipeline to pharmacological (psychedelics, modafinil, propofol anaesthesia) and clinical (schizophrenia) fMRI datasets. Propofol anaesthesia occupied the low-entropy end of the axis; psychedelic states and schizophrenia occupied the high end. The ordering tracks combined modulations of the level and content of consciousness, ranging from reduced awareness under anaesthesia to heightened arousal and expanded experience of psychedelic states and the disorganised processing of schizophrenia. Crucially, this result was not reducible to fluctuations in mean functional connectivity, supported by convergent reorganisation of higher-order association cortex under psychedelics and anaesthesia, alongside a distributed loss of network specificity in schizophrenia. These findings provide empirical support for an entropic continuum of brain states and identify the temporal diversity of large-scale network reconfiguration as a primary axis of conscious dynamics.

Theoretical and Computational Neuroscience

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Channelopathy and anticipated synchronization: effect of the W1204R (Na_v1.1) epileptogenic mutation in an SRI microcircuit

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Anticipated synchronization (AS) is a regime where a receiver neuron fires before the sender that excites it, preserving causality. Although a sender-receiver-interneuron (SRI) neuronal motif transitions from delayed synchronization (DS) to AS upon increasing inhibitory conductance, it remains to be elucidated whether this depends on the neuronal excitability class. Here, three models are contrasted within the SRI circuit: Hodgkin-Huxley (HH) and two GEFS+ variants based on Na_v1.1 channel kinetics (control and the W1204R epileptogenic mutation). Excitability analysis reveals that HH is Class 2 (subcritical Hopf bifurcation), whereas the GEFS+ variants are Class 1. The W1204R mutation shifts the transfer (f-I) curve without altering its excitability class. For a rigorous parametric comparison, the models were evaluated at equivalent operating points by matching the receiver's intrinsic frequency. Under these conditions, the parameter space was analyzed to determine the DS-AS transition thresholds according to the excitation-inhibition balance. Using phase response curves (PRC), the plane defined by the operating point and the synaptic conductance ratio was characterized. These findings demonstrate how the dynamic divergences of the models modulate synchronization regimes, highlighting the role of intrinsic excitability in the propagation of epileptogenic activity.

Theoretical and Computational Neuroscience

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The user as a whole: emotional factors influencing the experience with brain-computer interfaces

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While motor imagery brain-computer interface (MI-BCI) rehabilitation yields lasting upper-limb motor recovery after stroke, how the User eXperience (UX) evolves, within individual sessions and across consecutive days, remains poorly understood. Here we investigated the variations of users' answers to UX questionnaires when training with a MI-BCI. 12 healthy naive users performed 5 application sessions (5 runs, 20 trials each), where some questionnaires were administered before using the BCI, while others after the BCI task was completed. To understand the relationship between emotional factors and the ability to control a BCI, the questionnaires collect information related to emotional arousal, use of stimulants, motivation, engagement, agentivity, anxiety and level of comfort perceived. Another publicly available dataset was used to understand results replicability. This metadata information aims to be used as predictors of the control capability and to provide perspective on the performance evolution. The participants reported being intensely engaged in the task, considered the feedback clear and useful, and the game motivating and reliable. Preliminary results indicate that those who did not change the imagery strategy throughout the sessions had better performances than those who actually did so. Understanding of the UX impact of the BCI controlling capability can significantly change our understanding of protocol designing for proper user engagement.

Theoretical and Computational Neuroscience

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Emulating Wilson-Cowan neural mass dynamics with grey-box Neural ODEs: a progressive-complexity study of unmodelled behaviour

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Neural mass modelling is a powerful tool in computational neuroscience. The Wilson-Cowan (WC) model is a well-established, low-dimensional description of population dynamics. Its simplicity, however, disregards subtler phenomena that may be present in the real plant. This work investigates a preliminary grey-box replication of neural mass dynamics using Neural ODEs. A WC-structured backbone is combined with a learnable NN correction for unmodelled behaviour. At this stage, data is generated by a WC simulator with refractoriness and optogenetic actuator dynamics. Fidelity is measured by rollout error on held-out stimuli. Each disturbance is isolated in a progressive-complexity protocol. The actuator lag adds a hidden state with its own memory, which no state-based correction can represent, while refractoriness, a pure function of the state, is capturable. Under refractoriness alone, a memoryless correction already reproduces the dynamics, and expanding the backbone with the physical form of the disturbance improves performance. . Under actuator dynamics alone, memoryless corrections fail. Only augmenting the model with a first-order filter of learnable time constant restores fidelity. The memory of the omitted physics, rather than its magnitude, determines whether accurate reproduction is achieved. This gives a criterion for when state augmentation is necessary. Future work will validate this on experimental recordings.

Theoretical and Computational Neuroscience

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Bio-inspired metrics for synthetic neuromorphic systems

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Neuromorphic computing proposes an alternative to traditional computing by developing hardware that integrates and processes information through mechanisms analogous to biological neurons.The main motivations for this research are to develop more compatible hardware for artificial neural networks, and to to study diverse topics of neuroscience. Such hardware requires properties compatible with brain-inspired computation, such as spiking behavior, network dynamics, scale-free morphology, and many others. The goal of this work is to develop metrics that quantify the resemblance of these neuromorphic systems to biological neurons. We present the results of this analysis in high density silver nanowires networks, which are promising material for neuromorphic applications. First, we characterized their morphology and identified fractal-like properties applying a box-counting algorithm to optical images. Second, we observed spike-like electrical responses to external stimuli, which were compared with neuronal activity generated by the Izhikevich model. We are currently extending this analysis by studying a biological computer developed by Cortical Labs, which is a platform that runs in a culture of human neurons. Particularly, we are investigating correlation metrics, focusing on the spike time tiling coefficient proposed by Cutts and Eglen. With these metrics we aim to provide a framework for comparing the neuromorphic potential of diverse biological and artificial systems.

Theoretical and Computational Neuroscience

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Modeling Synaptic Integration of Tactile Inputs in a VB Thalamocortical Neuron

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Ventrobasal (VB) thalamic neurons are the primary relay of somatosensory information to the cortex. In vivo, they operate in a high-conductance state shaped by continuous, asynchronous synaptic activity, yet must reliably detect and transmit transient sensory signals. Understanding how intrinsic membrane properties enable these neurons to distinguish phasic sensory inputs from ongoing synaptic noise is therefore essential for elucidating normal and pathological sensory processing. We developed a biophysically detailed, multicompartmental model of a VB neuron using Python and NEURON to investigate this process. To reproduce key features of the in vivo synaptic environment, we implemented a hybrid input paradigm combining stochastic background activity with a simulated tactile stimulus. Background network activity was represented by independent, uncorrelated Poisson processes driving balanced excitatory and inhibitory synaptic inputs. Superimposed on this ongoing activity, a simulated mechanical stimulus, such as von Frey filament indentation, was modeled as a synchronous, phasic burst of presynaptic activity with Gaussian temporal dispersion to capture biological variability in mechanoreceptor recruitment and axonal conduction. This framework enables us to examine how changes in intrinsic membrane conductance associated with neuromodulation or disease affect the detection, integration, and fidelity of tactile signals at the single-neuron level.

Theoretical and Computational Neuroscience

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Towards Label-Free Identification of Electrographic Seizure Patterns: A Machine Learning Anomaly Detection Approach

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The electrographic seizure pattern (ESP) identification problem is usually addressed as a supervised classification problem. Nevertheless, in a clinical setting, access to human-labeled data can be limited due to the tedious and time-consuming process of ESP annotation. In addition, when working on longitudinal data, such annotations represent a practical burden for proper patient monitoring. In this work, we address this problem with a semi-supervised machine learning anomaly detection approach. We used intracranial electroencephalographic (iEEG) recordings from patients with drug-resistant epilepsy treated with Responsive Neurostimulation (RNS). From iEEG recordings without ESP, we extracted time-frequency features to train ensembles of one-class support vector machine (OCSVM) classifiers. Training data comprised no-ESP iEEG recordings from the first period after RNS implantation (baseline). The trained classifiers were then used to identify iEEG recordings with ESP as those classified as outliers. The models were initially assessed using baseline recordings and subsequently evaluated on longitudinal data. We investigated the impact of training data regularity and size on model performance and introduced a metric to assess training data quality for OCSVM training. Overall, we present a complete pipeline for ESP identification based on anomaly detection, opening new avenues for the development of robust, reliable, and fast subject-specific ESP detectors.

Theoretical and Computational Neuroscience

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Organizational Networks as Collective Processing Systems: An Agent-Based Modeling Framework for Structural Analysis

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Complex adaptive systems, from neural circuits integrating sensory stimuli to organizational networks, share a fundamental property: collective patterns emerge from local interactions among individual units. In neuroscience, distributed sensing relies on agents integrating information through local rules, where no central controller is required. We propose that this framework is analogous to Organizational Network Analysis (ONA). This work explores how Agent-Based Modeling (ABM) can provide a robust methodology to simulate organizational dynamics, moving beyond descriptive network snapshots. In this conceptual framework, each individual is represented as an agent with communication ties that define the informal network structure, rather than the formal hierarchy. We investigate how an agent's position within the network — specifically regarding central nodes and bridges connecting disjoint functional areas — influences the propagation of information and organizational signaling. By applying an ABM approach, we aim to design a model capable of mapping how structural network features relate to collective organizational outcomes. This study establishes a methodological bridge between computational neuroscience principles and ONA, providing a platform to simulate decentralised coordination phenomena. Empirical validation using real-world organizational data is proposed for subsequent development.

Theoretical and Computational Neuroscience

V-118

Generation of transient sequences in excitatory-inhibitory neural networks and their relationship to the motor gestures of birdsong

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Birdsong requires the generation of highly structured motor sequences with precise temporal organization. Neural activity in song-related circuits shows stereotyped temporal patterns tied to specific motor gestures (Amador et al., 2013). Reproducible sequences can emerge in randomly connected neural ensembles (Huerta & Rabinovich, 2004), suggesting network connectivity as a mechanism for sequence generation. Recent work has also described respiratory motor gestures as excitable transients (Andrada & Mindlin, 2025), linking neural dynamics to motor output. Here, we study electromyographic (EMG) signals from syringeal muscles, which show sequences of one to four pulses with roughly fixed width and short inter-pulse delays. We propose a reduced model of the HVC circuit based on excitatory-inhibitory pairs, each representing a population of RA-projecting neurons and its associated HVC interneuron population, operating in an excitable regime. Each pair generates a stereotyped transient, transmitted through a two-stage synaptic filter; propagation requires near-simultaneous coincidence of multiple presynaptic inputs. Units are connected through an Erdős-Rényi random graph, letting us study how topology shapes the propagation and timing of transient sequences. This minimal architecture reproduces sequences of one to four transients with temporal characteristics compatible with those observed experimentally.

Theoretical and Computational Neuroscience

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Intracranial EEG and Mutual Information: Identifying the Preictal State

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Refractory epilepsy represents a significant clinical challenge due to the resistance of certain patients to pharmacological treatments capable of suppressing the seizures inherent to the disease. Although surgical removal of the affected areas may be a solution, this option is not always feasible, forcing patients to live with a limited quality of life. The use of intracranial electrodes iEEG allows obtaining high resolution signals both spatially and temporally, which have allowed the identification of three main brain states: basal, postictal and preictal. Early detection of the preictal state is crucial, as it can predict a seizure minutes before it occurs. In this study, mutual information (MI) was used to analyze statistical dependencies, both linear and nonlinear, between multichannel iEEG time series. both linear and nonlinear, between multichannel time series of $iEEG$. MI was applied to measure the transmission of information between different neuronal rhythms in status epilepticus, acting as an objective biomarker with potential for early diagnosis of seizures. Finally, MI calculations between different frequency bands were used to train neural networks that were able to predict the preictal state with an accuracy of 81%. This approach represents a promising tool to improve the quality of life of patients with refractory epilepsy through early seizure prediction.

Theoretical and Computational Neuroscience

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Size of the basin of attraction as a key factor to achieve homeostasis in a mathematical model of synaptic plasticity

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Many functions and regimes of the cerebral cortex are characterized by patterns of self-sustained neural activity produced by recurrent excitatory connections. Mathematical models of synaptic plasticity traditionally depend on the pre-existing level of neural activity; therefore, if the initial state during development is silent, modifying the synaptic weights is, in principle, unachievable. To understand the emergence of a stable activity from the mostly silent state in early developmental stages, we addressed this problem using a firing-rate neural model with rectified linear activation functions (ReLU). We performed an exhaustive exploration of the neural model's parameter space (synaptic weight values). Tens of millions of combinations of the four local synaptic weights (self-excitation, self-inhibition, and cross-connections) were simulated. The dynamical analysis focused on quantifying the size of the silent state's basin of attraction in two scenarios: early and late development stages. We found that a significant percentage of combinations (in both the early and late models) meet the condition of having a basin of attraction small enough to align with experimental criteria. Particularly, the basin of attraction in the early developmental model can be smaller than in the late one. This finding shows that, within a certain region of parameter space, the network has an intrinsic ability to "take off" from the silent state via spontaneous fluctuations.

Theoretical and Computational Neuroscience

V-119

DtMF: Debí… ¿tirar más fotos? tener Más Fijaciones — Modeling Human Variability and Same-Image Target-Presence Comparisons in Visual Search

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Computational models of visual search have become increasingly successful at predicting observers' fixation patterns during free viewing. A recent approach combining deep neural networks for bottom-up information processing with Bayesian top-down integration achieved the best performance across many datasets in the ViSioNS benchmark. However, two important limitations remain. First, comparisons between target-present and target-absent search are often based on different sets of images, making it difficult to disentangle effects of target presence from differences in scene content. To address this, we built a new dataset and framework in which target-present and target-absent trials can be directly compared under matched visual conditions. Second, existing metrics focus on average performance, although observers' scanpaths in the same scene are not identical. We therefore investigated whether variability across observers could be reproduced by introducing structured stochasticity in the initial prior (saliency map) and in the expected-information map at each fixation. Across different noise parameters, introducing internal noise not only captured observer variability but also improved model performance. We conclude that stochasticity is inherent to human information processing and propose that future models should be evaluated both by their average performance and by their ability to reproduce human variability.

Theoretical and Computational Neuroscience

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Automated speech and language markers of childhood autism in restricted interest based conversational tasks

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Automated speech and language analysis has demonstrated potential for identifying the linguistic and acoustic characteristics of language in autistic children. However, most studies use traditional assessment tools to extract markers, which are resource-intensive. This study used brief conversation to elicit natural communication about general and restricted interests (GI and RI) in 72 participants (35 autistic and 37 non-autistic, age between 6-15 years old). Acoustic and linguistic markers were then extracted and analyzed using group-level comparisons and machine-learning classification. Results revealed group differences in pitch variability, disfluencies, fluency, lexical diversity, and third-person pronoun use. Most alterations were found in RI rather than GI interviews. Machine-learning models integrating speech and language features achieved high classification accuracy (AUC = 0.88 vs. 0.82). The RI-based conversational tasks are promising for ASD diagnosis due to their objectivity, affordability, scalability, and sensitivity and could complement traditional assessment.

Theoretical and Computational Neuroscience

D-119

Nonlinear path integration explains speed-dependent field shifts in hippocampal place and time cells

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Place and time cells encode spatial location and elapsed time in the hippocampal formation. Recent experiments in CA1 have revealed speed-dependent shifts in the receptive fields of these cells, interpreted as evidence for mixed encoding of space and time. Here, we propose that such shifts can instead arise from nonlinear path integration, without explicit temporal coding. We first show that a Continuous Line Attractor model in which velocity is transformed by a saturating function reproduces speed-dependent shifts in estimated position. We then train a Recurrent Neural Network on a 1D path-integration task. After training, the network spontaneously develops place cells with speed-dependent field shifts and a concave relationship between simulated and internally represented speed, despite neither feature being imposed during training. Analysis of the trained network reveals two direction-selective populations and a non-selective population that is progressively silenced by increasing speed, effectively acting as a brake on the integrator. This emergent mechanism produces the saturation of internally represented speed and the resulting shifts in place fields. Together, our models show that speed-dependent place-field shifts can emerge from nonlinear path integration, without requiring explicit temporal coding.

Theoretical and Computational Neuroscience

V-120

Sleep-stage dynamics beyond the power spectrum: A surrogate-referenced multiscale ordinal analysis

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Sleep stages are commonly characterized by their EEG spectra, but spectral analysis cannot reveal whether brief voltage fluctuations follow a preferred temporal order. This study investigates whether such temporal organization varies across sleep stages and persists after controlling for amplitude distributions and power spectra. Using an open multi-night dataset, ordinal patterns were used to characterize short EEG segments according to the ordering of their values. Entropy, statistical complexity, and Fisher information provided complementary measures of this organization. Each window was compared with IAAFT surrogates preserving its amplitude distribution and Fourier magnitude, with inference performed at the participant level. Residual temporal organization was consistently observed across stages and temporal scales, with the strongest combined signature in N2 at intermediate subsecond scales. Complexity and Fisher information further distinguished N3 from N2 when entropy alone did not. Synthetic benchmarks suggested that a slowly amplitude-modulated linear oscillator better reproduced the empirical profile than a canonical chaotic system. Thus, sleep EEG exhibits stage-dependent temporal organization beyond conventional amplitude and spectral structure, without implying a unique mechanism or deterministic chaos.

Theoretical and Computational Neuroscience

S-119

Brain Age Estimation in Young Adults from Resting-State fMRI: Comparison of Functional Connectivity, Spectral Amplitude Features, and Regularized Regression Models

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Brain age is an estimate of the brain's biological age, derived from neuroimaging data using machine learning algorithms, that allows quantification of brain ageing. The difference between predicted and chronological age, known as Brain Age Gap (BAG), can serve as a biomarker of deviations from typical ageing. Estimating brain age in young adults, where age-related differences are subtle, poses specific challenges. We developed a reproducible pipeline using the Human Connectome Project (HCP S1200), comprising 1,003 adults aged 22–37 years with resting-state functional magnetic resonance imaging (rs-fMRI). Time series from 50 brain networks were obtained using independent component analysis (ICA). Multiple BOLD signal representations were evaluated, including functional connectivity, ALFF, fALFF, and low-frequency subband variants. Ridge, ElasticNet, and Lasso regression were compared using grouped cross-validation while preserving family structure. Functional connectivity showed the best overall performance, while spectral representations incorporating multiple low-frequency subbands outperformed the original ALFF representation. Ridge consistently outperformed ElasticNet and Lasso, suggesting that age-related information is distributed across multiple functional features. These results indicate that low-frequency rs-fMRI information is relevant to brain ageing in young adults, with functional connectivity providing an informative representation for Brain Age estimation.

Theoretical and Computational Neuroscience

S-123

Agent-Based Modeling (ABM) as a Complementary Framework to Differential Equations for Collective Sensory Processing: An Exploratory Study

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Introduction: Complex adaptive systems, particularly neural circuits that integrate sensory information, exhibit collective patterns emerging from local interactions between individual units (collective sensing). This work explores when agent-based modeling captures phenomena that population-level differential equations cannot describe, and how both frameworks articulate in a multiscale approach. Methods: We propose representing each sensory unit as a discrete agent with its own activation threshold and local interaction rules with immediate neighbors (direct coupling and imitation). The main guiding case models the propagation of a sensory disturbance through a population of sensory channels. As an illustration of the framework's extensibility, this same scheme could be transferred to economic agents to model expectation contagion or herd behavior in markets with incomplete information. Expected Results: We expect to obtain a conceptual design of the ABM and a formal approach to its continuous limit (mean-field). We aim to identify under what conditions local rules give rise to phenomena like partial or asynchronous stimulus propagation that a purely aggregate description does not capture with the same resolution. Conclusions: This framework specifies when ABM provides unique insights into collective sensory processing dynamics that a population-level differential equations approach could not show. Keywords: Agent-Based Modeling, Computational Neuroscience.

Theoretical and Computational Neuroscience

V-121

ApoE Variants in Sei Whale (Balaenoptera borealis): From the perspective of Cetaceans and 'Alzheimer's-like' Pathology

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Alzheimer’s disease study has been limited by the scarcity of natural models replicating ispontaneous disease development. Natural models of “Alzheimer’s-like” pathologies could expand our understanding disease mechanisms and their environmental interactions, offering translational insight and more accurate experimental models. Recent evidence of Aβ plaques and Tau tangles in cetaceans suggests an “Alzheimer’s-like” pathology in this group, whose research interest is expanded by their longevity, prolonged postmenopause, and oxidative damage protection mechanisms; factors underlaying the pathology. ApoE, the main genetic risk factor for sporadic Alzheimer's, remains structurally uncharacterized in cetaceans. Following a 2015 sei whale (Balaenoptera borealis) mass stranding in Chile, two novel ApoE variants (S22R, S112R) were identified in structurally relevant regions via AlphaFold-predicted structures, potentially influencing neurodegeneration analogously to pathogenic human ApoE variants.

S-120

Reading movement from posture: Machine learning approach

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With the advent of high-speed cameras and the widespread use of artificial intelligence, software tools can now extract trajectories and body parts from videos, changing how behavior and neuroethology are studied. A key idea is that an animal's posture or sequence of postures contains information about its behavior and intentions. Knowing an animal's body movements over a given period, one might expect to predict its future movement using equations. However, the high dimensionality and many interactions involved make a general analytical solution difficult. However, many animals can do this and take advantage of it in their own behavior, without needing to formulate or solve equations. Machine learning offers an alternative by identifying patterns across different situations and using them to make predictions. We investigate whether an animal's displacement and rotation can be predicted from its previous postures. Using freely swimming zebrafish larvae, we extracted body-part trajectories with DeepLabCut and trained machine learning algorithms to predict displacement and rotation from a preceding time window. Our results show good predictive performance, allowing the animal's trajectory to be predicted even a few seconds into the future. However, performance is strongly affected by errors in posture estimation. This work provides a starting point for developing more general approaches and exploring further improvements and applications of the algorithm.

Tools Development and Open Source Neuroscience

D-121

Immersive Virtual Reality and EEG Recording System to Detect Neurophysiological Signatures Related to Cognitive Behavior

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Immersive virtual reality (VR) enables ecologically valid environments for brain–machine interface and cognitive neuroscience research, but studying neurophysiological signatures of behaviour in VR requires precise synchronization between experimental events, behavioural variables, and EEG recordings. We present a reproducible, open-source synchronization platform for immersive EEG–VR experiments using a Meta Quest 3/3S headset and an 8- or 16-channel OpenBCI EEG system. The platform integrates Unity-based VR event generation and Lab Streaming Layer (LSL) acquisition, with low-latency communication via ESP32-based external pulse generators. Unity event markers are converted into unified timestamps across EEG, VR, and behavioural streams, enabling automatic alignment of neural activity with trial onset, visual transitions, navigation, responses, feedback, and movement variables. EEG was sampled at 250 Hz and the VR stream at 72 Hz. Repeated measurements yielded a mean synchronization offset of 18.10 ± 1.77 ms (n=144), a 49.7% reduction in offset and 69.3% reduction in jitter versus the fastest system in the literature. The platform offers a scalable, reproducible framework for time-sensitive neuroscience, including brain–computer interfaces, spatial navigation, and event-related potential analyses.

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Tools Development and Open Source Neuroscience

V-122

Development of a Controlled Electrical Stimulation System for the Study of Behavioral Responses in Zebrafish Larvae

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The habenula (Hb) is a brain structure that plays an important role in negative reward processing. We aim to study how social isolation during early development affects habenular function in larval zebrafish. In particular, we want to analyze habenular neuronal responses to mild electric shocks of socially raised and isolated larval zebrafish using in vivo calcium imaging while we record tail motor responses. As a first step towards these aims we developed a stage platform for individual larvae that allowed applying controlled and reproducible electrical stimuli while recording brain activity and tail movements. The project involved designing a recording chamber for use with larvae approximately 4 mm in length and configuring an electrical stimulator capable of delivering current pulses while allowing the experimenter to control their amplitude, duration, frequency, and number of pulses. Our electrical stimulator can deliver a constant current of up to approximately 0.8 mA which is independent of experimental variations of the load resistance. The circuit can also reverse the polarity of the pulses to prevent capacitive effects generated by the aqueous medium in which the larva is immersed. The optimal operating range of the circuit was characterized, and the fish responses were statistically quantified as a function of the variable pulse parameters.

Tools Development and Open Source Neuroscience

S-121

Addressing Domain Shift in Automated Brain Tumor Segmentation: Evaluating TumorSynth on a Latin American Clinical Data.

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The translation of deep learning models for brain tumor segmentation to public healthcare systems is hindered by domain shift, particularly in heterogeneous clinical cohorts. This study presents a zero-shot analysis of a promising model TumorSynth using local data. We evaluated these methodologies on the local FLENI dataset for segmentation accuracy and the public LUMIERE dataset for automated Response Assessment in Neuro-Oncology (RANO) classification. Results on the FLENI dataset indicate that the model achieved a median Dice coefficient of 0.90 for the whole tumor. Conversely, the contrast-agnostic model successfully identified active tumor regions and edema but encountered significant difficulties in accurately resolving necrotic and non-enhancing with median Dice score of 0.60. For longitudinal monitoring, both automated volumetric approaches exhibited significant limitations in RANO classification, frequently misclassifying progressive disease as stable disease and yielding F1-scores near random chance levels. Furthermore, they underscore that relying solely on automated volumetrics remains insufficient for robust clinical-level disease progression assessment.

Tools Development and Open Source Neuroscience

D-122

Two-Dimensional Structured Illumination System for Epi-Illumination Microscopy

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In this work, a two-dimensional structured illumination system integrated into an epi-illumination microscope was designed, constructed, and calibrated. A DMD projector was used as the illumination source, together with a lens system consisting of a camera lens and an achromatic biconvex lens, designed to collimate the white-light beam entering the microscope's rear aperture. A Python-based algorithm was developed to acquire sample images, segment them using the Segment Anything Model (SAM), and generate masks based on color similarity using the K-means clustering algorithm. To ensure spatial alignment between the projected mask and the sample, the system was calibrated using a homography transformation. For both the 4× and 10× microscope objectives, wavelength-selective illumination was successfully projected onto a square sample region. However, significant chromatic aberration was observed in the projection, which represents an aspect to be addressed in future work.

Tools Development and Open Source Neuroscience

V-123

Unsupervised Categorization of Animal Behavioral Patterns Using Deep Neural Networks

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Automated quantification of animal behavior can reveal behavioral patterns that are difficult to identify through manual scoring. RAINSTORM was recently developed in our lab as a tool for analyzing rodent exploratory behavior based on pose estimation. This project extends RAINSTORM to support reproducible unsupervised behavioral quantification. This approach reduces reliance on predefined human categories while enabling the detection of subtle differences in behavioral organization that may not be evident through visual observation. The original workflow was reorganized to enable systematic data preparation, model integration, evaluation, and reuse. Unsupervised models inspired by VAME and Keypoint-MoSeq were implemented and compared using either pose data alone (pose_ego) or enriched with contextual information from regions of interest (ego_roi). Models were evaluated based on internal segmentation, behavioral state usage, label stability, and agreement with a reserved human reference. Native VAME with pose_ego achieved the best internal motif separation (silhouette score: 0.28 vs. −0.13), whereas official VAME with ego_roi showed greater agreement with the human reference (ARI: 0.083 vs. 0.058). The latter was selected as the operational configuration for subsequent analyses. Overall, this work provides a reproducible framework for training, comparing, validating, and reusing unsupervised behavioral quantification models, facilitating automated analysis of animal behavior.

Tools Development and Open Source Neuroscience

S-122

Curcumin-based nanoformulation as a potential treatment for peripheral neuropathies

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Curcumin, a natural polyphenol of rhizome Curcuma longa, exhibits anti-inflammatory, antioxidant and neuroprotective properties, partly through the modulation of brain-derived neurotrophic factor (BDNF). Peripheral neuropathies are highly prevalent disorders, affecting approximately 2-3% of the general population and up to 24% of individuals over 55 years of age, and still effective therapies remain limited. Based on our experience evaluating regenerative strategies in experimental models of peripheral nerve injury, we propose a curcumin-based nanoformulation as an alternative neuroregenerative approach. Considering the poor solubility and bioavailability of curcumin in biological fluids, curcumin-loaded poly lactic co-glycolic acild (PLGA) nanocapsules were synthetized and characterized by DLS, NMR and IR. To assess the potential regenerative effects of curcumin, scratch assays were performed in primary dorsal root ganglia (DRG) cultures. The formulation containing 0.5 mg/mL curcumin in chloroform yielded homogeneous PLGA nanocapsules with an encapsulation efficiency of approximately 80%. Preliminary results from the scratch assay suggest that this formulation may promote wound closure in DRG cultures. These findings support the development of curcumin-based nanoformulations as promising therapeutic approaches for peripheral neuropathies, potentially combining neuroregenerative, antioxidant, and anti-inflammatory effects to improve clinical outcomes.

Tools Development and Open Source Neuroscience

D-123

Webcam-based eye-tracking for online assessment of smooth pursuit and saccade performance

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Webcam-based eye-tracking is a scalable alternative to traditional eye-trackers, but its precision requires validation for clinical deployment. As methodological validation for ongoing studies involving Mild Cognitive Impairment (MCI) patients, we evaluated an online protocol to capture subtle gaze dynamics during static fixation, smooth pursuit, and saccadic paradigms online in a control sample . Participants were enrolled via LIAA's DataPruebas (N=49). Excluding 8 subjects with poor calibration, the remaining sample (N=41, 34.8 ± 14.1 years) showed a mean Euclidean error of 0.20 ± 0.07 (normalized to screen height) during fixation. Smooth pursuit yielded comparable errors (euclidean: 0.22, horizontal: 0.12, vertical: 0.16). Despite higher error margins than state-of-the-art eye-trackers, this approach identified subtle variations in saccadic behavior. Prosaccade (PS) accuracy was significantly higher than that of antisaccade (AS) for strictly correct (69 vs. 60%) and correct or corrected trials (91 vs. 83%). Timing and kinematics presented significant differences: correct AS exhibited longer latencies than correct PS, whereas incorrect AS had shorter latencies than correct ones. The system also detected variations in amplitude and velocity, revealing corrected PS had higher amplitudes and faster gaze velocities than strictly correct trials. These findings support webcam-based eye-tracking as a sensitive tool for oculomotor assessment in scalable cognitive testing.

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