Sociedad Chilena de Neurociencia

XX Reunión Anual de la Sociedad Chilena de Neurociencia

Hotel Hippocampus, Concón. Chile

Del 23 al 25
de Octubre 2024

LIBRO DE RESÚMENES

PROGRAMA

	Wednesday 23	Thursday 24	Friday 25
9:00-11:00	Registration	A1: The Intersection Between High Schools, Neuroscience, and Academia/EduTech **Timothy Marzullo**	S4: Gender perspective in Neuroscience: deepen the current view and confronting future challenges. **Carolina Oliva / Vania Figueroa**
11:00-11:30		*Coffee break*	*Coffee break*
11:30 -12:30		S2: Aging and Neurocognitive Disorders Insights through Multimodal Profiling **Leonel Medina / Adrian Palacios**	S5: Decoding BrainMechanisms of Stress Resilience **Alexies Dagnino**
12:30 -13:30			
13:30-15:00	*Lunch Break*	*Lunch Break*	*Lunch Break*
15:00-17:00	S1: Genetic, molecular, and cellular basis of Neurodevelopmental Disorders **Christian Cea**	Young Neuroscientists Symposium (YNS)	Oral Communication I Oral Communication II

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<tr><td>17:00-17:30</td><td>Coffee break</td><td>Coffee break/ Foto Congreso</td><td>Coffee break</td></tr>
<tr><td>17:30-18:30</td><td>Conversatorio con el SEREMI de Ciencia de la Macrozona Centro</td><td rowspan="2">S3: Perspectives on meaning processing from a psycho and neurolinguistic approach

María Francisca Alonso</td><td>Asamblea de socios
Elqui 3</td></tr>
<tr><td>18:30-19:30</td><td>PL1: Ulrike Heberlein</td><td>Best Poster and Oral Communication Award Ceremony
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<tr><td>19:30-20:30</td><td rowspan="2">Poster Session I</td><td rowspan="2">Poster Session II</td><td>Conferencia Mario Luxoro
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AUSPICIADORES

TCL Group

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LA TIENDA CIENTIFICA SCIENTIFIC DECO

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INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

PLENARY LECTURES

Flies, alcohol and sex: An interplay of nature and nurture

Ulrike Heberlein[1]

(1)HHMI-Janelia Research Campus. USA.

Alcoholism is a major problem in medicine and society, affecting approximately 10% of the population in their lifetime. Effective treatments are not available. Progress has been hampered by complex genetics and complex interactions between genes and the environment. Our lab decided to tackle this difficult problem using the fruit fly Drosophila melanogaster, the mother of modern genetics since the early 1900s. We started out by simply exposing flies to alcohol and to our utter amazement, they acted a lot like intoxicated people: they became disinhibited, got clumsy and eventually passed out. Flies also show tolerance, a hallmark of addiction, find mild intoxication rewarding, and they drink until they are wasted. Using the powerful genetics of Drosophila, we identified many genes and their mechanisms of action, that affect alcohol-related behaviors. A large portion of these genes have been validated in mammals including humans and are potential targets for therapy. More recently, our focus has shifted from genes to environmental factors. For example, we found that sexually rejected males drink a lot more than mated males and we identified a molecular mechanism through which the environment talks to the genome. Finally, reward circuits evolved for natural rewards such as food, sex, and social interaction. We identified a circuit that signals to a female fly whether she has successfully mated. This, in turn, leads to modified behaviors that include egg-laying or further mating. In summary, we have shown that Drosophila is an excellent model system to unravel the genetic and neural underpinnings of reward systems and their interaction with past experiences. The experimental accessibility of Drosophila allows us to tackle these complex problems with incredible precision.

Serendipity of a scientific drift: What I have learned about visual perception and other herbs.

Pedro Maldonado [1,2]

(1) Universidad de Chile, Neurociencia, Medicina, Independencia 1027, Santiago, Chile
(2) Centro Nacional de Inteligencia Artificial, CENIA, Independencia 1027, Santiago, Chile

The research trajectory of a scientist is subject to unpredictable events and encounters. Still, a constant in my career is collaborative work, mixing a central question with the perspective of others who question or enrich the research focus. In this presentation, I will talk about my scientific experience, from participating in the laboratory of H Maturana and F Varela to the current experience of living in a collective laboratory. I will talk about the mechanisms of perception, from the neuron doctrine to the synchrony of neural networks and active perception. I will describe how our conception of perceptual phenomena has been changing and what perspectives and challenges we face to better understand the brain, incorporating theoretical components in perception, consciousness, and artificial intelligence.

Keywords: Perception, Maturana, Varela, Cognition, Artificial Inteligence

Funding: Supported by ANID, the Sociedad Chilena de Neurociencia, Guillermo Puelma Foundation, and the National Center for Artificial Intelligence CENIA FB210017.

SYMPOSIA

SYMPOSIUM 1:
Genetic, molecular, and cellular basis of Neurodevelopmental Disorders

Chair: Christian Cea

Mutations in tao, the homologue of TAOK1 autism candidate gene, leads to autism-like behaviors in adult Drosophila melanogaster

Angelina Palacios Muñoz [1,3,4], Liliana Bustos [3], John Ewer [2,3], Isaac García [1,3,4]

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(2) Universidad de Valparaíso, Facultad de Ciencias, Valparaiso, Chile
(3) Centro Interdisciplinario de Neurociencia de Valparaíso, Universidad de Valparaíso
(4) Centro de Investigación en Ciencias Odontológicas y Médicas (CICOM), Facultad de Odontología, Universidad de Valparaíso

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder, characterized by impaired social interactions and stereotyped, repetitive behaviors. More than 200 high-confidence risk genes have been implicated in ASD, yet the functional relevance of many remains unclear. Additionally, research has predominantly focused on children and young adults, leaving a significant gap in understanding the impact of aging on individuals with ASD. We focus on the *thousand-and-one amino acid kinase 1* (*TAOK1*) gene, which encodes TAO1, a serine/threonine-protein kinase, disrupted in ASD patients. *TAOK1* gene is critical for cytoskeletal regulation, neuronal morphogenesis, and synapse development. However, the neural mechanisms through which *TAOK1* deficiency leads to ASD remain largely unexplored. To address this, we utilized the fruit fly, *Drosophila melanogaster*, with genetic deletions in *tao* (the fly gene most similar to *TAOK1*). We observed that hypomorphic mutant and RNAi-mediated knockdown of *tao* in the nervous system resulted in autistic-like behaviors, including deficits in social interactions (based on courtship behavior), hyperactivity, and impaired sleep (without affecting the circadian control of sleep) in young and old flies. Furthermore, the knockdown of *tao* using different drivers reduced mushroom body areas and affected *Drosophila* postsynaptic structures in young and aging flies. Our findings suggest that *TAOK1* is essential for regulating social interaction behaviors across the lifespan, providing new insights on the behavioral abnormalities observed in ASD patients, and highlighting the importance of examining the effects of aging on this disorder.

Keywords: Autism, Behavior, Drosophila melanogaster, genetic.

Funding: Centro de Investigación en Ciencias Odontológicas y Médicas (CICOM)

Interplay between mGluR- and GABAAR-mediated neurotransmission underlying the Excitatory-Inhibitory Balance in a Fragile X Syndrome mouse model

Christian Cea Del Rio [1]

(1) Centro de Investigación Biomédica y Aplicada (CIBAP), Escuela de Medicina, Facultad de Ciencias Medicas, Universidad de Santiago de Chile, Santiago, Chile.

Fragile X Syndrome (FXS) is the most common inherited form of intellectual disability and a leading genetic cause of autism spectrum disorder. It results from a mutation in the *FMR1* gene, leading to a deficiency of the Fragile X Messenger Ribonucleoprotein (FMRP), which is essential for synaptic plasticity and neural circuit development.
A key feature of FXS is hyperexcitability, presenting as heightened sensory sensitivity, anxiety, and seizures. This hyperexcitability is linked to imbalances in excitatory and inhibitory neurotransmitter systems. Specifically, the loss of FMRP disrupts metabotropic glutamate receptors (mGluRs) and GABAergic pathways, causing excessive mGluR-mediated signaling and insufficient GABAergic inhibition. These pathways are critical in regulating synaptic transmission and plasticity during neurodevelopment.
Our research shows that both mGluR and GABAAR follow abnormal developmental trajectories in the FXS mouse model. These disruptions affect mGluR-mediated inhibitory plasticity, particularly long-term depression of inhibition (LTDi), which is severely reduced in adult FXS mice but is determined earlier in neurodevelopment. We also found decreased mGluR-mediated intracellular calcium levels early in development, potentially explaining the altered LTDi, which may later adjust as a compensatory mechanism to counteract hyperexcitability.
These findings highlight the importance of the early neurodevelopmental interplay between mGluR and GABAergic pathways in the altered excitatory-inhibitory balance seen in FXS. Pharmacological strategies targeting these pathways could help address the neurodevelopmental challenges of FXS, offering potential for more effective treatments.

Keywords: Neurodevelopment, GABA, Plasticity, Fragile X Syndrome, Excitatory-Inhibitory Balance

Funding: DICYT 022401CDRDICYT 022001CDRFondecyt 11150816IBRO Return to Home Fellowship

Neurovascular dyscoupling in Schizophrenia: An hiPSC-derived neurodevelopmental study.

Verónica Palma [1], Bárbara S Casas [1], Stevens Rehen [2], Sebastian Arizábalos [1], Maria Jesus Garrido [1], Benjamín I. Reuse [1], Catalina Prieto [1], Jesús Juárez [1], Ignacio Casanova [1], Magdalena Sanhueza [1], Sofía Puvogel[1], Kris Blanchard [1], Yerko Suazo [3], Katherina Llanos [3]

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(2) Federal University of Rio de Janeiro and D'Or Institute, Brazil.
(3) Instituto Psiquiátrico Dr. José Horwitz Barak, Servicio de Salud Metropolitano Norte, Santiago, Chile.

Schizophrenia (SZ) is a chronic debilitating neuropsychiatric disorder with a lifetime risk of ~ 1% worldwide. Increasing evidence is tracing SZ's origin to embryonic neurodevelopment, where the brain is formed concomitantly with a vast and complex vascular network, structuring the neurovascular unit (NVU). However, how neurovascular coupling emerges developmentally and contributes to SZ is unclear. We have worked in the modeling of early neurovascular interactions in SZ using induced pluripotent stem cells (hiPSC), reprogramed from healthy controls (HC) and SZ patients (SZP) and differentiated into the main cellular components of the NVU: Neurons, astrocytes and brain endothelial cells (BEC). We have studied cell-cell interactions, their functional and molecular alterations, and their secretome effect on angiogenesis, brain barrier formation, and neural activity. SZP-hiPSC derived BEC show a decreased response to angiogenic stimuli and present alterations in their blood-brain barrier capacities. SZP hiPSC-derived astrocytes reveal a chronic inflammatory profile with broad effects on their secretome, inducing vascular alterations when assayed both *in vitro* and *in vivo*. SZP hiPSC-derived long-term neuronal cultures show changes in functional

connectivity dynamics, suggesting that alterations in neuronal communicational dynamics are already present during early development in SZ. Overall, these findings indicate the presence of inherent deficiencies in both neural and vascular components, resulting in defective crosstalk in the formation of the NVU that possibly contributes to the etiology of SZ. Current investigations aim to correlate these results with clinical research on HC versus SZP for developing novel therapeutics.

Keywords: Schizophrenia, hiPSC, brain development, neurovascular union, Blood-brain barrier

Funding: Fondecyt # 1190083, 1221522 (VP) & ANID PhD fellowship # 21150781 (BC)

Acknowledgments: Acknowledgement: Gabriela Vitória, Marcelo Costa (Federal University of Rio de Janeiro and D'Or Institute, Brazil)

Impaired cognitive flexibility in a mouse model of OCD

Francisca Henriquez-Belmar [1], Carlos Ancatén-González [1], Nicolás Ardiles [1,2], Sebastián Estay [1], Andrés E. Chávez [2,3], **Pablo R. Moya** [2,4,5]

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(5) Centro de Estudios Traslacionales en Estrés y Salud Mental C-ESTRES, Valparaíso, Chile

Obsessive Compulsive Disorder (OCD) is a chronic neuropsychiatric disorder affecting 1-2 % of the population worldwide. Individuals with OCD can have impaired executive functions including cognitive flexibility and inhibitory control. Genetic variants that increase *SLC1A1* gene expression have been previously associated with OCD in case-control studies. *SLC1A1* gene encodes the neuronal glutamate transporter EAAT3 that regulates glutamate spillover and affects synaptic transmission. We evaluated executive functions in operant conditioning and visuospatial learning paradigms in a mouse model of OCD (EAAT3glo/CaMKII mice) with increased forebrain expression of the EAAT3. We found that EAAT3glo/CaMKII mice have impaired cogntive flexibility and working memory, as well as deficits in inhibitory control. In addition, by electrophysiological recordings we demonstrate a role for EAAT3 in regulating heterosynaptic plasticity mechanisms that are implicated in reversal learning. Collectively, our results suggest that EAAT3 levels are relevant for proper executive functioning, highlighting the relevance of this model for translational studies of OCD and positioning EAAT3 as a novel target for drug development.

Keywords: GLUTAMATE TRANSPORTER, EAAT3, REVERSAL LEARNING, COGNITIVE FLEXIBILITY, OBSESSIVE COMPULSIVE DISORDER

Funding: FONDECYT REGULAR GRANT 1231012; C-ESTRES (CIDI UV)

SYMPOSIUM 2:
Aging and Neurocognitive Disorders Insights through Multimodal Profiling

Chairs: Leonel Medina - Adrian Palacios

Otoacoustic emissions as a biomarker of neurodegeneration.

Carolina Delgado Derio [1,2], Paul Delano [1], Vicente Medel [3], Gonzalo Farias [1,2], Rodrigo Vergara [4], Cristina De Gatica [1], Ximena Garcia [6], Mauricio Cerda [5], Cristian Muñoz [5], Carlos Navarro [5], Victor Vidal [1]

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(4) Universidad San Sebastian, Sede Valdivia
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Hearing loss is one of the major risk factors for dementia, especially when hearing thresholds exceed 40 dB in the pure tone average. Otoacoustic emissions refer to acoustic waves produced by the outer hair cells of the cochlea, which are associated with the amplification of sounds of interest. They are used in clinical practice as an objective indicator of cochlear integrity and are commonly employed for hearing assessment in newborns.
Our team has been investigating the relationship between hearing loss and cognitive decline in Chilean adults from the Andes cohort. We have found that the loss of Distortion Product Otoacoustic Emissions (DPOAEs) is behaviorally linked to the decline in cognitive abilities, particularly those related to language and executive functions, as well as to a loss of motivation and functional decline. Neuroimaging studies further reveal that this loss correlates with atrophy in areas of the extended language network (insula, anterior cingulate cortex, amygdala) in individuals without cognitive impairment. Moreover, the loss of DPOAEs is associated with mild cognitive impairment and hippocampal atrophy. This makes DPOAEs a promising peripheral biomarker for the early stages of neurodegeneration.

Keywords: hearing loss, dementia, otoacustic emissions, risk factor, biomarkers

Funding fondecyt 1220607

The role of cardiometabolism in shaping age-related structural and functional brain decline

Vicente Medel [1]

(1) Universidad Adolfo Ibáñez, Latin American Brain Health Institute, BrainLat, Diagonal Las Torres 2640, Santiago, Chile

The brain operates at multiple domains, which require rapid state transitions to cater the ever-changing environmental demands. These transitions use a critical amount of metabolic energy, which is impaired in aging. Emerging theories emphasize the role of bodily-level cardiometabolic processes on these adaptive regulations across the lifespan. While aging affects brain structure and function alongside an increase in body cardiometabolic decline, the relation between these processes across age remains less understood. To study this relation, we examine different brain datasets to explore the role of cardiometabolism on

modulating the appearance of white-matter hyperintensities -a known neuroimaging biomarker of vascular burden-, alongside age-related changes of canonical functional and structural brain measures on MRI and EEG. Our findings suggest that the appearance of white-matter hyperintensities across aging is closely related to fMRI-BOLD and EEG dynamics, as well as structural MRI ventricular enlargement and atrophy of the Locus Coeruleus, the main noradrenergic structure in the nervous system. Finally, we theorize that astrocyte metabolism plays a key role in linking body cardiometabolism and brain health, shedding light to new perspectives on brain function and its disorders in aging.

Keywords: EEG, fMRI, White-Matter Hyperintensities, Cardiometabolism, Aging

Funding: PAI-UAI

Acknowledgments: We thank all the co-authors of the papers and draft presented in these talk.

Aging and Neurocognitive Disorders - Insights through Complexity Analyses

Leonel Medina Daza [1]

(1) Universidad de Santiago de Chile, Departamento de Ingeniería Informática, Santiago, Chile

Interest in entropy-based tools for biological signal analysis has surged since the introduction of the multiscale entropy (MSE) method. This approach quantifies the disorder, or entropy, of physiological outputs across multiple time scales, resulting in an MSE curve that estimates the system's complexity. According to the complexity-loss theory, aging and disease degrade this complexity, a notion supported by recent findings in conditions such as depression, Parkinson's disease, schizophrenia, and Alzheimer's disease. In this talk, we will provide a concise overview of the fundamentals of complexity analysis in electrophysiological signals and explore their relevance to neurodegenerative disorder diagnosis. We will demonstrate the utility of MSE tools using micro-electroretinogram recordings from healthy and transgenic mice (5XFAD, Tg^{XBP1}, and Tg^{XBP1}/5XFAD) obtained via multi-electrode arrays in response to various visual stimuli. We will highlight the potential of non-traditional retinal electrophysiology assessment in developing novel diagnostic methods for Alzheimer's disease through the eye. Additionally, we will share insights into detecting Parkinson's disease by analyzing the complexity of autonomic activity measured through heartbeat signals. The MSE analyses show great promise and could appeal to a broad neuroscience audience. For researchers examining biological system complexity, MSE tools offer valuable applications across a range of biomedical challenges, potentially paving the way for innovative diagnostic techniques and further research opportunities.

Keywords: Multiscale entropy, Complexity, Electroretinogram, Neurodegenerative diseases, Heart rate variability

Funding: ANID Exploración 13220082

The Retina: A Tool for Detecting Early Signs of Aging and Neurodegenerative Diseases.

Adrián Palacios Vargas [1]

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The retina, an extension of the central nervous system, is recognized as a non-invasive biomarker for the early detection of neurodegenerative diseases, including Alzheimer's disease (AD). We are employing various physiological methods to elucidate retinal changes associated with neurodegeneration using both the Tg5xFAD transgenic mouse for AD and Octodon degus, a natural model of aging and AD. Young Tg5xFAD (2-3 months) manifested hyperactivity in RGC, elevated firing rate responses to natural image stimuli, which is correlated with increased glutamate levels in the ganglion cell layer, suggesting that early-stage RGC dysfunction may serve as a biomarker for the onset of neurodegeneration. However, older Tg5xFAD (6-7 months) shows hypoactivity along with increased levels of GABA in the inner plexiform layer. Furthermore, multiscale entropy analysis of retinal microelectro-retinogram signals revealed in the Tg5xFAD, compared to the wilde type mice a reduction in signal complexity, sugesting the retina as a sensitive marker of neurodegenerative alterations. These findings indicate a progressive imbalance in excitatory and inhibitory neurotransmission, reflecting the transition from early to advanced stages of AD. Concurrent studies in Octodon degus further corroborated the role of the retina as an early indicator of neurodegeneration, and using chromatic pupillometry, we observed age-related declines in pupillary light reflex, particularly in response to blue light, which was correlated with cognitive decline. These combined results underscore the potential of retinal imaging and electrophysiological evaluations in the early diagnosis and monitoring of neurodegenerative diseases.

Keywords: Retina, Neurodegeneration, Aging, Early Biomarker, Physiology

Funding: ANID: Fondecyt 1200880, Exploración #13220082, FONDEQUIP EQM190032

SYMPOSIUM 3:

Perspectives on meaning processing from a psycho and neurolinguistic approach

Chair: María Francisca Alonso

Thought disorder and semantic coherence relations in discourse

Pedro Alfaro Faccio [1]

(1) Pontificia Universidad Católica de Valparaíso, Instituto de Literatura y Ciencias del Lenguaje, Filosofía y Educación, El bosque 1290, of. C5-2, Viña del mar, Chile

In Psychiatry, schizophrenic speech disturbances are interpreted as a manifestation of disturbances in thinking (Ehlen et al., 2023). This perspective suggests a correlation between impairments in language production and comprehension and deficits in the patients' cognitive processes (Cabana et al., 2011). Empirical studies have characterized the speech of individuals with schizophrenia through both manual and computational methodologies, identifying symptoms such as pressured speech, discursive disorganization, and reduced content, which are indicative of Thought, Language, and Communication Disorders (Andreasen, 1986; Barch & Berenbaum, 1997; Ehlen et al., 2023). However, these findings present both methodological and theoretical challenges: first, the structural approach—encompassing phonological, morphological, lexical, and syntactic analyses—fails to distinguish features specific to schizophrenia from those associated with other disorders; second, they contradict the notion that cognitive properties are directly reflected in linguistic structures. In response to these issues, a semantic approach may offer a viable alternative, considering that EQZ discourse is characterized by maintaining a topic -perseveration- and moving away from it in an evident way -tangentiality. This presentation aims to analyze the semantic connectivity within the discourse of individuals diagnosed with schizophrenia to better characterize its internal coherence and incoherence. As a preliminary step, we will examine the relationships between discourse segments utilizing Renkema's (2009) model applied to thirteen oral narratives produced by patients during a retelling task.

Keywords: schizophrenia, language structure, semantics, discourse

Funding:Proyecto Fondecyt 1230532

Perspectives on meaning processing from a psycho- and neurolinguistic approach.

María Francisca Alonso [1]

(1) Universidad de Valparaíso, Escuela de Fonoaudiología, Centro del investigación del desarrollo en Cognición y Lenguaje, Facultad de Medicina, Angamos 655, Viña del Mar, Chile

Language is dynamic, variable, and adaptable to societies in both meaning and form. The study of language meaning, or semantics, presents numerous complexities. Different time scales exist in both language and the neural patterns associated with language processing. The meanings of individual words can sometimes differ from the meanings of the sentences that contain them, and brain activity patterns reflect this complexity. At the most basic level, the comprehension of a word represents the simplest form of meaning processing. Sentences introduce additional elements that confound meaning processing, as roles are assigned to each component within the sentence. When non-literal language is involved, social knowledge becomes key to processing the meaning. Conceptualization is further complicated by the disciplinary knowledge stored in semantic memory. These processes undergo changes throughout the life cycle, and aberrant patterns can be observed in pathological conditions. In this symposium, we will explore the meaning of words from the lexical level to the interpretation of non-literal idiomatic expressions, such as idioms, in both behavioral and neural terms. Our investigations will span different stages of the life cycle—from children to youth, adults, and older adults—and we will show different methods, including psycho- and neurolinguistic approaches (e.g., EEG, fMRI). We will analyze the meaning, concreteness, processing, and production of language, along with its associated brain networks.

Keywords: Language, Semantic network, Psychosis, fMRI

Financing: Fondecyt regular 1230532

Age-Related Differences in the Processing of Spanish Idioms

Begoña Góngora [1,2]

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(2) Centro de Investigación del Desarrollo en Cognición y Lenguaje

Language is one of the most complex cognitive functions, evolving continuously throughout the human lifespan. Although extensive research has examined the effects of aging on language comprehension and production, the cognitive mechanisms underlying the processing of figurative language are insufficiently understood. In the current Study, we assess the effect of aging on idioms processing by integrating behavioral and electrophysiological measures. This research received ethical approval from the research ethics committees of Universidad de Valparaíso. 50 volunteers were recruited, divided into two groups (Healthy elders group: n=32; Young Adult Group: n=18), all of whom provided informed consent before beginning their participation in the project. A total of 36 participant completed the experimental Spanish Idiom Comprehension Task, in which sentences (idiomatic IC, literal LC, control CC, and filler FF) are presented on a screen word by word. Each participant was instructed to mentally read the sentences and answer the questions by pressing buttons, while their brain activity was recorded by electroencephalography (EEG). Behavioral measures, including response times and accuracy rate, were analyzed alongside electrophysiological data, specifically the amplitudes of the frontal Positive-Negative Potential (PNP) event-related component (ERP). The results of the study indicated that older adults exhibited lower accuracy rates and longer response times compared to younger adults. Furthermore, both the IC and LC conditions showed significant differences from the CC condition in the amplitude of the late PNP component. These results suggest that distinct mechanisms underlie the processing of figurative language respect to literal language.

Keywords: aging, figurative language, idioms processing, event related potential, Language

Funding: FONDECYT DE INICIACIÓN 11170654

Language Processing in Children with Typical Development and Children with Developmental Language Disorder (DLD): Interaction Between Visual and Linguistic Modalities

Andrea Helo [1,2,3], Ernesto Guerra [3], Carmen Julia Coloma [1,3]

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(2) Universidad de Chile, Departamento de Neurociencias, Faculta de Medicina, Av. Independencia 1027, Santiago, Chile
(3) Universidad de Chile, Centro de Investigación Avanzada en Educación, Instituto de Estudios Avanzados en Educación, Periodista José Carrasco Tapia 75, Santiago, Chile

Our research examines the interplay between language processing and visual attention in children with both typical and atypical language development. We use eye-tracking and event-related potential (ERP) techniques to explore how factors such as semantic consistency, perceptual features, and vocabulary skills influence visual exploration throughout development. Additionally, we investigate how preschoolers, both with and without Developmental Language Disorder (DLD), activate object shape during spoken word recognition and how grammatical structures are processed in children with DLD.
Our findings reveal that object shape plays an important role in language development, with typically developing preschoolers activating shape representations during word recognition more efficiently than children with DLD. We also observe a clear relationship between language skills and how children visually explore their environment, suggesting that stronger language abilities are linked to more effective visual exploration. Finally, we showed that the processing of simple grammatical elements is delayed in children with DLD, but it follows a developmental trajectory similar to that of typically developing children, highlighting a shared, yet slower, progression.
This research deepens our understanding of the mechanisms underlying language comprehension, grammatical processing, and visual attention, emphasizing the importance of object shape and visual exploration in language development.

Keywords: Language development, Developmental language disorder, Visual exploration, Eye-movements

Funding: Fondecyt de Iniciación 11180334, Fondecyt Regular 1241884, Programa de Cooperación Internacional REDI170285.

Acknowledgments: Funding from ANID/PIA/Basal Funds for Centers of Excellence Project FB0003

SYMPOSIUM 4:

Gender perspective in Neuroscience: deepen the current view and fronting future challenges.

Chair: Carolina Oliva - Vania Figueroa

This symposium was sponsored by Proyecto FDI AE UAU22101 MINEDUC, Proyecto InES Género INGE210017 ANID, and IBRO Diversity Grant.

Tailoring the Exclusion in Neuroscientific Research or How to Face Real Solutions from Partial Data.

Carolina A. Oliva[1], Vania Figueroa[1]

(1) Centro para la Transversalización de Género en I+D+i+e (CTGénero), Unidad de Igualdad, Vicerrectoría de Investigación y Doctorados, Universidad Autónoma de Chile.

At the CTGénero, we encourage equal access to scientific careers and promote the inclusion of gender perspective in every step of investigation, from the formulation and hypothesis to the data compilation, analysis and results, including equity in citations. Integrating the gender dimension in research and innovation adds value to excellence, creativity and opportunities, allowing us to advance in the questioning of gender norms and stereotypes rethinking standards and reference models, improving the social relevance of knowledge, technology, and the innovations derived from them, which would contribute to the production of goods and services more appropriate. In this symposium, we will offer the opportunity to discuss the impact of the investigation in neuroscience discussing the biases we face in neuroscience: gender inequities in academia, in editorial committees, in reference letters, citations, and the biomedical research with sexual bias that includes disproportionated use of males or no-sex. Through different topics, we will i) analyze how scientific knowledge has moved with evident dismiss of inclusion and diversity, ii) how we can tackle the lack of information, iii) how to re-think problems to generate real results, iv) and to support multidisciplinary and intersectional studies as methodologies that allows the best approach to complex problems. Finally, we will discuss of how better understanding of health issues in women, aged, and underrepresented groups, can contribute to policy debates providing recommendations based on research findings and expertise.

How and Why to Account for Sex and Gender in Brain and Behavioral Research?

Lise Eliot[1]

(1) Stanson Toshok Center for Brain Function and Repair, Chicago Medical School, Rosalind Franklin University.

Long overlooked in research, sex and gender are now expected to be included as key variables in all levels of brain and behavioral analysis. Still, many neuroscientists do not understand the difference between "sex" and "gender," the complexity and nuance of each, or how to best include them as variables in research designs. This talk will outline rationales for considering the influence of sex and gender in both human and non-human species, with a focus on strengthening the rigor and reproducibility of such analyses. It will address the use of appropriate statistical methods as well as controls for key covariates of sex (e.g., pubertal timing, total brain volume) and gender (e.g., income, caregiver stress, discrimination). Finally, we will discuss the interpretation and communication of sex and gender-related findings about the brain, which have often been misconstrued by neuroscientists and the lay public a like.

Unlocking How Sex Steroid Hormones Regulate Ion Channels.

Karen Castillo[1]

(1)Centro Interdisciplinario de Neurociencia de Valparaíso, Instituto de Neurociencia, Facultad de Ciencias, Universidad de Valparaíso

Ion channels play a role in a number of physiological and pathophysiological processes. In mammals, ion channels play a key role in regulating a multitude of essential physiological processes, including hormones and neurotransmitter secretion, sensory transduction, and muscle and nerve excitation. Sex steroid hormones (SSH) regulate the activity of ion channels through the canonical transcriptional pathways; however, ion channels can also function as ionotropic receptors for SSH. Furthermore, SSH can bind to specific domains within ion channels, thereby modifying their gating properties and eliciting rapid cellular responses. This can be achieved either by inducing the expression of ion channel-interacting proteins or by direct binding to channels. The impact of SSH on ion channels appears to be a crucial mechanism through which steroids fulfill numerous physiological functions in the cardiovascular and nervous systems, as well as in non-excitable tissues. It is well established that 17b-estradiol (E2) regulates the gating and conduction of BK channels through direct binding to the auxiliary subunit b1. β1 plays a pivotal role in the modulation of arterial tone and blood pressure through vascular smooth muscle cells, with implications for female cardiovascular control and cardiac protection. The thermally sensitive heat (TRPV1) and cold receptor (TRPM8) channels have been identified as estrogen and testosterone receptors, respectively. Their activation may play a role in a pleiotropic response with physiological significance in females and males, including effects on animal behavior and pain. The significance and relevance of ion channels regulation by SSH will be further discussed.

Sex differences in the brain hippocampus during aging: mitochondria as a central target.

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Aging is thought to coincide with gradual and progressive changes in brain function and behavior over a lifetime. This includes age-related spatial memory and mitochondrial function impairment, but the contribution of sex differences to the grade of cognitive decline and mitochondrial dysfunction remains elusive. Here, we evaluated hippocampal memory and its correlation with mitochondrial function during the aging process of male and female mice. 3 and 20-month-old C57BL/6J male and female mice were used in this study. We used a battery of behavioral tests to evaluate hippocampal-dependent memory, novel object recognition, novel object localization, and Morris water maze. Mitochondrial function was evaluated by the measurement of ATP production, mitochondrial membrane potential, mitochondrial ROS, mitochondrial calcium homeostasis and mtDNA content. Key proteins related to mitochondrial function were evaluated by western blot. Our results reveal that although most aged individuals present memory loss, a smaller percentage do not exhibit cognitive decline, and this correlates with enhanced mitochondrial function. However, differences between aged female and male mice in both cognitive and mitochondrial structure and function in the hippocampus are observed. Thus, mitochondrial changes in both structure and function in the hippocampus will predict the degree of cognitive impairment in aging, and therefore mitochondrial-targeted interventions will be used as age-related alterations.

Acknowledgments: FONDECYT 1221178 VRID-Puente21/01-USS and Centro Ciencia & Vida, FB210008 to CTR.

SYMPOSIUM 5:
Decoding Brain Mechanisms of Stress Resilience

Chair: Alexies Dagnino

The role of astrocyte-derived small extracellular vesicles in central and peripheral inflammation - potential contributors to stress-induced bowel inflammation

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Introduction: Stressors are perceived and interpreted by the brain, initiating adaptive physiological and behavioral responses. The stress response has been linked to peripheral- and brain inflammation (neuroinflammation). In turn, stress-induced neuroinflammation might be related to peripheral immune disorders, such as inflammatory bowel diseases. We studied the role of brain astrocyte-derived small extracellular vesicles (ADEVs) in peripheral immune regulation and in the brain-to-gut axis under stress conditions.

Methods: Rats were stressed by movement restriction. Primary astrocyte cultures were incubated in the presence of the stress hormone corticosterone or vehicle to obtain Cortico- or Ctrl-ADEVs by ultracentrifugation. ADEVs were analyzed by proteomics and their modulatory effect on microglia activation was assessed. DiR-labelled ADEVs were administrated into the tail vein to visualize their body distribution and to study their immune regulatory functions. Histological analysis of the intestine and flow cytometry was performed in blood cells, disaggregated mesenteric lymph nodes (MLN) and Peyer´s patches (PP).

Results: ADEVs have an immunomodulatory action on brain microglia and on peripheral macrophages. They carry the gut-targeting receptor CCR9R, reaching the intestine, and regulate stress-induced changes on the Treg/Th17 ratio of the MLN and PP, both *in vivo* and *in vitro*.

Discussion: ADEVs are potent immune regulators, including the Gut-Associated Lymphoid Tissue (GALT). These results hold translational potential for using ADEVs as regulators of stress-induced neuroinflammation and intestinal inflammation.

Keywords: stress, extracellular vesicles, inflammatory diseases

Funding: Fondecyt# 1200693 and 1240604; Basal funding for Scientific and Technological Center of Excellence, IMPACT, #FB210024

Genetically driven resilience: increased expression of EAAT3 confers behavioral, neurochemical, and plasticity resilience to chronic stress in a mouse model.

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INTRO: Depression is a disabling and highly prevalent psychiatric illness. Multiple studies have linked glutamatergic dysfunction with the pathophysiology of depression, but the exact alterations in the glutamatergic system that contribute to depressive -like behaviors are not fully understood. Recent evidence suggests that a decreased level in neuronal glutamate transporter (Slc1a1/EAAT3), known to control glutamate levels and limit the activation of glutamate receptors at synaptic sites, may contribute to the manifestation of a depressive phenotype. AIMS: To determine if increased EAAT3 expression at excitatory synapses can reduce the susceptibility of mice to develop depressive -like behaviors when challenged to a 5 -week unpredictable chronic mild stress (UCMS) protocol. METHODS: Mice overexpressing EAAT3 in the forebrain (EAAT3OE) and control littermates were subjected to 5-week UCMS protocol, and then assessed for depressive -like behaviors, long -term memory performance, dopamine neurotransmission and hippocampal synaptic plasticity. RESULTS: After UCMS, EAAT3-OE mice did not exhibit depressive -like behaviors or memory alterations observed in control mice. Moreover, we found that EAAT3-OE mice did not show the alterations in dopamine release in the nucleus accumbens nor impaired long -term synaptic plasticity in the CA1 region of the hippocampus as observed in control mice after UCMS. DISCUSSION Our findings demostrate that forebrain EAAT3 6 at behavioral and phyisiological level, to the deleterious effect of chronic stress, highlighting the importance of neuronal EAAT3 in the pathophysiology of depressive -like behaviors

Keywords: chronic stress, resilience, glutamate, glutamate transporter, depression

Funding: FONDECYT REGULAR GRANT 1231012 (ANID CHILE); C-ESTRES (CIDI UV)

Pharmacological modulation of stress resilience targeting glucocorticoid and mineralocorticoid receptors: A new frontier for mental illness

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Stress resilience is associated with the ability to fine-tune stress coping and it is proposed that the balance of glucocorticoid (GR) and mineralocorticoid (MR) receptors in the brain could modulate this process. We previously demonstrated that in rats, resilience to stress is lost two weeks after chronic social defeat stress (CSDS). Therefore, in this study we evaluated whether pharmacological modulation of GR and MR has an impact on loss of stress resilience. Adult male *Sprague-Dawley* rats were exposed to the CSDS paradigm. Those rats that were selected as stress resilient based on physiological and behavioral markers were injected intraperitoneally during two weeks with vehicle (sesame oil), GR and MR agonist (corticosterone), GR antagonist (dazucorilant) or MR antagonist (spironolactone). Interestingly, dazucorilant and spironolactone attenuated plasma corticosterone levels and counteracted adrenal cortex hypertrophy compared with vehicle- or corticosterone-treated rats. At the behavioral level, dazucorilant and spironolactone promoted social behavior and active coping in the forced swimming test as well as an antidepressant effect when compared with vehicle or corticosterone treatments. Although this study cannot determine whether the effects we observed can be

explained by a peripheral and/or central action of the compounds used, these results suggest that GR and MR antagonists attenuated the loss of resilience to stress, opening a new pharmacological target for the treatment of stress-related disorders, such as major depressive disorder.

Keywords: Stress, Resilience, Depression, glucocorticoid receptor, mineralocorticoid receptor

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Acknowledgments: This work has been funded by Interdisciplinary Centre for Health Studies (CIESAL) and Corcept Therapeutics Inc.

Effects of Psychosocial Stress on Oscillatory Patterns and Pupillary Activity in Humans: Potential Indirect Measures of LC-NE System Reactivity

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Psychosocial stress has significantly increased in modern lifestyles, negatively impacting global mental health. Deficits in attentional control are key features of stress-related disorders and pathological anxiety. Evidence suggests that alterations in the locus coeruleus-norepinephrine (LC-NE) system may underlie the effects of stress on top-down attentional control. However, the impact of psychosocial stress on attentional processes and its underlying neural mechanisms remains poorly understood.
This study investigates the effects of psychosocial stress on attentional processing and associated brain signatures. Evoked potentials and pupillary activity were recorded in response to an auditory oddball paradigm before and after applying the Montreal Imaging Stress Task (MIST). Additionally, electrocardiogram (ECG), salivary cortisol levels, and subjective anxiety/stress perceptions were measured at various experimental stages. The control group underwent the same physical and cognitive effort without the psychosocial stress component.
The results revealed that stressed subjects exhibited a decrease in P3a and P3b amplitudes, phasic pupillary response, and correct responses. In contrast, they showed an increase in Mismatch Negativity (MMN). N1 amplitude decreased only in the control group after the MIST. Furthermore, a significant correlation was found between changes in P3b amplitude and both pupillary dilation and salivary cortisol levels.

Our findings suggest that under social-evaluative threat, the basal activity of the LC-NE system increases, heightening alertness while reducing the voluntary attentional resources available for the cognitive task. These results contribute to a better understanding of the neurobiological basis of attentional changes in pathologies associated with chronic psychosocial stress.

Keywords: Attention, Acute Psychosocial Stress, Pupil Diameter, Locus Coeruleus-Noradrenergic System, EEG

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The Intersection Between High Schools, Neuroscience, and Academia/EduTech

Chair: Timothy Marzullo

Bringing High School Students into Scientific Publication with Electrophysiology

Timothy Marzullo [1]

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Normally high school students learn about the scientific process through lectures and prepared laboratory experiments where the results are known beforehand. Professional science is not done this way, but through the design of novel experiments, the analysis of the literature, and scientific publishing. Most students only learn about this process during late undergraduate education, but it is possible for high school students to contribute original scientific research to the scientific community through proper leadership. The key factors are 1) scientists willing to work on a long term basis with high school students and 2) high schools willing to take a risk on unproven scientific protocols. Through partnerships between universities, high schools, and small businesses, more horizontal transfer of knowledge can occur at all levels of science education. We have successfully replicated this model in both Chile and Serbia. Systemic, cultural, and financial challenges/opportunities will be discussed to further improve scientific productivity at the pre-university level.

A Library of Electrophysiological Responses in Plants: A Model of Transversal Education and Open Science

Étienne Serbe-Kamp [1]

(1) LMU, Philosophy of Mind

"A Library of Electrophysiological Responses in Plants: A Model of Transversal Education and Open Science" highlights a transformative approach to both plant science and education. This study explores how hands-on learning, facilitated through the recording and analysis of plant signals, fundamentally changes the way students engage with science. By demonstrating that plants are dynamic organisms capable of generating electrical responses to environmental stimuli, the research opens new avenues for interactive, experiential learning in the classroom. Students actively participated in scientific discovery, shifting from passive learning to collaborative engagement, fostering a deeper understanding of plant biology and a stronger connection to the natural world.

Keywords: Educación de ciencia, Electrofisiología, Plantas, Potenciales de electricidad

From the laboratory to the school: challenges and opportunities

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Science permeates almost every aspect of our lives and is essential for addressing and solving the key challenges that humanity faces, both now and in the future. Science education is therefore fundamental for understanding science and cultivating habits of mind, such as scientific thinking. My laboratory has been working to develop initiatives and educational tools aimed at fostering scientific thinking and neuroliteracy within the school community. In this presentation, I will discuss the challenges, opportunities, and outcomes of these efforts. First, I will present a project using neuroscience as an innovative framework to develop scientific thinking skills and attitudes. Working with an interdisciplinary research group composed of neuroscientists, educators, and psychologists, we created scientific resources —funded by the Ministry of Science— to promote neuroliteracy in preschool children. These resources include "Mi primer libro del cerebro" and the audiovisual series "Valentina descubre el Cerebro."
Second, I will discuss the impact of NeuroFest 2024 on the school community. NeuroFest 2024, the first neuroscience-themed science fair in Chile, was an event supported by the Chilean Neuroscience Society that brought together more than 700 students and teachers. Finally, I will share insights on the coordination and impact of the Biotechnology Elective course for high school students. This practical course, taught at the Faculty of Science of the Universidad de Chile by professors from the Biology Department, aims to bring students closer to the fields of biotechnology and research.

Keywords: Scientific thinking, neuroscience and education, neuroliteracy

Llevar el futuro a estudiantes escolares a través de vínculos académicos, científicos y empresariales.

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Creemos que para motivar e incentivar a los jóvenes a querer aportar e innovar en el futuro, es importante exponerlos a variados ámbitos culturales y profesionales, que no suelen estar en las experiencias escolares cotidianas. Por eso, como director del Colegio Alberto Blest Gana, he impulsado hacer una colaboración interdisciplinaria, con distintas áreas que consideramos claves para el desarrollo de Chile: en el mundo se la ciencias hemos trabajado con el departamento de ciencias de Universidad de Chile (Mil Genomas) y Universidad Católica (Biología Sintética), además de empresas científicas como Backyard Brains y Lab4U.
También entendemos que el entusiasmo juvenil y el deseo de resolver problemas pueden ser desafiantes y generar frustración cuando no se logran los resultados inmediatos, lo que termina en estrés. Está observación nos llevó a incluir técnicas de Mindfulness en nuestros estudiantes: los talleres de meditación y reconocimiento de emociones han sido fundamentales en este proceso.
Finalmente, nuestra forma distinta de enseñar ha llamado la atención de la prensa nacional e internacional, lo que nos ha abierto las puertas a finalmente trabajar con casi todas las universidades y empresas de ciencia de Chile. En esta charla vamos a discutir cómo este modelo puede ser replicado en otras instituciones y además, compartiremos métodos para conseguir financiamiento público y privado que sirva para nutrir este tipo de colaboración entre el mundo científico, empresas y colegios.

Keywords: Innovación, Colegio, Educación, Neurociencia, Intervención

YOUNG NEUROSCIENTISTS SYMPOSIUM

Chair: Tomás Ossandón

OCRL1 regulates the endocytic trafficking of ApoER2 and Reelin signaling

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Lowe Syndrome (LS) is an uncommon X-linked condition characterized by kidney dysfunction, cataracts, and various anomalies within the central nervous system (CNS). The specific mechanisms that contribute to neurological dysfunction in LS are not well understood, although some phenotypic features resemble those seen in conditions involving Reelin signaling deficiencies, a pathway important for CNS development and neuronal function.
In this research, we examined the function of OCRL1, an inositol polyphosphate 5-phosphatase produced by the OCRL gene, which is mutated in LS. Our focus was on how OCRL1 affects endosomal trafficking and receptor recycling in human neuronal cells. We specifically investigated the consequences of OCRL1 deficiency on the trafficking and signaling of ApoER2/LRP8, a receptor for the Reelin ligand. Our results indicated that the absence of OCRL1 disrupts the intracellular trafficking of ApoER2, resulting in lower receptor expression and diminished levels at the plasma membrane. Furthermore, human neurons lacking OCRL1 exhibited deficiencies in responses triggered by ApoER2/Reelin signaling. These findings emphasize the vital role of CRL1 in managing ApoER2 endosomal recycling and its influence on the ApoER2/Reelin signaling pathway, shedding light on potential mechanisms behind the neurological symptoms associated with LS.

Keywords: ApoER2/LRP8; Reelin; endosomal pathway; Lowe Syndrome.

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Remote Control of Genetically Targeted Neurons with Magnetogenetics: Electrophysiological Validation and Applications

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Magnetogenetics is a set of techniques that render genetically targeted cells magnetically sensitive through the expression of magnetically sensitive ion channels. Due to the ability of magnetic fields to freely penetrate biological tissue, magnetogenetics has been proposed for potential biomedical applications. However, its efficacy has been debated due to a lack of evidence from electrophysiological measurements. Here, I present electrophysiological validation of a magnetogenetic technique called FeRIC (Ferritin Iron Redistribution to Ion Channels), which uses radiofrequency magnetic fields to activate exogenous magneto-sensitive ion channels. We successfully addressed the challenge of interference between radiofrequency fields and patch-clamp recordings. We demonstrate that in cultured cells expressing the cation-permeable ion channel TRPV4-FeRIC, magnetic field stimulation evokes inward currents and decreases membrane resistance due to TRPV4-FeRIC activation. In hippocampal cultured neurons expressing TRPV4-FeRIC, magnetic field stimulation depolarizes the neuronal membrane potential and increases spike activity. Conversely, in neurons expressing the chloride-permeable TMEM16A-FeRIC, magnetic field stimulation hyperpolarizes the neuronal membrane potential and decreases the firing rate of action potentials. Our results demonstrate that FeRIC magnetogenetics can be used to control both neuronal membrane potential and neuronal excitability. Furthermore, I will discuss future directions for magnetogenetics in neuroscience and present new unpublished results in which we use FeRIC magnetogenetics to modify synaptic circuits.

Keywords: magnetogenetics, membrane potential, TRPV4, TMEM16A, ferritin

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Left prefrontal regions mediate the influence of executive functions on language processing in primary progressive aphasia

Andrea Gajardo Vidal [1,2]

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Previous neuropsychological studies have shown that executive functioning (EF) contributes to performance on language tasks that pose high cognitive demand. Furthermore, functional neuroimaging studies have provided neurobiological evidence that language tasks involve an interaction between language-related and domain-general executive control regions. Finally, it has been suggested that enhanced activity (or increased connectivity) in executive control networks may support language recovery in stroke patients. Here, we sought to investigate cross-sectionally and longitudinally the relationship between EF and language, and the neural substrates of that relationship, in a large cohort of 197 patients with primary progressive aphasia (PPA). First, we found a significant, positive relationship between EF and performance on two of the most demanding language tasks: sentence comprehension (SentComp) and speech production (SpProd). Second, we identified two clusters located within the left middle frontal gyrus and left superior frontal gyrus that mediate this relationship. Third, resting-state-fMRI data of healthy controls showed that these two regions are part of the fronto-parietal executive-control network. Finally, the SentComp and SpProd scores of the patients with better EF compared to those with worse EF were significantly better across the two time points and declined significantly less over time, even after controlling for potential confounds such as severity and education. Therefore, we conclude that EF supports sentence processing in PPA, primarily through two left prefrontal regions that are part of the fronto-parietal executive-control network. Our findings also indicate that the brain regions involved in EF might play a "compensatory" role as language abilities decline in PPA.

Keywords: Language, Neurodegenerative diseases, Neuroimaging, Executive functioning
Meanor, Evan W. Miller, Richard H. Kramer, and Chunlei Liu

Educational disparities in brain health and dementia across Latin America and the United States

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Education influences brain health and dementia, yet its impact across regions, specifically Latin America (LA) and the United States (US), remains unclear. We address this issue using magnetic resonance imaging (T1-weighted and functional resting recordings) from 1,412 participants, including controls and patients with Alzheimer's disease and frontotemporal dementia from LA and the US. We studied the association between education, gray matter volume, and functional connectivity while controlling for age and sex. Lower educational levels in LA were associated with reduced gray matter volume and lower functional connectivity compared to the US, explaining 24-98% of the geographical differences. Additionally, machine learning algorithms that classified clinical conditions by region identified education as the second most important factor, surpassed only by cognition. These algorithms indicate that even the data of gray matter volume and functional connectivity in different brain areas are less important than education. Our findings emphasize the importance of incorporating educational factors into the diagnosis, care, and prevention of dementia, especially in LA. Furthermore, this evidence supports the need for public policies to enhance educational levels as a preventive measure to address the anticipated rise in dementia rates in the region.

Keywords: education, MRI, salud cerebral, demencia

Acknowledgments: Agredecimiento especial al equipo del Instituto Latinoamerica de salud cerebral

ORAL COMMUNICATIONS I

Chairs: Magdalena Sanhueza-Julio Alcayaga

Cognitive, synaptic, and mitochondrial improvement following mtUPR activation in the aged hippocampus

Matías Lira [1], Alejandra Catenaccio [1], Cheril Tapia Rojas [1]

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Introduction: In aging, progressive changes lead to cellular impairment and functional decline in several tissues, especially the brain. The hippocampus is particularly vulnerable to aging, where mitochondrial dysfunction and abnormal protein accumulation occur. The mitochondrial unfolded protein response (mtUPR) is a genetic program that oversees the proteostatic state of the mitochondria; thereby, it is triggered when unfolded proteins are accumulated within the organelle to cope with this unfolded protein load. We have determined that mtUPR is defective in the hippocampus of aged mice; thus, activating mtUPR could benefit the hippocampal functional state.

Materials and methods: Aged (20-month-old) male mice were treated for 5 weeks with doxycycline to activate mtUPR.

Results: mtUPR activation, indicated by increased levels of mitochondrial chaperons and proteases, improves mitochondrial function with concomitant restoration of spatial memory. Specifically, the hippocampus of doxycycline-treated mice shows a more robust neuronal architecture and mitochondrial ultrastructure related to an increased bioenergetic state, reduced overload of abnormal proteins, and increased learning and memory capacity.

Discussion: Altogether, by activating mtUPR in aged mice, we improved spatial memory and its associated cellular processes. This pharmacological activation of mtUPR offers a potential treatment approach that could significantly improve cognitive decline in aging.

Keywords: memory, mitochondria, aging, mtUPR

Funding: FONDECYT 1221178 and Centro Ciencia & Vida, FB210008 to CTR, FONDECYT 3240174 to ML.

Exploring the control of unitary conductance of the inhibitory ligand-gated ion channels by phosphorylation events: Implication on inhibitory neurotransmission and actions of clinical relevant drugs.

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The inhibitory GABA type A ($GABA_A$Rs) and Glycine (GlyRs) receptors are members of the pentameric ligand-gated ion channels (pLGICS) family. They play a critical role in the fast inhibitory neurotransmission contributing to the phasic and tonic control of the neuronal excitability. The functional pentamer is formed by the arrangement of five subunits surrounding a central chloride-permeable pore. Each subunit is composed by an extracellular domain (ECD), a transmembrane domain (TMD) and a large intracellular domain (ICD). The function of the $GABA_A$R and GlyRs can be allosterically modulated by several protein kinases, targeting specific serine residues located in the ICD. The impact of kinase activation on the channel function is varied, and seems to relay on the specific subunit composition. For example, PKA activation reduce the glycine-activated currents in GlyR containing only the alpha3 subunit. For the $GABA_A$R case, the effects are more controversial, since PKA or PKC activation lead to either a potentiation or an inhibition of GABA-activated currents, depending on the subunit composition. Overall, the alteration of phosphorylation/dephosphorylation balance have suggested as one mechanism that underlies some pathophysiological states such as cerebral ischemia, epilepsy, drugs abuse and chronic pain. However, the molecular mechanism explaining the impact of phosphorylation events on the function of $GABA_A$R and GlyRs remain still controversial. In this line, biophysical, biochemical and functional results from our group have shown that the phosphorylation of serine residues located in the ICD reduce the unitary conductance of both $GABA_A$R and GlyRs, suggesting an conserved molecular mechanism of allosteric modulation.

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Accessory Olfactory Bulb: How different is an experimental model of atypical social interaction?

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Fragile X Syndrome (FXS) is a neurodevelopmental disorder elicited by a mutation in the FMR1 gene which causes the silencing of the gene. The main symptoms of FXS include intellectual disability and social interaction difficulties. Behavioral studies performed in *Fmr1* KO mice (KO), an experimental model for FXS, revealed that while they can detect social olfactory cues, they cannot discriminate between cues from different males. This data suggests that neuronal coding of social cues might be altered in KO mice. To test this hypothesis, we explored the anatomical and functional differences in the accessory olfactory bulb (AOB) of KO mice. Briefly, pheromones activate sensory neurons in the vomeronasal organ that project to the glomerular layer of the AOB. Mitral cells (MC) project a single dendrite to one or more glomeruli and transmit the information upstream to the vomeronasal amygdala.
We observed no differences in the overall volume of the AOB between KO and wild-type (WT) mice, but we did find that the KO mice had a smaller glomerular layer. Neuronal reconstruction of MC revealed that KO's cells had a more complex dendritic tree. Altered electrophysiological properties accompanied anatomical differences. Specifically, we found that MC from KO is hypoexcitable compared to WT. They showed a decreased amplitude of spontaneous excitatory and inhibitory currents. Moreover, evoked action potentials in MC exhibit a higher failure rate compared to WT animals. Our results suggest that anatomical and electrophysiological differences may contribute to the observed social interaction deficits in KO.

Keywords: vomeronasal system autism social interaction

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Cortical Alterations in Pitt-Hopkins Syndrome: Exploring Genotype and Sex Differences in an Autism-Related Condition

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Pitt-Hopkins Syndrome (PTHS) is a neurological and developmental disorder. Individuals with PTHS may exhibit cognitive delays, intellectual disability, and autistic behaviors. The condition is caused by haploinsufficiency of the TCF4 transcription factor, different mutations produce the lack-function of this important gene-regulator. During embryonic development, TCF4 is highly expressed in the cerebral cortex of both humans and mice. A deficiency in TCF4 expression leads to changes in cerebral cortex thickness, abnormalities in cortical lamination, and impaired neuronal migration. In this study, we investigate cerebral cortex alterations during embryonic and postnatal development in PTHS, taking into account, for the first time, sexual dimorphism in HET and KO genotypes. PTHS model animals were analyzed at days E12 and E15, as well P0 and P14. We characterized changes in apical and basal progenitors, as well as populations of upper layer (UL) and deep layer (DL) neurons, using immunohistochemistry. Additionally, in-utero electroporation (IUE) was performed to restore TCF4 expression in the cerebral cortex. During early stages, we observed an increase in the neuronal-progenitor transition in PTHS animals, accompanied by a significant increase in the apical progenitor population. This defect was associated with a decrease in UL neurons and an increase in DL neurons at P0. The reintroduction of TCF4 during embryogenesis partially corrected these alterations. Furthermore, we describe changes in progenitor proliferation at the level of the MGE, which are linked to alterations in inhibitory neuronal populations, such as parvalbumin and somatostatin interneurons. Notably, all these alterations were more pronounced in males compared to females.

Keywords: PTHS, TCF4, ASD, Cerebral cortex

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Synergy and redundancy balance across layered connectomes: An information and network decomposition approach to C. Elegans structural and functional topology

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Neurons in the brain communicate in different ways, and thus connectomes can be conceived as overlapping dissimilar networks depending on the type of signal being transmitted. One way of disentangling such layers of connectomes is by the connectivity timescales, yielding four layers of paths (ordered from fastest to slowest): gap junctions, amino acid, monoaminergic, and peptidergic transmitters. *Caenorhabditis elegans*, a 302-neuron nematode, is an excellent model for exploring topological properties of the interaction between layers of networks because its full connectome is known. Combining functional and structural network topology metrics, partial network decomposition, and Phi-information decomposition we were able to characterize complementary (synergistic), redundant, and unique paths between nodes of the connectomes. Unique paths are predominant in all four layers, the highest redundancy is between electrical and amino acid transmission, and the highest synergy is found between electrical and peptidergic transmission.
Analysis of 'whole-brain' calcium dynamics during anesthesia and developmental sleep datasets show that integration of information measured by Integrated Information Theory of consciousness' Phi 2.0 decreases during quiescence but increases during anesthesia (both compared to wakefulness), yet the time-dependent synergistic components of the information dynamics decrease during both anesthesia and quiescence. This reveals the importance of a more nuanced analysis using partial information decomposition. High-order interactions (in groups of 3 to 15 neurons) show more synergy during wakefulness and in larger groups of neurons. A computational model is used to prove the contribution of specific neurons to the synergistic and redundant interactions considering the full topology of the network.

Keywords: network topology, connectomes, information theory, synergy, C. elegans

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Dopaminergic modulation in spiking neural networks allows selective attention in Ring attractor networks.

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Selective Attention (SA) is a critical cognitive task where, when presented with two equally interesting stimuli, an organism must redirect its neural resources to focus on the most relevant stimulus. This cognitive feature is ubiquitous across the animal kingdom. In vertebrates, the **Superior Colliculi** and in insects, the **Central Complex (Cx)** are known to support this behavior. Interestingly, both structures share a similar computational architecture known as a **Ring Attractor Network (RAN)**.
In insects, dopaminergic modulation of the Cx has been shown to influence SA by inhibiting the preference for a particular stimulus. However, the precise computational mechanisms by which dopaminergic modulation facilitates this selective process remain largely unexplored. It is hypothesized that ring networks may represent an evolutionary conserved mechanism underlying attentional processes.
To investigate this, I utilized a computational model of an RAN composed of AdEx neurons to study the network's response to both isolated and competing stimuli. The network exhibited a "bump" of activity, which was only present when there was a specific balance between inhibitory and excitatory currents. Under a competitive stimuli paradigm, the network's selection was biased by localized dopaminergic modulation of excitatory neurons. **These findings suggest that SA is mediated by a**

pooling mechanism, orchestrated through selective and specific dopaminergic modulation. *Future work will explore SA under different network topologies and firing patterns to further understand the robustness and versatility of this mechanism.*
Keywords: Selective attention, Ring Attractor Network, Dopaminergic Modulation, Drosophila, Computational Neuroscience

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Clustering analysis of age-related adaptations in retinal ganglion cells of the diurnal rodent Octodon degus.

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The retina is an intricate neural network essential for visual perception and recent research has identified close to 30 unique functional retinal ganglion cells (RGCs). These discoveries indicate a highly complex organization within the retina, where various neural circuits, such as bipolar cells, amacrine cells, and RGCs, interact dynamically to produce accurate visual signals. Advanced multielectrode array (MEA) recording techniques have been crucial in uncovering this complexity by capturing high-dimensional data representing the retina's diverse functional outputs. However, the nature of this data poses significant challenges for visualization and neural network analysis, requiring advanced computational methods. In this study, we utilized multiple clustering techniques to identify and classify different functional types of RGCs and to explore how these categories vary with aging and neurodegeneration. Specifically, we employed three distinct clustering methods: hierarchical agglomerative clustering, which organizes RGCs based on spike distance and effectively groups cells with similar spike patterns; the K-Nearest-Neighbor Graph Method; and an Autoencoder, both of which analyze features derived from temporal spike responses, offering a detailed view of the functional diversity among RGCs. For visualization, we used Uniform Manifold Approximation and Projection (UMAP), a robust tool for exploratory data analysis, to create meaningful representations of the complex datasets. This comprehensive approach provides a first thorough understanding of the functional organization of RGCs and illuminates how retinal output is affected by aging and neurodegenerative conditions. These findings have potential implications for developing targeted therapeutic strategies to preserve or restore visual function.

Keywords: Retinal ganglion cells (RGCs), Multielectrode array (MEA) recording, Clustering techniques

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Awake Sharp wave ripples and their coupling with prefrontal activity patterns are related to spatial navigation strategies.

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Goal-directed spatial navigation is an iterative process that involves gradually adjusting the navigation strategy to efficiently reach a spatial goal. Implementation of a navigation strategy may require consolidation and retrieval of stored spatial memory from previous experiences.
Awake-hippocampal-sharp-waves-ripples (aSWR) and their coupling with prefrontal activity have been related to spatial memory consolidation and retrieval, but their relationship to navigation strategy has not been examined.
To explore this relationship, we recorded local-field-potentials from the Hippocampus and Prefrontal cortex in mice during two goal-directed navigation tasks, the Barnes maze (BM) and the variable-cue Barnes maze (cvBM). In the BM task, animals learn the spatial location of a fixed escape hole, whereas in the cvBM task, the escape location is visually cued and changes on each trial.
Our results show that, in the BM task, animals use several navigation strategies that improve in efficiency with increasing exposure to the maze. However, in cvBM, animals consistently resort to the same escape navigation strategy regardless of maze exposure time.
During the implementation of efficient navigation strategies in BM, we observed an increase in the incidence of aSWRs, especially when the animal was searching for the target. In contrast, this result was not observed in the cvBM.
In addition, we found an increase in cortical theta amplitude before aSWR events, which was only observed when animals used an efficient navigation strategy in the BM.
Thus, our results imply that aSWRs may play a role in implementing efficient navigation strategies necessary to reach the goal.

Keywords: Hippocampus, Sharp wave ripples, Prefrontal cortex, Goal-oriented spatial navigation, Spatial navigation strategies

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The decline in spatial memory during aging is associated with impaired HPC-mPFC oscillatory coupling

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Aging has been associated with impairments in the acquisition and recall of goal-directed spatial memory. These functions are supported by the coordination of several brain regions, including the hippocampus (HPC) and the medial prefrontal cortex (mPFC). However, it is unclear whether the cognitive decline in goal-directed spatial memory during aging is related to impaired synchronization between the mPFC and HPC. To address this question, chronic electrodes were implanted in the mPFC and HPC of young adult and aged C57BL/6 mice and local field

potential was recorded in both groups during the spatial memory acquisition and recall in the Barnes maze task. The results showed that the aged mice group exhibited inferior performance compared to young mice during the acquisition and recall phases of spatial memory. Additionally, it was found that the performance of aged mice varied among subjects; some showed unimpaired performance, while others exhibited impaired performance. This performance of the aged mice was associated with a decrease in the coupling of theta band phase in the HPC and gamma band amplitude in the mPFC during memory acquisition. This suggests that the decreased ability of neural circuits in aged mice to synchronize their oscillatory patterns may contribute to impaired goal-directed memory acquisition. These findings may have important implications for the development of therapies aimed at improving or preserving cognitive function in aging.

Funding: Aging, Spatial memory, Synchronization

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ORAL COMMUNICATIONS II

Chairs: Paul Délano-Vicente Medel

Chewing modulates theta oscillation and functional connectivity of the frontocentral cortex in attentional and working memory paradigms

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Oral health has been shown to correlate with cognitive decline, which is increasingly recognized as a significant public health issue. Clinical studies link tooth loss with this condition, though it remains unclear whether the association is due to tooth loss itself or the inability to perform adequate chewing. This distinction is crucial as it could inform interventions to mitigate cognitive decline through improved oral care. In this study, 30 healthy participants (25-60 years old) right-handed, with complete dentition, and preserved cognitive state (MMSE ≥13 points) underwent a 2x2 experimental design, receiving either anesthesia (lidocaine 15% p/v) or a placebo. Within each condition, there were sub-blocks in which participants were required to chew gum (specially formulated with neutral flavor) for one minute before performing two tasks: a visual oddball (VO) attentional task and a two-back (2B) working memory task. There were no differences by age (25-40 and 41-60 years groups). Significant differences in task accuracy rate were observed when participants chewed gum before the tasks, with no effect from the anesthesia. Electrophysiological analysis revealed a statistically significant increase in theta-band spectral power in both tasks when chewing was involved between 350-550 ms after stimulus presentation in the VO task and 150-350 ms in the 2B test. The Phase Lag Index also showed increased functional connectivity in frontocentral electrodes for both tasks. These results suggest that chewing enhances functional connectivity in brain regions associated with attention and working memory. Somatosensory disruption does not impact this connectivity.

Keywords: Working memory, Attention, EEG, Functional Connectivity, Chewing

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Beyond the "Mona Lisa Smile": Behavioral and neuroelectrophysiological evidence for the influence of context on emotional recognition.

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"The Mona Lisa" by Leonardo da Vinci, has been studied extensively due to its enigmatic smile and the multiple interpretations it has elicited. Despite our ability to recognize faces, fully understanding the emotion conveyed requires considering context. This study focuses on analyzing emotional recognition in facial expressions and contextual images, including unimodal and bimodal perception. Two levels of complexity will be addressed: behavioral and electrophysiological (EEG). To analyze the behavioral level, a repeated measures anova between conditions will be performed for each experiments. At the physiological level, a between-group analysis will be performed for the following evoked potentials: N100, N200, P300 and N400. We recorded the electrical brain activity of 125 participants with a 64-channel EEG network from Electrical Geodesic Inc. At the behavioral level, we found statistically significant differences in accuracy and response time between positive, neutral and negative stimuli in both unimodal and bimodal perception. At the physiological level, EEG distinguishes between positive, neutral and negative stimuli at the early level (P100) for the emotional face recognition task and for congruence in both unimodal and bimodal perception. The findings will provide theoretical information on the role of facial expression in emotional recognition in natural contextual situations, thus, to understand the expression of another, taking the Mona Lisa as an icon, the context in which a facial expression is situated is necessary. They will also contribute to empirical knowledge of emotional processing at the brain level, comparing both levels of complexity with behavior.

Keywords: Emotion recognition, Perception emotion, Bimodal emotion perception, Emotions in context, Event related potential (ERP)

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The Default Mode Network's Role in Social Cognition and Psychosis Risk

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The Default Mode Network (DMN) is a critical neural network in the human brain, known for its activity during rest and its involvement in self-referential and introspective processes. In psychiatry, the DMN has garnered significant attention due to its implication in various mental health disorders. Research has shown that aberrant DMN connectivity and activity are associated with psychiatric conditions such as depression, anxiety, schizophrenia, and bipolar disorder. In schizophrenia, disrupted DMN connectivity correlates with symptoms like hallucinations and impaired self-referential thinking. The DMN plays a pivotal role in social cognition by supporting processes that involve understanding and reflecting on the thoughts, feelings, and intentions of others, allowing individuals to navigate complex social interactions and predict social outcomes. Disruptions in DMN connectivity and function can therefore impair social cognitive abilities, leading to challenges in social communication and relationships. This is particularly relevant in schizophrenia and in stages before the disease manifests itself, such as in a clinical high-risk (CHR) state or in individuals who present psychotic-like experiences (PLEs). Evidence shows that in early stages, disrupted DMN connectivity is exhibited, which affects social cognition. These impairments are crucial as they can exacerbate social withdrawal and isolation, which are common in psychosis. Identifying DMN dysfunction in CHR and PLE individuals could reduce the progression to full-blown psychosis. This symposium will explore the latest findings on DMN disruptions in CHR and PLE populations, highlighting the importance of early detection and targeted interventions to mitigate social cognitive impairments and improve outcomes in at-risk individuals.

Keywords: Redes neuronales, psicosis, Experiencias psicóticas subumbrales, detección temprana, cognición social

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Eardrum Oscillations are Evoked by Voluntary and Reflexive Saccades

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Eardrum oscillations around 30 Hz have been found in silent conditions in response to eye movements generated during simple saccade tasks. Interestingly, the amplitude and phase of these eardrum oscillations, measured with a microphone sealed within the ear-canals, correlate strongly with the amplitude and direction of saccades, mainly in the horizontal (azimuthal) plane. Various geometrical aspects of saccades have been explored to understand the mapping between saccade angles, and their corresponding eardrum oscillations, which can be utilized to reconstruct the saccades that generated them. The physiological function of these eardrum oscillations has only been speculated, and the only study reported on a hypothetical role in three-dimensional hearing found negative results.
In this work we studied if reflexive saccades, such as the fast-phase of the optokinetic nystagmus, also evoke eardrum oscillations, and even though we thought not, results revealed that reflexive saccades comparable in amplitude (6°) and direction (left-right) with voluntary saccades, evoke similar eardrum oscillations, but with less synchronization (more jitter in the peaks) and less amplitude.
We conclude that eye-movement-related eardrum oscillations (EMREOS) are a global phenomenon that synchronizes oculomotor output with evoked low-frequency acoustical oscillations that may interfere with incoming sounds differentially for each ear (as EMREOS have opposite phases between ears) and this could modulate interaural time and intensity differences employed for auditory localization of sound sources.
Finally, we present an undergoing study to evaluate subjective auditory spatial perception in response to spatialized sounds triggered by voluntary saccades in the horizontal plane.

Keywords: Eardrum Oscillations, Saccades, Optokinetic Nystagmus, Spatial Hearing, Audiovisual Integration

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The Neural Dynamics of Emotion Regulation: Exploring the Role of Attachment and Electrophysiological Responses

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Understanding the interplay between emotion regulation (ER) and attachment orientations is crucial for comprehending human affective processes. This study integrates findings from three investigations to explore how attachment orientations influence ER strategies using electrophysiological measures. A total of 174 adults participated in tasks involving cognitive reappraisal and expressive suppression, with brain activity recorded via EEG. Attachment orientations were assessed using the Experiences in Close Relationships-12 (ECR-12) questionnaire, and emotional regulation difficulties were measured with the Difficulties in Emotion Regulation Scale (DERS-E). Using Linear Mixed-Effects Model analysis our results showed that cognitive reappraisal generally resulted in lower Late Positive Potential (LPP) amplitudes, indicating reduced emotional intensity. Higher attachment anxiety was associated with increased LPP amplitudes during both reappraisal and suppression, suggesting heightened emotional responses. Increased frontal theta activity during reappraisal correlated with lower attachment anxiety, reflecting enhanced cognitive control. Interestingly, LPP amplitude moderated the relationship between attachment anxiety and emotional regulation difficulties, with greater LPP intensifying the association. These findings highlight distinct neural responses and suggest that attachment orientations significantly impact the efficacy of ER strategies, with implications for targeted interventions.

Keywords: Human Attachment, Emotion Regulation, Electrophysiological Dynamics, Cognitive Reappraisal, Expressive Suppression

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Reduction of Theta Oscillation in the Occipital Cortex and Pupil-Indexed LC-NE Activity Associated with Error-Monitoring During Learning

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Arbitrary associative learning enables the formation of associations between sensory inputs and actions. Traditionally, this process is associated primarily with the medial frontal cortex (MFC). However, recent studies indicate that sensory cortices also contribute to associative memory formation by processing both sensory and non-sensory information.
This study investigates whether the occipital cortex (OC) is involved in error-monitoring during associative learning, similar to the MFC. We recorded brain activity using a 128-sensor EEG in 29 subjects performing a deterministic visuomotor associative learning task. Additionally, pupil diameter was measured to index locus-coeruleus norepinephrine (LC-NE) system activity, assessing shifts from exploratory to exploitative behavior.
Results showed a reduction in theta band (3-7 Hz) power in both frontal and occipital regions as learning progressed, with changes occurring earlier in MFC sensors (300-500 ms) and later in OC sensors (600-900 ms). Increased coherence in the theta band between fronto-temporo-occipital regions diminished with enhanced learning. Furthermore, a reduction in pupil-indexed LC-NE system activity was observed as learning advanced.
These findings suggest that the OC is involved in error-monitoring, as evidenced by the reduction in theta power and fronto-temporo-occipital coherence as learning increased, albeit later than the MFC. The reduction in pupil-indexed LC-NE activity supports a transition from exploratory behavior, characterized by tonic LC activity, to exploitative behavior, marked by phasic selective LC activity.

Keywords: memory, eeg, pupil diameter, locus coeruleus, theta

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Neuroanatomy of word retrieval across stroke and neurodegenerative diseases

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The ability to retrieve a word one wants to say is a fundamental human skill that frequently breaks down after brain damage. Prior lesion studies of word retrieval have implicated a wide variety of discrete brain regions, often in and around the left temporal lobe. One important factor that arguably contributed to this inter-study inconsistency in the mapping between lesion and deficit is the spatial bias, and ensuing localization errors, that follow from the non-random distribution of brain damage: e.g., stroke-induced brain lesions are constrained by the anatomy of the vascular tree,

while neurodegenerative diseases affect (preferentially) vulnerable large-scale neural networks. Critically, lesion-deficit relationships observed across different etiologies with largely uncorrelated spatial biases would be much less likely to be contaminated by localization errors. Here, we embrace this logic to localize brain regions that are persistently necessary for successful word retrieval in two large samples of patients suffering from brain damage caused by stroke (n = 587) or neurodegeneration (n = 205). Our task of interest was object naming, and we covaried out variance unrelated to word retrieval ability when performing equivalent voxel-based lesion-deficit analyses on these two patient cohorts. Irrespective of analysis type (univariate versus multivariate) and etiology (stroke versus neurodegeneration), our lesion-deficit mapping approach identified a common region in the left mid-to-anterior superior temporal sulcus/middle temporal gyrus and underlying white matter. Our findings suggest that the entirety of this region is important for word retrieval, adding to the existing body of knowledge on the neurobiology of language processing.

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Spatio-temporal and electromyographic characterization of gait in individuals with parkinson's disease at different stages of progression.

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Introduction: Parkinson's Disease (PD) is the second most prevalent neurodegenerative disease in Chile and worldwide, with aging being the main risk factor for its development. Classic motor symptoms such as tremors, muscle rigidity, and bradykinesia are commonly recognized as the initial manifestations of the disease. In more advanced stages, one of the most frequent functional impairments is gait disturbance and postural control issues, which compromise independence and autonomy. At these stages, pharmacological treatment becomes less effective, increasing the relevance of physical therapy. The high variability in the progression of the disease creates a need to characterize the Chilean population diagnosed with PD to provide appropriate rehabilitation.

Method: A descriptive study is presented, characterizing a population of 35 subjects with a medical diagnosis of PD, including both men and women, aged between 50 and 83 years. The study aims to identify clinical characteristics according to disease stage and evaluate gait performance through joint kinematic analysis, spatio-temporal gait parameters, and electromyographic activity.

Results: Clinical characterization and gait performance results are presented for 35 subjects from the city of Valdivia, conducted during the year 2024.

Projections: The results of this study seek to understand the mechanisms related to gait dysfunction in PD. By characterizing a group of individuals with PD, it is possible to better identify the needs to improve the effectiveness of physiotherapeutic interventions.

Keywords: Parkinson disease, Gait Analysis, physical therapy

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Emergence and occupation of dynamical brain states in different states of consciousness using a biophysical model

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Healthy individuals and patients in Disorders of Consciousness (DoC) can be analyzed by how their dynamical activity wanders around and visits recurrent states of connectivity. This is characterized by clustering patterns of functional connectivity (FC) in time, and quantifying how much these patterns are "occupied" in each condition. Sorting the patterns according to their resemblance to the underlying structural connectivity reveals that DoC individual's brain dynamics stay more consistently around connectivity patterns closer to the structural connectivity than healthy individuals. How does structural connectivity give shape to these dynamics? Do DoC and healthy patients transition between states at the same rate?. To answer these questions, we use simulations coming from a biophysical model of brain activity, exploring structural connectivity alteration hypotheses. After fitting the model to CNT dynamics, we explore the exclusion of nodes from the network, which results in an improvement in the fit to DoC dynamics, that depends on network characteristics of the excluded nodes. Not only a lower global coupling fits the DoC dynamics better, but excluding more integrated nodes shifts the model's dynamics closer to those of DoC. Analyzing the transition rates between states for each individual, we gained insights into their stability in different conditions. Also, the model displays a richer repertoire of state jumps, number of states, and overall functional connectivity levels when fitted to healthy patients data than to DoC patients, as the empirical analysis suggests. This can help explain the structural determinants of different dynamic regimes in different brain states.

Keywords: Disorders of Consciousness, Computational Neuroscience, Whole-Brain Models, Brain Dynamics, Functional Connectivity

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POSTER SESSION I

Chairs: Koyam Morales - Carolina Oliva - Francisca Alonso

Exacerbated mitochondrial ROS production and oxidative damage in aged male compared with aged female C57BL6 mice

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Introduction: Aging is characterized by progressive changes leading to cellular deterioration in the organism, including the brain. The hippocampus is a brain structure affected by aging, losing its learning and memory functions as time progresses. Oxidative stress is the main hypothesis leading to aging and is triggered by reactive oxygen species (ROS), contributing to the accumulation of oxidized proteins. Mitochondria are the primary source of ROS; however, if oxidative damage and mitochondrial ROS production are different in the hippocampus of aged mice according to sex, it has not been fully studied.

Materials and methods: In our comprehensive study, we performed immunofluorescence using oxidative damage markers, including 4-HNE, in hippocampal slices from 3- and 18-month-old male and female C57BL/6 mice. In addition, we evaluated the levels of mitochondrial ROS content and production as well as the levels of several antioxidant enzymes in the hippocampus of these animals.

Results: Both male and female aged mice showed higher oxidative damage than adults. Interestingly, aged male mice showed more increased oxidized proteins related to females. This could be explained, almost partly, to exacerbated ROS produced by mitochondria, enhanced ROS content, and minor levels of oxidative enzymes in the hippocampus of aged males compared with aged female mice.

Discussion: Our findings suggest that oxidized proteins accumulate more in the hippocampus of aged males than in female mice, possibly due to differential mitochondrial dysfunction and a deficiency in the antioxidant mechanisms. Thus, mitochondrial ROS could be an important anti-aging target, mainly in aged males.

Keywords: Aging, Oxidative Stress, Sex-related differences, Hippocampus

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Axonal synthesis of an ER-shaping protein determines outgrowth after injury

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The regenerative potential of developing cortical axons after injury relies on intrinsic mechanisms like axon-autonomous protein synthesis, which remains incompletely understood. A critical emerging factor in this regenerative process is the bidirectional interaction between microtubule dynamics and the structural proteins of the axonal endoplasmic reticulum (ER). We propose that locally synthesized ER structural proteins may regulate microtubule dynamics and promote the outgrowth of injured cortical axons. This hypothesis is supported by RNA data mining, which identified Reticulon-1 as the only ER-shaping protein consistently present in axonal transcriptomes and found it to be downregulated following cortical axon injury. In experiments using compartmentalized microfluidic chambers, we show that local knockdown of Reticulon-1 mRNA enhances axonal outgrowth while reducing distal tubulin levels in injured cortical axons. Additionally, live-cell imaging reveals that injury-induced microtubule growth rate and length reductions are fully restored by axonal Reticulon-1 knockdown. Notably, inhibition of the microtubule-severing protein Spastin in axons completely blocks the effects of local Reticulon-1 knockdown on outgrowth and tubulin levels without affecting microtubule dynamics. Furthermore, we present evidence that the Reticulon-1C isoform is locally synthesized in injured axons and interacts with Spastin to inhibit its severing activity. Our findings uncover a novel injury-dependent mechanism where a locally synthesized ER-shaping protein dampens microtubule dynamics and limits the outgrowth of cortical axons.

Keywords: Axon, Injury, Local protein synthesis, reticulon-1, Spastin

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Early Disruption of Mitochondrial Proteostasis and Function Drives Premature Aging in SAMP8 Mice

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Introduction: Cellular proteostasis refers to the dynamic regulation of a balanced and functional proteome, achieved through various mechanisms and organelles. Mitochondrial networks play a critical role in maintaining proteomic integrity via a range of protein effectors, including chaperones, proteases, and the fusion/fission machinery, which collectively work to repair damage within the organelle. SAMP8 mice, an inbred strain known for developing a premature aging phenotype, exhibit severe cognitive impairment as early as 7 months. However, the specific mitochondrial changes preceding the onset of age-related characteristics in SAMP8 mice remain poorly understood.

Material and methods: Biochemical, histological, and cognitive assays were performed in SAMP8 mice from 2, 5, 7, and 12 months old to evaluate the mitochondrial structure and function and its relationship with age-related cognitive impairment.

Results: Our results demonstrate that SAMP8 mice exhibit altered levels of mitochondrial proteins essential for maintaining proteostasis and bioenergetic function. Additionally, diverse parameters related to mitochondrial energy production, redox balance, and calcium homeostasis suggest that mitochondrial dysfunction occurs early in the hippocampus, preceding cognitive impairment. The disruption of mitochondrial proteostasis, driven by an imbalance in proteases, chaperones, and other stress response proteins, appears to be a primary contributor to this dysfunction.

Discussion: Mitochondrial dysfunction is a crucial factor contributing, at least in part, to the cognitive impairment observed in SAMP8 mice. Specifically, the disruption of protein homeostasis within the mitochondria seems responsible for this dysfunction.

Keywords: SAMP8, mitochondria, hippocampus, memory loss, mitochondrial proteostasis

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Repetitive stress induces an increase of Neutral Sphingomyelinase 2 in the rat prefrontal cortex

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Introduction: Ceramide (Cer) is a signaling molecule and a key component of cellular membranes. Elevated ceramide levels are shown in the plasma of patients with stress-related disorders, as well as in the prefrontal cortex (PFC) and hippocampus (HP) of human postmortem brains. Neutral Sphingomyelinase 2 (NSM2) serves as a primary source of Cer in the brain by catalyzing the hydrolysis of sphingomyelin (SM), however, its cellular localization and regulation under long-term stress remains unknown. We propose that NSM2 is regulated by stress in neurons and/or astrocytes, impacting brain Cer levels.

Methods: We used movement restriction in adult Sprague Dawley male rats (n=13) to analyze the expression and activity of NSM2 in the PFC and Hp. In-vitro we immunolocalized NSM2 in neurons (stained with MAP2) and astrocytes (stained with GFAP) treated with the stress hormone corticosterone.

Results: Western Blot analysis showed an increase in the levels of NSM2 in the PFC, but not in the HP. This goes along with the increased enzymatic activity of NSM2 in the PFC. Besides, a higher NSM2/GFAP intensity ratio in PFC-derived cell cultures was observed, indicating that astrocytes may be sensitive to NSM2 regulation in these cells. This might affect the signaling capacities of Cer such as receptor recruitment, cell membrane permeability, or extracellular vesicle biogenesis.

Conclusion: Movement restriction induces an increase in the NSM2 expression and activity in the PFC, suggesting that NSM2 offers an attractive target for stress-related therapeutic interventions.

Keywords: Ceramide, Neutral Sphingomyelinase 2, Long-term stress

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Modulation of the TRPM8 channel degradation rate by S29 phosphorylation

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In mammals, environmental cold sensing by peripheral cold thermoreceptor neurons (CTNs) mainly depends on TRPM8, a polymodal TRP channel activated by cold, cooling compounds such as menthol, voltage, and osmolality rises. The regulation of TRPM8 function involves several mechanisms, including phosphorylation. We previously identified serine 29 phosphorylation as a critical player in downregulating TRPM8 function, leading to decreased responses to cold and menthol by reducing the number of active TRPM8 channels in the plasma membrane. To further understand how this post-translational modification regulates TRPM8 expression at the cell surface, we generated two stable HEK293 cell lines expressing wild-type mTRPM8-myc and mutant S29A-mTRPM8-myc channels. This allowed us to reproduce our previous observations where the S29A-mTRPM8-myc cell line exhibited higher responses to cold and menthol due to an increased maximum conductance (Gmax) and a leftward shift of the half-maximal activation voltage towards negative membrane potentials. To assess if the increase in the Gmax could be related to a decrease in the TRPM8 degradation rate when S29 phosphorylation is prevented, we evaluated the effect of chloroquine and bafilomycin A1, two lysosome inhibitors, in the TRPM8 protein levels by western blot analysis. We observed that the impact that lysosome inhibitors were more pronounced in cells expressing wild-type TRPM8 channels rather than S29A mutant channels, suggesting that preventing S29 phosphorylation reduces TRPM8 degradation. Since our findings underscore the role of S29 phosphorylation in regulating the cell TRPM8 expression levels, this mechanism should be considered when studying pathological conditions related to altered TRPM8 function.

Keywords: TRPM8, Phosphorylation, Degradation rate, Lysosome inhibitors

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Exploring the impact of astrocyte-derived extracellular vesicles on axonal protein synthesis

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Extracellular vesicles (EVs) are membranous structures released by various cell types, including glial cells in the central nervous system. Among these, astrocytes are the most abundant and play a crucial role in maintaining the cerebral microenvironment through direct contact with neighboring cells or by secreting factors, including EVs. In our laboratory, we have conducted multiple studies on the cargo of astrocyte-derived extracellular vesicles (ADEVs), identifying protein cargos related to the progression of protein translation and nucleic cargos like microRNAs (miRNAs) that target messengers associated with microtubule stability. Cortical neurons, highly dependent on microtubule dynamics, are polarized cells whose axonal projections may reach outstanding

dimensions. During development, axonal extension is supported by translational machinery that critically depends on their local interaction with the brain microenvironment. While the literature has documented the ability of neurons to internalize ADEVs in their somas, their local interaction with neuronal axons remains to be explored. Taking advantage of compartmentalized cultures in microfluidic chambers, we showed that axons autonomously internalize fluorescently labeled ADEVs and retrogradely transport them toward the cell body. This process depended on micropinocytosis and dyneins, respectively. By analyzing the somatic and axonal domains, we revealed that ADEVs differentially control local protein synthesis and the levels of microtubule-stability-associated proteins like GSK3B and post-translational modifications such as acetylated and tyrosinated tubulin. The potential of ADEVs to trigger axon-autonomous responses during development may have broader implications for developmental disorders and during regeneration that remain to be elucidated.

Keywords: ADEVs, axonal protein synthesis, cortical neurons, microfluidics, microtubule stability

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Deciphering the role of miR-26a in coordinating neuronal microtubule dynamics and mitostasis

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Microtubule dynamics and mitochondrial function, or mitostasis, are essential regulators of neuronal activity and overall function. However, the interplay between these two critical processes remains inadequately understood. MicroRNAs (miRNAs) are small non-coding RNAs that play crucial roles in regulating gene expression post-transcriptionally, influencing various cellular processes, including those in the nervous system. In this study, we investigated the role of miR-26a, a specific miRNA, as a potential coordinator of microtubule dynamics and mitostasis in neuroblastoma cells. Using Western blot (WB) analysis, we demonstrated that upregulation of miR-26a leads to a significant increase in dynamic microtubules, as indicated by elevated levels of tyrosinated tubulin. Conversely, inhibition of miR-26a resulted in decreased levels of tyrosinated tubulin. Further exploration using a combination of WB and confocal microscopy revealed that miR-26a upregulation significantly reduces mitochondrial biomass, while its inhibition causes an increase in mitochondrial content. These findings were corroborated by live cell imaging, which allowed simultaneous quantification of mitochondrial dynamics and microtubule end dynamics. Our results begin to elucidate the novel connection between microtubules and mitochondria, shedding light on a relationship that is critically disrupted in several neurodegenerative disorders.

Keywords: neuroblastoma, microtubule dynamics, mitostasis, miR-26a

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Age-Related Development of Cognitive Flexibility in a Sample of Latin American Children

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Cognitive Flexibility (CF) involves the ability to switch between different concepts, adapt behavior to changing demands, and shift perspectives to consider multiple facets of a situation. This adaptability is crucial for problem-solving, learning, and everyday functioning. CF is a key component of Executive Functions (EFs), which are cognitive processes essential for coordinating and controlling thoughts and actions to achieve specific goals. EFs improve with age due to brain maturation during childhood. This study aims to elucidate the relationship between CF performance and developmental stages in 87 children (38 girls) aged 6 to 12 years, identifying potential critical periods for CF acquisition and optimization. We employed the subtests of CF from the Battery of Executive Function Assessment (BEFE, *Batería de Evaluación de las Funciones Ejecutivas*), which include the Verbal Semantic Fluency and Phonological Fluency tests, and an adapted version of the Wisconsin Card Sorting Test (WCST). Results indicated positive correlations between CF performance and age. Notably, verbal fluency optimization was observed at ages 11 and 12, while the adapted WCST subtest showed performance optimization between ages 10 and 12. These findings suggest that CF development follows a distinct pattern during these years, with critical periods of optimization.

Keywords: Cognitive Flexibility, Executive Functions, Neurodevelopment, Neuropsychological Assessment

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Long-term effects of maternal observational stress during the lactation period on anxiety-like and social behaviors in adulthood

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The maternal period is essential for brain development and highly demanding in the lives of mammals. Living stressful experiences as well as observing them during the lactation period can have significant consequences for both the dams and offspring. The aim of this study was to determine in an animal model the long-term effects of observational stress during the lactation period on anxiety-like behavior and social behavior of the offspring. In our laboratory we developed a rat model of observational stress called maternal vicarious social defeat stress (VSDS). On postnatal day (PND) 3, dams and pups observed a defeat stress session between two male Long-Evans and Sprague-Dawley rats. Each SDS session lasted 30 minutes and was repeated for 7 days. In adulthood, the female and male offspring (PND 110) were assessed for anxiety-like (elevated-plus maze) and social behaviors (social three chamber test). Notably, offspring of dams exposed to VSDS were more anxious than controls while social behavior deteriorated. These results suggest that brain areas that modulate anxiety and sociability, such as the amygdaloid complex and the nucleus accumbens, were vulnerable to dam's observational stress during the lactation period, and the long-term effects on anxiety and social behavior persist into the offspring's adulthood.

Keywords: stress, social defeat, maternity, development, observational

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Mozart Reads Salieri: Perceived Difficulty is Associated with Pupil Diameter in Musicians During Sight-Reading

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Mental workload can be defined as the amount of deliberate mental effort required to achieve a specific outcome. There is limited information on how mental workload manifests in musicians and what factors might influence it while they read and perform musical pieces. In this work we aimed to determine whether the complexity of musical scores influences the increase in mental workload, as measured by pupillometry, during sight-reading. Twenty musicians aged 15 to 30, who were proficient in reading sheet music and playing the piano, were recruited. The assessment involved reading musical scores of varying difficulty levels, presented in random order. Pupil diameter, perceive difficulty and perceive performance was recorded. As expected, perceive performance was highly correlated with perceived difficulty. In addition, participants exhibited a greater increase in pupil diameter when reading more difficult scores compared to easier ones. These findings contribute to understanding the relationship between mental workload and the cognitive demands placed on musicians during sight-reading, a crucial skill in musical performance. Future research will explore which specific characteristics of musical scores influence mental workload and how this, in turn, might lead to postural adjustments that could potentially result in injuries.

Keywords: music, mental workload, performance, human factor

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Tympanic oscillations associated with saccades occur in the absence of visual input

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During active sensing, the changes of activity in the sensory organs result from self-initiated motor actions. This motor activity precisely modulates early sensory cortices such as V1, A1, and S1. It has been observed that active sensing is a multi-modal phenomenon. Recently, it was reported in humans and monkeys that the eardrums move when saccades are performed, with the phase and amplitude of tympanic oscillation being dependent on the direction and amplitude of the saccades. For instance, when performing a saccade to the right, the ipsilateral eardrum bulges while the other eardrum contracts. Is this phenomenon dependent on visual activity? Because direct connection from motor to early sensory areas has been reported, we hypothesized that the tympanic movement associated with movement would not depend on retinal visual activity. We recruited subjects to perform voluntary saccades while tympanic movements were measured through intra-aural microphones, and eye movements were measured through electrooculography. We observed the expected tympanic movement associated with the saccades, which were also observed during voluntary saccades performed with the eyes covered. Our results indicate that during active sensing, tympanic oscillations associated with saccades do occur in the absence of visual input, demonstrating a central role for motor action in multimodal sensory sampling.

Keywords: Eardrums, Saccade, Active sensing

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Socio-affective skills in early childhood educators: A behavioral study.

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Teaching behavior corresponds to a form of cooperative skill that facilitates the learning of others. This behavior becomes particularly complex in humans, leading to what is known as pedagogical teaching. It has been poorly understood from the perspectives of cognitive science and neuroscience.
Interestingly, in preschool educational settings active listening and empathy are crucial for effective communication. However, it remains unclear whether preschool teachers with formal training exhibit significant differences in these competencies compared to individuals without such training. In this study, we compared the performance of experienced preschool teachers (N = 30, age range =28-61 years) with a matched control group of non-teachers (N = 30, age range =30-64 years) using the Active-Empathic Listening Scale (AELS) and the Interpersonal Reactivity Index (IRI). Additionally, fluid intelligence (Raven's Progressive Matrices) and crystallized intelligence (Peabody Picture Vocabulary Test, PPVT) complement the affective measures.
The results revealed that preschool teachers scored significantly higher on the AELS, demonstrating a greater ability to understand the relational aspects of discourse ($p=0.0005$), effectively process messages ($p<0.0001$), and provide verbal and non-verbal feedback ($p =0.0002$). They also obtained higher scores on the perspective-taking IRI subscale ($p =0.0113$), indicating a greater ability to understand and resonate with others' viewpoints. On the other hand, while fluid intelligence did not show differences between the groups ($p=0.34$), preschool teachers scored lower on crystallized intelligence ($p<0.0001$). Finally, these findings suggest that experience as a preschool teacher enhances active listening and empathy skills without impacting the development of abstract thinking or vocabulary enrichment.

Keywords: socio-affective, teacher, cognitive

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A triple-blind Neurofeedback Protocol for Depression, based on a "Subject-Independent" Brain State Classifier

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Background: Most neurofeedback (NF) studies are based on the idea that patients can achieve a healthy brain state by receiving feedback from their own abnormal brain function. The goal of this study is to use an EEG-based NF system to guide patients with depression towards a healthy brain state, but using neural information from healthy individuals.

Methods: A "brain state classifier" was created based on EEG Common Spatial Patterns and Support Vector Machine, using brain data from 19 healthy women. This "subject-independent" classifier was integrated with an EEG-NF system.
Twenty patients participated in this NF protocol, attempting to emulate the "healthy" brain, through feedback from the classifier. The experimental group received real-time visual feedback from the classifier, aiming for a positive emotional state, with information that responded to brain classification: "healthy" or "non-healthy" state. The control group received non-contingent feedback. Patients, the technician, and the clinical psychologist were blind to whether the feedback was contingent (experimental group) or not (control group).
Results: A significant improvement in "classification" accuracy was observed towards the end of the training in the experimental group. Most subjects in the experimental group also showed clinical improvement, faster than the control group. Our results demonstrate the feasibility of using an EEG NF system with a subject-independent classifier to help patients with depression reach a "healthy brain state."

Keywords: depresión, neurofeedback

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Evaluating the coupling between the prefrontal cortex and lateral hypothalamus in a rodent model of binge eating

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Feeding behavior is a complex process involving homeostatic, physiological, and cognitive mechanisms. Palatable food (PF) can disrupt these processes, contributing to eating disorders such as binge-eating (BE), which is characterized by impaired cognitive control over feeding. While feeding behavior is regulated by the lateral hypothalamus (LH), the medial prefrontal cortex (mPFC) modulates the LH and plays a key role in the cognitive control of feeding.
We hypothesized that BE may be associated to an impairment in the mPFC-LH coupling during PF consumption. To investigate this, we subjected adult female mice to intermittent access to PF to induce BE. Control animals were subjected to ad libitum access to PF. Cognitive control of feeding was assessed using a modified version of the dark-light box test (DLB) before and after BE induction. Neural activity (local-field potential and single unit) was recorded from the mPFC and LH during BE induction and DLB.
Preliminary results show that intermittent access to PF leads to binge-like behavior and modifies feeding patterns. In DLB, binge animals consume more PF in lit compartment following BE induction, but no significant differences were observed in the time spent in lit compartment compared to control group. Finally, characterization of LFP in mPFC-LH reveals gamma events in both regions during BE induction.
These results provide an initial approach to elucidating neurophysiological changes in mPFC-LH coupling during BE episodes.

This research will contribute to the understanding of the neural mechanisms of BE.

Keywords: cognitive control, in vivo neurophysiology, binge eating, hypothalamus, prefrontal cortex

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The Effectiveness of Immersive Virtual Reality for Spatial Learning Tasks in Two Diverse Age Groups

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Spatial learning is a critical function for our effective functioning in the world. Despite the importance of this function, its study has been limited to unrealistic contexts, hindering a deep understanding of its underlying mechanisms. Today's technological advancements allow us to study this phenomenon in environments close to natural ones, with the potential to perform physiological measurements that help us understand its mechanisms in humans. In this work, we aimed to evaluate the box room task implemented in an immersive virtual reality system for studying spatial learning in humans. The sample consisted of healthy children and older adults, without neurological or psychiatric alterations. All participants successfully completed the task without any problems associated with the use of immersive virtual reality. Although in different ways, both children and older adults showed improvements in the three established performance measures used to assess their performance over the course of the rounds: time, travel distance, and number of errors. Our results support the effectiveness of the box room task implemented in an immersive virtual reality system for studying spatial learning and navigation in humans. The flexibility in its implementation positions the task as a valuable research tool for investigating spatial cognition in a wide variety of populations with diverse characteristics and in

various contexts.

Keywords: virtual reality, spatial learning, spatial navigation, neuroscience

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Implementation of a Calculus Teaching Method and its Impact on High Cognitive Abilities

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Calculus, a cornerstone of mathematics that explores continuous change through differentiation and integration, is pivotal to higher education in engineering and STEM careers. However, in these fields, the teaching of calculus has diverged from its real-world applications. As a result, its instruction presents challenges, with many students grappling with its complexity, leading to discouragement and dropout, highlighting the need for innovative teaching strategies. Grounded on the nexus between calculus and higher cognitive functions, this research evaluates the efficacy of a contextualized calculus teaching method in enhancing understanding and applying calculus and seeks to determine its impact on broader cognitive functions, specifically, perceptual reasoning, working memory, and processing speed. Perceptual reasoning is critical for interpreting and organizing visual information, an essential skill in problem-solving and engineering tasks. Working memory supports the manipulation of information necessary for complex calculations and logical reasoning, while processing speed impacts the efficiency with which these cognitive tasks are performed. Employing a pretest-retest design with control and intervention groups, we merge cognitive evaluations, including subtests from the Wechsler Adult Intelligence Scale, with calculus performance assessments in a sample of 85 university students aged 18 to 20, enrolled in a Calculus I course across various engineering disciplines. Our results revealed the intervention group exhibited enhanced calculus performance and improvement in the perceptual reasoning index, especially in block design subtest, reflecting enhanced visuospatial skills. This study offers valuable perspectives for improving calculus instruction and potentially improving students' cognitive capabilities by implementing contextualized teaching methodologies.

Keywords: Calculus, Education, Engineering, Cognitive Functions, Perceptual Reasoning

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Childhood Maltreatment: Effects on Brain Activity in Adulthood During Psychosocial Stress. A Study Using Functional Magnetic Resonance Imaging (fMRI).

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Background: Adverse childhood experiences (ACEs) can influence stress responses in adulthood. This study examines brain activity differences during a psychosocial stress task in adult women with high and low scores of childhood maltreatment.

Methodology: Sixty women (aged 18-40) without active psychiatric conditions participated in the experiment, divided in two groups: 31 with low scores of maltreatment (control group, mean ACE = 7.4) and 29 with high scores of maltreatment (experimental group, mean ACE = 23.7). ACEs were measured using the Maltreatment Adversity Chronological Experience (MACE) questionnaire. The Montreal Imaging Stress Task (MIST), which involves solving math problems under stress and non-stress conditions, was used for stress induction. BOLD signals during this task were measured with a Siemens 3T MRI and processed using FEAT (FSL), with a threshold of Z>2.3 and p=0.001.

Results: No significant behavioral differences were observed in MIST performance. However, under stress, the experimental group showed significant greater activations in the posterior cingulate gyrus, precuneus, bilateral temporal gyrus, and superior frontal gyrus, compared to the control group. Without stress, this group exhibited

Keywords: fMRI, Childhood maltreatment, Stress

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Eye movements behavior during crossmodal visuo-auditory search.

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In active sensing, auto-initiated movements contribute to coordinating multimodal sensory activity. Many studies reported the predominance of visual over the auditory system when there is a mismatch of visual and auditory stimuli. We tested this assumption during a search task where a joint visual and auditory stimulus is presented on a corner of a computer monitor after a visual fixation in a center fixation point. The corner stimuli could change

immediately after the onset of the saccade, meaning that the visual or auditory stimuli' location could differ during the execution of this first saccade. We examined the eye movement behavior to determine if the saccade landed in the original location of the visuo-auditory stimuli when the visuo-auditory stimulus remained in the same place or changed location. We found that the first saccade landed in the original stimulus location, even when the visual or auditory stimulus changed location during the saccade. We also found that after the first fixation to the stimulus, a secondary saccade was directed to a changed location, but primarily when this changed stimulus was visual but not auditory. These results confirm the predominance of visual over the auditory system when there is a mismatch of visual and auditory stimuli.

Keywords: active sensing, crossmodality, eye movements, vision, audition

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Maternal High-Fat Diet Exposure Impairs Offspring Cognitive Function and Hippocampal GABA Transmission

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Background: Maternal obesity (MO) during pregnancy is a growing global health issue, with evidence linking it to long-term effects on offspring health and development. The hippocampus, critical for cognitive function, is particularly vulnerable to nutritional changes during fetal development. While maternal high-fat diet (mHFD) exposure has been associated with cognitive impairments, its impact on hippocampal synaptic transmission is not well understood.

Aim: This study investigates the effects of mHFD during gestation and lactation on offspring cognitive function and hippocampal synaptic transmission.

Methods: Female mice were fed a mHFD (60% of calories from fat) from pre-pregnancy through lactation. Offspring were evaluated using novel object recognition (NOR) and object location memory (OLM) tests. Electrophysiological recordings from CA1 pyramidal neurons assessed synaptic transmission and plasticity.

Results: Offspring exposed to mHFD showed impaired cognitive performance, reflected by reduced discrimination indices in NOR and OLM tests. Electrophysiological analyses revealed enhanced inhibitory synaptic efficacy and reduced long-term potentiation (LTP) in hippocampal slices.
Conclusions: Exposure to mHFD during critical developmental periods leads to cognitive deficits in offspring, potentially through disrupted hippocampal synaptic plasticity and an excitatory/inhibitory imbalance. These findings offer mechanistic insights into MO-associated cognitive disorders and may guide future therapeutic strategies.

Keywords: Maternal Obesity, Inhibitory Transmission, Hippocampus, Plasticity, Neurodevelopment

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Iso -N, N-dimethyltryptamine, and derivatives enhance hippocampal synaptic plasticity.

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Most symptoms that characterize major depressive disorder (MDD) converge on cognition, memory, and synaptic impairment. The use of psychedelic compounds has gained attention in the last few years, especially in patients refractory to antidepressant treatments. Nevertheless, the high comorbidity of MDD with other neurological disorders could increase the risks of exposure to hallucinogenic compounds. An alternative is the use of iso- forms of N, N-dimethyltryptamine (DMT) which do not generate a murine response considered to be a surrogate of human hallucinogenesis while stimulating the growth of dendritic spines in neuronal cultures. We studied the effects of iso-DMT, 5-methoxy-iso-DMT, and 6-methoxy-iso-DMT on the Learned Helplessness (LH) murine model of depression. The model is generated by footshock exposure for two consecutive days, inducing behaviors like anxiety and poor spatial-referential memory. Regarding hippocampal neurotransmission, we found that LH mice present smaller field potentials and reduced long-term potentiation (LTP) of CA3-CA1 synapses compared to non-stressed animals. Acute exposure to the derivatives (10 µM) recovers the hippocampal LTP of the LH mice but does not enhance the LTP in non-stressed animals. The exposure of brain slices of non-stressed animals to non-saturating stimulus protocols is not enough to induce LTP, but pretreatment with 5-methoxy-iso-DMT (10 µM) generates LTP. Intraperitoneal administration of 5-methoxy-iso-DMT (10 mg/kg) to non-stressed animals increases hippocampal LTP, suggesting a role in glutamatergic neuromodulation. In conclusion, exposure to iso-DMT derivatives enhances hippocampal synaptic plasticity and recovers the impairment in LH mice, but more evidence is required to test their antidepressant properties.

Keywords: Depression, Hippocampus, Synaptic plasticity, Psychedelics

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Prenatal stress impairs fetal subpallial neuro/gliogenesis

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Psychological distress during pregnancy or prenatal stress (PS) increases the risk of poor neurodevelopmental outcomes in the offspring. However, PS-induced alterations in fetal neurodevelopment (i.e., neuronal/glial differentiation and maturation) are poorly understood. In this work, using a repetitive maternal restraint stress rat model, we assessed PS-induced morphological and molecular changes in the offspring developing brain, focusing on subpallial neuro/gliogenesis (i.e., the site where cortical GABAergic interneurons and some oligodendrocyte precursor cells (OPCs) are born). Pregnant rats were split at embryonic day (E)0.5 in control and stress (repetitive restraint) groups. Rats from the stress group were confined daily (2h/day) to movement restriction from E8.5. One subgroup of rats was euthanized at E17.5, and embryos were recovered. Another subgroup was subjected to the stress protocol until parturition and pups were euthanized at postnatal day (P)9. Microscopic brain morphological analyses were performed in the subpallium and the cortex. In addition, neuronal differentiation was evaluated in the brain cortex by qRT-PCR, WB assays, and immunofluorescence. Our results showed that PS induced changes in the fetal subpallial neurogenic process, leading to a decrease in the number of cortical interneurons at E17.5 and P9. Interestingly, the expression of specific GABAergic neuron markers such as somatostatin showed a significant decrease at P9. On the other hand, differentiation assays suggest an impairment of neuronal (GABAergic interneurons) and glial (OPCs) differentiation of subpallial progenitors. Together, these findings suggest that PS impairs fetal subpallial neuro/gliogenesis, altering neuron/glia differentiation processes and decreasing cortical interneuron populations.

Keywords: Maternal distress, interneurons, brain development, fetal programming

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Mitochondrial enhancement and concomitant restoration of synaptic structure and cognitive function in the hippocampus of aged SAMP8 mice following Red630 Light Transcranial LED Therapy (RL-TCLT)

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Introduction: Mitochondrial dysfunction is a crucial factor in aging, leading to synaptic and memory impairment in the hippocampus. RL-TCLT, an innovative and non-invasive strategy, employs a 630 nm wavelength to deliver photons that activate sensitive molecules within brain cells, promoting neurotherapeutic effects and providing tissue therapy for neurological conditions. However, its cellular targets and effects on age-related memory loss remain poorly understood.

Materials and Methods: We treated 7-month-old Senescence-Accelerated Mouse-Prone 8 (SAMP8) mice with RL-TCLT for 125 seconds daily over 5 weeks. Then, in the hippocampus, we assessed mitochondrial function, synaptic structure, adult neurogenesis-related proliferation and differentiation (using Ki67 and DCX staining), as well as hippocampal-dependent spatial and recognition memory.

Results: RL-TCLT activates mitochondrial function in the hippocampus, as indicated by increased oxygen consumption, ATP production, and cytochrome c oxidase (COX) activity, with reduced ROS production and sensitivity to calcium overload. Additionally, RL-TCLT increased synaptic proteins, promoted the formation of mushroom spines, and enhanced dendritic arborization, suggesting improved synaptic plasticity. Nevertheless, the synaptic improvement seems unrelated to adult neurogenesis because no changes in the densities of Ki67+ or DCX+ cells were observed in the dentate gyrus of animals exposed to RL-TCLT. Finally, RL-TCLT-mediated mitochondrial and synaptic effects contribute to enhanced hippocampal-dependent memory.

Discussion: Our findings indicate that RL-TCLT stimulates mitochondrial function and improves synaptic structure without affecting hippocampal neurogenesis, suggesting that the increased dendritic arborization does not involve newborn neurons. Altogether, these changes enhance hippocampal function, counteracting the harmful effects of aging and protecting the brain against age-related processes.

Keywords: LED Therapy, Aging, Mitochondria, Hippocampus
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Cardiometabolic state links neurovascular burden with brain structure and function: evidence from EEG and MRI

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Aging affects brain structure and function alongside metabolic and vascular processes leading to energetic impairments. While local neurometabolic dysfunction in aging is well-documented, the influence of systemic cardiometabolic and vascular markers on

brain structure and function remains less understood. We examine the link between cardiometabolic dysfunction (measured by an allostatic load index) and neurovascular burden (measured by white matter hyperintensities) with brain changes, including ventricular and hippocampal volume, as well as EEG activity, across age. Analyzing data from 196 healthy individuals across age (20-75 years), we found a significant positive correlation between allostatic load index and white-matter hyperintensities, irrespective of age. White matter hyperintensities are also positively linked with ventricular enlargement, but not hippocampal atrophy. The allostatic load index mediated the relationship between white-matter hyperintensities and ventricular volume. Regarding brain function, changes in the spectral aperiodic exponent but not periodic alpha power were linked to white matter hyperintensities and the allostatic load index. Such index mediated the relationship between spectral aperiodic exponent and white matter hyperintensities. Thus, findings suggest that the cardiometabolic state, as measured by an allostatic load index, plays a crucial role in brain health across age, particularly influencing ventricular enlargement and increased aperiodic activity.

Keywords: Cardiometabolic state, White matter hyperintensities, neurovascular burden, aperiodic activity

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Alterations in Neural Connectivity in "Jumping to Conclusions" Paradigms in Patients with Schizophrenia

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Schizophrenia is a highly disabling chronic disorder with a significant impact on the quality of life of those who suffer from it. One of the most relevant symptoms, which has been associated with adverse outcomes in psychosocial functioning and worse clinical results, is cognitive impairment. Among the various cognitive symptoms, decision-making processes are particularly important to study. One of the key decision-making processes studied in schizophrenia is the "Jumping to Conclusions" (JTC) bias, which is characterized by making more hasty decisions during probabilistic reasoning tasks.
A major hypothesis regarding the origins of schizophrenia is the neural connectivity hypothesis, which postulates that disrupted neuronal synchrony plays a role in the pathogenesis of the disorder. This disruption can be investigated using electroencephalography (EEG). However, despite the heterogeneity of schizophrenia's pathophysiology, the neurobiological underpinnings of JTC in this condition, particularly in its early stages, remain unclear. This is especially relevant as some studies have linked JTC with the onset and propensity for delusions in patients with schizophrenia. These studies suggest that delusions may arise from a tendency to make inferences based on insufficient evidence, highlighting the need for further research in this field.
In this analytical case-control observational study, we aim to contribute to the understanding of the neurobiological alterations associated with JTC, focusing on the cognitive component, through the use of EEG in patients diagnosed with schizophrenia.

Keywords: Schizophrenia, Cognitive symptoms, Decision-making, Jumping to Conclusions, Electroencephalogram (EEG)

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Age-Related Changes in Electroretinogram Parameters

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The electroretinogram (ERG) is a valuable tool for assessing retinal function and holds promise as a non-invasive biomarker for neurodegenerative diseases such as Alzheimer's and Parkinson's disease. However, establishing robust ERG-based diagnostic tests for these conditions necessitates a clear understanding of how the physiological ERG response is affected by normal aging. Characterizing age-related changes in ERG parameters will enable researchers to differentiate between normal aging and pathological changes associated with neurodegeneration. This study investigated the impact of age on the amplitude and latency of ERG signals in a normal population. A cohort of fifty participants, recruited from the University of Santiago de Chile and stratified into young, young adult, and adult (with and without presbyopia) age groups, underwent a comprehensive ophthalmological assessment, including electroretinography (ERG) recording using a portable ERG device (LKC Technologies). Statistical analysis revealed significant differences in ERG parameters across age groups. Notably, the latency of A and B waves was significantly prolonged in the adult groups (both with and without presbyopia) compared to the young group ($P<0.0001$). Additionally, amplitude reductions in A and B waves were observed in the adult groups compared to the young group. These findings demonstrate that both the amplitude and latency of the ERG are influenced by age, underscoring the importance of considering age-related changes when evaluating the potential of ERG as a biomarker for neurodegenerative diseases.

Keywords: Electroretinogram (ERG), Retinal function, Aging, Amplitude, Latency

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Sociodemographic heterogeneity in enlarged perivascular spaces? A comparative study of the glymphatic system in Latin America and the US

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This study investigates perivascular spaces (PVS) as part of the glymphatic system by analyzing data from the RedLat database, which includes subjects from Chile, Argentina, Brazil, Peru, Mexico, and Colombia, alongside US samples (N=780). The primary objective was to conduct a comparative analysis of PVS number across Latin American and US samples and between control subjects, Alzheimer's disease (AD) patients, and frontotemporal dementia (FTD) patients. An automated method was employed to quantify PVS in the white matter. By integrating data from diverse geographic regions, this research aims to explore potential regional differences in glymphatic system performance, which could be influenced by varying environmental, genetic, and lifestyle factors. The findings will provide valuable insights into the potential global variations in brain health indicators, particularly in the context of neurodegenerative diseases like AD and FTD. Understanding these differences could contribute to more precise approaches in the diagnosis and treatment of dementia across different populations. Additionally, this study underscores the importance of considering regional and cultural factors in the study of brain health, emphasizing the need for further exploration of global differences in glymphatic function and their implications for neurodegenerative diseases.

Keywords: Glymphatic System, Neurodegenerative Diseases, Perivascular Spaces, Sociodemographic Heterogeneity

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The role of noradrenaline in Amyotrophic Lateral Sclerosis

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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by neuronal damage in motor cortex, brainstem, and spinal cord. Higher levels of noradrenaline have been described in ALS patients, but its impact is certainly unknown. Cell death caused by noradrenaline was proposed in several tissues. In fact, mitochondrial apoptosis was described in rat brain as a possible mechanism of neuronal death induced by high noradrenaline levels acting on alpha1-adrenoceptors (ADRA1s). These findings support a plausible role of noradrenaline overstimulation on ADRA1s in ALS neurodegeneration. Besides, inhibition of phenyletanolamine N-methyltransferase (PNMT) enzyme, which catalyze noradrenaline to adrenaline conversion, was suggested to increase noradrenaline levels and cause neuronal dysfunction in mice. However, the effect of high noradrenaline levels acting on ADRA1s in ALS context has not been investigated before. Ingenuity Pathway Analysis (IPA) software predicts that ADRA1A and ADRA1D participate in ALS and our transcriptomic analysis from public data also sustain noradrenaline involvement. Our unprecedented results showed a significant gene expression alteration of ADRA1s and corticosterone receptors *Nr3c1* and *Nr3c2* in SOD1^{G93A} mice specially in brainstem, supporting the relevance of brainstem and a noradrenaline signaling alteration in ALS. Moreover, our results indicate for the first time a significant decrease in *Pnmt* gene expression in mutant mice, pointing out PNMT as a new target in the study of ALS. Thus, modulation of noradrenaline signaling using ADRA1s antagonists, and regulation of noradrenaline levels through overexpression of *Pnmt* could lead to the development of potential therapies for the disease.

Keywords: Amyotrophic Lateral Sclerosis, noradrenaline, alpha1-adrenoceptors, phenyletanolamine N-methyltransferase

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Adolescent NMDAR Hypofunction Disrupts mPFC GABAergic Transmission and Synaptic Plasticity.

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Background: The medial prefrontal cortex (mPFC) is crucial for cognitive functions, including attention, decision-making, and working memory. During adolescence, GABAergic interneurons play a vital role in mPFC maturation. Disruptions in interneuron development during this period have been implicated in neuropsychiatric disorders, but their long-term impact on adult synaptic plasticity remains unclear.

Methods: We used subanesthetic doses of ketamine to investigate the effects of adolescent NMDAR hypofunction on adult mPFC synaptic plasticity. Electrophysiological and pharmacological techniques were employed to measure spontaneous and evoked inhibitory postsynaptic currents (IPSCs) and spike timing-dependent plasticity (STDP).

Results: In layer II/III pyramidal neurons of adult mPFC slices from ketamine-treated (Ket) mice, we observed:
A reduction in the frequency of spontaneous and miniature inhibitory postsynaptic currents (sIPSCs and mIPSCs) in Ket-treated mice.
An increased paired-pulse ratio of evoked IPSCs in Ket-treated slices, indicating altered GABA release.
Normal t-LTP induction, but reversed t-LTD (potentiation instead of depression) in Ket-treated mice.

Conclusions: Adolescent NMDAR hypofunction impairs GABAergic interneuron maturation and function, reducing GABA release and disrupting the excitation-inhibition balance in the adult mPFC. This alteration reverses the temporal dependence of STDP-LTD, significantly impacting synaptic plasticity. These findings provide insight into the long-term consequences of adolescent NMDAR dysfunction on mPFC circuit development and may contribute to our understanding of neuropsychiatric disorders.

Keywords: ketamine, synaptic transmision, neuroplasticity, STDP, Prefrontal cortex

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Intranasal probenecid reduces the inflammatory phenotype of astrocytes —but not microglia— in a preclinical model of multiple sclerosis

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Multiple sclerosis (MS) is an irreversible, chronic and inflammatory demyelinating disease of the central nervous system (CNS) characterized by the loss of myelin (i.e. demyelination). The demyelinated regions (or lesions) are focal brain areas that undergo an inflammatory gliosis leading ultimately to neuronal death. Pannexin 1 (Panx1) channels are ubiquitously expressed in CNS, facilitating ATP release from intracellular to extracellular space in neurons and glial cells. Panx1-channel activity has been largely involved in neuroinflammatory and neurodegenerative diseases, including MS. However, the mechanisms underlying the role of these channels have not been fully described. Here, we investigate the effect of intranasal Probenecid, a Panx1-channel blocker, on astrocytes, microglia and oligodendrocytes in a preclinical model of MS, based on the stereotaxic injection of lysolecithin (LPC, a demyelinating agent) into CNS white matter tracts. As expected, at the peak of demyelination both astrocytes and microglia showed an inflammatory phenotype associated with myelin loss. However, when animals were treated with nasal Probenecid, both myelin loss and the astrocytic gliosis response were reduced significantly, while microglia were not susceptible to this treatment. Together, these results suggest an association between the Panx1-channel activity and the inflammatory response of astrocytes during demyelination in a pathological context such as MS.

Keywords: Pannexin 1, Inflammation, Myelin, Glia, Astrocytes

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Evaluation of treatment with metformin, insulin, lixisenatide, and photobiomodulation in an in vitro model of diabetic retinopathy

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Diabetes Mellitus affects 10% of the global population. Upon diagnosis, 15-20% of people present with diabetic retinopathy (DR), a microangiopathy characterized by neuronal apoptosis, retinal inflammation, oxidative stress, and vision loss. Current treatments involve invasive procedures, making it urgent to improve the therapeutic landscape. Photobiomodulation (PBM) has been shown to reduce inflammation, oxidative stress, and neuronal apoptosis in various retinal pathologies. However, in DR, the effect of PBM has not been compared with diabetes medications. The aim of this study was to evaluate the impact of PBM and conventional treatments for diabetes mellitus: insulin, metformin, and lixisenatide, in organotypic retinal cultures exposed to high glucose concentrations. Using confocal microscopy, TEM, MitoSOX assay, and immunofluorescence for the assessment of NF-kB, VEGF, and GFAP, the progression of damage under different conditions was evaluated. The results suggest that lixisenatide is effective in preventing the thinning of the ganglion cell layer and reducing mitochondrial superoxide. On the other hand, photobiomodulation reduced DNA fragmentation and increased NF-kB expression, suggesting it may inhibit neuronal apoptosis and promote NF-kB-mediated neuroprotective signaling.

In conclusion, lixisenatide is the most effective drug for inhibiting early neuronal degeneration in DR. Additionally, photobiomodulation could provide retinal neuroprotection, suggesting that research on the combined effects of both treatments would be of great interest.

Keywords: Photobiomodulation, Diabetic retinopathy, Diabetes mellitus

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Antioxidant activity and neuroprotective effects of Xenophyllum poposum from the Atacama Desert: Implications for Parkinson's Disease

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Parkinson's disease (PD) is the second most common neurodegenerative disorder among elderly people, characterized by non-motor and motor symptoms. Motor symptoms (MS) emerge after the progressive loss of 40-50% of dopaminergic neurons (DNs) from *Substantia Nigra* (*SN*). Multiple cellular and molecular mechanisms contribute to PD pathogenesis. Evidence suggests that oxidative and nitrosative stress (OxS/NS) plays a pivotal role in the degeneration of DNs. Current treatments for PD target MS management instead of halting neuronal degeneration, which begins long before the onset of MS. Therefore, alternative therapies are required to prevent, halt, or slow down the neurodegenerative progression of PD. Exogenous antioxidants have been proposed as a strategy to neutralize radical species implicated in OxS/NS. *Xenophyllum poposum* (*Xp*), an endemic plant from the Atacama Desert, has been traditionally used by Andean communities for medicinal purposes. The presence of flavonoids and p-hidroxyacetophenones derivatives in *Xp* suggests its potential antioxidant and anti-inflammatory activities. However, studies on its biological activity and neuroprotective effects remain limited. This study shows that *Xp* hydroalcoholic extract (HAE-Xp) has a higher *in vitro* antioxidant capacity than other extract sub-fractions, with no cytotoxic effect observed on Schneider-2 and SHSY-5Y cells at different concentrations. Preliminary experiments using a *Drosophila* PD model, revealed that HAE-Xp treatment partially improved the climbing ability of PD flies. These findings indicate that *Xp* extracts may exert a neuroprotective effect in a PD fly model, likely through its antioxidant activity, highlighting the use of this model for rapid screening of potential therapeutic compounds for PD.

Keywords: Parkinson's disease, neurodegeneration, Xenophyllum poposum, antioxidant, Drosophila melanogaster

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Reactive Astrogliosis and Epilepsy: Modulation of network dynamics by astrocytes

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Astrocytes modulate synaptic transmission, actively participating through gliotransmission, and having effects on working memory and behavior. Morphological and functional alterations of astrocytes, a phenomenon called reactive astrogliosis, have been described in several pathologies of the nervous system. In particular, reactive astrogliosis has been observed in patients with epilepsy, and empirical evidence suggests that modulation of astrocytic activation is related to the development of seizures. However, it is not understood how neuron- astrocyte interactions at the synaptic level produce changes at the level of brain microcircuits, and how this may be related to the neuronal hyperactivity and hyper synchronization observed in epileptogenic activity. In this work we develop a computational model of networks with neuron-astrocyte interactions capable of simulating the dynamics of a cortical neuronal microcircuit. To understand the effect of reactive astrogliosis on the emergence of network dynamics, we studied the effect of an increased overlap of astrocytic territories, the dysfunction of gliotransmission at the synaptic level, and impairment of neuronal intrinsic adaptation mechanisms. These alterations lead to epileptic-like network dynamics, with neuronal hypersynchronization and changes in the spectral power of the local field potential. This suggests that the alteration of astrocyte-synaptic interaction can modulate the occurrence of high frequency oscillations in brain microcircuits in the context of epilepsy.

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The TASK-1/TASK-3 channels activator JG-C3-98 reduces painful sensitivity induced by acute irritant stimulation and chronic peripheral nerve injury

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The K2P channels TASK-1 and TASK-3 have a crucial role in primary afferents of the somatosensory system, contributing to the regulation of cold sensing, mechanosensitivity, and pain. We have previously shown that activating TASK-1/TASK-3 channels using JG-C3-98 shifts the thermal threshold of cold thermoreceptor neurons to higher temperatures and reduces the maximal mechanically evoked responses of mechanosensitive neurons in culture. In this study, we have explored the effect of local TASK-1/TASK-3 activation by JG-C3-98 in mice *in vivo*. Using acute irritant stimulation of peripheral nerve endings with allyl isothiocyanate (AITC), we found that activating TASK-1/TASK-3 channels by local administration of JG-C3-98 in the hind paw decreases the AITC-evoked nociceptive responses. In addition, in a model of neuropathic pain induced by chronic constriction of the sciatic nerve, we observed that cold allodynia resulting from this form of peripheral nerve damage is also reduced by local administration of JG-C3-98 in the hind paw. Altogether, these results suggest that this novel and specific activator of TASK-1 and TASK-3 channels could be a potentially effective pharmacological tool to tackle these forms of acute and chronic pain.

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Empathy Across the Lifespan: A Comparative Study of Sensorimotor and Physiological Responses in Young and Older Adults

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Background: Empathy evolves across the lifespan, profoundly influencing social relationships and overall well-being. Recent studies indicate that older adults display stronger empathic responses compared to young adults. While most research on changes in empathy over time has relied on psychometric approaches, this study aims to compare the physiological and sensorimotor responses between young and older adults.

Method: 91 healthy participants (44 young adults and 47 older adults) watched one-minute videos designed to evoke negative empathy (athletes experiencing accidents during extreme sports), positive empathy (athletes achieving sports goals), and neutral responses (home furnishings). Data were collected using a force platform and electrodermal and heart electrodes. Self-report questions were administered after each stimulus to assess emotional self-perception (valence and arousal).

Results: Results from sensorimotor analysis revealed that the older adult group showed significantly higher values in postural variables compared to the young group, with increased postural instability, larger sway amplitude, and higher sway velocity. In addition, older adults had higher scores in the self-perception of empathic stimuli (valence and arousal) than young adults. In contrast, young adults exhibited more intense physiological responses, including heart rate variability, respiratory cycle variation, and electrodermal activity.

Conclusions: Older adults experience a more intense sensorimotor response when confronted with various empathic situations. In contrast, young adults tend to show greater physiological activation in response to empathic stimuli, which could be linked to changes in the sympathetic nervous system associated with aging.
Keywords: Empathy, Lifespan, Sensorimotor responses, Physiological responses, Aging

Adolescent Sucralose Intake Impairs Adult Prefrontal Cortical Inhibitory Synaptic Transmission in Mice.

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Background: Adolescence represents a critical period of neurodevelopment, during which the prefrontal cortex (PFC) undergoes substantial remodeling and energy demands increase significantly. Non-caloric sweeteners (NCS), particularly sucralose, have been widely adopted as a means of addressing concerns about excessive caloric intake. Nevertheless, the impact of NCS on adolescent neurodevelopment remains understudied.

Objective: To investigate the impact of adolescent sucralose consumption on adult PFC inhibitory synaptic transmission in adult mice.
Methods: We administered sucralose to adolescent mice and assessed PFC GABAergic transmission in adulthood using electrophysiological techniques.

Results: The intake of sucralose by adolescent mice resulted in a significant reduction in both spontaneous and evoked inhibitory synaptic transmission frequency in the adult PFC.

Conclusions: The findings of this study suggest that the consumption of sucralose during adolescence impairs GABAergic transmission in the adult PFC, potentially affecting synaptic plasticity. This underscores the need for caution in the use of NCS among adolescents and highlights the importance of further research on the neurodevelopmental effects of NCS.

Implications: These results contribute to the growing body of evidence regarding the potential risks of NCS consumption during critical developmental periods and may inform future dietary guidelines for adolescents.

Keywords: sucralose, cortexprefrontal, adolescence, GABAergic transmission

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Effect of chronic administration of Riluzole and methylphenidate on hippocampal behavior and synaptic function in a mouse model of attention deficit

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Attention-deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children, characterized by hyperactivity, impulsivity, and impaired attention, most often treated with methylphenidate (MPH), atomoxetine, or D-amphetamine. Recently, using the prenatal nicotine exposure (PNE) model of ADHD, we found that PNE mice have decreased numbers and delayed maturation of dendritic spines on hippocampal CA1 neurons. We also found that MPH restores the learning and memory deficits and synaptic plasticity observed in ADHD mice by inducing spine maturation and insertion of calcium-permeable AMPA receptors, restoring the abnormal behavior associated with the disorder without restoring the lower density of dendritic spines. We therefore hypothesized that a combination of a spinogenic drug with MPH could provide a more complete recovery of the deficits found at the neuronal level in this ADHD model. Riluzole, a glutamate modulator that increases oxidative metabolism and brain-derived neurotrophic factor (BDNF) production and is used as a neuroprotectant in amyotrophic lateral sclerosis (ALS), has been proposed as a spinogenic in the hippocampus. Furthermore, Riluzole did not restore TBS-dependent LTP in these animals. Taking this evidence into account, we propose to study the effect of Riluzole/MPH co-treatment on the recovery of cognitive and synaptic plasticity impairments in ADHD mice. To understand the cellular and molecular mechanisms underlying the effect induced by Riluzole plus methylphenidate, our proposal focuses on investigating the synergistic action of Riluzole and MPH on ADHD behavior and synaptic plasticity, combining behavioral, pharmacological, electrophysiological, cellular, and molecular approaches comparing controls, PNE, and treated animals.

Keywords: Sinaptic Platicity, Hippocampus, ADHD, Methylphenidate, Riluzole

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Wireless electrocochleography in awake chinchillas: A model to study crossmodal modulations at the peripheral level

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The electrocochleography (ECochG) has been a primary tool in audiologic medicine and neurotology. This wouldn't be possible without the development of this tool in animal models. In our laboratory, the ECochG has opened the path to a deep understanding of the auditory efferent pathway. Using chinchillas as a model, we provided evidence of the corticofugal modulation of auditory-nerve and cochlear responses during visual attention and working memory, but at this point, we did not have recordings of corticofugal modulation in peripheral structures of the auditory pathway during cross-modal (auditory and visual) stimulation. For this, we developed a wireless ECochG system to record compound action potentials of the auditory nerve (CAP), cochlear microphonics (CM), and round-window noise (RWN) in awake chinchillas during a cross-modal stimulation paradigm. We obtained quality recordings from 4 awake chinchillas with the wireless system to compare with the recordings of 6 anesthetized chinchillas with a wired system. We did not find significant differences in CAP and CM amplitudes in response to cross-modal stimulation, com-

pared with single auditory stimulation. On the other hand, RWN recordings, which are related to the spontaneous activity of the auditory nerve, were modulated by the cross-modal stimulation, suggesting that this type of modulation can modulate the spontaneous activity of the auditory nerve, but not the evoked one. Given the small sample size, these results should be interpreted cautiously. Future experiments are necessary to support these conclusions. Moreover, we introduce the wireless ECochG in animal models as a useful tool for translational research

Keywords: Electrocochleography, auditory pathway, efferent modulation, crossmodal stimulation

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TRPA1 channels and sex specific differences in mechanical hypersensitivity in a mouse model of painful diabetic neuropathy

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Diabetes mellitus is a chronic disease characterized by elevated glucose levels in the bloodstream and insulin deficiency that can lead to diabetic neuropathy (DNP), often resulting in neuropathic pain. In primary sensory neurons, several TRP channels have a crucial role in detecting and transducing innocuous and noxious chemical, thermal, and mechanical stimuli in physiological and pathological states. Among them, TRPA1 channels are pivotal in nociceptor function and have been implicated in neuropathic pain. However, the specific role of this polymodal channel in the development of painful DNP remains unclear. In this study, using a mouse model of type I diabetes mellitus (T1DM) induced by streptozotocin (STZ) and combining behavioral assays and functional recordings in cultured dorsal root ganglion (DRG) neurons, we investigate the molecular and cellular mechanisms underlying peripheral hypersensitivity in painful DNP. We found that hyperglycemia in this model of T1DM was predominantly observed in male mice, and mechanical hypersensitivity significantly increased in males during the first two weeks post-STZ treatment. In contrast, female mice exhibited lower glucose levels and delayed disease progression, showing a late onset of mechanical hypersensitivity correlating with their slower rise in glucose levels. In male mice, Ca^{2+} imaging of DRG neurons revealed an increase in the neuronal population responding to the TRPA1 agonist AITC in the second week of T1DM. These preliminary findings suggest a sexual difference in the development of mechanical hypersensitivity in T1DM, potentially linked to an increase in the functional expression of TRPA1 in a subset of primary somatosensory neurons.
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Dynamic changes of phrenic inspiratory bursts in neonatal mice

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The recruitment of phrenic motor neurons (PMNs) depends on the balance between their intrinsic electrophysiological properties and external influences such as ionic environment and synaptic inputs, in particular the Respiratory Pattern Generator (RPG). The activity of PMNs in response to stimuli applied to the RPG has not been systematically compared. We recorded the phrenic inspiratory bursts in the *en bloc* preparation from neonatal mice before, during, and after stimulation of the RPG with different neuromodulators. We evaluated classical respiratory rhythm variables and we analyzed the spectral time frequency domain of the inspiratory activity using continuous wavelet transformation and complexity calculations. The administration of D-serine (100 µM), or substance P (1 µM), or the hypercapnic acidosis of the superfusion medium bathing the brainstem produced similar changes in the respiratory rhythm variables: increased respiratory frequency, due to a shorter expiratory time, with no changes in inspiratory time, amplitude, and area under the curve of the integrated inspiratory signal. However, these stimuli produced selective effects upon the inspiratory burst. With D-serine and substance P, the high energy recruitment of PMNs occurred at the first and second half of the burst (possibly slow (S) and fast fatigue-resistant (FR) fibers) whereas with hypercapnia, PMNs were recruited at the beginning of the inspiratory burst, with discharge frequencies possibly of slow (S) fibers. These results reveal stimulus-dependent responses of the neuronal network that controls breathing, with no variation in the number of active MNFs, but rather the time course of their recruitment, i.e., inspiratory respiratory muscle contraction.

Keywords: phrenic motor neurons, wavelet transform, complexity, hypercapnia, control of respiratory rhythm

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Characterization of Cx36 in the mouse Medial Amygdala

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Introduction: The medial amygdala (MeA) is crucial for regulating social and emotional behaviors. It integrates and processes social information through projections to various brain regions, such as the hypothalamus. Both the MeA and hypothalamus are sexually dimorphic, which accounts for differences in social behavior between males and females. Additionally, these regions have a high density of electrical synapses containing connexin 36 (Cx36), indicating a highly synchronized neuronal network. In this study, we characterized Cx36-expressing neurons in the amygdala and investigated the structural changes in Cx36 following social isolation.

Methods: Female mice were either controls or subjected to 2 months of social isolation. The mice were then either dissected or perfused with paraformaldehyde (PFA). Connexin 36 (Cx36) levels were assessed using quantitative RT-PCR (qRT-PCR) and immunohistochemistry on frozen coronal sections. The number and area of Cx36 puncta were quantified using Imaris software.

Results: Under normal conditions, Cx36 was highly expressed

in calbindin- and NPY-positive neurons. After 2 months of social isolation, although the density of Cx36 clusters increased in the region, the total number of clusters decreased compared to socialized mice.

Discussion: Our results suggest that social isolation leads to the remodeling of Cx36 puncta, likely as a form of neuronal plasticity, by preserving only the essential electrical synaptic connections.

Keywords: Social Behaviour, Amygdala, Electrical Synapses, Connexin

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Role of NKCC1 cotransporter on synaptic plasticity of the dentate gyrus in an animal model of autism

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In autism spectrum disorder (ASD) there are alterations in social interaction, spatial memory, and cognitive mapping, which are related to hippocampal function.

In animal models of ASD, in CA3 hippocampal neurons GABA is excitatory after birth due to a higher intracellular chloride concentration, similar to temporal lobe epilepsy, due to the cation chloride cotransporters NKCC1 and KCC2, involved in the influx and efflux of this anion, respectively.

Given that a significant proportion of patients with ADS present epileptic seizures, we study the participation of NKCC1 in excitatory GABA in the dentate gyrus on synaptic plasticity, in the animal model of valproate.

In acute brain slices, extracellular field recordings were performed not to perturb intracellular chloride concentration. Input-output relationships of fEPSP showed a shift to the right in the presence of NKCC1 blocker bumetanide in control and VPA animals, suggesting that this cotransporter is involved in excitatory neurotransmission. Long-term potentiation (LTP) in VPA animals showed a faster induction and a higher potentiation level compared to the control group, suggesting higher excitability. This effect was decreased by blocking NKCC1, suggesting its participation in excitatory plasticity. In both groups, the LTP induction altered the paired-pulse ratio stimulation due to a presynaptic component in LTP unaffected by bumetanide.

These results show that NKCC1 activity is present in the dentate gyrus in control animals and affects some synaptic plasticity parameters in VPA group, which can explain some of the synaptic alterations in this condition.

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Unraveling the role of glycine receptor in immune inflammatory response: A molecular characterization on macrophage cell line.

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Macrophages, the surveillance cells of the innate branch of the immunity system, play a critical role in the regulation of diverse physiological processes, from tissue regeneration to the development of inflammatory responses. In a functional point of view, depending on the tissue-specific micro-environmental stimulus, they can be derived in macrophages type M1 (pro-inflammatory) or type M2 (anti-inflammatory). For this purpose, they express a wide variety of functional receptors in the plasmatic membrane, where recently the role played by members of the superfamily of ligand-activated pentameric ion channels (pLGIC), has gained a significant relevance. Even though several experimental data has been reported the expression of the glycine receptor (GlyR), in different macrophages populations, the physiological role in these cells is still unknown. In the present work we characterize the expression and function of GlyRs using the RAW264.7 macrophage line as a cellular model using immunostaining, molecular and electrophysiological techniques. In addition we tested the expression of GlyRs under activation conditions using endotoxin (LPS) treatment. We detected the expression of alpha2 and alpha3 subunits by RT-PCR without the expression of alpha1 or beta subunits. Also, our immunocytochemical experimental results show that the RAW264.7 macrophage expresses GlyRs at the level of the plasma membrane. Overall, our experimental data increase the knowledge about the role of the GlyRs, a receptor typically inherent to the central nervous system, in the activation of the immune response mediated by macrophages.

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Control of unitary conductance of the GABA type A receptors (GABAARs) by phosphorylation: Impact on the function and sensitivity to allosteric modulators.

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The gamma-aminobutyric acid type A receptors ($GABA_A$Rs) belong to the family of pentameric ligand-gated ion channels (pLGICs). The functional pentamer is formed by the arrangement of five subunits surrounding a central chloride-permeable pore. Each subunit is composed by an extracellular domain (ECD), a transmembrane domain (TMD) and a large intracellular domain (ICD). The function of the $GABA_A$Rs can be modulated by several protein kinases targeting serine residues located in the ICD. Even though several experimental data had shown that phosphorylation reduced the maximum currents in the $GABA_A$Rs, the molecular mechanism underlying this effect is still controversial. One of the most plausible explanation for this phenomena is the reduction in the unitary conductance of the channel. To test whether the introduction of a negative charge in the ICD impacts on the unitary conductance of the $GABA_A$Rs composed by alpha 1, beta 2 and gamma 2 subunits, we performed single-channel electrophysiological recordings in $GABA_A$Rs carrying the phosphomimetic mutation S410E in the beta 2 subunit. Interestingly, the phosphomimetic mutation reduced the unitary conductance of the channel but displayed no impact at the macroscopic level. Furthermore, we tested the effects of two recognized GABAergic positive allosteric modulators (PAMs), propofol and allopregnanolone. Remarkably, both PAMs potentiated the phosphomimetic mutants through a mechanism that involved the recovery of reduced unitary conductance. Overall, our results suggest that the inhibition of the $GABA_A$Rs function by phosphorylation events could be explained by a significant reduction in the unitary conductance. Moreover, the reduced conductance can be restored by PAMs.

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Generation of a reverse genetic system to evaluate functional alterations of PrP(C) induced by the deletion of the C-terminal portion of helix 2

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Prion diseases are fatal neurodegenerative pathologies caused by prions, which induce changes in the normal cellular prion protein (PrP^C), leading to an abnormal conformation known as PrP^{Sc}. During pathogenesis, prions replicate through an autocatalytic process in which PrP^{Sc} induces the conformational change of PrP^C, resulting in the accumulation of large aggregates. Numerous studies have been conducted to identify key regions in the pathogenic conversion, with one strategy being the modification of the PrP^C sequence. In fact, serial deletions in the C-terminal end of the H2 of PrP^C, to determine if the integrity of the residues in the protease-resistant domain is necessary for prion conversion, have shown that the conversion ability and strain-specific information transfer are preserved despite the shortenings. Other observations regarding these mutants showed that while they retained their ability to convert to PrP^{Sc}, they exhibited some alterations in their conversion pattern and strain permissiveness. These observations suggest that anomalies in the mutants pre-exist the conformational change and could affect the normal function of PrP^C. To determine the effect of the C-terminal deletion of H2 on the function of PrP^C, we used RK13 cells to stably express the deletions Δ193-196 and Δ193-197 obtained by site-directed mutagenesis, as a model to characterize the function of PrP^C. Our studies suggest that these mutants exhibit altered cell adhesion patterns.

Keywords: prion-disease

Funding: Fondecyt 1211095

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POSTER SESSION II

Chairs: Cheril Tapia Rojas - Sebastián Loyla - Constantino Dragicevic

The Role of the Spine Apparatus in Voltage Compartmentalization of Cortical Synapses

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Dendritic spines are specialized postsynaptic compartments that play a fundamental role in central nervous system communication. Spines serve as biochemical insulators, integrating and segregating postsynaptic chemical responses, while also functioning as electrical compartments. This electrical isolation may be attributed to their morphology and organelle content, which includes a small head and a thin neck. The mechanisms underlying this electrical compartmentalization are unknown, but the internal content of the dendritic spine could explain this effect. We studied the presence of an organelle called the spine apparatus that corresponds to a domain of the smooth endoplasmic reticulum which extends from the dendrites and invades the neck of some spines. While its molecular composition is largely unknown, a protein called synaptopodin has been described associated with this organelle. To analyze the role of the spine apparatus in voltage compartmentalization in dendritic spines, we designed synaptopodin probes to specifically label the spine apparatus *in vivo* and employed optogenetics combined with voltage imaging measurements to test spine compartmentalization. These constructs were electroporated *in utero* into CD1 E15 embryos to allow their expression in pyramidal neurons of the somatosensory cortex. In adult animals, in vivo voltage imaging was obtained using two-photon microscopy, and subsequently, histological processing of brain tissue to characterize these sensors and probes by high-resolution confocal imaging. By using these tools, we will define how specialized intracellular organelles, such as the spine apparatus, contribute to the modification of the electrical properties of dendritic spines.

Keywords: Dendritic Spines, Spine Apparatus, Synaptopodin, Voltage Imaging, Two Photon Microscopy

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Differential contribution of residues of the Voltage Sensor Like Domain in the TRPM8 responses to chemical agonists

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TRPM8 is the main molecular entity responsible for detecting cold temperatures in the somatosensory system. This ion channel is activated by cold, cooling compounds such as menthol, voltage, and osmolality rises. TRPM8 is also involved in several pathologies, including cold hypersensitivity in response to axonal damage, dry-eye disease, and several forms of cancer. Although the potential for therapies focused on TRPM8 modulation is promising, the clinical use of known agonists and antagonists has faced some challenges, requiring the development of novel modulators. The rational design and the high-throughput virtual screening could be successful strategies for this task, but they require a comprehensive understanding of how agonists and antagonists modulate TRPM8. To this end, we built a comparative model of human TRPM8 and identified relevant residues for the binding of the TRPM8 agonists menthol, WS-12, and icilin. Our analysis involving molecular docking, molecular dynamics simulations, and binding free energy calculations revealed that several residues of the Voltage Sensor Like Domain (VSLD) play a significant role in the binding of these compounds. To experimentally validate their involvement, we mutated these residues and evaluated the impact of these mutations on the TRPM8 responses using Ca^{2+}-imaging and patch-clamp analysis. Our results showed that these mutations displayed different effects on their responses to WS-12, icilin, and menthol without causing major alterations in TRPM8 cold activation. These findings provide critical clues about the specific contribution of each residue in the TRPM8 activation by these compounds, which would be helpful in the future design of TRPM8 modulators.

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Role of Cdk5 kinase in modulating TRPV1 and TRPA1 and its relevance to afferent activity in murine nodose ganglion neurons.

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Nodose ganglion neurons (NGns) innervate internal organs, like the lungs, heart, and gastrointestinal tract, conveying afferent signals to the central nervous system (CNS). NGns express the transient receptor potential (TRP) channel vanilloid 1 (TRPV1) and ankyrin 1 (TRPA1), which, upon activation by temperature, acidity, and irritant chemicals, increases calcium influx and afferent activity, initiating CNS reflex responses. In addition, Cyclin-dependent kinase 5 (Cdk5) can phosphorylate TRPV1 and TRPA1, thus modulating their function in afferent pathways, like nociception in other sensory ganglia. Our group previously showed that Cdk5, its activator p35, TRPV1, and TRPA1 channels are present in most NGns, suggesting their involvement in sensory modalities besides nociception. We aim to determine whether Cdk5-mediated regulation of TRPV1 and TRPA1 could modulate afferent activity in the NG. Using immunofluorescence and Western blotting, we assessed the expression and co-localization of these proteins in control mice and TNF-a conditional transgenic mice, where Cdk5 activity is elevated. Preliminary results reveal the presence of Cdk5, p35, TRPA1, TRPV1, and phospho-TRPV1 (specifically phosphorylated by Cdk5) in most NGns. Using immunofluorescence,

we found that Cdk5 co-localizes with TRPV1 or pTRPV1 in 30% of NGns, while Cdk5 co-localizes with TRPA1 in 20% of NGns. Additionally, we found a significant increase in immunolocalization of Cdk5 (39%), p35 (148%), TRPA1 (38%), TRPV1 (124%), and phospho-TRPV1 (54%) in NGns of TNF-a conditional transgenic mice as compared with control adult mice. These results suggest that Cdk5 is present and active in NGns and could modulate TRPV1- and TRPA1-mediated responses in visceral afferent pathways.

Keywords: Nodose ganglion, TRPV1 receptor, TRPA1 receptor, Cdk5 kinase, Autonomic nervous system

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Immunomodulatory Role of Astrocyte-Derived Extracellular Vesicles in Macrophage and Microglial Activation Under Stress Conditions

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The traditional view of the brain as isolated from the peripheral immune system is no longer tenable. Stress-induced disorders, such as major depressive disorder, involve the infiltration of blood-derived macrophages into the brain, leading to the activation of resident microglia. During this process, astrocytes release extracellular vesicles (ADEVs), which may play an immunomodulatory role. This study investigates the impact of ADEVs on microglia and macrophages under stress conditions. To emulate stress in vitro, human astrocytes (CCF-STTG1) were incubated with cortisol, and cort-ADEVs were recovered. These were used to stimulate microglial (HMC3) cell lines and monocyte-derived human macrophages to perform flow cytometry and RT-qPCR analyses. In rats, repetitive stress was induced through 10-day movement restriction. Results showed that incubation of macrophages with control ADEVs reduced the M1 (inflammatory) phenotype and increased the M2 (anti-inflammatory) phenotype compared to untreated cells. Similarly, pre-incubation of microglia with control ADEVs diminished the inflammatory response to LPS, a response further enhanced by cortico-ADEVs. The miRNAome of ADEVs revealed Macrophage Immunometabolism Regulator protein (MACIR) as a key miRNA-regulated target, with LPS stimulation reducing MACIR expression in microglia. MACIR was also downregulated in the hippocampus of stressed rats. These findings suggest that ADEVs have an overall anti-inflammatory effect, potentially counteracting stress-induced brain adaptations. MACIR emerges as a novel target for modulating macrophage and microglial activation during stress, offering new insights into the immunomodulatory mechanisms of ADEVs in the brain.

Keywords: neuroinflammation, stress, extracellular particles

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Immunomodulatory Role of Astrocyte-Derived Extracellular Vesicles on Microglial Phagocytosis in Response to Porphyromonas gingivalis Virulence Factors

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Astrocyte-derived extracellular vesicles (ADEVs) have recently emerged as critical modulators of neuroinflammation, the inflammatory response in the central nervous system. These vesicles contain microRNAs such as miR-26a, crucial in opposing neuroinflammation by downregulating relevant protein targets. Peripheral pathogens like *Porphyromonas gingivalis* (*Pg*), an oral pathogen associated with chronic periodontitis, and their virulence factors lipopolysaccharide (LPS) and outer membrane vesicles (OMVs) may trigger neuroinflammation by activating brain microglial cells. In turn, over-activated microglia may migrate and engulf synapses, contributing to neuronal damage. We hypothesize that ADEVs attenuate the microglial phagocytosis induced by *Pg* virulence factors depending on miR-26a. Microglial cell line HMC3 was employed to analyze the effects of ADEVs on microglial phagocytosis of rat brain synaptosomes under *a* neuroinflammation model induced by *Pg* OMVs and LPS. We showed that ADEVs significantly decrease microglial synaptosome phagocytosis induced by *Pg* LPS and OMVs. Mimicking and inhibiting miR-26a activity with synthetic oligonucleotides significantly modify synaptosome phagocytosis of microglia induced by virulence factors and its regulation by ADEVs. These results highlight the potential of ADEVs and miR-26a to modulate neuroinflammation induced by *Pg* virulence factors.

Keywords: Neuroinflammation, microglia, extracellular vesicles, astrocytes, phagocytosis

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Sex-related differences in Lonp1 proteolytic activity and its relationship with unfolded proteins and mitochondrial dysfunction in the hippocampus of aged C57BL/6J mice

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Introduction: Aging is a process characterized by mitochondrial dysfunction and the accumulation of abnormal proteins in the hippocampus; however, the sex differences related to these distinctive aging features are still unknown. The link between these processes could be the mitochondrial protease Lonp1. Lonp1 is responsible for maintaining the mitochondrial proteome and, consequently, the functionality of mitochondria. We investigated Lonp1 expression and proteolytic activity in the hippocampus of aged mice, focusing on sex differences and their correlation with mitochondrial dysfunction and abnormal protein accumulation in the hippocampus.

Material and methods: Total lysates and mitochondria-enriched fractions were isolated from the hippocampus of 3- and 20-month-old female and male C57BL/6J mice. Biochemical analyses and fluorescence and luminescence assays were performed to assess mitochondrial function indicators and levels of some mitochondrial chaperones and proteases, including Lonp1. In addition, we indirectly and directly measured the proteolytic activity of Lonp1.

Results: We observed that 20-month-old mice showed accumu-

lation of unfolded proteins, decreased mitochondrial function and expression of chaperones and proteases, including Lonp1. Proteolytic activity of Lonp1 is also reduced in the aged hippocampus. Interestingly, a more severe reduction in several chaperones and proteolytic activity of Lonp1 was observed in aged male mice.

Discussion: We propose that aging affects protein homeostasis and mitochondrial function differently between sexes, with male C57BL/6J mice potentially being more vulnerable to age-related mitochondrial dysfunction. These findings underscore the need to explore sex-specific mechanisms that could inform targeted therapies for age-related conditions.

Keywords: Aging, Lonp1, Mitochondrial Dysfunction, Sex-related differences

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A library of electrophysiological responses in plants. Conduction velocity across species

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Electrical signaling is ubiquitous across life domains. We have previously demonstrated the presence of wound or tactile electrophysiological responses in a variety of both rapid movement (Sensitive Mimosa, Venus Fly Trap) and non-rapid movement plants (Tomato, Mint, Rosemary, etc.). Here, we measured the conduction velocity of impulse propagation in the same group of species plus others. We found that rapid movement plants had conduction velocities >3x faster (~30 mm/s) than non rapid-movement plants (~5-10 mm/s). We also note that plant conduction velocities are up to 10,000x slower than neuron conduction velocities (1-90 m/s). Whether plant impulse propagation is passive or active is an area of continued investigation.

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Anxiety and social behavior as predicting factors of empathic behavior in rats

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Psychopathy is an antisocial personality disorder mainly characterized by lack of empathy, guilt or remorse and a insensitive to the harm caused to anothers. Since it is not considered a disease, rather a personality disorder and the causes are still unclear, no treatment still exist which males it a problem for individual and society.
The present study aims to identify behavioral predictors of low empathic behavior, a cardinal sign of psychopathy. To test this idea adult rats were tested for anxiety levels, locomotion and social interaction behavior to then explore the relationship between this behavioral variables and the level of empathic behaviour which was measured by conducting an operating conditioning task were rats can decide either or not to damage a companion.
We found that animals with higher locomotion or higher number of social interactions are those with lower empathic behavior, while no relationship was found with anxiety levels.

Keywords: Psychopathy, Empathy, Anxiety, Locomotion, social interaction
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Sensory Multibrain Stimulation Enhances Cooperative Behavior

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Most hyperscanning studies show inter-brain coupling between individuals engaging in social interactions, posing such inter-brain coupling as a mechanism supporting social activity. However, as social interactions afford similar stimulation for the involved subjects, it has proven difficult to test whether the observed synchrony corresponds to a genuine neural mechanism or is rather spurious due to similar stimulation. To address this problem, we implemented for the first time a multibrain sensory stimulation paradigm, which allowed us to manipulate interbrain coupling between interacting partners in terms of frequency and phase. We added flickering stimuli to a classical cue-target cooperation task to visually entrain sixteen same-sex dyads in four blocks. At each block, participants were entrained at 16 Hz or 40 Hz, and either synchronously or asynchronously (delayed flickering onset) between them. Sixteen same-sex control dyads performed the same task without any entrainment. We found that: i) overall cooperation rates were significantly higher for the entrained group compared to control group; ii) cooperation rates under 16 Hz synchronous entrainment was significantly higher than under 16 Hz delayed-onset and iii) 40 Hz entrainment protocols had no effect over cooperation rates. Additional permutation tests against shuffled pseudo-dyads further confirm the observed differences. Using fine-controlled, rhythmic sensory stimulation, we demonstrate that affecting the degree of interbrain coupling between interacting partners yields clear changes in their interpersonal behavior, thus supporting the notion that inter-brain coupling is not a spurious phenomenon and, conversely, is a genuine neural mechanism supporting social interactions.

Keywords: interbrain coupling, multibrain stimulation, cooperation, hyperscanning, sensory entrainment

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The role of tectofugal pathway in avoidance behaviour

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Detection and avoidance of threats are necessary features of instinctive, defensive behaviors. Regarding vision, evidence indicates that the superior colliculus (SC) and its ascending tectofugal pathway are critical components of the neural architecture organizing defensive maneuvers. Moreover, abnormal activation of this pathway might be involved in social phobias and several anxiety disorders, which underlines the importance of understanding the neural processes by which this pathway detects threats and elicits adaptive responses. In particular, the functional roles of the thalamic relays of the SC, the rostral (PulR) and caudal (PulC) pulvinars, are far from clear. In this study, we made extracellular recordings from these nuclei, in head fixed, awake mice, while different visual stimuli were presented on video monitors, covering most of the visual field. We found that neurons in the caudal pulvinar had large receptive fields and responded strongly with sustained firing to small moving targets and to expanding discs simulating an approaching threatening stimulus. Interestingly, they also responded to stimuli presented in the monocular field of either eye, possibly as a result of the bilateral projection from the superior colliculus to this nucleus. Further experiments will compare these results with recordings in PulR, which does not receive a binocular projection from the SC, and in the posterior temporal area (TP), the primary cortical target of the caudal pulvinar. Overall, our results support the participation of PulC of the tectofugal pathway in defensive behaviors and highlight the possible role of binocular interactions in shaping these behaviors.

Keywords: tectofugal pathway, caudal pulvinar, awake mice, Avoidance behavior, visual system

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Executive Functions and their Relationship with Age: Insights from a Novel Neuropsychological Assessment Battery in Children - A Pilot Study.

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Executive functions (EFs) are cognitive processes that help individuals manage and coordinate their thoughts and actions to achieve goals. EFs include planning, organizing, initiating, and monitoring actions, and have been found to improve with age due to the maturation of the brain, especially during childhood. Therefore, our correlational study sought to determine the relationship between the performance in executive functions and age in 79 children (36 girls, 45.6%) throughout development, between the ages of 6 and 12 (mean = 9.25; SD = 2.05), using a battery designed in Chile: BEFE (*Batería de Evaluación de las Funciones Ejecutivas*: Executive Function Assessment Battery) based on traditional neuropsychological tests to evaluate Working Memory, Inhibitory Control, Cognitive Flexibility, and Planning skills. Our results showed various correlations between the variables age and performance in various behavioral parameters, demonstrating an increase in the number of correct responses (positive correlation) and/or a decrease in errors (negative correlation) with age (6 to 12) in the subtests that correspond to dimensions of Cognitive Flexibility (Semantic and Phonological Fluency, Card Sorting Game, and Tracing Tasks), Inhibitory Control (ENA-F and Sentence Completion), Working Memory (Audio-verbal WM Forward and Ordering, and Visuospatial WM Forward and Backward), and Planning (La Portada de Antofagasta and FISA Maps). These results are consistent with previous empirical evidence and support the notion of a developmental relationship between EF performance and age. Additionally, this study contributes to understanding EF development in culturally specific contexts, highlighting the importance of contextually relevant assessment tools in evaluating cognitive development.

Keywords: Executive functions, neurodevelopment, neuropsychological assessment.

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Coupling of Pupil Linked Arousal and Neural Scale-Free Dynamics under Variable Cognitive Load

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Pupil diameter is a known indicator of alertness, shedding light on attention mechanisms. According to the Posner and Petersen model, attention comprises distinct networks: alertness, orientation, and executive control. The executive network particularly links attentional capacities with executive functions. This study investigates the relationship between pupil-linked arousal and neural scale-free dynamics under varying cognitive load. Prior research emphasizes the significance of aperiodic brain activity in capturing fluctuations in excitation-inhibition (E/I) balance, crucial for cognitive processing. We integrate EEG and pupillometry to examine whether the aperiodic exponent—a measure of 1/f noise in the power spectrum—correlates more strongly with pupil diameter as cognitive load increases, thereby elucidating the link between the LC-NE system and neural gain.
Participants perform a working memory task with varying cognitive load while EEG and pupil data are recorded. We aim to determine how shifts in the aperiodic component of neural activity correspond to changes in pupil-linked arousal. We hypothesize that under higher cognitive load, characterized by increased task demands, the aperiodic exponent will correlate more strongly with pupil diameter, suggesting that scale-free dynamics provide a robust marker for arousal-driven neural modulation.
Preliminary results (n = 16) show that higher cognitive load significantly increases pupil dilation, consistent with previous research. We expect EEG findings to reveal decreased low-frequency and increased high-frequency activity, predominantly affecting the aperiodic component, especially in frontal cortical regions. If confirmed, these findings will enhance our understanding of how cortical arousal mechanisms are reflected in scale-free neural activity and influence cognitive performance.

Keywords: aperiodic activity, arousal, norepinephrine

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Integration of cognitive and somatic activity during deliberation reflected in pupillary dynamics.

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Decision-making is an essential process in daily life, present in both trivial and complex contexts with potentially significant impacts. Although there are various theoretical and experimental approaches to this process, a clear consensus on how we make decisions has yet to be reached. One perspective focuses on the underlying mechanisms, suggesting that mental simulations are activated during the evaluation of options, creating future scenarios. The evidence supporting this theory has focused on cognitive processes such as episodic memory and visual imagery, studied through neuroimaging and EEG, primarily exploring cortical activity. This work focused on the study of decision-making, specifically the autonomic response recorded through pupillometry during preferential decision tasks. The hypothesis was that evaluating options during decision-making generates changes in autonomic activity, manifested through the modulation of pupillary dynamics. An experimental design was implemented that involved preferential decisions about foods familiar to the target population, explored pupillary dynamics in different phases of the decision-making process, and compared responses under different conditions related to the evaluation of alternatives. Pupillary dynamics about preferred and non-preferred options, decision difficulty, and mental imagery were studied. The results suggest differences in pupillary dilation related to preference, the replication of pupillary activity patterns when viewing and imagining alternatives, and modulation of pupillary activity linked to mental imagery. Although no statistically significant differences were found, these findings highlight the importance of integrating autonomic nervous system activity in the study of decision-making.

Keywords: decision making, imagery, pupillometry, mental simulations, autonomic nervous system

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Vagus nerve stimulation and basal forebrain in a mouse model of Fragile X Syndrome

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Vagus nerve stimulation (VNS) has been used as a therapeutic tool to treat epilepsy and depression. Recently, it has been used to treat symptoms in individuals with other neurological conditions, including autism spectrum disorder (ASD), such as social interaction and mood alteration. However, the neurobiological bases of VNS stimulation effect are still elusive. Some evidence suggests that VNS mediates the release of acetylcholine in the brain by activating the basal forebrain (BF), a central cholinergic modulatory and regulatory region. Interestingly, the olfactory system receives vast cholinergic and GABAergic projections from the BF, critical for olfactory discrimination by creating appropriate odor-object representations. Moreover, it has been shown that ASD individuals exhibit anatomical and functional abnormalities in the BF and cholinergic systems. Therefore, in this work, we explored the effect of VNS and basal forebrain activity in a mouse model (*Fmr1* KO) of ASD, Fragile X Syndrome (FXS). *Fmr1 KO* mice have olfactory discrimination deficits and higher thresholds for odorant detection. Thus, we performed single-cell extracellular recordings in the BF of *Fmr1* KO and WT controls while they were actively sniffing during an odor habituation/dishabituation test and studied whether VNS could improve olfactory behavior in these mice. Our preliminary results show a statistically significant increase in BF activity for FXS mice in a free-roaming, caged, and stimulus-free environment. We also found that direct VNS lowers mean arterial pressure and heart rate. A less invasive procedure stimulating the ear vagal afferents, auricular VNS, also tends to decrease mean arterial pressure and heart rate.

Keywords: autism, single cell extracelullar recording, behavior

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Influence of prior activity on inhibitory control failures in children with attention deficit/hyperactivity disorder

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Inhibitory control (IC) is a crucial executive function that enables the suppression of natural impulses and the selection of more appropriate behaviors in various contexts. Deficits in IC are associated with impulsive behavior and difficulties in inhibiting distractions, commonly observed in several clinical disorders, including Attention Deficit Hyperactivity Disorder (ADHD). This study analyzed IC and electrophysiological modulations in children with ADHD using a Go/Nogo task with slow and fast interstimulus intervals (ISIs). The sample included 26 children diagnosed with ADHD and 23 typically developing (TD) children as a control group, all aged between 7 and 13 years.
Results showed that children with ADHD exhibited lower accuracy in correctly inhibiting responses and greater variability compared to the TD group. The EEG analysis identified two event-related potential (ERP) components, N100 and P200, related to perceptual processing and attention. ADHD children showed a reduced amplitude of the N100 component and an increased amplitude of the P200 component in correctly inhibited responses, suggesting greater allocation of attentional resources in these situations. Additionally, TD children adjusted their reaction times according to cognitive load. In contrast, ADHD children did not show significant changes in response speed, indicating deficits in modulating responses based on task demands.
These findings suggest alterations in early perceptual processing of stimuli in incorrectly inhibited responses and deficits in response modulation according to task demands in the ADHD group. This contributes to a better understanding of the neurophysiological basis of ADHD and may have important implications for developing therapeutic interventions.

Keywords: ADHD, inhibitory control, EEG, ERP

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Evaluation of Communication Protocols in Heart-Computer Interfaces for Real-Time Auditory Perception Experiments

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The relevance of brain-computer interfaces (BCIs) has increased significantly, serving roles in rehabilitation, enhancement, and research. In research, neuromodulation can be used as an independent variable to assess the effect of specific biological phenomena on psychological processes. This study explores how communication protocols impact the implementation of a closed-loop system in a heart-computer interface, focusing on analyzing cardiac activity to trigger events in auditory perception experiments.
This work aims to compare the effectiveness and consistency of TCP/IP and LPT communication protocols in implementing a closed-loop system for real-time detection of R-peaks in cardiac activity and their application in the synchronization of auditory stimuli.
Cardiac activity was analyzed using a bipolar lead with Biosemi, employing a TCP/IP communication protocol for real-time detection of QRS complex characteristics, with a focus on R-peak detection. The height of the R-peaks (delta from the baseline) was measured, and the period of occurrence was calculated. These parameters were used to classify cardiac activity in real-time, enabling the transmission of triggers from the recording computer to the stimulus presentation computer. The synchronization system was implemented using a second TCP/IP port and a parallel port in independent trials.
The results indicated that while the LPT port demonstrated greater consistency in signal transmission, its accessibility is limited by hardware availability. In contrast, the TCP/IP protocol showed greater speed in triggering events that do not require extreme precision, such as initiating an experiment.

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An insular view of psychopathy: vasopressin antagonist injection in the insular cortex regulates empathic behavior

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Psychopathy is a personality disorder characterized by antisocial behavior and moral transgression, associated with a lack of empathy towards the distress of others and a high rate of criminality. Clinical interest in psychopathy has increased in recent decades due to the progressive rise in the rate of premeditated crimes, not only in Chile but worldwide. Despite various approaches, there is still no effective treatment for psychopathic individuals, partly because the neurophysiological mechanisms underlying this disorder remain unclear.
In this research, we explore the modulatory role of vasopressin, a neuropeptide involved in the regulation of social behavior, within the insular cortex, region where structural and functional abnormalities have been associated with psychopathic traits and empathic dysfunction. To explore this antecedent, rats were trained in an operant conditioning task in which one of them (the operant) had to decide either to damage or not a companion. Our results showed that blocking vasopressinergic transmission through bilateral injection of an AVP1a vasopressin receptor antagonist in the anterior portion of the insula, induced a dose-dependent decrease in empathy during the task, compared to saline-injected control rats. More specifically, when rats were injected with the antagonist they were more likely to choose to press the lever that gave a foot shock to their companion, despite the other lever was harmless and gave the same reward. This provides new evidence that helps understading a critical aspect of psychopathic disorders and the identification of a potential therapeutic target.
Keywords: Behavior, Empathy, Psychopathy, Insular cortex, Vasopressin

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Short-term effects of high-sugar diets on adult brain neurogenesis

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Introduction: Neurogenesis is the formation of new neurons. In adult mammals, it primarily occurs in the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG). Recently, potential neurogenic niches have been identified in the amygdala (AMY) and hypothalamus (HYP). The AMY in the temporal lobe is crucial for emotions and social behavior, while the HYP regulates the endocrine system and energy balance. This study investigates the impact of high-sugar diets on adult neurogenesis in mice.

Methods: Two-month-old female and male mice were injected daily with BrdU intraperitoneally for 7 days at the start of their diets. They were then maintained on one of three diets: normal chow, high glucose, or high fructose, for an additional month. Weekly weight measurements and glucose tolerance tests were conducted. Neuronal differentiation was assessed in brain sections from the AMY, HYP, and DG using BrdU and NeuN markers, and the POMC-eGFP transgenic mouse line.

Results: Analysis showed the DG had the highest percentage of BrdU+/NeuN+ cells, followed by the AMY, with the HYP showing the lowest. High-sugar diets led to a decrease in BrdU+/NeuN+ cells across all three regions.

Conclusion: High-sugar diets reduce normal neurogenesis rates in the DG, HYP, and AMY.

Keywords: Neurogenesis, Energy balance, Glucose, Fructose

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Childhood Maltreatment: Effects on the Integrity of Cerebral White Matter in Adult Women

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Introduction: Adverse childhood experiences (ACEs) can alter the structure of cerebral white matter during childhood. This study investigates whether these alterations persist into adulthood.

Methods: Sixty-seven women aged 18 to 40 years, without active psychiatric conditions at the time of measurement, were evaluated. They were divided into two groups: 38 with high levels of maltreatment (experimental group, mean MACE = 23.7) and 29 with low levels (control group, mean MACE = 7.4). ACEs were measured using the Maltreatment Adversity Chronological Experience (MACE) questionnaire. Diffusion tensor imaging (DTI) was performed using a Siemens Skyra 3 Tesla scanner with a 2D EPI sequence and a DTI scheme with 90 sampling directions, a b-value of 1000 s/mm², a resolution of 1.875 mm, and a slice thickness of 2.47 mm. The integrity of white matter tracts was assessed by measuring fractional anisotropy (FA), where higher values indicate better integrity.

Results: Compared to the control group, the experimental group showed higher FA values in the left thalamus, along with decreased FA values in the left superior frontal gyrus and the left medial lemniscus and/or left spinothalamic tract.

Conclusion: The results suggest that childhood maltreatment is associated with persistent changes in cerebral white matter in adulthood. The structural differences may reflect adaptations or vulnerabilities that persist into adulthood, indicating a long-lasting impact of ACEs.

Keywords: Fractional anisotropy, childhood maltreatment, DTI, white matter

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Astrocyte-Derived Extracellular Vesicles Modulate Fetal Neurodevelopment Under Prenatal Stress Conditions.

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Prenatal stress (PS) during pregnancy increases the risk of poor neurodevelopmental outcomes in the offspring. However, the signals communicating stress from mother to fetus are poorly understood. Maternal brain astrocytes are reactive to stress conditions and astrocyte-derived extracellular vesicles (ADEVs) can reach peripheral blood; thus, potentially acting as mother-to-fetus "stress signals". Using a repetitive restraint rat model of PS, we examined the effect of ADEVs on fetal neurodevelopmental processes. Stressed pregnant rats were confined daily (2h/day) to movement restriction from E7.5 to E14.5 or E16.5. ADEVs were obtained from control and corticosterone-treated cultured astrocytes and injected into pregnant dams (4 injections; every 48h from E7.5). Fetal neural proliferation/differentiation assays were performed at E15.5 and E17.5 by BrdU assays, Western blot and immunofluorescence. Our results showed that PS reduced the number of intermediate progenitor cells at E15.5 and E17.5 in the pallium, suggesting premature neuronal differentiation. Expression of the maturation marker MAP2 increased in the restraint group at E15.5 but decreased at E17.5, indicating PS-induced impairment in neuronal maturation. Remarkably, ADEVs treatment showed a preventive effect, modifying the expression of neuronal differentiation markers in prenatally stressed animals. Together, our findings suggest that PS accelerates neuronal differentiation; thus, leading to a premature depletion of neural progenitors and a reduction of maturing neurons at later developmental stages. Circulating ADEVs counteract and/or modulate the effect of PS on fetal neurogenic processes.

Keywords: Prenatal stress, extracellular vesicles, neurodevelopment

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Prenatal stress and neurodevelopment: in vitro study of the effect of astrocyte-derived extracellular vesicles (ADEVs) on neural stem/progenitor cells proliferation and differentiation.

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Prenatal stress (PS) increases the risk of poor neurodevelopmental outcomes in the offspring, though the mechanisms are not fully understood. Maternal brain-derived extracellular vesicles may act as mediators of maternal-fetal stress communication, transferring cargo that alters the physiology of recipient cells. In this context, astrocyte-derived extracellular vesicles (ADEVs) can influence the biology of peripheral cells and tissues. In fact, ADEVs have been detected in the peripheral blood plasma, and their

cargo change under stress conditions. Nonetheless, their role in PS-induced changes in fetal neural stem/progenitor cells (NSPCs) and neurogenesis remains unknown. In this study, we assessed the effect of ADEVs on NSPCs proliferation and differentiation using an in vitro approach. For this, NSPCs were isolated from the pallium of rats at embryonic day (E)14.5, cultured as neurospheres, and divided into 5 experimental groups: (i) Control, no treatment; (ii) DMSO, (iii) Corticosterone (5 µM), (iv) ADEVs, and (v) ADEVs from astrocytes previously treated with corticosterone. Treated groups received 1 pulse of treatment every 24 hours (a total of 3 pulses). Cultures were analyzed after treatments by Western blot and immunofluorescence in adherent (differentiation) or suspension (proliferation) conditions. In proliferation conditions**,** ADEVs-treated NSPCs showed an increase in the number and diameter of neurospheres, along with an increased expression of NSPC markers, such as Nestin and SOX2. Interestingly, under differentiation conditions, ADEVs treatment stimulated cell differentiation, as assessed by the expression of neuronal lineage markers. These findings highlight the potential role of ADEVs as mediators/modulators of mother-to-fetus communication under stress conditions.

Keywords: Prenatal stress, Neural Stem/Progenitor Cells, Astrocyte-derived extracellular vesicles.

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Pupil dynamics in visuospatial processing in early stages of alzheimer's disease.

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INTRODUCTION: Alzheimer's disease (AD) is the most frequent cause of dementia in the world and can initially present as amnestic mild cognitive impairment (aMCI). Neurodegeneration affects visuospatial navigation (VN) areas and autonomic nervous system structures. Evidence suggests that changes in pupillary dynamics (PD) may reflect neuronal damage in AD. However, the impact of VN on PD in early stages of the disease remain unknown.

METHOD: We evaluated 26 subjects (13 control, 13 aMCI) using neuropsychological batteries. We analyzed behavioral and PD variables during a VN task (Virtual Morris Water Maze). Temporal segmentation of PD was performed to differentiate pupillary reflexes from cognitive exploration responses. Pupillary diameter, contraction velocity and spectral power were measured.

RESULTS: Subjects with aMCI showed worse performance in VN since they took longer to complete the task (aMCI=91.1±17.7s. Control=54.4±6.4s, $p<0.01$) and higher error rates (aMCI=88%. Control=50%, $p<0.05$). In the initial stage of the task, both contraction diameter (ΔaMCI = -1.17, ΔControl=-1.65, $p<0.01$), dilation diameter (ΔaMCI = 1.39, ΔControl=1.78, $p<0.05$), and contraction velocity (ΔaMCI = 0,0031 ΔControl=0.018, $p<0.01$) were lower in subjects with aMCI, difference that increases during the exploration. The change in the spectral power of the PD frequencies during the exploration was significant only in the aMCI group towards frequencies <2Hz.

DISCUSSION: The deterioration of PD in subjects with aMCI is accentuated during cognitive effort in VN with respect to the differences in the pupillary reflex between the groups, which may suggest that autonomic dysregulation begins early during the neurodegeneration of AD.

Keywords: Alzheimer's disease, visuospatial navigation, pupillary dynamics

Impaired Availability and Action of Thyroid Hormones in an Animal Model of Alzheimer's Disease

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Alzheimer's disease (AD) is a neurodegenerative disorder associated with thyroid hormones (TH) T3 and T4, with T3 playing a role in regulating key genes involved in AD pathophysiology and reduced TH levels observed in AD patients. This study aims to examine TH availability and action in the brain of the 5XFAD transgenic mouse model of AD compared to Wild Type (WT) mice. A total of 32 mice, aged 7 months (16 WT and 16 5XFAD, with 8 males and 8 females in each group), were used. Mice were perfused with saline (0.9% NaCl), and their brains were extracted and frozen for subsequent radioimmunoassay (RIA) and qPCR analysis to determine TH concentrations and actions, respectively. Results showed that 5XFAD mice had reduced plasma levels of T3 and T4, though no significant differences were found in the cerebral cortex, hippocampus, or cerebellum, nor in female brain tissues. Despite normal TH levels in brain tissue, the Hairless gene, regulated by T3, exhibited low mRNA expression in the hippocampus of both sexes and high expression in the cerebellum of females. Dio3 mRNA, which degrades T3 and T4, was low in the cortex and hippocampus of males, while Dio2 mRNA, which converts T4 to T3, was elevated in the cerebellum of females and the hippocampus of males, indicating a potential compensatory mechanism.
In conclusion, 5XFAD mice demonstrate peripheral but not central hypothyroidism, likely due to local compensation by Dio2 and Dio3, though there is dysregulated expression of T3-regulated genes, suggesting further mechanisms need exploration.

Keywords: Thyroid Hormones, Alzheimer's Disease

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Impact of prenatal and postnatal androgenization on female rat prefrontal cortex neuroinflammation, working memory and social behavior.

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Polycystic ovary syndrome is a prevalent disorder in women of reproductive age, characterized by hyperandrogenism being a risk factor for neuropsychiatric disorders. The aim of this study was to determine in an animal model the impact of prenatal and postnatal exposure to androgens on the prefrontal cortex, working memory and social behavior. *Sprague-Dawley* rats were used to generate a model of prenatal and pubertal androgenization. Dams were exposed to dihydrotestosterone (DHT) in the prenatal androgenization model. Female offspring rats were re-exposed to DHT during puberty via implantation of Alzet osmotic pumps. The model was validated by measuring anogenital distance and alterations in the estrous cycle. Prenatally androgenized rats had impaired social behavior compared with the vehicle group. In addition, rats that were androgenized both prenatally and at puberty took longer to perform the working memory test (T-maze). The androgenized rats showed an increase in Iba-1 levels in the prelimbic cortex relative to control animals. The results suggest that pre- and postnatal androgenization induces neuroinflammation in the prefrontal cortex, which could explain the impairment of working memory and socialization in androgenized rats.

Keywords: polycystic ovary syndrome working memory

Financing: FONDECYT Regular Grant number 1210261.

Effectiveness of a stress management intervention on academic performance and cortisol levels in students of the Polythecnical Naval Academy of Chile: A pilot study

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Students at the Chilean Naval Polythecnic Academy experience signficant stress in three areas: academic load, military responsibilities and family life. We aimed to evaluate a psychoeducational stress management intervention by measuring academic performance and peripheral (nail) cortisol levels.

Methods: The intervention consisted of techniques from mindfulness practice, positive self-talk and improving concentration skills, following the "Mental Skills Training" model with six training sessions, including two stress exposure events. Forty students at risk of academic failure were selected. The control group (n= 20) had a similar structure of activities but did not receive the psychoeducational intervention. The intervention grouop (n=20) participated in a stress management program twice a week for three weeks. Cortisol levels in nails were determined before and after intervention using ELISA method.

Results: Cortisol levels, measured before and after the intervention, showed a significant increase in the control group ($p=0.001221$, Wilcoxon matched-pairs rank test). In contrast, cortisol levels remained unchanged over time in the experimental group. When considering academic performance, the experimental group had a 85% approval rate, compared to a 50% found in the control group, with statistical significance of $p < 0.05$.

Conclusion: this study validates the effectiveness of psychoeducational interventions in a military context, and urges for improved stress management policies that are culturally aadaptive and individual-focused.

Keywords: stress, cortisol, academic performance, mental skills

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Social play behavior in prepubertal offspring impacted by vicarious social defeat stress on lactating rats

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Social play behavior in early life is an indicator of social interaction development. The neurobiology of social play has been well documented, however the mechanism involved in alterations in early life social play by maternal stress via observable social adversity during lactation, remains unknown. The aim of this research was to develop an animal model of observational stress in lactating rats to study changes in social play behavior during the prepubertal period and the underlying neurobiology in the offspring. Vicarious social defeat stress (VSDS) is a model, where a third-party rodent observes an aggressive supine pinning (social defeat) of an intruder rodent by a resident rodent, which generates robust physiological and behavioral effects on observers. Social play behavior was evaluated by manual scoring by Ethovision XT of nape-attacks, pinning, evading, and chasing at PND 24, between 2 unfamiliar same sexed and aged pups socially isolated 12 hours prior and placed in a clean foreign chamber with wooden bedding to interact. A sexual dimorphism was found in the effects of VSDS on social play in pups. At the molecular level, the oxytocinergic system is a candidate for its strong role in modulating social play behavior via neuronal substrates such as the Amygdala, Ventral Tegmental Area, and Nucleus Accumbens. We're currently evaluating the impact of VSDS on oxytocin and its receptor in pups. This research holds great relevance for understanding early life stressors, remodeling of neuro circuitry, and impact on social play for social interaction development.

Keywords: Oxytocin, SocialPlay, Neurodevelopment, Early Life Stress

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Discovery and profiling of new genes associated with ALS, first approaches.

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Amyotrophic lateral sclerosis (ALS) is a rare motor neuron disease with no cure, leading to complete paralysis as neurons disconnect from muscles. Environmental and lifestyle factors, such as exposure to cyanotoxins, smoking, and head traumas from sports or accidents, have been linked to ALS. Approximately 90% of ALS cases are sporadic, while the remaining 10% are familial. Genetic studies, including Genome-Wide Association Studies (GWAS) and RNA sequencing (both bulk and single-cell), have identified thousands of genes associated with ALS. Although these genes may appear to play individual roles, a systems biology approach using biological networks reveals intricate connections among them.In our research, we applied a network-based approach to identify new candidate genes by examining "seed genes" already associated with ALS. By testing the transcript levels of ten candidate genes in the spinal cord and frontal cortex of an ALS mouse model, we determined transcriptional dysregulation at various disease stages. Further validation was performed using Western blots on a neuromuscular synaptic gene of interest. These findings suggest that the newly identified genes could play different roles in ALS pathology, providing new insights into the disease.Future cellular studies of these genes could enhance our understanding of ALS, potentially leading to the development of genetic markers, treatments, or preventive measures. Our research expands the knowledge of ALS and could aid in the fight against the disease by identifying new candidate genes that may contribute to its pathology.

Keywords: ALS, System Biology, Biological Networks

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Non-rem sleep characterization of patients with long covid and brain fog

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The long COVID syndrome has emerged as a consequence of the COVID-19 pandemic. One of the most common symptoms is "brain fog," which is a group of cognitive alterations, but doesn't have an accurate definition.
Many studies described the relationship between sleep and the cognitive process to show that sleep has an essential function in memory consolidation, attention, and other cognitive aspects. Non-REM sleep plays a vital role in cognitive function, and REM sleep is crucial for procedural and emotional aspects.
Despite the significant prevalence of sleep disorders in patients with long COVID-19, exists limited studies using polysomnography or electroencephalography during sleep. Patients with long COVID have structural and functional alterations in slow-wave production areas in deep Non-REM. There are no detailed descriptions of the performance of cerebral activity in this population. The main objective is to determine the integrity of Non-REM sleep in patients with long COVID and brain fog. The expected result is that patients show alterations in the temporal organization, proportion, and structure of Non-REM sleep due to damage caused by SARS-CoV-2 infection.

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Unsupervised Segmentation of Electroencephalographic Signals Compared with Standard Visual Staging for Sleep Studies in Patients with Persistent COVID.

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The staging of the sleep-wake cycle, essential in sleep studies, is traditionally performed through Polysomnography using visual inspection based on international standards. However, these guidelines capture only a limited range of signal characteristics, with minimal contribution from modern analytical methods.
In response to these limitations, the research proposed a new framework for analyzing electroencephalogram signals from sleep studies through unsupervised analysis using clustering techniques. The goal is to achieve a temporal segmentation of sleep states that statistically aligns with the expert-conducted visual polysomnographic staging.
The analysis included records from patients with persistent COVID symptoms from the FONDECYT 1231901 project, along with 10 patients without sleep disorders from public databases. A time-frequency analysis was performed using the central EEG derivation, focusing on frequencies from 0 to 30 hertz. One-second epochs were used, with an initial clustering via K-means using the signal spectrogram, followed by a second clustering via Agglomerative Clustering based on contextual features. The correspondence between the traditional and unsupervised approaches was assessed using Cohen's Kappa.
This research lays the foundation for developing cutting-edge analytical tools that provide complementary information to sleep studies and potentially detect pathological markers through an unsupervised framework.

Keywords: SLEEP, DATA DRIVEN, CLUSTERING, UNSUPERVISED, AUTOMATIC SLEEP STAGING

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The glymphatic system's role in linking cardiometabolic health to cerebral small vessel disease and frailty in Chilean healthy older adults

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Cardiometabolic factors are linked to structural brain changes throughout life, particularly during late adulthood, and are associated with cerebral small vessel disease (cSVD), a common cause of dementia. cSVD is characterized by neuroimaging markers such as white matter hyperintensities (WMH) and enlarged perivascular spaces (PVS). PVS are integral components of the glymphatic system, a brain waste clearance pathway increasingly recognized for its role in cSVD pathogenesis. This study explores the relationship between cardiometabolic factors, measured via an allostatic load index (ALI), cSVD markers, and gait speed (GS), an index of frailty. We hypothesized that ALI would significantly relate to cSVD markers, and impact GS as a frailty index. Our sample consisted of 87 healthy Chilean elderly (mean age 73.5 years, 58 women), ALI was calculated from blood pressure, body mass index, cholesterol, and glucose levels. PVS were quantified using an automated method. We found a significant positive correlation between ALI and PVS, and between PVS and GS. Mediation analysis revealed that ALI has both direct and indirect effects on the relationship between PVS and GS, indicating a complex interplay where the influence of PVS on GS is not solely mediated by ALI. No association was found between ALI, GS, and WMH volume. All in all, this research highlights the intricate connections between cardiometabolic health, glymphatic system dysfunction, and frailty indexes in older adults, emphasizing differential contributions of cSVD markers.

Keywords: Cerebral Small Vessel Disease, Glymphatic System, Perivascular Spaces, White Matter Hyperintensities, Gait Speed

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Cochlear dysfunction as an early biomarker of cognitive decline in normal hearing and mild hearing loss

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Age-related hearing loss is an important risk factor for cognitive decline. However, audiogram thresholds are not good estimators of dementia risk in subjects with normal hearing or mild hearing loss (<40 dB) which is the most common hearing range in older people. Here we propose to use distortion product otoacoustic emissions (DPOAEs) as an objective and sensitive tool to estimate the risk of cognitive decline in older adults with normal hearing or mild hearing loss. We assessed neuropsychological, brain magnetic resonance imaging, and auditory analyses on 120 subjects > 64 years of age. We found that cochlear dysfunction, measured by DPOAEs-and not by conventional audiometry-was associated with cognitive state and brain atrophy in the group with mild hearing loss (25 to 40 dB) and normal hearing (<25 dB). Our findings suggest that DPOAEs may be a non-invasive tool for detecting neurodegeneration and cognitive decline in the older adults, potentially allowing for early intervention. We continue analyzing data from a larger group of subjects (approximately 300) and studying which characteristics of DPOAEs are most relevant to detect incipient cognitive impairment.

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Dissecting Cortical Network Dynamics: The Impact of Motor Thalamus Inactivation and Noradrenaline Receptor Blockade on Synergy, Redundancy, and Information Processing in Primary Motor Cortex

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The dynamic interplay of cortical networks is crucial for motor function, which depends on the efficient processing and integration of neural information. Synergy and redundancy are key to understanding this process. Synergy reflects the collective contribution of multiple elements that exceed their individual inputs, while redundancy indicates overlapping information that supports robustness. Our goal is to understand how synergy and redundancy reconfigure depending on the network's activity or the specific function it aims to fulfill.
Analyzing data from a biophysically detailed multi-scale model of the primary motor cortex (*M1*), this study explores the effects of motor thalamus inactivation (*MTh-i*) and noradrenaline receptor blockade (*NA-b*) on neural information dynamics. We analyzed firing rates across 15 distinct cell populations, during three behavioral states: initial quiet, movement, and subsequent quiet. High-order statistics (HOS) metrics were applied, utilizing O-information to dissect synergistic and redundant interactions, and the Integrated Information Decomposition (ΦID) framework to assess changes in information dynamics.
Our preliminary findings reveal that *MTh-i* and *NA-b* significantly increase redundancy and decrease synergy, particularly during movement, indicating less efficient neural processing. The ΦID analysis showed that information storage and transfer peaked during movement under control conditions, signifying optimal neural coordination. In contrast, the impaired conditions reduced these metrics, disrupting motor control and neural communication.
Additionally, *MTh-i* primarily disrupts movement-related information processing, while *NA-b* affects both movement and quiet stages. These insights deepen our understanding of cortical function underscoring the importance of these analytical tools in identifying potential therapeutic targets for neurological disorders.
Keywords: Neural Information Dynamics, High-order Statistics, Synergy, Redundancy, Cortical Model

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Empathy for pain in Parkinson's Disease: Exploring the integration Between Neurophysiological Responses and Phenomenological Experience (Bodyssence) Through Varela's Neurophenomenological Program

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Background: Empathy for pain involves a dynamic interaction between neurophysiological responses and phenomenological experience, a process referred to as ´*Bodyssence*´. Although research has identified alterations in empathy among Parkinson's patients, understanding how these bodily and subjective attributes interact remains limited. This study aims to explore ´*Bodyssence*´ in empathy for pain by examining the integration of phenomenological experiences and neurophysiological responses in Parkinson's patients through Varela's neurophenomenological approach.

Method: Forty-five patients with mild to moderate Parkinson's disease watched videos of athletes suffering falls during extreme sports while standing on a force platform and wearing electrodermal and heart rate electrodes. To explore the integration of physiological and subjective experience, we employed both first-person (phenomenological) and third-person (postural control, electrodermal response, heart rate) approaches, focusing on pre-fall and post-fall phases of the videos.

Results: First-person analysis revealed two empathic phenomenological structures: bodily resonance and transparency resonance. The comparison of neurophysiological data according to the grouping of phenomenological structures (repeated-measures ANOVA) showed that the bodily resonance group exhibited greater anteroposterior postural movement than the transparency group ($F(1,41) = 4.55$, $p = .039$) in the pre-fall phase, but not in the post-fall phase. No significant temporal window or interaction effects were found.

Conclusions: This study, following Varela's neurophenomenological approach, identifies two distinct ´*Bodyssences*´ manifest in empathy for pain in Parkinson's patients. The integration of first-person and third-person data reveals that empathy varies based on experiential structure, underscoring the sensory-motor system's key role. These findings deepen our understanding of how neurodegeneration impacts empathy in this population.

Keywords: empathy, Parkinson's disease, Bodyssence, neurophenomenology, sensory-motor system

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A glimpse into the functional connectivity of cortical networks in vitro through calcium imaging

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Studying the organization of small neuronal groups in vivo is extremely challenging due to difficult access and because connectivity is influenced by interactions with surrounding tissues and the organism's overall development. Neuronal cultures provide versatile, simplified, and controlled models to study the principles of neural network self-organization. Despite their relative simplicity, under appropriate conditions, cultures exhibit a variety of collective behaviors that recapitulate many features of in-vivo neural networks, including the generation of synchronized activity patterns, rhythmic oscillations, and transient burst events. These in vitro models allow for precise manipulation and observation of neuronal behavior, becoming valuable tools for exploring the mechanisms underlying collective phenomena in the brain. We performed calcium fluorescence recordings in cortical cultures from mice and rats to monitor the activity of large neuronal populations with single-cell resolution. We examined functional connectivity (correlation between activity patterns) and synchronization between nearby/distant neurons and assessed whether there is recurrent activity over time. We quantified functional coupling between neurons and its temporal evolution by constructing static (average) and dynamic connectivity matrices, respectively. In basal conditions, neuronal populations in our networks exhibited stable or transient correlated events (in-phase or anti-phase). Reducing the extracellular Mg^{+2}/Ca^{+2} ratio increased activity and correlation, which became more robust by enhancing transmission via NMDA receptors by adding glycine. Our preliminary results pave the way to explore synaptic plasticity processes and assess whether synchrony/recurrence is linked to the formation of neuronal ensembles analogous to those observed during memory formation and consolidation.

Keywords: network self-organization, functional connectivity, cortical neuronal cultures, neural collective behavior, calcium imaging

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State-space evoked potentials as markers of pain and analgesia

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Although pain is ultimately a subjective experience, tools to objectify it are clearly useful to understand the neurobiological basis of this perception, to differentiate pain phenotypes and to understand the different factors that contribute to its occurrence, including emotional and psychosocial ones.
Electroencephalography (EEG) and event-related evoked potentials (ERP) have been proposed as a plausible alternative for the measurement of perceived pain. However, conventional EEG/ERP approaches have a low signal-to-noise ratio and thus require significant amounts of data (stimulations) to achieve an acceptable estimate of the effect. In this work we present a new method to analyze ERPs using a new state-space model (EE-ERP). 10 human volunteers were subjected to varying and random levels of transcutaneous electrical painful stimulation. The stimuli were presented again under increasing levels of analgesia. The EEG signal was recorded and analyzed with this new model. When comparing EE-ERPs with traditional ERPs, we observed that EE-ERPs correlate with the pain reported by the subjects in the different conditions in a clearly superior way to traditional ERPs, since they are more precise and require fewer repetitions of the stimulus to obtain them.
The superiority of EE-ERPs over traditional ERPs may have important implications for understanding the biological bases underlying pain, as well as serving as a tool for pain research and treatment.

Keywords: Dolor, Electroencefalograma, Potenciales evocados, Modelo estado espacio, Analgesia

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Spatio-temporal description of slow waves and its coupling with fast oscillatory activity in the canonical cortical circuit of the avian pallium.

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Mammalian slow waves (SW) are spontaneous episodic oscillations of great amplitude and low frequency which appear during quiescent states, like non-REM sleep or deep anesthesia. Slow wave activity appears to be coupled with faster oscillatory activity (ripples, gamma oscillations) during its negative deflections. This type of activity involves the activation of the columnar cortical circuits, thus, constitutes a tool to unravel the operation of these circuits. Recently, comparable SW activity has been described to occur in the pallial telencephalon of birds, during sleep and deep anesthesia. In parallel, recent anatomical studies have shown that the avian sensory pallium is organized according to a laminar/columnar/recurrent motif comparable to that of the mammalian cortex. However, to date no studies in birds have address the possible occurrence of SWs in the columnar sensory local circuitry. In the present work we describe, in anesthetized pigeons, the presence of SW activity along the sensory columns of the visual pallium, by means of simultaneous recordings columnarly oriented across laminae. We found that SWs co-occur with fast

oscillatory activity (ripples; 80-120Hz) seemingly originated in the thalamorecipient lamina. Also, spike discharges and local field potentials recorded across lamina during SW episodes are temporally correlated with ripples. These results suggest that in birds, as in mammals, the columnar pallial circuitry is activated during SWs and ripples, and its neuronal elements contribute to generate or at least to modulate its spatio-temporal shape.

Keywords: Slow wave oscillations, spontaneous activity, bird sleep, canonical cortical circuitry, avian pallium

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PKA and Epac control differentially the neurotransmitter release probability and synaptic facilitation in the Drosophila motoneuron synapses

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Defects in cAMP signaling cascade impair the learning and memory processes of *Drosophila* mutants. Flies carrying defects on the adenililcyclase (*rut*) and cAMP-phosphodiesterase (*dnc*) coding gene exhibit abnormal learning index and retention and short-term synaptic plasticity. Motoneuron synapses of this fly miss post tetanic potentiation (PTP), display lower neurotransmitter release (NTR) Ca^{2+}-dependence and also exhibit abnormal spontaneous postsynaptic currents. Furthermore, these flies exhibit abnormal sensory and motor end-terminal sprouts as well. Here, we present a study of the effect of cAMP on the motoneuron NTR, addressed to understand the involvement of the cAMP cell signaling cascade on *Drosophila* motoneuron synapse function. Our results show that cAMP gradually affects motoneuron synaptic plasticity; modulates the Ca^{2+}-independent spontaneous NTR; increases the NTR probability through the Exchange protein directly activated by cAMP (Epac) activation. Our results suggest that, cAMP increases reached by neural activity, induce PKA-dependent spontaneous NTR increases, which became to improve synchronic NTR probability (SNTR). Consequently, the SNTR increase causes synapses sensitization as well as shift the NTR Ca^{2+}-dependence, which reduce the dynamic range of synaptic plasticity. Therefore, the behavior alteration by *Drosophila* learning and memory mutant, flies (*dnc* and *rut*) should be due to loss of cAMP synaptic modulation ability.

Keywords: Synaptic Facilitation, NTR, cAMP, Epac

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Connexin and Innexin over time: Impact of gap junctions in BBB during mouse and fly aging.

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Introduction: The blood-brain barrier (BBB) plays a crucial role in protecting the brain by regulating the exchange of substances between the blood and the central nervous system. As we age, this barrier undergoes changes that may contribute to cognitive decline and an increased risk of neurodegenerative diseases. Proteins such as connexin 43 (Cx43) in mammals and innexin 1 (Inx1) in flies are essential for BBB functionality. This study investigates how aging affects the expression and distribution of these gap junction proteins, offering insights into how alterations in the BBB might impact brain health over time.

Methods: Female Mus musculus C57BL/6 mice and *Drosophila melanogaster* Inx2:V5 flies were used for analysis. In mice, the hypothalamus was dissected and sectioned, while in flies, the whole brain was used. Immunofluorescence was employed to evaluate the distribution and levels of the proteins. Quantification and analysis of protein distribution were performed using Imaris and ImageJ software.

Results: In mice, tanycytes of the third ventricle and cells associated with hypothalamic blood vessels expressed Cx43. Cx43 clusters showed a decrease in area with age. In flies, Inx1 clusters in the BBB increased in volume with aging, while fluorescence intensity remained constant.

Conclusion: Changes in the distribution of Cx43 and Inx1 gap junction plaques in the BBB and the parenchyma-ventricle interface suggest potential effects on central nervous system homeostasis with aging. These changes could lead to a progressive loss of barrier function, potentially contributing to neurodegenerative decline.

Keywords: Blood Brain Barrier, Aging, Gap Junctions, Innexin1, Connexin43

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Tracing the Early Development of the Avian Trigeminal Pallial Circuit

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The avian trigeminal system features a direct pathway from the hindbrain to the telencephalon, a unique feature among birds. The principal sensory trigeminal nucleus (PrV), located in the pons, receives primary somatosensory inputs from the rostrum and forms the quinto-frontal tract, which projects to the basorostralis area (Bas) in the dorsal ventricular ridge (DVR), bypassing the thalamus. Despite this unique route, the trigeminal DVR is organized similarly to its visual and auditory counterparts, with dorsoventral laminae of highly interconnected cell groups arranged in a columnar, reciprocal, and homotopical manner. These laminae include Bas, the intermediate nidopallium (NI) just dorsally to Bas, and the ventral mesopallium (MV) above. Our previous work showed that in the visual DVR, the thalamus-DVR and intra-DVR cytoarchitectonic organization and connectivity develop early and independently of external visual inputs in chick embryos (Reyes-Pinto et al., 2024). Here, we use *ex-vivo* biocytin injections and immunolabeling to explore whether similar patterns occur in the trigeminal DVR. From embryonic day 8 (E8), somatosensory MV expresses the transcription factor Satb2, a trait shared with visual and auditory regions. By E10, the somatosensory DVR shows columnar, reciprocal connections between Bas

and MV. Additionally, the PrV is cytoarchitectonically defined with its fibers extending towards Bas. Thus, by the time PrV afferents reach Bas, the trigeminal DVR displays its characteristic columnar organization, suggesting that intra-DVR circuitry 1) arises early in development and 2) is primarily guided by intrinsic processes rather than external sensory inputs.

Keywords: Sensory forebrain, Trigeminal system, Avian, Circuits, Development

Financing: FONDECYT REGULAR 1210069

From Obesity to Cognitive Decline: MRI Reveals the Hidden Crisis of Sedentary Lifestyle in Chile.

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Chile has experienced a significant rise in obesity over the past thirty years, leading to its status as the second country in Latin America with the highest growth in obesity rates. This situation is strongly connected to sedentary living, unhealthy eating patterns, and emotional issues, forming a pattern that is hard to change. A lack of physical activity is not just a main cause of obesity, but also increases the chances of chronic illnesses and cognitive decline. In Chile, the high rate of physical inactivity is a major burden on both public health and the economy. This study emphasizes the importance of creating a holistic strategy that incorporates nutrition, mental health, and physical activity to tackle the problem of sedentary lifestyle and its widespread effects on Chilean society. In order to do this, neuroimaging techniques were used to compare 71 participants (43 active and 28 sedentary classified based on IPAQ), revealing notable variances in the size of the left hippocampus, particularly in regions CA1, CA3, CA4, and Dentate Gyrus, along with other distinct subfields. These regions play a role in the development of verbal memory, sequential learning, and planning, all of which are essential for daily tasks and are impacted in age-related neurodegenerative diseases. This discovery highlights the significance of including personalized physical activity regimens that suit each person's needs and abilities, as it has a direct effect on overall biopsychosocial health and happiness.

Keywords: Sedentary lifestyle, Mental Health, Hippocampus, Obesity

Dynamics of Otoacoustic Emissions During Acoustic Residual Inhibition in Tinnitus

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Background and Aim: Tinnitus is a phantom sound perception in the absence of stimulation; it affects quality of life and has a prevalence of up to 10%. Recent studies suggest its cerebral nature, but the neurophysiological mechanisms involved remain uncertain. Our research aims to elucidate cortico-cochlear oscillatory dynamics during tinnitus using the *residual inhibition paradigm*, which temporarily suppresses tinnitus via broadband noise stimulation.
Methods: We are recruiting individuals aged 18 to 50 from the Universidad de Chile Clinical Hospital. All participants provided informed consent. Eligibility criteria include chronic tinnitus lasting more than three months, unilateral presentation, and normal auditory thresholds. Participants are subjected to a 15-minute electroencephalographic (EEG) protocol using the residual inhibition paradigm and recording distortion product otoacoustic emissions (DPOAE). The primary comparison focuses on spectral power related to both cortical and cochlear activity.

Results: Preliminary results confirm the protocol's feasibility in capturing EEG signals, DPOAE, and subjective tinnitus intensity during the residual inhibition paradigm. So far, 10 subjects have been recruited. We observe a tendency for distinct cortico-cochlear changes, such as heightened low-frequency power in cochlear activity (<10 Hz) particularly after prolonged auditory masking, among other results.
Conclusion: This study aims to clarify the neurophysiological mechanisms of tinnitus, with a particular focus on the role of the efferent auditory system. By using the residual inhibition paradigm, we seek insights that could lead to personalized treatments. The integration of cortical and cochlear dynamics represents a novel approach to understanding this complex condition.

Keywords: Tinnitus, Auditory Efferent System, Electroencephalography, Otoacoustic Emissions

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Development of a tool to study PRNP gene polymorphisms within the population of Biobío and Ñuble Regions

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Creutzfeldt-Jakob Disease is a neurodegenerative disorder caused by the prion pathogen: an altered form of the PrPC protein, which is naturally found in the body and is highly expressed in the nervous system. This altered form has infectious properties, as it induces structural changes in normal PrPC, spreading throughout the nervous system. There are three forms of the disease: sporadic, iatrogenic, and familial, with the latter accounting for 10% of cases. Although global incidence is low, with 1 case per million people per year, the Biobío and Ñuble regions of Chile report rates up to 10 times higher. It is hypothesized that this high prevalence in Chile is mainly due to the familial form, which is associated with mutations in the PRNP gene. More than 40 mutations have been described in this gene, with varying frequencies and geographic distributions. In Chile, the most common mutation is E200K, which has also been reported in other countries with high rates of the disease, suggesting a common historical origin linked to Sephardic Jewish migrants. The objective of this study is to generate a genetic registry through the development of a PRNP gene library representative of the population in the Biobío and Ñuble regions, with the aim of establishing a tool to determine the frequency of polymorphisms and their association with this disease. This work has direct implications for human health, enabling key public health decisions to be made in Chile.

Keywords: creutzfeldt-jakob, PRNP

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TGF-β1-signaling is required for Nrf2-antioxidant pathway activation in a murine model of multiple sclerosis

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Multiple sclerosis (MS) is an irreversible progressive disease characterized by the loss of myelin, the presence of glial cell-mediated neuroinflammation, and an overproduction of reactive oxygen species (ROS). These alterations have been linked to impairments of the Nrf2 signaling pathway, a critical antioxidant factor that prevents mitochondrial failure, oxidative damage, and neuroinflammation in the brain. Additionally, it is well known that TGF-β1 is a major cytokine involved in the inflammatory response in MS. However, it is not clear how this signaling contributes to the Nrf2 activation and together in the pathogenesis and progression of MS. We studied the participation of the TGF-β1 in the activation of Nrf2 pathway in neuroinflammation, mitochondrial function, and behavior of an animal model of MS obtained by feeding mice with 0.25% cuprizone (CPZ)-a demyelinating agent- and treated with a TGF-β1 receptor 1 blocker (galunisertib, GAL). After the in vivo treatment with GAL, Nrf2 and TGF-b1 we performed studies of protein expression, mitochondrial function and mice behaviour. At 3 weeks, animals subjected to cuprizone treatment showed a decrease of Nrf2 expression in both treated and untreated animals with a decrease in ATP levels in animals treated with GAL. At 5 weeks, an increase in protein levels of Nrf2 was observed in cuprizone-fed animals and this increase was reduced in animals treated with GAL. Finally, a decrease in locomotor and memory activity was observed in animals treated with GAL, suggesting a protective role of TFG-β1 in the cognitive and locomotor impairment induced by cuprizone.

Keywords: Myelin, Remyelination, TGF-β1, Nrf2, Multiple Sclerosis

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