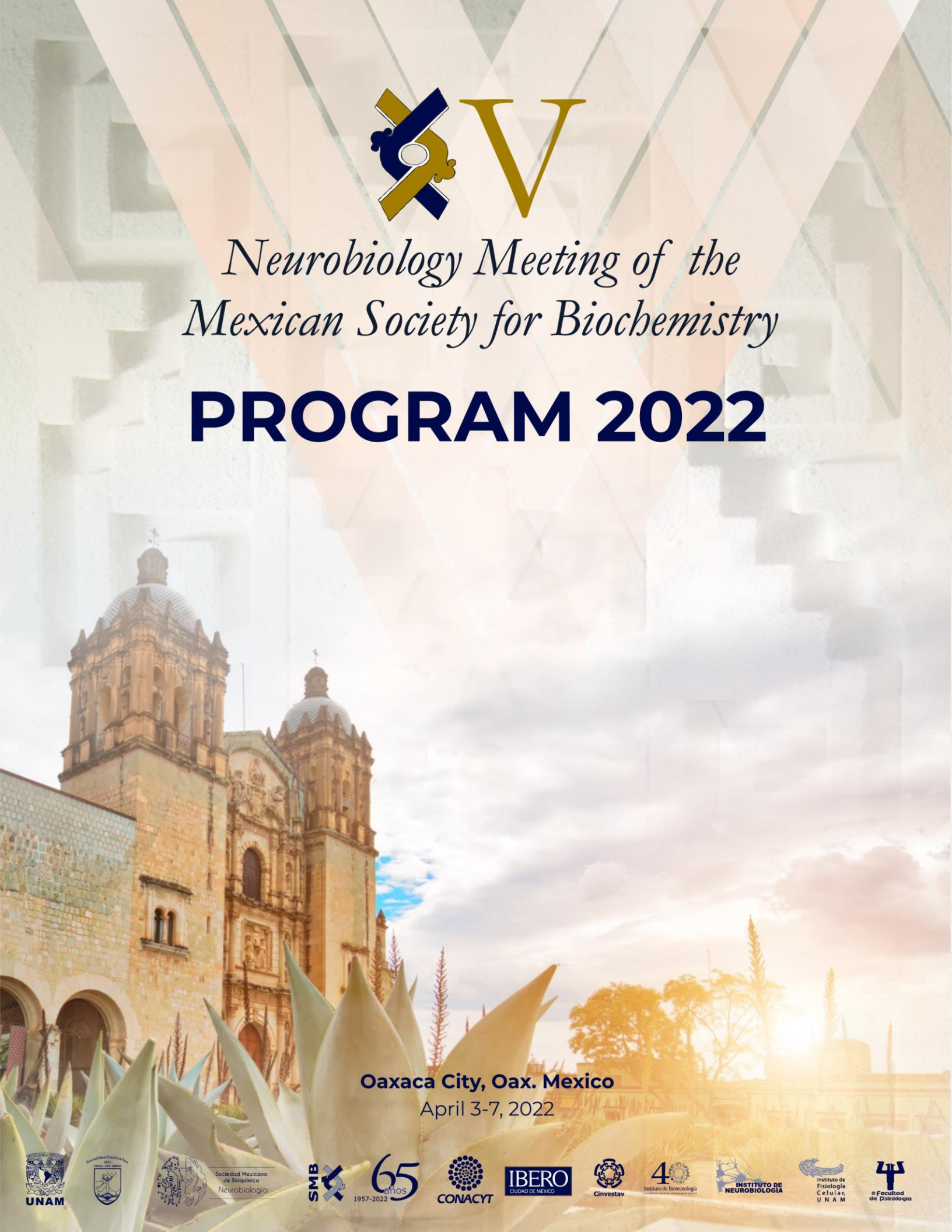
V

Neurobiology Meeting of the Mexican Society for Biochemistry

PROGRAM 2022



Oaxaca City, Oax. Mexico

April 3-7, 2022

Sociedad Mexicana
de Bioquímica
Neurobiología

SMB

PROGRAM

IV Neurobiology Meeting of the Mexican Society for Biochemistry

Mision de los Angeles Hotel, Oaxaca City, Oaxaca, México
April 3-7, 2022

Organizing Committee:

Leonor Pérez Martínez, Instituto de Biotecnología, UNAM in Cuernavaca.
Yazmín Macotela, Instituto de Neurobiologia, UNAM in Queretaro.
Oscar Galicia, Departamento de Psicologia, Universidad Iberoamericana in Mexico City.
Oscar Zamora, Facultad de Psicologia, UNAM in Mexico City.
Arturo Ortega, Cinvestav, IPN in Mexico City.
Gustavo Pedraza, Instituto de Biotecnología, UNAM in Cuernavaca.
Iván Velasco, Instituto de Fisiologia Celular, UNAM and Instituto Nacional de Neurologia y Neurocirugia in Mexico City.

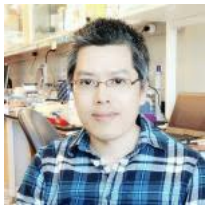
SUNDAY, APRIL 3

Pre-Meeting course
Organoids and single-cell sequencing in Neuroscience

Organizers: Dr. Leonor Pérez-Martínez / Dr. Iván Velasco
Instituto de Biotecnología, UNAM / Instituto de Fisiología Celular, UNAM and Instituto Nacional de Neurología y Neurocirugía.





9:00-10: 00 *Computational methods used for single-cell sequencing of brain cells*
Dr. Jiaqian Wu / Dr. Raquel Cuevas-Díaz Durán
The University of Texas Health Science Center at Houston, MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, USA / Tecnológico de Monterrey, Monterrey, México

10:00-11:00 *Building multilevel atlases one cell at a time using patch-seq technology*
Dr. Violeta Lopez-Huerta
Instituto de Fisiología Celular, UNAM, Mexico City

11:00-11:30 *Coffee break*

11:30-12:30 *Understanding the nervous system of C. elegans one neuron at a time*
Dr. Julián Valdés
Instituto de Fisiología Celular, UNAM, Mexico City

12:30-13:30 *Reactive astrocyte heterogeneity in inflammation and neurodegenerative disease*
Dr. Shane A. Liddelow
Neuroscience Institute, NYU Grossman School of Medicine, New York, NY, USA.

13:30-14:30 **Lunch**

14:30–15:30 *Modeling human brain development and disorders using brain organoids*
Dr. Zhexing Wen
Emory University School of Medicine, Atlanta, GA, USA

15:30–16:15 *Round table*

SUNDAY, APRIL 3

Open House for the public / Día de Puertas Abiertas

Chair: Dr. Gustavo Pedraza
Instituto de Biotecnología, UNAM



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11:00-11:30 ***De vacas y vacunas. La historia de cómo los humanos logramos domesticar a las pandemias***
Dra. Karla F. Meza Sosa
Instituto de Biotecnología, UNAM

11:30-12:00 ***¿Cómo puede dañar la COVID-19 a tu cerebro?***
Dr. Juan Carlos González-Orozco
Instituto de Fisiología Celular, UNAM

12:00-12:30 ***Generación de nuevas neuronas en el cerebro de adultos ¿Qué son las células troncales neurales?***
Dra. Itzel Escobedo Ávila
Instituto de Fisiología Celular, UNAM

12:30-13:00 ***Diferentes acercamientos para estudiar la conducta animal***
Dra. Citlalli Netzahualcoyotzi Piedra
Instituto de Fisiología Celular, UNAM

13:00-13:30 ***Alexa, ¿van a destruirnos los robots? Presente y futuro de la inteligencia artificial***
Dr. David Valle García
Instituto de Biotecnología, UNAM

13:30-14:00 ***Todo lo que querías saber sobre la marihuana pero temías preguntar***
Dr. Oscar Galicia
Universidad Iberoamericana, Ciudad de México

SUNDAY, APRIL 3

IV Neurobiology Meeting

17:45-18:00 **Welcome ceremony**

18:00–19:00 **Opening Talk**

"What do reactive astrocytes (really) do?"

Dr. Shane A. Liddelow
Neuroscience Institute, NYU Grossman School of Medicine, New York, NY, USA

Chair: Dr. Leonor Pérez-Martínez
Instituto de Biotecnología, UNAM

19:00 **Welcome cocktail**

MONDAY, APRIL 4




9:00–11:00 **Symposium I**

EPIGENETICS, GENE REGULATION AND NEURODEVELOPMENTAL DISEASES

Chair: Dr. Leonor Pérez-Martínez
Instituto de Biotecnología, UNAM

Environmental effects on C. elegans behavior, from hiperglycemia to starvation

Dr. Julián Valdés
Instituto de Fisiología Celular, UNAM, México

Dynamic landscape of chromatin accessibility and transcriptomic changes during differentiation of human embryonic stem cells into dopaminergic neurons
Dr. Raquel Cuevas-Díaz Durán
Tecnológico de Monterrey, Monterrey, México

In vivo gene editing to study neurodevelopmental disorders
Dr. Violeta Lopez-Huerta
Instituto de Fisiología Celular, UNAM, México

Modeling Fragile X syndrome with 3D human brain organoids
Dr. Zhexing Wen
Emory University School of Medicine, Atlanta, GA, USA

11:00 – 11:20
Mapeo neuronal en 3D a alta velocidad. Technical presentation
I.Q. Alejandro Olvera
Product Application & Sales Support Team. CARL ZEISS.

11:20 – 11:40 **Coffee break**

11:40 – 12:40

Plenary Lecture I

Integrative study of gene expression and transcriptional regulation in the CNS
Dr. Jiaqian Wu
The University of Texas Health Science Center at Houston / MD Anderson Cancer Center, Houston, USA

Chair: Dr. Iván Velasco
Instituto de Fisiología Celular, UNAM

12:40–13:40 **Four oral presentations selected from the abstracts I**

Chair: Dr. Oscar Zamora
Facultad de Psicología, UNAM, Mexico City

Peroxiredoxin 5 overexpression decreases oxidative stress and dopaminergic cell death in a Parkinson´s Disease cellular model
Ana Patricia Duarte Jurado
Facultad de Medicina. Universidad Autónoma de Nuevo Léon

Social support and cognitive function in people living with HIV
Enrique Berra Ruiz
Facultad de Ciencias de la Salud. Universidad Autónoma de Baja California

Proteogenomic of Primary Brain Tumors Using Liquid Biopsies, for Diagnosis and Precision Medicine
María del Carmen Abrahantes Pérez
Laboratorio de Oncología Traslacional de Precisión. Instituto Nacional de Medicina Genómica

Stabilization of basal dopamine in inorganic nanoreservoirs for controlled delivery in Parkinson's disease
Francisco J. Padilla-Godínez
Instituto de Fisiología Celular, UNAM. / UAM - Xochimilco

13:40 -15:00 **Lunch**




15:00–17:00 **Symposium II**

BEHAVIOR AND PHARMACOLOGY

Chair: Dr. Oscar Galicia
Departamento de Psicologia, Universidad Iberoamericana, Mexico City

The role of neuropeptides in social behavior and reproduction in ants
Dr. Ingrid Fetter-Pruneda
Instituto de Investigaciones Biomédicas, UNAM, Mexico City

Endocannabinoids in juvenile stages of development modulate gene expression changes that affect learning and time perception
Dr. Mario Buenrostro Jauregui
Departamento de Psicología. Universidad Iberoamericana, Mexico City

Genome-wide detection of transcriptional determinants of neurological decline
Dr. Humberto Gutiérrez
Instituto Nacional de Medicina Genómica, Secretaría de Salud, Mexico City

Prepronociceptin-expressing neurons in the extended amygdala signal darting away from an aversive odor
Dr. Jose Rodríguez-Romaguera
The University of North Carolina at Chapel Hill, USA

17:00 – 17:05 **1 min talks for poster advertisings**

Chair: Dr. Arturo Ortega
Cinvestav, México City

Striatal Cholinergic Interneurons Contribute to Specific Behavioral Updates in a Classical Conditioning Task
Hector Alatriste-León
Instituto de Fisiología Celular, UNAM

Light and temperature cycles as zeitgebers in the circadian locomotor activity rhythm of the snake Crotalus molossus
Angel Bernardo Villarreal Medina
Instituto de Biología, UNAM

Evaluation of Superoxide dismutase enzyme activity in the prefrontal cortex of neonatal rats subjected to postnatal stress
Dennis Paniagua Camacho
Centro de Investigación Biomédica del Noreste. IMSS

Exogenous hydrogen sulfide improves hypertension induced by traumatic brain injury in rats through vasopressor sympathetic outflow inhibition and H2S-synthesizing enzymes restoration
Saúl Huerta de la Cruz
Departamento de Farmacobiología. Cinvestav Sede Sur

Analysis of density and distribution of astrocytes and microglial cells at the hippocampal formation of autistic-like C58/J mice.
Carlos Noé Vázquez-Moreno
Instituto de Investigaciones Biomédicas, UNAM

17:05 – 19:00 **Poster Session I (Even numbers)**

TUESDAY, APRIL 5





9:00 – 11:50 **Symposium III**

NEUROIMMUNE INTERACTIONS

Chair: Dr. Yazmín Macotela
Instituto de Neurobiología, UNAM, México

Maternal microbiome modulation of brain development processes
Dr. Helen Vuong
University of California Los Angeles, USA

Microbiota-gut-brain axis and behavior across the lifespan
Dr. Livia Hecke Morais
California Institute of Technology, USA

Gut Microbiome neuroactive compounds in children from an Indigenous Me´phaa community and Mexico City
Dr. Isaac González Santoyo
Facultad de Psicología, UNAM

10:30 – 10:50 **Coffee break**

Neuronal regulation of lung infection and pulmonary defense
Dr. Pankaj Baral
Kansas State University, USA

Neuroimmune interactions during experimental pulmonary tuberculosis
Dr. Rogelio Hernández-Pando
Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán”, Mexico City

11:50 – 12:10 *Technical presentation*

Líneas Celulares autenticadas como herramientas para las Neurociencias / Authenticated Cell Lines as a Tool for Neurosciences Research
M. en C. Francisco Calderón Estrella. CIENTÍFICA SENNA

12.10 – 13:10 **Plenary Lecture II**

Microbiota and neuroimmune interactions in gut homeostasis and CNS inflammation
Dr. Dan R. Littman,
Skirball Institute, USA

Chair: Dr. Gustavo Pedraza
Instituto de Biotecnología, UNAM, México

13:10 - 14:30 **Lunch**

14:30–15:30 **Four oral presentations selected from the abstracts II**

Chair: Dr. Oscar Zamora
Facultad de Psicología, UNAM, Mexico City

Transcriptional adaptive responses to ischemia linked to DNA methylation in astrocytes
Luis B. Tovar-y-Romo
Instituto de Fisiología Celular. UNAM

Characterization of layer 5 sensorimotor cortex neurons projecting to red nucleus and pons
Verónica López Virgen
Instituto de Neurobiología. UNAM

Spinal a6GABAA receptor activation induces antinociception under physiological and pathological conditions
Erick J. Rodríguez-Palma
Departamento de Farmacobiología. Cinvestav Sede Sur

An enriched environment restores metabolic homeostasis by reducing inflammation in the adipose tissue and hypothalamus of obese mice
María del Sol Diaz de Leon Guerrero
Instituto de Biotecnología.




15:30 – 17:30 **Symposium IV**

GLIAL CELLS IN HEALTH AND DISEASE

Chair: Dr. Arturo Ortega
Cinvestav, México City

Glutamate transporters: non-traditional roles in CNS myelination
Dr. Babette Fuss
Virginia Commonwealth University, USA

A functional signature in the developing cerebellum: evidence from a preclinical model of autism
Dr. Daniel Reyes-Haro
Instituto de Neurobiología, UNAM campus Juriquilla, México

Modulation of Tissue Injury and Repair by Microglia During Autoimmunity
Dr. Astrid Cardona
University of Texas, San Antonio, TX, USA

Astrocytes in aging: The case of the aryl hydrocarbon receptor and neurodegeneration
Dr. Mónica Torres Ramos
Instituto Nacional de Neurología y Neurocirugía, Mexico City

17:30 – 17:35 **1 min talks for poster advertisings**

Chair: Dr. Oscar Galicia
Departamento de Psicologia, Universidad Iberoamericana, Mexico City

The Suprachiasmatic nucleus controls sleep delay-induced hyperglycemia.
Gabriela Hurtado-Alvarado
Instituto de Investigaciones Biomédicas. UNAM

Maternal immune activation impairs morphophysiological properties of CA1 pyramidal neurons from dorsal hippocampus of the offspring
Ernesto Griego Melo
Departamento de Farmacobiología. Cinvestav Sede Sur

Analysis and comparison of protein content of serum derived exosomes obtained from patients with Major Depressive Disorder (MDD): responders versus non-responders to pharmacological treatment
Diana Gutierrez Buenabad
Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz". Facultad de Psicología. UNAM

Sympathoadrenomedular system mediates anti-inflammatory and glycemic reflex to endotoxin
Esteban Santacruz-Martínez
Instituto de Investigaciones Biomédicas. UNAM

In Vivo Transfection in a Murine Model of Tubulinopathy
Diego Carmona Montiel
Departamento de Ingeniería Química, Electrónica y Biomédica.Universidad de Guanajuato

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17:35 – 19:30 **Poster Session II (Odd numbers)**

19:30-20:00 ***Having a beer with the speakers***

WEDNESDAY, APRIL 6

9:00 – 12:00 **Free time**

12:00 – 13:00 **Four oral presentations selected from the abstracts III**

Chair: Dr. Yazmín Macotela
Instituto de Neurobiologia, Queretaro, Mexico.

Neurotoxicity induced by methylmercury in an in vitro model and its relationship with the development of Alzheimer's disease.
Angela Alvarez Dominguez
Universidad Autónoma de San Luis Potosí

Chronic copper exposure as an in vivo model of non-genetic Parkinson's disease
Alfredo González Alcocer
Facultad de Medicina. Universidad Autónoma de Nuevo Léon

Changes in the number and morphology of dendritic spines in the hippocampus and prefrontal cortex of the C58/J mouse model of autism
Isabel Barón Mendoza
Instituto de Investigaciones Biomédicas. UNAM

Putative single nucleotide polymorphisms associated with Alzheimer's disease by artificial intelligence strategy
Erick Cuevas Fernández
Universidad Autónoma del Estado de Morelos

13:00 – 14:00 **Plenary Lecture III**

Transgenerational inheritance of epigenetic signatures in mice
Dr. Yuta Takahashi
The Salk Institute, San Diego, CA, USA

Chair: Dr. Leonor Pérez-Martínez
Instituto de Biotecnología, UNAM

14:00 - 15:30 **Lunch**



15:30 – 17:30 **Symposium V**

THE SCIENTIFIC LEGACY OF LATE PROFESSOR RICARDO TAPIA

Chair: Dr. Lourdes Massieu / Dr. Clorinda Arias
Instituto de Fisiología Celular / Instituto de Investigaciones Biomedicas, Mexico City

Ricardo Tapia. A pioneer of Neurochemistry in Mexico
Dr. Lourdes Massieu
Instituto de Fisiología Celular, UNAM, Mexico City

Non-canonical gating control by the cytoplasmic T1 domain of Kv channels
Dr. Manuel Covarrubias
Thomas Jefferson University, Philadelphia, USA.

Electrophysiological biomarkers of epileptogenesis: new insights about its utility in the neurobiology of the hippocampus and clinic
Dr. Laura Medina-Ceja
Universidad de Guadalajara, Mexico

17:30 – 18:30 **Closure Lecture**

Death after a long journey; how local circuit neurons adjust their numbers
Dr. Arturo Álvarez-Buylla
University of California San Francisco, USA

Chair: Dr. Yazmín Macotela
Instituto de Neurobiología, UNAM

18:30 - 18:40 **Closing Ceremony**

19:00 – 20:00 **Business Meeting**

20:30 - **Farewell Dinner**

THURSDAY, APRIL 7

9:00 - 11:00 **Breakfast**

12:00 **Departure**

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Pre-Meeting Workshop:
Organoids and single-cell sequencing
in Neuroscience

Hotel Misión de los Ángeles, Oaxaca City, Oax. Mexico
April 3-7, 2022

Deadline for abstract submission:
February 25, 2022

OBRAS DEL ARTISTA PLÁSTICO OAXAQUEÑO MARIANO GÓMEZ RAMÍREZ

Organizing Committee:

Leonor Pérez Martínez, Instituto de Biotecnología, UNAM

Yazmín Macotela Guzmán, Instituto de Neurobiología, UNAM

Martín Gustavo Pedraza, Instituto de Biotecnología, UNAM

Oscar Zamora Arévalo, Facultad de Psicología, UNAM

Oscar Galicia Castillo, Departamento de Psicología, Universidad Iberoamericana

Arturo Ortega Soto, Departamento de Toxicología, Cinvestav

Iván Velasco, Instituto de Fisiología Celular, UNAM

Iván Velasco, Instituto de Fisiología Celular, UNAM

UNAM · Sociedad Mexicana de Bioquímica Neurobiología · SMB · 65 años 1957-2022 · CONACYT · IBERO Ciudad de México · Cinvestav · Instituto de Biotecnología · Instituto de Neurobiología · Instituto de Fisiología Celular, UNAM · Facultad de Psicología

Posters Session I Even numbers

Monday April 4. 17:05 – 19:00

COGNITION & BEHAVIOR

2	*Striatal Cholinergic Interneurons Contribute to Specific Behavioral Updates in a Classical Conditioning Task* **Hector Alatriste-León.** Cellular Physiology Institute. UNAM
4	*Early behavioral characterization of the murine model of autism induced by valproic acid* **Noé Samuel Bravo Rivero**. Facultad de Psicología, SUA, UNAM
6	*Short-memory disfunction induced by haloperidol in the thalamic reticular nucleus in the rat* **Christian A Evangelista Arzate**. Escuela Nacional de Ciencias Biológicas. I.P.N.
8	*Perception of regular and irregular stimuli in single trials in humans* **Marina Fuentes Dávila.** Instituto de Neurobiología, UNAM
10	*Lateral habenula participation during aversive sugar memory formation, as well as after flavor familiarization* **Jocelyn Lucero Lomeli-Castillo.** Instituto de Neurobiología, UNAM
12	*Establishing the link between Speech-to-speech Synchrony and General Auditory-Motor synchronization skills* **Cecilia Mares.** Instituto de Neurobiología, UNAM
14	*Effect of High-fat diet on the Central Nervous System in CD-1 mouse* **César A. Mendoza-Calles**. Instituto de Ciencias de la Salud. Universidad Veracruzana
16	*Starvation increases attraction to odorants through CRH-1/CREB activity in the nervous system and intestine of Caenorhabditis elegans.* **Francisco Pinta Castro**. Instituto de Fisiología Celular, UNAM
18	*Involvement of CB2 receptors of the anterior cingulate cortex on the modulation of palatable food intake in rats with binge-type behavior* **Juan Carlos Rodríguez-Aguilar.** FES Iztacala. UNAM
20	*Light and temperature cycles as zeitgebers in the circadian locomotor activity rhythm of the snake Crotalus molossus* **Ángel Bernardo Villarreal-Medina.** Instituto de Biología. UNAM

DEVELOPMENT & AGING

22	*The amniotic epithelium confers a bias to human embryonic stem cells to differentiate toward the neuroectoderm lineage* **Daniela Ávila González.** CIATEJ / INPER
24	*The role of GDNF in the axonal growth of motor neurons and in the establishment of the neuromuscular junction* **José Fernando Becerra Vélez.** Instituto de Fisiología Celular. UNAM
26	*Axonal degeneration in an in vitro model of neuronal senescence* **Gisselle A. Campos-Martínez.** Instituto de Fisiología Celular, UNAM

28	*TRa1andTRb1expression in the neurogenic nicheof the hippocampus* **Edna Ahtza Esparza Arellano.** Neuroscience Lab. University of Guanajuato
30	*Taurine plays a key role in the differentiation process of neural progenitor cells from SVZ through GABA receptor interaction* **Nadia Estefanía Gutiérrez-Castañeda.** Facultad de Medicina, UNAM
32	*Generation and characterization of human midbrain organoids* **Angel Polanco.** Instituto de Fisiología Celular, UNAM
34	*Generation of mouse and human embryonic stem cells for doxycycline inducible GDNF expression.* **Melanie Trinidad Peralta.** Instituto de Fisiología Celular, UNAM

TEACHING & SCIENTIFIC KNOWLEDGE DISSEMINATION

36	*How to give good public engagement talks? A pilot workshop aimed at researchers and students at IFC* **Camila del Río Castro.** Instituto de Fisiología Celular, UNAM

EPIGENETICS

38	*Identification of Enhancer Regions of Midbrain Dopaminergic Neurons using Histone Modification ChIP-Seq* **Mayela Giacomán-Lozano.** Tecnológico de Monterrey, Escuela de Medicina y Ciencias de la Salud
40	*DNA methyltransferases as an epigenetic barrier in Müller cells reprogramming* **Victoria-Chávez Rebeca Yael.** Dept. de Farmacobiología. Cinvestav Sede Sur

STRESS

42	*Effect of chronic stress on the expression of mucins and cytokines in different intestinal regions of female BALB/c mice* **Jennifer Karume1 Gutiérrez-Galicia.** Escuela Superior de Medicina. IPN
44	*Maternal consumption of trans-resveratrol, epigenetic and behavioral effects in prenatally stressed rats* **Gerardo Vega Juárez.** Instituto Nacional de Perinatología
46	*Evaluation of Superoxide dismutase enzyme activity in the prefrontal cortex of neonatal rats subjected to postnatal stress* **Dennis Paniagua Camacho.** Centro de Investigación Biomédica de Michoacán, IMSS
48	*Brain and peripheral oxidative damage during the development of obesity* **Elena Salazar-Hernández.** Universidad Autónoma de Guerrero
50	*Exposure to acute stress in young offspring from mothers with maternal immune infection acts as a risk factor for the development of depressive-like behaviors in adulthood* **Gabriela Abigail Valle-Castillo.** Instituto Nacional de Psiquiatría “Ramón de la Fuente Muñiz”

GENE EXPRESSION

52	*Gene data mining and Protein-Protein interaction analysis for Alzheimer's Disease and Diabetes Mellitus and identifies their potential molecular links* **Ricardo Castillo Velázquez.** Universidad Autónoma de San Luis Potosí
54	*Identification of transcripts, proteins and microRNAs that are differentially expressed at early phases of brain regeneration in the Mexican axolotl* **Arturo Emiliano Martínez-Hernández.** Instituto de Fisiología Celular. UNAM
56	*Transcriptional adaptation to ischemia in the brain endothelium mediated by the Early B-cell factor* **Jaime Emiliano Rogerio-Ríos.** Instituto de Fisiología Celular, UNAM
58	*Transcriptional effect of enriched environment exposure in a murine colitis model* **David Valle García.** Instituto de Biotecnología. UNAM

GLIA

60	*In Vitro and Computational Studies of Perezone and Perezone Angelate as Potential Anti-Glioblastoma Multiforme Agents* **Maricarmen Hernández Rodríguez.** Escuela Superior de Medicina. IPN
62	*Alterations in the physiology of Müller glial cells under diabetic retinopathy conditions in vitro* **Alan Emmanuel Medina Arellano.** Facultad de Medicina, UNAM
64	*Differential expression of astrocytic fibrillary glial acidic protein during brain aging in rats* **Brian Iván Morales-López.** Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suarez
66	*Flouride exposure modulates SLC7A11 (xCT) in radial glial cells* **Andrea Ocharán.** Departamento de Toxicología. Cinvestav. IPN
68	*Thrombospondin-1 (TSP-1) expression in brain mouse during postnatal development.* **Arturo Esteban Pérez Miguel.** Facultad de Psicología. UNAM,
70	*Effect of 5 Hz transcranial magnetic stimulation on hippocampal oligodendrocytes in chronically stressed female Swiss-Webster mice* **Allan Rico Becerra.** Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz"
72	*Differences in the localization of AQP1 and expression patterns of AQP isoforms in rat and mouse sciatic nerve and changes in rat AQPs expression after nerve crush injury* **Edith Segura-Anaya**. Laboratorio de Neurociencias. Facultad de Medicina. UAEMEx
74	*Analysis of density and distribution of astrocytes and microglial cells at the hippocampal formation of autistic-like C58/J mice.* **Carlos Noé Vázquez-Moreno.** Instituto de Investigaciones Biomédicas. UNAM

METABOLISM

76	*Obesity and its relationship with the appearance of peripheral insulin resistance and brain insulin resistance in C57BL/6 mice.* **Oscar Ezequiel Bahena-Cuevas**. FCQB. Universidad Autónoma de Guerrero

78	*Aerobic training decreases peripheral sensitivity and inflammation in T2D mice.* **Saúl Ernesto Cifuentes Mendiola**. FES Iztacala. UNAM
80	*Metabolomic profile of dopaminergic neurons derived from induced pluripotent stem cells of Parkinson's disease patients.* **Xóchitl Flores-Ponce**. Instituto de Fisiología Celular. UNAM
82	*Effect of cysthationine-gamma-lyase/hydrogen sulfide system modulation on vascular dysfunction induced by insulin resistance in male Wistar rat thoracic aorta* **Araceli Sánchez-López**. Departamento de Farmacobiología, Cinvestav – Coapa
84	*Sulpiride, a D2 dopamine receptor antagonist improves glucose tolerance, insulin sensitivity and reduces visceral adipocyte hypertrophy in obese mice* **Dina Iathzil Vázquez-Carrillo**. Instituto de Neurobiología. UNAM

NEUROENDOCRINOLOGY

86	*Short-term administration of tibolone reduces inflammation and oxidative stress in the hippocampus of ovariectomized rats fed high-fat and high-fructose* **Christian Guerra-Araiza**. Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social
88	*Oxytocin/vasopressin-related neuropeptide distribution in ovaries of Pogonomyrmex barbatus ant* **María Fernanda Vergara Martínez**. Instituto de Investigaciones Biomédicas, UNAM

NEUROPHARMACOLOGY

90	*Effect of probiotics on fluoxetine and sertraline antidepressant activity in learned helplessness models in mice.* **Patricia Aguirre-Bañuelos.** Universidad Autónoma de San Luis Potosí
92	*Analysis of the effect of two hypoglycemic agents on long-term memory in diabetic BALB/c mice* **Carolina Carrillo-Calderón**. Autonomous University of Coahuila
94	*Bunodeopsis globulifera toxins induce [3H]-glutamate release in rat cortex and decrease viability of human neuroblastoma cell line SH-SY5Y* **Aleida Jeannette Flores Pérez.** Posgrado en Ciencias del Mar y Limnología. UNAM
96	*Exogenous hydrogen sulfide improves hypertension induced by traumatic brain injury in rats through vasopressor sympathetic outflow inhibition and H_2S-synthesizing enzymes restoration* **Saúl Huerta de la Cruz**. Departamento de Farmacobiología, Cinvestav Coapa
98	*Identification of the locus underlying synaptic potentiation mediated by TrkB receptor activation in CA3 pyramidal cells of the hippocampus* **Roberto Olvera-Guillen**. Departament of Pharmacobiology, CINVESTAV
100	*Orally administered silybin improves most of the biochemical and behavioral outcomes in the MPTP-induced parkinsonism murine model* **Ricardo Jair Ramírez-Carreto.** Unidad de Investigación en Medicina Experimental, UNAM
102	*Anticonvulsant and nervous system stimulant effect of Ehretia tinifolia extracts* **David Osvaldo Salinas-Sánchez**. Universidad Autónoma del Estado de Morelos

104 *NPY-Y1 receptors in dorsal periaqueductal gray modulate food, sucrose and alcohol consumption in pre-exposed and free food and water access rats*
Priscila Vázquez-León. Facultad de Psicología. UNAM

INTEGRATIVE NEUROPHYSIOLOGY

106 *Enrichment environment improves memory and synaptic plasticity in cognitively impaired animals due to chronic exposure to a high-fructose and high-fat diet.*
Ernesto Saúl Gutiérrez López. Instituto de Fisiología Celular. UNAM

108 *Cortical effects of facial palsy in motor planning of facial expressions in a murine model*
Elías Perrusquia Hernández. Faculty of Higher Studies Iztacala. UNAM

110 *Dietary restriction blocks epileptogenesis by preventing the increase in low-frequency bands and IL-1β expression by hippocampal kindling*
Josué Denichi Sánchez Hernández. National Institute of Neurology and Neurosurgery M.V.S.

NEUROIMMUNOLOGY

112 *Influence of maternal immune activation on synaptic transmission mediated by metabotropic glutamate receptors at the mossy fiber-CA3 synapse.*
Johaly del Carmen Anguiano Buenfil. Departament of Pharmacobiology. Cinvestav

114 *Effect of thermal stimulation on macrophage subpopulations in a murine sepsis model*
Mario Alberto Bautista-Hernández. Centro Médico Nacional Siglo XXI, IMSS

116 *Catecholaminergic neuroimmunological system in the dental pulp*
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118 *Effect of dopamine type 2 receptor activation on neuroinflammation in a mouse model of sleep deprivation*
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120 *Activation of Toll-like receptors in combination with vincristine in glioblastoma cells*
Orlando Daniel Moedano-Hernández. Hospital Infantil de México Federico Gómez.

122 *The p38 MAP kinase mediates BDNF neuroprotective functions against β–Amyloid peptides and inflammatory cytokines*
Alejandro Ramírez Olvera. Instituto de Biotecnología, UNAM

124 *Differential expression of BDNF, RANTES and EOTAXIN-1 in serum-derived exosomes and in serum and from major depressive diagnosed patients*
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128	*Establishment of a CRISPR based-system for ataxin-7 transcript interactome characterization* **Rodolfo Daniel Ávila-Avilés.** Department of Genetics and Molecular Biology. Cinvestav IPN
130	*Tibolone administration decreases oxidative stress in plasma and spinal cord in a traumatic spinal cord injury animal model* **Guadalupe Bautista Poblet**. Hospital de Especialidades. Centro Médico Nacional SXXI. IMSS
132	*Early dysregulation of Wnt signaling in the hippocampus of 3xTg-AD model* **Diana Elizabeth Colín Martínez.** Instituto de Investigaciones Biomédicas. UNAM
134	*Role of NOX in NLRP3 inflammasome regulation during cerebellar granule neuron death.* **Karen S. Cruz-Hernández.** Instituto de Fisiología Celular. UNAM
136	*Inhalation of vanadium pentoxide (V2O5) induces memory and cytoskeleton alterations in brain structures related to Alzheimer disease.* **Claudia Dorado-Martínez**. Facultad de Estudios Superiores Iztacala, UNAM
138	*Hyperphosphorylated Tau relates to reduced hippocampal excitability in the young rTg4510 mouse model of tauopathy* **Carlos Antonio García-Carlos.** Instituto de Neurobiología. UNAM
140	*Autophagy Inducers Trehalose and Metformin Prevent Congnitive and Motor Dysfunction by Protecting Dopaminergic Neurons from Paraquat Toxicity* **Yareth Gopar-Cuevas.** Universidad Autónoma de Nuevo León, Facultad de Medicina
142	*Temporality in the expression of alpha-synuclein and dopaminergic neuronal death after intracerebral lipopolysaccharide injection* **Alma Karen Lomeli-Lepe**. (CUCBA), Universidad de Guadalajara
144	*Differential expression of synaptic plasticity of the medial and lateral perforant path to the dentate gyrus in a neurodevelopment model of schizophrenia: effects on spatial memory* **Luis A. Márquez.** Departament of Pharmacobiology, Cinvestav-Sede Sur

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146	*Neuronal differentiation of the N1E-115 cell line promoted by aminated biomaterial coatings synthesized by plasma polymerization*. **Estephanny Jocelyn Alvarado Muñoz.** Universidad Autónoma Metropolitana Plantel Xochimilco
148	*Environmental enrichment influences social interaction and agonistic behavior in the offspring of pregnant dams exposed to immune activation with the viral mimetic Poly I:C implication of neurogenesis and sex.* **Valeria Flores-Torres.** 1Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz
150	*Short time of social instability stress does not induce depressive-like behavior but evidences low social interaction with increased negative social behavior and dendritic remodeling in the dentate gyrus of female C57Bl6 in environmental enrichment* **Ana Cecilia Luis-Castañeda.** Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz
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160 *Artificial early and late memory signals induce taste avoidance memory, plastic and neurochemical changes*
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3	*Natural sweeteners decrease short-term memory capacity in male and female C57BL6 mice* **Cristina Balcón Pacheco**. Univ. of Guanajuato Campus Irapuato Salamanca
5	*Bimodal Encoding in a Neuronal Population of the Dorsal Premotor Cortex during Working Memory* **Andrea Fernanda Campos Pérez.** Instituto de Fisiología Celular, UNAM
7	*Environmental Enrichment and a Cooperative Social Behavior Task* **Gabriela Lizbeth Franco Olivares.** Facultad de Psicología. UNAM
9	*Effect of dopamine type 2 receptor activation in long-term memory in a murine REM sleep deprivation model.* **Stephany García Velasco**. Facultad de Medicina UNAM
11	*Maternal enrichment increases infantile spatial amnesia mediated by postnatal neurogenesis modulation.* **Grecia López-Oropeza.** Department of Cell Biology, Faculty of Sciences, UNAM
13	*The role of 5-HTRs of the Nucleus Accumbens in Sociability* **Magda Karina Martínez Mata.** Instituto de Fisiología Celular, UNAM
15	*Effects of Disruptors on a Retrospective Temporal Discrimination Task: An Approach through Signal Detection Theory* **Mario Pérez Calzada.** Facultad de Psicología. UNAM
17	*Emotional dysregulation in women with endometriosis presenting cyclical and non-cyclical chronic pelvic pain* **Dulce Carolina Rodríguez-Lozano**. INPER-Facultad de Química. UNAM
19	*Striatal circuitries for motor control and action selection* **Daniela Trejo-Saavedra**. Instituto de Neurobiología, UNAM
21	*The effect of optogenetic-induced synaptic plasticity in LC-CA1 pathway on memory* **Arenski Vázquez-Lechuga**. Instituto de Fisiología Celular. UNAM

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23	*Evaluation of ketogenic diet as a non-invasive strategy to improve autophagy and memory function in aged 3xTg-AD and WT mice* **Lorelei Ayala-Guerrero**. Instituto de Fisiología Celular. UNAM
25	*Sucrose Consumption During Late Adolescence alters Dendritic Orientation of Doublecortin Positive Neurons of The Ventral Dentate Gyrus in Adulthood* **Pablo Edson Bustamante Nieves.** Instituto Nacional de Pediatría

27	*Generation of knock-down and knock-out hESC lines for SCL to study GABAergic differentiation* **Jorge Luis Díaz-Ruiz.** Instituto de Fisiología Celular, UNAM
29	*Effect of sonic hedgehog on the axonal growth of human dopaminergic neurons* **García-Gutiérrez Paola.** Instituto Nacional de Neurología y Neurocirugía
31	*Prolactin receptor deficiency promotes a hypomyelinating phenotype in the corpus callosum of suckling and prepubertal mice* **Ana Luisa Ocampo-Ruiz**. Instituto de Neurobiología, UNAM
33	*The chronoarchitecture of the cerebral cortex could be linked to the emergence of the senescent phenotype* **Ana Karen Ramírez Reyes**. Instituto de Investigaciones Biomédicas, UNAM
35	*Effect of D-serine on cognitive reserve in aged rats* **Bárbara Vázquez-Prieto.** ENES - Unidad Juriquilla. UNAM

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43	*Participation of the Sympathetic Nervous System in the Modulation of Components of Intestinal Homeostasis in Mice Underwent Stress* **Fabiola Guzmán-Mejia.** Universidad Autónoma Metropolitana Xochimilco
45	*Mechanisms of Neurotoxicity Induced by Exposure to Low Doses of Permethrin* **Sonia Nava-Salazar.** Instituto Nacional de Perinatología
47	*Development of binge eating behavior in Female Wistar Kyoto rats: a better model with construct and appearance validity* **Daniela Sarai Rodriguez-Rangel.** Cinvestav-Sede Sur
49	*Mitochondrial dynamics under glucose deprivation and glucose reintroduction in cortical neurons and its possible regulation by the ketone body βhydroxybutyrate* **Ashley Salcido-Gómez.** Instituto de Fisiología Celular. UNAM

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51	*Identification of the exons retained in the mRNA of the Sulfonylurea receptor 1 in the brain and other rat tissues* **Penélope Aguilera.** Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez
53	*DISC1 interactome genes are associated with psychosis in patients with schizophrenia and bipolar disorder in the Mexican population* **Araceli Gutiérrez-Rodríguez.** Instituto Nacional de Medicina Genómica
55	*Potential role of lncRNAs as modulators of pluripotency and dopaminergic neuronal differentiation* **Ismael Portillo Pantoja.** Instituto de Fisiología Celular, UNAM
57	*An enriched environment prevents the cognitive decline in the Alzheimer´s disease mouse model 5XFAD by modulating the microglia neuroprotective phenotype* **Kenya Paola Romero Burgos.** Instituto de Biotecnología. UNAM

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59	*Evidence for a neuroinflammatory process in the hippocampus of the autistic-like mouse strain C58/J throughout development* **Juan Francisco Duarte-Campos.** Instituto de Investigaciones Biomédicas. UNAM
61	*Characterization of Mice Cerebellar Microglia Primary Cultures* **María Isabel Martínez Hernández.** Departamento de Toxicología. Cinvestav IPN
63	*Glutamine transport systems expressed in the U373MG glioblastoma cell line* **Laura Isabel Méndez-Aldana.** Departamento de Toxicología. Cinvestav. IPN
65	*Protective and antioxidant effects in glial cells of phenolic compounds* **José Manuel Nájera-Maldonado.** FCQB. Universidad Autónoma de Guerrero
67	*Expression of exosomal miR-29a in astrocytes exposed to high glucose* **Claudia Paola Pérez-Macedonio.** FCQB. Universidad Autónoma de Guerrero
69	*Stimulation with TNF-α and glutamate induces the release of Wnt5a and Wnt7a in Astrocyte-derived exosomes* **Rosa Isela Rendón-Meza.** Instituto de Investigaciones Biomédicas. UNAM
71	*Characterization of EAATs in human endothelial cells and astrocytes: contribution of the BBB to glutamate efflux* **Fredy Sánchez Cano.** Neurotoxicology Lab. Dep. of Toxicology. Cinvestav-IPN
73	*Aryl hydrocarbon receptor as a new EAAT1/GLAST regulator* **Janisse Silva-Parra**. Departamento de Toxicología. Cinvestav. IPN
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79	*Prolactin modulates enterocyte intestinal maturation in lactating mice* **José Luis Dena-Beltrán**. Instituto de Neurobiología. UNAM

81	*Regulation of the transcription factor TFEB by the ketone body β-hydroxybutyrate in neurons and its impact on mitophagy* **Juan Carlos Gómora-García**. Instituto de Fisiología Celular, UNAM
83	*Metabolic profile of CPA: Implications for Glioma's Treatment* **America Vanoye Carlo**. Laboratorio de Neurociencias, Instituto Nacional de Pediatría

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85	*Prolactin Modulates Sexual Pheromone Perception and Accessory Olfactory Bulb Cell Activation In Female Mice* **Viridiana Cerbantez Bueno**. Instituto de Neurobiología. UNAM
87	*Differential regulation of pituitary growth hormone expression and release by several neuropeptides among vertebrates* **Valeria Alejandra Urban Sosa**. Instituto de Neurobiología. UNAM
89	*Oxytocin/vasopressin-related neuropeptide distribution in developmental stages and castes in the ant Pogonomyrmex barbatus brain* **Carlos Zavaleta Zamora**. Instituto de Investigaciones Biomédicas, UNAM

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91	*Anxiolytic and hypnotic effect of methanolic extract of Malphigia mexicana* **Dante Avilés-Montes.** Universidad Autónoma del Estado de Morelos
93	*Sea anemone Bartholomea annulata venom actives $GABA_A$ CHANNEL-receptors* **Antonia Colom-Casasnovas.** Instituto de Ciencias del Mar y Limnología. UNAM
95	*Effect of hydrogen sulfide on the vascular dysfunction induced by severe traumatic brain injury in rats* **Félix Iván López-Preza**. Center for Research and Advanced Studies. Cinvestav
97	*Pharmacological evidence of the mechanisms involved in the hydrogen sulfide-induced peripheral neuronal modulation of the vascular tone* **Grecia Josefa Medina-Terol.** Departamento de Farmacobiología. Cinvestav Coapa
99	*Characterization of hollow titanium dioxide nanospheres as a release device of biomolecules with the potential to induce axonal growth of human dopaminergic neurons* **Emma Ortiz-Islas**. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez
101	*Silica nanoparticles functionalized with folic acid and loaded with antineoplastic drugs for glioblastoma multiforme* **Citlali Ekaterina Rodríguez-Pérez**. Molecular Neuropharmacology and Nanotechnology lab National Institute of Neurology and Neurosurgery
103	*Functional expression of the oligodendroglial α3β2γ1 GABAA receptor in HEK293 cells* **María Berenice Varela Correa**. Instituto de Neurobiología, UNAM
105	*Effects of pioglitazone in an experimental animal model of Attention-Deficit/Hyperactivity Disorder* **Daniela Vázquez-González**. Hospital Infantil de México Federico Gómez

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109	*In Vivo Wireless Optogenetic Control of Skilled Motor Behavior* **Diana L. Rodríguez-Muñoz**. Instituto de Fisiología Celular. UNAM
111	*Neuronal representation of oral ethanol administration in orbitofrontal cortex of sedated naïve mice* **Karla Ivonne Zepeda-Reyes.** Faculty of Higher Studies Iztacala. UNAM

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113	*KChIP3 impairs memory in the Alzheimer's disease mouse model 5XFAD* **Bolivar Jesús Arcos-Encarnación**. Instituto de Biotecnología UNAM
115	*Analysis and comparison of protein content of serum derived exosomes obtained from patients with Major Depressive Disorder (MDD): responders versus non-responders to pharmacological treatment* **Diana Gutierrez-Buenabad.** Facultad de Psicología. UNAM
117	*Maternal immune activation impairs morphophysiological properties of CA1 pyramidal neurons from dorsal hippocampus of the offspring* **Ernesto Griego Melo.** Departament of Pharmacobiology, Cinvestav
119	*Effect of maternal immune activation on central nervous system and function* **Karla F Meza-Sosa.** Instituto de Biotecnología, UNAM
121	*TNFR2 inhibit Long-term potentiation in single-synapses and promote memory loss in a familial Alzheimer´s disease mouse model* **Jorge Luis Ochoa-Almazán**. Instituto de Biotecnología. UNAM
123	*Sympathoadrenomedular system mediates anti-inflammatory and glycemic reflex to endotoxin* **Esteban Santacruz-Martínez**. Instituto de Investigaciones Biomédicas. UNAM
125	*Exposure to an Enriched Environment Attenuates Mouse Experimental Colitis* **Tomás Villaseñor Toledo**. Instituto de Biotecnología, UNAM

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127	*Structural and dynamics analysis of the polyQ tract in the Ataxin-7 protein* **Rodolfo Daniel Ávila-Avilés.** Cinvestav IPN
129	*Effect of the ketone body β-hydroxybutyrate on autophagy activation induced by glucose deprivation in cultured cortical neurons* **Karla Gabriela Avilez Poblador**. Instituto de Fisiología Celular. UNAM
131	*In Vivo Transfection in a Murine Model of Tubulinopathy* **Diego Carmona Montiel**. Neuroscience Laboratory, DCI, University of Guanajuato
133	*Effect of tibolone on inflammation and motor recovery in a model of traumatic spinal cord injury* **Angélica B. Coyoy Salgado**. Hospital de Especialidades. Centro Médico Nacional SXXI. IMSS - CONACyT
135	*Characterization of cellular markers of senescence during the progression of Alzheimer's disease pathology in the brain of 3xTg-AD mice* **José Eduardo Domínguez Rivas**. Instituto de Investigaciones Biomédicas, UNAM

137	*Dopamine concentration and mitochondrial function modifications in a Parkinson's disease model by manganese inhalation* **Cesar Alfonso Garcia-Caballero**. Facultad de Estudios Superiores Iztacala, UNAM
139	*Post-translational modifications on tau protein after neuronal exposure to palmitic acid* **Valeria Melissa García-Cruz**. Instituto de Investigaciones Biomédicas. UNAM
141	*Contribution of brain microvasculature to remyelination after an ischemic injury via extracellular vesicles* **Fernando Hernández-Real**. Instituto de Fisiología Celular. UNAM
143	*Temporal expression of circadian clock proteins in glioma C6* **Emely Maqueda-Martínez.** Instituto de Investigaciones Biomédicas. UNAM
145	*Protective effect of the ketone body, β-hydroxybutyrate on ischemic brain injury. Role of reticular stress and autophagy* **Teresa Montiel**. Instituto de Fisiología Celular. UNAM

CELLULAR PLASTICITY & NEURAL CIRCUITS

147	*The persistence of antidepressant-like effects of rTMS at 5Hz is associated with microglial modifications in the hippocampal neurogenic niche in rodents exposed to unpredictable chronic mild stress.* **Dana Vianey Castro-de Aquino.** Instituto Nacional de Psiquiatría
149	*Neurogenesis-dependent and/or independent mechanisms underlying the antidepressant-like effect of 5Hz repetitive transcranial magnetic stimulation (rTMS) in mice exposed to chronic mild stress* **Andrea Granados-Juárez.** Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz
151	*Repetitive transcranial magnetic stimulation (5 Hz) decreases the depressive-like behavior, modifies the structural dendritic plasticity, and induces global epigenetic changes in the frontal cortex and hippocampus in a model mouse of chronic stress.* **Juan David Meneses-San**. National Institute of Psychiatry "Ramón de la Fuente Muñiz"
153	*Memory impairment in adulthood after neonatal excitotoxicity is related to changes in NMDA receptor NR2 subunit protein expression* **Mónica E. Ureña-Guerrero.** (CUCBA), Universidad de Guadalajara

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155	*The Krüppel-like factor 13 (KLF13) is a New Regulator of the JAK/STAT Signaling Pathway in Hippocampal Neurons* **José Ávila-Mendoza.** Instituto de Neurobiología. UNAM
157	*Analysis of phosphatidylethanolamine binding protein 1 (PEBP1) interactions with other proteins during brain cerebral focal ischemia in rat hippocampus* **Jorge Daniel Corzo-Toledo.** Cinvestav – IPN
159	*PTP1B regulates cell cycle progression through a Cdk3/Rb dependent manner in human glioblastoma cells* **Olga Villamar-Cruz.** Facultad de Estudios Superiores-Iztacala. UNAM

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161 *Functional role of cortical glutamatergic neurotransmission in conditioned taste preference*
Karla Gabriela Medina-Medina. Instituto de Fisiología Celular. UNAM

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163 *Increase of 5-HT levels is induced both in mouse brain and HEK-293 cells following their exposure to a non-viral tryptophan hydroxylase construct.*
Emiliano Tesoro-Cruz. Hospital de Infectología, Centro Médico Nacional “La Raza”, IMSS / IFC UNAM

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V

Neurobiology Meeting of the Mexican Society for Biochemistry

Pre-meeting course

Abstracts

Computational methods used for single-cell sequencing of brain cells

Raquel Cuevas-Diaz Duran[1], Jiaqian Wu[2,3,4]

[1]Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Monterrey, Nuevo Leon, Mexico.

[2] The Vivian L. Smith Department of Neurosurgery, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, United States

[3]Center for Stem Cell and Regenerative Medicine, UT Brown Foundation Institute of Molecular Medicine, Houston, TX, United States.

[4]MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, Houston, TX, United States.

Single-cell sequencing technologies are transforming our understanding of the transcriptomic and epigenomic identities of brain cells and their interplay in health and disease. As the capacity and accuracy of experimental conditions grow, more analysis tools are becoming available and the selection of data analysis methods requires a better understanding of the underlying statistical assumptions. Here, we review key computational steps used in a typical single-cell sequencing analysis including data preprocessing, normalization, feature selection, dimensionality reduction, visualization, and downstream applications such as clustering, cluster characterization, trajectory inference, and kinetics of transcription among others. We highlight the implementation of single-cell technologies in neuroscience.

Building multilevel atlases one cell at a time using patch-seq technology

Violeta Giselle López Huerta
Physiology and Neurodevelopment Department. Instituto de Fisiología Celular, UNAM. Ciudad Universitaria. Mexico

The era of single cell omics is revolutionizing the field of neurobiology. Single cell transcriptomics offers a comprehensive, objective way to study neurons and neural circuits and has become a cornerstone of neuroscience. However, it is necessary to have an integral approach combining other techniques to have a biological validation and deeper meaning of the big data that transcriptomics offers. Patch-seq is a powerful technique that allows a targeted study of single neurons at the transcriptomics, physiology and morphological levels. As a multimodal approach it bridges the molecular and physiology levels of complexity in neural networks. In this class we will review the opportunities as well as the challenges it presents.

Understanding the nervous system of *C. elegans* one neuron at a time

Julián Valdés

Departamento de Biología Celular y del Desarrollo, Instituto de Fisiología Celular, Universidad Nacional Autónoma de México, Mexico City.

The free-living nematode *Caenorhabditis elegans* has been a model organism for over 50 years powering seminal discoveries in developmental, molecular and cell biology as well as neurosciences. This nematode has a constant number of cells and each cellular division has been mapped from the one-cell embryo to the 959 somatic cells in the adult hermaphrodite. The nervous system of *C. elegans* is composed of 302 neurons and 56 glial cells distributed in the ganglia in the head, tail and ventral nerve connected by approximately 5000 chemical synapses, 2000 neuromuscular junctions and 500 gap junctions. Worms use neurotransmitters acetylcholine, GABA, glutamate, serotonin, dopamine, octopamine and tyramine allowing the sensory neurons to detect a plethora of environmental stimuli like food, predators, pathogens, temperature, and light among others and letting the animals to adapt their behavior accordingly. *C. elegans* also shows different forms of associative and non-associative learning in addition to long-term memory. More recently, the whole connectome of *C. elegans* has been fully characterized at an astonishing resolution by electron microscopy as well as the transcriptional profiling of each neuron by single-cell RNA-seq. We will review these recent achievements that now make it possible to study the complete nervous system of an animal as an integrated unit and open up the possibility to investigate its interaction with the environment as a whole.

Modeling human brain development and disorders using brain organoids

Zhexing Wen

Emory University School of Medicine, Atlanta, GA, USA

With the rapid development of stem cell technology, the advent of three-dimensional (3D) cultured brain organoids has opened a new avenue for studying human neurodevelopment and neurological disorders. Brain organoids are stem-cell-derived 3D suspension cultures that self-assemble into an organized structure with cell types and cytoarchitectures recapitulating the developing brain. In recent years, brain organoids have been utilized in various aspects, ranging from basic biology studies, to disease modeling, and high-throughput screening of pharmaceutical compounds. Here I will discuss how to combine the cutting-edge brain organoid technology with sing-cell sequencing and other approaches to study human brain development and delineate the molecular mechanisms underlying neurodevelopmental disorders.

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Open House for the public

Abstracts

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How COVID-19 can affect your brain?

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Área: Docencia y divulgación

Abstract:

The COVID-19 pandemic has caused several troubles to our country both socially and economically. At the level of individual health, people who acquire the disease commonly have affectations in the respiratory system, however, they can also develop complications in other organs such as the kidneys, heart, blood vessels and brain. In this last organ, it has been documented in many patients, regardless of whether they have mild or severe symptoms, the presence of mental and cognitive abnormalities, including memory loss, decreased attention span, restlessness, delirium and even risk of brain stroke, abnormalities that can persist even long after recovery from respiratory symptoms. Due to this, it is still important to inform to the general public about all the effects of COVID-19 in order to prevent its spread.

Keywords: COVID-19, pandemic, brain.

Different approaches to study animal behavior

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Topic: Open House for the public (science communication)

Animal models are used in experiments in the behavioural neurosciences that aim to contribute to the better undertanding, prevention and treatment of diverse motor, cognitive and affective disorders in human beings. The aim of this talk is to provide a brief overview of the most commonly used animals models and behavioral tests in neurosciences, as well as to show the key relevance of their coordinated and effective use. We will start explaining that animal behavior is regulated by national and international legislation that provide a framework for performing more humane animal research. Then, we will procede to describe different animal models (c. elegans, frut fly, zebrafish, guinea pig and mice/rats) making enphasis in the advantages and limitations of each to study different aspect of behavior.

***Keywords**: Animal use, 3R, behavioral evaluations*

IV

Neurobiology Meeting of the Mexican Society for Biochemistry

Plenary
Abstracts

Opening Talk

"What do reactive astrocytes (really) do?"

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The study of astrocyte reactivity requires careful identification of heterogeneity via transcriptomic profiling, followed by identification using cell based systems to model their functional alterations compared to physiologically 'normal' astrocytes. Further validation by confirmation in rodent models of disease and in human cells and postmortem tissue provides corroboration of biologically important reactive astrocyte sub-states.

We recently completed a large well-powered scRNAseq analysis of astrocyte reactivity profiles following acute systemic inflammation, highlighting several transcriptomically defined sub-states. Further, using integration with other published datasets we find specific disease-associated substates in rodent models of Alzheimer's disease, demyelination, and an acute stab wound. Following, we produced in vitro models to further study the functional alterations of these substates of reactive astrocytes, and used snRNASeq from human post-mortem Alzheimer's disease patients for cross-specific integration.

We define transcriptomic differences in astrocytes and oligodendrocytes in Alzheimer's disease at the single nuclei level and localize human Alzheimer's-associated transcription profiles to strategic location in the inflamed mouse brain.

Systematic analysis of astrocytes after spinal cord injury unveils heterogeneity and important regulatory genes in astrogliosis

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To better understand the functions and interactions of the cell types in the brain, we have previously purified representative populations of neurons, astrocytes, oligodendrocyte precursor cells, newly formed oligodendrocytes, myelinating oligodendrocytes, microglia, endothelial cells, and pericytes from mouse cerebral cortex, collaborating with Dr. Ben Barres group. We generated a transcriptome database for these cell types by RNA sequencing (http://jiaqianwulab.org/resource.htm; https://www.brainrnaseq.org/). Recently, we have comprehensively investigated the molecular changes in the injury environment and the astrocyte-specific responses by astrocyte purification from injured adult spinal cords from acute to chronic stages. In addition to protein-coding genes, we have systematically analyzed the expression profiles of long non-coding RNAs (lncRNAs) (>200 bp), which are regulatory RNAs that play important roles in the CNS. Bioinformatic and functional analyses identified a highly conserved lncRNA *Zeb2os*, and we demonstrated it plays an essential role in reactive astrogliosis through the *Zeb2os/Zeb2/Stat3* axis. Viral mediated knockdown of *Zeb2os* in subacute stage of spinal cord injury (SCI) led to reduced astrogliosis, lesion size and pSTAT3 in injured animal models (PMID: 33535036). Overall, these studies provide valuable insights into the molecular basis of reactive astrogliosis and fill the knowledge gap regarding the functions of lncRNA in astrogliosis and SCI.

Currently, my group is dissecting molecular and cellular constituents of astrocyte lineage cells and progenitors in neurological injury and disorders using single cell sequencing, advanced comparative bioinformatics and functional tests. Studies from us and others indicate that astrocyte lineage cells are highly heterogeneous in gene profiles and morphology (PMID: 33589835). How diverse constituents of these cells contribute to neurological disorders remains elusive. Understanding astrocyte lineage cell states and roles can open new avenues for the development of improved therapeutics.

RORγt$^+$ immune cells as integrators of microbiota and gut neuroimmune interactions

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Multiple constituents of the intestinal commensal microbiota interact with host immune system cells to promote mutually beneficial functions. Among these, bacterial pathobionts, such as *Helicobacter hepaticus* (Hh), co-exist with the mammalian host under homeostatic conditions, but promote inflammatory bowel disease following diverse perturbations of host immune functions. Hh induces microbe-specific regulatory T cells (iTreg) and follicular helper cells (Tfh) at homeostasis. However, when iTreg cell differentiation is perturbed, Hh instead induces pathogenic Th17 cells and colitis. We sought to determine which antigen-presenting cells (APCs) convey Hh-directed signals for iTreg cell differentiation. We unexpectedly found that antigen presentation by CCR7-dependent migratory RORγt$^+$ cells, potentially type 3 innate lymphoid cells (ILC3), is both required and sufficient to instruct microbiota-specific iTreg cell differentiation. In contrast, pathogenic Hh-specific Th17 cell differentiation required neither CD11c- nor CCR7-expressing APCs, while Tfh cells were dependent on antigen presentation by CD11c$^+$ cells. Our results thus highlight the existence of defined APC subsets that respond to microbiota to direct the differentiation of distinct CD4$^+$ T cell programs. Insights from these studies may allow for future manipulation of APCs to achieve desired compositions of antigen-specific T cells for therapeutic applications. The lymphoid tissue inducer-like ILC3 also form intestinal cryptopatches that are innervated by enteric neurons producing vasoactive intestinal peptide (VIP). In response to feeding, activation of these neurons results in inhibition of ILC3 function with, reduced production of microbiota-dependent IL-22. As a consequence, there is enhancement of a lipid-transport program in intestinal epithelial cells, as well as reduced production of anti-microbial peptides, with blooming of Firmicute bacteria. The VIPergic neuron:ILC3 axis thus balances selective microbiota growth with nutrient acquisition. We are currently investigating the potential role of this neuroimmune circuit in regulation of microbiota-specific T cell differentiation.

Dan Littman's laboratory has made multiple contributions towards our understanding of mechanisms that promote immune system development and roles in physiological homeostasis, particularly through interactions with microbiota and with cells of the peripheral and central nervous systems. He received Ph.D. and M.D. degrees from Washington University in St. Louis, and was Professor of Microbiology and Imm unology at the University of California, San Francisco, before joining NYU, where he is the Kimmel Professor of Molecular Immunology at the Skirball Institute and an Investigator of the Howard Hughes Medical Institute. Dr. Littman is a member of the U.S. N ational Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences, past president of the American Association of Immunologists, and recipient of several scientific awards, including the Ross Prize in Molecular Medicine and the Vilcek Prize in Biomedical Sciences.

Transgenerational inheritance of epigenetic signatures in mice

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We have sought to deeply explore the physiological and pathological functions of DNA methylation using our unique DNA methylation editing technique. We previously demonstrated that insertion of CpG-free DNA, which doesn't contain any CG sequences, into targeted CpG islands (CGIs) induces *de novo* methylation of the entire CGI in human pluripotent stem cells (PSCs) (Takahashi, *Science*, 2017). The acquired methylation is stably maintained even after CpG-free DNA removal, extensive passaging, and differentiation. Thus, this approach allows for targeted CGI methylation editing. Using this approach, we have successfully generated a PSC model with a cancer-related epimutation and corrected aberrant imprinting in iPSCs derived from Angelman syndrome patient. More recently, we have established the first DNA methylation-edited mice using our DNA methylation editing strategy. We found that the introduced methylation in obesity-related CGI could be stably maintained during the development of mice and resulted in extreme obesity. More importantly, we demonstrated that the acquired DNA methylation of targeted CGIs is transmitted from parent to offspring. Taken together, our approach enables us to generate epigenetically modified animals, which could allow for detailed investigation of the physiological and pathological roles of epigenetics and mechanisms of transgenerational epigenetic inheritance in mammal.

Death After a Long Journey; How Local Circuit Neurons Adjust their Numbers

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Neural Stem Cells become regionally specified very early in development. Their location determines the types of neurons they will generate. This often results in a dislocation between the site of neuronal birth and the brain region where neurons will be incorporated into functional circuits. Therefore, many young neurons are required to migrate extremely long distances to reach their ultimate destination. An extreme example of this process is the migration of GABAergic inhibitory neurons into the cerebral cortex. Whereas the excitatory cortical neurons are born in the underlying cortical epithelium, inhibitory cells are born in the ventral forebrain, in the medial and caudal ganglionic eminences (MGE & CGE), far from the developing cerebral cortex. How do inhibitory and excitatory neurons adjust their numbers to properly balance neural circuits? This is essential to establish a proper excitatory-inhibitory balance which is key to brain function and to prevent neurological deficits and epilepsy. Previous work from our laboratory identified a period of programmed cell death (PCD) when approximately 40% of the MGE-derived cINs are eliminated. Surprisingly, this period of cIN elimination is in part controlled by an intrinsic mechanism within MGE-derived cells and is not dependent on the trophic support from the excitatory cells already present in the cortex. Clustered Protocadherins (Pcdhs) are homophilic cell-adhesion molecules expressed in a combinatorial manner in single neurons. Three clusters of Pcdhs genes (α, β, and γ) encode 58 distinct isoforms. I will discuss our findings on the contribution of the different Pcdh clusters and isoforms to the regulation of cIN programmed cell death. I will also discuss co-transplantation studies of Pcdh mutant and wild-type young cINs which reveal both self, and non-self autonomous mechanisms in the regulation of programmed cell death. The new data indicates that Pcdhs are key intrinsic regulators of cIN survival precisely during the period of PCD.

IV

Neurobiology Meeting of the Mexican Society for Biochemistry

Symposia

Abstracts

Environmental effects on *C. elegans* behavior, from hyperglycemia tostarvation

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In its natural ecosystem, the nematode *Caenorhabditis elegans* is exposed to diverse environmental stimuli ranging from different food sources, toxic chemicals, temperature, starvation and pathogens. The nematodes have an extraordinary capacity to sense molecules such as odorants that allow them to adapt their behavior and survive the changing environment. Additionally, they can establish long-term memory of the favorable environments in favor of survival. In our laboratory, we have established that long periods of starvation during larval stages result in alterations in the preference to odorants, these changes are dependent on the insulin pathway as well as the transcription factor CREB that is activated in neurons and intestine cells after starvation. On the other hand, exposing the nematodes to a high-glucose environment not only affects their odorant preference but impairs the establishment of long-term memory with the odorant benzaldehyde having a transgenerational effect. Our results highlight the intricate relationship between different environments and neuronal circuits as well as the crosstalk between neurons and intestine cells in the worm.

Dynamic landscape of chromatin accessibility and transcriptomic changes during differentiation of human embryonic stem cells into dopaminergic neurons

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Chromatin architecture influences transcription by modulating the physical access of regulatory factors to DNA, playing fundamental roles in cell identity. Studies on dopaminergic differentiation have identified coding genes, but the relationship with non-coding genes or chromatin accessibility remains elusive. In the current research we used RNA-Seq and ATAC-Seq to profile differentially expressed transcripts and open chromatin regions during early dopaminergic neuron differentiation. We performed hierarchical clustering of differentially expressed genes and found 6 groups of genes enriched in functions related to dopaminergic neuron differentiation. Interestingly, we observed a decrease in open chromatin regions upon differentiation and found that these regions yielded specific functional enriched pathways and gene-sets. Additionally, a motif analysis resulted in the identification of transcription factors and structural nuclear proteins that potentially regulate dopaminergic differentiation. We also found changes in protein and mRNA abundance of the CCCTC-binding factor, CTCF, which participates in genome organization and gene expression. Our work provides a unique resource of transcription factors and regulatory elements, potentially involved in human dopaminergic neuron cell fate commitment.

In vivo gene editing to study neurodevelopmental disorders

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Neurodevelopmental disorders are a set of diseases with high prevalence and complex etiology and symptoms. The latest evidence suggests a strong genetic component, interestingly, most times polygenicity accounts for all the diversity found in patients. Nevertheless, most known genes belong to few frequently affected molecular pathways suggesting convergence in the mechanisms and brain circuits underlying neurodevelopmental disorders. Recent advances in gene editing technology, such as CRISPR/Cas9, makes it possible to mutate several genes in targeted neuronal populations. Here we use CRISPR technology to identify genetic mediators that affect electrophysiological profiles of a brain region involved in neurodevelopmental disorders like autism spectrum disorder and attention deficit and hyperactivity disorders. We unveil a powerful tool to further investigate the molecular and physiological underpinnings of brain disorders.

Key words: CRISPR, gene editing, brain circuits

Modeling Fragile X syndrome with 3D human brain organoids

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Fragile X syndrome (FXS) is the most common inherited form of intellectual disability and a leading genetic cause of autism. FXS is caused by the loss of functional fragile X mental retardation protein (FMRP), an RNA-binding protein that can regulate the translation of specific mRNAs. Despite major progress to characterize underlying disease mechanisms in animal models that has led to several clinical trials, improvements of behavioral and cognitive outcomes in patients have unfortunately been unsuccessful, a strong need for human-specific models of FXS to understand the unique factors that underlie human disease and to test the efficacy of candidate compounds. Here we have developed an FXS human forebrain organoid model and observed the loss of FMRP led to dysregulated neurogenesis, neuronal maturation, and neuronal excitability. Bulk and single-cell gene expression analyses of FXS forebrain organoids revealed that the loss of FMRP altered gene expression in a cell type-specific manner. The developmental deficits in FXS forebrain organoids could be rescued by inhibiting the phosphoinositide 3-kinase pathway, but not the metabotropic glutamate pathway disrupted in the FXS mouse model. Furthermore, we identified a large number of human-specific mRNAs bound by FMRP. One of these human-specific FMRP targets, CHD2, contributed to the altered gene expression in FXS organoids. Collectively, our study revealed molecular, cellular, and electrophysiological abnormalities associated with the loss of FMRP during human brain development.

The role of neuropeptides in social behavior and reproduction in ants.

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Behavioral and reproducti ve division of labor are key features of insect societies. Where queens specialize in egg laying, workers perform all the tasks related to the maintenance and growth of the the colony such as collecti ng food, caring for the young and defending the colony. Division of labor in ant colonies is known to be associated with age, genotype, individual experience, size, and morphology and is characteri zed by both speciali zation and behavioral flexibility. However, many aspects of its molecular and neurobiological basis remain poorly understood. Here we asked what are the differences between queens and worker ants and between workers performing different tasks at the neurobiological level.

To identify differences in gene expression between queens and workers we performed brain transcriptomic analysis in seven distantly related species of ants. We found that the ant insulin gene, insulin-like peptide 2 (*ilp2),* is always unregulated in queens across all species tested. We showed that in the clonal raider ant, *ilp2* expression in adults responds to larval signals that inhibit reproduction, and that by increasing ILP2 levels through synthetic peptide injections we could override the larval suppression signals, inducing reproductive division of labor. This allowed us to propose a simple model to explain the emergence of ant social behavior via evolutionary innovations in insulin signaling.

To understand the differences between workers that perform different tasks in ants, we characterized the function of the oxytocin/vasopressin ortholog, inotocin. Oxytoci n is a highly conserved peptide that plays major roles in regulating social behavior across vertebrates. Our results in ants show that levels of inotocin correlate with age and with propensity to forage, and that pharmacologically increasing inotocin had an effect on behavior only in ants of a certain age and in a specific social environment, suggesting that inotocin signaling plays an important role in worker division of labor by modulating behavioral response thresholds to social cues, which could contribute to behavioral individuality in ants.

Endocannabinoids in juvenile stages of development modulate gene expression changes that affect learning and time perception.

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A cognitive impairment associated with marijuana consumption at an early age has been described in consumers. There are some doubts whether this impairment is due to alterations in the developing nervous system and/or by educational factors. We aim to assess the effect of anandamide in developing rats on both learning and performing a temporal bisection task in their adult stage. Also, we evaluate the gene expression of principal subunits of NMDA receptors in the hippocampus and prefrontal brain cortex and their relation to the learning and performance of the behavioral task.

Anandamide or vehicle was injected i.p. for 14 consecutive days to 21 (Young) and 150 (Old) day-old Wistar rats. Both groups were evaluated in a temporal bisection test, which included discriminating tones of different durations that the animals must classify as a short or long time. The gene expression of Grin1, Grin2A, and Grin2B was evaluated by PCR-Quantitative in both groups, after the extraction of mRNA from the hippocampus and prefrontal brain cortex. The young group which received anandamide shows impairment in the learning of the temporal bisection task ($p<0.05$) and a modification in the time of estimation ($p<0.05$). The supplementation with anandamide in the young group showed a decreased expression of Grin2b ($p=0.001$) versus the control vehicle group. However, the same young group (supplemented with anandamide) tested after the behavioral task, not showed a difference ($p>0.05$) versus the control vehicle group, in gene expression of all the genes evaluated in this study. A significantly high correlation ($r=0.775$; $p=0.025$) was founded between grin1 gene expression in the hippocampus and the number of sessions to learn the temporal estimation task, but only in the young group. The effect caused by anandamide in young rats can be observed in a long-term period in the hippocampus, and in the gene expression of NMDA protein receptor subunits, which are implicated in learning mechanisms.

Keywords: cannabinoids; endocannabinoid system; behavior; learning; temporal bisection task

Genome-wide detection of transcriptional determinants of neurological decline

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Modern Neuropharmacological development requires a deeper understanding of the intricate molecular underpinnings of complex phenotypes, including neural development, aging-related neurological decline and behaviour.

Genome-wide approaches have become an essential tool to gain more comprehensive insights into the wider molecular circuitries underlying complex biological traits, both in health and disease. Here we set out to detect networks of transcriptional determinants of cognitive decline as well as long term functional maintenance in neural tissue. By combining genome-wide coexpression approaches with phenotypic associations in mouse models of AD as well as human data on postmitotic cellular longevity, derived from a range of tissues, we identify gene network signatures associated with either cognitive decline in AD as well as as motor deterioration in Parkinson´s and Huntington´s disease, in addition to brain ageing. Our results demonstrate wider and coherent transcriptional machineries, normally associated with neurological functional stability, that become compromised during the onset of age related functional decline in the nervous system.

Su línea de investigación se centra en el empleo de aproximaciones de genómica funcional, genómica comparativa y análisis de redes de coexpresión para la identificación de redes transcripcionales subyacentes a fenotipos complejos, con énfasis en aspectos del desarrollo, complejidad y/o deterioro funcional en varios sistemas, así como envejecimiento y el control de longevidad celular postmitótica en diversos tejidos yespecialmente en el sistema nervioso.
El objetivo de estas aproximaciones es la detección de determinantes y firmas transcripcionales con poder pronósitico y diagnóstico en un amplio espectro de condiciones patológicas, así como la identificación de blancos transcripcionales con potencial terapéutico en patologías de interés.
Cuenta con un sólido historial de publicaciones en revistas de alto impacto (índice H = 21), incluyendo Nature Neuroscience, Journal of Neuroscience, Developent, Proceedings of the Royal Society B y otras. Cuenta con una amplia red de colaboradores en varios países incluido el Reino Unido, México, Irlanda y España. Participa activamente en la enseñanza en todos los niveles de educación superior y es mi embro permanente (Permantent Fellow) de la Academia Británica de Educación superior. Ha dirigido un gran número de tesis de licenciatura (23), maestría (6) y doctorado (5) tanto en México como en el reino Unido y es miembro del Sistema Nacional de Investigadores (SNI) nivel 2.
Es egresado de la Licenciatura en Investigación Biomédica de la UNAM y obtuvo su Maestría y Doctorado en ciencias biomédicas en la misma institución. Llevó a cabo varias estancias posdoctorales en el Reino Unido (Universidad de St Andrews, Universidad de Edinburgo y Universidad de Cardiff), estudiando redes de señalización involucradas en la regulación del desarrollo y supervivencia neural. Fue investigador titular de tiempo completo en el Instituto de Fisiología celular de la UNAM e ntre 2010 y 2012, transfiriéndose posteriormente al Reino Unido con la posición de Senior Lecturer in Biomedical Sciences en la Universidad de Lincoln entre 2012 y 2019. Habiendo regresado recientemente a México es actualmente Investigador en Ciencias Médicas en el Instituto Nacional de Medicina Genómica.

Prepronociceptin-expressing neurons in the extended amygdala signal darting away from an aversive odor

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Dysregulation in the neural circuitry that encodes physiological arousal responses is thought to contribute to the manifestation of the maladaptive behaviors observed in neuropsychiatric disorders. We previously found that *prepronociceptin*-expressing neurons in the bed nucleus of the stria terminalis (*Pnoc*^{BNST} neurons) modulate rapid changes in physiological arousal upon presentation of motivationally salient stimuli. However, whether *Pnoc*^{BNST} neurons are necessary to regulate behavioral actions to motivationally salient stimuli is still unknown. Here, we investigated the role of *Pnoc*^{BNST} neurons in encoding behavioral responses to motivationally salient stimuli using *in vivo* calcium imaging and optogenetic approaches in freely behaving mice. We find that the bulk activity of *Pnoc*^{BNST} neurons increases when mice are near an aversive odor in comparison to a rewarding odor. However, optogenetic inhibition of *Pnoc*^{BNST} neurons does not affect the amount of time mice spend near an aversive odor. Further analysis revealed that a subgroup of *Pnoc*^{BNST} neurons that correlate with proximity to the aversive odor also correlate to darting away from the same aversive odor. Since these two behaviors are opposite to each other and since we previously found *Pnoc*^{BNST} neurons correlate with arousal responses, we believe these results may be due in part to the encoding of arousal responses that occur when mice approach and dart away from aversive stimuli.

Maternal microbiome modulation of brain development processes

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Changes in the gut microbiome, in response to environmental challenges such as infection, altered diet, and stress during pregnancy, have been increasingly associated with brain function and behavior. We investigate how depletion and selective reconstitution of the maternal gut microbiome influence fetal neurodevelopment in mice. Metabolomic profiling reveals that the maternal microbiota regulates levels of numerous small molecules in the maternal serum and embryonic brains. Moreover, maternal supplementation with select metabolites abrogates deficiencies in fetal neurodevelopmental processes and prevents abnormalities in sensory behavior in offspring from microbiome-depleted dams.

Microbiota-gut-brain Axis and Behavior Across the Lifespan

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Abstract

There is a growing appreciation of the importance of the bidirectional communication between our gut and brain on regulating the function and development of multiple physiological systems, including the central nervous system. Recently, the gut microbiota was demonstrated to interact with the gut-brain axis to regulate behavior which has driven a paradigm shift in our understanding of neuropsychiatric disorders. An individual's microbiota starts to develop mainly upon birth and continues to change throughout life. Studies in animal models have demonstrated that this initial colonization has a significant impact on development and behavior later in life. At the other extreme of life, changes in microbiota diversity and alterations in gut microbial metabolites have been implicated in neurodegenerative disorders, including Parkinson's disease. Further efforts into understanding the mechanisms that contribute to the major role of the gut-brain axis on programming brain health across the lifespan may allow the development of new treatment strategies.

Gut Microbiome neuroactive compounds in children from an Indigenous Me´phaa community and Mexico City.

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The bacterial gut microbiome (GM) performs a variety of ecosystem services that are essential for its host's health and function. One example is the production and degradation of neuroactive compounds by the GM, which impacts communication within the host's nervous system. The state of the GM has therefore been previously associated with several pathophysiologies of the nervous system. The host's lifestyles and age exert selective pressures on the GM that shape its diversity and abundance, and childhood is a particularly sensitive period for GM establishment and development. Here, we explored how lifestyle affects the composition and abundance of GM in children from two contrasting Mexican populations: inhabitants of Mexico City, the most industrialized city in Latin America, and members of the Mep'haa indigenous people living in traditional rural communities. We found that differences in the ecosystem structure of the GM between the two populations were associated with differences in the ability to synthesize or degrade neuroactive components that affect the function of the gut-brain axis. These results provide further knowledge about how changes in sociocultural practices in Latin American people have acted as selective pressures on the GM, and how these changes are associated with differences in neuroactive compounds that might be associated with pathophysiological states of the nervous system frequently present in people with urbanized lifestyles.

Neuronal Regulation of Lung Infection and Pulmonary Defense

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Summary:
Our lab studies the respiratory tract innervating neurons, inflammation and host immune responses to understand the pathogenesis of pulmonary infection and pneumonia. The respiratory tract is heavily innervated by sensory and autonomic (sympathetic and parasympathetic) neurons that constantly interact with external insults, including respiratory pathogens. Nociceptor neurons are a major sub-type of peripheral neurons that sense noxious/harmful stimuli and protect organisms from danger. Our work has discovered a critical role of nociceptor sensory neurons from the vagus nervous system in suppressing innate immunity against methicillin-resistant Staphylococcus aureus lung infection. However, the role of the peripheral nervous system and its crosstalk with the immune system in host defense against other respiratory pathogens have not been well defined. We use different respiratory pathogens to induce lethal pneumonia in mice to study the pathogenesis of lung infection. The overall goal of our research is to understand how neurons regulate pulmonary defense and immunopathology during respiratory illness and lung inflammation.

Highlights of my scientific career and research interests

I am an early-stage principal investigator leading efforts to uncover the fundamental mechanisms of interactions of our peripheral nervous system with the respiratory defense system during lung infection and pneumonia. I started my laboratory at Kansas State University (KSU) in 2020 with a major goal to define how neuronal signals regulate lung inflammation and host defense. My educational and research background are primarily in microbiology, innate immunity and infectious disease, with specific training and expertise in neuroscience, pulmonary immunology and host-pathogen interactions. I have a long-lasting research interest in molecular and cellular basis of infectious disease pathogenesis with more than 12 years of academic and professional experience. At the graduate level, I used microbiology, cell biology and immunology techniques to identify the mechanism that explains how virulent *Burkholderia pseudomallei* (BSL-3 pathogen) escape the host defense mechanisms and establish themselves inside macrophages. During my first postdoctoral position in Dr. Samithamby Jeyaseelan's laboratory at Louisiana State University, I studied the pulmonology of lung infections and learned the techniques and obtained the skillsets necessary to investigate lung infections in vivo. We demonstrated that the CXCL1 chemokine plays a crucial role in lung defense, granulopoiesis, and neutrophil mobilization during pneumococcal pneumonia in mice. My research during my second long-term postdoc in Dr. Isaac Chiu's laboratory at Harvard Medical School was focused on neuroimmune crosstalk in host defense and inflammation during lung, gut and skin infections. My work has discovered a critical role of nociceptor sensory neurons in suppressing innate immunity against methicillin- resistant Staphylococcus aureus lung infection (Baral et al., *Nature Medicine*, 2018). In contrast, our studies at Chiu laboratory discovered the host protective role of nociceptor neurons in fighting against *Salmonella typhimurium* gut infection in mice by modulating the microbiota homeostasis, levels of segmented filamentous bacteria and microfold (M) cell number in ileum. These studies have great potential to enhance our understanding of the peripheral nervous system in host defense and immunomodulation. My potential for scientific accomplishments and capability for innovative research is reflected by several primary peer-reviewed research papers and reviews in high-profile journals, including *Nature*, *Nature Medicine*, *Cell*, *Nature Communications*, *Nature Reviews Immunology*, *American Journal of Respiratory and Critical Care Medicine*, *Cell Host & Microbe*, *Blood, Mucosal Immunology* and *PloS pathogens*.

Neuroimmune interactions during experimental pulmonary tuberculosis

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The brain and the immune system are the major adaptive systems of the body. Both systems are constantly in communication, overlapping their biochemical language: neurons produce cytokines and express cytokine receptors, while immune cells produce neurotransmitters and express their receptors. Thus, cytokines can alter neural activity in the brain and neural activity can alter immunological processes. Both the hypothalamic-pituitary-adrenal axis, and the autonomous nervous system (ANS) are the major pathways involved in the cross-talk between the brain and the immune system. The lungs are densely innervated with nerve fibers from autonomic motor neurons or sensory neurons from vagal or spinal nerves that control the basal activity of bronchomotor tone, vasomotor tone and mucus secretion, and also can conduct afferent peripheral stimulus produced by lung inflammation. Thus, these autonomic nerve fibres send alerting signals when exposed to pathogen-associated molecular patterns (PAMPs) and cytokines that activate the sympathetic centers in the brain (locus coeruleus, hippocampus, hypothalamus). Sympathetic neurotransmission from the brain to the periphery is via projections from the paraventricular nucleus (PVN) of the hypothalamus and rostral medulla to preganglionic neurons of the spinal cord (T1-L2), which send nerves to superior cervical and stellate sympathetic ganglia. From these ganglia, a second projection innervate the blood vessels and airways. These sympathetic nerves release the neurotransmitter norepinephrine (NE) that binds to adrenergic receptors (ARs) expressed by various cell populations including immune cells. NE exerts different effects on T cells cytokine production depending on whether the naïve or effector cell is exposed to this neurotransmitter. Naive CD4T cells exposed to NE during the process of differentiation generated progeny Th1 cells that produced higher levels of IFN-γ acting on β-2AR, while less IFN-γ is produced if NE is added before T cell receptor (TCR) stimulation. The other branch of the ANS is the parasympathetic or cholinergic system, which is responsible for the coordinated synthesis, effects, and degradation of the neurotransmitter acetylcholine (ACh), an endogenous nicotinic receptor (nAChR) and muscarinic receptor (mAChR) agonist. In the lungs, vagal cholinergic sensory neurons are activated during inflammatory responses, inducing modulation of the immune response during normal and inflammatory conditions. Interestingly, ACh as well as NA can be produced by T lymphocytes and macrophages.

Tuberculosis (TB) is a bacterial infectious disease produced by the complex Mycobacterium tuberculosis (Mtb), which is usually acquired by the aereal route and produce significant abnormalities of the immune response and chronic inflammation. Using a model of progressive pulmonary TB in BALB/c mice the interaction with ANS was studied. There is a high production of NE during early infection by adrenergic nerves and lymphocytes located in the lungs and mediastinal lymph nodes, these cells highly expressed β2 adreno-receptors (β2AR) which by an autocrine mechanism promote Th-1 cell differentiation favoring protection. During advanced infection, the production of NE and β2AR sharply decreased, suggesting that adrenergic activity is less important during late TB. Regarding to the parasympathetic system, there is a high concentrations of ACh and expression of its synthesizing enzyme choline acetyltransferase (ChAT) during early infection in lung epithelial cells and macrophages. During late progressive TB, lung ACh upregulation was even higher and coincided with ChAT and α7 nicotinic receptor (nAChR) subunit expression in immune cells, which induced an anti-inflammatory immunosuppressive activity. The administration of nAChR antagonists increased pro-inflammatory cytokines, reduced bacillary loads and synergized with antibiotic therapy in multidrug resistant TB. Interestingly, in vitro studies revealed that Mtb produce ACh and incubation with ACh and nicotinic antagonists to Mtb cultures respectively induced or inhibited bacterial proliferation. Thus, Mtb possesses a cholinergic system and upregulates the lung non-neuronal cholinergic system, particularly during late progressive TB, favoring bacterial growth and immunomodulation within the lung that favor disease progression.

As a consequence of these chronic inflammation and constant afferent nerve stimulus from the infected lung, there is a long term stimulation of the brain that in the absence of infection produced neuroinflammation, with a marked increase in the synthesis of cytokines in the hypothalamus, hippocampus and cerebellum with changes in the synthesis of neurotransmitters. Moreover, there is neurodegeneration and neuronal death as infection progressed and neuropsychiatric abnormalities, such as cognitive impairment, and depressive- and anxiety-like behaviour. Thus, it seems that during pulmonary TB there is a significant neuroimmune interactions that could have beneficial or deleterious consequences depending of the phase of the disease.

Prof. Rogelio Hernandez Pando is MD, specialist in Pathology, with a PhD in Immunology from the Medicine School and Biomedical Research Institute at National University of Mexico, and postdoctoral studies at Bacteriology Department, School of Pathology University College of London UK. Since the last 15 years he has been the Chairman of the Experimental Pathology Section, Department of Pathology at National Institute of Medical Sciences and Nutrition in Mexico city, which is consider the best academic center in Medicine in Mexico. During the last 30 years, Dr. Hernandez Pando and his team have been working on the immunopathology of tuberculosis (TB) using murine models of progressive TB and latent TB infection, as a consequence of this work he

has been also working on the design and testing of TB immunotherapy and vaccination. At the present, Dr. Hernandez Pando has 385 publications in peer reviewed international journals, 33 book chapters, earned numerous research awards, he has supervised 61 postgraduate students and established a wide national and international TB collaboration network.

Glutamate transporters: non-traditional roles in CNS myelination

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Myelination of central nervous system (CNS) axons enables efficient signal propagation via saltatory conduction, and it provides metabolic support to ensure axonal integrity. Thus, the developmental establishment of CNS myelin by a highly specialized cell type, the oligodendrocyte (OLG), represents a critical component of building a fully functional CNS. Current models propose that myelination can be modulated by axonal electrical activity that is mediated, at least in part, by vesicular release of the excitatory amino acid glutamate along axonal segments. While good progress has been made in defining the effects of axonally released glutamate on progenitor cells of the OLG lineage, much less is known about the glutamate-responses in differentiating and pre-myelinating OLGs. We introduce here, sodium-dependent glutamate transporters as OLG expressed glutamate-responsive transmembrane proteins modulating CNS myelination. In our earlier studies, we demonstrated that activation of sodium-dependent glutamate transporters in differentiating OLGs promotes process outgrowth and branching. This aspect of OLG maturation is driven by actin cytoskeleton dynamics, and it is considered a critical step toward the initiation of CNS myelination. Mechanistically, activation of glutamate transport was found to initiate a signaling cascade involving reverse mode activation of sodium-calcium exchange and calcium influx. In continuing studies, we have started to investigate CNS myelination *in vivo* in conditional *Glt-1 (EAAT2/Slc1a2)* knockout mice and our data demonstrate that loss of GLT-1 in maturing OLGs attenuates CNS myelination within a developmental time window of heightened vulnerability for white matter alterations associated with adult behavioral and cognitive dysfunctions.

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A functional signature in the developing cerebellum: evidence from a preclinical model of autism

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Autism spectrum disorders (ASD) are pervasive neurodevelopmental conditions detected during childhood when delayed language onset and social deficits are observed. Children diagnosed with ASD frequently display sensorimotor deficits associated with the cerebellum, suggesting a dysfunction of synaptic circuits. Astroglia are part of the tripartite synapses and postmortem studies reported an increased expression of the glial fibrillary acidic protein (GFAP) in the cerebellum of ASD patients. Astroglia respond to neuronal activity with calcium transients that propagate to neighboring cells, resulting in a functional response known as a calcium wave. This form of intercellular signaling is implicated in proliferation, migration, and differentiation of neural precursors. Prenatal exposure to valproate (VPA) is a preclinical model of ASD in which premature migration and excess of apoptosis occur in the internal granular layer (IGL) of the cerebellum during the early postnatal period. In this study we tested calcium wave propagation in the IGL of mice prenatally exposed to VPA. Sensorimotor deficits were observed and IGL depolarization evoked a calcium wave with astrocyte recruitment. The calcium wave propagation, initial cell recruitment, and mean amplitude of the calcium transients increased significantly in VPA-exposed mice compared to the control group. Astrocyte recruitment was significantly increased in the VPA model, but the mean amplitude of the calcium transients was unchanged. Western blot and histological studies revealed an increased expression of GFAP, higher astroglial density and augmented morphological complexity. We conclude that the functional signature of the IGL is remarkably augmented in the preclinical model of autism.

Daniel Reyes-Haro, neurobiologist from Universidad Nacional Autónoma de México (UNAM), where he obtained his Ph. D. under the supervision of Dr. García-Colunga, in the group of Prof. Ricardo Miledi at Instituto de Neurobiología – UNAM. During this time he performed electrophysiological recordings to study potassium channels and neurotransmitter receptors expressed in primary cultures of astrocytes. Dr. Reyes-Haro continued his postdoctoral research at Max Delbrück Center, Berlín with Prof. Helmut Kettenmann, where he pair-recorded neurons and glial cells *in situ* from the calyx of Held synapse, an excellent model to investigate about neuron-glial communication. Later, he returned to Instituto de Neurobiología – UNAM where his team is currently studying the dysfunction of glial cells in murine models of anorexia and autism. He is also directing the organization of the Symposium on Physiology and Pathology of Neuroglia, an international-biannual event that is gathering leading researchers in the field since 2016.

Modulation of Tissue Injury and Repair by CNS Tissue Resident Macrophages during Autoimmunity

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Department of Molecular Microbiology and Immunology
The University of Texas at San Antonio

Abstract:
Microglia are implicated in the pathogenesis of chronic immune-related diseases such as multiple sclerosis (MS) and diabetic retinopathy. The fractalkine receptor (CX3CR1) limits the activation of pathogenic microglia and the human polymorphic variant hCX3CR1I249/M280 increases disease progression in models of MS. However, the role of microglia in repair mechanisms in the central nervous system remains unknown. Therefore, utilizing wild-type CX3CR1-KO and transgenic mice expressing the hCX3CR1I249/M280 variant, the study aims to determine the contribution of defective CX3CR1 signaling to neuroinflammation and tissue repair. For this, models of experimental autoimmune encephalomyelitis (EAE), cuprizone-induced demyelination/remyelination, and diabetic retinopathy were used.

hCX3CR1I249/M280 expressing mice displayed significant demyelination and microgliosis following acute cuprizone treatment. Nanostring gene expression analysis in demyelinated lesions showed that h*CX3CR1I249/M280* but not CX3CR1- deficient mice upregulated the cuprizone-induced gene profile linked to inflammatory, oxidative stress, and phagocytic pathways. Although CX3CR1-KO and fractalkine-KO mice displayed comparable demyelination and microglial activation phenotype to hCX3CR1I249/M280 mice, only CX3CR1-KO and CX3CR1-WT show significant myelin recovery one week from cuprizone withdrawal. Upon EAE induction, hCX3CR1I249/M280 expressing mice exhibited exacerbated EAE correlating with severe inflammation and neuronal loss.

Microglia activation, neuronal loss, vascular aberrations, and fibrinogen deposition were also detected in the mouse diabetic retina. CX3CR1-KO mice displayed increased microglial activation and fibrinogen deposition, correlating with increased neuronal loss. Visual acuity was compared in diabetic groups treated with the defibrinogenating agent ancrod to assess the effects of fibrinogen in retinal pathology. After ancrod treatment, diabetic mice appeared to improve visual acuity, which associated with reduced retinal microgliosis and less fibrinogen deposition. Using the CX3CR1Cre-ER:iDTR model to deplete microglia, results show that elimination and repopulation of resident microglia, at a time point of increased inflammation and neuronal damage, appeared neuroprotective by reducing microglia activation, decreasing vascular injury, and sustaining neuronal integrity in the diabetic retina.
Moreover, over-expression of sFKN using recombinant adeno-associated viruses (rAAVs) revealed that rAAV-sFKN minimizes microglial activation, reduces fibrinogen deposition, and rescues neuronal loss, compared to rAAV-mFKN. rAAV-sFKN retinas of diabetic and non-diabetic mice improved visual function in a two-choice visual discrimination task.

The results support the rationale that fractalkine acts as a neuroprotective signal, serving as an alternative therapeutic approach to minimize neuronal damage. Overall CX3CR1 pathway activity may be a key mechanism for limiting toxic gene responses in neuroinflammation.

Short BIO:

Dr. Astrid Cardona is a Professor of Immunology and founding Chair of the Department of Molecular Microbiology and Immunology at the University of Texas at San Antonio. Dr. Cardona received her bachelor's in science from the University of Antioquia in Medellin, Colombia. After receiving her Ph.D. in Microbiology and Immunology in 2002 at UT Health San Antonio, she continued her post -postdoctoral training at the Cleveland Clinic and joined the faculty at the University of Texas at San Antonio in 2009. Her research has centered on understanding the interactions between immune and nervous systems in neuroinflammatory models of infectious disease and autoimmunity

Dr. Cardona's research is focused on understanding the role of resident macrophages damage in tissue injury and repair in neuroinflammatory diseases, including Multiple Sclerosis, Diabetic retinopathy, and Neurocysticercosis. Dr. Cardona discovered a key neuronal-microglial communication signal mediated by the chemokine fractalkine and has developed several new models to confirm the neuroprotective effects of fractalkine and its mechanisms of action. She is also passionate about pedagogy, teaches immunology, and is engaged in mentoring undergraduate scholars and doctoral st udents. Dr. Cardona's research has been supported by the San Antonio Area Foundation, The US National Multiple Sclerosis Society, and the National Institutes of Health.

Astrocytes in aging: The case of the aryl hydrocarbon receptor and neurodegeneration

Mónica Adriana Torres Ramos

Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

Aging in the central nervous system (CNS) is distinguished by chronic inflammation. Astrocytes are cells involved in the brains' inflammatory response, and the aryl hydrocarbon receptor (AHR) participates in the modulation of the inflammation. Evidence in animal models shows that the appearance of aging features is associated with changes in AHR levels. We focus on evidencing the behavior and participation of AHR in the CNS of humans and mice during aging and neurodegenerative diseases such as Alzheimer's Disease (AD).

We evaluated AHR levels in human serum samples and post-mortem preparations from the hippocampal region of young donors and adults older than 60 years. Collaterally, we performed experiments in an animal model of young and aged wild-type and AHR-/- mice evaluating memory and inflammatory molecular changes (IL-6) and GFAP in the cortex and hippocampus. Also, we assess the behavior of AHR in two models of senescent astrocytes. Finally, as a search for possible therapeutic molecules, generated a 3D model *in silico* of the complete structure of human AHR and was evaluated the interaction of different ligands by molecular docking.

We found an increase in AHR expression in aging human post-mortem samples significantly up in AD, tissue and serum. The AHR co-localizes with astrocytes, and the images show that they shed vesicles with AHR into the extracellular space. AHR-/- mice have reduced memory that differs with sex. Furthermore, AHR levels and their localization are differential with advancing age and senescence of astrocytes. In the complete 3D structure of the human AHR, the recognition site is not the same for agonists and antagonists. Both the chemical structure of the ligand and the conformational changes of the AHR influence, thus having a better recognition for agonists with nonplanar aromatic rings.

Our results suggest that AHR is a relevant protein in human aging and AD and a potential therapeutic target for controlling neuroinflammation through astrocytes.

Ricardo Tapia. A pioneer of Neurochemistry in Mexico

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Dr. Ricardo Tapia was born on the 6th of February of 1940 in México city. Following his family tradition, he enrolled the Faculty of Medicine at the Universidad Nacional Autónoma de México (UNAM) and graduated in 1963. Soon after he joined the Faculty of Medicine, he met Dr. Guillermo Massieu who invited him to work in his laboratory at the Institute of Biology in 1961. Working with Massieu, he studied the effects of glutamate decarboxylase (GAD) inhibition in the brain and published his first paper, among many others, in 1962 when he only was 22 years old. From this moment he drops the medical practice and decides to dedicate himself to the study of the nervous system. He joined the doctorate Program in Biochemistry in 1964 and in 1969 became the first Doctor in Biochemistry at UNAM. This was the onset of a 60-year brilliant scientific career in Neurochemistry becoming an outstanding neuroscientist in Mexico and Latin America. He was an Emeritus Professor at UNAM and a co-founder of the Instituto de Fisiología Celular, where he worked for more than 40 years since his foundation in 1979. After spending one year as a visiting professor in the UK, he returned to México and stablished one of his most important fields of research on the role of GABA synthesis and the generation of epileptic seizures. From then on, he made substantial contributions on this field and others which include the regulation of neurotransmitter release from isolated synaptic terminals, the role of in vivo neurotransmitter release on excitability and neurodegeneration and its relevance to epilepsy, among others. His more recent studies were centered on excitotoxicity as a mechanism of the induction of death of motor neurons of the spinal cord and its role in amyotrophic lateral sclerosis.

Ricardo was a passionate man for neurosciences, a passion that he shared with many of the students that worked in his laboratory. He was a professor of the Faculty of Medicine for many years and tutor of graduate programs. He was a remarkable guide and mentor, training more than 60 undergraduate, masters and doctorate students. He promoted the creation of the Bachelor, Master and Doctorate Programs in Basic Biomedical Research and lead the Doctorate Program for several years. He was a determined promoter of neuroscience and a creator of a school of neurochemists in Mexico and other countries. Ricardo published more than 200 scientific papers which received more than 6000 citations and was the author of several books, including the book entitled “Las Células de la Mente” a popular book among many readers. He was a member of several international neuroscience societies, a member of the editorial board of prestigious neurochemistry journals and an author of many newspaper and cultural magazines articles. He received numerous awards including the “Premio Universidad Nacional

en Ciencias Naturales" and the "Premio Nacional de Ciencias y Artes". Besides his scientific interests he was also an active promoter of bioethics and founded the College of Bioethics in 2003. Ricardo Tapia's departure on the 8th of September of 2021 was an enormous loss for his ex-students, the Mexican scientific community and the cultural life in Mexico.

Non-canonical gating control by the cytoplasmic T1 domain of Kv channels

Manuel Covarrubias

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Canonical gating in voltage-gated K (Kv) channels involves an electromechanical mechanism in which the voltage sensors move in response to membrane potential changes, and this movement is coupled to the dilation and contraction of an intracellular gating cuff that surrounds an iris-like activation gate and thereby controls its opening and closing. A non-canonical mechanism, in contrast, involves direct and allosteric interactions between the voltage-sensors and elements of the pore domain. In this talk, I will present the new cryo-EM structure of Kv3.1 and demonstrate a novel non-canonical gating mechanism in which the specialized architecture of a secondary gating cuff from the cytoplasmic T1 domain controls the channel's activation gate. This mechanism may confer fast Kv3.1 channel gating, which is necessary to support fast spiking in GABAergic interneurons.

Electrophysiological biomarkers of epileptogenesis: new insights about its utility in the neurobiology of the hippocampus and clinic

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In models of Temporal Lobe Epilepsy (TLE) and patients, high frequency oscillations called ripples (R,100-250 Hz) and fast ripples (FR, 250-600 Hz) have been observed, particularly in the regions of the dentate gyrus (DG), CA3 and CA1 of the hippocampus. TLE is the main form of localized epilepsy, a highly drug-resistant disease that is generally treated using surgical intervention, being hippocampal sclerosis the most frequent pathophysiological evidence. This makes the hippocampal region of special interest to investigate the mechanisms related to the development and establishment of the disease. Hippocampus exhibits a high degree of neuroplasticity and great control of the temporal dynamics of its circuits to encode information, this property confers an intrinsic epileptogenicity because the loss of excitatory/inhibitory control, that might be fixed as a stable state in the main circuit of the structure, the trisynaptic circuit. There are several proposals of the mechanisms in the trisynaptic circuit that generate and underlie R and FR activity, and in particular FR is an activity observed before and during seizures commonly recorded in quiet wakefulness or slow-wave sleep states and related to clusters of pathologically associated neurons ascribed to a volume of approximately 1 mm^3 of tissue; this activity is considered as an electrophysiological biomarker of epileptogenic processes. Due to its area specificity and that are commonly found in seizure onset zone, FR activity has been used as a surgical reference to detect candidate areas for resection, with resulting seizure-free outcomes in patients. Although there is evidence around the changes needed in the neural circuit of the hippocampus to develop R and FR events, only a few of those hypothesis has been tested in an *in vivo* model, therefore the aims of the present talk will be: a) to describe the relevant results about these biomarkers in TLE models, b) to describe the causal dynamics needed in the trisynaptic circuit to develop FR in the hippocampus, and c) the implications of these studies to the clinic.

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Oral presentations

Abstracts

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Peroxiredoxin 5 overexpression decreases oxidative stress and dopaminergic cell death in a Parkinson´s Disease cellular model

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Area: Stress

Oxidative stress (OS) plays a prominent role in the pathogenesis of Parkinson's Disease (PD), where mitochondria disruption is responsible for overproducing reactive oxygen species (ROS). Post-mortem studies of PD patients' brains showed increased oxidative activity and decreased antioxidant enzymes in dopaminergic neurons. One of those enzyme families includes the Peroxiredoxins (Prxs), constituting a ubiquitous large family of thiol-dependent peroxidases that catalyze the reduction of hydrogen peroxide (H2O2), alkyl hydroperoxides, and peroxynitrite. Prx5 locates mainly in the mitochondria and cytoplasm. However, its expression is significantly low in the dopaminergic neurons, which may contribute to the vulnerability of these cells to nitro-oxidative attacks occurring in PD. In an *in vitro* PD model, we previously found that Prxs were hyperoxidized in response to the neurotoxin paraquat, turning them catalytically inactive and perpetuating the oxidative stress state. In the present study, we evaluate the redox state of the typical 2-Cys Prx subgroup. We found by eastern blot that oxidative stress is compartmentalized in different organelles, reflected by these enzymes' hyperoxidation pattern. Next, Prx5 was overexpressed in the SHSY-5Y dopaminergic cells using the adenoviral vector Ad-Prx5, confirmed by immunofluorescence. Using a mitochondrial fluorescent oxidative indicator, we demonstrated that Prx5 overexpression decreases mitochondrial oxidative stress produced by paraquat. Since mitochondrial oxidative stress usually diffuses to the cytoplasm, ROS were also evaluated in this cellular compartment by flow cytometry, showing a decrease mediated by Prx5 overexpression. Notably, the decrease in oxidative stress in the main subcellular compartments led to the overall cell protection against death in the PD model induced by paraquat, which was demonstrated by flow cytometry using Annexin V and propidium iodide. Therefore, Prx5 is an attractive therapeutic target for PD.

Keywords: Oxidative stress, Antioxidant enzymes, Peroxiredoxins

Social support and cognitive function in people living with HIV

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Area: Cognition and Behavior

The human immunodeficiency virus (HIV) is a neurotropic virus that affects the central nervous system (CNS). It has been reported that 40 to 50% of HIV-positive patients have cognitive impairment. Latinos living in the United States have been reported to be three times more likely to have HIV, tend to have worse characteristics of HIV, and are at higher risk for HIV-associated cognitive impairment. But curiously, rates of global cognitive impairment in latinos living with HIV had been reported up to 39% while up to 42% in white people living with HIV. In fact, the literature reports the hypothesis of the health paradox for Latin America in which the socio cultural resources of the Latin population, as social support, function as protective factors against diseases. Social support is defined as the degree of support provided to an individual, particularly in times of need, in order to make him feel loved and belonging to a social group whose members are willing to provide help or support in case of need (Jhonson y Sarason, 1979; Cobb, 1976). Various studies have identified that social support has a role in buffering stress and modulating immune function (Goodkin et al., 1996; Folayan et al., 2017; Hermanstyne et al., 2018), which leads us to propose the following objective.
The objective in this study was to examine the potential role of social support in modifying the effects of cognitive impairment in HIV. In the present study 42 people living with HIV (13 women) with a mean age of 40.2 (SD=10) years and from the board and care home “Las Memorias” participated in the study. The Perceived Social Support inventory and Social Support from Family and Friends were applied to them, in addition to a neuropsychological evaluation with the following tests: Wisconsin Card Sorting Test and Stroop Test.
Results: It was found that the perceived social support of both friends and others correlated positively with the performance of the WCST-64 task, specifically in the T score of the total errors (r=.34, p< .03 and r=.31, p<.04 respectively), without maintaining the relationship with perseverative errors. Regarding inhibition, a negative correlation was found between family support and the percentiles of the scores obtained in the Stroop-Word (r=-.39, p<.03) and Stroop-Color (r=-.38, p<. 03) task without relationship in the inhibition Stroop-Word-Color task (r=-.14, p>.40). On the contrary, a positive correlation was found between viral load and family support of the Family and Friends support scale (r=.31, p<.05), which indicates that the greater the family support, the higher the viral load. Using a multiple linear

regression model, it was found that the best description model of executive function is made up of years of schooling (Beta=.41), and perceived social support from friends (beta=.31) with a explained variance of r^2=.22.
In conclusion, social support is related to processing speed and cognitive flexibility and social support from friends and years of schooling interact with each other to predict executive function. In this sense, social support has important implications for the cognitive function of HIV patients.

Key Words: Cognition, Social Support, HIV.

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Proteogenomic of Primary Brain Tumors Using Liquid Biopsies, for Diagnosis and Precision Medicine

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Fields: Genetic Expression

Introduction: Primary brain tumors are a serious health problem, both in pediatric and adult patients. Their early diagnosis as well as personalized treatments are urgent to increase the survival of these patients. However, accessibility for taking samples of tumor tissue and monitoring response to treatment is a very invasive method, and in some cases it is not possible. For this reason, identification genetic expression pattenrns at liquid biopsies is a promising approach for achieving molecular characterization of these tumors to establish clinical directions.
Objective: To develop an integrated analysis of genic expression patterns identified in liquid biopsies of patients with brain tumors, useful for diagnosis and precision medicine in neuro-oncology.
Methods: An integrated analysis of the biomarkers associated with brain tumors present in liquid biopsies was carried out using the methodology of systematic reviews. Circulating microRNAs (miRs), extracellular vesicles (EVs), molecular fusions at different levels (DNA, RNA and proteins), and proteogenomic of glioblastomas were evaluated for identification genetic expression of common molecules useful for diagnosis and precision medicine in neuro-oncology.
Results: miR-21, miR-10b, and miR-15b were expressed in liquid biopsies: plasma, serum, and cerebrospinal fluid (CSF). The expression levels of MiR-21, miR-222, miR-221, miR-106a, miR-301a, miR-137, miR-205, miR-5194, miR-203 and miR-182 in samples from patients with glioblastoma were associated with a worse prognosis. In the case of molecular fusions, future research should be directed to the detection of the common molecules: BCOR-CREBBP, CREBBP-COLGA6L2, CREBBP-SRRM2, BCOR-L3MBTL2, EGFvIII and FAM13B-BRAF among pediatric and adult patients using liquid biopsies. In EVs, miR-21 expression was relevant both in exosomes and in other EVs. The oncogenic epidermal growth receptor EGFRvIII and the complement protein C3 were the protein molecules of greatest interest. In addition, tumor DNA loaded in EVs carries the tumor-associated mutations *IDH1R132H*, *IDH1A395*, and *EGFRvIII*, which are relevant to diagnostics and precision medicine. Interestingly, EV-borne miRNAs have clinical relevance for diagnosis, prognosis (miR-21, miR-222, miR-124-3p, miR-210, and miR-301A), and precision medicine (miR-21, miR-10b, and let 7-A), with emphasis on miR-21 as a useful biomolecule for global clinical guidance from peripheral blood. The main proteogenomic markers described in liquid biopsies from patients with glioblastoma were EGFR (and EGFRvIII), PI3KCA, NF1 and TP53. The genetic expression pattern associated to up-regulation of miR-21, EGFR, and IDH mutations is relevant in liquid biopsy.
Conclusions: Liquid biopsies have high added value in the era of genomic and precision medicine for early diagnosis, personalized medicine and the evolution of patients with primary brain tumors. miR-21, EGFR, and IDH mutations are a promising proteogenomic combination for diagnosis and precision medicine in neuro-oncology from liquid biopsies of patients with primary brain tumors.

Keywords: *Brain Tumor, Genetic Expression and Protogeonomic*

Stabilization of basal dopamine in inorganic nanoreservoirs for controlled delivery in Parkinson's disease

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Abstract: Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide. It is characterized by motor and cognitive disturbances resulting from the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc), whose progressions to the striatum (nigrostriatal pathway) constitute the control system of motor activity through the dopamine (DA) signaling. Historically, DA impairment in PD has been treated by administration of agonists and precursors, the latter mainly levodopa (L-DOPA). However, discontinuous administration of these drugs leads to the development of side effects, such as dyskinesias. Although advances in the controlled release of L-DOPA, as well as adjuvant delivery approaches, suggest the possibility of developing more effective treatments for PD, research to reverse DA depletion could take a more physiological approach by direct administration of DA. Nonetheless, the neurotransmitter presents several problems related to its stabilization and release *in vivo*, given its high reactivity and susceptibility to oxidation. Thus, the administration of DA requires effective controlled delivery technologies that allow its stabilization in its basal state and its controlled release at physiological rates in the required regions of the brain (*e.g.*, the SNpc). Historically, the use of inorganic nanostructures has offered promising results for drug stabilization and release. In view of the above, the present work reports the stabilization of DA in a nanoparticulated silicon dioxide matrix (nanoreservoir), which has been shown to be capable of stabilizing drugs and releasing them in a controlled manner. The nanoreservoir was characterized by different techniques to know its intrinsic physicochemical properties, including its morphology, topology, particle size, atomic stoichiometry, electronic structure, the molecular composition of its functional groups, specific area, pore size and distribution, crystalline structure, and thermal stability. The state of the stabilized DA (basal or oxidized) and its interaction with the matrix were also studied. The results corroborate that the DA could be conserved in its basal state during the synthesis of the nanoreservoir. Future work will study the release kinetics and its effect *in vitro* to understand the mechanism of action of the released DA. Once these questions are further explored, these nanoreservoirs could represent a novel and more physiological approach to the treatment of DA depletion in PD.

Keywords: dopamine, nanoreservoir, controlled drug delivery.

Funding: DGAPA-PAPIIT (IN211419) and CONACyT (A1-S-10064 and CVU 1037018).

Transcriptional adaptive responses to ischemia linked to DNA methylation in astrocytes

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Astrocytes are essential players in brain recovery after injury and are involved in neuronal survival, angiogenesis, neuronal plasticity, and functional recovery in the aftermath of an ischemic stroke. Despite DNA-methylation has a central role in neurovascular-related disorders like stroke, few studies have addressed the overall genetic and epigenetic changes at the molecular resolution. We set out to comprehensively describe transcriptional changes related to the epigenetic DNA-methylation in astrocytes in response to ischemia. We performed a genome-wide assessment of DNA-methylation in cultured human astrocyte-like CRL-1620 cells subjected to oxygen and glucose deprivation (OGD) for 4 h followed by recovery for 8 h, and correlated the methylated regulatory sites to gene expression assessed by RNA-seq. We describe different patterns of gene expression regarding adaptive changes immediately after OGD and recovery. We determined how several genes involved in neuronal death and recovery change their transcriptional regulation in an experimental stroke model produced by the transient occlusion of the middle cerebral artery (MCAO) in C57 mice. These genes changed their expression profile when DNA-methylation was inhibited with 5-azacytidine. We correlated these changes to promoter methylation analyzed by methylation-sensitive high resolution melting analysis at 1, 3, and 7 d after MCAO. Our results help to elucidate the overall changes induced by ischemia and reperfusion in terms of transcription and DNA-methylation in astrocytes after cerebrovascular accidents. Understanding the global regulatory changes driven by astrocytes in adapting to ischemia is essential for knowing how the damage caused after stroke is mechanistically resolved in the brain. This work is supported by DGAPA-PAPIIT IN207020 and CONACYT A1-S-13219.

Area: Glia
Keywords: astrocytes, ischemia, epigenetic adaptation

Characterization of layer 5 sensorimotor cortex neurons projecting to red nucleus and pons

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One major goal un neuroscience is to understand how different aspects of movements are regulated in parallel by the cerebral cortex. Output commands of cortical sensorimotor areas are driven by pyramidal tract neurons (PTNs) which projects to several subcortical structures. An open question is if PTNs are hierarchically organized generating different and specific output commands for sensorimotor integration. The aim of the present work is to characterize the PTNs of the motor cortex (M1) projecting to red nucleus (RN) and pons.

Wild-type C57BL/6 mice adults were simultaneously injected using retrograde tracers in RN and pons (Biotinylated dextran amine and Fluoro-Gold). To in vivo cell-attached recordings and biocytin fillings we implant a bipolar electrode in RN or pons and cortical recording in M1 following juxtasomal biocityn filling of PTNs. For analyze the Ca+ in M1 in vivo, we infected the neurons with a retrograde virus pGP-AAV-syn-jGCaMP7f-WPRE, and for the inhibition we infected the neurons with the retrograde virus AAV2/8-hSyn-Jaws-KGC-GFP-ER2 of in red nucleus or pons, and implant in M1 an optic fiber cannula, mice were trained to push a lever after a visual stimulus. The animals were perfused and 50-µm coronal sections were obtained from sensorimotor cortex (2.46 mm to -0.80 mm relative to bregma) and from the injection sites (-3.4 mm to -4.04 mm relative to bregma). Large scale fluorescence images with cellular resolution were obtained to quantify the number of retrogradely labeled cells and for the three-dimensional reconstruction of individual neurons.

PTNs were distributed broadly, intermingled, and segregated in M1. Using single cell 3D reconstructions in In vivo identified motor cortex PTNs projecting to mesencephalic red nucleus, or pons, we found morphological and electrophysiological characteristics for PTNs to RN and pons. Moreover, using photometry in both class of PTNs during a motor execution task, revealed a different relationship of this neurons with movement, similar, optogenetically inhibitions either kind projection, differentially affects forelimb movement onset and execution in a lever press task. The results indicates that PTNs are organized into different subsystems controlling in a coordinated manner distinct subcortical circuits related with different aspects of sensorimotor integration and thus, proper movement execution.

Key words: pyramidal tract neurons, sensorimotor cortex, movement, red nucleus, pons.

Spinal α_6GABA$_A$ receptor activation induces antinociception under physiological and pathological conditions

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Spinal GABAergic disinhibition is a mechanism that underlies neuropathic pain. Thus, rescuing the GABAergic inhibitory tone through activation of GABA$_A$ receptors is a strategy to reduce neuropathic pain. This study was designed to elucidate the role of the spinal α_6GABA$_A$ receptor in physiological conditions and neuropathic pain in female rats. We found that α_6GABA$_A$ receptor blockade or transient α_6GABA$_A$ receptor knockdown with a specific siRNA induces evoked hypersensitivity and spontaneous pain in naïve female rats. Moreover, western blot and immunohistochemistry analysis show that α_6GABA$_A$ receptor is expressed in nociceptive neurons of the dorsal ganglion root (DRG) and the laminae 2 to 5 of the spinal dorsal horn. Nerve injury reduces α_6GABA$_A$ receptor protein expression in the DRG and spinal dorsal horn; whereas intrathecal administration of positive allosteric modulators (PAMs) of the α_6GABA$_A$ receptor reduced tactile allodynia and spontaneous nociceptive behaviors in female neuropathic rats. Lastly, overexpression of the spinal α_6GABA$_A$ receptor with a purified *Gabra6* plasmid reduced tactile allodynia in neuropathic female rats. Our results suggest that the spinal α_6GABA$_A$ receptor plays an antinociceptive role under physiological conditions and neuropathic pain, suggesting that this receptor may represent an interesting target to develop a novel treatment for neuropathic pain.

Key words: Neuropathic pain, GABA$_A$ receptor, Nociception

Acknowledgments: The National Council for Science and Technology (CONACyT) supported this study (Grant No. A-S1-40015). CONACyT scholarship was given to EJRP (615618).

An enriched environment restores metabolic homeostasis by reducing inflammation in the adipose tissue and hypothalamus of obese mice

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Obesity is a worldwide health issue that is characterized by the development of a low grade chronic inflammatory process in different tissues. This obesity-associated inflammation increases immune cell recruitment and activation in the adipose tissue, leading to the development of insulin resistance and metabolic alterations. In the brain, this inflammatory process leads to insulin and leptin resistance, inhibiting the ability of the hypothalamus to maintain energy balance. However, several studies have shown that inhibiting different inflammatory pathways, including the IKK/NF-κB, JNK or inflammasome pathways, can lead to a decrease in food intake and improved insulin sensitivity in obesity models. Here we decided to study an enriched environment as a non-invasive therapy to treat the metabolic alterations caused by obesity. An enriched environment has been widely studied for having beneficial effects in the central nervous system, where it increases neurotrophin levels, long-term potentiation, as well as learning and memory in murine models. Additionally, and enriched environment has been shown to decrease inflammation in the brain and to regulate the activation of the immune system. Given these data we determined if an enriched environment could restore energy balance in mice that already presented metabolic alterations using a model of diet-induced obesity. We found that an enriched environment decreased food intake, increased glucose tolerance and insulin sensitivity in mice that still presented obesity. We also found that the enriched environment decreased hepatic steatosis and increased insulin signaling in the liver. In the adipose tissue the enriched environment inhibited the recruitment of macrophages and decreased the levels of inflammatory cytokines, while increasing the levels of lipolysis and browning markers. Finally, we found that the enriched environment decreased the protein levels of key mediators of the JNK and IKK/NF-κB pathways in the hypothalamus. Overall, we found that an enriched environment can reduce inflammation and ameliorate the metabolic alterations caused by obesity. We propose that the enriched environment could be used as a novel therapeutic approach to treat obesity-related metabolic alterations.

This work was partially supported by grants from CONACyT (IFC 2016-2282 and CF-2019 40792) and DGAPA-PAPIIT (IN213119 and IN211719).

Area: Neuroimmunology

Keywords: Obesity, Enriched environment, Inflammation

Neurotoxicity induced by methylmercury in an *in vitro* model and its relationship with the development of Alzheimer's disease.

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Introduction: Alzheimer's disease (AD) is a progressive, irreversible chronic-neurodegenerative disorder of multifactorial origin. One of the histopathological hallmarks is the deposition of amyloid plaques composed mainly of amyloid-β peptides (Aβ) (1). Although little information is known about the molecular mechanisms that contribute to the generation of Aβ, the alteration in the expression of modulatory microRNAs (miR) of the BACE1 enzyme has been demonstrated in sporadic AD (2). Furthermore, research suggests that exposure to mercurial compounds, mainly methylmercury (MeHg), could contribute to the pathogenesis of AD. **Objective:** To evaluate the expression of miR-29a and miR-29b-1 and correlate it with the activity of BACE1 in an in-vitro model of N2a neurons exposed to methylmercury to establish a probable mechanism related to the development of AD. **Results:** It was established that the intoxication conditions to obtain 80% cell viability are cells cultured in a medium without serum exposed to 0.3 µM of MeHg for 24 h. In this work, we evaluated the effects of organic mercury on the expression of miR29a and miR29b-1 in cells exposed to 0.1, 0.3, and 1 µM of MeHg for 24 h (n= 6) through the T-qPCR technique. Our results indicate that the expression of miR29a in the treated group with 0.1 µM of MeHg has decreased respect the control group (**p<0.01), and for mRNA 29b1 a non-statistically significant reduction in expression was observed for the control in the group treated with 0.01 µM of MeHg. The BACE1 activity was determined by FRET-type assay from cell lysates exposed to 0.01, 0.3, and 1 µM MeHg, finding a decrease in BACE1 activity in the group treated with 1 µM MeHg compared to the control (* p<0.0140). **Discussion and Conclusion**: At low concentrations, exposure to MeHg decreases the expression of miR-29a and miR-29b-1 at the post-transcriptional level, however, at concentrations of 1 µM MeHg cells increase miR expression level, probably to generate a compensatory mechanism that could influence the decrease in BACE1 activity, regulating the generation of Aβ peptides.
Keywords: Methylmercury (MeHg), Alzheimer's Disease (AD), MicroRNAs.

Bibliography:

1. Mutter J, Curth A, Naumann J, Deth R, Walach H. Does inorganic mercury play a role in Alzheimer's disease? A systematic review and an integrated molecular mechanism. J Alzheimers Dis. 2010;22(2):357-74.
2. Hébert SS, Horré K, Nicolaï L, Papadopoulou AS, Mandemakers W, Silahtaroglu AN, et al. Loss of microRNA cluster miR-29a/b-1 in sporadic Alzheimer's disease correlates with increased BACE1/beta-secretase expression. Proc Natl Acad Sci U S A. 2008;105(17):6415-20.

Chronic copper exposure as an *in vivo* model of non-genetic Parkinson's disease

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α-Synuclein gene multiplication and point mutation are associated with familial and sporadic Parkinson's disease (PD). However, the environment is also critical in neurodegenerative diseases development, and exposure to chemical contaminants, toxins, and transition metals, including copper, can be harmful. Excessive or deficient copper levels can be detrimental, and precise homeostatic control is essential. In addition, the cerebrospinal fluid and blood of PD patients have shown increased levels of copper. Therefore, occupational exposure to copper is related to a high risk of developing PD. In addition to this, we have previously shown that α-synuclein, wild or mutated, requires an environmental factor, such as exposure to copper to increase its cytotoxicity. However, the effect of chronic copper exposure on the neurodegenerative process has not been explored *in vivo*. Therefore, we aimed to elucidate whether prolonged copper treatment reproduces the features of PD. Over ten months, male C57BL/6 mice were treated with CuSO4 at 0, 100, 250, and 500 ppm in drinking water ad libitum. Since the motor function is impaired in PD, we tested whether copper exposure affects mice's gait. The results demonstrated that chronic copper exposure alters the motor function and induces dopaminergic cell death, astrocytosis, and microgliosis in a dose-dependent manner. Furthermore, the protein α-synuclein, associated with PD pathogenesis, was also increased in response to copper. Alterations in the protein degradation systems, the proteasome, and autophagy, previously observed *in vitro*, were confirmed *in vivo*, where protein ubiquitination and the autophagy marker LC3-II were increased in response to copper. Finally, nitrosative stress levels were evaluated by detecting nitrated proteins, finding that copper increases protein nitration in a concentration-dependent manner. Therefore, our chronic copper exposure animal model reproduces several PD features and may help understand how environmental factors increase the risk of developing this disorder.

Keywords: *Parkinson's disease, autophagy, copper*

Changes in the number and morphology of dendritic spines in the hippocampus and prefrontal cortex of the C58/J mouse model of autism

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Introduction. The etiology of autism spectrum disorder (ASD) has a broad range of neurobiological characteristics, including modifications in the neuronal structural plasticity, such as alterations in the number and morphology of dendritic spines. The mentioned changes could be associated with the atypical brain communication found in people with autism. The C58/J inbred mouse strain displays low sociability, impaired learning, diminished cognitive flexibility, and pronounced stereotyped behavior; along with polymorphisms in ASD-associated genes involved in neurotransmission and synaptic function. Hence, the C58/J strain is a suitable model for the study of idiopathic ASD.

Objective. This project aimed to evaluate the differences in the number and structure of the dendritic spines in the pyramidal neurons of the hippocampus and the prefrontal cortex of C58/J mice, as well as the polymorphisms in genes with a role in the regulation of neuronal structural plasticity.

Methodology. The morphology of the dendritic spines in Golgi-Cox-stained neurons (approximately 6000 spines per mouse strain) was assessed through three categorizing approaches based on spinal dimensions. Single-nucleotide polymorphisms (SNPs) were *in-silico* detected using the Mouse Phenome Database. Gene Ontology enrichment analysis was performed, and the ASD association of the polymorphic genes was evaluated in the SFARI database.

Results. Changes in the number and morphology of dendritic spines were found in a brain region-dependent manner: a decrease in spine density in the prefrontal cortex, and a higher frequency of immature phenotype spines in the hippocampus. The *in-silico* analysis of C58/J mice's genome showed SNPs in genes collectively involved in structural plasticity modulation and potentially associated with ASD risk. The above suggests a relationship between the genome of the C58/J strain, its autistic-like behavior, and the observed anomalies in dendritic spines' morphology. Thus, the C58/J strain might be useful as *in vivo* model for studying changes in structural plasticity associated with idiopathic ASD.

Keywords: Autism, dendritic spines, animal model. **Area:** Neuropatología.

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Putative single nucleotide polymorphisms associated with Alzheimer's disease by artificial intelligence strategy.

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Area: Tecnología e Innovación

Alzheimer's disease (AD) is a major neurocognitive disorder generally responsible for the loss of memory and cognitive abilities. Neurodegeneration is one of the main causes of these events. The etiology of the disease is multiple, and it is estimated that 80% of the disease is due to genotype. Single nucleotide polymorphisms (SNPs) are estimated to originate every 300 base pairs and exist in at least 1% of the population, with approximately 600 million SNPs in databases. These genetic variations are relevant because they have explained and helped to estimate the risk of suffering a disease, as well as to track the response to a drug and to know the ancestry of an individual. Currently about 0.4% of SNPs have been associated with disease through genome-wide association studies. There are 935 statistically significant SNPs associated with AD. Using a last generation machine learning algorithm, XGBoost, we generated a artificial intelligence model with the ability to classify SNPs, thus proposing putative AD-associated SNPs that could propose new disease mechanisms. In the laboratory we have been developed methodologies for the use of these SNPs in gene regulation and the Neurovascular Unit, within the context of AD.

Keywords: SNP, Alzheimer's disease, Machine Learning.
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Neurobiology Meeting of the Mexican Society for Biochemistry

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Neurobiology Meeting of the Mexican Society for Biochemistry

Cognition & Behavior

UNAM · Sociedad Mexicana de Bioquímica Neurobiología · SMB 65 años 1957-2022 · CONACYT · IBERO Ciudad de México · Cinvestav · Instituto de Biotecnología 40 · Instituto de Neurobiología · Instituto de Fisiología Celular UNAM · Facultad de Psicología

Striatal Cholinergic Interneurons Contribute to Specific Behavioral Updates in a Classical Conditioning Task

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Investigation area: Cognition and Behavior

The identification of changes in environmental conditions allows animals to update their memories and adapt their behavior to new rules. The striatum, the main input to the basal ganglia, is implicated in the control of movements, learning mediated by reinforces and behavioral flexibility. Cholinergic interneurons (ChIs) have been suggested to control the behavior´s update of animals to new contingencies in instrumental conditioning, but little is known about how these neurons participate to adapt behaviors to changes in classical conditioning. Hence, this study aims to evaluate the contribution of ChIs and spiny projections neurons (SPNs) activity on the behavioral flexibility of mice in a classical conditioning task.

Preliminary results: We standardized a head-fixed task with four different auditory stimuli paired to four different outcomes (stim 1-big drop, stim 2-small drop, stim 3-neutral, stim 4-air puff), and after verifying the proper acquisition of the tones (monitoring anticipatory responses), we switch the tones-outcomes in a reverse mode. As the first experiment and to evaluate the contribution of striatal activity on the behavior update, we optogenetically inhibited the striatum, using AAV-Syn-Arch, during the switch of the tones. Later as a second experiment, and to evaluate the ChIs contribution on the behavior update, we optogenetically inhibited the ChIs, using AAV-DIO-Arch in ChAT-Cre mice. Finally, to investigate how the dynamic of striatal projection cells is modulated during the switch of tones, we recorded the striatal activity by expressing the genetically encoded calcium indicator (GCaMP6f) and monitored the striatal activity by micro-endoscopes.

Our preliminary results suggest that the SPNs and mainly ChIs contribute to specific updates depending on the values of the outcome's changes in a classical conditioning task.

Key words: behavioral flexibility, optogenetics, striatal circuits.

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Analysis of Neuronal Activity in Prefrontal Cortex and Modeling with Recurrent Neural Networks during Bimodal Detection Task

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Área: Cognición y Comportamiento

The use of cognitive tasks has helped better our understanding of cognitive phenomena such as percepcion, attention, and decision making. Here, we use a novel task named bimodal deteccion. In this task the monkey has to sense stimuli that are near the threshold of detection coming from to possible sources: tactile or auditory.

Neurons in the prefrontal cortex show coding for the percepted stimuli and the decision in an unimodal detection task. In order to analyze the coding of a population of neurons, electrode arrays are implanted in the monkey's dorsal and ventral prefrontal cortex. Spike sorting is used to get the individual spikes of each neuron. This is generally done with the geometric features of the wave, principal component analysis (PCA), or wavelet analysis. In conjunction with these classical methods, we use a nonlinear dimension reduction method called UMAP to perform the spike sorting. Once the firing rate of each neuron is obtained, single neuron and population analysis are used to understand how the network performs the task.

Recurrent neural networks (RNN) can be used to model cognitive tasks, and make predictions of how the biological network will behave. To this end, population analysis serves to compare both networks. By projecting the neuronal activity that lies on a large dimension space into a lower dimension space with methods as PCA, it is possible to study the trajectory of the network in various epochs of the task, between conditions, between hits or misses, etc. Therefore, the aim of this study is to compare the dynamical system that emerges from the RNN model and the biological network.

Nonlinear Spike Sorting; Artificial Neural Networks; Frontal Lobe Neural Coding

"Natural sweeteners decrease short-term memory capacity in male and female C57BL6 mice"

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Area: Cognition and behavior.

The current lifestyle of the population has increased the demand for easily accessible processed foods including those containing sweeteners. Recently, these have been associated with the increased of incidence of neurodegenerative diseases like as anxiety, autism, depression, among others (Toews *et al;* 2018, Carocho, 2017; Guzman *et al.,* 2017; Liuchonak *et al*; 2019). There is currently evidence supporting the serious effect of sweetener consumption on the gut-brain axis mainly through intestinal dysbiosis and other molecular mechanisms (Pearlman *et al;* 2018, Shiano *et al*; 2018, Zmora *et al;* 2018). Some neuromodulatory metabolites from the microbiota include precursors and metabolites of tryptophan, serotonin (5-hydroxytryptamine, 5-HT), GABA, catecholamines, and 4-ethylphenylsulfate modulate gut bacteria leading to behavioral changes and impaired memory in treated mice with commercial sweeteners (Clemmensen *et al.,* 2017, Lee and Dixon, 2017., Holzer and Farzi 2019., Nicolanni *et al.,* 2019). In rodents, the Morris Maze test is widely used to determine the latency period (time it takes for the mouse to reach the platform) which decreases over the days (Dubois., 2020). The objective of this study is to investigate the impact on short-term memory retention capacity in a murine model treated with sweeteners of natural origin. A comparative experimental study was carried out with *C57BL6* male and female mice of 6 weeks of age (N= 144; n=12), fed with a standard diet (Labdiet 5001,) and 5 mg/kg/d/mL allulose (ALU), 0.5 mg/kg/d/mL monk fruit (FM), 0.1 mg/kg/d/mL partially hydrolyzed agave syrup (AG), 1 mg/kg/d/mL glycyrrhizin (GLI) and 5 mg/kg/d/mL xylitol (XILI), for 20 weeks. The sweeteners were added to the drinking water. Food and drinking water were offered *ad libitum*. The Morris Maze test was performed at the end of the experimental period, with an acquisition phase (day 1) and a retention phase (day 2), after 48 hours, determining the latency period. Data analysis was performed with a Kolmogorov test for normality, one-way analysis of variance (ANOVA), and Tukey's analysis of difference of means with a Statistica 8.0 software. Data were represented as total seconds (mean ± SEM).

Our results indicate that on day 1, male mice from the AG group (176.80 ± 0.58 s) decreases significantly compared to FM (112.54 ± 0.47), GLI (60.84 ± 0.43 s), XILI (99.40 ± 0.46 s), CON (77.81 ± 0.40 s) p= 0.0001, and ALU (130.09 ± 0.36 s) p=0.007 respectively. In addition, the GLI group decreases significantly compared to FM, ALU

p=0.0001, XILI p=0.002. In female mice, significant differences were found between the AG group (878.12 ± 0.95 s) compared to the FM (278.31 ± 0.69 s), ALU (454.30 ± 0.74 s), GLI (442.11 ± 0.67 s), XILI (175.75 ± 0.48 s) groups, CON(155.93 ± 0.64 s) p=0.0001. In addition, the FM group decreases significantly compared to ALU, GLI, XILI and CON (p=0.0001), while ALU decreases significantly compared to XILI and CON (p=0.0001); finally GLI decreases significantly compared to XILI and CON (p=0.0001).

On the second test day, the male mice from the CON group (30.23 ± 0.31 s) obtained a shorter latency period in comparison with the AG (145.23 ± 0.47 s), ALU (132.56 ± 0.54 s), GLI (113.04 ± 0.53 s) (p=0.0001), FM (84.70 ± 0.38) (p=0.002) and XILI (93.27 ± 0.31) (p=0.0003), showed significant differences. In addition, FM group showed significant differences with AG group (p=0.0004) and FM with respect to CON group (p=0.008), finally AG group and XILI (p=0.003), found significant differences. In the case of females mice, the AG group (879.31 ± 1.19 s) had differences between FM (532.57 ± 1.19 s), ALU (656.70 ± 0.73 s), GLI (142.02 ± 0.75 s), XILI (141.65 ± 0.59 s) and CON group (88.32 ± 0.41 s) (p= 0.0001); in addition the FM group and GLI, XILI and CON groups (p=0.0001) showed significant differences in latency periods. Finally, differences between ALU compared with XILI and CON (p=0.0001). The results of this study revealed that females and males treated with Agave Syrup (AG) have a significantly longer latency period compared to the other treatment groups which suggests that this sweetener alters the capacity of retention and short-term memory.

Keywords: Agave syrup, allulose , monk fruit, short-term memory, C57BL6.

Early behavioral characterization of the murine model of autism induced by valproic acid

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Área: Cognición y Comportamiento

Autism spectrum disorder (ASD) is considered a neurodevelopmental disorder with neurobiological origin. It is characterized by presenting symptoms related to difficulties in social interaction, repetitive and stereotyped behaviors, language problems and communication deficits (Lord et al., 2018; Morales et al., 2013; Calderón, 2002).

Although 95% of ASD cases are idiopathic, some well-defined causes of the disorder have been described. For example, exposure to valproic acid (VPA) during pregnancy has been shown to increase the risk of autism in children. In addition, rodents prenatally exposed to this drug show behavioral characteristics of the human condition (Sztainberg & Zoghbi, 2016). Therefore, the VPA-induced ASD model represents a robust model and a valuable tool to investigate the neurobiology underlying autistic behavior, as well as to detect new therapeutic alternatives. It is worth mentioning that this model could represent the cases of idiopathic ASD that are of environmental/epigenetic origin, mostly reported in clinical practice (Nicolini, C., & Fahnestock, M. 2018).

We characterize the early behavioral expression of the core symptoms of the VPA-induced ASD model, including ultrasonic vocalizations (USV), social Interaction, repetitive behaviors, and somatosensory responses in female and male mice from postnatal day 4th to 21st. Our results, shows different time symptoms expression as well as, sex related phenotypes. These results will be a prominent tool to further neurobiological research of the ASD core symptoms and the discovery of new potential therapeutic targets.

Keywords: Neurodevelopmental disorders, ASD, Mouse disease models.
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Bimodal Encoding in a Neuronal Population of the Dorsal Premotor Cortex during Working Memory

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Area of the project: Cognition and Behavior (Cognición y Comportamiento)

The Dorsal Premotor Cortex (DPC) of primates has historically been considered as an area dedicated to motor control. However, recent studies have found that this area is also involved in a wide range of cognitive processes, such as decision-making and working memory. This conception of the DPC is relatively new, so there are still questions about how the neurons of this cortex encode information from stimuli from different sensory modalities during the execution of cognitive tasks. In this work, it is considered whether the DPC is capable of integrating and retaining information from vibrotactile and acoustic stimuli in working memory during a frequency discrimination task. To address this approach, the electrical activity of a neuronal population in the DPC of the right hemisphere of a trained *Rhesus* monkey was recorded while performing a frequency discrimination task. This task consisted of the comparison of two consecutive stimuli of variable frequency and that could both be of the same modality (tactile-tactile or acoustic-acoustic) or cross-modality (tactile-acoustic or vice versa). It was found that the performance of the animals did not vary between the different conditions of the task, suggesting that the subjects are capable of abstracting the frequency value regardless of the sensory modality of the stimulus. Principally, it was found that an overwhelming majority of DPC neurons are capable of retaining stimulus frequency information during the working memory period regardless of their sensory modality, that is, they exhibit bimodal encoding. These results support the cognitive role of the DPC in working memory processes and reject the idea that this is a cortex with a purely motor role.

Keywords: Dorsal Premotor Cortex; Bimodal Encoding; Working Memory.

Short-memory disfunction induced by haloperidol in the thalamic reticular nucleus in the rat

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Área: Cognición y Comportamiento

Anterior and mediodorsal thalamic nuclei have been linked to memory and learning disfunctions (Aggleton & Nelson, 2015; Cross et al. 2012; Pernaudeau et al. 2018). Nevertheless, role in memory of thalamic reticular nucleus (TRN), a key thalamic structure to control the information interchange between thalamus and cortex, has scarcely been studied. TRN has a common dopaminergic innervation from substantia nigra compacta with globus pallidus and striatum named as extrastriatal innervation (Anaya-Martinez et al. 2006). Functional relevance of this innervation has evaluated by local 6-hydroxidopamine lesions in TRN and globus pallidus producing anxiety and memory alterations, respectively (Picazo et al. 2009; Baron-Quiroz et al. 2021). So, in this work the effect of acute dopaminergic blocking in TRN on short memory by haloperidol was assessed. All animal procedures were performed in accordance with national and international guidelines for care and use of laboratory animals (NOM-062-ZOO-199 & NIH Guide). Adult male Wistar rats were used (n=6-8/group) to test their performance on novel object recognition task (NORT) and locomotor activity. In NORT short-memory was evaluated measuring the exploration time of a novel object and another previously known and using these times to calculate an new object recognition index (NORI). First the systemic effect of haloperidol was evaluated at doses of 0.04, 0.07, 0.1 and 0.7 mg/kg observing a reduction of NORI at 0.1 and 0.7 mg/kg. Only 0.7 mg/kg affected locomotor activity. Subsequently intracerebral cannulas directed to TRN were implanted in the proper stereotaxic coordinates calculated using Paxinos & Watson rat brain atlas (2014). After surgical recuperation period the unilateral injection of 200 μM of haloperidol elicited a statistically significant reduction on NORI without effects on locomotor activity. These results shows that dopaminergic D2 block in TRN reduces short-memory in recognition tasks implying that dopaminergic activity of extrastriatal way to this nucleus and globus pallidus is need it for a correct performance in recognition memory. Finally, it could be possible that damage to this innervation it would be related to the cognitive disfunction showed by Parkinson patients in early stage.

Short-memory; Reticular thalamic nucleus; Dopamine

Environmental Enrichment and a Cooperative Social Behavior Task

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Area: Cognition and behavior.

The consequences from housing and breeding early experiences have been explored in animal models through environmental enrichment (EE), and Wistar rats are the most used strain in these protocols. EE has been effective at increasing performance in tasks related to spatial learning, however, scarcely have tried to integrate tasks about social behavior. In addition, the contemporary perspective of cooperation/coordination is formulated as a kind of social behavior given from the interaction between individuals. In this context, this research proposed to assess 1) if housing in EE or control conditions modify the subjects execution concerning the interaction within a cooperation/coordination task and 2) if the strain and their physiological characteristics influenced the execution in the task. We worked with 12 Wistar (W) and 12 Long Evans (LE) rats separated in four groups, one control and one under EE conditions for each strain (n=6, 21 postnatal days -PND- and 35-50g at the beginning of experiment). The results were based on different parameters from the cooperative social behavior task, showing significant differences in number of reinforcers, relative response rate (RRR), relative reinforcement rate (RRr), latencies, effectiveness and relative rate of contact time in session (RRCTS) for our rats. Finally, we concluded that EE can influence the cooperative social coordination and a multi-variate behavioral research in cooperation/coordination task will play an important role in the success of many species of rodents by examining relationships between environmental variables and social and individual behavior from animals.

Keywords: Environmental Enrichment (EE), cooperation, coordination.

Perception of regular and irregular stimuli in single trials in humans

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Area: Cognition and Behavior

Despite the importance of perceiving the temporal regularity in a sequence of repetitive sensory events, the mechanism used by our brain to estimate temporal regularity is not entirely understood. To test two possible hypotheses, we program a model capable to predict with high efficiency, what the subjects will answer in a regularity discrimination task and in how long they will do it, trial by trial.

In the discrimination task the subjects had to perceive trains of sensory pulses (visual, auditory, or tactile) and decide whether they appeared at regular or irregular intervals. In our model two simultaneous processes are competing; an irregular decision is made when an irregular decision variable reaches the upper decision bound and the regular decision variable moved towards the lower bound if throughout the stimulus there is not enough evidence in favor of the irregularity.

After testing two possible hypothesis using our model and the values observed by the subjects in each trial, results suggest that instead of waiting for a single large temporal deviation in the stimuli, the participants accumulate evidence in favor of irregularity (when the difference between the duration of the current interval and the duration of the previous one is different from zero) during the whole stimuli leading to the irregular decision when the amount of evidence exceeds a bound. After comparing trial by trial and obtain the optimal values of each parameter of the model (bounds, noise, slope, and decay constant of the accumulated evidence) for each subject, the psychometric and chronometric curves of the model and the subjects had a very good fit. We can assure that our model is a good predictor of this regularity discrimination task and therefore reinforce the hypothesis that our brain could evaluate all the stimulus and accumulates evidence of irregularity in order to make a decision of this type.

Key words: rhythm; decision-making; sensory perception.

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Effect of dopamine type 2 receptor activation in long-term memory in a murine REM sleep deprivation model.

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Several animal studies show the role of Rapid Eye Movement (REM) sleep on long-term memories formation. Spatial memory, a hippocampus-dependent episodical memory, is impaired in sleep-deprived animals, and this cognitive deficit is associated with reduced levels of Brain Derived Neurotrophic Factor (BDNF), decreased neuroblasts proliferation, and differentiation in brain. These events, along with synaptic plasticity, are crucial for memory consolidation and evocation, where Dopamine (DA) seems to play a key role. Interestingly, dopaminergic D_1-D_5 receptors are required for plasticity persistence in the hippocampus and novelty-associated memory enhancement. Furthermore, DA neurons in locus coeruleus may enhance memory formation when DA is co-released from the hippocampus. Thus, this study aimed to determine if activation of D2 and D3 DA receptors with Quinpirole positively modulates behavioral paradigms such as anhedonia and episodic memories in REM sleep deprived mice.

Two-month-old male CD1 mice were used for the experiments. All animals were kept in a room with controlled illumination (12:12 h light/dark cycle) and temperature (18-22◦C) to enable acclimatization. Animals were kept in the room where experiments were performed one day before the assays. Quinpirole (Sigma-Aldrich, St. Louis, MO) was freshly prepared for every administration. Quinpirole (2µg/kg/day i.p.) was injected for 3 days (the REM sleep deprivation period). The multiple platform method was used to induce REM sleep deprivation. Briefly, 6 platforms (8.5 cm height, 2.5 cm diameter) were placed in a water-filled tank. Spatial memory was assessed by the Morris Water Maze (MWM) test; this task is well-known for evaluating hippocampal-dependent memories. Evocation test was assessed 72 h after the last training. Animals were sleep-deprived during this period between acquisition and evocation. Additionally, novel object recognition was also tested. Animals were habituated in an arena containing two identical objects; 24 h later, evocation was tested, replacing one object with a novel one. The recognition index was determined to evaluate the task performance. Anhedonia was measured by sucrose consumption.

The data show that REM sleep deprivation caused memory evocation deficit in MWM and novel object recognition tests. In contrast, Quinpirole co-administration during the sleep deprivation period significantly attenuated this effect. This tendency was observed in both behavioral tasks. On the other hand, Quinpirole prevented the anhedonic condition induced by REM sleep deprivation. Our results showed that D2 receptor activation improves the cognitive deficit and anhedonia induced by REM sleep deprivation.

Palabras clave: REM sleep deprivation, Dopamine, memory.

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Lateral habenula participation during aversive sugar memory formation, as well as after flavor familiarization

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Introduction: The habenula (Hb), located in the epithalamus, is a phylogenetically conserved structure in all vertebrate animals. The Hb is divided into medial habenula and lateral habenula (LHb). LHb has a critical role in aversion-mediated learning and behavior (aversive signal processing), responding to cues that predict adverse events and aversive outcomes. Also, pharmacological inactivation of LHb neurons seems to render animals indifferent to a given behavioral outcome. LHb has broader connections to the limbic and basal ganglia input and input to various structures that transmit internal state information and connect to some structures involved with taste memory. On the other hand, the glutamatergic system is highly involved in associative learning. The activity mediated by NMDA (N-methyl-D-aspartate) receptors regulates the formation of conditioning taste aversion (CTA) since its antagonism in various brain structures prevents CTA. Deep brain stimulation of LHb significantly reduces sucrose self-administration on rats. In contrast, LHb injury increased sucrose-seeking behavior and a delayed extinction response to substituting sucrose for water. Thus, it is important to study the participation of the habenula during CTA of a highly appetitive stimulus such as sugar. **Objectives**: To evaluate LHb function, we made bilateral NMDA lesions just before sugar aversive memory formation (CTA), as well as during latent inhibition of CTA, after high sugar familiarization. **Materials and Methods**: Adult male Wistar rats (250-310 g initial weight) were liquid deprived and habituated to a single daily liquid presentation (20min/day). During CTA acquisition day, 30 minutes before sugar presentation, rats were bilaterally injected in the LHb with NMDA (10 µg/µl). The consumption of sugar (10% water solution) was recorded during acquisition, retrieval, and three extinction sessions. For sugar familiarization experiment (latent inhibition of CTA), rats were permanently exposed to sugar for 21 days, and after this prolonged consumption, they were subjected to CTA procedure. **Results:** The bilateral NMDA lesion of the LHb did not affect the CTA, but a tendency of differences was observed during aversive memory extinction. **Conclusions:** LHb lesions do not significantly alter sugar aversive conditioning; however, the more posterior LHb lesions tend to increase CTA. Furthermore, the results suggest a decrement of latent inhibition of CTA induced by the LHb lesion.

Keywords: Habenula, aversion, glutamate.

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Area: Cognition and Behavior

Maternal enrichment increases infantile spatial amnesia mediated by postnatal neurogenesis modulation.

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Area: Cognition and Behaviour

Infantile amnesia, the inability to form long-lasting episodic memories, is a phenomenon extensively known but with no clear understanding of its origins. Recent research showed that high rates of hippocampus postnatal neurogenesis degrade episodic-like memories in infants a few days after memory acquisition.

Additionally, new studies indicate that exposure to an enriched environment in mice leads to a high hippocampal neurogenesis level in their offspring. Nevertheless, it is still unclear how this intergenerational trait affects the persistence of hippocampal memories. To address this question, we evaluated the spatial memory of the offspring of enrichment female mice after weaning. Ten days after spatial learning, we tested memory retention, and we found that the offspring of enriched dams showed an increase in spatial memory failure, an observation that correlates with high rates of proliferation in the hippocampus. Moreover, to determine the causal relationship between hippocampal neurogenesis and memory failure, we ablated hippocampal neurogenesis with temozolomide (TMZ), which rescued spatial memory retrieval. Finally, neuronal activity in the hippocampus, evaluated by the immediate early gene (IEG) c-Fos expression showed engram modifications between groups. This shows that the large addition of newborn neurons added to the circuit can modify memory engrams and cognitive performance. In conclusion, the intergenerational increase of hippocampal neurogenesis leads to plastic changes that exacerbate spatial infantile amnesia.

Keywords: Postnatal Neurogenesis, Infantile Amnesia, Hippocampus

Establishing the link between Speech-to-speech Synchrony and General Auditory-Motor synchronization skills

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Cognición y Comportamiento

Auditory-motor synchronization (AM-synch) is the ability to temporally align a train of motor gestures to a rhythmic auditory stimulus. In humans, it is an innate skill that has been shown to predict performance on different language-related tasks; across species, it has only been observed in vocal learners. In light of this link between AM-synch and speaking abilities, Assaneo and colleagues explored the phenomenon in the context of speech. They designed a behavioral protocol, the Spontaneous Speech Synchronization Test (SSS-test), in which participants are instructed to continuously repeat the syllable "tah" while concurrently listening to a rhythmic train of syllables. Using this simple test showed that the general population can be segregated into two groups: while some participants are compelled to spontaneously align the produced syllabic rate to the perceived one (high synchronizers), the rate of other participants is not modulated (low synchronizers). Strikingly, individuals classified as 'high' or 'low' synchronizers have structural and functional brain differences, with important consequences regarding speech processing and language learning skills. This initial work invites the following questions: where does the predictive power of the test come from? Is the bimodal distribution of the synchronization measurement a consequence of the speech motor gestures or the acoustic properties of the stimulus? To answer these questions, in the present study we evaluate the level of AM-synch for different motor gesture-stimulus combinations. Motor gestures, as well as the stimulus, can be speech-related (whispering "tah"/train of syllables) or speech-unrelated (clapping/train of tones). Participants completed eight synchronization blocks, two for each motor gesture-stimulus combination. On each block, participants were instructed to continuously repeat the motor gesture (whisper or clap) at the same rate as the auditory stimulus (train of syllables or train of tones) until the end of the stimulus. All stimuli lasted 1 minute, the rate started at 4.3 Hz (i.e., 4.3 syllables or tones per second) and it increased in 0.1 Hz every 10 seconds until it reached 4.7 Hz. Preliminary results show that, while the bimodal distribution is recovered for the clapping-to-syllables combination, it dissolves (most participants were able to synchronize) when the stimulus included tones, regardless of the motor gesture. This result shows that the previously reported 'high' vs. 'low' synchronizers segregation is a consequence of the acoustic features of the stimulus and is independent of the nature of the motor response. Additionally, individuals classified as low synchronizers during a first assessment with the SSS-test, show a significant increase of their synchronization abilities to the train of syllables, when the SSS-test is completed after the clapping to tones block. This suggests that synchronization abilities can be temporarily enhanced if previously entrained by a more efficient stimulus. Building upon these results, further work will be conducted to identify the precise acoustic characteristics that would grant the previously observed bimodal outcome in the synchronization test and to explore whether a temporal enhancement of synchronization abilities translates to better performance in language-related tasks.

Speech, Auditory-motor Synchronization, Language

The role of 5-HTRs of the Nucleus Accumbens in Sociability

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Introduction: 5-hydroxytryptamine (5-HT) has been found to modulate reward, mood, emotional and social behavior (SB). Furthermore, the 5-HT system has been found to be altered in several psychiatric entities, including sociability disorders, as well as depression, anxiety, schizophrenia and autism spectrum disorder. In view of that, the 5-HT system and particularly its receptors (5-HTRs), as promising pharmacological targets, have been widely studied. It is however not totally clear what is the role of 5-HT in SB. On the other hand, the nucleus accumbens (NAc) has an important role in sociability both in humans and rodents, and some studies have suggested that intra-accumbal 5-HTRs could be essential to explain the neurobiology of SB. It is however not totally clear what is the role subserved by selected 5-HTRs in sociability within this region. **Objective:** To develop a project aimed to study the involvement of 5-HTRs in sociability within the NAc. **Methods:** A survey of the literature was made on the role of 5-HTRs in SB, paying particular attention to its role in the NAc and to see how this behavior has been methodologically evaluated in rodents. PubMed was the principal searching engine but Science Direct, Mendeley, Google Scholar, Science Research and Semantic Scholar were also used. “Serotonin”, “5-HT”, “accumbens”, “nucleus accumbens”, and “social behavior” were the principal words used in this search. **Results:** **Behavioral methodology**. Maternal care, empathy and prosocial behavior, social reward and social interaction were found suitable models to study the role of 5-HTRs on SB. **Role of accumbal 5-HTRs on SB**. Four principal 5-HTRs were found to have a role in SB, namely 5-HT1A, 5-HT1B, 5-HT2A and 5-H2C receptors. Acquired information indicated that the reported results varied depending upon the particular behavior evaluated, the rodent model used, the objective of the research, and whether they were either beneficial or harmful for sociability. They were also depending on whether the receptors involved were acting either in a direct way or through a crosstalk with other neurotransmission systems. **5-HT1A receptors**. Although numerous studies concluded that this receptor participates in SB, its role has been found secondary to a reduction in aggression and anxiety. **5-HT1B receptors**. Beside that this receptor seems to have a role in the modulation of social reward, the results obtained have failed to completely explain its role on this behavior. 5-HT2A receptors. Numerous studies using different animal models, drugs and protocols, as well as genetic studies showing different polymorphisms, have suggested that 5-HT2A receptor seems to be the most promising receptor to study the role of SB neuromodulation, especially within the NAc. **5-HT2C receptors**. No convincing evidence was found for the participation of this receptor in SB. However, since colocalization of 5-HT2A and 5-HT2C receptors has been reported within NAc it results tempting to study their intra-accumbal interactions in the modulation of SB. **Conclusion:** According to the information gathered, it has been considered that a promising approach to evaluate the involvement of 5-HT on the accumbal modulation of SB will be to study by means of the social interaction test the effects of the intra-accumbal infusion of M100907, a 5-HT2AR antagonist. **Key words:** social behavior, serotonin, 5-HT2AR.

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Effect of High-fat diet on the Central Nervous System in CD-1 mouse

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Cognitive dysfunction is a neurological disorder characterized by the gradual loss of one or more cognitive domains but retaining the ability to perform daily activities. Several factors contribute to cause this disorder, such as substance consumption, metabolic disorders, among others. Emerging research has demonstrated that high consumption of food rich in saturated fat and refined sugars is capable to produce changes in memory and learning processes. Moreover, cognitive disfunction have been reported more frequently in obese women than in men.

The aim of our work was to determine the effect of the hypercaloric diet on mice performance on the radial eight-arm maze (RAM) test. For that purpose, eight-week-old female CD-1 mice were randomly assigned into two independent groups: control (CTL, n=9) and high-fat diet (HFD, n=9). Over 13 weeks HFD mice had free access to hypercaloric diet and 40% sucrose solution and standard feed and water for the CTL group. In week 14, the RAM test was performed, and the following parameters were evaluated: a) latency to find palatable stimulus; 2) number of errors in working memory; and 3) the number of errors in reference memory.

We found that there is a significant effect of diet on weight gain and glucose levels, from week five until the end of the behavioral test. In the acquisition phase, through the eight testing days, both groups showed the same latency. However, in the analyses we observed a significance decrease since day three of the task. On working memory errors there were no changes between groups, but from day two a decrease was seen, until the eighth day. Finally, on errors in reference memory there were no changes neither between groups nor in days. In the retention phase, we found no changes in any of the parameters analyzed.

These results suggest that the increase in body weight and glucose levels causes slight changes in spatial and short-term memory after 13 weeks of hypercaloric diet.

Keywords: High-fat diet, Radial eight-arm maze test, Female CD-1 mice

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Effects of Disruptors on a Retrospective Temporal Discrimination Task:

An Approach through Signal Detection Theory

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An adequate integration of information from different temporal events is fundamental for organisms to adapt optimally into the environment. There are processes related to memory which consider the integration of temporal information, specifically, processes related to retrospective memory.

Previous research on retrospective temporal discrimination have established the existence of some disruptors that have an impact on behavioral timing, mainly manipulations of reinforcement magnitude, pre-feeding and others disruptors (Akdoğan & Balcı, 2016; Barrón et al., 2020; Cambraia et al., 2020; Galtress, Marshall & Kirkpatrick, 2012; Ward & Odum, 2006). These findings have shown evidence of changes in the shape and location of psychophysics curves. However, disruptors such as feeding during intertrial interval (ITI) or feeding during the presentation of stimuli to be estimated have been less explored. Also, the specific relationship between these motivational variables and temporal discrimination, in terms of how they are linked to the alteration of temporal control processing, has not been explored yet.

The aim of this study was to analyze how changes in temporal discrimination occur in a temporal bisection task by altering the value of the reinforcer using the following manipulations: delivery of reinforcement during ITI, delivery of reinforcement during the presentation of the stimulus to be estimated, and through differential extinction. 12 Wistar male rats were trained in a temporal bisection task. Subjects were divided into 3 groups, determined by different pairs of durations (0.4”-1.6”, 2.0”–8.0”, 5.0”–20.0”). The subjects were exposed to 10 generalization sessions both for baseline and for the experimental manipulations, which consisted in a) delivering free food during ITI, b) delivering free food during the presence of the stimuli to be estimated to the subjects and finally c) we using an extinction disruptor for each duration, short and long, separately.

Our analyses were focused on two issues, the first one about classical psychophysical and the second one about Signal Detection Theory. Our results indicate that the parameters behaved as a function of experimental manipulations in the condition b) delivering free food during the presence of the stimuli to be estimated, and condition c) differential extinction. We can suggest retrospective temporal discrimination and motivational variables are related.

Keywords: Retrospective Temporal Discrimination Task; disruptors of timing; signal detection.

Starvation increases attraction to odorants through CRH-1/CREB activity in the nervous system and intestine of *Caenorhabditis elegans.*

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To survive starvation, organisms have a diverse array of responses ranging from metabolic adaptation to behavioral changes. Although these metabolic adaptations have been broadly characterized, a thoroughly analysis of the molecular mechanisms involved the regulation of behavior after starvation is still lacking. Starvation has notable long-term repercussions in the nematode *Caenorhabditis elegans,* our experiments showed that adult worms subjected to 3h starvation or a 6-day starvation during the first larval stage resulted in an increase in attraction to the odorant butanone. Chemotaxis assays in various mutants show that the transcription factor *crh-1,* an ortholog of the cAMP response element-binding protein (CREB), are necessary for the occurrence of changes in the preference for butanone following starvation. It was also demonstrated that CRH-1 is activated in neurons and the intestine of the worm after the 6 days of starvation. Moreover, tissue-specific RNAi of *crh-1* suggests that CRH-1/CREB is needed both in the intestine and nervous system to increase attraction to butanone after starvation. To further shed light on this requirement, we propose to perform a ChIP-seq of the histone mark H3K27ac in wild-type and CREB-knockout worms, in feeding conditions or after starvation. These data would contribute to our understanding of the regulation of behavior by insults such as starvation in animals and the inter-tissue communication that is behind it.

Keywords: Starvation, CREB, inter-tissue communication.

Area: Cognition and behavior. Epigenetics.

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Emotional dysregulation in women with endometriosis presenting cyclical and non-cyclical chronic pelvic pain

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Endometriosis is a medical condition characterized by glands and stroma presence outside uterine cavity in regions such as the bladder, ureter, fallopian tubes, peritoneum, ovaries, and even in extra pelvic sites. One of the main clinical problems of endometriosis is the chronic pelvic pain (CPP) that considerably affects the patients' quality of life. Patients with endometriosis may experience CPP in a cyclic manner or in (80% of cases) a non-cyclical manner defined as non-menstrual pain. Psychopathological conditions such as anxiety and depression can modify the response to pain; however, this has not been evaluated in women with endometriosis with different types CPP. Therefore, the aim of this work was to determine if there are differences pain levels and emotional dysregulation in patients with cyclical and non-cyclical CPP. 50 women diagnosed with endometriosis presenting cyclical and non-cyclical CPP answered several batteries made up of Visual Analog Scale, General Health Questionnaire, Beck´s Depression Inventory, Hospital Anxiety and Depression Scale, Generalized Anxiety Inventory, and State Trait-Anxiety Inventory. Results demonstrated that patients with non-cyclical CPP exhibited higher levels of general discomfort, depression, and anxiety (trait-state, and generalized anxiety) compared to patients with cyclical pain. No differences were observed in pain intensity, but the relative risk of this parameter in patients with non-cyclical CPP was associated with a higher probability of presenting emotional dysregulation (anxiety or depression) as risk factors. Our data suggest that patients with non-cyclical CPP present a higher emotional dysregulation than those with cyclical pain.

Key works. Chronic pelvic pain, anxiety, depression

This work was supported by Project 2019-1-51, Instituto Nacional de Perinatología.

Involvement of CB2 receptors of the anterior cingulate cortex on the modulation of palatable food intake in rats with binge-type behavior

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The experimental evidence suggests that neurobiological alterations in the endocannabinoid system may contribute to obesity and some pathological forms of eating. Researchers in this field observed that people suffering from obesity express elevated plasmatic endocannabinoid tone. In animal models, studies consistently report that in rats with binge-like behavior experimentally induced, particular areas of the brain show alterations of endocannabinoid tone. The nucleus accumbens receives modulatory activity from several areas, including the prefrontal cortex, specifically the anterior cingulate cortex (ACC). Since the ACC expresses cannabinoid CB2 receptors, it is possible that the cannabinoid signaling mediated by CB2 receptors modulates some of the behavioral and motivational processes of non-homeostatic feeding. Part of the cognitive processing of non-homeostatic eating involves structures such as the ACC, which modulates emotional aspects, action-result learning, and decision-making. The ACC participates in behaviors related to food foraging, then an abnormal brain activity in the ACC may be related to the craving for food observed in obese and eating disorders patients and laboratory animals. Accordingly, this study aimed to evaluate the effects of CB2 receptors activation in the ACC on a palatable diet intake (PD) of male Wistar rats with induced binge-like behavior. The standard diet (SD, chow) was available ad libitum, while the PD (evaporated milk added with 10% sucrose) was provided 60 min per day, during 35 days in the light phase of the light/dark cycle. We measured the daily SD consumption (24 h) and the SD intake during the 60 min previous to the presentation of the PD. Then, we measured the consumption of PD (60 min). On day 20, when the consumption of the PD stabilized (variations less than 20% in 3 consecutive sessions), microinjection cannulas were stereotaxically implanted in the ACC. A group of rats had continuous access to the palatable diet, and two different groups of rats had interrupted access to the palatable diet after day 21 for 8 or 4 days post-surgery. Subsequently, rats received intra-ACC injections of the CB2 receptor agonist (GW838972A, 0.25 µg/µl), the CB2 receptor antagonist (AM630, 0.75 µg/µl) or both (GW838972A, 0.25 µg/µl + AM630, 0.75 µg/µl) 15 min before the access to the PD and food intake was measured (SD and PD, 60 min). We found that the protocol of limited access to the PD induced binge-like behavior (energy intake >50% from the total daily caloric intake in 60 min), and activation of CB2 receptors in the ACC decreased PD intake only in the group with interrupted access to the PD for four days after surgery. In conclusion, ACC CB2 receptors contribute to the modulation of PD intake in specific conditions, and restriction to the diet may modify how CB receptors contribute to regulation of non-homeostatic feeding.

Keywords: Endocannabinoids, anterior cingulate cortex, binge-like behavior

Striatal circuitries for motor control and action selection

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The ability to organize actions into coherent behavioral sequences is essential for survival. To face environmental challenges and to improve performance, animals must be able not only to make decisions based on sensory stimuli but to adapt their actions according to the outcomes. It has been proposed that the basal ganglia (BG) provide specific estimations of perceptual decision variables, implement action selection rules, and evaluate/modify such processes throughout learning. Detailed knowledge has been accumulated on how the direct and indirect pathways of the striatum (input nucleus of the BG) are involved in movement and execution of motor plans. Recently, it has been observed that: *i)* the activity patterns of these pathways are complementary and critical for motor control, and *ii)* during the initiation and execution of sequences of actions, each pathway participates in different motor processes. Furthermore, it has been proposed that to learn sequences and convert them into habitual behaviors, a reinforcement learning mechanism is implemented in the striatum. However, the exact computational functions of both pathways regarding the integration and execution of complex motor plans remain unclear.

In this study, we developed an action-selection behavioral paradigm with different levels of complexity, where subjects must perform a series of actions (*nosepokes*) to obtain a reward. We found that when mice have to choose between two actions -in the absence of cues indicating which will be rewarding- cell-specific ablation of the direct pathway impaired the ability to establish causal action-reward relationships; whereas the ablation of the indirect pathway did not affect this ability but made them inflexible to modify their choices when actions stoped to be rewarded. Strikingly, when animals had to concatenate two consecutive actions to obtain a reward, the ablation of either pathway generated similar behavioral deficits, disabling them to generate coherent sequences, and establishing a significant bias towards the closest action (in time) to the reward.

Our data indicate that both pathways participate in a differentiated manner in action selection and reinforcement learning of simple sequences, and raises a relevant question about the function of these pathways for the acquisition/execution of motor sequences with higher computational demands.

Área: Cognición y Comportamiento

Keywords: *dorsal striatum, action selection, reinforcement learning*

The effect of optogenetic-induced synaptic plasticity in LC-CA1 pathway on memory

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Área: Cognición y Comportamiento

Learning is the process of acquiring new information through experience, while memory is the encoding and storage of this information for later recall. Both processes allow the adaptation and updating of previous knowledge. The formation of a new memory involves changes in the strength of the synapses, called synaptic plasticity. The most accepted model for synaptic plasticity is long-term potentiation (LTP), and it is proposed to be one of the mechanisms that underlie learning and memory.

The hippocampus is critical for memory encoding and consolidation, and it contains place cells that encode the spatial location of objects. Furthermore, some studies demonstrate that it plays an essential role in novelty detection and contextual encoding. Moreover, it has been demonstrated that catecholaminergic terminals modulate hippocampal memories. In vivo microanalysis of free-moving mice performing an object location memory (OLM) task revealed that there is an increase in dopamine (DA) and norepinephrine (NE) release in the dorsal hippocampus. They also demonstrated that depletion of the catecholaminergic terminals in the dorsal hippocampus impairs OLM. Thus, DA and NE play an essential role in contextual memory.

The dorsal hippocampus receives many catecholaminergic terminals from the Locus coeruleus (LC). LC optogenetic stimulation can induce LTP in the dentate gyrus and CA1. Nevertheless, so far, it is not clear if there is a relation between LTP induction through activation of catecholaminergic terminals from LC to CA1 and the behavioral outcome of mice in a memory task. Thus, we propose that optogenetic-induced LTP in the LC-CA1 pathway will improve hippocampus-dependent memory consolidation. We selectively activate LC catecholaminergic terminals by inflicting a Cre-inducible virus in TH-Cre mice that express a light-activated protein channel, rhodopsin (ChR2).

Overall, we found that optical stimulation of LC terminals to CA1 can induce LTP. After the Morris water maze (MWM) and Barnes maze (BM) standardization. We found that mice tested ten days after the last training session had a poor performance in both tasks, indicating that the memory trace at this time point is not easily retrieved. However, mice that received the Opto-LTP induction protocol significantly improved memory performance. In conclusion, this project provides direct evidence that hippocampal LTP induced by optogenetic activation of LC catecholaminergic terminals to CA1 enhances the memory trace evaluated by MWM and BM.

Key words: memory, hippocampus, LTP, optogenetics

Light and temperature cycles as zeitgebers in the circadian locomotor activity rhythm of the snake *Crotalus molossus*

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Area: Cognition and behavior

In ectothermic organisms, the most common zeitgeber that synchronizes the circadian locomotor activity rhythm is the light/dark cycle; however, the importance of the temperature as a synchronizer is still uncertain. Therefore, we evaluated the effect of cold cryophase and thermophase cycles in the daily locomotor activity of the snake *Crotalus molossus*. We found that snakes synchronized to the thermophase and are most active during high temperatures; however, to test if temperature has a major influence over light, snakes were exposed to both zeitgebers. In a first experiment, snakes underwent a 12-hour light /12-hour dark cycle, with the dark phase during the thermophase. As a result, snakes synchronized primarily to the light cycle, remaining active during the dark phase at a warm temperature. In a second experiment, to test if snakes would be active during the dark phase despite cold temperatures, we overlapped the cycles, with the dark phase starting six hours after the cryophase. We found that snakes remained synchronized and performed their activity in the dark phase, but showed less movement when temperatures are low. We concluded that both light and temperature are important zeitgebers entraining circadian locomotor activity rhythms in *C. molossus* and that temperature cycles by themselves can entrain activity rhythms when photic cues are absent. Our experiments supported that light remains the most important synchronizer of activity rhythms.

Keywords: Locomotor activity, circadian rhythm, reptiles

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Neurobiology Meeting of the Mexican Society for Biochemistry

Development & Aging

UNAM · Sociedad Mexicana de Bioquímica · Neurobiología · SMB · 65 años 1957-2022 · CONACYT · IBERO Ciudad de México · Cinvestav · 40 años Instituto de Biotecnología · Instituto de Neurobiología · Instituto de Fisiología Celular UNAM · Facultad de Psicología

IV Neurobiology Meeting
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The amniotic epithelium confers a bias to human embryonic stem cells to differentiate toward the neuroectoderm lineage

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Human embryonic stem cells (hESC) derive from the epiblast differentiate into cell lineages from mesoderm, endoderm and ectoderm (pluripotency). On the other hand, the neural lineage or neuroectoderm is the first to be specified in the human epiblast once morphogenesis begins. Previously, we demonstrated that human amniotic epithelial cells (hAEC) derive and maintain hESCs in an undifferentiated state. We evaluated if the hESC-hAEC co-culture could represent a different pluripotent state than conventional conditions (grow on a layer of mouse embryonic fibroblasts, MEF), simulating the post-implantation stage embryo where the amniotic epithelium interacts with the epiblast before morphogenesis. Our data demonstrate that hESC-hAEC condition presents a downregulation expression of genes associated with the endoderm and mesoderm lineages. In contrast, there is an increase in the expression of genes from the ectoderm lineage, specifically from the anterior neuroectoderm (FEZ1, LHX5, SIX3, RIX, OTX1/2). When challenged to differentiate towards the neural lineage, hESC-hAEC showed an increase in generated neural progenitors (SOX2+, NESTIN+) and mature neurons (MAP2+) in comparison to hESC-MEF. To elucidate the possible mechanism(s), we analyzed the phosphorylated kinase proteomes, which showed an upregulation of the SRC kinase, STAT3, ERK and AKT signaling pathways. Later, each one was inhibited by a specific small molecule and the expression of neural genes, as well as their potential for neural differentiation, were evaluated. PI3K/AKT pathway inhibition did not produce a decrease in neural induction in hESC-hAEC condition. However, the ERK, STAT3 and SRC individual inhibition induced a reduction in the differentiation towards the neuroectoderm in hESC-hAEC. There were no alterations in the conventional condition hESC-MEF when inhibiting the SRC and ERK pathways. Our results suggest that interaction hAEC-hESC promotes a biased potential to neuroectoderm by specific signaling pathways (SRC and ERK).

Keywords: human pluripotency, neuroectoderm, differentiation

Área: Desarrollo y Envejecimiento

Evaluation of ketogenic diet as a non-invasive strategy to improve autophagy and memory function in aged 3xTg-AD and WT mice.

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Aging is a biological process characterized by a progressive loss of physiological functions and an accumulation of damage at the molecular, cellular, and tissue level over time that increases the probability of death. This deterioration represents a risk factor for developing cancer, diabetes, cardiovascular and neurodegenerative diseases. One of the most frequent neurodegenerative diseases in old age is Alzheimer's disease (AD). A common feature between physiological aging and AD is that in both exist an accumulation of senescent cells. *Cellular senescence* is a phenotype characterized by cell cycle arrest and a lack of response to mitotic and apoptotic stimuli. It can be caused by different stressors, including the failure of autophagy. Autophagy is a catabolic process responsible for degrading intracellular components into essential biomolecules within lysosomes to maintain cellular homeostasis and prevent the accumulation of unnecessary proteins and damaged organelles. Its failure has been associated with neuronal senescence induction in aging and memory alterations in aging and AD models. For this reason, stimulating autophagy could be a promising intervention strategy to prevent neuronal senescence and improve cognitive abilities in elderly and AD subjects. Previous reports have shown that the consumption of ketogenic diets (KD) improves the memory of mice with physiological aging and AD. In addition, the presence of ketone bodies improves autophagic flux and neuronal viability *in vitro.* So, we propose that modulating autophagy *in vivo* through KD consumption could prevent the senescent phenotype of neurons and astrocytes and reduce the cognitive deficiencies associated with physiological aging and AD. To test this hypothesis, we analyzed hippocampal and cortex-dependent memory tasks such as Morris's water maze and object recognition memory from males and females in physiological aging (6 and 13 months) and AD mice model (3xTg-AD, 6 and 13 months) exposed to a KD (75.1% fat, 8.6% protein and 3.2% carbohydrates) or control diet (CD, 13.6% fat, 28.9% protein and 57.4% carbohydrates). The metabolic and cognitive results will be discussed in the meeting.

Key Words: Ketogenic diet; Autophagy; Alzheimer´s disease.

Area: Development and Aging

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The role of GDNF in the axonal growth of motor neurons and in the establishment of the neuromuscular junction

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Area:

Desarrollo / Developmental biology

GDNF is a neurotrophic factor which promotes neuronal differentiation and increases dopaminergic and motor neurons (MNs) survival. In this work, we differentiated MNs from mouse embryonic stem cells with continuous expression of GDNF (mESC-GDNF), as well as with control cells. Differentiated MNs were placed on microfluidic chambers to assess their axonal growth and the establishment of neuromuscular junctions with myotubes derived from C2C12 myoblasts. Axonal growth and interactions between the axons of MNs and myotubules were analyzed with epifluorescence and confocal microscopy. We found that MNs derived from mESC-GDNF extended their axons to reach the chamber with muscle cells, in contrast to MNs derived from control mESC, which did not reach myotubes. Among the interactions found between MNs expressing GDNF and myotubes, a few co-localized with bugarotoxin, which binds to acetylcholine receptors, suggesting the formation of a neuromuscular junction. Thus, GDNF expression allowed MNs to reach myotubes, and establish putative synaptic contacts, although further experiments *in vivo* and *in vitro* will provide more information about the role of GDNF on the establishment of the neuromuscular junction.

This work was supported by grants from PAPIIT-UNAM IN213719 and IN219122.

Key words: Stem cells / Glial cell Derived Neurotrophic Factor / Neuromuscular junction

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Sucrose Consumption During Late Adolescence alters Dendritic Orientation of Doublecortin Positive Neurons of The Ventral Dentate Gyrus in Adulthood

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Area: Development and Aging

Abstract:

The high availability of sucrose for the population makes this carbohydrate susceptible to an immoderate consumption specially in the adolescent population which is actually one of the groups with the highest consumption of sucrose among all. Preclinical studies demonstrate that sucrose consumption during early adolescence promotes depressive and anxious behaviors that correlate with decreased neurogenesis on the dentate gyrus (DG) of the hippocampus. Surprisingly, there is a lack of information concerning to the effect of sucrose consumption on the ventral DG during late adolescence (LA) even though this portion modulates emotional behaviors including depression and anxiety. Thus, we tested whether sucrose intake during LA decreases neurogenesis in the ventral DG of the hippocampus and causes abnormalities in the spatial distribution on the cells involved in this process. Adolescent male Wistar rats were divided in three groups. One group had free access to a bottle of water and sucrose 10 % from LA to adulthood, namely from post-natal day 42 to post-natal day 82 (Sucrose group or Suc group); the second group had access to water and sucrose 10% only during the LA period, namely from post-natal days 42 to 52, after which sucrose was withdrawn (Restricted group or Res group). The third group had access to only water during the entire experiment (Control group or Ctrl group). Rats did not show difference on the number of proliferating Ki67+ cells at the subgranular zone and the hilus of the DG. However, we observed an increased number of doublecortin (DCX) cells with horizontal dendritic arborizations at the Suc and Res groups when compared with the control group ($p<0.05$), suggesting an altered orientation. Finally, no ectopic distribution of DCX cells was appreciated. These results suggest that sucrose consumption during LA does not impair the neurogenesis rate on the ventral DG, but it could impair the synaptic connections of granular neurons due to the wrong orientation of DCX immature neurons.

Keywords: Sucrose consumption, neurogenesis, ventral hippocampus.

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Axonal degeneration in an *in vitro* model of neuronal senescence

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Area: Development and aging

During aging, senescent cells accumulate and are responsible of deleterious traits. Cellular senescence is a cell state characterized, among other features, by lysosomal dysfunction and the secretion of growth factors, cytokines, metalloproteinases, etc., collectively known as senescence associated secretory phenotype (SASP), that alter the surrounding tissue. Neurons with senescent features also accumulate in old brains. In previous work we demonstrated that neuronal senescence occurs as a consequence of autophagy dysfunction.

Autophagy is a process of selective engulfment of intracellular components into double membrane vesicles that are delivered to the lysosome for degradation. As autophagy depends on vesicular transport and cytoskeleton integrity, in this work we wonder whether axonal degeneration could be the trigger of autophagy dysfunction leading to neuronal senescence.

Axonal degeneration is the selective elimination of axons in a cell-autonomous way, and occurs in some neurons during aging and neurodegenerative diseases. It includes induction, cytoskeleton fragmentation, membrane permeabilization and disintegration. In some instances, axonal degeneration is mediated by the RIPK1-RIPK3-MLKL pathway.

We will present data showing that during an *in vitro* model of neuronal senescence axonal degeneration occurs. Preliminary results suggest that RIPK1-RIPK3-MLKL pathway is activated and could trigger axonal degeneration leading to neuronal senescence. We are currently studying whether it is mediated by autophagy dysfunction.

Key words: autophagy, neuronal senescence, necroptosis

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Generation of knock-down and knock-out hESC lines for SCL to study GABAergic differentiation

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Area: Development and aging.

The transcription factor SCL (Stem Cell Leukemia) is widely described in the hematopoietic system as a master regulator in differentiation and developmental processes. It is also expressed in some regions of the central nervous system (CNS), having a fundamental role in the differentiation to GABAergic neurons. However, its study is limited to animal models since the development of the human nervous system is difficult to study due to the limitation of non-invasive techniques or the variable availability of fetal tissue donated for research. The possibility of studying the involvement of this transcription factor in human cells would be of great importance to generate more information on CNS development and differentiation. Among several strategies, one of the most widely used is the differentiation in culture of pluripotent cells of human origin; these cells can be induced to form neural ectoderm and subsequently neurons with various phenotypes. Here we aimed to study the effect of SCL downregulation and loss of function in human embryonic stem cells (hESC) by generating two cell lines, a knock-down line with interfering RNAs and a knock-out line, obtained through the CRISPR/Cas9 system, in H9 cells. The obtained lines had the morphology of hESC and grown in the presence of antibiotic of selection, also expressed the green fluorescent protein (*GFP*) as a reporter gene. The knock-down line did not express *SCL*, as confirmed by RT-qPCR. These lines will be used to discern the role fo SCL in GABAergic differentiation.

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Key words: SCL; human embryonic stem cells; GABAergic differentiation.

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TRa1 and TRb1 expression in the neurogenic niche of the hippocampus

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Area: Development and aging

Thyroid hormones (TH) are essential for fetal and post-natal nervous system development, playing a vital role in maintaining adult hippocampal neurogenesis. Thyroid hormones mediate their genomic effects by binding to TH receptor (TR) isoforms alpha and beta. Previous data demonstrate a differential expression of *Thra1* and *Thrb1* along the neurogenic cellular population of the subgranular zone (SGZ). However, it remains to determine which of the distinct populations of the dentate gyrus (DG) expresses one or both TRs in physiological conditions. Thus, in this work, we analyzed the expression of TRα1 and TRβ1 in the neural stem cells (NSCs), the glia-like cells (GLCs), and the granular neurons (GNs) in the adult mouse brain that will help us elucidate the more complex mechanisms acting in the neurogenic process of this niche.

TRα1 and TRβ1 expression was analyzed in coronal sections (30 um) of 4 months old adult mice by fluorescence immunohistochemistry. To identify the different cellular populations, we marked them with antibodies against specific markers: GFAP, SOX2, NeuN, and Calbindin. A confocal fluorescence microscope (Zeiss LSM 710) was employed for image obtention, and ImageJ and Zen 3.3 (blue) were used for image analysis.

Our results show that GLCs and GNs expressed both TRα1 and TRβ1 in the SGZ. However, the GLC population expressed varying levels of each receptor, suggesting a differential expression among NSCs and mature astrocyte populations. In contrast, GNs show a similar level of both receptors.

In conclusion, for the first time, we demonstrate a differential expression of TRα1 and TRβ1 among the neurogenic population of the adult hippocampus. Further identification should be performed to better characterize the pattern of TH receptors in NSCs and mature astrocytes.

Keywords: Neurogenesis, hippocampus, thyroid hormones.

Effect of sonic hedgehog on the axonal growth of human dopaminergic neurons

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Area: Development and Aging

Abstract:
Parkinson's disease (PD) is a neurodegenerative disorder characterized by the premature death of dopaminergic neurons (NDA), causing motor symptoms. Currently, the treatment is palliative. Cell replacement therapy consists on restoring lost NDAs and is considered as a viable therapeutic option; however, transplanted neurons are required to extend their axons to their innervation target, thus chemoattractants molecules are required to guide axonal growth and form the corresponding connections. SONIC HEDGEHOG (SHH) has been shown to be an important guiding molecule in the development of various neural circuits, and it promotes chemoattraction of NDA during embryonic development. In this work we evaluated the chemoattractant activity of SHH on axons of dopaminergic neurons derived from embryonic stem cells (CTEh). We used the CTEh H9-EGFP transgenic cell line that constitutively expresses the green fluorescent protein, so axons from NDA could be identified to evaluate their behavior when stimulated. The CTEh was cultivated in an area of 9.5 cm2 until reaching a confluence of 80%. Subsequently, the differentiation of CTEh to NDA was induced through the double inhibition of SMAD combined with the induction of the floor plate, followed by a maturation and survival phase. The differentiated cells were characterized by specific markers of NDA (FOXA2 and tyrosine hydroxylase) by immunofluorescence. Next, the NDAs on day 28 of differentiation were dissociated and seeded in axonal growth chambers, where one group was exposed to a SHH gradient and the other was set as the control group. To evaluate the effect of SHH on the axonal growth of NDA, the microchannels occupied by the axons were quantified daily by epifluorescence microscopy. Neurons exposed to Shh did not show a defined attractive or repulsive growth pattern inside the microchannels. However, the percentage of dopaminergic axons attracted to the axonal compartment showed a tendency to an increase in SHH-stimulated neurons.

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Key words: Axonal growth; hedgehog; dopamine neurons

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Taurine plays a key role in the differentiation process of neural progenitor cells from SVZ through GABA receptor interaction

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Area: Neurodesarrollo y envejecimiento

Neurogenesis occurs throughout the life of mammals, and two main neurogenic zones have been described in adult mammals, the hippocampal subgranular zone and the subventricular zone (SVZ) of lateral ventricles where intrinsic and extrinsic factors regulate this process. In the adult brain, neurogenesis constitutes an important process for neuronal plasticity. Stem cell niches respond dynamically to environmental changes, thereby providing the appropriate number of neurons that support the adaptation of the animal to new conditions. Neuronal differentiation is a complex process characterized by the initial formation of immature neurites, commonly called "neurite outgrowth." During neurite outgrowth, a diverse array of ligands, including neurotransmitters, stimulate neurite outgrowth upon binding to their cognate receptors. Taurine, a neuroactive molecule, plays a central role in the proliferation, differentiation, and migration of neural progenitor cells. However, the mechanism of action of taurine is not well understood. In this work, we explored the interaction of taurine with the GABA receptors as a probable mechanism to regulate the differentiation process of the SVZ neural progenitor. Immunofluorescence assays were performed on cells isolated from SVZ of CD1 mice (P8) in the absence or presence of taurine. Our results show that neural progenitor cells express Nestin, a progenitor cell marker; however, no signal for DCX was observed, confirming that cells obtained from the SVZ are neural progenitors. In cultures exposed to differentiation conditions with taurine, the number of DCX+ cells was increased.

Morphometric analysis revealed a significant difference in cell morphology. Compared to control and GABA-treated cells (positive control), taurine-treated cells exhibited increased dendritic branching and marked complexity in dendritic arborization. Taurine actions were sensitive to picrotoxin, indicating active participation of $GABA_A$ receptors. Also, the treatment with CGP55485 antagonist of $GABA_B$ receptors increased dendritic complexity and branching. Additionally, we measured the electrophysiologic properties of the control, GABA-, and taurine-treated cells with patch-clamp whole-cell recordings. A remarkable observation was that taurine-treated cells developed electrophysiologic behavior characteristics of mature neurons. Our results provide information regarding the role of taurine as a morphogen in the neurogenic processes throughout the interaction with ionotropic and metabotropic GABA receptors and their role as a central player in the maturation processes of NPCs into functional neurons. This work represents an advance in the morphometric effect and suggests a functional effect of taurine in the neuronal differentiation process through GABA receptors.

Keywords: Taurine, neurite outgrowth, GABA receptors.

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Prolactin receptor deficiency promotes a hypomyelinating phenotype in the corpus callosum of suckling and prepubertal mice

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In central nervous system (CNS), oligodendrocytes (OLs) are responsible for myelination, a fundamental phenomenon that promotes optimal action potential conduction and allows the assembly of complex neural circuits. The hormone prolactin (PRL) plays a regulatory role in CNS myelination during pregnancy, however it is unknown whether PRL participates in myelination during neonatal development. In pregnant mice lacking an allele of the PRL receptor (Prlr), there is a lower rate of OLs precursor cell proliferation and decreased myelin production. Moreover, systemic PRL treatment promotes myelin repair in a model of female spinal cord demyelination. In this work, we explored the effect of Prlr deficiency during early postnatal development. We evaluated myelination in suckling mice (Postnatal day (P) 12), age at which pups are exposed to high concentrations of PRL via breast milk, and in prepubertal stage (P28). Using wild type (Prlr-WT) and Prlr null mice (Prlr-KO), we analyzed myelination by Black Gold II (BGII) staining, immunofluorescence (IF) against myelin basic protein (MBP), volumetric assessment and gene expression by rt-qPCR. In addition, we explored locomotion by open field. In the corpus callosum (CC) of both suckling and prepubertal Prlr-KO mice, BGII staining revealed a hypomyelinating phenotype. In suckling mice, volumetric analysis showed less volume in this area and IF showed less MBP expression compared to Prlr-WT mice. Furthermore, evaluation of CC mRNA expression of some myelin proteins showed a significant reduction in the expression of myelin proteolipid protein (PLP) and myelin oligodendrocyte glycoprotein (MOG) in Prlr-KO mice compared to Prlr-WT. In open field, prepubertal Prlr-KO mice traveled less distance and showed less velocity in ambulatory movements compared to Prlr-WT. Taken together, these data indicate that lack of Prlr, leads to hypomyelination in the CC, disfavors myelin sheath transcriptional elements and triggers locomotor alterations. *Keywords: Prolactin, Hypomyelination, Corpus Callosum.* *Area: Development and aging*

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Generation and characterization of human midbrain organoids

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Area:

Desarrollo y envejecimiento

Brain organoids are three-dimensional cell cultures resembling the microenviroment and cell organization during embryonic development. In this work, we standardized the generation of human midbrain organoids (hMO) derived from embryonic stem cells and evaluated its potential as *in vitro* midbrain developmental model. We characterized different markers of specification, differentiation and maturation of dopaminergic neurons like LMX1A, FOXA2 and TH. We also observed that hMO showed cell populations of neural precursors with cell markers as FOXA2, LMX1A, NESTIN and KI67 in neural rosettes-like structures. We were able to generate midbrain organoids with similar structural characteristics and cell phenotypes to that of an embryonic development stage of the midbrain, so we conclude midbrain organoids could be used as good model for the study of the generation of in vitro dopamine lineage. In further studies, we will test if chemical gradients with morphogens have an impact in hMO generation.

This work was supported by grants from PAPIIT-UNAM IN213719 and IN219122.

Keywords: Midbrain development; Brain organoids; Dopaminergic induction.

The chronoarchitecture of the cerebral cortex could be linked to the emergence of the senescent phenotype

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The prevailing neurodegeneration model proposes neuronal death as the origin of behavioral and cognitive dysfunctions. Nevertheless, some studies have shown that patients with Parkinson's and Alzheimer's disease exhibit cognitive impairment in the absence of neuronal death. These data suggest that during the initial and intermediate phases of neurodegeneration, neuronal death couldn't explain the symptoms. In regard of this, it's important to remember that during the nervous system development, neuronal death and pruning of connections lead to cognitive functions improvement. Therefore, events that favor the conservation of neurons in numbers greater than those required, could cause a malfunction of the neural circuits. An alternative mechanism to explain the dysfunction observed in the early stages of neurodegeneration is cellular senescence. A cell in a senescent state is characterized by being resistant to apoptosis, secreting pro-inflammatory factors, and favoring the decline of regenerative potential, therefore we can propose that neurodegeneration could be the result of the accumulation of dysfunctional cells in a senescent state, and not a consequence of cell death. From this proposal, the question that arises is: which cells are more susceptible to acquiring the senescent phenotype and where are they located? It's known that the neurodegenerative process occurs asynchronously in the cerebral cortex, the entorhinal and motor cortices being the most affected during the early stages of this process. Interestingly, the cells that make up both cortices during adulthood are those cells that originated early during embryonic development. On the contrary, the somatosensory cortex, which isn't very sensitive to damage by neurodegeneration, is mainly made up of cells that originated in the last embryonic days. Taking the foregoing into account, the main goal of this study was to establish whether neurons of early embryonic origin express the senescent phenotype in advance. In this way, the asynchronous neurodegeneration pattern of the cerebral cortex could be explained by the cellular chronoarchitecture that's established during the embryonic period.

To solve the hypothesis, 4 groups of mice embryos were administered with BrdU between 11-14 embryonic day, when neurogenesis is active to form the cerebral cortex. Each group was administered on a single embryonic day and the animals were sacrificed at 60 pnd. To analyze the fate and cellular organization of the somatosensory, entorhinal, and motor cortices, coronal slices of the brain were processed by BrdU immunohistochemistry. At the same time, to determine if the senescent phenotype was present in the cells, the activation of the lysosomal enzyme senescence-associated β-galactosidase (SA-β-gal) was evaluated. The patterns of both brands were subsequently compared to establish whether the cells of early embryonic origin expressed the senescent phenotype in a higher proportion. Preliminary results show that the patterns of senescence and cell origin aren't coincident, even though in the analyzed sections senescence marks can be observed in the regions of interest. However, cellular senescence is a complex biological phenomenon, in which different cellular and molecular mechanisms occur simultaneously and could even precede the lysosomal activity detected by SA-β-gal, therefore it's not feasible to rule out the hypothesis using a single senescence marker. In future experiments, will be necessary to analyze additional cell senescence biomarkers, like DNA damage or cell cycle markers.

Key words: senescence, cerebral cortex, neurodegeneration

Generation of mouse and human embryonic stem cells for doxycycline inducible GDNF expression.

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Embryonic stem cells (ESCs) have been postulated as an unlimited source of clinically relevant cells for cell therapy of various diseases. Transplantation of ESC-derived dopaminergic neurons (DaN) has been proposed as an alternative to existing pharmacological treatments for Parkinson's disease (PD), a neurodegenerative disease caused by DaN loss from the *substantia nigra pars compacta*, reducing dopamine supply to the striatum. In animal models of PD, transplantation of DaN differentiated from ESC provide recovery of the motor symptoms associated to the dopaminergic lesion. However, only a low percentage of grafted neurons survive in the brain. Glial cell line-derived neurotrophic factor (GDNF) is a survival factor for DaN in vitro and in vivo. By forcing GDNF expression, we have found enhanced dopaminergic differentiation, neuroprotection against 6-OHDA and improvement of motor symptoms in hemi-parkinsonian rats. However, overexpression of GDNF may lead to compensatory and counterproductive mechanisms such as reduced TH transcription. In this work, two clones were generated from the R1 mouse ESCs line (R1rtTA-GDNF), which expresses the tetracycline response element (rtTA) constitutively, and GDNF in a doxycycline-regulated manner when under the Tet operator (TetO). Transfection was performed using lipofectamine, clones were selected for dual antibiotic resistance and genotyping was performed by PCR. Both lines were treated with doxycycline for 48 hours and GDNF expression was observed by immunocytochemistry. We started to engineer human embryonic stem cells with the CRISPR-Cas9 system for targeted integration of rtTA and TetO-GDNF by transfecting the vectors into H9 cells. The plasmid with rtTA and TetO-GDNF is being constructed by molecular cloning. The transgenic cells can be used for regulated expression of GDNF in different contexts of differentiation and survival of dopamine neurons.

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Keywords: Glial cell line-derived neurotrophic factor; dopaminergic neurons; doxycycline.

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Effect of D-serine on cognitive reserve in aged rats

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Aging-related cognitive decline is associated with structural and functional changes in the brain. However, the temporal course and the degree of the detriment of cognitive functions are not homogeneous among senescent individuals and some people will perform better than others. One of the theories explaining these differences is the cognitive reserve, where differences in neuronal resources (brain anatomy and physiology that mediate cognitive processes) allow some individuals to cope better than others. NMDA receptors have a pivotal role in many cognitive functions like memory, attention, and learning, besides the binding of glutamate, it requires the binding of the co-agonists D-serine. During aging, D-serine levels are decreased which has been linked to cognitive deficits. Results from our group have shown that D-serine supplementation in aged rats improves cognitive flexibility. However, it is not clear if this effect can be extended to young middle-aged rats and if the D-serine effect would depend on the initial cognitive status. In a longitudinal study, the present work aims to characterize the effect of oral D-serine supplementation on the decline of cognitive flexibility in middle-aged rats (12 months old). Middle-aged rats were trained in a reversal-learning task and were quantified the number of perseverations as an inverse measure of cognitive flexibility. We first showed that middle-aged rats had lower performance than young rats (6 months), indicating that the rats have cognitive flexibility decline at this age. The rats were then randomly assigned into two groups, 1) The D-serine group, which was supplemented with D-serine (300 mg/kg of weight) in the drinking water for two months before the cognitive flexibility test and 2) the control group, which follows the same procedure but receives only regular drinking water. Rats from both groups were followed for 6 months and had a second evaluation of cognitive flexibility performance when they were 18 months old. We found that control middle-aged rats improve their performance in the second evaluation, however, rats that have good performance in the cognitive flexibility task at 12 months and were supplemented with D-serine, significantly decreased the cognitive flexibility. These results indicate that the D-serine effect depends on the initial cognitive status and that supplementation in high performers is a detriment for cognitive functions.

Keywords Cognitive reserve, D-serine, Aging

Áreas: Envejecimiento y Desarrollo

V

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How to give good public engagement talks?
A pilot workshop aimed at researchers and students at IFC

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Área: Docencia y divulgación

It is increasingly common that scientists from diverse sociocultural backgrounds acknowledge the importance of acquiring the proper skills to clearly communicate their research to different audiences (Massarani, 2018; Orozco, 2018; Pham, 2016; Varner, 2014). Nonetheless, very few scientists receive formal or informal training on these skills as part of their scientific education (L. D. Mercer-Mapstone & Kuchel, 2016; L. Mercer-Mapstone & Kuchel, 2015; Varner, 2014). Several courses and workshops on public science communication have been developed since the 1980's (Massarani, 2018), although there is little to none consensus on the topics to be addressed, how they should be taught, and how to evaluate their impact (Rodgers et al., 2018; Rodgers, Wang, & Schultz, 2020; Rubega et al., 2020; Sánchez-Mora & Macías-Nestor, 2018; Ziegler et al., 2021).

I designed and developed a workshop at the Cellular Physiology Institute at UNAM where four researchers and their undergraduate students worked in pairs to create 4 public engagement talks about their research. The aim of the workshop was to both motivate researchers and students to participate in future public engagement events, and to improve their communication skills.

To evaluate the success of these goals, we applied two short surveys. The first one, addressed at the workshop's participants to know their general perceptions about the training, and the second aimed at the publics of the talks, who evaluate the talks (Rodgers et al., 2018, 2020; Rubega et al., 2020; Varner, 2014).

Based on the 50 responses obtained by the public, the audience liked the event and said to have easily understood the talks. They also said that they would like to attend similar events in the future. On the other hand, most of the workshop attendees said they enjoyed the event and the workshop, especially the chance to collaborate with their lab co-mates in a science communication activity. They reported to have acquired new tools and methods to both plan and give public engagement talks. Most of them said that they would use what they learnt for future events and that they would recommend their peers to attend other editions of the workshop.

Overall, these results suggest that a short workshop that promotes teamwork between researchers and students, provides the attendees with the proper communication skills to give an effective public engagement talk and motivates them to attend future public engagement events.

Keywords: science communication, workshop, evaluation

Malnutrition and the serotoninergic System: the consequences of a poor nutrition during pregnancy in the development of the Brain.

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Área: Dilvulgación

The development of the brain has been widely studied looking for the underlying mechanisms that control the process. Brain development involves a series of well-regulated changes including the production, maturation and organization of several types of brain cells.

However, some of those stages are susceptible to alterations due to external factors, one of them being the lack of nutrients during the development. Several reports in humans describe that fetal malnutrition relies on two main causes: maternal nutrition and placental insufficiency. Maternal nutrition is one of the most studied due to consequences and because the oxygen and nutrients that support fetal growth and development rely on the entire nutrient supply line, beginning with maternal consumption and body size.

Malnutrition is a worldwide problem affecting adults, children, and even unborns. All countries are affected by one or more forms of malnutrition, making it one of the biggest health problems worldwide (WHO, 2020). This condition refers to any disorder of nutritional status resulting from a deficiency or excess of nutrient intake that could result in a pathological condition.

Currently, malnutrition is one of the principal nongenetic factors affecting the developing brain and may adversely alter the organism's ability to interact with its environment. In particular, malnutrition appears to affect the serotonergic system of the brain, specifically in the hippocampal formation due to the numerous serotonin receptors in this área.

But, why is this so important? Well, Serotonin has a major role in modulating some neuropsychological processes, especially when it comes to hippocampal activity given that it has been highly discussed the relation of this neurotransmitter to sleep-wake cycles, depression and learning-memory processes.

Since during early development (gestation, lactation and early childhood) nutrients provide the energy and raw materials necessary for the maturation and functionality of the organism, therefore the quantity and quality of these is essential, which is why the perinatal environment is one of the essential factors for its optimal development.

Making this information more accessible to the population would raise awareness of nutrition before and during pregnancy, allowing to mitigate or prevent pathologies associated with alterations of the development and maturation of the nervous system, that could lead to malfunctions of systems like the serotoninergic.

Key words: Malnutrition, Development, Serotoninergic System.

V

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Epigenetics

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Identification of Enhancer Regions of Midbrain Dopaminergic Neurons using Histone Modification ChIP-Seq

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Parkinson's Disease (PD), the second most common neurodegenerative disease, is characterized by the loss of midbrain dopaminergic neurons (mDA). Human pluripotent stem cells have been successfully induced into midbrain dopaminergic neurons using a floor-plate based strategy, which mimics mDA neuron development. This differentiation process occurs alongside extensive epigenetic remodeling. It has been shown that many disease-associated genetic variants, such as single nucleotide polymorphisms (SNPs), are located within non-coding genomic regions, highlighting their importance as regulators of gene expression. Enhancers are important regulatory regions that are distal to the transcription start site, usually found within intergenic or intronic regions and enriched in the histone modifications H3K27ac and H3K4me1. Additionally, enhancers have been found to be highly tissue-specific and enriched in cell-type specific transcription factor motifs. To gain insight on the regulatory regions involved in mDA neuron cell specification, we adopted the induction process of DA neurons and obtained histone modification maps for H3K27ac and H3K4me1 at day 0 and 28 of differentiation by chromatin immunoprecipitation followed by sequencing (ChIP-Seq). Following the ChIP-Seq analysis pipeline, we were able to identify putative active enhancers in D0 embryonic stem cells and D28 mDA neurons.

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Area: Epigenetics

Key words: Dopaminergic neurons, ChIP-Seq, histones

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Tn5 enzyme production and characterization for CUT&Tag profiling of epigenetic modifications in human embryonic stem cells

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Area: Epigenetics

Abstract: Embryonic stem cells (ESC) are characterized for their ability of self-renewal and differentiation. ESC has been widely used as developmental models for the study of differentiation processes and has been successfully induced into midbrain dopaminergic neurons (mNDA) using a floor-plate based strategy which mimics mNDA development. Differentiation processes are accompanied by major epigenic changes such as histone post-translational modifications which have a critical role in regulating gene expression. Chromatin immunoprecipitation followed by sequencing (ChIP-seq) is the most used technique for mapping epigenetic features genome-wide; nevertheless, this method has limitations, like high background, low signal and requires large numbers of cells for each assay. In recent years, enzymatic techniques for massively mapping chromatin features have gained importance. The cleavage under target and tagmentation (CUT&Tag) is a technic that uses a Tn5 enzyme fused to protein A or G, and allows the identification of chromatin features in an efficient and low-cost fashion. In this work, we produced a Tn5 enzyme fused to both, protein A and protein G to perform CUT&Tag in ESC, which can be later differentiated into mDA. We validated Tn5 enzyme activity by *in vitro* assays and the target specific activity by using ESC knockout cell lines. We generated and sequenced CUT&Tag libraries for H3K27ac and H3K4me1 in the human ESC line H9.

This work was supported by grants from PAPIIT-UNAM IN213719, IN219122.

Key words: Differentiation; Histones; Pluripotency.

DNA methyltransferases as an epigenetic barrier in Müller cells reprogramming

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Epigenetic

Muller cells are the major type of glial cells in retina. Among their multiple functions, their capacity to dedifferentiate and acquire a “progenitor-like” phenotype and their role in retinal regeneration as a respond to damage or injury stands out in vertebrates as zebrafish. However, in mammals this regenerative ability is absent.

DNA methylation is a process widely involved in Müller glia dedifferentiation and it has even been considered as an epigenetic barrier for retinal regeneration in mammals. DNMT3a (an enzyme related with the establishment and maintenance of DNA methylation and involved in the self-renewal ability of several stem cells) shows ambivalent expression kinetics in regenerative and no-regenerative species. While in regenerative species DNMT3a expression remains in basal levels after injury, in mammals it seems to increase.

In order to identify the possible functional role of DNMT3a in mammalian Müller glia dedifferentiation we designed a CRISPR/dCas9-KRAB system to specifically inhibit DNMT3a in mouse Müller primary cultures. We demonstrate that 72 hours after CRISPR/dCas9-KRAB system transfection in Müller cells DNMT3a expression decreased by 90% while the neural pluripotent-related genes Lin28, Ascl1 and Nestin expression increased. We also show that DNMT3a inhibition raises cell proliferation and viability, two stem cells characteristics. In addition, we observed morphological changes in cell cultures after transfection that may be related to cell dedifferentiation.

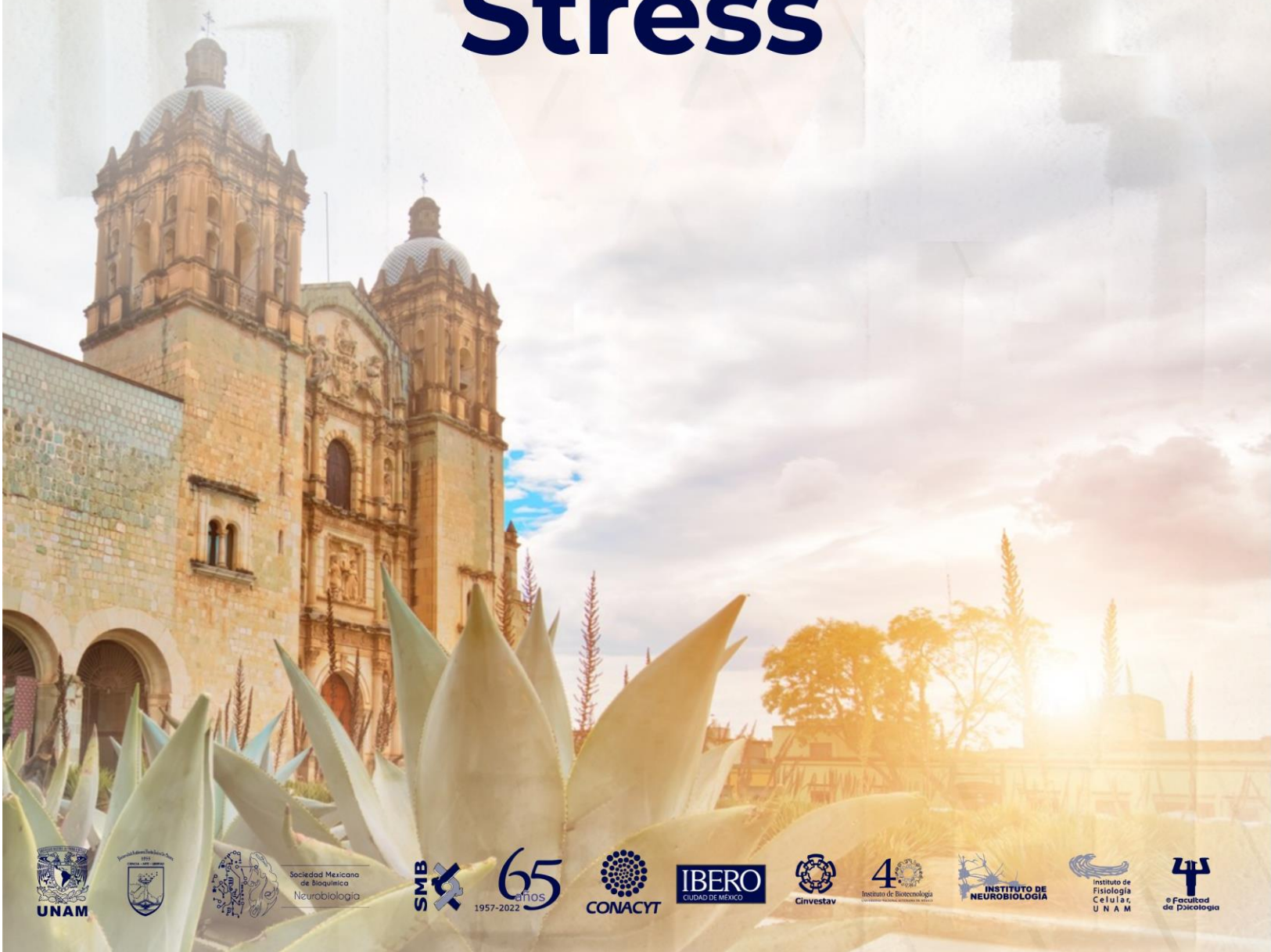
We concluded that DNMT3a is widely involved in murine Müller glia dedifferentiation and we speculate that it could be envisioned as a therapeutic target to improve the functional regeneration in mammalian retina. The next step is drive dedifferentiated Müller cells into neuron-like cells and also identifies the role of DNMT1 and DNMT3b in this process.

Key words: Müller glia, dedifferentiation, DNA methylation.

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Stress



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Neuronal death induce by potassium deprivation (K5) and ST has differential effects in Drp1 phosphorylation.

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Introduction: Reactive oxygen species (ROS) have been suggested to be involved in multiple pathophysiological processes. Several sources of ROS have been described in the cell, including NADPH oxidases (NOX) and mitochondria, both of which have been shown to be important in the physiological and pathological processes of neurons. In addition to the observed increase of ROS levels during neuronal death, a change in mitochondrial morphology has been described. These changes are known as mitochondrial dynamics and consist of the hyper connection or shortening of mitochondrial networks. The shortening is known as mitochondrial fission (or fragmentation) and is regulated by the Drp1 protein. It is not known whether the ROS produced by the mitochondria are related to the regulation of Drp1 activity. **Objective:** To know the role of mitochondrial ROS in the death of cerebellar granular neurons (NGC) and evaluate the regulation of mitochondrial dynamics during this process. **Experimental strategy:** We used isolated cerebellar granule neurons (CGN) maintained in a medium with 25 mM KCl (K25) for 7 days *in vitro*. To induce neuronal death, KCl was reduced to 5 mM (K5) or cells were treated with staurosporine (ST, 0.5 µM). The level of cytoplasmic ROS (ctERO) and mitochondrial ROS (mtERO) were determined at different times by using dihydroetidium (DHE) or MitoTracker Red CM-H2XRos, respectively. The metabolic activity was estimated by the reduction of MTT. To determine the changes in mitochondrial morphology, mitochondria were stained with MitoTracker Green and images were obtained with an epifluorescence microscope. The levels of total and phosphorylated Drp1 in residue Ser616 were determined by Western blot at different times after K5 and ST stimuli and were used as an indicative of Drp1 activation. To evaluate the role of mitochondrial ROS, some cultures were pretreated with the mitochondrial antioxidant MitoTempo (10 µM). **Results:** Although neuronal death was observed after 12-24 h of treatment, an increase in the levels of ctERO and mtERO was detected from the first minutes of the treatment. Similarly, a decrease in MTT reduction was also observed early and were maintained from 24h. The decline of the MTT reduction was partially inhibited by the mitochondrial antioxidant. An increase in the number of fragmented and rounded mitochondria was observed in both death conditions (ST and K5). It was also observed that the phosphorylation of Drp1 (Ser616) increased in the K5 condition, but decreased in the NGC treated with ST. The K5-induced phosphorylation of Drp1 (Ser616), was completely inhibited by MitoTempo, an effect that was not observed in ST-treated neurons. **Conclusions:** The generation of mtERO is an early event in the neuronal death process, prior to the generation of ctERO and the activation of the apoptotic program. mtERO seem to be necessary for the neuronal death process, but not for mitochondrial fragmentation, although fragmentation is induced during the death process. Mitochondrial fragmentation and neuronal death appear not to be mediated by phosphorylation of Drp1 at residue Ser616, suggesting that mitochondrial fragmentation could be carried out by different mechanisms, depending on the apoptotic condition.

This work was supported by CONACYT (285184) and DGAPA-PAPIIT, UNAM (IN212019)

Keywords: Neuronal death, mitochondrial dynamics, ROS (reactive oxygen species)

Effect of chronic stress on the expression of mucins and cytokines in different intestinal regions of female BALB/c mice.

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Area: Stress

Introduction: Mucins are the main component of the intestinal mucus layer that is secreted by goblet cells and constitutes one of the host's first lines of defense. Chronic stress exposure results in alterations of brain-gut interactions, produces a long-term alteration in the quantity and structure of intestinal mucin, and induces an inflammatory response, altering intestinal permeability.
Objective: To evaluate the effect of chronic stress on genic expression of mucins and its relationship with the expression of pro- and anti-inflammatory cytokines.
Methodology: Female mice of the BALB/c strain of 7-8 weeks were divided into a control group (n=6) and a stressed group (n=6), which were subjected to a board-immobilization stress model for 2 h/day for 4 days. Mice were sacrificed with exposure to inhaled isoflurane and duodenum, ileum and colon were dissected and washed with saline solution to obtain the total mucosa by scraping for the extraction of total RNA; which was subsequently performed RT-qPCR to evaluate the gene expression of mucins (MUC2 and MUC5ac) and cytokines TNF-α, IFN-γ, IL-6, IL-10 and IL-18. Data were normalized to the endogenous GAPDH gene and relative expression was calculated by the 2-ΔΔCT method. Results of each group were compared with the Student's T-test.
Results: Regarding the expression of MUC2, a significant increase was observed in the duodenum (p=0.007) and a decrease in the colon (p=0.002) compared to the control. With respect to MUC5ac, a significant increase in its expression was observed in the duodenum (p=0.002) and the ileum (p=0.007) compared to the control. In turn, stress also significantly increased the expression of TNF-α (p=0.002), IL-6 (p=0.004), IL-18 (p=0.002) and decreased the expression of IL-10 (p=0.007) in the duodenum. At the level of the ileum, stress significantly increased the expression of IL-6 (p=0.0025) without changes in the rest of the cytokines. Meanwhile, in the colon region, stress significantly increased IFN-γ (p=0.0022) and IL-6 (p=0.004) and decreased the expression of IL-18 (p=0.002) and TNF-α (p=0.01), compared to the control group.
Conclusions: Stress has a differential impact on the gene expression of MUC2, observing that, in the region of the duodenum, it increases until it reaches the colon where its expression decreases. This effect in colon may explain the lower concentration of mucus, increasing contact between antigens and the epithelium that promote inflammation, such as inflammatory and allergic conditions. The expression of MUC5ac could be related to the propulsion of the gastrointestinal tract and to a regulatory response. Further insight into the complex mechanisms involved in mucin changes in response to stress is needed, which could lead to new approaches in understanding functional gastrointestinal disorders.

Keywords: intestinal mucins; cytokines; stress.

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Participation of the Sympathetic Nervous System in the Modulation of Components of Intestinal Homeostasis in Mice Underwent Stress

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Area: Stress

Introduction: Stress modulates the gut barrier components through the Autonomic Nervous System (ANS) pathways but the role of neurotransmitters released by the Sympathetic Nervous System (SNS) - a branch of the ANS - is not fully known. **Aim:** To determine some components of the gut barrier including mucopolysaccharides monolayer content and immunoglobulin A (IgA) response as well as epithelial transudation marker such as albumin in the proximal region (PX) and colon (COL) of stressed mice, using DSP-4, a neurotoxin that depletes the amount of catecholamine from the terminal nerve fibers of SNS. **Methodology**. Eight-week-old female BALB/c mice were intraperitoneally injected with 50 mg/kg of DSP-4 or sterile isotonic saline solution as vehicle; thereafter mice were stressed by board immobilization 2 h/4 days or unstressed. On day 4, the animals were sacrificed, samples of the PX region and COL were collected to obtain intestinal lavages to quantify IgA and albumin by ELISA; from each tissue segment, the mucopolysaccharide was quantified with the alcian blue stain. **Results**: IgA response within DSP4-treated groups, was increased in stress vs unstress group in PX and within the stressed groups, in DSP4 vs vehicle in colon. Albumin amount in both stress and unstress groups was decreased in DSP4 vs vehicle-treated groups. Mucopolysaccharide concentration within unstressed groups was increased in DSP4 vs vehicle-treated group in PX and within the stressed groups was reduced in DSP4 vs vehicle-treated groups in colon. **Conclusion**. The results demonstrate that the SNS has divergent modulatory outcome on the analyzed markers of the gut barrier in the proximal region and colon.

Key words: Stress, Gut Barrier, Sympathetic Nervous System

Maternal consumption of trans-resveratrol, epigenetic and behavioral effects in prenatally stressed rats

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During the pregnancy process, a high level of stress and anxiety is generated to the future mother with adverse effects for her and her baby. If the stress level becomes excessive, this will generate prenatal stress that will produce an intrauterine environment unfavorable for fetal development that can negatively impact offspring increasing the risk of developing physiological dysfunctions and neurological impairment.

It has been reported that oxidative stress and prenatal stress can produce depression and several neurological diseases by modifying genes involved in the neurodevelopment as the brain-derived neurotrophic factor (BDNF), which plays a crucial role in neurogenesis and neural plasticity. The nuclear factor erythroid 2-related factor 2 (Nrf-2) and other genes that stress could modify; recent studies have shown that Nrf-2 regulates the transcription of BDNF by binding to its exon I promoter. Furthermore, the inhibition of Nrf2-induced BDNF transcription may play a role in the pathophysiology of depression. Also, the activation of Nrf2-induced BDNF transcription promoted antidepressant-like effects. It has been reported that epigenetic changes may be transferred to the offspring and lead to the development of several metabolic and neurological diseases

Because trans-resveratrol (tRV) exhibits a potent anti-oxidative effect and decreases vulnerability to depression by increasing BDNF expression, in the present work, we propose to evaluate the effect of the maternal consumption of tRV on epigenetic and behavioral changes in prenatally stressed rats. The anxious and depressive behaviors were evaluated using the plus maze and forced swimming models, respectively. In addition, the expression and methylation status of genes encoding BDNF and Nrf-2 in the hippocampus and hypothalamus were evaluated. Preliminary results indicated that rats subjected to prenatal stress and without treatment showed a significant increase in the time spent in closed areas associated with anxious behavior. On the other hand, rats treated with tRV showed better performance in the forced swimming test than controls, showing a significant increase in the number of escalation episodes and a decrease in immobility related to an antidepressant behavior. Epigenetics and behavioral results will provide us with valuable information regarding the effect of the tRV in the prevention of the damage produced by prenatal stress and thereby his possible use as a therapeutic alternative.

Key words: *Prenatal stress, Depression, Trans-resveratrol*

Mechanisms of Neurotoxicity Induced by Exposure to Low Doses of Permethrin

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Permethrin (PERM) is a pyrethroid commonly used as a pesticide. Clinical and experimental evidence suggests alterations in the nervous system due to permethrin exposure; however, the physiopathological mechanisms are not fully understood. This work aimed to analyze the effects of sublethal administration of PERM on bioenergetic processes, neuroinflammation, oxidative stress markers, and morphological changes at the neuronal level to explore the cellular mechanism responsible for neuronal damage. Male Wistar rats treated with PERM at 150 and 300 mg/kg (sublethal dose) were used. The effects of PERM were evaluated in different brain regions; lipoperoxidation, antioxidant enzyme activities, protein carbonyls, mitochondrial O_2 consumption, pro-inflammatory cytokine expression, and histopathological analysis in the hippocampus were determined. An increase in lipoperoxidation and carbonyl proteins was observed at the two doses studied after PERM administration, in a dose-dependent manner, in the different brain regions (cortex, hemispheres, cerebellum, and medulla), when compared to control animals. The antioxidant enzymes glutathione peroxidase, reductase, S-transferase, catalase, and superoxide dismutase showed increased in enzymatic activity in all the structures studied, with a dose-dependent effect. Cytokines (IL-1β, IL-6, and TNF-α) increased in a dose-dependent in the different brain regions. Administration of both doses of PERM showed neuronal damage in the hippocampus. Neuronal degeneration and cell death were observed when using 150 mg/kg dose. Both doses of PERM promote mitochondrial uncoupling, reduced oxidative phosphorylation, and significantly decreased respiratory parameters state 3-associated respiration in complex I and II. Exposure to PERM at sublethal doses induces the production of reactive oxygen species, facilitating imbalance in the antioxidant system and increasing the expression of pro-inflammatory interleukin genes with mitochondrial functional and morphological impairment.

Keywords: permethrin; neurotoxicity; bioenergetics; neuroinflammation

Area: Stress

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Evaluation of Superoxide dismutase enzyme activity in the prefrontal cortex of neonatal rats subjected to postnatal stress.

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Abstract

The adversities experienced at an early age, such as abandonment, child abuse, etc., can affect the psychological, cerebral, emotional and physiological. Animal models, such as maternal separation (MS), are used to detect brain changes originated after stress exposure. Our aim was to evaluate the activity of the enzyme superoxide dismutase (SOD) in the prefrontal cortex of rat pups in the presence of acute and chronic stress. Material and Methods: 76 Sprague-Dawley rat pups were divided in four groups of males and females (n=8): basal control (CB), stress control (CS), basal MS (MSB) and stress MS (MSS). The separation of the pups from their mothers was carried out for 180 minutes for 15 days. The rats were sacrificed under basal or stress conditions at the end of the period and the prefrontal cortex was removed. Superoxide dismutase (SOD) activity was quantified using a modification of Beyer's 1987 method. Results: a three-way ANOVA analysis was performed to compare SOD activity under basal, acute and chronic stress conditions between males and females. Basal Control (CB, SC) Vs basal MS presented a significant increase (BMS, SMS): $F(1, 122) = 21.08$, $P<0.0001$. The second factor, euthanasia in basal conditions Vs acute stress, showed a significant increase in the EMS group: (CB, BMS Vs CE, SMS) $F(1, 122) = 34.94$, $P<0.0001$. In the third factor, no significant increase was found, $F(1, 122) = 0.007923$, $P = 0.9292$. The interaction of the groups resulted in (CB and CS Vs BMS and SMS) X (CB, BMS Vs CS, SMS): $F(1,122) = 44.85$, $P<0.0001$. Finally, a significant increase was found only in the SMS group, and comparing the CB, CS, SMB groups, no significant increase was found compared to the CB group. The activity of SOD did not show a significant difference in the control groups, but it did show a significant difference greater in the SMS group than in the rest of the groups: CB, CE and BMS. Conclusion: When postnatal stress is generated in the CE, SMB, SME groups, only the SME group showed a distinctive increase, which indicates that there is an increase in reactive oxygen species in rats.

Keywords: Stress, maternal separation, oxidative stress, superoxide dismutase (SOD)

Development of binge eating behavior in Female Wistar Kyoto rats: a better model with construct and appearance validity

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Binge eating disorder (BED) is the more prevalent eating disorder worldwide. The main symptoms are: 1) the presence of binge eating episodes, defined as the consumption of large amounts of food in a short time; 2) a sense of lack of control over eating, and 3) the lack of any compensatory behavior to prevent weight gain. The binge-eating episodes are usually characterized by eating in the absence of hunger, feeling uncomfortably full, eating much more rapidly than usual, and the presence of discomfort feelings after the episode. BED is more prevalent in women and has elevated comorbidity with other psychiatric disorders such as anxiety, depression, bipolar disorder, and substance use disorder.

Because the Wistar Kyoto (WKY) strain of rats has high levels of stress response and is prone to developing anxiety and depressive-like behavior, it could offer an animal model for binge eating with more significant construct and appearance validity than the traditional one.

We implemented an intermittent access model in female WKY and Sprague Dawley (SD) rats, using shortening or sugar syrup (30%) as palatable food. We evaluate the development of binge eating-like behavior, the consumption pattern during palatable food access, the effect of sex hormones on the development of binge eating-like behavior, and the presence of anxiety-like behavior.

Even though both strains developed binge eating behavior, considering only the caloric ingestion, the WKY rat strain consumes more shortening than SD in a shorter time, emulating a binge eating episode better. Also, the WKY strain was the only one that developed an anxiety-like behavior associated with the intermittent access model, similar to one of the comorbidities observed in binge eating patients. The sexual hormones did not affect the parameters evaluated in the binge eating-like behavior in any strains.

In conclusion, the WKY rat strain offers a better construct and appearance validity to the binge eating model than the SD strain.

Key Words: Binge Eating, Wistar Kyoto, Anxiety-like behavior

Area: Estres

Brain and peripheral oxidative damage during the development of obesity

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Area: Stress

Introduction: Obesity is the disease characterized by increased body weight due to the growth of white adipose tissue, mainly due to excessive consumption of fat in the diet. This also generates inflammation and oxidative stress. During oxidative stress, this generate damage to lipids and proteins, producing malondialdehyde (MDA) and carbonylated proteins (PCO), respectively. In obesity, oxidative stress has been associated with the development of insulin resistance in muscle, adipose tissue, liver, and brain, which is associated with its comorbidities. Thus, it is important to determine oxidative damage at the brain level and the relationship with oxidative damage in white adipose tissue and plasma during the development of obesity. Therefore, the objective of this work was to determine the oxidative damage in the brain, white adipose tissue and plasma, during the development of obesity in mice. **Methodology:** 3-month-old C57BL/6 mice were fed with high-fat diet (HFD), low-fat diet (LFD), and standard diet; for 1, 2 and 3 months (n=6). The evaluation of oxidative damage was carried out in the cerebral cortex, white adipose tissue and plasma, determining amount of malondialdehyde, carbonylated proteins and the enzymatic activity of glutathione peroxidase. **Results:** In the case of plasma, in 2- and 3-month groups, the amount of MDA was higher in HFD-fed mice than in standard diet-fed mice. Whereas, in the 1-month-old group, the amount of PCO was significantly higher in the HFD-fed mice. In the 2-month group, GPx enzyme activity was significantly lower in HFD-fed mice than in standard diet-fed mice. In white adipose tissue, the amount of MDA was slightly higher in mice fed HFD and LFD, in all three groups (1, 2 and 3 months) than in mice fed standard diet. Furthermore, in the 1-month group, the amount of PCO was significantly higher in HFD-fed mice than in HFD-fed mice. In the 1-month and 2-month groups, Gpx activity was slightly lower in mice fed HFD than the ones in standard diet. Finally, in the 1-month group, the amounts of MDA and PCO in the cerebral cortex were significantly lower in the HFD-fed mice than in the standard-diet-fed mice. Whereas, Gpx enzyme activity in the 1-month group was significantly lower in LFD-fed mice and slightly lower in HFD-fed mice than control mice. **Conclusion:** In the cerebral cortex, there is no development of oxidative damage, in this model. While, in white adipose tissue there is greater lipid oxidative damage in mice fed HFD, from the first month. In plasma, the damage begins in the second month with the same diet.

Keywords: Obesity, stress, oxidative damage.

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Mitochondrial dynamics under glucose deprivation and glucose reintroduction in cortical neurons and its possible regulation by the ketone body β-hydroxybutyrate

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Brain relies on circulating glucose as its main energy source; thus, a dramatic reduction in brain glucose can cause cellular damage, which can culminate in neuronal death. Since neurons are highly energy-consuming cells with an oxidative metabolic profile, mitochondrial health is indispensable for neuronal survival after hypoglycemic and ischemic events which are associated with glucose depletion in brain. Mitochondria responds to cellular demands through distinct processes (like fission, fusion, transport, biogenesis, and mitophagy), which together are known as mitochondrial dynamics. The ketone bodies (KB) acetoacetate and β-hydroxybutyrate (BHB), can be consumed by brain mitochondria, where they can be converted to acetyl-coA for ATP production; therefore, KB can prevent neuronal damage induced in glucose deprivation models both *in vivo* and *in vitro*. Multiple mechanisms of action of KB can underlie their protective actions; however, their effects on mitochondrial dynamics in neurons is still not clear. Thus, we aimed to determine the effect of BHB on fission, fusion and mitophagy, in response to glucose deprivation/reintroduction (GD/GR) in cultured cortical neurons. Results suggest that GD induces both mitochondrial fission and mitophagy, without affecting mitochondrial fusion. While mitophagy is inhibited and mitochondrial morphology is apparently recovered during GR. BHB showed no effect on either mitochondrial fission or fusion, although it apparently inhibited the BNIP3/NIX pathway of mitophagy during GD, as a decreased NIX-LC3 interaction was observed in cultures incubated with BHB. Together, results suggest a lack of effect of BHB on mitochondrial fission of fusion, but it apparently prevented mitophagy during the lack of glucose period, possibly due to a better preservation of the energy state of the cells. The impact that the effect of BHB on mitophagy may have on neuronal survival remains to be elucidated.

Keywords: Energy failure, Ketone Bodies, Mitochondrial Dynamics

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Exposure to acute stress in young offspring from mothers with maternal immune infection acts as a risk factor for the development of depressive-like behaviors in adulthood

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Abstract.
Epidemiological studies have reported that the offspring of mothers who suffered an infection during pregnancy may be susceptible to develop behaviors associated with depression, which is exacerbated in adulthood after being exposed to an acute stressor present in adolescence. Depression is a neuropsychiatric disorder that causes neurochemical, morphological, and behavioral alterations. One of the processes that are altered in depression is the generation of new neurons and glial cells in the dentate gyrus of the hippocampus. We thus here investigated the effect of maternal immune infection on the development of depressive-like behaviors associated with alterations in neurogenesis, as well as alterations in microglia and astrocytes, in offspring of mothers treated with Poly IC (polyinosinic acid-polycytidylic) during the gestational stage, as well as offspring that were exposed or not to a stressful situation (forced swimming) during early adolescence. The results indicate that mice, of mothers administered with Poly IC, exposed to a stressful situation during adolescence have decreased dendrite complexity of doublecortin cells in the dentate gyrus of the hippocampus. Also, we analyzed the effects in microglia and astrocytes. However, neither microglial nor GFAP+ cell density was seen in the hippocampal dentate gyrus in offspring of mothers administered Poly IC. Finally, our data may suggest that exposure to a stressful situation during adolescence is able to cause alterations in neurogenesis in offspring of mothers exposed to Poly IC. The differences between males and females will be discussed.

Keywords: maternal immune infection, Poly IC, and neurogenesis.
Área: glia and stress

V

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Gene Expression

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Identification of the exons retained in the mRNA of the Sulfonylurea receptor 1 in the brain and other rat tissues

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Área: Expresión Génica

Abstract

Medical expenses for hospitalization and maintenance of stroke survivors represent a high cost to the Ministry of Health. Notwithstanding, health policies has focused on control of risk factors, it has not been effective in reducing the number of cases in our population. Therefore, it is essential to effort basic research on the identification of therapeutic targets. The Na^+-channel integrated by the sulfonylurea receptor 1 (SUR1) and the Transient Receptor Potential Cation Channel Subfamily M Member 4 (TRPM4) is involved in edema formation after cerebral ischemia. Remarkably, an undescribed short isoform of SUR1 (sSUR1) is overexpressed in the brain exposed to ischemia. This small protein has a comparable size to the one expressed in heart and other tissues, which has been described as an unspecific protein. Importantly, resveratrol prevents the overexpression of sSUR1 and reduces cerebral edema in a model of stroke in rat. Therefore, the main objective of this work was to identify the mRNA of the sSUR1 expressed in the brain and compared with those expressed in different tissues including the heart. To identify the exons retained in the mRNA of the tissues, seven pairs of oligonucleotides were designed and used in RT-PCR reactions. The fragments amplified correspond to the different domains of the protein SUR1. Exons (E): E1 and E2, located in the NH2 terminal region; E5 and E6, in the transmembranal domain 0 (TM0); E10 and E11, in the TM1; E14 and E15, in the Nucleotide binding domain 1 (NBD1); E17 and E18, in the NBD1; E23 and E24 in the TMD2, and E30 and E31 in the TM2/NBD2. Interestingly, we found that each tissue has a unique profile of expression. The lung expressed one out of the seven fragments analyzed (E14-E15), while the brain, the pancreas, the heart, the liver, and the kidney have a similar profile since they do not amplified with the primers designed for E1-E2 and E30-31. Additionally, the heart does not amplified E14-E15, the kidney E17-E18, the liver E5-E6 and E17-E18, and the pancreas E17-E18 and E35-E36. Accordingly, the protein profile of expression is also different for each tissue. Identification of the complete sequence of the mRNA will allowed overexpressing *sSUR1 in vitro*, favoring the understanding of its function in the ischemic brain.

Key words: Sulfonylurea receptor, ischemia, edema

Gene data mining and Protein-Protein interaction analysis for Alzheimer's Disease and Diabetes Mellitus and identifies their potential molecular links

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Area: Neurobiology, Bioinformatics.

Keywords: data mining, Alzheimer, Diabetes mellitus type 2, protein-protein interaction.

Abstract

Objectives: Alzheimer's disease (AD) and type 2 Diabetes Mellitus (DM2) are chronic-degenerative pathologies with complex molecular processes that today are associated due to failures in insulin metabolism and a process of cognitive deterioration, in the This study uses systems biology tools to find and identify the main biological processes, signaling pathways and concentrating proteins associated with the AD-T2DM binomial utilizing information present in databases and scientific publications (data mining).

Methods: The data collection was carried out through the mining of various specialized databases in proteins as well as in scientific literature present in the NCBI database with the help of the PubTator platform, later the protein-protein interaction networks (PPI) using String-db.org, to later continue with the analysis of gene ontology and signaling pathways through the EnrichR platform, likewise EnrichR was used in conjunction with the Molecular Complex Detection Tool (MCODE) to determine the most relevant hub elements on PPI networks.

Results: In the present work, a total of 1411 proteins related to the AD-T2DM binomial were found. Within the analysis of gene ontology processes such as cytokine-mediated signaling. (GO: 0019221), cellular response to cytokine stimulation (GO: 0071345), positive regulation of intracellular signal transduction (GO: 1902533) are shown as highly associated with the AD-T2DM binomial. At the level of signaling pathways, those related to cancer, lipids, atherosclerosis, PI3K-Akt, AGE-RAGE are highly related to the AD-T2DM binomial. The most important elements (hub proteins) were determined using two methodologies, finding that MAPK3 EGFR AKT1 AR STAT3 MAPK1 is the main kinases and transcription factors associated with the AD-T2DM binomial, while SCR and UBC PRKCA PRKACA are shared with AD and T2DM respectively. The second analysis methodology showed that the proteins IL1A MMP3 IL1B CCL20 IL18 CCL2 CCL5 HGF CSF2 MMP1 CCL4 FGF2 IL12B TIMP1 MMP9 POMC LBP TN are the most important within the PPI of AD-T2DM.

Conclusion: In this work, we found a considerable amount of genetic data suggesting that inflammatory processes are the main links between AD and T2DM in addition to insulin dysregulation. The PPI prediction showed specific molecules for AD and shared bonds in T2DM and AD-T2DM which could be of interest for experimental validation. on the other hand, the methodological part of data mining could be applied to the study of links between different pathologies by contributing to the analysis of large amounts of information in a much faster way.

DISC1 interactome genes are associated with psychosis in patients with schizophrenia and bipolar disorder in the Mexican population

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Abstract:
Introduction. Psychosis is a disabling clinical phenotype observed in various psychiatric disorders. Genetic variants of the DISC1 interactome have been identified in genome-wide association analysis (GWAS) studies in psychosis. However, the association with psychosis at different statistical approaches (i.e., gene and gene-set level, besides genetic variants) of this interactome in mestizo populations, specifically the Mexican population, is unknown.
Methodology. We use DNA samples from cases with psychotic disorders and control individuals. Then, we process the samples through genotyping microarrays. After, we performed quality control of the genomic data, the genetic annotation, and the association analysis at the genetic variant, gene, and gene-set level. Finally, we perform *in silico* prediction, functional validation, and pathway enrichment analysis.
Results. We identified an association with psychosis phenotype in both psychiatric disorders of one single variant, the intronic variant rs6754640 of *NRXN1* (Neurexin 1) gene. However, at a gene level, we found an association of the genes *NRG1 (Neuregulin 1*), *PCM1* (Pericentriolar Material 1), *GRIA2* (Glutamate Ionotropic Receptor AMPA Type Subunit 2), and *DISC1* (Disrupted-In-Schizophrenia 1) with the phenotype. Finally, the gen-set analysis showed an association with cillium organization and regulation of cellular component organization, cytoskeletal rearrangements processes; besides, ionotropic glutamate receptor signaling pathway, glutamate receptor signaling pathway, and regulation of cation channel activity, which participate in glutamatergic neurotransmission. The associated biological processes include all the genes before mentioned except PCM1.
Conclusions. Among the genes of DISC1 interactome associated with an increased risk of developing psychosis in Mexican patients, we found mainly those involved with cytoskeletal rearrangements for cell migration, a relevant mechanism for neurodevelopment, and glutamatergic neurotransmission. These findings support the neurodevelopmental and glutamatergic hypothesis in psychosis according to results observed in Mexican patients. These results could influence future clinical approaches in this population.
Area: Genetic expression
Keywords: psychosis, *DISC1*, interactome

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Identification of transcripts, proteins and microRNAs that are differentially expressed at early phases of brain regeneration in the Mexican axolotl

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Since Spallazani first conducted studies in salamanders in 1768, these salamanders have been thoroughly studied for their remarkable regenerative capacities, including the outgrowth of a new identical limb after amputation and -more remarkably- the regeneration of the central nervous system after a mechanical injury or chemical ablation of cells. This phenomenon might be used as a model in regenerative medicine, hoping that the generated knowledge could ameliorate or heal brain affectations such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and others. The present study aimed to unravel the molecular pathways involved in the early stages of brain regeneration in juvenile neotenic axolotls. We performed mechanical extraction of a piece with a diameter of 1 mm of brain tissue at dorsal pallium and then allowed the axolotls to recover for up to 6 hours, collecting the surrounding tissue for analysis. To characterize the differential expression of transcripts and proteins, we performed RNA-sequencing of mRNA and miRNA, as well as mass spectrometry to identify proteins. We were able to identify 43 differentially expressed mRNA comparing control vs regenerative tissue. These genes are related to chromatin remodeling, axonal regrowth, and cytoskeleton regulation. In addition, we also identified 32 conserved miRNAs, the majority of the reported as "onco-miRNAs" as they play a role as inhibitors of tumor suppressants. Finally, we found 171 differentially expressed proteins related to cytoskeleton stabilization, extracellular matrix remodeling, and DNA acetylation. We conclude that stage-specific patterns, starting as soon as 30 minutes post-injury, involve mRNAs, miRNAs and proteins at the early stages of brain regeneration.

This work was supported by grants from Conacyt 265793 and PAPIIT-UNAM IN213719.
Key words: Brain regeneration; Proteomics; Transcriptomics.

Potential role of lncRNAs as modulators of pluripotency and dopaminergic neuronal differentiation

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Research area: Neurodevelopment

Long non-coding RNAs (lncRNAs) are a very diverse group of transcripts that are mainly characterized by being greater than 200 nucleotides in length, do not code for proteins and are expressed in a more tissue-specific manner than protein-coding genes. In past decades they were considered "transcriptional noise" since it was believed that the functional product of genes were proteins. Nowadays, it is known that lncRNAs can modulate very important cellular processes, including the maintenance of pluripotent stem cells (PSCs, cells with the ability to self-renew and differentiate into any cell type of the adult body) and differentiation through diverse mechanisms. Differentiation is of great interest for regenerative medicine, since it might lead to clinical applications. Protocols have been established to obtain dopaminergic neurons (nDAs) from PSCs; these neurons die in Parkinson's disease. Although these protocols are efficient, other cell subtypes are generated, so it is imperative to understand the molecular mechanisms that regulate differentiation towards a specific lineage. For this reason, the objective of the present work was to identify novel lncRNAs that may regulate the pluripotent state of PSCs and the dopaminergic differentiation process. In this way, from the transcriptomic profile of this process, differentially expressed lncRNAs were selected for validation by RT-qPCR (AC019155.2, LINC00678, ESRG, DIO3OS, AC018563.1 and MIR124-2HG) and through bioinformatic analysis they were associated with important cellular processes: the overexpressed lncRNAs in the pluripotent state were enriched in processes related to cell cycle and PSCs regulation. Furthermore, expression patterns of a significant fraction of them were highly correlated with epigenetic factors. On the other hand, lncRNAs overexpressed in nDAs were associated with neuronal fate commitment and dopaminergic neuronal differentiation, some of them highly positive correlated with spatially close coding genes that participate in the development of the nervous system.

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Keywords: lncRNA; stem cell; Parkinson's disease.

Transcriptional adaptation to ischemia in the brain endothelium mediated by the Early B-cell factor 1

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Ischemic stroke is one of the leading causes of death and disability worldwide. After the stroke, the brain undergoes cellular and molecular adaptations including angiogenesis in the brain vasculature, which involves physiological modifications that are molecularly driven by proteins such as vascular endothelial growth factor (VEGF). The main regulator for VEGF expression under ischemic conditions is hypoxia-inducible factor 1 (HIF1); however, the activation of VEGF expression is very complex and many other transcriptional regulating sites exist in the proximal promoter region of the *VEGF* gene. We analyzed the 3 kbp proximal promoter region of *VEGF* and identified potential binding sequences for transcription factors, among them early B-cell factor 1 (EBF1), whose locus has been previously linked as a risk factor for cardiovascular disease and is known to be highly expressed in the blood-brain barrier endothelium. To characterize the molecular adaptations driven by EBF1 in response to ischemia in the brain vasculature, we performed chromatin immunoprecipitation analyses followed by next-generation sequencing for EBF1 association sites on a genome-wide scale in rat brain microvascular endothelial cells (BMEC) challenged to oxygen and glucose deprivation (OGD) and recovery. We determined how EBF1 association to these sites changes in response to ischemia and recovery to depict a general profile of molecular adaptations driven by this factor. The identification of gene targets of EBF1 beyond VEGF in ischemic responses will allow for the characterization of vascular adaptive changes at the level of gene regulation in the brain endothelium. This work is supported by DGAPA-PAPIIT IN207020 and CONACYT A1-S-13219.

Area: Expresión Génica

Keywords: Stroke, brain vasculature, gene regulation

An enriched environment prevents the cognitive decline in the Alzheimer´s disease mouse model 5XFAD by modulating the microglia neuroprotective phenotype

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Alzheimer's disease (AD) is the most common age-related neurodegenerative disease and is the leading cause of dementia worldwide. It is characterized by the extracellular accumulation of β-amyloid (βA) peptide plaques, intracellular accumulation of neurofibrillary tangles (NFTs), and by both synaptic and neuronal loss. These pathological marks result in memory impairment.

Recently, it has been discovered by single-cell RNA analysis, a population of microglia that displays a unique transcriptional and functional profile in neurodegenerative diseases known as disease-associated microglia (DAM). Two-step activation mechanism regulates switching from homeostatic to stage 1 DAM (DAM1; Trem2-independent) and stage 2 DAM (DAM2; Trem2-dependent). Increased expression of genes associated with the stage 1 DAM results in the loss of microglial homeostatic genes. Interestingly, the stage 2 DAM presents phagocytic activity and is beneficial for AD. These observations suggest that blocking specific checkpoints to promote the stage 2 DAM might constitute a therapeutic approach to treat AD.

Previous studies have demonstrated that an enriched environment (EE) paradigm exerts a neuroprotective effect. The enriched environment consists of housing conditions that promotes social interaction as well as sensory, cognitive and motor stimuli leading to a number of brain regions activation. Importantly, Alzheimer's disease (AD) mice models exposed to the EE paradigm show delayed βA peptide plaque deposition, increased hippocampal neurogenesis, increased microglial phagocytic activity, and improved learning and memory capacity. In the present study, the AD mouse model 5XFAD was housed to an EE. The EE prevented the cognitive decline and improves motor skills and anxiety behavior in the 5XFAD mice. Interestingly, the EE neuroprotective effect correlated with the expression of DAM2 specific genes. In particular, the EE accelerated the transition to the DAM2 phenotype as the expression of *Trem2* and *Tyrobp* genes were increased whilst the expression of *Cx3Cr1* was decreased. These data point out that the EE exerts a neuroprotective effect by modulating the microglia activation state at the gene expression level.

Gene expression can be affected by modifications in the epigenetic landscape in response to environmental changes. Current experiments are aimed to evaluate whether the neuroprotective effect of the EE on the 5XFAD mice results from modulating epigenetic marks. This is of particular importance to evaluate how environmental factors and lifestyle changes modulate the phenotypic response of microglia to effectively contain and delay cognitive deterioration.

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Area: Gene expression

Keywords: Alzheimer's disease, enriched environment, epigenetics

Transcriptional effect of enriched environment exposure in a murine colitis model

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Using different disease models, it has been shown that enriched environment can enhance the response to several stresses, improve homeostasis and enhance central nervous system functions. Despite the clear phenotypic effect of enriched environment exposure, gene networks that govern such changes have not been fully explored. To understand the effect of enriched environment at a molecular level, we used RNA-seq in a murine colitis model to analyze the transcriptional changes upon colitis induction and the consequences of enriched environment exposure. Through differential gene expression as well as reconstruction of gene networks and differential network connection analyses, we uncovered a set of pathways that are altered by enriched environment and point to an interesting function of neural cells at the gut-brain axis.

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Glia

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Evidence for a neuroinflammatory process in the hippocampus of the autistic-like mouse strain C58/J throughout development

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Area: Glia

Autism spectrum disorder (ASD) comprises a complex and heterogenous array of neurodevelopmental disorders that are characterized by communication and language impairments, as well as repetitive behaviors or restricted interests.

Neuroinflammation refers to a detrimental group of processes that include activation of immune-related cells associated to the central nervous system (CNS), along with a sustained production of proinflammatory molecules, which can have a negative impact in the general physiology of the brain. Microglia constitute the primary type of immune cells in the brain parenchyma, which sets them as the main bridging element between the immune system and neurons as well as other glial cells. Recently, neuroinflammatory cues have been linked to the onset and maintenance of neurodegenerative diseases and neurodevelopmental disorders, such as ASD. For instance, individuals with ASD show microglia with hypertrophic morphologies; besides an elevated content of proinflammatory cytokines and chemokines across different areas of the CNS. However, the relation between neuroinflammation and the observed neuronal and behavioral traits in autistic individuals remains to be fully understood.

Several animal models have been proposed for studying the molecular alterations implicated in the development of autistic-like traits. The inbred mouse strain C58/J shows a low social preference along with repetitive behaviors. Here we found that male adult mice of the C58/J strain show a significant increase in the density of microglia in the CA1 region of the hippocampus. We also found that there are distinct subsets of morphological types of microglia in the same brain region of these mice. We observed there is a significant increase in the hippocampal content of the cytokines IFN-γ and TNF-α, besides an increase of the CCL2 chemokine. Along this line, we discovered there is an imbalance in the hippocampal content of the enzymes inducible nitric oxide synthase (iNOS) and arginase-1 (Arg-1). The same molecules are currently being evaluated in embryos on the 17.5 gestational day to determine if inflammatory disruptions occur early during development and persist until the adult stage.

Keywords: autism spectrum disorder, microglia, neuroinflammation.

In Vitro and Computational Studies of Perezone and Perezone Angelate as Potential Anti-Glioblastoma Multiforme Agents

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Area: Glia

Glioblastoma multiforme (GBM) represents the most malignant type of astrocytoma, with a life expectancy of two years. It has been shown that Poly [ADP-ribose] polymerase 1 (PARP-1) protein is over-expressed in GBM cells, while its expression in healthy tissue is low [1]. In addition, perezone, a phyto-compound, is a PARP-1 inhibitor with antineoplastic activity [2]. In consequence, in the present study, both *in vitro* and computational evaluations of perezone and its chemically related compound, perezone angelate, as anti-GBM agents were performed. Hence, the anti-proliferative assay showed that perezone angelate induces higher cytotoxicity in the GBM cell line (U373 IC_{50}= 6.44 μM) than perezone (U373 IC_{50}= 51.20 μM), by induction of apoptosis. In addition, perezone angelate showed low cytotoxic activity in rat glial cells (IC_{50}= 173.66 μM). PARP-1 inhibitory activity (IC_{50}= 5.25 μM) and oxidative stress induction by perezone angelate were corroborated employing *in vitro* studies. In the other hand, the performed docking studies allowed to explain PARP-1 inhibitory activity of perezone angelate, and ADMET studies showed its probability to permeate cell membranes and the blood-brain barrier, an essential characteristic of drugs to treat neurological diseases. Finally, it is essential to highlight that the results confirm perezone angelate as a potential anti-GBM agent.

Keywords: Phyto-compounds, computational studies, drug-likeness, anti-neoplastic activity, glioblastoma multiforme.

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References:

1. Galia, A.; Calogero, A.E.; Condorelli, R.; Fraggetta, F.; La Corte, A.; Ridolfo, F.; Bosco, P.; Castiglione, R.; Salemi ,M. PARP-1 protein expression in glioblastoma multiforme. Eur J Histochem **2012**, 56, e9.
2. Hernández-Rodríguez, M.; Mendoza Sánchez, P.I.; Macias Perez, M.E.; Rosales Cruz, E.; Mera Jiménez, E.; Nicolás Vázquez, M.I.; Ruvalcaba, R.M. *In vitro* and computational studies showed that perezone inhibits PARP-1 and increase ROS levels in K562 cells. *Arch Biochem Biophys* **2019**, 19, 225-234.

Characterization of Mice Cerebellar Microglia Primary Cultures

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Microglia cells are the primary resident immunocytes in the cerebellum, continuously function as immune system supervisors to sustain cerebellar homeostasis. Recent studies have demonstrated that cerebellar microglial have a uniquely hyper-vigilant immune phenotype compared to microglia from other brain regions. These findings suggest that microglia contributes to cerebellar vulnerability in ataxia and probably in the toxic effects of xenobiotics. Cerebellar development may be particularly sensitive to such insults, as cerebellar maturation occurs over a relatively long developmental time. Human cerebellar development extends from the early embryonic period until the first postnatal years. Elimination of immature, functional redundant synapses during postnatal development is essential for the formation of the functional cerebellar network. While the unique character of cerebellar microglia has only recently been identified, cerebellar astrocytes and in particular Bergmann glia are well known for their unique interaction with Purkinje cells (PC) and their plausible regulation of glutamatergic synapses. Additionally, the cerebellum is a target for metal neurotoxicity, such as manganese (Mn). It has been shown that Bergman glia cells are affected by acute exposure to Mn, causing decreased glucose uptake and increased phosphorylation of the ERK1/2. The establishment of the molecular and cellular process triggered by xenobiotics is fundamental for the development of public health policies. Therefore, the development of suitable *in vitro* models is important, herein we describe a protocol to isolate and characterize cerebellar microglia from post-natal mice. After the removal of the meninges and the mechanical and enzymatic cell dissociation, the suspension was cultured in a T-75 flask for 15 days and then microglia was purified by shaking the flasks. Cerebellar microglia grow for 10 days and increase rapidly on days 14–18. *Iba1* was used to microglia marker for immunofluorescence studies. In conclusion, an easy to follow protocol for primary cerebellar microglia cultures was developed.

Keywords: Microglia, cerebellum, culture

Alterations in the physiology of Müller glial cells under diabetic retinopathy conditions *in vitro*

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Area: Glia

Diabetic retinopathy (DR) is the most common related diabetes microvascular disease. Recent studies have discovered a relationship between dyslipidemia and progress in DR. In this study, we investigated the role of high glucose (G25), palmitic acid (lipid increased significantly in diabetic patients, PA), and co-treatment (G25/PA) in Müller glial cell (MG) viability, morphology, VEGF presence, and $GABA_AR$ subunit expression and function. MG primary cultures from CD1 mice were exposed to 25 mM Glucose (G25), 250 µM PA, and G25/PA for 24, 48, 72, or 96 hours. Cell viability was measured by trypan blue. Cell morphology changes and VEGF synthesis was evaluated by immunofluorescence (IF). mRNA expression of $GABA_AR$ subunits was evaluated by RT-PCR and electrophysiological GABA-induced response by patch-clamp experiments. We found that PA and G25/PA reduce cell viability in MG cultures after 72 hours of exposition, G25 was unable to generate these effects. Only PA induces morphological changes in this retinal cell, altering cellular and nuclear areas. We detect a significant increase of VEGF in MG cultures exposed to G25, PA, or G25/PA. The bioinformatics prediction showed that α1 is an important subunit in $GABA_AR$ assemble in MG. Interestingly, PA and G25/PA, but not G25, downregulate alfa1 subunit mRNA expression. Moreover, our preliminary data indicate that the MG electrophysiological response to GABA is also critically diminished in G25/PA. These results together suggest that G25/PA, and not G25, induce several events observed in animal models and human DR patients, such as VEGF increase, morphological changes, and lower cell viability. Likewise, we also observed an alteration in the function of the $GABA_AR$ expressed in MG by G25/PA, that mimics two of the main pathological processes during DR, hyperglycemia and hyperlipidemia. Further experiments are necessary to determine the mechanism by which G25/AP is capable of downregulating $GABA_AR$, as well as the physiological consequences that these events would have on the retina.

Keywords: Retina, Diabetic retinopathy, GABA.

Glutamine transport systems expressed in the U373MG glioblastoma cell line

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Field of study: Biochemistry, Cancer, Neuroscience

Aside from the high glucose consumption by glioma cells, glutamine is a compulsory amino acid for the survival of these transformed cells. Therefore, it is not surprising that Glutamine transporters are overexpressed in cancer cells. Glutamine is needed to either synthesize metabolites that can enter the tricarboxylic acid cycle or to generate glutamine pools that are used for exchange for other important molecules. Among the main glutamine transporters, those which have Na+- dependent activity, are usually coupled with other plasma membrane transporters essential for cell growth and survival. The gene expression regulation of glutamine transporters both at the transcriptional and translational levels has not been fully characterized in human glioma cell lines, like the one used in this study, U373 MG. The signaling pathways responsible to augment their expression in cancer cells are dysregulated in most types of cancer studied thus far. Through the utilization of L-[^{3}H] Glutamine uptake assays, amino acid competition experiments, and western blot assays we aim to characterize the main glutamine transport systems in U373MG glioblastoma cells. Both system A and system N are present in this cell line and functional experiments suggest an apparent major role of system N transporters.

Key words: glutamine transporters, glioblastoma, cell metabolism

Differential expression of astrocytic fibrillary glial acidic protein during brain aging in rats

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Área: Glía

Introduction

Astrocytes are the most abundant cells in the CNS; glial fibrillary acidic protein (GFAP) is characteristic of this cell type. Differences in GFAP expression during brain development and aging modify astrocytic functions affecting brain physiology. Also, the GFAP increase alters astrocyte´s functions and morphology in response to brain damage stimuli, in a process known as astrogliosis. It has been described that those differences in GFAP expression during brain aging indicate changes in astrocytic functions that affect brain pathophysiology.

Objective

To evaluate the levels of GFAP expression during the aging in rats

Methods

We used brain slices of 30 µm thick from 3-, 9-, and 15-months old rats. Immunofluorescence was performed using the flotation technique for four different anti-GFAP antibodies (GFAP-pan, GFAP-GA5, GFAP-C19, and GFAP-9259) to evaluate the possible changes in GFAP in aging. The study was focused on the dentate gyrus and Cornu ammonis (CA) of the hippocampus. Images were captured with a Cell Imagen multimode Reader (Cytation 5™, BioTek™) and a confocal microscope (Nikon™ ECLIPSE Ti2). The analysis of fluorescence intensity was using ImageJ and NIS-Elements Viewer (Cargill et al., 2012).

Results and Discussion

The experimental images show that GFAP increases at nine months compared to the three-month control and decreases at 15 months. The results suggest that the GFAP decrease could favor astrocytes atrophy in old age, which probably contributes to aging neurodegeneration. However, it should thoroughly explore the mechanism and functional outcome of GFAP decline during aging.

Keywords: GFAP, astrogliosis, neurodegeneration

Protective and antioxidant effects in glial cells of phenolic compounds

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The present work belongs to the area of glia.

Introduction: The glia has a role of support and immunomodulatory for neurons, it has been shown that in neurodegenerative diseases, the pathological neuro-glial interactions generated an “aggressive” cellular environment. Dysfunction in glial cells is associated with a variety of neurological diseases with shared molecular and cellular alterations, which include, glutamate (Glu) toxicity, oxidative stress, and inflammation. There is no cure for neurodegenerative diseases, so the use of alternatives, such as phenolic compounds that have shown antioxidant and anti-inflammatory activity.

Methodology: The anti-radical capacity of 6 phenolic compounds (1,2-dihydroxybenzene, resorcinol, 1,2,4-benzenetriol, phloroglucinol, pyrogallol, hydroquinone) was evaluated by DPPH and ABTS method. We evaluated the glial protective effect of phenolic compounds against glutamate toxicity *in vitro* in a C8-D1A mouse astrocyte cell line, using cell viability (MTT) and nuclear integrity (immunofluorescence) assays.

Results: We identify that the compounds 1,2-dihydroxybenzene, pyrogallol, and hydroquinone had higher anti-radical activity 4.98 ± 1.67, 4.89 ± 2.81, and 5.63 ± 2.17 µg/mL, respectively. Cellular damage was induced with Glu at concentrations of 0.62-80 mM, showing a significant decrease in astrocyte viability ($p<0.05$) from 5 mM and nuclear condensation was observed. The compounds phloroglucinol and 1,2 dihydroxybenzene showed a protective effect from 3.12 µg/mL to Glu-induced damage.

Conclusion: Phloroglucinol and 1,2 dihydroxybenzene were the compounds with the best glial protective effect at high concentrations while pyrogallol, resorcinol and hydroquinone showed a protective effect at low concentrations.

Keywords: Glial protection, Phenols, Glutamate damage.

Flouride exposure modulates SLC7A11 (xCT) in radial glial cells

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Glutamate (Glu) is the main excitatory neurotransmitter of the central nervous system (CNS) and exerts its actions by activating membrane receptors and transporters. Under physiological conditions, extracellular levels of glutamate are regulated by amino acid transporters (EAAT) and the glutamate-cystine exchanger (xCT) present in glial cells. Müller cells are the glial cells responsible for retinal Glu transport and metabolism, damage to these cells might result in an excitotoxic insult. Flouride, a pollutant present in contaminated groundwater and oral care products, has deleterious effects on the structure and function of the CNS. A correlation between elevated drinking water Fluoride levels and reduced scores in intelligence quotient has been reported. Exposure to this xenobiotic increases reactive oxygen species (ROS) which modifies the expression and function of several proteins. The xCT exchanger is at the interface between excitatory signaling and oxidative stress through its involvement in glutathione (GSH) synthesis. This exchanger is inducible and one of the mechanisms described to regulate its protein levels is the binding of the RNA binding protein HuR to its 3´-UTR region. The signaling cascades involved in this regulation is currently unknown. This work aims to delineate the signaling pathways (s) involved in the regulation of xCT in response to Fluoride exposure in human retina MIO-M1Müller glial cells.

Keywords: Glutamate-Cystine exchanger (xCT), radial glial cells, Fluoride, RNA binding proteins, *HuR,* Glutamate

Expression of exosomal miR-29a in astrocytes exposed to high glucose

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The present work belongs to the area of glia.

Background: High glucose can lead to neuronal damage as well as glial cell reactivity. Astrocytes play metabolic and support roles that affect the function of neurons at the local and network levels. These cells can release exosomes, crucial nanovesicles in cell communication. Exosomes can attenuate neurodegeneration in the brain or exacerbate damage depending on the cargo molecules such as miRNAs and proteins. An increase of miR29a is involved in ameliorating inflammation and decreasing apoptosis.

Methods: Astrocytes from the C8-D1A cell line were treated with 5.5 and 25mM glucose concentrations for 7 days. The Anthrone method was used to assess glycogen levels in astrocytes and was performed assay to evaluate glucose consumption. Subsequently, astrocyte-derived exosomes were isolated from the conditioned medium by ultracentrifugation. Characterization of the exosomes was performed by transmission electron microscopy and CD9 and Annexin V detection by western blot. In addition, the RNA was extracted from exosomes and used for RT-PCR real-time to quantify miR-29a expression.

Findings: High glucose concentrations (25 mM) decreased astrocyte viability. In addition, astrocytes increased glycogen stores and glucose uptake in response to the high glucose. We confirmed that the extracellular vesicles isolated from the conditioned medium corresponded to exosomes Also, exosomes from astrocytes treated with high glucose showed increased expression of exosomal miR-29a.

Conclusions: High glucose stimulation induces metabolic changes like increased glucose uptake and glycogen storage in astrocytes. Furthermore, increased the expression of miR-29a in exosomes derived from astrocytes,

Keywords: High glucose, miR29a, astrocytes

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Thrombospondin-1 (TSP-1) expression in brain mouse during postnatal development.

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Thrombospondin 1 (TSP-1) belongs to a family of large multidomain oligomeric glycoproteins that participate in a variety of biological functions as part of the extracellular matrix. Through their associations with various binding partners, TSP-1 mediates complex cell-cell and cell-matrix interactions in processes as diverse as angiogenesis, inflammation, osteogenesis, cell proliferation, and apoptosis. During embryogenesis, TPS-1 plays a very important role in the development of many organs of the body, including bones, muscles, heart, and central nervous system (CNS). In the brain, TSP-1 is secreted by astrocytes promoting the formation of new dendritic spines and synapses. However, the expression of TSP-1 during postnatal development is not well characterized. In this work, we analyze TSP-1 expression in the cortex and hippocampus in mice of postnatal day 7 (P7), P23, and P29. The results show that TSP-1 secretion is similar between P7 and P29, however, a significant increase was observed on P23 in both cortex and hippocampus. TSP-1 levels were not associated with an increase in TSP-1 synthesis or the number of astrocytes. The increase in TSP-1 correlates with an increase in the expression of the synaptic marker PSD95. Our results suggest that increased TSP-1 levels could be involved with brain plasticity mechanisms during postnatal development.

Key Words: Thrombospondin-1 (TSP-1), astrocytes, development

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Stimulation with TNF-α and glutamate induces the release of Wnt5a and Wnt7a in Astrocyte-derived exosomes

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Astrocytes are critical regulators of brain function. They provide trophic and metabolic support to neurons, dynamically modulate information processing and signal transmission. Astrocytes respond to a variety of signals including hypoxia, glucose deprivation, neurotransmitters, and cytokines. When astrocytes are activated by glutamate, changes in intracellular calcium ion concentrations occur. On the other hand, astrocytes respond to tumor necrosis factor (TNF-α), treatment with a morphological transition to polygonal morphology and a shift to an inflammatory phenotype. Activated astrocytes release extracellular vesicles that, due to their size (50 nm to 100 nm), are considered exosomes that contain different signaling molecules. However, the role of astrocytes in the production of Wnt signaling components has been poorly explored and whether these proteins are released via exosomes to modulate neuronal function is still unknown. Therefore, in this work we study the production and abundance of Wnt5a and Wnt7a ligands in exosomes derived from cultured astrocytes exposed to TNF- α or glutamic acid. The relative expression of *Wnt5a* and *Wnt7a* was evaluated by RT-qPCR. Exosomes were isolated and the relative abundance of Wnt5a and Wnt7a proteins was determined by western blotting. Our results show that astrocytes modify the expression of *Wnt7a* and *Wnt5a* genes in response to proinflammatory or excitatory stimuli. Furthermore, these cells produce Wnt5a and Wnt7a proteins that are released through exosomes, that may play a fundamental role in neuronal structure and function.

This work was supported by DGAPA, PAPIIT IN202318

Keywords: Reactive astrocytes; Exosomes; Wnt signaling.

Area: Glia

Effect of 5 Hz transcranial magnetic stimulation on hippocampal oligodendrocytes in chronically stressed female Swiss-Webster mice

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Area: Glia

Introduction

Major depressive disorder (MDD) is the main contributor to mental health problems, with an estimated prevalence of 3.8% worldwide[1]. Due to its importance in healthcare and the limitations of studies with patients, multiple animal models have been developed to study depressive-like behavior and its neurobiological basis. Among those models, the chronic unpredictable mild stress model (CUMS)[2] produces alterations in behavior and structural plasticity in the brain[3]. Regarding to the later, the hippocampal neurogenic niche alterations impact on the generation of new neurons. In addition to microglia, astrocytes and new neurons, oligodendrocytes are relevant to form myelin sheaths that enwrap axons, provide metabolic support to axons and are important for neuroplasticity in the hippocampus. Thus, it has been proposed that oligodendrocytes have a functional role in depression[4,5]. Although pharmacological therapy represents the first line of MDD treatment, its negative secondary effects and the resistance of several patients to antidepressants[6] have sustained the research for alternatives, such as repetitive transcranial magnetic stimulation (rTMS), which has showed efficacy in MDD treatment protocols[7] alone, combined with fluoxetine[8] and in animal models of depression to revert depressive behavior and alteration in the neurogenic niche[9]. Nevertheless, there is a lack of knowledge about its neurobiological effects. In this study, we assessed the effects of rTMS in behavior, adult hippocampal neurogenesis and oligodendrocytes using the CUMS model.

Methods

We divided 36 Swiss Webster mice in six groups: 1) control group without CUMS, 2) CUMS 3) Sham for rTMS, 4) CUMS plus rTMS, 5) CUMS plus fluoxetine (FLX), 6) CUMS plus rTMS/FLX. The CUMS was applied for eight weeks. During the experiment, the coat state was evaluated once a week. Also, mice underwent to additional behavioral tests such as rotarod, open field test (OF), elevated Plus maze (EPM), novel suppressed feeding (NSF), forced swim test (FST) and splash test (ST). Later, we euthanized the mice, and the brain was cut to get 40 µm wide brain slices for the immunodetection of markers for oligodendrocytes (Olig2 and CNPase), cell proliferation (KI67), survival (CldU) and doublecortin (DCX).

Results

We found significant effects of CMS on some behaviors related to depression. Also, we found significant effects of rTMS on behavior, cell proliferation, survival, immature neurons. Regarding to oligodendrocytes, we found that rTMS increased the number of Olig2 positive cells within increased immunoreactivity of CNPase.

Keywords: rTMS, oligodendrocytes, neurogenesis

References

1. WHO. (September 13, 2021). Depression. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression
2. Willner, P. (2017). The chronic mild stress (CMS) model of depression: History, evaluationand usage. *Neurobiology of Stress* 6, 78-93, https://doi.org/10.1016/j.ynstr.2016.08.002.
3. Fenton, E., Fournier, N., Lussier, A., Romay-Tallon, R., Caruncho, H., & Kalynchuk, L. (2015). Imipramine protects against the deleterious effects of chronic corticosterone on depression-like behavior, hippocampal reelin expression, and neuronal maturation. *Prog.Neuro-Psychopharmacol. Biol. Psychiatry* 60, 52–59. https://doi.org/10.1016/j.pnpbp.2015.02.001.
4. Wang, J., Qiao, J., Zhang, Y., Wang, H., Zhu, S., Zhang, H., Hartle, K., Guo, H., Guo, W., He, J., Kong, J., Huang, Q., & Li, X. M. (2014). Desvenlafaxine prevents white matter injury and improves the decreased phosphorylation of the rate-limiting enzyme of cholesterol synthesis in a chronic mouse model of depression. *Journal of neurochemistry*, *131*(2), 229–238. https://doi.org/10.1111/jnc.12792
5. Zhou, B., Zhu, Z., Ransom, B.R. & Tong, X. (2021). Oligodendrocyte lineage cells and depression. *Mol Psychiatry* 26.**,** 103–117. https://doi.org/10.1038/s41380-020-00930-0
6. Little, A. (2009). Treatment-resistant depression. *Am. Fam. Physician* 80, 167–172
7. George, M. (2010). Transcranial magnetic stimulation for the treatment of depression.Expert Rev Neurother 10,1761–72. doi: 10.1586/ern.10.95
8. Yu, F., & He, R. (2021). The effect of fluoxetine combined with repetitive transcranial magnetic stimulation on the psychological emotions and cognitive and neurological functions of acute post-stroke depression patients. *American journal of translational research*, *13*(10), 11883–11889.
9. Feng, S., Shi, T., Yang, F., Wang, W., Chen, Y., & Tan, Q. (2012). Long-lasting effects of chronic rTMS to treat chronic rodent model of depression. *Behavioural Brain Research*, 232(1), 245-251. https://doi.org/10.1016/j.bbr.2012.04.019.

Characterization of EAATs in human endothelial cells and astrocytes: contribution of the BBB to glutamate efflux

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The blood-brain barrier is a selective barrier that protects and isolates the Central Nervous System. It is made up of endothelial cells that form the cerebral capillaries, it acts as a physical and selective barrier due to the tight junction complexes between these cells. The blood-brain barrier has various functions, among the most important the supply of glucose and amino acids, through various transporter systems is the most important. The entry and/or exit of glutamate, the major excitatory amino acid, is linked to neuronal death in pathologies such as cerebral ischemia. At high levels, glutamate exerts potent neurotoxic properties, triggering irreversible brain damage. It is well established that glutamate homeostasis in the cerebral interstitial fluid is maintained mainly by the activity of the transporters present in the glial cells, but it does not take into account the possible involvement of the blood-brain barrier endothelial cells in this process. Here, we characterized the sodium-dependent glutamate transport in the human endothelial and astrocytic cell lines HBEC-5i and U-87MG. We evaluated the Na^+-dependent [^{3}H] D-Asp uptake. Our results provide evidence for the functional expression of sodium-dependent glutamate transporters in both cell lines. Michaelis-Menten kinetics assay showed Vmax and K_M values similar to what has been previously reported for these cells in non-human primary cultures. These findings support the notion that the blood-brain barrier itself may participate in regulating brain L-glutamate concentrations.

Endothelial cells, blood-brain barrier, glutamate

Differences in the localization of AQP1 and expression patterns of AQP isoforms in rat and mouse sciatic nerve and changes in rat AQPs expression after nerve crush injury

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In the peripheral nervous system aquaporins (AQPs) have been reported in both peripheral neurons and glial cells. Previously we described the precise localization of AQP1 in the rat sciatic nerve, which is present in both Remak and myelin Schwann cells, and is enriched in the Schmidt-Lanterman incisures. In this work, we found that AQP1 in mouse is only present in Remak cells, showing a different localization between these species. However, after nerve crush injury the level of AQP1 mRNA expression remains constant at all times studied in rat and mouse. We then performed RT-PCR of nine AQP (AQP1-9) isoforms from rat and mouse sciatic nerve, we found that in rat only five AQPs are present (AQP1, AQP4, AQP5, AQP7 and AQP9), whereas in mouse all AQPs except AQP8 are expressed. Then, we studied the expression by RT-PCR of AQPs in rat after nerve crush injury, showing that AQP1, AQP4 and AQP7 expression remain constant at all times studied, while AQP2, AQP5 and AQP9 are upregulated after injury. Therefore, these two closely related rodents show different AQP1 localization and have different AQPs expression patterns in the sciatic nerve, possibly due to a difference in the regulation of these AQPs. The expression of AQP1 in Remak cells supports the involvement of AQP1 in pain perception. Also, in rat the upregulation of AQP2, AQP5 and AQP7 after nerve injury suggests a possible role for these AQPs in promoting regeneration following injury.

Keywords: Aquaporins; Schwann cells; Wallerian degeneration.

Aryl hydrocarbon receptor as a new EAAT1/GLAST regulator

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Glutamate (Glu) is the main excitatory neurotransmitter in the vertebrate Central Nervous System, exerts its effects by activating specific membrane receptors expressed in neurons and glial cells. Extracellular Glu levels are tightly regulated by a family of high-affinity sodium-dependent transporters known as excitatory amino acid transporters (EAAT), which remove Glu from the synaptic cleft and internalize it mainly into the glial compartment. When Glu is inefficiently removed, a phenomenon of cellular death can occur due to the over activation of Glu receptors, this effect is known as excitotoxicity. Glial Glu transporters are essential for glutamatergic neurotransmission and prevent excitotoxicity, and a deficiency in the expression of these transporters has been correlated to the development of pathologies such as Amyotrophic Lateral Sclerosis (ALS), Alzheimer's disease, and others. Glu transporters are regulated at several levels, including transcription of their gene, mRNA stability and maturation, post-translational modifications, and membrane traffic. In this work, we focused on the transcriptional regulation of the slc1a3 gene. Using the well-characterized in vitro model of chick cerebellar Bergmann glial cells that express exclusively GLAST/EAAT1, we describe here the effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), an Aryl hydrocarbon receptor (AHR) agonist, exposure in the transporter function. Using a [^{3}H]D-Aspartate uptake activity assay, we found a reduction of the effect in the presence of the RNA Pol II blocker Actinomycin D. In silico analysis of the reported chick slc1A3 promoter revealed the presence of two xenobiotic response (XRE) DNA binding sites. These results strengthen the notion of the importance of glial cells in the regulation of glutamatergic signaling.

Key Words: GLAST, Aryl hydrocarbon receptor, Glia

Analysis of density and distribution of astrocytes and microglial cells at the hippocampal formation of autistic-like C58/J mice.

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Area: Glia

Autism spectrum disorder (ASD) comprises a set of neurodevelopmental disorders, which affect communication, social interaction, and present repetitive behaviors. Although ASD etiology remains unclear, there is increasing evidence indicating that glial cells, such as astrocytes and microglia, are functionally deregulated in ASD, promoting its pathophysiology. Indeed, some findings show that astrocytes and microglia present anomalous overactivation and spatial distribution patterns in ASD across different brain areas. Importantly, no previous studies have evaluated these cell populations in the hippocampus of individuals with ASD.

Recent findings from our laboratory showed a decrease in the astrocytic density at the CA1 hippocampal region of the autistic-like mouse strain C58/J and an increase in the microglial density at the same region compared to a wild-type mouse strain. To further characterize glial populations in the hippocampal formation of C58/J adult male mice, here we aimed to evaluate astrocytic and microglial density in the dentate gyrus, as well as the spatial distribution of these populations within the CA1 and dentate gyrus strata. Our data show an increased astrocytic density in the dentate gyrus of autistic-like C58/J mice, while there is no difference in the microglial density in the same area. Additionally, there is an increase in the mean fluorescence intensity of GFAP and Iba-1 in the dentate gyrus of autistic-like mice. Interestingly, when the strata of CA1 were analyzed independently, all strata showed a significant increase in the microglial density, with a higher increase in the stratum pyramidale, along with a more contiguous spatial distribution between the microglia in this stratum. Furthermore, we found an increase in the hippocampal content of MCP-1 (CCL2) chemokine in the C58/J mice, suggesting that the alterations found in density and distribution of microglial cells could be related to a different migration pattern in the CA1 hippocampal region of autistic-like mice. Similarly, spatial distribution of astrocytes and microglia are being evaluated in the dentate gyrus.

Key words: Autism spectrum disorder, Microglia, Hippocampus

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Human olfactory epithelium-derived astrocytes transplantation into the striatum of neonatal mice

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The olfactory epithelium (OE) is distinguished by a continuous regeneration of olfactory sensory neurons and glial cells that persists into adulthood. These events (neuro and gliogenesis) are possible due to local stem cells known as globose and horizontal basal cells. The easy access of these cells in the nasal cavity of adult human donors is considered a great advantage to isolate neural progenitor cells (NPCs) that could be used in therapeutic applications such as autologous transplants. The aim of this work is to evaluate the potential of OE NPCs to derive astrocytes and their ability to survive after grafting them in the striatum of neonatal mice. To achieve this goal, OE cells in culture were assayed for the expression of astrocyte molecular markers and calcium activity after induction with ScienCell® astrocyte differentiation medium and the calcium activity determined by *in vivo* imaging using the calcium indicator Fluo-4AM. Subsequently, cells were transduced with an adenovirus carrying the green fluorescent protein (AdV-GFP) and grafted into neonatal P1-3 CD1 mice striatum and evaluated morphologically every week for one month. The expression of GFAP was also assessed in the grafted cells.

The results show that differentiated cells express in culture the astrocytic markers GFAP, S100β and Aldh1l1, moreover, they present basal calcium activity. The cells survived at least one month after transplantation in the striatum developing complex morphologies and preserved the expression of GFAP indicating that they maintain the astrocytic identity. These findings suggest the capability of OE NPCs to obtain astrocytes which may be useful for cell therapy in neurodegenerative disorders.

Key words: olfactory epithelium, neural progenitor cells, astrocytes. **Area:** Glia.

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Neurobiology Meeting of the Mexican Society for Biochemistry

Metabolism

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Obesity and its relationship with the appearance of peripheral insulin resistance and brain insulin resistance in C57BL/6 mice.

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Area: Metabolism

Introduction: Insulin resistance (IR) is a condition that characterizes metabolic disorders, such as obesity and type 2 diabetes mellitus, which causes altered metabolism due to lack of response to the presence of insulin, mainly in insulin-dependent tissues, such as the brain and adipose tissue. IR in the brain was recently related to the development of neurodegenerative diseases in obese people, however the mechanisms of damage that derive from the establishment of insulin resistance in the brain are not known, and if it predisposes to the establishment of alterations in peripheral tissues, during obesity.
The **aim** of our study was to determine if the establishment of peripheral insulin resistance (PIR) is related to the presence of cerebral insulin resistance (CIR) in an obesity model.
Methodology: The effect of the high-fat diet (HFD) administration on the establishment of obesity was determined by the difference of about 40% of the body weight of the mice fed standard diet (C) and low-fat diet (LFD). PIR in HFD mice was determined by measuring blood glucose levels, by incision in the mouse tail, every 30 minutes after administration of glucose and insulin. The effect of insulin administration in the preoptic area on core body temperature in mice was measured by radiotelemetry, to determine the establishment of CIR.
Results: Mice developed obesity and weight gain after 1, 2, and 3 months of consuming HFD. The glucose tolerance curves (GTC) and insulin (ITC) show that the group exposed to HFD had RIP at the third month of exposure, because the fasting glucose level during the GTC was above 150 mg/dl. Furthermore, the glucose level does not decrease when insulin is administered, compared to group C. On the other hand, insulin injection in the preoptic area does not induce an insulin response in the LFD groups (at the first and second month of diet) and HFD (at the third month), which shows the presence of CIR. Exposure to 10 °C caused an increase in body temperature in the HFD group in the second month.
Conclusions: Our results show that HFD causes PIR and CIR, while LFD causes CIR in the first and second months.

Key words: Insulin, insulin resistance, obesity, hypothalamus, POA, hyperthermia.

Coconut and Sucrose Diets Alter GABA in Overweight rat brain

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The relative amounts of carbohydrate and fat in the diet have an important modulating effect on the development of the obesity. Coconut milk (CO) contains medium chain triglycerides (MCT), and sucrose is rich in carbohydrates. The **aim** was to compare the effect of dietary sucrose and fat in the form of coconut fat on GABA, calcium and ATPase activity on rat brain regions. The aim was to compare the effect sucrose and fat (coconut fat) on gamma amino butyric acid (GABA) and calcium levels in the brain regions of rats. Methods. We investigated the effect of CO or sucrose 15% in adult rats. The administration of the treatments was as follows: Group A (control) - only water; group B - sucrose solution 15%; group C - coconut water; and group D - coconut milk. Blood glucose and triglycerides increased significantly ($p<0.05$) in the group that received coconut milk (group D). Calcium showed a significant increase ($p<0.01$) in all the brain regions of the animal groups treated with sucrose solution 15% (group B). In the groups that received the administration of coconut water (C) or coconut milk (D), calcium levels increased only in the hemisphere regions. Treatment with coconut water (C) or coconut milk (D) induced a significant increase ($p<0.002$) in GABA levels in hemisphere and cerebellum/medulla oblongata regions. The present results suggest that dietary coconut induces changes both in the fatty acid composition of the lipid components. In addition, it seems to exercise an impairment action on GABAergic metabolism.

Keywords: Coconut, sucrose, GABA, Brain.

Aerobic training decreases peripheral sensitivity and inflammation in T2D mice.

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Introduction. Type 2 diabetes mellitus (T2D) is a metabolic disorder that leads to the development of diabetic peripheral neuropathy, which is the most frequent microvascular complication in patients with T2D. It has recently been suggested that aerobic exercise may be an effective strategy to reduce pain and peripheral sensitivity associated with diabetic neuropathy. Diabetic peripheral neuropathy is related to the chronic inflammation characteristic of T2D. Our objective was evaluated the aerobic training on peripheral mechanical and thermal sensitivity and inflammation in T2D mice. ***Material and methods.*** Four-week-old male C57BL/6J mice were divided into 6 experimental groups (n=6): sedentary control, control + low-intensity aerobic training (LI), control + medium-intensity aerobic training (MI), sedentary T2D, T2D + LI and T2D + MI. T2D was induced through a high-carbohydrate diet administered throughout the experiment and low-dose streptozotocin administered at 10 weeks of age. The aerobic training was on automated wheels with velocity control as LI (8 m / min) and MI (18 m / min), performed it for 2 months. Weight, body mass index (BMI), glycemic profile, and serum cytokine profile were monitored. The thermal and mechanical sensitivity was evaluated by hot plate and Von Frey tests, respectively. The tests were performed before, one month and two months after training. Inflammation was evaluated with serum TNF-α concentration. ***Results.*** Mice with T2D developed hyperglycemia, insulin resistance, systemic inflammation, and thermal and mechanical hyperalgesia; while low and medium intensity aerobic training decreased blood glucose concentration, insulin resistance, serum TNF-α and had less thermal and mechanical hyperalgesia with values like healthy mice. In addition, we found a negative correlation between response latency to mechanical and thermal stimuli with serum TNF-α concentration. ***Conclusions.*** Low- and medium-intensity forced aerobic training in mice with T2D decreases glycemia, insulin resistance and restores warm mechanical and thermal perception by modulating systemic inflammation.

Area: metabolism

Keywords: Diabetic neuropathy, Aerobic exercise, Inflammation.

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Prolactin modulates enterocyte intestinal maturation in lactating mice

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During lactation, the pituitary hormone PRL is key for mammary gland development and function, and it is present in maternal milk, however, the role of maternal PRL in the pups is largely unknown. During suckling, the pup´s gut is exposed to high quantities of PRL from maternal milk, thus we hypothesize that the intestine is a target of maternal PRL to promote postnatal health. In this work, we aim to determine the effect of PRL on the maturation of the pup´s intestinal enterocytes. Neonatal intestinal maturation is characterized by increased numbers of crypts and villi length, and changes in the expression of carbohydrates processing enzymes on enterocytes, such as reduced lactase (Lct) and increased saccharase isomaltose (Si) as lactation progresses. In addition, the transition from neonatal to adult intestinal epithelium involves changes in argininosuccinate synthetase 1 (Ass1), which expression is high in suckling enterocytes and is involved in arginine synthesis, and adenosine desaminase 1 (Ada1) which expression is highest at weaning, catabolizes adenosine to inosine and it is associated with activation of immune cells. To evaluate the action of PRL on postnatal intestinal maturation, we used PRL receptor null mice (*Prlr*-KO) and their wild type pairs (*Prlr*-WT) at postnatal day 14, a middle window in the lactation period. The small intestine (duodenum, jejunum and ileum) was processed for histological techniques and morphometric analysis. Morphometry showed that ileum´s villi length is greater in KO than in WT mice, a feature of increased maturity. Consistently, *Prlr*-KO mice showed a phenotype of precocious intestinal maturation, as evidenced by reduced jejunum expression of *Lct* and *Ass1* (markers of intestinal immaturity) and increased expression of *Si* and *Ada1* (markers of intestinal maturity), when compared to *Prlr*-WT mice. These results support our hypothesis that PRL regulates enterocyte function in lactating pups to favor the absorption of milk components. Future research will focus on understanding the mechanisms of action of milk prolactin on postnatal enterocytes, and the health consequences from the precocious intestinal maturation observed in *Prlr*-KO mice, particularly on immune function and neuroendocrine development.

Area: metabolism
Key words: Maternal milk, prolactin, lactation, intestinal maturation.

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Metabolomic profile of dopaminergic neurons derived from induced pluripotent stem cells of Parkinson's disease patients.

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Topic: Metabolism

Parkinson's disease (PD) is caused by the progressive and selective loss of dopaminergic neurons in the *substantia nigra pars compacta* (*SNpc*), which results in motor alterations. Most PD cases (~90%) are idiopathic, although it is believed that aging, exposure to toxins or other environmental factors contribute to pathogenesis. The remaining 10% are familial PD cases, where different mutations in several genes have been identified. The proteins encoded by genes associated with PD are involved in a variety of molecular pathways such as α-Synuclein proteostasis, mitochondrial function, oxidative stress and neuroinflammation, suggesting that mitochondrion plays an important role in the development of this pathology. Therefore, the objective of this project is to generate PD patient-derived induced pluripotent stem (iPS) cell lines to identify metabolic changes through dopaminergic neuronal differentiation. Here, we generated and characterized three iPS cell lines from two patients with idiopathic PD, and another from a patient with familial PD carrying the p.A443AfsX481 mutation in *PINK1*. Dermal fibroblasts collected by skin punch biopsy, under informed consent, were reprogrammed into iPS cells using integration-free reprogramming methods. The generated iPS cell lines express pluripotency markers, maintain a normal karyotype and display the ability to differentiate into all three germ layers. We next differentiated this PD patient-derived iPS cell lines into midbrain dopaminergic neurons as described in Kriks *et al*., (2011). At day 28 of *in vitro* differentiation, we observed TH+ dopamine neurons. This population will be analyzed using Proton Nuclear Magnetic Resonance (^{1}H NMR) to evaluated metabolic changes through PD dopaminergic neuron differentiation.

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Keywords: Dopaminergic neurons, Parkinson's disease, Metabolomics.

Regulation of the transcription factor TFEB by the ketone body β-hydroxybutyrate in neurons and its impact on mitophagy

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Autophagy is a conserved pathway that delivers cytoplasmic content to lysosome for degradation. Specifically, the degradation and removal of damaged or unwanted mitochondria is named mitophagy and neurons are highly dependent on an optimal mitochondrial turnover. The transcription factor TFEB, is a master regulator of autophagy, lysosome biogenesis and mitophagy genes and the stimulation of its activity has been associated with beneficial effects in several neurodegenerative diseases. TFEB translocation to the nucleus is regulated by the activity of sirtuins, which are deacetylases highly regulated by changes in NAD^+ levels and cellular metabolism. Therefore, NAD^+ levels can regulate sirtuin activity and autophagy. The ketone body β-hydroxybutyrate (BHB), is synthesized in the liver from fatty acids and released to the circulation to be used in other organs including the brain as an energy substrate, when glucose supply is limited. BHB metabolism induces an increase in the NAD^+/NADH ratio in the cytosol and generates ATP. In addition to its metabolic activity, BHB, has been suggested as a signalling molecule with many actions, and previous studies have shown that BHB can stimulate autophagy in neurons under glucose deprivation conditions. However, the mechanisms involved are not completely clear. Here, we have investigated whether BHB can stimulate TFEB activation and promote mitochondrial renewal through mitophagy, in healthy neurons. Thus, we tested the effects of BHB long-term exposure on TFEB nuclear translocation and expression of its downstream genes, the activation of autophagy and mitophagy and the intracellular levels of NAD^+ in cortical cultures. Results show that neurons incubated with BHB exhibited increased nuclear levels of TFEB associated with the augmented expression of autophagy and lisosomal genes. Using cloroquine, a compound that blocks lysosome degradation, we observed that BHB stimulates the autophagy flux and the degradation of mitochondrial proteins. In addition, using confocal microscopy a higher colocalization of autophagosome and mitochondria was observed in neurons treated with BHB, suggesting the induction of mitophagy. Also, our results show that pre-exposure BHB reduces neuronal death induced by glucose deprivation. To assess the possible mechanism involved, we observed that BHB increased the NAD^+/NADH ratio and sirtuin 2 levels. Furthermore, inhibition of sirtuin 2 reversed the protective effects of BHB. In conclusions results suggest that BHB can regulate sirtuin activity and stimulate the activation of mitophagy, which promotes neuronal survival under energy stress conditions. *Ketone body, autophagy, mitophagy.*

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Effect of cysthationine-gamma-lyase/hydrogen sulfide system modulation on vascular dysfunction induced by insulin resistance in male Wistar rat thoracic aorta.

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Hydrogen sulfide (H_2S) is a novel gasotransmitter synthesized from L-Cysteine (L-Cys) by three enzymatic pathways. In blood vessels, cysthationine-gamma-lyase (CSE) is mainly expressed and regulates vascular function. This enzyme may be affected by insulin resistance. It has been demonstrated that insulin resistance leads to vascular dysfunction and represents the major mechanism underlying type 2 Diabetes Mellitus. The aim of this study was to determine the effect of chronic administration of sodium hydrosulfide (NaHS; inorganic H_2S donor), L-Cysteine (L-Cys; H_2S producing enzymes substrate), and DL-Propargylglycine (DL-PAG; CSE inhibitor) on the vascular function induced by insulin resistance in male Wistar rat thoracic aorta. For that purpose, animals were divided into two main sets that received for 20 weeks: (1) tap water (Control group; n=6); and (2) 15% p/v fructose in drinking water (Insulin resistance group; n=30). Then, the insulin resistance group were divided into 5 subgroups (n=6 each) which received daily i.p. injections during 4 weeks of: (1) nothing (no administration); (2) vehicle (PBS, 1 ml/kg); (3) NaHS (5.6 mg/kg); (4) L-Cys (300 mg/kg); (5) DL-PAG (10 mg/kg). After 20 weeks, metabolic (oral glucose tolerance test, insulin, and Matsuda index) and hemodynamics variables by tail-cuff method as well as vascular function by *in vitro* experiments were determined. We observed that insulin resistance induced by fructose leads to: (1) an increase in blood pressure (without affecting heart rate); (2) hyperinsulinemia; (3) a decrease in Matsuda index; and (4) a decrease in vasorelaxation responses with no effect on contractile responses compared to control group. Interestingly, after 4 weeks of treatment, NaHS decreased blood pressure and restored vasorelaxation responses with no effect on metabolic variables while L-Cys improve contractile and vasorelaxation responses when compared to vehicle. On the other hand, DL-PAG induced a slight increase in systolic and median blood pressure with any effect on contractile or relaxant responses as well as metabolic variables compared to vehicle. Taken together, these results suggest that chronic treatment with NaHS and L-Cys improve vascular dysfunction and hypertension by insulin resistance and may have a potential therapeutic application.

Palabras clave: Hydrogen sulfide, insulin resistance, transsulfuration.

Metabolic profile of CPA: Implications for Glioma's Treatment

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Gliomas in children are primarily treated with therapeutic schemes that include the prodrug cyclophosphamide (CPA). Chemotherapeutic schemes with medium and high doses of CPA result in greater disease-free survival compared to the low-dose regimen. The use of CPA in high doses also implies an increase in the toxicity caused by this compound, mainly to kidneys and heart but also to brain tissue. Several cytochrome P450 (CYP450) enzymes are involved in the metabolic activation of CPA in humans, including CYP2B6 and CYP3A4. The CYP2B6 isoform is the main responsible for the transformation of the prodrugs to 4-OH-CPA, which is turned into alkylating DNA molecule with antitumor effect. CYP3A4 is an abundant enzyme in the liver that also catalyzes the hydroxylation of CPA but also participates in CPA dechloroethylation reactions resulting in the formation of chloroacetaldehyde (CAA). CAA is a metabolite closely related to the systemic toxicity of CPA especially to neurotoxicity phenomena. Nicotine has been reported as a specific inductor of CYP2B6 in the central nervous system (CNS), without the expression of the enzyme in the liver being affected. An increase of CYP2B6 expression could improve the antitumoral activity of CPA and reduce the neurotoxic and nephrotoxic effect during the treatment of gliomas. Our main goal is to study whether the induction of CYP2B6 in the CNS contributes to optimize the conversion of CPA into its 4-OH metabolite reducing the formation of CAA. In the present work, we characterize the systemic metabolism of CPA, both in healthy animals and animals with glioma development, finding relevant differences that may contribute to the CPA toxicity observed in patients.

Key words: gliomas, CYP2B6, cyclophosphamide

Sulpiride, a D2 dopamine receptor antagonist improves glucose tolerance, insulin sensitivity and reduces visceral adipocyte hypertrophy in obese mice.

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Sulpiride, a second-generation antipsychotic, acts by inhibiting dopamine D2 receptors in the pituitary gland, resulting in increased systemic prolactin (PRL) levels. The hyperprolactinemic effect of antipsychotics has been associated with the development of obesity and its related metabolic alterations in patients. In contradiction, recent studies have shown that low PRL levels are associated with obesity, hyperglycemia, and insulin resistance in humans and rodents. Obese rats show lower PRL levels and an adverse metabolic profile, which is improved by PRL treatment. Furthermore, mice null for PRL receptor (*Prlr*) develop exacerbated obesity and hypertrophic adipocytes in visceral adipose tissue (VAT), supporting that prolactin action is beneficial for metabolic homeostasis. In this work, we aimed to evaluate the PRL-elevating side effect of sulpiride, as a possible therapy against metabolic alterations derived from obesity. For this, C57BL/6 8-week-old mice fed a high-fat diet (HFD) for 8 weeks to induce obesity, were administered daily with 30 mg/kg of sulpiride during the last 4 weeks of the diet. Sulpiride increased PRL levels to around 70 ng/mL in control and obese mice, a level reported to be metabolically beneficial. In obese mice, sulpiride treatment decreased hyperglycemia, insulin resistance, triglyceride levels, and energy expenditure, without affecting body weight or caloric intake. In VAT, sulpiride decreased adipocyte hypertrophy and the expression of *Hif1a* (a marker of hypoxia), while increased the expression of *Prlr*, *InsR* and *Glut4* (markers of insulin sensitivity). In control mice, sulpiride did not alter any of the metabolic parameters evaluated. Given that the dose of sulpiride used and the resulting level of PRL observed in our mice didn´t cause adverse metabolic effects, but on the contrary improved metabolic outcomes in obesity conditions, it suggests that the side effects observed when sulpiride is used as an antipsychotic could be related to the high levels of prolactin achieved in the patients. In conclusion, this work shows that sulpiride could be used to reduce metabolic alterations derived from obesity, particularly when obesity is accompanied by low PRL levels.

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Key words: Sulpiride, obesity, PRL

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Neuroendocrinology

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Prolactin Modulates Sexual Pheromone Perception and Accessory Olfactory Bulb Cell Activation In Female Mice

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Olfactory cues from opposite sex can induce neuroendocrine changes to promote sexual maturation and reproduction in female mice and prolactin (PRL) is one of the hormones involved. These signals are processed by the olfactory bulb (OB), mainly by the accessory olfactory bulb (AOB) region with a less contribution of main olfactory bulb (MOB). Previous reports showed expression of the prolactin receptor (PRLR) in the OB, but there was no clear evidence of the role of PRL within the OB in these reproductive events. In this work, we evaluate, by using qRT-PCR, the mRNA expression of PRL and the long isoform of PRLR (*Prl* and *Prlr-l)* along with the expression of the PRLR-L, through Western blot in the OB of female mice and serum PRL levels using ELISA. We evaluated three maturational stages: onset of puberty, sexual maturation (first ovulation) and adulthood. We found that although *Prl* and *Prlr-l* and serum PRL remain constant during these stages, the expression of PRLR-L in AOB is lower in adulthood compared with previous ages. Later, we evaluate the role of PRL in the processing of sexual pheromones. For this, acutely PRL treated adult female mice in estrous were exposed to sexual experienced male soiled bedding. Using immunohistochemistry, we quantified the number of positive cFos cells, a cell activation marker, the AOB and MOB and their first central projections, the medial amygdala (MeA) and the piriform cortex (PirC), respectively. Our results show that within the AOB, PRL prevents the increased mitral cell activation expected for the exposure pheromones; additionally, PRL promotes a higher activation in the anterior AOB, which is involved in the processing of sex pheromones. In this condition, PRL also promotes more activation in mitral cells in the dorsal MOB. In the central projections PRL augmented the cell activation of MeA but no in PirC. Finally, we evaluate the exploration trajectory of the mice during the pheromone exposure; finding that PRL augmented their exploration of the sexual olfactory stimulus. In conclusion, our results suggest that PRL might participate in the sexual maturation, since the PRLR expression is higher before adulthood; however, once adults, PRL could be participating in perception and behavioral responses triggered by male pheromones. This response could be mediated by the mitral cells within the AOB and MOB, but also by the MeA.
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Short-term administration of tibolone reduces inflammation and oxidative stress in the hippocampus of ovariectomized rats fed high-fat and high-fructose

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Background: Studies in animal models have shown that chronic consumption of a hypercaloric diet affects the hippocampus, a brain region critical for learning and memory processes. Various signaling pathways participate in neurodegeneration, where inflammation and oxidative stress are critical events. Also, neurodegeneration worsens with age, mainly after menopause. Hormone replacement therapy (HRT) helps to ameliorate menopause symptoms. Tibolone (TB) is a synthetic hormone with estrogenic, progestogenic, and androgenic effects on different tissues. **Aim:** We determined the effect of short-term TB administration on oxidative stress markers in the hippocampus of ovariectomized rats fed a high-fat-and-fructose diet (HFFD). **Methods:** Adult female rats were divided randomly into the following groups: intact and ovariectomized (OVX) groups were fed with a standard diet, OVX groups were fed with an HFFD consisting of 10% lard supplemented chow and 20% high-fructose syrup in the drinking water and administered vehicle or TB (1 mg/kg for seven days). Bodyweight, triglycerides and cholesterol, oxidative stress and inflammation markers, and the activity and expression of antioxidant enzymes were quantified in the hippocampus of each experimental group. **Results**: We observed that short-term TD administration significantly reduced body weight, AGEs, MDA levels, increased SOD activity, and GPX, improved in GSH/GSSG ratio, and reduced inflammation markers (IL-6 and TNF-α). **Conclusions:** Our results suggest that short-term administration of TB ameliorates oxidative stress and reduces inflammation caused by HFFD and early estrogenic decline. Keywords: Overnutrition; hippocampus; high-fat-and-high-fructose diet; oxidative stress; inflammation; estrogenic decline

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ÁREA: NEUROENDOCRINOLOGIA

Differential regulation of pituitary growth hormone expression and release by several neuropeptides among vertebrates

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The complex regulatory mechanisms that control pituitary growth hormone (GH) expression and secretion show important changes during vertebrate evolution, which involve differential roles of several peptides that act as either stimulatory or inhibitory GH secretagogues. Here, we analyzed the effect of various neuropeptides upon GH regulation in hemi-pituitary cultures derived from three vertebrate models: reptiles (green iguana), birds (chicken) and mammals (rat). Results showed that GHRH significantly stimulated both GH mRNA expression and GH secretion in rat and iguana, whereas in chicken only GH secretion was augmented. TRH increased GH secretion only in iguana, but stimulated GH mRNA expression in chicken and iguana. PACAP stimulated GH secretion in chicken and iguana, and GH mRNA expression in all three species. Ghrelin increased GH secretion in chickens and iguanas, but decreased it in rats, while it lowered GH mRNA levels in rats and iguanas. GnRH stimulated both GH mRNA expression and GH release in chicken pituitary cultures, whereas in iguana it only increased GH secretion. On the other hand, SST directly inhibited GH mRNA expression in iguana, whereas in the other species it significantly inhibited GHRH-stimulated GH secretion. It is known that the transcription factor Pit-1 regulates GH expression. We found that Pit-1 expression was increased by GHRH and TRH in rat and chicken pituitary cultures, while in iguana both GHRH and PACAP stimulated it with a greater increase. Furthermore, we analyzed the structure of GH promoters in each species to identify binding sites for Pit-1, and found that the rat GH promoter has 5, chicken 5, and anole, a close-related reptile to the iguana, has 8. We then analyzed the GH promoter activity of each species using the transfection-luciferase reporter assay and found the following response order: chicken > iguana > rat in cells transfected with the corresponding GH promoter. In conclusion, these results indicate that GH regulatory mechanisms have evolved differentially in vertebrates, and that variations in responsiveness to neuropeptide secretagogues could be explained, at least partially, by differences in the structure of the GH gene promoter between species.

Keywords: GH, regulation, vertebrates
Area: Neuroendocrinology
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Oxytocin/vasopressin-related neuropeptide distribution in ovaries of *Pogonomyrmex barbatus* ant

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Área: Neuroendocrinología

The neuropeptides oxytocin and vasopressin and their receptors are one of the best-studied signaling systems in vertebrates, where they are known to play major roles in regulating social and reproductive behaviors as well as memory and learning. However, their role in invertebrates is poorly understood because they are absent in the common insect model organisms fruitflies and honeybees. On the other hand, ants possess an oxytocin/vasopressin-related neuropeptide orthologue called inotocin, which provides a great opportunity to study its potential role in modulating social and reproductive behavior.

In the brains of ants, it has been demonstrated that the expressions of inotocin and its receptor change according to age, and it correlates with the propensity to perform certain tasks associated with age and caste. Division of labor in ants, is also known to correlate with ovarian activity; therefore, we are interested in knowing if inotocin has any role in the modulation of ovarian activity in ants of different ages and castes. In the present work, we compared the localization of inotocin in ovaries of young and old adult workers of the red harvester ant *Pogonomyrmex barbatus*, as well as in queens using immunofluorescence and microscopy techniques. We identified inotocin staining in the ant ovary, with qualitative variations between certain experimental groups.

Key words: inotocin, ants, ovaries

Oxytocin/vasopressin-related neuropeptide distribution in developmental stages and castes in the ant *Pogonomyrmex barbatus* brain

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Neuroendocrinology

Neuropeptidergic transmission systems such as the ones mediated by the oxytocin/vasopressin-related peptides are known to be essential for social behavior in various animal species and are conserved among many taxa, in both vertebrates and invertebrates. The distribution and function of the insect orthologue, inotocin, has been described in some ant species and has been implicated in the modulation of foraging behavior, resistance to desiccation, cuticular hydrocarbon synthesis and metabolism. Nevertheless, the distribution and presence of this peptide in ant neural tissue in different developmental stages and castes remains unknown. In the present work, we studied the immunostaining pattern of inotocin in red harvester ants, *Pogonomyrmex barbatus*, in different castes and developmental stages. We found that inotocin is present in the brains of larvae, pupae, young and old workers, and queens. Specifically, we found two cellular bodies and punctae of neuropeptide in the subesophageal zone in pupae, in young and old workers, and in queens. We also found punctae in other neuropils in the supraesophageal ganglion, including the mushroom bodies, optical lobe and the protocerebrum. These results suggest that inotocin distribution in ant nervous tissue is species specific and could play a broader role in modulating behaviors or physiology, regulated by different parts of the brain as well as during different developmental stages.

Neuropeptides, Social Insect Behavior, Oxytocin/vasopressin-related

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Neuropharmacology

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EFFECT OF PROBIOTICS ON FLUOXETINE AND SERTRALINE ANTIDEPRESSANT ACTIVITY IN LEARNED HELPLESSNESS MODELS IN MICE.

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Area: Neuropharmacology

Depression is a mental pathology, whose incidence is increasing globally and nationally. One of the most accepted hypotheses as etiology is the decrease in serotonin and other catecholamines in the brain pathways. Pharmacological treatment is serotonin reuptake inhibitors drugs (SRIs) administration like fluoxetine and sertraline, in order to increasing the amount of this mediator at the synaptic space in the pathways involved. However, at a clinical level, it has been reported that only in treatment with SRIs is it effective in 40% of diagnosed patients and that is why new treatments are being sought from combination with other drugs or alternative therapies. In this sense, and based on the evidence that the microbiota is connected to the brain and that some probiotics could have an impact on the balance of mediators such as serotonin and its metabolic predecessor, such as tryptophan, its use is proposed in order to achieve an antidepressant effect. In this study, the antidepressant effect of fluoxetine and sertraline administered alone or in combination with a commercial mixture of probiotics was evaluated using models of depressive behavior in mice, as well as the quantification of serotonin and tryptophan in brain and digestive areas.

The methodology consisted of 48 mice into six groups, of which group 1 and 2 received only the administration of water and probiotic ($2X10^8$ CFU) respectively, groups 3 and 5 received the administration of fluoxetine (18 mg /Kg) and sertraline (30 mg/K) and groups 4 and 6 received, in addition to the probiotic, fluoxetine and sertraline, respectively. The administration of probiotics was for 23 days in the drinking water and the administration of fluoxetine and sertraline in the last 7 days of treatment. Once this period was over, antidepressant behaviors were evaluated using the tail suspension and forced swimming tests. Subsequently, the mice were euthanized and the brain structures of the hypothalamus and brain stem were obtained, as well as the section of the jejunal intestine, serotonin and tryptophan were quantified by a high-resolution chromatography method. This study was approved by FCQ-UASP Ethical committee.

An antidepressant effect was observed due to the administration of the probiotic and whose effect is additive with the effect produced by fluoxetine and sertraline, however, this effect does not correspond to an increase in serotonin and tryptophane in brain areas such as the hippocampus, brain stem and jejunum, since perhaps other pathways are participating.

Clave words: probiotics, depression, fluoxetine, sertraline.

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Anxiolytic and hypnotic effect of methanolic extract of *Malphigia mexicana*

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Work area: Neuropharmacology

Introduction. *Malphigia mexicana* (Malpighiaceae) is a tree native to Mexico and its fruits are edible. It is used in traditional Mexican medicine to treat different diseases. Pharmacological studies of some plants of the Malphighiaceae family have shown sedative, antidepressant, anxiolytic, anticonvulsant, nootropic and learning enhancement effects (Huerta-Reyes et al., 2013). **Aim of the study**. To evaluate the pharmacological effect of the methanolic extract of *M. mexicana*, on the nervous system in *in vivo* models. **Material and methods**. The dried and ground material (150 g) was extracted with methanol (500 mL) by maceration for 3 days/3 times. The solvent was eliminated under reduced pressure distillation with a BUCHI R-215 rotary evaporator. The methanolic extract (EMMm) was administered to male CD-1 mice (100, 200, 400, 600 mg/kg, p.o., 24,18 and 1 h before testing) the negative control received only saline (p.o.). The tests to evaluate the effect at the central nervous system level were: Forced Swimming Test (FST), Elevated Plus Maze Test (EPM), Open Field Test (OFT) and Pentobarbital-induced Sleep Test (PST). A High Performance Liquid Chromatography (HPLC) analysis of EMMm was conducted on a Waters 2695 liquid chromatographer equipped with a Waters 2996 photodiode array detector. **Results and discussion**. A yield of 9.7% was obtained. In the EPM test the doses 100, 200, 400, 600 mg/kg of EMMm significantly increased the percentage of entries to the open arms when comparing to the negative control group ($p<0.001$), the doses 200, 400, 600 mg/kg significantly increased the percentage of time spent in the arms when comparing to the negative control group ($p<0.001$). In the OFT the doses 200, 400, 600 mg/kg significantly increased the number of total crossings when comparing to the negative control group ($p<0.001$), the doses 100, 200, 400, 600 mg/kg significantly increased the number of rearings when comparing to the negative control group ($p<0.001$). In the PST the EMMm doses 100, 200, 400, 600 mg/kg induced the loss of the righting reflex of mice modifying the latency and duration of pentobarbital-induced sleep significantly when comparing to the negative control group ($p<0.001$). The EMMm presented 6 peaks in the HPLC chromatogram and were compared with standards identifying Kaempferol glycoside and Quercetin glycoside and the other peaks according to their absorption correspond to other flavonols. These pharmacological effects may be due to the presence of flavonoids of the flavonol type, among which Kaemferol glycoside and Quercetin glycoside were identified, which have shown the same effects in other plants (Aguirre-Hernández et al., 2010; Pérez-Ortega et al., 2008). **Conclusions**. The EMMm exerted an anxiolytic-like effect in the EPM tests by modifying the parameters of percentage of entries to the open arms, percentage of permanence in the open arms, and in the OFT test by increasing the number of total crossings and rearings. The EMMm induced a hypnotic effect in the PST by producing loss of the righting reflex and modifying the latency and duration of pentobarbital-induced sleep.

Key words: anxiolytic, hypnotic, *Malphigia mexicana*.

References

Aguirre-Hernández, *et al*. (2010). HPLC/MS analysis and anxiolytic-like effect of quercetin and kaempferol flavonoids from Tilia americana var. mexicana. *J Ethnopharmacol, 127*(1), 91-97. doi: 10.1016/j.jep.2009.09.044

Huerta-Reyes, *et al*., (2013). Heteropterys cotinifolia: a neuropharmacological and phytochemical approach with possible taxonomic implications. *ScientificWorldJournal, 2013*, 870468. doi: 10.1155/2013/870468

Pérez-Ortega, *et al*. (2008). Sedative and anxiolytic efficacy of Tilia americana var. mexicana inflorescences used traditionally by communities of State of Michoacan, Mexico. *J Ethnopharmacol, 116*(3), 461-468. doi: 10.1016/j.jep.2007.12.007

Analysis of the effect of two hypoglycemic agents on long-term memory in diabetic BALB/c mice

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Area: Neuropharmacology

Alzheimer's disease (AD) is a neurodegenerative disease characterized by an insidious onset and gradual development of cognitive dysfunction. AD has recently been considered the third type of diabetes. Some epidemiological studies suggest that metformin treatment prevents cognitive decline in diabetics. Additionally, the use of salicylic acid as a hypoglycemic agent reduces cognitive impairment and decreases the prevalence of AD. Interestingly, the administration of streptozocin (STZ) in rodents mimics some relevant aspects of AD. Therefore, in this study, the effect of metformin and salicylic acid on long-term memory in diabetic BALB/c mice was evaluated. For this, 45 mice weighing between 20-30 g, treated with STZ (175 mg/kg, i.p.) were used. The animals were divided into two groups to which metformin and salicylic acid were administered orally for 5 days. All animals were subjected to the object recognition test before and after STZ treatment. The results of the object recognition test revealed that exploration time was longer on object 2 in all healthy animals, unlike diabetic animals whose exploration time was reduced by 54% indicating memory loss. This memory loss was reduced by 34, 13, and 30% with pretreatment salicylic acid (2.25 mg/kg) and metformin (200 and 800 mg/kg), respectively. However, with doses of salicylic acid 12.5 mg/kg and metformin 400 mg/kg, memory loss was greater by 79 and 60%, respectively. These results suggest that salicylic acid (2.25 mg/kg) and metformin (200 and 800 mg/kg) prevent STZ-induced memory loss at specific doses.

Keywords: Alzheimer´s disease; hypoglycemic agents; novel object recognition test

SEA ANEMONE *Bartholomea annulata* VENOM ACTIVES GABA$_A$ CHANNEL-RECEPTORS

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Neuropharmacology

The phylum Cnidaria are comprised of a large number of species, which include jellyfishes, corals and sea anemones. A characteristic of this phylum is the production of structures called nematocysts, these are capsules containing venom mainly used as weapons for hunting and defense. The main toxins identified in the venom are cytolysins and neurotoxins. Specifically in sea anemones, some neurotoxins have already been purified and characterized. Most neurotoxic substances reported act on sodium and potassium voltage-dependent ion channels expressed in the nervous system from different species, and have a potential therapeutic use. In this study we look for the effects caused by *B. annulata* venom, a representative of the Metridioidea superfamily that has not been studied so far. For this, different strategies were performed in order to identify possible molecular targets. First, effects of the crude extract (CE) were evaluated using electrophysiology in *X. laevis* frog oocytes, using either native oocytes or oocytes injected with rat brain mRNA that expressed diverse membrane proteins from the mammalian nervous system. Native oocytes did not respond to CE (n=3), while mRNA-injected oocytes (n=40), consistently generated a rapid activating smooth inward current response associated to an increase in membrane conductance. Current-Voltage (I-V) curves indicated that the current response elicited by CE was mainly carried by Cl^-. Several characteristics of the response recalled those commonly observed by activation of channel-receptors to GABA (GABA$_A$R). Thus, a direct action of CE on GABA$_A$R was confirmed on oocytes that were injected with the mRNA to express the receptors conformed by $\alpha1\beta2\gamma2$ (n=7), $\alpha3\beta2\gamma1$ (n=7) or $\rho1$ (n=7) subunits from mammals. Using ELISA assay, it was found that CE contained low nanomolar GABA concentration, amount that did not explain the activation of the GABA$_A$Rs tested, thus, this suggested that *B. annulata* venom contained a GABA$_A$R agonist, alternatively, CE could contain a potent allosteric modulator. This effect has not been reported for venoms from other cnidarians, and further experiments will be required to identify the toxin(s) responsible for this novel effect.

Key words: sea anemones, neurotoxins, GABA$_A$Rs

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Bunodeopsis globulifera toxins induce [3H]-glutamate release in rat cortex and decrease viability of human neuroblastoma cell line SH-SY5Y

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Animals venom is an important source of bioactive compounds, which disrupt the physiology of their prey or predators, mainly affecting the cardiac and neuromuscular systems, which is why they are of great interest to the research. Cnidarians (jellyfish and sea anemones, for example) produce potent toxins that can cause cytolytic and neurotoxic damage. Sea anemone neurotoxins can quickly immobilize their predators and have been described as having a high selectivity ion Na^+ and K^+ channels, so the study of these toxins has been directed to the development of future treatments for neurological diseases associated with ion channel dysfunction. *Bunodeopsis globulifera* is an abundant sea anemone in the Mexican Caribbean Sea, has been reported to cause serious injuries to the skin to those who have contact with this organism and is considered highly toxic specie.

B. globulifera was collected in the reef lagoon of Puerto Morelos, Q. Roo., and the crude extract (CE) was obtained by maceration and lyophilization. The biological activity assays in *Ocypode quadrata* crab, it was observed that the administration of the CE causes difficulty in controlling movement and death. By electrophoresis it was recorded that CE contains compounds between 5 and 150 kDa; those of low molecular weight suggest the presence of neurotoxic compounds, which are the objective of this study. In neurotoxicity assays, the release of [3 H] -glutamate in rat cortex using EC (50 µg/mL) significantly increased the release from the depolarizing pulse (30 mM KCl). On the other hand, EC also increased the release of [^{3}H] -glutamate relative to the basal release. Subsequently, the CE stimulated basal release was evaluated in the presence of EDTA (1 mM), where [$_3$H]-glutamate release was lower than baseline, indicating that the toxin stimulated release involves a calcium dependent mechanism, probably the target are sodium channels or directly opening of calcium channels. Locomotor activity in mice was decreased significantly by intraperitoneal administration of CE (100 and 500 mg protein/mL per kg). Finally, cell proliferation and apoptosis were evaluated in the presence of CE in the human neuroblastoma SH-SY5Y cell line and found that CE (10, 25, 50, 75 and 100 µg protein/mL) promoted a significant increase in cell proliferation; however, the CE also induces apoptosis (60%). The CE obtained from *B. globulifera* provoke neurotoxic effects on *Ocypode quadrata*, on rodents and on the human neuroblastoma SH-SY5Y cell line.

Key words: Sea anemone toxins, glutamate release, neuroblastoma cells.

Exogenous hydrogen sulfide improves hypertension induced by traumatic brain injury in rats through vasopressor sympathetic outflow inhibition and H_2S-synthesizing enzymes restoration.

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Area: Neuropharmacology

Traumatic Brain Injury (TBI) represents a critical public health problem worldwide that affects central and peripheral nervous systems regulating the cardiovascular system. Up to date, the therapeutic approaches for the treatment of TBI-induced cardiovascular impairments are limited. In this regard, hydrogen sulfide (H_2S), a novel gasotransmitter synthesized by cystathionine-γ-lyase (CSE), cystathionine-β-synthase (CBS), and 3-mercaptopiruvate sulfurtransferase (3-MST) enzymes, has been proposed as a neuro- and cardio-protective molecule. Therefore, this study was designed to determine the effect of subchronic treatment with NaHS (an H_2S donor) on H_2S-synthesizing enzymes, hemodynamic, and vasopressor sympathetic outflow impairments induced by TBI. For that purpose, animals were submitted to a severe TBI by the lateral fluid percussion injury model. The changes in CBS, CSE, and 3-MST protein expression in the hypothalamus and brainstem were measured by western blot, meanwhile, the hemodynamic variables and sympathetic activity were assessed by the plethysmographic method and the pithed rat model, respectively. Injured animals were treated with i.p. daily injections of NaHS, an H_2S donor, (3.1 and 5.6 mg/kg) during 7 days after TBI, starting one day after TBI induction. After severe TBI, the animals showed: (1) a decrease in CBS and CSE protein expression in the hypothalamus and brainstem; meanwhile, 3-MST protein expression diminished in the hypothalamus but not brainstem compared to the sham group; (2) an increase in heart rate, systolic, diastolic and mean blood pressure; (3) progressive sympathetic hyperactivity; and (4) a decrease on vasopressor responses induced by noradrenaline ($\alpha_{1/2}$-adrenoceptors agonist) and UK 14,304 (selective α_2-adrenoceptor agonist). Remarkably, NaHS administration (3.1 mg/kg) restored CBS and CSE but not 3-MST protein expression in the hypothalamus at day 7 post-TBI and re-established only CSE in brainstem 7 and 28 days after TBI. Furthermore, NaHS administration (3.1 and 5.6 mg/kg) after TBI prevented the development of the impairments in hemodynamic variables and decreased the sympathetic hyperactivity, as well as the noradrenaline-induced vasopressor responses. Taken together, our results show that NaHS: (1) restores CBS and CSE protein expression in a time- and tissue-dependent manner with no effect on 3-MST expression, and (2) ameliorates the hemodynamic and sympathetic system impairments observed after TBI. These findings shed further light on the potential therapeutic role of H_2S for systemic cardiovascular impairments observed after TBI.

Keywords: hypertension; traumatic brain injury; hydrogen sulfide

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Effect of hydrogen sulfide on the vascular dysfunction induced by severe traumatic brain injury in rats.

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Area: Neuropharmacology

Traumatic brain injury (TBI) is a condition that affects the central nervous system and leads to systemic impairments. Particularly in the cardiovascular system, the blood pressure is altered after a TBI. Indeed, hypertension is one of the most frequent comorbidities in TBI survivors. Moreover, hypertension is related to a decrease in hydrogen sulfide (H_2S) synthesis. Therefore, this study aimed to assess the effects of I.P. subchronic administration with NaHS, an exogenous H_2S donor, on the TBI-induced vascular impairments. Animals underwent a lateral fluid percussion injury, and thoracic aortas were obtained seven days after TBI induction. The vascular function was measured using isolated organ bath chambers. The Sensorimotor function was evaluated using the Neuroscore test. After seven days of the severe TBI induction, animals showed 1) a decrease in body weight, 2) sensorimotor dysfunction, and 3) vascular dysfunction characterized by a decrease in the vasorelaxation induced by carbachol and an increase in contraction induced by norepinephrine. Interestingly, NaHS subchronic administration (3.1 mg/kg; I.P.; every 24 h for seven days, starting 24 h after TBI induction) avoided TBI-induced vascular dysfunction by restoring carbachol-dependent vasorelaxation and norepinephrine-induced vasoconstriction with no effect on the body weight or sensorimotor impairments. These results suggest the use of NaHS as a therapeutic strategy to avoid post-TBI vascular dysfunction.

Keywords: hydrogen sulfide; vascular dysfunction; traumatic brain injury.
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Pharmacological evidence of the mechanisms involved in the hydrogen sulfide-induced peripheral neuronal modulation of the vascular tone

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Area: Neuropharmacology

Hydrogen sulfide (H_2S) is a gasotransmitter that modulates the peripheral transmission regulating the vascular tone. In this respect, it has been demonstrated that H_2S inhibits the vasopressor sympathetic outflow and stimulates the non-adrenergic noncholinergic (NANC) neurotransmission. However, the mechanisms that underlie these effects have not been investigated. Therefore, this study aims to evaluate the role of K^+ in H_2S-induced sympatho-inhibition, as well as the role of TRPA1 and TRPV1 channels in the increase of NANC transmission induced by H_2S. For that purpose, 54 male Wistar rats were anesthetized and pithed. The animals were divided into two main groups to evoke responses with the selective electrical stimulation of: (1) the vasopressor sympathetic outflow (T_7-7_9); and (2) the NANC neurotransmission (T_9-T_{12}). Group 1 received i.v. administration of K^+ channel blockers: (1) tetraethylammonium (non-selective; 16.5 mg/kg); (2) 4-aminopyridine (K_V; 5 mg/kg); (3) $BaCl_2$ (K_{IR}; 65 mg/kg); (4) vehicle (bidistilled water; 1 ml/kg); (5) glibenclamide (K_{ATP} channels; 10 mg/kg); or (6) glibenclamide vehicle (DMSO, NaOH 0.1 N and glucose 10%; 1 ml/kg) in presence of NaHS 310 μg/kg·min continuous infusion. On the other hand, group 2 received i.v. administration of TRPA1 and TRPV1 channel blockers: (1) HC030031 (TRPA1 channels; 18 μg/kg); (2) capsazepine (TRPV1 channels; 100 μg/kg); or (3) vehicle (DMSO 10%; 1 ml/kg) in the presence of NaHS 18 μg/kg·min continuous infusion. The sympatho-inhibition induced by NaHS was completely reversed by tetraethylammonium and glibenclamide, and to a lesser extent, by 4-aminopyridine and $BaCl_2$ administration. Furthermore, the increase of vasodepressor responses induced by NaHS was abolished by HC030031, a TRPA1 blocker, and remained unaffected after capsazepine, a TRPV1 blocker. These data suggest that: (1) H_2S-induced sympathoinhibition is mediated by K_{ATP} channels, and to a lesser extent, K_V and K_{IR} channels activation; and (2) activation of TRPA1 channels, but no TRPV1 channels, are responsible for the increase in the NaHS-induced NANC neurotransmission.

Keywords: hydrogen sulfide; potassium channels; TRPA1 channels.

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Identification of the locus underlying synaptic potentiation mediated by TrkB receptor activation in CA3 pyramidal cells of the hippocampus

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Area: Neuropharmacology

Brain-derived neurotrophic factor (BDNF) and its endogenous receptor, the tropomyosin receptor kinase B (TrkB), are widely expressed in the central nervous system, with the higher concentrations found in the region comprised of the dentate gyrus and hippocampal area CA3. Here, we studied the effects of TrkB activation on the excitatory postsynaptic current evoked at the mossy fiber - CA3 pyramidal neuron synapse (MF-EPSC). Whole-cell patch-clamp recordings were performed in acute hippocampal slices; bath perfusion of the TrkB specific agonist, 7,8-DHF, induced a concentration-dependent potentiation of the MF-EPSC that was depressed in the presence of the mGluR2-agonist, DCG-IV. Likewise, blockade of TrkB with the antagonist ANA-12 abolished the effects of 7,8-DHF. Nanomolar perfusion of 7,8-DHF increased the MF-EPSC amplitude without altering the paired-pulse ratio. When postsynaptic cells were held at -100 mV, 7,8-DHF failed to increase the MF EPSC amplitude, suggesting a postsynaptic mechanism for synaptic potentiation. On the other hand, millimolar concentrations of 7,8-DHF triggered a more robust potentiation, decreased the paired-pulse ratio, and was insensitive to voltage manipulations of the postsynaptic cell, indicating a presynaptic locus behind the synaptic potentiation. Our results provide novel information regarding the cellular locus underlying synaptic potentiation mediated by activation of TrkB receptors in the MF-CA3 synapse.

Key words**:** Synaptic plasticity; presynaptic mossy fiber potentiation; BDNF-TrkB

Characterization of hollow titanium dioxide nanospheres as a release device of biomolecules with the potential to induce axonal growth of human dopaminergic neurons

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Area: Neuropharmacology

Abstract:
Parkinson's Disease (PD) is characterized by the degeneration of the nigrostriatal pathway, which mainly consists of the loss of axons from dopaminergic neurons (DANs) that connect the substantia nigra (SN) and the striatum. Surprisingly, DANs have been detected in the SN of PD patients even after twenty years from initial diagnosis. These findings motivate the development of new strategies to regenerate the axons of DANs remaining in the SN and to direct DANs axonal growth toward the striatum for the regeneration of the nigrostriatal pathway. To achieve these goals, there is a need for the advancement of release devices with the capability to deliver factors that promote axonal growth and create a gradient between biomolecules and DANs, hence also directing axonal growth. In this work, hollow titanium dioxide nanoparticles (hTiO2) are synthesized and tested as release devices of creatine. First, hTiO2 are incubated with creatine, a neuroprotective molecule that promotes the axonal growth of corticospinal tract neurons. Then, the release of creatine is studied and characterized through transmission electron microscopy (TEM), Fourier-transform infrared analysis (FTIR), and ultra-violet spectrometry (UV). Preliminary results show that not only the hTiO2 morphology changes after the release of creatine, but the creatine remains in close proximity to hTiO2 and the concentration of creatine increases over time. After 24h incubation time, creatine is found to induce an increase on the viability of human DANs, but does not show an effect on axonal growth when compared to controls. These preliminary results suggest that hTiO2 are able to release creatine over time, but creatine alone cannot induce axonal growth of DANs. The potential usefulness of hTiO2 as a delivery device is encouraged by the results. Therefore, further studies must be performed to identify a biomolecule that not only is compatible with hTiO2, but is also capable of inducing axonal growth of DANs.

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Key words: Axonal growth; Drug release; Nanoparticles.

Orally administered silybin improves most of the biochemical and behavioral outcomes in the MPTP-induced parkinsonism murine model

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Parkinson's Disease (PD) is the second most frequent neurodegenerative disease with motor dysfunction secondary from lost dopaminergic neurons in the nigrostriatal axis in old patients. Actual choice therapy consists of levodopa; however, its long-term use promotes treatment resistance and secondary effects. Hence, it is necessary to find new therapeutic alternatives, such as neuroprotective agents. Among these alternatives is silymarin, due to its neuroprotective role by exerting its antioxidant, anti-inflammatory, anti-apoptotic properties, and its dopamine (DA) preserving effect in MPTP-treated mice.

To elucidate the role of silybin (Sb), the primary bioactive compound in silymarin, in the neuroprotection of silymarin in the PD context, Sb was administered orally to determine dopamine levels, biochemical markers, and behavior.

Mice received 30 mg/kg of MPTP intraperitoneally for five consecutive days to induce the PD model. On the same days, Sb was co-administered orally to evaluate its dose-dependent conservation of striatal DA at day seven post-treatment. The best DA conservative dose of Sb was used to evaluate the Sb effect on biochemical context: BDNF, TNFα, IL10, lipid peroxidation, and mitochondrial reduction capacity. Sb's effect on bradykinesia, gross and fine motor skills, equilibrium, and muscle strength were evaluated using pole, traction, beam, and nest building tests.

Results showed that oral Sb at 100 mg/kg dose conserved DA levels about 60%, higher Sb doses did not modify DA content, so 100 mg/kg was elected as the best dose to compare biochemical and behavioral tests. Sb preserved BDNF content, diminished TNFα to basal levels, and reduced lipid peroxidation in the striatum and substantia nigra in the MPTP mice. Sb preserved mitochondrial function in the substantia nigra of the MPTP group but had no effect in the striatum. Behaviorally, the Sb-treated MPTP group improved turning down and landing behavior in the pole test, demonstrating better gross motor skills and reduced bradykinesia in mice. Fine motor skills improved on Sb-treated MPTP mice, demonstrated in the beam test, where mice reduced their relative error index and higher escape ratio in beam and traction tests. Also, Sb improved equilibrium and muscle strength in MPTP mice.

100 mg/kg of Sb showed to be a potential alternative in PD treatment by exerting anti-inflammatory, antioxidant effects, BDNF and DA preservatory effects, and improving motor behavior in MPTP treated mice.
Key words: Silybin, Parkinson's disease, Neuroprotection.

Silica nanoparticles functionalized with folic acid and loaded with antineoplastic drugs for glioblastoma multiforme

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Glioblastoma multiforme is known as the most frequent and malignant tumor of the central nervous system, which develops and originates from glial cells of the brain. Despite the advances in the treatment, the median survival of patients is around 15 months. In this study we show the synthesis, characterization, drug release and biological effect of silica nanoparticles functionalized with folic acid and loaded with cisplatin or temozolomide as a targeted release system to glioblastoma cancer cells. The SiO_2 nanoparticles were synthesized by the Stöber method using hexadecyltrimethylammonium bromide as the templating agent, which was finally removed by calcination at 550 °C. The folic acid was chemically anchored to the silica nanoparticles surface by a carbodiimide reaction. Homogeneous and well-defined nanoparticles with well distributed and homogeneous porosity were obtained. The spectroscopic results show the proper functionalization of the nanoparticles; SiO_2 nanoparticles showed high surface area and large pore size. An *in vitro* cisplatin and temozolomide release test were evaluated using artificial cerebrospinal fluid. The cytotoxic effect of temozolomide-SiO_2 nanoparticles was dose-dependent and clearly increased the effect of the drug alone in two human glioblastoma cell lines U87 and LN18. These results, suggest that these mesoporous silica nanoparticles obtained offer new properties such as targeted delivery, controlled release, improved bioavailability, and cellular uptake. Further the functionalization with folic acid can differentiate between cancer and healthy cells.

Área: Neurofarmacología

Palabras clave: glioblastoma multiforme, temozolomide, cisplatin

Anticonvulsant and nervous system stimulant effect of *Ehretia tinifolia* extracts

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Work area: Neuropharmacology

Introduction. *Ehretia tinifolia* (Boraginaceae) is a tree native to the humid and sub-humid tropical regions of the American continent. In traditional Mexican medicine it has been used to calm the nervous disorders (Niembro, *et al*., 2010). **Aim of the study**. To evaluate the pharmacological effect of two extracts of *E. tinifolia* on the central nervous system. **Material and methods.** Dried and ground material (150 g) was extracted with methanol and acetone (500 mL, each separately) by maceration for 3 days/3 times. The solvent was eliminated by distillation under reduced pressure with a BUCHI R-215 rotary evaporator. The methanolic extract (EMEt) was administered to male CD-1 mice at doses of 100, 200, 400, 600 mg/kg, p.o., 24,18 and 1 h before the test, the negative control received only saline (p.o.). The models to assess central nervous system activity were: Forced Swimming Test (FST), Elevated Plus Maze Test (EPM), Open Field Test (OFT) and Pentobarbital-induced Sleep Test (PST). The acetone extract (EAEt) was administered to male CD-1 mice at doses of 50, 100, 150, 200, 250 mg/kg, p.o., 24,18 and 1 h before the test, and subjected to Pentylenetetrazol-induced Seizure Test (PTZt). A High-Performance Liquid Chromatography (HPLC) analysis of EMEt was conducted on a Waters 2695 liquid chromatographer equipped with a Waters 2996 photodiode array detector. **Results and discussion**. The yield of EAEt is 3.06% and of EMEt is 8.36%. In the FST the doses 100, 200, 400, 600 mg/kg of EMEt significantly increased immobility time when compared to the negative control ($p<0.001$). In the OFT the doses 200, 400, 600 mg/kg significantly increased the total number of crossings when compared to the control ($p<0.001$) and the doses 100, 200, 400, 600 mg/kg significantly increased the number of rearings when compared to the negative control ($p<0.001$). In the EPM test the doses 200, 400, 600 mg/kg of EMEt significantly increased the percentage of entries to the open arms ($p<0.05$), the doses 100, 200, 600 ($p<0.05$) and 400 ($p<0.001$) mg/kg, significantly increased the percentage of time spent in the open arms compared to the negative control group. In the OFT the doses 200, 400, 600 mg/kg of EMEt significantly increased the total number of crossings ($p<0.001$), the doses 100, 200, 400 and 600 mg/kg significantly increased the number of rearings, compared to the negative control group ($p<0.001$). In the PTZt, the doses 50, 100, 150, 150, 200, 250 mg/kg of EAEt induced a significant decrease in the frequency of clonic seizures when compared to the negative control ($p<0.001$) and protected 100% of the survival of the mice, a significant result when compared to the negative control group ($p<0.001$). EMEt extract, presented 5 peaks in the HPLC chromatogram and were compared with standards identifying ferulic acid and the other peaks according to their absorption correspond to other phenolic compounds. The pharmacological effect of EMEt and EAEt on the nervous system may be due to the presence of phenolic compounds such as ferulic acid, which has been reported to have potential in the treatment of neurological diseases due to its antioxidant and neuroprotective capacity (Thapliyal et al., 2021). Ferulic acid has been shown to have an anticonvulsant effect in the PTZ-induced seizure model (Amini-Khoei et al., 2021). **Conclusion**. EMEt extract, exhibits a central nervous system stimulant effect by modifying spontaneous motor activity in the FST, EPM and OFT models. EMEt extract, did not induce a hypnotic effect in the PST. EAEt extract, showed an anticonvulsant effect by decreasing the frequency of clonic seizures and reducing the mortality of mice to zero.

Key words: anticonvulsant, stimulant, *Ehretia tinifolia*.

References

Amini-Khoei, et al. (2021). *J Basic Clin Physiol Pharmacol*. doi: 10.1515/jbcpp-2020-0496

Niembro, et al. (2010). *Árboles de Veracruz. 100 especies para reforestación estratégica.* Xalapa, Veracruz, México: Seretaría de Educación-Gobierno del Estado de Veracruz.

Thapliyal, et al. (2021). *Neurochem Res, 46*(5), 1043-1057. doi: 10.1007/s11064-021-03257-6

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Functional expression of the oligodendroglial α3β2γ1 $GABA_A$ receptor in HEK293 cells

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The $GABA_A$ receptor ($GABA_AR$) is the ionotropic receptor activated by γ-aminobutiric acid (GABA). There is evidence that GABAergic signaling modulates the myelination process through $GABA_AR$ activation expressed in oligodendrocytes (OLs). Recently, our data strongly suggested that the $GABA_AR$ in OLs is composed by α3β2γ1 subunits. When the properties of the α3β2γ1 receptor were explored in detail using heterologous expression in *Xenopus laevis* oocytes, most characteristics were similar to those described for the endogenous $GABA_A$ receptor, however, some absolute values were distinct.

To explore the properties of the OLs $GABA_A$ receptor in a closer cellular microenvironment, in this study the coding sequences of rat α3β2γ1 subunits were subcloned into the pcDNA3.1 vector and transfected in HEK293 cells. Then, cells were monitored electrophysiologically using the patch-clamp technique in whole-cell configuration, to compare the pharmacological and functional characteristics of the expressed receptors with those obtained in the *Xenopus laevis* oocytes and with the endogenous receptor.

The results showed expression of a $GABA_AR$ composed by α3β2γ1 subunits since it had low sensitivity to GABA, it was inhibited by Zn^{2+} and potentiated by β-carbolines and diazepam, characteristics of the endogenous $GABA_AR$ in OLs. The results shown should be taken into consideration when studies of heterologously expressed receptors from OLs are carried out, since they showed that pharmacological and functional characteristics of this receptor may be different compared with the endogenous receptor depending on the expression model used.

Neuropharmacology

Keywords: $GABA_A$ receptor, Oligodendrocytes, HEK293, Xenopus oocyte.

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NPY-Y_1 receptors in dorsal periaqueductal gray modulate food, sucrose and alcohol consumption in pre-exposed and free food and water access rats

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ABSTRACT

Periaqueductal gray (PAG) is a well-documented midbrain region on integrated defensive responses and anxiety-like behavior. Recently PAG was linked to drugs/alcohol consumption, mainly in the relapse state and associated with anxiety. Interestingly, NPY is probably the major endogen neuropeptide with orexigenic action mediated mainly by NPY-Y_1 and NPY-Y_5 receptors. Herein, we addressed the role of the NPY-Y_1 receptors in the dorsal (D)-PAG on food, sucrose and alcohol consumption in water and food free access male Wistar rats. A twice repeated sucrose-fading paradigm since juvenile age as the alcohol intake initiation procedure was performed in other group of rats. Present results show that injected intra D-PAG NPY significantly increased both the food and sucrose intake and decreased the alcohol consumption in a free-choice sucrose and alcohol fluid access model. Furthermore, intra D-PAG of a selective NPY-Y_1 receptor antagonist BIBP3226 produced the opposite effects that those by NPY. Our results suggest that NPY-Y_1 in D-PAG may be a target for the orexigenic and alcohol intake preventive actions of NPY.

Keywords: Periaqueductal gray, NPY, BIBP3226, alcohol intake.

Effects of pioglitazone in an experimental animal model of Attention-Deficit/Hyperactivity Disorder

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Attention-Deficit/Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder in childhood, highly prevalent, multifactorial, and clinically heterogeneous, characterized by symptoms such as hyperactivity, impulsivity, and inattention. The worldwide prevalence of ADHD is estimated to be 5.9% in children and adolescents. ADHD has been associated with an imbalance in the dopaminergic pathway, involving it in the pathophysiology. Recently, there has been an increasing interest in the mitochondrial dysfunction and oxidative stress in ADHD and its potential to contribute to the pathophysiology of the disorder (BBA Clinical, 6:153, 2016; Antioxidants, 9, 1039, 2020; Antioxidants, 9 (2), 176, 2020). Pharmacotherapy with psychostimulants such as methylphenidate (MPH) is currently the most common treatment for ADHD, however, it has been shown that MPH produces changes in the neurotransmission of several brain regions involved in motivation, behaviour, cognition, appetite, and stress, likewise favoured the increase of oxidative stress, and altered the activity of several antioxidant enzymes (J. Neurosci. 27:27, 2007; Brain Res. 1078:189, 2006; Neurochem. Res. 33:1024, 2008). Therefore, seeking adjuvant therapies with drugs commonly used in the clinic that could help to counteract oxidative and/or bioenergetic damage in ADHD, we have studied whether pioglitazone which is a PPARγ agonist, has neuroprotective mechanisms through the activation of antioxidant pathways or mitochondrial biogenesis in neonatal 6-OHDA lesioned rats as a model of ADHD. Therefore, at postnatal day 7 rats were lesioned at the right striatum with 6-OHDA. Afterwards, at postnatal day 25, behavioural tests were performed before pioglitazone was administered. Next, after 14 days of pioglitazone treatment, we repeated these behavioural tests to assess the effect of pioglitazone. Our data showed that pioglitazone did not show significant changes in the behavioural tests performed but showed an increase in the expression of proteins involved in the mitochondrial biogenesis in the striatum, prefrontal cortex, hippocampus and cerebellum; In addition, an increase was observed in the expression of Nrf2 mainly in the striatum, prefrontal cortex and cerebellum; however, there was no change in other antioxidant enzymes. Thus, pioglitazone treatment exhibited partial inhomogeneous beneficial effects on mitochondrial biogenesis and in the Nfr2 pathway in the brain of neonatal 6-OHDA lesioned rats but, appears to not affect the behavioural activity.

Keywords: ADHD; pioglitazone; mitochondrial biogenesis; 6-hydroxydopamine
Area: Neurofarmacología

V

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Enrichment environment improves memory and synaptic plasticity in cognitively impaired animals due to chronic exposure to a high-fructose and high-fat diet.

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Cognition and behavior; Cellular plasticity and neural circuits; Metabolism; Integrative Neurophysiology.

Abstract:

Metabolic deregulations like the excessive accumulation of body fat, hyperglycemia, and overweight are considered a risk factor for the development of cognitive and neuronal plasticity impairment. The mechanisms underlying these declines are unknown. However, several studies indicate that chronic exposure to high-calorie diets affects spatial memory, neuronal plasticity and reduces the catecholaminergic levels in hippocampus. Catecholamines act as neuromodulators for the formation of declarative memory and neuronal plasticity. Increasing catecholaminergic levels with an intra-hippocampal microinjection of nomifensine in rats that were chronically exposed to high-calorie diets recovers memory and synaptic plasticity, showing that the restoration of dopaminergic activity can reverse the deterioration of recognition memory and long-term plasticity. However, it is not known whether implementing an alternative treatment that increases catecholamines in hippocampus such as environmental enrichment, reverse the negative effects of chronic consumption of these diets on synaptic plasticity and memory. To test this hypothesis, a group of male mice were exposed to a high-fructose and high-fat diet for 6 months and compared to a control group of male mice exposed to standard diet for the same number of months. Cognitive performance was evaluated with the object location memory task and neuronal plasticity was evaluated by long-term potentiation on the perforating to dentate gyrus pathway. The high-fructose and high-fat diet caused an increased in adiposity and glucose intolerance, constituting a model of metabolic deregulation. The behavioral results indicate an impairment of the spatial memory and long-term potentiation shows a deficiency in the synaptic strength in mice with high-fructose and high-fat diet. In addition, a 6-month enrichment environment consisting in a constant replacement of toys of different sizes, colors, shapes, and textures in mice with high-fructose and high-fat diet produced an increase in synaptic strength like controls. Likewise, mice with metabolic deregulations treated with enriched environment behaved similarly to controls in spatial recognition memory tests. These results show that the enriched environment prevents the deterioration of recognition memory and long-term plasticity. These results will help to lay the foundations for the development of a treatment for the deterioration of memory associated with chronic consumption of a hypercaloric diet.

Key words: Hypercaloric diets; Enrichment environment; Memory improvement.

The Suprachiasmatic nucleus controls sleep delay-induced hyperglycemia.

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Sleep during the correct circadian period is critical for health. In experimental rodents, sleep delay can induce glucose intolerance, which mechanisms are still unknown. The suprachiasmatic nucleus (SCN) regulates circadian rhythms promoting a decrease in circulating glucose coinciding with the onset of the sleep phase and high SCN neuronal activity. Specifically, vasopressin (VP) release from the SCN, rises in the cerebrospinal fluid two hours before the onset of the resting period. We recently demonstrated that the communication of VP-SCN neurons with the arcuate nucleus (ARC) is essential to promote low systemic glucose levels before sleep onset.
We hypothesized that glucose intolerance observed during acute sleep delay, is mediated by changes in VP-SCN signaling to the ARC. To investigate this, we induced sleep delay by placing adult male Wistar rats in a slowly rotating wheel (one revolution every 3 minutes) for 2 hours at the beginning of their rest phase. We found this to induce basal hyperglycemia, a decrease in VP-SCN neuron activity measured by c-Fos, as well as the VP immunoreactivity. In the ARC, the glucose transporter GLUT1 was also decreased. Our data agree with previous findings in which administration of an VP receptor antagonist results in GLUT1 decreasing and the ARC and increasing systemic glucose levels.
VP-SCN neuronal activity is easily disturbed and that alterations in its input to target brain areas including the ARC could be responsible of hyperglycemia and, probably other metabolic disturbances such as insulin resistance. Our study contributes to the understanding of how sleep restriction, social jetlag or shift work impair metabolism by the disrupting the communication between the circadian system and hypothalamic regions involved in metabolic regulation.
Keywords: suprachiasmatic nucleus; arcuate nucleus; glucose

Area
Integrative Neurophysiology

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Cortical effects of facial palsy in motor planning of facial expressions in a murine model

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Facial palsy can be defined as the partial or complete loss of function of some or all of the structures innervated by the facial nerve, a fundamental structure for the communication of emotions. Thus, the functional impairment (as occurs in facial palsy) can significantly lose the quality of life. Interestingly, rodents use their orofacial musculature to express long-lasting internal states and convey emotions through facial expressions. In murine models, it has been observed that pyramidal neurons of the anterolateral motor cortex (ALM) project to subcortical structures to control facial movements (facial retraction and vibrissae movements). It is considered a structure that anticipates, prepares, plans, and executes movements, mainly in the licking and vibrissae movements. Facial palsy alters the face musculature; in murine models, angles formed by the vibrissae movements are lost, and there is an inability to close the eyelids of the eye; that at the cortical level, it is represented as electrophysiological changes in the primary motor and somatosensory cortex; specifically prolonged disinhibition in both hemispheres and a decrease in the firing rate of pyramidal neurons. As can be seen, facial palsy has cortical effects that control the movement of the facial muscles, resulting in a loss of the generation of facial expressions, which are voluntary movements that are anticipated, planned, and send information to executing centers through the ALM. However, alterations in these processes have not been studied in depth when there is experimental facial palsy and how it correlates with the loss of the correct execution of facial expressions. Extracellular neuronal activity of ALM is evaluated with an array of electrodes; at the same time, the facial expressions and whiskers movements of mice (a control group, one with reversible facial paralysis and other with irreversible facial palsy) were video-recorded while they were subjected to a behavioral predictive consumption of a solution rewarding (sucrose) task. Video recordings were made daily until recovery from the reversible pattern of palsy. The results show that reversible facial palsy is maintained from the time of injury up to 11 days later. In the case of the irreversible model, loss of motion persists throughout the experimental protocol. Two models of palsy show a loss in the vibrissae dynamics movements of the study subjects. This loss of vibrissae movements correlates with the inability to generate facial expressions related to consuming a rewarding substance. To conclude, the neural correlates of these two results with alterations in ALM will be sought, which will lead us to demostrate that the preparation, anticipation, planning and execution of facial expressions caused by facial palsy are affected.

Key words: Facial palsy, antero-lateral motor cortex, facial expressions

In Vivo Wireless Optogenetic Control of Skilled Motor Behavior

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Área: Neurofisiología Integrativa

Motor-skilled behavior is present during most of the movements we perform in everyday life, and it is known to be affected in several brain disorders. Reaching and grasping objects is part of our routine movements, and it is one of the first motor skills acquired during early development and refined during later years. In mice, the single pellet reach-to-grasp task is characterized for several phases that can be analyzed separately.

Optogenetics has been a dominant tool for dissecting the contribution of neuronal subpopulations, as it enables selective and targeted activation or inhibition. The combination of optogenetics with behavioral assays sheds light on the underlying mechanisms of specific brain functions. However, traditional wired systems restrict animals' behaviors during tasks. Our protocol combined a wireless optogenetic approach with high-speed videography in the reach-to-grasp task, to dissect the contribution of neuronal subpopulations in the striatum to fine motor behavior.

For this protocol a Cre-dependent adeno-associated virus was injected and an LED cannula was placed into the dorsolateral striatum of Drd1-Cre transgenic mice. After recovery, mice were trained to reach for and grasp a single food pellet from a small plastic shelf located outside the test chamber. On test day, the LED cannula was manually activated to stimulate Drd1-expressing neurons during the reaching phase, while it was recorded with high-speed videography for later kinematics analysis. Upon the completion of the experiment, the placement of the LED cannula was histologically confirmed.

Our results showed that the contralateral activation of D1 dopamine expressing spiny projection neurons (SPNs) reduced grasping success and increased the traveled distance compared to control conditions. These differences lead to the incapability of mice to target the pellet. While the activation of ipsilateral SPNs increased the trajectory dispersion without affecting reaching success, distance traveled and velocity.

The possibility of selectively manipulating neuronal populations in freely moving animals with minimal invasive techniques makes it possible to dissect the contribution of specific neuronal types in precise behavioral tasks. Conserved brain structures are known to participate in the different phases of the reach-to-grasp task, so revealing the neural circuitry underlying this behavior will increase our understanding of motor control.

Keywords: optogenetics, reach-to-grasp, motor skills

Dietary restriction blocks epileptogenesis by preventing the increase in low-frequency bands and IL-1β expression by hippocampal kindling

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Epileptogenesis and epilepsy results from the over-expression of Interleukin 1 Beta (IL-1β) and the activation of IL-1R1/TLR4 and NMDA receptors. Among the alternative therapies to treat epilepsy are those of metabolic nature such as dietary restriction (DR). DR induces the production of beta-hydroxybutyrate (β-HB) that blocks inflammasome protein 3 preventing the formation of caspase-1 and the subsequent maturation of IL-1β. The objective of this work was to evaluate the effect of dietary restriction on epileptogenesis. Adult Wistar rats were used. Four experimental groups were made: Group AL, fed ad libitum throughout the experimental period, Group RA/AL, fed with food restriction for 21 days and subsequently ad libitum until the end of the study, Group AL/RA fed ad libitum for 21 days to then be fed with food restriction until the end of experiment and Group RA, fed with food restriction throughout the experimental period. The hippocampal kindling model was used to induce epileptogenesis. The concentration of ketone bodies in blood was quantified. Electroencephalographic recordings were made during the kindling process. At the end of the experimental phase the animals were sacrificed, brain was removed and processed for IL-1β immunohistochemistry. Dietary restriction produced an increase in ketone bodies in the blood [$F(3, 112) = 13.88$, $P<0.0001$]. Food restriction induced antiepileptogenic effects since it inhibited behavioral presence of generalized seizures acording to the Racine scale [$F(35, 1008) = 21.92$, $P<0.0001$] respect to the AL group in rats in process kindling. On the other hand, the antiepileptogenic effect of the DR was associated with a decrease in delta bands and an increase in alpha and beta bands [$F(3, 560) = 1653$, $P<0.0001$], associated with a decrease in IL-1β expression. These results support the hypothesis that ketone bodies produced by food restriction such as β-HB, could modulate the inflammatory signals, which contributes to understanding the molecular mechanisms involved in the control of epileptic seizures. We can conclude that dietary restriction could be an auxiliary preventive therapeutic tool to control or delay the epileptic or epileptogenic process respectively.

Keywords: Epileptogenesis, Inflammation, Food Restriction.

Neuronal representation of oral ethanol administration in orbitofrontal cortex of sedated naïve mice.

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Área: Neurofisiología integrativa

Abstract

The orbitofrontal cortex (OFC) is a structure related to compulsive behavior, characteristic in the development of addictions. OFC changes its neuronal activity to acute and chronic exposure to ethanol which has appetitive and aversive taste qualities. OFC could encode concentrations-dependent taste elements of ethanol when administered orally for the first time (naïve mice); however, it has not been demonstrated. To answer this question, we evaluated OFC neurons that respond to oral stimulation with ethanol; a temporal analysis protocol was used (*in three window times: earl, middle and late*) in C57BL/6 mice under sedation. The neurons in OFC respond to the different concentrations of ethanol administered. A modulation map dependent on the time stage analyzed is shown. On a population basis, an increase in firing rate is observed at an early stage after stimulation with different ethanol concentrations. Finally, percent of neurons in OFC through the windows time and modulations in response to managed solutions can be showed. These results show that OFC's neuronal modulation depends on the time stage and the concentration of ethanol administered in sedate naïve mice, i.e., animals that had never consumed this substance.

Key Words: Ethanol, Taste, Electrophysiology.

V

Neurobiology Meeting of the Mexican Society for Biochemistry

Neuroimmunology

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Influence of maternal immune activation on synaptic transmission mediated by metabotropic glutamate receptors at the mossy fiber-CA3 synapse.

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Area: Neuroimmunology/Neuropathology disorders.

Maternal immune activation (MIA) caused by exposure to pathogens during critical periods of neurodevelopment is a significant risk factor for behavioral deficits and psychiatric illness in the offspring. The MIA-resulting effects include cognitive and behavioral abnormalities, a phenomenon mimicked by bacterial endotoxin or lipopolysaccharide administration. However, dysregulation of the neuronal activity, including the glutamatergic transmission between dentate gyrus and area CA3 of the hippocampus, is barely explored under this pathological situation. Indeed, this work explored synaptic alterations of the glutamatergic transmission at the hippocampal mossy fiber to CA3 pyramidal cell synapse (MF-CA3). Extracellular recordings performed in acute hippocampal slices obtained from MIA-induced animals revealed that MIA triggers a decrease in the synaptic strength of the MF-CA3 transmission and decreased paired-pulse facilitation. Consistent with this finding, the ratio between the presynaptic fiber volley and the MF-EPSP amplitude is reduced in MIA-induced animals. Also, frequency-facilitation of the MF-EPSP, a key feature of this glutamatergic synapse, exhibited decreased levels in the MIA-induced animals. In another group of experiments, pharmacological stimulation of group I metabotropic glutamate receptors (mGluRs) with DHPG induced depression of the synaptic response, whereas MIA-induced animals exhibited a biphasic effect: a stronger but temporary depression, followed by potentiation of the MF-CA3 synaptic response. On the other hand, long-term depression (MF-LTD) induced with low-frequency stimulation and mediated by activation of presynaptic group II mGluRs, did not exhibit further alterations in MIA-induced animals. Together, these results suggest a dysregulation in the presynaptic MF terminals and altered functionality restricted to the postsynaptic metabotropic glutamate receptors expressed in area CA3 of the rat hippocampus.

Keywords: Maternal immune activation, glutamatergic transmission, Mossy Fibers, hippocampus.

KChIP3 impairs memory in the Alzheimer's disease mouse model 5XFAD

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Alzheimer's disease (AD) has become a priority public health problem, due to the trends of increasing cases that are expected for the next 30 years. Today it is known that the deposition of senile plaques is one of the causes by which the inflammatory environment is exacerbated, inducing neuronal death in brain regions involved in learning and memory. However, the molecular mechanisms underlying this inflammatory process are poorly understood. In this sense, increased levels of KChIP3 in the brains of postmortem AD patients and in AD mouse models have been reported. KChIP3 is a neuronal protein able to interact with the presenilins 1 and 2 of the γ secretase complex which is responsible for generating the beta amyloid peptides (βA). In addition, KChIP3 is also a transcription factor that regulates positively and negatively gene expression. Therefore, here we propose that KChIP3 participate in the development of AD on one hand, by stimulating βA deposition, and on the other hand, through its transcriptional activity maintaining an inflammatory state that negatively impacts cognitive functions. To test this hypothesis, we knock out the expression of KChIP3 in the AD mouse model 5XFAD (5XFAD/KChIP3 KO). We characterized the phenotype of the 5XFAD/KChIP3 KO mouse by evaluating in the brain, the pro- and anti-inflammatory profile, the accumulation of the insoluble βA plaques and the learning and memory capacity by a number of memory and learning paradigms.

To characterize the molecular mechanisms regulated by KChIP3 fulling AD progression, we performed quantitative proteomic analysis (iTRAQ) from hippocampus samples derived from WT, 5XFAD, KChIP3 KO and 5XFAD/KChIP3 KO animals. The proteomic data were confirmed by an *in vitro* approach (FASS-LTP) to evaluate long-term potentiation (LTP), a form of synaptic plasticity considered as the cellular mechanism for memory formation. Current experiments are aimed to further confirm the KChIP3 mediated AD progression.

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Area: Neuroimmunology.

Keywords: Neuroinflammation, KChIP3, Alzheimer´s disease

Effect of thermal stimulation on macrophage subpopulations in a murine sepsis model

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Área: Neuroinmunología

Previous anti-inflammatory strategies against sepsis, a leading cause of death in hospitals, had limited efficacy in clinical trials, in part because they targeted single cytokines and the experimental models failed to mimic clinical settings. Neuronal networks represent physiological mechanisms selected by evolution to control inflammation, that can be exploited for the treatment of inflammatory and infectious disorders. We report that ST36 acupunctural point activation with thermal stimulation (fire needling) controls systemic inflammation and induces macrophage anergy in polymicrobial peritonitis. To characterize the effect of thermal stimulation at ST36 (TE-ST36) on serum TNFα, survival rates, and macrophage and polarization, a sepsis model was induced in C57/BL6 mice using cecal ligation and puncture (CLP). The septic mice were subsequently treated with TE-ST36 (CLP+ST36), and serum samples were collected and analyzed for cytokines levels. The serum TNFα levels in the CLP+ST36 group were significantly lower (p<0.0001) compared with the group without treatment, however, the survival rates were significantly lower (p<0.05). On the other hand, spleen samples were obtained in order to evaluate macrophage polarization by flow cytometry. Immunophenotype of macrophages (F4/80+) M1, M2, and M2a subpopulation was determinate in the experimental groups. The percentage of M2a macrophages were in CLP-ST36 was significantly higher compared (p<0.01) with the group without treatment. In conclusion, in CLP mice model, the thermal stimulation induces anergy of spleen macrophages that diminish the cytokines levels and survival rates.

Key Words: Neuroimmunology, Thermal stimulation, Macrophages

Catecholaminergic neuroimmunological system in the dental pulp

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Área: Neuroinmunología

Neuroimmunology is relatively a recently developed scientific discipline, which studies the inter-relationship between the nervous and the immune system. Neuroimmune control pathways have been extensively described in various pathological models *in vivo*. In the last 10 years, various communication pathways have been discovered that can modulate the inflammatory response. The nervous system may play an important role in defense mechanisms and local tissue remodeling. However, at the moment, there is poor knowledge about those mechanisms in the human dental pulp. When pulpal inflammation occurs, it triggers a painful response due to this tissue is highly innervated. In addition, multiple subpopulations of immune cells with specialized functions have been reported. Therefore, both systems may be in communication through these neuroimmune control mechanisms. This project aimed to evaluate the expression of neurotransmitters receptors in innate immune cells from dental pulp and their plausible relationship with neuroimmune control pathways. We hypothesized that the catecholaminergic neuroimmune pathway in dental pulp is present. That could demonstrate by determining the expression of catecholamines surface receptors on immune cells from pulp tissue as well as the anatomical interaction of these systems. In addition, we hypothesized that there is an effect of catecholaminergic neurotransmitters on cell differentiation and the production of pro- and anti-inflammatory cytokines in innate immune cells from dental pulp tissue. That could demonstrate by determining the expression of catecholaminergic receptors on the surface of immune cells of dental pulp by immunohistochemistry. Dental pulp tissue samples were incubated with primary antibodies at appropriate dilution, specific markers associated with immune lineage cells, and antibodies for α2, β2 catecholaminergic receptors. The results showed the presence of catecholaminergic receptors in the human dental pulp.

Keywords: Dentistry, Dental pulp, Neuroimmunology

Maternal immune activation impairs morphophysiological properties of CA1 pyramidal neurons from dorsal hippocampus of the offspring

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Area: Neuroimmunology/Neuropathology

Maternal immune activation (MIA) is nowadays associated with an increased risk for neuropsychiatric disorders in the offspring. Mouse models of MIA employing immunogenic molecules, whether lipopolysaccharide (LPS) or poly I:C, induce neurobiological and behavioral alterations relevant to schizophrenia and autism spectrum disorders. However, the effects of these models on the neurophysiology and geometric properties of neurons have been barely explored. Therefore, we analyzed cellular and synaptic physiology and the morphology of CA1 pyramidal neurons from the dorsal hippocampus of the offspring of LPS- and saline-treated dams. Compared to control cells, CA1 pyramidal neurons from LPS-treated dams display increased intrinsic excitability, characterized by a higher membrane resistance and firing frequency. Also, we found changes in the kinetics of the action potential waveform, such as the hyperpolarization of the firing threshold and broadening of the action potential spike. Increased excitability is partially explained by decreased A-type potassium current functionality. To assess the morphological properties of CA1 pyramidal neurons, we performed a complexity analysis of digital reconstructions from biocytin-filled neurons. We found a decrease in dendritic intersections, the total length of dendritic cable, and the dendritic complexity index. Lastly, we analyzed spontaneous excitatory and inhibitory synaptic activity by analyzing the excitation/inhibition balance (E/I-balance) of CA1 pyramidal neurons. Compared to control cells, CA1 pyramidal neurons from offspring of LPS-treated dams exhibited increased amplitude of spontaneous excitatory postsynaptic currents (sEPSC) without changes in the sEPSC frequency. On the other hand, this group of neurons exhibited decreased frequency of inhibitory postsynaptic currents (sIPSC), without changes in the sIPSC amplitude. Together, these results suggest that LPS-induced MIA triggers significant rearrangements of CA1 pyramidal neurons morphophysiology, leading to hippocampal hyperexcitability. These alterations may modify the computational and integration capabilities of CA1 pyramidal neurons, which could explain some cognitive symptoms of MIA-associated neuropsychiatric disorders.

Key words: maternal immune activation, hippocampus, morphophysiology.

Analysis and comparison of protein content of serum derived exosomes obtained from patients with Major Depressive Disorder (MDD): responders versus non-responders to pharmacological treatment

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Major Depressive Disorder (MDD) is the most prevalent mental disorder worldwide. The pathophysiology involves a multisystem imbalance including neurotransmitters imbalance, hyperactivity of Hypothalamic-Pituitary-Adrenal axis, poor regulation of the immune response and dysregulation of neurogenic processes. Around 30% to 40% of patients receiving fist-line antidepressants do not respond. Lack of response has been linked to increase of pro-inflammatory molecules, defects in anti-inflammatory mechanisms, and oxidative stress. In addition, comorbidity with other diseases such as diabetes, cancer, neurodegenerative illness are also factors related to poor response to treatment. In recent years, exosomes (extracellular vesicles) have gained interest in the investigation of multiple pathologies including mental disorders. They are involved in signaling and cellular communication and play important role in homeostasis, but also in the onset and course of different pathologies. These exosomes express receptors in their membranes and transport mRNAs, miRNAs, proteins and other molecules that can deposit in other cells.

The aim of this study is to analyze and compare the content of exosomes from blood serum obtained from patients with MDD before and after 8 weeks of treatment with fluoxetine. The results indicated the presence of two groups: responders versus non-responders to fluoxetine. The protein content of the exosomes of both groups will be shown and discussed. Also, the results will be statistically analyzed and correlated with clinical data in order to identify changes in protein levels associated with response to treatment.

Key words: Depression. Exosomes. Pharmacological Treatment

Area: Neuroinmunology

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Effect of dopamine type 2 receptor activation on neuroinflammation in a mouse model of sleep deprivation

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Neuroimmunology

The proinflammatory stategenerated during sleep deprivation (SD), seems to be a determining factor in the development of neurodegenerative processes. It is important to investigate mechanisms that reduce or attenuate the inflammatory effects derived from sleep disorders. A new proposal is that the neurotransmitter Dopamine may trigger and modulate the progress of the immune response by activating different receptors present on immune cells. The purpose of this study was to determine if D2 receptor activation attenuates the pro-inflammatory response derived from rapid eye movement (REM) sleep deprivation in mice. Two-month-old male CD1 mice were used in the experiments. All animals were kept in a room of controlled illumination (12:12 light/dark cycle) and temperature (18–22°C). Animals were kept in the room where experiments were performed on the day before sleep deprivation to enable acclimatization. The D_2 receptor agonist Quinpirole (Sigma-Aldrich, St. Louis, MO) was freshly prepared for every administration. Quinpirole (2µg/kg/day i.p.) was injected for 3 days (during the sleep deprivation period). The multiple platform method was used as REM sleep deprivation model. Briefly, 6 platforms (8.5 cm height, 2.5 cm in diameter) were placed in a water-filled tank. Mice were placed on the platforms for 3 days. To determine inflammatory state ELISA tests were used to assess cytokines levels. Iba-1 and GFAP were immunolabeled in frozen brain slices.

We found that SD mice showed morphological signs of microglial activation and enhanced levels of pro-inflammatory cytokines (TNFα and IL-1) in both the hippocampus and plasma. On the other hand, Quinpirole attenuated the increased levels of cytokines and reduced the microglial activation. These results suggest that D2 receptor activation may be involved in neuroinflammation mechanisms generated by REM sleep deprivation.

Neuroinflammation, Sleep deprivation, Dopamine

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Effect of maternal immune activation on central nervous system and function

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Gestation represents a critical period in which environmental alterations can cause profound and sustained defects in the development of progeny's central nervous system (CNS). Accordingly, maternal immune activation (MIA) has been identified as an important risk factor for the appearance of several neurodevelopmental disorders (NDD) including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and Tourette syndrome (TS). Moreover, schizophrenia-related phenotypes are also more prevalent in the progeny of MIA-exposed mothers. MIA can be triggered by both acute and systemic chronic inflammation. In this study, we used an acute inflammation-MIA mice model by simulating a viral acute infection through the administration of Poly(I:C) and established a systemic chronic inflammation-MIA mice model by feeding a high fat diet (HFD) to mothers during gestation. Interestingly, the adult male offspring of acute-MIA mice presented a decreased response to pleasure (anhedonia) when compared to the response of non-MIA mice offspring. In contrast, adult offspring of chronic inflammation-MIA mice, did not show any sign of anhedonia when compared to non-MIA mice offspring independently of sex. As other characteristics of human behavior including sociability, anxiety and exploratory capacity can be altered in people within the ASD and schizophrenia patients; we are also interested in determining if there is any difference in the behavior of both acute- and chronic-MIA offspring. Moreover, given that some NDD present different symptoms between women and men, we will also analyze the results of our behavioral tests: open field test (to measure anxiety and exploratory capacity) and three-chambers test (to measure sociability) by sex.

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Area: Neuroimmunology
Keywords: Inflammation, neurodevelopment, neurodevelopmental disorders

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Activation of Toll-like receptors in combination with vincristine in glioblastoma cells

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Introduction. Glioblastoma is a highly invasive, therapy-resistant primary brain tumor with the highest mortality rate among all primary brain malignancies. Therefore, there is an urgent need to explore the exact molecular mechanisms of glioblastoma progression and develop new and effective treatment strategies to improve patient prognosis. Immunotherapy has become an important part of the treatment of some cancers. The activation of the immune system through Toll-like receptors (TLRs) could be an area of opportunity. The TLR agonists imiquimod, resiquimod (R848) and ODN1826 have been shown to be an effective adjuvant therapy to chemotherapy against several types of cancer. Currently treatment consist of surgical resection followed by chemotherapy and radiotherapy. Vincristine (VCR) is chemotherapeutic medication that inhibits proliferation by depolymerizing mitotic spindles, causing cell cycle arrest and apoptosis.

Material and methods: we use the U373 cell line to determine the effect of TLR activation in combination with VCR on cell viability and migration. We performed MTT assays to determine the effect of synthetic TLR7, TLR8, and TLR9 agonists (imiquimod, R848, and ODN, respectively; 3 µg/mL) and VCR (200 and 300 ng/mL) on cell viability. We also performed migration assays (wound healing) to determine the effect of the synthetic agonists previous mention (3µg/ml) and PDTC (200, 300 and 500 µM) on the cell migration.

Results: we observed a decrease in the viability of glioblastoma cells in the presence of VCR at both concentrations; however, the addition of TLR agonists has no effect. We also performed migration assays with TLR agonists, we observed that the administration of agonists plus VCR decreases cell migration capacity.

Conclusions. The administration of TLR agonists in combination with VCR does not affect glioblastoma cell viability. However, TLR agonist administration decreased cell migration, mainly imiquimod, which had the greatest effect on cell migration.

Keywords: glioblastoma, TLRs, vincristine

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Area: Neuroinmunología.

TNFR2 inhibit Long-term potentiation in single-synapses and promote memory loss in a familial Alzheimer´s disease mouse model.

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Alzheimer's disease (AD) is the most common type of dementia, characterized by the accumulation of β–amyloid (βA) peptides and neurofibrillary tangles[1].
Different research groups, including ours, using mouse models for AD have shown that the neuroinflammatory process controlled by the inflammasome plays an essential role in the development of AD[2]. Although, TNF and its receptors (TNFR1 and TNFR2) have been also implicated in this process[3], the specific roles of each TNFR in AD development is not clear, since it has been suggested that TNF signaling trough TNFR1 lead to neurodegeneration while signaling through TNFR2 is neuroprotective[3]. However, we found that caspase-1-dependent neuroinflammation resulting from the presence of βA peptides increased TNFR2 levels in the hippocampus of the 5XFAD. These data and data recently published[4] suggest that TNFR2 can also promote neurodegeneration.

Given that synapse-encoded long-term potentiation (LTP) is the major correlate of memory, we isolate a crude fraction enriched in pre and postsynaptic particles and evaluated, by flow cytometry the presence of both TNF receptors. In agreement with the fact that the presence of βA peptides increased the TNFR2 protein levels in the whole hippocampus of 5 months old 5XFAD mice, we found that TNFR2 levels increased in synapse from 5xFAD mice in a caspase-1-dependent manner. Interestingly, in the surface of hippocampal synapses of Wt mice TNFR2 was the predominant TNFR. Furthermore, LPS-mediated peripheral inflammation also increases TNFR2 levels on hippocampal synapses. Our results led us to carry out experiments to evaluate the role of TNFR2 on LTP in single-synapses using FASS-LTP (Fluorescence analysis of single-synapse long-term potentiation)[5]. TNF exposure prevented LTP-firing, using a specific blocking antibody (100ng/ml) against TNFR2, demonstrate that in hippocampal synapses, TNF trough TNFR2 inhibit LTP, since the block of TNFR2 signaling in 5xFAD mice of 5-month-old rescue the LTP firing. Finally, the bilateral intrahippocampal administration (AP, -2.06 mm; ML, ±2.30 mm; SV, -2.25 mm relative to the bregma) of a specific blocking antibody against TNFR2 (1μg) rescue the short-term memory and long-term memory of 5xFAD mice in novel object recognition test. Together out results indicate that inflammatory signals originated centrally or in the periphery promote the accumulation of TNFR2 on hippocampal synapsis were it blocks synaptic transition leading to cognitive deficits observed in AD. Thus, our data points to TNFR2 signaling as therapeutic target to improve cognitive functions in AD patients.

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Keywords: Alzheimer´s disease, TNFR2, Long-term potentiation (LTP).

1.- Labzin LI, Heneka MT, Latz E. (2018) Innate Immunity and Neurodegeneration. Annu Rev Med. 29; 69: 437-449. **2.-** Álvarez-Arellano L, Pedraza-Escalona M, Blanco-Ayala T, Camacho-Concha N, Cortés-Mendoza J, Pérez-Martínez L, Pedraza-Alva G. (2018). Autophagy impairment by caspase-1-dependent inflammation mediates memory loss in response to beta-Amyloid peptide accumulation *Journal of Neuroscience Research,* 96, 234-246. **3.-** Perry RT, Collins JS, Wiener H, Acton R, Go RC. (2001) The role of TNF and its receptors in Alzheimer's disease. Neurobiol Aging. 22(6):873-83. **4.-** Zhang K, Li Y, Guo Y, Zheng K, Yang Q, Xin Y, Wang X, Song Q, Chen T, Zhuo M, Zhao M. (2017). Elevated progranulin contributes to synaptic and learning deficit due to loss of fragile X mental retardation protein. Brain 120(12):3215-3232. **5.-** Prieto GA, Snigdha S, Baglietto-Vargas D, Smith ED, Berchtold NC, Tong L, Ajami D, LaFerla FM, Rebek J Jr, Cotman CW. (2015). Synapse-specific IL-1 receptor subunit reconfiguration augments vulnerability to IL-1β in the aged hippocampus. Proc Natl Acad Sci U S A. 8;112(36):E5078-87

"The p38 MAP kinase mediates BDNF neuroprotective functions against β-Amyloid peptides and inflammatory cytokines"

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Area: Neuroinmunología

In recent years, it has been accepted that the inflammatory environment established during microglial activation is an important driving factor of neurodegenerative pathologies. In Alzheimer´s disease, inflammatory cytokines produced in response to the accumulation of β-Amyloid peptides causes synaptic dysfunction and subsequent neuronal cell death. At the molecular level, the deleterious effects on neuronal function elicited by inflammatory signals is achieved, at least in part, by blocking the neuroprotective effect mediated by neurotrophic factors like BDNF. Under normal conditions, microglia through the production of BDNF promotes axonal growth, synaptogenesis and neuronal survival. However, during AD progression the BDNF levels decrease both in the brain and in the periphery, which strongly correlates with significative cognitive decline. Accordingly, *in vivo* experiments show that the exogenous administration of BDNF prevents cognitive decline and neuronal atrophy in AD mice models, which suggest that BDNF signaling can override the negative effect that inflammatory cytokines exert on learning and memory.

Our data shows that BDNF attenuates the deleterious effects that β-Amyloid peptides and TNF exert on SN56 cholinergic neurons. BDNF neuroprotective effect on cell viability and neuritic growth was concentration dependent. According with the fact that the stress kinase JNK mediates the neurodegenerative effects elicited by both β-Amyloid peptides and TNF and that, in an inflammatory environment, the p38 MAP kinase is able to shut down JNK activation, our results indicate that BDNF impairs JNK activity, neuronal death and neurite degeneration in a p38-dependent manner.

Together, our data suggest that BDNF, at early stages of AD development, sustains synaptic transmission and cognitive functions by impairing deleterious signaling pathways activated in neurons by β-Amyloid peptides and by inflammatory cytokines, whose production resulted also from microglia activation in response to the presence of β-Amyloid peptides. However, as the production of β-Amyloid peptides is constant and in consequence that of inflammatory cytokines, eventually inflammatory cytokines override BDNF neuroprotective effects fulling cognitive decline and neurodegeneration. Our results also suggest an anti-inflammatory function for BDNF.

Keywords: BDNF, p38, neuroinflammation.

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Sympathoadrenomedular system mediates anti-inflammatory and glycemic reflex to endotoxin

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Resumen

An immune challenge causes many changes in the physiology of the organism related to the regulation of the immune system and different organs of the body. It is generally accepted that the sympathetic nervous system, through sympathetic noradrenaline, regulates early cytokine production. This is supported by experiments involving betablockers and splanchnic nerve ablation, all this triggered by prostaglandin synthesis. Nevertheless, the splanchnic nerve also innervates the adrenal gland and can induce adrenaline secretion. Because beta-blockers also block the effects of adrenaline, there is a possibility that the sympathetic inflammatory reflex can be mediated by adrenaline. To test this possibility, we executed adrenal de-medullation (AdMX), removing adrenaline from the circulation while leaving the sympathetic nervous system intact, and determined the contribution of adrenaline to the inflammatory reflex in response to an intravenous injection of LPS in rats. Adrenalin also stimulates glucose production, and LPS can cause transitory hyperglycemia, we also explored the possibility that cytokine production and hyperglycemia have a common mechanism. The results demonstrated that after LPS injection, AdMX animals had higher circulating TNF levels and lacked blood glucose increase. Transitory hyperglycemia was prevented by prostaglandin inhibition through administration of indomethacin and was shown to be induced by direct administration of PGE2 but not in AdMX. Consequently, the glycemic effect of prostaglandins is through the release of adrenaline. Altogether, we demonstrated that adrenaline mediates the anti-inflammatory reflex and concomitantly regulates glycemia during an acute immune challenge.

Keywords: Inflammatory reflex, adrenaline, glycemia

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"Differential expression of BDNF, RANTES and EOTAXIN-1 in serum-derived exosomes and in serum and from major depressive diagnosed patients"

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ABSTRACT

Major Depressive Disorder (MDD) is one of the most common and debilitating neuropsychiatric disorders around the world. Traditionally MDD is related to neurochemical basis and involved several alterations like chronic stress, inflammation, reduced neuroplasticity, among other. However, its etiology remains unclear. Interestingly, recent findings have pointed to a possible role of peripheral components on depression. In this regard, exosomes (nanometric size extracellular vesicles) have gained attention since they can act as mediators of intercellular communication especially because they contained proteins, peptides, and miRNAs. In addition, it is proposed that exosomes can contribute to neuropsychiatric disorders probably acting at the peripheral level but also at the central level. However, the protein cargo content in exosomes from depression diagnosed patients and how the pharmacological treatment impacts on their content is unknown. We thus here isolated exosomes from serum of control subjects (n=5; women), and depression diagnosed patients (n=5; women). The expression of proteins related to exosomes was analyzed by western blot and the content of cargo proteins in the exosomes was characterized with a proteomic microarray, and protein-protein interactions (PPI) *in silico* analysis was performed. The exosomes analysis and characterization indicate that the nanovesicles contains 120 different proteins at least, such as chemokines, cytokines, and growth factors. We observed differences in BDNF, RANTES and EOTAXIN-1 expression among healthy controls, and depression diagnosed patients, and from the PPI analysis, a complex interaction network with other 14 proteins involved in molecular pathways and cell signaling inflammation, stress, metabolic diseases, among others. Differences in protein expression and PPI analysis in exosomes, in the serum from which exosomes were isolated and furthermore the differences in psychiatric, clinic and biochemical parameters among healthy controls and depression diagnosed patient's will be shown and discussed.

Keywords: Exosomes, depression, proteins. **Topic**: Neuroimmunology

Exposure to an Enriched Environment Attenuates Mouse Experimental Colitis

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The Enriched Environment (EE) paradigm is defined as housing conditions which promote sensory, visual, cognitive, motor and social stimulation. It has been shown that the EE exerts beneficial effects on the brain at cellular and functional levels in in homeostatic and pathological conditions. It promotes neurogenesis and synaptogenesis in the hippocampus through increasing the expression of different neurotrophins such as Brain-Derived Neurotrophic Factor (BDNF). In addition to the central nervous system, the functions of the immune system are also modulated by exposure to an EE, improving phagocytosis, chemotaxis and attenuating the inflammatory response induced by lipopolysaccharides. In this work, we show that exposure to an EE attenuates inflammation in the colon. After dextran sodium sulfate (DSS) or Trinitrobenzenesulfonic acid (TNBS) treatment, animals exposed to an EE showed reduced weight loss, reduced colon shortening and disease activity score than animals housed in a normal environment. Furthermore, the colon of animals exposed to an EE showed reduced epithelial damage, less immune cellular infiltrate, reduced myeloperoxidase activity and secreted lower TNF, IL-6 and IL-1β levels than animals housed in a normal environment. In contrast, colon explants from mice exposed to an EE and treated with DSS or TNBS produced higher levels of the anti-inflammatory cytokine IL-10, than the colon explants from animals housed in standard conditions. Congruent with the fact that exposure to an EE prevented the raise of IL-18 levels observed in the colon of mice with colitis, the number of goblet cells in these mice were higher than the number of globlet cells found in the colon of mice with colitis housed under standard conditions. In agreement with the fact that exposure to an enriched environment attenuates inflammation and reduces epithelial damage in the colon, we found that animals exposed to the EE presented low LPS levels in circulation, compared with animals housed in normal conditions. Together, our results show that brain stimulation by exposure to an enriched environment attenuates inflammation in the gut mucosa, resulting in improved intestinal epithelial barrier functions.

Key words: somatosensorial stimulation, enriched environment, colitis, BNDF, inflammation

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Encoding signs of orofacial neuropathic pain from facial expressions in mice

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The characterization of trigeminal nerve injury relies mainly on the evaluation of mechanical withdrawal threshold. Nevertheless, neuropathic pain is also reflected in several spontaneous pain-related responses that relied in supraspinal processes. The analysis of facial expression has surged as a promising alternative to the evaluation of pain-related behaviors. We proposed the use of machine-learning algorithms that accurately encode facial expressions with high time-precision to detect spontaneous pain-like facial reactions and quantify the intensity of the facial expression elicited by mechanical stimuli. The facial expression of mice was videorecorded in a head-fixed system during a stimuli-free period and during mechanical stimulation with three different Von Frey filaments one day before and four days after a unilateral mental nerve injury. Each frame was then processed to obtain its main characteristics by extracting the Histograms of Oriented Gradients (HOGs). These descriptors were compared to a prototypical pain-like facial expression to quantify the spontaneous pain-like facial reactions and the intensity of the response evoked by mechanical stimulation. We found that mental nerve injury promotes an increase in spontaneous facial pain-like expressions and mechanical hyperalgesia reflected in a higher similarity to the prototypical pain-like facial expression regardless of the intensity of the mechanical stimuli applied. Machine vision is a useful tool to evaluate both evoked and spontaneous pain after mental nerve injury with high sensitivity and temporal precision that can be applied to the study of neural circuits involved in the establishment of chronic pain

Área: Neuropatología

Keywords: Facial expressions, trigeminal injury, artificial intelligence.

Structural and dynamics analysis of the polyQ tract in the Ataxin-7 protein

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Polyglutamine (PolyQ) tracts are sequences of several glutamine residues, frequently referred as causative entities of numerous neurodegenerative conditions that include Huntington's disease, dentatorubral pallidoluysian atrophy, spinal and bulbar muscular atrophy, and the spinocerebellar ataxias (SCA) types 1, 2, 3, 6, 7 and 17.

SCA7 is an autosomal dominant neurodegenerative disorder clinically characterized by cerebellar ataxia associated with progressive macular dystrophy, dysarthria, spasticity, ophthalmoplegia, and total blindness. The disease primarily affects the cerebellum and retina, but also many other central nervous system structures as the disease progresses. SCA7 is caused by CAG trinucleotide expansion in exon 3 of the ATXN7 gene that generates a polyQ tract in the encoded ataxin-7 protein. In this work, we performed a structural and dynamics analysis of ataxin-7 carrying a polyQ tract of different lengths.

To this end, we modeled a region of ataxin-7 constituted by a polyQ tract containing 10, 20, 30 or 40 glutamines flanked by the native proximal residues alanine-alanine-alanine-arginine on the amino-terminal domain, and the proline-proline-proline residues on the carboxy-terminal domain of each peptide ($A_3R\mathbf{Q}_{10}P_3$ / $A_3R\mathbf{Q}_{20}P_3$ / $A_3R\mathbf{Q}_{30}P_3$, and $A_3R\mathbf{Q}_{40}P_3$). By using the I-Tasser server, we predicted the 3D structure of each peptide. Molecular dynamic simulation was performed during a period of 500ns, and the stability of each CAG tract during this period was examined by determination of the root mean square deviation (RMSD), radius of gyration (Rg) and the root mean square fluctuation (RMSF) parameters. Then, clustering analysis were performed to determine the structures adopted during the molecular dynamics simulation. Subsequently, secondary structure and H-bonds analysis were performed. Our data indicated that the polyQ tract folds into an α-helix structure stabilized by H-bonds. Interestingly we observed an increased stability and rigidity in the protein structure in a polyQ length-dependent manner. Our structural results support experimental evidence indicating an association between the presence of polyQ expansions and loss of function of the Ataxin-7 protein, possibly by altering its interaction patterns.

Keywords: PolyQ tract; Ataxin-7; molecular dynamics simulation.

Neuropathology

Establishment of a CRISPR based-system for ataxin-7 transcript interactome characterization

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Spinocerebellar ataxia type 7 (SCA7) is an autosomal dominant neurodegenerative disorder clinically characterized by cerebellar ataxia associated with progressive macular dystrophy, dysarthria, spasticity, ophthalmoplegia, and total blindness. SCA7 is caused by a CAG repeat expansion in the coding region of the ATXN7 gene. CAG tract ranges from 4 to 18 in general population, and from 36 to 460 in affected individuals. To date, there is no cure for SCA7, therefore, a better knowledge of the underlying pathological mechanisms is crucial to advance into novel therapy strategies. Ataxin-7, the encoded product of the ATXN7 gene, is part of a chromatin remodeling and transcriptional coactivator complex. In SCA7, mutant protein tends to form nuclear inclusions altering transcriptional regulation and cellular pathways that leads to neurodegeneration. Although the involvement of the mutant ataxin-7 is well recognized in SCA7, to date other potential pathophysiological mechanisms have not been explored. Growing experimental evidence suggests a role for the CAG-expanded mRNAs as toxic entities. The formation of nuclear aggregates by mutant transcripts that sequester other RNAs and/or proteins have been observed in other polyglutamine diseases. In order to analyze the molecular complexes associated with the mutant RNA of the ATXN7 gene, we proposed a methodology based on the use of the CRISPR/dCas13a system. By using an inactive nuclease and crRNAs to target specific ATXN7 transcripts, we will be able to purify mRNA complexes and to identify new associated RNAs and proteins in a MIO-M1 retina cell model of SCA7. By using bioinformatic tools that consider the secondary structure of both normal and mutant ATXN7 transcripts, two crRNAs were designed and subsequently cloned into a pc0040-LwaCas13a-crRNA-backbone plasmid. In parallel, MIO-MI SCA7 cells, expressing the wild-type or mutant ATXN7 transcript, were transfected with the pC035-dLwCas13a-msfGFP plasmid to induce the dCas13a protein stable expression. We present the preliminary results of the application of this cutting-edge methodology in our SCA7 in vitro models. Our results will help us to establish new pathophysiological mechanisms by the identification of the ataxin-7 transcript interactome, to eventually propose new therapeutic approaches for this complex disease.

Keywords: SCA7; mRNA; CRISPR/Cas13.

Neuropathology

Effect of the ketone body β-hydroxybutyrate on autophagy activation induced by glucose deprivation in cultured cortical neurons

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Area: Neuropathology

As glucose is the main source of energy in the nervous system, neurons are highly vulnerable to dysregulation in its metabolism or disruptions in its supply, which can lead to brain injury, as observed during acute hypoglycemia or cerebral ischemia. One of the main adaptive cell responses induced in the brain during nutrient deprivation is autophagy, a lysosomal-dependent degradation process. Even though autophagy has been observed to promote cell survival, its defective or excessive activation under acute excitotoxicity and glucose deprivation can lead to neuronal death, as identified in different in vivo and in vitro models in our laboratory.

Alternative energy substrates such as ketone bodies (KB): acetoacetate (AcAc), and β-hydroxybutyrate (BHB) can be used as energy fuel in the brain when glucose is unavailable and protect neurons against cell death. Nevertheless, the mechanisms involved in its protective effects are yet to be well understood. In previous studies from our group, it has been shown in both in vitro and in vivo models that under glucose deprivation (GD), impaired autophagosome degradation contributes to neuronal death. In these conditions, addition of the D isomer of BHB (D-BHB) stimulates the autophagic flux due to improved autophagic degradation. In addition, in the in vivo model of hypoglycemia, it has been recently observed that D-BHB can downregulate excessive autophagy activation by decreasing AMPK activity, which increases neuronal viability. However, whether BHB can downregulate autophagy initiation in neurons exposed to GD is still unknown.

In the present study we aimed to investigate the role of the mTOR/AMPK pathway in the activation of autophagy during periods of glucose deprivation (GD) followed by periods of glucose reintroduction (GR) in cultured cortical neurons, and the possible regulatory effect of the ketone body D-BHB. The changes in total protein and their phosphorylation status of the autophagy proteins, ULK1, mTOR and AMPK, and in the abundance of BECN1, SQTSM1/p62 and LC3-II/LC3-I, were monitored at different times after GD and GR. Results indicate that autophagy is activated in the GD period, as suggested by an increase in AMPK (pAMPK T172) and a decreased in mTOR (mTOR pS2448). Meanwhile, during GR there is no reactivation of autophagy but rather degradation of autophagosomes. D-BHB showed no effect on autophagy initiation, but accelerated autophagic degradation, therefore restoring the autophagic flux.

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Keywords: Autophagy; hypoglycemia; ketone bodies

Tibolone administration decreases oxidative stress in plasma and spinal cord in a traumatic spinal cord injury animal model

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Brackground: Traumatic spinal cord injury (TSCI) causes irreversible damage to neurological and motor function. Oxidative stress increases damage to important biomolecules that in turn impair motor activity causing progressive neurodegeneration in the spinal cord. There is currently no treatment capable of reversing the damage and promoting functional recovery of patients without generating side effects. Tibolone (Tib) is a treatment currently used for menopause and has been shown to have a neuroprotective effect by acting as an antioxidant. **Aim:** To evaluate the effect of Tib on oxidative stress in the medulla and plasma in an animal model of traumatic spinal cord injury. **Metodology:** Forty-eight male rats of the *Sprague dawley* strain were randomly distributed in 6 groups: 1) Control (water), 2) Laminectomy, 3) TSCI, 4) TSCI + 0.1 mg/kg weight of Tib, 5) TSCI + 1 mg/kg weight of Tib, 6) TSCI + 10 mg/kg weight of Tib. The administration of the different doses of Tib was performed at 30 min, 24 hours and 48 hours post-surgery and the animals were sacrificed at 72 hours. Biochemical techniques were used for the quantification of superoxide dismutase (SOD) activity and for the quantification of carbonyls, and malondialdehyde (MDA) levels in plasma and spinal cord. **Results:** It was observed that the administration of Tib at a dose of 0.1 mg/kg after TSCI increased SOD enzyme activity in spinal cord homogenates, when compared to the TSCI group without treatment. However, in plasma, SOD enzyme activity did not show significant differences. The administration of Tib at a dose of 0.1 mg/kg after TSCI significantly decreased the levels of MDA and carbonyls in plasma and in spinal cord homogenates. **Conclusions:** The results obtained in the present work show that the dose of Tib that had the best effect in decreasing oxidative stress markers in plasma and spinal cord after injury was 0.1 mg/kg, which is similar to that reported for estradiol and suggests an estrogenic effect of this synthetic hormone in the TSCI model.

Key words: oxidative stress, traumatic spinal cord injury, tibolone.

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In Vivo Transfection in a Murine Model of Tubulinopathy

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Introduction. Hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC) is a central neurodegenerative disease caused by mutations in the TUBB4A protein. Magnetic resonance imaging (MRI) shows atrophy and hypomyelination. Our group has proposed the *taiep* rat as a model to study this group of diseases. This animal shows the same MRI signs as human patients and carries a tubulin. Due to the lack of pathology material from human patients, the animal model allows us to study and understand the pathophysiology of this tubulinopathy and, in addition, to propose therapeutic strategies such as gene therapy, for example. The subventricular zone (SVZ) harbor one of the most important neurogenic zones. Under physiological conditions, neural stem cells (NSCs) of the adult brain can generate new neurons and new oligodendrocytes capable of migrating from SVZ to the white matter of the striatal tracts, corpus callosum, or olfactory bulbs. This regenerative capacity opens the possibility for cell or gene therapy. However, one of the main challenges is introducing signals into the NSCs to modify or guide their cellular fate.

Objective. To study the effects of the TUBB4A mutation using biophotonic and to analyze the *in vivo* transfection efficiency in the neurogenic zone of the SVZ of the rat.

Materials and methods. We used male *taiep* rats and healthy controls (WT) between 10 and 11 months. After anesthesia, the rats were transcardially perfused, the brain removed and processed for fluorescence immunohistochemistry. Neurofilaments, myelin, and cell nuclei were identified. For *in vivo* transfection, male rats of 3 months were used. The injections with the non-viral PEI vector complexed with CMV-eGFP (*cytomegalovirus immediate early promoter Functional Enhanced Green Fluorescent Protein*) using an N/P ratio of 6 were performed in the right lateral ventricle following stereotaxic coordinates. Brains were analyzed 5 days after transfection. The samples were observed under a confocal microscope and analyzed with FIJI. All experimental procedures were authorized by the bioethics committee of the University of Guanajuato.

Results. The *taiep* rat exhibits atrophy of the corpus callosum, basal ganglia and cerebellum, accompanied by hypomyelination. It was also found transfection in the SVZ. In addition, the morphology of transfected cells suggest the transfection of astrocytes, transitional cells, and neuroblasts.

Conclusions. TUBB4A mutation causes hypomyelination and demyelination of the corpus callosum and atrophy of the caudate-putamen. Furthermore, for the first time, it was possible to transfect the neurogenic niche of the SVZ using a non-viral vector. All this confirms that the *taiep* rat is an ideal model for studying H-ABC and can be used in gene therapy trials.

Keywords. tubulinopathy, *taiep* rat, transfection.

Early dysregulation of Wnt signaling in the hippocampus of 3xTg-AD model

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Área: Neuropatología

Alzheimer disease (AD) is the most common age-related dementia. This neurodegenerative disease is characterized by progressive loss of cognitive abilities synaptic damage, and accumulation of extracellular senile plaques and intraneuronal neurofibrillary tangles. The etiology of AD remains unknown, although downregulation of Wnt signaling has been reported in patients, suggesting this pathway is as a possible participant in Alzheimer's pathology. In vivo experimental evidence indicates that inhibition of canonical Wnt triggers synaptic loss and accumulation of Ab y p-tau and induces cognitive decline. Postmortem analysis of brain samples from AD patients showed elevated levels of Wnt canonical inhibitor, Dkk-1, as well as decreased levels of the agonists Wnt7a, Wnt2b and Wnt6, suggesting a reduced Wnt signaling, at least at the final stages of the pathology. However, it has not yet been determined whether alterations in the Wnt pathway are the cause or consequence of disease progression. Therefore, the present study aims to describe the status of Wnt signaling along the expression of pathological markers of AD in the 3xTg-AD model to assess the therapeutic potential of Wnt signaling activation, through silencing of Dkka-1 and/or by the administration of agonist, Wnt7a. We have observed that the hippocampal Dkk1 levels increase according to disease progression in 3xTg-AD mice compared to control mice. In addition, hippocampal Wnt7a levels diminished compared to the control group throughout aging. Both alterations are evident as early as since 3-months of age, when the hallmarks of AD are not yet clearly expressed. These results suggest that Wnt signaling may participate early in AD pathology and open the possibility that the activation of this pathway could be a therapeutic tool to delay the disease.
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Kay works:
Neurodegeneration, Alzheimer disease, Wnt signaling.

Effect of tibolone on inflammation and motor recovery in a model of traumatic spinal cord injury

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Traumatic spinal cord injury (TSCI) is an important health issue, there are approximately 2.5 million people in the world who suffer from TSCI and this number increases 130,000 each year. Causes include vehicle accidents, violence, accidental falls, and other traumatic events. The pathophysiology of TSCI can be divided in primary and secondary phase. The primary phase refers to the instantaneous mechanical damage that occurs in the injury. The secondary phase is marked by changes in the cellular metabolism and in the genetic expression, which result in a prolonged period of tissue destruction. Inflammation contributes to the secondary injury through the non-specific activation of the innate immune response, which activates immediately after the stimulation by the TSCI.
It is important to develop a treatment for TSCI, endogenous steroids have neuroprotective effects and therefore the idea of their therapeutic use to reduce the secondary injury of TSCI is promising, however they exert undesirable secondary effects. Consequently, the use of synthetic steroids, such as tibolone, has been proposed, since it exerts the neuroprotective effects of sexual hormones, but does not promote the development of cancer.
In the present study, we evaluated the effect of tibolone in the regulation of neuroinflammation, its impact in the preserved tissue, and its effect to promotes recovery of motor function after TSCI.
Adult male sprague Dawley rats with TSCI were divided into 3 groups (n = 5): Vehicule (V); tibolone 1 mg/kg (TIB 1); tibolone 2.5 mg/kg (TIB 2.5). Three hours, three, seven and fourteen days after TSCI we quantified the concentration of pro and anti inflammatory cytokines in the spinal cord injured. Others rats were divided into 2 groups (n =10): V, TIB 1. Eight weeks after TSCI, we evaluated
preserved tissue and functional recovery by BBB scale.
The results showed that the treatment with tibolone regulate the neuroinflammation modifying the concentration of some pro and anti inflammatory cytokines, conserved more nervous tissue and promoted recovery of motor function after TSCI.

Cytokines, neuroprotection, steroid hormones
Area: Neuropatología

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Role of NOX in NLRP3 inflammasome regulation during cerebellar granule neuron death.

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Introduction: The NLRP3 inflammasome was described in immune cells and plays a central role in inflammatory processes and is known to be involved in both acute neuronal damage and several neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease and multiple sclerosis. Induction of NLRP3 by these conditions leads to the activation of caspase-1, which in turn facilitates the maturation of pro-IL-1β and pro-IL-18 that are secreted to recruit other immune cells to the site of infection to offer a timely response and restore tissue homeostasis. Some of the cellular perturbations that are able to induce NLRP3 activation include potassium efflux, lysosomal damage, reactive oxygen species (ROS) production, increased levels of the thioredoxin-interacting protein (TXNIP) and mitochondrial dysfunction. We have previously demonstrated that cell death of cerebellar granule neurons (CGN) induced by potassium deprivation triggers an early increase of ROS and TXNIP levels. Interestingly, in an excitotoxicity model of cell death CGN show an increase in ROS and NLRP3 levels, suggesting a possible involvement of the NLRP3 inflammasome in neuronal death. However, no much information is available about this possibility, as well as the implication of NOX activation in the NLRP3 inflammasome assembly induced by these conditions in neurons.

Objective: To evaluate the role of the NOX activation in the NLRP3 inflammasome activity and their involvement of CGN death induced by excitotoxicity and potassium deprivation.

Materials and methods: We used cultured CGN from 8-day-old Wistar rats maintained in a medium with 25mM of potassium (K25) for 7 days *in vitro*. Later, neuronal death was produced by treating neurons with a reduction of extracellular KCl to 5mM (K5); excitotoxic death was induced by addition of 300 µM of glutamate. Cell viability was evaluated by the MTT reduction assay, as well as calcein/propidium iodide incorporation; the ROS production was measured by DHE (dihidroethidium oxidation); the levels and localization of the components of the NLRP3 inflammasome were measured by Western blot analysis and immunocytochemistry, respectively; the determination of pro-cytokines and cytokines were carry out by PCR and ELISA assay.

Preliminary results: The viability of CGN in the potassium deprivation model showed a significant decrease of 50% after 24 hours of treatment measured as MTT reduction. These results were confirmed when neuronal death was measured by the calcein/ propidium iodide assay. Similar results were obtained in the preliminary experiments of excitotoxicity. Work is underway to confirm the levels of ROS, TXNIP and cytokines.

This work was supported by CONACYT (285184) and DGAPA-PAPIIT, UNAM (IN212019)

Keywords: NLRP3 inflammasome, excitotoxicity and potassium deprivation.

Area: Neuropathology

Characterization of cellular markers of senescence during the progression of Alzheimer's disease pathology in the brain of 3xTg-AD mice

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Alzheimer's disease (AD) is the most common neurodegenerative disease associated with brain aging. It is characterized by the accumulation of extracellular β-amyloid-containing plaques, intraneuronal tau-containing neurofibrillary tangles, chronic neuroinflammation, metabolic dysfunction and a progressive synaptic loss, accompanied by clinical manifestations of cognitive decline. One of the proposed mechanisms that drive the aging process is the accumulation of senescent cells in the brain, which are mainly characterized by cell cycle arrest, apoptosis resistance and the acquisition of a senescence associated secretory phenotype (SASP), composed of inflammatory cytokines and chemokines. Recently, the presence of distinct cellular types in the brain with a senescent phenotype has been observed in samples from human AD's brains and from transgenic mouse models of the disease. However, there has not been a thorough characterization of the presence of distinct markers of senescence in the main areas affected by the disease throughout the pathological progression. To this end, we evaluated senescence in neurons and astrocytes in the hippocampus and cerebral cortex of mice of the 3xTg-AD model at different ages: young (2-4 months), middle-aged (9-11 months) and aged (15-18 months). Through immunofluorescence and western blot analysis, the levels of three senescence markers were analyzed: the cell cycle inhibitors $p16^{INK4a}$ and $p21^{Waf1/Cip1}$ and the DNA damage-associated histone γ-H2A.X. Additionally, inflammatory markers, such as microglial and astrocytic activation and cytokine levels, were measured in the same brain areas. Our preliminary results show two main findings: 1) an age-related increase in inflammatory markers and reactivation of astrocytes and microglia and, 2) a significant increase in older animals in the number of cells positive to the different senescence markers, mainly in the neuronal layers of the hippocampus. Our results suggest that accumulation of senescent cells is associated with the pathological progression and increased neuroinflammation in the 3xTg-AD mice, that may aggravate AD's pathology.

Key words: senescence, neurodegeneration, aging

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Inhalation of vanadium pentoxide (V_2O_5) induces memory and cytoskeleton alterations in brain structures related to Alzheimer disease.

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Alzheimer disease (AD) is the most common neurodegenerative pathology worldwide; it has been reported that approximately 15 million people suffer from this disease, the incidence annually increases 0.5% in 65-year-old people and 8% in 85-year-olds; although it was described more than 100 years ago and there is a lot of research being done about this pathology, it has been challenging to find an animal model that replicates all the characteristics of the neurodegenerative process of AD. Previous experiments in our laboratory have shown that chronic exposure to vanadium pentoxide (V_2O_5) in rats causes morphological and behavioral changes similar to those seen in AD. To this end, 20 male Wistar rats were randomly divided into one control and one experimental group (n = 10) with an initial 180-200 g weight. The experimental group was exposed to V_2O_5 0.02M for one h, three times a week, for six months. For behavioral changes, the two groups were trained in the T-maze test that assesses spatial behavior and an open-field test for 10 mins. Both groups were evaluated once a month for six months. After six months of inhalation to measure histological alterations, the frontal cortex, hippocampal CA1, entorhinal cortex, and amygdala regions underwent argentic Bielskschovsky impregnation, and Congo red staining analyzed. Memory results in the T-maze show memory impairment since the group had been exposed for three months to V_2O_5. During the open field test, differences were observed in the locomotion pattern of the experimental group. Motor activity decreased (fewer lines crossed) while freezing increased. Freezing behavior in control rats is nearly absent; this immobility behavior appears in rats exposed to V_2O_5 from the first month. Bielskschovsky impregnation and Congo red staining showed that affected neurons have the same morphological characteristics as the neurons of patients with AD (i.e., the affected cells are shaped like a "flame"), and structures similar to fibrillary tangles are observed.

Keywords: Vanadium pentoxide, Neurodegeneration, Alzheimer disease.

Post-translational modifications on tau protein after neuronal exposure to palmitic acid.

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Area: Neuropathology

Alzheimer´s Disease (AD) is one of the most common neurodegenerative diseases and is characterized by the extracellular deposition of the amyloid-β peptide and the intraneuronal accumulation of neurofibrillary tangles composed by hyperphosphorylated forms of tau protein. Epidemiological studies have shown an important correlation between the presence of metabolic alterations and the increased risk for developing cognitive impairments due to the high consumption of saturated fatty acids such as palmitic acid (PA). Cumulative evidence has demonstrated the participation of PA in the development of neuronal insulin resistance, increments of intracellular calcium, ROS production, activation of several protein kinases as well as the reduction in the NAD+/NADH ratio, which results in the decrement of content and activity of the deacetylase sirtuin-1 (Sirt1). All these processes may have an impact in post-translational modifications of tau protein through dysregulation of protein kinases and deacetylases. Thus, in this work we studied the effects of PA exposure in human neuroblastoma cells on tau phosphorylation and acetylation at different AD-related epitopes (S199/202, S214, S396) and K280 and the protein kinases involved. At present we have demonstrated that neurons differentiated from human neuroblastoma MSN exposed to high but nontoxic concentrations of PA increased the levels of tau phosphorylation and acetylation through activation of GSK3-β and classical PKCs, and reduction of Sirt1 activity. These results provide evidence of how the metabolism of saturated fatty contributes to biochemical alterations of the tau protein.

This work was supported by CONACYT A1-S9559
Keywords: tau protein, palmitic acid, phosphorylation, acetylation.

Dopamine concentration and mitochondrial function modifications in a Parkinson's disease model by manganese inhalation

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Parkinson's disease (PD) is a worldwide health problem and the change in the population pyramid has been suggested that in the next decades will increase their incidence, so it is necessary to have new experimental models that allow us to analyze possible pathophysiological mechanisms and thereby design effective interventions. Even though current animal models have been useful, none of them completely reproduce this disorder, most of them are acute and the degeneration degree of dopaminergic neurons that they cause correspond to advanced stages of the disease. In our laboratory found that inhalation of manganese chloride ($MnCl_2$) and manganese acetate ($Mn(OAc)_3$) produced alterations in fine motor skills and balance tests that are reversed with L-dopa, besides we found a decrease in the immunoreactive neurons to TH in the substantia nigra, these disturbances were gradual and bilateral, similar to what was report in humans with PD.
The present work aimed to evaluate dopamine concentrations and its metabolites together with evaluation of modifications of mitochondrial complex IV in the substantia nigra, striatum and globus pallidus. For this were used CD1 male mice with an initial weight of 30g, divided into two groups: one group was exposed to deionized water (control group, n= 20), while the second group (n= 20) was exposed to a mixture of $MnCl_2$ 0.04 M and $Mn(OAc)_3$ 0.02 M by inhalation in an acrylic box, 1 hour, 2 times per week. To evaluate dopamine concentrations and its metabolites in basal ganglia the mice were sacrificed at 5 months of exposition (n=5 controls and 5 experimental); to evaluate mitochondrial activity, mice were sacrificed at 3, 5 and 8 months (n=5 controls and n=5 experimental mice for each time). According to our results, animals exposed to Mn showed a significant decrease in dopamine concentration and its metabolites in the substantia nigra, striatum and globus pallidus, therefore there was a significant decrease in mitochondrial activity complex IV from the five months of exposition.
In summary, Parkinson's model by manganese inhalation is a useful tool for the study of PD, because decrease in dopamine in these nuclei and the alteration of mitochondrial complexes are an important part of the pathophysiological changes observed in humans with this disease; so that, our model could allow study mechanisms and evaluation of new interventions that seek to improve the symptoms and quality of life of patients.

Keywords: Parkinson disease, Experimental model, Manganese

Hyperphosphorylated Tau relates to reduced hippocampal excitability in the young rTg4510 mouse model of tauopathy

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Area: Neuropathology

ABSTRACT

Tau hyperphosphorylation at several sites, including those close to its microtubule domain (MD), is considered a key pathogenic event in the development of Alzheimer's disease (AD). Nevertheless, we recently demonstrated that at the very early disease stage, Tau phosphorylation (pTau) at MD sites promotes neuroprotection by preventing seizure- like activity. To further support the notion that very early pTau is not detrimental, the present work evaluated the impact of pTau in the young rTg4510. Our results showed that at this very early stage the hippocampal neurons from p30-35 rTg4510 mice accumulate pTau protein and exhibit frequency reduction in hippocampal oscillatory activity. Moreover, we found a significant reduction in the somatic area of pTau positive pyramidal and granule neurons in the young rTg4510 mice. Despite this, increased number of dendrites per cell in granule neurons was found. Altogether, this study provides further evidence that pTau remodels hippocampal function and morphology.

Keywords: Alzheimer's disease, Tau, tauopathies.

Autophagy Inducers Trehalose and Metformin Prevent Congnitive and Motor Dysfunction by Protecting Dopaminergic Neurons from Paraquat Toxicity

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Area: Neuropathology

Parkinson's Disease (PD) pathological characteristics include dopaminergic neuronal loss in the substantia nigra at the central nervous system, the subsequent dopamine level reduction affecting motor function, mitochondrial damage, oxidative stress, and disruption of the protein degradation pathways mediated by the proteasome and autophagy. Autophagy plays an essential role in neuronal maintenance since its impairment leads to neurodegeneration, while its stimulation has a protective effect. Therefore, studying the potential neuroprotective effect of different autophagy-inducing molecules such as trehalose and metformin is crucial. Trehalose induces autophagy through mTOR-dependent and independent pathways and metformin only through the mTOR-dependent pathway. We previously demonstrated that autophagy induction with trehalose and metformin has an antioxidant effect and improves mitochondrial activity on SH-SY5Y dopaminergic cells protecting them from paraquat (PQ) toxicity. Hence, we evaluated the effect of both autophagy inducers in an animal PD model. C57BL6 mice were pretreated with trehalose (2%) or metformin (500 mg/kg) in drinking water *ad libitum* one week before PQ (10 mg/kg) intraperitoneal co-administration for seven weeks. Cognitive function was evaluated through the nest building test. Trehalose and metformin-pretreated mice followed by PQ treatment built higher quality nests (full dome-shaped) than those that received only PQ. The gait test assessed the motor function; no significant difference in stride width was observed among the treatment groups; however, PQ-treated mice showed a smaller stride length compared to mice from the control group, whereas the mice that received the autophagy inducers and PQ showed a very similar stride length to the control group. Therefore, trehalose and metformin prevent cognitive and motor functions deterioration in the PD animal model. Notably, pretreatment with trehalose and metformin protected from PQ-induced dopaminergic neuronal death, demonstrated through tyrosine hydroxylase detection by immunofluorescence and confirmed by western blot. Astrocytes were also analyzed, observing that PQ induces astrocytosis, which was prevented by pretreatment with both autophagy inducers. Therefore, trehalose and metformin represent autophagy inducers with a promising potential for treating neurodegenerative diseases such as PD.

Keywords: *Parkinson's disease, autophagy, neuroprotection*

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Contribution of brain microvasculature to remyelination after an ischemic injury via extracellular vesicles

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Neuropathology.

Ischemic stroke is one of the leading causes of death and disability worldwide. Among the many different cellular and molecular mechanisms that are activated upon the ischemic insult, the decrease of energy metabolism causes a general state of axon demyelination in the infarct core and penumbra. Axon myelination is essential in the conduction of action potentials, and it is also a source of trophic input for neuronal survival and maintenance. Mature oligodendrocytes are the cells responsible for axon myelination in the central nervous system, a process that bears a high metabolic demand. It is becoming increasingly evident that oligodendrocytes' function is intimately related to the vascular physiology in the brain, which is mainly carried out by brain microvascular endothelial cells (BMEC). We have previously found that extracellular vesicles (EV) released by BMEC carry F3/Contactin, a non-canonical activator of the Notch pathway that is mechanistically involved in myelination. Here, we evaluated the influence of BMEC-derived EV in the reconstitution of myelin structures affected by stroke in an *in vitro* model of ischemia-induced demyelination in rat cerebellar organotypic slice cultures subjected to oxygen and glucose deprivation. We found that BMEC-EV produced under normoxic and hypoxic conditions promote the restoration of myelin sheaths in the cerebellar white matter. Our preliminary data shows that the brain endothelium is capable to influence axon myelination via the release of EV. The underlying molecular mechanisms are currently being investigated. This work is supported by DGAPA-PAPIIT grant IN207020 and CONACYT A1-S-13219.

Key words: stroke, remyelination, exosome

Temporality in the expression of alpha-synuclein and dopaminergic neuronal death after intracerebral lipopolysaccharide injection

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Area: Neuropathology

Abstract

Introduction: Alpha-synuclein (α-syn) is a marker for synucleinopathies, which have early stages whose consequences are visible long after, so understanding the initial cellular and molecular events in these conditions is relevant. In this sense, the aim of this work was to determine the temporality in the initial expression of α-syn after a stimulus with lipopolysaccharide (LPS) in the substantia nigra (SN). In addition, the expression of thyroxine hydroxylase (TH) was analyzed to explore the viability of dopaminergic cells in response to post-stimulus events in that region.

Methodology: Male Wistar rats (200-250 g) were used and injected with LPS (2.5 µg) (LPS group) or vehicle (SHAM group) via intra-nigral. The results were compared with animals without any procedure (Naive group). The expression of the α-syn and TH proteins was measured by western-blot at 3-, 5-, and 7-days post-injection (DPI) of LPS or vehicle.

Results: The LPS induced an increase in α-syn expression on the ipsilateral side to injection from 3 DPI, which is maintained at 7 DPI ($p<0.05$), compared to the Naive and SHAM groups. Furthermore, the expression of TH was observed decreased at 5 and 7 DPI ($p<0.05$).

Conclusions: These results show that the initial expression of α-syn stimulated by LPS is a sudden event, and once this happens, the tendency to increase in its expression is slow, which is consistent with the gradual development of the synucleinopathies. On the other hand, the decrease in TH expression suggests that there is a death of dopaminergic neurons, which is probably related to the initial increase of α-syn.

Keywords: Alpha-synuclein; thyroxine hydroxylase; synucleinopathies

Temporal expression of circadian clock proteins in glioma C6

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Neuropathology

Central and peripheral clocks of organisms generate circadian rhythms of approximately 24 hours, which coordinate physiological processes with the rhythmically changing environment. The daily light-dark photoperiod synchronizes the master circadian pacemaker, located in the suprachiasmatic nuclei (SCN) of the brain, which in turn synchronizes the central clock of the organism as well as the peripheral clocks in each cell.
Endogenous circadian rhythms are established by two transcription-translation negative feedback loops, in which the positive limb is composed of ARNTL and CLOCK, which form heterodimers, with its transcriptional output linked to metabolism, immune regulation and other cellular pathways. The ARNTL-CLOCK complex drives the rhythmic expression of the proteins PER1/2/3 and CRY1/2 (the negative limb of the feedback loop), which form a complex to inhibit ARNTL-CLOCK transcriptional activity.
Gliomas are solid tumours of the central nervous system that originate from different glial cells. Glioblastoma multiforme (GBM) is the most common and aggressive type of malignant brain tumour. Growing evidence indicates that disruption of circadian rhythms may be a risk factor for the development of gliomas. However, temporal expression of proteins that govern circadian rhythms in glioma cells is yet to be explored.
Using immunofluorescence staining, we examined the expression of the period 2 (PER2) protein in C6 glioma cells, a murine glioblastoma model, at two different times: ZT1 and ZT13.
Our results revealed an increased number of positive cells with a higher cellular fluorescence at the core of the tumour, compared to the sham group. Because the circadian clock regulates the expression of cell cycle-related genes, we suggest that disturbances in PER2 may disrupt the regulation of the circadian clock, thus enhancing the survival of cancer cells and promoting carcinogenesis.

Key words: glioma, circadian clock, PER2

Protective effect of the ketone body, β-hydroxybutyrate on ischemic brain injury. Role of reticular stress and autophagy.

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Brain ischemia is the leading cause of disability and a frequent cause of death worldwide and to date there is no effective treatment to prevent ischemic brain injury. The ketone bodies (KB) have been recently suggested as therapeutic tools for the treatment of acute neurological disorders and neurodegenerative diseases, due to their metabolic activity and several other actions that can improve neuronal survival. Both the ketogenic diet (KD) and the exogenous administration of the KB, Beta-hidroxibutirato (BHB), have been shown to reduce global and focal brain ischemic injury, but the mechanisms involved are not completely clear. We have investigated whether the epidural infusion post-ischemia of the physiological and the non-physiological enantiomers of BHB (D-BHB and L-BHB, respectively) can reduce the infarct size in a model of focal ischemia in the rat, and whether protection is associated with the activation of the unfolded protein response (UPR), autophagy and lysosomal integrity. The accumulation of unfolded proteins leads to proteotoxicity and activates the UPR, which drives the global block of protein synthesis and cell death if unresolved. Impaired autophagy also contributes to proteotoxicity due to failure in protein degradation. We observed that infusion of D-BHB notably reduced the infarct size and the number of degenerating neurons, while L-BHB infusion showed no effect. The effect of D-BHB infusion is associated with attenuated activation of the PERK/eIF2α/ATF4 branch of the UPR and with a decrease in the accumulation of the autophagy proteins LC3-II and SQSTM1/p62 in the striatum and cerebral cortex. D-BHB also inhibited the cleavage of the lysosomal membrane protein LAMP2, associated with the autophagosome and lysosome fusion, increasing lysosomal permeability. Results highlights proteotoxicity and impaired autophagy as an important contributor to the progression of brain injury after MCAO and suggests that protection afforded by D-BHB treatment post-ischemia involves UPR downregulation and improvement of lysosomal degradation.

Keywords: Ketone body, reticular stress, autophagy, ischemia.

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Differential expression of synaptic plasticity of the medial and lateral perforant path to the dentate gyrus in a neurodevelopment model of schizophrenia: effects on spatial memory

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During early postnatal development, the transient hypofunction of the NMDA receptor-mediated synaptic transmission induces schizophrenia-like behavior, and this phenomenon is well documented in the hippocampus. However, dysregulation of the NMDA-mediated synaptic transmission conveyed by the entorhinal cortex and the dentate gyrus (DG) is barely explored. Here, using a model of schizophrenia induced by neonatal NMDA receptor blockade (daily administration of 0.2 mg/kg MK-801 during postnatal day P7 to P11), we investigated in acute hippocampal slices changes in the synaptic transmission and neuronal plasticity at the medial perforant path (MPP) and lateral perforant path (LPP) to DG synapses in juvenile (P30-35), and adult male rats (P90-115). We found that synaptic strength decreases at the MPP–DG synapse of juvenile MK-801 treated animals, whereas synaptic strength increases at the LPP–DG synapse. In addition, a physiologically-relevant theta-burst stimulation protocol delivered to the perforant path failed to induce LTP at the LPP–DG synapse and induced a blunted response at the MPP–DG synapse of the MK-801 treated animals, indicating that the information processing of the DG exhibits dysregulation and possibly, cognitive impairment. Therefore, we evaluated the performance of MK-801 treated rats in the Barnes maze, a hippocampus-dependent task of spatial memory. Compared to control animals, the juvenile MK-801 treated animals exhibited impaired performance. Adult MK-801 treated animals exhibited impaired performance in the Barnes maze. These results suggest that spatial and contextual information processing mediated by the MPP-DG and LPP-DG synapse are differentially affected during the early phase of schizophrenia, and these alterations persist in the adult stage of development.

Keywords: Synaptic plasticity, dentate gyrus, schizophrenia

Area: Neuropathology

Neuronal differentiation of the N1E-115 cell line promoted by aminated biomaterial coatings synthesized by plasma polymerization

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Plasma-synthesized amine-based polymers have been used in various types of biomedical devices as coatings, in membranes, as immobilizers of molecules and coatings of cell support scaffolds. In this work, amino monomers (pyrrole and allylamine) were used to generate different plasma synthesized polymers and copolymers with different physicochemical characteristics due to the variation in synthesis power (20, 30 and 40 watts) used as coatings on slides that functioned as support for a mouse neuroblastoma derived cell line. The polymeric materials were physicochemically characterized by X-Ray Photoelectron Spectroscopy (XPS), Infrared Spectroscopy (IR-ATR), Chemical Derivatization using 4-Trifluoromethyl benzaldehyde and Contact Angle measurement to identify chemical differences due to power variation. The neuronal differentiation effect was evaluated by seeding the N1E-115 cell line on the materials and controls without polymer using a differentiation stimulus that was interrupted at 72 hours. The neuronal networks formed on the materials were analyzed by performing immunofluorescence against βIII-Tubulin, images were obtained by confocal microscopy and analyzed with ImageJ with NeuronJ Plug-In and CellProfiler programs to obtain the differences in dendrite length, differentiation index by Sholl analysis normalized by counting cell nuclei.
Significant differences in neurite length were shown in two of the materials, in contrast, the differentiation index was significantly different from the control in most of the materials. The materials showed differences in percentages of primary and secondary amines, as well as in the oxidized states (C≡C and C≡N) that were appearing in higher amounts as the synthesis power increased, which may explain the differences in the degrees of cell differentiation and proliferation.

Area: Plasticidad Celular y Circuitos Neurales

Key words: polymers, differentiation, plasma.

The persistence of antidepressant-like effects of rTMS at 5Hz is associated with microglial modifications in the hippocampal neurogenic niche in rodents exposed to unpredictable chronic mild stress.

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Repetitive transcranial magnetic stimulation (rTMS) as a therapeutic intervention for depression has been shown to have positive results in patients suffering from major depression, especially in patients with resistance to pharmacological treatment. There is a close relationship between neurogenesis and the effects of rTMS. In rodents exposed to chronic unpredictable mild stress (CUMS) treated with rTMS (5Hz), the stimulation is linked to pro-neurogenic effects in the hippocampus and a decrease in depressive-like behaviors such as anhedonia and hopelessness. However, although the relationship of hippocampal neurogenesis in the antidepressant effect is known, the molecular and cellular mechanisms that lead to the persistence of its antidepressant and plastic level effects in the hippocampus have not been fully elucidated. In this sense, it was of interest to know whether rTMS can modulate other cell types, such as microglia since the overactivation of these cells has been correlated with the generation of a pro-inflammatory environment in the depressive disorder, which affects the production of factors that modulate the proliferation or survival of different cells within the neuronal lineage. Therefore, it was important to determine whether 5Hz rTMS can reverse the morphological alterations of microglial cells in the hippocampus of rodents exposed to CUMS, and whether these modifications persist over time. We used Balb/c females exposed to CUMS for 15 continuous weeks, treated with the first set of stimulation at 5Hz for 4 weeks, then started maintenance sessions at 5Hz for 5 more weeks. To perform microglial cell detection, immunolabeling with IBA-1 and TMEM119 was performed, and the number of IBA-1$^+$ or TMEM119$^+$ cells in the granule cell layer and throughout the subgranular zone of the hippocampal dentate gyrus was quantified, and morphometric data of these cells were estimated. Our results indicate that 5Hz rTMS reverses the alterations in microglial cells caused by chronic stress, promoting their proliferation in the granular cell layer of the dentate gyrus and, this effect is maintained for at least 7 weeks, despite continued exposure to chronic stress. It was also observed that exposure to CUMS induced changes in the morphology of microglia, such as a reduction in the number and length of processes. However, treatment with 5Hz rTMS was able to reverse these effects and modulate their persistence for at least 7 weeks. In addition, the alterations produced by CUMS and the benefits of rTMS on hippocampal neurogenesis will be shown and discussed.

Keywords:
Repetitive transcranial magnetic stimulation, depression, neurogenesis.

Área: Plasticidad celular y circuitos neurales.

Environmental enrichment influences social interaction and agonistic behavior in the offspring of pregnant dams exposed to immune activation with the viral mimetic Poly I:C implication of neurogenesis and sex.

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Environmental enrichment (EE) consists of the improvement of physical and psychological well-being. In rodents, EE induces behavioral and structural neuroplastic modifications that influence the way they face stress and social behavior. Interestingly, the offspring of pregnant dams exposed to immune activations shows alterations in social behavior with important affectation in the ventral hippocampus. Those alterations caused by the pregnant dams exposed to immune activation on the offspring are prevented by the exposure to EE in C57Bl6 mice. Interestingly, hippocampus is a brain region in which the generation of new neurons occurs. Those newborn neurons are related to learning and memory processes but also to support the effects of stress. Also, EE modulates the generation of new neurons in the hippocampus and some studies have pointed to the regulation of glial cells (microglia and oligodendrocytes) as part of the plastic modifications caused by EE exposure. Thus, in this study we hypothesized that the intervention with EE in the offspring of pregnant dams exposed to immune activation will reverse social behavior with modifications in the hippocampal neurogenic niche in females and male Balb/C mice. The offspring of dams exposed or not to immune activation during pregnancy at embryonic day 12 (E12) were assigned to different groups: 1) control, 2) EE, 3) Poly I:C or 4) Poly I:C/EE. The exposure to EE or standard housing conditions was from postnatal day 22 to 32. On postnatal day 34, males and females evaluated in social behavior test. Then, mice were sacrificed to dissected out the brain. Left hemisphere was destinated for immunohistochemistry and from the right hemisphere, we dissected out the hippocampus. The results of our study suggest that the EE intervention during adolescence improved sociability in female Balb/C mice than in female mice exposed to standard conditions of housing. Similar results were seen in male Balb/C mice exposed to EE during adolescence. The full discussion of social/agonist behavior and their correlation with increased neurogenesis will be exposed.

Keywords: Environmental enrichment · Neurogenesis · Poly I:C · Hippocampus

Neurogenesis-dependent and/or independent mechanisms underlying the antidepressant-like effect of 5Hz repetitive transcranial magnetic stimulation (rTMS) in mice exposed to chronic mild stress

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Introduction: Depression is one of the most common affective disorders. It is characterized by lack of interest in daily activities, anhedonia, suicidal thoughts, poor emotional reactivity. Symptoms must be present in the subject for a minimum period of two weeks to be diagnosed as depression and are diminished by antidepressant drugs, electroconvulsive therapy, and repetitive transcranial magnetic stimulation (rTMS). The latter is a non-invasive brain stimulation treatment approved by the Food and Drug Administration (FDA) in 2008 for major depressive disorder. Despite its approval, the mechanisms underlaying its benefits are not completely known. Recent studies have pointed to the regulation of hippocampal neurogenesis as one of the mechanisms by which rTMS produces the benefits. However, some behavioral benefits of rTMS could be associated with other structural neuroplasticity related events. Thus, the aim of this study was to determine the neurogenesis dependent- or independent effects of rTMS in a chronically stressed mouse model.

Methodology: Thirty-five female Balb/C mice were exposed to a protocol of chronic unpredictable mild stress. Rodents were assigned to one of the five groups: 1) control without stress, 2) stress group, 3) stress plus rTMS, 4) stress plus temozolamide (25mg/kg) and 5) stress plus temozolamide followed by rTMS. At the end of the stress protocol mice underwent to several behavioral test related to learning and memory or depression. Finally, brains were dissected out to perform immunohistochemistry for markers of the neurogenic process or for Golgi-Cox impregnation for the analysis of dendrites and dendrite spines in granular cells.

Results: The results of our study indicate that rTMS requires neurogenesis to revert behavior related to despair but not for self-care. Although, rTMS seems to be independent of neurogenesis to improve learning and memory in chronically stressed mice. Further results and limitations will be discussed.

Conclusion: Our results point to that neurogenesis is one of the important mechanisms by which rTMS is carrying out its antidepressant effect. Although, the benefits on learning and memory involved other neuroplasticity related events.

Keywords: Neurogenesis, repetitive transcranial magnetic stimulation (rTMS), and depression.

Area: Cellular plasticity and neuronal circuits.

Short time of social instability stress does not induce depressive-like behavior but evidences low social interaction with increased negative social behavior and dendritic remodeling in the dentate gyrus of female C57Bl6 in environmental enrichment

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It has been shown that the risk of developing stress-related behavioral disorders such as depression is twice as high in women than men. Social stress appears to be the leading cause of the origin of this disorder. Emerging evidence suggests that the social instability stress (SIS) model could be a suitable framework for investigating this stress related to depression in females. On the other hand, it has been seen that environmental enrichment (EE) modulates hippocampal neurogenesis and behavior, resulting in an increase dendritic remodeling in the hippocampal dentate gyrus (DG) and that this, in turn, contributes to greater adaptability to stressful exposures in environment-enriched mice. Therefore, it is important to know the neuroplastic mechanisms associated with the behavioral effects generated by the SIS.

In this regard, we carried out an instability stress protocol trial using C57BL/6 mice females together with the forced swimming test, sociability test, and Golgi cox technique to know the mechanisms of dendritic remodeling associated with behavioral effects produced by the stress paradigm. We designed a standard housing experiment with a subsequent short time of social instability stress protocol on animals that were or were not pre-housed in EE. Subsequently, we exposed them to forced swim, sociability test and then made the analysis of dendrite spines and neurogenesis events occurring in the dentate gyrus of the hippocampus.

Our results showed that stress due to social instability can modify social behaviors, especially the preference of mice to seek new individuals with whom to interact, and those mice exposed to the social instability protocol decreased the exploration time. On the other hand, the protocol of the paradigm of instability carried out for a week does not increase the despair in the mice significantly, however, the enriched group showed a decrease in immobility time that may be associated with the effect of enrichment to cope stress in this test.

We conclude that the immobility time in the forced swim test decreased in those mice with the EE experience. Nevertheless, there was a decrease in sociability for all groups after the social instability protocol with interesting differences in negative social behavior. The differences in dendrite spines, doublecortin, oxytocin, social behavior will be discuss.

Key concepts: Social instability stress (SIS), Environmental Enrichment (EE) and Dendritic remodeling.

Repetitive transcranial magnetic stimulation (5 Hz) decreases the depressive-like behavior, modifies the structural dendritic plasticity, and induces global epigenetic changes in the frontal cortex and hippocampus in a model mouse of chronic stress.

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Depression is one of the main mood disorders affecting the world's population. It is estimated that more than 300 million people worldwide suffer from depression, a figure that has been accentuated by the recent COVID-19 health crisis and is expected to grow in the coming years. It has been reported that there are several neurobiological alterations in the brains of patients with depression, ranging from changes in the activity and volume of cortico-limbic system structures, reduced neurogenesis and synapse formation, as well as dendritic atrophy in the hippocampus (Hp) and prefrontal cortex (PfCx). These morphofunctional changes in the brain of patients with depression and in animal models of stress have been associated with the alteration of epigenetic mechanisms that regulate brain plasticity, such as DNA methylation and histone acetylation. Also, it has been reported that repetitive transcranial magnetic stimulation (rTMS) is able to reduce the symptoms caused by depression. At the neurobiological level, it has also been described that rTMS is able to regulate the expression of neurotrophins, induce long-term potentiation, and the formation of new neurons in the Hp. However, there are no published data on the effect of this technique at the epigenetic level in the context of depression. It is for this reason that the aim of this work is to evaluate the antidepressant effect of rTMS (5 Hz) and its involvement in dendritic remodeling and in the regulation of global DNA methylation and histone H2B acetylation in PfCx and Hp. For this purpose, female Balb/C mice were exposed to the chronic unpredictable stress (CUS) to generate depressive-like behaviors assessed by the coat state, sucrose preference test and forced swim test. After of the stress protocol and behavioral assessment, the mice were sacrificed, and brain samples were obtained for histology and DNA extraction. By Golgi-Cox staining, dendritic remodeling was evaluated at the micro- and macrostructural level in the dentate gyrus (DG) of the Hp and in the CxPf. By immunohistochemistry, immunoreactivity of synapse proteins (synaptophysin and neurogranin) and H2B acetyl-histone was determined. In addition, N-5-methylcytosine levels (global DNA methylation) were quantified by ELISA. Our data indicate that stress generates depressive-like behaviors (reduced self-care, anhedonia, and hopelessness) and that rTMS and Flx reverse this effect. At the neuroplastic level, we found that our antidepressant treatments reverse the reduction in dendritic spine density as well as stress-generated atrophy in dendritic arbors, in addition to favoring dendritic spine maturation and synapse protein expression differentially in CxPf and Hp. At the epigenetic level we found that rTMS induces DNA methylation in the dentate gyrus, but Flx does not, while in CxPf the Flx showed an increase in histone H2B acetylation compared to EMTr. In conclusion, these data provide evidence that rTMS has an antidepressant effect comparable to that of Flx, in addition to acting by promoting dendritic remodeling and the expression of synapse proteins in the cortico-limbic system. These neuroplastic changes may be associated with the increased DNA methylation found in GD. It is recognized that it is required to explore in detail whether there is a direct association between these changes in epigenetic marks and the neuroplastic phenomena reported in this work, in addition to exploring the regulation of possible candidate genes that may explain the mechanism of action of rTMS at the level of brain plasticity.

Keywords: rTMS, epigenetic, depression.

Plastic changes in the sexual reward circuit induced by motivated behaviors in male rats

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Area: Cellular plasticity and neural circuits

Synaptic plasticity is the result of changes in the number and strength of synaptic connections due to the processing of different stimuli. Sexual experience can influence synaptic plasticity in the CNS in many ways, to date there are no studies that have demonstrated this. In male rats, motivational and executive mechanisms are fundamental in sexual behavior. To evaluate these mechanisms we used the Partner Preference Test (PPT) and the Sexual Incentive Motivation (SIM). The objective of the project was to determine by immunofluorescence techniques and stereology the plastic changes derived from the activation generated by the acquisition of experience in the SIM and PPT in amygdala (AMY), hippocampus (HPO), ventromedial hypothalamus (VMH) and olfactory bulbs (OBs), related structures with sexual reward circuits.

Material and methods. 15 male Wistar rats (300-350 gr) will be used. They were divided into 3 groups: control group (CG), PPT and SIM. As stimuli, ovariectomized female rats will be used in advance of behavioral tests and sexually expert males. After 10 weeks of the behavioral tests, the brains were extracted, 30 µm sections were made and those corresponding to the structures of interest were selected. Images were obtained with confocal microscopy from -2-12 to -3.60 mm with respect to Bregma in AMY, HPO and VMH and in the OBs from 5.2 to 6.7 mm. To avoid bias, capture parameters were established in the CG and applied to the experimental groups. In each image the sites of interest (ROIs) were delimited and intensity data were obtained. We average the intensity values of 4 coordinates (3 µm each coordinate) by ROI and determine the volumetric value of each structure.

Results. Behavioral test show that the sexual experience acquired during 10 weeks in both, PPT and SIM increases the time that the male spends with the female as was expected, as well as a decrease in mounting and intromission latencies and an increase in the number of mounts and intromissions. We found significant differences in synaptophysin expression in the dentate gyrus between the PPT and the control group and in the amygdala and the main olfactory bulb between SIM and the control group.

Conclusion. We can concluded that sexual behavior as motivated behavior induces plastic changes in brain structures belonging to the sexual reward circuit.

Key words: synaptophysin, sexual behavior, synaptic plasticity.

Memory impairment in adulthood after neonatal excitotoxicity is related to changes in NMDA receptor NR2 subunit protein expression

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Area: Synaptic Plasticity and Neural Circuits

Abstract

NMDA receptors (NMDARs) are essential transducers of excitatory glutamate-mediated neurotransmission. They have a heterotetrameric structure classically composed of two NR1 subunits combined with two NR2A-D subunits or with one NR2A-D and one NR3A-B subunit. The NR1-NR2A and/or NR2B combinations appear more frequently in the hippocampus where NMDARs have been widely implicated in memory and learning, but also in excitotoxic neuronal death when they are overactivated. Neonatal monosodium glutamate (MSG) treatment induces excitotoxicity and early changes in the NR1 and NR2 subunits expression level. However, the expression level of NR1, NR2A, and NR2B proteins in adulthood after neonatal MSG treatment and their relationship to memory and learning remained unknown. In this work, newborn male Wistar rats were randomized into two groups: MSG-treated animals (4 g/kg body weight on postnatal days (PD) 1, 3, 5, and 7) and untreated (control) animals. At PD60, 6 animals from each group were euthanized to obtain hippocampal total protein extract, and the expression level of the NR1, NR2A and NR2B proteins was analyzed by western-blot approach in the extracts. In addition, other animals (9 for each group) were subjected to the Barnes maze and object recognition tests to assess memory and learning. The results obtained show that neonatal MSG treatment does not significantly modify the expression level for the NR1 and NR2A proteins, but the treatment does significantly increases the expression level for the NR2B protein. In addition, behavioral tests indicate that short-term working and spatial memory are significantly impaired in MSG-treated animals. These findings suggest conformational and functional modifications in NMDARs as part of the long-term effects of neonatal excitotoxicity elicited by the MSG treatment, which appears to be related to learning impairment, but it should better determined to improve therapeutic approaches applied after excitotoxicity.

Keywords: NMDA receptors – Excitotoxicity – Memory

Muscarinic modulation of firing pattern in two types of parafascicular thalamic nucleus neurons.

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Background: The Parafascicular nucleus (Pf) is part of the intralaminar thalamic nuclei associated with different functions such as attention, learning, sensory processing, pain perception and motor action selection. Electrophysiologically, the neurons composing this nucleus have been separated into two populations characterized by the presence of only one or two components in the after hyperpolarizing potentials (AHPs) following a single action potential. Despite the important cholinergic input received by the Pf nucleus, the functional effects of acetylcholine have not been clearly established. Therefore, the aim of the present work was to establish which are the changes in the electrophysiological properties of the Pf nucleus neurons in response to the activation of cholinergic receptors, as well as, to determine the ionic conductance and the cholinergic receptors involved in this modulation.

Methodology: The spontaneous activity of neurons was recorded using the patch-clamp technique in whole cell mode in current clamp in 300 µm thick horizontal slices of CD1 mice 25 to 30 days postnatal. Agonists for cholinergic receptors and antagonists of different types of ion channels were used to identify the mechanism of action of acetylcholine in the PF nucleus.

Results: The results of the work show that pharmacological activation of cholinergic receptors, by using the agonist carbachol, exclusively affects neurons that present the AHPs with two components reducing the amplitude and duration of the slow component. These electrophysiological changes were associated to calcium-dependent potassium channels (KCa) SK-type, because the pharmacological blockade of these channels with apamine, occluded the effect produced by the activation of cholinergic receptors. Likewise, it was identified that calcium entry through L-type channels is a necessary factor for the activation of SK-type KCa channels. Finally, it was observed that the cholinergic receptors involved in this modulation are muscarinic type.

Discussion and Conclusion: The above data indicate that cholinergic modulation of the Pf nucleus presents a differential effect on the neuronal populations that compose it, which is based on the electrophysiological effect of cholinergic muscarinic receptor activation and the fact that, SK-type KCa channels are one of its final effectors by increasing the firing frequency. This could imply functional and behavioral differences associated with the afferents that this nucleus presents, whose main output is towards the striatal nucleus of the basal ganglia.

Area of work: Cellular Plasticity and Neuronal Circuits.

Keywords: Parafasicular nucleus, After Hyperpolarizing Potentials, Acetylcholine.

The Krüppel-like factor 13 (KLF13) is a New Regulator of the JAK/STAT Signaling Pathway in Hippocampal Neurons

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The Krüppel-like factors (KLFs) have emerged as important regulators of neuronal proliferation, differentiation and axon regeneration. They constitute a family of eighteen transcription factors characterized by three C-terminal C2H2 zinc finger motifs that recognize GC/GT rich sequences in DNA. Our work focused on KLF13, which is known to act predominantly as a transcriptional repressor by associating with chromatin within proximal promoters of its target genes. Recently, it has been described that KLF13 directly represses transcription of genes involved in neurotrophic factor signaling pathways in mouse hippocampal neurons, including the JAK-STAT pathway, which mediates the actions of several cytokines, growth factors and hormones. In the nervous system, it transduces extracellular signals into transcriptional programs to regulate survival, axon regeneration, synaptic plasticity and neuroinflammation. Growth hormone (GH), in part by activating the JAK-STAT pathway, has been shown to have some of these neurotrophic activities. Therefore, here we analyzed the GH-induced JAK-STAT activity in the adult mouse hippocampus-derived cell line HT22 to test the hypothesis that KLF13 crosstalks with the JAK/-STAT pathway to regulate its activity. We used our previously engineered HT22 cell lines: the TRTO-*Klf13,* in which the *Klf13* expression is induced by addition of doxycycline; and the CRISPR/Cas9 genome edited *Klf13*-KO HT22 cell line. Our results confirmed that KLF13 directly regulates the expression of several genes involved in the JAK-STAT pathway: *Stat3, Stat5b, Socs1* and *Socs3* were repressed while *Stat5a* was induced by forced expression of *Klf13*. We also found that expression of some of these genes (*Socs1*) was dysregulated in KLF13-deficient neurons. We then analyzed the effect of GH on mRNA levels of its main mediator, IGF1, and found that KLF13 depletion led to an enhanced effect of GH on *Igf1* expression. As a proxy for analyzing JAK-STAT activity, transfection-reporter assays were conducted using two sensor plasmids to track pathway activity either by STAT3 or STAT5. We found that forced expression of KLF13 increased baseline of STAT5 activity, which was enhanced by GH treatment, while in HT22-*Klf13*-KO cells the basal and GH-induced activity of STAT5 were lower compared with control. By contrast, KLF13 blocked the GH-induced activity of STAT3, while *Klf13* depletion caused an enhanced effect of GH on STAT3-mediated pathway activity. These findings support the notion that KLF13 has a bifunctional effect on the GH-induced JAK/STAT activity by enhancing or inhibiting the STAT5 or STAT3 branch, respectively.

Keywords: Krüppel-like factors; JAK/STAT; growth hormone; hippocampus

Areas: Signal transduction; Gene expression; Neuroendocrinology

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I

The role of miRNAs in the signaling pathway activated by Zika virus leading to microcephaly

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Development of central nervous system (CNS) requires complex sequential processes, that involves an orchestrated sequence of genetic, environmental, and biochemical factors. Alteration at any step of this organized series of events can lead congenital damage like microcephaly. Microcephaly results of a depletion of the radial glia population, either by cell death or premature differentiation. Through case reports, it had been stablished that maternal Zika infection during pregnancy can induce microcephaly and accumulating evidences have shown that Zika virus (ZIKV) can infect human neural stem and progenitor cells, astrocytes, microglia and neural cells disrupting differentiation, proliferation, apoptosis and cell cycle process.

Post-transcriptional gene regulation is an important mechanism that controls neuronal development and CNS function; where participation of miRNAs, small non-coding RNAs molecules that suppress expression of target genes, are essential both embryonic and adult stages. Given that miRNAs are essential for the fine tuning of neurogenesis and that ZIKV infection impairs neurogenesis and brain development, in the present study, we investigated whether the antiviral response against ZIKV alters the expression of miRNAs involved in neurogenesis.

We identified two-time dependent antiviral responses triggered by ZIKV infection in the neuronal cells line, mHypoE-N1. The first one is mediated by NF-κB pathway. ZIKV infection promoted NF-κB translocation to the nucleus at 24 hours post-infection (hpi) when compared with non-infected cells. Simultaneously, the STAT3 pathway was induced and picked at 72 hpi. According with previous data indicating that NF-κB can induce miRNA-125a expression while STAT3 can promote miR-7 expression, we found that ZIKV regulates miRNA-125a and miRNA-7a expression in a time dependent manner. miRNA-125a expression was increased at 24 hpi meanwhile miRNA-7a was increased after 48 hpi. Current experiments are aimed to identify the miRNA-125a and miRNA-7a target genes in mHypoE-N1 cells.

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Area: Transducción de señales
Keywords: NF-kβ pathway, miRNA-7, Zika virus.

Analysis of phosphatidylethanolamine binding protein 1 (PEBP1) interactions with other proteins during brain cerebral focal ischemia in rat hippocampus

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Introduction: Focal Cerebral ischemia (FCI) is the sudden loss of blood flow of a specific area in the brain. FCI is among the leading causes of morbimortality and the main cause of disability worldwide. PEBP1 (also called RAF kinase inhibitory protein) is a scaffold protein involved in the regulation of signaling pathways for cellular response of different tissues during normal and pathological conditions. During FCI, reactive oxygen species production increases due to the copper, zinc, and selenium mobilization among other molecular processes. Under oxidative stress, PEBP1 is involved in the regulation of ferroptosis, interacting with GPX4 and lipoxygenases 15LO1/15LO2. Due to this and other activities, it is considered that PEBP1 may have neuroprotective functions, but they have not been enough characterized.

Objective: Analyze the interaction of PEBP1 with other proteins, including those involved in antioxidant regulation during FCI to assess its neuroprotective role.

Methods: FCI was induced in Wistar rats for 30 to 90 min with/without 24 h of reperfusion (R). Hippocampus total proteins were analyzed by 12% SDS-PAGE and Western Blot (WB) using specific anti-PEBP1 and anti-PEBP1(S153) antibodies. To identify PEBP1 interaction with other proteins during FCI we used co-immunoprecipitation (co-IPP) and Mass spectrometry (MS). In addition to investigate PEBP1 interaction with antioxidant proteins we search STRING interactome database and did molecular docking with candidate molecules.

Results: The expression and phosphorylation of PEBP1 augmented at 60 min FCI/R and diminished after 90 min. PEBP1 was detected as a double band (between 37 and 25 kDa) by WB. Using Co-IPP and MS, interaction of PEBP1 with dynein and desmin was detected. PEBP1 interaction with catalase, GPX4 and SOD3 was detected and supported by interactomes and molecular docking.

Conclusions: Brain ischemia induces changes in expression and phosphorylation of PEBP1 in hippocampus. During FCI, PEBP1 interacts with Catalase, GPX4 and SOD3 possibly modulating an antioxidant response. Interaction of PEBP1 with dynein and desmin could suggest that, as a scaffold protein participate in the intracellular mobilization of molecules.

Keywords: Ischemia, PEBP1, Hippocampus

Alterations in signaling by DHA and its association with dendritic complexity in hippocampal neurons of an autistic-like mouse

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Area: Signal transduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders characterized by persistent deficits in social communication and interaction, as well as the presence of restricted and repetitive patterns of interest and behavior. Diverse studies in subjects with ASD and murine models demonstrated alterations in morphology and reduction of dendrites in hippocampus.

Treatment with docosahexaenoic acid (DHA) in primary neuronal cultures changes the neural complexity, promoting the growth of dendrites and axons. Supplementation with DHA has been used as a complementary treatment in children with ASD demonstrating improvement in symptoms such as low sociability, however its effects in neuronal cytoarchitecture are unknown.

DHA is a ligand of GPR40 and GPR120, its stimulus can activate pathways such as PI3K/AKT and PKC/Erk. GPR40 protein overexpression has been implicated with an increase in complexity of the dendritic arbor in cell culture, but the activation of its signaling pathway and its effect on dendritic complexity in ASD are unknown. Thus, in this study we aim to analyze the effect of DHA treatment in the GPR40 and GPR120 signaling pathways, and its repercussion in dendritic complexity in primary hippocampal cultures of the strain C58/J an ASD murine model.

First, we analyzed the basal content of GPR40 and GPR120 receptors, as well as the phosphorylation levels of AKT and Erk, and the trophic factor BDNF. We found a lower quantity of GPR40 and BDNF in the autistic-like strain compared to the wildtype strain C57BL/6J, and an increase in total but not phosphorylated Erk.

To study the role of GPR40 and GPR120 in the activation of AKT and Erk, the primary cultures were treated with DHA 10µM for 5 min and with the receptor antagonists DC260126 (for GPR40) and AH7614 (for GPR120). We found that the stimuli with DHA increased AKT and Erk phosphorylation in the wildtype strain through GPR40 activation, meanwhile GPR120 was only implicated in the phosphorylation of AKT. Interestingly the same conditions of treatment with DHA couldn't activate the kinases in the autistic-like strain, showing alterations in the signaling pathway.

It was previously demonstrated by our laboratory that the neurons of the hippocampus in the adult C58/J mice had a lower dendritic complexity compared to C57BL/6J. We wanted to confirm these changes in the hippocampal primary culture and analyze if the treatment with DHA could increase the complexity of the dendritic arbor in both strains. We found that the C58/J strain had a lower complexity of the dendritic arbor than the C57BL/6J strain and, that the treatment with DHA 10µM for 6 days increases the complexity and length of the arbor in the wildtype strain and only the length in the autistic-like strain.

Thus, these results show that there are changes in the content and signaling pathway of GPR40 as well as the dendritic complexity in the hippocampal cultures of the autistic-like strain C58/J compared to the wildtype strain, and that the treatment with DHA could affect the length of the dendritic arbor in the C58/J strain.

Key words: Docosahexaenoic acid (DHA), GPR40, dendritic arbor

PTP1B regulates cell cycle progression through a Cdk3/Rb dependent manner in human glioblastoma cells

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Glioblastoma (GB) represents an important health problem due to its high rate of mortality and the lack of an effective therapy. Therefore, the identification of new potential drug targets may provide novel therapeutic strategies for the treatment of these tumors. Recent evidence indicates that Protein Tyrosine Phosphatase 1B (PTP1B) is overexpressed in different types of cancer. However, the role of this enzyme in GB development remains unclear.
Using a SILAC-based strategy we identified the Cyclin-dependent kinase 3 (Cdk3) as a novel PTP1B substrate. Local docking and molecular dynamics studies revealed stable interactions between PTP1B's catalytic domain and Cdk3. In addition, an *in vitro* phosphatase assay confirmed that PTP1B dephosphorylates Cdk3 at Tyr15. Interestingly, these two proteins interact in the nuclear envelope of HEK293-T cells, as well as in the nucleus and cytoplasm of human GB cell lines. Finally, our results showed that pharmacological inhibition of PTP1B promotes a delay in cell cycle progression. Mechanistically, PTP1B inhibition significantly reduces Cdk3 activity, with the consequent repression of E2F transcriptional activity in an Rb dependent-manner, and the down-regulation of E2F target genes Cdk1, Cyclin A, and Cyclin E1. These findings delineate a new signaling pathway from PTP1B to Cdk3, needed for efficient cell cycle progression in an Rb-E2F dependent manner in human GB cells and suggest new therapeutic strategies for the treatment of this type of tumors.

Keywords: Protein Tyrosine Phosphatase 1B, Cell Cycle, CDK3, Cancer, Glioblastoma.

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Artificial early and late memory signals induce taste avoidance memory, plastic and neurochemical changes

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Área: Transmisión sináptica

The basolateral nucleus of the amygdala (BLA) and the insular cortex (IC) are brain structures anatomically connected that are involved in the formation and expression of Conditioned Taste Aversion (CTA). There is some evidence suggesting a neurochemical modulation of the IC made by BLA; such modulation entails waves of neurotransmitters' release during and after the association of a novel taste with gastric malaise and is equally determinant for CTA consolidation. Nevertheless, high-specificity approaches are still required for a better understanding on the functional role of this BLA-IC interaction in the establishment of aversive memories. We designed a set of experiments using optogenetics to determine whether stimulation of the BLA-IC pathway might induce CTA in the absence of a gastric malaise inductor. Male Wistar rats were bilaterally injected with an adeno-associated virus encoding channelrhodopsin (ChR2) and a fluorescent protein (EYFP) into BLA, and optical fibers were implanted aiming IC in pursuance of manipulate the aforementioned projections. Blue light (473 nm) pulses (20 Hz) were applied in a double-stimulation protocol after saccharin consumption in order to emulate the activity observed during and after the CTA association. The results show a reduced saccharin intake during long-term memory test, similar to the effect observed when the taste stimulus is paired with gastric malaise. Next, we aimed to explore the mechanisms by which the optogenetic manipulation may generate this avoidance memory; monitoring of neurochemical activity within IC reveals an increase in extracellular levels of glutamate concurrent with both stimulations of the pathway exclusively in animals expressing the opsin. Moreover, electrophysiological recordings of the BLA-IC projection indicate that, as observed in behavioral experiments, a double stimulation leads to a sustained augmentation in the strength of excitatory postsynaptic potentials, thus providing evidence of plastic changes expressed as long-term potentiation. Interestingly, inactivation of glutamatergic NMDA receptors before the double stimulation prevents the enhancement of synaptic communication, demonstrating the relevance of this neurotransmitter as well as its associated signaling activity for the reactivation process and, at the same time, for consolidation of a taste avoidance memory.

Keywords: Amygdala, Insular Cortex, Glutamate.

Functional role of cortical glutamatergic neurotransmission in conditioned taste preference

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Área: Transmisión sináptica

Taste recognition memory is essential for animal's survival, this ability allows them to distinguish nutritious from toxic substances. Particularly, taste preference memory has an important adaptive role since the organisms have to associate tastants with positive postingestive effects. Currently it is known that insular cortex (IC) has a functional role in the integration of taste and visceral signals. However, there is scarce information about the neurochemical processes of cortical brain structures involved in taste and positive postingestive signaling necessary for conditioned taste preference (CTP) establishment. Therefore, we evaluated the neurochemical signaling of a novel taste and positive visceral stimuli within the IC during the acquisition of a CTP. First, we developed a taste preference conditioning protocol in male Wistar rats through the presentation of a novel taste that is paired with the administration of i.p. glucose. Accordingly, we performed a dose-response curve in which two bottles containing 30 mL of saccharin (0.3%) were given to animals and 15 min later different doses of glucose were injected intraperitoneally. Our results show that the administration of glucose 350 mg/kg induces a long-term conditioned preference for saccharin. Subsequently, by implanting microdialysis probes in free-moving animals, we monitored the changes in norepinephrine and glutamate release within the IC during saccharin intake and glucose administration. The results show that saccharin presentation induces an elevation of norepinephrine. Interestingly, glucose administration promotes an increase in both norepinephrine and glutamate release. To assess whether glutamate signaling has a functional role during CTP establishment, we administered NMDA receptor antagonist (APV) into the IC immediately before i. p. glucose and evaluated long-term memory 72 hours later in a two-bottle session test. Our results demonstrate that NMDA receptors blockade within the IC hinders CTP establishment. Additionally, we evaluated whether the blockade of NMDA receptors impairs memory acquisition or consolidation processes; to achieve this, we administered APV 30 minutes after the acquisition session. Short-(4 hrs) and long-(72 hrs) term memory were assessed. Results show that NMDA receptors blockade within the IC impairs long-term memory but spares short-term memory. These results suggest that glutamatergic signaling within the IC plays an important role in the establishment of CTP. Additionally, our results prove that the activation of NMDA receptors is related to the consolidation of taste preference memories.

Keywords: Insular cortex; glutamate; taste preference

Cerebral biomarkers measurement in serum from Parkinson's disease patients with a high output technique (nano not blot) and its further analysis using artificial intelligence tool

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Among neurodegenerative disorders, Parkinson's disease is the second most prevalent, preceded only by Alzheimer's disease. Although it is rapidly evolving, epidemiological projections point to more than 12 million people affected by 2040. Diagnosis still relies upon clinical features since no studies can refute or confirm its presence. Different studies have looked for a biomarker to diagnose Parkinson's disease (PD) accurately, even at pre-symptomatic stages; however, to date, no study has accomplished this objective. The importance of having a novel technique in clinical practice will improve medical treatments and provide further benefits in using medications with potential neuroprotective properties and disease modification effects. We have developed a new approach called "nano dot blot" to monitor several cerebral biomarkers associated with the PD, such as NF-L, GFAP, S100B, PSD95, and Debrin-1 in serum. The reliability of this method and its translational potential is proposed in this work, once first was validated in experimental animals. With this method it is possible to test several replicates of each sample in a high throughput format to evaluate a large number of patiens in a short time. We determined the level of these biomarkers in 25 PD patients and 23 healthy persons. The results were analyzed with a classical statistical package, and significant alterations were evident in PD patients concerning control. In addition, the data collected were processed in a single-blind model by using min-max normalization. Then, K-means was applied to obtain a possible first indication of clustering at the data. Something quite interesting is the fact that with a k=2, data is splitted into healthy and no healthy patients with accuracy of 97%. Finally, the real number of clusters, suggested by the elbow method and confirmed by 2D UMAP projection, is basically four indicating degrees from non-disease to full blown Parkinson. Thus, making the clustering method a great tool for analysis of possible degrees of Parkinson.

Area: Technology and innovation

Key words: Biomarkers, nano dot blot, artificial intelligence

Increase of 5-HT levels is induced both in mouse brain and HEK-293 cells following their exposure to a non-viral tryptophan hydroxylase construct.

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Abstract

Tryptophan hydroxylase type 2 (Tph2) is the rate-limiting enzyme for serotonin (5-HT) biosynthesis in brain. Dysfunctional Tph2 alters 5-HT biosynthesis, leading to a deficiency of 5-HT, which could have repercussions on human behavior. In the last decade, several studies have associated polymorphisms of the *TPH2* gene with suicidal behavior. Additionally, a 5-HT deficiency has been implicated in various psychiatric pathologies, including alcoholism, impulsive behavior, anxiety and depression. Therefore, the *TPH2* gene could be an ideal target for analyzing the effects of a 5-HT deficiency on brain function. The aim of this study was to use the construct pIRES-hrGFP-1a-Tph2-FLAG to treat CD1-male mice and to transfect HEK-293-cells and then to evaluate whether this treatment increases 5-HT production. 5-HT levels were enhanced 48 h post-transfection, in HEK-293 cells. Three days after the ocular administration of pIRES-hrGFP-1a-Tph2-FLAG to mice, putative 5-HT production was significantly higher than in the control in both hypothalamus and amygdala, but not in the brainstem. Further research will be needed on the possible application of this treatment for psychiatric diseases involving a Tph2 dysfunction or serotonin deficiency.

Área a la pertenece el trabajo: Tecnología e Innovación

Palabras clave: 5-HT; depression; TPH2 gene; tryptophan hydroxylase 2; transfection; gene therapy.