23 Jornadas Académicas

Septiembre 26 al 30
2016

Instituto de Neurobiología
UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO

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Ing. Ramón Martínez Olvera
Ing. Sandra Hernández García
Unidad de Cómputo
CONFERENCIA INAUGURAL

Septiembre 26, 10:00 h.
Dr. William Lee
Coordinador de la Investigación Científica, UNAM

Programa de Conferencias

Septiembre 26, 12:00 hrs.
"Scalar dynamics of cortico-basal ganglia circuits involved in motor timing"
Dr. Mehrdad Jazayeri
Massachusetts Institute of Technology, USA

Septiembre 27, 12:00 hrs.
"Prediction as a Humanitarian and Pragmatic Contribution from Human Cognitive Neuroscience"
Dr. John Gabrieli
Massachusetts Institute of Technology, USA

Septiembre 28, 12:00 hrs.
"The basal ganglia in action"
Dr. Henry Yin
Center for Cognitive Neuroscience
Duke University, USA

Septiembre 29, 12:00 hrs.
"Global vs. local mechanisms: How ion channels respond to temperature and pressure"
Dr. Dan L. Minor
University of California, San Francisco

Septiembre 30, 12:00 hrs.
"A putative participation of melanin-concentrating hormone in neurogenesis during the lactation period"
Dr. Jackson Cioni Bittencourt
Laboratory of Chemical Neuroanatomy
Dept. of Anatomy ICB/USP, São Paulo, Brazil
Programa de Actividades

PRESENTACIONES ORALES, ALUMNOS DE POSGRADO

SEPTIEMBRE 27, 10:00 hrs.
Departamento de Neurobiología Conductual y Cognitiva

Milené Roca
*Electroencephalographic characterization of subgroups of children with learning disorders.*
Laboratorio de Neurorretróalimentación.
Tutor Dra. Thalia Fernández Harmony.

Laura Cuaya
*Cerebral activity in dogs during perception of human faces.*
Laboratorio de Conectividad Cerebral.
Tutor Dr. Luis Concha.

Cristina Siller
*Glucocorticoids interact with endocannabinoids in the dorsal striatum during memory consolidation of an inhibitory avoidance task.*
Laboratorio de Neurobiología del Aprendizaje.
Tutor Dra. Gina L. Quirarte.

SEPTIEMBRE 28, 10:00 hrs.
Departamento de Neurobiología del Desarrollo y Neurofisiología

Rafael Oliwares Moreno
*Anatomical and functional segregation of the Corticospinal System.*
Laboratorio de Integración Sensoriomotora.
Tutor Dr. Gerardo Rojas Piñón.

Jaime Cadena Valencia
*Oscillatory activity of supplementary motor area reflects temporal judgment of periodic events.*
Laboratorio de Sistemas Sensoriales y Planeación Motora.
Tutor. Dr. Víctor de Lafuente.

Arturo González Islà
*Combination of moderate exercise and Lithium prevents Amyloid Beta-Induced Hippocampal Dysfunction: Role of GSK3B.*
Laboratorio de Circuitos Neuronales.
Tutor. Dr. Fernando Peña.

SEPTIEMBRE 29, 10:00 hrs.
Departamento de Neurobiología Celular y Molecular

María Guadalupe Ledesma Colunga
*Prolactin protects against joint inflammation and bone loss in arthritis.*
Laboratorio de Endocrinología Molecular.
Tutor: Dra. Carmen Clapp.

Angélica Sofia Martinez Ramirez
*EMT and migration in ovarian carcinoma cells are regulated by UTP and adenosine.*
Laboratorio de Fisiología Celular.
Tutor Dr. Francisco Vázquez.

Christian Molina Aguilar
*Time caloric restriction inhibits the neoplastic transformation of cirrhotic liver in rats treated with diethylnitrosamine.*
Laboratorio de Fisiología Celular.
Tutor Dr. Mauricio Díaz Muñoz.
23° Jornadas Académicas
Jueces Participantes

Aguilar Ramírez Manuel
Alcántara González David
Areliano Ostoa Rogelio
Arnold Edith
Ayala Sumuano Jorge
Barrios Álvarez Fernando
Becerra González Marymar
Bedos Marie
Bittencourt Jackson C.
Bolaños Aquino Edgar
Bosch-Bayard Jorge
Carranza Salas Martha E.
Castañeda García Carolina
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Concha Loyola Luis
De Lafuente Flores V. Hugo
Díaz Miranda Sofía
Espino Saldaña Ángeles Edith
García Horsman Patricia
Gasca Martínez Deisy
González Santos Leopoldo
Harmony Baillet Thalía
Hernández Ríos Nydia

Hernández Sámano Arisai del Carmen
Juárez María Elena
Martínez Cabrera Gema
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Mendoza Trejo Soledad
Merchant Nancy Hugo
Mondragón Rodríguez Siddhartha
Moreno Carranza Bibiana
Orozco Rueda Pavel Ernesto
Palma Tirado Lourdes
Pasaye Alcaraz Erick Humberto
Peña Rangel Teresa
Ramos Aguilar Ma. Eugenia
Regalado Ortega Mirelda
Robles Juan Pablo
Rodríguez Cruces Raúl
Rodríguez Ortíz Luis
Rojas Hortelano Eduardo
Vázquez Cuevas Francisco
Vázquez Martínez Olivia
Vera Rivera Ángela Gabriela
SESIÓN 1: Septiembre 26, 16:00 a 19:00 h.
Carteles Exhibidos: 1 al 34

SESIÓN 2: Septiembre 27, 16:00 a 19:00 h.
Carteles Exhibidos: 35 al 67
NOTA. EL TRABAJO 47 HA SIDO DESCARTADO

SESIÓN 3: Septiembre 28, 16:00 a 19:00 h.
Carteles Exhibidos: 68 al 102
NOTA. EL TRABAJO 102 APARECE EN ORDEN ALFABÉTICO POR PRIMERO AUTOR

Los resúmenes incluidos en esta Memoria son responsabilidad de sus autores.
1. PHARMACOLOGICAL HYPERPROLACTINEMIA PROTECTS AGAINST DIABETIC RETINOPATHY IN RATS

Departamento de Neurobiología Celular y Molecular, Instituto de Neurobiología, Universidad Nacional Autónoma de México (UNAM), Campus Juriquilla, Querétaro, México.

Increased retinal vasopermeability (RVP) occurs early in diabetes and is crucial for the development of sight-threatening diabetic retinopathy (DR) and diabetic macular edema. The hormone prolactin (PRL) is proteolytically processed to vasoinhibins, a family of PRL fragments that inhibits the excessive RVP related to DR. Here, we investigate whether pharmacologically-induced hyperprolactinemia, by serving as a source of ocular vasoinhibins, reduces the pathological RVP in diabetic rats. Daily intraperitoneal (i.p.) injections of the dopamine D2 receptor antagonist sulpiride leading to hyperprolactinemia, were administered for 15 days, starting at 2 or 4 weeks after inducing diabetes with a single i.p. injection of streptozotocin (STZ). RVP was evaluated by the Evans blue method. Sulpiride induced hyperprolactinemia in a dose-dependent fashion, with the highest dose (20 mg/Kg) leading to maximal serum PRL levels (117±10.6 ng/mL). Treatment with 20 mg/Kg of sulpiride reduced and blocked diabetes-induced increase in RVP when treatment began at 2 and 4 weeks after STZ, respectively. Sulpiride had no effect on the RVP in the non-diabetic controls. High levels of circulating PRL protect against the progression of DR, perhaps through its intraocular conversion to vasoinhibins. Sulpiride is a prokinetic drug used in diabetic patients that may be desirable to target DR and diabetic macular edema.

We thank to Fernando López Barrera, Martín García, Alejandra Castilla, Nydia Hernández Ríos, Antonio Prado, and Daniel Mondragón. Supported by CONACYT grant 247164. (M)

2. AUDITORY EVOKED POTENTIALS TO ECOLOGICAL AND NON-ECOLOGICAL SOUNDS IN AWAKE MACAQUE

Ayala YA, Prado L, Luna R, Merchant H
Department of Behavioral and Cognitive Neurobiology. Institute of Neurobiology, UNAM.

To understand how key acoustic features of behaviorally relevant sound such as vocalizations or syllables are processed in the brain we assessed brainstem and cortical evoked potentials to simple (click) and complex sounds (/da/, full-length and excerpts of coo vocalizations). The /da/ syllable is widely used in clinical practice for assessing languages and hearing impairments and coo calls are harmonic sounds given during social interactions. Scalp responses (10/20 EEG system; Cz, Fz, Pz, F3, F4) to alternating-polarity stimulus were recorded in two awake adult macaques under free-field acoustic stimulation. Three brainstem peaks (P1-P3) with latency and amplitude sensitive to the rate and intensity of stimulation were elicited by the broad-band click stimulus. Two additional waves (P5 and P6) occurring in the range of middle-latency evoked potentials reflecting activity from midbrain and primary auditory cortex were also observed. The / da/ syllable elicited an analogous waveform to the one previously described in human studies containing all the onset (V, A) and frequency-following response components (C-F) but with an additional positive peak occurring at 9.2. This peak at 9-10 ms was consistently evoked for all stimuli. Excerpt- (100 ms) and full-length versions (497-571 ms) of three different calls elicited three common peaks with latencies below 20
msec. Full-length vocalizations elicited three additional peaks between 20-50 ms reflecting cortical activation. Furthermore, peaks sensitive to amplitude changes and to the offset of the full-length vocalizations were observed. In the frequency domain, coherency analysis revealed that the fundamental frequency (114-669 Hz) and its harmonics of the vocalizations are captured by the EEG responses. Overall, results indicate that scalp-recorded activity convey the overall morphology and timing of complex sounds. The similarity between macaque and human evoked potentials to /da/ stimulus, enable animal recordings as a tool for studying the encoding of spectro-temporal elements of speech. Data indicates that macaque brain is capable of phase-lock to frequencies larger than the upper limit (250 Hz) previously described in single and multiunit activity as well as in epidural recordings. Likewise, behaviorally relevant sounds elicited stronger responses than other containing same spectral information.

Acknowledgements:
CONACyT (236836) and PAPIIT grant (IN201214-2) to HM. DGPA-UNAM fellowship to YAA. Authors thank to Raúl Paulín for his technical assistance.

3. CHARACTERIZATION OF SEXUAL BEHAVIOR IN THE PRAIRIE VOLE (MICHROTUS OCHROGASTER)

Aguilar TE¹, Diaz NF², Young LJ³, Paredes RG¹ and Portillo W¹.
¹ Instituto de Neurobiología, UNAM. México, ²Instituto Nacional de Perinatología, Isidro Espinosa de los Reyes. Mexico and ³Emory University, Atlanta Georgia. USA.

The prairie vole (Michrotus ochrogaster), is a monogamous mammal. It has been shown that mating for 6h induces a pair bond that in most cases is permanent. However, the characterization of the components of sexual behavior haven’t been described in detailed. The current study further evaluates in detailed sexual behavior in prairie voles. To this end, female and male sexual behavior was recorded during one session of twenty four hrs. For females, lordosis response was measured and reported as the lordosis coefficient (LC). Male sexual behavior was registered including the number and latency to mount (NM, ML respectively), to intromit (NI, IL) and to ejaculate (NE ,EL). In addition the interintromition interval (III) and postejaculatory interval (PEI) were calculated. Sixteen voles (eight males and eight females), with no sexual experience were used in this study. All females were ovariectomized and supplemented with estradiol during seven days to induce and maintain sexual receptivity along the behavioral test. Females prairie voles do not exhibit estrous cycles, and behavioral estrus is induced by contact with an unfamiliar stimulus male. In this study some of the sexual parameters were similar to those reported in rats and mice. This research was supported by grants CONACYT 252756, 167101,253631; Fronteras 374; UNAM-DGAPA-PAPIIT IN203615, IN210215; Instituto Nacional de Perinatología 212250-3230-21216-05-15. We thank Francisco Camacho and Deisy Gasca for their technical assistance. (M)

4. BEHAVIORAL EVALUATION OF DIFFERENT DOSES OF MANGANESE (MN) TO BE USE AS A CONTRAST MEDIUM IN FMRI STUDIES

Aguilar, Josué A¹; Paredes, Raúl G. ¹; Bedos, Marie¹; Gasca M, Deisy²; Hernández G, Flavio¹; Carbajal M, Cristal¹.
Laboratorio de conducta sexual y plasticidad¹; Unidad de Análisis Conductual². Instituto de Neurobiología UNAM, Campus Juriquilla. Querétaro, México.

MRI is a technique that allows us to identify anatomical and physiological modifications in the central nervous system (CNS) in vivo. It has the great advantage of performing longitudinal studies, using each subject as
his own control. Manganese-enhanced magnetic resonance imaging (MEMRI) is a technique that takes advantage of the paramagnetic proprieties of manganese. Mn reduces longitudinal relaxation time (T1) and increases signal activity where Mn accumulates. Nevertheless, high concentrations of Mn could lead to toxicity, affecting mainly motor activity. In our laboratory we are interested in studying the modifications of the CNS after sexual experience in rats. We have previously shown that when female rats are allowed to control (pace) the sexual stimulation that they receive during a sexual encounter, several behavioral and physiological changes occur that favor reproduction. We want to identify what brain regions are activated and if brain connectivity is modify in female rats that pace the sexual interaction. In the present pilot study we tried to identify the Mn dose that allow us the use of MEMRI and avoid the neurotoxic effect of Mn in the female rats.

We use 15 female Wistar rats, 250-300grs, without previous sexual experience. They were ovariectomized and supplemented with hormonal treatment and randomly assigned to the following groups: control (saline), MnCl2 8mg/kg and MnCl2 16mg/kg. Females were given different doses of MnCl2 and tested for sexual behavior, activity wheel and rotarod motor activity once a week for 10 weeks. MnCl2 was administered on sessions 1, 5 and 10. The preliminary results indicate that the dose of 8 mg/kg of MnCl2 can be used for future studies because that dose does not produce behavioral alterations.

Acknowledgments:
Francisco Camacho. This research was supported by CONACYT 253631, Fronteras 374 and PAPITT IN210215. (L)

5. ELECTROENCEPHALOGRAPHIC DIFFERENCES BETWEEN PHYSICALLY ACTIVE AND PASSIVE ELDERLY SUBJECTS

Alatorre-Cruz GC¹, Fernández-Harmony T², Sánchez-López J³, Silva-Pereyra J¹, Castro-Chavira SA², Sánchez-Moguel SM², González-López M².
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Aging is often accompanied by structural and functional changes; however, electroencephalographic abnormalities observed in baseline electroencephalogram (EEG) could be associated with behavioral or cognitive alterations. Structured physical activity improves cognitive performance in elderly subjects; still, non-structured physical activity is also present in daily life of healthy elderly. Non-structured physical activity results from performing every day activities without any programming for purposes of physical performance. We hypothesized that healthy elderly subjects with more unstructured physical activity will show lower EEG power in slow frequency bands and higher EEG power in fast frequency bands. A total of 98 elderly subjects were assessed using the Yale Physical Activity Survey (YPAS); then, a Cluster Analysis yielded two groups: Physically Active, and Physically Passive. Physically Active subjects obtained higher values in the performance domain of the Wechsler Adult Intelligence Scale (WAIS) than Physically Passive subjects. EEGs were recorded using the 10-20 system during rest with eyes closed. The EEG spectra was calculated in each lead, and absolute power with geometric power correction was obtained for each frequency band: delta (1.5-3.8 Hz), theta (3.9-7.5 Hz), alpha (7.6-12.5 Hz) and beta (12.6-19.9 Hz); subsequently, Z values from comparisons to norms were computed. A multivariate permutation analysis was conducted to look for differences between groups in Z values of EEG absolute power. The Physically Active group showed significantly (p<0.05) higher EEG alpha power and lower delta power in frontotemporal leads, mainly in the left hemisphere. Increased theta powers in left temporal and right frontal regions were also observed in the Physically Passive group. As we hypothesized, subjects with more physical activity presented faster EEG activity. More alpha activity in anterior leads could be a sign of functional compensation to perform cognitive
processes, which would explain the higher WAIS scores. Physical activity seems to promote changes in EEG, compatible with improvement in cognitive performance, which probably reduces the risk of future cognitive decline. To our knowledge, this is the first report relating physical activity and quantitative EEG in this population.

Acknowledgements:
Héctor Belmont, Leonor Casanova, Lourdes Lara, Bertha Esquivel, Teresa Álvarez, and Grant IN225414 from PAPIIT-DGAPA. (D)

6. EARLY ASSESSMENT OF SELECTIVE VISUAL AND AUDITORY ATTENTION WITH EEAS IN INFANTS WITH ANTECEDENT OF INTRAUTERINE GROWTH RESTRICTION AT EIGHTH MONTHS OF AGE TREATED WITH NEUROHABILITATORY THERAPY

Alonso Soto F.D, Carrillo-Prado C., Carbajal-Valenzuela C.C., Barrera-Reséndiz J. E., Pedraza-Aguilar M.C., Juárez-Colín M. E., Harmony T.

Introduction. Intrauterine growth restriction (IUGR) has been defined as the rate of fetal growth that is below normal in light of the growth potential of a specific infant. IUGR has been related with sensory, motor and cognitive development impairment. Selective visual and auditory attention is the ability to extract relevant information from a specific stimulus while ignoring distracting stimuli that compete for the limited resources of the central nervous system. Diminished selective attention leads to learning disable which makes necessary its early detection. The Escala de Evaluación de Atención Selectiva (EEAS) allow us to early assess selective attention in infants.

Objective. The aim of this study was to early assess selective visual and auditory attention in male and female infants with IUGR antecedent in neurohabilitatory therapy at 8 months of corrected age.

Results. Sixteen infants (8 males and 8 females) with IUGR antecedent, mean birth weight of 1670 gr (range: 1230-2050) and mean gestational age of 34 weeks (range: 29-36 weeks), were evaluated with the EEAS at 8 months of corrected age. All infants were attending neurohabilitatory therapy. Male infants score was 89.64 ± 12.85 in visual scale (VS) and 90.17 ± 2.52 in auditory scale (AS). Female infants score was 96.67 ± 4.21 in VS and 91.96 ± 1.65 in AS of the EEAS. This results show normal outcomes of visual and auditory selective attention in infants at 8 months of corrected age with IUGR antecedent treated with neurohabilitatory therapy assessed by the EEAS.

Conclusion: The EEAS represents an alternaty to early assessment of selective auditory and visual attention which is necessary in infants with IUGR.

Acknowledgment.
Projects: PAPIIT IN 204613 y CONACYT 218556, 166772. (L)

7. INFLUENCE OF PARENTAL INTERACTION AND PROLACTIN TREATMENT DIMINISHING KAINIC ACID-INDUCED NEURODEGENERATION IN THE HIPPOCAMPUS OF MALE MICE

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It has been shown that the hippocampus (HP) of lactating female dams is less sensitive to excitotoxic damage by kainic acid (KA) than that of virgin rats (Cabrera et al, 2013). Part of this effect is attributed to the pituitary hormone prolactin (PRL) which diminishes KA-induced neurodegeneration when administered to
virgin female rats (Tejadilla et al, 2010). However, we know neither the effects of exogenously administered PRL on neuroprotection in males nor if paternity itself can provide such a protection through changes in the hormonal milieu especially via PRL. To address these questions, male virgin adult mice CD-1 were paired with female virgin adult mice and co-housed throughout pregnancy. On the day of parturition (P0) the animals were randomly assigned to two groups: a) the pregnancy group (Pr), in which the males were removed from the home cage where they were co-housed with the female until parturition, placed in an individual cage and injected with 100 ng KA / 1 μl saline 0.9% (SAL) or with 1 μl SAL i.c.v. on day P1, and b) the paternity group (P), in which the males were allowed to stay in the home cage, interact with the lactating female and the pups until day P7, and underwent the i.c.v injection with KA or SAL on day P8 shortly after the evaluation of parental behavior. PRL effects were analyzed in male virgin adult mice by injecting a daily dose of 8 μg of ovine PRL/100 μl of sterile SAL s.c. for 7 consecutive days, followed by i.c.v. injection of KA or SAL. The control group consisted of male virgin adult mice housed individually subjected to KA or SAL i.c.v. injections. All animals were sacrificed 48 h after the i.c.v. injection and the cerebral tissue was processed for histology to measure neurodegeneration by Nissl and Fluoro Jade C in the CA 1, CA 3 and CA 4 subfields of the HP. Male mice treated with PRL showed less neurodegeneration in the regions analyzed compared to SAL controls. Additionally, both P and Pr groups had diminished levels of cell death after KA-lesioning. These results indicate that PRL has a neuroprotective effect on the HP of male mice subjected to excitotoxic lesion and that experiencing the environment of pregnancy and paternity can show similar protective effects.

Grant support: UNAM-DGAPA-PAPIIT-IN202315 and CONACYT scholarship 406166. (D)

8. ANALYSIS OF THE EFFECTS OF VASOINHIBINS ON HIPPOCAMPAL NEURONS

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1 Departamento de Neurobiología Celular y Molecular. Instituto de Neurobiología, Universidad Nacional Autónoma de México (UNAM), Campus UNAM-Juriquilla, Querétaro, México. 2 CONACYT Catedrática–Instituto de Neurobiología-UNAM.

Vasoinhibins (Vi) are a family of peptides derived from the hormone prolactin that have been shown to act on endothelial cells inhibiting angiogenesis, vasodilation and vasopermeability. Furthermore, Vi can participate in the modulation of some functions of the central nervous system (CNS) such as stimulating vasopressin secretion and promoting anxiety and depression behaviors. The hippocampus has been implicated in these behaviors; thus, in the present study we explored whether Vi are generated in this structure and if they affect hippocampal neurons. Extracts from hippocampus were evaluated for the presence of Vi as well as for the intrinsic capacity of this tissue to cleave prolactin to generate Vi. To explore the actions of Vi on hippocampal neurons, primary fetal hippocampal neuron-enriched cultures were isolated from the brain of E16 mice and seeded on plates treated with poly-L-lysine. Hippocampal cultures were treated on the first day in vitro (DIV1) with increasing concentrations of Vi (5-20 nM) for up to 72 hours (DIV2-DIV4). Vi were found in the hippocampus, and incubation of prolactin with extracts from hippocampus resulted in the proteolysis of this hormone to yield Vi, both revealed by Western blot. Incubation of hippocampal neuron-enriched cultures with Vi reduced in a dose-dependent manner the cell number, as well as the metabolic activity, evaluated by microphotography image analysis and MTT assay, respectively. Altogether these findings show that Vi are produced locally in the hippocampus and are able to affect its neurons, suggesting a possible site for the reported actions of Vi on anxiety and depression.

Acknowledgments:
We thank Gabriel Nava, Fernando López, Alejandra Castilla and Nydia Hernández for their technical assistance. Supported by CONACYT grants 251 and 251509. (D)
9. EFFECTS OF LONG TERM INTERMITTENT AND WITHDRAWAL SUGAR OR HIGH FRUCTOSE CORN SYRUP 55 CONSUMPTION IN TASTE PREFERENCE AND NEW AVERSIVE LEARNING

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Summary
Currently, sugar and high fructose corn syrup (HFCS-55 that is: 55 % fructose, 42 % glucose and 3 % higher saccharides) consumption is increasing around the world. This access increase of carbohydrates has an impact in human eating behavior. Recent works reports that the chronic intermittent sugar or glucose consumption elicits a high preference to taste, because their consumption may active the brain reward system like drugs. Thus the objective of this work was to evaluate in Wistar male rats the effect of the intermittent chronic consumption withdrawal of sugar or HFCS-55, on taste preference, and during a new aversive learning with the same taste. Thus, intermittent group, had access to food and sweet solution (10% sugar or 8% HFCS) only for 6 hours a day, during 21 days; the continuous group had permanent access to sweet solution and chow; and the control group had permanent access to chow, all groups had permanent access to water. After 21 days, rats were deprived of sweet solution during 1 or 3 days. Then the taste preference and the ability to acquire conditioned taste aversion (CTA) were also evaluated. Rats under intermittent sugar consumption and 1 day of withdrawal, showed more taste preference compared with control group, however they don’t showed difference compared with continuous group, in contrast rats under intermittent HFCS-55 consumption and 1 or 3 days of withdrawal showed more preference compared with control group, they don’t showed difference compared with continuous group. Moreover, rats under intermittent sugar consumption and 1 day of withdrawal, required more CTA training sessions compared with rats under intermittent sugar consumption and 3 days of withdrawal. In general rats under continuous or intermittent sugar or HFCS55 consumption and their withdrawal showed a higher latent inhibition than control group. These results indicate that the chronic intermittent exposition withdrawal of sweet taste generates a significant taste preference; furthermore, the continuous or intermittent HFCS-55 or sugar chronic consumption after withdrawal induced higher latent inhibition. Altogether these results indicate that the intermittent sweet consumption withdrawal generates higher taste preference and reduces new aversive learning for the same sweet taste.

Acknowledgments:
Technical assistants Gabriela Vera and Alejandro Rangel-Hernández. Research supported by DGAPA-PAPIIT IN209911, and CONACyT 152208. (D)

10. EFFECT OF GH TREATMENT AFTER HYPOXIC-ISCHEMIC INJURY IN CHICKEN CEREBELLAR CELL CULTURES

Baltazar-Lara M.R., Armenta M.E., Ávila-Mendoza J., Martínez-Moreno C.G., Carranza-Salas M., Arámburo C., Luna M.
Departamento de Biología Celular y Molecular, Instituto de Neurobiología, UNAM Campus Juriquilla, Querétaro, México.

The central nervous system (CNS) is highly sensitive to injuries induced by oxygen and nutrient privation (hypoxia-ischemia, HI). Severe cerebral dysfunctions such as cerebral palsy are associated with prolonged hypoxia. Under HI conditions, the CNS produces neurotropic factors as an endogenous neuroprotective strategy to reduce cell death. Several studies have shown that growth hormone (GH) is upregulated in different brain areas after damage by hypoxia. There is increasing evidence that suggest that exogenous GH treatment is able to induce neuroprotection and neuro-regeneration. In this study evaluated the effect
of GH administration after an acute HI injury in embryonic chicken cerebellar cultures as determined by cell viability. Furthermore, we evaluated the cerebellar expression of GH and IGF-1 mRNAs in normal and HLG condition. Primary embryonic cerebellar cultures were maintained in hypoxic conditions (0.5-5% O2) and incubated with low glucose levels (1 g/L) (HLG, hypoxia-low glucose) for 12 h and 24 h. Cell cultures were treated with 1 nM recombinant chicken GH (rcGH) to prevent cell death by HI. We observed a significant increase in cell viability (72.1±6.8%) compared to cells exposed to HLG (56.5±3.8%) without GH treatment after 24h. Interestingly after 12 h of HLG, this GH protective effect was not observed since treated cells did not show significant difference (72.6±4.6%) in comparison with untreated cells (61.7±5.3%). After 12 h of HLG conditions, cerebellar cell cultures increased GH and IGF-I mRNA expression (1.79-fold and 1.54-fold, respectively). Exogenous GH (1 nM) significantly decreased (P < 0.01) GH mRNA expression (1.02-fold) as well IGF-I mRNA expression (1.02-fold). GH gene silencing by small interfering RNA (siRNA) decreased both, GH mRNA expression (0.799-fold) and IGF-I mRNA (by 0.546-fold) expression. These results suggest that administration of GH after HI injury has a positive effect on cell viability, although its addition induced a negative feedback upon GH and IGF-I expression. Moreover, GH and IGF-I mRNA expression increased by HLG conditions. Our evidence strongly suggests that autocrine/paracrine GH in the cerebellum is a neuroprotective factor and its actions could be mediated by IGF-I.

Acknowledgements:
Financial support PAPIIT-DGAPA UNAM (IN206115) and technical support: Gerardo Curtois, Nydia Hernández. (M)

11. CHANGES INDUCED BY HYPOXIC CONDITIONING IN GFAP+ CELLS FROM THE ROOF OF THE FOURTH VENTRICLE

Becerra González M., Varman Durairaj R., Martínez Torres A.
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Introduction. Cerebellum is known for its role in motor control. It harbors a uniform cytoarchitecture composed of neuronal (granular, Golgi, Lugaro and Purkinje) and glial (astrocytes and Bergmann) lineages. We recently reported the presence of a cellular niche composed of diverse cell phenotypes located on the roof of the fourth ventricle that spans lobes I and X. The niche includes glial fibrillary acidic protein (GFAP+), and nestin+ cells distributed along the antero-posterior axis. Niches of GFAP+ and nestin+ cells in the lateral ventricles are well known neuronal or glial precursors that have the ability to respond upon hypoxic conditioning (HC). Yet, little cell proliferation has been demonstrated in cerebellum.

Aims. To evaluate the distribution of GFAP+ cells on the roof of the fourth ventricle, and to determine whether they respond to HC.

Methods. 25 days-old transgenic male mice expressing the enhanced green fluorescent protein under the GFAP promoter (GFAP-eGFP) underwent a three-cycle session of oxygen deprivation. Brains were collected at days 1 to 7 after HC. Distribution of the glial component was assessed by standard histological techniques and confocal microscopy, and western blot analyses evaluated changes in the levels of GFAP expression after HC.

Results. The organization of Bergmann glia cells was altered, somas were displaced and processes disorganized. Within the niche of GFAP+ cells of the roof of the fourth ventricle the expression of eGFP decreased after HC, but rebounded by day 7. This was confirmed by means of Western blot using antibodies against GFAP.

Conclusions. HC induces morphological changes in the Bergmann glial cells. It also reduces the expression levels of eGFP, which returns to normal levels after seven days. Consistently, expression of GFAP is reduced by HC and returns to normal levels within the same period of time. In general, the changes in the glial cells from cerebellum are a response to low levels of oxygen. Whether the GFAP+ cells proliferate and
differentiate as well as the molecular mechanisms of the cellular response under HC conditioning remain to be elucidated.

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12. GENERATION AND CHARACTERIZATION OF LENTIVIRAL VECTORS TO OVEREXPRESS VASOINHIBINS IN VIVO

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The formation of new blood vessels (angiogenesis) and vascular regression contribute to promote and modulate physiological liver growth, respectively. Liver growth is altered in pathological conditions; it occurs in response to toxic injury and infection and liver regeneration is restricted in liver steatosis and cirrhosis. Understanding the role of angiogenesis inhibitors could help promote adequate liver growth and function under disease. Vasoinhibins are a family of antiangiogenic peptides derived from the proteolysis of the hormone prolactin. In this work we generated and characterized lentiviral vectors to overexpress vasoinhibins (LV-Vi) in vivo. The vasoinhibin sequence (1-123 amino acids of prolactin coding region in which Cys58 was mutated to Ser) was obtained and cloned into the lentiviral genome plasmid downstream of the cytomegalovirus (CMV) promoter and upstream of the woodchuck posttranscriptional regulatory element (WPRE). Then, HEK293T/17 cells were transfected with three plasmids (the lentiviral vector genome containing the vasoinhibin sequence, the sequences of gag and pol that encode for the capsid and nucleocapsid proteins, respectively; and the env sequence that encodes for the glycoproteins of the lentiviral vector envelope). Later, the media from the transfected cells was collected and centrifuged to concentrate de viral particles. Finally, HEK293T/17 were transduced with the LV-Vi vector and the genomic DNA and conditioned media were collected to evaluate the integration and expression of the vector, by end-point PCR and Western blot, respectively. Our results indicate that the LV-Vi vector is efficiently integrated and expressed and can be further used to transduce liver cells in vivo in order to evaluate the effect of vasoinhibins on liver growth and regeneration. We hypothesize that vasoinhibins will delay liver growth during postnatal development and hepatic regeneration after a partial hepatectomy.

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13. OSCILLATORY ACTIVITY OF SUPPLEMENTARY MOTOR AREAS REFLECTS TEMPORAL JUDGMENT OF PERIODIC EVENTS

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The perception of periodic events is essential for an animal to respond to imminent changes in the environment. In order to coordinate a timed response, the motor system must encode and compute temporal patterns. A key circuit associated with the timing of motor responses is the cortico-basal ganglia-thalamo-cortical circuits. For example, the amplitude of Gamma oscillations in the putamen is associated with the encoding of time intervals in the order of milliseconds. Also single unit activity in the supplementary motor areas (SMA) shows increments in the firing rate as a function of the length of a time interval. However it is not
known if the structures mentioned above are also recruited when animals have to time events in the absence of the execution of motor commands. We trained 2 rhesus monkeys in a task with 2 phases. First, monkeys have to attend to a visual stimulus that changes its position periodically over time. In the second phase the stimuli vanishes and monkeys have to estimate the current position of the stimulus as a function of elapsed time. Go signal requesting the estimated position is displayed at random times. While monkeys performed the task, Local field potentials (LFP) where recorded in the SMA. We found that Gamma band amplitude in the SMA covaries as a function of the elapsed time and the frequency of the stimulus. Even in the absence of the stimulus, Gamma band increment rhythmically according with the estimated position of the stimulus over time. The rhythmical patterns observed in SMA suggest that this structure is important to integrate temporal patterns even in the absence of a motor response. Also Gamma amplitude may be related with the temporal judgement of perceived durations in the range of milliseconds. (D)

14. MODULATION OF LONG TERM FACILITATION BY MICROGLIA
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Microglia is an immune cell located in the central nervous system (CNS). This cell-type can be “activated” during neuroinflammatory processes but also regulates neuronal circuits function under physiological conditions. Microglial activation or inhibition regulate the activity of neuronal networks by the release of both anti-inflammatory or pro-inflammatory molecules. For example, the basal activity of the respiratory rhythm generator, the Pre-Bötzinger Complex (preBötC), is modulated by microglial activity. The preBötC exhibit a plastic phenomenon called Long Term Facilitation (LTF) in response to cycles of intermittent hypoxia (IH), which consists of an increase in respiratory rhythm frequency that can persist for 90 minutes. Considering that IH also activates microglia, here we studied whether microglia could modulate the LTF in the preBötC in vitro. Thus, we recorded the activity of the PreBötC in brainstem slices and induced LTF in the presence of microglial activators, such as lipopolysaccharide and fractalkine, or microglial inhibitors, such as minocycline and fucoidan. Surprisingly, our results show that both microglial activation and inhibition block LTF generation in vitro, which suggest that basal microglial activity is required for the induction of this plastic phenomenon and that pro-inflammatory microglial-activation could interfere with the plastic properties of the respiratory rhythm generator. (M)

15. FOLLOW-UP OF MOTOR EXPRESSION NEUROLOGICAL WARNING SIGNS IN PREMATURE INFANTS WITH NEUROHABILITATORY TREATMENT
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Background: Preterm is used to describe the babythat is born before 39 weeks, this population presents specific central nervous system organization and development vulnerabilities, later presenting a high risk of motor, sensory and cognitive disabilities. The motor expression neurological warning signs (MENWS) are neurological disorders that differ from the normal pattern of development presented by postures and movements associated with disorders in the function of the nervous system. Premature infants who present these adverse factors for neurological damage it is convenient to treat them early and in a multidisciplinary way with neurohabilitatory treatment.
Objective: To report the manifestation of MENWS in preterm infants who receive neurohabilitatory treatment. Method: Descriptive, observational, longitudinal, retrospective study, realized at Neurodevelopmental Research Unit. Premature infants with MENWS from year 2010-2015 were included. Results: A sample of 175 premature infants of 26-38 gestational age weeks (GAW), the mean for GAW is 33.09 gestational age weeks (SD= 3.37), 96 male and 79 female participated in the study. Of the 175 preterm, 10 presented/1 MENWS; 29/2; 53/3; 58/4; 25/5, with a mean of 3.34 (SD= 1.09). The manifestation of MENWS in corrected age weeks was: reflex hyperextension (µ=20.64), adducted thumb (µ=21.64), fisted hands (µ=24.14), scissor gait (µ=34.34), toe-walking gait (µ=37.16). The toe-walking gait is the most frequent and the one that shows later of all MENWS in 158 premature infants; in contrast, reflex hyperextension is the least frequent and manifested earlier in 64 premature infants. Conclusion: It is observed that MENWS were evolving in a cephalocaudal direction, showing a similar evolution to the one observed in signs present in upper and lower extremities. Acknowledgements: Macías-López M, González-Palmerín D, PAPIIT IN 204613, CONACYT 218556 and 166772. 

16. SELF ESTEEM OF MEXICAN CHILDREN WITH LEARNING DISORDER

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Specific Learning Disorder (SLD) is a deficit of reading, writing and/or calculus abilities; it affects academic performance and daily activities. It is reported that children in different countries use academic achievements and failures as indicators of self-esteem (judgement that the person has about herself/himself). It is expected that children with SLD have lower self-esteem than children with Normal Academic Performance (NAP). Objective: To explore if mexican children with SLD have low self-esteem, testing with standardized specific test of reading, writing and arithmetic. Method: 22 children with SLD and 18 children with NAP. All children had normal neurological exam, Intelligence Quotient (IQ) greater than 75 (IQ was assessed by WISC-IV), mother with at least elementary school education, and per capita income greater than 50 percent of the minimum wage. Children with an ADHD diagnosis or another psychiatric alteration were excluded. The reading, mathematics, and written expression subtests from the standardized Neuropsychological Scale for Children (Escala Neuropsicológica Infantil, ENI) were used to classify the groups. The Piers-Harris Self-concept Test was used to assess self-esteem. Scores from both groups were compared by a Non Parametric Multivariate Permutation Analysis. NAP group had higher global and specific scores than SDL group. As in other countries, mexican children with SLD have low self-esteem. In the future it would be interesting to explore if Neurobiofeedback may improve self-esteem. Acknowledgments:

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17. EFFECT OF FAMILIARITY IN THE INTERPRETATION OF PRAGMATIC LANGUAGE IN HEALTHY MEXICAN SUBJECTS


In pragmatic language the real meaning of a message is not literal, but figurative, and its interpretation needs non-verbal resources and context (Escandell, 1996). The graded salience hypothesis (Giora, 2003),
states that familiarity plays an important role. The study of pragmatic language in neuroscience has focused primarily on pathological populations. We designed a functional magnetic resonance imaging (fMRI) task to assess the effect of familiarity in the interpretation of pragmatic language, and its neural correlates, in healthy Mexican subjects, using proverbs as a model. We present the procedure we followed to obtain the experimental stimuli.

We selected 521 Mexican proverbs from different anthologies, arranged them in 20 booklets, and distributed them to 599 students from different colleges in the city of Queretaro. The participants answered Likert scales to assess comprehensibility (1=easy to comprehend, 4=difficult to comprehend), familiarity (1=novel, 4=familiar), literality (1=literal meaning, 4=figurative meaning), and emotional valence (1=positive, 4=negative). For a different screening, we created 240 literal phrases, arranged them in 2 booklets, and gave them to 29 students from different schools in the city of Queretaro. The students graded the phrases only on comprehensibility and emotional valence, using the same Likert scales. Both samples were composed of males and females, 18 to 30 years old, and had finished high school.

We selected proverbs that were rated by more than 50% of the judges as comprehensible (score=1) and neither literal nor metaphorical (scores 2 or 3). Then we chose two groups of proverbs: those with a familiarity score of 1 or 2 (novel), and those with a familiarity score of 4 (familiar). We also selected the literal phrases that were rated by more than 50% of the judges as comprehensible (score=1) and emotionally neutral (scores 2 or 3).

As a result, we obtained three groups of experimental phrases: familiar proverbs (n=30), novel proverbs (n=24), and literal phrases (n=80). These stimuli were used to design a task using PsychoPy (Pierce, 2007) that is currently being used in our fMRI experiment.

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References:

18. CONSOLIDATION OF GROSS MOTOR DEVELOPMENT MILESTONES IN INFANTS WITH ABO INCOMPATIBILITY AND MULTIFACTORIAL JAUNDICE TREATED WITH NEUROHABILITATION

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Introduction: Neonatal jaundice, clinical manifestation of hyperbilirubinemia, is a consequence of the retention of indirect bilirubin (IB) due to an imbalance in the production and elimination of bilirubin. This condition also can result from a hemolytic disease, such as blood group incompatibility. When jaundice occurs in the second day of life, with a maximum of 12 to 15 mg/dL, it is necessary monitoring to rule out pathological jaundice, as the IB can cross the blood-brain barrier causing neurological disorders. Neurohabilitation is a diagnostic and therapeutic method that involves intensive repetition of sensorimotor patterns, avoiding the appearance of neurological sequelae.

Objective: To describe the Gross Motor Development (GMD) in infants with multifactorial and ABO incompatibility jaundice that had indirect bilirubin levels ≥15 mg/dL treated with Neurohabilitation.
Methodology: Quantitative, descriptive transversal and retrospective study. 38 infants were included, with an average gestational age of 35.78 weeks, average weight 2476 g, IB ≥15mg/dL (15-38 mg/dL), which were divided in two groups. Group 1 (G1): 22 patients with multifactorial jaundice (average IB: 20.41 mg/dL), Group 2 (G2): 16 patients with ABO incompatibility jaundice (average IB: 24.60 mg/dL). They received neurohabilitatorio treatment on average three times a day during the first year.

Results: G1: 40.90% achieved the cephalic control in time expected for their age and G2: 35.71%; G1: 66.66% achieved crawling and 75% walking in adequate time; G2: 57.14% consolidated the crawling and 64.28% achieved walking in optimal time; 4 patients in G2 developed chronic bilirubin encephalopathy: 2 consolidated GMD milestones in time close to normal, 2 did not.

Conclusion: It is possible that an early intervention through Neurohabilitation and multidisciplinary team, has contributed to a motor development as close to normal, reducing neurological sequelae that can develop infants with hyperbilirubinemia.

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19. CELL PROLIFERATION IN THE MEDIAL PREOPTIC AREA OF THE HYPOTHALAMUS AFTER PACED MATING IN FEMALE RATS

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Cell proliferation and neurogenesis are processes that occur in the adult mammalian brain. In the subventricular zone (ZSV) progenitor cells that migrate through the rostral migratory stream (RMS) reach the olfactory bulb (BO) and integrate into neural circuits. Cell proliferation that occurs in the ZSV is largely mediated by olfactory stimuli. These stimuli play a significant role in sexual behavior. We have previously shown that in the female, the possibility of controlling sexual stimulation (paced mating), induces changes in cell proliferation in the olfactory bulb. The Medial preoptic area (mPOA) plays an important role in sexual behavior of both, males and females in several species of mammals. In the present study, we evaluated if paced mating induces cell proliferation in the mPOA. We used female rats (Wistar) of approximately 250 g without sexual experience. They were ovariectomized and treated with estradiol (25 mg / rat) and progesterone (1 mg / rat). Rats were injected intraperitoneally with 5-bromo-2- deoxyuridine (BrdU, a marker of DNA synthesis) at a concentration of 100 mg / kg. BrdU was injected one hour before the behavioral test, at the end of the test, and one hour after the behavioral test. Females were randomly assigned to one of four different groups: females left in their home cage; females exposed to a sexually receptive female without the possibility of physical contact; females that mated for 1 hr without pacing their sexual interaction and females that mated pacing their sexual contacts. At the end of the experiments animals were sacrifice and BrdU was detected by immunohistochemistry methods. Our results showed no significant differences between groups. These results indicate that paced mating promotes cell proliferation in the AOB but not in the mPOA suggesting that plastic changes induced by mating are brain region specific.

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20. SEXUAL EXPERIENCE INDUCES PLASTIC CHANGES IN THE OLFACTORIAL BULB

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Unlike other rodents; ovariectomized female mice during their first sexual experience display low receptivity levels (lordosis; spine curvature while elevating the head and the tail to facilitate the male intromission), even if they are hormonally supplemented. Lordosis increases as the female gets more sexual experience in repeated tests. The physiological mechanisms controlling this change in behavior have not been described. The aim of this study is to determine if sexual experience induces brain plastic changes such as axonal growth or an increase in the number of astrocytes in the olfactory bulbs, which are important for sexual behavior.

In order to evaluate our hypothesis we used 20 female mice, ovariectomized and supplemented with estradiol benzoate (50µg) and progesterone (300µg) 48 and 4 hours respectively; mice were randomly assigned to one of the following groups: (A) females with no sexual experience (B) females with one sexual experience, (C) females with three sexual experiences, and (D) females with six sexual experiences. Behavioral test were done once a week for one hour.

All animals were sacrificed 24 hours after the last behavioral test and brains were collected, sliced in 30µm sections and the accessory olfactory bulb (AOB) was recovered. Then, we perform an immunofluorescence staining to visualize axonal growth (GAP-43; Growth Associated Protein) and astrocytes (GFAP; Glial Fibrillary Acidic Protein). The number of GFAP positive cells was counted and GAP-43 was analyzed by densitometry in the glomerular, mitral and granular layers of the AOB. For the statistical analyses GFAP positive cells were analyzed by a Kruskal-Wallis and the densitometric analyze by an ANOVA.

Our results demonstrate that sexual experience increases the expression of GAP-43 in the mitral layer of the AOB after six weeks of sexual experiences. GFAP shows a fluctuating expression in the glomerular layer during those weeks, no significant differences were found neither in the mitral or granular layer. These results suggest that sexual experience is necessary for the formation and maintenance of brain circuits involving sexual behavior.

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21. CEREBRAL ACTIVITY IN DOGS DURING PERCEPTION OF HUMAN FACES

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Dogs are a unique model in the study of face recognition, because they not only have the capacity to discriminate between dog faces but they have also developed a remarkable capacity to extract valuable information from human faces. We have explored the cerebral correlates of face processing in seven dogs through fMRI.

In the first stage of the project, we presented as stimuli images of objects, human faces and dog faces. We found a posterior to anterior pattern of cerebral activity depending of the kind of visual stimuli: occipital cortex responds to all categories, while temporal cortex responds to all facial stimuli, regardless of species, and the frontal cortex responds preferentially to human faces. Our findings are consistent with the importance of temporal cortex in face processing in humans, non-human primates and sheep. And the activity in the frontal cortex related to human faces could be the brain correlate of the differential behavioral patterns that dogs show towards human faces.
Also because of the importance of human emotions for dogs, in the second stage of the project, we explored the cerebral correlates of emotion recognition in human faces. We begin by testing of one emotion in eight dogs: happiness in faces. We found brain activity related to happy human faces in several regions, including temporal cortex, frontal cortex and caudate.

Finally, there is behavioral evidence that shows that dogs are capable of discriminate expression of emotions in human faces. We tested whether a particular pattern of activity can be found in the dogs’ brain that correlates with a specific emotion in a human face, that is to say, if we can distinguish the emotion that the dogs are observing just by analyzing the patterns of activity in their brains. We used a block design with four emotions in humans: happiness, sadness, fear and anger. Four dogs participated in this experiment. Using multivariate pattern analysis, we were capable to predict above of chance ($p < 0.05$) from the pattern of activity of all the brain the emotion that dogs were observing. Our findings show that at the cerebral level dogs can discriminate basic emotions in human faces; this may reflect the adaptation of dogs to an anthropogenic niche.

We would like to thank the technical assistance of the MRI unit, especially Dr. Erick Pasaye for their help in the acquisition of the images. (D)

22. IODINE NUTRITION IN PREGNANT-LACTATING WOMEN AND THEIR NEWBORNS FROM SAN ILDEFONSO, AMEALCO, QUERETARO: A PROSPECTIVE STUDY

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Iodine deficiency during pregnancy and lactation may generate, cretinism, intellectual impairments and growth retardation among others. Exclusively breastfeed newborns rely on maternal breast milk iodine for normal development. Optimal iodine nutrition is measured through urinary iodine excretion. The aim of this study was measure iodine urinary concentration (UIC) in pregnant and lactating women from San Ildefonso; a socioeconomically depressed area to determine iodine sufficiency status before and after giving birth in addition to UIC from their newborns to compare with their mother’s data. 22 pregnant women and their newborns were recruited. The UIC was measured with a standard spectrophometric method based in Sandell-Kholtoff reaction.

According to WHO, UNICEF a median of UIC $\leq 150$ μg/L in pregnant and lactating women indicates a insufficient iodine intake whereas in newborn a iodine deficiency cut-off value is defined as a median of UIC $\leq 100$ μg/L. Median (interquartile range; IQR) UIC in pregnant woman was 140 (113-213) μg/L and in the same group of woman after given birth was 124 (70-147) μg/L. This reduction of UIC was statistically significant ($p=0.04$). Median UIC in newborns was 417 (239-843) μg/L. On the other hand, a positive and significant correlation between UIC of lactating women and newborns was found (Pearson r: 0.508; $p<0.05$). Our results indicate that iodine intake in pregnant and lactating women is insufficient whereas iodine intake in newborns is excessive which suggest a high iodine concentration in breast milk.

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23. SERONEGATIVE CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS), A CASE REPORT AND REVIEW OF THE LITERATURE


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A 29-year-old female, was admitted in emergency room for acute cerebellar ischemic stroke, secondary to left vertebral artery (LVA) dissection; a week before she presented generalized headache, 9/10 VAS. Treatment initiated with acetylsalicylic acid (ASA) 100 mg p.o.q.d and atorvastatin 80 mg p.o.b.i.d. Antecedents: cholecystectomy at 28-y-o without complications. No fetal losses, use of contraceptive patch since 27-y-o. Laboratory tests: leucocytosis 14.4x103/μL, creatinine 0.8 mg/dL. Echocardiogram showed patent foramen ovale. Magnetic resonance (MR) showed right chronic periventricular stroke and left acute ischemic cerebellar stroke. Cerebral angiography showed estenosis <40% NASCET in third proximal segment V1 of LVA, and free intraluminal clot in segment V3; treated with intraarterial thrombolysis with 30 mg of recombinant tissue plasminogen activator and 28 mg intravenous. Further neurologic deterioration presented when admitted to ICU, Glasgow 9 and lateral medullary syndrome. MR DWI showed infarction of the lateral portion of medullary tegmentum, mesial region and left occipital lateral lobe; T2* showed hemorrhagic transformation in the territory of the left posterior inferior cerebellar artery. Patient was treated with induced coma, endotracheal intubation, average blood pressure of 80-100 mm Hg, mannitol 0.25 mg/kg, ASA 100 mg/Clopidogrel 75 mg po qd. The third day patient presented fever (37.8°C), CRP 97 mg/L, procalcitonine 4.7 ng/mL, without infection foci, ESR at 43 mm/h and positive rouleaux. The forth day the patient presented livedo reticularis, tachycardia (150 bpm), Torax angioCT demonstrated pulmonary embolism in segment 10 of right lung. Total anticoagulation with enoxaparina was started. On the fifth day patient presented intracranial hypertension. MR showed generalized cerebral edema with brainstem and IV ventricle compression, and tonsillar herniation, treated with suboccipital craniotomy. The diagnosis of CAPS was suspected and treated with gammaglobuline at 1g/kg/d and prednisone at 80 mg p.o q.d. On the sixth day patient presented acute kidney injury AKIN 1, creatinine 1.33 mg/dL, developed diabetes insipidus, treated with desmopresin, mannitol was suspended.

Laboratory tests showed normocytic normochromic anemia, plateletes 212 x 103/μL; partial thromboplastin time 27.5 s; reumatoid factor, anticardiolipin IgG and IgM, anti-beta2GP1, lupus anticoagulant, Anti-dsDNA antibodies, ANA’s and VDRL were all negative. Brain death was diagnosed on the seventh day. Necropsy was not performed.

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24. RELATIONSHIP BETWEEN WORKING MEMORY, IQ, AND TEMPORAL PROCESSING DURING DIFFERENT SYNCHRONIZATION-CONTINUATION TASKS IN HEALTHY HUMAN SUBJECTS

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Temporal performance during rhythmic tapping to an auditory metronome is more accurate and precise than tapping to a visual metronome. This asymmetry, that has been well described in humans, is not present in some conditions such as deafness, where has been shown that the individuals performance is better
in visual than in auditory modality. On the other hand, it is well known that the IQ (Intelligence Quotient) is highly correlated with working memory and other executive functions; however, there are few studies relating tapping performance to a metronome with the subjects’ cognitive abilities. Thus, the purpose of this study is to evaluate the timing performance during a synchronization-continuation tapping task (SCT) where subjects will tap in synchrony to a sensory metronome with a different modality (auditory or visual) and with a different dynamic property (static, short duration stimuli producing empty intervals vs. moving/dynamic stimuli producing filled intervals) and to correlate the temporal performance in the four versions of the SCT with the cognitive skills described above. Twenty healthy human subjects (twenty to thirty-year-old) will be tested in the following neuropsychological tests: PASAT (Paced Auditory Serial Addition Test) and subtests of BANFE-2 (Neuropsychological battery of executive functions and frontal lobes) for the assessment of working memory and attention, as well as the WAIS-IV (Wechsler Adult Intelligence Scale) for IQ. Furthermore, the subjects will perform the SCT with the four different metronome conditions, in different experimental sessions. The preliminary results suggest better timing performance with static auditory than static visual metronomes during the SCT. Moreover, the visual dynamic condition produced a synchronization behavior that was nearly as accurate as in the auditory conditions. Furthermore, there was a significant correlation between the timing performance during the SCT and the working memory and IQ of the subjects. These results support the notion that visual timing improves when a moving visual stimulus is used to drive tapping performance, and that there is a relation between the cognitive skills and the timing abilities during rhythmic synchronization in human subjects. (D)

25. DECREASED PROLACTIN LEVELS INDUCED BY AN OBESOGENIC DIET IN LACTATING MOTHERS CONTRIBUTE TO METABOLIC ALTERATIONS IN THEIR OFFSPRING


Maternal obesity during lactation generates insulin resistance (IR) in the offspring. We have shown that prolactin (PRL), a critical hormone for the regulation of lactation is reduced in the circulation of obese rats and treatment with the hormone improves IR in those animals, however little is known about the effects of PRL on the offspring metabolism during lactation. In this study, we evaluated whether a high fat diet (OD) in lactating mothers reduced PRL levels in serum and milk, and if this diminution contributes to IR in their offspring. We used lactating Wistar rats fed with control diet (CD) or OD, treated or not with PRL delivered by subcutaneous osmotic mini pumps (OD+PRL). Alternatively, the offspring from OD dams where treated orally with PRL (oPRL) or vehicle. The OD generated a significant reduction in milk PRL levels of 39% and 46% at days 7 and 21 of lactation, respectively. Whereas the OD+PRL resulted in higher levels of milk PRL at day 7 and increased serum PRL levels at day 21 (p<0.05). In addition, offspring from mothers on OD showed increased body weight gain and visceral adipose tissue (VAT) mass compared to offspring from mothers on CD, while PRL treatment in mothers (OD+PRL) or in offspring (oPRL) resulted in lower VAT mass compared to offspring from mothers on OD. Furthermore, an OD in mothers, generated IR in their offspring, as shown by higher levels of glucose during an insulin tolerance test (ITT), whereas both types of PRL treatment resulted in an amelioration of offspring IR. In conclusion, maternal obesity during lactation results in reduced milk PRL levels and IR in their offspring. PRL treatment restores milk PRL levels and promotes insulin sensitivity in the offspring from mothers fed an OD.

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26. ISCHEMIC STROKE AS A COMPLICATION OF TAKAYASU’S ARTERITIS CASE REPORT AND REVIEW OF THE LITERATURE

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OBJECTIVE: To present a case of Takayasu’s Arteritis (TA) diagnosed through non-invasive and invasive neuroimaging. An 18-year-old female with the antecedent of left nephrectomy, when she was fourteen, secondary to renovascular hypertension (SRH), afterward controlled.

MATERIALS & METHODS: Attended emergency department after 1 hour of evolution of left faciocorporal hemiparesis. History and physical examination showed NIHSS score of 9; laboratory findings were normal. MR Diffusion Weighted Imaging (DWI) and Digital Subtraction Angiography (DSA) were performed.

RESULTS: DWI showed restriction of the right caudate, angioMR showed occlusion of the internal carotid artery (from C1 to C6 segments) and middle cerebral right artery (MCRA) from distal segment M1. Cranial CT showed hyperdensity of the MCRA in the segments M1 to M3. DSA showed stenosis of the brachiocephalic trunk, chronic complete occlusion (CCO) of the right subclavian artery (SA) at its proximal segment, stenosis at the ostium of the vertebral artery (VA); acute occlusion of the right common, internal and external carotid arteries; CCO of the ostium of left VA. Both SA filled by counterflow of the corresponding VA. Intraarterial treatment was performed with 30mg of recombinant tissue Plasminogen Activator obtaining a revascularization TICI 2A. Due to SRH history, DSA was performed, showing 50% occlusion of the right renal artery. According to the Ishikawa criteria, TA was diagnosed. Five days after stroke, the patient fully recovered was discharged with Dabigatran 150mg po, bid; and Methotrexate 15mg once a week.

DISCUSSION: TA is a large-vessel vasculitis with a granulomatous inflammation onset the vasa vasorum. Incidence of 2.6 per million, female:male ratio 8:1, initiating under 50 years-old. Biphasic physiopathology: early active inflammatory (EAI) and late chronic phase (LCP). The EAI characterizes by a vague course, with constitutional features. In 50% of the patients is subclinical, hindering diagnosis. If remission within 3 months is not achieved, it might progress to an occlusive LCP, with obliteration and inflammation of the aorta and its branches. Immunosuppressive therapy and vascular surgery are required in 80% of patients.

CONCLUSION: TA is a rare disease of difficult diagnosis and treatment, which has diminished the mortality rate in 2010, to 2.8% at 10 years, owing to the new therapeutic modalities.

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27. BEHAVIORAL AND NEUROENDOCRINE CHANGES ASSOCIATED TO CHRONIC STRESS: HYPOTHALAMUS-PITUITARY-ADRENAL AXIS DYSREGULATION

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Stress can be defined as the physiological response to real or emotional threatening stimuli. Even when the main purpose of stress response is to preserve the individual’s integrity enhancing the chances for
survival, the exposure to intense or chronic stress is associated to the development of a wide variety of mood disorders such as post-traumatic stress syndrome, long-term anxiety and major depression, aside to other systemic diseases. Brain regions such as prefrontal cortex, amygdala and hippocampus are involved in processing stressful inputs, though hypothalamus-pituitary-adrenal (HPA) axis is considered as the main neuroendocrine integrator in central nervous system. Under normal conditions HPA axis is started by the secretion of corticotropin releasing factor (CRF) which induces the hypophyseal release of adrenocorticotropic hormone (ACTH) to bloodstream, action that promotes the secretion of cortisol by the adrenal gland. Similar to cortisol, corticosterone in rodents is the hormone that regulates HPA axis activation through a negative feedback. The aim of this work was to evaluate plasma level of ACTH and corticosterone in 48 adult male Wistar rats (230-250 g) exposed to a daily episode of restraint stress or handling for 15 days, and further exposure to a final stress challenge of 0, 10, 30 or 60 minutes of restriction in a Plexiglas cylinder. Our results showed differences hyperactivity in spontaneous motor behavior of chronic stressed animals in comparison to handling controls. We also found a significant increase of the adrenal glands weight ($P < 0.01$) in chronic stressed animals in comparison to controls, and significant differences decrease in ACTH ($P < 0.01$) and corticosterone plasma level ($P < 0.05$) at 30 and 60 minutes after the final restriction challenge. These results suggest that the exposure to chronic stress might exacerbate spontaneous motor behavior, and dysregulate ACTH and corticosterone release in rodents.

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28. AN AAV2 VECTOR ENCODING PROLACTIN REVERSES BLOOD RETINAL BARRIER PATHOLOGY WHEN ADMINISTERED INTRAVITREALLY TO DIABETIC RATS

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Prolactin (PRL), the hormone essential for lactation, is converted by proteolytic cleavage to vasoinhibins, a family of PRL fragments that inhibit diabetes-induced blood retinal barrier breakdown (BRBB) by targeting both the inner (vascular endothelial cells) and outer (retinal pigment epithelium) components of the BRB (Garcia et al., JCI, 2008; Arredondo-Zamarripa et al., Front Cell Neurosci, 2014). Because elevated PRL circulating levels upregulate retinal vasoinhibins (Arnold et al., Diabetes, 2010), we reasoned that the intravitreal administration of an adeno-associated virus type 2 vector encoding PRL (AAV2 PRL) would reduce BRBB in diabetic rats by serving as a source of vasoinhibins. The AAV2 PRL vector was injected intravitreally before or after inducing diabetes with streptozotocin (STZ) in rats. The ability of the vector to reduce BRBB was examined by the Evans blue method four or six weeks after STZ injection. AAV2 PRL transgene expression and the levels of endogenous vasoinhibins were compared between the retinas of diabetic rats and non-diabetic controls. The AAV2 PRL vector inhibited the diabetes-mediated increase in BRBB when injected after, but not before, diabetes was induced. Expression of the PRL transgene was higher in the retinas from diabetic rats. Also, vasoinhibin levels were higher in the retinas of diabetic rats compared to the non-diabetic controls. We conclude that the AAV2 PRL vector inhibits BRBB by enhancing the intraocular generation of vasoinhibins. This effect depends on the conditions of the diabetic rat retina, which include an elevated transgene expression due to increased cell entry by the vector (Díaz-Lezama et al., Lab Invest, 2016) and, very likely, the enhanced activity of the cleaving enzymes that convert PRL to vasoinhibins. Experiments addressing this last possibility are underway.
We thank Fernando López-Barrera, Martín García, Alejandra Castilla, Gabriel Nava, Daniel Mondragón, Antonio Prado, for their technical assistance. Research was supported by CONACYT grant 247164.(D)

29. EXPRESSION PATTERN OF THE CALCIUM SENSOR mctp GENES IN ZEBRAFISH AND ANALYSIS OF THE PHENOTYPE AFTER SUPPRESSION BY CRISPR/Cas9

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MCTPs (Multiple Calcium-2 Domain Proteins with two transmembrane regions) are related to calcium sensor proteins important in synaptic function, such as synaptotagmins and ferlins. MCTPs have not been characterized and their function remains unknown, although it has been shown that they bind calcium in vitro. MCTPs are widely expressed in brain and muscle. Zebrafish is a powerful biological model due to important experimental advantages over other vertebrates for studies of in vivo cell biology and its genome has a large degree of evolutionary conservation in comparison to the human, in addition it is amenable to a wide range of genetic manipulations. Therefore, in this work, we aimed to determine the expression pattern of the mctp genes and to analyze the phenotype of zebrafish after knocking out their expression. Methods: We determined by RT-PCR the expression of mctp genes; we cloned and sequenced the open reading frame of the four mctp genes expressed in zebrafish; and evaluated the effect of silencing the expression using the CRISPR/Cas9 system. Results: We found that the zebrafish genome has four mctp genes (1a, 1b, 2a and 2b) and that the four genes are expressed from early development and in adult brain and heart. A high frequency of single nucleotide polymorphisms (SNPs) and alternative splicing events were detected. Silencing mctp1b by CRISPR/Cas9 did not show evident effects on embryonic development, whereas silencing of mctp2b blocked the proper development of embryos. There seems to be different functional participation of these genes, at least during early stages of development.
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30. IODINE AND SALT INTAKE IN MEXICAN ADULTS: A PILOT STUDY

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Iodine is a trace element, which is an essential component of thyroid hormones. In Mexico table salt iodization is mandatory since 1963 and thus salt is one of the main sources of iodine. According to the Institute of Medicine (USA) it is recommended a dietary allowance (RDA) and estimated average requirement (EAR) of iodine, in female and male adults of 150 μg/day and 95 μg/day; respectively. On the other hand, more recently the WHO recommended, and in order to prevent cardiovascular disease, a reduced table salt intake <5g/day. The 24-h urine collection is the gold standard for estimating the consumption of both iodine and salt, because 90-95% of iodine and dietary sodium are excreted in urine. However, it is an inconvenient method that usually does not apply for large groups of people. The aim of this study was to determine the relation between iodine and salt consumption through 24-h urine samples in Mexican adults. Six adults between 20-40 years old, 5 females and 1 male, residing in the municipality of Querétaro accepted voluntarily to participate. Participants were requested to collect a 24-h urine sample. Sodium quantification was performed using an ion selective electrode and iodine by a spectrophotometric method based in the Sandell-Kolthoff reaction.
We found that salt intake was above the recommendation by WHO, with an average salt consumption of 8.9 g/day, but with an average iodine consumption of 126 μg/day, which is below the RDA, but above EAR. The correlation between iodine and salt consumption was high (Spearman r = 1.0; p = 0.0014). According to this findings, reducing salt intake to <5 g/day, like the WHO recommends, might affect iodine intake. Thus we suggest that in order to guarantee iodine sufficiency, the concentration of iodine in salt should be increased. This study was supported by the grant FOFL-UAQ FME201602.

31. LEFT-RIGHT ASYMMETRY IN GENE EXPRESSION IN THE MOUSE EMBRYONIC TELENCEPHALON

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Structural and functional Left-Right asymmetry occurs in vertebrates in several internal organs including the brain. Brain asymmetry and laterality have been observed in fish, birds and mammals. In mammalian embryos, the specification of Left-Right asymmetry is initiated by ciliary motion at the Hensen’s node causing a vectorial flow of extracellular fluid and by releasing morphogenic signals that activate the Nodal cascade in the left Lateral Plate Mesoderm (LPM). Our hypothesis is that brain asymmetry and laterality are also related to asymmetric gene expression at early stages of development. To identify genes with asymmetric expression in the embryonic mouse telencephalon we analyzed the transcriptome of the left (LV) and right telencephalic vesicles (RV) of E10.5 CD1 mouse embryos. We detected 529 genes whith increased expression in the RV and 368 genes whith increased expression in the LV. Only 31 genes were expressed exclusively in the RV and 5 genes in LV. Most of the genes identified have been associated to embryogenesis, development of the nervous system or are non coding RNAs. The genes Kdm5d, Eif2s3y, Uty and Ddx3y had the highest asymmetry and were expressed predominantly on the RV. These four genes are located in the same region in the Y chromosome and are known to display sexual dimorphism. (D) Funding: PAPIIT203713, CONACyT232722, 238566, 271787, FOMIX249744. Acknowledgements: Antaramian Salas, A., Lara-Ruvalcaba A., Aguilar-Bautista L., Caballero Pérez, J., García Servín, M., Castilla, A., Martínez R., and Hernández, O.

32. KINEMATIC ANALYSIS OF THE HUMAN THORACIC AND LUMBAR SPINE

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We developed an kinematic analysis protocol in order to evaluate spine functionality. We calculate the position of the vertebrae of patients. Subjects were asked to sit comfortably, the feet height was adjusted to get an 120° angle between trunk and thighs. Then following seven maneuvers were performed ten times for every subject.

Trunk flexion (TF): the subjects placed their hands on the neck and made a trunk flexion then returning to the original position. Trunk flex and rotation (TFR): with the hands on the neck, the patient try to touch his knees with to opposite elbow. Trunk rotation (TR): the hands were put on the opposite shoulder, crossing the forearms over the chest, then the subjects lateralized their spine. Trunk Lateralization (TL): same position as
in TR but the required movement is an axial rotation of the trunk.
Last three maneuvers were made towards the left and to the right. For motion caption we put three infrared reflecting markers that forms a triangle and one of its vertex is over the spinous process of a vertebra. Triangles were put on the skin and over the following vertebrae: C7, T4, T8, T12, S2. Using the plane defined by the triangles we constructed reference systems inside the rotation axis of the spine; then we calculated the angles of motion.
Angular ranges were measured and using the data of 27 subjects we normalized the values. Five index define the range of motion of the spine, if they are greater than one we consider a functional motor state of the spine and viceversa. We consider that this parameters and the kinematic protocol of the spine will be a powerful diagnostic tool for many pathologies, particularly for chronic pain in the lower spine. (A).

33. METABOLIC AND CHRONOBIOLOGIC ANALYSIS IN TWO MODELS OF RESTRICTED FEEDING SCHEDULES WITH OR WITHOUT CALORIE RESTRICTION

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Introduction: Biological clocks in mammals can be synchronized by external stimuli such as light-dark cycles and the food access schedules. Daytime 2 h restricted food access (DRF2) in rodents promotes the presence of an alternative clock called feeding entrainment oscillator (FEO), which induces food anticipatory activity and phase shift in clock genes. DRF2 implies calorie restriction and changes in glucose and insulin daily profiles and lipid handling. However, it is not clear if those changes are promoted by the food access synchronization or by the calorie restriction.

Objective: To compare the influence of DRF with different calorie restriction level in metabolic and chronobiologic parameters.

Materials and methods: Male Wistar rats were randomly assigned to 3 groups: DRF2, DRF5 and ad libitum feeding (AL) during 3 weeks. Daily locomotor activity, food ingestion and body weight gain were recorded. A 24-h glycemia and corticosterone profile, and a glucose tolerance test and serum insulin at the end of the protocol were assayed. Perigonadal adipose tissue (PGAT) were analyzed by H&E stain and liver clock genes mRNA expression was analyzed by qPCR.

Results: DRF2 rats ingested 40% less calories than AL at the end of the protocol, while DRF5 only 10% less. DRF2 induced corporal weight loss as well as in several metabolic organs, and a larger number but smaller size adipocytes in PGAT with signals of inflammation (crown-like structures). DRF2 and DRF5 induced shift phase of clock genes and the presence of food anticipatory activity, then FEO installation, as well as 24-h hypoglycemia and hypoinsulinemia profile compared with AL. In contrast, DRF5 did not induce an additional peak before food access of corticosterone as in DRF2.

Conclusions: DRF is a potent circadian entrainment that promotes an alternative clock known FEO, which is present independently of the calorie ingestion. Improvement in metabolic parameters achieved by synchronization induced by DRF does not require calorie restriction.

This study was supported by grant IN202515 from PAPIIT, UNAM, México. (M)
34. GENOMIC REARRANGEMENTS TRANSCRIBED INTO MITOCONDRIAL RNA IN CANCEROUS TISSUE AND THE EFFECT OF ANTICANCER TREATMENTS IN THE GENERATION OF DELETIONS IN MITOCONDRIAL RNA

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Breast cancer is the most common malignancy and the leading cause of death in Mexico by cancer between the women, estimating that 80% of cases are ductal carcinoma, which is characterized by gene deletions. To evaluate the expression of RNA species containing deletions, RNA samples from cancerous and non-cancerous tissue of patients with breast cancer and treated with iodine or a mix of 5-fluorouracil, epirubicin and cyclophosphamide (FEC) or both, were massively sequenced by Illumina platform. Transcriptomic data was aligned to a reference genome with Blat and analyzed by additional bioinformatic tools and algorithms. We found an universe of 4,843 common deletions between samples from healthy tissue and cancerous tissue; whereas, 26 deletions increased their frequency in cancerous tissue. These deletions were located in ATPase6, NADH subunits 1, 2, 4, 4L, 5 and 6, cytochrome c oxidase (I, II and III) and cytochrome b; that they are part of the complex of the mitochondrial respiratory chain. When analyzing RNA from patients treated with iodine, FEC, or both, we that patients treated with FEC presented 33 deletions significantly increased in 20 genes as to the patients treated with iodine were 71 deletions increased in 25 genes. Finally in patients subjected to iodine and FEC, a total of 389 deletions increased their frequency affecting 30 genes of the mitochondrial RNA. The increase in deletions of mitochondrial RNA could correlate with a higher sensitivity of cancer cells to the anti-cancer drugs.

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35. RENAL VASCULATURE EVALUATION THROUGH 3.0T MR ANGIOGRAPHY IN POTENTIAL RENAL DONORS IN MEXICO

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Introduction: Renal transplantation improves the patient's quality of life and post-transplant life expectancy; with a mortality rate of 2.0/100 patients per year among patients with living-donor transplantation, compared to a 6.3/100 among patients receiving dialysis. The annual cost per patient of peritoneal dialysis is $66,087 US dollars, home Haemodalysis is $54,505; living donor kidney transplant is $34,028; immunosuppressive drug therapy cost in subsequent years is $27,086.

Objective: Determine anatomic variants among potential living donors within the state of Querétaro, Mexico; which will aid in the selection of the suitable kidney for donation, as well as pre-surgical mapping.

Material and Methods: From August 2012 to April 2016, fifty-three arterial and venous magnetic resonance angiography (MRA) studies were performed on potential kidney donors. MRA were performed on the scanners: Phillips Achieva 3.0T TX and General Electric Discovery 3.0T MR750, using the contrast media Gadobutrol. The MRA were evaluated by two radiologists: HMBC and LRLC, then were compared with surgical findings.

Results: Total population studied 53 patients with a mean age of 42 years (±12.24, age range 20-68), 26 men (48.1%), 27 women (51.9%). A total 36 transplants have been performed where the kidneys have sought 18 women (50%), 18 men (50%). The anatomical variants identified by MRA and the surgical finding were as follows: a) only bilateral artery (61.1%); and two case (5.5%) early division in the right renal artery, and one case (2.7%) right accessory renal artery, left accessory renal artery, retro-aortic left renal vein and left upper polar renal artery. With a percentage of reliability of surgical finding Magnetic Resonance Angiography 77.7%.

Conclusions: The use of MRA among living donors allows for the evaluation of renal vasculature. Due to the fact that no-ionizing radiation is employed, MRA is a non-invasive alternative technique to AngioCT or Digital Subtraction Angiography. The cost-effectiveness of renal transplantation has shown to be superior to the renal replacement therapy. (L)

36. COMBINATION OF MODERATE EXERCISE AND LITHIUM PREVENTS AMYLOID BETA-INDUCED HIPPOCAMPAL DYSFUNCTION: ROLE OF GSK3β

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We have previously shown that amyloid beta (Aβ)-induced inhibition of hippocampal network activity involves the activation of a signal-transduction pathway that recruits the serine/threonine kinase GSK3β.
Lithium (Li+), which is used for bipolar disorder treatment, inhibits GSK3β and several of the deleterious effects of Aβ. However, Li+ produces several undesired side effects that have limited their use in the elderly. Thus, we, and others, have been exploring different therapeutic strategies to inhibit GSK3β with less side effects. Recently we have shown that exercise prevents Aβ-induced inhibition of hippocampal activity by inhibiting GSK3β. Altogether these findings suggest that GSK3β can be inhibited by both pharmacological and non-pharmacological means. Here we tested the possible synergic effects of a subtherapeutic dose of Li+ combined with voluntary exercise against Aβ-induced deleterious effects on memory, hippocampal theta (θ) activity and GSK3β activation. Our results show that a subtherapeutic dose of Li+ combined with moderate exercise prevents the Aβ-induced memory and hippocampal θ activity deficits, which correlates with a diminished GSK3β activation. These results may have clinical application considering that both lithium and exercise are been separately tested on clinical trials for Alzheimer’s disease treatment with mild therapeutic outcomes. Thus, it is possible that the combination of pharmacological and non-pharmacological approaches would render greater benefits against AD or other Aβ-related dementias. (D)

37. SEMANTIC PRIMING IN HEALTHY ELDERLY AT RISK OF COGNITIVE DECLINE. AN EVENT-RELATED POTENTIALS STUDY

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Event-Related Brain Potentials (ERPs) have been widely used to study different aspects of cognition. Several differences have been reported in the amplitude and latency of the N400 component -which is related to language processing, specifically at the semantic level- between young and old adults, as well as between healthy elderly and those with cognitive decline. On the other hand, an increased absolute power of the theta frequency band (3.5-7 Hz) of the electroencephalogram (EEG) has proven a good predictor of cognitive decline in the medium-term (approximately seven years). Since the normal cognitive characterization of healthy elderly is often done with behavioral and psychometric measures, the aim of this study was to examine whether there are differences in terms of semantic processing between two groups of healthy elderly using ERPs. The control group consisted of those participants with a normal EEG (i.e. within the norms for their age) and the experimental group consisted of those with an increased theta power. We found that the semantic priming effect was present in both groups, which was evident in both the behavioral and electrophysiological measures. There were no significant differences in terms of the latency or mean amplitude of the N400 component between groups. However, we observed a significant difference in the mean amplitude of a late positive complex (LPC), which was larger for the Theta group. Moreover, the group-condition interaction showed a significant effect on the latency of the LPC. There were no differences in terms of behavioral measures between the groups. There appear to be differences in the way that both groups carry out the linguistic processing at the semantic level, which may be a result of compensatory mechanisms that lead to a correct behavioral performance, and that are not due to differences in the sensory and perceptual levels. This could be an indicator of an ongoing subclinical pathological process and contributes to increase the predictive power of the EEG for these disorders.

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38. THE PSYCHOMOTOR DEVELOPMENT EVALUATION TEST IN CHILDREN FROM 1 TO 36 MONTHS. PRELIMINARY RESULTS

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All changes in cognitive, emotional, motor and social skills that an infant goes through in all different stages: infancy, early and middle childhood, and adolescence, are considered in psychomotor development. The Psychomotor Development Evaluation Test aims to be a screening test that can be able to detect disturbances in Gross Motor Skills (GMS), Fine Motor Skills (FMS), Cognitive (C), and Language (L) abilities. Motor development has been considered to be a prerequisite for other functions like cognitive abilities. The objective is to analyze the preliminary results of a group of normal infants to establish percentiles, and to describe the correlation that every section holds with each other, in children from 1 to 36 months that were evaluated with the PDET. 1057 evaluations (n=819) were obtained, and divided in the months when they were performed. A Shapiro-Wilk test for analysis of a normal distribution of each month of the GMS, FMS, C, and L showed that 18 months for GMS (n=509) and FMS (n=504), 20 for C (n=538), and 22 for L (n=608), had a normal distribution. For every one of these months, percentile 5, 50, and 90 were calculated and plotted. The correlation between GMS-C (r=0.982, p<0.01) and GMS-L (r=0.973, p<0.01), FMS-C (r=0.972, p<0.01) and FMS-L (r=0.963, p<0.01), was positive. To achieve a normal distribution, and for the percentile graph to be more accurate, on all 36 months the sample should be increased, in order to gain variability in data. PDET should also undergo validity evidence evaluations to ensure an accurate screening.

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39. EFFECT OF MICROINJECTION OF ANISOMYCIN IN THE PREFRONTAL CORTEX ON MEMORY CONSOLIDATION OF LEARNING WITH HIGH AND LOW LEVELS OF REINFORCEMENT

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The prefrontal cortex, particularly its most ventral regions, i.e., prelimbic cortex (PLCx) and infralimbic cortex, has been associated with mnemonic, emotional, and cognitive processes, as well as in the modulation of encoding of fear memory. In this work we studied the participation of PLCx in the process of memory consolidation. It has been found that with moderate intensities of an aversive reinforcer, administration of inhibitors of protein synthesis during the consolidation phase, in different regions such as the striatum and hippocampus, can cause an amnestic effect; however, with higher intensities of the reinforcer memory is protected against this amnestic effect. To date there are no published data regarding this protective effect after interference with protein synthesis in PLCx normal activity. In the present experiment anisomycin (31.25 mg / 0.5 ul,) or saline (vehicle), was administered in PLCx cortex of male rats of the Wistar strain 30 minutes before training in an inhibitory avoidance task, with a moderate (1.0 mA), intermediate (2.0 mA) or intense (3.0 mA) reinforcer. Anisomycin produced an amnestic state only in the group that had been trained with 1.0 mA. Results of control manipulations demonstrated that the amnestic effect was not due to state-dependency, or to any alteration in acquisition. These data indicate that the normal activity of the PLCx is essential for memory consolidation of moderate learning, but not in conditions of intense training.
40. T3 AND T2 DIFFERENTIALLY REGULATE THE EXPRESSION OF GENES ASSOCIATED TO THYROID FUNCTION IN CEREBELLUM


Thyroid hormones (TH) are key regulators of physiological process and are essential for growth and development in vertebrates. Specifically in the cerebellum, TH regulate the expression of genes that play critical roles in neuronal differentiation, neurite growth, sinaptogenesis, neuronal migration and lamination during cerebellar development. For TH to exert their actions, at least three functional events need to occur: 1) the facilitation of TH transmembranal movement, mediated by the organic anion transporter polypeptide (OATP1C1), and more specifically by the monocarboxylate transpoter (MCT8); 2) the tissue-specific activation/inactivation of the prohormone thyroxine (T4) to produce either the bioactive 3,5,3-triiodothyronine (T3) or the inactive rT3, catalyzed by deiodinases D2 and D3, respectively, and 3) the binding of bioactive TH to nuclear thyroid hormone receptors type alpha and beta (THRA and THRB) which function as ligand dependent transcription factors to regulate the expression of TH-dependent genes. In concert with their thyroid-associated function, these genes are known to be tightly regulated by T3 in most studied tissues. However, we have previously described that as T3, 3,5-diiodothyronine (T2) is also bioactive. Indeed, T2 has been shown to regulate gene expression in liver but its actions upon other tissues have never been explored.

In this study, we analyzed the effects of the bioctive TH, T3 and T2 upon the regulation of OATP1C1, MCT8, D2, D3, THRA and THRB by treating cerebellum organotypic cultures from juvenile tilapia (Oreochromis niloticus) (n=12 individuals; 4/pool) with 0.1, 1, 10 and 100 nM of T2 or T3 administered for 24 h in the culture medium. We analyzed mRNA expression by RT-qPCR. Of the 6 analyzed genes, our results showed that D3 did not respond to any treatment, while OATP1C1 only responded to T2. Furthermore, T2 was a more potent regulator of the expression of MCT8 and THRB, while D2 and THRA are more acutely regulated by T3. Our results demonstrate that T2 is an important regulator of thyroid hormone homeostasis in cerebellum, supporting the notion that not only T3, but also T2 is physiologically relevant for cerebellar function. (D)

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41. CATEGORIES IN THE BRAIN, HOW DOES THE SOMATOSENSORY SYSTEM REPRESENT EVERYDAY OBJECTS?


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Introduction

There is evidence that the parietal cortex has several regions that process specific characteristics of an object when the object is explored with the hand. Additionally, it is known that the lateral occipital complex (LOC) is a structure that integrates visual information to create representations of whole objects. Our experiment aimed to identify regions that encode information about a stimulus category using multivariate pattern analysis (MVPA).
Methods
Ten healthy right-handed participants took part in the study. Functional images were acquired on a 3-T Philips Achieva TX scanner. Each participant underwent 12 scans that consisted in the tactile presentation of 120 everyday objects divided in 10 categories of 12 different objects each.

Results
To assess if the categories could be differentiated by the pattern of activity of the brain, we perform a full-brain searchlight analysis. We found at a group level that parietal and LOC regions had a prediction accuracy above chance (t-test, p < 0.01).

Conclusions
We found that stimulus category could be predicted from the pattern of activity of LOC and also the parietal regions of both hemispheres. Extending previous results, we found that LOC contains category-specific patterns of BOLD activity, suggesting that LOC could be encoding high level characteristics of the stimulus. Our findings suggest that LOC processes multimodal information about the objects at a categorical level.

We would like to thank the technical assistance of the MRI unit, especially Dr. Erick Pasaye for their help in the acquisition of the images. (D)

42. GABAρ3 EXPRESSION IN ASTROCYTES FROM THE MEDIAL NUCLEUS OF TRAPEZOID BODY


The Medial Nucleus of Trapezoid Body (MNTB) is part of the auditory circuit and its function is to detect changes in the intensity of sound to discriminate their origin. The MNTB contains axosomatic glutamatergic synapses, that contacts glial cells such as astrocytes and NG2 glia. Additionally, GABAergic transmission occurs during postnatal development in the MNTB prior to the opening of the ear canal in mice (postnatal day 12 = P12). The presynaptic terminal (Calyx of Held: CoH) expresses GABA-B receptors that modulate glutamate release, whereas the expression of GABA-A receptors (including the GABAρ subunit) occurs in postsynaptic neurons. However the expression of GABAρ in glial cells of the MNTB is unknown. The aim of this study was to investigate whether GABAρ3 subunit is expressed during postnatal development and whether astrocytes express it in the MNTB. Methods: RT-PCR.- GABAρ3 expression was investigated in ventral brainstem slices containing the MNTB of CD-1 mice at different ages (P3, P9, P12, P18, P30 and P60). Immunofluorescence.- histological sections (40µm) of brainstem of GFAP-eGFP transgenic mice (P9, P12 and P18) were used to assess the expression of GABAρ3 in astrocytes. Results.- GABAρ3 mRNA was detected from P3 to adulthood (P30). GABAρ3 + cell density showed a peak around the time of ear opening (P12 > P9 and P18). Finally, a fraction of astrocytes express GABAρ3. Conclusions: 1) The expression of GABAρ3 mRNA was observed from early postnatal development of the MNTB beginning at P3. 2) The density of GABAρ3+ cells peaks during the time period of opening of the ear canal (P12). 3) A fraction of MNTB astrocytes expresses GABAρ3. The expression pattern of GABAρ3 suggest a potential involvement in the synaptic refinement of MNTB.

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43. CONSOLIDATION OF GROSS MOTOR MILESTONES IN INTRAUTERINE GROWTH RESTRICTION INFANTS, TREATED WITH NEUROHABILITATION

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Introduction: Intrauterine growth restriction (IUGR) is defined as failure to achieve the endorsed growth potential, is associated with signs of abnormal fetoplacental function. IUGR infants are associated with adverse perinatal neurodevelopment outcome, including several complications, acidosis, hypoxia, hyperbilirubinemia, low birth weight and prematurity, higher risk of brain injury, neurobehavioral disorders and cerebral palsy. Milestones gross motor are an important number of global postural skills, are divided in observable stages according to the development of the human nervous system. Meanwhile neurohabilitation treatment is a diagnostic and therapeutic method which proposes decreasing the sequelae of perinatal brain damage, to take advantage the brain plasticity of the immature nervous system to improve the optimal neurodevelopment and motors skills in infants.

Objective: Observe differences in consolidation corrected age gross motor milestones between IUGR infants treated with neurohabilitation compared to healthy infants.

Method: Cross-sectional study, we evaluated the consolidation of 7 principal gross motor milestones: head control, seated position, protection reaction, dragging movement, crawling movement, postural autonomous movements and gait in 34 infants divided into 2 groups, IUGR infants (n=21) and Control group infants (n=13) using the Evaluation of Psychomotor Development Format (FEDPm acronym in Spanish).

Results: Differences between IUGR infants and Control infants, head control (p>0.05), seated position (p>0.05), protection reaction (p>0.05), dragging movement (p>0.05), crawling movement (p<0.05), postural autonomous movements (p>0.05) and gait (p>0.05).

Conclusions: Consolidation corrected age gross motor milestones are not different between IUGR infants treated with neurohabilitation and healthy infant.

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44. TRANSCRIPTOMIC ANALYSIS OF CONOTOXINS OF THE MARINE SNAILS CONUS BRUNNEUS AND CONUS PRINCEPS FROM THE MEXICAN PACIFIC

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Marine snails of the genus Conus are predators that paralyze their prey with a venom cocktail containing hundreds of peptides that target diverse neuromuscular ion channels and receptors. The mixture is unique to each species, providing a rich source of bioactive peptides (“conotoxins”) with pharmacological and medical relevance. No comprehensive transcriptomic analysis has yet been reported for Conus species from the Mexican Pacific coast. We examined the transcriptomes of the venom glands from specimens of the vermivorous species C. brunneus and C. princeps, collected off the Nayarit and Jalisco coasts, respectively. Approximately 2.1 x 10⁷ paired-end Illumina reads for each species were assembled using Trinity to generate 28,234 (C. brunneus) and 63,479 (C. princeps) transcripts. These assemblies were analyzed with ConoSorter, filtered for size and N-terminal hydrophobicity, and annotated using Blast2GO to identify transcripts encoding conotoxins belonging to distinct gene superfamilies and classes. ConoPrec was used to further assign and confirm superfamilies. A total of 79 putative toxin precursors were identified.
from C. brunneus representing 19 known toxin and 2 possibly new toxin superfamilies. From C. princeps 63 candidate toxins were found belonging to 16 known and several potentially new superfamilies. In addition, putative toxins from uncommon families (conodipines, conopressins, and conoporins) were identified, further establishing the breadth of toxin diversity in these species.

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45. A CASE OF OPHTHALMIC ARTERY OCCLUSION AND RECURRING AMAUROSIS FUGAX

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OBJECTIVE: to present a case report of ophthalmic artery (OA) occlusion evaluated through neuroimaging and physiologic studies. A female 33-year-old, suffered five years ago a first episode monocular Amaurosis Fugax (AF) in the right eye, lasting 30 seconds, with spontaneous ad integrum recovery (SAIR), she did not receive reatment. Right hemicranial headache during last 3 months, intensity 7/10 of visual analogue scale, oppressive, without irradiation; nor exacerbated, neither allaying. Five days later, a new episode of AF, binocular, appeared lasting 45 minutes with SAIR.

Antecedents: polycystic ovary syndrome under hormonal treatment (2012-14). Hypermetropia and astigmatism since 4 years ago.

MATERIALS & METHODS: Anamnesis, complete physical examination (neurologic and ophthalmological). Blood count, coagulation tests, blood chemistry, liver and thyroid tests, carcinoembryonic antigen. Antithrombin III, protein C and S, factor V, homocysteine, antiphospholipid antibodies (anti-β-2 glycoprotein IgM e IgG) and antinuclear antibodies were normal. HIV and VDRL were negative. Imaging studies: Carotid Doppler Ultrasound and transthoracic echocardiography were normal. Indirect ophthalmoscopy, visual field, and fluorangiography were normal. Brain Magnetic Resonance image simple and with contrast showed: right OA path was not recognizable. Left OA had tortuous course and beaded appearance. Cerebral angiography showed the absence of right OA in its proximal 1/3, patency of distal 2/3 through collateral vascularization from ipsilateral branches of external carotid artery. idiopathic occlusion of the ophthalmic artery (IOA) was diagnosed and treated with acetylsalicylic acid 100 mg po and nimodipine 30 mg po, quotid.

DISCUSSION: OA is a branch of internal carotid artery in charge of eye and orbit, it has 3 branches: 1) Ocular, retina and ciliary; 2) Orbital, lacrimal and muscular; and 3) extraorbital, supraorbital, anterior and posterior ethmoidal, nasal, palpebral, medial frontal and supratrochlear arteries. Etiologies: a) traumatic; b) retrobulbar anesthesia; c) depot corticosteroid treatment; d) autoimmune diseases; e) neoplasms; f) atherosclerotic disease; g) fibromuscular dysplasia; h) placement of medical devices; and i) idiopathic. IOA is rarely observed (3% to 5%), it can indicate posterior neovascularization in 5%.

CONCLUSION: OA occlusion is an entity that requires a multidisciplinary approach in order to establish etiology, allowing the physician to give a specific treatment and avoid blindness and / or brain stroke. (L)
46. ASTROCYTES FROM CEREBELLAR WHITE MATTER EXPRESS GABA-A RECEPTORS DURING EARLY POSTNATAL DEVELOPMENT

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Abstract

Background: The white matter of the cerebellum has a population of GFAP+ cells with neurogenic potential restricted to early postnatal development (P2-P12), these astrocytes are the precursors of stellate cells and basket cells in the molecular layer. On the other hand, GABA is known to serve as a feedback regulator of neural production and migration through tonic activation of GABA-A receptors.

Aim: To investigate the functional expression of GABA-A receptors in the cerebellar white matter astrocytes at P7-9 and P18-20.

Methods: Immunofluorescence for α1, α2, β1 subunits & GAD67 enzyme in GFAP-EGFP mice (n=10 P8; n= 8 P18). Calcium Imaging: horizontal acute slices were incubated with Fluo4 AM in order to measure the effect of GABA-A or GATs antagonist bicuculline or nipecotic acid on spontaneous calcium oscillations, as well as on GABA application evoked responses.

Results: Our results showed that α1 (3.18%), α2 (10.4%) and β1 (not detected) subunits were not predominantly expressed in astrocytes of white matter at P8. However, GAD67 co-localized with 54% of GFAP+ cells, suggesting that a fraction of astrocytes could synthesize GABA. Moreover, calcium imaging experiments showed that white matter cells responded to GABA. This response was antagonized by bicuculline suggesting functional expression of GABA-A receptors.

Conclusions: Together these results suggest that GABA is synthesized by half astrocytes in white matter at P8 and that GABA could be released locally to activate GABA-A receptors that are also expressed in cells of the white matter of the cerebellum, during early postnatal development. (D)

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48. PROLACTIN PROTECTS AGAINST JOINT INFLAMMATION AND BONE LOSS IN ARTHRITIS

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Prolactin (PRL) reduces joint inflammation, pannus formation, and bone destruction in rats with polyarticular adjuvant-induced arthritis (AIA). Here, we investigate the mechanism of PRL protection against bone loss in AIA and in monoarticular AIA (MAIA). Joint inflammation and osteoclastogenesis were evaluated in rats with AIA treated with PRL (via osmotic minipumps) and in mice with MAIA that were null (Prlr-/-) or not (Prlr+/+) for the PRL receptor. To help define target cells, synovial fibroblasts isolated from healthy Prlr+/+ mice were treated or not with T-cell-derived cytokines (Cyt: TNFα, IL-1β, and IFNγ) with or without PRL. In AIA, PRL treatment reduced joint swelling, lowered joint histochemical accumulation of the osteoclast marker, tartrate-resistant acid phosphatase (TRAP), and decreased joint mRNA levels of osteoclasts-associated genes (Trap, Cathepsin K, Mmp9, Rank) and of cytokines with osteoclastogenic activity (Tnfα, Il-1β, Il-6, Rankl). Prlr-/- mice with MAIA showed enhanced joint swelling, increased TRAP activity, and elevated expression of Trap, Rankl, and Rank. The expression of the long PRL receptor form increased in arthritic joints, and in joints and cultured synovial fibroblasts treated with Cyt. PRL induced the phosphorylation/activation of
signal transducer and activator of transcription-3 (STAT3) and inhibited the Cyt-induced expression of IL-1β, IL-6, and Rankl in synovial cultures. The STAT3 inhibitor S31-201 blocked inhibition of Rankl by PRL. PRL protects against bone loss in inflammatory arthritis by inhibiting cytokine-induced activation of RANKL in joints and synoviocytes via its canonical STAT3 signaling pathway. Hyperprolactinemia-inducing drugs are promising therapeutics for preventing bone loss in rheumatoid arthritis.

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49. ADC MEASUREMENT IN LATERALY MEDULLARY INFARCTION (WALLENBERG SYNDROME)

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BACKGROUND:
The stroke of the vertebrobasilar system (VBS) represents 20% of ischemic vascular events. When the territory of the posterior inferior cerebellar artery (PICA) is affected, lateral medullary infarction (LMI) occurs, typically called Wallenberg syndrome; it accounts for 2-7% of strokes of VBS. Given the diversity of symptoms that causes, it is a difficult disease to diagnose. The reference exam to evaluate cerebral blood flow is digital subtraction angiography (DSA); however, it is an invasive method. Magnetic resonance imaging (MRI) is a noninvasive study and the sequence of diffusion (DWI) can detect early ischemic changes, after 20 minutes of ischemia onset, it also allows to locate and determine the extent of the affected parenchyma. Measurement of the apparent diffusion coefficient (ADC) is a semiquantitative parameter that confirms or rule out the presence of infarction, although the diffusion sequence (DWI) has restriction signal.

OBJECTIVE:
To measure the ADC values in patients with LMI and compare their values with the contralateral healthy tissue.

MATERIALS AND METHODS:
The database of Unit Magnetic Resonance Unit of studies carried out from January 2010 to July 2016 was revised to include cases diagnosed by MRI with LMI. The images were acquired in two resonators of 3.0 T (Phillips Achieva TX and General Electric Discovery 750 MR). DWI sequence with b value of 1000 was used to look after LMI, then ADC value measurement of the infarcted area and the contralateral area was performed in the same patient. Two groups were identified: a) infarction and b) healthy tissue. Eleven patients, 5 female (45.5%) and 6 males (54.5%), were included. A descriptive statistic was performed and infarction and healthy tissue were analyzed with U-Mann-Whitney test.

RESULTS:
In the restriction areas observed in DWI, ADC values were measured; the infarction tissue has a median of 0.54X10-3 mm2/s, interquartile range 0.41-1.0X10-3 mm2/seg; the healthy tissue has a median of 0.24X10-3 mm2/seg, interquartile range 0.19-0.56X10-3 mm2/seg. The U-Mann-Whitney test has a statistical significance of p<0.05.

CONCLUSION:
ADC measurement allows to confirm or rule out LMI in patients with the clinical suspicion of Wallenberg syndrome. It also serves to eliminate other diseases that showed restriction in DWI; for example, neoplasm, pontine myelinolysis, acute disseminated encephalomyelitis, multiple sclerosis and diffuse axonal injury. (L)
50. ENDOVASCULAR CAROTID STENTING IN A PATIENT WITH PREVIOUS STROKE, ISCHEMIC HEART DISEASE, AND SEVERE AORTIC VALVE STENOSIS


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OBJECTIVE:
We present a case report of a 74-year-old feminine patient who suffered from right superior gyrus stroke, ischemic heart disease, and severe valve aortic stenosis, in whom it was needed to identify which problem had to be treated first. Family antecedent of breast, pancreas, and prostate cancer in first order relatives; smoking 5 packages/year during >20 years, occasional alcoholism, right inguinal hernioplasty, hypertension and dyslipidemia of 3 years of evolution, under treatment.

She presented angor pectoris at rest, lasted 3 minute long and has spontaneous recovery, 7 days later she had brain stroke at superior right frontal gyrus, developed hemiparesis with left crural predominance.

MATERIALS & METHODS:
Anamnesis, complete physical examination, laboratory, as well as heart and brain imaging were performed. Severe aortic valvular stenosis diagnosed by echocardiogram with 0.6 cm² valvular area, average gradient of 38 mmHg and maximum of 66 mmHg; light mitral stenosis with valvular area of 1.8 cm², without left atrium dilatation, maximum gradient of 8 mmHg; PSAP 30 mmHg, US Carotid Doppler showed atherosclerotic plaques in the proximal posterior wall of the bulb right internal carotid artery (RICA) that determinates a maximum stenosis of 70%. Aggressive management with antihypertensive (Metoprolol 100mg po quotid), lipid-lowering (Atorvastatin 80mg po qd) and anticoagulant (Dabigatran 110mg po quotid).

RESULTS:
Endovascular carotid stenosis treatment is prioritized. An autoexpandable carotid stent (Wallstent®) was placed in the RICA without complications, a diagnostic coronary angiography was performed, it showed coronary diseases in 2 vessels a) severe focal stenosis in the anterior descending coronary artery of 70% b) large moderate stenosis in proximal circumflex artery of 60%, as well as diffuse of the coronary tree. A dual antiplatelet scheme was administered (acetylsalicylic acid 100mg/clopidogrel 75mg po quotid) and dabigatran was reinitiated 110mg po quotid.

CONCLUSION:
Due to the previous brain stroke, carotid stent placement was considered the first therapeutic to perform. The global clinical data showed the patient was a good candidate for valvular aortic transcatheter implant.
51. EVALUATION OF THE PLATELET AGGREGATION VARIABILITY INDUCED BY THE P2Y12 RECEPTOR IN PATIENTS WITH CORONARY DISEASE UNDERGOING ANTIPLATELET TREATMENT: A PILOT STUDY

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INTRODUCTION: The central role of the platelet in the acute coronary syndrome (ACS) constitute the basis for the use of antiplatelet therapy that inhibit the P2Y12 receptor (P2Y12R). This receptor participates in the platelet activation by inducing its aggregation. P2Y12R inhibition allows us to decrease the risk of thrombosis and further restenosis after a Stent implant, a common treatment for ACS. However, antiplatelet therapy may induce bleeding because only a standard dose is used in all patients, and it is important to determine the risk of adverse effects like bleeding or thrombosis.

OBJECTIVE: to determine the variability of platelet aggregation in patients with ACS undergoing antiplatelet treatment.

MATERIAL & METHODS: patients with a clinical diagnosis of ACS that underwent a percutaneous coronary intervention and that were treated with antiplatelets drugs (inhibitors of P2Y12R) were included. Platelet aggregation was evaluated based on the interaction among the P2Y12R (VerifyNow™; Accriva Diagnosis) with the use of ADP (20 micromol) and E1 prostaglandin (22 nmol) as P2Y12R agonists.

RESULTS: basal platelet aggregation was of 191±60 PRU (platelet reactive units), P2Y12R inhibited platelet aggregation was of 45±37 PRU, and a high variability on the delta was observed in the basal units compared to the P2Y12R inhibited values (from 213 to 40 PRU).

CONCLUSIONS: a high variability was observed in the basal platelet aggregation and after the P2Y12R inhibition in patients diagnosed with ACS. It is fundamental to identify the factors related to this variation, among them possibly genetic factors. (M)

52. ANATOMICAL CHARACTERIZATION OF THALAMO-STRIATAL PATHWAYS

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Summary
The basal ganglia (BG) are a group of subcortical nuclei involved in motor control, learning and execution of habits and procedural memories. The BG receive massive projections from the cortex and the thalamus. Previous studies have demonstrated the existence of proprioceptive and somatosensitive representations in the dorsal lateral striatum (DLS: one of the input nuclei of the GB) but the precise origin (cortex or thalamus) or function of these representations is still unknown. Using microinjections of neuronal retrograde and anterograde tracers in rats, we have determined that besides the corticostriatal projection (primary sensory cortex, S1), the DLS receives topographically organized projections directly from the ventro-postero-lateral nucleus of the thalamus (VPL). Our data suggest the somatosensitive information arrives to the DLS from two pathways S1-DLS and VPL-DLS, understanding the electrophysiological characteristics and the specific behavioral role of each will be the subject of future investigations.

Acknowledgments:
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53. DEVELOPMENTAL ENZYMATIC REGULATION OF THE PROLACTIN/VASOINHIBIN AXIS IN THE HIPPOCAMPUS OF THE MICE

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Prolactin (PRL) and vasoinhibins are two families of hormones associated in a functional axis. Vasoinhibins, named for their inhibitory effects on angiogenesis, vasopermeability, and vasodilation, are synthesized through the proteolytic cleavage of PRL, sharing the N-terminal region. They range in molecular mass between 11 and 18 kDa, depending on the specific sites of action of the proteases involved in their generation, which include cathepsin D, matrix metalloproteinases (MMP), and bone morphogenic protein-1 (BMP-1). PRL and vasoinhibin species are detected in the rat hypothalamus, and other regions of the central nervous system (CNS), where they trigger opposite effects.

For instance, the intracerebroventricular administration of PRL attenuates stress-induced neuroendocrine and anxiety responses, while vasoinhibins induce anxious and depressive behaviors in rats. In the present study we are exploring the activity of the converting enzymes, particularly cathepsin D and MMP, in the hippocampus in different stages of the life cycle. For that purpose the hippocampus from 16 days old embryos (E16), neonates (N) and adult (A) mice were obtain and lysated in a lysis buffer (1M Tris-HCl, EGTA 0.2M, EDTA 0.2M, 1% Igepal, 0.1M Na3VO4, 0.05M NaF, 5mM Na4P2O7, 0.26M sucrose). Then, 6 μg of the lysates were incubated with 50 ng of rat prolactin in a pH 5 (0.1M Citric acid, 0.15M NaCl, 0.01M CaCl2) or 7 (0.05 M Tris-HCl, 0.15M NaCl, 0.01M CaCl2) buffer during 24h at 37°C in the presence or not of enzymes inhibitors such as pepstatin A or galardin, that inhibit the action of cathepsin D and MMPs, respectively. The levels of PRL and vasoinhibins were observed by immunobloting.

Our current results show that the hippocampus express enzymes that cleaves PRL into vasoinhibins at the three stages of development tested.

A hippocampal cathepsin D cleaves PRL into a vasoinhibin of 16kDa in the three stages analyzed. Also, although as a preliminary observation, a MMP seems to produce a vasoinhibin of 18kDa that appears to be restricted to the embryonal stage. Altogether these findings show that a developmental-related regulation of the PRL-vasoinhibin axis operates in the hippocampus of the mice.

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54. A TOOLBOX KIT FOR OPTOGENETIC CONTROL OF NEURAL TRANSMISSION IN Caenorhabditis elegans

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C. elegans is a free-living roundworm nematode approximately 1 mm long. Its relatively small nervous system is composed of only 302 neurons and the neuronal synaptic connectivity is well known; therefore it is a powerful model for the study of neuronal networks. Several plasmid systems encoding for light sensitive proteins capable of switching on and off neural transmission have been developed for the analysis of synaptic transmission in C. elegans. The aim of this work was to develop a device to control the LEDs used
for optogenetic protocols. Additionally, an instructions manual was prepared as guide in the use of the device and for programing new protocols. Two transgenic strains of *C. elegans* were used: EG5025 oxxIs351 [unc-47p::channelrhodopsin::mCherry + lin-15(+) + Litmus] that expresses the channelrhopsin in neurons of the GABAergic system, and EG5096 oxxIs364 [unc-17p::channelrhodopsin::mCherry + lin-15(+) + Litmus] that expresses the channelrhodopsin in the cholinergic system. For coupling the LED system to the recording microscope a circuit and an adapter were designed and 3D printed, software was programmed to run the activation/inactivation protocols. Blue and yellow LEDs were tested in periods of 10 sec. It was found that the transgenic worms expressed the fluorescent protein mCherry in the correct set of neurons. The LEDs were accurately controlled by the software, and when tested in both strains of worms, the incidence of blue light immediately paralyzed the worms, whereas incidence of yellow light did not show any evident effect. These tools will permit to design new experiments to determine the functional connectivity of the GABAergic and cholinergic systems in *C. elegans*. (L)

55. BRAIN CHANGES DUE TO SEXUAL EXPERIENCE IN THE FEMALE MICE, C-FOS EXPRESSION IN THE MEDIAL PREOPTIC AREA AND THE VENTROMEDIAL HYPOTHALAMUS

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When female are receptive they display a lordosis posture in response to a male mount which facilitates penetration. Sexually naïve female mice show low levels of sexual receptivity in their first sexual experience. In subsequent tests and after repeated hormonal treatment they will show an increase in lordosis response. The aim of this study is to evaluate if sexual experience induces plastic changes that involved the increase in cell activity, evaluated by the expression of the early gene c-fos in areas involved in the control sexual behavior, such as the Medial Preoptic Area (MPOA) and the Ventromedial Hypothalamus (VMH).

In this study 54, CF1 female mice were ovariectomized and hormonally supplemented. Females were randomly assigned to 1 of 2 groups: Experienced females (n=20), which received 6 mating sessions; and Naïve females (n=18), which had no previous sexual experience. Each group was sub-divided in 3 other subgroups: Mating group, which receive an extra mating session; Olfaction group, which was exposed to bedding impregnated with male secretions; and Control group, which were exposed to clean bedding 90 min after the last test. Animals were euthanized and perfused, and their brains were collected and sliced. Brain sections were immunostained for C-fos, using Nissl as a counterstaining.

Our behavioral results showed that, as expected, females increase their Lordosis Quotient with repeated sexual experience. Preliminary immunohistoquimical data shows that only the experienced females that mated had more IR-cells in the VMH than the experienced ones exposed to clean bedding (p=0.018). Despite not reaching statistical significance, sexually experienced females had more IR-cells than naïve ones in the VMH; when exposed to male odors or males itself. Opposite effects were observed in the MPOA where sexually naïve females showed more IR-cells compared to the experienced ones when exposed to male odor or the males itself.

We can conclude that the differential activation of the VMH, a brain region involved in the control of Lordosis, facilitates this response when females acquire sexual experience.

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56. SCALP-EEG AND SOURCE-EEG SPECTRA DURING A WORKING MEMORY TASK IN CHILDREN WITH LEARNING DISABILITIES

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Working memory (WM) deficits are one of the main problems in children with learning disabilities (LD), who also frequently show a slower electroencephalogram (EEG) resting activity than healthy children. EEG is useful as well to examine the neurophysiology and temporal dynamics of cognitive processes, therefore in this study we compared the EEG spectra of LD children and healthy controls while performing a working memory task. A second objective was to compare the results of the traditional scalp-EEG with an inverse method (e-Loreta) of source-EEG imaging, a type of analysis employed to improve the EEG spatial resolution by diminishing the influence of artifacts like volume conductor and the reference electrodes. Fifteen LD children and 16 controls with good academic achievement were included in this study, and performed a modified version of the Sternberg WM task. The EEG was recorded at 19 electrodes (10-20 system) referred to linked earlobes. The spectrum (from 1.25 to 50 Hz) was analyzed on 800ms samples corresponding to the retention phase of the WM task. For the current sources analysis, we selected the 19 cortical areas nearest to the electrodes. Behavioral results showed LD children had less correct responses than controls. As for the EEG results, the sources-EEG method demonstrated greater statistical differences than the scalp-EEG at comparing the groups of children. In the EEG-source spectra, LD children showed less high frequency activity (beta and gamma, >13 Hz) in frontal cortical areas, and a greater amount of theta (4-8 Hz) and alpha (8-12 Hz) activity in all cortical regions, mainly in the posterior areas of the brain. In conclusion, source-EEG was better at distinguishing the groups of children, by reducing the influence of artifacts. LD children showed a slower EEG than controls, inadequate alpha activity suppression, and less recruitment of high frequency activity in frontal areas. These results could help to explain their low efficiency in WM tasks that might underlie their poor performance in academic abilities like reading, writing and mathematics.

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57. EMT AND MIGRATION IN OVARIAN CARCINOMA CELLS ARE REGULATED BY UTP AND ADENOSINE

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Nucleotides and nucleosides are signaling molecules that have a variety of roles mediating paracrine or autocrine activities by acting through specific membrane receptors. Their participation in cancer has been studied but it is still not clear. In this work, we studied the role played by UTP and adenosine in the migration of ovarian carcinoma-derived cells SKOV-3. Stimulation of carcinoma-derived SKOV-3 cells with UTP (100 µM) increased migration (~57%), while apyrase (10 U/mL), an ectonucleotidase that catalyzes dephosphorylation of nucleotides, decreased basal migration (~47%). P2RY2 was found to be the receptor mediating these effects since knock down of this receptor blocked the UTP-induced cell migration, and was dependent on EGFR transactivation. UTP effect on migration was also associated with epithelial to mesenchymal transition (EMT), it was associated with an increase of snail and twist expression, known EMT inductors, as well as an increase of vimentin expression, a marker protein for mesenchymal phenotype.
In turn, the inhibitory effect of apyrase over SKOV-3 basal migration was associated with an enrichment of E-cadherin in the cell contacts, suggesting the establishment of an epithelial phenotype. This observation strongly suggests the possible role of adenosine inhibiting the invasive ability.

To analyze the effect of extracellular adenosine over cell migration, we studied the effect of a set of drugs that modify its activity, adenosine 5'-(α,βmethylene) diphosphate (APCP), an inhibitor of the enzyme that turns AMP into adenosine (NT5E); adenosine deaminase (ADA), the enzyme that catalyzes the desamination of adenosine to inosine; dipyridamole (DPR), an inhibitor of the adenosine uptake mediated by equilibrative nucleoside transporters (ENT). By blocking NT5E enzyme with APCP and degrading adenosine with ADA, migration was unaltered even in the presence of apyrase. However incubation with DPR induced a reduction of basal migration (≈36%), that was even more accentuated with adenosine (100 µM) (≈64%), suggesting that extracellular adenosine could be acting upon ADORA receptors.

Our results suggest that released nucleotides acting upon P2RY2 receptors are inductors of mesenchymal phenotype, while adenosine acting over an ADORA receptor could have antagonistic effects by promoting an epithelial phenotype in ovarian carcinoma cells. (D)

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58. IDENTIFICATION OF MOLECULAR TARGETS OF PEPTIDE TOXINS FROM THE VENOM OF THE TURRID SNAIL POLYSTIRA ALBIDA FROM THE GULF OF MEXICO

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For more than 40 years, conotoxins (peptides from the venoms of marine snails belonging to the Conidae family) have been studied, since they are a valuable source of molecular tools to distinguish subtypes of ion channels and receptors of excitable cells. However, the venoms of another family (Turridae) of snails have been poorly studied, despite this group represents more than 90% of the biodiversity of the Conoidea superfamily. Thus, the turrid snails may be the greatest source of molecular tools to understand the function of channels and receptors. Thus far, only preliminary evidence from a few Turridae and Terebridae (another Conoidean family) species has been obtained of inhibitory activity at nicotinic acetylcholine receptors (nAChRs). The aim of the present study was to identify toxins with effects on nAChRs from the turrid snail Polystira albida, collected in the Gulf of Mexico. We prepared an extract from venom glands of this species and fractionated it by reversed-phase high performance liquid chromatography (HPLC). We tested the HPLC fractions on the human α7 nAChR subtype expressed in Xenopus laevis oocytes. To date, 8 out of the 37 fractions tested have been determined to have antagonistic activity at the α7 receptor; one fraction reduces the acetylcholine-elicited current by ~24% at a concentration of 8.4 µM, and slowly dissociates from the receptor, allowing the current amplitude to return to control values after ~20 min of wash.

Our results constitute the first report of chromatographic fractions of venoms from non-Conidae species acting upon defined nAChRs. When purified and biochemically characterized, the active turritoxins contained in these fractions could be useful as molecular tools to study the function of the human α7 subtype, whose malfunction has been shown to be implicated in neurodegenerative disorders such as Alzheimer’s disease. (D)
59. NEUROPHYSIOLOGY OF TIME PERCEPTION IN THE PRESUPPLEMENTARY MOTOR AREA OF THE Rhesus Monkey

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Neuroimaging studies in humans suggest that the presupplementary motor area (pre-SMA) is a major component of the network engaged in processing temporal information during motor and perception tasks. To study the role of this node, we recorded single unit activity in the pre-SMA of two monkeys performing a relative temporal categorization task. In this task, the monkeys had to assign different interval durations to ‘short’ or ‘long’ categories according with previously learned prototypes. In each 96-trial run of the task, one of three sets of eight different intervals was presented to the monkey. For each set, the shortest four values were considered as ‘short’ and the remaining four as ‘long’. Employing linear regression analysis, multiple regression models and analyses based on the signal detection theory we show that a subpopulation of pre-SMA neurons show ramping activity during the presentation of the interval, which suggests the participation of these cells in the tracking of elapsed time. By the other way, the activity of a particular group of pre-SMA neurons was associated to the explicit representation of the limit between temporal categories. In addition, the activity of different groups of neurons was modulated by the categorical decision of the monkeys or by the consequences of such decisions. These results support the role of the pre-SMA in time perception. In particular they show that the pre-SMA not only represent elapsed time but also the temporal categorical boundaries needed to guide the subject’s choice as well as the consequences of such choices. Probably these groups of neurons interact in order to improve the subject’s capacity to categorize time intervals during the temporal categorization task.

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60. KIR CURRENTS IN OLIGODENDROCYTES FROM THE OPTIC NERVE ARE INSENSITIVE TO INTRACELLULAR H⁺

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Oligodendrocytes (OLs), the myelinating cells in the central nervous system, express inwardly rectifying K⁺ currents (named Kir currents). It is known that functional Kir channels are composed by tetramers in homomeric or heteromeric conformations, and depending on the subunits involved, the channels might be modulated by factors such as the ATP or intracellular H⁺ concentration. Also is well known that Kir 4.1 subunit is involved in OLs maturation, given that KO model for this subunit shows Kir current absence as well as an increase in the number of immature OLs causing general hypomyelination that includes the optic nerve. Nevertheless, the molecular identity of the Kir channel expressed in OLs remains unknown, it is plausible that channels might be either homomers of Kir 4.1 or heteromers with Kir 2.1 and Kir 5.1 subunits. Kir currents through these channels are inhibited by intracellular H⁺ whit the next potency: Kir 4.1/5.1 >> Kir 4.1 >> Kir 2.1. Thus, a systematic study about the Kir current sensitivity to intracellular H⁺ in OLs would provide information related to channel identity. Unexpectedly, using electrophysiology we found that Kir currents in OLs from the rat optic nerve were insensitive to H⁺ (pH range of 5.0-8.0). Kir current insensitivity to H⁺ was not provoked by lost of cytoplasmic components (a common effect when the standard patch-clamp technique is used), since the use of “perforated” patch-clamp technique gave the same result. Moreover, Kir subunits cloned from OLs that were expressed in Xenopus oocytes showed H⁺ sensitivity which matched
with that reported in other cell types. These results strongly suggested that Kir current $H^+$ sensitivity in Ols was regulated by extrinsic factor(s), since current activity in an acidic environment did not correspond with Kir channels composed of 4.1 subunits. Among many possibilities, it might be that Kir $H^+$ sensitivity is regulated through postranscriptional subunit modifications or by accessory molecules.

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61. TIME CALORIC RESTRICTION INHIBITS THE NEOPLASTIC TRANSFORMATION OF CIRRHOTIC LIVER IN RATS TREATED WITH DIETHYLNITROSAMINE


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The Hepatocellular cancer is the most common type of primary liver cancer. Cirrhosis is the principal risk factor in the generation of this malady. Protocols of caloric restriction and restricted feeding schedules have been proved protective in experimental carcinogenic models. We tested the influence of a time-caloric restriction protocol (2 h of food access during the daytime for 18 weeks) in an experimental model of cirrhosis-hepatocarcinoma (replicating the pathologic clinic sequence of both diseases), produced by the weekly administration of diethylnitrosamine. Our results indicate the time caloric restriction reduced the hepatomegaly and prevented the increase in blood leukocytes promoted by diethylnitrosamine. Strikingly, food restriction preserved hepatic functional and histological characteristics by preventing the anisocytosis and hypercelularity in cirrhotic areas compared with the group fed Ad Libitum. Tumoral masses of the restricted group were poorly undifferentiated of liver tissue; consider an advanced state of HCC. However, time caloric restriction enhanced collagen deposits. As to the cancerous process, food restriction prevented systemic inflammation and the increase of carcinoembryonic antigen, besides favouring the occurrence of diffuse multinodular tumor; histologically, it prevented tissue inflammation, the regenerative process and neoplastic transformation. Time caloric restriction promoted circadian synchronization in cirrhotic and cancerous liver sections as well as elevated levels of the clock protein BMAL1. We conclude that time caloric restriction prevents the neoplastic transformation of tumoral lesions induced by diethylnitrosamine, probably by circadian entrainment together with the caloric restriction. (D)

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62. SEXUAL ACTIVITY AND PROSTATE CANCER IN THE TRAMP MURINE MODEL

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Prostate cancer is the most frequently diagnosed neoplasia in occidental men. Sexual activity is an important stimulus for maturation and function of the prostate, but its role on prostate cancer is not clear. Epidemiological
research shows that a frequent sexual activity could reduce the risk to develop prostate cancer. In the TRAMP (transgenic adenocarcinoma mouse prostate) model, we have shown that continuous sexual activity for 2 months reduces the number of pre-cancer lesions (cribriform pattern) and increases the prostate T3 levels. In a xenotransplant (LNCaP cells) model of prostatic carcinoma was shown that T3 reduced tumor growth, whereas T4 increased invasive capacity and VEGF secretion in LNCaP cells. The purpose of this study was to analyze the effect of sexual activity on T3/T4 ratio, on gene expression of proteins that control cell proliferation (TIS21, CCND1, cyclin D1), VEGF secretion (HIF-1α, VEGFα), testosterone and estrogen levels. Eight week-old TRAMP mice were subdivided in two groups: inactive or sexually active. These latter cohabited with receptive females for 5 weeks. Mice were sacrificed by decapitation, serum was collected to determinate hormone levels (ELISA) and prostates were preserved for histological processing or analysis of gene expression (PCR real time). Results showed that sexual activity increased serum T3/T4 ratio but had no effect on testosterone or estrogen levels. Sexual activity induced functional hyperplasia and it correlated with increased expression of CCND1. In addition, sexual activity reduced the incidence of acini with cell invasion to lumen, but it did not modify the expression of HIF-1α/VEGFα genes. Further analysis should be considered to analyze if the T3/T4 ratio in tumors could be relevant on this protection.

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63. PROLACTIN STIMULATES POSTNATAL LIVER GROWTH

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Prolactin (PRL) stimulates normal liver growth and liver regeneration after partial hepatectomy in adult rats by promoting hepatocyte proliferation and liver angiogenesis (Moreno-Carranza et al., 2013, Am J Physiol Regul Integr Comp Physiol, 305(7):R720). The liver grows during the early postnatal period, and PRL levels are high in neonates. However, the effect of PRL on liver growth during postnatal development is unknown. Here, we studied postnatal liver growth in PRL receptor null mice (PRLR−/− on a C57BL/6 background) and in wild type (PRL+/+) mice treated with PRL or rendered hyperprolactinemic by lentiviral vector-mediated delivery of PRL (LV-PRL). Compared to wild type counterparts, PRLR−/− mice showed significantly (p <= 0.05) smaller liver to body weight (LBW) ratios at all times tested (1, 4, 6, and 20 weeks after birth) and lower hepatic expression of cyclin D1 and of vascular endothelial growth factor (VEGF). Consistent with PRL promoting liver growth after birth, the intra-peritoneal injection of PRL to PRLR+/+ mice, twice a day from postnatal day 1 to 4, significantly (p=0.02) increased the LBW ratio on day 5 after birth. Moreover, the intravenous delivery of the LV-PRL vector to 4-weeks old wild-type mice elevated PRL circulating levels ten-fold and resulted in increased LBW ratios, enhanced proliferation of hepatocytes [evaluated by proliferating cell nuclear antigen (PCNA)-positive nuclei], and higher hepatic expression of STAT3, cyclin D1, cyclin E, VEGF, and of the endothelial cell markers CD31 and von Willebrand factor. These results support the role of PRL as a physiological promoter of postnatal liver growth acting by stimulating hepatocyte proliferation and liver angiogenesis.

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Autism is considered a neurodevelopmental disorder characterized by impaired communication and social interaction, as well as repetitive and stereotyped behaviors. Recent fMRI studies showed a decrease in the thickness and volume of the corpus callosum of autistic children and adults (Wolff et al., 2015). The corpus callosum (CC) is the largest commissure in mammals. After postnatal day 5 (P5), 99% of the cell somata correspond to glial cells in rats (Reyes-Haro et al., 2013). Microglia is a sensor and a reactive element in events of neuroinflammation, as well as being involved in the maturation of synaptic circuits (Reyes-Haro et al., 2014). If the reduced volume of autistic CC correlates with a change in cell density, is unknown. The aim of this study was to investigate if microglia density of CC is modified in a murine model of autism, known as prenatal exposure to valproic acid (VPA). Methods: 1) VPA or saline solution injection (500 mg/Kg) of pregnant rats (E12.5), 3 per experimental group. 2) DAPI staining and immunofluorescence studies for Iba-1 were performed on male brain sagittal sections (30 um; at P6) to estimate microglia density in the genu of CC. Results: 1) Glial cell density was reduced 45% in the genu. 2) Microglia density was reduced 46% in the genu. 3) The ratio of activated/resting microglia was reduced 32%. We conclude that microglia density of the genu is affected by autism. These results could be related to the etiology of autism in humans. (L)

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The diabetic macular edema (DME) is the leading cause of blindness in people with diabetes. It results from the increment of permeability through the blood-retina barrier (BRB). Despite recent advances in treatments for DME, the available therapies are expensive and show low effectiveness in treating severe or diffuse DME. The cationic channel “Transient Receptor Potential Vanilloid 4” (TRPV4) is the only member of the TRP family involved in endothelial permeability regulation and it is expressed in the retina. However the expression of TRPV4 on both the inner and outer component of the BRB, i.e. endothelial cells and retinal pigment epithelium (RPE), remains to be demonstrated. Further, selective inhibition of TRPV4 using pharmacology has been recently shown to mitigate the pulmonary edema by reducing the permeability through the blood-lung barrier. Therefore we aim to determine the presence of TRPV4 in the BRB and assess if TRPV4 inhibition mitigates the increase of BRB permeability and water retention that associates with diabetes.

Immunofluorescence analysis showed TRPV4 expression in both capillaries and the RPE of mouse retinas. Next, we determined the rate of permeability through the BRB in diabetic rats using the Evans blue assay. We found that intravitreal injection with the selective TRPV4 antagonist GSK2193874 reverted the increase in diabetic-induced BRB permeability. Water movement in the retina was measured in images sensitive to diffusion obtained from ex vivo preparations from mice. We found that water diffusion was greater in diabetic
mice compared with non-diabetic animals, and that this increase was prevented in diabetic trpv4−/− mice. In view of these data, we then aimed to define if TRPV4 directly targets the RPE. To this end, we evaluated the transepithelial electrical resistance (TEER) in human RPE (ARPE-19) cell monolayers subjected to chronic exposure to high glucose levels. We showed that high glucose exerts a three-phase effect that includes a short-term increase (3 days), a medium-term stabilization (7 to 21 days), and a long-term reduction (28 days) in TEER. Both the increase and decrease in TEER were prevented when GSK2193874 was applied.

Conclusion: TRPV4 inhibition could be of therapeutic interest for controlling BRB breakdown associated with DME and other retinopathies.

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66. LEVOSULPIRIDE INCREASES THE LEVELS OF PROLACTIN IN THE VITREOUS OF PATIENTS WITH DIABETIC RETINOPATHY

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Diabetic retinopathy (DR) is the first cause of blindness and is determined by the ischemia-induced proliferation of new blood vessels (angiogenesis) in the retina that extend and bleed into the vitreous eventually leading to retinal detachment. Studies in rodents showed that the hormone prolactin (PRL) is incorporated into ocular tissues where it gets cleaved to vasoinhibins, a family of PRL fragments that inhibit ocular vasopermeability and angiogenesis. Therefore, inducing hyperprolactinemia may represent a novel therapy against DR. Levosulpiride, an antagonist of dopamine D2 receptors used in diabetic patients for its prokinetic effects in the digestive track, leads to hyperprolactinemia as a side-effect. Here, we tested whether the oral administration of levosulpiride increases PRL levels in the vitreous of patients with DR undergoing vitrectomy for medical reasons. PRL was measured by immunoassay (IMMULITE 2000 XPI). Treatment with levosulpiride (25 mg DISLEP, 3 times a day) for 7 days increased circulating (117.1±11.3 vs. 9.9±3.4 ng/ml, P<0.0001) and vitreous (1.6±0.7 vs. 4.2±0.8, p<0.04) PRL levels relative to placebo. PRL levels in the vitreous directly correlated with PRL values in the circulation (r=0.62, P<0.04) of the whole study population (5 patients treated with placebo and 6 levosulpiride). These findings show for the first time the presence of PRL in human vitreous and the ocular incorporation of systemic PRL in patients with DR. Current studies are evaluating the levels of vasoinhibins in the vitreous and extending the analysis to a larger group of patients. Our work is consistent with levosulpiride being a potential treatment targeting DR.

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67. ANATOMICAL AND FUNCTIONAL SEGREGATION OF THE CORTICOSPINAL SYSTEM

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The descending corticospinal (CS) projection has been considered a key element for motor control, which results from direct and indirect modulation of spinal cord pre-motor interneurons in the intermediate gray matter of the spinal cord, which in turn influences motoneurons in the ventral horn. The CS tract (CST) is
also involved in a selective and complex modulation of sensory information in the dorsal horn. However, little is known about the organization of CS projections that may encode different cortical outputs to the spinal cord. Here we use retrograde tracing and 2 photon calcium imaging to analyze anatomical distribution and functional interactions between different populations of CS neurons in rodents. Our results show that at least two different and partially intermingled populations of CS neurons in the sensorimotor cortex projects in parallel to dorsal horn and intermediate zone of the same segment. This sensorimotor segregation of CS system has long been suggested, but has never been conclusively shown; thus our findings implies that the CST is composed of hierarchically organized subsystems controlling different segmental neural circuits that are part of sensory and pre-motor pathways, representing a new and additional level of sensorimotor integration.

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68. THE HEDONIC VALUE OF THE CONTEXT MODULATES THE TASTE MEMORY FORMATION: EFFECTS OF AN APPETITIVE STIMULUS DURING INHIBITORY AVOIDANCE

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Context and flavor are directly interacting during learning, thus the aim of this research was to study how both stimuli are learned together and if they potentiated or inhibited in inhibitory avoidance (IA) learning. Accordingly, we evaluated if an appetitive stimulus (sugar) presented during IA training has an effect on the aversive learning and the effect of context pre-exposure with sugar on latent inhibition of IA. Rats were pre-exposed to a new context (IA chamber), and allowed to drink a sugar solution (10%) inside the dark compartment of the chamber. Next day, IA training was conducted with or without sugar presentation; 24 h later IA memory was evaluated. The results demonstrated that IA chamber pre-exposure, with a reinforcer did not affected incidental memory formation. However, during IA retrieval, animals whether pre-exposed or not, had the same entry latency indicating a weak latent inhibition of IA. Furthermore, the group that was pre-exposed to sugar presented a lower sugar intake latency, and had a significant increase on consumption along the trials that did not change regardless the electric shock, in contrast with the non pre-expose group that showed higher intake latency and a decrease in consumption. These results suggest that the initial/novel context where taste memory is formed, modulates the appetitive response.

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69. TILAPIA TRANSCRIPTOME ANALYSIS REVEALS TISSUE-SPECIFIC REGULATION BY THYROID HORMONES 3,5-T2 AND 3',3,5-T3

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Abstract
Thyroid hormones (THs) act mainly through their nuclear receptors (TRs). T3 is considered the primary bioactive TH because of its high affinity for TRs. However, our data in teleosts have shown that 3,5-T2 (T2) can also regulate gene expression as well as promote the recruitment of a different transcription factor population to the TR bound to the TH-response elements. In these vertebrates, the effects of T2 are mediated by a long (L-) TRβ1 isoform, in contrast to T3 that only activates the short (S-) TRβ1. In concert, T3 and T2 differentially regulate the expression of S- and L-TRβ1, respectively in vivo. To determine the functional relevance of these unique receptor mediated signaling pathways, we performed a transcriptome analysis in cerebellum, thalamus-pituitary and liver of tilapia treated with equimolar doses of T2 or T3 (25 nM). A total of 169, 154 and 2863 genes were differentially expressed (FDR < 0.05) in the cerebellum, thalamus-pituitary and liver, respectively. We identified genes that were regulated by both THs, as well as those that were uniquely regulated by T3 or T2. In consonance, many different pathways were affected. Among the most representative were transcription, immune system, and cell maintenance, emphasizing thus the relevance of T2 action in fish physiology. Furthermore, conserved response in liver between mammals and teleosts
highlight the importance of T2 action at least in teleosts, as an important transcriptional regulator. (D)
We thank Adriana González Gallardo and Anaid Antaramian for technical support.
This work was supported by CONACYT 219833, PAPIIT IN201614.

70. NOVEL POSITIVE ALLOSTERIC MODULATOR SITE FOR ENDOGENOUS β-CARBOLINES ON THE GABA<sub>α</sub> RECEPTOR

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The γ-aminobutyric acid (GABA) is a major neurotransmitter in the central nervous system, GABA acts mainly through activation of pentameric receptor-channels permeable to Cl- ions, known as GABAA receptors. In oligodendrocytes (OLs), GABA<sub>α</sub> receptor expression is determined by its interaction with neurons, thus, it has been proposed its role during the myelination process, and in fact this phenomenon is altered when gabaergic signaling is deficient. Functional characteristics of the GABAA receptor in OLs from the optic nerve indicated a specific combination of the subunits conforming the receptor, given that behaved different to receptors from either neurons or other glial cells. An important difference is related to the effect of butyl-carboline-3-carboxylate (β-CCB), an endogenous β-carboline. β-CCB is a substance described as an inverse agonist on the main GABAA receptor from neurons, acting on the benzodiazepine binding site, while it has been shown that β-CCB potentiates the response in OLs. Here, GABAA receptors cloned from OLs, were heterologously expressed in *Xenopus laevis* oocytes, and observed that β-CCB indeed acted as a potent enhancer of the GABA response. First, different combinations for the subunits cloned were expressed and analyzed electrophysiologically. Our results showed that α3β2γ1 subunit co-expression mimicked the functional and pharmacological pattern described for the receptor in OLs, and that β-CCB was a positive allosteric modulator of the response with an EC<sub>50</sub> = 4 ± 1.9 µM. This effect was not antagonized by flumazenil, a potent antagonist of the classic benzodiazepine binding site, thus, suggesting that β-CCB acted through a novel modulator site on GABA<sub>α</sub> receptors from OLs.
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71. IL–1β INDUCES GENOMIC REARRANGEMENTS THAT TRANSCRIBED IN THE MITOCHONDRIAL RNA IN CANCER CELLS

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Cancer cells accumulate numerous and frequent molecular alterations that causes genomic instability. Interleukin 1 beta (IL-1β) induces cell signaling pathways that increase malignancy of cancer cells, invasion and metastasis; nevertheless, little is known at the molecular levels of genomic rearrangements that occur during this cellular transition. To evaluate the possibility of genomic recombinations that occur in the mitochondrial transcriptome, we analyzed in cultured breast cancer cells, induced to epithelial-mesenchymal
transition with IL-1β, the prevalence of deletions in mitochondrial RNA. The transcriptome of MCF-7 cells induced and non-induced with IL-1β was massively sequenced and analyzed by means of bioinformatic algorithms for finding deletions and changes in their frequency. We found little variability in the deletion frequency between two cell conditions, also we found 30.4% of deletions shared between both experimental conditions, affecting a total of 22 genes mitochondrial in addition to regulatory region of the mitochondrial genome (D-loop), the most affected the cytochrome c oxidase I (COI) gene followed by the ribosomal subunit 16S, and then all the genes associated with cellular energy production, that is: cytochromes, NADH dehydrogenase, and ATPase 6, and other deletions in mitochondrial tRNA, indicating that IL-1β induces changes in mitochondrial transcriptome of MCF-7 cells; however, at this moment, we cannot be able to evaluate the effect of these deletions in the MCF-7 cell biology.

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72. PROLACTIN PROTECTS RAT CORTICAL ASTROCYTES AGAINST OXIDATIVE STRESS

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Astrocytes maintain brain homeostasis by protecting synaptic integrity, providing metabolic support for neurons, regulating inflammatory responses, and increasing survival under oxidant conditions. Several types of stress and injury in the brain induce mitochondrial dysfunction and oxidative stress leading to astrocyte death. Prolactin (PRL) is a stress-related hormone limiting gliosis and degeneration of neural retina (Arnold et al. JN 2014). Here, we investigate whether PRL protects brain astrocytes against oxidative stress and cell death. Primary cultures of cortical astrocytes were isolated from the brain of neonatal Wistar rats. The long PRL receptor isoform was detected in cortical astrocytes by qRT-PCR. Astrocytes were treated with increasing concentrations of PRL (1-100 nM) 24 hours after being exposed to oxidative stress induced with 400 μM hydrogen peroxide (H2O2) for 3 hours. Incubation of cortical astrocytes with PRL inhibited H2O2-induced cytotoxicity, evaluated by the MTT assay, in a dose-dependent manner. These findings indicate that PRL can act directly on astrocytes to protect them against oxidative stress injury. (L)

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73. EFFECTS OF PERINATAL UNDERNUTRITION ON PYRAMIDAL NEURONS OF THE ANTERIOR CINGULATE: ITS CORRELATION WITH THE MATERNAL RESPONSE OF RATS

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Perinatal undernutrition (PU) in the rat elicits long-term physical and behavioral consequences. The physiological and metabolic abnormalities associated with PU have been widely studied, but the negative consequences on the mother-litter interactions are still under investigation. The aim of this study was to analyze the pup retrieval and nest building responses of dams with PU and its correlation with the morphology of the pyramidal neurons of the anterior cingulated cortex.
The experimental underfed group (UG) consisted of undernourished dams fed with a caloric food restriction diet during the pre- and neonatal periods, while the control group (CG) was fed ad libitum. At postnatal (PN) day 90 rats were mated, and after the delivery the retrieval of pups (grasping body area and latency), and the nest building (shape and size) at PDs 4, and 12 were evaluated. The analysis of the anterior cingulate pyramidal neurons was performed by using the Golgi-Cox technique. The perimeter and area of the perikarya and the dendritic arbor density measurements were obtained.

At PDs 4, and 12 the UG dams showed significant prolonged retrieving latencies, carrying the pups by improper body areas, and with deficient nest building organization, compared with the CG dams. Furthermore, at PDs 4 and 12, pyramids from the UG dams showed significant reductions in the area, perimeter and the dendritic arborization than the cingulate neurons of CG dams.

The deficiencies in the maternal responsiveness of the UG mothers may partly reflect the long term synaptic and functional alterations at the telencephalic structures of the maternal circuitry, highly vulnerable during this time-window of life.

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74. CHRONIC ADMINISTRATION OF NICOTINE PARTIALLY REVERTS THE EFFECTS OF IBOTENIC ACID IN A MODEL OF SCHIZOPHRENIA

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Schizophrenia is a chronic neuropsychiatric disease affecting 1% of worldwide population. It is well known that schizophrenics tend to smoke heavily, 3-4 times more than the general population. The α7 receptor has been associated with this disease, and is considered a potential target mediating the nicotine pro-cognitive effects. The main goal of this work was to evaluate the effects of chronic administration of nicotine in the Neonatal Ventral Hippocampal Lesion (NVHL) experimental model of schizophrenia. For this purpose ibotenic acid was injected in the hippocampus of rat pups (postnatal day 7). In the 50th postnatal day, working memory was evaluated in a radial arm maze, and after 2 weeks of training chronic administration of nicotine was introduced (IM, 5 mg/kg, twice a day). The results showed that in NVHL animals the working memory was impaired, and treatment with nicotine improved their task execution. Rapid Golgi staining showed that in NVHL animals the area and diameter of the soma of granular neurons of the hippocampus was reduced; in addition, pyramidal neurons of the cortex showed a reduction in the area and diameter of the soma, as well as in the length of dendrites. Interestingly, administration of nicotine reverted the effects on cell morphology of the NVHL animals. Western blot analysis revealed that the level of expression of α7 receptor in hippocampus of NVHL and control animals is similar, whereas in the cortex of NVHL animals with nicotine treatment the expression was increased. Our data suggest that nicotine acts as a pro-cognitive drug in the NVHL, supporting the hypothesis that subjects with schizophrenia smoke at higher rates as an attempt to self-medicate. This effect may be mediated in cortical regions due to the effect on the cellular morphology of the pyramidal neurons, as well as the increment in the expression of the α7 receptor.

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75. ENHANCED MITOCHONDRIAL PRESENCE OF GLUCOCORTICOID RECEPTOR IN THE STRIATUM DURING THE CONSOLIDATION OF A PROCEDURAL MEMORY

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Glucocorticoids administrated into the striatum enhance memory consolidation. This effect is accomplished through the activation of the glucocorticoid receptors (GRs). Recent work indicates that mitochondria play a major role in neuronal plasticity and behavior; it has been reported experimental evidence that suggests that mitochondrial functions are involved in memory consolidation. Furthermore, there is a relationship between mitochondrial activity and glucocorticoids, as GRs translocate into mitochondria and affect its functions. However, it is not known the full dynamics of GRs translocation into mitochondria and its influence on memory consolidation. To study this topic, we trained independent groups of rats on a cued-water maze task and dissected the striatum at different times after training (0.5, 1.5 and 6.0 h) to isolate the mitochondria fraction. In this subcellular fraction we evaluated the temporal course of the translocation of GR by the western blot technique. We also studied an intact group that remained in its home-cage, and a swim group, that was exposed to the water maze task but without the platform or the cue. Our results showed that training in the cued-water maze task induced GR translocation into the mitochondria of the striatum, having a significant increase at 0.5 and 1.5 h after training in comparison with the intact group. On the other hand, the levels of GR within mitochondria of the swim group had a single peak at 6.0 hours after exposure. We conclude that there is a different temporal course of the GR translocation into mitochondria of the striatum of the trained groups, different from that of the swim group, which suggests that this process is associated in procedural memory consolidation.

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76. THALAMO-STRIATAL INTERACTIONS DURING THE LEARNING AND EXECUTION OF COGNITIVE AND MOTOR HABITS

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The sensorimotor striatum (in rodents the dorsolateral striatum, DLS) has been classically implicated in the learning and execution of cognitive and motor habits but the underlying network-level mechanisms remain largely unknown. Understanding the precise role of the different inputs arriving to the DLS is a fundamental step to start unraveling such mechanisms. For example, it is well know that somatosensory information arrives to the DLS from the primary sensory cortex (S1) and preliminary data in our lab indicates that this kind of information also arrives from the ventro-postero-lateral nucleus of the thalamus (VPL). To investigate the functional role of these projections we performed pharmacological disconnections between the DLS and the VPL in rats and evaluated the animals in two behavioral protocols. Specifically, rats where trained to perform a motor coordination-dependent task in the rotarod or a motor coordination-independent, cognitive task in the T-maze. Preliminary results indicate that DLS-VPL disconnection before training on the T-maze protocol induced no changes in performance (learning or extinction). In contrast, after learning the rotarod protocol, DLS-VPL disconnection induced severe deficits in the first post-disconnection sessions followed by relearning curves. Ongoing work using magnetic resonance imaging (MRI) will help to evaluate the extent
of damage caused by the lesions on each animal. While future investigations will focus on the S1-DLS projections, our data suggest that VPL-DLS interactions are necessary for motor coordination but not for the "cognitive" role of the DLS. (A)

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77. GENERATION OF A TRANSGENIC ZEBRA FISH LINE THAT EXPRESSES THE GENETICALLY ENCODED CALCIUM INDICATOR GCaMP6s IN NEURONS

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Transposon technologies for gene engineering can be used for stable genomic insertion of DNA in a regulated and highly efficient manner. Recently, the Tol2 transposon has been applied for the integration of highly sensitive sensors of metabolic activity, such as the genetically encoded calcium indicators (GCaMPs). These proteins consist of a calcium binding domain from calmodulin, a bipartite version of the green fluorescent protein and the phage M13. GCaMPs can be genetically targeted to express in different cell types for studies in living organisms. Thus, the aim of this project was to generate a transgenic line of zebrafish (Danio rerio) that expresses the GCaMP6s calcium sensor in neurons of the central nervous system.

We used the following plasmids: a) pTol2-elavl3-GCaMP6s, that carries the gene of the calcium sensor under control of the ELAVL1 promoter. ELAVL1 is a neuron-specific RNA-binding protein: b) pCS2FA-transposase encoding for the Tol2 transposase that was in vitro transcribed. Plasmid and Tol2 RNA were co-injected into fertilized wild-type (TABWIK) zebrafish eggs at the one-cell stage and expression assessed by epifluorescence and confocal microscopy, basal activity of GCaMP6 was recorded and contrasted with emission induced by a high concentration of potassium.

The efficiency of transgenesis was about 80% as assessed by epifluorescence microscopy. Expression of GCaMP6s was observed 24 h post-injection throughout the neural tube, the olfactory bulb, ventrolateral optic tract and spinal cord. When a high concentration of potassium was included in the water, the intensity of the fluorescent signal increased considerably; consistent with higher neuronal activity. In conclusion, the preliminary observations show that the genetically encoded calcium sensor GCaMP6s was successfully introduced in the genome of zebrafish, it is expressed in neurons and its activity raised by high potassium.

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78. PROLACTIN PROTECTS AGAINST THE DIABETES INDUCED BY STREPTOZOTOCIN IN MICE


The hormone prolactin (PRL) regulates metabolic homeostasis. It promotes the proliferation, survival, and insulin production of pancreatic β-cells, its levels are reduced in the circulation of patients with diabetes and in obese children, and lower systemic PRL levels correlate with an increased prevalence of diabetes and a higher risk of metabolic syndrome. Here, we investigated the protective effect of PRL against diabetes by comparing the incidence and severity of the disease induced by multiples intraperitoneal injections of streptozotocin (STZ) in mice that were null (PRLR-/-) or not (PRLR+/+) for the PRL receptor. Diabetes was
defined by blood glucose levels >180 mg/dL. Incidence of diabetes was maximal at week 2 after STZ injection and similar between the two groups of mice (64.7% and 66.6% for PRLR/-/ and PRLR+/+, respectively). Starting on week 3-post-STZ, PRLR+/+ mice showed a gradual recovery from diabetes that was maximal (75%) at the end of the study (11 weeks post-STZ). In contrast, in PRLR/-/ mice the recovery from diabetes started at week 11 post-STZ, when 37.5% of the mice showed lower glucose levels (153.5±10.25 mg/dL).

Also, three diabetic PRLR/-/ mice died before the end of the experiment and glucose reached higher levels in mice null for the PRL receptor (473.3±46.41 mg/dL and 263.5±25.6 mg/dL for PRLR/-/ and PRLR+/+, respectively). The reduced recovery and the increased severity of diabetes observed in the absence of the PRL receptor may be due to a reduction in the population of functional pancreatic β-cells. The area of pancreatic islets is reduced in diabetic PRL receptor null mice relative to wild type mice (5094±922.4 μm² vs. 17801±1847 μm²). All together, these findings support the protective effect of PRL against diabetes.

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79. THE USE KILLER TOXIN OF Saccharomyces cerevisiae AS BIOLOGIC CONTROL OF PATHOGEN STRAINS WITH IMPORTANCE IN BIOMEDICAL RESEARCH

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Some strains of Saccharomyces cerevisiae have the characteristic of secrete toxins, the most studied are K1, K2, K28 this toxins have a lethal effect in sensitive strains. Subsequent to genome S. cerevisiae sequencing, they found that the receptor of the toxin are the potassium channel TOK1. In yeast the toxin K1 induce a channel activation that event increase the open probability. In consequence the cells are deplated of potassium ion and membrane depolarization, after the cell dies. Interestingly, the toxin product strain have a protect mechanism this is produced an immature toxin (pptoxK1) localized in intracellular TOK1 structure. In this way, S. cerevisiae present a dual toxicity-resistance system, to study mechanisms of interaction at molecular level.

Subsequent studies have important evidence about the expression homologous protein like TOK1 in strains of the Candida, Aspergillus and Neurospora suggesting that dual toxicity-resistance system are conserved in the evolution.

Results obtained from in sillico analyses shown that homologous genes to TOK1 are present in Klebsiella pneumoide, Staphylococcus aureus and Listeria monocytogenes. Microbiological studies indicates that K. pneumoide, S. aureus and L. monocytogenes recognized K1 toxin from Saccharomyces cerevisiae, this data suggest that a possible interaction of the K1 toxin in these prokaryotes that have an important role in biomedical research.

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80. EFFECTS OF ANOREXIA ON GLIAL DENSITY OF THE PREFRONTAL CORTEX

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Anorexia nervosa is an eating disorder that primarily affects adolescent females; knowledge about the neurobiology of anorexia is limited. The rat model of dehydration induced anorexia (DIA) mimics reductions in voluntary food intake and severe weight loss. The aim of this study was to investigate whether anorexia modifies the density of nerve cells in the prefrontal cortex. Methods: Three independent experimental series of ten female Wistar rats (180-200g) per group were used for this study: a) Control: received food and water ad libitum b) DIA: received a saline solution (NaCl 2.5%) and food ad libitum c) Forced Food Restricted (FFR) group received water and the same amount of food as the DIA group. Body weight, food consumption and food intake were recorded for 5 days. Subsequently, the rats were sacrificed, brain tissue sections (30 μm) were obtained for immunofluorescence studies and density of astrocytes (GFAP), neurons (NeuN) and microglia (Iba1) was estimated for the three experimental groups. Western blot studies tested if GFAP, vimentin and nestin expression were modified by anorexia. Results: The astrocyte and neuronal densities were reduced by anorexia (-20 and -18% respectively), while a similar reduction was observed for the FFR group (-19% and -17%). On the other hand, the density of microglia was not affected by anorexia. Nevertheless, anorexia significantly increased reactive microglia (+239%), and a similar increase was also observed for the FFR group (+229%). Finally, Western blot studies showed a decrease in the expression of GFAP (-91% and -86%), while an increase in vimentin (+93% and +89%) and nestin (+86% and +82%) expression was observed for DIA and FFR respectively. We conclude that astrocyte and neuronal densities are reduced, while reactive microglia is increased by anorexia.

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81. DETECTION OF BONE METASTASES THROUGH DIFFUSION-WEIGHTED WHOLE-BODY IMAGING WITH BACKGROUND BODY SIGNAL SUPPRESSION (DWIBS)

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Background: Cancer is the third leading cause of mortality worldwide. Approximately 70% of patients with cancer have bone metastases (BM) at their time of death. 18F-NaF Positron emission tomography/computed tomography (18F-NaF PET/CT) is considered the gold standard in the diagnosis of BM. The aim of the study is to compare the diagnostic accuracy of the Diffusion weighted imaging with background suppression (DWIBS) against 18F-NaF PET/CT.

Materials and methods: Patients were recruited from public and private institutions. Those who met the inclusion criteria underwent DWIBS, then PET/CT; such studies were interpreted by a medical radiologist and a nuclear medicine physician, respectively.

Results: The diagnostic performance of DWIBS compared to 18F-NaF PET/CT showed sensitivity of 86.8% (confidence interval [CI] 95%, 71.9 - 95.6), specificity of 51.6% (CI 95%, 33.1 - 69.9), positive predictive value (PPV) of 68.8% (CI 95%, 53.8 – 81.3), negative predictive value (NPV) of 76.2% (CI 95%, 52.8 –
91.8), positive likelihood ratio 1.79 (CI 95%, 1.2 – 2.6), negative likelihood ratio 0.25 (CI 95%, 0.1 – 0.6) and prevalence of 55.0% (CI 95%, 42.6 – 67.1).

Conclusion: DWIBS has excellent sensitivity and NPV, whereas specificity and PPV are regular. Nonetheless, the data remain uncertain due to the reduced sample size (69 patients) at the cutoff date. Our goal to achieve is 112 patients, expecting valid results for further analysis.

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82. STRUCTURAL ANALYSIS OF VASOINHIBINS: A MOLECULAR DYNAMIC SIMULATION APPROACH

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Vasoinhibins are endogenous angiogenesis inhibitors and potential agents for anticancer therapies. These peptides are generated when the hormone prolactin (PRL) loses its fourth $\alpha$-helix (H4) by proteolysis. The antiangiogenic effects are restricted to vasoinhibins, which suggest that conformational changes occur and new bioactive domains are created upon PRL proteolysis. However, the structure of vasoinhibins is unknown. The aim of this study was to predict the structure of these molecules and to identify newly formed domains through a molecular dynamic (MD) simulation approach. A classical MD simulation was performed using the Gromacs 5.1 package executed by the High Performance Computing Cluster Horus with 135 processors. We found that if the H4 is missing, the hydrophobic nuclei of PRL is exposed and this results in a rapid compression of the protein that buries the hydrophobic nuclei again. Such compression largely occurs by a movement of the loop1 (L1), which seals the gap left by the removal of H4. Consequently, some residues in L1 (R48, F50, H59, Q73 and K78) are more solvent-exposed in vasoinhibins than in full-length PRL and may represent a vasoinhibin antiangiogenic domain. This study provides insights into the structure of vasoinhibins that may help understand their structure-function relationship, develop a vasoinhibin quantitative assay, and design new agonist and antagonist drugs of their antiangiogenic properties.

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83. ELECTROENCEPHALOGRAPHIC CHARACTERIZATION OF SUBGROUPS OF CHILDREN WITH LEARNING DISORDERS

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Electroencephalographic alterations have been reported in subjects with learning disorders (LD), but there is no consensus regarding what characterizes their electroencephalogram (EEG). Our objective was to determine if there were subgroups within a group of students with specific LD in 2 or more domains and if these subgroups had specific electroencephalographic patterns.

85 subjects (31 female, 8-11 years) who scored low in at least 2 subscales -reading, writing and arithmetic- of the Infant Neuropsychological Evaluation were included. A cluster analysis formed 3 subgroups according to
their performance: Group 1 (higher scores than Group 2 in reading speed and reading and writing precision), Group 2 (better performance than Group 1 in composition) and Group 3 (lower scores than Groups 1 and 2 in the 3 subscales). EEG was recorded in 19 leads (10-20 system) during rest with eyes closed, EEG spectra was calculated and absolute power (AP) with geometric power correction was obtained every 0.39 Hz. A one-way ANOVA test was done to compare EEG measurements from the 3 groups, using a randomization test to correct significance threshold.

G3 had higher AP in frequencies in delta and theta range at left frontotemporal sites than G1 and G2. Higher AP in frequencies within the alpha band was observed in G2 than G3 and G1 at left occipital site. G3 had higher AP in frequencies in the beta range than G1 in parietotemporal areas and than G2 in frontopolar and temporal sites, mainly left. G1 had more AP within the beta frequencies than G2 in the left frontopolar site. G3 had lower values of gamma AP than the other groups in the left hemisphere, gamma activity was higher in G1 than in G2 in frontopolar and temporal areas.

This group of children with LD proved to be very heterogeneous. Three subgroups were found within this group, which have different cognitive profile, as well as a different EEG pattern. It is important to have these differences in mind while planning interventions with children with LD.

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84. NEUROANATOMICAL AND NEUROCHEMICAL TARGETS OF ATRAZINE EXPOSURE IN THE MALE RAT

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Atrazine (ATR) is an herbicide extensively used to control weeds and it is a potential toxicant for the dopaminergic system. Alterations in dopaminergic markers after ATR administration in rodents have been described. It has been observed that ATR exposure causes hypoactivity shortly after its administration. Also, GABAergic markers have been suggested to contribute to the disruption of hypothalamic release of GnRH in rats. In order to understand how acute ATR administration induces hypoactivity, we assessed the brain areas responsive to ATR using c-Fos, and we also measured the levels of gamma-amino-butyric acid (GABA) and glutamate, as markers of neuronal activity and neurochemical alterations, respectively. Two groups of Sprague-Dawley male rats received a systemic injection of 1% methylcellulose (MC; vehicle) or 100 mg ATR/kg body weight (under deep anesthesia), and 90 minutes after injection, rats were perfused with saline and paraformaldehyde (4%) for c-Fos, and TH immunohistochemistry in brain areas. In other two groups of rats, locomotor activity was recorded for 90 minutes after administration of 1% MC or ATR, then the brain was removed and dissected for GABA and glutamate determination. We found statistically significant increases in the number of c-Fos positive cells in the amygdala, subthalamic nucleus, substantia nigra, superior colliculus, and thalamus, but contrary to what we expected, no increases in c-Fos activation on catecholaminergic cells in SN, VTA or LC were observed. GABA and glutamate levels in the brain areas assessed were not affected. These findings suggest that the hypoactivity observed after ATR administration is the result of activation of non-dopaminergic cells and is not related to significant changes in glutamate and GABA tissue levels.

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85. DIFFERENTIAL EFFECT OF MOLECULAR IODINE IN MAMMOSPHERE CULTURE OF BREAST CANCER MCF-7 CELLS

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Mammary cancer (MC) is the malignant tumor with highest incidence worldwide and the first cause of death in women. It is estimated that 90% of MC have the potential to generate metastasis. In recent years several studies have focused on improving the conventional chemotherapeutic treatment by using natural molecules to limit chemoresistance and avoid significant increases in toxicity. Molecular iodine (I2) is a chemical form of iodine that exerts significant antineoplastic effects on several cancer cells, and whose actions could be mediated by the induction of differentiation mechanisms. There are many theories to explain the way carcinogenesis arises and progresses. Among them, cancer stem cell (CSC) theory proposes that only the stem cells present in the mature tissue, after converted into carcinogenic cells, possess tumor-initiating properties and metastatic potential. Putative CSC have been described and characterized in MC, where the CD44+/CD24- surface marker profile has been considered a canonical CSC characteristic. Moreover, in vitro mammary cancer MCF-7 cells cultured under serum-free, non-adherent conditions lead the selection of highly enriched CSC by the formation of spherical cell clusters called MCF-7 mammosphere (MCF-7/M) with high invasive capacity. On the present work we used this approach to evaluate the effects of I2 in cell proliferation and mammosphere formation. Results showed that after 72 hours 90% of the MCF-7/M culture adopt a mammosphere pattern and exhibit high expression of CD44 marker. I2 supplementation is accompanied by decrease in cell proliferation in CSC and parental cancer cells; it also impairs mammosphere formation in a dose-response manner. Cytometric analysis showed that MCF-7/M culture exhibited a dominant CD44+/CD24- sub-population and I2 supplement exerted a differential selection through the phenotype CD44+/CD24-. All these results suggest that I2 maintains its antiproliferative effects in CSC and parental cancer cells by forcing their differentiation into a less invasive phenotype and thereby inhibiting their tumorigenic capacities. Studies analyzing this hypothesis are currently ongoing.

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86. HEMODINAMIC RESPONSE DURING A VISUAL ORIENTING-ATTENTION TASK IN PREMATURE INFANTS AT 4, 8 AND 12 MONTHS

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Attention problems are a common behavioral difficulty in preterm infants. In this population, research suggests rates of 3 to 6 times higher for Attention Deficit Hyperactivity Disorder. It has been reported that at seven years, preterm infants present deficits in different attention tasks. Orienting attention is the ability to prioritize sensory input by selecting a modality or location; it involves parietal (PC) and frontal cortex (FC). Nowadays it has not been realized a study that describes the participation of PC and FC during a visual orienting attention task (VOAT) in preterm infants. Objectives: 1) To describe concentration of cerebral oxygenated hemoglobin (HbO) in PC and FC during a VOAT in preterm infants at 4, 8 and 12 months. 2) To describe the visual attention development using the Visual Attention Scale Test (VAST). Hypothesis: 1) Increased concentration of HbO in PC and FC in VOAT. 2) Increased percentage of correct answers in VAST.
while increasing age. Method: The neuroimaging technique of near-infrared spectroscopy (NIRS) was used. Task consisted in the presentation of visual images that change positions, appearing in the center, left and right side of a monitor. Results: The highest HbO concentration was found in FC in right hemisphere only in 12 months old group. The lowest percentage of correct answers in VAST was in the 4 months group. Conclusion: The VOAT involves the FC, which shows focalized activity only at 12 months in preterm infants. Contrasting with infants born in term this activity is present at 4 months. (D)

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87. CORTICAL NETWORK FOR INTERNAL REPRESENTATION OF TIME

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Experiments with humans and non-human primates have related a motor cortico-thalamic-basal ganglia circuit with the production of rhythmic movements. This experiments use a synchronization-continuation task (SCT) that needs a rhythmic finger-tapping movement to evaluate the performance of the subjects. A key remaining question is if this network is still involved when the rhythmic stimulus is internally represented (i.e. without movement). To evaluate this, we designed a variation of the SCT that does not need any movements to be performed. Our SCT version consisted in presenting a visual stimulus that changed position at regular intervals (synchronization phase). After three presentations, the stimulus stopped appearing and the subjects had to keep imagining the changes in position as a function of time (continuation phase). We measured the BOLD signal of 10 subjects while they performed the task. The results show that our SCT version recruits the thalamus, basal ganglia, parietal and premotor cortices. Furthermore, we compared the activity between the synchronization and continuation phases to see if they are functionally different processes. This analysis revealed that the thalamus, visual and parietal cortices are more active during the synchronization phase, but the premotor cortex is more active during the continuation phase. Our results support the hypothesis that for time perception a cortico-thalamic-basal ganglia circuit is needed and that this network has to be flexible depending on the demands of the task.

We would like to thank the technical assistance of Edgar Bolaños. (D)

88. ANALYSIS OF THE MUTATIONAL LOAD IN THE HUMAN MITOCHONDRIAL GENOME

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Mitochondria are subcellular organelles specialized in energy production by oxidative phosphorylation. Some of the most important proteins for this process are encoded in the mitochondrial genome. Mutations in this genome are related to neuromuscular diseases in human and their diagnosis is difficult due to the heterogeneous nature of the pathologies and to limitations in current molecular methods. The purpose of this work is to analyze the mutational load in healthy individuals using Next Generation Sequence technology as a first step to develop diagnostics tools for the detection and quantitation of mitochondrial mutations. To this end, we isolated mitochondrial DNA from dental pulp cells and peripheral blood cells for massive
re-sequencing. Additionally, we cloned the mitochondrial DNA in plasmids as control for sequencing errors. These samples will be sequenced with the Illumina HiSeq 2500 platform followed by bioinformatic analysis of mutations. The results will be validated by cloning and Sanger sequencing. The analysis of deletions in mitochondrial DNA will reveal their abundance and diversity in healthy individuals and will serve as a baseline for future studies aimed to detect and quantitate mutations associated to neuromuscular disorders. (M)

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89. PROLACTIN PROMOTES INSULIN SENSITIVITY AND ADIPOSE TISSUE FITNESS DURING OBESITY

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Obesity is characterized by excessive accumulation of body fat resulting in dysfunctional adipose tissue and insulin resistance. Recently, there is evidence that low levels of the hormone prolactin (PRL) correlate with prevalence of obesity, type 2 diabetes and metabolic syndrome in humans and rodents; however it is not known whether low levels of PRL contribute to the development of these metabolic diseases. In the present study we evaluated whether PRL promotes insulin sensitivity and adipose tissue fitness during obesity. We used 3 models: Male Wistar rats, fed a control (CD) or a high fat diet (HFD) treated or not with PRL, 2) C57BL/6 mice lacking PRL receptors (Prlr-/-) fed with CD or HFD, and 3) evaluation of possible correlations between serum PRL levels and expression of markers of adipose tissue function in humans. Prolactin improves insulin sensitivity. While HFD-induced obese rats showed reduced serum PRL levels, PRL treatment improved their insulin sensitivity. Conversely, Prlr-/- mice showed aggravated insulin resistance and glucose intolerance induced by a HFD, compared to their wild type pairs. In agreement, patients with insulin resistance had low serum PRL levels compared to insulin sensitive subjects. PRL also preserves the functionality of the adipose tissue. In obese rats, PRL treatment prevented adipocyte hypertrophy and increased their hyperplasia, while Prlr-/- mice fed a HFD showed higher adipocyte hypertrophy. The possible mechanisms by which PRL exerted these effects in rats involve increasing Pparg and Xbp1s expression in visceral adipose tissue and elevating serum adiponectin levels, factors known to promote adipose tissue fitness and insulin sensitivity. Also, in humans, serum PRL levels correlated positively with the expression of markers of adipose tissue functionality such as PPARG and GLUT4. In conclusion, PRL is a novel promoter of adipose tissue functionality and insulin sensitivity and increased PRL levels have therapeutic potential against metabolic alterations induced by obesity.

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Aquaporins belong to one of the largest groups of the major intrinsic protein (MIP). It is well known that aquaporins play a role in the osmotic regulation; because of this, channels allow the movement of water through the membrane, so the maintenance of water homeostasis is achieved by aquaporins. These channels are found in the membrane of a great variety of organisms, such as humans and yeast. Although aquaporins are understood just like exclusive water channels, there are two groups of aquaporins, the first group is called orthodox aquaporins because only water can pass, the other group is called aquaglyceroporins which also allows the flow of small solutes as glycerol. In eukaryotes, different aquaporins are commonly found in the membrane. It is known that in Saccharomyces cerevisiae, there exist two aquaporins, which are AQY1 and AQY2, and these aquaporins are found in the membrane. We have the hypothesis that one of these aquaporins plays the role of water efflux and the other plays the role of water inflow. Thus, we have the aim to show what is the aquaporin that plays the role of water efflux and water inflow. To find out we use three strains of S. cerevisiae, the first strain is the wild type, which has the two aquaporins, the second strain is ∆AQY1, which has only the AQY2 aquaporin, and the third strain is ∆AQY2, which has the AQY1 aquaporin. An osmotic shock was applied to 250 µg of yeast cells to measure the wet weight before and after every osmotic shock. The results show so far, that ∆AQY1 loses a little bit of water after the osmotic shock; the ∆AQY2 loses more water than ∆AQY1. These results provide us information about the role of each aquaporin, because it's shown in our experiments that AQY1 has a major water efflux activity than AQY2.

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tapping variability change). This behavioral scores were correlated, across subjects, with the difference in Pre-Post BOLD signal in the aforementioned areas. TC correlated positively with R-CrusI, R-Hippocampus, R-Brainstem, L-BA2 and L-IPL. LS correlated negatively with L-V3. In conclusion, we found a time learning transfer of the IDT on the temporal performance of the continuation phase of the SCT. This generalization was associated with an increase in BOLD signal in visual areas, the intraparietal sulcus, the cortical-basal ganglia circuit and the cerebellum during the internally produced tapping condition of the SCT. (D)

102. IDENTIFICATION OF GENES AND GENETIC NETWORKS ASSOCIATED WITH ADIPOGENESIS IN VISCERAL AND SUBCUTANEOUS ADIPOSE TISSUE

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Obesity is the accumulation of excessive fat stores, mainly in the adipose tissue (AT), and is associated with the development of many diseases, particularly when expansion occurs in visceral adipose tissue (VAT), but not in the subcutaneous depot (SAT). AT expansion is the result of hyperplasia or increase in adipocyte precursor cell number and their differentiation into mature adipocytes (adiogenesis), and of hypertrophy or enlargement of existing mature adipocytes by triglyceride accumulation. Most of the studies on the molecular events of adiogenesis have been carried out using in vitro models, whereas the molecular networks governing in vivo adiogenesis are still poorly understood. In this work, we have asked whether the transcriptional cascade of adiogenesis differs between VAT and SAT. Using in silico analysis, we combined previously available information from two independent gene microarrays containing gene expression analysis from 1) preadipocytes and 2) adipocytes, from VAT and SAT, to identify genes and gene networks that differ between VAT and SAT in this in vivo adiogenesis model. Data analysis was performed using ambient R and gene network analysis using GOrilla (Gene Ontology enRICHment analySis and visuAlization tool) platform. The expression matrix determined a total of 5964 genes that were included in the analysis in both VAT and SAT. 32.4% vs 28.5% of the genes were upregulated and 50.2% vs. 45.3% downregulated in mature adipocytes compared to preadipocytes in VAT vs. SAT, respectively. Different gene expression patterns were observed between VAT and SAT when comparing the preadipocyte to the adipocyte stage. Gene expression networks from VAT and SAT were found to be involved in different biological processes: downregulated genes showed differences in pathways related to hormonal regulation, signaling pathways and structural organization, among others. Whereas upregulated genes were involved in pathways related to several biochemical routes and metabolism, with differences between VAT and SAT. In conclusion, intrinsic differences exist in the transcriptional mechanisms that occur in adiogenesis between VAT and SAT, that might be involved in the different metabolic phenotypes of these fat tissues. (M)

92. GLUCOCORTICOIDS INTERACT WITH ENDOCANNABINOIDS IN THE DORSAL STRIATUM DURING MEMORY CONSOLIDATION OF AN INHIBITORY AVOIDANCE TASK

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Glucocorticoids released during an emotionally arousing experience enhance memory consolidation. The endocannabinoid system of the hippocampus and the amygdala interacts with glucocorticoids in modulating memory consolidation. Previous findings from our group showed that corticosterone administration into the dorsal striatum enhances memory of inhibitory avoidance training. Moreover, the cannabinoid receptor type 1 (CB1R) is also highly expressed within the striatum. Therefore, our objective was to assess whether glucocorticoids interact with the endocannabinoid system of the dorsal striatum in modulating memory consolidation of inhibitory avoidance training. Male adult Wistar rats with bilateral cannulae in the anterodorsal striatum, were trained on the inhibitory avoidance task and had a retention test 48 h later. We found that the CB1R antagonist AM251 (0.28 or 0.56 ng/µl) administered into the striatum immediately after the training experience, dose-dependently impaired memory retention. Contrarily, the CB1R agonist WIN55-212 (50 or 100 ng/µl) administered posttraining, dose-dependently enhanced memory retention; this latter effect was blocked by the pretraining administration of the corticosterone synthesis inhibitor metyrapone (50 mg/kg, i.p.). Corticosterone administered either systemically (3 mg/kg, i.p.) or intra-striatally (10 ng/0.5 µl) posttraining enhanced memory retention; however, the corticosterone effect was blocked by a previous administration of an otherwise non-amnesic dose of AM251 (0.28 ng/0.5 µl) into the striatum. Our findings provide evidence for the broad interaction of endocannabinoids with glucocorticoids that modulate memory, now assessed in the striatum. These findings further indicate that, like in the amygdala and hippocampus, the endocannabinoid system acts downstream of glucocorticoids to enhance memory consolidation of an emotional aversive training experience.

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93. PARTICIPATION OF THE BLOOD-BRAIN BARRIER IN THE HIPPOCAMPAL NEUROPROTECTION OF THE LACTATING RAT

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Diminish sensitivity of the hippocampus to a kainic acid (KA) lesion is present in the lactating rat. Due to the capacity of KA altering blood-brain barrier (BBB) permeability, here we aim to determine whether lactation condition would protect the BBB permeability after treatment with this excitotoxin. Changes in the concentration of the tight junctions of the BBB, induced by lactation or a KA-lesion, are also investigated and compared to those in virgin rats. Adult virgin or lactating (8-10 pups, postpartum day 15) female Wistar rats (250–300 g), were lesioned with an ip (10 mg/kg bw) or icv (100 ng/1 µL) injection of KA and were perfused 24 h after. Control groups received a similar volume of vehicle. BBB permeability was assessed by a 500 µL-intravenous injection of fluorescent tracer FITC-conjugated dextran (40 kDa, 100 mg/mL, N=3) or of 4% Evan’s blue Dye (EVD) (N=5), given at 24 hrs after administration of KA. Leakage of dextran was evaluated under the microscope by fluorescent intensity, while extravased EVD was determined by spectrophotometry at 680 nm. The expression of proteins of tight junctions, claudin 5 and occludin was assessed by immunohistochemistry in fixed tissue and by Western blot in the half of vertical dissected brain samples. The analysis of BBB permeability to EVD showed increased permeability in virgin versus lactating rats in basal conditions, and increased further in KA-lesioned virgin rats but not in KA-lesioned lactating rats. Also, the permeability analysis of FITC-dextran showed significant changes in the hippocampus subfields CA3 and CA1 of the hippocampus of virgin rats that received a KA injection. No changes were detected in
lactating rats. The analysis by Western blot of the content of claudin-5 and occludin, showed a decrease of claudin-5 in lactating rats either basal or lesioned conditions, and no changes were detected in the virgin rats. Content of occludin did not change in any of the experimental conditions. These results showed that decreased permeability caused by lactation is not affected by the neurotoxin, thereby suggesting a protection in the lactating rats. (D)

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94. GABA_3 EXPRESSION IN THE AUTISTIC CEREBELLUM

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Autism is a psychiatric disorder where stereotyped and repetitive behavior as well as reduced social interaction and communication are observed. The prevalence of this disorder is 1/100 and consistent loss of cerebellar Purkinje cells (PC) is known. The cerebellum maintains connections with cognitive and affective areas of the prefrontal cortex. The loss of PCs is reproduced in the murine model of autism with prenatal exposition to valproic acid (VPA model). The PCs express GABA_1-3 subunits with a major expression of GABA_3. Aim: Test if GABA_3 expression is modified in the VPA model. Methods: 1) VPA injection (500 mg/Kg, IP) to pregnant mice (E12.5) to induce autism. 2) Olfactory test to male offspring at P8 to estimate latency to rich the home bed. 3) Double immunofluorescence in horizontal slices (40 μm) to estimate the PC density. 4) Western blot to determine the calbindin and GABA_3 expression. Results: 1) Latency to rich the home bed was significantly increased in VPA group (170%, p<0.0001), indicating an impairment in the olfactory discrimination, suggesting an “autistic behavior” in the VPA group. 2) Immunofluorescence studies showed that calbindin and GABA_3 intensities were significantly decreased in the Purkinje layer (-20%, p<0.05 and -22%, p<0.05, respectively). 3) The PCs density was significantly reduced in VPA group (-27%, p<0.001). 4) Calbindin and GABA_3 expression was significantly reduced in VPA group (-22% and -26%, respectively, p<0.0001). In conclusion, GABA_3 expression is reduced in the autistic cerebellum due to a decreased density of PCs. This results could be related to the autism etiology in humans.

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95. EXPRESION OF THE CALCIUM SENSOR PROTEIN MCTP THAT IS RELEVANT FOR PROPER LOCOMOTION OF THE NEMATODE Caenorhabditis elegans

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The multiple calcium-2 domain (C2) and transmembrane region proteins (MCTPs) have three conserved C2s, and one or two transmembrane regions. Although their ability to bind calcium has been already probed, their function and cellular distribution are yet unknown. The nematode Caenorhabditis elegans has only one mctp gene, thus it is an approachable experimental model to test the function of this family of proteins. The aim of this work was to determine the expression pattern of the C. elegans mctp gene that encodes for this putative calcium sensor protein. The following studies were performed: 1) bioinformatic analysis of the promoter; 2)
96. PERINATAL UNDERNUTRITION ALTERS SOCIAL TRANSMISSION OF FOOD PREFERENCE IN ADULT WISTAR RATS. PRELIMINARY RESULTS

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Perinatal undernutrition (PU) causes morphological and metabolic alterations in brain structures that regulate cognitive processes as well as social interaction. The social transmission of food preference (STFP) is a useful test of associative memory essential for social development. This study evaluates the effects of undernutrition on the STFP in adult Wistar male rats. Undernutrition in pregnant mothers was made by giving different percentages of a balanced diet of Purina chow. After birth, the underfed group (UG) was treated by rotating 12 h two dams with the galactophorous ducts tied. Weaning was at postnatal day 25, followed by an ad libitum diet until day 90 of age. The control group (CG) remained on a balanced diet until the day 90 of age. During the phase I of the test the demonstrator rat (DEM) ate a cue flavor 1 h; in the phase II a DEM and an observer rat (OBS) interacted in a cage during 30 min, and recorded to evaluated seven behavioral parameters. In the phase III an OBS ingested food (the cue and a novel flavor) for 12 h and was weighed. The results showed that in phase II the UG had higher frequency of head contacts (HCF) and sniffing the muzzle (SM) than CG (p <0.05). In the phase III the UG rats ingested different amount of cue flavor at 1, 4, and 12 h (p <0.05). In this paradigm undernourished rats showed more HCF and SM to recognize the cue stimulus, being that these are the essential parameters associated with the olfactory stimulus for social interaction. The findings suggest that PU interferes with the functioning of brain structures such as the olfactory bulb and other brain areas underlying cognitive functions for associative memory.
Partly supported by DGAPA, UNAM IN200413. (L)

97. STRUCTURAL AND FUNCTIONAL CHARACTERIZATION OF GLUTAMATE DEHYDROGENASE UNDER THE RESTRICTED FEEDING OSCILLATOR

Departamento de Neurobiología Celular y Molecular. Instituto de Neurobiología, Universidad Nacional Autónoma de México.

Background. Glutamate dehydrogenase (GDH) is an important enzyme that catalyzes the reversible oxidative deamination of glutamate into alpha ketoglutarate and ammonia, participates in protein metabolism and detoxification of ammonium. It is known that feeding behavior in many species exhibits a clear daily rhythm
and restricted feeding (RF) schedules becomes a strong entraining stimulus. Regarding to hepatic GDH, little is known about the existence of biological rhythms and food influence in its expression or activity.

Objective. The aim of this study was to evaluate the daily pattern of heptic GDH on rats under a protocol of daytime RF schedule.

Methods. Adult male Wistar rats were maintained in a 12:12 h light-dark cycle in a controlled temperature environment and were distributed randomly in the following groups: RF: food access for 2 h (from 12:00 to 14:00 h) every day, during 3 weeks, AL: ad libitum feeding, Fa: fasting during 22 h, Re: fasting during 22 h with subsequent refed 2 h later for only one day. Groups of 4 rats were sacrificed at 3 h intervals, during a 24-h period. Daily variations of liver GDH were studied in terms of mRNA expression by RT-qPCR, protein expression by Western-blot, activity by spectrophotometric analysis and location in hepatic acinus by immunohistochemical analysis.

Results. RF promoted higher levels of mitochondrial GDH protein and activity, as well as a loss of 24-h rhythmicity, in comparison to AL conditions. RF enhanced GDH promoted a shift phase in mRNA rhythm and serum activity, but without effect in its expression in hepatocytes surrounding central and portal veins.

Conclusions. These results demonstrate that the GDH is under a temporal regulation with a great capacity to adapt to different feeding conditions. In addition, these results be part of the adaptations in nitrogen metabolism and energy produced in the liver during RF.

This study was supported by grant IN202515 from PAPIIT, UNAM, México

Category: M

98. CHANGES IN PRO-OXIDANT REACTIONS IN A MODEL OF HIPOFUNCTIONAL LIVER PRODUCED BY PORTACAVAL ANASTOMOSIS IN RAT

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Antecedents: Portacaval anastomosis (PCA) is an experimental protocol to generate a dysfunctional liver condition. By means of a surgical procedure, the portal circulation is directly connected to the cava vain, resulting in the arrival of all nutrients to the systemic blood. As a consequence, PCA is characterized for a reduction in the hepatic functions as well as modifications in histological properties of the liver. High proportion of pro-oxidant reactions take place in the hepatic tissue in response to the elevated metabolic rate. However, it is not known how the pro-oxidant reactions are affected in the liver of organisms after several weeks of surgical PCA.

Objective: The present study was aimed to assess oxidative status in homogenate and subcellular fractions of liver and serum of rats beetwen 8–13 weeks with PCA.

Methods: Lipid peroxidation from homogenate and subcellular fractions of liver and serum were quantified by TBARS. Lipid peroxidation in vivo was also determined by means of conjugated dienes detection in homogenate and subcellular fractions of liver.

Results: Preliminar results showed 24% less weight gain in PCA group in comparison with sham group. Also, PCA group showed a smaller liver with 38% reduction in the ratio liver weight/body weight compared
with sham group. As to pro-oxidant reactions PCA did not modify the basal production of TBARS in serum. When the assay was supplemented with Fe2+, TBARS levels showed significant differences with a 40% minor of pro-oxidant reactions in the PCA group compared with the sham group. However, the Fe2+/basal ratio did not show any change. In homogenate, it was observed an evident reduction in the levels of pro-oxidant reactions in the basal production of TBARS. The diminution in lipid peroxidation was also present when the assay was supplemented with Fe2+. PCA produced a similar effect in the liver cytosolic fraction. Finally, the level of conjugated dienes did not show differences between both groups in homogenate and cytosolic fraction of liver.

Conclusion: Within the metabolic modifications, we found a significant reduction in the pro-oxidant potential of the hepatic tissue (TBARs) but without effect in the in vivo lipoperoxidative activity (conjugated dienes).

Acknowledgments: The authors thank Raúl Aguilera, Fernando López and Christian Molina for her helpful assistance. (L)

99. CELLULAR COMMUNICATION MEDIATED BY NUCLEOTIDES IN HEPATIC FIBROSIS

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Introduction: Hepatic fibrosis is characterized by the excessive accumulation of extracellular matrix components, including collagen, as result of a chronic liver disease. When damage occurs, the liver cells release pro-inflammatory signaling molecules, resulting in a continuous state of inflammation and aberrant scarring that drives the liver into a fibrotic state. One of the signaling pathways involved in the regulation of inflammatory and cellular responses to stress is the activation of purinergic receptors by adenosine triphosphate (ATP) and its metabolites. However, the role of purinergic communication on fibrotic processes is not well understood. We have hypothesized that ATP could act a promoting-damage mediator in the onset of this pathological state.

Methods: We administered CCl4 during 4 weeks as model of hepatic fibrosis in C57BL6 mice of 6 weeks of age. After demonstrating the establishment of fibrosis by Masson’s trichrome stain, we proceeded to identify purinergic receptors by PCR. To observe receptor activation slices of hepatic tissue were stimulated with ATP (1 µM) at different times (1, 5, 30 and 60 min) and analyzed to detect the phosphorylation of p42/p44 MAPK by Western Blot. In an effort to extend the aim of this experiment, we began to standardize the protocol on primary cultures of hepatocytes to study purinergic responses.

Results: We observed a clear tendency for a differential expression of the mRNAs of the receptors in the CCl4-induced fibrotic state, since P2YR1 seems to increase in animals treated with the halogen and P2YR12 appears to be diminished in this group. When stimulated with ATP, hepatic slices presented an increase in the phosphorylation of p42/p44 MAPK at 1 and 5 min of exposure and gradually returns to basal levels. In isolated hepatocytes ATP produced a nearly 4-fold increase in the phosphorylation of p42/p44 MAPK compared with its control; however the comparison between fibrotic and healthy hepatocytes remains to be done. These results suggest that there is a differential effect of the purinergic receptors in hepatic fibrosis.

Funded by PAPIIT-UNAM, number IN205114. (M)
100. AMYLOID BETA PEPTIDE MODULATES STATUS EPILEPTICUS IN RATS

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Alzheimer’s Disease (AD) is a neurodegenerative pathology and the most common cause of dementia. A key histopathological feature of AD is the progressive accumulation of senile plaques mainly composed of amyloid beta peptide (Aβ). AD patients and transgenic animal models of AD exhibit greater incidence and prevalence of epileptic seizures. However, the direct influence of Aβ on the induction of seizures is still unknown. Thus, we aimed to evaluate the effect of Aβ on the induction of convulsive seizures and status epilepticus (SE). Adult male rats were intracisternally injected with Aβ or vehicle and stainless steel bipolar electrodes were stereotaxically implanted into the right ventral hippocampus for electrical recordings. Three weeks after the Aβ injection, seizure activity and SE were induced by the administration of lithium/pilocarpine. SE was finished two hours after the SE onset by diazepam administration. Brain slices were obtained from these animals and the activity of CA1 pyramidal layer was recorded. The animals injected with Aβ showed a reduced latency to SE manifestation. The magnitude of the hippocampal activity during the SE, evaluated through power spectrum analysis, was higher in animals injected with Aβ, which correlated with increased spontaneous hippocampal activity recorded in brain slices. These results demonstrate that Aβ sensitizes neuronal circuits to develop hyperexcitability which could be the basis for the increased occurrence of spontaneous recurrent seizures in AD. (M)

101. ADJUVANT EFFECTS OF MOLECULAR IODINE WITH DOXORUBICIN CHEMOTHERAPY IN CANINE MAMMARY CANCER: CLINICAL SIGNS, CHEMORESISTANCE AND INVASION

Zambrano E.X.; Landaverde Q.B.; Dueñas B.A.; De Paz C.M.A.; Hernández A.G.; Solorio P.B.; Trejo M.M.; Pérez G.L.; Aceves C.
1Departamento de Neurobiología Celular y Molecular, Instituto de Neurobiología, Universidad Nacional Autónoma de México; 2Facultad de Estudios Superiores Cuautitlán, Universidad Nacional Autónoma de México and 3Facultad de Ciencias Naturales, Universidad Autónoma de Querétaro, México.

Canine mammary cancer is an important veterinary health interest and also represents an excellent model of spontaneous carcinogenesis due to its similarity with its human counterpart. Molecular iodine (I2) exhibit apoptotic and differentiation effects in several cancer cells and co-administration with doxorubicin (DOX) avoid chemoresistance and cardiac toxicity in preclinical and clinical studies. In this study, the effect of daily I2 (0.05%) supplement was analyzed with the standard or slow schedule DOX 30 mg/m2 in 27 canine patients with cancer mammary gland. Eligibility criteria included signed informed consent, normal hepatic, renal and cardiovascular function. The standard scheme includes four cycles of DOX every 21 days administrated intravenously during 20 minutes, while in the modified schedule; DOX has applied four cycles every 15 days during 60 minutes of infusion. The patients exhibited diverse tumor type, clinical stage and degree of malignancy. Results showed that the modified versus standard scheme prevents deterioration of the general health condition (70 vs. 80% Karnofsky scale, respectively) and I2 supplementation further attenuated clinical signs of DOX toxicity such as severe vomiting and hemorrhagic diarrhea, hyporexia, lethargy and myelosuppression. Although none of the protocols applied accomplished with the standard therapeutic requirement (at least 50% decrease in tumor size), patients treated with I2 + modified scheme showed a significant reduction in the tumor epithelial fraction, as well as decreased expression of markers of chemoresistance (MDR1 and Survivin) and invasion (uPA). Moreover, this combination produced synergetic induction of apoptosis (Bax/Bcl2 index) and enhanced expression of peroxisome proliferator-
activated receptors type gamma (PPARγ). The endocrine evaluation shows that any combinations affect thyroid function (serum T3) or estrogen receptor alpha expression and cellular localization. In conclusion, we propose an I2/DOX low infusion schedule to treat canine mammary cancer to decrease side effects and to improve therapeutic outcome. Further investigations are actually in consideration to analyze if I2 supplement allows diminish in DOX dose without loss therapeutic efficacy.

The authors appreciate the technical support of Alexander Bontempo, Evangelina Delgado and Maria Juana Cardenas Luna. Investigation supported by PAPIIT-UNAM IN200813 and 201516; CONACYT 245255. (D)
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