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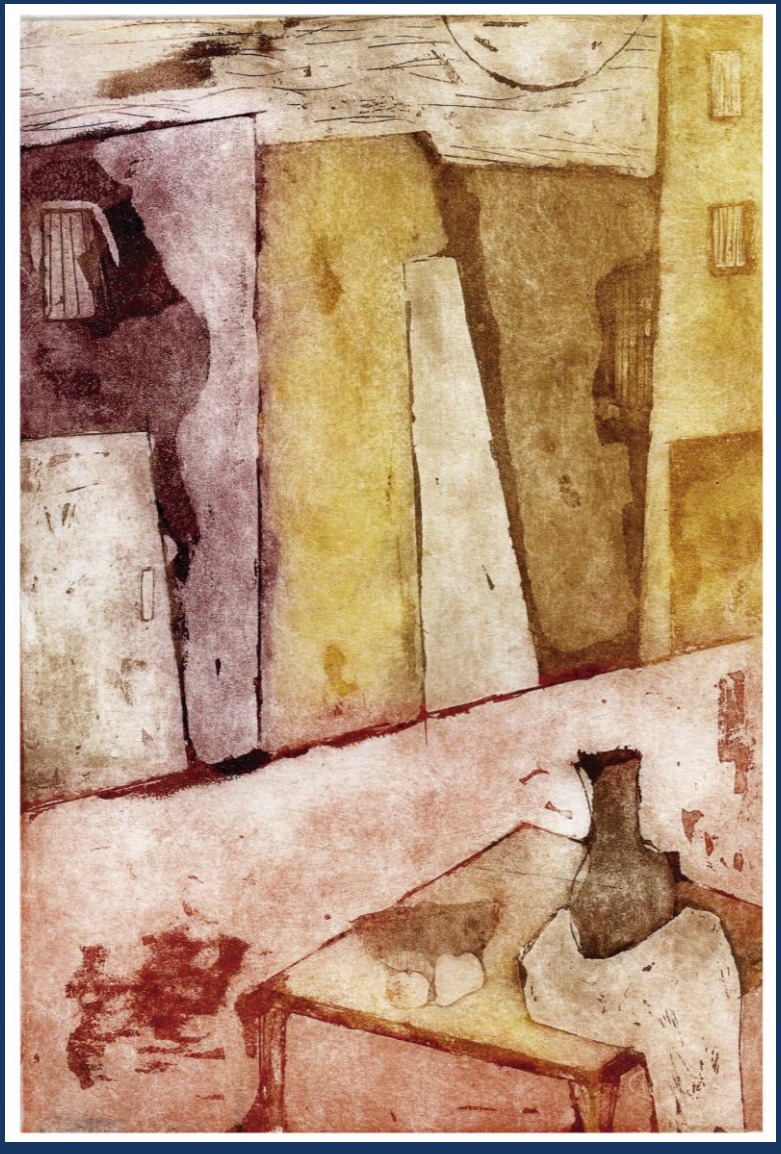

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La Tapa (Ver pág. 4)
Atardecer en la tarde
Antonella Ricagni

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LXIV Reunión Anual de la
Sociedad Argentina de Investigación Clínica (SAIC)

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XXI Reunión Anual de la
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XXXI Reunión Anual de la
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IX Reunión Anual de la
Asociación Argentina de Nanomedicinas
(NANOMED-ar)

VI Reunión Científica Regional de la Asociación Argentina de Ciencia y Tecnología de Animales de Laboratorio (AACyTAL)

con la participación de
The Histochemical Society

13 - 16 de noviembre de 2019
Hotel 13 de Julio - Mar del Plata

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estrogen receptor: ERalpha or GPR30. cPKC activation precedes that of ERalpha. cPKC probably uses intermediaries to phosphorylate ERalpha. Several kinases can be phosphorylated by cPKC and are able to phosphorylate the ERalpha, among them we find GSK3ß. The aim of this study was to evaluate the role of GSK3ß in the E17G-induced alteration of Mrp2 activity. IRHC were treated with GSK3ß inhibitors Li (3 mM) or BIO (1 µM) and then exposed to E17G (100 µM). To investigate in which pathway GSK3ß participates, IRHC were exposed to BIO and inhibitors of ERalpha (ICI182,780, ICI, 1 µM), cPKC (Gö6976, Gö, 1 µM) or PI3K (Wortmannin, W, 100 nM) before exposure to E17G. All preparations were incubated with CMFDA (intracellularly converted in gluthation-methylfluorescein [GMF], substrate of Mrp2). IHRC accumulating GMF in their canalicular vacuoles (cVA) were counted and compared to control IHRC. Results (% Control): GSK3ß inhibition (Li+E17G: 71 ± 7b; BIO+E17G: 70 ± 5b) partially prevented the effect of E17G (48 ± 4a) on cVA of GMF. The preventive effects of W (W+E17G: 75 ± 5b) and BIO on the decrease in cVA induced by E17G were additive (BIO+W+E17G: 91 ± 1a,c). Contrarily, the preventive effects of ICI (ICI+E17G: 69 ± 3b) or Gö (Gö+E17G: 77 ± 3b) did not modified BIO protective effects (BIO+ICI+E17G: 72 ± 2b) and (BIO+Gö+E17G: 77 ± 10b). a: significantly different from Control; b: significantly different from E17G and Control; c: significantly different from E17G+BIO and E17G+W. BIO, Li, W, Gö, and ICI did not affect % cVA. ($p<0.05$, n= 3). GSK3ß inhibition protects against E17G-induced impairment of Mrp2 transport, indicating a role of the kinase in estrogen cholestasis. Co-inhibition studies suggest that GSK3ß participates in the same pathway of ERalpha and cPKC and in different pathway of PI3K (downstream of GPR30).

0875 - ATRIAL NATRIURETIC PEPTIDE (ANP) ENHACES ANTIOXIDANT CAPACITY IN EXPERIMENTAL ACUTE PANCREATITIS

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Abstract/Resumen: We previously reported ANP attenuates the severity of acute pancreatitis by reducing trypsinogen activation and the inflammatory response. Recent studies support that endoplasmic reticulum (ER) stress and oxidative stress (OS) precede these events. Indeed, we showed that ANP attenuates ER stress and stimulates ER-dependent apoptosis. ER stress is intimately related to OS in the pathophysiology of numerous diseases. Given that the exocrine pancreas is rather susceptible to OS due to the extremely weak expression of antioxidant enzymes, in the present we sought to establish whether ANP affected OS in experimental AP by studding the main antioxidant (enzymatic and non-enzymatic) defense. AP was induced in Sprague-Dawley strain rats (200-220 g) by four repetitive cerulein injections (40 µg/Kg). Thirty minutes before the first cerulein injection animals were infused with either saline (control) or ANP (1 µg/Kg/h) for 60 min. Following euthanasia (60 min after the last cerulein injection) pancreatic samples were harvested for further assays (CICUAL-FFYB #4107/18). ANOVA followed by a Student's t test modified by Bonferroni was used for statistical analysis. Results are expressed as the means±S.E.M. and p values of 0.05 or less were considered statistically significant. AP induces OS as previously reported. ANP stimulated Nrf-2 nuclear translocation (assessed by immunohistochemistry) which is a transcription factor that induces the expression of antioxidant enzymes ($p<0.001$). ANP also enhanced the activity of superoxide dismutase (SOD) ($p<0.05$), catalase ($p<0.01$) and glutathione transferase. Furthermore it also restored reduced glutathione and total glutathione levels (assessed by HPLC- tandem mass spectrometry) to control values ($p<0.05$). Present findings show that ANP enhances the antioxidant defense capacity of the exocrine pancreas in AP, further supporting its beneficial role in the disease.

Neurociencias / Neurosciences III

Chairs: Claudia Bregonzio | Analía Reinés

0324 - EFFECT OF LITHIUM IN PYRAMIDAL NEURONS OF CORNUS AMMONIS

Georgina Paula OSSANI (1) | Ana Margarita UCEDA(2) | Osvaldo Juan PONZO(3) | Néstor Rubén LAGO(4) | Miguel RIUDAVETS(5) | Diego Javier MARTINO(6)

UBA, FAC MED, DEPTO PATOLOGÍA, CPEA; HOSPITAL ALEMÁN; CONICET (1); UBA, FAC MED, DEPTO PATOLOGÍA, CPEA; HOSPITAL ALEMÁN (2); UBA, FACULTAD DE MEDICINA, DEPARTAMENTO DE FISIOLOGÍA, LABORATORIO DE ENDOCRINOLOGÍA (3); UBA, FACULTAD DE MEDICINA, DEPTO DE PATOLOGÍA, CENTRO DE PATOLOGÍA EXPERIMENTAL Y APLICADA (4); FLENI, DEPTO NEUROPATOLOGÍA; CORTE SUPREMA DE JUSTICIA, MORGUE JUDICIAL, LAB HISTOPATOLOGÍA (5); UNIVERSIDAD FAVALORO, FUNDACIÓN INECO, INCYT; CONICET (6)

Abstract/Resumen: Lithium (Li) is a first-line drug for long-term prophylactic treatment of bipolar disorder (BD). However, mechanisms by which lithium exerts its mood-stabilizing effects are not very clear. A decrease in the overall volume of the hippocampus (H) by imaging studies has been described in patients with BD, it has also been reported that treatment with Li would reverse this effect, highlighting its neuroprotective effect. The aim of this work was to evaluate the effect of Li on pyramidal neurons within Cornu Ammonis (CA) subregions of the H. Wistar male rats (n= 16) were randomized into two groups: control group (CG) fed ad libitum powered standard diet and experimental group (EG) fed ad libitum the same diet supplemented with 60 mmol of lithium/kg diet for 1 month. Lithium serum levels were measured and reached therapeutic values in EG (0.57 ± 0.18 mmol/L). The brains were removed for histopathological analysis, fixed, and cut coronally. From each brain we selected a section (Bregma -2.8 mm) and stained with cresyl violet. First, we took serial pictures of the entire CA region with a 60x objective starting at the midline (CA1-2-3). Serial photos were divided into 4 groups, and the first 5 photos from each of them were selected for the analysis. Then, using the Image J Software we measured the area of the cell body and nucleus of CA pyramidal neurons on each selected picture. The criteria for selecting neurons to be measured included a well-defined nucleus and nucleolus. All assessments were performed blinded to Li treatment. We observed that the mean size (µm²) of the neuronal soma and nucleus of pyramidal neurons in the third group were significantly larger: CG= 140 ± 24 vs. EG= 174 ± 36, t= -2.15, p= 0.049 for cytoplasm; and CG= 75 ± 12 vs. EG= 92 ± 16; t= -2.28, p= 0.038 for nuclear size. This sub-region could correspond to CA2 subfield. Our results support the theory that lithium acts at the H level producing an increase of the cell and nuclear area of the pyramidal neurons in a specific sub-region of the CA.

0337 - EVIDENCE OF CANNABINOID MODULATION IN NUCLEAR SIGNALING

Virginia Lucía GAVEGLIO | Norma María GIUSTO | Susana Juana PASQUARE

INIBIBB-CONICET, DEPTO. BIOLOGÍA, BIOQUÍMICA Y FARMACIA-UNS

Abstract/Resumen: The endocannabinoid system (ECS) is a signaling mechanism involved in many pathophysiological processes, especially in the nervous system. Former studies from our lab demonstrated the presence of the different components of the ECS in nuclei from rat cerebellum and cerebral cortex (CC). We detected diacylglycerol lipase and monoacylglycerol lipase activities which are involved in maintaining the levels of the endocannabinoid 2-arachidonoyl-glycerol. In addition, we demonstrated a nuclear CB1 protein expression by Western Blot and immunocytochemistry. CB1 is a GPCR receptor that triggers different signaling cascades, modulating intracellular Ca^{2+} levels, ERK1/2 phosphorylation, and other second messengers at the plasma membrane. Nevertheless, we also observed an increase in ERK phosphorylation in isolated nuclei from rat cerebral cortex (CCN) incubated with a CB1 synthetic agonist (WIN 55-212-2). Phosphorylated ERK could be involved in activating MSK1/2, a nuclear kinase that phosphorylates histone 3 (H3). The aim of this work was therefore to study how a cannabinoid agonist modulates ERK1/2 and H3 phosphorylation in CCN. To this end, CC from Wistar rats were dissected and homogenized, and highly purified nuclei (CCN) were isolated on a sucrose-density ultracentrifugation. CCN were subsequently incubated at 37 °C with WIN and ERK1/2 and H3 signaling cascades were studied by Western Blot. Interestingly, it was observed that ERK1/2 and H3 phosphorylation increased in nuclei treated with WIN 5 µM for 30 min with respect to controls ($p<0.05$). As expected, this was reversed by pre-incubating for 10 min with a MEK inhibitor (U0126, 10 µM), however, no changes were observed when a CB1 antagonist (SR141716, 1 µM) was used ($p<0.05$). Taken together, these results demonstrate that cannabinoids at nuclear level could modulate H3 phosphorylation by ERK1/2 signaling. This indicates a potential role of these lipids in chromatin regulation and gene expression in cerebral cortex.

0339 - SILDENAFIL EFFECTS ON MEMORY AND FUNCTIONAL AND STRUCTURAL PLASTICITY IN THE HIPPOCAMPUS

Maria Florencia CONSTANTIN | Emilce ARTUR DE LA VILLARMOIS | Gastón CALFA | Mariela Fernanda PÉREZ

FACULTAD DE CIENCIAS QUÍMICAS, UNC, DEPARTAMENTO DE FARMACOLOGÍA, IFEC-CONICET

Abstract/Resumen: Sildenafil (SILD) is a drug widely used in clinical practice for its inhibitory effects on phosphodiesterase type 5 (PDE-5), that generate increases in cGMP levels, indirectly enhancing the signaling pathway activated by nitric oxide (NO/ GC / GMP). SILD crosses the blood brain barrier, and PDE-5 is expressed in the brain. In the hippocampus (HP), NO increases glutamate release, which is essential for long-term potentiation (LTP) maintenance, a phenomenon of synaptic plasticity that underlies the formation of learning and memory. An acute exposure to SILD improves memory consolidation in mice and previous results from our laboratory showed a facilitation in the generation of LTP in HP 2 hours later, however little is known about the persistence of these changes in that structure and its correlation with learning and memory processes. The objective of the work is to evaluate the effect of SILD on the acquisition of HP-dependent memories and characterize the persistence of the functional and anatomical changes produced in this structure 24 hours, 7 and 30 days after the administration of SILD. For this purpose, male Wistar rats were administered with SILD or saline before training in the "step-down", object recognition test and Y maze, and 4 or 24 hours later the memory acquisition was evaluated. Immediately after the test, 7 or 30 days later, the animals were sacrificed for electrophysiological and neuroanatomic experiments of dendritic spine density. Our results showed that animals administered with SILD have a longer latency time in the step-down test compared to the control group, but a lower rate of exploration of the new object in the object recognition test, while preliminary data on Y maze showed no changes arm discrimination rate compared to control group. On the other hand, SILD improves the synaptic plasticity of HP, reducing the threshold to induce LTP at all times measured, and increases the density of total spines in the HP. These results indicate that SILD would have selective effects on different types of memories, and would induce persistent changes in the functional and structural plasticity of the HP, which temporarily coincide with the effects on memory. It is necessary to carry out new studies on the impact of acute or chronic use of SILD on different types of memories to justify the use of this drug in pathologies related to cognitive deficits.

0350 - ADMINISTRATION OF MGLU2/3R AGONIST IN A MODEL OF CHRONIC CEREBRAL HYPOPERFUSION

Juan TURATI (1) | Amanda NUNES SANTIAGO(2) | Lila CARNIGLIA(1) | Julieta SABA(1) | Carla CARUSO(1) | Daniela DURAND(1) | Rúbia Maria WEFFOR DE OLIVEIRA(2) | Mercedes LASAGA(1)

INBIOMED- INSTITUTO DE INVESTIGACIONES BIOMÉDICAS. UBA-CONICET (1); DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS - STATE UNIVERSITY OF MARINGÁ (2)

Abstract/Resumen: Chronic cerebral hypoperfusion (CCH) resembles central changes in aging-related vascular dementias and Alzheimer´s disease (AD). Our group has demonstrated, in vitro, that astroglial subtype 3 metabotropic glutamate receptors (mGlu3R) present protective actions against neurotoxic agents including Aß. However, contradictory results were reported when mGlu3R ligands were administered in vivo. We examined the effect of the mGlu2/3R agonist, LY376298 (LY) 1 mg/kg i.p., in middle aged rats with CCH. The effect of mGlu2/3R agonist in neuron cell death and glial activation of the hippocampus were determined by immunohistochemistry. Moreover, the expression of GRM2, GRM3 (mGlu2/3R genes), GFAP and BDNF was studied by RT-qPCR technique. NeuN expression presents a decreased in CCH animals ($p<0.05$), that was reversed with the LY ($p<0.05$), only when the CA1 hippocampus subregion was studied. GFAP mRNA levels remained unchanged, but GFAP immunolabeling decreased in CCH rats ($p<0.05$) and increased in CCH+LY animals ($p<0.05$). We observed that the expression of GRM3 increased in CCH+LY ($p<0.05$), whereas GRM2 decreased ($p<0.05$) with the surgery compared to control animals. BDNF mRNA levels also increased in CCH animals ($p<0.05$). To conclude, our results suggest that the in vivo administration of an mGlu2/3R agonist increased neuron viability produced by CCH, which could be linked to increased mGlu3 receptor levels.

0439 - EXPERIMENTAL FEBRILE SEIZURES IN YOUNG POSTNATAL RATS: GENDER DIFFERENCES IN LONG-LASTING EFFECT ON THE EPILEPTIC THRESHOLD AND GLIAL RESPONSE.

Alicia Raquel ROSSI | Florencia RODRIGUEZ | Paula SARCHI | Alberto Javier RAMOS

IBCN, FACULTAD DE MEDICINA, UNIVERSIDAD DE BUENOS AIRES

Abstract/Resumen: Febrile seizures occurs in 3–5 % of children between 6 months and 5 years of age. Retrospective studies in adult epilepsy patients show an initial precipitating injury, usually febrile seizures, during childhood. Using an animal model of hyperthermic seizures (HS), we have previously shown that male HS-exposed animals exhibit a significative reduction in the convulsive threshold compared with controls and moderate reactive gliosis with an atypical astrocyte distribution in the pyriform cortex and other brain structures. Here we investigate consequences of early HS exposure in adolescent female rats compared to males. Rat pups (10-11 postnatal days old, PND) were placed in a glass chamber, and their core temperature was raised by a regulated stream of moderately heated air (39-42 °C). Body temperature was measure at baseline, seizure onset and every 2 min during the seizures. Hyperthermic temperatures (39.5–42.5 °C) were maintain for 30 min. The seizures onset was monitored behaviourally, and consisted of an acute sudden