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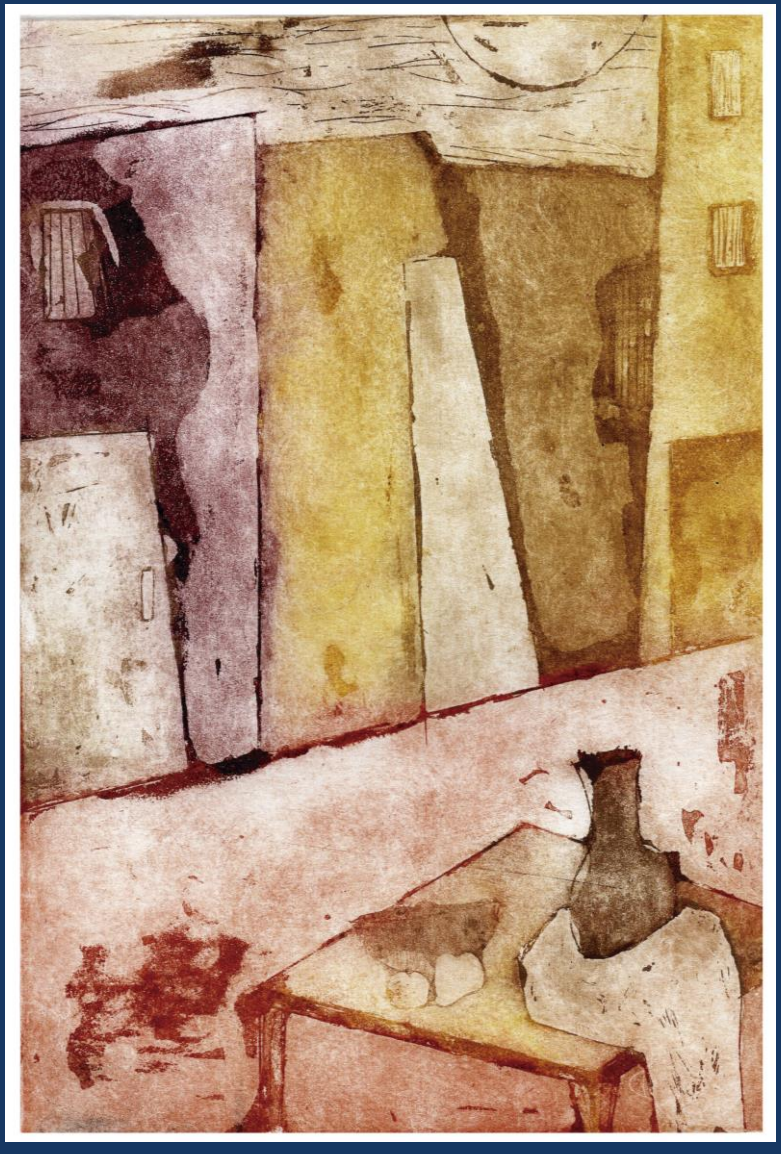

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medicina

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

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

con la participación de
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arrest of hyperthermia-induced tonic freeze postures and occasional oral automatism (biting and chewing) and often body flexion. Rats were then placed on a cool surface, monitored for 5 min before being returned to their mothers. At PND37-39 rats were exposed to repeated pilocarpine subconvulsive doses (10 mg/kg every thirty minutes). Another group of animals (PND35) was deeply anesthetized, fixed and brains processed for immunohistochemistry. We observed that, contrary to the males, the females did not develop SE after four repeated doses of pilocarpine and histological analysis of their brains exhibited lower reactive gliosis compared to males. Our results suggest that HS exposure early in the postnatal brain development produce long-lasting effects in males, which could be related to their future susceptibility to develop epilepsy.
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0441 - NITRIC OXIDE AND APOPTOSIS DUE TO AFTER-EFFECTS OF ACUTE ETHANOL EXPOSURE IN BRAIN CORTEX

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Abstract/Resumen: Alcohol hangover (AH) is defined as a combination of mental and physical symptoms experienced the day after a single episode of heavy drinking, starting when blood alcohol concentration approaches to zero. We previously evidenced bioenergetics alterations and oxidative stress in brain cortex synaptosomes from AH mice. The aim of the present work was to study the after-effects of acute ethanol administration on nitric oxide (NO) metabolism, mitochondrial calcium uptake and induction of apoptosis. Mice received an i.p. injection of ethanol (3.8 g/kg body weight, AH group) or saline (control group) and were sacrificed 6 h afterwards. Synaptosomal NOS activity and total NO levels were determined, as well as the expression of nNOS, iNOS, PSD-95 and the NR2B-subunit of NMDA receptor. Mitochondrial calcium uptake, permeability transition (MPT) and the expression of apoptotic markers were analyzed in mitochondrial fractions. Results showed a 35-37 % decrease in NOS activity and total NO content in AH mice ($p<0.05$), both in the absence and presence of glutamate and calcium. Protein expression of nNOS and PSD-95 were 19 and 15 % decreased, respectively ($p<0.05$) while no changes were observed in iNOS protein expression. Furthermore, a 60 % decrease in NMDA receptor protein expression ($p<0.01$) was found in AH synaptosomal membranes. Impairment of calcium handling and MPT induction were observed in AH mitochondria ($p<0.05$) together with a 21 % increase and 18 % decrease in Bax and Bcl-2 protein expression ($p<0.05$), respectively. Moreover, a 4-fold decrease in cytochrome c mitochondria/cytosol ratio was found due to AH ($p<0.01$). In conclusion, alcohol after-effects include changes in NO synthesis probably related to the observed decrement in NMDAR and PSD-95 protein expression at synaptic membranes. Impairment of mitochondrial capacity to accumulate calcium due to mitochondrial dysfunction and oxidative stress can lead to cell death by the activation of apoptotic signalling pathways.

0452 - MODULATION OF METABOTROPIC AND IONOTROPIC FUNCTIONS OF THE NICOTINIC α7 RECEPTOR BY THE INTRACELLULAR DOMAIN

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Abstract/Resumen: The α7 receptor is a nicotinic receptor present in the nervous system and in non-neuronal cells. It has been demonstrated that α7 not only mediates fast synaptic transmission in neurons, but also regulates inflammatory responses in immune cell, neurite growth and neuronal protection, as well as cancer cell proliferation. The concept of α7 as a dual metabotropic/ionotropic receptor is attracting increasing attention. A key role in this dual nature is played by the receptor intracellular domain (ICD), which contains sites for phosphorylation and intracellular signaling. To explore the relationship between metabotropic and ionotropic activities we expressed α7 in mammalian cells and performed single-channel recordings to determine the channel properties and western blot to determine signaling pathways triggered by α7 activation. Single-channel recordings of human α7 from cells exposed to inhibitors of Src family kinases showed increased open durations and frequency of opening events. The effects were recapitulated using a receptor carrying mutations of the two ICD tyrosine residues, thus indicating that phosphorylation modulates receptor ionotropic activity. Cells exposed to the specific α7 agonist, PNU-282987, showed an increase of ERK1/2 phosphorylation, which was abolished by exposure to a tyrosine kinase inhibitor. PNU-282987 was not able to trigger ERK phosphorylation neither from cells expressing the double mutant receptor lacking tyrosine residues nor from cells co-expressing α7 and the ICD domain. Finally, the exposure of cells co-expressing α7 and ß2 adrenergic receptors to nicotine (α7 agonist) and isoproterenol (ß2 agonist) decreased phosphorylation of CREB, a known effector of the ß2 adrenergic receptor. This study indicates that the phosphorylated state of α7-ICD plays a role in the dual metabotropic/ionotropic receptor responses. It also opens doors for future studies exploring the role of the ICD as a modulator of the crosstalk between α7 and G-protein coupled receptors.

0752 - EXTRACELLULAR PROTEOLYSIS OF THE HORMONE GHRELIN GENERATES A SPECIFIC SUBSET OF GHRELIN-DERIVED PEPTIDES WITH DIFFERENTIAL BIOACTIVITIES

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Abstract/Resumen: The stomach-derived hormone ghrelin is a peptide of 28 residues acylated with an octanoic acid at Ser3. The N-terminal sequence of ghrelin along with the octanoyl group are essential to act on the ghrelin receptor. Here, we tested the hypothesis that ghrelin can be extracellularly cleaved in order to generate ghrelin-derived peptides with differential bioactivities. Initially, we incubated ghrelin with plasma and then performed MALDI-TOF MS analysis. We found that ghrelin is mainly cleaved in the region extended from residue 11 to 16. Then, we incubated ghrelin with liver carcinoma HepG2 cells or with extracellular medium derived from these cells, and also found that ghrelin cleavage occurs in the same "hot cleavage region" of its sequence. Since ghrelin1-14 was derived from ghrelin proteolysis, we then tested the ability of this shorter version of ghrelin to act in the brain and stimulate appetite in mice. We found that ghrelin increases food intake (0.29 vs. 0.07 g in vehicle-injected mice, p-value 0.0008) while ghrelin1-14 failed to do it (0.005 g). Similarly, ghrelin increases the levels of the marker of neuronal activation c-Fos in the ARC (48.0 vs. 12.0 cells/side/section in vehicle-injected mice, p-value 0.0036) while ghrelin1-14 was unable to induce neuronal activation (16.1 cells/side/section). In addition, ghrelin1-14 failed to impair the orexigenic effect of full-length ghrelin. Thus, these data support the existence of a proteolytic extracellular mechanism that generates ghrelin-derived peptides with different bioactivity than ghrelin. Moreover, the liver may be involved in this mechanism