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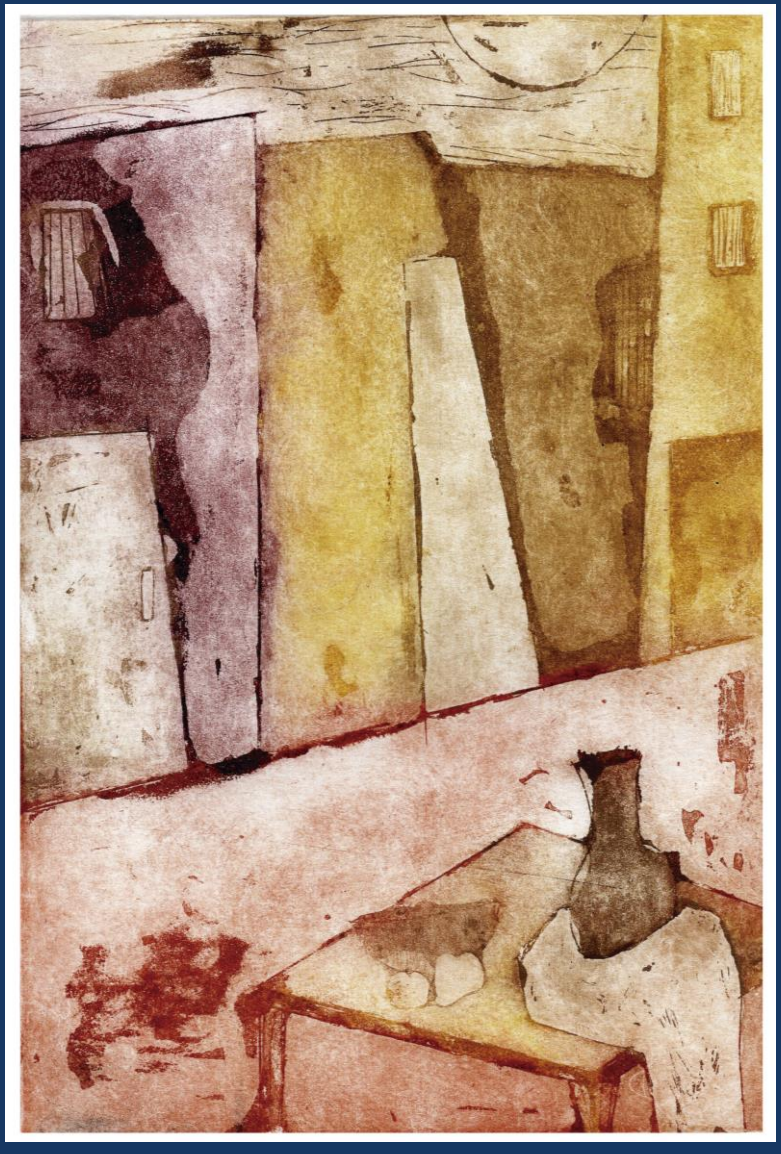

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Abstract/Resumen: In previous studies we evaluated the interaction between the CB1 cannabinoid receptors and the endogenous opioid system studying the antinociceptive effect of morphine (MOR) by using the acetic acid (AA)-induced writhing test in CB1 knockout (KO) adolescent male and female mice. The aim of the present study was to evaluate the motivational (anxiety like-behaviour) and cognitive (memory consolidation) responses associated to the AA-induced visceral pain model in adolescent CB1 KO mice of both sexes. The anxiety like-behaviour associated to visceral pain was measured by the elevated plus maze (EPM). CB1 KO and WT mice were pre-treated with MOR (1, 3 or 9 mg/kg i.p.) or saline (SAL) injection, 20 minutes before the AA (1.5 %, 10 ml/kg i.p.) or SAL administration. Immediately after, the time spent and number of entries to the open arms were registered during 20 min. The memory consolidation associated to visceral pain was determined using the novel object recognition (NOR) test and expressed as a differentiation index (DI). During the training phase of NOR test, CB1 KO and WT mice were placed in an open field with two identical objects for 9 minutes and right after, mice were pretreated with MOR (1, 3 or 9 mg/kg) or SAL injection 20 minutes before AA or SAL administration. On the test phase, 24 hs after, one of the two identical objects was randomly replaced by a different object. Time spent exploring either novel or familiar object, were measured and the DI was calculated. In the EPM test only MOR 1 mg/kg attenuated the AA-induced anxiogenic like effect expressed as the % of time in the open arms in CB1 KO ($p<0.05$), but not in WT male mice. In the NOR test no significant changes were observed in any of the experimental groups. Our results suggest that CB1 receptors could modulate the anxiety-like behaviour associated to AA-induced visceral pain in males. On the other hand, memory consolidation process would not be affected by the AA-induced visceral pain.

0586 - BEHAVIORAL AND BIOCHEMICAL TESTS IN AN ANIMAL SCHIZOPHRENIA MODEL.

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Abstract/Resumen: In this study, behavioral and biochemical tests were performed on an epigenetic model of schizophrenia, with the aim of revealing alterations characteristic of the disease. For this purpose, Swiss albino mice were administered with methionine 5.2 mmol/kg for 30 days. After this period, they were subjected to a task of object recognition, based on the etiological paradigm of novel preference. The procedure consists of exposing a lot of 5 animals to a first session with two identical objects placed in an open field during 10 min and then 24 h later these animals were exposed again to two objects, one of which was in the first session and the other with which the animal has not been. The results showed that the animals touched the object with their noses 84 ± 14 times (control) 60 ± 13 times (treated) in the first session and 57 ± 14 times (control) and 72 ± 21 times (treated) in the second session, without any significant differences among the groups. However, control animals interacted more often with the novel object (65 %) than 46 % of the treated animals, indicating that the animals subjected to the schizophrenia model showed changes in the memory involved in the recognition of the objects. We have previously observed that lipid peroxidation of the cerebral cortex increased in animals subjected to the epigenetic model. In this case, the determination of substances reactive to 2-thiobarbituric acid was carried out by the modified method of Yokohawa (Yokohawa et al. 1973) subsequent to the administration of chlorpromazine 3 mg/kg, vapreotide (somatostatin analogue) 100 mcg/kg or both produced significant reductions of 43, 48 and 60%, respectively; in the cerebral cortex lipid peroxidation. In addition, no changes were observed in the control animals. These results suggest that certain modifications of the disease would be represented in this model allowing its use for the testing of new antipsychotic agents.

0678 - DIAZEPAM-INDUCED TRANSCRIPTIONAL REGULATION OF GABAA RECEPTOR ALPHA1 SUBUNIT GENE VIA L-TYPE VOLTAGE-GATED CALCIUM CHANNEL ACTIVATION IN RAT CEREBROCORTICAL NEURONS

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Abstract/Resumen: GABA-A receptors are targets of different pharmacologically relevant drugs, such as barbiturates, benzodiazepines, and anesthetics. In particular, benzodiazepines are prescribed for the treatment of anxiety, sleep disorders, and seizure disorders. Prolonged activation of GABA-A receptors by endogenous and exogenous modulators induces adaptive changes that lead to tolerance. For example, chronic administration of benzodiazepines produces tolerance to most of their pharmacological actions, limiting their usefulness. The mechanism of tolerance is still unknown. We have previously demonstrated that chronic diazepam administration in rats result in tolerance to the sedative and anxiolytic effects which is accompanied with a decrease in the interactions between GABA and benzodizepine binding sites (uncoupling) in cerebral cortex. The aim of this work was to investigate the molecular mechanism of benzodiazepine tolerance in an in vitro model of primary neuronal cultures from rat cerebral cortex. The exposure of cultured neurons to diazepam for 48 h produced a 40 % uncoupling ($p<0.05$) which was prevented in the presence of nifedipine, an inhibitor of L-type voltage-gated calcium channels (L-VGCCs). Benzodiazepine treatment also induced a 45 % decrease ($p<0.05$) in GABA-A receptor alpha1 subunit mRNA levels ($p<0.05$) that was inhibited by nifedipine. We hypothesized that the adaptive changes of GABA-A receptors induced by sustained exposure to benzodiazepine are mediated by a signaling pathway that involves activation of L-VGCCs. Results from calcium mobilization and nuclear run-on assays suggested that benzodiazepine exposure produces an increase in the calcium influx through L-VGCCs that activates an intracellular signaling cascade finally leading to the transcriptional repression of alpha1 subunit gene expression. Insights into the mechanism of benzodiazepine tolerance will contribute to the design of new drugs that can maintain their efficacies after long term treatments.

0723 - ELECTROPHYSIOLOGICAL AND MOLECULAR EVALUATION OF TWO NMDAR ANTAGONISTIC PEPTIDES, POSSIBLE CANDIDATES IN NEUROPROTECTION PROCESSES.

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Abstract/Resumen: Glutamate (E), an excitatory amino acid of the central nervous system (CNS), acts through different receptors, among which is the N-methyl-D-aspartate receptor (NMDAR). The NMDAR is responsible for allowing the flow of Ca2 + ions into the postsynaptic neuron, playing an important role in synaptic plasticity. One of the most relevant pharmacological