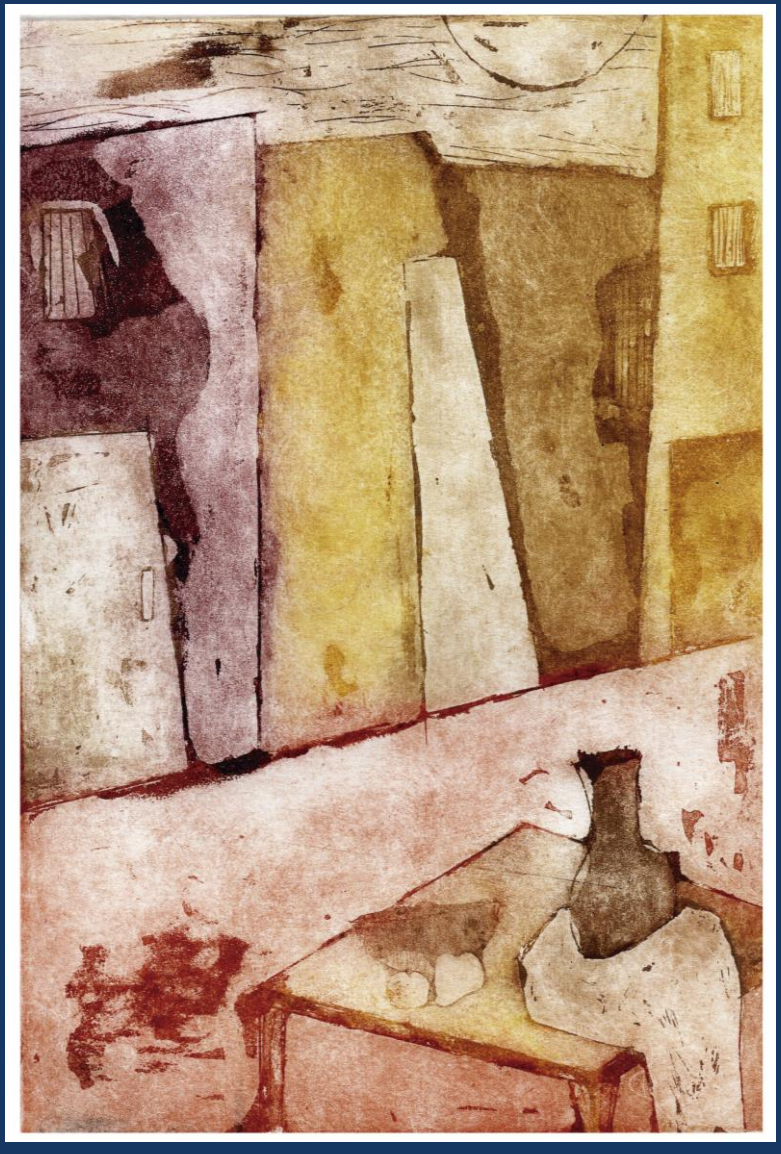
2019

medicina

BUENOS AIRES VOL. 79 Supl. IV - 2019

80° Aniversario



MEDICINA

Volumen 79, Supl. IV, págs. 1-338

kidneys from the inflammatory damage associated with consumption of high fat diets and obesity.

Supported by UBACYT 20020170100586BA, 20020160100132BA, and PIP-CONICET 11220170100585CO grants.

Reproducción / Reproduction IV

Chairs: Julieta Aisemberg | Luis Canosa

0547 - PHARMACOLOGICAL ACTIONS OF ALLOPREGNANOLONE OVER THE OVARIAN PHYSIOPATHOLOGY WITH DIFFERENT EXPERIMENTAL MODELS

Antonella CACERES (1) | Maria de Los Ángeles SANHUEZA(1) | Laura Tatiana PELEGRINA(2) | Myriam Raquel LACONI(1)

INSTITUTO DE MEDICINA Y BIOLOGÍA EXPERIMENTAL DE CUYO (IMBECU) (1); UNIVERSIDAD DE MENDOZA (2)

Abstract/Resumen: Allopregnanolone (ALLO) is a neurosteroid derived from progesterone; its actions in the CNS are well known. ALLO modulates GABA neurotransmission with antidepressant, anxiolytic, anticonvulsant and anesthetic effects. ALLO levels fluctuate under stress and throughout the menstrual cycle, pregnancy and menopause. The objective of this work was to evaluate ALLO action over the female rat ovarian physiopathology, from the global effect on the CNS to the action on the granulose cells. We designed different experimental models in order to differentiate four levels of action. After a dose/response curve we found that ALLO 6 µM, a pharmacological dose, was capable of disrupting the hypothalamus-hypophysis-ovarian axis causing significant ovarian morpho-physiological changes (augmented follicular atresia, $p<0.001$; cyst formation, $p<0.001$; corpora lutea apoptosis, $p<0.001$; and inhibited ovulation, $p<0.001$) through the central interaction with GABAAR. This dose changed the ovarian total expression of the progesterone receptor ($p<0.01$). The ex vivo culture of GMS-NOP-ovary system, proved the peripheral effect of ALLO over the ovarian steroidogenesis augmenting P4 secretion ($p<0.05$) through the adrenergic innervation. The local intra-bursal administration of ALLO affected the ovarian morpho-physiology (augmented follicular atresia, $p<0.001$ and corpora lutea diameter, $p<0.05$), through GABAAR, but failed to inhibit ovulation. Finally, the in vitro primary culture of ovarian granulose cells treated with ALLO showed a significant decrease in the PCNA antigen ($p<0.05$). ALLO at pharmacological dose is able to affect the rat female reproductive physiology. This is the first evidence of the global ALLO actions on the reproductive axis that allow us to assess the power of ALLO effects over reproductive parameters utilizing different administration routes. ALLO is a molecule with a great versatility and with a great pharmacological potential in female reproductive physiology.

0561 - HYPERTHYROIDISM ENHANCES FETAL AND PLACENTAL GROWTH AND PLACENTAL IMMUNE CELL INFILTRATION

María Belén SÁNCHEZ | María Tamara MORENO SOSA | Flavia Judith NEIRA | Elisa Olivia PIETROBON | Marta SOAJE | Susana Ruth VALDEZ | Graciela Alma JAHN | Juan Pablo MACKERN OBERTI

INSTITUTO DE MEDICINA Y BIOLOGÍA EXPERIMENTAL DE CUYO (IMBECU)

Abstract/Resumen: Thyroid dysfunctions cause reproductive disorders as fetal deaths, preterm birth and preeclampsia. Whether thyroid hormones (THs) exert any function in placental immune cells is unknown. Therefore, the aim of our work was to assess the influence of hyperthyroidism on placental immune cells as well as the impact on reproduction in pregnant rats. To this end, 10-12 weeks old Wistar rats were injected with a daily dose of T4 (0.1 or 0.25 mg/kg s.c) to induce hyperthyroidism (hyper) or vehicle in control animals. Rats were mated 8 days after starting T4 treatment and euthanized on day 19 (G19) and 20 (G20) of gestation. Placenta samples were minced to reach single cell suspension. Then, resident placental immune cells (CD45+) were analyzed by flow cytometry and mRNA content of hormone receptors by qPCR. Also, placental and fetus weights and fetus number were measured. Hyper mothers delivered more fetuses compared to controls ($p<0.001$). The offspring of hyper 0.25 mg/kg mothers weighed more in G19 and G20 ($p<0.001$). The placentas of the hyper 0.25 mg/kg mothers were heavier than controls only in G19 ($p<0.001$). Furthermore, we showed a decrease in the expression of progesterone, estrogen and ß2 thyroid receptors in hyper 0.1 mg/kg ($p<0.05$; $p<0.01$). On G19, the percentage of leukocytes was significantly higher in both hyper groups ($p<0.05$ for 0.1 mg/kg; $p<0.01$ for 0.25 mg/kg). On G20 we showed an increase in leukocyte infiltrate respect to G19 in the control ($p<0.001$) but not in the hyper group. These results suggest that T4 administration accelerates fetal development and changes the placental sensitivity to ovarian steroids by modulating their receptors expression and advances the increase in placental resident leukocytes. To our knowledge, this is the first report that shows the modulation of resident immune cells by thyroid hormones.

0623 - CYCLIC AMP EFFLUX THROUGH MRP4 REGULATES MOTILITY AND ACTIN POLYMERIZATION IN BOVINE CRYOPRESERVED SPERMATOZOA.

Nicolas CHIARANTE (1) | Carlos Agustín Isidro ALONSO(1) | Raquel LOTTERO(1) | Jessica PLAZA(2) | Carlos DAVIO(3) | Marcelo MIRAGAYA(2) | Silvina PEREZ MARTINEZ(1)

CEFYBO, UBA-CONICET (1); INITRA, UBA (2); ININFA, UBA-CONICET (3)

Abstract/Resumen: Capacitation is a key process involved in the acquisition of sperm fertilizing competence. The importance of cAMP during capacitation has led us to study the role of the MRP4 transporter, multidrug resistance-associated protein 4 that extrudes cAMP from cells. We previously described that MRP4 mediates cAMP efflux in bovine spermatozoa and that extracellular cAMP activates signaling pathways associated to capacitation. Here we deepen the study of cAMP efflux in the acquisition of sperm fertilizing ability in this species using MK571, a compound that inhibits MRP4. We evaluated capacitation by LPC-induced acrosome reaction and the ability of sperm to be released from oviductal epithelia. Both events were decreased when the MRP4 inhibitor (50 µM) was added ($p<0.05$). Immunofluorescence evidenced that MRP4 is localized in the acrosomal and post-acrosomal regions, and mid-piece of the flagellum at 15 min capacitation time. At 45 min, localization was preferentially acrosomal. As a result of MRP4 localization in the flagellum, we assessed the involvement of this protein in sperm motility during capacitation. A decrease in parameters associated to sperm motility (progressive motility, VCL, STR, ALH and BCF), measured by computer assisted sperm analysis, was observed in spermatozoa incubated for 15 and 45 min with MK571 ($p<0.05$). Since actin cytoskeleton plays essential roles in the regulation of sperm motility, we studied actin polymerization (F-actin). An increase in F-actin (assessed by Alexa 488-phalloidin) was observed in sperm at 15 but not at 45 min incubation time. This increase was detected in sperm's heads as well as in their tails. When MRP4 was inhibited, F-actin decreased, in a process that was reverted with extracellular cAMP 10 nM in the flagellum but not in the head ($p<0.05$). Our results support the importance of cAMP efflux through MRP4 in sperm capacitation and suggest that this process is involved in the regulation of sperm motility.

0657 - EVALUATION OF GROWTH HORMONE RECEPTOR AND INTRACELLULAR SIGNAL