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

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REUNIÓN ANUAL DE SOCIEDADES DE BIOCIENCIA 2019

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

**LI Reunión Anual de la
Asociación Argentina de Farmacología Experimental (SAFE)**

**XXI Reunión Anual de la
Sociedad Argentina de Biología (SAB)**

**XXXI Reunión Anual de la
Sociedad Argentina de Protozoología (SAP)**

**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

EDITORES RESPONSABLES

**Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi**

ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2019

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CHIEF EDITORS

**Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi**

determined by RT-qPCR. HpC mRNA content of TRs, STAT5b (activator of PRL signaling) and SOCS1 (suppressor of PRL signaling) decreased from G19 to L12 in Co and HyperT rats ($p < 0.05$). HyperT induced increases of TRa2 ($P < 0.05$ vs Co) and TRb2 in L2 ($p < 0.01$ vs. Co) without changes in others isoforms. HyperT increased STAT5b in G19 ($p < 0.05$ vs. Co). ERa and PRLR mRNAs were unchanged by treatment or reproductive state while GR increased in L12 in both groups ($p < 0.05$ vs. G19). These results indicate a physiological decline in HpC responsiveness to thyroid and PRL hormones in the transition from pregnancy to lactation in Co, while the increases observed in TRa2, TRb2 and STAT5b described in HyperT rats may be involved in the persistence of high HHA axis reactivity.

Endocrinología/ Endocrinology III

Chairs: María Sonia Baquedano | Silvina Gutiérrez Oschmann

0066 - THE PHTHALATE DEHP DOWNREGULATES THE PITUITARY ESTROGEN RECEPTOR ALPHA EXPRESSION AND IMPACT ON LACTOTROPH AND GONADOTROPH CELL PROLIFERATION

Pablo Aníbal PÉREZ | Jonathan TOLEDO | Liliانا Del Valle SOSA | Ana Lucía DE PAUL | Alicia Ines TORRES | Silvina GUTIÉRREZ

CENTRO DE MICROSCOPIA ELECTRÓNICA-FACULTAD DE CIENCIAS MÉDICAS. INICSA-CONICET

The normal functioning of the pituitary gland is the result of a balanced mechanism capable of rhythmically control the proliferation and hormonal secretion of different endocrine cell populations in response to endogenous factors such as Estrogen (E2) acting through estrogen receptors (ER). Also, it has been shown that exogenous agents as phthalates, substances used for plastics manufacture, might act as endocrine disruptors in several tissues, simulating E2 effects. The purpose of this study was to analyze the Di-2-ethylhexyl phthalate (DEHP) effect on pituitary ERa expression and its impact on cell proliferation. We used Wistar female rats prenatally treated with DEHP. At 21 days of postnatal life pituitary glands were extracted and intracellular ERa (ERa) and membrane ERa (mERa) positive cells were quantified by flow cytometry (FC). Also, primary pituitary cell cultures were stimulated with DEHP, E2 or DEHP+E2 for 72 h. The lactotroph and gonadotroph proliferation was quantified by double immunostaining (ki67+PRL or Ki67+bLH). The percentages of ERa+ and mERa+ cells were quantified by FC. ANOVA Fisher ($p < 0.05$). Our results showed that DEHP prenatal exposition significantly reduced the cell number that express ERa (DEHP: 73 ± 4.6 vs. control: 86.4 ± 0.5 %) and mERa (DEHP: 5.7 ± 0.8 vs. control: 8.9 ± 0.2 %). In vitro, DEHP decreased ERa+ pituitary cells (DEHP: 79.2 ± 1.1 vs. control: 86 ± 1.2 %) and mERa+ pituitary cells (DEHP: 8.2 ± 1.3 vs. control: 11.5 ± 1.5 %). In lactotrophs, DEHP inhibited the Ki67 expression (DEHP: 21.1 ± 2.2 vs. control: 27.1 ± 2.1 %). Also, DEHP reversed the E2 proliferative effect observed in this cell type (DEHP: 25.4 ± 1.2 vs. 30.7 ± 1.9 %) In gonadotrophs, DEHP inhibited Ki67+cells (DEHP: 20.0 ± 4.2 vs. control: 28 ± 2.5 %), without modifying E2 effect. These observations suggest that DEHP impacts on the pituitary gland during the development, downregulates ERa expression and affects the lactotroph and gonadotroph proliferation in adulthood.

0158 - LONG-TERM EFFECTS OF SUCROSE CONSUMPTION ON GLYCEMIA AND RAGE EXPRESSION IN JUVENILE VERSUS ADULT RATS.

María Sol KRUSE | Mariana REY | María Claudia GONZALEZ DENISELLE | Héctor COIRINI

IBYME-CONICET

Excessive consumption of sucrose in early stages of development has deleterious neurobiological and behavioral effects in adulthood. Among these disturbances, difficulties in memory retrieval by early sucrose exposure were previously described. Here, we examined the glycemic levels of the animals and their response to an intraperitoneal glucose overload. We found that sucrose consumption increased the AUC (area under the curve derived from the oral glucose tolerance test) in both young and adults (two-way ANOVA, $F_{Treat(1,34)} = 7,658$; $p = 0.0091$. Fisher's LSD post hoc test, $p = 0.047$ and $p = 0.040$, respectively) but only consumption during youth maintained this effect in the long term (two-way ANOVA, $F_{Treat(1,34)} = 4,445$; $p = 0.0429$. Fisher's LSD post hoc test, $p = 0.020$). RAGE expression was also assessed by Western blot. Age differences were detected by two-way ANOVA in the two brain areas examined, the mPFC and the vHIP, but only in the mPFC differences by treatment were observed (two-way ANOVA, $F_{Treat-Age(1,20)} = 2,327$; $p = 0.001$). Surprisingly, sucrose exposed animals in their youth showed decrease of RAGE while adults raised these values in the mPFC (Fisher's LSD post hoc test, $p = 0.037$ and $p = 0.002$, respectively). When all animals were pulled together, there was a negative correlation of the exploration ratio of the memory recognition test and the RAGE levels in the mPFC ($F(1,14) = 7,225$; $p = 0.0434$; $r^2 = 0.59$) indicating that higher RAGE values relate with poorer novelty recognition on the final task of the memory test. Similarly, the basal plasma glucose levels also correlated with lower exploration ratio on the final recognition task ($F(1,21) = 5,744$; $p = 0.0264$; $r^2 = 0.223$). When basal glycaemia was analyzed together with mPFC RAGE levels, a positive correlation was observed ($F(1,18) = 5,693$; $p = 0.0289$; $r^2 = 0.251$). In summary, these results suggest that sucrose induced-hyperglycemia is detrimental for the memory a phenomenon that is related with the RAGE pathway in the mPFC.

0210 - THE KALLIKREIN-KININ SYSTEM IN THE PITUITARY GLAND IS INVOLVED IN LACTOTROPH FUNCTION AND CONTROLLED BY DOPAMINE AND ESTRADIOL

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INSTITUTO DE BIOLOGÍA Y MEDICINA EXPERIMENTAL (IBYME-CONICET) (1); INSTITUTO DE BIOCENCIAS, BIOMEDICINA Y BIOTECNOLOGÍA (IB3-CONICET) (2)

TGFB1 is a potent inhibitor of lactotroph cell proliferation and prolactin (PRL) secretion and Tissue Kallikrein (KLK1) was described as an important activator of latent TGFB1 in vivo. The Kallikrein-Kinin System (KKS) is complex; kininogens are cleaved by KLK1, releasing kinins, which exert their effect through its receptors B1R and B2R. Whereas B2R is constitutively expressed, B1R is inducible in pathological conditions. We have previously found that the pituitary expression of most components of the KKS, as well as local TGFB1 activity, is reduced in prolactinomas. Then we postulate that the recovery of pituitary KKS, could improve local TGFB1 activity counteracting prolactinoma development. To this end, we first deepen the study of the pituitary KKS regulation by dopamine and estradiol and the pituitary cell types expressing kinins receptors. Female mice lacking the dopamine receptor type 2 (Drd2KO, prolactinoma) vs. WT counterpart were used. 1- Double immunofluorescences were performed to assay B2R expression in different pituitary cell-types in WT females. We found that lactotrophs, somatotrophs and gonadotrophs express B2R. 2- Adult females were injected with E2 valerate (0.2 mg/kg, s.c.), cabergoline (DA agonist, 2mg/kg, i.p.), sulpiride (DA antagonist, 5mg/kg, i.p.) or vehicle (castor oil or saline) and were sacrificed after 3 hours. Pituitary expression of KKS components was evaluated by RTqPCR. We found that E2 exerts a negative regulation of klk1, b2r and b1r expression in WT females, but this control is lost in Drd2KO. On the contrary, DA exerts a positive regulation of klk1 expression but negatively regulates b2r expression in WT females. We conclude that the positive DA-regulation exercised on the pituitary KLK1 expression is lost in the

Drd2KO pituitary, reducing KLK1 local activity, reducing TGFβ1 activation, and contributing to prolactinoma development. The improvement of pituitary KKS activity could represent a novel treatment for resistant prolactinomas.

0226 - DEREGULATION OF THE PITUITARY SMAD-INDEPENDENT ACTIVIN SIGNALLING PROMOTES PROLACTINOMA DEVELOPMENT.

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Activins are known inhibitors of lactotroph function. Pit-1 is a pituitary-specific transcription factor that plays an important role in regulating PRL expression. Despite pSMAD2/3 is known as the activins-canonical intracellular signalling, it was described that activin represses Pit-1 expression in lactotroph cells in a Smad-independent mechanism. We have previously demonstrated that decreased pituitary activin expression is involved in prolactinoma development. In the present work we have studied the activin-signalling pathways involved. We used two different animal models of prolactinomas: female mice lacking dopamine type 2 receptor (Drd2-/-) and female mice overexpressing the β subunit of the human chorionic gonadotrophin (hCGβ+). We used wild-type (wt) mice as controls. Despite the reduced activin expression found in prolactinomas vs wt pituitaries, we found unexpectedly increased pSMAD3 expression (Western blot) in prolactinomas. But nevertheless, by using double immunostaining, we observed that pSMAD3 co-localizes mainly in FSH+ cells, but not in PRL+ cells. Then we focused on the activin alternative pathway involved in prolactinoma development. Our results show that wt female pituitaries present high activin expression concomitant with strong expression of p-p38 in lactotroph population (double IHC). However, activin expression is decreased in prolactinomas concomitant with decreased p-p38 expression in PRL+ cells, increased Pit-1 mRNA expression (q-RT-PCR) and tumor development. This highlights the importance of the activin inhibitory action on lactotroph function and places the activin system and the p38 MAPK pathway as new targets in the treatment of dopamine agonist resistant prolactinomas. Key words: pituitary, prolactinoma, activins, p-p38 pathway

0268 - EFFECTS OF THE CHRONIC TREATMENT WITH L-3,4-DIHYDROXYPHENYLALANINE (L-DOPA) ON THE NEUROENDOCRINE STRESS RESPONSE

Santiago Jordi ORRILLO (1) | Mercedes IMSEN(1) | Alfonsina LIZARRAGA(1) | Ana Clara ROMERO(1) | Fernanda DE FINO(2) | Milagros PEÑA(3) | Alejandra ABELEDO MACHADO(3) | Sandra ZÁRATE(1) | Jimena FERRARIS(1) | Graciela DÍAZ-TORGA(3) | Daniel PISERA(1)

INBIOMED-UBA-CONICET (1); INSTITUTO DE INVESTIGACIONES FARMACOLÓGICAS, UNIVERSIDAD DE BUENOS AIRES-CONICET (2); INSTITUTO DE BIOLOGÍA Y MEDICINA EXPERIMENTAL (IBYME-CONICET) (3)

Stress evokes a complex response mediated by two systems: the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic-adreno-medullar (SAM) axis. Glucocorticoids and catecholamines secreted from the adrenal glands and sympathetic nerves are the main hormone effectors of the physiological adaptations observed during stress. Moreover, prolactin (PRL) is another pituitary hormone secreted under stressful stimuli. Catecholamines are synthesized from the hydroxylated precursor L-Dopa. This agent is also used with therapeutic purposes, e.g. in Parkinson's disease. In the present research, we studied the effects of L-Dopa on the response to a stressor. Adult male Wistar rats (300 g) were

chronically treated (24 days) with LBOCAR (L-Dopa (75 mg/day) - Carbidopa (7.5 mg/day)) orally in drinking water and stressed by immobilization during the last 9 days of treatment. We first explored the activity of the SAM axis. Circulating noradrenaline increased in rats treated with LBOCAR (p<0.05; HPLC), while its content in the adrenals showed no significant alteration. Serum adrenaline (A) levels augmented by LBOCAR treatment or stress (p<0.05; HPLC). Also, the adrenals from stressed animals showed higher content of A (p<0.05). Next, we studied the reactivity of the HPA axis. Chronically stressed rats displayed a lower ACTH secretion (ELISA) and a downregulation of POMC expression (qPCR) in the anterior pituitary (p<0.05). In addition, LBOCAR treatment induced a reduction in serum ACTH and POMC levels (p<0.05). As expected, serum corticosterone (ELISA) peaked under chronic stress, an effect that was inhibited by treatment with LBOCAR (p<0.05). Finally, pituitary PRL gene expression (qPCR) was downregulated by LBOCAR treatment with a more pronounced effect when rats were also stressed (p<0.05). In summary, our results suggest that L-Dopa alters the neuroendocrine stress response by enhancing SAM axis activity and declining HPA axis reactivity and PRL expression.

0298 - SEXUAL DIMORPHISM OF THE KISSPEPTIN AND DOPAMINERGIC SYSTEMS IN THE HYPOTHALAMUS OF THE SOUTH-AMERICAN PLAINS VIZCACHA (L. MAXIMUS).

Alejandro Raúl SCHMIDT | Santiago Andrés CORTASA | Sofía PROIETTO | María Clara CORSO | Victoria FIDEL | Kevin FEEHAN | Pablo Ignacio Felipe INSERRA | Julia HALPERIN | Alfredo Daniel VITULLO | Verónica Berta DORFMAN

CENTRO DE ESTUDIOS BIOMÉDICOS, BIOTECNOLÓGICOS, AMBIENTALES Y DE DIAGNÓSTICO-UNIVERSIDAD MAIMÓNIDES

Vizcacha shows the highest sexual dimorphism among rodents. It presents atypical reproductive features as natural polyovulation up to 800 oocytes per estral cycle, inhibition of follicular atresia and ovulation during pregnancy with new corpora lutea formation. Brain dimorphism occurs during the embryogenesis and such process is modulated by the hormonal environment they are exposed, which modifies their structure and neurochemical composition. Within hypothalamic structures, this process affects the anteroventral-periventricular nucleus (AVPV) and the arcuate nucleus (ARC) among others. The aim of this work was to characterize the hypothalamic dimorphic sexual nuclei in the vizcacha focusing on the neurochemistry of cellular composition. Adult non-pregnant female (FM) and male (M) vizcachas were used (n=6/group). The localization of AVPV and ARC was determined by Nissl staining, and estrogen receptor alpha (REalpha), tyroxine hydroxylase (TH) and kisspeptin (Kiss) expression were studied by immunohistochemistry. Sexual dimorphism was observed at macroscopic level, being the brain weight/body weight ratio higher in FM than in M (0.47%, t test, p<0.05). In addition, Nissl staining showed a significantly increased AVPV area in FM with a significantly increased number of REalpha, TH and Kiss immunoreactive neurons and immunoreactive cell area (p<0.05). In ARC, TH showed similar variations than AVPV, however, Kiss did not show differences between sexes. AVPV of both sexes showed colocalization of REalpha with Kiss and with TH, whereas in ARC, REalpha colocalized with Kiss. Estradiol plays an important function in the establishment of brain sexual dimorphism through the REalpha which plays a key role in the sexual dimorphism maintenance. In consequence, the expression level of REalpha should support TH and Kiss expression in the AVPV nucleus in female vizcachas. The association of REalpha with Kiss and TH would be important as part of the indirect GnRH regulation pathway. Supported by FCFF, CONICET-PIP110/14 and MICyT-PICT1281/2014 grants.