by means of body weight, eye opening, climb ability and grip strength. At PND 44, we assessed anxiety and locomotor activity. At PND 46, we obtained brain samples to study the expression of genes related to cholinergic system. Results showed lower body weight and delayed eye opening in both C57BL/6J-treated mice, while opposite effects were observed in communication analysis. ApoE mice only showed genotype differences in all the parameters evaluated. Cholinesterase activity was not altered by prenatal exposure to CPF. Therefore, at that developmental stage, C57BL/6J mice are more sensitive to CPF exposure than apoE mice, however the different apoE isoforms present different maturation patterns which condition the behavioral response.

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P0027 / #3605

Topic: AS01 Nervous System Development and Related Disorders

PARTIAL SLEEP DEPRIVATION ALTERS THE DEVELOPMENT AND COGNITIVE ABILITY OF ZEBRAFISH LARVAE

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Sleep deprivation is characterized by an insufficient act of sleeping, causing a reduction in performance and alertness. The zebrafish sleep is characterized by a diurnal circadian rhythm and adjusted with degrees of inactivity gradually increasing the excitation. Considering the importance of sleep in the early stages of development and its possible effect in adult life, in this study, we evaluated the influence of a partial sleep deprivation (PSD) protocol on the development of zebrafish larvae and its possible effects on the memory of the adults. Thus, we modify the light and dark cycle, over three consecutive days, to induce PSD in larvae with 5 days post-fertilization (dpf) (CEUA/PUCRS: 9511). The protocol was performed by extending the light phase in 19 h and 5 h in dark. The control group was maintained in the cycle of the laboratory, 14 h in light and 10 h in dark. During the PSD protocol, we analyzed the heartbeat rate and the exploratory and optomotor behaviors. After the end of the protocol, the animals were kept in a normal light and dark cycle until reached 180 dpf, when memory analysis was performed. The results showed that larvae submitted to 24 and 48 h of PSD presented a reduction in the heartbeat rate. For the analysis of exploratory behavior, we observed a reduction in distance at 48 and 72 h and movement at 72 h of PSD. The indirect analysis of cognition, performed through the optomotor behavior, showed that animals submitted to 72 h of PSD presented a better cognitive performance. Memory analysis performed at 180 dpf showed that PSD in the early stages of development did not alter the memory of adult animals. The results show that PSD can significantly affect the development and cognition of animals, but these changes do not extend into adulthood.

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P0028 / #2741

Topic: AS01 Nervous System Development and Related Disorders

SYNAPTIC IMBALANCE AND THE NITRIC OXIDE PATHWAY IN THE VPA MOUSE MODEL OF AUTISM

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Although many progresses have been made in the knowledge of autism, there is still a long way to understand its molecular, cellular, neuroanatomical, and behavioural bases. One of the main neuronal alterations observed in this disorder is an imbalance between excitatory and inhibitory activity. In this sense, nitric oxide (NO) participates in the modulation of excitatory/inhibitory neurotransmission by interacting with both glutamate and GABA. Until now, little is known about how the nitrergic system works in the autistic brain. In this study, we investigated the nitrergic system in the valproic acid-induced mouse model of autism (VPA). We focused on olfactory bulb (OB) since NO plays a relevant role in this area, and because olfaction is crucial in terms of survival and social interaction, at least in rodents. Besides, the importance of sensorial dysregulations in humans with autism is largely known, which also highlights the study of olfaction. We carried out histochemistry for nicotinamide adenine dinucleotide phosphate diaphorase (NADPH-d) and immunohistochemistry for the neuronal isoform of nitric oxide synthase (nNOS) to analyse the activity/expression of elements involved in NO production. Finally, we determined total NO levels through quantification of its metabolites, nitrite (NO_2^-) and nitrate (NO_3^-), using the Griess technique. Our preliminary results indicate a relevant decrease in NADPH-d activity, nNOS expression, and NO_2^- and NO_3^- presence. This leads us to think that NO production could be significantly reduced in the OB of the VPA model. Examining the nitrergic system and its relationship with glutamate and GABA will shed light on the research field of autism spectrum disorders. Alterations in this system, as a regulator of neuronal excitability, could be participating in or aggravating the important excitatory/inhibitory imbalance described for autism. E-mail: cabedonavarro.valeria@usal.es; ddiaz@usal.es; jralonso@usal.es Support: MICINN (PID2019-106943RB-I00), JCyL (SA129P20), USAL

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P0029 / #2702

Topic: AS01 Nervous System Development and Related Disorders

THE EFFECT OF MATERNAL CORTISOL ON OFFSPRING'S BRAIN DEVELOPMENT

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Exposure to adverse childhood experiences (ACEs) can result in altered regulation of the hypothalamic-pituitary-adrenal (HPA) axis as evidenced by altered cortisol levels. Stress-induced increase in maternal glucocorticoid levels during pregnancy may lead to fetal glucocorticoid overexposure which can affect brain development, and alter HPA axis development. The present study investigated whether maternal cortisol levels impact neonate cortisol levels and brain development. Salivary cortisol was collected from mothers and their offspring on the same day that the neonates performed a brain MRI scan. Multiple linear regressions were conducted for 14 bilateral subcortical regions (hippocampus, amygdala, caudate, putamen, globus pallidus, thalamus, and accumbens) as dependent variables with maternal cortisol as the independent variable and controlled for post-menstrual age (PMA) and infant sex. The subcortical regions were segmented using a validated infant MRI platform (finneas.ai). The results were corrected for multiple comparisons using the Bonferroni correction ($p < 0.004$; 14 different models). The correlation between maternal and infant salivary cortisol levels was also explored. A total of 130 dyads (mothers and neonates) were included in the analyses. The average age for the mothers was 27.03 (±5.17) years-old and for the neonates was 43.7 (±1.64) days (postmenstrual age – PMA) at MRI. Average maternal cortisol level was 5.23 (±4.27) ng/mL and the neonate's salivary cortisol was 8.87 (±7.42) ng/mL. Maternal cortisol level was negatively correlated with the volume of the left hippocampus ($p < 0.004$). There was a strong correlation between maternal and neonate cortisol levels ($p = 0.0001$). Our results suggest synchronicity between maternal and neonatal cortisol, suggesting an influence of maternal stress in offspring HPA axis development. Moreover, our data demonstrated that increased maternal cortisol is related to offspring brain development, specifically in the left hippocampus, a brain region rich in glucocorticoid receptors.

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P0030 / #4175

Topic: AS01 Nervous System Development and Related Disorders

HISTONE H4 ACETYLATION INVOLVEMENT IN SEXUALLY DIMORPHIC AROMATASE EXPRESSION OF DEVELOPING MOUSE BRAIN

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During early development, sex chromosome complement (SCC) regulates a sexually dimorphic gene expression in limbic regions of the mouse brain. Furthermore, aromatase and ERβ expression are higher in amygdala neurons of XY than XX embryos at embryonic day (E) 15, before of critical period of hormone-induced brain masculinization. Epigenetic has been proposed as mediator of hormonal and genetic sexual differentiation of the brain. We aimed to study the role of SCC on the epigenetic mechanisms involved in brain sexual differentiation. Four core genotypes mouse model (FCG) was employed to evaluate by RT- qPCR the epigenetic machinery involved in DNA methylation and histone deacetylation in amygdala at E15. Moreover, the epigenetic regulation of aromatase and ERβ expression was analyzed by Chromatin Immunoprecipitation (ChIP-qPCR) from E15 amygdala primary neuronal cultures segregated by sex using anti-Acetyl-H3 and -H4 antibodies. Independent cultures were performed to evaluate the effect of pharmacological inhibition of DNA methylation (using zebularine) on the aromatase gene expression by RT-qPCR. We found that SCC regulate the sexually dimorphic expression of *de novo* DNA methyltransferase 3a and 3b, and histone deacetylase 2 and 8 with higher expression in XX than XY embryos. Zebularine did not change aromatase expression levels neither in male nor female cultures. However, ChIP assays showed an enrichment of Acetyl-H4 in the male aromatase promoter that was not observed in female cultures. The ERβ promoter did not show a significant enrichment of the explored marks. In summary, the acetylation of H4 could be contributing to relax chromatin structure in male amygdala neurons, thereby facilitating the access of the transcriptional machinery to the aromatase gene promoter leading to the higher expression previously observed in males. These results contribute to a better understanding of the role of epigenetics in the establishment of brain sex differences independently of hormonal masculinization.

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