SUMO conjugation to tau, indicating that it is not a tau SUMO-E3 ligase. Finally, our preliminary autophagic flux assays revealed that PIAS4 might be blocking selective autophagy degradation of tau.
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213. (317) **CHRONIC EXPOSURE TO FLUOXETINE DURING PRE-PUBERTY IMPAIRS RAT SOCIAL INTERACTION IN A SEX-DEPENDENT MANNER**

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Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), has been approved to treat major depressive and obsessive-compulsive disorders in pediatric patients along with some off-label uses. Several concerns were raised when it was determined that Fluoxetine could lead children to suicidal thoughts and behaviors. Although well characterized for adults, little is known about the effect of Fluoxetine on pediatric patients. The aim of this work was to evaluate the effect of early exposure to Fluoxetine on social interaction, stereotypical and exploratory activities, and anxiety. Male and female Wistar rats were daily administrated (sc.) with Fluoxetine (10 mg/kg) or saline between postnatal days (PND) 16-35 and behaviorally evaluated at PND 30-35. Concerning social behavior, Fluoxetine treatment in males dramatically reduced social play behavior measured as the number of pinnings and social preference evaluated in a three-chamber task. On the contrary, Fluoxetine did not modify these behaviors in females. Also, only in male, Fluoxetine treatment increased stereotypical behaviors measured as the number of self-grooming events and enhanced anxiety-like behavior indicated by a reduction in the time spent in the open arms of an elevated plus-maze. Notably, while in males Fluoxetine treatment did not affect exploratory activity, in females it decreased the number of hole-pokings. Regardless of sex, Fluoxetine treatment did not modify locomotor activity and increased serotonin immunoreactivity in the hippocampus These results strongly indicate that pre-puberal rat exposure to Fluoxetine targets social interaction, exploration, stereotypical and anxiety-like behaviors in a sex-dependent manner. Our results also highlight male vulnerability to modulation of serotonin levels during infancy and pre-puberty.

214. (320) **MILD VPA BEHAVIORAL PHENOTYPE IN FEMALE RATS: EVIDENCE OF STRUCTURAL SYNAPSE REMODELING IN THE MEDIAL PREFRONTAL CORTEX AND THE HIPPOCAMPUS**

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Autism spectrum disorders (ASD) are a group of severe neurodevelopmental disabilities of unknown etiology, characterized by social interaction deficits and increased stereotyped behaviors. Although ASD incidence is four times higher in boys than in girls, sex differences have not been clarified. The rat model of autism induced by prenatal exposure to valproic acid (VPA) has been characterized in males (MVPA), while female rat VPA (FVPA) phenotype is still controversial. The aim of this work was to further characterize the behavioral profile of FVPA and explore structural synapse markers, cell adhesion molecules and microglia morphology in the medial prefrontal cortex (mPFC) and the hippocampus. At early postnatal days (PND)7-15, and similar to MVPA, FVPA showed growth and maturation deficits: delayed eye opening, lower body weight, altered negative geotaxis, higher latencies to nest seeking response and a deficit in swimming performance. At PND30-35, like MVPA, FVPA showed a reduced number of interactions in the social play behavior test, but they exhibited distinctive pinning features. Contrary to MVPA that showed an exploratory deficit and increased stereotypical activities, FVPA matched control female rat behavior. Notably, at PND35, mPFC of FVPA and MVPA showed an increase in synaptophysin (SYN) and neural cell adhesion molecule (NCAM) and a similar ramified/unramified microglia (Iba+) ratio. However, the polysialylated form of NCAM (PSA-NCAM) was increased in FVPA but decreased in MVPA. In the hippocampus, both FVPA and MVPA showed reduced SYN labeling and increased NCAM but only FVPA displayed a higher proportion of unramified microglia. Also, PSA-NCAM levels were preserved in FVPA but reduced in MVPA. To sum up, FVPA exhibit a mild behavioral phenotype accompanied with a distinctive microglia profile and NCAM/PSA-NCAM ratio that may facilitate structural synapse remodeling and plasticity.

215. (411) **$GABA_A$ RECEPTOR MODULATION BY KETONE BODIES**

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Ketone bodies are produced from the β-oxidation of fatty acids during ketogenesis. In humans, acetyl-CoA is the end product of fatty acid catabolism. Three types of ketone bodies can be synthesized from acetyl-CoA: acetone, β-hydroxybutyrate and acetoacetate. Ketogenesis is increased under conditions of low glucose (eg, fasting), low insulin or excessive alcohol consumption. This increase also occurs during certain diets, with low carbohydrate and high fat consumption, indicated to reduce the probability of seizures in epileptic patients or to alleviate the alcohol withdrawal syndrome. Additional beneficial effects of ketogenic diets have been described in models of Alzheimer's disease and amyotrophic lateral sclerosis. The actions of ketone bodies on neurotransmission have been poorly explored and the mechanisms responsible for the therapeutic benefits of ketogenic diets remain under study.
Recently Pflanz et al. (2019) studied for the first time the effects of ketone bodies on ligand-activated ion channels and described acetone as a positive modulator and β-hydroxybutyrate as a negative modulator of GABAAα1β2γ2 receptors. In this context, we studied the modulatory effects of ketone bodies on GABAergic neurotransmission, evaluating the sensitivity of different subtypes of GABAA phasic and tonic receptors. Human $GABA_A$ρ1, $GABA_A$α1β2, $GABA_A$α5β3 y $GABA_A$α4β3δ were expressed in *Xenopus laevis* oocytes and chloride currents were recorded by two-electrode voltage-clamp. Results with acetone (100 to 300 mM) showed inhibitory effects on GABAAρ1 and potentiating effects on GABAAα1β2, GABAAα5β3 and GABAAα4β3δ responses (~EC10). Acetone effects on oocytes baseline were controlled in every experiment. Further experiments will be carried out to characterize acetone modulation and evaluate β-hydroxybutyrate effects on these receptors.

216. (413) **METABOLISM AND EFFECTS OF TESTOSTERONE IN THE SPINAL CORD FROM WOBBLER-ALS MICE AFTER TREATMENT WITH EXOGENOUS TESTOSTERONE**

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Amyotrophic lateral sclerosis (ALS) patients present motoneuron degeneration leading to muscle atrophy, dysphagia and dysarthria. The Wobbler (WR)-ALS mice, a recognized model of this disease, shows a selective loss of motoneurons, astrocytosis and