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Microglia were immunolabeled for Iba1 to study morphology under basal conditions and after exposure either to a pro-inflammatory (lipopolysaccharide) or a phagocytic (synaptosomes) stimulus. While cortical microglia from male VPA animals showed a pro-inflammatory profile and an intrinsic resistance to phagocytic stimuli, hippocampal microglia from male VPA animals matched microglia from controls under basal condition and showed a preserved response to pro-inflammatory and phagocytic stimuli. In the case of microglia isolated from females, both cortical and hippocampal microglia from VPA rats evidenced morphological changes under basal conditions but both were able to respond to pro-inflammatory and phagocytic stimuli. To sum up, microglia from male and female VPA rats show sex-dependent changes which may contribute to sex-differences in ASD.

**405.** (256) **A DEFICITARY MODEL OF CDK5 DOES NOT IMPAIRS NEURONAL DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELLS**

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CDK5/P35 is a complex involved in neuronal homeostasis and development that was described as a critical player for neuronal survival. Besides, its deregulation is linked with neurodegenerative pathologies such as Alzheimer Disease and Parkinson Disease. For that reason, we generated a deficitary CDK5 genetic model in neurons derived from human pluripotent stem cells. For this purpose, we used CRISPR/Cas9 technology to generate human embryonic and induced pluripotent stem cells (hESCs and hiPSCs, respectively) KO-CDK5 lines. CDK5 protein expression levels were analyzed by western blot in samples obtained from clones where indels caused by CRISPR/Cas9 editing were detected by DNA sequencing. We obtained CDK5-/- clones for H9 hESCs and FN2.1 hiPSCs lines and a CDK5+/- clone for H9 hESCs line. Then, neural stem cells (NSC) were derived from the CDK5 KO clones using a commercial neural induction medium and their phenotype was validated by immunofluorescence staining using antibodies that recognize specific lineage markers (SOX-1, SOX-2, NESTIN and PAX-6). Finally, NSC obtained from the heterozygous CDK5+/- KO H9 hESCs clone were differentiated into neurons using a 2D-based protocol and their phenotype was validated by immunofluorescence staining of neuronal specific markers (TUJ-1 and MAP2). In conclusion, we managed to obtain NSC-neurons from CDK5-/- and CDK5+/- clones, determining that CDK5 is not essential for NSC generation. Besides, neuronal differentiation was achieved for H9 CDK5+/- clone, indicating that the CDK5 deficiency does not impair the generation of NSC-derived neurons. This result allows us to account with a CDK5-deficient model to further study its participation in neuronal homeostasis dysfunctions.

**406.** (266) **ASTROCYTIC INSULIN SIGNALING AND INFLAMMATION IN EXPERIMENTAL ALZHEIMER'S DISEASE**

Melisa Bentivegna[1,2]; Amal Gregosa[1,2], Soledad Rossi[1], Ángeles Vinuesa[1,2]; María Marta Bonaventura[1], Carlos Javier Pomilio[1,2] Jessica Presa[1,2]; Victoria Lux[1], Flavia Eugenia Saravia[1,2]; Juan Beauquis[1,2]
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Insulin resistance (IR) and chronic inflammation are associated with the development of cognitive disorders and neurodegenerative diseases such as Alzheimer's (AD). However, it is not clear whether there is a causal link between these factors, which one appears earlier in the pathology or if either one of them is triggered by the increasing circulating levels of Aβ or amyloid deposits in early AD. Our objective was to study the metabolic and inflammatory status of a model of AD, the PDAPP-J20 mouse at the age of 8 months. We also treated a WT group with a high fat diet (HFD) as a positive control for IR. Our hypothesis was that in early stages of AD, the brain develops IR with astrocytes showing reactivity and impaired insulin signaling. Final body weight, glycemia and insulinemia were not affected by genotype or HFD. The open-field test showed an anxious-like behavior in transgenic and in HFD-fed mice. Insulin signaling measured by pAkt/Akt ratio was decreased in the hippocampus of AD mice ($p<0.05$) but not in the hypothalamus or the liver. Pancreatic IL1β and COX2 levels were unchanged. Insulin receptor puncta colocalizing with GFAP+ cells in the hippocampus by fluorescent immunolabeling showed a decreasing tendency in transgenic animals while astrocytic reactivity markers GFAP and S100b were increased ($p<0.05$). Finally, we evaluated the effect of fibrillar Aβ or palmitate on C6 astrocytes in vitro. Astrocytes exposed to Aβ showed increased nuclear translocation of NFkB and decreased AKT phosphorylation ($p<0.05$), suggesting inflammatory activation and impaired insulin signaling, respectively. Our results show that inflammation and insulin signaling impairment in the hippocampus are found in an early stage of experimental AD. The inflammatory context triggered by increased circulating Aβ or amyloid deposits in the brain could affect astrocytic insulin receptors, hence decreasing insulin signaling and affecting their neuroprotective capacity.

**407.** (267) **DIETARY RESTRICTION AS A FASTING MIMETIC IN AGED MICE. METABOLIC, COGNITIVE, AND NEUROINFLAMMATORY EVALUATION.**

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Aging is a physiological process that involves cognitive decline, decreased autophagic flux, and increased oxidative stress. Dietary restriction is a multitarget strategy that has been linked to several benefits, inducing autophagy flux, decreasing oxidative stress and inflammation, and improving metabolism. These effects establish dietary restriction as a possible approach to delay physiological aging and to prevent or treat aging-related diseases. In a previous work, we evaluated a protocol of periodic dietary restriction (PDR) in an animal model of familial Alzheimer's disease. Now, we have studied the effects of this strategy on aged female mice (16 month-old), evaluating metabolic, cognitive, and neuroinflammatory changes.
PDR involved 5 days of dietary restriction (DR) alternated with 9 days of ad libitum (AL) food intake for 7 weeks. During the DR period, mice ate 60% of their habitual intake.
Animals under PDR showed similar body weight and glycemia to AL mice. During DR periods, circulating ketone bodies increased (1WAnova-Sidak, basal vs DR $p<0.001$) suggesting a fasting-like effect. Additionally, we evaluated cognitive performance by the novel object location recognition test. No changes were observed between AL and DR animals, but both groups' performance was worse than that of 5 month-old mice, evidencing an age-related cognitive decline. We assayed S100b/GFAP by immunofluorescence in the hippocampus and analyzed morphological astrocytic parameters. S100b, an astrocytic pro-inflammatory marker, was diminished in DR mice (vs AL). However, GFAP immunoreactivity was unchanged. These preliminary results evidenced fasting-like effects in mice exposed to DR. Further, cognitive impairment in aged mice was corroborated, and a possible modulation of the pro-inflammatory S100b with DR. Future perspectives point to evaluating glial morphology in depth, and autophagy as a possible main mechanism for DR.

**408.** (268) **ADMINISTRATION OF ANASTRAZOLE, AN AROMATASE INHIBITOR, REDUCES THE PROTECTIVE EFFECTS OF TESTOSTERONE TREATMENT IN AN ANIMAL MODEL OF AMYOTROPHIC LATERAL SCLEROSIS**

Esperante Iván[1], Meyer María[1], Lara Agustina[1], Lima Analia.[1], Roig Paulina[1], De Nicola Alejandro Federico[1,2b] and Gonzalez Deniselle María Claudia[1,2a]
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Amyotrophic lateral sclerosis (ALS) is characterized by progressive degeneration of upper and lower motoneurons leading to muscle weakness and motor impairment. The Wobbler (WR) mouse, a recognized model of ALS, shows a selective loss of motoneurons, astrocytosis and microgliosis in cervical spinal cord (CSC). ALS presents in men at younger ages than women, but increases after menopause. Testosterone (T) exerts its effects via androgen (AR), or estrogen receptors after bioconversion into several metabolites. Previous work has shown that T reduces gliosis and improves clinical score in male WRs. Now, we investigated the effects of cotreatment of T + anastrazole, an aromatase inhibitor (AI), on: 1) mRNA expression of myelin oligodendrocyte glycoprotein (MOG) and proteolipid protein (PLP)- 2) CD11B mRNA, a marker of microglia, 3) % AR-immunoreactive (IR) cells in ventral horn. T was implanted in 10mm silastic tubes for 2 months. AI was given in DMSO 10% by Alzet osmotic pumps (1mg/kg/day) s.c. starting 1 week before T. Four groups were prepared: a) WRs or (b) controls receiving empty silastic tubes + vehicle-pumps, c) WR+T (silastic tubes filled with T) + vehicle-pumps and d) WR+T+AI. Pituitary weight, a gland sensitive to estradiol, is greater in WRs ($p<0.05$ vs. control) and smaller in WR+T+AI ($p<0.05$ vs WR). MOG mRNA rose in WR+T ($p<0.05$ vs WR) but not PLP. However, both myelin genes were significantly reduced in WR+T+AI ($p <0.01$ vs. WR+T). CD11B was reduced by T in WRs ($p<0.05$ vs. WR), but WRs and WR+T+AI showed higher expression ($p<0.05$ vs. controls or WR+T). The % AR-IR cells were low in WRs and WRs+T+AI ($p<0.01$ vs. controls), but increased in WR+T ($p<0.01$ vs WR). The mRNA for the steroidogenic acute regulatory protein (StAR) increased in WRs ($p<0.05$ vs control) and was still higher in WR+T and WR+T+AI ($p <0.05$; $p <0.01$ vs WRs). These data support that estrogen-derived aromatase may play a role in androgen neuroprotection.

**409.** (271) **SHORT AND LONG-TERM ASSESSMENT OF NOISE EXPOSURE ON HIPPOCAMPAL OXIDATIVE STRESS IN ADOLESCENT FEMALE AND MALE RATS**

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Previous studies from our laboratory have shown that noise exposure was able to trigger behavioral and neurochemical alterations in the Central Nervous System (CNS) of adolescent male rats when evaluated at short-term, whereas results in females have not been obtained yet. In addition, long-term measurements have not been performed. Therefore, the aim of the present work was to investigate the effects of noise exposure in the hippocampus (HC) of adolescent female and male rats on biochemical parameters evaluated at short and long-term. Male and females PND28 Wistar rats were separated into different cages and at PND 33 a subgroup was exposed to noise (2h, 95-97 dB). HC was dissected at short (PND 33) and long-term (PND 39) to assess reactive oxygen species (ROS) levels and catalase activity (CAT). Results showed an increase in ROS levels in females (sham: 0.004±0.001; noise: 0.123±0.005) and males (sham: 0.019±0.004; noise: 0.054±0.003) and an increase in CAT activity only in males (sham: 0.0004±0,0002 noise: 0.001±0.0001) when evaluated at short term. In contrast, long-term results showed a decrease in CAT activity in females (sham: 0.001±0.0004; noise: 0.0003±0.0007), whereas no significant differences were found in males. No differences were found in either group in ROS levels. These results suggest that noise exposure may induce short-term changes in oxidative markers that seem to disappear at long-term and to be sex-specific. In conclusion, adolescence seems to be a period of vulnerability to different stimuli capable of generating oxidative imbalance in the hippocampus, which could underlie some of the behavioral changes previously observed.

**410.** (276) **INFLUENCE OF PERSONALITY TRAITS, ALCOHOL EXPECTANCIES AND COVID-19 LOCKDOWN ON ALCOHOL CONSUMPTION IN STUDENTS OF THE UNIVERSITY OF BUENOS AIRES**

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University students (US) often consume alcohol for recreational purposes being exposed to various negative consequences that this substance produces. Different factors have been associated with increased alcohol consumption (AC), such as personality, alcohol expectancies and social isolation (e.g. COVID-19 lockdown). Thus, the aim of this work was to evaluate the AC pattern and the potential influence of personality, alcohol expectancies and lockdown in students from the University of Buenos Aires.
A sample of 1776 US completed an online survey that assessed the amount and frequency of AC before and during the first year of COVID-19 pandemic. In addition, US responded to the BIG-5 and CEA-A questionnaires to assess personality traits and alcohol expectancies.
Results showed that students' AC was highly prevalent both before and during the lockdown. In addition, men consumed significantly more alcohol than women per occasion ($F1,3523=12.83$) and month ($F1,3523=21.10$), but women had more episodes of heavy drinking ($\chi2=40.68$). When comparing both time periods, the amount and frequency of AC decreased during lockdown (F3,3523= 36,67 and F3,3523= 14,15). Moreover, positive and significant correlations were observed between AC and personality traits such as agreeableness (rs= 0.08 to 0.11) and responsibility (rs=
0.06 to 0.13) in women, and extraversion (rs= 0.13) and agreeableness (rs= 0.16 to 0.21) in men. Finally, results showed positive and significant correlations between AC and all alcohol expectancies evaluated (positive and negative), in both sexes (rs= 0.11 to 0.37).
In conclusion, this study suggests that AC is highly prevalent in US, which is worrying given the negative consequences associated with it. Furthermore, factors such as personality and alcohol expectancies could promote AC, whereas lockdown decreased it. Finally, the knowledge about risk and protective factors for AC is important for the development of interventions aimed at preventing and reducing AC.

**411.** (282) **ASSOCIATION OF FOLATE PRODUCTION AND IMMUNE MODULATION BY SELECETED BACTERIA IN PARKINSON'S DISEASE MODELS**

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Parkinson's disease (PD) is a neurodegenerative process that affect motor functions and involves an inflammatory response and B group vitamins' deficiency. Folate depletion with hyperhomocysteinemia are related with immune activation; however, the association between folate (vitamin B9) and the immune system in PD requires further research. Aim: To evaluate the effect of folate-producing and immunomodulatory lactic acid bacteria (LAB) in PD models. Methods: *Streptococcus thermophilus* (*St.*) CRL808 (folate producer