strain), and *St.* CRL807 (immunomodulatory strain) were evaluated individually using *in vitro* and *in vivo* PD models. N2a neuronal cells were differentiated to dopaminergic neurons with di-butyryl cyclic AMP and then exposed to the neurotoxin 1-methyl-4-phenylpyridinium (MPP+) in presence of intracellular extracts from LAB or the commercial vitamin B9. Cell viability, IL-6 production and reactive oxygen species (ROS) were determined. *In vivo*, LAB were administered to mice injected with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Motor capacity, tyrosine hydroxylase (TH) in brain, and cytokines in serum were evaluated. Results: Neurotoxic effect of MPP+ decreased in cells cultured with both LAB intracellular extracts. This result was related with significant ($p<0.05$) decrease of ROS formation and IL-6 release by the neurons. Mice given LAB improved motor skills altered by MPTP and significantly ($p<0.05$) increased the number of TH+ neurons in the brain. The LAB effect was associated to decreased pro-inflammatory cytokines such as IL-6 and TNF-alpha and increased levels of IL-10 in the serum of the mice. Conclusions: LAB selected as folate producers and as immunomodulators have the potential to be used as adjuvants in PD, improving both vitamin deficiency and the inflammatory state associated with this pathology, which translates into less loss of dopaminergic neurons and better motor skills.

412. (290) **GLUN2A REDUCED EXPRESSION CHANGES MOLECULAR COMPOSITION AND STRUCTURE OF SYNAPSES WHICH WOULD BE RELATED TO CERTAIN TYPES OF EPILEPSIES**

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For several years, NMDA receptors (NMDAR) have been involved in memory and learning processes as well as in a wide range of neurodevelopmental disorders, as epilepsies. NMDAR are heterotetramers composed by two GluN1 obligatory subunits and two regulatory subunits, being GluN2A and GluN2B the most expressed in hippocampus and other cognitive related structures. During development and synaptic maturation, there is a shift in GluN2A/GluN2B expression ratio. This change was called the developmental switch and modifications in this relationship were associated to learning and memory as well as to different pathologies. Recently, grin2a (the gene that codifies for GluN2A) mutations were related to complex syndromes that include the development of seizures and or epilepsy. In this work, we induced a knockdown in GluN2A expression (GluN2A-KD) after developmental switch *in vitro* and *in vivo*. Results showed that NMDAR total amount and GluN2A/GluN2B ratio was decreased in GLuN2A- KD cultures. Moreover, downregulation of GluN2A *in vitro* increased dendritic branching and the number of dendritic spines, which in consequence, rise neuronal excitability. On the other hand, in vivo, GluN2A silenced expression in hippocampus, induced an impairment in contextual fear conditioning memory and a change in spatial-exploration. In addition, rats where GluN2A hippocampal expression were silenced, showed increased seizure susceptibility, both in time and intensity. Altogether, these results led us to conclude that the decrease in GluN2A expression would be related to epileptogenic mechanisms.

413. (367) **GLATIRAMER ACETATE REVERTED CHRONIC STRESS-INDUCED ALTERATIONS IN BEHAVIOUR, REGULATORY T CELLS IN SPLEEN AND TGF-β LEVELS IN HIPPOCMPUS OF BALB/C MICE**

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In previous reports we found that chronic mild stress (CMS) exposure induces a decrease in learning and memory in female BALB/c mice. This cognitive deficit correlated with a decrease in CD4+CD25+FOXP3+ and an increase in CD4+CD25-FOXP3+ regulatory T cells (Tregs) in CMS mice spleen. No differences in the CD4+CD25+FOXP3+ and CD4+CD25-FOXP3+ Tregs were found in lymph nodes in stressed mice. Tregs have an important role in maintaining self-tolerance through the inhibition of effector T cells. The main cytokines involved in this mechanism are IL- 10 and TGF-β, both released by Treg cells. Moreover, glatiramer acetate (GA) (synthetic amino acid polymer that can safely simulate the protective and reparative effects of autoreactive T cells) reverted the behavior and the neuroimmune alterations induced by CMS. In this context, the aim of this work was to evaluate the GA effect on the Treg cells in spleen and ARNm levels of TGF-β and IL-10 in hippocampus of CMS mice. Here, we show that CMS mice presented a poor learning performance in Y-maze and open field test. The Treg were evaluated by flow cytometry. The decrease of CD4+CD25+FoxP3+ (control-PBS vs. CMS-PBS: $p<0.05$) and the increase of CD4+CD25-FoxP3+ (control-PBS vs. CMS-PBS: $p<0.01$) cells in spleen of CMS mice were reverted by GA treatment (CMS-PBS vs. CMS-GA: $p<0.05$ and CD4+CD25-FoxP3+= CMS-PBS vs. CMS-GA: $p<0.01$, respectively). The mRNA expression by qRT-PCR indicated an increase in the mRNA levels of TGF-β in hippocampus in CMS mice respect to control mice ($p<0.05$). This levels were reverted by GA in CMS mice ($p<0.05$). No differences in the mRNA levels of IL-10 were found in hippocampus of stressed mice. Our findings indicate that GA revert the chronic stress effects on the immune system through a mechanism that involves Treg cells possibly by the release of TGF-β. This suggests Treg cells participation in the cognitive deficit observed in chronic stressed female mice and this can be reverted by GA.

414. (393) **REGIONAL DIFFERENTIAL EFFECTS OF HORMONE-REPLACEMENT TREATMENTS ON MITOCHONDRIAL DNA REPAIR MECHANISM ARE NOT EXERTED THROUGH GENE EXPRESSION REGULATION IN THE BRAIN**

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The brain is highly susceptible to mitochondria dysfunction and oxidative stress due to its high demand of energy and low antioxidant capacity. Mitochondrial DNA (mtDNA) is specially vulnerable to oxidative damage and Base Excision Repair (BER) is the main mtDNA repair mechanism. Ovarian hormone loss during natural or induced reproductive senescence is associated with mitochondrial alterations, synaptic decline and increased risk of age-related diseases. The aim of this work was to assess whether hormone-replacement treatments affect the expression of BER enzymes to explain previous results regarding the differential activity of such enzymes in the hippocampus (Hp) and cerebral cortex (Cc) of hormone-treated ovariectomized (OVX) rats.

To this aim, adult OVX or sham-operated (SHAM) rats were s.c. with empty or containing estradiol (E) and/or progesterone (P) silastic capsules. After 12 weeks, cDNA was obtained from total RNA extracted from the Hp and Cc and amplified by qPCR using specific primers for BER enzymes.

The expression of DNA glycosylases was either lower o similar to SHAM group in both Hp and Cc of OVX rats (NEIL1 $p<0,01$; NEIL2 $p<0,05$; UNG1 $p<0,01$; OGG1 ns; Student´s t test). Similar results were obtained for the rest of the enzymes of the pathway (AP endonuclease1, γ-polymerase and lygase3 $p<0,05$, Student´s t test). Hormone treatments did not affect the expression of OGG1, NEIL2 or UNG1 in any brain region, but increased the expression of NEIL1 only in the Hp (E+P $p<0,05$; ANOVA). On the other hand, P alone or combined with E, increased the expression of the rest of the enzymes of the pathway in both brain regions ($p<0,05$; ANOVA).

Our results show that OVX decreases the expression of BER en-

zymes in both brain regions and that there is no association between ARNm levels and the activity of such enzymes in hormone-treated rats. Thus, hormones exert their regional differential action on BER pathway through a mechanism not involving gene regulation.

415. (397) **METFORMIN TREATMENT IS ASSOCIATED WITH IMPROVED COGNITION AND REDUCED PATHOLOGICAL BIOMARKERS IN DIABETIC PATIENTS WITH PRODROMIC ALZHEIMER'S DISEASE ENROLLED IN THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI) STUDY**

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Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive cognitive decline, with no effective treatment available to this day. AD hallmarks include aberrant Amyloid-β and Tau accumulation in the brain, the presence of chronic neuroinflammation and alterations in brain metabolism. Evidence suggest a possible shared pathophysiology between Type 2 Diabetes Mellitus (T2D) and AD, as impaired insulin signaling. Some therapeutic strategies employed on T2D subjects could be beneficial on AD patients. Here, we evaluated the effect of the antidiabetic drug metformin on patients enrolled in ADNI, an observational and longitudinal study including patients from all around the world. We employed data from patients diagnosed with mild cognitive impairment (MCI) due to AD and we performed a principal component analysis focusing on biomarkers associated to AD measured in cerebrospinal fluid (CSF). We concluded that MCI metformin-treated patients were globally characterized as subjects with a better CSF biomarkers profile than the mean population of MCI patients ($p<0.05$). On the other hand, control subjects and T2D patients were paired by age, gender, ApoE allele and years of education, defining three groups: MCI, MCI+T2D and MCI+T2D+metformin. We evaluated the effect of T2D and metformin treatment employing the PACC score, and composites defined from standardized ADNI variables to evaluate the memory and learning function. We found that MCI+T2D patients have a worse cognitive performance than MCI patients ($p<0.01$), but this deleterious effect was not observed in MCI+T2D+metformin patients. These cognitive variations were associated with changes in cortical thickness and hippocampal volume obtained from Magnetic Resonance Images ($p<0.001$). To summary, our study shows a beneficial effect of metformin treatment on cognitive performance, CSF biomarkers profile and neuroanatomical measures in MCI due to AD patients.

416. (419) **PLASMA BIOMARKERS FOR THE EARLY DETECTION OF ALZHEIMER'S DISEASE USING A MACHINE LEARNING BASED LOGISTIC REGRESSION MODEL**

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Alzheimer's Disease (AD) is the most common type of dementia. Clinical and basic research hope for early interventions to cure or stop the progression of the disease. However, patients seeking help mostly present mild to advanced cognitive decline. While it would be helpful to look for early signs of AD, specific tests are not routinely done and present elevated costs. Notably, evidence shows that blood biomarkers are altered through the progression of the disease. Here, we used patients' plasma biomarkers data available from Alzheimer's Disease Neuroimaging Initiative (ADNI) from healthy controls (HC), patients with mild cognitive impairment (MCI) and AD to develop an automated classifier. The total of patients selected was 544 (55 HC, 379 MCI, 110 AD) all having associated demographic and cognitive information. We used a total of 146 routine blood tests results, such as transferrin and CRP, and did not include AB, Tau of=r pTau.
There was no difference in representativity of females, age, education level or ethnia between groups. We separated the data into a train set and a hold-out set. We performed cross validation with the train sets with 5 folds and a grid search for hyper parameters optimization to train a logistic regression model. Employing the train set, our model presented a ROC curve with an AUC for HC prediction of 0.86, MCI
0.81 and AD 0.79. When tested with the hold-out, the AUC of the ROC curves were HC: 0.81, MCI: 0.77 and AD: 0.77. Only 2% of MCI patients were misclassified as HC, and none AD patient was classified in the HC group. Feature importance analysis showed pregnancy associated plasma protein as the most relevant parameter, in accordance with literature. While the number of patients between groups is unbalanced, our classifier has a very good predictive power and successfully minimizes type 2 errors. In the future, it would be important to increase the number of subjects to train and test the model with balanced groups.

417. (424) **MYELINATION PROCESS DURING THE EMBRYOGENESIS OF *LAGOSTOMUS MAXIMUS*, A PRECOCIAL RODENT**

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Myelin is a protein synthesized by oligodendrocytes forming a multilaminar membrane around the axons of the CNS. This membrane acts as an insulator increasing the speed of stimulus transmission. Myelination is a continuous process that begins when axons reach a diameter of approximately 1 μm and follows a structural sequence with a caudo-rostral, dorso-ventral and center-to-periphery progression which varies between species. The aim of this study was to analyze the myelination process during the embryogenesis of the South America plains vizcacha, *Lagostomus maximus*, an hystricomorph rodent native from Argentina, and to compare it with this process in rat, mouse and guinea pig. Brains of 24 embryos, distributed between 51 embryonic days (e.d.) and 2 days postnatal, were used and studied by Klüver-Barrera histological technique. The onset of the myelination process was observed around mid-pregnancy. Inside the brain, the myelination process began around 72 e.d. up to 118 e.d. in the cortex; at the same time, the myelination extended towards connection fibers beginning in the external cingulate at 106 e.d. and gradually progressing towards the internal cingulate from 112 e.d. onwards. At 124 e.d., the internal and external capsule, and optic chiasm were myelinated. After that, striosomes of the corpus striatum and the fornix columns were myelinated at 133 e.d. At birth time (155 e.d.), all the intra-hemispheric white matter structures were myelinated, but the inter-hemispheric connections of the corpus callosum and the anterior commissure were not myelinated yet. These results show that both the onset of the myelination process and its progression during embryonic development are framed in the precocial character of *L. maximus.* The onset of this process in vizcacha agreed with that in guinea pig, and was in contrast to the postnatal onset in rat and mouse. Grant: Fundación Científica Felipe Fiorellino.

418. (428) **EVALUATION OF CIRCULATING MONOCYTES AND PROINFLAMMATORY CYTOKINES IN PATIENTS WITH MOOD DISORDERS**

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