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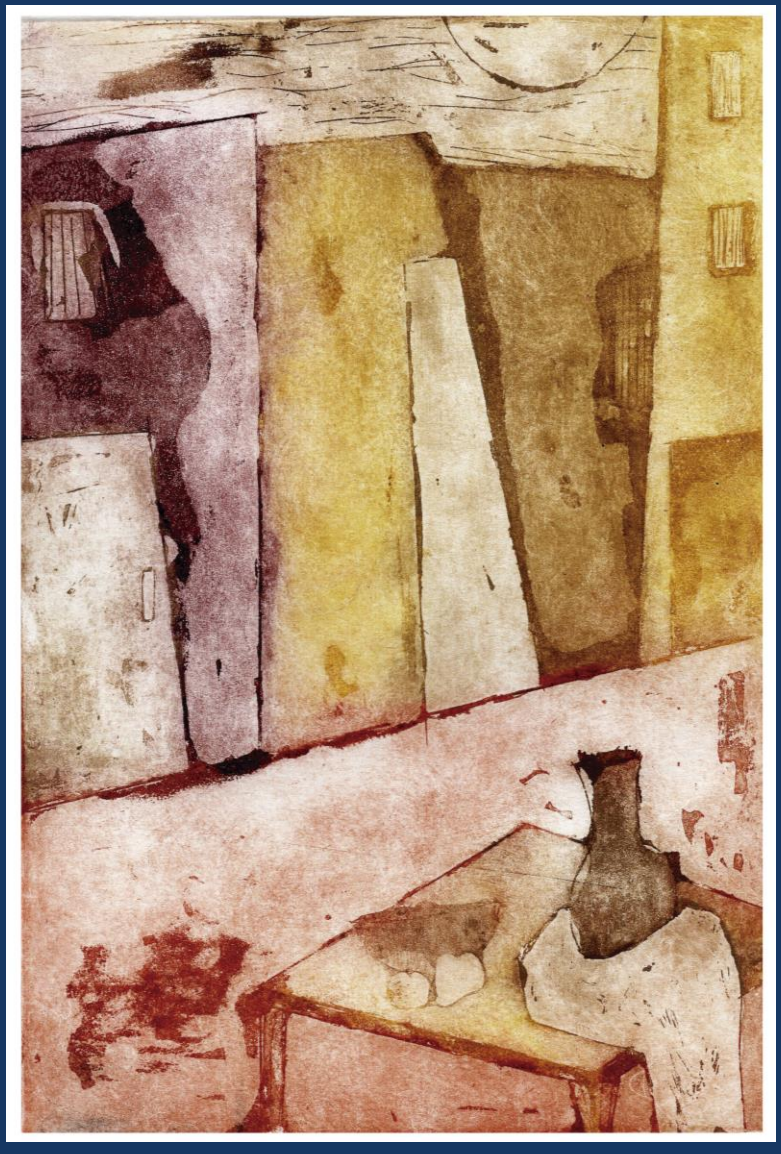

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con la participación de
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neovascularization promoting factor VEGF increased in MGs under HG ($p<0.01$) and reverted to control values when SIRT6 was overexpressed. Furthermore, SIRT6 silencing resulted in the increment of VEGF levels supporting the idea of SIRT6 as a direct modulator of this factor. We also found that HG induced a decrease in the neural factor BDNF levels while this effect was reverted in SIRT6 overexpressing MGs. However, BDNF levels did not show variations in SIRT6 siRNA expressing cells compared to controls. Moreover, and in accordance to our previous findings in diabetic animals, retinas from mice with conditional deletion of SIRT6 in the CNS exhibited increased levels of VEGF and lower levels of BDNF than WT ($p<0.01$). Our results suggest that HG would induce a neurodegenerative response in MGs that would be epigenetically regulated by SIRT6.

0360 - MUSCLE TROPHISM AFTER TESTOSTERONE TREATMENT IN THE WOBBLER MOUSE, AN SPONTANEOUS MODEL FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS).

Iván José ESPERANTE (1) | Agustina LARA(1) | Maria MEYER(1) | Laura GARAY(2) | Federico DE NICOLA(3) | Ignacio JURE(1) | Analia LIMA(1) | Paulina ROIG(1) | Alejandro F DE NICOLA(2) | Deniselle Maria GONZALEZ(4)

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Patients suffering amyotrophic lateral sclerosis (ALS) present muscle atrophy in upper and lower limbs and difficulties in swallowing and dysarthria in association to motoneuron degeneration. Wobbler mice (WR) are animal models of ALS showing selective loss of motoneurons, astrocytosis and microgliosis in the ventral horn of the cervical spinal cord, brain stem and motor cortex. The incidence of ALS is greater in men than in fertile women; however, it increases after menopause. Therefore, sex steroid hormones could be involved in disease susceptibility or outcome. Previously, we demonstrated that testosterone treatment to WRs reduced astrocytosis and increased glutamine synthetase immunoreactivity, an enzyme necessary for maintaining glutamate concentration in synaptic cleft. Now, we investigated the effect of testosterone treatment on myelination and muscle trophism. Treatment consisted of 10 mm silastic tubes containing crystalline testosterone s.c. for 2 months to male symptomatic WR. Non-treated WR or control received an empty silastic tube s.c. Testosterone serum levels and seminal vesicles weight were significantly higher in testosterone-treated WRs compared to empty silastic-treated WRs ($p<0.01$). Luxol fast blue (LFB) staining was used to identify myelin. We quantified the % of area stained over a threshold in white matter of the cervical cord. Significant group differences were shown by ANOVA ($F(3,16)= 29.86$, $p<0.001$) in the % of stained area for LFB in the ventro-lateral funiculus (VLF). Lower LFB staining was shown in WRs (mean ± SEM-WR: 27.56 ± 5.57 vs. control: 87.40 ± 0.92; $p<0.001$), while higher values were demonstrated after testosterone treatment (WR+testosterone: 41.94 ± 5.62 vs. WR, $p<0.05$). As regards to biceps muscle mass, one way ANOVA also indicated significant group differences ($F(3,24)= 7.55$, $p<0.01$). WRs showed biceps atrophy (WRs: 0.62 ± 0.08 mg/g body weight vs. controls: 0.86 ± 0.04, $p<0.05$). However, greater mass was shown in testosterone-treated WRs in comparison to empty silastic-treated WRs (WR+testosterone: 1.05 ± 0.08, $p<0.01$ vs. WR). No effect of testosterone treatment was found in controls. These preliminary data showed protective effects of testosterone in motoneuron degeneration.

0368 - REGION-SPECIFIC ASTROCYTES EXERT DIFFERENTIAL NEUROPROTECTION IN AN IN VITRO MODEL OF HUNTINGTON'S DISEASE

Julieta SABA | Federico LÓPEZ COUSELO | Juan TURATI | Lila CARNIGLIA | Daniela DURAND | Mercedes LASAGA | Carla CARUSO

INBIOMED- INSTITUTO DE INVESTIGACIONES BIOMÉDICAS. UBA-CONICET

Evidence shows that there is significant heterogeneity in astrocytes, as regards morphology, gene expression and function. In this work we investigated the action of astrocytes from two areas involved in Huntington`s disease (HD): the striatum and the cortex. We have previously demonstrated that BDNF exert protective and antioxidant effects on astrocytes treated with 3-nitropropionic acid (3-NP) a toxin widely used to model HD in vitro. First, we determined TrkB expression and ERK activation in cortical and striatal cultured primary rat astrocytes treated with BDNF (50 ng/ml) + 3-NP (15 mM) for 24 h. We showed before that cultured astrocytes do not express TrkB-full length (TrkB-FL) protein; therefore TrkB-truncated (T1) isoform expression was assessed by Western blot. In cortical and striatal astrocytes BDNF and BDNF+3-NP increased protein expression of TrkB-T1 expression ($p<0.001$). 3-NP alone did not modify protein levels of this receptor. Also, in cortical and striatal astrocytes BDNF increased levels of pERK while 3-NP per se decreased them compared to control group ($p<0.05$). In astrocytes treated with BDNF+3-NP, ERK activation was also increased ($p<0.001$). To study neuroprotection, we used cortical and striatal astrocyte conditioned medium (ACM) to treat ST14A-Q120 cells, a cell line derived from embryonic rat striatal cells which express the N-terminal fragment of mutant human Htt with a 120 glutamine region (120 CAG repeats). ACM from striatal astrocytes treated with BDNF protected ST14aA-Q120 from 3-NP induced death ($p<0.001$), whereas ACM from treated BDNF cortical astrocytes did not modify 3-NP effect on ST14A-Q120 cells. These data suggest that striatal treated astrocytes with BDNF secrete soluble neuroprotective factors. Furthermore, only ACM from 3-NP+BDNF treated striatal astrocytes increased viability of ST14A-Q120 cells compared to ACM-3-NP. A better understanding of astrocytes heterogeneity would help elucidate astrocyte functions and how their malfunction contributes to neurodegenerative diseases.

0387 - STUDY OF NEUROPROTECTIVE FACTORS MEDIATED BY OMEGA 3 AND COGNITIVE STIMULATION IN THE FACE OF MILD AMNESIC COGNITIVE IMPAIRMENT IN PATIENTS RESIDING IN THE CITY OF CÓRDOBA-ARGENTINA.

Tatiana CASTRO ZAMPARELLA | Paula ABATE | Magdalena Marcela CÁCERES | Veronica BALASZCZUK

INSTITUTO DE INVESTIGACIONES PSICOLÓGICAS IIPSI UNIDAD EJECUTORA DEL CONICET-UNC

General description: Neurodegenerative and vascular desease have a high prevelance in older adults. In Latin American countries, with low economic resources, goals in public health should be based on preventive and educational actions, promoting brain protection factors. Background shows that the diet based on food rich in essential fatty acids Omega 3 (O3) contributes to the prevention of neurological clinical conditions. Objective: To study neuroprotective factors mediated by the dietary supplement (O3) and cognitive stimulation in patients with mild amnesic cognitive impairment from the city of Córdoba, Argentina. We conducted observational case-control studies. Non probabilistic sample of adults between 60 and 80 years both sexes of the city of Córdoba, Argentina. n= 20 Pre-post evaluation of blood lipid profile, brain magnetic resonance with hippocampal volumetry and complete neurocognitive evaluation battery. Treatment for 24 weeks with O3 capsules (1,000 mg) and 24 weeks of treatment with cognitive stimulation workshops. Supplementation with O3 is expected to mitigate or protect against the progression of mild amnesic cognitive impairment in the sample of adults/older adults and even more increases this effect along with cognitive stimulation.

Discussion and conclusions: Little is known about the protective effects of O3 in Argentina. Currently, this country has a high aged population, therefore, the risk of cognitive and demential pathologies is very frequent. Hence, health trends are set to prevent and provide life´s quality for the adult population.

0840 - MODULATION OF GLIAL AUTOPHAGY BY PERIODIC DIETARY RESTRICTION AS A POTENTIAL THERAPEUTIC STRATEGY IN AN ANIMAL MODEL OF ALZHEIMER'S DISEASE.

Amal Patricio GREGOSA MERLINO | Ángeles VINUESA | Carlos Javier POMILIO | Melisa BENTIVEGNA | Jessica PRESA | Flavia Eugenia SARAVIA | Juan BEAUQUIS

IBYME-CONICET

Alzheimer's disease (AD) is the leading cause of dementia for which there are no effective treatments. Dietary restriction (DR) has been proposed as a potential therapeutic strategy for age-associated diseases. Our objectives were to analyze memory and hippocampal alterations in an animal model of familial AD, the PDAPP-J20 transgenic mouse (Tg) and to evaluate the effects of a periodic DR protocol (3 cycles of 40 % DR for 5 days and ad libitum (AL) diet for 9 days). We observed cognitive impairment, impaired adult neurogenesis and progressive amyloid beta (Aß) deposition in the hippocampus of AL-fed Tg mice. Periodic DR was associated to cognitive improvement, increased hippocampal neurogenesis, and reduced hippocampal amyloid load. Through immunofluorescence for LC3 (autophagosomes) and GFAP (astrocytes), we found that autophagy is modulated in Tg mice with a high proportion of LC3 localized in astrocytes (2-way ANOVA, $p<0.01$ for genotype effect). We also found that astrocytes contained Aß co-localizing with LC3. From these results we hypothesized that the reduction in amyloid plaques associated to DR would be partly mediated by astroglial autophagy. Therefore, we evaluated the C6 astrocyte line exposed to fibrillar beta amyloid (fAß, 2, 6 or 24 h) and previously nutrient restricted (NR; 2 % FBS) or not (10 % FBS) for 6h. Exposure to fAß for 2 h showed that LC3 was increased after bafilomycin treatment, an inhibitor of autophagosome-lysosome fusion, indicating a functional autophagy (Aß NR 0.4 ± 0.14 vs. Aß NR BAF 2.24 ± 0.38, $p<0.001$). At 6 and 24h of Aß exposure, LC3 levels rose in Aß but not in Aß+NR cells (Aß vs. Aß+NR, 6 h $p<0.001$, 24 h $p< 0.05$) and this effect was lost if bafilomycin was administered in the last 2 hours (Aß+NR vs. Aß NR BAF, 6 h $p<0.05$, 24 h $p<0.05$) suggesting that autophagy was blocked by Aß but conserved with prior NR. We conclude that NR could prevent autophagy alterations that occur in response to Aß and could be a potential therapeutic strategy in AD.

0843 - EFFECTS OF A HIGH-FAT DIET IN A MOUSE MODEL OF ALZHEIMER´S DISEASE.

Melisa BENTIVEGNA | Angeles VINUESA | Carlos POMILIO | Jessica PRESA | Amal GREGOSA | Flavia SARAVIA | Juan BEAUQUIS

IBYME-CONICET; CÁTEDRA DE QUÍMICA, CICLO BÁSICO COMÚN, UBA

Insulin resistance and obesity, associated to the consumption of hyperlipidic diets, are considered risk factors for the development of cognitive disorders and neurodegenerative diseases such as Alzheimer's disease (AD). Insulin resistance, inflammation and cognitive dysfunction are common manifestations in the context of both neurodegenerative and metabolic pathologies. Our objective was to study the effects of the exposure to a moderately high-fat diet (HFD), from 6,5 to 8 months of age, on cognitive performance and hippocampal glial and neuronal changes in a transgenic model of AD, the PDAPP-J20 mouse. Interestingly, HFD exposure did not induce changes in body weight at the end of the protocol. Although we found that diet had no effect on glucose blood levels, transgenic mice showed decreased glycemia compared to non-transgenic groups ($p<0.05$). We found a tendency towards decreased hippocampal insulin signaling, measured by Western blot of pAkt/Akt, in HFD-treated animals, suggesting an effect of this diet on insulin sensitivity. The analysis of the open-field test showed an anxious-like behavior in transgenic mice fed a control diet and also in HFD-fed transgenic and non-transgenic mice (Distance travelled in the center of the arena= NTg 20.63 vs. Tg 12.67 %, $p<0.005$; CD 20.21 vs. HFD 13.09 % $p<0.01$), evidencing similar effects of the genotype and also of the HFD on animal behavior. Our results show that HFD induced behavioral and brain metabolic alterations in adult mice, sharing similarities with PDAPP-J20 mice that model Alzheimer's disease.

0854 - DEXAMETHASONE BLOCKS MOTOR IMPAIRMENT AND BRAIN MORPHOLOGICAL CHANGES INDUCED BY THE MIXTURE OF TAURINE AND ALCOHOL IN A MICE MODEL OF ALCOHOL HANGOVER.

Alipio PINTO | Silvia CARBONE | Jorge GOLDSTEIN | **Rodolfo Angel CUTRERA**

IFIBIO

It has been proposed that inflammatory mechanisms could be involved in alcohol hangover (AH). In previous work we demonstrated that at the beginning of AH mice treated with alcohol (OH) and taurine (TAU), the main component of energy drinks, showed behavioral and morphological changes in the brain. The aim of this work was to study if the pretreatment with dexamethasone (DEXA) could block the motor disabilities and the neural stress produced by TAU in an experimental model of AH. Mice (n= 8-12) were ip pretreated with DEXA (7.5 mg/kg) 24 h before the i.p. injection of OH (3.8 mg/kg) and/or TAU (190 mg/kg). Controls were injected with saline. The Tight rope (TR) and Hanging wire (HW) tests were used to study neuromuscular coordination and muscle tension, respectively. Another group of mice (n= 8) were perfused and the brains were subjected to immunofluorescence with an anti-GFAP antibody (glial fibrillary acidic protein) and an anti-MBP antibody (myelin basic protein) to identify reactive astrocytes and myelin sheath respectively. All the studies were performed 6 h after treatment with OH and/or TAU (beginning of AH). It was observed that DEXA blocked significantly (ANOVA-Tukey, $p<0.001$): A) In HW test, the decrease in latency to fall (sec) in OH and OH+TAU groups; B) In TR test, the loss of neuromuscular coordination (sec) in animals with OH and a tendency to improve the performance in DEXA+OH+TAU. It was also observed a significant increase ($p<0.001$) in astrocytic reaction and a significant decrease in MBP in OH, TAU and OH+TAU treated mice compared to the control ones. On the other hand, DEXA significatively achieved to block the astrocytic reaction in OH+TAU treated mice and the reduction of MBP in TAU and OH+TAU treated mice. These results suggest that an inflammatory process may be mediated by the decrease in muscle tension and morphological changes in the brain caused by combined treatment with OH and TAU evidenced at the beginning of AH in mice.

0900 - NEUROPROTECTIVE EFFECT OF FK506 AGAINST OXIDATIVE STRESS

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IBYME-CONICET (1); LABORATORY OF NUCLEAR RECEPTORS, DEPARTMENT OF BIOLOGICAL CHEMISTRY OF THE FCEN-UBA (2)

Immunophilins are proteins that bind immunosuppressive drugs. Those that bind cyclosporin A (CsA) are cyclophilins (ej, CyPA), and those that recognize the macrolide FK506 are FKBPs (FK506-binding proteins), a subfamily to which FKBP51 (51-kDa) and FKBP52 (52 -kDa). Both FKBPs were described in steroidal receptor heterocomplexes with Hsp90, Hsp70 and p23. FKBP51 and FKBP52 have 60 % similarity and 75 % homology. Previous laboratory studies showed that FK506 has regulatory effects on neurodifferentiation through both FKBPs, such that overexpression of FKBP52 or silencing