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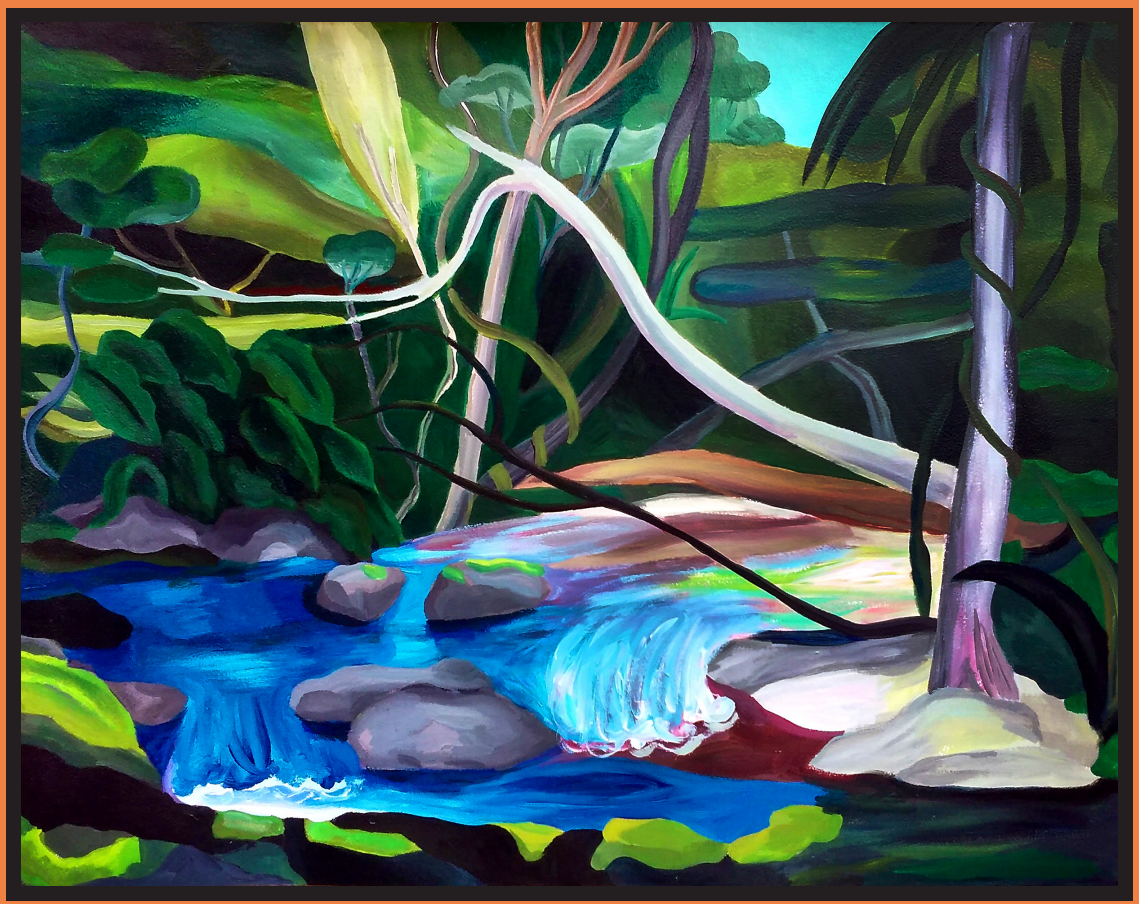

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15-17 de noviembre de 2023
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duction (H2DCF-DA: 2-fold, p<0.05). Moreover, Mn-exposed HT22 cells exhibited shorter mitochondria (p<0.05) with fewer ramifications (p<0.05). The area (p<0.05), perimeter (p<0.05), and circularity (p<0.05) of mitochondria were also affected. Preliminary results showed an increment in LC3 levels after Mn exposure (western blot: 2.8-fold); however, bafilomycin A1-treated cells exhibited similar levels, suggesting autophagic flux impairment. Colocalization analysis of GFP-Sec61β (ER) and DsRed2Mito revealed that Mn increases ER-M contacts (M2: p<0.05). Furthermore, we detected an accumulation of lipid droplets in HT22 cells exposed to Mn (Red Nile staining). In summary, Mn-induced mitochondrial dysfunction is accompanied by alterations of ER-M contacts and lipid dyshomeostasis. Understanding the role of MAMs in Mn-induced neurodegeneration may contribute to discovering novel therapeutic targets to treat this and other neurodegenerative disorders.

P1-NEUROSCIENCES

WEDNESDAY 15TH NOVEMBER 14:00-15:30

CHAIRS: CARLOS POMILIO
SOLEDAD PORTE ALCÓN
MARIELA FERNADA PÉREZ

229. 33. **PHYTOCANNABINOIDS DECREASE NEUROINFALMMATAION AND IMPROVE LOCOMOTOR OUTCOME FOLLOWING SPINAL CORD INJURY**

Julián Del Core[1], Alejandro F De Nicola[1,2] , Florencia Labombarda[1,2]

1 Laboratorio de Bioquímica Neuroendócrina, Instituto de Biología y Medicina Experimental, CONICET. 2 Departamento de Bioquímica Humana, Facultad de Medicina, UBA.

Neuroinflammation is involved both in secondary damage and functional deficits after traumatic spinal cord injury (SCI), so its regulation represents a therapeutic target. In this regard, Tetrahydrocannabinol (THC) and Cannabidiol (CBD), the main phytocannabinoids of *Cannabis Sativa*, emerge as anti-inflammatory molecules. In the present study we used a model of SCI in rats to evaluate the effects of oil extracted from a resin composed of THC: CBD 1:1 (CAN). SCI rats received an oromucosal dose (20mg/kg/day) during 15 days post-injury (dpi) and they were sacrificed in the acute (3dpi) and chronic phases (60dpi). By Real Time RT-PCR, pro-inflammatory (TNFα, IL-1β, IL-6) and anti-inflammatory (TGFβ, ARG-1, MRC) markers were determined during the acute phase. After SCI, the expression of all pro-inflammatory markers was increased compared to sham rats (p<0.001, ANOVA one-way), while the expression of anti-inflammatory molecules remained as sham values. Unlike, CAN treatment decreased the expression of pro-inflammatory molecules (p<0.05 vs SCI rats, ANOVA one-way) and increased the expression of anti-inflammatory ones (p<0.01 vs SCI rats, ANOVA one-way). Moreover, confocal analysis of a double immunohistochemistry (Iba-1 and ARG-1) showed that CAN treatment increased the number of microglial cells (Iba-1+ cells) which express ARG-1 (an anti-inflammatory marker, p<0.05 vs SCI rats, ANOVA one-way). Finally, we evaluate functional recovery at the chronic phase. Rotarod analysis showed that CAN treatment increase the latency to fall compared to SCI rats (p< 0.05, ANOVA one way). Regarding horizontal ladder, SCI rats increased the number of hindlimb foot misplacements compared to sham rats (p<0.05, ANOVA one way), while CAN treatment reduced the value of this parameter (p<0.05 vs SCI rats, ANOVA one way).These results suggest that THC and CBD offer a promising perspective in reducing acute neuroinflammation promoting functional recovery after SCI.

230. 59. **UPREGULATION OF CHOLESTEROL METABOLISM AS A HALLMARK OF MIDBRAIN NEURODEGENERATION INDUCED BY IRON OVERLOAD**

Athina Maniscalchi*[1], Oriana Benzi Juncos[1,2], Melisa Conde[1,2], Melania Funk[1,2], Natalia Alza[1,3], Gabriela Salvador[1,2]

[1]Instituto de Investigaciones Bioquímicas de Bahía Blanca, Universidad Nacional del Sur (UNS), Consejo Nacional de Investigaciones Científicas y Técnicas. [2]Departamento de Biología, Bioquímica y Farmacia, UNS. [3]Departamento de Química, UNS

Iron (Fe) accumulation in specific brain areas and ferroptosis are associated with various neurodegenerative disorders. We have previously established an *in vivo* model of Fe overload (C57BL/6 mice treated with Fe 333 mg/kg) with midbrain neurodegeneration and lipid cacostasis. Our aim was to study the link between lipid metabolism alterations and ferroptosis taking into account neuroglial metabolism. In midbrain of Fe-overloaded animals, we detected a decrease in the expression of *SLC7A11* and an increase in *ACSL4* (p<0.001), both markers of ferroptosis. We found that cholesterol (chol) was elevated in midbrain of Fe-treated mice, coincidentally with *SREBP2* and *ABCA1* upregulation (p<0.001). In addition, increased levels of *CPT1c* (p<0.001) were observed after Fe overload, indicating an enhanced β-oxidation for the removal of fatty acid released by lipolysis. In the open field test, Fe-overloaded mice displayed motor impairment, with a lower rearing activity, a shorter time spent in the central square, and a longer time in the periphery (p<0.001). Next, we investigated chol metabolism in dopaminergic neurons and astrocytes exposed to Fe overload with ferric citrate ammonium (FAC). Chol content in neurons (N27), astrocytes (C6), and mouse primary glial culture was increased both in intracellular compartments as well as in secretomes after Fe treatment (p<0.001). This rise correlated with an increase in chol *de novo* synthesis and transport, respectively, by means of *HMGCR* and *ABCA1* upregulation (p<0.001). To study the link between chol accumulation and ferroptosis, cells were exposed to the inhibitor ferrostatin (FER). We found that FER reduced chol levels when cells were exposed to FAC (p<0.001). Our findings indicate that altered chol metabolism could be a biomarker of midbrain neurodegeneration triggered by ferroptosis, with motor impairment as a final outcome.

231. 65. **NEURONAL DIFFERENTIATION OF MURINE NEUROBLASTOMA N2A CELLS IS DIFFERENTIALLY INDUCED BY SELECTIVE INHIBITION OF CLASS I OR CLASS IIA HDACS**

Stephanie Junge[1], Alejandra Bernardi[1], María Sofía Villalba[1], Francisco J. Urbano[2] and Veronica Bisagno[1]

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[2]IFIBYNE-CONICET, Universidad de Buenos Aires, Argentina.

Histone deacetylases (HDACs) are vital enzymes for regulating chromatin functions. Their primary role is to eliminate acetyl groups allowing histones to wrap the DNA more tightly. This study aims to investigate the in vitro application of selective inhibitors targeting class I/IIa HDACs. HDAC inhibitors (HDACi) are upcoming interesting targets due to their involvement in epigenetic/non-epigenetic regulation, and their potential as use as anti-cancer agents. All statistical differences were tested using ANOVAs. We used N2a cell cultures, a fast-growing mouse neuroblastoma cell line, capable of differentiating into neurons. They were cultured for 4 or 7 days in vitro (d.i.v.) using a 24-well plate in a DMEM with low serum (0.5%) condition and treated with HDACi MS275 (class I) and MC1568 (class IIa), at high or low concentrations. Equivalent DMSO concentrations were used as control. Whole cell patch-clamp recordings were performed to study neuron-like characteristics. Results showed a severe decrease in cell viability 4 d.i.v with MS275 (high), further corroborated by dapi staining. The same tendency was observed at 7 d.i.v (p<0.05). None of the inhibitors (low) affected cell viability. Cells showed a positive mark for tyrosine hydroxylase (TH) and MAP2. Moreover, at 4 d.i.v., patch-clamp recording showed an increase in voltage-gated ionic channel expression; 70% of the cells treated with Class I HDACi at low concentration showed positive voltage-gated ionic current versus only a 30% increase in DMSO (p<0.05). Both groups of HDACi at high concentrations showed lower levels of capacitance compared to DMSO. In summary, treatment with HDACi increased N2a differentiation at 4 days in vitro. Survival and voltage gated ionic channel were affected. These results suggest that HDACi are arresting tumoral growth, leading to a N2a