sual evoked potentials (mfVEP) in multiple sclerosis (MS) and compare with healthy controls. Also we sugest a new method for the evaluation of the morphology of mfERG signals to discriminate between registries of control subjects and patients with multiple sclerosis. The multifocal mfERG tecnique allows to obtain objective and qualitative measurements about retinal function using different types of visual stimuli. The standard paradigm of visualization consists of apply an m-frame whose excitation is governed by the sequence m, with a period between frames of 13.3 ms.
Methods: Fifty-eight eyes were included: 14 of healthy controls and 44 of subjects with MS (of whom 17 had presented a previous episode of optic neuritis). The BCVA ETDRS was recorded to the 100 contrast, 2.5 and 1.25%, SC with CSV1000 test (at 3, 6, 9 and 12 cycles per degree) and Pelli Robson. The pERG, mfERG and mfVEP electrophysiology tests were performed with the Roland Consult's Reti-port / scan device. Index of discrimination, quantify the ability to discriminate between controls and MS patients. This capacity was evaluated using Receiver Operating Characteristic (ROC) analysis. A ROC curve shows sensitivity against the False Positive Rate (FPR=1-specificity) for all possible decision thresholds. Area under the ROC curve (AUC) quantify the overlaps between the distributions in controls and MS of a parameter. AUC value of 0.5 implies that the distributions in both diagnosed groups overlap. AUC values above 0.9 indicate high diagnostic accuracy. Individual mfERG responses for the 61 hexagons were grouped all together (SUM), into five concentric rings centered on the fovea for analysis and also in four cuadrants (upper-nasal, lower-nasal, upper-temporal and lower-temporal).
Results: Patients with MS showed a significant reduction of VA at 100% contrast ($p = 0.013$), 2.5% ($p < 0.001$) and 1.25% ($p = 0.008$), CSV-1000 was also affected at 3 ($p = 0.017$), 9 ($p = 0.017$), and 12 cycles per degree ($p = 0.048$), and also Pelli Robson ($p < 0.001$). The mfERG showed in MS patients a significant affectation for amplitude and latency at the inferonasal and superonasal quadrants ($p = 0.045$ and 0.042 respectively), and the overall values of the mfPEV sown abnormalities at N1 and P1 amplitudes ($p = 0.019$ and $p = 0.039$, respectively). According to our experiment, quadrant upper-nasal is the most sensitive to appreciate the evolution of MS. Taking as reference the average value of available AUC values, the group of sectors that has a higher AUC between control subjects and patients with MS corresponds to upper-temporal (AUC= 0.6475) and ring 3(AUC=0.64), also average value reflects a greater discrimination between signals on N1 amplitude density (AUC=0.641) and P1 amplitude (AUC=0.635).
Conclusions: Patients with MS have a clear impairment of visual function in both psychophysical and electrophysiological tests. According to our experiment, quadrant Q1 is the most sensitive to appreciate the evolution of MS.

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P.297 Peripubertal treatment with cannabidiol reverses behavioral alterations in Δ9-THC animal model of schizophrenia

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Several studies suggest that disturbances in the development of central nervous system could lead to schizophrenia (SCZ), a psychiatric disorder with severe symptoms in cognitive and social domains [1]. While a variety of studies emphasize the role of the endocannabinoid system (ECS) in the neurodevelopmental dysregulation during perinatal and adolescent periods, mostly arising from well-known long-lasting negative effects of delta-9-tetrahydrocannabinol (Δ9-THC), the main psychoactive compound of Cannabis sativa [2,3], very little attention is dedicated to the positive potential of the ECS modulation in these sensitive periods as a preventive intervention. Given that preventive antipsychotic treatment seems to reduce the risk of transition to psychosis in vulnerable individuals [4], we hypothesized early modulation of ECS could be a potential novel therapeutic strategy.

In the present study, we aimed to investigate 1) the potential effects of perinatal administration of Δ9-THC on a) behavioral phenotype resembling schizophrenia to assess negative and cognitive symptoms in social interaction (SI) and novel object recognition (NOR) tasks at adulthood, b) mRNA expression of D3 receptors (D3R), alterations of which were observed in preclinical and human studies of SCZ, and 2) if the early pharmacological intervention with cannabidiol, major non-psychotropic phytocannabinoid of Cannabis sativa, could reverse the schizophrenia-like phenotype.

Timed-pregnant Sprague-Dawley rats were perorally administered with Δ9-THC (5mg/kg/day) or vehicle (sesame oil, CTR, 1 ml/kg/day) from gestational day 15 to postnatal day (PND) 9 [5]. From PND 19 to PND 39 the offspring of THC-exposed mothers were treated intraperitoneally with cannabidiol (30 mg/kg/day) or vehicle (saline, 5 ml/kg/day).

At adult age, rats perinatally exposed to Δ9-THC engaged in less social behavior than the control group ($p < 0.001$), as defined by the reduced time of interaction in the social interaction (SI) test, while the number of interactions, as index of locomotor activity, was not affected. Peripubertal treatment with cannabidiol reversed Δ9-THC-induced social deficit ($p < 0.001$) at adulthood, without any effect on motor activity.

Early exposure to Δ9-THC also impaired cognitive performance in the novel object recognition (NOR) test. Discrimination index indicated inability to recognize the novel object in Δ9-THC group, compared to apparent recognition in control animals ($p<0.001$). Peripubertal cannabidiol treatment was able to reverse this deficit ($p<0.01$).

At molecular level perinatal Δ9-THC exposure did not affect D3R mRNA expression, while peripubertal cannabidiol treatment significantly decreased gene expression of D3Rs in the prefrontal cortex ($p<0.001$).

Our results support the hypothesis that perinatal Δ9-THC exposure could lead to late behavioral abnormalities resembling a schizophrenia-like phenotype. These Δ9-THC-induced abnormalities do not seem to be related to altered D3Rs gene expression in prefrontal cortex of tested animals. Results of our presented experiment suggest that early pharmacological intervention with cannabidiol at peripubertal age could be a promising therapeutic approach to prevent the development of social and cognitive aspects of schizo-affective disorders.

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P.298 Lack of microglial Interleukin-6 ameliorates the brain's response to traumatic brain injury

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Introduction: Traumatic brain injury (TBI) has a relevant impact on the population's health in terms of disability and death. It implies different pathophysiological events at the lesion site, and minutes or days after, secondary injury, changes in intracranial pressure and blood perfusion could take place.

Interleukin-6 (IL-6) is a pleiotropic cytokine that controls the immune system and influences the central nervous system both in normal and pathological conditions. IL-6 plays a critical role in the cold injury method, a murine model of TBI, characterized by an increment of the blood-brain barrier permeability followed by vasogenic brain edema, and resulting in tissue damage with infiltration and activation of inflammatory cells and cell death [1]. In fact, the inflammatory response is led by cytokines such as IL-6, as findings using Il6-deficient mice showed a significantly reduction of glia activation and macrophage recruitment as well as a lower number of neurons [2,3].

Neurons, microglia, astrocytes and other CNS cells synthesize and respond to IL-6. However, little is known about how microglial IL-6 could contribute the pathophysiological response to TBI.

Material and methods : In this study, we used microglial knock-out Il6 mice (Il6MicΔ), by crossing Il6lox/lox [4] x CX3CR1CreER [5], which is tamoxifen-inducible model, and as a control, their Il6loxflox littermates. One month after tamoxifen injections (1mg/day for 5 days), Il6MicΔ and Il6lox/lox (n=4) were lesioned, under isoflurane anesthesia, in the right fronto-parietal cortex with size-controlled dry ice for 30 seconds. Furthermore, sham-operated Il6MicΔ and Il6lox/lox mice (n=4) were also included. One day after, animals were euthanized and the ipsilateral cortex was dissected, snap-frozen in liquid nitrogen and stored at -80°C.

Total RNA was isolated using a kit RNAeasy Mini Kit and its concentration and dye incorporation was measured using a UV-VIS spectrophotometer. Then, hybridization to SurePrint G3 Mouse Gene Expression Microarray (ID G4852B, Agilent Technologies) was conducted following manufacturer's two-color protocol (Two-Color Microarray-Based Gene Expression Analysis v.6.5), and dye swaps (Cy3 and Cy5) were performed for RNA amplified from each sample. Microarray chips were then washed and immediately scanned using a DNA Microarray Scanner.

We used a two-way ANOVA, with genotype and cryolesion as main factors, to detect differentially expressed (DE) genes. The DE candidate genes were additionally filtered with at least a log-2 fold change. Then, we carried out a gene ontology (GO) enrichment to identify the functional categories of these DE genes.

Results: We obtained 128 annotated genes significantly affected by the interaction (p-value < 0.05). We generated a heat-map for the visualization of the gene expression per condition of these genes.

GO analysis showed that cryolesion produced a clear induction of genes involved in immune system processes, inflammatory response, regulation of leukocyte and T cell migration, regulation of mononuclear cell proliferation, an-