chewing) and often body flexion. Rats were then placed on a cool surface, monitored for 5 min before being returned to their mothers. At PND35 rats were deeply anesthetized, fixed and brains processed for immunohistochemistry and morphometrical studies. We observed an increase in the area occupied by S100B + cells in females, although there was an increase in the number of S100B cells in both sexes. On the other hand, reactive microgliosis was more prominent in males compared with females. Our results strongly suggest that males are more susceptible to HS exposure and this could be related to their future susceptibility to develop epilepsy.
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203. (205) **ASTROGLIAL PHENOTYPES IN TRAUMATIC BRAIN INJURY AND THEIR RELATIONSHIP WITH NEURONAL DEGENERATION**

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Astrocytes are key players in the Central Nervous System injury. By not completely defined pathways, reactive astrocytes may suffer a pathological remodeling engaging a pro-inflammatory phenotype that is very stable and promote further neuroinflammation and neurodegeneration. We here aimed to define the spatio-temporal distribution of astroglial phenotypes after traumatic brain injury and the consequences for neuronal survival and behavioral parameters. Following a stereotaxic stab wound injury (0.8 mm needle, coordinates 2 mm posterior and lateral to Bregma; 1 mm depth) performed in C57BL/6 mice and immunohistochemistry on brain sections, we classified GFAP reactive astrocytes in five different phenotypes defined using Sholl analysis (Auzmendi et al., Molec. Neurobiol. 2019). While at 1 day post-injury (DPI) GFAP+ astrocytes were not different from contralateral non-injured hemisphere, at 3DPI and 7DPI highly reactive phenotypes colocalized with altered neurons in lesion penumbra. At 14DPI highly reactive astrocytes and altered neurons were abundant only in the lesion core. Pro-inflammatory gain of function paradigm was achieved by administering LPS (5 mg/Kg i.p) in lesioned animals, and that resulted in a greater number of complex reactive astrocytes at 7DPI ($p<0.05$) and a population of C3+ astrocytes. On the other hand, loss of function paradigm with chemical NFkB blocker sulfasalazine (150 mg/kg i.p) significantly reduced highly reactive astrocytes ($p<0.05$) and showed reduced neuronal death. Animal motor deficits were analyzed by computer-assisted open field, but at 7DPI we were unable to detect significative differences among groups probably due to the small lesion size. We conclude that increased GFAP+ higher complexity astrocytes are associated with increased neuronal death and that NFkB pathway is likely to be involved in the pathological conversion to the pro-inflammatory-neurodegenerative phenotype.
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204. (214) **MICROGLIA AS THE TRIGGERING SPARKLE FOR CHROMATIN REMODELING IN PRO-INFLAMMATORY ASTROCYTES**

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Conversion of astrocytes to a pro-inflammatory phenotype leads to exacerbated neuroinflammation and neurotoxicity, therefore understanding this mechanism has become a main interest as a novel pharmacological target. We here aim to understand an epigenetic mechanism which may lead to a sustained astrocyte response expanding inflammation and neuronal death.
We exposed primary cultures of cortical astrocytes containing different amounts of microglia (below 1% and up to 20%) to 25 ng/ml Lipopolissacharide (LPS) for different periods of time to promote pro-inflammatory conversion. Astroglial and microglial morphology was analyzed using immunofluorescence. Nuclear localization of p65 subunit was assessed as parameter of NFkB activation using immunofluorescence for p65/GFAP/DAPI or p65/IBA/DAPI. As an indicator of chromatin remodeling, we studied the levels of acetylated histone 3 at lysins 9 and 14 (H3K9K14ac) using immunofluorescence for H3K9K14ac/GFAP/DAPI. This epigenetic mark is known to be promoted by NFkB activation. Pro-inflammatory conversion of astrocytes was confirmed by analyzing expression of pro-inflammatory cytokines.
Results show that LPS-induced astroglial conversion towards a pro-inflammatory phenotype evidenced by changes in morphology, activation of NFkB and cytokine expression is microglia-dependent. This astroglial pro-inflammatory phenotype correlates with global changes in nuclear H3K9K14ac only when they are co-cultured with microglia.
Our work evidences a mechanism of gene regulation by chromatin remodeling which may underlie long term cellular changes in astrocyte phenotype conversion. Our results suggest a global reconfiguration of the chromatin which could be pharmacologically targeted to reduce neuroinflammation. **PICT-2018-00920 (joven), ISN-CAEN_2020 (category B),** ***PICT 2017-2203, PICT 2015-145.***

205. (220) **PRELIMINARY EFFECT OF THE ADMINISTRATION OF *E. COLI* LIPOPOLYSACCHARIDE (LPS) ON THE ASCORBYL RADICAL ($A^{\cdot}$) CONTENT IN BRAIN FROM RATS OVERLOADED WITH FE**

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The aim of this study was to evaluate the effect of LPS in brains from rats treated with acute Fe-dextran. Sprague Dawley rats were intraperitoneally injected with a single dose of Fe-dextran (500 mg/kg) and LPS (4 mg/kg). The nitric oxide (NO) content was determined in blood by Electronic Paramagnetic Resonance Spectroscopy (EPR), with hemoglobin at 77K. The administration of LPS significantly increased ($p\leq0.01$, ANOVA) the NO content in the blood of the control animals (1.9 ± 0.1 AU), in the presence of either Fe-dextran, or LPS or LPS+Fe-dextran (1.5-, 10.5- and 14.2-folds, respectively). After 6 h of treatment, the administration of Fe-dextran or Fe-dextran+LPS, showed a significant increase of the Fe content in total brain, determined by acid mineralization, in the absence (20-fold), and in presence of LPS (17-fold). The labile Fe pool (LIP) content, determined using calcein, was increased 6 h after Fe administration, and returned to control values after 8 h. The content of $A^{\cdot}$, determined by EPR, significantly increased after 6 h, in animals overloaded with Fe-dextran in the absence of LPS (41%, $p<0.05$), without changes in the brains of animals treated with LPS or with LPS+Fe-dextran, as compared to the control values. These results suggested a protective effect against the production of $A^{\cdot}$ of the simultaneous acute administration of Fe-dextran and LPS. This effect could be due to (i) the ability of NO generated by the LPS to chelate Fe with the formation of complexes which would favor the gradually incorporation of the metal, and decreasing its catalytic capacity, or (ii) since Fe-dextran administration leads to an increase in the nuclear levels of Nrf2/keap1, the activation of the antioxidant response mediated by changes in the glutathione metabolism related enzymes would occur, which could be a critical factor in the observed response. Further studies are necessary to identify the mechanisms underlying this treatment.

206. (226) **REVERSIBLE ALTERATIONS IN GLIAR FIBRILAR ACIDIC PROTEIN (GFAP) AND TYROSINE HYDROXYLASE (TH) EXPRESION AFTER ACUTE ACETAMINOPHEN (APAP) INTOXICATION IN BRAIN AREAS INVOLVED IN LOCOMOTION AND MEMORY REGULATION.**

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