**Metabolic alterations and inflammatory cytokines in mesial Temporal Lobe Epilepsy with or without hippocampal atrophy: a preliminary study.**

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**Introduction:** Mesial temporal lobe epilepsy (mTLE) is one of the most prevalent forms of focal epilepsy in adulthood and most of them become refractory to the pharmacological treatment. Proton magnetic resonance spectroscopy (1H-MRS) is able to detect subtle changes in brain tissue and might be a useful tool to better understand mTLE [1]. The aim of the present work was to investigate changes in 1H-MRS metabolites in relation to response to antiepileptic drugs (AED) and hippocampal atrophy (HA) in mTLE patients. We analyzed N-acetylaspartate+N-acetyl-aspartate-glutamate (NAA+NAAG/Cr) and glutamate (Glu/Cr). Moreover, we quantified preliminarily data on cytokines in order to better characterize inflammatory process inmTLE.

**Materials and Methods:** We included 58 mTLE patients with poor AED response, 47 with good AED response and 47 healthy controls (mean values of metabolites from right+lef thippocampi). 1H-MRS data was acquired in a 3T scanner (Philips Achieva) using a single voxel PRESS (Point Resolved Spectroscopy) sequence with repetition time (TR) = 2000msec and echo time (TE) = 35msec. Spectra were then quantified ipsi- and contralateral to the lesion using LCModel (MRI negative patients were lateralized according to EEG) [2]. We also performed a preliminary multiplex essay (xMap) of eight regulatory mediators: TNF-Alfa, BDNF and interleukins (IL) 1β, 4, 6, 10, 12 and 13 in patients (n = 57) and healthy controls (n = 29). We used SPSS (IBM, Version 22.0) for statistical analysis. Metabolic data was compared between groups using MANCOVA co-varying for age and the t Test was used to evaluate data on cytokines.

**Results:** We found an ipsilateral decrease of NAA+NAAG/Cr in refractory group when compared to responders and controls (p = 0.021 and p = 0.0001, respectively). NAA+NAAG/Cr was also decreased in contralateral hippocampus of refractory group compared to controls (p = 0.004). Moreover, we observed a decrease in Glu/Cr in refractory patients ipsilateral to the lesion when compared to controls (p = 0.008). Regarding xMap analysis, only BDNF and IL-8 were quantified (the other cytokines were under the detection range of the essay kit). This analysis reached no significant difference between groups (p > 0.05).

**Discussion:** The results found are probably due to pharmacological response than the presence of HA [1]. Cytokines data are preliminary and resulted from a pilot study to guide next analysis. Nonetheless, IL-8 might be expressed by microglia and reactive astrocyte [3] thus next step is evaluating the relationship between metabolic data measured by 1H-MRS and cytokine levels.

**Conclusion:** Metabolic alterations seems to be related to the pattern of AED response when ipsilateral to the lesion. However, alterations in NAA might go beyond the lesion and affect both hippocampi [1]. Further analysis is required to investigate whether there is or not an association between metabolic alterations and regulatory mediators levels.

**References:** [1] Pimentel-Silva, LR et al., Journal of Epilepsy and Clinical Neurophysiology21 (4): 136-43, 2015; [2] Provencher SW, Magn. Reson. Med. 30: 672–679, 1993.[3] Pernhorst et al., Seizure 22(8):675-8, 2013.