Hippocampi and epilepsy in MS patients: a diffusion weighted imaging study with NODDI.

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TARGET AUDIENCE – Scientist and clinicians with interest in the application of advanced diffusion models to multiple sclerosis

PURPOSE –

The linkage between Multiple Sclerosis (MS) and epilepsy has recently come to the attention of researchers, as the prevalence of epileptic episodes in MS population is higher than in the healthy population[1]. Literature suggests the critical involvement of the hippocampi in MS[3]; in this work we exploit the application of Diffusion Weighted MRI (DW-MRI) to the hippocampi to investigate possible tissue impairment in patients with MS and temporal lobe epilepsy.

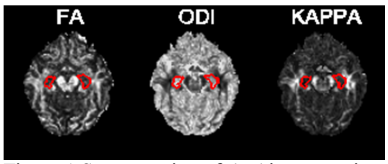

Figure 1 Segmentation of the hippocampi on FA, ODI and KAPPA maps.

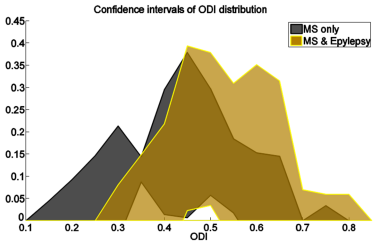

Figure 2 Confidence interval of the ODI histograms on the right hippocampus for the two groups. Epileptic group exhibit higher average dispersion index.

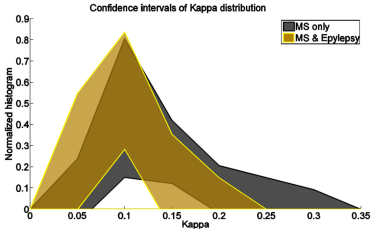

Figure 3 Confidence interval of the KAPPA histograms on the right hippocampus for the two groups. Epileptic group exhibit lower average kappa values.

METHODS:

Classic single-shell DW acquisitions only allow reliable analysis of White Matter (WM) using the diffusion tensor model, while the use of a multiple shells acquisition design in conjunction with "Neurite Orientation Dispersion and Density Imaging" (NODDI)[4] model overcomes these limitations. In fact, single-shell DW indices like fractional anisotropy (FA) although able to reveal modifications of WM, due to their macroscopic nature are not capable to describe the microstructural complexity of dendrites and axons. Moreover, the classic single-shell DW model is not well suited for the analysis of gray matter (GM). The NODDI model decomposes the multiple shells DW signal in the sum of three compartments and allows a more sophisticate interpretation of the acquired data, disentangling the signal from free water (CSF), intra-cellular compartment and extra-cellular compartment. The model provides maps of the fraction of intra-cellular volume fraction (FICVF), orientation dispersion index (ODI), fractional isotropy (FISO) and of the concentration parameter of the anisotropic compartment (KAPPA) , that provide a more comprehensive structural description than FA. Both diffusion tensor and NODDI models were used in order to investigate their ability in detecting possible tissue impairment in the hippocampi of MS with epilepsy. Region of Interest (ROI) of the hippocampi was extracted using the Hammers Atlas[5] that provides the segmentation of anatomical structures. The ROI was then moved to the native diffusion space of each subject using a nonlinear transformation computed by the Advanced Normalization Tools (ANTs)[6]. The structural T1 weighted image was used in the process as an intermediate step.

4 patients affected by MS and 4 patients affected by MS presenting temporal lobe epileptic episodes underwent MRI with a 3T Philips Achieva MRI scanner equipped with a 8 channels coil. For each subject a T_{1w} scan (isotropic resolution 1x1x1mm^3 TR/TE 8/4.3ms) and a two shells DW sequence (isotropic resolution of 2x2x2mm^3, 7 B_0, 32 directions b=700s/mm^2, 64 directions b=2000s/mm^2) were acquired. DW-MRI data was pre-processed with Tortoise[7] to remove motion and eddy currents artefacts. FA was computed on the low b-value sequence with FSL using the linear DTI model, while we fitted the NODDI model on the complete dataset using the Matlab toolbox available at (http://mig.cs.ucl.ac.uk). For each index (FA, FICVF, ODI, KAPPA, FISO) a two samples t-test was performed on both the left and right hippocampi using all the voxels of each group as input vectors . The p-values of the tests for ODI were 6.1E-6 for the right hippocampus and 0.0005 for the left hippocampus, while the p-values for Kappa were 3.91E-7 and 0.003 respectively. The t-tests were also repeated testing the average values of the subjects in each group and confirmed the statistical difference with $p<0.05$.

RESULTS: For each of the mentioned maps we computed a mean value for each subject keeping the right and left hippocampi separated, then a two samples t-test was performed. The tests showed statistical difference (i.e. $p<0.05$) for the ODI and KAPPA indices both on the left and right hippocampi; details are reported in Table 1.

	Left Hipp	Right Hipp
MS-ODI	0.49 (0.11)	0.53 (0.10)
Epileptic MS ODI	0.55 (0.11)	0.44 (0.11)
MS – Kappa	0.11 (0.04)	0.10 (0.03)
Epileptic MS Kappa	0.09 (0.03)	0.13 (0.05)

Table 1 Average values (and SD) for the ODI and Kappa maps in the two groups.

DISCUSSION: NODDI is able to model the signal providing a more accurate and specific quantitative description of the tissue microstructure in the hippocampi than the classic diffusion tensor model. While the FA index did not detect any modification between epileptic and non-epileptic hippocampi in MS subjects, both ODI and KAPPA appeared to be more sensible, reporting statistical difference in the coherence of the fibers inside the structure. ODI and KAPPA are strictly related, as KAPPA is a parameter of the statistical distribution governing the anisotropic compartment, therefore the statistical difference on both indices was not surprising. In particular, the right shifting of the ODI distribution in the epileptic group is linked to the reduction of fibers coherence that may be justified with the disruption of local structure.

CONCLUSION: The combination of multi-shell DW-MRI acquisition schemes and a three-compartment tissue model like that implement by NODDI might be able to provide a deeper characterization of tissue specific alterations than the classic DTI acquisition. We found that a possible link between epileptic episodes in MS patients and some alterations in the hippocampi might exist. Although at this first stage only ODI and KAPPA appeared to be sensible to MS lesions, the role of the intra cellular volume fraction and isotropic fraction will be investigated with further analysis.

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