Voxel-based Diffusion-Tensor-Imaging demonstrates hippocampal sclerosis

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Introduction: The typical diagnostic MR criteria of hippocampal sclerosis (HS) are disturbed internal architecture, hippocampal volume reduction and increased signal in T2-weighted images. There is a good correlation between these criteria and the histopathological diagnosis of HS, nevertheless, some patients with pathologically proven HS fail to display these MR criteria, and in others the changes are mild, and not clearly different from unspecific hippocampal changes. Diffusion tensor imaging (DTI) has unique sensitivity to molecular environment and provides information about the microstructure of cerebral tissue. Previous studies have suggested hippocampal DTI changes (2-3) in epilepsy. However, evaluation of its sensitivity in this area has been complicated by heterogeneity of patient groups and by limitations in analysis methods used. This study aims to use a voxel-based approach to analyse a relatively homogeneous group of HS patients. The common analysis framework also allows voxel-wise comparison with corresponding T2 and volume.

Methods: Subjects: 11 patients with unilateral left HS determined from our comprehensive epilepsy surgery program at Austin Health were investigated (mean age: 36, 7 men). Results were compared with a control group of 15 healthy subjects (mean age: 29, 6 men).
Imaging: The three imaging methods were performed at a 3T GE scanner: (i) DTI was performed with a 28 direction spin echo EPI sequence. The imaging parameters were as follows: TR/TE=5.8sec/83ms, 96×96 matrix, voxel size: 2.2×2.2×2.5mm, 50 contiguous slices, 3 pass interleaving, b=1100s/mm^2, 5 repeats of b=0 image, 28 directions; (ii) T2 mapping was carried out with a multi-echo CPMG sequence (8 echoes, TE=29-231ms, TR=6sec, 256×128, voxel size: 1.8×0.9×5mm, 24 slices); (iii) The structural scan was a T1-prepared high-resolution 3D-FSPGR sequence (voxel size 1×2×2mm).
Image analysis: The DTI images were analysed with the FSL package (fMRIB, Oxford). The fractional anisotropy (FA), Trace and principal eigenvalue (EV1) were obtained as invariant measures of anisotropy and mean diffusivity respectively. T2 maps were generated as previously described (4).
Voxel-based analysis: Voxel based analysis of the DTI, T2 and volume data was carried out by normalising the appropriate images to standard space. For the DTI analysis, a target template was created from the B0 images from each subject. The individual B0 images were normalised to this template and the warping parameters applied to the DTI parameter images. A final warp from template space to standard space was then applied. T2 analysis was carried out according to the voxel based relaxometry (VBR) procedure outlined in (4). Voxel-based analysis of the volume data followed the optimised VBM approach for gray matter (GM) (5). In all cases, spatially normalised images were smoothed with a 5mm kernel (the expected hippocampal lesion size). For the statistical analysis, age was used as a covariate of no interest. Areas of significant change are reported for $p<0.0005$ (uncorrected). Masks of the left hippocampus and the left anterior temporal lobe (ATL) (excluding the hippocampus) were generated and were used to compare counts of significant voxels.

Results: Figure 1shows 2 coronal slices with overlayed statistical differences for the DTI voxel-based analysis (FA: control>patients; Trace: patient>controls; EV1: patients>controls). Significant areas of FA reduction were observed in two principal areas of white matter: the genu of the corpus callosum and in the ipsilateral uncinate fasciculus (Fig. 2). This is the main white matter tract connecting the temporal lobe with the other parts of the brain. The Trace displayed an extensive area of increase in the anterior temporal lobe of the patient group. In addition, a significant portion of the tail and inferior body of the hippocampus displayed a significant Trace increase. The principal eigenvector (EV1) was increased over an even more extensive region of the hippocampus, with little change observed in the ATL. The T2 was significantly increased in a smaller, more anterior portion of the hippocampus and over large areas of the ATL in both GM and WM. The VBM analysis indicated volume changes that were principally localised to the lateral portion of the tail and body of the hippocampus, not distinguishable from the ventricular space. Table 1 lists voxel counts in the hippocampal and ATL masks.

Discussion & Conclusions: This study suggests that in unilateral HS patients focal Trace and principal eigenvector changes can be detected in the presumed epileptogenic region. These changes were more pronounced than abnormalities of T2 or GM volume, suggesting the potential of this method in the identification of this pathology. Additionally, extensive temporal lobe WM changes were detected with FA, Trace and T2. Reflecting the differences between these methods, the uncinate fasciculus, the major temporal lobe white matter tract, was identified with FA, the core of the white matter and the hippocampal formation with the Trace and EV1, and the gray-white matter junction with T2. This highlights that these different methods are suited to detect different aspects of the abnormalities associated with HS, and may be best used in conjunction. A previous DTI study has assessed TLE patients using ROI analysis and did not observe temporal lobe changes (2). This difference in observations may be explained by patient selection and methods used, highlighting the need for further studies of this topic. Our results suggests that there is an important role for DTI to play in the research and clinical evaluation of epilepsy.

References: (1) Briellmann R.S. et al, Neurology 58 :265 (2002); (2) Arfanakis K. et al, MRI, 20:511 (2002) ; (3) Assaf B.A. et al., AJNR, 24:1857 (2003) ; (4) Pell G.S. et al, NI (2004); (5) Good C. et el, Neuroimage, 14:21-36 (2001)

	FA ↓	Trace ↑	EV1 ↑	T2 ↑	Volume ↓
Hc	0	84	103	67	102
ATL	69	148	12	711	42

Table 1 Counts of significant voxels in the hippocampal and ATL masks

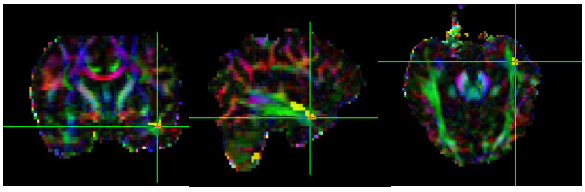

Fig. 2 Orthogonal overlay of FA result on standard DTI color map showing the area of signal change in the uncinate fasciculus (in yellow)

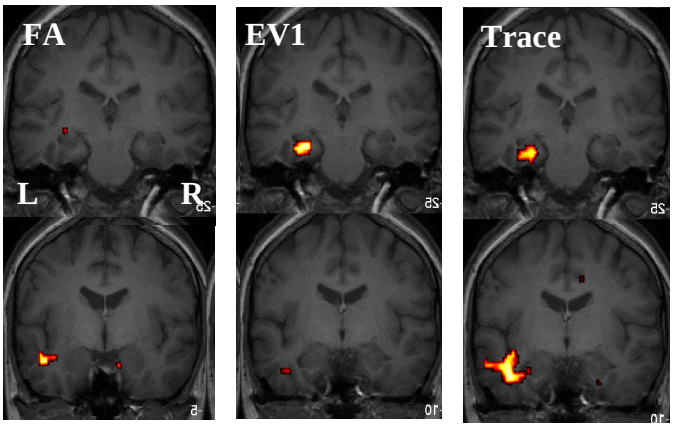

Fig 1 (to the right) Display of statistical overlays on 2 slices on the standard brain showing results of the DTI voxel-based-analysis. Images are displayed in neurological orientation. Contrast between patients and controls (see results).