Combined Voxel-based analysis of volume and T2-relaxometry in temporal lobe epilepsy

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Introduction: Hippocampal sclerosis (HS) is the most common abnormality found in the temporal lobes of patients with temporal lobe epilepsy. The typical diagnostic MR criteria of HS are volume reduction and increased signal in T2-weighted images. There have been many studies of the significance of these separate findings in HS, but their relationship could not be directly assessed due to the approaches commonly used for their analysis. The assessment of volume changes is possible by the voxel-based statistical technique of voxel-based morphometry (VBM). To date, analysis of T2 data has been carried out by manual placement of regions of interest (ROIs) over predefined areas of anatomy. We have introduced a voxel-based approach for the analysis of T2 data (voxel based relaxometry, VBR) (1). This technique shares with VBM the use of a common space for comparison of the images. The relationship of the volume and T2 changes can thereby be studied in the same subjects in a manner that has not before been possible.

Methods: Subjects: 16 patients with typical HS determined from our comprehensive epilepsy surgery program at Austin Health were investigated. 10 patients in this group had been diagnosed with left HS and the remaining patients had right HS. Results were compared with a control group of 49 healthy subjects.
Imaging: Structural and T2 scans were performed at a 3T GE scanner. The structural scan was a T1-prepared high-resolution FSPGR sequence. T2 mapping was carried out with a multi-echo CPMG sequence (8 echoes, TE=29-231ms, TR=6sec, slice thickness=5mm, FOV=24cm, 256×128).
Analysis: T2 maps were generated by fitting the two to 2 models: (i) The standard mono-exponential (T2r) and (ii) a mono-exponential model with inclusion of a baseline (T2b) (1). This latter fit incorporates the long-T2 CSF compartment into the baseline so that the T2 values in the mesial temporal area are less affected by partial voluming effects resulting from atrophy and proximity to the ventricles. VBR(T2b) and VBR(T2r) denote the use of the method with each of these measures of T2. VBM (structural) analysis followed the optimised approach of (2). Images were spatially normalized, segmented and then smoothed (8mm kernel). VBR analysis was carried out according to the procedure outlined in (1) (8mm smoothing kernel). Areas of significant volume and T2 changes between control and patient groups are reported for $p<0.005$ (uncorrected). Conjunction analysis was used to assess the degree of concurrent volume and T2 changes. A mask of the mesial temporal area was created in standard space and was used to compare counts of significant voxels in this region between the two techniques. Significant areas of extra-hippocampal signal changes were also assessed. In order to look at any underlying differences of the different images used in the two analyses, variance maps were calculated of the control group for each method.

Results: *VBM*: Regions of grey matter volume reduction (patients relative to controls) were observed in the ipsilateral hippocampus of the left and right HS subjects. The region was concentrated around the lateral edge of the hippocampus in an area close to the lateral temporal horn (see figure 1). In the right HS group, changes extended anteriorly. Small areas of volume change in the amygdala were evident in both groups. *VBR (T2b)*: Left hippocampal T2 increases (patients relative to controls) extended from anterior to posterior hippocampus in left HS and from middle to posterior hippocampus in right HS. *VBR(T2r)* changes were more extensive and, as expected, extended to the surrounding CSF. For both VBM and VBR, significant extra-hippocampal areas included ipsilateral anterior temporal lobe. Table 1 displays the voxel counts including areas of concurrent changes between the morphometry and T2 methods. Fig. 1 shows the results of VBR(T2b) and VBM methods for the left HS group. Fig. 2 shows the results of the conjunction analysis. The normalised variance map of the smoothed grey matter data used for VBM were significantly more heterogeneous in the mesial temporal area than the corresponding maps of the T2 data used for VBR analysis. For a mesial temporal region, the variance was approximately 50% lower than the corresponding structural value.

Discussion & Conclusions:
The concentration of the VBM change close to the lateral horn may reflect some of the deficiencies of the method. VBR changes were more localised to the hippocampal grey matter and were greater in extent and significance in this preliminary group of subjects. Areas of signal coincident signal change between structural and T2 methods were small in extent. This number increased when the T2r measurement was used for VBR and this is likely due to its sensitivity to CSF contamination in the voxel. Conjunction analysis is a statistical approach to the assessment of coincident significance and detected a greater extent of the hippocampus that the logical operation shown in Table 1. The variance maps, however, reflect an underlying difference in signal heterogeneity that needs to be considered in any statistical comparison. The consequences of tissue change in the sclerotic hippocampus are not well understood. The ability to compare the two analyses in a common framework is therefore a substantial step forward in the continuing investigation of HS and other pathologies.

References: (1) G.S. Pell et al, Neuroimage (in Press)
(2) C. Good et el, Neuroimage, 14:21-36 (2001)

	Whole brain	Hippocampal Region
VBM [left]	6266	246
VBR(T2b) [left]	40218	2914
Overlap with VBM	*492*	*0*
VBR(T2r) [left]	30983	6076
Overlap with VBM	*2111*	*231*
VBM [right]	9537	44
VBR(T2b) [right]	15970	959
Overlap with VBM	*36*	*0*
VBR(T2r) [right]	51142	1653
Overlap with VBM	*118*	*0*

Table 1 : Count of significant voxels in VBR and VBM analyses including overlapping voxels

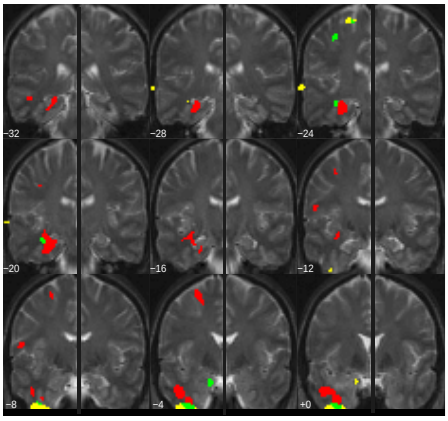

Fig. 1: Areas of significant signal change for VBM (yellow), VBR(T2b) (red) and overlapping voxels (green) for the left HS group ($p<0.005$ uncorrected)

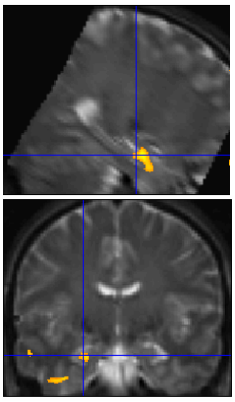

Fig.2: Result of conjunction analysis of VBM and VBR(T2b) contrasts ($p<0.005$ uncorrected) for the left HS group