Non-invasive imaging of endogenous magnetic particle deposits in biological tissue using magnetic resonance imaging

H. Pardoe[1], G. S. Pell[1], G. D. Jackson[1]

[1]Brain Research Institute, Melbourne, Victoria, Australia

Introduction:

For cryptogenic and idiopathic epilepsies, the anatomical basis of the epilepsy is, by definition, not discernible through standard visual inspection as there are no obvious structural abnormalities associated with these forms of epilepsy. Subtle variations associated with different forms of these epilepsies may, however, be detectable using voxel based morphometry and may provide information concerning the cortical and subcortical networks and regions involved.

Methodology:

Subjects: The Connecticut Study of Epilepsy in Children is an on-going prospective community-based study of 613 children enrolled when initially diagnosed with epilepsy (1993-1997). The primary aim of the study is to monitor outcomes of epilepsy in children over the course of their development into adulthood. Epilepsy syndromes have been carefully characterized in this cohort. This provides an ideal setting in which to apply morphometric analysis techniques to investigate structural brain structural variations using voxel-based morphometry (VBM). Here we focus on Childhood Absence Epilepsy (CAE), Cryptogenic Localization Related Epilepsy (CLRE) and Benign Rolandic Epilepsy (BRE). The results of the VBM analysis are compared with results reported in a previously published fMRI study of regional BOLD signal decrease in idiopathic generalised epilepsy (IGE) subjects [1].

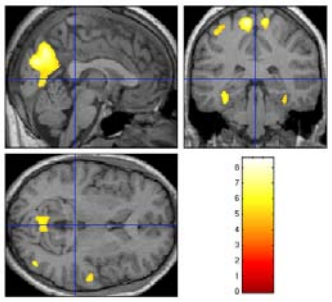

Figure 1. Areas of significant gray matter volume decrease in CAE subjects overlaid on a standard normalised MR image.

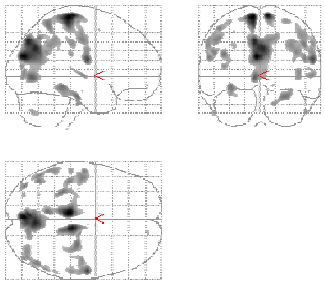

Figure 2. Areas of significant gray matter volume decrease in CAE subjects (as shown in Figure 1).

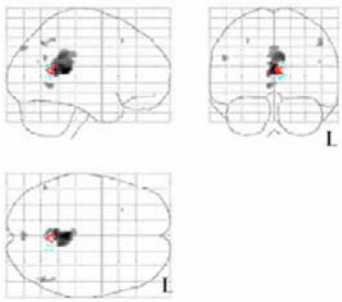

Figure 3. Areas of spike related deactivation in IGE subjects studied using fMRI. Figure from [1].

Imaging and VBM analysis: Approximately 8-9 years after study entry, study participants were invited to have a brain MRI as part of the study. The imaging protocol included an inversion-recovery 3D Gradient Echo MR imaging sequence on a 1.5 T Siemens Sonata MR scanner (voxel size $0.86 \times 0.86 \times 1.6$ mm). Control scans were imaged using an inversion-recovery 3D Gradient Echo MR imaging sequence on a 3T GE LX Horizon scanner (voxel size $0.48 \times 0.48 \times 2$ mm). VBM analyses were carried out according to the procedure outlined in [2]. Areas of significant gray matter volume reduction in the patient group are reported for $p < 0.05$ (FWER corrected).

EEG activated fMRI: Functional MRI sequences were recorded on a 3T GE LX Horizon scanner using gradient-echo echo-planar imaging with whole brain coverage (voxel size $1.87 \times 187 \times 4$ mm, 1mm gap). EEG was acquired in the scanner and an imaging sequence was manually triggered upon observation of epileptiform activity. For full details of the fMRI methdodology see [1].

Results :

To date images have been analysed from 10 CAE (mean age 14.6, 5 male); 17 CLRE (mean age 16.4, 7 male) and 8 BRE (mean age 16, 1 male) subjects. Results were compared with a control group of 109 subjects previously imaged at the Brain Research Institute, Australia (Mean age 31.8, 54 Males). Figures 1 and 2 indicate brain regions in which there is a significant gray matter volume decrease in CAE subjects compared to controls, as detected by VBM. The largest difference is seen posteriorly in the cuneus and precuneus, with some volume changes detected in the hippocampus and posterior cortical regions. In the CLRE subject group significant gray matter volume decreases were observed in similar regions to those in the CAE subject group, with additional volume decreases observed in the pons. In the BRE subject group significant gray matter volume decreases were confined to the cuneus. Figure 3 indicates grouped analysis results from a previous study [1] of patients with idiopathic generalised epilepsy indicating the location of spike-triggered fMRI decreases in BOLD signal. BOLD signal decreases were observed in the posterior cingulate and posterior parietal regions, including the cuneus.

Discussion & Conclusions:

The similarity in regions of gray matter decrease in epilepsy subjects, as measured using VBM, and decrease in BOLD signal in epilepsy subjects displaying epileptiform activity, as measured using fMRI, provide compelling evidence for a link between functional changes in the brain that occur during seizures and structural variations that are present in different epilepsy syndromes. The congruity of the measured regions in the independent experiments validates the biological plausibility of the observed VBM results.

Furthermore the subtle differences of structure that are indicated by the VBM analyses of different epilepsy syndromes suggest that VBM has the potential to elucidate syndrome-dependent brain structure variation. Of considerable importance for determining inter-syndrome structural variations using VBM is a large, well-defined epilepsy subject cohort. The potential for longitudinal structural scans would provide valuable information regarding the correlation between seizure activity and structural changes in the brain. The subject cohort investigated in this study will provide ideal data for the investigation of this relationship.

One potential factor that may need to be accounted for in order to confirm the validity of the VBM results is the fact that the control scans were acquired on a different MR scanner to the epilepsy subjects. The effect of different scanners and imaging parameters on the accuracy of VBM results is an area of current investigation by our research group. The importance of investigating the effect of imaging parameters on VBM results extends beyond the validation of the results presented in this study. Large scale clinical studies may involve the acquisition of imaging data over a long time period or large geographical distances, and so imaging on the same scanner using the same imaging sequence may be impractical. Therefore a detailed investigation of the effects on varying imaging parameters on VBM results will be of considerable use. The correlation between regions of decrease in BOLD signal in fMRI studies and significant regions of gray matter volume decrease as indicated by VBM analysis of epilepsy subject suggests that the result observed in this study likely reflect real structural change.

1. Archer, J.S., et al., *fMRI "deactivation" of the posterior cingulate during generalized spike and wave.* Neuroimage, 2003. 20(4): p. 1915-22.
2. Good, C.D., et al., *A voxel-based morphometric study of ageing in 465 normal adult human brains.* Neuroimage, 2001. 14(1 Pt 1): p. 21-36.