Altered Memory Network Organisation in Left Temporal Lobe Epilepsy Associated with White Matter Structural Changes

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Introduction: Temporal lobe epilepsy (TLE) is associated with specific localised hippocampal atrophy and metabolic and white matter changes extending beyond the mesial temporal lobe (MTL). Surgical resection of the seizure focus may cure intractable unilateral seizures arising from the MTL, but carries a risk of postoperative decline in episodic memory. Although functional reorganisation of language functions has been demonstrated in patients with left hemisphere TLE (LTLE) (e.g Adcock et al 2003), the existence of plasticity within the memory network remains uncertain. The emergence of refractory seizures may involve abnormal connectivity within the MTLs as a result of dendritic sprouting. Consequently, LTLE may not induce large-scale functional reorganisation, but rather impact on structural coherence, or coherence of functional timeseries between different voxels across subjects, between the MTLs and other regions involved in memory processing. The aim of this study was to test whether (i) LTLE is associated with hemispheric reorganisation of memory functions, (ii) LTLE is associated with altered structural coherence in the memory network, and (iii) functional memory changes relate to altered structural integrity of white matter pathways.

Methods: 11 LTLE patients and 10 healthy volunteers performed a functional MRI task of complex visual memory encoding (previously described by Rombouts et al (2001)), known to engage bilateral MTL structures in healthy volunteers. All data were acquired on a 3T Siemens-Varian. Blood-Oxygen-Level-Dependent (BOLD) data were acquired in 50s blocks of "new" compared with "familiar" items (TR=3s, TE=30ms, 5mm slice thickness). Whole-brain diffusion images (60 gradient directions, 2.5mm slice thickness) were also available for 9 of the 11 LTLE patients. Whole-brain, cluster-based fMRI general linear model (GLM) data analysis ($p<0.05$) was conducted using FMRIB's Expert Analysis Tool (FEAT) following standard preprocessing steps and 5mm FWHM smoothing. Model-free structural coherence analysis was conducted using Tensor Independent Component Analysis (TICA) (Beckmann et al 2005). Fractional Anisotropy (FA) measures were calculated with FMRIB's Diffusion Tool, and fed into Tract-Based-Spatial-Statistics (TBSS) (Smith et al 2006). To identify regions where FA correlated with task-related BOLD signal change, percent signal change was extracted from a region of significantly different structural coherence identified with TICA, demeaned, and incorporated as a covariate in permutation testing on the TBSS FA skeleton using both cluster-based thresholding and threshold-free cluster enhancement using 100-1000 iterations.

Results: Group FEAT analysis revealed extensive bilateral MTL activation in both LTLE patients and healthy controls during complex scene encoding. No significantly increased activation of the contralesional (right) hemisphere was found in patients relative to controls using standard GLM analysis. TICA, however, revealed significantly increased structural coherence in patients relative to controls between the MTLs and a region encompassing the left gyrus rectus, medial and posterior orbital gyri (Figure 1). FA along the right uncinate/inferior longitudinal fasciculus correlated with percent signal change in this left inferior frontal region (using both cluster-based thresholding and threshold-free cluster enhancement permutation testing) (Figure 2).

Discussion: Reductions in anisotropy have been reported in multiple regions including the ipsilesional uncinate in TLE (e.g. Rodrigo et al 2007). Our results extend these findings by relating localised measures of white matter integrity to functional changes within the memory network in patients with LTLE. Using more sensitive, objective measures of functional and structural organisation, our results indicate (i) memory reorganisation in LTLE involves subtle changes within the normal anatomical network, involving altered structural coherence rather than hemispheric reorganisation between medial temporal and orbitofrontal regions and that (ii) these functional changes in orbitofrontal activity correlate with white matter integrity in the contralesional limbic projection fibres. Further analysis will be conducted with additional permutation test iterations.

References: Adcock J.E. et al (2003) NeuroImage 18(2) :423-438; Rombouts S.A et al (2001) NeuroImage 14(1) : 67-76 ; Beckmann, C.F. et al. (2005) NeuroImage 25(1) : 294-311 ; Smith S.M et al (2006) NeuroImage 31 : 1487-1505

Figure 1

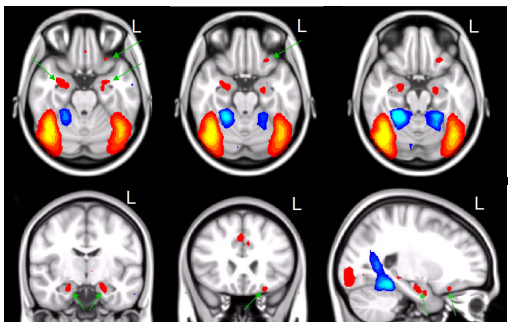

Figure 2