Hard-wired or Soft-wired ? Evidence for the Structural Plasticity of White Matter Networks Following Anterior Temporal Lobectomy

M. Yogarajah[1], N. Focke[2], S. Bonelli[1], P. Thompson[1], C. Vollmar[1], A. McEvoy[3], M. Symms[1], M. Koepp[1], and J. Duncan[1]
[1]MRI Unit, National Society for Epilepsy, Chalfont St Peter, Bucks, United Kingdom, [2]University of Goettingen, Germany, [3]University College London Hospital, United Kingdom

Introduction Temporal lobe epilepsy (TLE) is the most common cause of medically intractable partial epilepsy, and in approximately 80% of patients with TLE, seizures are refractory to drug treatment. For this group of patients, anterior temporal lobe resection (ATLR) is now a well-established and effective means of treatment. Though up to 80% of these patients may be rendered seizure free by surgery, up to 40% are also at risk of postoperative decline in language functioning. We used diffusion tensor imaging in a longitudinal study in order to investigate the reorganisation of white matter that occurs after epilepsy surgery and how this relates to neuropsychological outcome.

Methods: We scanned 46 patients with TLE (26 left 20 right) before, and 4 months after ATLR. All patients underwent neuropsychological assessment including the Mc Kenna Graded Naming Test, IQ and verbal fluency tests pre- and postoperatively. fMRI was used to lateralise language.

MRI acquisition was performed on a 3T GE Excite II scanner. Standard imaging gradients with a maximum strength of 40mT/m and slew rate 150T/m/s were used. All data were acquired using a body coil for transmission, and 8 channel phased array coil for reception. The DTI acquisition was a single-shot EPI sequence, cardiac gated, with TE=73ms. Sets of 60 contiguous 2.4mm-thick axial slices were obtained, covering the whole brain, with diffusion sensitizing gradients applied in each of 52 non-collinear directions (maximum b value of 1200mm2/s (δ=21ms, Δ=29ms, using full gradient strength of 40mT/m)) along with 6 b=0 scans. The field of view was 24cm, and the acquisition matrix size was 96x96, zero filled to 128x128 during reconstruction so that the reconstructed voxel size was 1.875 x 1.875 x 2.4 mm3.

FSL was used for all image processing. After eddy-correction of the images, the main diffusion tensor and its eigenvalues ($\lambda 1$, $\lambda 2$, $\lambda 3$) and eigenvectors were estimated for each voxel, along with the summary parameters fractional anisotropy (FA), mean diffusivity (MD), parallel diffusivity ($\lambda \parallel$) and perpendicular diffusivity ($\lambda \perp$). In order to align all FA data into a common space, the following procedure was applied separately for left and right TLE groups. Firstly, all patients' preoperative FA images were aligned to the FMRIB58_FA standard space template supplied with FSL. Then each patient's postoperative FA image was co-registered to its preoperative FA image with the aid of a de-weighting mask drawn over the area of resection in the mean b=0 image. Finally, the warps derived from each of the two steps were combined, and the resulting warp was applied to the native, postoperative FA image in each subject. In this manner in each subject the pre- and postoperative images were aligned in a common space. Following this, voxelwise statistical analysis of the FA data was carried out in the left and right TLE groups separately, using TBSS (Tract-Based Spatial Statistics). A permutation-based, non-parametric approach was used to carry out a paired t-test in order to assess the location and extent of significant increases and decreases in the FA between pre- and postoperative scans in each group. Threshold free cluster enhancement (TFCE) was used to correct results for multiple comparisons, and results were considered significant for $p < 0.05$.

In order to verify and further explore results, all significant pre- and postoperative clusters were de-projected and inverse-normalised into their native images. The mean pre- and postoperative FA, $\lambda \parallel$ and $\lambda \perp$ values were then compared using paired t-tests. SPSS was used to test for a correlation between the change in language function and diffusion parameters after surgery. Selected native clusters were also used to seed tractography in order to investigate the morphological nature of the observed morphometric changes. Thresholded tractography maps were then normalised to the FMRIB58_FA template, and averaged to form a group commonality map.

Results Both left and right TLE patients demonstrated similar patterns of a decrease in FA ipsilateral to the resection, and to lesser extent contralaterally (see figure 1). Left TLE patients also demonstrated a widespread increase in FA (mean 8%) in a single cluster extending over the anterior, posterior and superior corona radiata, the posterior limb and dorsal part of the anterior limb of the internal capsule, and the external capsule ($p \leq 0.01$) These changes were absent in right TLE patients. Comparison of pre- and postoperative native clusters confirmed these findings, which were due to an increase in $\lambda \parallel$ ($p=0.002$) and decrease in $\lambda \perp$ ($p=0.003$) after ATLR. A comparison of hand drawn, pre- and postoperative masks over the internal and external capsule in the native FA images further validated these findings ($p=0.001$). A significant correlation was noted between the percentage change in verbal fluency and $\lambda \parallel$ in this cluster after surgery ($r=0.398$ $p=0.027$) such that the greater the increase in $\lambda \parallel$ after surgery the better the outcome. This remained significant after correction for IQ and language dominance ($r=0.457$ $p=0.016$). There was also a significant correlation between pre- and postoperative $\lambda \parallel$ in this cluster and postoperative GNT scores ($r=0.388$ $p=0.030$ and $r=0.480$ $p=0.009$ respectively), but not preoperative GNT scores. Tractography from this cluster highlighted a network of corticostriatal and motor connections, and a ventral connection between language areas in the posterior superior temporal gyrus and the inferior frontal lobe via the external capsule (figure 2).

Figure 1 – TBSS results in left TLE group. Postoperative decreases in FA are in blue and increases in FA are in red-yellow

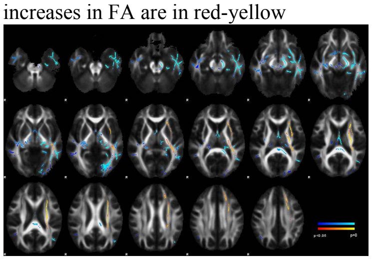
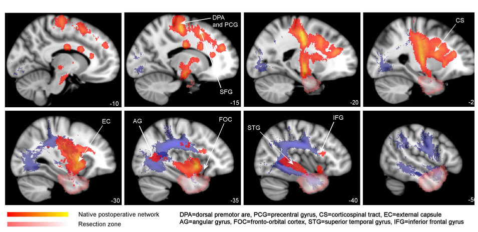


Figure 2 – Commonality map in left TLE group (20% threshold)



Discussion This study demonstrates the structural consequences of ATLR on white matter networks in patients with TLE. Although areas of decreased FA were evident postoperatively in both left and right TLE patients, there were also significant postoperative increases in FA in left TLE patients. The location of these changes, their correlation with language function, and their presence in left TLE patients only, suggests that they may be related to structural plasticity underlying language function after surgery. Tractograpahy confirms that these regions are part of the ventral language network[1] which is medial to the arcuate fasciculus/superior longitudinal fasciculus and may therefore be less prone to damage after surgery than the latter structure which extends into the anterior temporal lobe (figure 2). Surgery and damage to the dorsal language system may cause an increase in connectivity in the evolutionarily, older ventral system. This finding has important implications for the understanding of brain plasticity in response to injury, and our understanding of cognitive outcome after ATLR. The use of white matter functional connectivity as an additional landmark for ATLR may aid pre-surgical planning, and minimise postoperative deficits.

[1]Saur D et al. Ventral and dorsal pathways for language. Proc.Natl.Acad.Sci U.S.A 2008; 105: 18035-18040.