Decrypting cryptogenic partial epilepsy using white matter fractional anisotropy analysis

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Introduction

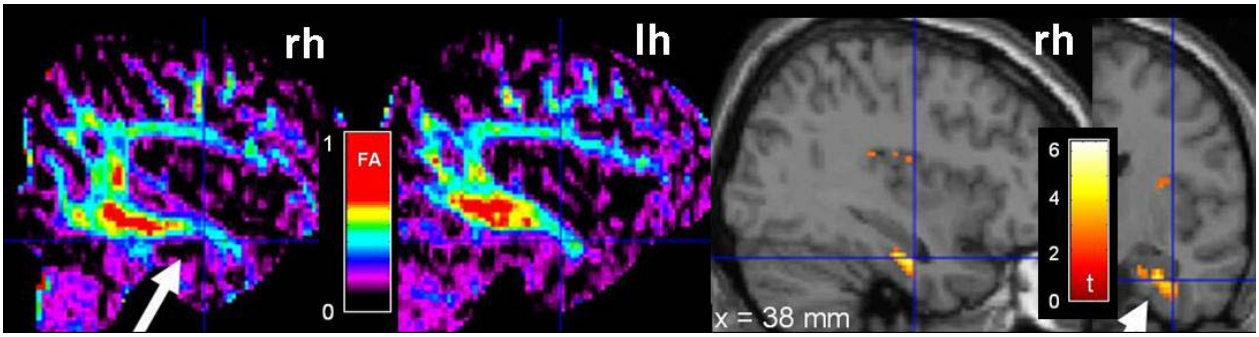
Magnetic resonance imaging (MRI) is a crucial tool in the evaluation of patients with partial epilepsy (PE) for the preoperative etiologic characterization of epileptic regions. However, conventional structural MRI fails to identify a cerebral lesion in approximately 25% of patients with refractory focal epilepsy, and surgical treatment of these patients with negative MRI is often associated with a poor outcome. Diffusion tensor imaging (DTI) is a relatively new noninvasive MRI technique that is sensitive to microstructural abnormalities of cerebral white matter (WM). The amount of nonrandom water diffusion within WM tissue is quantified by fractional anisotropy (FA). This measure provides unique in vivo information about the pathological processes that affect water diffusion as a result of brain microstructural damage. The objectives of the present study were to (i) identify focal FA abnormalities in MRI-negative patients with PE and to (ii) correlate FA changes with electroclinical information (e.g. duration of epilepsy, frequency of seizures, and duration of anti-convulsion mediation).

Methods

We studied 67 healthy volunteers and nine age-matched patients with cryptogenic partial seizures. All patients underwent medical and neurological examination, interictal EEG, long-term video EEG monitoring, and conventional MRI (T1-weighted, T2-weighted and FLAIR). No patient showed evidence of abnormal brain morphology (structure or volume) or tissue signal integrity using conventional MRI. All patients and controls underwent DTI analysis (3T, EPI, 20 diffusion directions (two b-factors, 0 s/mm^2 and 1000 s/mm^2, TR=9,8 s / TE=98 ms, voxel size: 0.89 x 0.89 x 3.6 mm, 2 averages, scanning time 7:46 min)). Voxel-by-voxel FA differences between patients and controls were evaluated using SPM5. Differences in FA values between the patient and control groups were statistically evaluated by analysis of covariance, modelling the factor age as co-variable to account for the age dependency of FA (ANCOVA, $P < 0.001$, uncorrected; min. cluster size 20 voxels; smoothing 8 mm). ROI analyses were also performed in several predefined WM regions.

Results

Significant widespread FA reduction was observed preferentially in temporal, parietal, callosal and brainstem regions when all nine patients were compared to controls. When patients were compared to controls on an individual basis, voxel-based analyses revealed widespread symmetrically bilateral extratemporal temporal lobe FA reduction in all patients. Furthermore, asymmetrical temporal lobe FA reduction was consistently ipsilateral to the electroclinical focus. The Figure depicts significant FA reduction of the right medial temporal WM region in a patient with a well circumscribed right epileptogenic focus. ROI analyses were consistent with voxel-based analyses, showing FA abnormalities in temporal, parietal and callosal regions, without significant alterations in cerebellar, thalamic or occipital regions. There were no significant relationships between FA and duration of epilepsy, age of onset of epilepsy, frequency of seizures, duration of anti-convulsion medication or other clinical data.



Discussion

Our findings extend previous studies that identified FA changes in patients with known hippocampal sclerosis. We have identified FA alterations in temporal lobe regions consistently ipsilateral to the seizure focus in patients with no observable brain abnormality on conventional MRI. We suggest that WM FA analysis may represent an effective method of lateralising a neuroanatomical abnormality underlying the seizure focus during pre-surgical evaluation of PE. In order for this potential to be realised, patients need to be further investigated to correlate pre-surgical FA alterations with post-surgical outcome, as only then will a direct relationship between microstructural alterations and the epileptogenic zone be established. We furthermore have demonstrated widespread multi-lobar FA abnormalities in patients with PE, thus indicating that microstructural abnormalities extend far beyond the epileptogenic zone in these patients, which is consistent with other research on macrostructural abnormalities in patients with PE.