A Preliminary Diffusional Kurotsis Imaging Study of Temporal Lobe Epilepsy

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Introduction

Gray and white matter abnormalities have been extensively investigated in medial temporal lobe epilepsy (MTLE) [1]. Diffusion tensor imaging (DTI) studies have reported reduced fractional anisotropy (FA) and increased mean diffusivity (MD) in the limbic system of patients with MTLE, as well as extra-limbic abnormalities [2]. Diffusional kurtosis imaging (DKI) is an extension of DTI that enables simultaneous quantification of Gaussian and non-Gaussian diffusion in the brain [3]. Non-Gaussian diffusion measures are sensitive markers of tissue microstructure and as such provide complementary information to DTI metrics. DKI quantifies non-Gaussian diffusion by estimating the kurtosis of the water diffusion displacement distribution. The goal of this preliminary study is to investigate the non-Gaussian diffusion signature of MTLE as measured with DKI and to compare this to that of DTI.

Methods

DKI scans were obtained from ten patients with left MTLE (mean age ± std dev = 40.4 ± 17.6 years; 7 female) and twenty age- and sex-matched healthy volunteers (mean age ± std dev = 37.1 ± 13.1 years; 14 female). The patients were diagnosed with MTLE based on a history of partial epilepsy and the presence of unilateral hippocampal sclerosis on conventional diagnostic MRI or ictal video-electroencephalography demonstrating unilateral temporal seizure onset. Diffusion-weighted images were obtained on a Siemens 3T Verio scanner using a twice-refocused echo planar sequence with three diffusion weightings (b = 0, 1000 and 2000 s/mm^2) along 30 diffusion encoding directions with NEX=1 (NEX=10 for b = 0). Other imaging parameters were TR = 8500 ms, TE = 98 ms, FOV = 222×222 mm^2, matrix size = 74×74, parallel imaging factor of 2, slice thickness = 3 mm, and 40 axial slices. Parametric maps of the standard DTI metrics of MD, axial diffusivity $D_{\parallel}$, radial diffusivity $D_{\perp}$, and FA, as well as the additional DKI metrics of mean kurtosis (MK), axial kurtosis $K_{\parallel}$, and radial kurtosis $K_{\perp}$ were obtained using methods described elsewhere [4]. FA maps were spatially normalized to standard space using the FMRIB Software Library (FSL) [5] and the resulting transformation was applied to normalize the other maps. Following spatial normalization, standard and skeleton-based voxelwise analyses were performed using Nonparametric Mapping (NPM) [6] and Tract-Based Spatial Statistics (TBSS) [7], respectively. Multiple-comparison corrections were performed by false discovery rate thresholding in NPM and permutation testing in TBSS.

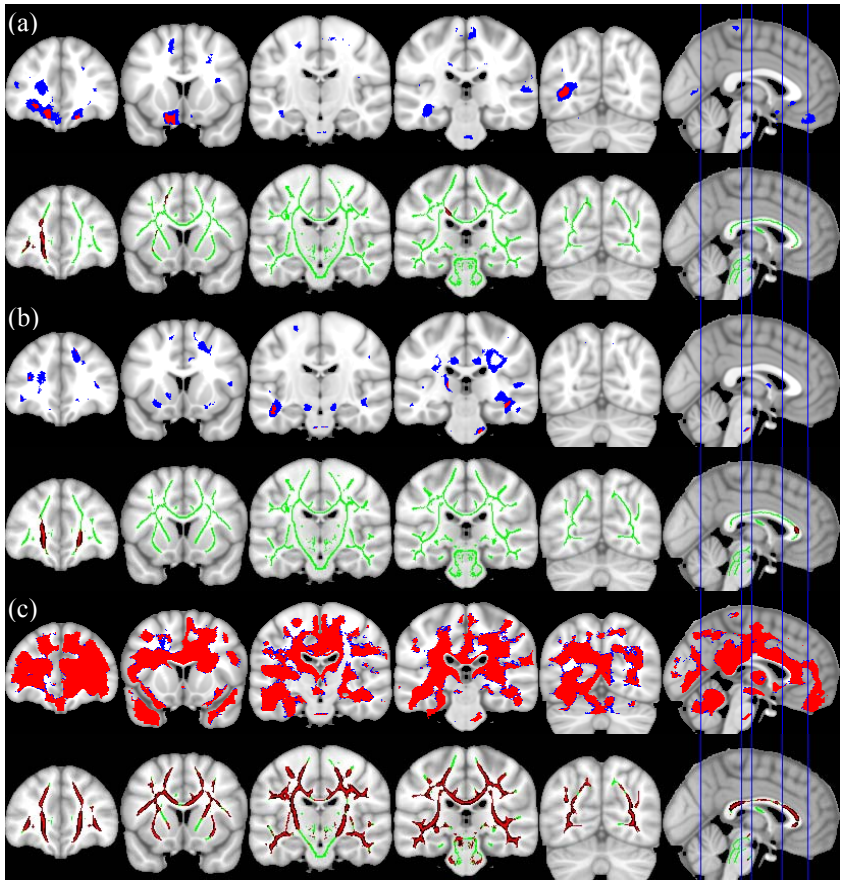

Figure 1. Voxelwise and TBSS maps of (a) increased MD; (b) decreased FA; and (c) decreased MK in patients with left MTLE compared to matched healthy subjects shown in neurological convention. In voxelwise maps, voxels corresponding to two-sided uncorrected $p < 0.05$ are marked in blue, and voxels with FDR-corrected $p < 0.05$ are shown in red. In TBSS maps, the FA skeleton with FA > 0.3 is shown in green and voxels with one-sided permutation-corrected $p < 0.05$ are marked in red.

Results

Figure 1 shows the results of voxelwise analyses for MD, FA, and MK. MD and FA identified small areas of abnormalities clustered around the hippocampus, the corpus callosum and corona radiata, as well as the frontal regions. Conversely, MK showed widespread limbic and extra-limbic abnormalities, with a higher intensity around peri-hippocampal and peri-limbic regions. Table 1 summarizes the fraction of statistically significantly different voxels between the patients and controls as identified with various diffusion metrics. Both standard and TBSS analyses identified appreciably more significant voxels with MK and $K_{\perp}$ than with DTI measures, whereas no voxels were found to show increased $K_{\parallel}$ in patients.

Discussion

We investigated the non-Gaussian diffusion signature of MTLE as characterized with DKI and compared this to that of DTI. Our preliminary results suggest that while DTI measures showed limited limbic and frontal abnormalities in MTLE, DKI metrics identified widespread group differences in temporal and extra-temporal regions. These observations suggest that MTLE may be associated with a pervasive and previously unrecognized pattern of compromised cerebral tissue microstructure as revealed by DKI. By providing a potentially more sensitive marker of brain pathology in MTLE, DKI may enable improved monitoring of disease progression and more effective treatment planning.

References: **1.** Keller SS & Roberts N, Epilepsia 2008; 49:741. **2.** Bonilha L, et al. Epilepsia 2010; 51:519. **3.** Jensen JH, et al. MRM 2005; 53:1432. **4.** Tabesh A, et al. MRM 2011; 65:823. **5.** Smith SM, et al. NeuroImage 2004; 23:208. **6.** Rorden C, et al. NeuroImage 2007; 35:1531. **7.** Smith SM, et al. NeuroImage 2006; 31:1487.

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Table 1. Percentage of significantly different voxels between the diffusion maps of patients and controls at the corrected significance levels indicated in the Figure 1 caption. The percentages are reported for increased MD, $D_{\perp}$, and $K_{\parallel}$, and decreased $D_{\parallel}$, FA, MK, and $K_{\perp}$ in patients. For voxelwise analysis of MD and MK maps, the percentage was calculated relative to the number of parenchyma voxels with average MD < 1.5 μm^2/ms. For axial and radial metrics as well as for FA, it was calculated relative to the number of white matter voxels with average FA > 0.25. For TBSS, the percentage was calculated relative to the number of voxels in the FA skeleton with FA > 0.3.

Metric	Significant voxels (%) (voxelwise)	Significant voxels (%) (TBSS)
MD	0.42	5.8
$D_{\parallel}$	0.11	6.9
$D_{\perp}$	0.58	2.5
FA	0.23	2.8
MK	42	81
$K_{\parallel}$	0	0
$K_{\perp}$	76	79