

LONGITUDINAL DIFFUSION TENSOR IMAGING OF FORNIX DEGENERATION FOLLOWING EPILEPSY SURGERY

M. Liu¹, D. Gross², B. Wheatley³, and C. Beaulieu¹

¹Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada, ²Neurology, University of Alberta, Edmonton, Alberta, Canada, ³Neurosurgery, University of Alberta, Edmonton, Alberta, Canada

INTRODUCTION: White matter fiber degeneration caused by neuronal injury is characterized by axonal alterations in the acute phase and myelin loss in the chronic phase. Unlike conventional MRI, diffusion tensor imaging (DTI) may be sensitive to this process as shown in animal models^{1,2} and humans^{3,4}. The observed reduction of fractional anisotropy (FA) is often the result of decreased parallel (λ_{\parallel}) diffusivity early on and increased perpendicular (λ_{\perp}) diffusivity later on which can be related to axonal degeneration and myelin breakdown, respectively⁵. A previous study of epilepsy patients with surgical transection of the corpus callosum has confirmed this pattern and time course of water diffusion at 1 week and 2-4 months after injury consistent with the known stages of Wallerian degeneration⁴; however, the DTI changes within the first week of injury are unknown as are whether these findings hold true for a different tract injured by a different surgical procedure. To address this issue, DTI analysis of the fimbria-fornix was acquired on three patients with medically intractable temporal lobe epilepsy (TLE) who underwent anterior temporal resection (including a portion of the fimbria-fornix) at several time points: before the surgery, 3-4 times within a week after surgery and 2-4 months later.

METHODS: Three patients with medically intractable TLE were studied with DTI: Patient 1, a 33-year-old man was scanned before surgery and 1, 2, 3, 6 days, 2 months, 4 months after left temporal resection; Patient 2, a 55-year-old woman was scanned before surgery and 2, 3, 6, 7 days, 2 months after left temporal resection; and Patient 3, a 45-year-old man was scanned before surgery and 1, 5, 6 days, 2 months after right temporal resection. DTI was performed on a 1.5T Siemens Sonata scanner using axial fluid-attenuated inversion recovery (FLAIR) DTI (26 slices, 2x2x2 mm³, scan time=8:23min) with coverage of the fornix. Tractography of the fornix was performed using the FACT algorithm in DTIstudio⁶. For each time point within the first week, the crus of the fornix (Figure 1) ipsilateral to the surgery side was traced by tractography using parameters FA>0.25 as a start threshold and FA<0.25 or angle >70° as a stop threshold. Three regions of interest for fiber selection were drawn on the color maps derived from the FLAIR DTI⁷. Because the fornix degenerated dramatically at 2-4 months after surgery and tractography failed to trace this white matter bundle consistently, the chronic scans were nonlinearly registered to the pre-surgical scans using MEDINRIA to query the DTI parameters of the co-registered fornix. FA, apparent diffusion coefficient (ADC), λ_{\parallel} and λ_{\perp} were quantified over all voxels in the ipsi-lateral fornix at each time point.

RESULTS: The diffusion parameters of the ipsilateral fornices were dynamic and showed unique changes over time for each measure (Figure 2). The FA stayed relatively constant within the first few days after surgery but was reduced at 6-7 days relative to the pre-surgical values per subject. In contrast to the relatively stable FA early on, the injured fornix in all three patients showed a considerable decrease of both λ_{\parallel} and λ_{\perp} at the first one or two days after surgery which led to a dramatic decrease in ADC (reduced by 11%, range: 8%-16%). λ_{\parallel} showed the largest reductions acutely and remained below the pre-surgery level until the end of the week for all three patients. Interestingly, λ_{\perp} was also reduced acutely, to a lesser extent, but by 7 days it was reversing the trend (i.e. pseudo-normalizing). At the 2-4 months post-operative stage, FA was reduced markedly, λ_{\parallel} was elevated relative to week one in 2 of the 3 patients, but was still lower in 2 cases relative to pre-surgical values, and λ_{\perp} was elevated in all cases.

DISCUSSION: Animal models have suggested that parallel and perpendicular diffusivities may reflect unique aspects of tract pathology (e.g. axon versus myelin) after injury¹. Our results in human subjects are in agreement that longitudinal diffusion is markedly affected acutely; however, we also observed reductions of perpendicular diffusion early on within the first week. A previous longitudinal human DTI study after corpus callosum transection showed that parallel diffusion was reduced at 1 week, but gave the impression that perpendicular diffusion was static and unchanged at 1 week post-injury, but they did not measure within the first week after surgery, which is challenging in post-surgical patients. It is not clear what the early diffusion reductions reflect but possibilities include reduced cytosolic streaming or neurofilament/microtubule dissolution. The chronic findings of much elevated perpendicular diffusivity agree with the earlier work suggesting that it is related to myelin degradation. DTI appears capable of following the complex axonal degeneration process in human brain.

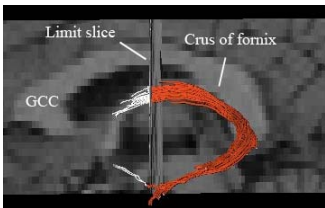


Figure 1 (Left): Ipsilateral crus of fornix from patient 1 with TLE derived from tractography at the pre-surgical time point. A coronal limit slice was placed at the separation of crura of fornix to restrict the analysis within single crus. For point of reference, GCC is the genu of corpus callosum.

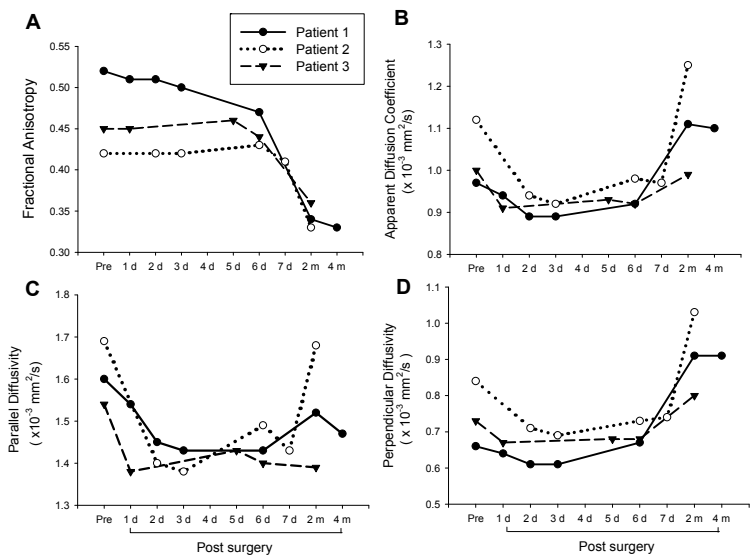


Figure 2: Time course of averaged DTI parameters of the ipsilateral crus of fornices from three patients with TLE. The time point prior to surgery serves as a reference. FA showed small reductions within the first week with a much bigger reduction at 2-4 months. A dramatic reduction particularly of λ_{\parallel} as well as λ_{\perp} occurred in the first two days post-operative. λ_{\parallel} remained low at the subsequent time points within a week and recovered slightly at 2-4 months. λ_{\perp} reached a minima ~ day 3 and recovered at the end of the first week then continued to increase to a higher level than pre-surgical stage at 2-4 months.

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