Diffusion Tensor Imaging demonstrates the evolution of axonal degeneration after corpus callosotomy

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INTRODUCTION: Axonal degeneration is characterized by a series of events caused by neuronal or axonal injury that ultimately lead to the fibrosis and atrophy of the affected neuronal fibers. Conventional MRI cannot identify the spread of degeneration along white matter within the first four weeks[1, 2]. Contrarily, previous studies using diffusion tensor imaging (DTI) have demonstrated white matter abnormalities in the acute phases of axonal degeneration in animal models[3] and in humans following stroke[4]. However, the unpredictable nature of stroke makes it impossible to obtain diffusion measurements prior to the injury and the injury itself is typically heterogeneous. The well-localized and complete nature of the lesion inflicted to the white matter during corpus callosotomy serves as a unique opportunity to study the evolution of axonal degeneration in-vivo.

METHODS: Three patients with medically intractable epilepsy (33, 40 and 53 years old) were included in the study. The three patients were scanned before surgical transection of the anterior two thirds of the corpus callosum. Six to nine days after surgery, the patients were scanned again, and once more after two to four months. DTI was performed on a 1.5 T Siemens Sonata using a single-shot EPI-based sequence (63 slices, 2 mm thickness with no inter-slice gap; TR=10 s, TE=88 ms; 6 diffusion directions, b=1000 s/mm^2; 8 averages; 96x128 matrix, zero-filled to 256x256; FOV=256x256 mm; scan time=9:30 min). Quantitative diffusion maps were created in DTIstudio (Johns Hopkins University) and included fractional anisotropy (FA), mean apparent diffusion coefficient (ADC), parallel diffusivity ($\lambda_\parallel = \lambda_1$) and perpendicular diffusivity ($\lambda_\perp = (\lambda_2+\lambda_3)/2$). Using the non-diffusion weighted volumes, the post-operative data sets were linearly co-registered to their pre-operative images and the transformations were extended to their corresponding diffusion maps. The genu and body (transected during surgery) and the splenium (not affected during surgery) of the corpus callosum were depicted with tractography on the pre-operative data sets (using the FACT algorithm[5]). The tracts were used to extract quantitative parameters from the pre-operative and registered post-operative diffusion maps. Voxels with an FA value < 0.25 in any of the images were not analyzed in all the data sets from that subject (in order to avoid measuring the surgical lesion itself).

RESULTS AND DISCUSSION: The splenium of the corpus callosum, which was not transected during surgery, showed little variability in diffusion parameters measured following surgery, as compared to its pre-surgical values (coefficient of variability = 1-4%). In all patients, the genu and body of the corpus callosum (transected during surgery) showed a dramatic decrease of diffusion anisotropy at one week post-surgery followed by a further reduction at two to four months (Figure 1). However, inspection of diffusivity both parallel and perpendicular to the tracts showed a different underlying mechanism for the reduction of FA at the two post-operative time points (Figure 2). At one week after surgery, there was a considerable decrease in $\lambda_\parallel$ and a slight increase in $\lambda_\perp$ driving the reduction in FA and yielding a normal mean diffusivity. On the other hand, $\lambda_\parallel$ showed a pseudo-normalization at 2-4 months, while $\lambda_\perp$ was considerably increased, further decreasing FA and producing an increased ADC. The most dramatic changes in diffusion parameters were seen in the areas closest to the resection, suggesting a centrifugal spread of the degeneration. The first stage of axonal degeneration in the CNS is characterized mainly by fragmentation of the axons with relatively intact myelin sheaths. This stage occurs rapidly (several hours to days) and is irreversible. A few weeks following the injury, the myelin sheaths become degraded in a slow and progressive fashion, which can last for months and even years. As has been previously demonstrated in an animal model, the fragmentation of axons can be indirectly assessed by reductions in $\lambda_\parallel$, while myelin degradation produces changes mainly in $\lambda_\perp$[3]. Our present findings in humans are in agreement with animal models and show that DTI can be used to diagnose and characterize axonal degeneration in-vivo even in its early stages.

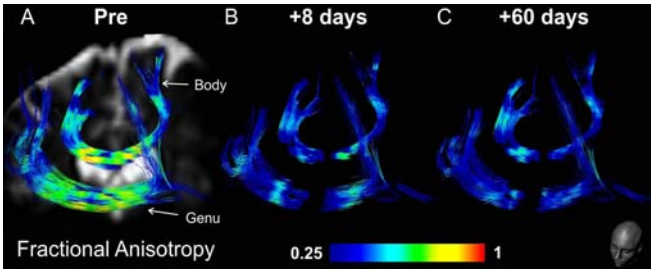

Figure 1. Diffusion anisotropy changes due to axonal degeneration following corpus callosotomy. The genu and body of the corpus callosum were depicted using tractography. The high FA values seen pre-operatively (A) decrease considerably at one week following surgery (B), and remain low at two months (C). All three patients had similar changes.

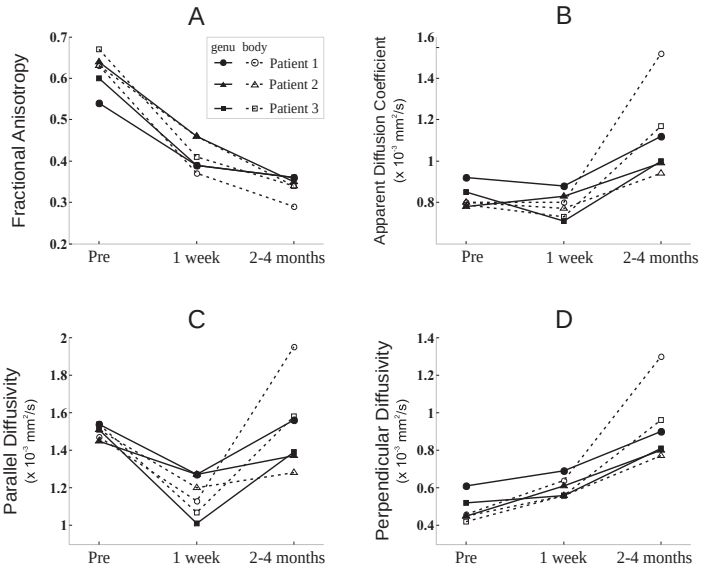

Figure 2. Diffusion parameters in the transected portions of the corpus callosum. Average diffusion measurements along the tracts within ±20 mm from the midline. Fractional anisotropy (FA) shows a marked decrease at one week following surgery, accompanied by nearly normal bulk diffusivity (ADC). Reduction in FA at this time point is due to a reduction in parallel diffusivity ($\lambda_\parallel$), with only a slight increase in perpendicular diffusivity ($\lambda_\perp$), consistent with axonal degradation. At 2-4 months post-surgery, ADC is elevated and FA shows a further decrease; however, the FA decrease is now due to a marked increase in $\lambda_\perp$ and a pseudo-normalization of $\lambda_\parallel$, consistent with myelin degradation.

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