

Focal Wallerian Degeneration of Corpus Callosum in Large Middle Cerebral Artery Stroke: Serial Diffusion Tensor Imaging

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Introduction: Degeneration of white matter fibers distal to a primary lesion, referred to as Wallerian degeneration (WD), is a common finding in many central nervous system diseases¹. WD is characterized by disintegration of axonal structures within days after injury, followed by degradation of myelin and atrophy of the affected fiber tracts². Diffusion tensor imaging (DTI), a noninvasive modality, is capable of examining the organization of fibers in compact white matter fiber tracts such as corpus callosum (CC). The degree of diffusion anisotropy depends on the level of organization of fiber tracts and the degree of hindrance to water diffusion by neurotubules, axonal membranes and myelin sheaths³. When white matter tracts degenerate, as occurs in cerebral infarction, a decrease in anisotropy is observed⁴. CC white matter tracts are significantly influenced by cortical damage, however only a few reports are available describing the cortico-callosal relationship in stroke patients⁵. The purpose of these longitudinal DTI studies is to demonstrate focal WD changes in the CC that reflect the underlying cortico-callosal topography in patients with large middle cerebral arterial (MCA) territory stroke.

Materials and Methods: Subjects: Eight patients (seven males, one female; 47.3±11.0 years (mean±SD); range: 34 to 65 years) with symptoms of large MCA territory stroke were included in the study. The involvement of complete MCA territory and absence of magnetic resonance imaging (MRI) signal abnormalities on both T1- and T2-weighted images in other cerebral regions besides the MCA region of the involved hemisphere were the inclusion criteria. These patients underwent DTI scans at different time points; 6-8 weeks, 10-12 weeks and beyond 6 months of stroke onset. Eight healthy age-matched controls with a mean age 43.9±7.4 years (seven males, one female) were investigated using the same MRI protocol at different time points.

Image Acquisition and Data Processing: Conventional MRI and DTI were acquired on a 1.5 Tesla MRI scanner using standard quadrature birdcage head coil. DTI data were acquired using a single-shot echo planar dual spin echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slices=34-38/slice thickness=3mm/interslice gap=0/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=8/diffusion weighting b-factor=1000 s mm⁻². The DTI data was processed as described elsewhere⁶ for region of interest (ROI) and tracking analyses. The CC was divided into seven segments based on a single sagittal slice using the scheme proposed by Witelson⁷. For ROI analysis of fractional anisotropy (FA) and mean diffusivity (MD), rectangular boxes varying from 2×2 to 6×6 pixels were placed on seven segments of CC. Areas of seven segments of CC were measured by placing free hand ROI depending on sampling area on the T2-weighted images. We also performed fiber tracking in order to visualize the changes in the callosal fibers connectivity in these patients at three different time points.

Results: In controls, no significant temporal changes in FA and MD were observed in any of the seven segments of CC indicating the stability of measurements. In patients, a significant reduction in FA values was observed from first to the third study in the different segments of CC, indicating temporal degeneration in CC1 (rostrum; p=0.055), CC2 (genu; p=0.024), CC3 (rostral body; p=0.010), CC4 (anterior mid-body; p=0.003), and CC7 (splenium; p=0.054) respectively. However, significant temporal elevation in MD values was observed in only the CC3 (rostral body; p=0.020) and CC4 (anterior mid-body; p=0.035) segments of CC. Mean regional callosal cross-sectional areas showed no significant change in controls with time, however, significant changes were observed in patients over time in CC2 (genu; p=0.006) and CC4 (anterior mid-body; p=0.052) segments only.

Discussion: This is the first longitudinal DTI study that investigates the time course of focal changes in CC in large MCA territory stroke patients. Disintegration of axonal structures and myelin sheath as occurs in WD result in loss of anisotropy on DTI. Structural changes in WD evolve over time with progressive disintegration of fiber structures followed by gliosis². Our results, indicate significant temporal decline in FA values in rostrum, genu, rostral body, anterior mid-body and splenium of CC suggesting that cortico-callosal fibers are the most affected fibers secondary to lesion related focal WD changes in CC segments. The temporal degeneration of callosal fibers seen on fiber tract maps further confirms this contention (Figure). Our study also showed significant elevation in MD values in rostral and anterior mid-bodies. This could be due to a cumulative loss of cell membranes, perhaps the most important barriers for movement of water, caused by delayed damage of glial cells or axons. This was associated with significant region specific-size reduction consistent with atrophy only in the last study beyond 6 months in genu and anterior mid-body, while significantly lower FA values were seen as early as 6 weeks of stroke onset. This suggests that changes in FA were observed much earlier than atrophy. This significant size reduction confirms an important loss of callosum structural components due to interruption of cortico-callosal fibers secondary to WD.

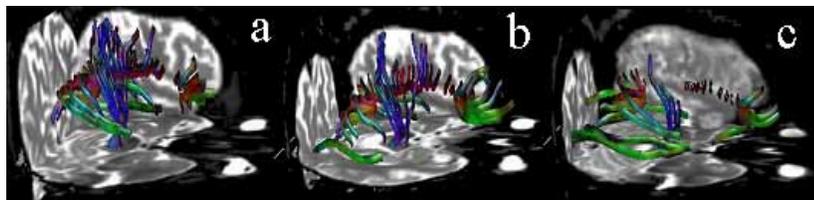


Figure. DTI fiber tracking (a, b, and c) on a patient showing the three dimensional views of the callosal fibers at the three different time points (6, 10, and 24 weeks) of stroke onset.

- References:** 1. Kuhn MJ, et al. *Radiology* 1989;172:179-182. 2. Johnson AC, et al. *Arch Neurol Psychiat* 1950;64:105-121. 3. Beaulieu C, et al. *Magn Reson Med* 1994;31:394-400. 4. Zelaya F, et al. *Magn Reson Imaging* 1999;17:331-348. 5. De Lacoste MC, et al. *J Neuropathol Exp Neurol* 1985; 44:578-591. 6. Hasan KM, et al. *J Magn Reson Imaging* 2005;21:735-743. 7. Witelson SF. *Brain* 1989;112:799-835.