

Postoperative Cerebral White Matter Changes in Diffusion Anisotropy Associated with Alterations in Cognitive Function after Carotid Endarterectomy: A Tract-Based Spatial Statistics Study

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INTRODUCTION:

Carotid endarterectomy (CEA) reduces the risk for stroke events in appropriately selected patients.¹ A recent study has shown that 10% of patients undergoing CEA experience an improvement in cognitive function after surgery.² Although postoperative normalization of metabolism in the cerebral cortices has been reported in these patients,³ it remains unknown whether the cerebral white matter (WM) is altered in association with an improvement in cognitive function. Diffusion tensor imaging (DTI) is widely used to detect microstructural alterations in WM, most commonly using fractional anisotropy (FA).⁴ Recently, a novel method called tract-based spatial statistics (TBSS)⁵ has been introduced for further quantitative analyses of DTI. Here, we utilized TBSS to evaluate subtle changes in FA values of the cerebral WM, which can occur in relation to improved cognitive function after CEA.

METHODS:

Ninety-three patients underwent DTI before and after CEA. DTI was performed using a 3T MRI scanner (Signa HDxt, GE) with a single-shot EPI sequence with the following parameters: TR/TE, 10000/62 ms; pixel size, 0.47 × 0.47 mm²; averages, 3; and *b*-value, 1000 s/mm². Postoperative cognition of patients was categorized as improved or unchanged on the basis of a previously described definition.² DTI data from 89 eligible patients were analyzed using TBSS with nonlinear registration to the most representative map. After generating skeletonized FA maps (based on FA > 0.2), FA values were compared between the preoperative and postoperative groups by using skeleton-based region of interest (ROI) and voxel-wise statistical approaches. In the former approach, The ROIs were defined as the intersection between the skeleton and cerebral WM labels based on the Harvard-Oxford subcortical structural atlas using FSL (FMRIB Software Library), as illustrated in Fig. 1. Mean FA values in the cerebral hemispheres of the affected and unaffected sides were calculated and compared between the pre-CEA and post-CEA images. The latter approach involved a nonparametric randomization method using FSL. Statistical significance was determined using a threshold-free cluster extent algorithm at *P* < 0.05, which was corrected for multiple comparisons by using a family-wise error rate. We also assessed the reproducibility of TBSS analyses by using DTI data of 10 healthy subjects who were scanned twice.

RESULTS:

In the 11 patients who showed postoperative cognitive improvement, mean FA values in the bilateral cerebral WM showed a significant increase after CEA (*P* < 0.01, Fig. 2), while no significant increase was found in the remaining patients who did not show any postoperative cognitive improvement. In the voxel-wise statistical approach, FA values increased in the ipsilateral cerebral WM as well as the contralateral frontal WM only in the patients showing improved cognitive function after CEA (Fig. 3). There were no significant differences in FA values between the 2 scans of the 10 healthy subjects.

DISCUSSION:

Our quantitative study using TBSS indicated that an increase in FA values of the bilateral cerebral WM is closely related to an improvement in cognitive function after CEA. Furthermore, a significant increase in FA values not only in the affected side but also in the unaffected frontal WM may suggest recovery of impaired myelin/axonal metabolism as well as secondary activation of frontal lobe functions. In conclusion, TBSS can detect increases in FA values in the bilateral cerebral WM, particularly in the frontal lobes, and these increases are associated with cognitive improvement after CEA.

REFERENCES:

[1] Cahurvedi S, et al. *Neurology* 2005;65:794-801. [2] Yoshida K, et al. *Neurol Med Chir (Tokyo)* 2012;52:154-160. [3] Chida K, et al. *Cerebrovasc Dis* 2010;29:343-351. [4] Sundgren PC, et al. *Neuroradiology* 2004;46:339-350. [5] Smith SM, et al. *Neuroimage* 2006;31:1487-1505.

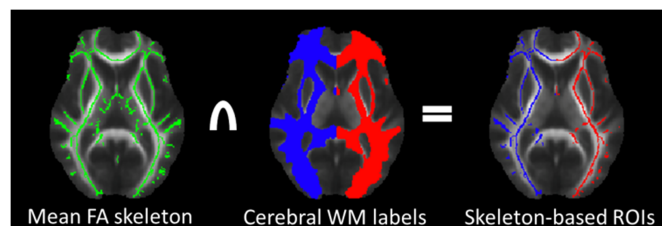


Fig. 1. Skeleton-based ROIs for evaluating the cerebral WM.

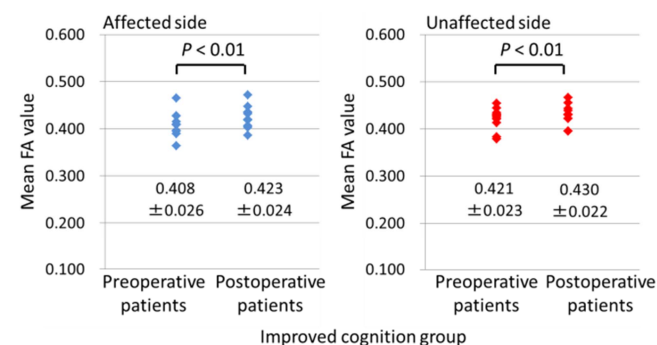


Fig. 2. Comparison between preoperative and postoperative mean FA values in patients with improved cognitive function after CEA.

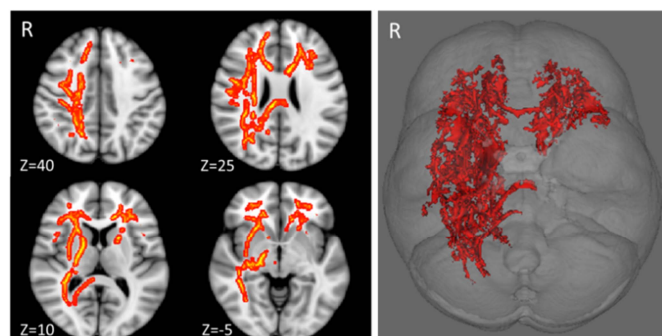


Fig. 3. TBSS analyses of FA maps. The left panel shows the locations where FA values were significantly increased after CEA in patients with postoperative improvement of cognitive function (red areas). The right panel shows axial 3D image of the same data.