Remote Effect of Acute Ischemic Stroke Revealed by Microstructure and Fiber Density Analysis

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INTRODUCTION Microstructural impairments were associated with the process of ischemic stroke [1, 2, and 3]. Previous researches showed elevated fractional anisotropy (FA) in the ipsilateral to the stroke lesions during the hyperacute phase and reduced FA during the rest phases [1, 2]. The FA reductions in stroke lesions and in regions downstream from the infarct such as the cerebral peduncles (CP) and pons were reported at 1 day to 1 year after stroke onset [2, 4].Such a long time range might contain a mixed status of the FA changes. In this study, we narrowed the time range into 5 days after symptom onset of the initial ischemic stroke, and characterized the differences in FA, mean diffusivity (MD), fiber density (FD) between affected ipsilateral CP and unaffected contralateral CP.

METHODS Fourteen subjects diagnosed with acute, unilateral ischemic stroke were consecutively recruited (10 males, 4 females, aged 62±15.7 years). All the lesions were single and remote to the ipsilateral CP. Diffusion tensor imaging (DTI) was performed within 5 days from the symptom onset of the disease. To obtain the bilateral CP masks, the initial masks were first constructed using the JHU_MNI template (http://cmrm.med.jhmi.edu/cmrm/atlas/human_data/file/JHUtemplate_newuser.html), followed by spatial normalization to the space of the DTI image for each subject. The deformed masks were then treated as the regions of interest (ROIs) (Figure 1). MD and FA were measured in the ROIs based on the DTI data using DTIStudio (https://www.dtistudio.org/). Fiber reconstruction was done with the method of probabilistic tractography provided by the MRtrix (http://www.brain.org.au/software/mrtrix/), from which fiber densities in the ROIs were calculated. The MD, FA and FD between the bilateral CP were investigated with Paired *t*-test using PASW (PASW 18, SPSS Inc., Chicago, IL). In order to facilitate the display of results, the relative values of these parameters were calculated as follows: $rX = X_{affected\ side} / X_{unaffected\ side}$, where X indicates the measured MD, FA and FD.

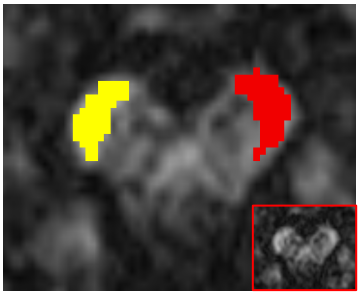

Figure 1.The shapes and localization of the ROIs in the axial plane of one subject.

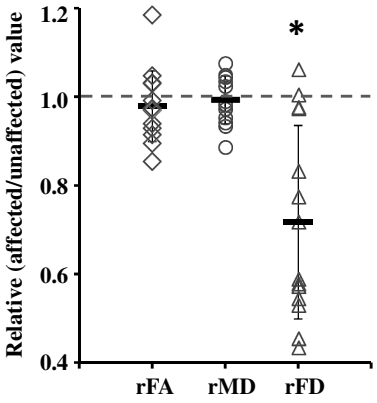

Figure 2.The three relative value in CP. Tetragons, circles and triangles respectively represented the all individual values of rFA, rMD and rFD * Significant difference between ipsilateral and contralateral fiber count.

RESULTS The measured MD, FA and FD for the bilateral CP were summarized in the Table 1.

Table 1 Measured mean diffusivity (MD), fractional anisotropy (FA), fiber density (FD)

	MD (mm^2/s)	FA	FD (per voxel)
Ipsilateral CP	87.50±11.07	0.61±0.07	361.76±66.47
Contralateral CP	87.91±7.98	0.62±0.05	528.43±109.58

There was no significant difference in MD or FA between the bilateral CP, while FD in the CP ipsilateral to the ischemic lesion was substantially less than that in the contralateral CP ($p<0.001$, Figure 2).

DISCUSSION AND CONCLUSION The insignificance in the difference of MD and FA of the bilateral CP may attribute to the independent evolution of axial and radial diffusivity. Reduction of the FD in the ipsilateral CP suggested that ischemic stroke causes axonal damage remote to the lesion as early as in 5 days after the disease onset during which changes of MD and FA may not be detectable. FD may serve as a sensitive index identifying remote white matter damage in acute ischemic stroke.

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