Tractography of white matter based on diffusion tensor imaging in ischaemic stroke involving the corticospinal tract: a preliminary study

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ABSTRACT

Diffusion tensor MR imaging (DTI) provides information on diffusion anisotropy in vivo, which can be exhibited three-dimensional white matter tractography. Five healthy volunteers and five right-hand affected patients with early subacute ischaemic infarction involving the posterior limb of the internal capsule or corona radiate were recruited in this study. We used 3D white matter tractography to show the corticospinal tract in both volunteer group and stroke group. Then we compared parameters of the corticospinal tract in patients with that in normal subjects and assessed the relationships between the fiber number of the corticospinal tract in ipsilesional hemisphere and indicators of the patients' rehabilitation using Pearson correlation analysis. The fractional anisotropy (FA) values and apparent diffusion coefficient (ADC) values in the ipsilesional corticospinal tract may significantly reduce comparing with the volunteer group. In addition, the stroke patient with less fiber number of the ipsilesional corticospinal tract may bear more possibilities of better motor rehabilitation. The FA values, ADC values and fiber number of the corticospinal tract in the ipsilesional hemisphere might be helpful to the prognosis and prediction of clinical treatment in stroke patients.

Keywords: Tractography, Corticospinal tract, Stroke, Brain infarcts, Diffusion tensor imaging (DTI)

1. INTRODUCTION

Motor deficit is the most prominent symptom in ischemic stroke, and recovery of motor function modulated by carefully treatment has been observed during first several months after stroke onset [1-3]. However, the neural mechanisms

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underlying the motor rehabilitation are not well understood. Diffusion tensor MR imaging (DTI) provides information on diffusion anisotropy in vivo, which can be exhibited three-dimensional white matter tractography [4, 5]. The DTI also provides an effective tool to safely explore the brain activities and changes evoked by motor rehabilitation in ischaemic stroke patients.

Although functional magnetic resonance imaging (fMRI) as an in-vivo neuroimaging technique, has excelled at depicting the functional alterations of motor recovery in stroke patients, many cellular functions and disease processes that occur at the microscopic level do not affect conventional fMRI parameters [1, 6, 7]. DTI is a newly developed technique with which anisotropic diffusion can be demonstrated noninvasively. Diffusion anisotropy can be expressed by invariant indices such as fractional anisotropy (FA) or apparent diffusion coefficient (ADC) [5, 8]. White matter tractography is a powerful method to anisotropic diffusion which can be obtained from a DTI data set. Fibre tract maps would be created, based on similarities between neighbouring voxels in the shape and orientation of the diffusion ellipsoid [9].

Some studies on human stroke analysed invariant anisotropy indices and demonstrated reduced diffusion anisotropy in white matter ischaemia [5]. It is of interest, however, whether stroke affects an important axonal projection such as the corticospinal tract when neurological deficits suggest its involvement. Precise imaging localisation of stroke reinforces neurological findings, and demonstration of stroke and neuronal fibre tracts on the same images might be helpful. White matter tractography may be applied to show axonal projections and other brain components simultaneously. We applied the technique to demonstration of the corticospinal tract in patients with ischaemic stroke thought on examination and conventional MRI to involve the tract. Our purpose was to investigate the feasibility and use of white matter tractography in stroke, focusing on analysis of the FA values and ADC values in the ipsilesional corticospinal tract between the volunteer group and stroke group.

In the present paper, we performed tractography of the corticospinal tract based on diffusion tensor imaging in both ischaemic stroke patients and normal subjects. The comparasion of FA values and ADC values between patients and volunteers or between the ipsilesional hemisphere and contralesional side was done. We also explored relationships between the fiber number of the corticospinal tract in the ipsilesional hemisphere and clinical scores of the patients' rehabilitation. We hypothesized that the stroke patient with less fiber number of the ipsilesional corticospinal tract may bear more possibilities of better motor rehabilitation.

2. METHOD AND MATERIALS

2.1 Subjects

We studied five healthy volunteers (three male, aged 51±1.3 years) and five right-hand affected patients (three male, aged 53 ± 5.2 years) with ischaemic stroke referred for MRI with early subacute infarction involving the posterior limb of the internal capsule or corona radiata. The clinical and demographic data were tabulated in Table 1, and the patients were inquired again for stroke rehabilitation studies one month later. The infarcts were identified on the pattern of signal change on T2-weighted and isotropic diffusion-weighted images and apparent diffusion coefficient maps. No patient presented signs or history of somatosensory deficits of the healthy hand or other neurological or psychiatric disease, deafness and/or blindness, prior cerebrovascular disease, brainstem stroke, or multiple cerebral lesions. All of them were right-handed and provided written informed consent to participate in this study. All subjects were in accordance with the declaration of Helsinki.

Table 1 Clinical and demographic data

Patients Number	1	2	3	4	5
Localization of infarct	IC CR	IC	IC CR	IC	IC
MMT (0-5)	3; 4	4; 4	3; 4	4; 5	4; 5
MRS (0-5)	4; 3	2; 1	4; 3	2; 1	2; 0
NIHSS (0-15)	6; 1	4; 0	9; 4	1; 0	1; 0
ADL (0-100)	20; 65	45; 100	20; 65	60; 100	100; 100
FMA (0-100)	6; 39	35; 65	11; 38	40; 59	47; 66

IC = internal capsule; CR = corona radiate; MMT = manual muscle test; MRS = Modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; ADL = Activity of Daily Living; FMA = Fugl-Meyer Assessment; values after ';' represent measurements after one month.

2.2 DTI data acquisition and analysis

DTI was performed on at 3.0 Tesla Achieva X-series Philips scanner (Philips, Netherlands). A custom-built head holder was used to prevent head movements. The patients underwent a DTI scan 6 h–10 days after onset of the stroke. We used single-shot spin-echo echoplanar sequence, TR = 2925ms, TE = 60 ms, acquiring 30 interleaved contiguous 5 mm axial images covering the entire brain, with field of view 224 mm×224 mm and matrix 128×128 interpolated to 256×256. Diffusion gradients were applied in 15 noncollinear directions with the b = 800 s/mm2 as the peak diffusion gradient. After the functional run, high-resolution structural information on each subject was acquired using 3D MRI sequences with a voxel size of 1 mm^3 for anatomical localization (TR = 2510 ms, TE = 15 ms, matrix = 384 × 512, FOV = 230 mm × 230 mm, FA = 30°, thickness = 5 mm).

All the volumes were realigned to correct for head motions using the least-squares minimization. After realignment of 15 diffusion-weighted volumes to the unweighted image (b = 0 s/mm^2) of each subject and eddy current distortions were corrected by affine registration. Diffusion tensors were calculated and 3D fibre-tract maps were created in the DTI native space using DTIstudio (www.DtiStudio.org). The Fiber Assignment by Continuous Tractography (FACT) method [10] was used with a FA threshold of 0.2 and a principal eigenvector turning angle threshold of 45° between two connected pixels. The posterior limb of the internal capsule was served as a seed ROI and derived from the normalized MNI space, the inverse transformation of the spatial normalization was applied to acquire the seed ROI in the native DTI space. For the affected cerebral hemisphere, the seed was on an uninvolved region of the corticospinal tract. Mean FA values, number of fibers and mean ADC values on the tract were also extracted from each subject. Two sample t-test was performed on FA values or ADC values between bilateral hemispheres or between volunteer group and stroke group respectively. The fiber number of the ipsilesional corticospinal tract was correlated with the difference of neurological examinations between post-treatment and the first measurement using Pearson correlation analysis. The statistical test and correlation analysis steps were carried out using Matlab 7.6.0 (2008a) (Math works Inc., Natick, MA).

3. RESULTS

Table 2 showed that in healthy volunteers, FA values of the left corticospinal tract were larger than that of the mirror side ($p < 0.05$), indicating that more fibers were working in the left corticospinal tract compared with the right hemisphere. In stroke patients, FA values of the left corticospinal tract were smaller than that of the right side ($p < 0.05$), suggesting that the left corticospinal tract was damaged. We also performed a contrast of ADC values in the corticospinal tract between left and right hemispheres in both volunteers and patients. Table 3 showed that ADC values of the corticospinal tract between left and right hemispheres were significantly different in stroke group ($p < 0.05$), but no significant difference was found in volunteer group. The ADC values in the ipsilesional hemisphere of stroke patients were lower than that in the same side (left hemisphere) of volunteers, indicating that some abnormal infarcts affected the anisotropy of white matter in the lesional corticospinal tract. There were no significant differences for ADC values in the right side between stroke patients and volunteers. Furthermore, the ADC values of the left corticospinal tract in stroke patients were lower than that of the mirror side ($p < 0.05$), while for the volunteer group was not significant ($p > 0.05$).

Table 2 Comparison of FA values of the corticospinal tract between left and right hemispheres.

Group	**Left (mean ± SD)**	**Right (mean ± SD)**	***p***
Volunteer Group	0.5795 ± 0.0258	0.4712 ± 0.0206	< 0.05
Stroke Group	0.4388±0.0676	0.4592±0.0507	< 0.05
p	< 0.05	> 0.05	

Table 3 Comparison of ADC values in the corticospinal tract (10-10 m2/s) between left and right hemispheres.

Group	**Left (mean ± SD)**	**Right (mean ± SD)**	***p***
Volunteer Group	7.7620 ± 0.5936	7.6200 ± 0.6164	> 0.05
Stroke Group	6.1500±1.9624	8.1840±0.5346	< 0.05
p	< 0.05	> 0.05	

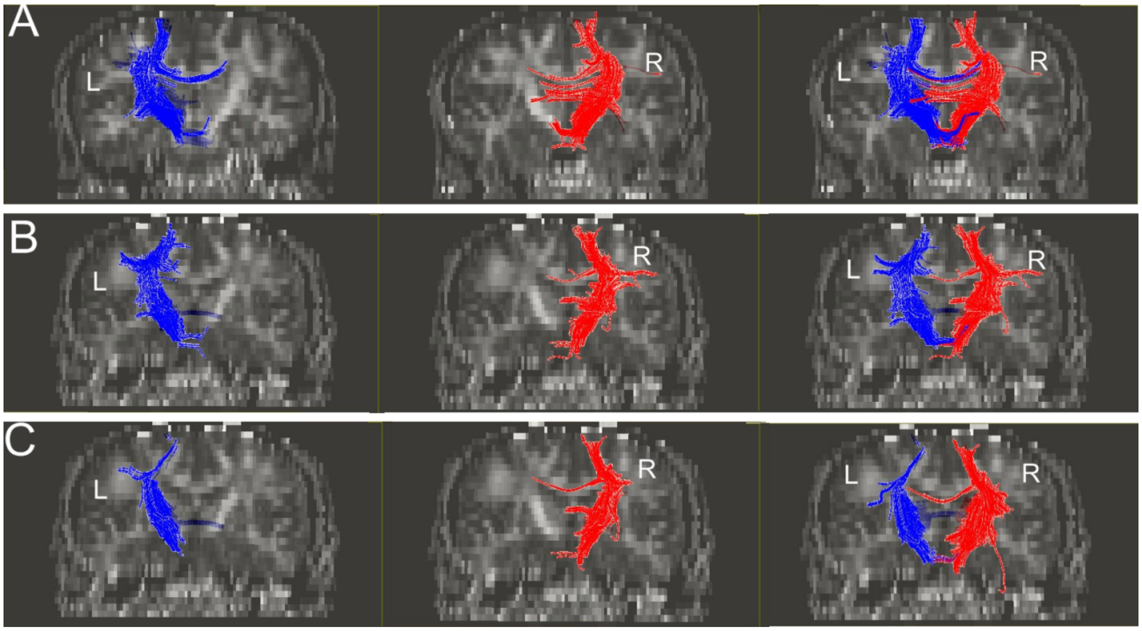

Figure 1 The corticospinal tract of one volunteer (A) and two stroke patients (B, C). Blue represents the corticospinal tract in left hemisphere, and red indicates right.

Tractography of the corticospinal tract in both volunteers and stroke patients was performed. Fig. 1A showed the bilateral corticospinal tracts of a normal subject, the left and right tracts were intact visually. Both Fig. 1B and Fig. 1C showed corticospinal tracts in stroke patients (patient 2 and 3), and the fiber number in the left hemisphere (blue color) in Fig. 1C was obviously less than that of Fig. 1B. From clinical assessments in Table 1, the patient 2 recovered better than patient 3, suggesting that the fiber number of the corticospinal tract in the ipsilesional hemisphere may affect the restoration of stroke patients. The fiber number of the ipsilesional hemisphere in five patients was significantly correlated with their individual difference of NIHSS scores between post-treatment and pre-treatment using Pearson correlation analysis ($r = 0.994$, $p < 0.05$). Although no significant correlations were observed between the fiber number and the difference of ADL scores or FMA scores, there was still a negative trend between them from Fig. 2.

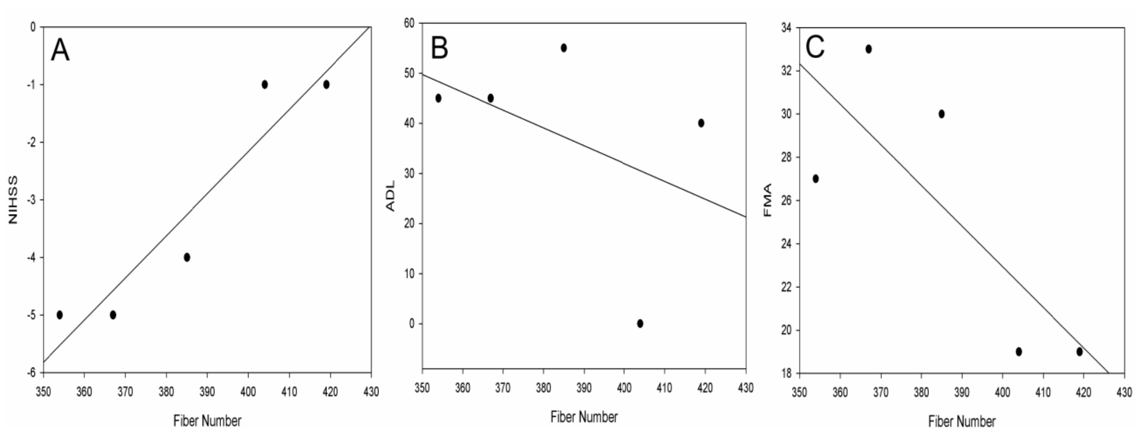

Figure 2 The number of fibers in the affected hemisphere of five patients was correlated with the difference of clinical evaluation between post-treatment and the first measurement using Pearson correlation analysis. NIHSS = National Institutes of Health Stroke Scale; ADL = Activity of Daily Living; FMA = Fugl-Meyer Assessment.

4. DISCUSSIONS

In this study we performed tractography of the corticospinal tract based on diffusion tensor imaging in both ischaemic stroke patients and normal subjects. For the first time, we explored relationships between the fiber number of corticospinal tract in the ipsilesional hemisphere and indicators of the patients' rehabilitation using Pearson correlation analysis. We also calculated the FA values, ADC values and tracked the corticospinal tracts of volunteers and patients, and all results sufficiently supported our hypothesis.

We depicted the corticospinal tract repeatedly and symmetrically in involved or uninvolved hemispheres in both stroke group and volunteer group. Its course was consistent with anatomical descriptions, and we inferred that what we were showing did represent the corticospinal tracts [4, 5]. The technique provided information which could not be obtained from coronal images alone, displaying the corticospinal tracts simultaneously, so that the integrality of the corticospinal tract could be observed by eye. This may be useful in ischaemic stroke, which frequently affects the internal capsule and corona radiata. The observed correlation between involvement of the tract and prognosis indicates that the fiber number of the corticospinal tract to an infarct might affect with recovery of motor function [11].

The FA values of the left corticospinal tract were larger than that of the mirror side in healthy volunteers ($p < 0.05$), indicating that more fibers were working in the left corticospinal tract compared with the right hemisphere. It was consistent with previous literatures [12, 13]. ADC values of the corticospinal tract between left and right hemispheres were significantly different in stroke group ($p < 0.05$), but no significant difference was found in volunteer group. The ADC values in the ipsilesional hemisphere of stroke patients were lower than that in the same side (left hemisphere) of volunteers, indicating that some abnormal infarcts affected the anisotropy of white matter in the lesional corticospinal tract [5, 11, 14, 15]. From Fig. 1 we observed that the fiber number of the corticospinal tract in the ipsilesional hemisphere may affect the restoration of stroke patients. The fiber number of the ipsilesional hemisphere in five patients was significantly correlated with their individual difference of NIHSS scores between post-treatment and pre-treatment using Pearson correlation analysis ($r = 0.994$, $p < 0.05$). The result may indicate that less fiber number of the ipsilesional corticospinal tract may bear more possibilities of better motor rehabilitation for stroke patients.

Despite the population in this paper was small, the significant Pearson correlation we have shown are encouraging. Although further studies are needed, it seems likely that favourable recovery of gross motor functions could be expected in patients without obvious involvement on white matter tractography. The technique seems suitable for qualitative assessment of motor rehabilitation in stroke patients, which might be helpful in prognosis of patients with stroke.

From these preliminary observations, we proposed that the stroke patient with less fiber number of the ipsilesional corticospinal tract may bear more possibilities of better motor rehabilitation. The FA values, ADC values and fiber number of the corticospinal tract in the ipsilesional hemisphere might be helpful to the prognosis and prediction of clinical treatment in stroke patients.

5. CONCLUSIONS

In the current study we performed tractography of the corticospinal tract based on diffusion tensor imaging in both ischaemic stroke patients and normal subjects. The FA values and ADC values in the ipsilesional corticospinal tract may significantly reduce comparing with the volunteer group. In addition, less fiber number of the ipsilesional corticospinal tract may predict better motor rehabilitation. The FA values, ADC values and fiber number of the corticospinal tract in the ipsilesional hemisphere might be helpful in prognosis of gross motor function. Our findings may provide additional evidence to support the effects underlying recovery of motor function in stroke patients.

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