Motor outcome according to the integrity of the corticospinal tract determined by diffusion tensor tractography in the early stage of corona radiata infarct

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Abstract

Diffusion tensor tractography (DTT) is useful for exploring the state of the corticospinal tract (CST). An accurate estimation of the integrity of the CST in the early stage of a cerebral infarct would enable a determination of motor recovery. DTT was performed to classify CST integrity following a corona radiata infarct to evaluate if the procedure could characterize the motor outcome of the affected hand. Fifty-five patients with completely paralyzed hands due to a corona radiata infarct were recruited for the study, and DTT images were obtained within 7–30 days after a stroke. The DTI findings for the patients were classified into four groups. In type A, the CST was preserved around the infarct; in type B, the CST originated from a cortex other than the primary motor cortex; in type C, the CST was interrupted at the infarct; in type D, the CST failed to reach the infarct due to degeneration. Six months after a stroke, the motor function of the affected hand was evaluated with the motricity index (MI) for the hand, the Medical Research Council score (MRC) for finger extensors and the modified Brunnstrom classification (MBC). These indices were significantly influenced by the DTT type (p < 0.05). The highest MI, MRC and MBC were seen in the DTT type A patients; the lowest MI, MRC and MBC were seen in the DTT type D patients (p < 0.05). The integrity of the corticospinal tract determined by DTT obtained during the early stage of a corona radiata infarct seems to be helpful in predicting the motor outcome of the affected hand.

Keywords: Cerebral infarct; Diffusion tensor imaging; Prognosis; Motor function

An accurate estimation of prognosis is very important in terms of rehabilitation for stroke patients. Many studies have tried to predict motor outcome in hemiparetic stroke patients using clinical findings [16,30] radiological measurements [3,7,12,17,19,24,28,33], electrophysiological methods [14,15,22] and functional neuroimaging [20,28]. However, these studies have an inherent weakness in that they were unable to visualize the corticospinal tract (CST), the most important structure for motor control, especially for fine motor control of the hand in humans [6,9,35].

Diffusion tensor imaging (DTI) allows the orientation and integrity of white matter tracts to be determined by virtue of its ability to image water diffusion characteristics [2,17,19]. Diffusion tensor tractography (DTT), derived from DTI, has a unique advantage as it is able to visualize the architecture and integrity of the CST in three dimensions [1,21,27,29,34]. The validity and reliability of DTT for the CST has been well demonstrated in previous studies [5,8,13,26,27]. Therefore, integrity of the CST in patients with a subcortical lesion may be estimated by DTT, which may be helpful in a prediction of motor prognosis in patients with a subcortical infarct. Recently, a few studies
have demonstrated that DTT has a predictive value for motor outcome in stroke patients [7,24].

In the current study, we have investigated if the integrity of CST classified by DTT obtained during the early stage of a corona radiata infarct can be used to predict outcome of the affected hand.

Fifty-five patients were included in this study. All of the patients provided written informed consent prior to the study, and the local ethics committee approved the study protocol. Inclusion criteria were the following: (1) complete weakness of the affected hand (finger flexors and extensors) at the time of stroke onset; (2) an infarct at the level of the corona radiata which explained the hand weakness (at least included the posterior half of the middle third and adjacent to the lateral wall of the lateral ventricle of the corona radiata) [18,23,32], confirmed by a neuroradiologist; (3) DTT was performed within 7–30 days of stroke onset. Exclusion criteria were the following: (1) patients with previous stroke history; (2) patients who showed apraxia, sensory problems, or severe cognitive problems (Mini-Mental State Examination < 25); (3) large middle cerebral artery or lacunar infarct patients.

Motor function of the affected hand was measured twice: at stroke onset and at 6 months after the onset. The motricity index (MI) for hand, the Medical Research Council score (MRC) for finger extensors and the modified Brunstrom classification (MBC) was used to determine the motor function for the affected hand [4,10,11]. The MI for the hand is as follows: 0 = no movement; 1 = beginning of prehension; 2 = prehension of the object without gravity; 3 = prehension of the object against gravity; 4 = prehension against slight manual resistance applied to the object; 5 = prehension against resistance identical of the resistance overcome by the healthy hand [10]. The MRC score for the finger extensors is as follows: 0 = no contraction; 1 = palpable contraction, but no visible movement; 2 = movement without gravity; 3 = movement against gravity; 4 = movement against a resistance lower than the resistance overcome by the healthy side; 5 = movement against a resistance equal to the maximum resistance overcome by the healthy side. The MBC is as follows: 1 = unable to move fingers voluntarily; 2 = able to move fingers voluntarily; 3 = able to close hand voluntarily, unable to open hand; 4 = able to grasp a card between thumb and medial side of index finger, able to extend fingers slightly; 5 = able to pick up and hold a glass, able to extend fingers; 6 = able to catch and throw a ball in a near-normal fashion, able to button and unbutton a shirt [4,11]. The reliability and validity of MI, MRC and MBC are well established [4,10,11].

Diffusion tensor images were acquired using a 1.5-T Philips Gyroscan Intera system equipped with a Synergy-L Sensitivity Encoding (SENSE) head coil using a single-shot spin echo-planar imaging sequence. For each of the 32 non-collinear and non-coplanar diffusion-sensitizing gradients, we acquired 60 contiguous slices parallel to the anterior commissure-posterior commissure line. The imaging parameters used were as follows: matrix = 128 × 128 matrix, field of view = 221 mm × 221 mm, TE = 76 ms, TR = 10,726 ms, SENSE factor = 2, EPI factor = 67, b = 600 mm² s⁻¹, NEX = 1 and a slice thickness of 2.3 mm. We also evaluated fiber connectivity using fiber assignment by continuous tracking (FACT), a 3-D fiber reconstruction algorithm contained within the Philips PRIDE software [27]. The termination criteria used were FA < 0.2, and an angle change >45° according to a previous study for the optimal trackability threshold of FA [25]. We lowered the FA to 0.1 at the interval of 0.05 to confirm whether the motor fibers existed through or around the lesion in the affected hemisphere. A seed ROI was drawn in the CST portion of the anterior mid-pons on a 2-D FA color map and another ROI was drawn in the CST portion of the anterior low pons on a 2-D FA color map. Fiber tracts passing through both ROIs were designated as the final tracts of interest. The DTT findings for the patients were classified into four groups: Type A, the CST was preserved around the infarct, namely, the tract originated from the affected hemisphere including the primary motor cortex and passing around the infarct to the medulla; Type B, the CST was similar to type A, except the fiber originated from another cortex (primary sensory cortex, posterior parietal cortex, premotor cortex and prefrontal cortex), but not the primary motor cortex; type C, the CST was interrupted at the infarct; and type D, the CST did not reach the infarct due to degeneration (Fig. 1).

Because of the small and different numbers of the four DTT type groups, non-parametric statistical analysis tools from SPSS 12.0 were used—the Kruskal–Wallis test with Dunn’s post hoc test, and the Pearson’s chi-squared test. The level of significance was set to p < 0.05.

The study included 34 male and 21 female patients, and the study population was divided into four types by the DTT findings: 27 type A, 9 type B, 9 type C and 10 type D. Twenty-one of the 55 patients had an infarct in the right hemisphere, and the other 34 patients had an infarct in the left hemisphere. The distribution of age (mean ± S.D., 59.85 years ± 2.26) and days to DTT (18.11 days ± 7.70) between the four DTT type groups were not significantly different (Kruskall–Wallis test; p = 0.211, p = 0.091).

The MI and MRC, scores measured on the day of the stroke onset were all zero in the four DTT groups. The MBC score was 1 in all of the patients examined. Therefore, on an initial evaluation, we were not able to find any significant differences between the DTT types. On a second evaluation, the MI score distribution among the four different DTT types were significantly unequal (Fig. 2; Pearson’s chi-square test p = 0.003) and the MI score was significantly influenced by the DTT type (Kruskal–Wallis test, p = 0.0002); the median score was greatest for DTT type A (25% ~ median ~ 75% — 3.0–4.0–5.0) and smallest for the type D group (0.5–1.0–1.5) (Dunn’s post-hoc test: p < 0.05). The patients who had recovered equal or more than to prehend an object against gravity (MI score 3–5) were 96.3% for type A, 66.7% for type B, 55.6% for type C and 10.0% for type D. Twenty percent of the type D patients showed no recovery on the MI at all.

The MRC score distribution was similar to the MI distribution. A significant uneven MRC distribution among the four groups (Fig. 3; Pearson’s chi-square test, p = 0.000) was seen, and a significant influence of the DTT type for the MRC score (Kruskal–Wallis test, p = 0.0001) was noted. The median score was greatest for DTT type A.
(25% ∼ median ∼ 75%—3.0–4.0–4.0) and smallest for the type D group (0.0–0.0–0.5) (Dunn’s post hoc test, $p < 0.05$). The patients who had recovered equal or more than to extend the fingers against gravity (MRC score 3–5) were 96.3% for type A, 66.7% for type B, 55.6% for type C and 10% for type D. Eighty percent of the type D patients showed no recovery on the MRC score at all.

The final MBC distribution was also similar to the MRC score and MI distribution. A significant uneven MI distribution among the four groups (Fig. 4; Pearson’s chi-square test, $p = 0.000$) was seen, and a significant influence of the DTT type for the MBC score (Kruskal–Wallis test; $p < 0.0001$) was noted. The median score was greatest for DTT type A (25% ∼ median ∼ 75%—5.0–6.0–6.0) and smallest for type D (1.0–1.0–2.0) (Dunn’s post hoc test; $p < 0.05$). The patients who had recovered equal or more than to pick up and hold a glass and extend fingers (MBC 4–5) were 96.3% for type A, 66.7% for type B, 44.4% for type C, and 10% for type D. Sixty percent of the type D patients showed no change of the MBC at all.

In the current study, we have investigated if the integrity of the CST classified by DTT type obtained during the early stage of a corona radiata infarct can predict the motor outcome of the affected hand. We were able to measure DTI parameters (FA and apparent diffusion coefficient values) along with the CST pathway if the CST integrity was maintained as in the patients with type A or B findings using the ROI method. However, in the patients with type C or D findings, it was impossible to measure the DTI parameters accurately as the CST was completely

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**Fig. 1.** Classification of diffusion tensor tractography: (A) T2-weighted MR images, (B) Coronal images of diffusion tensor tractography (DTT), (C) combined axial (at the infarct level) and coronal images of DTT and (D) axial images (at the primary motor cortex level) of DTT.
disrupted at the corona radiata level. Therefore, we performed this study using DTT data without DTI parameter data.

In order to focus the clinical perspective to the functional evaluation of the affected hand, the scoring tools MI, MRC score, and MBC were chosen. As the baseline scores of all the patients in this study was essentially “zero”, the scores measured on the 6th month also described the amount of motor recovery that occurred in each patient. The motor recovery was greatest in the DTT type A group, and was smallest in the DTT type D group, whether it was measured with the hand MI, finger extensor MRC score, or MBC. Therefore, motor recovery for the affected hand during the first 6 months after a infarct was significantly different according to the initial DTT findings of the damaged CST ($p<0.05$). For example, over 90% of the patients in the DTT type A group had recovered to the extent to prehend an object, to extend the fingers against gravity, and to pick up and hold a glass and to extend fingers. On the contrary, only 10% of patients in the DTT type D group were able to complete those functions. As an early prediction for motor recovery of the paralyzed hand has great value in stroke rehabilitation, the clinical application of the DTT technique will empower clinicians with a better rehabilitation strategy.

There have been two DTT studies that have attempted to demonstrate a predictive value for motor outcome in stroke patients. Konishi et al. reported that the degree of CST involvement measured by DTT evaluated within 3 days of symptom onset was highly correlated with a motor deficit and the clinical outcome at 3 months in patients with an acute lenticulostriate infarct [24]. The latest DTT study is our previous study for patients with an intracerebral hemorrhage [7]. Using similar experimental settings, we compared the results for a cerebral infarct versus a cerebral hemorrhage. The average MBC score in DTT type A was 5.56 (S.D. 0.85) in the infarct group and 5.80 (S.D. 0.42) in the hemorrhage group, the Mann Whitney comparison was not significant ($p=0.5207$). The score for DTT type B was 4.67 (S.D. 1.23) in the infarct group and 3.42 (S.D. 2.11) for the hemorrhage group, this difference was not significant ($p=0.2394$). Therefore, our two studies have showed that the lesion type was not a significant factor in the relationship between the DTT type and motor outcome.

We believe that this DTT method can be applied to other stroke patients with subcortical lesions to predict motor outcome. The current study has the limitation that the DTT analysed in this study was not the CST for only the hand although we tried to predict the motor outcome of the affected hand. Therefore, further studies that can discriminate the fibers according to the somatotopy should be warranted. Other further studies combined with transcranial magnetic stimulation are required for more accurate knowledge of the CST state because transcranial magnetic stimulation has been the most actively researched tools for predicting motor outcome and it can provide important information about the CST status through the presence or characteristics of motor evoked potentials [14,15,31].

In conclusion, the current study has demonstrated that the integrity of CST classified by DTT at the early stage of a corona radiata infarct can be helpful in the prediction of motor outcome for the affected hand.
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References

[10] G. Demeurisse, O. Demol, E. Robaye, Motor evaluation in vascular hemi-
