Diagnostic sensitivity of traumatic axonal injury of the spinothalamic tract in patients with mild traumatic brain injury

Sung Ho Jang, MD\textsuperscript{a}, Seong Ho Kim, MD\textsuperscript{b}, Hyeok Gyu Kwon, PhD\textsuperscript{c}\textsuperscript{*}

Abstract
Diffusion tensor tractography (DTT) can detect traumatic axonal injury (TAI) in patients whose conventional brain magnetic resonance imaging results are negative. This study investigated the diagnostic sensitivity of TAI of the spinothalamic tract (STT) in patients with a mild traumatic brain injury (TBI) suffering from central pain symptoms, using DTT.

Thirty-five patients with central pain following mild TBI and 30 healthy control subjects were recruited for this study. After DTT-based reconstruction of the STT, we analyzed the STT in terms of configuration (narrowing and/or tearing) and the DTT parameters (fractional anisotropy and tract volume).

Thirty-three (94.3\%) patients had at least 1 DTT parameter value at 1 standard deviation below the control group value, and 20 (57.1\%) patients had values at 2 standard deviations, below the control group value. All 35 patients showed STT abnormalities (tearing, narrowing, or both) on DTT.

A high diagnostic sensitivity of TAI of the STT in patients with mild TBI was achieved. However, the small number of subjects who visited the university hospital and the limitations of DTT should be considered when generalizing the results of this study.

Abbreviations: DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FA = fractional anisotropy, MRI = magnetic resonance imaging, ROI = region of interest, SD = standard deviation, STT = spinothalamic tract, TAI = traumatic axonal injury, TBI = traumatic brain injury, TV = tract volume, VAS = visual analogue scale.

Keywords: diffusion tensor tractography, mild traumatic brain injury, sensitivity, spinothalamic tract

1. Introduction
Traumatic brain injury (TBI) is a major cause of neurological disability in adults, and 70\% to 90\% TBI patients are classified as mild TBI.\textsuperscript{[1] In addition, diffusion axonal injury is the predominant mechanism of TBI caused by shearing forces by acceleration, deceleration, or rotation of the brain.\textsuperscript{[2–3]} TBI causes widespread microscopic axonal damage at the border between the gray and white matter, such as the corpus callosum, brainstem, and cerebellum.\textsuperscript{[1–5]} Chronic pain is a common sequela of mild TBI, with an up to 75\% prevalence.\textsuperscript{[6,7]} Various pathophysiologic mechanisms of chronic pain in patients with mild TBI have been suggested, with central pain caused by brain injury being a major pathophysiological mechanism.\textsuperscript{[8–14]} The precise diagnosis of central pain is clinically important because its management and prognosis differ remarkably from pain attributed to other pathophysiological mechanisms.\textsuperscript{[18]} In particular, diagnostic precision is important for patients with mild TBI whose conventional brain computed tomography or magnetic resonance imaging (MRI) results are negative.\textsuperscript{[19–21]}

The spinothalamic tract (STT) is a sensory pathway that projects to several cortices, such as the primary somatosensory cortex, mid-cingulate cortex, and supplementary motor area via various thalamic regions, including the ventro-posterolateral nucleus and pulvinar nucleus and it is responsible for touch, temperature, and pain.\textsuperscript{[22–24]} In detail, the pulvinar nucleus connects to the sensory cortex, superior colliculus, primary visual cortex, and amygdala and is related to pain modulation.\textsuperscript{[24–26]}

After introducing diffusion tensor imaging (DTI), several studies using diffusion tensor tractography (DTT), which is used to reconstruct neural tract images from DTI data, have demonstrated that traumatic axonal injury (TAI) of the STT causes central pain in patients with mild TBI.\textsuperscript{[8–15]} These studies focused on the prevalence of central pain caused by TAI of the STT, or they have provided a case description of patients with mild TBI.\textsuperscript{[8–13]} However, there are no reports on the diagnostic sensitivity of TAI of the STT following mild TBI. This study hypothesized that DTT...
could have high diagnostic sensitivity for TAI of the STT in patients with mild TBI. Therefore, this study investigated the diagnostic sensitivity of TAI for STT in patients with mild TBI.

2. Methods

2.1. Subjects

Among 127 patients with mild TBI (September 2013–January 2017), 35 patients (male: 9, female: 26, mean age: 42.5 ± 9.8 years, range: 21–58 years) with TBI were recruited for this study. In addition, 30 healthy control subjects (male: 16, female: 14, mean age: 36.1 ± 11.0 years, range: 20–56 years) with no previous history of neurological, physical, or psychiatric illness were recruited. The following inclusion criteria were applied to patient recruitment: loss of consciousness for <30 minutes, posttraumatic amnesia for ≤24 hours, and an initial Glasgow Coma Scale score of 13 to 15\(^{19,27}\); presence of central pain characteristic of neuropathic pain: stimulation-independent pain; shooting, lancinating, burning, electric shock-like sensation, and characteristic of neuropathic pain: stimulation-independent pain; no specific lesion was observed on brain MRI (T1-weighted, T2-weighted, and fluid attenuated inversion recovery images); more than 1 month after the onset of TBI; age at the time of head trauma: >20 years-old; no radiculopathy or peripheral neuropathy on electromyography and nerve conduction study; no musculoskeletal problem (e.g., myofascial pain syndrome, complex regional pain syndrome, or heterotopic ossification); and no history of previous head trauma, neurologic or psychiatric disease. This study was conducted retrospectively and written consent was obtained from all control subjects. The study protocol was approved by the Institutional Review Board of the Yeungnam University Hospital.

Demographics, clinical data, and DTT parameters for all subjects are summarized in Table 1. The average loss of consciousness, posttraumatic amnesia, and Glasgow Coma Scale values were 4.8 ± 8.0 minutes, 7.6 ± 13.1 minutes, and 14.9 ± 0.4 units, respectively. The mechanisms of injury for TBI were as follows: motor vehicle accident, 25 patients (71.4%); pedestrian accident, 6 patients (17.1%); fall, 3 patients (8.6%); bicycle accident, 1 patient (2.9%).

2.2. Clinical evaluation

The patients’ central pain was evaluated using the visual analogue scale (VAS) and the highest score was selected. The reliability and validity of the VAS have been well-established.\(^{32}\) The average VAS score of the patients was 6.2 ± 1.6 (Table 1).

2.3. Diffusion tensor imaging

DTI scanning was performed at an average of 9.6 ± 8.9 months after the onset of TBI using a 1.5T Philips Gyroscan Intera (Philips, Ltd., Best, The Netherlands). Seventy contiguous slices were acquired with 32 gradients. Imaging parameters of DTI were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm; repetition time = 10,398 ms; echo time = 72 ms; b = 1000 s/mm\(^2\); number of excitations = 1; and a slice thickness = 2.5 mm.

2.4. Fiber tracking

Fiber tracking was performed using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Diffusion Software (www.fmrib.ox.ac.uk/fsl) with the default tractography option.\(^{33}\) To reconstruct the STT, the seed region of interest (ROI) was given at an isolated STT area (posterolateral to the inferior olivary nucleus and anterior to the inferior cerebellar peduncle in the medulla).\(^{34}\) Two target ROIs were placed on a portion of the ventro-postero-lateral nucleus of the thalamus and on the primary somatosensory cortex on the axial images.\(^{34}\) A

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**Table 1**

Demographic, clinical data, and diffusion tensor tractography parameters of the patient and control groups.

|                      | Patient | Control |
|----------------------|---------|---------|
| Sex (male:female)    | 9:26    | 16:14   |
| Mean age, yr         | 42.5 (9.8) | 36.1 (11.0) |
| LOC, min             | 4.8 (8.0) | –       |
| PTA, min             | 7.6 (13.1) | –       |
| GCS score            | 13      | 1       |
|                      | 14      | –       |
|                      | 15      | 33      |
| VAS score            | 6.2 (1.6) | –       |
| Mechanism of injury  | Motor vehicle accident 25 | –       |
|                      | Bicycle accident 1 | –       |
|                      | Pedestrian accident 6 | –       |
|                      | Fall 3 | –       |
| Mean duration to DTI (mos) | 9.57 (8.86) | –       |
| DTT parameters for STT | FA Right 0.395 (0.040) | 0.408 (0.025) |
|                      | Left 0.406 (0.032) | 0.411 (0.031) |
|                      | Both 0.400 (0.036) | 0.409 (0.028) |
|                      | TV Right 1546.11 (978.22) | 1667.90 (482.55) |
|                      | Left 1716.80 (987.56) | 1737.53 (461.93) |
|                      | Both 1631.46 (979.53) | 1702.72 (469.65) |

Values represent mean (±standard deviation).

DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FA = fractional anisotropy, GCS = Glasgow Coma Scale, LOC = loss of consciousness, PTA = posttraumatic amnesia, STT = spinothalamic tract, TV = tract volume, VAS = visual analogue scale.
threshold of 2 streamlines was applied when obtaining the fiber tracking results. The tracking analyzer was blinded to all patient and control data, and data analyses were performed randomly. The fractional anisotropy (FA) and tract volume (TV) values for the STT were determined for both hemispheres. The observed abnormalities were classified as narrowing, tearing, or narrowing and tearing (Fig. 1).

2.5. Statistical analysis

SPSS software (SPSS for Windows, Version 15.0; SPSS Inc., Chicago) was used for statistical analysis. Before statistical analysis, we tested the normality of the DTT parameter values for the patients and controls; the data for both the patients and controls met the normality conditions. For group analysis, an independent t test was used to compare the FA and TV values between the patient and control groups. The null hypothesis of no difference was rejected if the P values were less than .05. The statistical power of the sample size was calculated using G*power 3.1 and showed a 0.5 effect size, 0.05 α error probability, and 0.64 power (1-β error probability). For individual analysis, and because the injured hemisphere in patients varied according to the injury mechanism, all patients were divided into 2 hemispheres and compared with similarly divided control groups. DTT parameter values lower than 1 or 2 standard deviations (SDs) of the control value mean were defined as indicative of an injured STT. For definition of the configuration of the STT, tearing was defined as any deficit of continuity in the entire pathway of the STT, while narrowing was defined as the thinness of the whole pathway of the STT compared to the thickness of the STT of the control subjects.

3. Results

Group-based analysis showed that the FA and TV values for the STT did not differ significantly between the patient and control groups (P > .05) (Table 1). Table 2 presents a summary of the results of the prevalence of STT injury based on the DTT parameters and configurations. Thirty-three patients had a DTT parameter lower than 1 SD from the mean parameter value in the control group, and 20 patients had a parameter lower than 2 SDs. In detail, the individual FA values in 21 and 7 patients, and the individual TV values of 21 and 14 patients were lower than 1 SD and 2 SDs, respectively, from the mean FA and TV values of the control subjects.

Figure 1. Results of diffusion tensor tractography for the spinothalamic tract (STT) in the patient group. Narrowing (red arrows) and tearing (blue arrows) of the STT are defined as abnormal compared with a normal control subject.
control group. Three patients had a decrease of 1 SD in both the FA and TV values compared to the control group.

Regarding the DTT configuration of the STT, 35 patients showed the STT abnormality (tearing and narrowing). Of those, 24 patients showed narrowing of the STT, and 21 patients revealed tearing of the STT. Furthermore, 9 patients revealed both tearing and narrowing of the STT.

### 4. Discussion

This DTT-based study investigated the diagnostic sensitivity of TAI when assessing the STT in patients with mild TBI. Thirty-five patients with central pain after mild TBI were enrolled in this study, and the following results were obtained; there is high diagnostic sensitivity for TAI of the STT, that is, 100% sensitivity for a torn or narrowed configuration of an injured STT as the individual patient denominator in the patient group. By contrast, 94.3% (1 SD decrease) and 57.1% (2 SD decrease) sensitivity were associated with the FV and TV parameters as the individual patient denominator in the patient group.

Several studies reported that an analysis of DTT parameters is better than an analysis of the DTI parameters when using an ROI-method to detect a neural injury in an individual patient. Two DTT (FA and TV) and DTT-derived configurations (narrowing, tearing, or both) of the STT were analyzed. The FA value indicates the degree of directionality of water diffusion within a range of 0 (completely isotropic diffusion) to 1 (completely anisotropic diffusion). Furthermore, the FA values indicate the white matter organization. In particular, FA indicates the degree of directionality of the white matter microstructures such as axons, myelin, and microtubules. By contrast, TV, which reveals the number of voxels within a neural tract, indicate the number of fibers within a neural tract. Therefore, changes in the DTT parameters, such as a decrease in FA or TV values, can indicate an injury to the STT. Moreover, narrowing or tearing of the STT, as visualized on DTT results, can indicate an injury to the STT. In this study, a higher sensitivity was obtained when assessing the configuration of the STT (100%) than the sensitivities (94.3% – 1 SD and 57.1% – 2 SD) obtained from assessing the FA and TV parameters. Hence, configurational analysis of the STT has better diagnostic sensitivity for an STT injury than an analysis of the directionality (FA) or fiber number (TV) of a TAI in the STT of patients with mild TBI.

All subjects in the patient group suffered neuropathic pain; however, no definite brain lesions were observed on conventional brain MRI. Radiculopathy and peripheral neuropathy were also ruled out. Therefore, it appears that injury of the STT was related to the occurrence of central pain in the patient group. TAI appeared to be the most likely pathogenetic mechanism for STT injury. After introducing DTI, many studies reported an injury to the neural tracts in patients with mild TBI; however, regarding the sensitivity associated with diagnosis of TAI of a neural tract following mild TBI, a few studies reported high sensitivity (100%) of the configurational analysis of the corticoreticulospinal tract and corticospinal tract. These results are similar to those in the above studies. Further DTT-based studies on the diagnostic sensitivity of TAI of other neural tracts should be encouraged.

Since the introduction of DTI, several studies reported an association of central pain with TAI of the STT in patients with mild TBI. In 2015, the previous study reported central pain in 68.75% of all patients with mild TBI, injuries that had been diagnosed as STT injuries based on DTI parameters. By contrast, the current study recruited new patients except for those included in Kim et al and investigated the diagnostic sensitivity of TAI in terms of DTT-based configuration and parameters for the STT in patients with mild TBI. Other studies described an association between the injury of the STT and central pain in individual patients following mild TBI. The current study is the first original DTT-based study to assess the diagnostic sensitivity of TAI for the STT in patients with mild TBI. However, there are limitations to this study that should be considered. First, the study included a small number of subjects. In addition, only patients with central pain who visited the rehabilitation department of a university hospital were recruited. Therefore, among all patients with mild TBI, patients with severe clinical manifestations might have been recruited. Second, the diagnostic specificity of TAI was not estimated because the majority of the patients with mild TBI usually have some pain. Because the possibility of central pain could not be excluded in patients with other kinds of pain following mild TBI, the specificity estimation could be biased and misleading. Third, although DTT is a powerful anatomic imaging tool, which can demonstrate gross fiber architecture, it can produce both false positive and negative results caused by crossing fibers or partial volume effect. Further studies with larger numbers of subjects and studies that include an assessment of the diagnostic

### Table 2

| Injury of the spinothalamic tract in terms of individual values of diffusion tensor tractography parameters and configurations categories. |

| DTT parameters | Hemisphere (total: 70) | Patient (total: 35) |
|----------------|-----------------------|---------------------|
| FA TV Both (FA + TV) Total | FA TV Both (FA + TV) Total |
| 1 SD | 25 (35.7%) | 26 (37.1%) | 4 (5.7%) | 47 (67.1%) | 21 (60.0%) | 21 (60.0%) | 0 | 23 (32.9%) | 7 (20%) | 14 (40.0%) | 0 | 20 (57.1%) |
| 2 SD | 7 (10.0%) | 16 (22.9%) | 0 | 23 (32.9%) | 7 (20%) | 14 (40.0%) | 0 | 20 (57.1%) |

| DTT configurations category | Hemisphere (total: 70) | Patient (total: 35) |
|-----------------------------|-----------------------|---------------------|
| Narrowing | 34 (48.6%) | 24 (68.6%) |
| Tearing | 28 (40.0%) | 21 (60.0%) |
| Narrowing + tearing | 9 (12.9%) | 9 (25.7%) |
| Total | 53 (75.7%) | 35 (100%) |

1 SD: when the value was decreased 1 standard deviation below that of controls.
2 SD: when the value was decreased 2 standard deviations below that of controls.

DTT = diffusion tensor tractography, FA = fractional anisotropy, SD = standard deviation, TV = tract volume.
specificity of TAI of the STT should be encouraged. Moreover, studies overcoming DTT imaging limitations will be necessary.

In conclusion, the high diagnostic sensitivity of TAI of the STT was detected for assessing the STT in patients with mild TBI. The DTT for the STT is useful for diagnosing TAI in patients with central pain after mild TBI. Moreover, the DTT protocol for the STT provides reliable methods to quantify the FA and TV of the STT.

Author contributions
Data curation: Seong Ho Kim.
Funding acquisition: Sung Ho Jang.
Methodology: Hyeok Gyu Kwon.
Resources: Seong Ho Kim.
Supervision: Sung Ho Jang.
Visualization: Hyeok Gyu Kwon.
Writing – original draft: Hyeok Gyu Kwon.
Writing – review & editing: Sung Ho Jang.

References
[1] Cassidy JD, Carroll LJ, Peloso PM, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004;28–60.
[2] Adams JH, Graham DI, Murray LS, Scott G. Diffuse axonal injury due to nonmissile head injury in humans: an analysis of 45 cases. Ann Neurol 1982;12:557–63.
[3] Meythalal JM, Pederuzzi JD, Eleftheriou E, Novack TA. Current concepts: diffuse axonal injury-associated traumatic brain injury. Arch Phys Med Rehabil 2001;82:1461–71.
[4] Chung SW, Park YS, Nam TK, Kwon JT, Min BK, Hwang SN. Locations and clinical significance of non-hemorrhagic brain lesions in diffuse axonal injuries. J Korean Neurosurg Soc 2012;52:377–83.
[5] Maxwell WL, Pavlishock JT, Graham DL. A mechanistic analysis of nondisruptive axonal injury: a review. J Neurotrauma 1997;14:419–40.
[6] Sherman KB, Goldberg M, Bell KR. Traumatic brain injury and pain. Arch Phys Med Rehabil Clin N Am 2006;17:473–90. viii.
[7] Nampaparampl DE. Prevalence of chronic pain after traumatic brain injury: a systematic review. JAMA 2008;300:711–9.
[8] See JP, Jang SH. Injury of the spinothalamic tract in a patient with mild traumatic brain injury: diffusion tensor tractography study. J Rehabil Med 2014;46:374–7.
[9] Kim JH, Ahn SH, Cho YW, Kim SH, Jang SH. The relation between injury of the spinothalamocortical tract and central pain in chronic patients with mild traumatic brain injury. J Head Trauma Rehabil 2015;30:E40–6.
[10] Jang SH, Park SM, Kwon HG. Relation between injury of the periaqueductal gray and central pain in patients with mild traumatic brain injury: observational study. Medicine (Baltimore) 2016;95:e4017.
[11] Jang SH, Lee HD. Central pain due to spinothalamic tract injury caused by indirect head trauma following a pratfall. Brain Inj 2016;30:933–6.
[12] Jang SH, Kim SH, See JP. Spinothalamic tract injury due to primary brainstem injury: a case report. Am J Phys Med Rehabil 2016;95:e42–3.
[13] Jang SH, Kwon HG. Degeneration of an injured spinothalamic tract in a patient with mild traumatic brain injury. Brain Inj 2016;30:1026–8.
[14] Jang SH, Lee HD. Severe and extensive traumatic axonal injury following minor and indirect head trauma: a case report. Brain Inj 2017;31:416–9.
[15] Jang SH, See JP. Central pain due to spinothalamic tract injury by head trauma caused by a falling object. Ann Rehabil Med 2016;40:1149.
[16] Devulder J, Crombez E, Mortier E. Central pain: an overview. Acta Neurol Belg 2002;102:97–103.
[17] Oték H, Defrin R. The characteristics of chronic central pain after traumatic brain injury. Pain 2007;131:330–40.
[18] Tenovuo O. Central pain due to brain trauma—a neglected problem in neglected victims. Pain 2007;131:241–2.
[19] Alexander MP. Mild traumatic brain injury: pathophysiology, natural history, and clinical management. Neurology 1995;45:1253–60.
[20] De Kruijck JR, Twijnstra A, Leffers P. Diagnostic criteria and differential diagnosis of mild traumatic brain injury. Brain Inj 2001;15:599–106.
[21] Jang SH. Diagnostische history of traumatic axonal injury in patients with cerebral concussion and mild traumatic brain injury. Brain Neurorehabil 2016;9:1–8.
[22] Kishi M, Sakakibara R, Nagao T, Terada H, Ogawa E. Thalamic infarction disrupts spinothalamic projection to the mid-cingulate cortex and supplementary motor area. J Neurrol Sci 2009;281:104–7.
[23] Apkarian AV, Hodge CJ. Primate spinothalamic pathways: III. Thalamic terminations of the dorsolateral and ventral spinothalamic pathways. J Comp Neurol 1989;288:493–511.
[24] Kraseu T, Brunecker P, Pirtt S, et al. Thalamic sensory strokes with and without pain: differences in lesion patterns in the ventromedial posterior thalamus. J Neurrol Neurosurg Psychiatry 2012;83:776–84.
[25] Chou XL, Fang Q, Yan L, et al. Contextual and cross-modality modulation of auditory cortical processing through pulvinar mediated suppression. Elite 2020;9.
[26] Fang Q, Chou XL, Peng B, Zhong W, Zhang Ll, Tao HW. A differential circuit via retino-colliculo-pulvinar pathway enhances feature selectivity in visual cortex through surround suppression. Neuroon 2020;105:355–69.e6.
[27] Ruff RM, Iverson GL, Barth JT, Bush SS, Broshek DK. NAN Policy and Planning Committee Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. Arch Clin Neuropsychol 2009;24:3–10.
[28] Woolf CJ, Mannion RJ. Neuropathic pain: aetiology, symptoms, mechanisms, and management. Lancet 1999;353:1595–64.
[29] Dworkin RH, Backonja M, Rowbotham MC, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. Arch Neurol 2003;60:1524–34.
[30] Kilt H, Finnerup NB, Jensen TS. Central post-stroke pain: clinical characteristics, pathophysiology, and management. Lancet 2009;6:578–68.
[31] Barad M, Michael MD, Mackey S. Imaging the CNS correlates of neuropathic pain. Continuum (Minneap Minn) 2009;5:30–46.
[32] Miller MD, Ferris DG. Measurement of subjective phenomena in primary care research: the Visual Analogue Scale. Fam Pract Res J 1993;13:15–24.
[33] Smith SM, Jenkinson M, Woolrich MW, et al. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage 2004;23(Suppl 1):S208–19.
[34] Jang SH, Kwon HG. Anatomical location of the medial lemniscus and spinothalamic tract at the pons in the human brain: a diffusion tensor tractography study. Somatosens Mot Res 2013;30:206–9.
[35] Shenton ME, Hamoda HM, Schneiderman JS, et al. A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. Brain Imaging Behav 2012;6:137–92.
[36] Brandstack HW, Kurki T, Lapo J, Kauko T, Tenovuo O. Reproducibility of tract-based and region-of-interest DTI analysis of long association tracts. Clin Neuroradiol 2016;26:199–208.
[37] Assaf Y, Pasternak O. Diffusion tensor imaging (DTI)-based white matter mapping in brain research: a review. J Mol Neurosci 2008;34:51–61.
[38] Neil JJ. Diffusion imaging concepts for clinicians. J Magn Reson Imaging 2008;27:1–7.
[39] Jang SH, Chang CH, Lee J, Kim CS, See JP, Yeo SS. Functional role of the corticospinal pathway in chronic stroke patients. Stroke 2013;44:1099–104.
[40] Pavlishock JT. Traumatically induced axonal injury: pathogenesis and pathobiological implications. Brain Pathol 1992;2:1–12.
[41] Hill CS, Coleman MP, Menon DK. Traumatic axonal injury: mechanisms and translational opportunities. Trends Neurosci 2016;39:311–24.
[42] Lee HD, Jang SH. Injury of the corticospinal pathway in patients with mild traumatic brain injury: a diffusion tensor tractography study. Brain Inj 2015;29:1219–22.
[43] Jang SH, Kim SY. Injury of the corticospinal tract in patients with mild traumatic brain injury: a diffusion tensor tractography study. J Neurotrauma 2016;33:1790–5.
[44] Parker GJ, Alexander DC. Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue. Philos Trans R Soc Lond B Biol Sci 2005;360:893–902.
[45] Lee SK, Kim DI, Kim J, et al. Diffusion-tensor MR imaging and fiber tractography: a new method of describing aberrant fiber connections in developmental CNS anomalies. Radiographics 2005;25:53–65. discussion 66–8.
[46] Yamada K. Diffusion tensor tractography should be used with caution. Proc Natl Acad Sci U S A 2009;106:E14author reply E15.