The Nigrostriatal Tract between the Substantia Nigra and Striatum in the Human Brain: A Diffusion Tensor Tractography Study

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Objectives: The nigrostriatal tract (NST) connect from the substantia nigra pars compacta to the striatum. A few previous studies have reported on the NST in the Parkinson’s disease using a probabilistic tractography method. However, no study has been conducted for identification of the NST using streamline DTT technique. In the current study, we used streamline DTI technique to investigate the reconstruction method and characteristics of the NST in normal subjects.

Methods: Eleven healthy subjects were recruited in this study. The NST from the substantia nigra of the midbrain and the striatum of basal ganglia was reconstructed using DTI data. Fractional anisotropy, apparent diffusion coefficient (ADC) values and fiber numbers of the NST were measured.

Results: In all subjects, the NST between the substantia nigra of the midbrain and the striatum. Mean values for FA, ADC, and tract volume were 0.460, 0.818, and 154.3 in the right NST, and 0.485, 0.818, and 176.3 in the left NST respectively.

Conclusions: We reconstructed the NRT from the substantia nigra of the midbrain and the striatum of the basal ganglia using streamline tractography method. We believe that the findings and the proposed streamline reconstruction method of this study would be useful in future researches on the NST of the human brain.

Keywords: Diffusion tensor imaging, Diffusion tensor tractography, Nigrostriatal tract, Dopaminergic pathways

INTRODUCTION

The nigrostriatal tract (NST), which is one of the major bilateral dopaminergic pathways that link the brainstem to the striatum, connects from the substantia nigra pars compacta in the midbrain to the dorsal striatum.1,2 It is major dopaminergic pathways in the human brain, and belong the basal ganglia motor loop which is critical as part of a system in the production of movement.3 The degeneration of the NST is led to be the cause of the motor symptoms of Parkinson’s disease including tremors, rigidity, hypokinesia, and postural imbalance.4,5

Recent developments in diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), have allowed for the three dimensional visualization and localization of the various neural tracts in the human brain.6-8 A few previous studies have reported on the NST in the Parkinson’s disease using a probabilistic tractography method.9-10 Although a streamline DTI technique is a powerful anatomic imaging tool in a clinical field and it can be applied in native space, without registration to a template,11,12 no study has been conducted for identification of the NST using streamline DTT technique.

In the current study, we used streamline DTI technique to investigate the reconstruction method and characteristics of the NST in normal subjects.

METHODS

1. Subjects
Eleven right-handed healthy subjects (males: 7, females: 4, mean age: 29.2 years, range: 20-38 years) with no previous history of neurological, physi-
cal, or psychiatric illness were recruited for this study. All subjects understood the purpose of this study and provided written, informed consent prior to participation. The study protocol was approved by our local Institutional Review Board.

2. Data acquisition
A 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips, Ltd, Best, The Netherlands) with single-shot echo-planar imaging was used for acquisition of DTI data. For each of the 32 gradients, 70 contiguous slices were acquired parallel to the anterior commissure-posterior commissure line. Imaging parameters of DTI were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm²; repetition time = 10,398 ms; echo time = 72 ms; parallel imaging reduction factor = 2; echo-planar imaging factor = 59; \( b \) = 1,000 s/mm²; number of excitations = 1; and a slice thickness of 2.5 mm.

3. Fiber tracking
Eddy current-induced image distortions were removed using affine multiscale two-dimensional registration in the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL: www.fmrib.ox.ac.uk/fsl). DTI-Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD, USA) was used to evaluate NSTs. For reconstruction of the NST, a first region of interest (ROI) was manually drawn on the substantia nigra on the FA map at midbrain, and a second ROI was placed on the striatum on the FA map. In a nigrofugal tracing study, traversing of nigrostriatal projections from the globus pallidus to the striatum was demonstrated. Moreover, the NST from the posterior putamen have been found to form a discrete bundle coursing through the globus pallidus to converge at the substantia nigra. Fiber tracking was started at the center of a seed voxel with a fractional anisotropy (FA) of > 0.15 and ended at a voxel with a fiber assignment of > 0.15 and a tract turning-angle of < 70°, with an option of cut operation on the axial images. FA, apparent diffusion coefficient (ADC) values and fiber numbers of the NST were measured in both hemispheres.

4. Statistical analysis
SPSS software version 15.0 (Chicago, SPSS Inc.) was used for the analysis. An independent t-test was used for determination of variances in the value of FA, ADC, and fiber numbers of the NST between the right and left hemispheres. Statistical significance was accepted for \( p \) values of < 0.05.

### RESULTS
In all subjects, the NST between the substantia nigra of the midbrain and the striatum were reconstructed (Figure 1). Mean values for FA, ADC, and fiber number were 0.460, 0.818, and 154.3 in the right NST, and 0.485, 0.818, and 176.3 in the left NST respectively. No significant differences were observed in FA, ADC, and fiber number between the both hemispheres in the NST \( p > 0.05 \) (Table 1).

### DISCUSSION
In the current study, the NST in the normal human brain was reconstructed between the substantia nigra of the midbrain and the striatum, using the streamline tractography technique. Determination of ROIs is
fundamental to analysis for the DTT. We selected ROIs for reconstruction of NST: the substantia nigra on the midbrain, and the striatum. We found that the NST originated from the substantia nigra on the midbrain and terminated in the striatum of basal ganglia. Therefore, we believe the reconstruction of this neural tract to be precise and reproducible using streamline tractography technique.

Since introduction of DTT, a few studies DTT studies have been conducted on the NST in the Parkinson’s disease. Andica et al. reported on degeneration of the NST in the patients with Parkinson’s disease using generate tractography. In 2008, Camp et al. investigated that the substantia nigra and did not include the nigrostriatal fiber tract in the Wistar rats brain. However, these studies described the reconstruction of the NST using probabilistic tractography method. The probabilistic tractography takes into account intra-voxel crossing fibers, estimates the pathways which originate at seed voxel and provides quantitative information about the probability of structural connectivity that a white matter tract in the human brain. The stream line tractography method is the most intuitive way to reconstruct a 3D trajectory from a 3D vector field by following the local vector orientation, and it has advantage in simplifying visualization considering medical application. To the best of our knowledge, this is the first DTT study to reconstruct the NST in human brain using streamline tractography method. However, limitations of DTI should be considered. DTI may underestimate fiber tracts, due to crossing fiber or partial volume effect, and it is difficult to reflect all fibers, particularly small fibers.

In conclusion, we reconstructed the NST from the substantia nigra of the midbrain and the striatum of the basal ganglia using streamline tractography method. We believe that the findings and the proposed streamline reconstruction method of this study would be useful to neuroscience clinicians in clinical practice and future researches on the NST of the human brain. Conduct of further complementary studies involving larger case numbers is warranted. In addition, we suggest further studies are required for the clinical studies which are related with the NST injury.

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