An Anatomic Review of Thalamolimbic Fiber Tractography: Ultra-High Resolution Direct Visualization of Thalamolimbic Fibers Anterior Thalamic Radiation, Superolateral and Inferomedial Medial Forebrain Bundles, and Newly Identified Septum Pellucidum Tract

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Key words
- Affective disorders
- Alzheimer disease
- Anterior thalamic radiation
- Deep brain stimulation
- Depressive disorder
- Diffusion tensor imaging
- Inferomedial medial forebrain bundle
- Limbic system
- Magnetic resonance Imaging
- Parkinson disease
- Septum pellucidum tract
- Superolateral medial forebrain bundle
- Track density imaging
- Tractography
- Ultra high field MRI

Abbreviations and Acronyms
AC: Anterior commissure
ALIC: Anterior limb of the internal capsule
ATR: Anterior thalamic radiation
DBS: Deep brain stimulation
Fx: Fornix
imMFB: Inferomedial medial forebrain bundle
MRI: Magnetic resonance imaging
PC: Posterior commissure
PLIC: Posterior limb of internal capsule
slMFB: Superolateral medial forebrain bundle
SPT: Septum pellucidum tract
TDI: Track-density imaging

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BACKGROUND: **Images obtained through ultra-high-field 7.0-tesla magnetic resonance imaging with track-density imaging provide clear, high-resolution tractograms that have been hitherto unavailable, especially in deep brain areas such as the limbic and thalamic regions. This study is a largely pictorial description of the deep fiber tracts in the brain using track-density images obtained with 7.0-T diffusion-weighted imaging.**

METHODS: **To identify the fiber tracts, we selected 3 sets of tractograms and performed interaxis correlation between them. These tractograms offered an opportunity to extract new information in areas that have previously been difficult to examine using either in vivo or in vitro human brain tractography.**

RESULTS: **With this new technique, we identified 4 fiber tracts that have not previously been directly visualized in vivo: septum pellucidum tract, anterior thalamic radiation, superolateral medial forebrain bundle, and inferomedial forebrain bundle.**

CONCLUSIONS: **We present the high-resolution images as a tool for researchers and clinicians working with neurodegenerative and psychiatric diseases, such as Parkinson disease, Alzheimer disease, and depression, in which the accurate positioning of deep brain stimulation is essential for precise targeting of nuclei and fiber tracts.**

INTRODUCTION

The introduction of ultra-high field 7.0-T magnetic resonance imaging (MRI) has enabled the visualization of many deep brain structures with markedly improved resolution. In diffusion tractography, further progress has been made by performing track-density imaging (TDI) using ultra-high field MRI (1, 4, 5). In addition, the clinical importance of tractography has increased as highly precise neurologic treatments such as deep brain stimulation (DBS) become more common (7).

A widely accepted conceptual illustration of overall fiber connections in the thalamolimbic area is shown in Figure 1, in which several newly discovered fibers are seen together with classic fibers such as the fornix (Fx) and stria terminalis. The 4 newly identified fibers—septum pellucidum tract (SPT), anterior thalamic radiation (ATR), inferomedial medial forebrain bundle (imMFB), and superolateral medial forebrain bundle (slMFB)—are indicated with red boxes. A coronal image and its corresponding tractogram are shown for reference in Figure 2. Except for these 4 new fibers, this tractography diagram is a well-known scheme that has been the standard connectivity diagram for decades; however, the in vivo human imaging correlate has not been definitively proven.

Many affective disorders may be associated with the fibers identified in this study, including major depressive disorder, obsessive-compulsive disorder, drug addiction, and posttraumatic stress disorder (8, 10, 15, 16). This group of disorders is responsible for significant morbidity and potential mortality, and the accurate localization of these tracts may provide novel means for effective therapeutic intervention with minimal side effects. The comprehensive in vivo human tractograms presented here are the first of their kind, and their

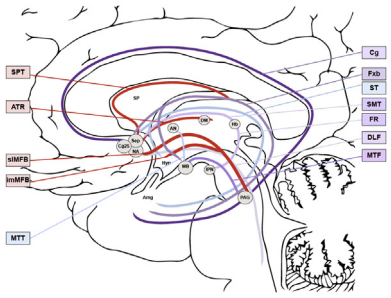

Figure 1. Fibers and connections in the thalamolimbic region. Newly identified tracts include the septum pellucidum tract (SPT), anterior thalamic radiation (ATR), superolateral medial forebrain bundle (sIMFB), and inferomedial medial forebrain bundle (imMFB). Amg, amygdala; AN, anterior nucleus of the thalamus; Cg, cingulum; Cg25, subgenual cingulate; DLF, dorsal longitudinal fasciculus; DM, dorsomedial nucleus of the thalamus; FR, fasciculus retroflexus; Fxb, fornix body; Hb, habenula; Hyp, hypothalamus; IPN, interpeduncular nucleus; MB, mammillary body; MTF, mammillotegmental fasciculus; MTT, mammillothalamic tract; NA, nucleus accumbens; PAG, periaqueductal gray; Sep, septal area; SMT, stria medullaris thalami; SP, septum pellucidum; ST, stria terminalis.

potential applications in neurosurgery and other clinical areas could be vast, especially in the treatment of psychiatric disorders with DBS, wherein accurate targeting—not only of nuclei but also of fibers—is of utmost importance.

METHODS

The subject in this study was a healthy 30-year-old male volunteer. MRI diffusion-weighted data were obtained through conventional diffusion-weighted imaging with a 7.0-T MRI scanner (7.0T; Siemens, Erlangen, Germany). Diffusion-weighted imaging was performed with single-shot diffusion-weighted echo planar imaging with the following parameters: repetition time/echo time = 6000/83 ms; matrix = 128 × 128 (field of view = 230 mm × 45 slices); 1.8 mm isotropic resolution; 64 (+1) diffusion-weighted directions; b-value = 0 and 2000 seconds/mm^2; 3 repeats; generalized autocalibrating partially parallel acquisition with factor 3; bandwidth = 1562 Hz/Px; and total acquisition time = 19 minutes (6 seconds × 65 × 3 repeats). Diffusion-weighted images acquired using echo-planar imaging have geometric distortion artifacts caused by strong local susceptibility and Bo field inhomogeneity, especially when using ultra-high-field MRI. The diffusion-weighted imaging data were corrected for geometric distortions using a combined dimensional point spread function mapping method (21). Corrected diffusion-weighted images were processed with a TDI image processing technique, which included spherical deconvolution with voxel division 0.18 mm. The final nominal image was made with 0.18-mm plane resolution, after which the image data were color-coded (2, 3). This analysis was performed using the MRtrix software package (Brain Research Institute, Melbourne, Australia).

Identification of Fibers

Identification of fibers was performed through double-axis and triple-axis correlation as shown in Figure 3: a sagittal image versus a series of coronal images (Figure 3A), a coronal image versus a series of sagittal images (Figure 3B), and a coronal image versus a series of axial images (Figure 3C). Interaxis correlation is a manual method for colocalizing structures seen on TDI maps using perpendicular lines placed on coronal, sagittal, and axial images. Intersecting interaxis lines are manually and visually correlated between the orthogonal planes. Using this methodology, we can identify structures traversing in 1 direction (in a single color-coded track density), which would otherwise be difficult to localize. These structures can be confirmed in multiple planes.

Readers can use the triple-axis correlations to observe the fibers and nuclei themselves, in much the same way as one uses a neuroanatomy textbook such as Schaltenbrand and Wahren (23). To that end, we have included "correlation lines" on each pair of compared images. For example, in Figure 4, the solid white correlation lines on either image are located at the level of the plane of the comparison image; that is, the line on the sagittal image corresponds to a coronal slice at +2 mm, and, inversely, the line on the coronal image corresponds to a sagittal slice at +5 mm. Perpendicular dashed lines are drawn between the 2 lines to confirm colocalization of fibers. Additionally, intersecting red lines on each image indicate the center of the anterior commissure (AC)−posterior commissure (PC) line, which passes through the center of the anterior and posterior commissures. The AC-PC line was used to define 0 mm on the sagittal and axial planes, and the orthogonal line passing vertically through the center of the AC-PC line was used to define 0 mm on the coronal plane.

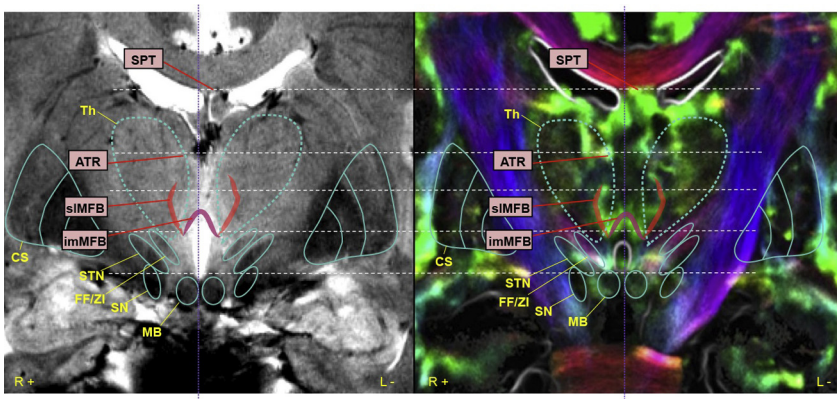

Figure 2. A 7.0-T coronal image (C. + 2 mm) with corresponding track density imaging tractogram. The superolateral medial forebrain bundle (sIMFB) and inferomedial medial forebrain bundle (imMFB) create a "W" shape at the midline; the sIMFB forms the lateral portions of the W, and the imMFB forms the middle portion. ATR, anterior thalamic radiation; CS, corpus striatum; FF/ZI, field of Forel/zona incerta; MB, mammillary body; SPT, septum pellucidum tract; SN, substantia nigra; STN, subthalamic nucleus; Th, thalamus.

RESULTS

Interaxis Correlation of Thalamolimbic Fibers

Sagittal Image versus Series of Coronal Images. In this section, a sagittal image (at S. + 5 mm) is correlated with a series