Statistical DSI brain tractography: a way to handle the kiss-cross uncertainty

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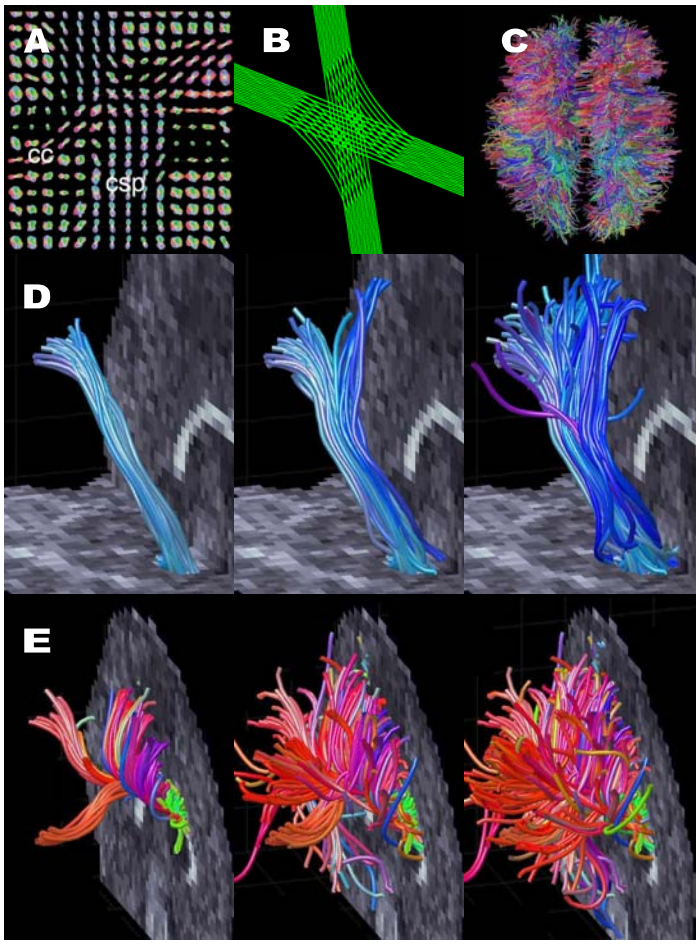
Introduction

Until recently the study of white matter axonal architecture was the neuropathologist's private domain, but the advent of diffusion magnetic resonance imaging and tractography algorithms has given a new breath to the field. The recent Diffusion Spectrum Imaging (DSI) [1] has shown its capacity to image multiple intra-voxel fiber directions (Fig. A), thus allowing DSI-based tractography algorithms to accurately image fiber crossings in the brain white matter (WM) [2]. However, most of these techniques are not able to detect all possible paths that could possibly intermix in a complex fiber kiss-crossing area (Fig. B). This is due to their inherent fiber generation model, which prevents the tracts from changing direction when an intersection occurs. In this study, we present a statistical DSI-based tractography algorithm which considers all possible fiber paths in the brain WM and creates a cortex connectivity graph to estimate the connection probability. As a first test case for our algorithm we take one of the most obvious members of brain WM regions with complex fiber intermixing: the centrum semi-ovale.

Material and Methods

The MR diffusion images of a brain are obtained on a healthy volunteer with a 3T Allegra scanner (Siemens, Erlangen, Germany), following a classical DSIscheme [3] using 515 diffusion encoding directions. We use a twice-refocused spin echo EPI sequence with $TR/TE/\Delta/\delta$ = 3000/154/66/60 ms and b-max = 17000 mm^2/s to acquire 37 slices of a 64 x 64 matrix with a spatial resolution of 3 x 3 x 3 mm^3.

The fiber tracking algorithm presented here is based on a streamline algorithm. The first step consists in reducing the orientation distribution function (ODF) of each voxel into a set of normalized direction vectors $V = \{\mathbf{v}^l, 0 \le l \le |V|\}$ corresponding to the local maxima of the diffusion. The fibers grow by expanding from a position $\mathbf{p}_i$ by a fixed step size μ along the vector $\mathbf{v}_i^{r_i}$: $\mathbf{p}_{i+1} = \mathbf{p}_i + \mu \mathbf{v}_i^{r_i}$. The vector $\mathbf{v}_i^{r_i}$ is randomly chosen among the subset of direction vectors $V_i^{'} = \{\mathbf{v}_i \in V_i \,|\, \|\mathbf{v}_i \times \mathbf{v}_{i-1}^{r_{i-1}}\| \le \sin(\alpha)\}$, with α a fixed tolerance angle (e.g. π/3) avoiding abrupt changes of direction. DSI tractography is performed by initiating fibers uniformly over the whole brain WM (Fig. C). We then place a 3D grid over the brain image, which corresponds to covering the brain with small Regions of Interest (ROI) of size 6x6x6 mm^3. Furthermore, we identify the brain gray matter (GM) by using a T1w based segmentation algorithm and consider as ROIs only the boxes that contain GM. We construct a graph where the vertices represent the set of ROIs defined above. A weighted edge between two vertices is drawn if there is at least one fiber that has its origin and destination in a pair of different ROIs. The edge weight corresponds to the probability of connection between ROIs, defined by: $n_{fb}\left[\bar{l}_{fb}(S_1 + S_2)\right]^{-1}$, with n_{fb} and $\bar{l}_{fb}$ respectively the number and the average length of the fibers connecting the pair of ROIs, and S_1, S_2 the cortical connection surface in each ROI. A thresholding of the graph edge weights is then performed, thus keeping the most probable connections.



Results

In Fig. D the cortico-spinal tract has been mapped by capturing the fibers running through the internal capsule and the cerebral peduncle. The callosal fibers passing in the region of the centrum semi-ovale have been selected by placing a ROI in the mid-sagittal plane centered on the corpus callosum (Fig. E). For both tracts different threshold levels have been applied on the edges of the weighted graph: a high one (left) selecting only the connections with the highest relative probability, an intermediate one (center), and a lower one (right) keeping around 90% of fiber population. According to known anatomy [4], we can see that the most probable connections within the cortico-spinal tract take their origin between the superior and inferior genu of the central sulcus and correspond to the motor fibers for the arm and hand (light blue). By decreasing the threshold level, the part of the pyramidal tract starting in the apical part of the precentral gyrus and middle part of the paracentral lobule and corresponding to the motor function of the trunk and legs becomes visible (dark blue). The fibers of the corpus callosum are widely distributed throughout the parietal cortex from the apex down to its lower limit at the lateral sulcus.

Discussion

The current method differs from standard tractography algorithms as it tries to explore all possible paths in the brain WM instead of generating only the fibers along the most probable direction, thus providing a way to handle the kiss-cross uncertainty. Typically, it is not clear whether fibers cross or kiss in a shallow crossing, but they probably do both in many instances such as the centrum semi-ovale, where the cortico-spinal tract fans out over the motor homunculus and the corpus callosum widely connects the parietal and frontal cortex. Moreover, we introduce a way to quantify the connection probability between two points of the brain GM in terms of intersections, which is used to measure the uncertainty of the connections between any pair of ROIs. Indeed, the connection likelihood between two brain areas is certainly dependent on the number of diffusion crossings that occur on its tract trajectory. The tests on the centrum semi-ovale have shown that the algorithm presented here allows us to accurately reconstruct the main fiber bundles. It is important to note that the threshold applied to the edges of the weighted graph does not only limit the number of fibers; it is also a useful tool for the identification of the most probable tracts. Thus, by varying the level of this threshold, the connectivity of any part of the brain can be mapped to the desired level of complexity. The analogy with standard image thresholding is obvious: high threshold level means capturing features of high SNR, i.e. of high confidence, while by decreasing the threshold one increases the sensitivity at the cost of introducing noise. The presented method is then very efficient to accurately image complex fiber kiss-crossing areas. However, even if DSI is able to solve variously oriented fascicles within a voxel, we are still limited by the resolution of this imaging technique, the diameter of an axon being well beyond the resolution of a current MRI scan.

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