How much confidence do we have in a MRI tractography experiment?

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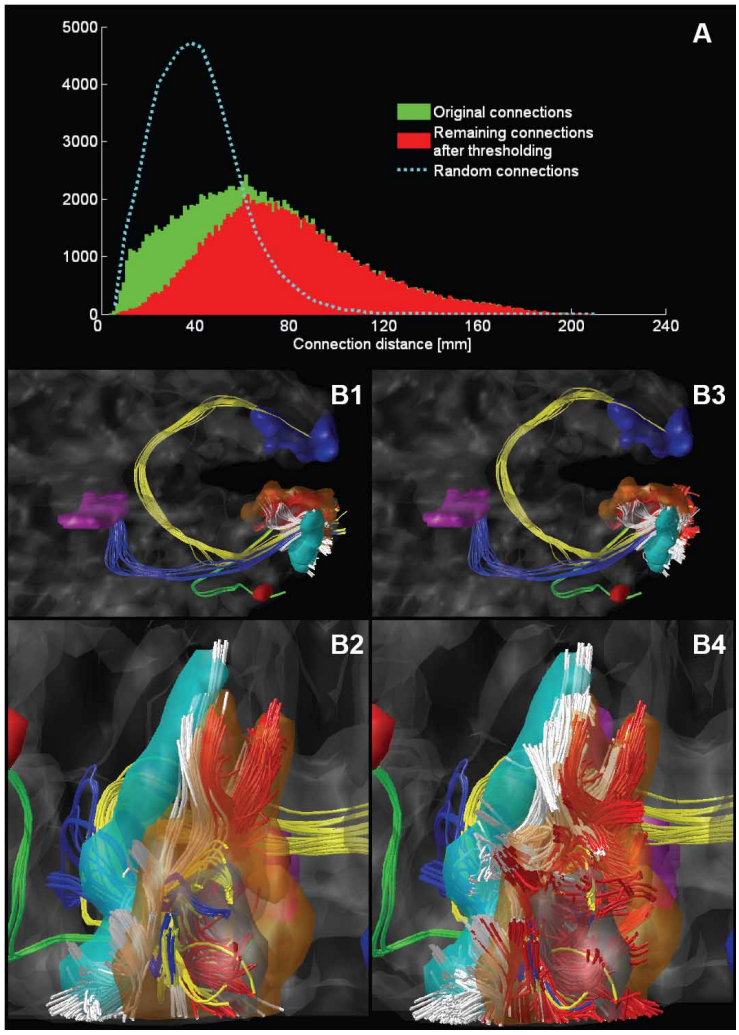
Introduction

Diffusion MRI tractography has proved to be a very powerful tool to study brain anatomical connectivity. However, researchers haven't paid much attention to the confidence one can attribute to a tractography solution. It is nonetheless essential to know whether a reconstructed tract results from the diffusion signal itself or from some random effect or noise. In this study, we introduce a way to estimate the contribution of noise in the tract construction by comparing the density of every gray matter to gray matter connection to a set of equivalent connections generated by a random process. This method provides for every connection a confidence level (p-value). We note that the latter varies greatly from connection to connection, while some connections exhibit a strong confidence others can hardly be discriminated from noise. The factors and the reasons of this variability are discussed and we further propose a method to filter out the connections likely to be the result of noise. As a first test case, we apply this method to the connectivity of the human visual system.

Material and Methods

The MR diffusion images of a human brain are obtained on a healthy volunteer with an Achieva 3T Philips scanner, following a classical DSI scheme [1] using 257 different encoding gradients (acquisition time 18 minutes). We use a diffusion weighted single shot EPI sequence with $TR/TE/\Delta/\delta$ = 3000/100/47.6/35 ms and b-max = 12000 mm^2/s to acquire 32 slices of a 128 x 128 matrix with a spatial resolution of 2 x 2 x 3 mm^3. In every brain voxel, the obtained 3D diffusion pdf is converted into an orientation distribution function, which is reduced into a set of direction vectors corresponding to the local maxima of the diffusion pdf. Both white and gray matter (WM and GM) are identified using a T1w based segmentation algorithm. The interface between WM and GM is partitioned into small, compact and equally sized regions of interest (ROIs) using a partitioning heuristic. DSI tractography is performed in WM using an algorithm especially designed for DSI data [2]. Then, we create the graph of brain connectivity [3]. Every ROI becomes a node in the graph, and an edge is constructed between two nodes if there is at least one fiber whose end-points lie in the corresponding ROIs. The edge weight is defined as $w(e) = \sum_{f \in F_e} 1/l(f)$, with F_e the set of fibers contributing to the edge e and $l(f)$ the fiber length. Moreover, 30 random datasets are created by applying a random reshuffling of the pdfs inside the WM of the original brain creating that way a tractography space by all means equal to the original dataset but with random orientations. For each of these datasets, DSI tractography is performed and the corresponding graph of brain connectivity is constructed using the ROIs computed with the original brain. Finally, a p-value is attributed to each edge, resulting from a sign test comparing its weight to the corresponding edge weights obtained with the reshuffled brains.



Results

Fig. A shows the distribution of the connection distance, defined as the shortest path through white matter between the origin and destination point of each connection. Original and random connections are represented respectively in green and cyan, while red stands for the remaining connections after the suppression of those likely to be the result of noise with a p-value > 0.05. In Fig. B, a part of the visual system white matter connectivity has been mapped, top (1, 3) and zoomed posterior (2, 4) views. The left part correspond to the results obtained after filtering out connections presenting a low confidence level, while the right part represents the whole set of connections. We can see the well known areas left and right V1 (gray and blue), V2 (orange), V3 (cyan), V5 (red) and the thalamus (magenta) [4]. Three long range connections are plotted: the optic radiation linking the thalamus to V1 (blue), V1 homotopic callosal projections (yellow) and V2–V5 (green), as well as the short connections V1–V2 (red) and V2–V3 (white).

Discussion

The distribution of the connection distance (Fig. A) shows that there are more short tracts in the random dataset compared to the original brain dataset. On the other hand, the number of connections of a given distance decreases faster with increasing distance in the random dataset than in the original brain dataset. Actually, long range connections are almost inexistent in the random dataset. This phenomenon can be easily understood by the observation that in a random dataset the probability of finding a path of coherently aligned directions of maximal diffusion is small. Actually the longer the path is, the less likely is its realization by chance, and this probability decreases quickly with the path length. Therefore, among all the short connections generated by the tractography algorithm in the original brain dataset, many are likely to be the result of noise only, which makes it difficult to differentiate the "real" connections. The level of confidence we have computed for every connection helps us to distinguish between connections in which we strongly believe, typically long distance connections, and connections that we are not sure to be able to distinguish from noise, typically short connections. We can threshold the connectivity matrix with a given confidence level in order to study and represent only the reliable tracts. This method, applied on the human visual system (Fig. B), gives the expected result. Indeed, we see no difference between the filtered and original version for long range connections, such as thalamus–V1, V1 homotopic and V2–V5, while a large proportion of short fibers, such as V1–V2 or V2–V3, are suppressed.

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