Potential Importance of Secondary Connections in Tractography

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Introduction: Pioneering work by Behrens et al demonstrated the potential of high angular resolution diffusion imaging (HARDI) for segmenting brain structures based on their anatomical connectivity (1). The methodology uses a "winner-takes-all" approach in which classification does not distinguish between slight or large differences in connectivity. However, secondary connections may be important but are masked by the winner-takes-all approach. We demonstrate this point by examining connectivity of the internal capsule (IC), a potentially significant target for deep brain stimulation (DBS) treatment of refractory depression (2).

Methods: One rhesus macaque was scanned under a Cleveland Clinic ethics board-approved protocol on a 3 Tesla TIM Trio (Siemens Medical Systems, Erlangen, Germany) with a high spatial resolution, high angular resolution diffusion imaging (HARDI) scan (1.5 mm isotropic voxels, 71 non-collinear diffusion weighting gradients with b=1000s/mm^2, eight b=0). The IC of the macaque was segmented based on highest connectivity to one of three nuclei: caudate, lentiform nucleus (LN), and thalamus (1). The regions were specified by ROIs hand-drawn on fractional anisotropy maps. Probabilistic tractography was run from each voxel in the IC to the entire brain followed by statistical correction for distance-related bias (3). Track density in each nucleus associated with a given IC voxel was then used for classification.

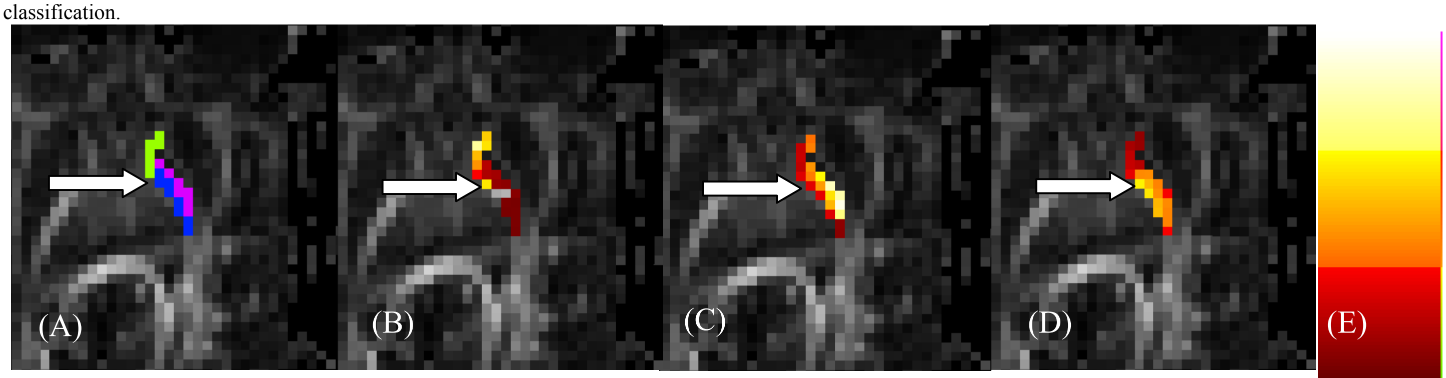

Figure 1: (A) segmentation of the internal capsule (IC) for an axial slice based on highest connectivity to caudate (green), lentiform nucleus (LN) (purple), and thalamus (blue). (B), (C), and (D) indicate connectivity to caudate, LN, and thalamus. Scale (E) runs from low (red) to high (white) track density in arbitrary but consistent units. The arrow indicates a voxel in which connectivity to caudate and thalamus is almost the same.

Results: Figure 1A shows a winner-takes-all segmentation of the IC. The arrow indicates a voxel classified as most connected to thalamus. However, the number of connections to caudate (B) and to thalamus (D) is nearly equal. Interestingly, this voxel has more connections to caudate than voxels in the IC classified as most connected to caudate by winner-takes-all. Therefore, secondary connections to this voxel are potentially important. Figure 2 gives a comprehensive summary of connectivity of all IC voxels classified as thalamus by the winner-takes-all approach. The arrow indicates the voxel discussed in figure 1. This voxel is not an anomaly as a number of other voxels are highly connected to caudate and LN.

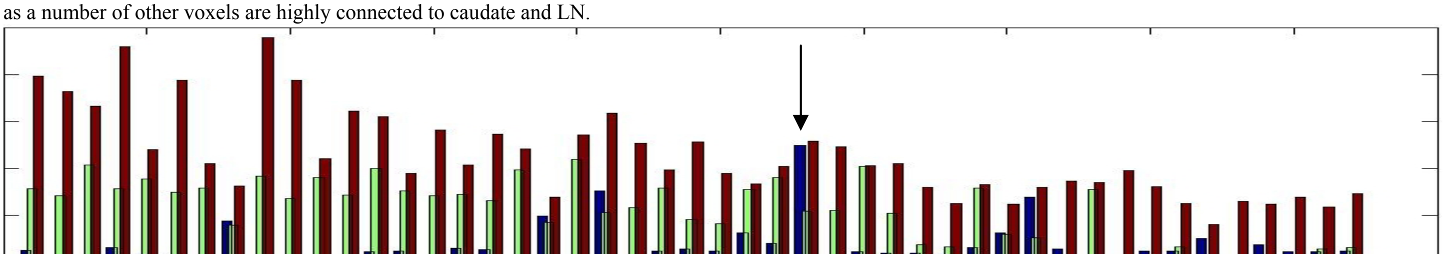

Figure 2: A bar graph of all the voxels classified as thalamus in the IC. Red corresponds to thalamus, blue to caudate, and green to LN. The arrow indicates the same voxel as that indicated by the arrow in figure 1.

Discussion: We have demonstrated that a more comprehensive approach may be necessary to perform segmentation by anatomical connectivity. The results agree with the fact that the spatial resolution of current HARDI acquisitions will inevitably lead to partial volume averaging between nearby regions with distinct connectivity. In a hypothetical scenario, optimal therapeutic benefit from DBS may result from targeting IC fibers most highly connected to caudate. The above example suggests that identification of regions of high therapeutic benefit may require an examination of secondary connections. Further work will examine methods for testing and visualizing the uncertainty of assignment in the segmentation methodology and their use in presurgical planning for DBS.

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References:

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