Cortical parcellation based on DTI connectivity--validation in the squirrel monkey brain

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INTRODUCTION

Diffusion MRI provides the potential to non-invasively parcellate the cortex into functionally distinct regions based on tractography-derived connectivity features [1-3]. However, the accuracy of the parcellation has not been established. This study validates DTI connectivity-based cortical parcellation by comparing the parcels to a histological gold-standard. The comparison reveals the potential and limitations of connectivity-based parcellation.

MATERIALS AND METHODS

Histological regions acquisition: A squirrel monkey brain was frozen and sectioned coronally at 50μm thickness using a microtome. The tissue blockface was photographed after every three sections to compose an intermediate space for registration from microscopy space to DTI space. Every sixth section was reacted for Nissl stain and photographed under a light microscope with 0.5X magnification. The borders of eighteen frontal and parietal cortical regions were identified based on architectonics of Nissl-stained neurons [4]. Each cortical region was then transformed to DTI space using deformation fields calculated via a modified multi-step registration procedure from light microscopy to DTI space [5,6]. More details can be found in previous study reports [7,8].

DTI parcellation: Before sectioning, the fixed monkey brain was scanned (PGSE multi-shot spinwarp imaging, TR=4.6s, TE=42ms, number of gradient directions=31, b≈1020s/mm^2, voxel size=0.3mm×0.3mm×0.3mm, data matrix=128×128×192) in 9.4Tesla scanner. FDT [9] was used to estimate fiber orientations and probabilistic tractography was seeded on each voxel at the white-gray matter (WGM) interface underneath the 18 cortical regions in DTI space. The cross correlation (CC) matrix was calculated, in which each element value is the correlation of the density maps of fibers originated from two seed points [1-3]. Three clustering algorithms were evaluated to partition the CC matrix: (1 "Grp") similarity to canonical tracts based on 18 histologically defined clusters, (2 "Kmn") naïve k-means, and (3 "Hrc") hierarchical clustering.

Comparison of DTI and histology: The histological regions and clusters are rendered on the WGM interface for visual comparison. To quantitatively assess the similarity between each cluster, C_i $(i = 1,2,\dots,n)$, and a histologically-defined region, R_j $(j = 1,2,\dots,m)$ in DTI space, three metrics were computed: *Dice* index (*i.e.*, $D_{i,j} = (C_i \cap R_j)/(C_i \cup R_j)$), *Hausdorff* distance (*i.e.*, $H_{i,j} = \max\left\{\sup_{c\in C_i}\inf_{r\in R_j} d(c,r), \sup_{r\in R_j}\inf_{c\in C_i} d(r,c)\right\}$) and surface distance (*i.e.*, $S_{i,j} = \text{mean}\left\{\text{mean}_{c\in C_i}\inf_{r\in R_j} d(c,r), \text{mean}_{r\in R_j}\inf_{c\in C_i} d(c,r)\right\}$). Then three global measures of similarity over all clusters, $\overline{D_{maxJ}}$ (*i.e.*, $\text{mean}_i\{\max_j D_{i,j}\}$), $\overline{H_{minJ}}$ (*i.e.*, $\text{mean}_i\{\min_j H_{i,j}\}$), and $\overline{S_{minJ}}$ (*i.e.*, $\text{mean}_i\{\min_j S_{i,j}\}$) were calculated to compare connectivity-based parcellation algorithms.

RESULTS

Fig.1 displays the histological regions, grouping result and DTI connectivity-based clusters rendered on the WGM interface of monkey brain. Table 1 shows the three metrics of global similarity between histological regions and connectivity-based clusters. Fig.2 illustrates the possible situation explaining the difference of patterns between histological and connectivity-based parcels.

(Abbreviation: PF-prefrontal cortex; PM-premotor cortex; M1-primary motor cortex; PA-anterior parietal cortex; PP-posterior parietal cortex; SMA-supplementary motor area; AC-anterior cingulate cortex; PV-parietal ventral and rostral areas; S2-secondary somatosensory cortex. Note that PV and S2 area are hidden in the dorsal view of Fig. 1)

CONCLUSION AND DISCUSSION

Compared with the 18 histological regions shown in Fig.1A, the clusters of k-means and hierarchical schemes in Fig.1CD roughly identified the boundary between PA and M1, AC and SMA, but gave an enlarged combination of PR and M1, followed by an eroded PF. SMA and AC were roughly separated although with some noise. Hierarchical clustering yields increased anterior-posterior (A-P) instead of medial-lateral oriented parcels as the number of clusters increases, as shown in Fig.1D-F. In these cases, DTI fiber density profiles originating from seed points distributed along the A-P direction are more similar than those of neighboring points in the medial-lateral direction. This might be due to the complex anatomy of crossing fibers (i.e., A-P fibers crossing medial-lateral fibers), which was not accurately detected by DTI tractography. Fig1B indicates that DTI connectivity profiles are consistent with true histological parcellation.

The results show that there is a reasonable parcellation of the connectivity data in which the fibers cluster in histologically defined areas. However, the intrinsic structure reveals finer parcellations in medial-lateral divisions. These may reflect somatotopic arrangements. Continuing studies are examining more individuals and cortical regions.

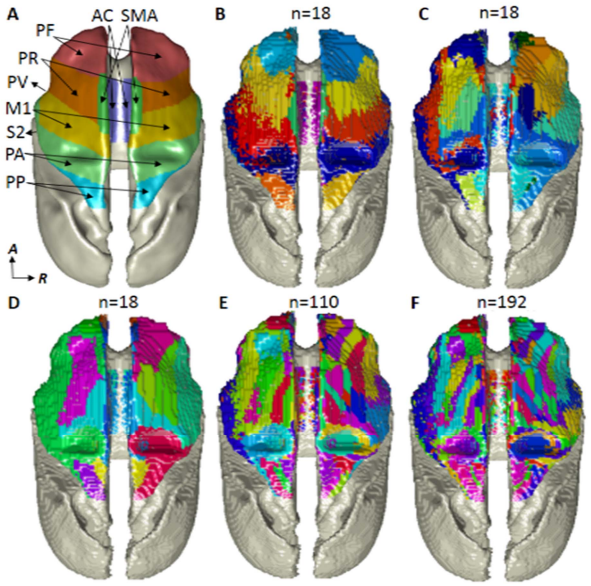

Fig.1. Dorsal view of histological regions (A), grouping result (B) and DTI connectivity-based clusters via k-means (C) and hierarchical (D-F) clustering methods rendered on the WGM interface of monkey brain (Silver color-WGM interface; other colors represent individual clusters of voxels).

Table 1. Three metrics of global similarity (*i.e.*, *Dice* index, *Hausdorff* distance in mm and surface distance in mm) between histological regions and grouping result, and connectivity-based parcels computed by clustering methods (*i.e.*, k-mean and hierar

	Grp n=18	Kmn n=18	Hrchy n=18
$\overline{D_{maxJ}}$	0.44	0.25	0.15
$\overline{H_{minJ}}$	8.0	8.0	7.1
$\overline{S_{minJ}}$	0.8	1.3	1.6

Fig.2. Example of fibers seeded on PR and M1 sharing the same pathways due to crossing, which may bias clusters toward A-P oriented parcels.

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