Validation of DTI measures of primary motor area cortical connectivity

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INTRODUCTION

By using fiber tracking techniques based on DTI, neural connectivity of specialized cortical regions can be examined noninvasively. However, accuracy of the result is not well validated. In this study, we reconstruct the 3D projection regions connected to primary motor cortex (M1) of squirrel monkey based on histological segmentation and quantitatively compare the location of fiber terminals derived from DTI tractography with the histological segmented projection regions.

MATERIALS AND METHODS

Data acquisition: We injected a bidirectional neural tracer (biotinylated dextran amine,BDA) at 8 sites covering the M1 region (left hemisphere) of squirrel monkeys. After sacrifice, we performed ex-vivo DTI imaging of the brain on a 9.4T (128×128×192) scanner using 32 gradient directions (b=1022ms/mm^2). The brain was sectioned in the coronal plane (50 micron thickness) and the block face was photographed after every third section. Every sixth section was reacted for BDA, producing 41 sections spanning a continuous part of brain.

Data process: We segmented the injection region and different projection regions on each BDA section by observing the location of neural cell bodies and terminals. To transfer these regions into MRI space, we applied an affine followed by thin-plate spline algorithm to co-register each BDA section with the corresponding block face slice in 2D and the adaptive bases algorithm[1] (ABA) to co-register the block face stack to the MRI stack in 3D. Finally, we performed FACT tractography[2][3] using the DTI data to find the locations of terminals of the DTI fibers penetrating the transformed injection region.

Data analysis: We define the coefficients A and A_i to evaluate the agreement of connectivity derived from DTI and histological segmentation: $A = N(T \in \sum S_i)/(N(T \in \sum S_i) + N(T \in \overline{\sum S_i}))$, $A_i = N(T \in S_i)/(N(T \in S_i) + N(T \in \overline{\sum S_i}))$, where T is a DTI fiber terminal, S_i is a segmented projection region, N is the number of DTI fiber terminals in a set, and the bar represents the complement of a set. To determine the influence of stop criteria in fiber tracking, we calculated the coefficient A for different stop criteria. The projection regions are the supplementary motor area (SMA), premotor cortex (PMc), putamen-caudate (Pu-Cd) and Claustrum (Cl).

RESULTS

Figure 1 displays the histological segmentation of injection and projection regions as well as DTI fiber terminals (pink points) in MRI space. Terminals distributed outside the projection regions indicate that DTI tractography may provide false positive connectivity to M1. Moreover, the projection regions without terminals (e.g.P_{Cl}) indicate false negative connectivity. Figure 2 shows quantitative comparisons of different projection regions. No DTI fibers terminate inside the segmented contralateral SMA, ipsilateral Pu-Cd and Cl, probably due to limitations of the FACT algorithm, especially incorrect tracking of crossing fibers and DTI image quality. Figure 3 describes the influence of stop criteria on connectivity agreement. A>0.5 along all the curves shows good agreement for the specified stop criteria. Also, 0.25 might be an optimized stop FA (SFA) for these five stop angles (SA), considering low false positive connectivity and high true positive connectivity.

CONCLUSION

The visualized and quantitative results show an approximate agreement of connectivity to M1 between histological segmentation and DTI tractography in this case. However, connectivities between M1 and different cortical projection regions are variable in agreement coefficients due to the limits of the tracking algorithm and DTI image quality. Moreover, it was found that the choice of stop criteria influences the agreement. Further efforts will include quantifying the histological projection density and comparing it with the distributed density of DTI fiber terminals. In addition, common probabilistic tracing methods will be evaluated by the same strategy.

REFERENCES

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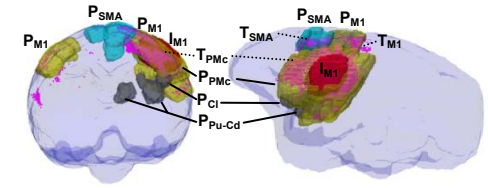

Fig.1: Visualized comparison of segmented projection regions with locations of DTI fiber terminals in MRI space (I-injection sites, P-projection region, T-DTI fiber terminals).

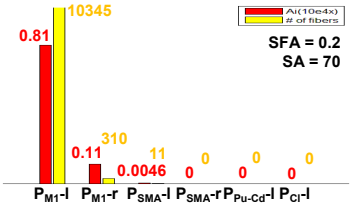

Fig.2:Agreement coefficient for different segmented projection regions and the number of DTI fiber terminals in the reference projection regions.

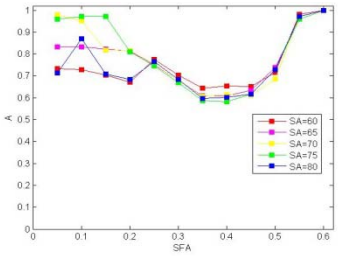

Fig.3: Agreement coefficients when using different stop criteria (SFA=0.05-0.6, SA= 60,65,70,75,80).