Comparison of Anatomical Connectivity Metrics

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Introduction: Tractography-based anatomical connectivity (tAC) can complement the information provided by resting state functional connectivity (rsFC) (1,2). However, the best way to define anatomical connectivity is unclear (3). We assess two metrics for tAC by comparison with rsFC in a multiple sclerosis (MS) model for disconnection: tract counts (tAC_{count}) and transverse diffusivity along a pathway (tAC_{TD}) (4). The results suggest that the latter may be a more appropriate metric for comparison with rsFC.

Methods: Eleven MS patients (seven female, age: 44.8 ± 9.5, MS functional composite (MSFC): 0.39 ± 0.53, Expanded disability status score (EDSS): 1.9 ± 1.5) participated in a Cleveland Clinic Institutional Review Board-approved protocol on a 3 tesla TIM Trio (Siemens Medical Systems, Erlangen, Germany). rsFC measures were taken between ROIs corresponding to left and right hand regions of motor cortex. ROIs were delineated by BOLD-fMRI activation from a complex finger tapping task. Probabilistic tractography was performed to map anatomical connections between the same ROIs. Details of the scans and the postprocessing pipeline are given in (1). tAC_{count} is defined as the fraction of tracks generated in the left ROI that connect to the right ROI. tAC_{TD} is defined as the mean transverse diffusivity along the white matter pathway defined by tractography. A threshold was placed to eliminate spurious contributions from TD in gray matter. High track counts are found in gray matter due to the lack of well-defined diffusion orientation and the weighted random walk nature of the tractography algorithm. A histogram of track densities with number of bins set to the square root of the number of track count values was generated, and voxels with track counts in the first bin of the histogram were excluded from the white matter pathway.

Results and Discussion: We find significant correlation between rsFC and tAC_{TD} (figure 1, R = -0.69, $p < 0.02$) but not between rsFC and tAC_{count} (figure 2, R = -0.19, $p > 0.5$). Myelination directly affects the efficiency of conduction of signals along axons and should therefore correlate with connectivity. As transverse diffusivity correlates with myelination (4), it serves as a viable alternative for measuring tractography-based anatomical connectivity. Note that multiple sclerosis patients with a wide range of disability scores were examined in order to provide a cohort of subjects with a range of connectivity values. The interpretations of the two tAC metrics are quite different. The count-based metric assesses how efficiently a given tractography algorithm draws curves between two regions, and such algorithms are highly sensitive to a number of algorithmic-dependent issues, including uncertainty in fiber orientation (5,6). The TD-based metric uses tractography to segment white matter into functionally specific pathways but then uses a physical measure as a surrogate for tissue integrity within that region. Although this study used MS patients to compare tAC measures, a previous report of the same tAC_{TD} measure in this pathway showed significant correlation to rsFC when combining age-matched healthy control subjects and patients(1), implying that the measure in healthy controls is statistically consistent with the finding in MS.

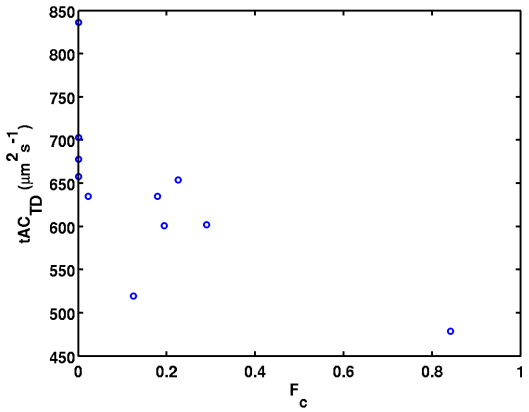

Figure 1: rsFC versus pathway TD

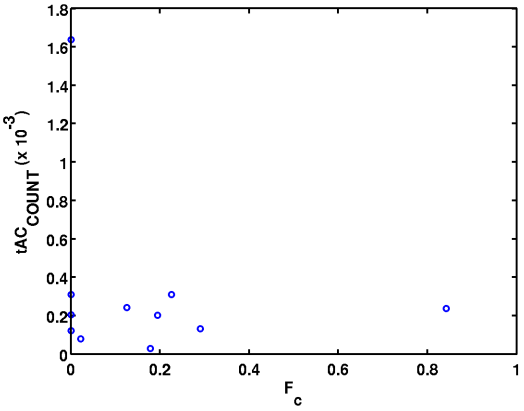

Figure 2: rsFC versus track count

Conclusion: White matter fiber pathway-specific measures of tissue integrity may provide a more robust metric for anatomical connectivity than more common track-counting measures.

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