

CORTICOSPINAL TRACT DISEASE AND SENSORY-MOTOR DISABILITY IN MULTIPLE SCLEROSIS

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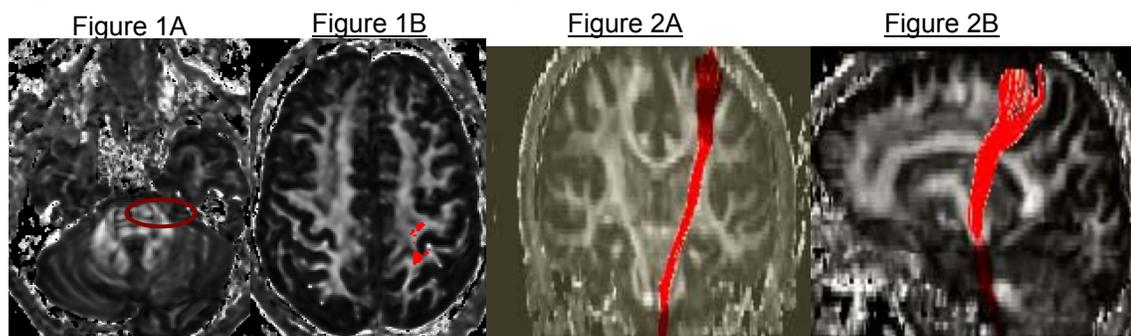
Introduction Diffusion tensor imaging (DTI) tractography is a unique tool for identifying the trajectory of white matter (WM) fibers and providing information about the integrity of specific tracts *in vivo*. By addressing specific WM tracts, DTI-tractography has the unique capability to study regional WM damage, its relationship with disease in other defined brain regions and its impact on disability related to specific neurological conditions. Among these conditions, is multiple sclerosis (MS). Although MS is a multi-focal and widely disseminated disease within the central nervous system, specific neurological impairments might arise from disproportional damage to particular tracts. We here exploited the dual capability of DTI in permitting: (1) topographically specific disease measures as well as (2) reliable quantification of disease outside visible lesions. We aimed at: (1) investigating the role of corticospinal tract (CST) specific disease in determining sensory-motor disability of MS patients; (2) assessing the relative role of focal and diffuse disease in the CST as possible source of sensory-motor disability of MS patients.

Methods Twenty-five patients with MS and 25 age- and sex-matched healthy volunteers (HVs) underwent a 3T MRI inclusive of DTI and evaluations of physical disability using the Expanded Disability Status Scale (EDSS) and the Timed 25-Foot Walk test (T25FW). MRI was performed on a 3T scanner (Signa Excite HDx, GE Healthcare, Milwaukee, WI) using an 8-channel head coil. The following sequences were acquired in the axial plane: i) FSE T2-w and SE T1-w with 54 contiguous slices of 2.4 mm thickness before and within 10 minutes of injection of a single dose of gadopentate dimeglumine (GD) (Magnevist, Berlex Labs, Cedar Knolls, NJ); ii) T1-w 3D Inversion Recovery Fast Spoiled Gradient Echo (IR-FSPGR) with 1.0 mm thickness; and iii) two DTI acquisitions using a single-shot, spin-echo echoplanar imaging (SS-SE-EPI) sequence with 54 contiguous slices of 2.4 mm thickness, TR / TE = 13000 ms / 76 ms, Matrix = 96 x 96 (reconstructed to 256 x 256), FOV = 240 x 240 mm², with ASSET acceleration factor of 2. The DTI acquisition consisted of 3 volumes with no diffusion gradients applied ($b = 0$) and 33 volumes with diffusion gradients applied in non-collinear directions, with $b = 1000$ s/mm². Differences between patients and HVs in BPF and age were assessed using an unpaired t-test with equal or unequal variance as appropriate. A linear mixed-effects model (LMM) assuming a compound symmetric covariance structure was used to investigate the difference between patients and HVs in CST-mean diffusivity (MD), fractional anisotropy (FA) and Eigenvalue-1 (E_{-1}). Spearman and partial correlation analyses using CST-T1-LV or WB-T1-LV as controlling variables were employed to assess the relations between DTI-derived metrics and the above measures of physical disability.

Results

Figure 1. Reference points

Figure 2. CST reconstruction



Higher MD ($p=0.004$) and E_{-1} ($p=0.043$) but similar FA were seen in patients compared to HVs. Spearman rank correlation analyses disclosed associations between mean FA and MD of the CSTs and EDSS ($p=0.011$, $r=0.500$), motor-EDSS ($p\leq 0.018$, $r\geq 0.469$) and T25WF ($p\leq 0.033$, $r\geq 0.428$) scores. When correcting for CST- and global lesion volume, only the association between CST-FA and EDSS ($p\leq 0.013$, $r\geq 0.546$) or motor-EDSS score ($p=0.032$, $r=0.468$) held true.

Discussion and Conclusion Our results provide some insight towards the understating of the complex interplay between focal lesions and diffuse neurodegeneration as source of disability in MS, while the confounding effect of the spatially disseminated disease distribution is taken into account. 3T tractography allowed quantification of regional changes in CST in patients with MS and showed that the impact of diffuse disease of the CST in the sensory-motor disability is greatly mediated by the regional (i.e., CST) lesion load.

Acknowledgement

This work was supported in part by the Intramural Research Program of the NINDS, NIH.