Quantifying the effects of lesions with the Tractography-based Lesion Assessment Standard (TractLAS)

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Target audience: Clinicians, stroke assessment and rehabilitation, diffusion imaging methods

Purpose: *Create a structural network-based standard model for quantifying the impact of lesions on the brain and behaviour.* In the clinical setting, structural brain lesions are visually assessed to classify their type, extent, and general location [1]. Lesion segmentation approaches can also be used to quantify location, volume, and extent as a first step towards investigating the impact of lesions on behaviour and functional outcomes [2]. While this approach has a number of benefits, it is not able to assess how lesions may impact the structural connections *between* regions (i.e., quantify the amount of structural disconnection). A network-based perspective could provide a more complete characterisation of the structural impact of lesions that can be used to better understand functional deficits and recovery trajectories [3]. However, fibre tractography through lesions is problematic and may result in metrics that are difficult or impossible to compare across individuals. To address these issues, we created a diffusion tractography atlas (TractLAS) that can be used to quantify the impact of lesions on brain connectivity.

Methods: We collected 1.5mm isotropic whole-brain diffusion imaging datasets from 13 healthy controls on a Siemens 3T scanner (60 directions, b=1000). Data was upsampled to 1mm and FA calculated and co-registration to create a template in MNI space. Transforms were applied to the diffusion data, b-vectors, and native T1w images to bring them into common space. Co-registered diffusion images from all individuals were concatenated and the fODF derived with MRtrix. A single-voxel WM/GM boundary mask was generated from the mean T1w image. The TractLAS was created by seeding/terminating in the boundary voxels with 50 million streamlines. GM atlases were then used to segment the GM/WM boundary voxels to create region-based connectivity matrices and facilitate comparison with functional data and measures of clinical outcome. To quantify the variability across subjects, we also performed tractography in individual space and warped the streamlines of all subjects into the standard space.

Results: We created a tractography standard consisting of probabilistic streamlines and co-registered FA and T1w images. Super-resolution tract-density images were generated to confirm that the fine details of white-matter trajectories are readily identifiable in our standard (Fig. 1A). To assess the impact of lesions in individuals, lesion masks were transformed into template space and the TractLAS was used to generate disconnection matrices for comparison with the unaffected matrix (Fig 1B). The individual disconnection network can be related to measures of clinical behaviour, brain function, and disease progression/recovery.

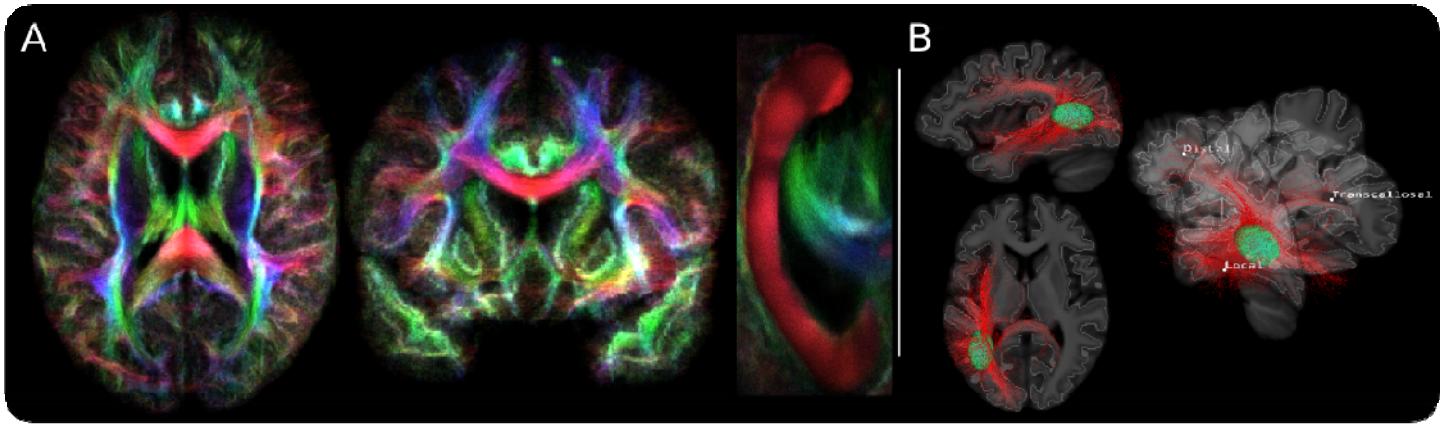

Figure 1. A: Tract-density images from the TractLAS. A single-voxel mask at the GM/WM boundary served as the seed and target mask. Top: 0.5mm (axial, coronal) and .1mm (saggital CC) colour-coded TDI - descending cortical spinal tract fibres are notably absent because they are not included in the GM mask. B: Depiction of streamlines disrupted by a simulated lesion spanning GM and WM in posterior temporal lobe. Streamlines (red; 1 in 1000 shown) disrupted by the lesion (green) are overlayed on the T1w template and tractography seed mask.

Discussion and Conclusion: We have created a standard model of structural connectivity that can be used to both assess and monitor the individual effects of lesions during disease progression and rehabilitation. Our model allows clinicians and researchers to generate individual structural disconnection maps which can be used to quickly identify affected white-matter tracts and connected regions. This network-based approach will help researchers and clinicians understand the complex functional effects of focal brain lesions.

References:

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