

Megatrack: A fast and effective strategy for group comparison and supervised analysis of large-scale tractography datasets

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Purpose: Diffusion tractography is unique imaging technique that allows the reconstruction and analysis of white matter connections from living human brains. While manual “dissections” performed by expert users may offer the best results in terms of anatomical accuracy [1], they are also extremely time consuming making difficult to extend this approach to large-scale datasets. On the contrary, automatic dissections or clustering approaches allow researchers to efficiently dissect a large number of datasets but at the expense of a decreased accuracy in the final dissection, leaving often little to no user interaction to control for artifactual components [2,3]. In this study we propose a novel supervised approach that drastically reduces the time required for manual dissections while preserving at the same time the ability to extract automatically tract specific measurements from large datasets. This approach, named Megatrack, generates a single “mega” tractography dataset by combining together and remapping in the same anatomical standard space streamlines from all subjects. In this way the user can accurately dissect all subjects simultaneously using the same anatomical references while still correcting for any potential spurious tract. By associating a unique streamline and subject ID code to each megatrack streamline, native space tracts can be directly recovered for each subject and tract-specific measurements automatically extracted. The proposed approach is applied here on two distinct datasets. First, one dataset of healthy adult subjects is used to assess the ability to recover realistic tract specific measurements. A second dataset from a motor neurone disease (MND) study is then used to compare the performances of the proposed method in detecting group differences against manual and automatic dissections.

Methods: In-vivo data. A normal adult dataset (20 healthy male subjects, age 28.6±5.6) and a MND dataset (49 subjects, age 51.7±10.5, 24 controls and 25 limb-onset MND patients, age and gender matched) were acquired using a 3T GE HDx MRI scanner (General Electric, Milwaukee, WI, USA) with the following parameters: voxel size 2.4x2.4x2.4 mm, 128x128 matrix, 60 slices, TE 104.5 ms, b-value 1300 s/mm², 32 DW-directions, 4 non-DW volumes using a spin-echo EPI sequence and peripheral gating with equivalent TR of 20 RR intervals.

Pre-Processing: Datasets were pre-processed for motion and eddy current distortion correction using ExploreDTI. To assess different tractography approaches, whole brain diffusion tensor tractography as described in [4] was applied on the normal adult dataset to dissect the long segment of Arcuate Fasciculus (AF). Spherical deconvolution tractography as described in [5] was applied instead on the MND dataset to dissect the left and right cortico-spinal tract (CST). For both datasets tracts were first manually dissected individually for each subject and tract specific measurements extracted (i.e. tract volume, FA, MD, Axial and Radial diffusivity). Multiple regions of interest were used to dissect each tract and exclude spurious components.

Megatrack processing. Affine and non-linear transformations from the diffusion space of each subject to the MNI space were calculated using flirt and fnirt from the FSL software package. Each tractography dataset was then remapped to MNI by applying the corresponding transformations to each streamline point (Figure 1). To maintain a manageable number of streamlines, while concatenating all datasets in the Megatrack dataset, a pre-filter ROI was applied to include only streamlines belonging to the brain region of the tract of interest. A unique ID for streamline and subject number was also assigned to each streamline at this step. Megatrack datasets were then dissected using standard manual dissection procedures. From the final dissected tract, each streamline and subject ID was extracted and used to automatically recover individual tracts in native space for each subject and extract from them tract-specific measures. With the exception of the manual dissection, all Megatrack processing was entirely scripted with no interaction from the user.

Automatic dissections were performed using template-based ROIs registered to each subjects. To dissect the CST, the pre-central gyrus and the anterior portion of the midbrain were used as inclusion ROIs while excluding surrounding cortical gyri, commissural and cerebellar tracts.

Results: Figure 2A shows, as example, the final Megatrack dissection for the left long segment of the Arcuate fasciculus from the normal adults dataset. Fig 2B shows the left CST from 49 subjects of the MND dataset. For both datasets, each Megatrack dissection required between 20 to 40 minutes. In comparison more days were required to dissect all subjects individually.

Table 1 shows mean and standard deviation of the tract measurements for the Arcuate fasciculus. Between Megatrack and the Manual approach, results are very similar on both left and right Arcuate and no significant differences were found.

Table 2 shows results for the MND dataset. As reported by previous neuroimaging and neuropathological investigations [6], in MND patients, the CST is known to show significant changes in its microstructural organization and in diffusion indices like FA and radial diffusivity. In this study, Manual, Megatrack and Automatic methods were all able to detect highly significant differences between patients and controls in these indices. However, by comparing the p-values or equivalently the observed power ($\alpha=0.01$) it is possible to observe also that while Megatrack shows similar results to Manual dissections, the Automatic approach seems slightly less sensitive to group differences probably due to less accurate dissections. More rigorous statistical analyses are required to confirm this point, however.

Discussion and Conclusions: By combining all streamlines from multiple subjects into a single dataset normalized to standard space it is possible to accurately dissect a large number of subjects in a very short period of time. Tract specific measurements obtained with the proposed method showed that results are comparable to manual dissections both as absolute values and as ability to detect group differences. In conclusion, we think that the proposed approach can be effectively used as a new and complementary approach for group comparison and analysis of large-scale tractography datasets.

References: [1] Aarnink et al., NeuroImage 86:404–416 (2014), [2] Lebel et al., NeuroImage 40:1044–1055 (2008), [3] Guevara et al., NeuroImage 61:1083–1099 (2012), [4] Basser et al., MRM 44:625–632 (2000), [5] Dell'Acqua et al., Hum Brain Mapp 34(10):2464–2483 (2013), [6] Tsermentseli et al., Cortex 48:166–182 (2012).

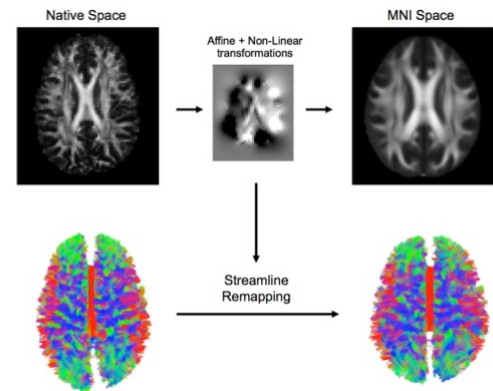


Figure 1

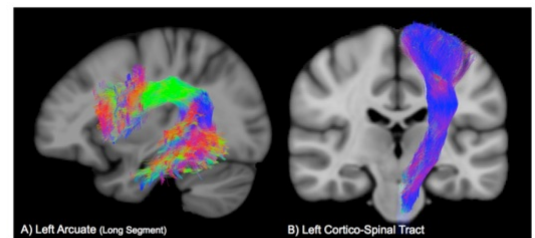


Figure 2

Arcuate fascicle – Long Segment (20 healthy subjects)

		Volume [ml]	FA	MD [$\times 10^{-3}$ mm ² /s]	Axial Diff. [$\times 10^{-3}$ mm ² /s]	Radial Diff. [$\times 10^{-3}$ mm ² /s]
Left	Manual	14.89 ± 3.92	0.50 ± 0.02	0.76 ± 0.02	1.21 ± 0.02	0.53 ± 0.02
	MegaTrack	14.72 ± 3.86	0.49 ± 0.02	0.76 ± 0.02	1.20 ± 0.02	0.53 ± 0.02
Right	Manual	7.68 ± 4.73	0.50 ± 0.02	0.75 ± 0.02	1.21 ± 0.04	0.52 ± 0.02
	MegaTrack	6.97 ± 4.22	0.49 ± 0.01	0.75 ± 0.02	1.20 ± 0.03	0.53 ± 0.02

Table 1

Cortico-Spinal Tract (MND dataset)

		Manual			MegaTrack			Automatic		
		F	p-value	obs. Power	F	p-value	obs. Power	F	p-value	obs. Power
Left	FA	16.27	0.0002	0.90	14.67	0.0004	0.87	9.05	0.0043	0.63
	Radial Diff.	15.15	0.0003	0.88	16.35	0.0002	0.91	10.34	0.0024	0.70
Right	FA	15.04	0.0003	0.88	15.68	0.0003	0.89	12.77	0.0009	0.81
	Radial Diff.	50.57	0.0000	1.00	10.84	0.0019	0.72	10.86	0.0019	0.72

Table 2