Group analysis of tractography images using early registration in primary dystonia patients

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Introduction
Primary torsion dystonia (PTD) is a chronic movement disorder manifesting clinically as focal or generalized sustained muscle contractions, postures, and/or involuntary movements [1]. The most common inherited form of PTD is associated with the DYT1 mutation [2]. PTD is thought to be a neurodevelopmental disorder affecting motor circuits (particularly striato-thalamic and cerebellar pathways), but the details are not yet worked out. Diffusion tensor imaging (DTI) has exquisite ability to visualize the white matter pathways and may be useful in understanding the underlying pathology in this disease. Prior studies using DTI have shown reduced fractional anisotropy (FA) in the subgyral white matter and in the vicinity of the superior cerebellar peduncle in DYT1 carriers [3]. Group analysis of the white matter tracts has been elusive to date due to the difficulty to register diffusion tractography maps from different subjects to a particular template. To overcome this problem we employed an early registration technique [4] where diffusion weighted images (DWI) are registered to a template before any processing.

Subjects and Methods
7 manifesting DYT1 mutation carriers, 4 non-manifesting DYT1 mutation carriers, and 7 age-matched normal control subjects were imaged in a 3 T clinical scanner. We acquired 72 slices of 1.8 mm thickness with FOV of 230 mm and data acquisition matrix of 128x128 which was zero-filled to an image matrix of 256x256. The apparent resolution of the diffusion weighted images was 0.9mmx0.9mmx1.8mm. TE was 68.3 ms and TR was 7000ms. In addition to a b=0 image, diffusion was measured in 55 directions with a b-value of 1000 s/mm². After data acquisition, diffusion weighted images were transferred to a workstation. All DWI had been registered to a template using FLIRT FSL [5]. The corresponding voxels from all the subjects in the group were used in the diffusion tensor calculation. The effect of rotation in the registration process were considered during the tensor calculation. Using the seed regions obtained from the previous DTI study [3], namely superior cerebellar peduncle, group tracts were computed.

Results
Figure 1 below shows a 3D plot of the tracts originating in the cerebellum involved in the disease process. To our knowledge this is the first time that part of a motor pathway involved in dystonia has been directly visualized. In DYT1 mutation carriers we could detect fewer fibers in the cerebello-thalamo-cortical pathways regardless of the diffusion anisotropy thresholds we used.

Discussion
The group analysis of diffusion tensor tractography maps determined parts of the motor pathways involved in a group of dystonia patients with DYT1 genotype. There is an increasing amount of evidence suggest the involvement of cerebellum in this disease. The disruption of outgoing pathways could lead to cortical hyperactivation, which is characteristic to dystonia.

Conclusions
Group analysis of diffusion tractography results are possible using early registration of diffusion weighted images. This analysis visualized group level white matter tract differences between dystonia patients and normals. This analysis can be useful in understanding the pathophysiology of primary dystonia.

References:
5) http://www.fmrib.ox.ac.uk/fsl