Application of probabilistic fiber tracking for the quantitative assessment of the connectivity pattern between basal ganglia and frontal cortex in children with Tourette Syndrome

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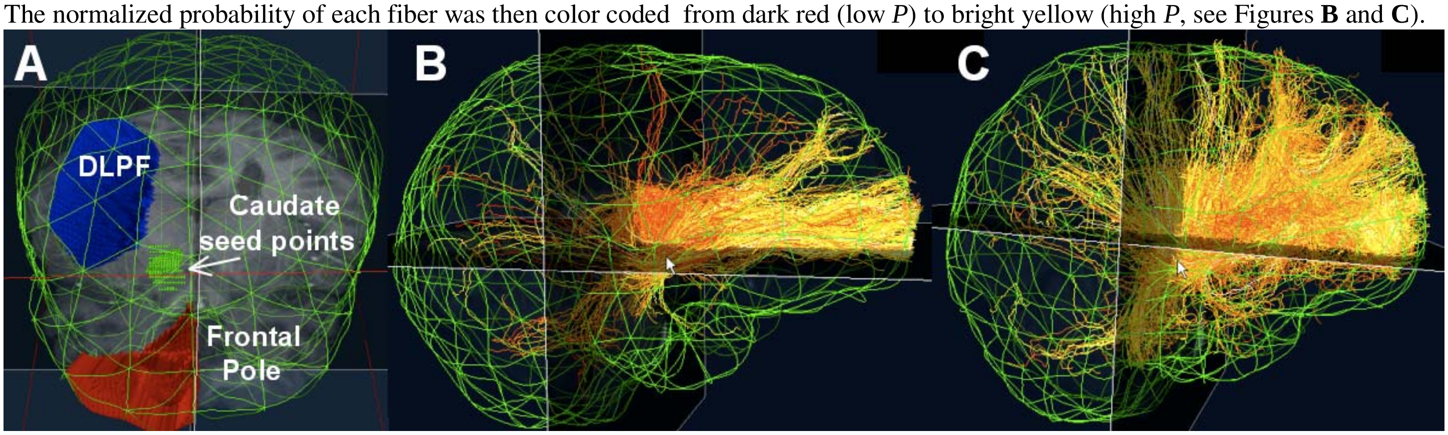
Introduction: In order to quantitatively assess fiber tract connectivity patterns in the developing brain, we have developed an integrative software environment based on conformal mapping of the cortical surface and probabilistic fiber tracking. We applied this computational framework in children with Tourette Syndrome (TS) and pediatric controls to obtain a more detailed understanding of aberrant white matter connectivity patterns in this patient group.

Methods: We studied a group of children with TS (N_1 = 6, 3M, 12.1 ± 3.3 yrs)) and a control group (N_2 = 6, 2M, 15.8 ± 1.7 yrs). All MR studies were performed using a GE 3T Signa unit and included a T1-weighted SPGR sequence as well as a diffusion-weighted dual spin-echo single shot echo-planar MR sequence with 6000/110/6 (TR/TE/NEX), 256x256 matrix, FOV of 240mm, 40 planes with a slice thickness of 3mm covering the whole brain. The DTI sequence consisted of an image volume with no diffusion weighting (B_0, b=0 s/mm^2) followed by the acquisition of image volumes in 6 gradient directions with a b-value of 1000s/mm^2. Regions of Interest (ROIs) encompassing the head of caudate were defined in high resolution T1-weighted images in both groups and these ROIs were then transferred into DTI space using a transformation matrix obtained through coregistration of T1 and B_0 image volumes. All data sampling and analysis was subsequently performed in the subject's native DTI space. Probabilistic fiber tracking was performed using a Bayesian framework (Friman et al., 2006) in which the local probability density function (PDF) in each voxel is based on the angular distribution of the primary eigenvectors in all 18-connect neighboring voxels. This PDF is then multiplied with a prior distribution giving preference for continuation in the previous-step direction (zero probability for turns > 90 degrees). The so obtained posterior distribution is then evaluated at 2562 predefined unit length vectors obtained by a fourfold tessalation of an icosahedron. Starting from a seed point, random samples were drawn from the posterior distribution creating fiber paths which were terminated when the local FA < 0.15. It has to be noted that this model assumes only one fiber direction in each voxel and any deviation from this model (such as fiber crossing/convergence) is translated into uncertainty in the posterior distribution leading to an increased probability of randomly sampled fibers to diverge into multiple directions. Cortical target regions for fiber tracking were created using a previously developed landmark-constrained conformal mapping algorithm (Zou et al., 2006) which allows a unique and accurate transformation of each subject's brain surface to a canonical spherical domain where finite elements are defined geometrically on the sphere. These finite elements are reversely mapped into native space and extended inside the brain, resulting in homotopic finite cortical volume elements across all subjects. For each seed pointing the caudate, 100 paths were created yielding a minimum of 15,000 paths originating from the source region. To quantify connectivity strength between the source (head of caudate) and target regions (frontal pole and dorsolateral prefrontal cortex (DLPF); Figure **A**), we calculated for each individual fiber path of length N the average probability along a fiber i as $p_i = (\Pi_N\ p_{ij})^{1/N}$ where p_{ij} is the randomly sampled probability of voxel j (j = 1,..N). Path probabilities p_i were then normalized to the sampling space (total number of fiber paths n) as $p_i' = p_i/\Sigma p_n$ and the probability of connection between two regions (*P*) was calculated as (Σ_k pi') with index k (k < n) representing all paths connecting the two regions. The normalized probability of each fiber was then color coded from dark red (low *P*) to bright yellow (high *P*, see Figures **B** and **C**).



Results: Fiber tract pattern in normal children showed a strong connection bilaterally between the head of caudate and the frontal pole (Figure **B**). In contrast, fiber tracts originating from the head of caudate in children with TS showed bilaterally a more diffuse projection pattern (Figure **C**). Quantitative analysis indicated similar connectivity strength of caudate/frontal pole fiber tracts in the TS (*P* = 0.27 ± 0.13) and control groups (*P* = 0.31 ± 0.14), however the connectivity strength of the caudate/DLPF fiber tracts was significantly increased in the TS group (*P* = 0.053 ± 0.04) as compared to the control group (*P* = 0.0087 ± 0.004, p = 0.024).

Conclusion: The presented method allows the quantitative evaluation of the connectivity strength between subcortical and cortical regions as well as the assessment of their connectivity patterns. Our findings suggest an abnormal connectivity pattern between the caudate and frontal lobe regions in children with TS as compared to control children.

References: Zou et al. IEEE Intern Conf Image Process, 2006: 1193 - 1198; Friman et al. IEEE Trans Med Imag 2006, 25: 965-978