Correlation of Quantitative Sensori-Motor Tractography with Clinical Grade of Cerebral Palsy

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Introduction: Cerebral palsy (CP) is the term used to describe a group of developmental disorders of movement and posture causing activity limitation or disability. During brain maturation, pyramidal tract and the somatosensory radiation are susceptible to injury leading to neurological deficits, often resulting in the classic clinical presentation of spastic diplegia/quadriplegia in children born preterm [1]. Neuroimaging studies using conventional magnetic resonance imaging (MRI) have shown that 70 to 90 % of affected children have structural brain abnormalities [2]. Serial DTI has been used to study the plasticity of the CST in spastic quadriparesis [3]. In most studies, DTI quantitative metrics have been obtained using region of interest (ROI) analysis. ROI based morphometric DTI analysis is limited to 2dimensions (D) and does not reflect the whole fiber bundle. The information about the direction of diffusion encoded by the eigenvalues and eigenvectors of the diffusion tensor has been used in DTI tractography to investigate the continuity of axonal orientation between voxels and thus to infer the paths of fiber tracts in 3D. In the present study, we analyzed fractional anisotropy (FA) and mean diffusivity (MD) values in sensory and motor tracts in children with spastic quadriparesis and age/sex matched controls. Our primary hypothesis was that both sensory and motor WM injury would correlate with clinical grade as defined using the Gross Motor Function Classification System (GMFCS).

Materials and Methods: The institutional research ethics committee approved the study. We examined 39 children (30 boys and 9 girls) CP who had spastic quadriparesis (mean age of 9 years) and 14 age and sex-matched controls. All of the children participated in this study were born at term (>37 weeks gestational age) and had no history of seizures. The diagnosis of CP was based on clinical observations. The major signs that collectively lead to the diagnosis of CP were: delayed motor milestones, abnormal neurologic examination, persistence of primitive reflexes, and abnormal postural reactions. All patients were assessed by standard clinical examination, video gait examination, GMFCS scale [4] and modified Ashworth scales (to measure spasticity). Patients were graded according to GMFCS scale. Out of 39 children, twelve children had CP with grade II, 22 children had grade IV CP, and remaining 5 children had grade V CP.

Whole brain conventional MRI (T2, T1 and FLAIR) and DTI were performed on a 1.5-Tesla GE MRI system. All imaging was performed in the axial plane and had identical geometrical parameters: field of view (FOV) = 240 × 240 mm², slice thickness = 3 mm, interslice gap = 0 and number of slices = 36.DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling. The diffusion tensor encoding used was a dodecahedral scheme with 10 uniformly distributed directions. Fiber assignment by continuous tracking (FACT) algorithm was used for reconstruction of fibers. The white matter fiber tracts were generated as described in detail elsewhere (5). The central sulcus was identified and marked on sagittal surface image reconstructed by 3D surface rendering of b0 image stack. By using 3D cross connectivity between three planes central sulcus was displayed on axial images. Free hand ROIs were drawn on axial T2-weighted image near the brain's vertex on the precentral and postcentral gyri, and the fibers generated from those ROIs were defined as motor and somatosensory tracts, respectively (Fig.1).

Statistical analysis: Bivariate analysis of correlation was performed to study the relationship between the sensory and motor tract specific DTI measures and clinical grade of CP with the assumption that there was no correlation between DTI measures and clinical grade (Ho=0). Alternatively, if a correlation of <0.001 is observed at α=0.05 and 90% power of the test, the null hypothesis was rejected. One-way analysis of variance (ANOVA) with multiple comparisons using Bonferroni, Post Hoc test was performed to evaluate the differences in tract specific DTI metrics among age/sex matched controls and patient groups in sensory and motor tracts. P values of ≤ 0.05 were considered to be significant.

Results: Significant inverse correlation between clinical grade and FA values was observed in both right* and left** motor (*r=-0.497, p=0.001; **r=-0.504, p=0.001) and sensory (*r=-0.621, p<0.001; **r=-0.693, p<0.001) tracts. Significant direct correlation between clinical grade and MD was observed only in left motor (r=0.368, p=0.032) tracts. When we pooled MD values from right and left hemisphere, significant direct correlation was observed between MD and clinical grade in both motor (r=0.342, p=0.004) and sensory (r=0.278, p=0.023) tracts.

Successive decrease in FA values was observed in right motor and right as well as left sensory tracts moving from controls to grade V through grade II and IV (Fig. 2). Though, no successive change in MD values in motor as well as sensory tracts was observed moving from controls to grade V through grade II and IV (Fig. 4), all the patient groups showed increased MD values compared to controls in both motor and sensory tracts.
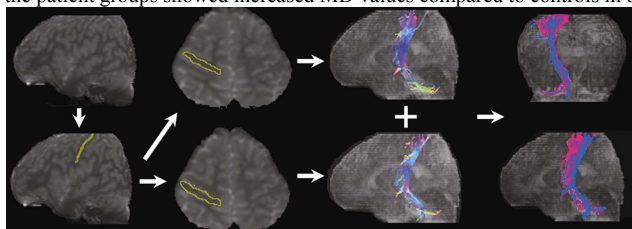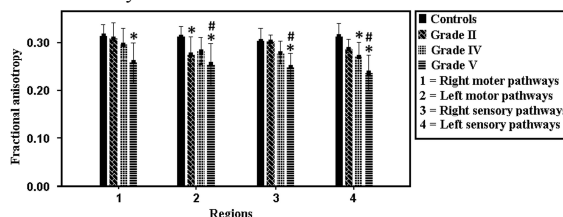

Fig. 1

Fig. 2

Fig.1: Demonstration of methodology used for motor (red) and sensory (blue) tracts reconstruction from 7-years-old control.
Fig.2: Bar graph shows differences of FA values in the motor and sensory pathways in control and patient groups. *Denotes the significance difference in patient groups compared to controls. # Denotes the significant difference between patient groups.

Discussion: This study demonstrates the correlation between clinical grades and DTI measures in motor and sensory pathways in children with CP. In this study 11 (28%) patients showed normal imaging even though they shared similar clinical profile with children who were abnormal on conventional imaging. This data suggests that conventional MRI is inadequate for the assessment of clinical grade. Significant inverse correlation of FA with clinical grades suggests that FA is a better measure than conventional MRI for the assessment of clinical grade in these patients.

Correlation of FA with clinical grade was much stronger in sensory tracts than motor tracts, which suggest that sensory tracts are probably more damaged in these patients and may play a role in the pathophysiology of motor disability in patients with CP. Instead of using an indirect approach to quantify sensory tracts i.e. thalamic radiation, in this study we quantified DTI measure of sensory tracts generated from primary somatosensory cortex. In contrast to Hoon et al.[6] we performed quantitative DTT analysis of whole sensory and motor tracts in these patients. In this study we extend our understanding of the pathophysiology of CP in children with spastic quadriparesis by showing that DTI measures in both motor and sensory pathways reflects the degree of motor deficits.

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