Quantitative Entire Brain Diffusion Tensor Imaging of Spina Bifida Meningomyelocele Children at 3.0T: Preliminary Evidence of Neurodevelopmental Brain Plasticity

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Introduction: Spina Bifida Meningomyelocele (SBM) is a common congenital neurodevelopmental disorder with a rate of 0.5-1 per 1000 live births **[1]**. SBM is caused by incomplete neural tube closure during the first 5-6 weeks of gestation and results in abnormal function and maturation of the spinal cord and brain **[1]**. SBM results in abnormal formation of the cerebellum (Chiari II malformation), posterior cortex, white matter, midbrain, and corpus callosum (CC). Hydrocephalus is common. Most of the sparse MRI-based literature on SBM brains highlights the role of volumetric assessment in characterizing the condition. There is little contribution of quantitative approaches that provide region-specific information about the neuronal plasticity that is known in the SBM brain. In this report, we present the first DTI evidence of brain plasticity in SBM. In this preliminary report, we have used an optimally designed entire brain DT-MRI protocol at 3.0 T in combination with conventional MRI sequences to document regional differences between healthy pediatric controls and children with SBM.

Methods: Subjects: 10 SBM children (9-20 years) and 19 (7-16 years) healthy pediatric controls were included in these studies. Parental consent was obtained to conduct the imaging and the psychometric evaluations. The sample included 6 girls and 4 boys of mixed ethnicity with an IQ range of 57- 97.

Conventional and DT MRI Acquisition: We acquired entire brain data using a Philips 3.0 T Intera system using a SENSE receive head coil. The MRI protocol included conventional MRI (spoiled 3d and FSE), phase sensitive MRI, in addition to a matching prescription of diffusion tensor MRI data. The DT-MRI data were acquired using a single-shot spin echo diffusion sensitized EPI sequence with the balanced Icosa21 encoding scheme **[2],** b=1000 smm^{-2}, TR=6.1 s, TE= 84 ms. To reduce EPI related image artifacts, we used a SENSE acceleration factor R=2. The slice thickness is 3mm with 44 axial slices covering the entire brain; fov=24 cm, and an image matrix of 256x256. The number of b~0 magnitude image averages was 8; in addition each encoding was repeated twice and magnitude averaged to enhance the signal-to-noise ratio. The total DTI acquisition time was approximately 7 minutes and resulted in SNR-independent DTI-metric estimation (SNR0~60, SNR (DW) ~ 20) and reproducible results.

Data Processing and Analysis: Diffusion weighted data were distortion corrected using the mutual information maximization approach **[3]**, compact fiber tracking was conducted as described elsewhere **[4]**; the details of the DTI processing are provided in **[5]**. The regions-of-interest represented 30 "normally appearing" white and gray matter structures that included contralateral caudate, putamen, internal capsule, corticospinal tract, and forceps minor. The procedure was done by trained raters and used anatomical landmarks from the conventional MRI sets (sagittal phase-sensitive inversion recovery). The ROI placement procedure was supervised by a radiologist and used a sophisticated system that fused DTI maps with conventional MRI. Statistical group comparisons were made using the t-test for unpaired groups (ANOVA). The transverse diffusivity was defined as the mean of the minor and medium eigenvalues. The transverse diffusivity was defined as the mean of the minor (third) and medium (second) eigenvalues ($(\lambda_t = (\lambda_2 + \lambda_3)/2)$ **[6].**

Results and Discussion: **Figure 1** illustrates representative DTI and phase sensitive sagittal MRI samples from three SBM children **(a, b, c)** compared to a healthy pediatric control **(d)**. Notice that the three groups of SBM can be classified based on the appearance of the CC. The first group **(a)** has dysgenesis of the CC and abnormal posterior temporal and parietal sectors of the brain. In this group the genu and frontal lobe connections are clearly depicted. The second group (**b**) has a hypoplastic CC, and the third group **(c)** has intact CC. **Figure 2** shows a representative sample of quantitative ROI group comparisons using the tensor fractional anisotropy (FA) metric in the right and left frontal minor forceps. Notice that the anisotropy is increased in the deep basal ganglia caudate nucleus head. A further analysis shows that the transverse diffusivities (λ_t) were reduced, indicating possible increase in myelination **[6]** in this structure that is involved in cognitive function and refinement of movement. **Figure 3a** shows the transverse group comparison for other structures (projection fibers cortico-spinal) that offer restriction to transverse diffusion such as the posterior limb of the internal capsule). In other structures (**Figure 3b**) that involve long association fibers, the trend is that of an increase in transverse diffusivity.

Discussion and Conclusion: This is the first non invasive report to document patterns of brain fiber connectivity and plasticity in children with SBM compared to healthy controls using fiber tracking and quantitative DTI metrics. We have demonstrated the utility of the DTI metrics, such as FA and the more specific transverse diffusivity to unravel subtle microstructural changes that are not otherwise directly observable by global MRI volumetry. Based on the transverse diffusivity analysis on animal models of dysmyelination **[6,7]**, an increase in FA and decrease in transverse diffusivity may be attributed to increased myelination as a compensatory mechanism in SBM. The increase in transverse diffusivity along association pathways may be attributed to reduced or impaired myelination along these long fibers. An increase in anisotropy in deep gray matter structures may be attributed to increased levels of myelination or more coherent dendrite proliferation that would enhance conduction. These findings are consistent with MRI volumetric studies of SBM showing normal volumes of gray and white matter in areas anterior to the genu of the corpus callosum **[8]** and are consistent with recent reports of preservation of procedural motor learning in SBM **[9]**.

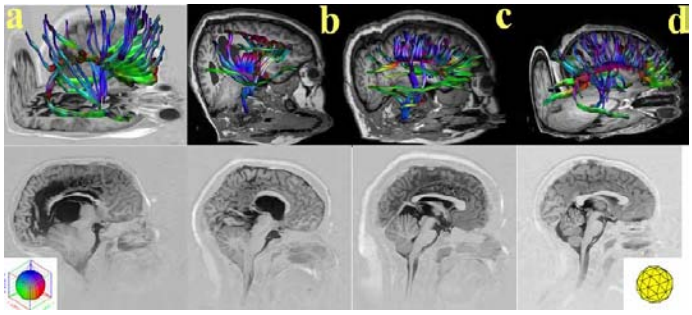


Figure 1. DTI based fiber tracking of the SBM brain showing the three SBM group characteristics **(a) agensesis (b) dysplastic (c) intact "normally appearing"** and **(d)** a healthy age-matched control compared to controls.

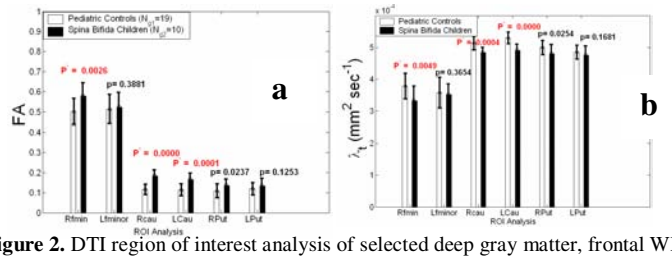
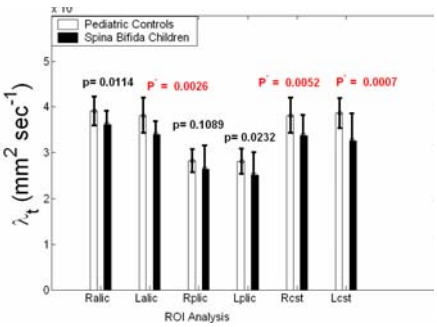
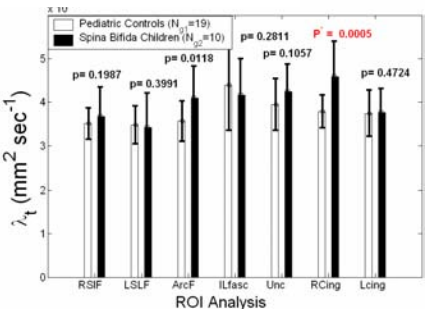


Figure 2. DTI region of interest analysis of selected deep gray matter, frontal WM structures **(a)** FA and **(b)** transverse diffusivity group comparison between the SBM children (N=10) and healthy controls (N_c=19).

Figure 3. (bottom left) DTI transverse diffusivity ROI group comparisons in some selected structures along projection (cst, internal capsule) and association pathways.





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