Diffusion Tensor Imaging Study of Adolescents with Spina Bifida

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Introduction

Spina bifida refers to a congenital birth defect caused by failure of normal closure of the embryonic neural tube. It is a common birth disorder affecting 3-5 per 10,000 newborns in North America. Numerous cerebral structural abnormalities in spina bifida children have been reported. These patients typically have Chiari II malformation and corpus callosum dysgenesis, often develop hydrocephalus and require shunt diversion. In addition to the apparent macrostructure abnormalities, microstructure abnormalities may also affect the cerebral development of children with spinal bifida. In this study, we performed diffusion tensor imaging (DTI) on 9 adolescents with spina bifida and 9 age matched controls. The goal of this study was to evaluate white matter microstructures in adolescents with spinal bifida.

Methods

Nine adolescents with spina bifida (15.1±1.5 years of age) and nine age matching controls (15.6±1.6 years) were recruited for the study. Consents were obtained from the parents and the Institutional Review Board approved the study. All subjects were scanned by a 1.5T Achieva MRI scanner (Philips Healthcare, Best, the Netherlands) with an 8 channel SENSE head coil. A 3D T1 weighted gradient echo pulse sequence was used to acquire whole brain anatomical data. Single shot spin echo EPI sequence with diffusion weighting gradients in 15 uniformly distributed directions was used to acquire DTI data. Other parameters for the DTI sequence include: TR = 6345 ms, TE = 75 ms, 2 averages, FOV 220*220 mm^2, isotropic voxels 2.5*2.5*2.5mm^3, reconstruction matrix size 128*128, 45 contiguous axial slices, and b = 1000 s/mm^2. After the scan, fractional anisotropy (FA) and mean diffusivity (MD) maps were calculated and exported to a workstation with MATLAB software (The MathWorks, Inc. MA, United States) for further region of interest (ROI) analysis. The diffusion weighted images were also processed by the FiberTrak package provided by the scanner manufacturer for visualization and quantitative analysis of major white matter tracts in the brain. Specifically, the genu and splenium of the corpus callosum, the left and right posterior limb of internal capsule were sketched in the axial FA maps for ROI analysis of FA and MD values; the corpus callosum in the mid-sagittal slice of the FA maps was sketched as a single ROI seed to track the callosal fibers; the anterior and posterior parts of cingulum in the coronal FA maps were sketched as multiple ROI seeds to track the limbic system fibers; the posterior limb of internal (PLIC) capsule and the corresponding hemisphere cortex in the axial FA maps were sketched as multiple ROI seeds to track the corticospinal fibers. The DTI tractography was based on the fiber assignment by continuous tracking (FACT) algorithm with a threshold for maximum angle change at 27 degree and a threshold for minimum FA values at 0.15. The number and length of the fiber tracts as well as the average FA and MD values in different tracts were calculated and compared between patients and controls. Group comparison was also performed between ROIs in the hemisphere with cerebral shunt (or shunt track) in the spina bifida patients and ROIs in hemispheres in control subjects. A two sample unpaired student t-test was used for all group comparisons.

Results

MRI results show that all 9 spinal bifida patients have mild to severe degree of Chiari II malformation. Many of the patients have corpus callosum dysgenesis with malformed/missing splenium/rostrum and some of them have thick genu and anterior commissure. Cingulate gyrus malformation was also observed in patients with abnormal corpus callosum. All 9 patients have at least one cerebral shunt and 3 of them have shunt (or shunt track) bilaterally. The shunts are remote from major white matter tracts such as corpus callosum and internal capsule, with rare exceptions. DTI study revealed significant difference between controls and patients in many white matter regions and tracts. Some of the ROI and Fiber Tracking (FT) analysis results are listed in the table below, and representative FT results are illustrated in the figure. Generally, when compare to controls, spina bifida patients have significantly elevated MD in multiple regions and major white matter tracts; the FA values are similar in the limbic fibers and corticospinal fibers, but are significantly lower in the corpus callosum; the number of white matter tracts is also significantly less in the corpus callosum and cingulum (data not shown), agree with the macroscopic abnormality of these structures. In addition, the FA and MD values in the PLIC of patients in the hemispheres with shunt are significantly different from that in the normal PLIC of controls. On the other hand, the FA and MD values in the PLIC of patients in the hemispheres without shunt are not significantly different from that in controls.

	Fractional anisotropy			Mean diffusivity (10^{-3} mm^2/s)		
	controls	patients	**P value**	controls	patients	**P value**
FT: callosal fibers	0.554±0.030	0.528±0.019	**0.049**	0.869±0.041	0.916±0.033	**0.012**
FT: limbic fibers	0.415±0.036	0.427±0.035	**0.338**	0.789±0.025	0.860±0.051	**0.008**
FT: corticospinal fibers	0.470±0.030	0.474±0.047	**0.784**	0.793±0.026	0.832±0.052	**<0.001**
ROI: genu	0.829±0.034	0.771±0.030	**0.001**	0.771±0.021	0.818±0.043	**0.011**
ROI: PLIC	0.736±0.033	0.699±0.042	**0.014**	0.736±0.024	0.762±0.039	**0.035**

Table: group comparison of FA and MD values between control and patients, Note the last row is based on comparisons between the hemispheres with a shunt in patients and the hemispheres in controls.

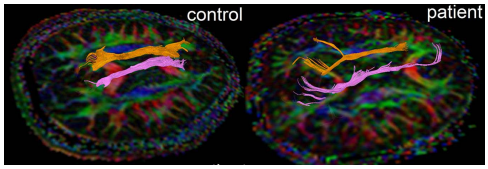

Figure: Limbic system fibers in the cingulum in one control (left) and one patient (right)

Discussion

DTI parameters such as MD and FA are sensitive to white matter microstructures since the water diffusion is greatly affected by the direction and integrity of axonal fiber bundles and myelin sheath in white matter. A few DTI studies have been performed on spinal bifida patients showing the abnormal development of the association fibers[1], anormalies of the corpus callosum and anterior commissure[2], as well as altered hemispheric fiber connection[3]. Our study provides new data demonstrating white matter microstructure abnormalities in the projection and limbic fibers. It is hypothesized that spina bifida affects the brain by disrupting structures such as corpus callosum during the first embryonic trimester and then affecting other structures especially white matter secondary to hydrocephalus and shunt diversion therapy. Our data combined with previous data may provide better understanding of brain development affected by spina bifida. In addition, our study revealed white matter DTI parameter differences between shunted and nonshunted (in controls) hemispheres suggesting that ventricular shunt therapy for hydrocephalus may be associated with abnormal white matter development independent of the effects of hydrocephalus alone.

References 1. Hasan KM et al, JMRI 27: 700-709 (2008); 2. Herweh C et al, NeuroImage 44:306-311 (2009); 3. Lee SK et al, AJNR 25:25-28 (2004)

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