Temporal Brain white matter maturation in Spina Bifida Cystica (SBC) with Diffusion Tensor Imaging

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Introduction: Spina Bifida cystica (SBC) is the most frequent congenital neurodevelopmental anomaly with a rate of 0.5-1 per 1000 live birth[1]**.** SBC results from incomplete closure of neural tube during 5-6 week of gestation**.** SBC is associated with congenital or developmental defects in brain macrostructure including the formation of cerebellum (Chiari II malformation), posterior cortex, white matter, midbrain and corpus callosum (CC) and results in functional deficitis[2]. Conventional MRI has been used routinely in neurodevelopmental disorders to rule out gray and white matter anomalies. However conventional MRI has its limitations such as demonstration of aberrant WM connections. DT-MRI can demonstrate the orientation and integrity of WM fibers by exploiting the anisotropic diffusion of water molecule in brain parenchyma. The aim of this study was to demonstrate differences in the age related changes in FA and MD in major WM tracts of the brain in SBC patients compared to age/sex matched controls.

Material and methods: The present study was performed on 23 SBC patients (14 male, age range 1-28 years) and 33 controls (22 male age range 1-29 years). Informed consent was obtained from patients or parents to perform MR Imaging. Conventional (T2, T1) as well as DT MRI were performed on a 1.5-Tesla GE MRI scanner. DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slice =30-34/slice thickness=3mm/interslice gap=0/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=8/ diffusion weighting b-factor=1000 s mm-2. The DTI data were processed as described in detail elsewhere[3]. The DTI-derived maps were displayed and overlaid on images with different contrasts to facilitate the region-of-interest (ROI) placement. The size of ROI was varied from elliptical to rectangular depending on the region size. ROI were placed in corpus callosum [genu and splenium (Spl)], internal capsule [anterior limb of internal capsule (ALIC), posterior limb of internal capsule (PLIC)], peri-ventricular WM [frontal white matter (FWM), occipital white matter (OWM)], and corticospinal tracts (CST) at the level of pons.

Result: In nineteen out of twenty three patients no abnormality was observed on conventional imaging. In the remaining three (n=3) patients, auqeductul obstruction in isolation was observed in two and also chiari I malformation was observed in one patient. FA values in SBC patients were higher than normal during the first 2 decade of life in the ALIC, PLIC, FWM, and CST. In these regions FA continued to decline with age and reached the level of controls by the age of 21 years (fig.1 a-d). In OWM the initial FA values were higher in SBC patients than controls and this difference remained between these two groups up to the age at which the patients and controls studied (fig. e). In corpus callosum (genu and spl) the initial FA values were similar in patients and controls but gap widened with age (fig. 1f-g). However the MD values did not show much differences in different ROIs in which FA differed between controls and patient group.

Discussion: Different patterns of FA changes (fig 1) and lack of change in MD (fig 2) in major WM tracts in SBC patients compared to controls demonstrate that the pattern of WM development in SBC is different from normal. The FA is one of the most commonly used diffusion indices, and reflects the molecular diffusion directionality and has been used to assess the maturity or plasticity in brain WM tracts[4]. It has been shown that stress during pregnancy can alter brain growth, development and behavior in the offsprings in both humans and laboratory animals[5, 6]. It has also been reported that accumulation of adrenocorticsteroids may directly influence the embryonic brain at a critical period and interfere with normal brain development [7]**.** Stress leads to alteration in circulating cortosteroids that affect the process of myelination[7].The underlying mechanism may play a role in SBC patients resulting in changes in brain white matter development. The increased FA values in SBC patients relative to controls may be due to increased myelination that leads to accelerated development. The increased FA values in white matter regions (ALIC, PLIC, FWM, OWM and CST) provide excellent examples of neural plasticity, restoration and reorganization in SBC patients. The WM tract development in genu and Spl of the corpus callosum have different developmental trajectory compared to other regions in patients with SBC and probably reflect different pattern of maturation.

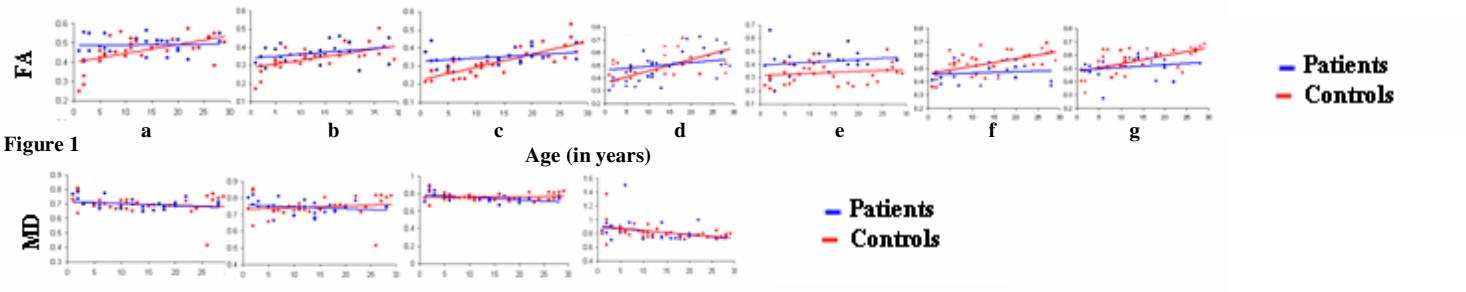

Figure 1

Figure 2

Figure 1: Pattern of FA in different regions [PLIC (a), ALIC (b), FWM (c), CST (d), OWM (e), genu (f), spl and (g)] of brain in SBC patients relative to controls**.**
Figure 2: Shows overlapping pattern of the MD values in WM [PLIC (a), ALIC (b), FWM (c), and spl (d)] SBC patients and controls.

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