Serial Quantitative Diffusion Tensor MRI of the Term Neonates with Hypoxic-ischemic Encephalopathy (HIE)

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Introduction: Perinatal hypoxic-ischemic encephalopathy (HIE) is the most frequent neurologic problem in term newborns and is a major cause of neurodevelopment abnormalities. HIE occurs in 0.2 - 0.4 % of full term neonates, and 25 % of the survivors exhibit permanent neuropsychological deficits[1] such as cerebral palsy, and severe mental retardation. Insufficient delivery of O_2 and glucose to brain triggers a sequence of biochemical events, which contributes to the energy failure leading to neuronal and glial cell injury or death.[2] Histologically and biochemically watershed zones are most vulnerable to HI injury because of least perfusion pressure. In the term infants' parasaggital cortex, thalamus, dorsal hippocampus, and subcortical white matter are all located within watershed zones and are the primary brain regions affected by insult.

Myelination delay is a well-known finding in neonates with perinatal brain damage. Conventional MR imaging techniques fail to detect the effect of the hypoxic-ischemic injury on myelination during the first four months of life due to incomplete myelination and the higher water content of the neonatal brain. In pediatric patients diffusion weighted imaging (DWI) may either underestimate or fail to detect some global hypoxic ischemic injury, its sensitivity appears to be affected by timing and pattern of injury. Diffusion tensor imaging (DTI) is a noninvasive modality that was applied in many research and clinical applications and in particular brain developmental studies.[3] The aim of this study was to determine the change over time of DTI measures [mean diffusivity (MD) and fractional anisotropy (FA)] in brain parenchyma in serially studied neonates with and without HIE, which may signify a poor neurological outcome.

Materials and Methods: Eleven full-term neonates (37 or more completed weeks of gestation) were examined and categorized into Sarnat stages on the basis of presence and severity of HIE. Out of them 5 had stage 1 HIE and 6 had stage 2 HIE. Five term neonates with normal neurological examination served as control subjects. Both patients and controls underwent serial DTI within 1 to 7 days postnatal and 12 to 14 weeks of age. Antecedent events thought to have contributed to hypoxic-ischemia in our group include difficult extraction, precipitous delivery, tight nuchal cord, and other unidentified in-utero causes of fetal distress (stresses leading to acute decrease in fetal movement).

Whole brain conventional MRI and DTI were acquired on a 1.5 Tesla GE MRI scanner using a standard quadrature head coil. DTI data was acquired using a single-shot echo planar dual spin echo sequence with ramp sampling. The acquisition parameters were: TR=8sec/TE=100ms/number of slices=30-34/slice thickness=3mm/interslice gap=0/FOV= 240mm/image matrix=256x256 (following zero-filling)/NEX=8/ diffusion weighting b-factor=700 s mm^{-2}. The DTI data were processed as described in detail elsewhere.[4] The DTI-derived maps were displayed and overlaid on images with different contrasts to facilitate the region-of-interest (ROI) placement. ROIs were placed on normal appearing white matter (periventricular white matter of cerebral lobes, genu, midbody, and splenium of corpus callosum, internal capsule, and cortico-spinal tracts) and deep grey nuclei (thalamus, putamen, and head of caudate nuclei) for FA and MD quantification in these patients. Change in FA and MD values with age in controls as compared to patients was analyzed by using univariate analysis of variance.

Results: On comparing FA change over time in pediatric patients with controls, a significant difference in FA change was observed in right anterior limb of internal capsule (RALIC), head of left caudate nuclei (LCN), and periventricular white matter of right parietal (RPWM), right occipital (ROWM), right temporal (RTWM), and left temporal lobe (LTWM). The difference between FA values with age was lesser in patients as compared to controls. A significant difference in MD change over time was observed in left posterior limb of internal capsule (LPLIC), right caudate nuclei (RCN), LCN, left putamen (LP), left thalamus (LTh), in patients as compared to healthy controls. On comparing 1st study with 2nd study in controls, significantly increased FA values was observed in RFWM, ROWM, RPWM, LPWM, RTWM and LTWM. While in patients with stage 1 and 2 HIE significantly increased FA values were observed only in RFWM, LFWM, RPWM, LPWM and LFWM, RPWM respectively.

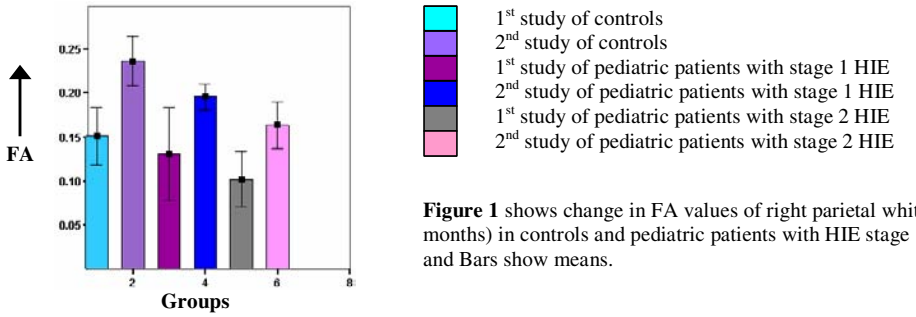

Figure 1 shows change in FA values of right parietal white matter at two time points (t = 0 and t = 3 months) in controls and pediatric patients with HIE stage 1 and 2. Error bar show mean +/- 1.0 SD and Bars show means.

Discussion: In this longitudinal study of the neonatal brain with and without HIE, we observed increasing FA and decreasing MD in periventricular white matter of normal controls as a function of age, which reflects normal process of myelination in normal white matter tracts.[5] In newborn with HIE, FA failed to increase significantly in periventricular white matter of right frontal, right occipital, right temporal, left temporal, and right parietal cerebral lobes. Difference in FA change in periventricular white matter over time in patients as compared to controls may suggest the delay in myelination or axonal damage seen in newborns with HIE. Our study suggests that detecting abnormal FA and MD values may allow for the earlier and more accurate diagnosis of HIE and will give predictive value for anatomic extant of cerebral injury as well as long-term neurofunctional outcome in these neonates.

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