DTI STUDY IN THE INFANTS BRAIN; METHODOLGY AND VALIDATION IN INFANTS WITH HYPOXIC-ISCHEMIC-ENCEPHALOPATHY

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Background / Aims: The ability to diagnose and evaluate abnormal MR signal in the infant's brain is challenging due to the rapid changes in the MR contrast during the neonatal period, the small number of normative data, and the dependence of the existing data on the acquisition parameters. Advanced MR sequences such as diffusion tensor imaging (DTI) and new analysis methods can improve the evaluation of brain impairment. The aim of this study is to present a methodology which enables the assessment, quantification and comparison between infants' brain. Neonatal hypoxic-ischemic encephalopathy (HIE) is associated with high morbidity and mortality rates and with long term motor and cognitive sequealae. Hypothermia is a neuroprotective treatment for infants with HIE[1-3]. The protocol includes a total body cooling to 33˚C for 72 hours within the first 6 hours of life. Several mechanisms for the neuroprotection of this therapy have been suggested[1,3] however, there is limited data regarding whole brain response to hypothermia. We present our preliminary results of DTI study in infants with HIE with and without hypothermic treatment compared with normal controls.

Methods: Seven infants with moderate to severe HIE (3 who got hypothermia; HIE-H, 4 normothermic HIE-N,) and 2 healthy infants ages 3 days-6 weeks were scanned using the 1.5T GE magnet. MR scans included conventional imaging and DTI (b=700 sec/mm^2, 33 diffusion directions and 2 repetitions). Mean fractional anisotropy (FA), mean diffusivity (MD), radial (Dr) and axial (Da) diffusivity maps were calculated using FSL (FMRIB) software. A brain infant template was created based on Cincinnati Children's Research Foundation (CCRF) white matter (WM), gray mater (GM) and CSF infant's template (Figure 1.a). Adult's atlases: JHU WM tractography atlas (Mori, Johns Hopkins University) and MNI structural atlas (Research Imaging Center, UTHSCSA, Texas), and subjects calculated maps, were normalized and realigned into the infant's template space. Volumes of interest (VOIs) included: the entire WM based on CCRF WM template with statistic threshold of 0.7 (Figure 1.b); Mean values of left and right corticospinal tract (CST) and Thalamus (Figure 1.c) based on the normalized JHU and MNI atlases, respectively. Mean VOI's diffusivity values and whole brain histogram were calculated and compared, while adjusting to age. Clinical data, of all infants, on birth, delivery and the postnatal period was collected.

Figure 1: Infant's brain template based on CCRF infant's templates; b. WM VOI-red; c. Left-CST-violet, Right-CST-green, Thalamus-blue.

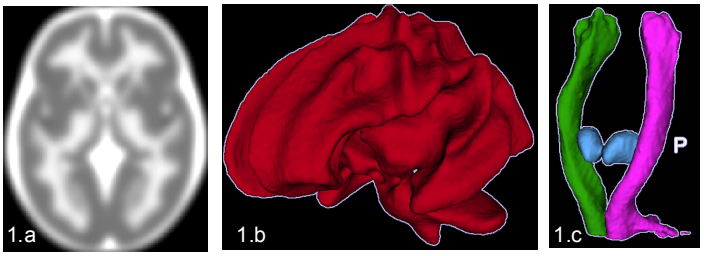
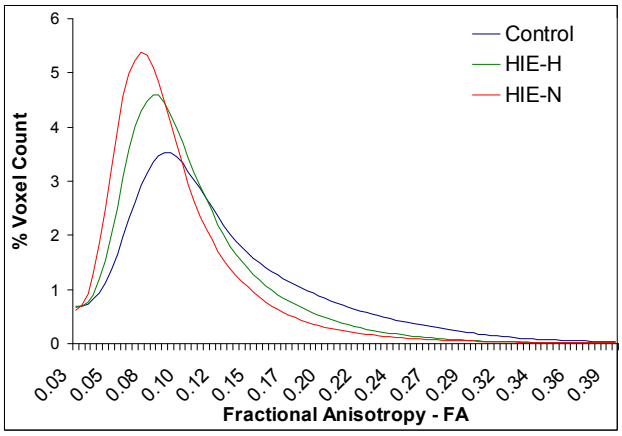


Figure 2: Whole brain FA histograms.



Results and Discussion: As expected, a general increase in FA and decrease in MD, Da and Dr were detected in all subjects in all VOIs during brain development. The HIE-H had lower MD, Da, Dr and higher FA values compared to HIE-N in the WM VOIs but not in the thalamus, even though the HIE-N infants had lower initial Apgar scores. The lowest MD, Da, Dr and the highest FA values were detected in the healthy subjects, in all VOI, compared to HIE subjects. Similar results were detected in the histogram analyses, demonstrating different distribution of the diffusivity histogram where: controls> HIE- hypothermia > HIE- normothermia with standard deviations values of 0.079, 0.062 and 0.056 respectively (Figure 2). In the healthy subjects and HIE-N, significant correlations were found between one minute Apgar score and whole brain WM FA values ($r=0.95$, $p<0.001$), CST and FA values ($r=0.85$, $p\leq0.04$), five minute Apgar score and CST-Da values ($r=0.78$, $p\leq0.04$), and whole brain FA distribution (std values) ($r=0.93$, $p<0.02$).

Conclusion: We proposed a methodology, similar to data published for adults, to study the neonatal brain. We created a standard space for all subjects, including templates and atlases adjusted to the infant's brain and achieved quantification and comparison of different imaging values in various anatomical areas. Preliminary results in HIE infants, demonstrate the applicability of this methodology for the pathological brain and its' sensitivity to the effect of therapeutic hypothermia in these infants.

References:

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