

Diffusion tractography in term neonates with hypoxic-ischemic encephalopathy: Projection Fiber System and corpus callosum involvement as predictors of neurodevelopmental outcome

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BACKGROUND: Perinatal hypoxic-ischemic encephalopathy (HIE) is still the leading cause of mortality and morbidity in term infant, being essential to obtain early and accurate assessment of the degree of injury to properly guide clinical management and predict outcome.¹ Advanced neuroimaging, such as diffusion-weighted imaging (DWI) can be of great help identifying abnormalities associated with hypoxic-ischemic injury (HII) that frequently could have been missed on conventional images within the first few days of life.^{2,3,4} In cases of diffuse injury, visual analysis has limited sensitivity due to the high water content of the neonatal brain and the normally lower apparent diffusion coefficient (ADC) compared to surrounding regions in most vulnerable areas. ADC values measured within regions of interest (ROIs) drawn on one image in various regions have been correlated with outcome, however, tract-based ADC measures, what would give a better representation of a specific white matter system, have not.^{5,6,7}

GOAL: To investigate the selective vulnerability of the projection fiber system (PFS) passing through the posterior limb of the internal capsule (PLIC) as well as interhemispheric connections (corpus callosum (CC), and its sub-regions the genu (GCC) and splenium (SCC)) using quantitative tractography, comparing to normal and correlating with neuromotor outcome at 1-2 years of age.

METHODS: We retrospectively included neonates (≥ 36 weeks of gestation) born between 2008 and 2010 who presented clinical evidence of perinatal HIE, and had a 3.0 Tesla MRI with DTI performed within 7 postnatal days were retrospectively included. Neonates with normal brain MRI with DTI performed the first week of life but without any criteria for HIE, and normal neurodevelopment were included as control group. Neonates with confirmed metabolic disorders, congenital malformations, chromosomal abnormality, congenital infection and neonatal stroke were excluded.

All MRI studies were performed on a Magnetom Tim Trio System 3.0 Tesla (Siemens) with a using 12-channel adult head coil and had a 35 directions DTI, b=750. Diffusion Toolkit was used for tract reconstruction using FACT algorithm and a 35 degree angular threshold.⁸ TrackVis was used to perform a manual ROI approach to select CST, CC, SCC, and GCC from the FA color map and to calculate ADC and FA values along the selected tracts from the ADC and FA maps.

Independent samples t-test was used to compare mean ADC and FA in LCST, RCST, CC, SCC and GCC between HIE patients and control population and between HIE patients with poor neuromotor outcome and good outcome. Motor outcome was assessed using the Gross Motor Function Classification System (GMFCS).⁹

RESULTS:

Inclusion criteria were met by 37 HIE and 9 controls. Mean age at MRI was 2.9 ± 1.5 and 4.2 ± 0.9 days respectively. Mean age at last follow-up was 12.7 ± 7.6 months.

HIE versus Control: Mean ADC in CST and CC was lower in HIE neonates but was significant only in CST. Mean FA in CST and CC was significantly lower in HIE patients.

HIE Good versus Bad Outcome: Outcome in HIE patients was poor in 10 and good in 27. The poor outcome group had significantly lower mean ADC in CST, GCC and SCC but not in the entire CC.

HIE Hypothermia vs No Hypothermia: Hypothermia was performed in 22. All hypothermia had significantly higher ADC in SCC. Mean FA was also higher in cooled in all tracts except in GCC but differences were not significant.

HIE without and with neonatal seizure (NS): HIE with NS had significantly lower mean ADC in SCC and GCC as well as CST. In addition, HIE with NS had elevated mean FA in these same tracts but this was only significant in the RCST.

HIE Hypothermia, with and without NS: Within the cooled group, those with NS had lower mean ADC in all the tracts but this was significant only in SCC and GCC but not in the entire CC. HIE with NS had higher mean FA in all selected tracts but this was only significant in the SCC.

CONCLUSION: Tract-based analysis demonstrated selective vulnerability of the CST in HIE compared to controls, with lower mean ADC correlating significantly with early neurologic outcome (neuromotor scores). Mean tract FA was also lower in HIE with poor motor outcome. Treatment with hypothermia was associated with a significant increase in mean ADC in SCC and significantly higher mean tract FA suggesting less metabolic compromise and preservation of white matter microstructure. NS were associated with lower ADC but higher FA in the SCC similar to other reports of transient seizure injury.

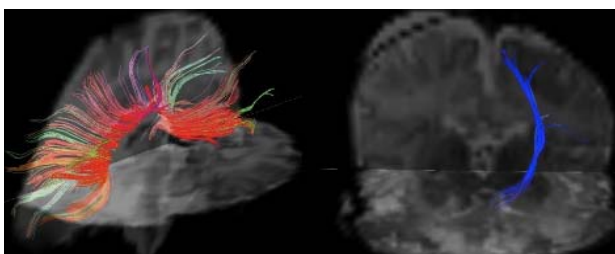


Figure 1: Three-dimensional images of the segmented white matter tracts superimposed on two-dimensional ADC maps. Left lateral view of callosal fibers passing through the genu, body, and splenium of the corpus callosum, and coronal view of the left corticospinal tract.

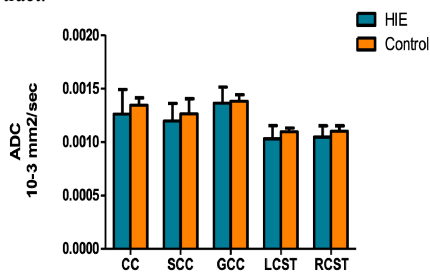


Figure 2: Bar Chart showing mean ADC and SD in CC, SCC, GCC, LCST and RCST in HIE patients (blue) and controls (orange). (*) indicates $p < 0.05$

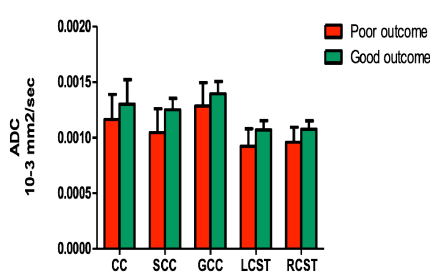


Figure 3: Bar chart showing mean ADC and SD in CC, SCC, GCC, LCST and RCST in HIE patients with poor outcome (red) and good outcome (green). (*) indicates $p < 0.05$

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