Differences between Early versus Late Magnetic Resonance Imaging in Infants with Neonatal Encephalopathy following Therapeutic Hypothermia

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Background and Aim

- MRI is the gold standard diagnostic test to define the nature of brain injury in infants with Neonatal Encephalopathy (NE).
- Conventional MRI is predictive of neurodevelopmental outcome.
- Early diffusion weighted MRI may assist in delineating injury in the first days of life.
- Clinical and imaging findings evolve considerably over the 1st week of life; early imaging may not reflect the true extent of brain injury.
- The aim of this study was to assess the value of combining early MRI with late MRI following therapeutic hypothermia (TH) for NE.

Methods

- Retrospective cohort study
- Infants who received TH for NE at the Brigham and Women's Hospital between 2016-2020.
- Infants had two MRIs:
  - Early - within the first week of life
  - Late - beyond the first week of life
- MRI findings were classified into normal or abnormal.
- Abnormal findings included diffusion restriction, evidence of parenchymal or germinal matrix hemorrhage, extra-axial hemorrhage, or other signal abnormalities.

Results

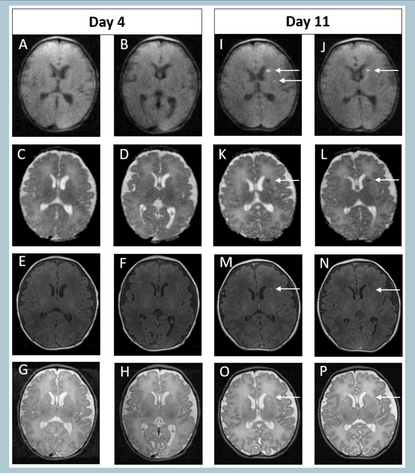
Infants:

- 94 infants with NE (40 mild, 49 moderate, 5 severe)
- Median gestation age was 39.3 weeks (IQR 37.5 – 40.2)
- Median birth weight was 3.2kg (IQR 2.6 – 3.6)

MRIs:

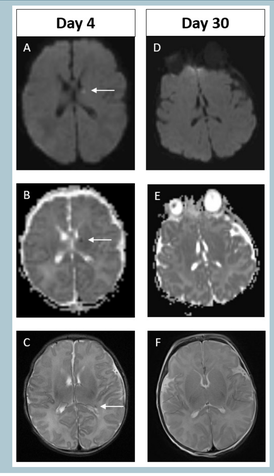
- First MRI scan was performed at a median age of 4 days (IQR 4-4) with repeat scan at a median age of 15 days (IQR 11-24).
- Changes were noted between early and late scans in 19 infants (20%)
  - Twenty-four infants (26%) had a normal early scan of which 3/24 (13%) had injury noted on repeat MRI
  - Seventy infants (74%) had abnormal findings noted on the early MRI, of which 5/70 (7%) had further evolution of injury and 11/70 (16%) had complete resolution of findings

Figure 1. Example of MRI images of normal early scan and abnormal late scan.



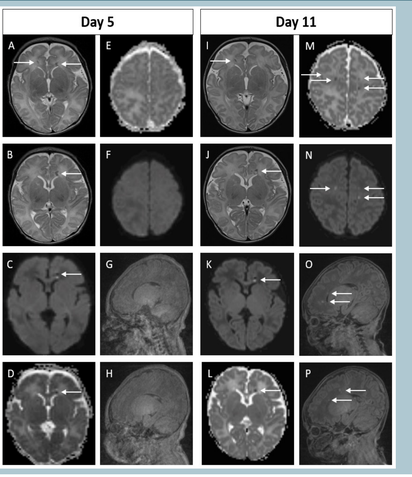
Images **A-H** on Day 4. Images **I-P** on Day 11. In the late scan, punctate foci of diffusion restriction in the left caudate head and left putamen are seen on DWI (**I** and **J**) and on ADC (**K** and **L**). Punctate foci seen in left external capsule on axial T1 (**M** and **N**) and T2 (**O** and **P**) weighted images. These findings are not evident on the early scan (**A – H**).

Figure 2. Example of MRI images of abnormal early scan and normal late scan.



Images **A-C** on Day 4. Images **D-F** on Day 30. In the early scan, punctate focus of diffusion restriction in the anterior, superior aspect of left thalamus is seen on DWI (**A**) and on ADC (**B**). Punctate focus of low signal intensity at left lateral ventricular atrium seen on axial T2 weighted image (**C**). These findings are not evident on the late scan (**D-F**).

Figure 3. Example of MRI images of abnormal early scan and evolved abnormalities on the late scan.



Images **A-H** on Day 5. Images **I-P** on Day 11. In the early scan, punctate foci of signal abnormality are seen bilaterally in the frontal periventricular white matter on the axial T2 weighted image (**A** and **B**) and on DWI (**C** and **D**). These findings are again seen on the late scan (**I-L**). In addition, new focal punctate white matter lesions are seen on DWI in the deep bilateral frontal white matter of the centrum semiovale (**M** and **N**) and in the right and left frontal periventricular white matter on sagittal T1 weighted images (**O** and **P**). These findings were not evident on the early scan (**E-H**).

Table 1. Summary of early and late MRI findings

Included infants n (%)	Early scan (≤7 days)	Imaging findings	Late scan (> 7days)	Imaging findings
21 (22)	Normal		Normal	
3 (3)	Normal		Abnormal	1 Micro-hemorrhages in white matter 2 White matter injury
59 (63)	Abnormal	32 Acute injury 5 Chronic injury 9 Parenchymal or germinal matrix hemorrhage 11 Extra-axial hemorrhage 2 Incidental findings	Abnormal	5 Evolution/worsening of injury 54 Stable/resolving injury
11 (12)	Abnormal	7 Acute injury 4 Chronic injury	Normal	

Conclusions

- In infants who received therapeutic hypothermia for NE, 20% had significant changes noted between their early and late MRIs.
- Relying solely on early MRI may overestimate injury in a proportion of infants and miss injury in another proportion.
- Caregivers should be aware of this limitation as it may impact prognostication.
- Combining early and late MRI following hypothermia allows for better characterization of brain injury.