Supplement 2: MR protocol and analysis

Protocol
Images were obtained in axial, sagittal, and coronal planes.
Sequences: conventional T₁-weighted spin echo (860/20), inversion recovery (3800/30/950) and T₂-weighted spin echo (3000/120). Diffusion-weighted images were not always obtained and not analysed in this study.
Sedation (oral chloral hydrate, 20-30mg/kg) used when necessary.
ECG, pulse-oximetry monitoring and ear protection used during scanning
An experienced neonatologist was always present.

Analysis of pattern of abnormal signal intensities

1. Basal ganglia and thalami (BG/T)
Mild: small areas of abnormal signal intensity (SI), often unilateral, involving ≤2 sites within the BGT
Moderate: abnormal SI involving >2 sites within the BGT, usually bilateral. Mild atrophy of the BGT was also classified as moderate BGT injury
Severe: bilateral extensive lesions throughout the BGT, focal lesions of very abnormal SI, or severe atrophic or cystic change.

2. White matter
Classified as mild, moderate or severe, defined below according to published criteria 2), and subdivided into diffuse, periventricular, and atrophic, defined below.
Mild: Increased T1 and T2 in periventricular WM.
Moderate: More extensive increased T1 and T2 in periventricular WM extending into deep and subcortical WM and/or presence of small focal lesions, haemorrhage or punctate WM lesions.
Severe: Widespread lesions, consistent with infarction or haemorrhage. Very severe long T1 and long T2 throughout with signal intensities approaching CSF.
Diffuse: non-atrophic involvement of the entire WM, seen as widespread abnormal SI of long T1 and long T2 throughout the WM extending up to the cortex.
Periventricular: abnormal SI in the periventricular WM
Atrophic: reduction in WM volume, with or without cystic breakdown.

3. **Posterior limb of the internal capsule (PLIC)**
   Classified as normal/equivocal/abnormal for infants of post-menstrual age (PMA) ≥37 weeks at scan, according to published criteria(3).

4. **Cortex**: Normal/abnormal, the latter being either loss of normal SI or highlighting (excessive low SI on T2-weighted and abnormal high SI on T1-weighted images). The abnormality was described as “focal” if limited to the central sulcus, insula or interhemispheric fissure, or “widespread” if more extensive.

5. **Brainstem**: Normal/abnormal (abnormal SI, atrophy, cysts, swelling, or poor myelination). Lesion site within the brainstem was documented.
6. **Cerebellum**: Normal/abnormal (any lesion noted in the cerebellum)

7. **Haemorrhage** was defined as regions of short T1 and short T2 within the ventricles or extracerebral space; occasionally when large and non acute these regions may develop a long T2 component.
References

