Reviewer’s report

Title: "Early identification of brain injury in infants with hypoxic ischemic encephalopathy at high risk for severe impairments: accuracy of MRI performed in the first days of life"

Version: 3
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Reviewer: Paul Govaert

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In a prospective observational cohort 15 newborns with HIE evaluated for therapeutic hypothermia had two sequential MR studies (1.5 T GE scanner): an ‘early’ one around the 4th day of life and a ‘late’ one during the second week of life. MRI was scored by two radiologists blinded to the clinical condition of the infants. The localisation, extension and severity of hypoxic-ischemic injury in early and late scans were highly correlated. This is important because in these first days of life MRI may provide prognostic information essential to orient management.

The paper reads fluently and the data are clearly presented. Some language errors need to be corrected [p4: during the entire process; p7: punctate lesions; p8: as pointed out by Wilkinson; p9: prognosis is based on …neuroimaging findings; p9: Thoresen et al.; p9: although it is still unclear; p9: moreover; p10: it is essential].

Major revisions to be made. The originality of this finding lies in the serial aspect of the MRI study. It is indeed relevant that in a centre with emphasis on clinical interpretation of HIE, the finding of relevant MRI support for care is important. For that reason the authors should rewrite the discussion focusing on papers who have done that and describe their findings. This list should perhaps focus on those papers where a scoring system was used (according to Hammersmith, Barkovich or Swarte et al. (not in the list of references)). The findings of serial MRI should be rewritten with in mind primary versus secondary injury (network injury in tracts and nuclei connected to sites of primary injury like thalamus and cortex). The second week diffusion changes should be compared to the first week ones just to learn about such network injury. It would also be useful to compare EEG findings with the reported patterns of MRI injury. Personally I would also like to correlate the lesion pattern with the presence of sentinel events (clear events pointing to an intrapartum cause of the asphyxial moment). The relevance of serial ultrasound imaging to depict deep grey matter injury may also need to be mentioned in the discussion and perhaps in the personal ultrasound findings of this cohort.

The paper is not in a position to compare cooling versus not cooling and therefore the discussion of shifting patterns following cooling is not relevant.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.