EEG based time points for longitudinal diffusion MRI studies in neonates with hypoxia-ischemia

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Introduction

Perinatal hypoxia-ischemia (HI) or birth asphyxia is one of the major causes of neonatal morbidity and mortality. Even when infants survive initial asphyxia, secondary damage processes, caused by the cascade of events triggered by reperfusion, can still result in encephalopathy [1]. Therefore, continuous monitoring is important for timely intervention and the possible prevention of permanent brain damage. MRI, and Diffusion Weighted Imaging (DWI) in particular, is often used for early detection of HI, but the lack of constant MRI availability and the necessity of infant sedation restrict the use of MRI for continuous monitoring. Furthermore, the outcome of DWI examinations is sometimes inconclusive because of the specific time dependence of measurable quantities (e.g. the diffusion coefficient decrease, subsequent renormalization, followed by an increase [2, 3]). Alternatively, the availability of EEG makes it suitable for continuous monitoring. The EEG signal is complex, because it is non-stationary, and influenced by many factors (e.g. maturational age, sleep-wake cycles, medication etc.). After a transient HI insult, reperfusion is often followed by epileptogenic activity that can be monitored by EEG. This epileptogenic activity could be obscured by similar EEG patterns originating from non-pathological circumstances. Therefore, interpretation of (changes in) the EEG signal can be complicated. It is hypothesized that combining EEG with MRI could possibly give more information about the development of the brain and of possible brain damage. The goal of this study is to develop protocols for the indication of diffusion MRI examinations based on continuous EEG monitoring of neonates with perinatal HI.

Methods

The study consisted of continuous EEG monitoring of neonates at risk, alternated by an MRI examination on predefined time points. MRI protocol: Philips Gyroscan 1.0 T, included T_1, T_2, IR-T_1 and DTI images in the axial plane. T_2 measurements with a double echo TSE sequence: $TE_1/TE_2/TR$ = 12.6/120/4381 ms; slice thickness 4 mm; slice gap 0.4 mm. DTI with a single-shot EPI sequence and Pulsed Field Gradients in 3 or 6 directions; voxel size 1.2x1.2x4 mm; slice gap 0.4 mm; b-values 0, 400 and 800 s/mm^2, as described in Van Pul *et al* [3]. Sedation with chloral hydrate was used in all patients. EEG protocol: Viasys NicoletOne EEG amplifier, with Ag/AgCl electrodes placed according to the full 10-20 system, a 512 Hz sampling rate and a filter frequency range of 0.5-70 Hz.

Included were 8 term newborns with suspected neonatal encephalopathy caused by perinatal HI. Excluded were perinatal infections, neuro-metabolic diseases and major congenital malformations. Perinatal HI was diagnosed when clinical symptoms of neonatal encephalopathy were present with 2 or more of the following risk factors: abnormal fetal heart rate pattern; umbilical artery pH < 7.10; meconium stained fluid; Apgar score 5 minutes < 7. The EEG was measured between day 1 and 8 after birth. MRI was performed between day 1 and 9 after birth, within 24 hrs from an EEG measurement.

Results

Figures 1 and 2 show representative DWI and EEG measurements. Fig. 1a shows a normal MR and EEG for a term neonate. From fig.1b, it can be seen that the DWI of the neonate with possible developmental delay shows no signs of ischemic damage, but displays decreased signal intensity in the frontal region, possibly due to little myelinisation. The EEG shows high amplitude δ-activity, mostly in the fronto-polar and frontal regions corresponding to the regions of decreased signal in the DW image. Fig. 2a shows increased signal intensity on DWI, characteristic for HI encephalopathy, in the globus pallidus and putamen, as well as pedunculus cerebri. The EEG shows paroxysmal (convulsive) slow waves, with varying location, although mostly with maxima in the C3 and C4 regions corresponding to the DWI abnormalities. Fig. 2b shows a DWI with cortical increased signal corresponding to elaborate HI encephalopathy. The EEG shows occasional θ- and α-activity, mostly located in the (right) temporal regions, on a flat line background. For the other neonates included in this study, similar agreements between EEG and DWI were observed.

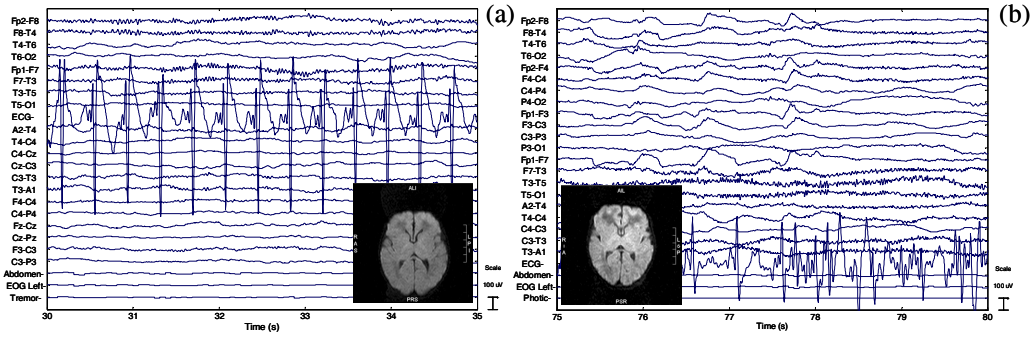

Fig. 1 Representative DWI and EEG data of normal neonate (a) and neonate with developmental delay (b).

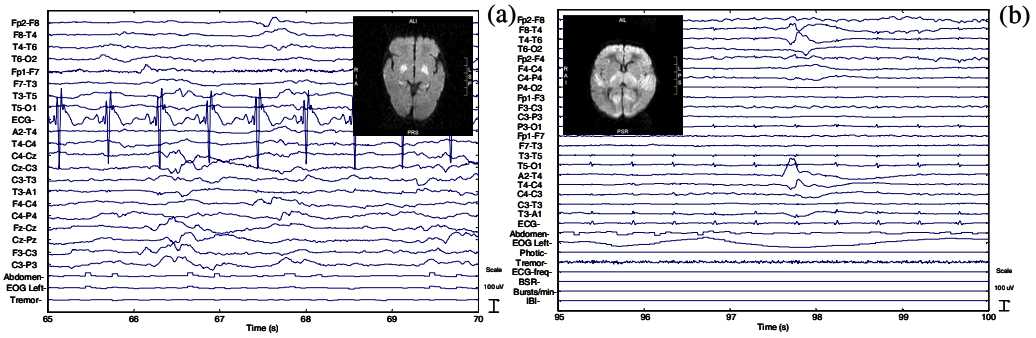

Fig. 2 Representative DWI and EEG data of neonate with focal (a) and global (b) HI encephalopathy.

Discussion

Preliminary results indicate an agreement between abnormalities in MR images and signal fluctuations at corresponding electrode locations. To be able to obtain a quantitative correlation between changes in MRI and EEG, further research and more clinical data is necessary. A confounding factor could be the use of medication, which often influences brain activity and therefore the obtained EEG signal, possibly masking HI effects. Currently, simultaneous EEG and MRI measurements in a rodent model of neonatal HI are being examined, allowing carefully controlled experimental conditions. These combined measurements could possibly provide more insight in the correlation of EEG and MRI.

References

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