

# Simultaneous EEG and MRI in a rodent model of neonatal hypoxia-ischemia

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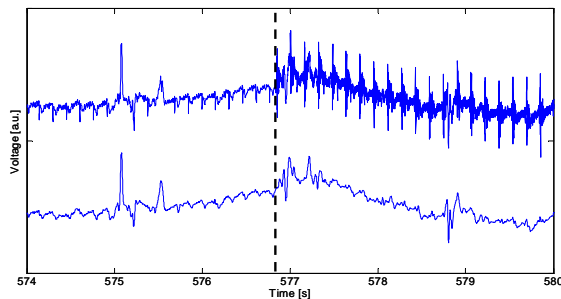
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## Introduction

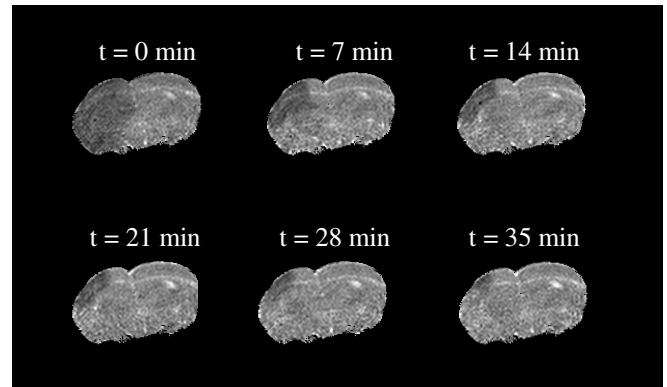
Premature neonates have a high incidence of hypoxia-ischemia (HI), which can lead to permanent neurophysiologic deficits. Therefore, these newborns are frequently monitored by means of EEG. However, clinical intervention strategies are mostly based upon MRI examinations. The time points of these studies usually depend on MRI availability. The aim of this study is to develop protocols for the indication of MRI examinations based on EEG monitoring. To aid in the development of these protocols, knowledge of the correlation of EEG and MRI is important. In order to investigate this correlation following a hypoxic-ischemic insult under carefully controlled experimental conditions, simultaneous EEG and MRI measurements in an experimental neonatal cerebral ischemia model were conducted. It is known that the developmental stage of the brain of neonatal rats with an age between 10 and 15 days closely resembles that of premature to term human neonates [1], the clinically relevant target group for this study. The MRI measurements include DTI, known for early detection of HI [2]. DTI based fiber tracking is sensitive to cellular changes, which are hypothesized to correlate to changes in neuronal functioning, as measured by EEG. Challenges in this setup are, amongst others, reduction of artifacts in the EEG signal due to MRI sequences, and artifacts in MRI images resulting from the EEG electrodes and leads.

## Methods

The HI model used in this study involved unilateral occlusion of the common carotid artery, followed by a temporary reduction of the inhaled oxygen percentage [3]. Following the carotid occlusion, rats were placed in the MRI scanner, EEG electrodes were positioned, and baseline MRI and EEG measurements were performed. Subsequently, the oxygen percentage was reduced to 10% for a period of time (HI), after which it was restored (reperfusion). During HI and reperfusion, MRI and EEG were continuously monitored. MRI examinations were conducted on a 4.7 T MRI scanner. Baseline measurements consisted of T<sub>2</sub>-weighted MRI and DTI, while evolution of the lesion during HI and subsequent reperfusion was monitored through repeated DWI measurements. The measurements were concluded with a second set of T<sub>2</sub> and DTI acquisitions. The EEG measurements were conducted using a homebuilt 10-channel amplifier, band pass filtered between 0.1 Hz and 250 Hz, a National Instruments<sup>TM</sup> NI USB-6211 DAQ with a sampling rate of 1000 Hz per channel and LabWindows<sup>TM</sup> programmed data acquisition software. Additional filters were built to reduce RF and magnetic field gradient induced artifacts. The ECG was derived from leads attached to the paws of the rat. Data processing and analysis was performed using Matlab<sup>®</sup>. Independent component analysis (ICA) was employed to remove ECG artifacts from the EEG signals.



**Figure 1:** EEG signal of the neonatal rat during an MR sequence (starting at the dashed line) before artifact reduction (top trace), and after ICA and filtering (bottom trace).



**Figure 2:** ADC images of the neonatal rat brain, acquired during the reperfusion phase following a period of hypoxia-ischemia.

## Results

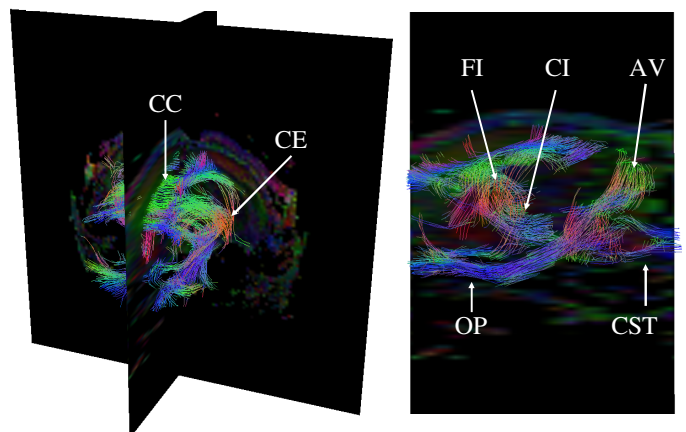
Effects of RF and magnetic field gradient artifacts on the EEG amplifier were effectively reduced by using low-pass filters specifically matching the properties of the MRI system. ICA in combination with digital filtering enabled efficient recovery of the EEG signal recorded during MR scans, as shown in figure 1. By properly selecting the EEG electrode material, imaging artifacts were also minimized. Preliminary EEG data was acquired using two channels, directly above the center of the hemispheres. To increase the spatial resolution of the EEG measurements, recordings using specially developed multichannel needle electrodes were successfully tested. Preliminary DWI data, acquired following a period of hypoxia-ischemia, is shown in figure 2. From this figure, it can be concluded that the developed setup allows for the study of reperfusion effects with sufficient time and spatial resolution. Figure 3 shows an example of fiber tractography, calculated from a baseline DTI dataset. In this figure, characteristic white matter structures are denoted.

## Discussion

This study demonstrates the feasibility of combined EEG and MRI measurements in a neonatal HI model. With the described setup, it is possible to follow the anatomical and functional impact of temporary HI-induced damage processes. Because significant biochemical and anatomical changes occur during maturation [4], which can influence the EEG, its correlation to MRI, and the sensitivity to HI [5], future work focuses on combined measurements as a function of gestational age, in order to assess effects of maturation on the susceptibility of the brain to hypoxia-ischemia.

## References

- [1] Romijn *et al*, Early Hum Dev. 1991 Jul;26(1):61-7. [2] Sotak *et al*, NMR Biomed 2002; 15(7-8):561-9. [3] Tuor *et al*, Exp Neurol 1998;150:321-8. [4] Ashwall *et al*, Pediatr Neurol. 1995 Apr; 12(3):191-6. [5] Rice *et al*, Ann Neurol. 1981 Feb; 9(2):131-41.



**Figure 3:** DTI-based fiber tractography in the neonatal rat brain, overlaid on color maps (green = LR, red = SI, blue = AP). Clearly visible are the corpus callosum (CC), capsula interna and externa (CI and CE), fimbria (FI), optical tract (OP), arbor vitae (AV) and corticospinal tract (CST)