Combined EEG and MRI measurements in a rat model of neonatal hypoxia-ischemia

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Introduction

Premature neonates have a high incidence (approximately 60%) of hypoxia-ischemia (HI), which can lead to permanent neurophysiologic deficits. For that reason these newborns are frequently monitored by means of EEG. However, clinical intervention strategies are mostly based on MRI examinations. The time points of these MRI studies are usually arbitrary, depending 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. To investigate this correlation under carefully controlled experimental conditions, it was decided to perform simultaneous EEG and MRI measurements on hypoxic-ischemic neonatal rats. It is known that the developmental stage of the brain of neonatal rats with an age in the range between 10 and 15 days closely resembles that of (premature to term) human neonates [1], the clinically relevant target group for this study. In this time frame, significant biochemical and anatomical changes occur [2], which can influence the EEG signal, its correlation to MRI, and the sensitivity to HI [3].

In this study a measurement setup has been developed to measure DWI and EEG in a neonatal cerebral ischemia model simultaneously, in order to find a correlation between changes in anatomy (as measured by MRI) and changes in function (as measured by EEG) following a cerebral infarction. It is hypothesized that there is a correlation between lesion volume and EEG amplitude, and possibly between the location of the lesion and the EEG frequency spectrum. Challenges in this setup are, amongst others, reduction of artifacts in the EEG signal due to MRI pulse sequences, and artifacts in MRI images resulting from the placement of EEG electrodes and leads.

Methods

The HI model used in this study is described by Tuor et al [4]: a unilateral occlusion of the carotid artery, followed by a temporary reduction of the inhalation oxygen percentage. Following the carotid occlusion, EEG electrodes are positioned, the rats are placed in the MRI scanner, and baseline MRI and EEG measurements are performed for 30 minutes. Subsequently, the oxygen percentage is reduced to 10% for a period of time (HI), after which it is restored (reperfusion). During hypoxia-ischemia and reperfusion, MRI and EEG are continuously monitored. MRI examinations are conducted using a 4.7 T MRI scanner, and consist of DWI, T_2 and PWI images in the coronal plane, while an MR angiogram is made pre- and post-hypoxia to verify the occlusion of the carotid artery and the decreased blood flow in the ipsilateral hemisphere. The EEG measurements are conducted using a homebuilt 10-channel signal amplifier, analog high-pass (0.1 Hz cut-off frequency) and anti-aliasing (250 Hz cut-off frequency) filters and LabWindows™ programmed data acquisition software. Data was logged using a National Instruments™ NI PCI-6229 DAQ with a 1024 Hz sampling rate per channel. Additional filters have been built to reduce RF and magnetic field gradient induced artifacts. This study was approved by the animal ethics committee, under the condition that the first pilot measurements are performed outside the MRI scanner, in order to be able to closely monitor the vital signs of the rats. Preliminary EEG data was acquired using 3 needle electrodes (2 active, 1 reference). The active electrodes were placed directly above the center of both hemispheres, while the reference electrode was placed in the neck. The ECG was derived from leads attached to the front and rear paws of the rat. Data processing and analysis was done using software written in Matlab®. Independent component analysis (ICA) was employed to remove ECG artifacts from the EEG signals. Histology will be performed to verify lesion locations and volumes.

Results

It could be shown that it is possible to reduce the effects of RF and magnetic field gradient artifacts on the EEG amplifier adequately by using low-pass filters specifically matching the properties of the MRI system. By selecting graphite EEG electrodes [5], the imaging artifacts could also be minimized.

Preliminary results of the EEG measurements are shown in figure 1. Fig. 1a and 1b show the frequency spectra of the EEG signals acquired during hypoxia-ischemia and during reperfusion respectively. From these figures, it can be seen that in both the ipsilateral (b) and the contralateral (a) side of the brain EEG activity is reduced following HI. During reperfusion, activity in the contralateral side is restored, while activity at the ipsilateral side remains depressed. Figure 1c and 1d show the EEG activity divided in customary frequency components. From these figures, it can be seen that following HI, the activity in the ipsilateral hemisphere, as well as the contralateral hemisphere, is mostly focused to lower frequencies (δ- and θ-activity). This effect is more pronounced in the ipsilateral side. After a longer period of HI, all activity ceases until reperfusion, restoring contralaterally, whilst remaining depressed ipsilaterally.

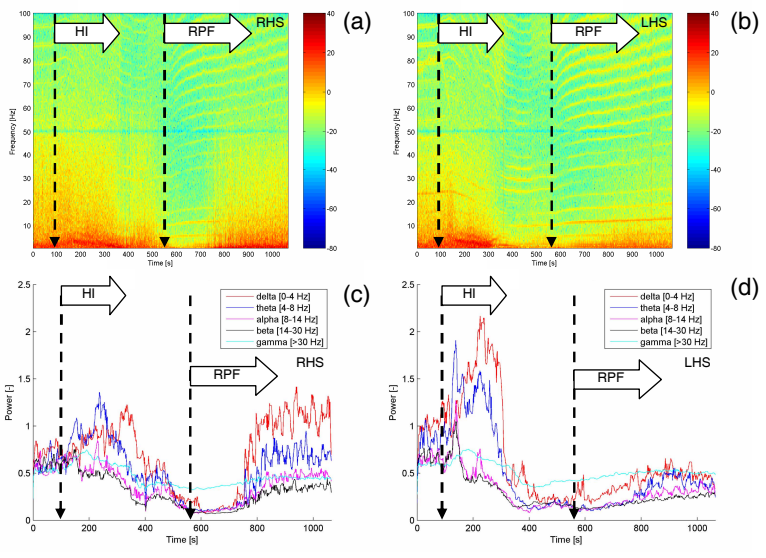

Fig. 1: Fourier spectra (a, b) and baseline normalized frequency component amplitudes (c, d) of EEG signals acquired during hypoxia-ischemia (HI) and reperfusion (RPF) for contralateral (RHS) and ipsilateral (LHS) hemisphere. Fourier spectra are plotted on a logarithmic relative intensity scale.

Discussion

In this study, it has been shown that EEG measurements on a rodent model of hypoxia-ischemia can be performed, and artifacts resulting from combining EEG and MRI can be adequately reduced. As it has previously been demonstrated that we are able to measure changes in brain tissue due to hypoxia-ischemia using MRI [6, 7], it can be concluded that it is feasible to perform combined EEG and MRI measurements in a neonatal HI model in which it is possible to follow the evolution of a unilateral encephalopathy. Future work will focus on combined measurements as a function of gestational age in order to assess the effects of maturation on the susceptibility of the brain to hypoxia-ischemia.

References

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