Simultaneous EEG and functional MRI

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Summary

Epilepsy is a neurological disease characterized by epileptic seizures. In the Netherlands about 120.000 persons have epilepsy. Most of them can be treated successfully with anti-epileptic drugs. However, 20 - 30 % of the patients does not respond to medication. These patients are potential candidates for epilepsy surgery, which aims to remove those brain regions that are responsible for the generation of seizures (i.e. epileptogenic zone). To create hypotheses about the location and extent of the epileptogenic zone several (non)invasive techniques are combined, ranging from electroencephalography (EEG) and magnetic resonance imaging (MRI) to neuropsychological tests.

In this context, we investigated the added value of a relatively new technique: simultaneous EEG and functional MRI (EEG-fMRI). EEG and fMRI are both techniques to measure neuronal activity. EEG measures electrical activity through electrodes at the scalp and is able to indicate the occurrence of epileptic activity [seizures or interictal epileptiform discharges (IEDs)] with good temporal resolution. However, the spatial resolution is relatively low, because the EEG signals represent a mixture of activity from different sources. fMRI, on the other hand, has a good spatial resolution. This technique provides an indirect measure for neuronal activity, which is based on changes in the ratio of oxy- and deoxyhemoglobin in the blood related to the occurrence op neuronal activity. Co-registration of EEG is necessary to determine whether changes in fMRI are related to epileptic activity. The epileptic events that are visible in the EEG during scanning are correlated with the fMRI time series yielding a correlation pattern indicating which brain regions were significantly more active during IEDs than in periods without visible IEDs in the EEG. The combination of EEG and fMRI provides a unique way to investigate epileptic networks with a high spatial precision.

The technical problems involved with the recording of EEG in the MRI environment are largely solved; under certain conditions and with special equipment it is safe to record EEG inside the MRI. However, the analysis and interpretation of the data are not straightforward. Therefore, the general aim of this thesis was to improve and to evaluate the potential of EEG-fMRI as a noninvasive technique in the presurgical evaluation of patients with medically intractable epilepsy.

Chapter 2 and 3 focus on the analysis of the fMRI data. In chapter 2 different analytical strategies for the correlation of EEG and fMRI were compared. The results suggest that the yield of EEG-fMRI is increased when a flexible approach is used, in which no assumptions are made about the precise underlying relation between EEG and fMRI, the hemodynamic response function (HRF). Since the HRF can vary over subjects and brain regions, the use of a more flexible approach, where the HRF is estimated from the data, increases the yield of fMRI.

Chapter 3 demonstrates that it is also important to correct the fMRI signals for variations in physiological functioning. These variations can be measured by a pulse oximeter at one of the subject's fingers. The variations in pulse height (VIPH) are related to respiration and cardiac output. VIPH appears to explain a large part of the fMRI signals, both in healthy volunteers and patients with epilepsy. Therefore, it is important to correct for these effects, especially when the subject has an abnormal breathing pattern during the experiment, as one of the patients with epilepsy in our study. When this physiological effect is taken into account the correlation pattern reduces from a very widespread correlation pattern to a pattern with a maximal BOLD response in the right temporal lobe. This region coincided with the resection area. The inclusion of VIPH regressors in the correlation model is not only important for the analysis of EEG-fMRI data of patients with epilepsy, but is relevant in general for resting-state fMRI studies, during which spontaneous brain activity is measured.

The yield of the EEG-fMRI analysis is dependent on the IEDs that are visible in the EEG. The detection of epileptic events is hampered by the presence of gradient and pulse artifacts in the EEG. Gradient artifacts result from switching of the gradients for slice selection, whereas pulse artifacts are related to the pulsation of the heart. Both types of artifacts can be removed off-line from the EEG with dedicated algorithms. Most of these algorithms are based on the average artifact subtraction principle, in which a template is created by averaging the artifact that is subsequently subtracted from the raw EEG data. In chapter 4 extensions of this approach are presented to further improve the correction of the EEG data. First, it appears that the gradient artifacts may differ slightly between scans. By clustering the artifacts and creating a template for each cluster, the correction was improved. Second, the pulsation artifacts appear to overlap from heartbeat to heartbeat. Therefore, the correction of the EEG data is improved when this overlap is taken into account.

Chapter 5 and 6 focus on the evaluation of the EEG-fMRI results. Most EEG-fMRI analyses yield a correlation pattern consisting of multiple activated brain regions. Our hypothesis was that these regions form an epileptic network including the onset and propagation of epilepsy related activity. For validation, the EEG-fMRI findings were compared to the results of invasive EEG data. These data are acquired either by depth electrodes implanted inside the brain tissue or by electrode grids placed on the subdural surface of the brain. In chapter 5 a semi-automatic procedure for the analysis of the invasive data is presented such that the EEG-fMRI findings can be compared systematically with the invasive EEG data. This method was tested for five patients who were implanted with depth electrodes. In chapter 6 the application of the same method was described for the EEG data of sixteen patients recorded from subdural grids. In all data sets there was at least one region that was concordant with active invasive electrodes during IEDs. Furthermore, the EEG-fMRI results were compared to the location of the seizure onset zone and resection area: the EEG-fMRI correlation pattern included the seizure onset zone in 83 % of the data sets and the resection area in 93 % of the data sets. For some patients, we were able to validate an epileptic network of onset and propagation regions.

Although in most patients relevant results are obtained with EEG-fMRI, in some patients no IEDs are detected in the EEG during scanning. This may have several explanations, for instance the limited scanning period (about 45 minutes) or an origin located in deep lying structures. When no IEDs are present, the data cannot be analyzed with the current EEG-fMRI approach. Chapter 7 is an explorative study to the use of independent component analysis (ICA), a data-driven approach independent of the EEG. The preliminary results suggest that it is possible to find epileptic networks with ICA, even in the absence of visible IEDs in the EEG. This finding provides further perspective for the use of resting-state fMRI in clinical practice.

In conclusion, the yield of EEG-fMRI increases with the methodological improvements presented in this thesis. Furthermore, the results of EEG-fMRI are clinically relevant, because EEG-fMRI is usually concordant with IEDs in the invasive EEG data and includes the seizure onset zone and resection area. For this reason, there is an important role for EEG-fMRI in the surgical planning, especially with regard to the determination of the implantation strategy. In comparison to other noninvasive techniques in the presurgical evaluation, EEG-fMRI will have an added value in patients in whom a focus from deeply lying structures or multifocal epilepsy is expected. In addition, EEG-fMRI is able to reveal the whole network from onset to propagation, which is more difficult to achieve with EEG alone.