Future perspectives

Usually, when a new medical technique is developed, its precise applicability in and value for clinical practice still need to be established, even when its theoretical improvement with regard to existing technologies may be quite obvious. One example of such a (relatively) new technique is multichannel EEG. In this thesis its value for clinical practice and - to a lesser extent - its feasibility in a clinical setting, have been investigated. Even though it is immediately clear that a 64- or 128-channel EEG recording provides much more information than a conventional EEG recording with up to 32 channels, the question remains whether this additional information is clinically relevant. More channels take more preparation time, which is less convenient for the patient, and more channels require a more expensive EEG recording system. Therefore, the main motivation for this thesis has been the question 'Does measuring more mean knowing more?'.

So far, multichannel EEG has only limited clinical neurological applications, as described in more detail in the introduction of this thesis. This might be partly due to the fact that many clinicians have the impression that multichannel EEG may be suitable for research purposes, but is not feasible in clinical practice. However, in the course of the research performed for this thesis and other projects more than 150 128-channel recordings have been performed in our department in patients with various disorders, ranging from movement disorders, to multiple sclerosis, dementia and mild head injury. This experience has learned us that the technique is well suited for recordings in patients, since - when the electrode cap is in experienced hands - preparation time can be limited to 20 minutes (for 64 channels) or 30 minutes (for 128 channels). Furthermore, placing (multichannel) caps is patient friendly and multichannel EEG recordings are cheap compared to imaging methodologies such as (f)MRI. Implementation of 64- or 128-channel EEG recordings therefore seems feasible for any clinical lab that is experienced in conventional EEG recordings.

Although there are only a few clinical applications, multichannel EEG has extensively been used for fundamental research (see introduction). In these studies results are limited to group comparisons, whereas estimates of sensitivity and
specificity are rare, even though high sensitivity and specificity are essential for introducing a technique in clinical practice. In this thesis we developed new analysis techniques for multichannel EPs, aiming at clinical introduction of the techniques. We showed that 128-channel recordings can measure SEP amplitudes more accurately than conventional recordings with only a limited number of electrodes. Theoretically, more accurate amplitude estimation should improve sensitivity and specificity for physiological and pathological changes in SEPs. We applied these techniques to multichannel SEPs obtained in patients with parkinsonian disorders to investigate if the use of these techniques can indeed improve the differential diagnosis. Unfortunately, for this group of patients this multichannel recording and analysis technique did not contribute to the differential diagnosis. Possible causes of this result may be sought at different levels.

First of all, assuming that 128-channel recording is sufficient (based on spatial sampling arguments (Spitzer et al., 1989)), the used analysis technique may not be optimal. Secondly, it is possible that underlying pathology is either not as expected or that the pathological effect of various parkinsonian disorders on SEP parameters is so small that it can not even be measured with 128-channel recordings.

A first possible improvement on the analytical level is to enhance the symmetry measure for application in parkinsonian disorders by calculating separate global field powers for frontal and parietal electrodes. In this way frontal SEP components, which are thought to be abnormal in patients with Parkinson’s disease (Mauguière et al., 1993; Bostantjopoulou et al., 2000; Garcia et al., 1995; Rossini et al., 1995), can be investigated separately from parietal components that are thought to be abnormal in patients with corticobasal degeneration (Brunt, 1995; Klodowska-Duda et al., 2006; Carella et al., 1997; Okuda et al., 1998; Monza, 2003; Takeda et al., 1998; Thompson et al., 1994).

On the other hand, for improvement at the recording level, it might be worthwhile to test other SEP protocols, such as double stimulation in which two nerves are stimulated simultaneously or stimulation during hand movements to induce the so-called gating effect (the modulation of sensory information processes during movement). Such protocols resulted in abnormal conventional SEPs in patients with dystonia and hand tremor (Restuccia et al., 2003; Tinazzi et al., 2000). Although our symmetry measure and amplitude estimation did not improve the differential diagnosis of parkinsonian disorders, these techniques can still be useful in other neurological applications. One of the clinical applications of the symmetry measure for multichannel SEPs may be the estimation of sensory impairment in stroke patients as prediction for clinical outcome (Rossini et al., 2003; Huang et al., 2004). The multichannel amplitude technique might also be useful for monitoring disease progression or estimating the effect of medication or surgical intervention in patients with e.g., multiple sclerosis, spinal cord compression, neuropathy, diabetes or amyotrophic lateral sclerosis.
In addition, other signal analysis techniques may be applied to both EPs and ERPs in general and to the SEP and attention and motor-related ERPs in this thesis in particular. For example, wavelet analysis (Chapter 2) might be useful for a more objective description and comparison of E(R)P waveforms. In this way, other features than amplitude and latency of the E(R)P waveform can be extracted and used for clinical purposes.

Furthermore, single trial analysis can be clinically relevant when pathological changes are associated with habituation, fatigue or other sources of intertrial variability. For example, in elderly subjects, it has already been found that the variability of single trial P3a amplitude is increased (Fjell and Walhovd, 2007).

The few existing neurological applications of multichannel EEG are based on source localization. This analysis technique can only be applied to multichannel recordings. As shown by Elting et al. (2006) this technique can differentiate the P3a and P3b peaks obtained with an oddball task. Not only these peaks, but also other peaks that overlap in time and space can possibly be separated using source localization techniques resulting in a better amplitude and latency estimation of the different peaks.

So far, the P300 is one of the few ERPs that is routinely used clinically. Another, less frequently used ERP is the Bereitschaftspotential or readiness potential (Shibasaki and Hallett, 2006). The use of multichannel recordings might increase the possible clinical applications of ERPs. However, while EPs reflect primary stimulus processing and are therefore reliable and easy to interpret, ERPs reflect many different processes and depend on subject attention and effort. Therefore, possibly new paradigms or recording protocols may need to be developed that are reliable and that control subject attention and effort.

Recently, MR-compatible multichannel EEG systems have become commercially available from multiple suppliers. By combining fMRI and EEG, the high temporal resolution of EEG can be combined with the high spatial resolution of fMRI, in principle providing more information about brain functioning than EEG or fMRI alone. So far, this combination has only been used clinically for localizing epileptic seizures. Yet, the combination of these techniques has the potential to be useful for other clinical problems as well. However, fMRI is an expensive technique compared to EEG and has some additional problems related to e.g. reliability of individual recordings. In addition, fMRI can not be performed in all patients, whereas EEG usually can. Thus, although potentially very powerful, much work remains to be done before individual EEG-fMRI recordings may be expected in clinical routine work-up.

Further development of neurological applications of multichannel EEG and EEG-MRI recordings requires close cooperation and considerable effort of neurologists, neurophysiologists and engineers. By using engineering, mathematical and
computational techniques, new developments may be expected in the future that can help solve clinical neurological problems. This thesis provides a step in this direction.