CHAPTER 9

Summary
The main part of this thesis focused on the influence of brain lesions on primary sensorimotor activity as studied with MEG (Chapters 2 to 5). MEG is a valuable clinical tool in the context of presurgical functional mapping, and usually describes the results of localizing the central sulcus or the sensorimotor cortex of the hand. However, apart from a localization tool, MEG can also provide more insight into alterations of sensorimotor cortical activity in the presence of intracranial lesions, and this had not been addressed in the available literature, especially with respect to the foot area.

In Chapter 2 we describe the results of posterior tibial nerve (PTN) stimulation in patients with a brain tumor, with special emphasis on interhemispheric differences of the different somatosensory evoked field (SEF) components in relation to clinical findings. MEG studies, using PTN SEFs in normal subjects, usually report four SEF components: at 37, 45, 60 and 75 ms, respectively. In our study, the underlying sources of these components were identified around the primary somatosensory (S1) foot area with dipole orientations rotating as a function of post-stimulus latency. In patients with intracranial lesions around the central sulcus (CS) we found that the main components were identified in the hemisphere contralateral to the stimulated nerve. Dipole location asymmetries were found, which is not an unexpected finding in the presence of space-occupying lesions, but the P45m dipole strength was also significantly increased in the affected hemisphere and the N60m component as well as in patients with motor deficits. This is the first report of increased neuromagnetic foot responses in the affected hemisphere of patients with lesions around the CS, especially in the presence of motor deficits. The findings suggest spatial and functional changes in the foot somatosensory network in the presence of intracranial lesions and could be used for further studies elucidating the somatosensory cortical activity changes in the presence of intracranial lesions.

In Chapter 3 we introduced a new source localization procedure (beamforming), to study whether movement-related oscillatory activity of the hand and foot is affected in patients with brain tumors around the CS. Voluntary movements are associated with suppression or event-related desynchronization (ERD) of the mu (7-11 Hz) and beta (13-30 Hz) rhythms in the contralateral sensorimotor areas of healthy subjects. Spatial mapping of the mu rhythm shows different sources in the primary somatosensory (S1) and primary motor (M1) cortex. The beta oscillations have been mainly observed in M1, but in S1 as well. In our study, we found that hand movements showed homotopic (i.e. activation somatotopically corresponding to the executed movement, e.g. hand movement – hand representation) and contralateral ERD in the sensorimotor cortex in the majority of cases for mu and to a lesser extent for beta rhythms. Foot movements showed an increased heterotopic distribution (i.e. activation not corresponding to the executed movement, e.g. foot movement – hand representation) with bilateral and ipsilateral ERD compared to hand movements. Despite the presence of a brain tumor, hand movements are usually localized in the hand area, but interestingly, movements of the foot showed a more complex spatial distribution. Possibly, a more widely distributed cortical motor network than the classic somatotopical distribution must explain heterotopic distribution of activation patterns.
A more detailed analysis of the influence of brain tumors on brain oscillations involved in motor control is described in Chapter 4. In the previous chapter we found that hand movements retain the normal functional-anatomical characteristics in brain tumor patients, however we also know that, at a different level, tumors may affect structural connectivity. Therefore, we studied whether the oscillatory activity associated with hand movements in M1 is affected in brain tumor patients without neurological deficit. We found a shift towards lower frequencies (‘slowing’), caused by an increase in mu and decrease in beta power both during resting state and during movements. This ‘slowing’ of oscillatory activity in resting state and during movement resembles findings in patients with monohemispheric stroke and Parkinson’s disease. Physiological modeling suggests that a loss of intracortical connectivity may account for our empirical findings. The findings may prelude clinical motor deficits and could be used as a potential diagnostic marker in the evaluation of glioma patients. Since the patients had no neurological deficits, the results also support studies demonstrating altered functional connectivity in remote areas. Finally, in Chapter 5 we describe the use of a clinical MEG protocol evaluating sensorimotor hand and foot function in a large group of heterogeneous patients with intracranial lesions and/or epilepsy to study whether differences in activation patterns between the hand and foot could be related to underlying pathology. We found that sensory stimulation (MN and PTN) is a very robust and effective way to identify S1 in all patient groups. Motor mapping of the hand is more successful than for the foot. The results of motor mapping showed in a small fraction of patients, ipsilateral localization, with differential occurrence in patient groups, especially with foot movements. The results may indicate differential functional reorganization in the presence of intracranial pathology. Multimodal imaging using MEG and fMRI has been described in a few studies, usually however, with different paradigms for both modalities, which could explain mismatches. In Chapter 6 we describe our results in eight healthy subjects using an identical MN stimulation paradigm for both MEG and fMRI to study which cortical areas, and in which temporal order, show activation. The results show that electrical MN stimulation with identical paradigms in MEG and fMRI does not give identical results, although in general there is good agreement between contralateral S1 and S2. Systematic localization differences were detected between the two functional imaging modalities, which vary from one brain region to another. The integration of MEG and fMRI shows systematic differences in terms of the spatial localization of specific active sources in the brain responses, which can be attributed to features intrinsic to each modality. This information should be taken into consideration, especially when the results are combined and used for e.g. intraoperative neuronavigation.

Anatomical structures, as identified by conventional MR- or CT-imaging can be used to localize functional brain areas, however, in the presence of infiltrating tumor, or other mass lesions, this may be challenging. The 3D-FLAIR sequence is frequently used in brain tumor surgery, especially in the treatment of low-grade gliomas to show the extent of tumor infiltration, but we found that 3D volume rendering showed a hypo-intense area at the CS region due to local signal intensity differences. To evaluate whether this structural
MRI technique could be used as an alternative imaging modality, we compared the structural and volume-rendered 3D FLAIR modality with functional and structural (MPRAGE) MRI in Chapter 7. We demonstrated the feasibility of a volume-rendered isotropic 3D FLAIR MR- scan, which may enhance the visualization of glioma in relation to the CS, however, CS identification was more successful on T1-weighted axial images. In selected cases, when functional imaging is not possible, volume rendering of the 3D FLAIR MR could be used to enhance 3D visibility of gliomas in relation to the CS as an alternative method in the presurgical and functional evaluation of neurosurgical patients.