NeuroImage: Clinical 10 (2016) 46–53

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Magnetoencephalographic study of hand and foot sensorimotor organization in 325 consecutive patients evaluated for tumor or epilepsy surgery

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ARTICLE INFO

Article history:
Received 14 August 2015
Received in revised form 30 October 2015
Accepted 4 November 2015
Available online 7 November 2015

Keywords:
Brain mapping
Brain neoplasms
Cortical reorganization
Epilepsy
Magnetoencephalography

ABSTRACT

Objectives: The presence of intracranial lesions or epilepsy may lead to functional reorganization and hemispheric lateralization. We applied a clinical magnetoencephalography (MEG) protocol for the localization of the contralateral and ipsilateral S1 and M1 of the foot and hand in patients with non-lesional epilepsy, stroke, developmental brain injury, traumatic brain injury and brain tumors. We investigated whether differences in activation patterns could be related to underlying pathology.
Methods: Using dipole fitting, we localized the sources underlying sensory and motor evoked magnetic fields (SEFs and MEFs) of both hands and feet following unilateral stimulation of the median nerve (MN) and posterior tibial nerve (PTN) in 325 consecutive patients. The primary motor cortex was localized using beamforming following a self-paced repetitive motor task for each hand and foot.
Results: The success rate for motor and sensory localization for the feet was significantly lower than for the hands (*motor_hand* 94.6% versus *motor_feet* 81.8%, $p < 0.001$; *sensory_hand* 95.3% versus *sensory_feet* 76.0%, $p < 0.001$). MN and PTN stimulation activated 86.6% in the contralateral S1, with ipsilateral activation < 0.5%. Motor cortex activation localized contralaterally in 76.1% (5.2% ipsilateral, 7.6% bilateral and 11.1% failures) of all motor MEG recordings. The ipsilateral motor responses were found in 43 (14%) out of 308 patients with motor recordings (range: 8.3–50%, depending on the underlying pathology), and had a higher occurrence in the foot than in the hand (*motor_foot 44.8%* versus *motor_hand 29.6%*, $p = 0.031$). Ipsilateral motor responses tended to be more frequent in patients with a history of stroke, traumatic brain injury (TBI) or developmental brain lesions ($p = 0.063$).
Conclusions: MEG localization of sensorimotor cortex activation was more successful for the hand compared to the foot. In patients with neural lesions, there were signs of brain reorganization as measured by more frequent ipsilateral motor cortical activation of the foot in addition to the traditional sensory and motor activation patterns in the contralateral hemisphere. The presence of ipsilateral neural reorganization, especially around the foot motor area, suggests that careful mapping of the hand and foot in both contralateral and ipsilateral hemispheres prior to surgery might minimize postoperative deficits.

1. Introduction

Magnetoencephalography (MEG) in combination with magnetic resonance imaging (MRI) has developed from a research tool into a useful and accepted clinical modality in the management of patients with epilepsy and brain tumors (Anderson et al., 2014; Castillo et al., 2004; Ganslandt et al., 1999; Knowlton, 2008). Using information obtained from MEG in the pre-surgical evaluation of epilepsy increases the success rate of epilepsy surgery (Knowlton, 2008), and MEG identification of the sensorimotor cortex has been validated by several groups using intraoperative measurements as a support to neurosurgical planning and intraoperative guidance of resection (Castillo et al., 2004; Ganslandt et al., 1999; Korvenoja et al., 2006; Schiffbauer et al., 2002; Tarapore et al., 2012).

Localization of the somatosensory cortex is typically achieved using dipole fitting applied to the 1st main peak of the somatosensory evoked field (SEF) following electrical simulation of the median (MN) or posterior tibial nerve (PTN). (Hari and Forss, 1999; Hari et al., 1996) The changes in oscillatory power in the beta band and mu rhythm following

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http://dx.doi.org/10.1016/j.nicl.2015.11.002

limb movement are typically localized using beam-former approaches (Cheyne et al., 2006; Hillebrand and Barnes, 2005), and have been shown to provide reliable preoperative localization of the hand motor cortex in patients with epilepsy and brain tumors (Nagarajan et al., 2008).

Localization of the hand primary motor and sensory cortex has been studied extensively using MEG, but less is known about the reliability of somatosensory and motor responses of the foot in a clinical setting, especially in the presence of intracranial lesions (Hari et al., 1996; Mäkelä et al., 2001; Nakamura et al., 1998; Willemse et al., 2007, 2010).

The clinical utility of MEG to map the sensorimotor cortex in surgical candidates depends on the ability to accurately and reliably lateralize and/or localize the primary sensorimotor cortex. In healthy subjects, the strongest activation is typically found contralateral to the side of stimulation or executed movement (Kakigi et al., 2000; Stippich et al., 2007). However, patients with brain lesions may have altered topographic organization of cortical functions, which can affect the results of non-invasive pre-surgical functional mapping (Lee et al., 2009; Staudt, 2010); the occurrence of such reorganization for patients with epilepsy is less clear, and may be related to underlying pathology. It is conceivable that different lesions affect the somatosensory network in different ways. Therefore, knowledge about the structural, as well as functional, changes in the network in the presence of intracranial lesions or epilepsy has clinical significance for pre-surgical planning.

In this paper, we retrospectively evaluated the results of our clinical MEG protocol in a large group of patients, eligible for epilepsy or tumor surgery, with respect to the success rate in locating the contralateral foot primary sensorimotor cortex in comparison to the hand. In addition, we studied whether differences between sensorimotor responses of the hand and foot could be related to underlying pathology.

2. Methods

The procedures with respect to recording and analysis of responses following electrical median nerve stimulation and hand movements have been described previously by Hillebrand et al. (2013).

2.1. Patients

Patients were referred from the VU University Medical Center but also externally from the University Medical Center Utrecht, Utrecht; Kempenhaeghe, Academic Center for Epileptology, Sleep Medicine and Neurological Learning & Development Disability, Heeze and SEIN, Dutch Epilepsy Clinics Foundation, The Netherlands. All 407 consecutive patients referred for clinical MEG from April 2010 until March 2014 were evaluated. All patients had at least MEG recordings with at least analysis of spontaneous activity. The majority of patients also had an additional motor and/or sensory paradigm tested as part of the routine clinical workup. Exclusion of 82 patients who had no sensory or motor paradigm tested, resulted in 325 patients for further analysis. The patients' diagnosis is summarized in Table 1.

As the patients were not subjected to procedures and were not required to follow rules of behavior other than routine clinical care, approval of the study by the institutional review board (Medical Ethical Research Committee, VU University Medical Center, Amsterdam, The Netherlands) and informed consent was not required according to the Dutch health law of February 26, 1998 (amended March 1, 2006), i.e. Wet medisch-wetenschappelijk onderzoek met mensen (WMO; Medical Research Involving Human Subjects Act), Division 1, Section 1.2.

2.2. MEG recordings

MEG recordings were obtained using a 306-channel whole-head neuro-magnetometer (Elekta Neuromag Oy, Helsinki, Finland) with subjects lying inside a magnetically shielded room during MEG recordings (Vacuumschmelze GmbH, Hanau, Germany). The head position relative to the MEG sensors was recorded continuously using the signals from four or five head-localization coils. The positions of the coils, as well as the outline of the participants scalp (~500 points), were digitized using a 3D digitizer (3Space Fastrak, Polhemus, Colchester, VT, USA). This scalp surface was used for co-registration with the patients anatomical MRI.

Table 1
Diagnosis for all patients.

Diagnosis	N_{all} (%)	$N_{included}$ (%)
Non-lesional epilepsy	168 (41.3)	134 (41.2)
Focal cortical dysplasia	50 (12.3)	45 (13.8)
Low grade glioma	50 (12.3)	39 (12)
Mesiotemporal gliosis	40 (9.8)	26 (8)
Stroke	19 (4.7)	18 (5.5)
DNET	11 (2.7)	9 (2.8)
Cavernoma	11 (2.7)	7 (2.2)
Traumatic brain injury	5 (1.2)	4 (1.2)
Developmental disorder	5 (1.2)	4 (1.2)
Tuberous sclerosis	5 (1.2)	2 (0.6)
High grade glioma	4 (1.0)	1 (0.3)
Cyst	4 (1.0)	4 (1.2)
Other	35 (8.6)	32 (9.8)
Total	407 (100)	325 (100)

DNET: dysembryoplastic neo-epithelial tumor.

2.3. Anatomical MRI and co-registration

Structural MR-images were available from previous studies or otherwise acquired with a 1.5 or 3.0 T MR scanner, where the axial slice distance varied from 1.5 to 3 mm. Co-registration of these T1-weighted MRIs with the MEG data was achieved by using surface matching software developed by one of the authors (AH), resulting in an estimated co-registration accuracy of approximately 4 mm (Whalen et al., 2008). A single best fitting sphere was fitted to the outline of the scalp as obtained from the co-registered MRI, which was used as a volume conductor model for the dipole fitting and beam-former analysis described below.

2.4. Somatosensory stimulation

MEG responses to electrical stimulation of the left and right median nerve (MN) and the left and right posterior tibial nerve (PTN) were recorded. Constant current square wave pulses (2 Hz, 0.2 ms duration, 500 epochs) were delivered trans-cutaneous at the wrist (MN) and the ankle (PTN) just above motor threshold.

2.5. Motor task

Subjects performed voluntary hand movements consisting of slow, unilateral, self-paced repetitive non-clenching opening and closing of the hand at about 1 Hz. The movements were performed for 15 repeats of 10 s movement followed by 10 s without movement. With foot movements patients were instructed to alternate flexion and extension at the ankle at about 1 Hz. Movement instructions were presented to the subject using a brief tone (movement) or brief burst of white noise (no movement). Movements were monitored on camera. Left and right movements of the hand and foot were performed in separate runs.

2.6. Analysis

The MEG recordings were analyzed according to standard clinical procedures for pre-surgical mapping of somatosensory and motor cortex by an experienced MEG/EEG technician, and evaluated by a team consisting of two experienced clinical neurophysiologists (HR and CJS), MEG/EEG technicians and physicists (AH).