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Cerebro-muscular and cerebro-cerebral coherence in patients with pre- and perinatally acquired unilateral brain lesions

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The cerebral networks involved in motor control were analyzed in four young hemi-paretic patients (21–25 years) with pre- and perinatally acquired brain lesions (3 with left periventricular brain lesions, 1 with left schizencephaly) by means of MEG source coherence analysis.

Previous TMS and fMRI studies on the same patients had investigated their residual ability to move the paretic hand by means of a reorganized primary motor cortex (M1) representation in the contralesional hemisphere. The purpose of this study is to identify the effects of such a cerebral reorganization and the related dynamic aspects which allow the patients to move the paretic arm.

Patients underwent a pinch grip task (1-N isometric contraction) using their paretic and non-paretic hands in alternation. MEG signals were recorded using a whole-head 151-channel magnetoencephalograph. EMG was simultaneously recorded as a reference for coherence calculations. 3D coherence mapping was performed in the β frequency range (14–30 Hz).

This approach confirmed the relocation of motor functions from the lesioned (left) to the contralesional (right) hemisphere. In case of left, non-paretic pinch grip, coherent activity originated from contralateral (right) M1 exclusively. In the case of right (paretic) grip, coherent activity in ipsilateral M1 as well as significant coherence of ipsilateral cerebellum with both muscle activity and M1 itself was detected in 3 out of 4 subjects. As expected, the patient with no cerebellar involvement during paretic hand contraction showed the worst motor performance in the grip task.

Coupling direction analysis demonstrated that throughout pinch grip the coupling direction goes from M1 to cerebellum.

The present study verified the assumption that the intact hemisphere takes over motor control from the paretic (ipsilateral) hand in the presence of early unilateral brain lesion. Moreover, the role of cerebellum in motor deficit compensation and its close interaction with ipsilateral primary motor cortex was studied in detail.

Keywords: MEG; Coherence; Brain lesions; Oscillations; Synchronization

Introduction

Brain activity is at least partially to be considered as a continuous transmission of frequency coded information. This approach has gained a general consensus in different neuroscience fields during the last years (Mima et al., 2001a, 2001b; Gross et al., 2001; Fox et al., 2005). In particular, in sensorimotor neurophysiology it is well known that motor activities involve distributed neuronal pools whose connection paths often extend over the whole brain (Gross et al., 2003). Neural mechanisms underlying preparation for movement and movement itself have been extensively studied by means of different imaging techniques (Salenius et al., 1997; Hülsmann et al., 2003; Hummel et al., 2005; Gerloff et al., 2006). While fMRI can provide excellent spatial resolution but only a rough idea of timing in cortical activities (Friston and Jezzard, 1994; Friston et al., 2003), MEG and EEG can offer an acceptable spatial resolution with a practically infinite time resolution (Hämäläinen, 1992). This is utterly important for the study of circuits which have an extension of many centimetres and which involve dynamics as fast as tens of milliseconds (Kilner et al., 2000).

Abbreviations: MEG, magnetoencephalography; EMG, electromiogram; M1, primary motor cortex; Cb, cerebellum; CMCoh, cerebro-muscular coherence; LCMVB, linear constrained minimum variance beamformer.

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Recently, spatial filter applications in MEG and EEG analysis (van Veen et al., 1997; Robinson and Vrba, 1997, 2001; Pasqual-Marqui, 2002) have proved to be a valuable tool to pass from the 2D space of the sensor surface to the 3D volume within the skull. These techniques can be used to investigate data in both time and frequency domain. Spatial filters in frequency space can successfully identify cortical areas which are coherent with a reference signal either internal or external to the brain (Gross et al., 2001; Schnitzler and Gross, 2005). In particular, the frequency coded relationship in the β range has been extensively studied by means of corticomuscular coherence (CMCoh) analysis (Conway et al., 1995). CMCoh is considered to reflect corticospinal activity during motor performance. Previous studies in humans (Mima and Hallett, 1999; Kilner et al., 2000; Mima et al., 2000; Gross et al., 2001; Mima et al., 2001a, 2001b) and non-human primates (Soteropoulos and Baker, 2006) have found the β frequency range (14–30 Hz) to be the frequency band most active during communication between M1 and muscles. Starting from this basis, studies on coherent oscillations of brain areas in the frequency domain by means of MEG have provided information on functional brain dynamics, providing new insights into motor system circuits (Pollok et al., 2003). In addition to the analysis on normal subjects, further coherence investigation has probed functional abnormalities in many pathological subjects with motor-deficits (Timmermann et al., 2003; Pollok et al., 2003).

In the present paper, the mechanisms underlying cerebral activity in four hemi-paretic patients while performing a grip task are reported. Underlying lesions were unilateral periventricular lesions acquired during pre- and perinatal period in three cases and schizencephaly in one. Previous clinical reports, TMS, MEG and fMRI studies on the same cohort of patients (Gerloff et al., 2006; Staudt et al., 2002, Staudt et al., 2004) have provided evidence that, as in healthy subjects, the patients' non-paretic hands were controlled by contralateral M1. However, corticospinal control over the paretic hand was exerted from the contralesional hemisphere, i.e. M1 ipsilateral to the grip hand.

To our knowledge the reorganization effects of motor circuitries in the contralesional hemisphere have never been studied in their dynamic aspect. Differences in motor system behavior are expected when the paretic hand is in use. In particular, we expect the reorganization process in these patients to be an anomalous organization of motor control for the impaired part of the body. Motor control activity is mainly located in the contralesional hemisphere, ipsilateral to the paretic hand. Such patients, in fact, have never been able to develop a normal contralateralization process. Ipsilateral cortico-spinal fibers for motor control are also present in normal subjects during perinatal stage, but they rapidly decay at a functional level because of the contralateralization process (Eyre et al., 2000). We expect, however, the process underlying motor control for the paretic hand to be different from the process for the non-paretic hand. More advanced procedures for the localization of coherently oscillating sources than in the study by Gerloff et al. (2006) were applied. In this way further results about the frequency coded mechanism underlying the organization and managing movement of the paretic hand were anticipated. Since in all patients both hands were able to move, despite the severe lesion in the left hemisphere, radical changes in the spatial organization of the active cortical areas were expected, as well as important changes in the connectivity patterns.

Subjects and methods

Patients

Four patients (mean age: 22 years range: 4 years; males: 2, females: 2) with congenital right hemiparesis were included in the study after giving informed consent. The patients suffered from pre- and perinatally acquired unilateral periventricular lesions having occurred in the early third trimenon of gestation (Fig. 1). Patient #2 was diagnosed with left hemispheric schizencephaly.

Schizencephaly is a brain malformation consisting of an abnormal cleft connecting the lateral ventricle with the subarachnoid space lined by abnormal (polymicrogyroc) cortex. All patients revealed a right hand impairment of moderate severity, showing an incomplete performance of sequential finger movements in a video-documented neurological examination (Staudt et al., 2002). Patients #1, 2 and 3 showed a right hand impairment classified by mark '2', which corresponds to slow/incomplete performance of sequential finger movements in a video-documented neurological examination. Patient #4 showed a hand impairment level marked with '3' which stands for 'complete inability to perform independent movements'. Mark '1' stands for 'normal performance'. The clinical data including a hand motor score are given in Table 1. The protocol was approved by the local ethics committee (Ethik-Kommission der Medizinischen Fakultaet der Eberhard-Karls-Universitaet, Tuebingen).

Patients sat on a comfortable chair with their arms placed on a rest and produced a precision grip by opposing thumb and index finger of the right or left hand in subsequent epochs. The patients had to generate a grip force of 1 N (isometric contraction) that was measured by a strain gauge whose output was recorded and fed back to the subjects by a visual signal every 12.5 s for 2 s. Particularly, the force generated by the subjects controlled the extent of a white rectangle that was projected onto a screen in the shielded room using a video beamer. A black rectangle corresponding to a force of 1 N was presented as reference.

MEG recording and pre-analysis

Magnetic brain activity and EMG activity (Fig. 2) were recorded during 25 intervals of 10.5 s duration interspersed between presentations of visual feedback signals. During the experiment, patients gazed at a fixation cross presented on the screen in front of them. MEG signals were recorded using a whole head magnetoencephalograph (151 channels Omega, VSM, Vancouver, Canada). EMG activity was recorded from four pairs of electrodes (In Vivo Metric, Healdsburg, USA) placed on the thenar (M. abductor pollicis brevis, APB) and forearm (M. extensor digitorum, ED) bilaterally. ED was also recorded because during thumb–index finger precision grip this muscle exerts a stabilizing effect on middle to little fingers. All signals were band-pass filtered with lower and upper frequencies of 0.1 and 108 Hz, amplified and digitized with a sampling rate of 312.5 Hz.

After removing the offset for all channels, i.e. the average activity across single trials, the EMG signal was rectified. Then, for each pair of MEG signals $m_i(t)$ and $m_j(t)$, complex spectra were calculated. A Fast Fourier Transform with a Hanning windowing over the single recording intervals was computed. FFT was calculated with a resolution of 512 points. With our digitization rate, such FFT resolution implies a frequency resolution of 0.61 Hz. The windows were overlapped by half of the FFT window. Successively, cross