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Motor representation areas in epileptic patients with focal motor seizures: A TMS study

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Summary
Purpose: This study used TMS mapping to investigate the motor representation of the abductor pollicis brevis (APB) muscles in a group of patients with focal epilepsy originating in central or pre-central region.
Methods: Eight epileptic patients and eight control subjects participated in the study. The coil was moved in 1.5-cm steps along a grid drawn on the subject's skull over the motor cortex of both hemispheres. At each site, six APB motor responses (evoked by TMS at 1.2 times the resting motor threshold) were recorded and averaged. The peak-to-peak amplitude was measured and plotted against the mediolateral and anteroposterior coil positions. The area of each APB muscle representation was measured and the position of the optimal point was calculated.
Results: The resting motor threshold was increased bilaterally in epileptic patients. The maps were distorted in most patients (but not in control subjects), as evidenced by an off-centre optimal point. Interhemispheric differences in APB map areas were greater in patients than in control subjects. However, whether these increases in map area were on the epileptic side or on healthy side depended on the given subject.
Conclusions: The changes in APB representation observed in epileptic patients demonstrate that reorganization occurs within the motor cortex. The heterogeneity of the present results is probably related to different locations of the epileptogenic and/or lesional areas and to a variety of compensatory phenomena that may occur, notably with respect to the disease duration.

Introduction

A growing body of evidence from animal models (Merzenich et al., 1984; Donoghue et al., 1990; Merzenich and Jenkins, 1993; Donoghue, 1995; Xerri et al., 1998) and neurophys-

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iological and neuroimaging studies in humans (Nelles et al., 1999; Pascual-Leone et al., 1999; Cramer et al., 2000; Hallett, 2001) supports the notion that the central nervous system undergoes changes and adaptations throughout life. Among reorganizational processes underlying this plasticity, the unmasking of existing but latent corticocortical connections by removal local tonic inhibition (Jacobs and Donoghue, 1991; Huntley, 1997; Sanes and Donoghue, 1997), the strengthening or weakening of existing synapses by processes such as long-term potentiation (LTP) or long-term depression (LTD) (Hess et al., 1996; Hess and Donoghue, 1996) and even sprouting of new dendritic connections and formation of new synapses (Toni et al., 1999) seem to be involved.

Transcranial magnetic stimulation (TMS) is a non-painful tool for studying brain function. Single- and double-pulse TMS allow to investigate the modulation of motor cortex excitability and the reorganization of topographic maps in the human sensorimotor cortex that may occur following motor learning (Liepert et al., 1998; Tyc et al., 2005) or injury to the peripheral or central nervous system (Cohen et al., 1991a). Changes in muscle map area are also present in certain diseases characterized by a disruption of motor cortex excitability. The cortical representation of hand muscles is modified in the affected hemisphere and sometimes in the contralateral hemisphere in focal hand dystonia (Byrnes et al., 1998) and primary tremor (Byrnes et al., 2005). In patients with hemi-Parkinson's disease, interhemispheric asymmetry in the first dorsal interosseous (FDI) cortical representation has been revealed by TMS mapping (Filippi et al., 2001), with a decreased map area in the clinically affected hemisphere during motor imagery. More recently, a shift in the map position was shown to occur in Parkinson's disease, and the interhemispheric difference in position was correlated with the severity of the symptoms (Thickbroom et al., 2006).

In epilepsy, TMS studies have mainly focused on excitability parameters and inhibitory phenomena by using motor threshold (MT), cortical silent period (CSP) and intra-cortical inhibition (ICI) and facilitation (ICF) techniques (for review, see Ziemann et al., 1998; Tassinari et al., 2003). In terms of functional reorganization, it has been demonstrated that stimulation of one side of the scalp evoked bilateral muscle responses in patients who had undergone resection of one hemisphere for the treatment of intractable epilepsy (Benecke et al., 1991; Cohen et al., 1991b). In one epileptic patient with focal dysplasia located in the central sulcus, evidence of the reorganization of motor function has been obtained by TMS mapping (Macdonell et al., 1999); TMS pulses in the affected hemisphere were unable to evoke any FDI MEPs. Group studies using functional magnetic resonance imaging (fMRI) have reported several cases of functional motor reorganization in epileptic patients with focal cortical dysplasia (Marusic et al., 2002; Janszky et al., 2003). However, some authors have also suggested that function might be conserved within dysplasic regions in several cases. However, to date, TMS mapping studies of the reorganization of motor function in groups of epileptic patients (compared with healthy subjects) have not been performed.

This study used TMS mapping to investigate the motor representation of distal arm muscles in a group of patients with unilateral focal motor epilepsy originating from central or pre-central regions. Our hypothesis was that the motor cortex undergoes representational adaptations in patients for whom the epileptogenic focus can be reliably localized within the motor cortex or involves a motor area.

Methods

We studied eight patients presenting epileptic disorders (four men and four women, mean age 28.9 ± 2.8 years and whose clinical features are summarized in Table 1) and eight healthy control subjects (four men and four women, mean age 31.8 ± 2.7 years). No seizure occurred during the 48 h preceding the experiment. To be included in the study, patients had to be free of any sensory or motor deficits other than epileptic seizures. Epileptic symptoms were assessed by an EEG and video recording over a 48 to 72-h period. Moreover, all patients underwent magnetic resonance imaging (MRI) as part of their clinical evaluation. In all patients, electroclinical findings suggested focal epilepsy originated in sensory and motor regions, and epileptic symptoms were sensorimotor. The upper limbs were affected in all but two patients. Among these two remaining patients, one had clinical signs restricted to the head and face (P1) while the lower limb was affected in the other (P6). The MRI examination revealed the presence of a dysplasia in four patients (P4, P5, P7 and P8). Three had a centro-rolandic dysplasia, and the last one an ulegyria. Patient P6 had an oligodendroglioma. No visible dysplasia or lesion was seen in patients P1 to P3 in whom localization of the epileptic locus was inferred from EEG exploration. All subjects and patients gave their informed, written consent to participation in the study, in accordance with the declaration of Helsinki and current French and European legislation. The experimental protocol was approved by the local ethics committee.

EMG recordings

Pairs of Ag—AgCl surface electrodes were placed over the belly of the right and left abductor pollicis brevis (APB) muscles. The diameter of the electrode's recording surface was 4 mm. Electrodes were attached to the skin with double-sided adhesive film and connected to optically isolated preamplifiers. A large reference electrode connected to the preamplifiers' common input was placed around the wrist. The EMG signals were amplified (1000×), high-passed at 10 Hz and low-passed at 1 kHz prior to sampling at 2 kHz with an A/D converter (micro 1401 MKII, Cambridge Electronic Design, UK).

Mapping the MCx with transcranial magnetic stimulation

Magnetic stimuli were applied over the scalp using a MagStim 200 electromagnetic stimulator with a figure-of-eight coil (MagStim Company, Whitland, UK). The external diameter of each half of the coil was 9.5 cm. The coil was held tangentially to the scalp, contralateral to the explored limb, at an angle of 45° to the sagittal plane with the handle pointing posteriorly. The subject wore a snugly fitting polyester cap on which a grid was drawn over the sensorimotor areas of the two hemispheres. The intersection points of the grid lines were spaced 1.5 cm apart and served as a visual reference for coil positioning by the experimenter. The coordinates of each intersection point on the grid were measured relative to the vertex. The mediolateral coordinate was measured as the distance from a reference line connecting the nasion to the inion, passing through the vertex. The anteroposterior coordinated was measured as the distance from the interaural line passing through the vertex. The coordinate system was numbered such that mediolateral coordinates were negative for the left hemisphere and positive for the right hemisphere. The anteroposterior coordinates were positive going towards the nose and negative going towards the occiput.