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Lateralization of cortical negative motor areas

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HIGHLIGHTS

- Negative motor areas were characterized with direct electrical brain stimulation in epilepsy patients during pre-surgical evaluation.
- The lateral fronto-central negative motor area controls contralateral upper limb movements.
- The mesial frontal negative motor area controls bilateral upper limb movements.

ABSTRACT

Objective: The lateral and mesial aspects of the central and frontal cortex were studied by direct electrical stimulation of the cortex in epilepsy surgery candidates in order to determine the localization of unilateral and bilateral negative motor responses.
Methods: Results of electrical cortical stimulation were examined in epilepsy surgery candidates in whom invasive electrodes were implanted. The exact localization of subdural electrodes was defined by fusion of 3-dimensional reconstructed MRI and CT images in 13 patients and by analysis of plane skull X-rays and intraoperative visual localization of the electrodes in another 7 patients.
Results: Results of electrical stimulation of the cortex were evaluated in a total of 128 patients in whom invasive electrodes were implanted for planning resective epilepsy surgery. Twenty patients, in whom negative motor responses were obtained, were included in the study. Bilateral upper limb negative motor responses were more often elicited from stimulation of the mesial frontal cortex whereas stimulation of the lateral central cortex leads to contralateral upper limb negative motor responses ($p < 0.0001$). Bilateral negative motor responses were exclusively found in the superior frontal gyrus whereas contralateral negative motor responses localized predominantly in the anterior part of the precentral gyrus ($p < 0.0001$).
Conclusions: Exact localization using 3-D fusion methods revealed that negative motor areas are widely distributed throughout the precentral gyrus and the mesial fronto-central cortex showing functional differences with regard to unilateral and bilateral upper limb representation.
Significance: The lateral fronto-central negative motor area serves predominantly contralateral upper limb motor control whereas the mesial frontal negative motor area represents bilateral upper limb movement control.

Abbreviations: NMR, negative motor response; PMA, primary motor area; PNMA, primary negative motor area; SSMA, supplementary sensorimotor area; SNMA, supplementary negative motor area; BP, bereitschaftspotential; SFG, superior frontal gyrus; PCG, precentral gyrus.

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1. Introduction

It is well established since the pioneering experiments of Penfield and Jasper that electrical stimulation of fronto-central areas of the human cortex may elicit paralysis or muscle atonia (Penfield and Jasper, 1954). These so called negative motor responses are defined as the inability to perform or sustain a voluntary movement with preserved consciousness when the cortex was stimulated at a stimulus intensity that did not produce any positive sign or symptom and was not associated with any afterdischarge (Lüders et al., 1995). Primary negative motor areas have been located by cortical electrical stimulation in the inferior frontal gyrus, just anterior to the primary facial motor area (Penfield and Jasper, 1954; Lüders et al., 1987, 1992; Lüders et al., 1995). This region was designated as the primary negative motor area with respect to the adjacent primary motor area. A further region was localized to the mesial part of the superior frontal gyrus and was designated as supplementary negative motor area with respect to the adjacent supplementary sensorimotor area (Fried et al., 1991; Lim et al., 1994). Recently, a broad distribution of the negative motor areas within the perirolandic region was demonstrated (Mikuni et al., 2006). In addition to electrical cortical stimulation, negative motor responses can also be elicited by epileptic seizure activity as for instance in negative myoclonus and in focal akinetic seizures (Noachtar et al., 1997; Noachtar and Lüders, 1999, 2000; Matsumoto et al., 2000). The localization of the seizure onset is located in close vicinity to negative motor areas in patients with focal akinetic seizures (Tinuper et al., 1987; Noachtar and Lüders, 1999; Villani et al., 2006). In addition, negative epileptic myoclonus is associated with hyperperfusion in the medial frontal gyrus as demonstrated by Single Photon Emission Computerized Tomography (SPECT) (Baumgartner et al., 1996). The mechanisms by which negative motor responses are generated have not yet been clarified. Electrophysiological studies and transcranial magnetic stimulation suggest that the silent period elicited by cortical activation is responsible for the generation of negative epileptic myoclonus (Rubboli et al., 2006). For the primary motor areas, it has been shown that inhibitory mechanism of the primary sensorimotor areas play an important role in eliciting negative motor phenomena (Ikeda et al., 2000).

This study investigated the topography of negative motor areas as identified by electrical stimulation comparing unilateral vs. bilateral upper limb motor inhibition with the localization of the subdural (epicortical) electrodes using 3-D reconstructed images of the cerebral cortex.

2. Patients and methods

2.1. Patients

Database screening of invasive recordings of patients with medically intractable focal epilepsy was performed between the years 1997 and 2008 and revealed a total of 20 out of 128 patients in whom negative motor responses were documented. The mean age at stimulation was 31 ± 11 years (range 9–53 years). All patients gave their written informed consent for the subdural implantation and electrical stimulation of the cortex. The lateral brain surface was studied in all of the 20 patients whereas the medial surface was examined in 7 patients. The demographic data of the patients are listed in Table 1. All patients gave their written consent to collection and analysis of the data obtained during EEG video-monitoring for scientific purposes.

2.2. Implantation of the subdural electrodes

Subdural electrodes were implanted into 20 patients referred for invasive presurgical evaluation in order to locate the epileptogenic zone and eloquent cortex. The exact localization of electrodes to be implanted was determined by non-invasive presurgical investigation techniques as EEG video monitoring, MRI, Positron Emission Tomography (PET), Single Photon Emission Computerized Tomography (SPECT) and clinical neuropsychology. Inert silicon grids and strips harbouring platinum electrode contacts of 3 mm in diameter were implanted subdurally. The centre to centre interelectrode distance was 10 mm.

2.3. Two-dimensional skull X-ray

Skull X-ray films were obtained after implantation in seven patients. The location of electrodes was established using an ubiquitous approach to estimate craniocerebral topography described previously (Lang, 1979; Gray, 1989). This method was transferred and applied for the skull X-ray films to determine the location. The exact localization was then compared and, if necessary, modified with the intraoperatively visible position of the electrode during the resection procedure.

Table 1
Demographic data of the patients.

Patient #	Diagnosis	Aetiology	Age at stimulation	Gender	Dominance
1	Lt. frontal epilepsy	Cortical dysplasia	39	M	Lt.
2	Lt. temporal epilepsy	Unknown	33	M	Lt.
3	Rt. parietal epilepsy	Unknown	9	F	Lt.
4	Rt. paracentral epilepsy	Gliosis	28	F	Lt.
5	Lt. frontal epilepsy	Cortical dysplasia	15	M	Lt.
6	Rt. frontal epilepsy	Cortical dysplasia	28	M	Lt.
7	Rt. frontal epilepsy	Cortical dysplasia	32	M	Lt.
8	Lt. frontal epilepsy	Gliosis	24	M	Rt.
9	Rt. parietal epilepsy	Cortical dysplasia	21	F	Lt.
10	Rt. paracentral epilepsy	Cortical dysplasia	17	M	Lt.
11	Lt. frontal epilepsy	Unknown	34	M	Rt.
12	Lt. frontal epilepsy	Reactive astrogliosis	44	M	Lt.
13	Rt. frontal epilepsy	Gangliogloma	32	M	Lt.
14	Lt. frontal epilepsy	Cortical dysplasia	33	F	Lt.
15	Lt. frontal and parietal epilepsy	Unknown	36	M	Lt.
16	Lt. temporal epilepsy	Posttraumatic contusion	53	F	Lt.
17	Rt. frontal epilepsy	Hamartoma	25	F	Lt.
18	Lt. frontal epilepsy	Cortical dysplasia	45	F	Lt.
19	Rt. frontal epilepsy	Unknown	41	F	Lt.
20	Lt. frontal epilepsy	Cortical dysplasia	26	M	Rt.