ELSEVIER

Clinical Neurophysiology 117 (2006) 33–40

www.elsevier.com/locate/clinph

Evidence for a wide distribution of negative motor areas in the perirolandic cortex

Nobuhiro Mikuni[a,*], Shinji Ohara[c], Akio Ikeda[b,c], Naoki Hayashi[a], Namiko Nishida[a], Junya Taki[a,c], Rei Enatsu[a], Riki Matsumoto[b], Hiroshi Shibasaki[b,c,1], Nobuo Hashimoto[a]

[a]*Department of Neurosurgery, Kyoto University Graduate School of Medicine, 54 kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan*
[b]*Human Brain Research Center, Kyoto University Graduate School of Medicine, Kyoto, Japan*
[c]*Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, Japan*

Accepted 23 August 2005
Available online 28 November 2005

Abstract

Objective: The perirolandic regions were studied by extensive electrical stimulation to clarify the topography and somatotopic distribution of negative motor areas (NMAs) and examine the clinical significance of these areas.
Methods: We evaluated the cortical function elicited by electrical stimulation in 30 patients with tumors or intractable epilepsy. The somatotopic distribution of NMAs was examined by localizing these regions using Talairach's bicommissural reference system. NMAs within the lesions of two patients were removed under local anesthesia.
Results: We obtained negative motor responses following the stimulation of 30 electrodes in 15 patients. On the lateral brain surface, the majority of NMAs for the upper extremities were distributed broadly throughout the premotor cortex, while NMAs for the tongue were only found in the inferior frontal gyrus of the dominant hemisphere. During removal of the NMAs within the lesions of two patients, we documented transient hand clumsiness in one patient.
Conclusions: NMAs were widely distributed throughout the perirolandic area, as well as the previously reported regions in the inferior frontal gyrus. These areas likely function in the control of skilled movements; dysfunction of such movements transiently follows resection of these regions, but is subsequently well compensated for after surgery.
Significance: The localization and consequences of resection of NMAs suggests their clinical significance in motor control.

Keywords: Negative motor area; Human; Location; Surgical resection; Electrical stimulation

1. Introduction

Direct electrical stimulation of cortex is one of the most reliable methods for mapping the functions of different cortical areas in humans. Electrical stimulation of the primary motor area elicits stimulation-evoked movements. In contrast, negative motor areas (NMAs) are defined as region in which electrical stimulation induces negative motor responses, an inability to perform voluntary movements or to sustain voluntary muscle contractions without a preceding positive motor response that occurs in the absence of a loss of awareness. Primary NMAs have been defined in the inferior frontal gyrus, just anterior to the primary facial motor area (Luders et al., 1987, 1992, 1995; Penfield and Jasper, 1954). Subsequently, supplementary NMAs were identified at a medial position in the superior frontal gyrus (Lim et al., 1994). The neurophysiological mechanisms governing negative motor responses remain unknown. To determine whether interference with reading resulted from speech deficits or negative motor effects, early studies of NMAs primarily examined selected areas that were positive for the reading aloud test (Lim et al., 1994; Luders et al., 1987, 1992, 1995). Therefore, a number of NMAs may also exist in other cortical areas that have yet to

* Corresponding authorTel.: +81 75 751 3459; fax: +81 75 752 9501.
E-mail address: mikunin@kuhp.kyoto-u.ac.jp (N. Mikuni).
[1] Present address: Takeda General Hospital, Kyoto, Japan.

1388-2457/$30.00 © 2005 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.clinph.2005.08.021

be recognized. To clarify the location and clinical significance of such NMAs, we examined the characteristics of negative motor responses elicited by electrical stimulation of the perirolandic regions. Furthermore, we documented the neurological symptoms caused by resection of NMAs under local anesthesia in selected patients.

Recently, a mirror neuron system was described in the posterior part of the inferior frontal gyrus in monkeys. This region plays a fundamental role in observation, understanding, and imitation of actions (Rizzolatti and Craighero, 2004). As the similarities and dissimilarities between this mirror neuron system and NMAs has not yet been examined in detail in humans, we examine that relationship here.

2. Patients and methods

Thirty patients with perirolandic lesions between the ages of 18 and 55 years were studied. This population included 18 individuals with brain tumors (diffuse or anaplastic gliomas) and 11 patients with epileptogenic cortical dysplasias. The lateral brain surface was studied in 26 patients, while the medial surface was examined in four patients. Tumors with an apparent anatomical shift on MRI were excluded because of possible anatomical distortion of the brain architecture by the lesion. Wada testing demonstrated that the lesions were localized on the dominant side in 15 patients (the right hemisphere in two patients and the left in 13 patients) and on the non-dominant side in 15 patients (the right hemisphere in 13 patients and the left in two patients). One patient displayed clinical deficits, with mild central facial palsy and clumsiness of the right hand due to a brain tumor of the precentral gyrus. No apparent clinical deficits were observed in the other patients.

2.1. Functional mapping

Subdural electrode grids were implanted into 16 patients (11 with epilepsy and five with tumors) to define epileptogenic areas and/or cortical functions. In the remaining 14 patients, all of whom had tumors in the perirolandic area, intraoperatively electrical stimulation was used to perform functional mapping. These procedures were approved by the Ethical Committee of Kyoto University Graduate School of Medicine (No. 79 and No. 443). Written informed consent was obtained from each patient. In all patients, negative motor responses were evaluated using 16–60 contact subdural grid electrodes, which covered the perirolandic area. All contacts, platinum constructs measuring 3 mm in diameter, had a center-to-center interelectrode distance of 1 cm. In one patient with epilepsy, custom subdural grid electrodes with an 8 mm center-to-center interelectrode distance were used for detailed functional mapping. A 50 Hz electric current was delivered in square waves of alternating polarity at a duration of 0.3 ms to a pair of subdural electrodes for 1 s. The current was then increased in 1 mA increments from the starting value of 2 mA to a maximum of 15 mA. The duration of electrical stimulation was then increased until reaching a maximum of 5 s. If after discharges were induced, the test was repeated at either the same current or a current reduced by 0.5–1 mA. At maximal current, each pair of electrodes was tested for stimulation-evoked movements, a negative motor response, and a language function.

Negative motor responses were defined as the inability to perform voluntary movement or to sustain voluntary muscle contraction without a loss of awareness upon stimulation of the cortex at an intensity that did not produce any preceding positive signs or symptoms and was not associated with the generation of afterdischarges (Luders et al., 1987, 1992, 1995). Patients were first asked either to stick out their tongue and move it from side to side or to perform bilateral, alternating rapid hand or foot movements requiring sustained muscle contraction of the distal extremities. After approximately 5 s of movement, we began electric stimulation without notification of the patient. If an inability to perform voluntary movements or to sustain voluntary muscle contractions could be confirmed by the examiner, elicited responses were checked at least twice to ensure reproducibility. Language functions, assessed by reading a paragraph, were then examined. If speech arrest or slowing occurred during stimulation, additional speech functions, including spontaneous speech, naming, and comprehension, were evaluated to determine if the speech dysfunction was due to a negative motor response. After determining which of the paired electrodes induced neurological deficits upon bipolar stimulation, referential stimulation localized each area more precisely and specified the nature of the function located at that electrode. Although all procedures were performed for all patients, the limited time of awake surgery only allowed the evaluation of negative motor responses at selected area surrounding the lesion. All elicited responses were recorded on video and later confirmed.

2.2. Localization of the subdural electrodes

The anatomical relationship of each electrode with the Sylvian fissure, the central sulcus, the precentral sulcus, and the lesion was determined by intraoperative photography. To identify the location of the subdural electrodes statistically, we used Talairach's bicommissural reference system on sagittal MRI sections (Talairach and Tournoux, 1988). The anterior commissure–posterior commissure (AC–PC) line, defined on median sagittal MRI sections, was reproduced on other sagittal sections (3 mm thick) with lines drawn perpendicular to the AC–PC line at the anterior (VAC) and posterior (VPC) commissures. The central sulcus was defined in relation to the VPC and the VAC on midsagittal and most lateral sections, respectively. A lateral skull radiograph and median sagittal MRI section were then traced on paper. Each electrode, identified on an intraoperative photograph, could be localized on according to its