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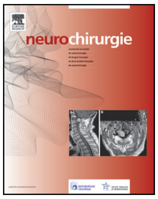

Original article

Intraoperative identification of the negative motor network during awake surgery to prevent deficit following brain resection in premotor regions

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ABSTRACT

Introduction. – Surgical resection in premotor areas can lead to supplementary motor area syndrome as well as a permanent deficit. However, recent findings suggest a putative role of the negative motor network in those dysfunctions. Our objective was to compare the functional results in two groups of adult patients who underwent the resection of a frontal glioma with and without resection of the negative motor networks.
Material and methods. – Twelve patients (total of 13 surgeries) were selected for awake surgery for a frontal glioma. Negative motor responses were monitored during surgery at the cortical and subcortical levels. Sites eliciting negative motor responses were first identified then spared ($n = 8$) or removed ($n = 5$) upon oncological requirements.
Results. – In the group with removal of the negative motor network ($n = 5$), all patients presented a complete supplementary motor area syndrome with akinesia and mutism. At 3 months, they all presented bimanual coordination dysfunction and fine movement disorders. In the group with preservation of the negative motor network ($n = 8$), all patients presented transient and slight disorders of speech or upper limb, they all recovered completely at 3 months.
Discussion. – The negative motor network is a part of a modulatory motor network involved in the occurrence of the supplementary motor area syndrome and the permanent deficit after resection in premotor areas. Then, intraoperative functional cortico-subcortical mapping using direct electrostimulation under awake surgery seems mandatory to avoid deficit in bimanual coordination and fine movements during surgery in premotor areas.

1. Introduction

Resections of tumors invading or close to the motor structures are classically performed using intraoperative brain mapping [1]. At a cortical level, Penfield and Boldrey, in 1937, described the somatotopic distribution of the positive motor responses after electrostimulation [2]. At a subcortical level, direct electrostimulation can also elicit positive motor responses and are therefore useful to identify the pyramidal pathway [3]. These techniques of cortical and subcortical motor mapping use direct electrostimulation to elicit a positive motor response through muscle contraction during awake surgery or motor-evoked potential under general anesthesia [1,3,4].

However, despite an effective monitoring of the primary motor cortex and the pyramidal tract, some studies showed that patients could experience postoperative deficit, such as in supplementary motor area (SMA) syndrome [5–10]. SMA syndrome consists of a complete akinesia with mutism when resection is performed in the dominant hemisphere, followed by a complete recovery in few days to weeks [5]. However, many authors have reported some slight permanent deficits, like bimanual coordination dysfunction

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or fine movement disorder of the upper limb [5,8,11,12]. These findings argue for the implication of other structures in motor control, which were not monitored during surgery. In fact, beyond the identification of the primary motor structures through positive motor responses, negative motor responses (NMR) have also been reported during stimulations in cortical motor areas [13–15]. They correspond to a complete inhibition of the movement, without loss of tonus or consciousness [14,15]. Despite many descriptions by Penfield in 1954 and Lüders et al. in 1987 and 1995 [13–15], the functional relevance remained a matter of debate, especially during cortical resections [16,17].

A recent study showed that it was possible to elicit NMR at a subcortical level and that resection up to these sites led to a slight transient deficit similar to a SMA syndrome [18]. The authors mentioned the existence of a modulatory motor network whose stimulation is able to generate an inhibition but also an acceleration of the movement. Since then, two studies have reported new findings regarding the anatomo-functional organization of the white matter pathways involved in this putative network, which tends to confirm its existence and role in the permanent deficit observed during resection in premotor areas [19,20]. Despite cortical resection of sites eliciting NMR led to no permanent deficit [16], the plasticity following resection of subcortical sites eliciting NMR still remains unknown.

We report a series of 12 patients who underwent 13 resections using intraoperative functional mapping under awake surgery for a glioma invading premotor areas. The goal of the surgery was to maximize the extent of the resection without impairing the quality of life [21]. However, some tumors harbored signs of anaplastic transformation or presented a progression in premotor structures after initial surgery. It has therefore been necessary to perform a larger resection, i.e. up to the cortical and subcortical primary motor structures to improve the onco-functional balance [22]. For each patient, negative motor structures were identified during surgery, by looking for speech inhibition, upper limb, lower limb or bimanual movement, depending on the somatotopy of this negative motor network (NMN) [20]. When the resection had to be performed beyond the NMN for oncological purposes, it was removed to find the primary motor structures whose stimulations elicited positive motor responses depending on the primary motor network [2].

Functional results between groups with and without resection of the NMN were analyzed. We report here for the first time the clinical consequences of the NMN resection and their relationship with the supplementary area syndrome in the light of the recent findings concerning the NMN.

2. Material and methods

2.1. Patients

Twelve patients presenting with a glioma of the frontal lobe were selected for surgical resection with a total of 13 procedures between December 2013 and November 2015. They all underwent a glioma resection by the same neurosurgeon using functional mapping with cortical and subcortical electrostimulation during awake surgery depending on the proximity of the glioma with the motor networks. A neurological examination was performed before and after surgery as well as a language and neuropsychological assessment.

Fine motor skills were assessed independently by the neurosurgeon and the neuropsychologist. The patients were first asked if they had previously experienced some dysfunction in their daily life. If a dysfunction was identified, the patient was asked to describe in which situation this dysfunction was a handicap. If the answer was negative, questions were more precise. Patients were then asked if they had any difficulties in performing bimanual or fine motor tasks, such as driving, buttoning a shirt, cooking, playing a music instrument, depending on their activities and work. Motor tasks completed the evaluation by asking the patient to perform repetitive synchronous and asynchronous rotations of the hands and thumb-fingers pinches (i.e. right thumb-index and left thumb-middle finger pinches each time with another finger). A dysfunction was considered positive when the patient spontaneously described a motor dysfunction corresponding to a bimanual or fine motor task, when they answered affirmatively to a question concerning bimanual or fine motor tasks, or when they could not perform a motor task. As the objective was to identify a dysfunction, even a slight one, only a qualitative assessment was performed.

This assessment was performed before and after surgery, during the first week and at 3 months.

Informed consents were obtained prior to surgery for all patients.

3. Methods

3.1. Intraoperative electrostimulation mapping

Resection was performed during awake surgery as already described in previous studies [3,23]. A intraoperative functional cortical and subcortical mapping was performed under local anesthesia by using direct electrostimulations. A bipolar electrode (tip-to-tip distance: 5 mm) delivering a biphasic current (pulse frequency: 60 Hz, single pulse phase duration: 1 ms, amplitude range: 1 to 4 mA, Nimbus*) was applied on the brain. Glioma macroscopic boundaries were first defined using intraoperative ultrasonography. Then, cortical mapping was started over the primary sensory-motor area (during a motor task) and the ventral premotor cortex (during a naming task) by progressively increasing the amplitude of stimulation of 0.5 mA (from a minimal level of 1 mA) until a functional response (involuntary movement, paresthesia, speech arrest or movement inhibition) was elicited, corresponding to the optimal threshold of stimulation. All functional sites were marked with a tag number. The resection was then performed at cortical and subcortical levels. Throughout the resection, functional boundaries were identified with electrostimulation, with the same electrical parameters. During surgery, motor and language tasks were performed by the patient. It consisted of repeating flexion and extension of the contralateral arm, hand, fingers and lower limb at approximately 0.5 Hz (namely one movement of flexion/extension every 2 seconds) while the patient performed a naming task during the same phase. In addition to the language mapping (i.e. by looking for phonological, semantic or syntactic disturbances), this task provided motor information about speech, such as articulation or face movement. This protocol of continuous double task (particularly the motor task) has been designed to take into account the patient tiredness during all the awake stage of surgery as reported in previous studies [18,19,24]. The intraoperative clinical assessment was performed by a neuropsychologist and a speech therapist.

A positive motor response was defined by a contralateral and involuntary muscle contraction during a cortical or subcortical stimulation. As mentioned previously, these sites corresponded to the primary motor network, namely the primary motor cortex and the pyramidal tract. A negative motor response was defined by a complete cessation of movement without loss of consciousness [14,15]. This movement could involve the upper or lower limb, face, speech or bimanual coordination. The movement was assessed using a visual inspection by the neuropsychologist or

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