

Right parietal cortex and calculation processing: intraoperative functional mapping of multiplication and addition in patients affected by a brain tumor

Clinical article

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Object. The role of parietal areas in number processing is well known. The significance of intraoperative functional mapping of these areas has been only partially explored, however, and only a few discordant data are available in the surgical literature with regard to the right parietal lobe. The purpose of this study was to evaluate the clinical impact of simple calculation in cortical electrostimulation of right-handed patients affected by a right parietal brain tumor.

Methods. Calculation mapping in awake surgery was performed in 3 right-handed patients affected by high-grade gliomas located in the right parietal lobe. Preoperatively, none of the patients presented with calculation deficits. In all 3 cases, after sensorimotor and language mapping, cortical and intraparietal sulcus areas involved in single-digit multiplication and addition calculations were mapped using bipolar electrostimulation.

Results. In all patients, different sites of the right parietal cortex, mainly in the inferior lobule, were detected as being specifically related to calculation (multiplication or addition). In 2 patients the intraparietal sulcus was functionally specific for multiplication. No functional sites for language were detected. All sites functional for calculation were spared during tumor resection, which was complete in all cases without postoperative neurological deficits.

Conclusions. These findings provide intraoperative data in support of an anatomofunctional organization for multiplication and addition within the right parietal area. Furthermore, the study shows the potential clinical relevance of intraoperative mapping of calculation in patients undergoing surgery in the right parietal area. Further and larger studies are needed to confirm these data and assess whether mapped areas are effectively essential for function. (<http://thejns.org/doi/abs/10.3171/2013.6.JNS122445>)

KEY WORDS • awake surgery • right parietal lobe • electrostimulation • functional mapping • addition • multiplication • functional neurosurgery

CALCULATION is based on distinct neural networks, which can be reproducibly identified in different subjects.^{2,3,24} A pivotal role in calculation is played by the parietal lobe. In the past 2 decades, neuroimaging and neuropsychological evidence was collected about the innermost mechanisms of calculation, and 3 main parietal circuits⁴ have been proposed as the basis of calculation processing. According to this model, intraparietal areas are bilaterally associated with core quantity organization, the left angular gyrus is associated with verbal processing of numbers, and the posterior superior parietal system is associated with spatial and nonspatial attention. In particular, a crucial role in quantity processing has been proposed for the horizontal segment of the intraparietal sulcus. With regard to electrostimulation mapping of calculation, some experiences have been reported on left parietal lobe mapping,^{7,13–15,21,23} while data on right pari-

etal mapping are anecdotal and discordant.^{20,25} This difference may be due to the much greater attention given to language mapping so far; however, impairment of mathematical skills can be the cause of serious personal and social difficulties. For this reason, the ability to perform calculation tasks ought to be regarded as a fundamental function. The parietal lobe is not only a frequent location of different neurosurgical conditions (such as gliomas, arteriovenous malformations, and others) but it is also a key area for the surgical approach of deeply seated lesions such as intraventricular or periventricular lesions.^{10,12,16} The potential clinical repercussions of new data providing evidence of the right parietal lobe as an eloquent area for calculation are therefore obvious in left-dominant patients, in whom the right, nondominant side is generally considered a reasonably safe surgical approach.

In this report, we present the results of intraoperative

mapping of right parietal cortex areas involved in calculation processes in 3 patients affected by brain tumors located in the parietal lobe. Our main aim was to evaluate the reliability of the technique to avoid permanent postoperative calculation impairment, and second, to investigate the different involvement of right cortical and intraparietal sulcus areas in calculation processes. Cortical mapping was focused on multiplication and addition. Last, our findings were compared with those in the relevant literature.

Methods

Patient Enrollment

Between December 2011 and April 2012, functional mapping for numerical processing tasks was offered to patients affected by brain tumors located in the right parietal area. Inclusion criteria were 1) a tumor located in the parietal lobe, 2) right-handedness assessment through the Italian version of the Edinburgh Handedness Inventory,¹⁹ and 3) a Karnofsky Performance Scale score of 100 (normal). Exclusion criteria were 1) preoperative impairment of numerical processing performance, and 2) preoperative motor impairment. Informed consent was obtained from all patients and their families. No ethics committee approval was required for this study because it was a purely observational work concerning an intraoperative technique that is routinely used in our institution. Furthermore, written informed consent was obtained in all patients according to hospital ethics guidelines.

Preoperative and Postoperative Assessment

Preoperative clinical examination results were normal in all cases. A neuropsychological assessment did not show linguistic impairments in spontaneous speech, word generation, repetition, picture naming, reading, or writing. Linguistic tests included the following: the fluency task from the Aachen Aphasia Test,¹¹ consisting of a semantic test and a phonological test; and the picture-naming test DO-80, which consists of 80 black and white pictures selected according to variables such as frequency, familiarity, age of acquisition, and level of education.¹⁷ Visual-spatial functions, executive functions, memory, praxis, as well as general cognitive functions were intact, as assessed by specific tests.¹⁸ Mood status was stable and no signs of depression or pathological anxiety were detected, as evaluated using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30)⁹ and Hospital Anxiety and Depression Scale²⁶ tests, respectively. The assessment of calculation skills according to the methods indicated by Delazer et al.⁵ showed a normal performance. In detail, the Number Processing and Calculation battery⁵ included 35 tasks assessing different counting abilities, such as number comprehension, numerical transcoding, calculation, arithmetic reasoning, and conceptual knowledge. The calculation abilities included tasks such as simple fact retrieval, rule-based processing, and oral and written calculation in all 4 operations (addition, subtraction, multiplication, and division). Over the 2 days prior to surgery, patients were

informed in detail about the intraoperative monitoring procedure of stimulation, introduced to the stimulus devices, and trained to perform the naming and calculating tasks.

Intraoperative Calculation Tasks

A speech therapist was always present in the operating room to administer the tests and to detect the mistakes. Language and sensorimotor functions were mapped first. Marked paper tags were placed on functional sites on the cortical surface.

For language mapping, patients were asked to perform counting (repeatedly, from 1 to 10) and picture naming (in which the patient was told to precede naming by reading a short sentence [“this is a...”] to check that there were no seizures). Each individual stimulation was separated by at least 1 picture administered without stimulation, and no site was stimulated twice in succession, to avoid seizures.

Numerical stimuli were presented visually, in Arabic digits, using a computer system with a display screen. Multiplication and addition were studied. Two different types of calculation tasks were administered to the patient: single-digit addition with a single operand (for example $4 + 7$, $8 + 6$, $5 + 7$) and single-digit multiplication with a single operand (for example 8×4 , 5×6 , 9×7). Each operation had to be solved within the 4-second time of the stimulation and was presented in the middle of the screen without the equal sign (“=”). The patient’s response was given orally. The patient was unaware of when electrical stimulation was performed. The administration procedure was as follows: a block of 14 additions was presented to the patient, in random order, using the electrostimulation in an alternate fashion, and repeated 3 times. A total of 21 trials with and 21 trials without stimulation were administered. Afterward, 3 blocks of 15 multiplications were administered using the same procedure, for a total of 22 tests with and 23 without stimulation.

Surgical Strategy

The surgical strategy was preoperatively planned on the basis of T1-weighted MR images after Gd administration. Tumor removal was performed using these functional landmarks as boundaries of the resection. A tailored craniotomy was performed on the basis of neuronavigation data through a linear incision; as a consequence, the parietal cortex was never completely exposed. Conversely, in all cases, sensorimotor areas were partially exposed to determine the intensity of stimulation. Because all tumors in this study were located on the right side, we did not have the usual opportunity to assess threshold of stimulation on language function through speech arrest. Even though it is undeniable that motor threshold is widely variable depending on the location of stimulation, the stimulation threshold we decided to choose was the minimal intensity able to evoke a sensorimotor response (arm movement or paresthesia). The occurrence of electroencephalography changes (known as afterdischarges) that might have contributed to disruption of mathematical function was continuously monitored. The cortical incision procedure was customized according to neuronavigation and cortical mapping data.

Functional mapping of the right parietal cortex

Intraoperative Mapping

The study entailed continuous electroencephalography, electrocorticography, and multichannel electromyography recordings (Eclipse 16-channel system, Axon). Cortical and subcortical mapping was performed by means of a bipolar stimulator (Spes Medica). A multipulse stimulation technique was adopted. The operating surgeon performed both cortical anatomical mapping (sulci/gyri identification) and tumor site assessment with the aid of MRI neuronavigation. Lettered tags were positioned on the cortical surface to draw the subcortical location of the tumor. Then, a functional cortical map was obtained using the method described by Duffau et al.^{6,8} A bipolar probe with 5-mm-spaced tips continuously delivering a low intensity, biphasic current with trains of 120 stimuli (pulse frequency 60 Hz, single pulse phase duration 500 msec) was applied to the cortex. The current intensity was determined with progressive increases of 0.5 mA (from a baseline of 1 mA) until a sensorimotor response was obtained. Sensorimotor mapping was performed and numbered tags were positioned on the cortical surface. In a second stage, patients were asked to perform counting and picture naming. In this stage as well, all functional sites were marked with numbered tags. In a third stage, calculation task tests were administered. All sites functional for calculation were marked with tags (“+” for addition and “x” for multiplication). Each cortical site (5 × 5 mm) of the whole cortex exposed by the bone flap was tested 3 times. A site was marked as functional for calculation only if 3 repeat stimulations provoked disruption of the tested function. Both the superior and inferior parietal gyri were stimulated in all 3 patients. Based on neuronavigation data, the intraparietal sulcus was then mapped in the part (or branch) needed to approach the tumor (Fig. 1). In all cases the horizontal segment of the intraparietal sulcus was exposed and stimulated.

Postoperative Assessment

The extent of resection was postoperatively evaluated with MRI within 72 hours from the surgical procedure. Neurological and specific neuropsychological assessment was performed at the 1st, 7th, and 30th day after surgery.

Results

Three patients (2 female, 1 male) underwent awake surgery with cortical stimulation for number processing (Table 1). Electrostimulation mapping was straightforward and well tolerated in all patients. No focal seizures occurred. The maximal current intensity of electrostimulation ranged from 2 mA to 3 mA; this was the actual peak-to-peak level of delivered current intensity, which was intraoperatively used in the presented setting.

Functional Mapping

All 3 patients were mapped during the cortical stimulation for sensorimotor function first, then for language, and finally for calculation tasks. Mapping data are summarized in Table 2. In all 3 patients, a total of 12 different specific sensorimotor sites were detected, while no

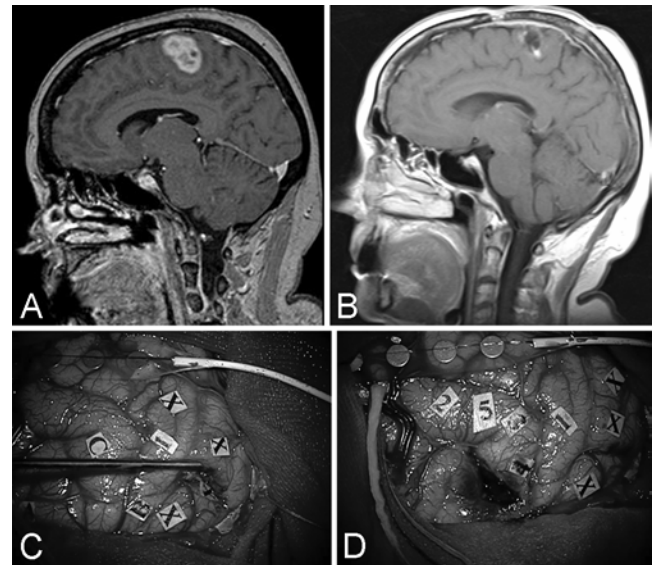


FIG. 1. Images obtained in Case 1. **A and B:** Preoperative (A) and postoperative (B) sagittal T1-weighted MR images with Gd enhancement. **C:** Intraoperative image obtained during functional mapping of the right parietal area. Lettered tags were positioned over the tumor, identified with MRI neuronavigation. Tag 1 marks the functional site for hand motor response (subsequently driving the intensity threshold of stimulation [3 mA]); X tags mark functional sites for multiplication on the superior, inferior, and intraparietal sulcus; B and C tags mark the subcortical site of the tumor identified by MRI neuronavigation. **D:** Final view. Tags 2 and 5 lie over the motor area in front of the corticectomy chosen for tumor removal.

functional sites for language were identified. A total of 9 sites were detected that were functional for calculation: 8 mapped for multiplication and 1 for addition. Overall, numerical processing interferences (functional sites for the task) were found in all 4 parietal regions explored by electrostimulation: 3 interferences (multiplication) in the angular gyrus, 3 interferences (2 multiplication, 1 addition) in the supramarginal gyrus, 2 interferences (multiplication) in the horizontal segment of the intraparietal sulcus, and 1 interference (multiplication) in the superior lobule. All sites functional for calculation were spared during tumor resection. Numerical processing stimulation was not used in the subcortical white matter. No intraoperative seizures occurred, and no afterdischarges were detected.

TABLE 1: Number of functional sites identified by intraoperative electrostimulation in the 3 patients*

Case No.	Age (yrs), Sex	Calculation		Sensorimotor
		Multiplication	Addition	
1	62, F	4	0	5
2	68, F	2	1	4
3	50, M	2	0	3
total		8	1	12

* All patients were right-handed and had high-grade gliomas in the parietal lobe. No functional sites for language were detected in any of the 3 patients.

TABLE 2: Localization of numerical processing sites*

Case No.	Angular Gyrus	Supramarginal Gyrus	HIPS	Superior Lobule
1	1 multi	1 multi	1 multi	1 multi
2	1 multi	1 add	1 multi	no
3	1 multi	1 multi	no	no
total	3 (multi)	3 (2 multi, 1 add)	2 (multi)	1 (multi)

* add = addition; HIPS = horizontal intraparietal sulcus; multi = multiplication.

Postoperative Course

The postoperative MR images showed complete tumor removal in all 3 patients. Discharge from the hospital occurred within 7 days after surgery in all cases. Neurological and specific neuropsychological assessments at the 1st, 7th, and 30th day after surgery were normal. In particular, all 3 patients had no postoperative numerical processing difficulties. The histopathological report confirmed the tumors to be Grade IV astrocytomas in all cases. All 3 patients underwent radiotherapy and chemotherapy with temozolomide after surgery.

Discussion

These findings provide new data in support of the role played by the parietal right cortex in calculation processing and of the usefulness of functional mapping in this area. There were 3 primary intraoperative results from our study.

First, multiple sites over the surface of the right parietal cortex were detected to be functional for multiplication. The inferior parietal lobule was most frequently involved. So far, no intraoperative data on the involvement of the right cortex in multiplication have been reported in the literature. Two reports have been published on this specific issue.^{20,25} In 1 case²⁵ the authors reported their experience with a patient affected by a right temporal glioma. However, multiplication was not impaired when the right parietal cortex was stimulated. In the other case,²⁰ the authors described a series of 5 patients affected by parietal astrocytoma, 4 with a left-sided tumor and 1 with a right-sided tumor. In left parietal tumor cases, 3 of 4 patients were found to have functional sites for multiplication. Conversely, in the patient with a right parietal tumor, multiplication was investigated but no functional sites were detected.

Second, our findings may prove the involvement of the right intraparietal sulcus in multiplication. Multiplication was impaired in 2 of 3 cases when the bottom of the horizontal segment of the intraparietal sulcus was stimulated. However, it must be remembered that the intraparietal sulcus was never entirely stimulated and mapped intraoperatively because of its partial exposure, on the basis of a planned approach guided by neuronavigation data. In both of the cases in which multiplication was impaired, the electrostimulation was performed on the bottom of the horizontal segment of the intraparietal sulcus. The intraparietal sulcus has been previously reported to be im-

portant in number processing and calculation.^{3,4} However, only 1 report on functional mapping of this type of sulcus has been published, focused on the left hemisphere.²⁰ In that case, multiplication was impaired with electrostimulation. To the best of our knowledge, intraoperative data on the right intraparietal sulcus have not been reported in the literature to date.

Third, 1 patient in our series was found to have a site functional for addition in the angular gyrus of the inferior parietal lobule. To our knowledge, addition was never previously explored using intraoperative mapping of the right parietal cortex. This intraoperative finding would confirm recent data acquired in neuropsychological settings or with transcranial magnetic stimulation.^{1,22}

In the right parietal lobe, no cortical or subcortical areas were found to be functional for language. These data need to be investigated further in depth, because the absence of language function in the right hemisphere could enable us to perform awake surgery in the right hemisphere using different tasks from language such as calculation, visual-spatial cognition, or others.

Conclusions

Two final considerations emerge from our results. First, intraoperative data confirmed both preoperative neuropsychological, radiological, and transcranial magnetic stimulation data previously reported in literature. Specifically, the data confirm that the right parietal cortex is involved in calculation, mainly in the inferior lobule and intraparietal sulcus areas. Second, we recognize that our findings cannot change the current neurosurgical practice; the small number of patients and the lack of subcortical mapping data are obvious limitations of the study. In addition, the present study does not clarify whether mapping findings could predict mathematical processing impairment when functional areas are removed or otherwise damaged. However, we documented how parietal areas can be highly eloquent for calculation and how they may be easily mapped and thus spared in the awake patient.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Della Puppa, De Pellegrin. Acquisition of data: Della Puppa, De Pellegrin. Analysis and interpretation of data: Della Puppa, De Pellegrin, d'Avella, Salillas. Drafting the article: Della Puppa, De Pellegrin, d'Avella, Gioffrè. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Della Puppa.

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