Right parietal cortex and calculation processing. Intra-operative functional mapping of multiplication and addition.

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Abstract

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

Methods: A calculation mapping in awake surgery was performed in three 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 three cases, after sensory-motor and language mapping, cortical and intra-parietal sulcus areas involved in single digit multiplications and additions were mapped using bipolar electro-stimulation.

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 two patients the Intra-Parietal Sulcus was functionally specific for multiplication. No functional sites for language were detected. ~~Tumor resection~~All sites functional for calculation were spared during tumor resection that was complete in all cases, without postoperative neurological deficits.

Conclusions: Our findings provide intra-operative data in support of an anatomo-functional organization for multiplication and addition within the right parietal area. Furthermore, we show the potential clinical relevance of intra-operative mapping of calculation in patients undergoing surgery in the right parietal area. Further and larger studies are needed in order to confirm ~~these~~our data and to assess whether mapped areas are effectively essential for function.

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Introduction

Calculation is based on distinct neural networks, that can be reproducibly identified in different subjects.[2,3,24] A pivotal role is played by the parietal lobe. In the past two decades neuroimaging and neuropsychological evidence was collected about the innermost mechanisms of calculation, and three main parietal circuits[4] have been proposed as the basis of calculation processing. According to this model, intra-parietal 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 non spatial attention. In particular, a crucial role in quantity processing has been proposed for the Horizontal segment of the Intra-Parietal Sulcus (HIPS). With regard to electro-stimulation mapping of calculation, some experiences have been reported on left parietal lobe mapping,[8,13,14,15,21,23] while data on right parietal mapping are anecdotal and discordant.[20,25] This may be due to the much larger attention paid so far to language mapping. Impairment of mathematical skills can be cause of serious personal and social difficulties, however. 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 (gliomas, AVMs, etc) but it is also a key area for the surgical approach of deeply seated lesions such as intra- or peri-ventricular 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, non-dominant, side is generally considered a reasonably safe surgical approach.

In this report, we present the results of intra-operative mapping of right parietal cortex areas involved in calculation processes in three patients affected by brain tumor located into the parietal lobe. Our main aim was to evaluate the reliability of the technique in order to avoid permanent postoperative calculation impairment; secondly, to investigate the different involvement in calculation processes of right cortical and intra-parietal sulcus areas. Cortical mapping was focused on multiplication and addition. Lastly, our findings were assessed against 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 tumor located in the right parietal area. Inclusion criteria were: tumor located into the parietal lobe, right-handedness assessment through the Italian version of the Edinburgh Handedness Inventory[19] KPS of 100. Exclusion criteria were: preoperative impairment of numeral processing performance, preoperative motor impairment. Informed consent was obtained from all patients and their families.

Preoperative and postoperative assessment

Preoperative clinical examination was 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 Aachener Aphasia Test[11] consisting of a semantic test and a phonological test; 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, as assessed by specific tests[18] were intact. Mood status was stable and no signs of depression or pathological anxiety were detected, as evaluated with the EORTC QLQ-C30[9] and HADS[26] tests respectively. The assessment of calculation skills according to the methods indicated by Delazer et al.[5] showed a normal performance. ~~Patients were specifically able to flawlessly read~~In detail, the Battery of Number Processing and ~~write Arabic numerals, to correctly perform~~Calculation (NPC)[5] included 35 tasks assessing different counting ability, such number ~~comparison~~comprehension, numerical

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transcoding, calculation, arithmetic reasoning and ~~to carry out~~conceptual knowledge. The calculation abilities included tasks such as simple fact retrieval, rule based processing, mental and ~~complex~~writer calculation in all four operations. Over the 2 days prior to surgery, patients were informed in detail about the intra-operative monitoring procedure of stimulation, were introduced to the stimulus devices and trained to perform the naming and calculating tasks.

Intra-Operative Calculation tasks

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

For the language mapping, the 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…" in order 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 8x4; 5x6; 9x7….). Each operation had to be solved within the four seconds time of the stimulation and was presented in the middle of the screen without the sign "="; the patient's response was oral. 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 electro-stimulation in an alternate fashion, and repeated three times. A total of 21 trials with and 21 trials without stimulation were administered. Afterwards, three blocks of 15 multiplications was administered with the same procedure, for a total of 22 tests with and 23 without stimulation.

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Surgical Strategy

The surgical strategy was preoperatively planned on the basis of T1-weighted MRI images after gadolinium administration. Tumor removal was carried out using these functional landmarks as boundaries of the resection. A tailored craniotomy was carried out on the basis of neuro-navigation data through a linear incision. As a consequence of this, the parietal cortex was never completely exposed. Conversely, in all cases, sensory-motor areas were partially exposed to determine the intensity of stimulation. Since located in the right side, we did not have the usual chance to assess threshold of stimulation on the language function through the speech arrest. Even though the fact that motor threshold is widely variable depending on the location of stimulation is undeniable, the stimulation threshold we decided to choose was the minimal intensity able to evocate a sensory-motor response (i.e. arm movement or parestesia). The occurrence of EEG changes (known as "after-discharges") that might have contributed to disruption of mathematical function was continuously monitored.

The cortical incision procedure was customized according to neuro-navigation and cortical mapping data.

Intraoperative mapping

The study entailed continuous electro-encephalography, electro-corticography and multi-channel electro-myography recordings~~.~~ ("Eclipse 16 channels", Axon, U.S.A.). Cortical and sub-cortical mapping was performed by means of a bipolar stimulator (Spes Medica, Italy). A multi-pulse stimulation technique was adopted. The operating surgeon performed both cortical anatomical mapping (sulci/gyri identification) and tumour site assessment with the aid of MRI neuro-navigation. Lettered tags were positioned on the cortical surface to draw the sub-cortical location of tumor. Then, a functional cortical map was obtained using the method described by Duffau et al.[6,7] A 5 mm-spaced tips bipolar probe continuously delivering a ~~biphasic~~low intensity, bifasic current

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~~was applied on the cortex for a period~~with trains of ~~four seconds (pulse~~120 stimuli (Pulse frequency of 60 Hz, single pulse phase duration of ~~0.3ms).~~500ms) was applied to the cortex." The current intensity was determined with progressive increases by 0.5-mA (from a baseline of 1 mA) until a sensory-motor response was obtained. A sensory-motor 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 case also, 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 the inferior parietal gyri were stimulated in all three patients. Then, Intra-Parietal Sulcus (IPS) was mapped in its part exposed on the basis of neuro-navigation data, as needed to approach the tumour (Figure 1). In all cases the HIPS 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 females, 1 male) underwent awake surgery with cortical stimulation for number processing (Table 1). Electro-stimulation mapping was straightforward and well tolerated in all patients. No focal seizures occurred. The maximal current intensity of electro-stimulation ranged from 2 to 3 mA. This was the actual peak to peak level of delivered current intensity, which was intra-operatively used in the presented setting.

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Functional mapping

All three patients were mapped during the cortical stimulation for sensory-motor function first, then for language, and finally for calculation tasks. Mapping data are summarized in (Table 2). In all three patients, a total of 12 different specific sensory-motor sites were detected, whilst no functional sites for language were identified. A total of nine sites functional for calculation were detected: eight mapped for multiplication and one for addition. The results are summarized in Table 2 . Overall, numerical processing interferences were found in all 4 parietal regions explored by electro-stimulation: 3 interferences (3 multiplication) in the angular gyrus, 3 interferences (2 multiplication and 1 addition) in the supramarginal gyrus, 2 interferences (2 multiplication) in the horizontal segment of the IPS, 1 interference (1 multiplication) in the Superior lobule. All sites functional for calculation were spared during tumor resection. Numerical processing stimulation was not used in the ~~subcortical~~sub-cortical white matter. No intra-operative seizures occurred, and no after-discharges were detected.

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Postoperative Course

The postoperative MRI showed complete tumor removal in all 3 patients. Discharge from hospital was within 7 days from 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 histo-pathological report was astrocytoma grade IV (sec. WHO) in all cases. All three patients underwent radiotherapy and chemotherapy with temozolamide afterwards.

DISCUSSION

Our 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. Our main intra-operative results were three.

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 intra-operative data on the involvement of right cortex in multiplication have been reported in literature. Two reports have been published on this specific issue.[20,25] In one case[25] the authors reported their experience on 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 five patients affected by parietal astrocytoma, four with a left and one with a right-sided tumour. In left parietal tumour cases, three out of four patients presented functional sites for multiplication. Conversely, in the patient with a right parietal tumour, multiplication was investigated but no functional sites were detected.

Second, our findings may prove the involvement in multiplication of the right IPs. Indeed, multiplication was impaired in 2 cases out of 3 when the bottom of the HIPS was stimulated. However, it must be borne in mind that the Intra-Parietal sulcus was never entirely stimulated and mapped intra-operatively because of its partial exposure on the basis of planned approach guided by neuro-navigation data. In both of the two cases in which multiplication was impaired, the electro-stimulation was carried out on the bottom of the HIPS. The Intra-Parietal Sulcus has been previously reported as important in number processing and calculation.[3,4] However, only one report on functional mapping of such sulcus has been published, focused on the left hemisphere.[20] In that case multiplication was impaired with electro-stimulation. Intra-operative data on the right IPS have not been reported in literature so far, to the best of our knowledge.

Third, in our series one patient presented a site functional for addition in the angular gyrus of the inferior parietal lobule (IFL). To our knowledge, addition was never explored before by intra-operative mapping of the right parietal cortex. This intra-operative finding would confirm recent data acquired in neuropsychological settings or with TMS.[1,22]

In the right parietal lobe, no cortical or sub-cortical areas were found to be functional for language. These data need to be investigated more in depth. However, they might be useful insofar they suggest to prefer mapping of other functions when awake surgery in right parietal areas of left dominant patients must be performed.

Two final considerations emerge by the present results. First, intra-operative data confirmed both preoperative neuropsychological, radiological and TMS data previously reported in literature. In particular, the right parietal cortex is involved in calculation, mainly in the Inferior Lobule and Intra-Parietal Sulcus areas. Second, we reckon that our findings cannot change the current neurosurgical practice. Indeed, the small number of patients and the lack of sub-cortical mapping data are obvious limits 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 awake patient.

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Illustrations

Figure 1: ~~**Patient#1:**~~ Pre-operative (Panel A) and post-operative (Panel B) sagittal GdT1-weighted MRI ~~**(a and b).**~~scan.

Panel C: Intra-operative ~~**images (c**~~image taken during functional mapping of the right parietal area. Lettered tags were positioned over the tumor, identified with MRI neuron-navigation; Tag 1= functional site for hand motor response (subsequently driving the intensity threshold of stimulation - 3mA); X Tags= functional sites for multiplication (on the superior, inferior and intraparietal sulcus).

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Panel D: Final view. Tags 2 and ~~d). (See text for details)~~5 lie over the motor area in front of corticectomy chosen for tumor removal

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Table 1: Clinical characteristics and functional mapping data of patients (R=Right; L=Left; HGG:High Grade Glioma; Multipl = Multiplication; Add = Addition). See text for details.

Table 2: Localization of numerical processing sites (HIPS= Horizontal Intra-Parietal Sulcus; M= Multiplication; A= Addition). See text for details.

We state that no ethics committee approval was required for our study, since it has been a purely observational work concerning an intraoperative technique which is routinely used in our Institution. Furthermore, informed consent was obtained in all cases from patients, according to the Hospital ethics guidelines.

All authors were equally involved in:

Conception and design, acquisition of data or analysis and interpretation of data.

Drafting the article or revising it critically for important intellectual content.

Final approval of the version published of the paper.

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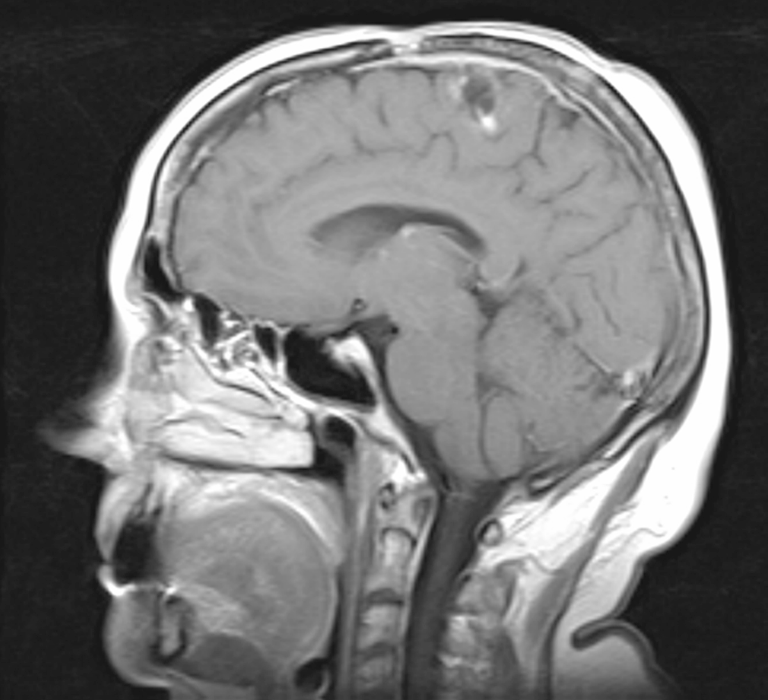

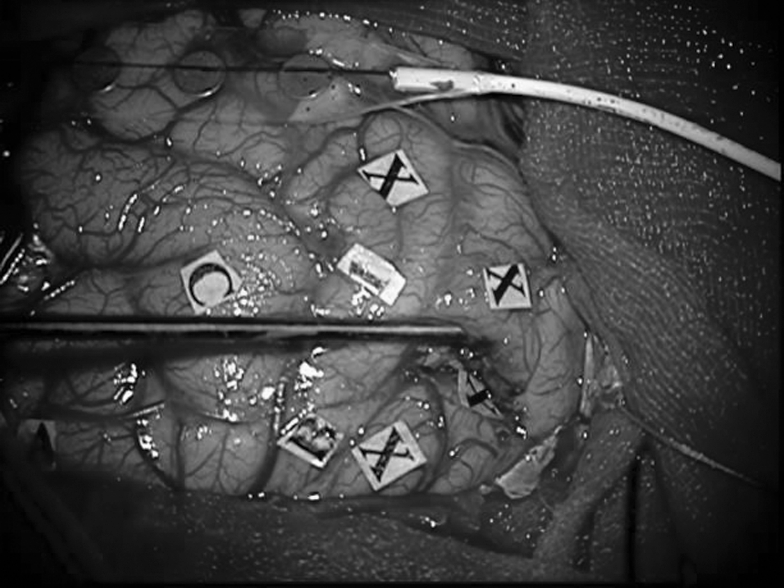

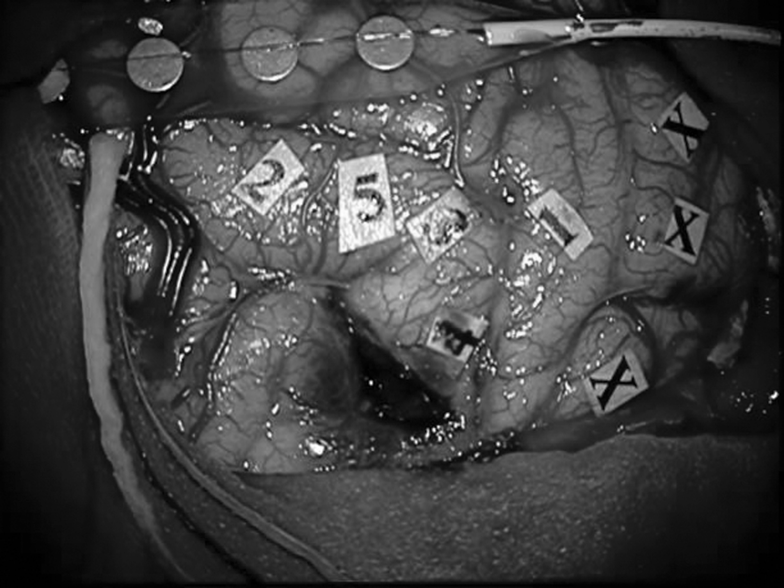
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Patient#	Age/sex	R/L	Site	Pathology	Calculation Multipl	Add	Language	Sensimotor
1	62/F	R	Parietal	HGG	4	0	0	5
2	68/F	R	Parietal	HGG	2	1	0	4
3	50/M	R	Parietal	HGG	2	0	0	3
Total					8	1	0	12

Patient #	Angular Gyrus	Supramarginal Gyrus	HIPS	Superior Lobule
1	1M	1M	1M	1M
2	1M	1A	1M	No
3	1M	1M	No	No
Total	3 (3M)	3 (2M; 1A)	2 (2M)	1 (M)