Acta Neurochir (Wien) (1999) 141: 1157–1167

Acta Neurochirurgica

Intra-Operative Direct Electrical Stimulations of the Central Nervous System: The Salpêtrière Experience With 60 Patients

H. Duffau[1], **L. Capelle**[1], **J.-P. Sichez**[1], **T. Faillot**[1], **L. Abdennour**[2], **J.-D. Law Koune**[2], **S. Dadoun**[2], **A. Bitar**[1], **F. Arthuis**[1], **R. Van Effenterre**[1], and **D. Fohanno**[1]

[1] Department of Neurosurgery 1, Hôpital de la Salpêtrière, Paris, France
[2] Department of Neuroanesthesiology, Hôpital de la Salpêtrière, Paris, France

Summary

Indications of surgical treatment for lesions in the central nervous system depend on the risk of a definitive neurological deficit, related to the benefit of resection. Detection of eloquent areas is then necessary because of major individual variability. Neuro-imaging functional techniques are in development and are beginning to be efficient for cortical sensorymotor mapping, but still lack sensitivity and specificity for language mapping, and remain unable to give real-time data during surgery and to perform sub-cortical mapping. The more precise and reliable method of functional mapping is represented by the intra-operative direct electrical stimulations (DES), which allow identification and preservation of essential pathways for motricity, sensibility and language, at each level of the central nervous system (cortico-subcortical). We report our experience of DES in the surgery of tumours and vascular malformations located in supratentorial brain eloquent areas, with a consecutive series of 60 patients operated on under general or local anaesthesia, from November 1996 until May 1999 in our department at La Salpêtrière Hospital.

Presenting symptoms in the 60 subjects (39 males, 21 females, mean age: 45 years) were seizures in 37 cases with normal clinical examination, and mild neurological deficit in 29 cases. MRI showed 60 supra-tentorial brain lesions: 30 precentral, 12 postcentral, 14 perisylvian in the dominant hemisphere, 4 deep-seated. All subjects underwent surgical resection using DES, with supratentorial cortico-subcortical mapping under general anaesthesia for motor areas detection in 43 cases and under local anaesthesia for sensori-motor and/or language tasks in 17 cases. The final histological diagnosis was 44 gliomas (31 low-grade and 13 high-grade), 9 metastasis, 3 cavernomas, 4 arteriovenous malformations (AVM). Resection was total or subtotal in 52 cases (87%) and partial in 8 cases (13%). 29 patients had no post-operative deficit, while the other 31 patients were impaired post-operatively, with in all cases, except 3, a complete recovery delayed for 15 days to 3 months (overall morbidity: 5%). The median follow up was 14 months.

Intra-operative direct electrical stimulations of the central nervous system constitute a reliable, precise and safe method, allowing the realization of a functional mapping useful for all operations of lesions located in eloquent areas. This technique allows a minimization of definitive post-operative neurological deficit, and concurrently an improvement in the quality of resection.

Keywords: Electrical stimulations; functional mapping; language; sensorymotor.

Introduction

Indications for surgical treatment of lesions located in the central nervous system depend on the risk of a definitive neurological deficit, related to the benefit of resection. Detection of eloquent neural structures is then mandatory, taking account of the major individual anatomo-functional variability both for sensori-motor [69] and language functions [32, 49], particularly in the presence of a lesion likely to induce a mass effect and/or a functional reorganization [61, 72]. Despite recent development of non invasive functional neuro-imaging (PETscan, functional MRI and Magneto-encephalography) which begin to be efficient for sensori-motor mapping [39, 45, 57, 73], these techniques still remain too imprecise for complex functions such as language mapping (75% of sensitivity and 80% of sensibility using PETscan [33] and 81% of sensitivity and 53% of specificity using fMRI [27]). Moreover, they do not give real-time data during surgery, and they are unable to perform a functional mapping of the white matter, which is equally important as the determination of eloquent cortical regions to avoid neurological sequelae. Finally, they allow detection of all the areas implicated in the realization of a task, but not the essential structures in these networks.

The more precise and reliable method nowadays is represented by intra-operative direct electrical stimulations (DES) of the central nervous system, which allows a safe real-time identification and hence preservation of essential pathways for motricity, sensibility, language and even memory [5, 6, 7, 8, 9, 12, 13, 16, 22, 25, 26, 31, 33, 36, 40, 47, 48, 49, 50, 52, 53, 54, 58, 59, 63, 68, 70]. This technique can provide intra-operative functional mapping at the cortical [6, 26, 31, 49, 70] and sub-cortical [7, 8, 22, 63] brain level, at the brainstem level [23, 44, 66, 67], and also at the spinal cord level [7, 24].

We report our experience of DES in the surgery of tumours and vascular malformations located in supratentorial eloquent brain areas, with a consecutive series of 60 patients operated on under general or local anaesthesia at La Salpêtrière Hospital, from November 1996 until May 1999.

Patients and Methods

Patient Population

All patients with lesions of the central nervous system close to an eloquent area seen in our institution between November 1996 and May 1999 were considered for entry into this prospective study. These cases included a wide variety of clinical presentations, lesion locations and histological types. Patients were excluded in case of severe pre-operative deficit. Paediatric surgery is not practiced at our institution.

When necessary, the dominant hemisphere was defined, to avoid the realization of an invasive Wada test, using neuropsychological examination associated with fMRI, which seems nowadays reliable for language lateralization determination [11, 19].

Operative Technique

In all surgical procedures, the location of the lesion was intra-operatively verified using ultrasonography [41] and/or an image-guided system (Surgiscope, Elekta*).

All subjects underwent surgical resection using DES. The principle consists in the direct application on the neural structures of a 5-mm spaced tips bipolar probe delivering a biphasic current with an intensity non-deleterious to the nervous system (current amplitude from 0.5 mA to 16 mA depending on the conditions of anaesthesia). A train of constant current biphasic square wave pulses was used with a pulse frequency of 60 Hz and a single pulse phase duration of 1 ms (Ojemann Cortical Stimulator, Radionics).

Supratentorial brain cortico-sub-cortical stimulations:

- Under general anaesthesia: direct cortical stimulations of the primary motor area performed without curarisation, induce a motor response of the contralateral corresponding limbs or face identified by an observer, allowing the reconstitution of an Homunculus as first described by Penfield [52], before the beginning of lesion removal. During resection, sub-cortical motor stimulations also allow the detection of the pyramidal pathways by generating movements, giving the deep boundaries of the removal. Moreover, the ability of *cortical* stimulations inducing at the end of the resection the same motor responses than before the lesion excision, at the same current intensity, allows the verification of anatomo-functional integrity of the entire motor pathways. Current intensity used varied from 6 to 16 mA.
- Under local anaesthesia: it is also possible to perform surgery on an awake co-operating patient without any pain or discomfort for him [16, 68], to study during operation not only essential cortico-sub-cortical areas of motricity, but also of sensitivity, language, and even memory. Patient is installed in the lateral position with great efforts to ensure that he could remain in this position for the duration of the procedure. Patient was during opening and closing of the craniotomy anaesthetized without intubation using Propofol [62] and Alfentanyl, with infiltration (Lidocaïne 1%) of the skin and the dura-mater as a regional field block. Patient is awakened before the opening of the dura, and the mapping performed.

For lesions located just behind the Rolandic region, cortical and sub-cortical stimulations of the primary somatosensory area induce paraesthesias on the contralatral hemibody which can be described by the awake patient. A motor mapping can also be realized as under general anaesthesia.

For language, on the contrary, electrical stimulations do not induce an activation but an inhibition of speech [46]. Then for lesions of the perisylvian region of the dominant hemisphere (fronto-opercular, temporal, insular and/or at the temporo-parieto-occipital junction), using language tasks such as counting and naming [49], we can determine before and during resection respectively cortical and sub-cortical essential eloquent areas which have to be preserved and are characterised on stimulation by speech arrest or anomia (Fig. 1, 2, 3, 4). Current intensity used range from 3 to 6 mA.

In all cases (under general or local anaesthesia, for sensori-motor or language mapping), the principle is to stop the resection as soon as a functional area (cortical and/or sub-cortical) detected using electrical stimulations is encountered. Although no margin is necessary between the edges of the surgical cavity and the sensori-motor sites, a margin of 7 mm must be preserved around the language areas [31] to avoid a definitive post-operative deficit.

Moreover, to avoid brain oedema, a bolus of Mannitol is systemically administered before dural opening. In case of intra-operative seizures, cortex irrigation with cold serum or Ringer allows immediate interruption of the epilepsy [60].

Results

Clinical, radiological, histological and treatment characteristics of the 60 patients are summarized in Table I.

There were 39 males and 21 females with an age range of 21 to 71 years (mean 45 years).

Presenting symptoms were seizures in 37 cases (61%) with normal neurological examination, progressive mild deficit in 21 cases (35%) (14 motor deficits, 4 somatosensorial disorders, 3 language disturbances) and 2 intracranial hypertension syndromes (4%). Concerning location, MRI revealed 30 precentral lesions (50%), 12 postcentral (20%), 4 left temporal (6%) (dominant hemisphere – DH –), 6 left fronto-opercular (10%) (DH), 2 left temporo-parieto-occipital (3.5%) (DH), 2 left insular (3.5%) (DH), 3 right insular (5%) (non DH), and one lenticulo-caudate lesion.

43 patients (71%) (with a central lesion or a lesion close to the internal capsula) underwent surgery under general anaesthesia with realization of a motor mapping using stimulations, while the other 17 patients (29%) were operated on awake under local anaesthesia: 3 with sensori-motor mapping (retrocentral lesion), and 14 with sensori-motor and language mapping (perisylvian lesion in the dominant hemisphere).

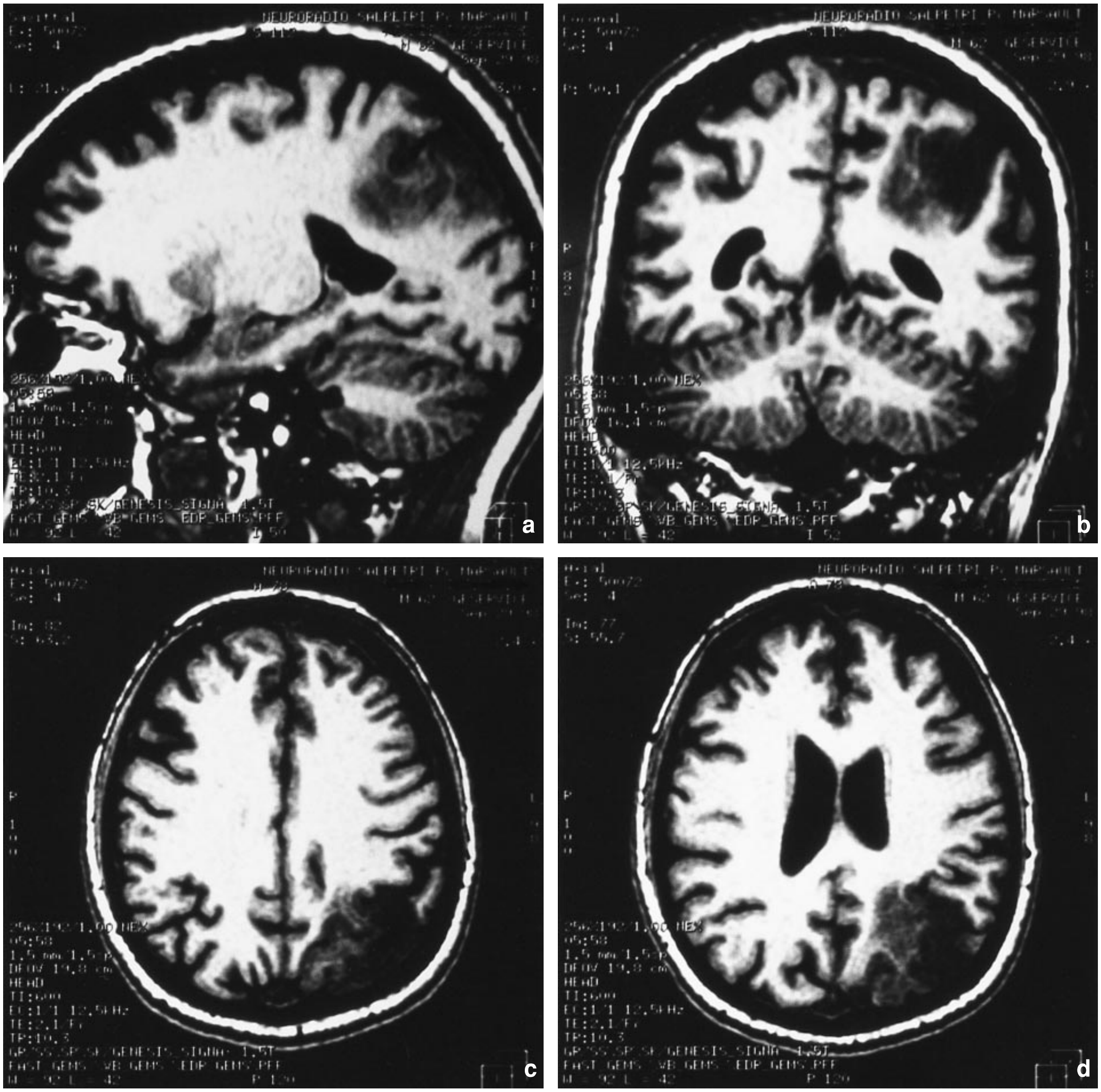

Fig. 1. Pre-operative sagittal (a), coronal (b) and axial (c and d) T1-weighted gadolinium-enhanced MRI showing a left parietal low-grade glioma extending to the temporo-parieto-occipital junction, diagnosed in a right-handed woman without any neurological deficit after generalized seizures

In all cases, eloquent areas were identified, without any ''negative'' brain mapping: it means that the motor sites were detected in the 60 patients, the somatosensory areas in the 17 awake patients, and the language (speech arrest and naming) sites in the 14 patients with specific language mapping. The resection was then *systematically* pursued up to contact with the eloquent cortical and sub-cortical areas detected by stimulations (with a 7 mm margin around the language sites already mentioned), to optimize the quality of the lesion removal. However, it was identified using intra-operative ultrasonography and/or neuronavigation a tumour residue infiltrating the functional areas (then without possibility of total removal) in 8 cases. Control cortical DES at the end of resection showed unchanged motor responses in all cases except 3: the threshold of electrical intensity was increased, nevertheless with a decrease of the motor response.

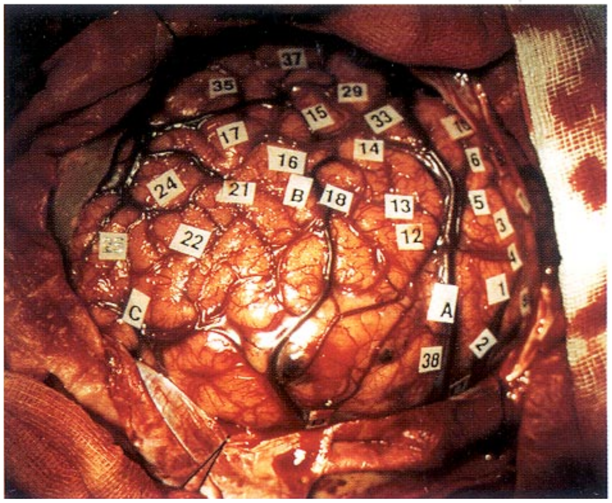

Fig. 2. Intra-operative view before resection. The letters A, B, C represent the limits of the tumour as identified by ultrasonography. The numbers mark the essential functional sites detected using direct cortical electrical stimulations under local anaesthesia on an awake patient: motor areas (2: arm, 1: forearm, 4: hand, 3 and 5: fingers, 6: face); somato-sensory areas (38: arm, 12: hand, 13: face); language areas (15 and 29: speech arrest during stimulations, 18 and 21: anomia during stimulations)

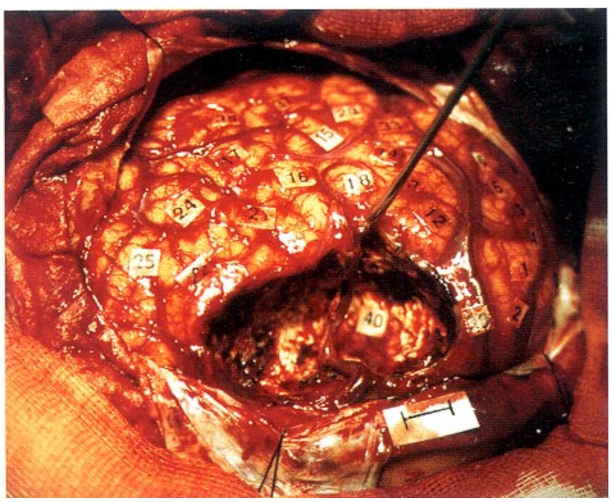

Fig. 3. Intra-operative view after the tumour resection. The primary motor areas (1 to 6) and somato-sensory areas (12, 13, 38) continue to give respectively motor and sensory responses during cortical stimulations, which means that the anatomo-functional integrity of the eloquent pathways is preserved. Moreover, the language areas (18, 21) were respected, with the sub-cortical stimulations allowing the identification of the corresponding descending language pathways [40]. The tumour removal was then stopped using functional boundaries

All procedures under local anaesthesia were well tolerated (median duration 5 hours), except in one case, where the patient was too tired to continue brain mapping during all the duration of the resection: surgery was then stopped, and the patient was re-operated on 2 months later with better co-operation.

No complication was noted due to the use of DES.

The histological examination showed 44 gliomas (31 low-grade and 13 high-grade), 9 metastasis, 3 cavernomas and 4 arteriovenous malformations (AVM).

29 patients had no postoperative deficit (48%), while 31 (52%) developed an immediate and transitory worsening of their neurological status (16 motor impairments in which 9 supplementary motor area syndromes [58], 12 language and 4 somatosensorial worsenings occurred): all these patients recovered within 15 days to 3 months, except 3 cases of high-grade gliomas – the 3 patients with the decrease of motor response during control cortical DES at the end of resection – (overall morbidity: 5%; postoperative mortality: 0). Nevertheless, in spite of normal objective neurological examination, approximately 10% of these patients complained of mild subjective discomfort after the surgery (particularly for left temporo-parieto-occipital lesions).

Quality of resection was systematically evaluated using immediate and/or delayed post-operative MRI (and angiography in the 4 AVM). Concerning the high-grade gliomas and metastasis, extent of removal was estimated on the basis of the contrast-enhancement. For all lesions, resection was considered subtotal in case of a residue with a volume less than 10 cc, and partial if the volume is more than 10 cc [10]. Resections were total in 31 cases (51%), subtotal in 21 cases (36%), and partial in 8 cases (13%) – because of infiltration of eloquent areas by the tumour.

The overall follow up for the 60 patients is 14 months.

Discussion

Principles

Although direct electrical stimulations are known for more than a century to induce alteration of brain function in animals [29] and humans [3], this method was used in neurosurgery only since 1930, first by Foerster [28], and then developed by Penfield who described the famous Homunculus [52, 53, 54]. Progressively, this technique expanded both geographically in the USA [5, 8, 9, 12, 13, 31, 36, 40, 47, 48, 49] and

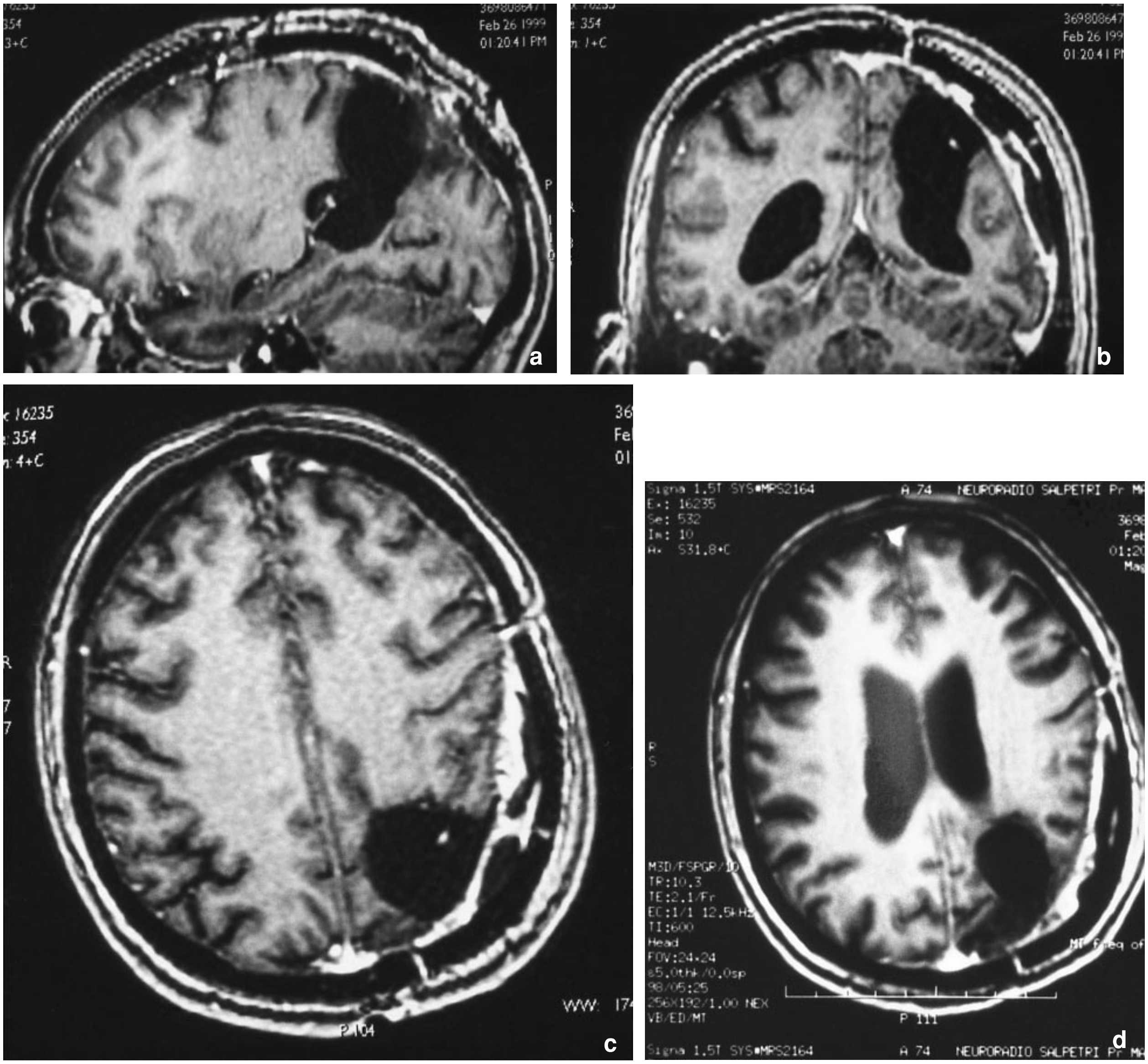

Fig. 4. Post-operative sagittal (a), coronal (b) and axial (c and d) T1-weighted gadolinium-enhanced MRI performed 3 months after the surgery, and showing a total resection. The patient presented a transitory right hemiparesia, right hemihypo-aesthesia and mild dysphasia during 15 days, with a complete recovery

likewise in Europe [22, 25, 26, 33, 70], the surgical indications were also widened for tumours [6, 7, 12, 22, 50, 58, 63, 68] and vascular lesions [13, 23].

The principle is based on the depolarisation of the local neurons and also of the passing pathways, inducing respectively local excitation or inhibition, plus the possibility of diffusion to more distant areas by orthodromic or antidromic propagation [56]. The result of DES seems then theorically unpredictable: the approach was consequently empiric. In practice, DES of the sensori-motor structures generate positive sensory and motor responses (predominance of the excitatory effect), while DES of the language (and memory) structures induce transitory blocking of the function (predominance of the inhibitory effect) [49, 53].

The recent use of a bipolar probe allowed the avoidance of local diffusion and a more precise mapping, as demonstrated with the optical imaging method [30], with an accuracy nowadays estimated around 5 mm.

Moreover, DES are safe for the central nervous system, as observed by the histological examination of resected structures first stimulated in vivo (lack of in-

Table I. *Clinical, Radiological, Histological and Treatment Characteristics of the 60 Patients Operated Using Intraoperative Direct Electrical Stimulations*

Lesions	Number of cases	Presenting Symptoms and signs						Location								Mapping			Transitory clinical worsening	Definitive sequelae	Quality of resection		
		seizures (normal examination)	deficit: motor	deficit: sensory	deficit: language	deficit: total	intracranial hypertension	precentral	postcentral	left fronto-opercular	left temporal	left TPO	left insular	right insular	lenticulo-caudate	GA motor	SM	LA SM+ lang			total	sub-total	partial
Supra-tentorial Brain Lesions																							
Low-grade gliomas	31	26	1	3	1	5		14	3	5	3	2	1	3		19	1	11	19		12	14	6
High grade gliomas	13	4	5	1	1	7	2	7	4		1		1			9	2	2	8	3	4	7	2
Metastasis	9	3	6			6		6	3							9			2		9		
Cavernomas	3	1	1		1	2		2							1	3			1		3		
AVM	4	3	1			1		1	2	1						3		1	1		4		
Total	60	37 (61%)	14	4	3	21 (35%)	2 (4%)	30 (50%)	12 (20%)	6 (10%)	4 (7%)	2 (3.5%)	2 (3.5%)	3 (5%)	1 (1%)	43 (71%)	3 (6%)	14 (23%)	31 (52%)	3 (5%)	31 (51%)	21 (36%)	8 (13%)

* 39 Males; 21 females; mean age: 45 years (21 to 71 years); median follow-up: 14 months.
GA General anaesthesia; *LA* local anaesthesia; *SM* sensory-motor; *Lang* language; *TPO* temporo-parieto-occipital.

flammation or other injury), and suggested by the follow up of patients [46]. No complication due to DES was noted in our series.

In addition, DES represent a reliable method: but the sine qua non condition is to identify the eloquent areas before any resection. Indeed, if a positive mapping assures the surgeon that the neural structures are functional and then must be preserved, a negative mapping does not guarantee the absence of eloquent sites. In this way, Taylor described in a recent study five patients with permanent worsening despite negative brain mapping [68]. Consequently, we perform in our experience systematically a wide boneflap, to expose the lesion and the functional regions both to be detected before the resection. Then, we obtained the identification of eloquent sites in all our procedures (100% of sensitivity of DES in our experience).

Moreover, at the end of removal, we used in all cases cortical stimulations to check the anatomo-functional integrity of the eloquent pathways, particularly for motor areas under general anaesthesia (then with the inability to ask the patient to realize each movement before the closure). Indeed, if these *cortical* stimulations induce, at the same current intensity than before resection the same motor responses at the same sites, it becames sure that the patient will recover full motor functions, even in case of an immediate post-operative deficit. This observation is illustrated by our results, since only 3 patients presented permanent worsening. These were 3 cases of high-grade gliomas with pre-operative deficit which made brain mapping less precise [8] (probably due to the fact that the tumour begins to infiltrate functional areas): in the attempt to perform the most extensive resection, the tumour excision was probably conducted too close to the eloquent sites, and the cortical stimulations at the end of the removal still induced motor responses but decreased and only with a higher current intensity. Then, the definitive post-operative impairment shows the good predictive value of direct cortical stimulations after resection, since the 57 other patients with unchanged motor responses during DES (with the same parameters than before resection) at the end of the lesion removal recovered (100% of specificity of DES in our experience).

However, if DES represent a reliable method for identifying and then preserving eloquent areas avoiding a *definitive* post-operative deficit, stimulations do not prevent and do not predict a transitory immediate neurological worsening when the resection is pursued close to the functional networks (31 patients in our series), because of:

(1) the post-surgical oedema;
(2) probably haemodynamic perturbations – to confirm using notably diffusion and perfusion-weighted MRI, a study started in our institution –;
(3) supplementary motor area (SMA) syndromes (9 cases in our experience) known to recover [58] and more recently known to occur only when the SMA-proper area is removed [37], independently of the results of DES identifying the primary motor area.

Indications

Tumour surgery. One of the most general principles in oncology is that survival is better if a larger surgical resection of the tumour is performed. This rule is also accepted in neuro-oncology, and usually applied to extracerebral lesions, but the main problem for intracerebral tumour remains the functionality of the brain. The aim becomes then to maximize the amount and hence the quality of resection of tumours from an oncological point of view, while minimizing the risk of definitive post-operative neurological deficit.

Prediction of functional organization of the brain areas using classical anatomical criteria is not reliable, because of the existence of an important individual variability in normal subjects [32] as in patients with a brain lesion [49], with an increase of this variability due to the mass effect and the possible functional reorganization by cerebral plasticity mechanisms [50, 61, 72]. Indeed, Uematsu reported that the primary motor area may extent more than 20 mm anterior to the central sulcus [69], making anatomical identification inadequate for a safe resection in this region. Concerning the language function, it is nowadays well-known that there are multiple essential cortical areas distributed differently from the Broca-Wernicke's model, without reliable anatomical landmarks, particularly for the surgery of the dominant hemisphere "perisylvian" lesions [31, 49]. Moreover, brain tumours may contain functional tissue in a patient without any deficit [50, 63]. The use of intra-operative DES allowing a real-time and accurate detection of the essential functional neural structures seems then mandatory.

Consequently, the application of this method to intracerebral glioma removal in an eloquent region may help to generate a new concept for their surgical management. Indeed, it becomes possible to perform a resection using functional instead of anatomical boundaries, namely to continue to resect the tumour but also the peritumoural tissue often infiltrated [17, 35], from which come the recurrences, until eloquent brain structures are encountered. This attitude then allows one to optimize the chances to improve the quality of life and the median of survival which depends on the extent of resection for low grade gliomas [1, 10, 34, 38, 42, 55, 65] as for high-grade gliomas [2, 14], while decreasing the risk of neurological sequelae.

Then, regarding morbidity, the use of intra-operative mapping generates five percent only of post-operative definitive neurological deficit for gliomas located in or near functional sites, in the main reports of the literature as in our experience [9, 12, 26, 31, 63, 68].

Concurrently, concerning the quality of resection of gliomas in eloquent areas, our experience shows approximatively 82% of total and subtotal resections verified on postoperative MRI, with in cases of partial removal (residue >10 cc), an interruption of the surgery because the tumour invaded functional tissue: our series then confirms the ability for gliomas to infiltrate eloquent regions without generating any deficit, as previously reported in the literature [50, 63]. Consequently, the classical surgical principle that debulking the tumour from within will avoid neurological worsening is inadequate.

The same attitude can be applied to the management of brain metastasis in eloquent areas, since more and more authors agree that there is tumoural infiltration around these lesions, suggested by 20% of local recurrence in the main series of the literature [18, 20, 51, 64]. This finding then gives arguments in favour of a larger removal than the metastasis itself, with a margin of some millimeters, raising the same problem of the limit of resection in functional regions than in the case of infiltrative gliomas, and showing the interest of DES.

Indeed, we have operated on 9 metastasis in eloquent areas using DES, without any post-operative deficit, and even with an improvement of the neurological status in 6 cases. Concurrently, all resections were "supra-complete".

Vascular surgery. – Cavernous angiomas

DES are useful during surgery of cavernomas in eloquent regions first for the determination of the best surgical approach (cortical mapping), and also for the improvement of the quality of resection (sub-cortical mapping). Indeed, it is nowadays well-known that around the cavernoma is a gliosis likely to contain associated telangiectasias, which represent the high risk of (re)bleeding in case of incomplete removal [15, 21]. Then, if the resection of the cavernous angioma is usually easy, the accurate definition of the interface between gliosis and the normal tissue is often difficult: DES become consequently very helpful in functional areas. Our 3 cases of cavernomas operated on using DES were totally resected without any clinical worsening, and with a histological diagnosis in one case of telengiectasias in the peripheral gliosis associated to the cavernous angioma.

– Arterio-venous malformations (AVM)

In the same way, the precise definition of the best surgical trajectory and of the boundaries between the malformation and the normal brain in an eloquent region is most of the time necessary, because of the more frequent existence of functional reorganization in AVM [43] (probably due to its congenital development). Moreover there is in this kind of vascular malformation inducing haemodynamic disturbances, an increased unreliability of pre-operative functional MRI even for motor cortical mapping [4], at the opposite of DES [13] (since they have an electrophysiological and not haemodynamic basis for recording).

Epilepsy surgery. Although DES were particularly used for this indication [47, 48, 49, 52, 53, 54, 71], we can not debate the place of intra-operative mapping in these cases because of lack of epilepsy surgery in our experience.

Perspectives

Combined recent technical improvement of the DES method and development of the neuro-imaging techniques should allow:

- A wider pre-operative battery of functional tasks, particularly for language, with the aim of a better selection of the intra-operative tests adapted to the patient and the location of the lesion (counting, naming, but also verb generation, calculation, reading, writing, memory, ... and even neuropsychological examination);
- A prospective study of the correlation between pre-operative functional imaging data and intra-operative DES data, to increase the sensitivity and

specificity of the neuro-imaging methods, especially for language, and then to benefit from a more reliable functional preplanning before surgery;
- A comparison of pre-, intra- and also post-operative functional mapping, correlated with clinical evolution, to understand better the mechanisms of functional reorganization induced by the lesion and by the surgery: this could allow for future patients to better anticipate the individual risk of transitory and definitive post-operative neurological disorders [37], since in our series, if the permanent worsening was only 5%, 52% of patients have presented a transitory impairment of their neurological status (sometimes with the persistence of mild subjective discomfort).

Conclusion

Direct electrical stimulations constitute an easy, reliable, precise and safe method, allowing the realization of a functional brain cortico-sub-cortical mapping useful for every surgical procedure of the central nervous system. This technique allows minimization of definitive post-operative neurological deficit, and concurrently an improvement in the quality of lesion resection.

References

1. Abdulrauf SI, Edvardsen K, Ho KL, Yang XY, Rock JP, Rosenblum ML (1998) Vascular endothelial growth factor expression and vascular density as prognosis markers of survival in patients with low-grade astrocytoma. J Neurosurg 88: 513–520
2. Ammirati M, Vick N, Liao Y, Ciric I, Mikhael M (1987) Effect of the extent of surgical resection on survival and quality of life in patients with supratentorial glioblastomas and anaplastic astrocytomas. Neurosurgery 21: 201–206
3. Bartholow R (1874) Experimental investigations into functions of the human brain. Am J Med Sci 67: 305–313
4. Beltramello A (1996) Motor cortex activation in a patient with arteriovenous angioma in the left region. Inter Neuroradiol 2: 155–156
5. Berger MS, Kincaid J, Ojemann GA, Lettich E (1989) Brain mapping techniques to maximize resection, safety and seizure control in children with brain tumors. Neurosurgery 25: 786–792
6. Berger MS, Ojemann GA, Lettich E (1990) Neurophysiological monitoring during astrocytoma surgery. Neurosurg Clin North Am 1: 65–80
7. Berger MS, Ojemann GA (1992) Intraoperative brain mapping techniques in neuro-oncology. Stereotact Funct Neurosurg 58: 153–161
8. Berger MS (1993) Lesions in functional ("eloquent") cortex and sub-cortical white matter. Clin Neurosurg 41: 444–463
9. Berger MS (1994) Functional mapping-guided resection of low-grade gliomas. Clin Neurosurg 42: 437–452
10. Berger MS, Deliganis AV, Dobbins JD, Keles GE (1994) The effect of extent of resection on recurrence in patients with low grade cerebral hemisphere gliomas. Cancer 74: 1784–1791
11. Binder JR, Swanson SJ, Hammeke TA, Morris GL, Mueller WM, Fischer M, Benbadis S, Frost JA, Rao SM, Haughton VM (1996) Determination of language dominance using functional MRI. A comparison with the Wada test. Neurology 46: 978–984
12. Black P, Ronner S (1987) Cortical mapping for defining the limits of tumor resection. Neurosurgery 20: 914–919
13. Burchiel K, Clarke H, Ojemann GA, Dacey RG, Winn HR (1989) Use of stimulation mapping and corticography in the excision of arteriovenous malformations in sensorimotor and language-related neocortex. Neurosurgery 24: 322–327
14. Ciric I, Ammirati M, Vick N, Mikhael M (1987) Supratentorial gliomas: surgical considerations and immediate postoperative results. Neurosurgery 21: 21–26
15. Cohen HCM, Tucker WS, Humphreys RP, Perrin RJ (1982) Angiographycally cryptic histologically verified cerebrovascular malformations. Neurosurgery 10: 704–714
16. Danks RA, Rogers M, Aglio LS, Gugino LD, Black PM (1998) Patient tolerance of craniotomy performed with the patient under local anesthesia and monitored conscious sedation. Neurosurgery 42: 28–36
17. Daumas-Duport C, Scheithauer BW, Kelly PJ. A histologic and cytologic method for the spatial definition of gliomas. Mayo Clin Proc 62: 435
18. DeAngelis LM, Mandell LR, Thaler HT, Kimmel DW, Galicich JH, Fuks Z, Posner JB (1989) The role of postoperative radiotherapy after resection of single brain metastases. Neurosurgery 24: 798–805
19. Desmond JE, Sum JM, Wagner AD, Demb JB, Shear PK, Glover GH, Gabrieli JDE, Morrell MJ (1995) Functional MRI measurement of language lateralization in Wada-tested patients. Brain 118: 1411–1419
20. Dosoretz DE, Blitzer PH, Russell AH (1980) Management of solitary metastasis to the brain: the role of elective brain irradiation following complete surgical resection. Int J Radiat Oncol Biol Phys 6: 1727–1730
21. Duffau H, Capelle L, Sichez JP, Faillot T, Van Effenterre R, Bitar A, Arthuis F, Fohanno D (1997) Early rebleeding from intracranial cavernous angiomas: report of 12 cases and a review of the literature. Acta Neurochir (Wien) 139: 914–922
22. Duffau H, Sichez JP, Capelle L, Bitar A, Faillot T, Arthuis F, Van Effenterre R, Fohanno D (1998) Interest of peroperative direct cortical and sub-cortical electrical stimulations during tumor surgery in functional cerebral area: the Salpêtrière experience. EANO. Versailles. J Neuro-oncol 39: 2 O10–101 (abstract)
23. Duffau H, Sichez JP (1998) Intraoperative direct electrical stimulation of the lamina quadrigemina in a case of a deep tectal cavernoma. Acta Neurochir (Wien) 140: 1309–1312
24. Duffau H, Capelle L (1999) Direct spinal cord electrical stimulations during surgery of intramedullary tumoral and vascular lesions. Stereotact Funct Neurosurg. 71: 180–189
25. Ebeling U, Schmid UD, Reulen HJ (1989) Tumour-surgery within the central motor strip: surgical results with the aid of electrical motor cortex stimulation. Acta Neurochir (Wien) 101: 100–107
26. Ebeling U, Schmid UD, Ying H, Reulen HJ (1992) Safe surgery of lesions near the motor cortex using intra-operative mapping techniques: a report on 50 patients. Acta Neurochir (Wien) 119: 23–28
27. Fitzerald DB, Cosgrove GR, Ronner S, Jiang H, Buchbinder B, Belliveau JW, Rosen BR, Benson RR (1997) Location of language in the cortex: a comparison between functional MR Imaging and electrocortical stimulation. AJNR 18: 1529–1539

28. Foerster O (1931) The cerebral cortex of man. Lancet 2: 309–312
29. Fritsch G, Hitzig E (1870) Ueber die elektrische erregbarkeit des grosshirns. Arch Anat Physiol 37: 300–332
30. Haglund MM, Ojemann GA, Blasdel GG (1993) Optical imaging of bipolar cortical stimulation. J Neurosurg 78: 785–793
31. Haglund MM, Berger MS, Shamseldin M, Lettich E, Ojemann GA (1994) Cortical localization of temporal lobe language sites in patients with gliomas. Neurosurgery 34: 567–576
32. Herholz K, Thiel A, Wienhard K, Pietrzyk U, von Stockhausen HM, Karbe H, Kessler J, Bruckbauer T, Halber M, Heiss WD (1996) Individual functional anatomy of verb generation. Neuroimage 3: 185–194
33. Herholz K, Reulen HJ, von Stockhausen HM, Thiel A, Ilmberger J, Kessler J, Eisner W, Yousry TA, Heiss WD (1997) Preoperative activation and intraoperative stimulation of language-related areas in patients with glioma. Neurosurgery 41: 1253–1262
34. Janny P, Cure H, Mohr M (1994) Low grade supratentorial astrocytomas. Management and prognostic factors. Cancer 73: 1937–1946
35. Kelly PJ, Daumas-Duport C, Kispert DB, Kall B, Scheithauer B, Illig J (1987) Imaging-based stereotaxic serial biopsies in untreated intracranial glial neoplasms. J Neurosurg 66: 865
36. King RB, Schell GR (1987) Cortical localization and monitoring during cerebral operations. J Neurosurg 67: 210–219
37. Krainik A, Sahel M, Lehéricy S, Duffau H, Cornu P, Capelle L, Valery CA, Frouin V, Le Bihan D, Marsault C (1999) Occurrence of motor deficit following surgical resection of the mesial frontal lobe: fMRI study of the role of the SMA-proper. 5th international conference on functional mapping of the human brain. Düsseldorf. Neuroimage 9: 6(S685)
38. Laws ER, Taylor WF, Clifton MP, Okazaki H (1984) Neurosurgical management of low-grade astrocytoma of the cerebral hemispheres. J Neurosurg 61: 665–673.
39. Lehéricy S, Duffau H, Cornu P, Capelle L, Sichez JP, Fohanno D, Philippon J, Le Bihan D, Marsault C (1998) Presurgical fMRI mapping of cortical motor areas in patients with brain tumors: comparison with intrasurgical stimulations. 4th international conference on functional mapping of the human brain. Montréal. Neuroimage 7: 4 (S457)
40. LeRoux PD, Berger MS, Haglund MM, Pilcher WH, Ojemann GA (1991) Resection of intrinsic tumors from nondominant face motor cortex using stimulation mapping: report of two cases. Surg Neurol 36: 44–48
41. LeRoux PD, Berger MS, Wang K, Mack LA, Ojemann GA (1992) Low grade gliomas: comparison of intraoperative ultrasound characteristics with preoperative imaging studies. J Neurooncol 13: 189–198
42. Loiseau H, Bousquet Ph, Rivel J, Vital C, Kantor G, Rougier A, Dartigues JF, Cohadon F (1995). Astrocytomes de bas grade sus-tentoriels de l'adulte. Facteurs pronostics et indications thérapeutiques. A propos d'une série de 141 patients. Neurochirurgie 41: 38–50
43. Maldjian J, Atlas SW, Howard RS, Greenstein E, Alsop D, Detre JA, Listerud J, D'Esposito M, Flamm ES (1996) Functional Magnetic resonance imaging of regional brain activity in patients with intracerebral arteriovenous malformations before surgical or endovascular therapy. J Neurosurg 84: 477–483
44. Morota N, Deletis V, Lee M, Epstein FJ (1996) Functional anatomic relationship between brain stem tumors and cranial motor nuclei. Neurosurgery 39: 787–794
45. Nyberg G, Andersson J, Antoni G (1996) Activation PET scanning in pretreatment evaluation of patients with cerebral tumours or vascular lesions in or close to the sensorimotor cortex. Acta Neurochir (Wien) 138: 684–694
46. Ojemann GA (1983) Brain organization for language from the perspective of electrical stimulation mapping. Beh Brain Sci 6: 189–230
47. Ojemann GA, Dodrill CB (1985) Verbal memory deficits after left temporal lobectomy for epilepsy. J Neurosurg 62: 101–107
48. Ojemann GA, Dodrill CB (1987) Intraoperative techniques for reducing language and memory deficits with left temporal lobectomy. Avances in epileptology Vol 16. In: Wolf P, Dam M, Janz D, Dreifuss F (eds) Raven, New York, pp 327–330
49. Ojemann GA, Ojemann JG, Lettich E, Berger MS (1989) Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg 71: 316–326
50. Ojemann JG, Miller JW, Silbergeld DL (1996) Preserved function in brain involved by tumor. Neurosurgery 39: 253–259
51. Patchell RA, Tibbs PA, Walsh JW, Dempsey RJ, Maruyama Y, Kryscio RJ, Markesbery WR, MacDonalds JS, Young B (1990) A randomizal trial of surgery in the treatment of single metastases to the brain. N Engl J Med 322: 494–500
52. Penfield W, Bolchey E (1937) Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60: 389–443
53. Penfield W, Erickson TC (1941) Epilepsy and cerebral localization. A study of the mechanism, treatment and prevention of epileptic seizures. Charles C Thomas, Springfield III
54. Penfield W, Rasmussen T (1950) Secondary sensory and motor representation. Macmillan, New York
55. Piepmeier JM, Christopher S, Spencer D (1996) Variations in the natural history and survival in patients with supratentorial low-grade astrocytomas. Neurosurgery 38: 872–879
56. Ranck JBJr (1975) Which elements are excited in electrical stimulation of mammalian central nervous system: a review. Brain Res 98: 417–440
57. Rezai AR, Hund M, Kronberg E, Zonenshayn M, Cappell J, Ribary U, Kall B, Llinas R, Kelly PJ (1996) The interactive use of magnetoencephalography in stereotactic image guided neurosurgery. Neurosurgery 39: 92–102
58. Rostomily RC, Berger MS, Ojemann GA, Lettich E (1991) Postoperative deficits and functional recovery following removal of tumors involving the dominant hemisphere supplementary motor area. J Neurosurg 75: 62–68
59. Sartorius CJ, Wright G (1997) Intraoperative brain mapping in a community setting – technical considerations. Surg Neurol 47: 381–388
60. Sartorius CJ, Berger MS (1998) Rapid termination of intraoperative stimuled-evoked seizures with application of cold Ringer's lactate to the cortex. Technical note. J Neurosurg 88: 349–351
61. Seitz RJ, Huang Y, Knorr U, Tellmann, Herzog H, Freund HJ (1995) Large scale plasticity of the human motor cortex. Neuroreport 6: 742–744
62. Silbergeld DL, Mueller WM, Colley PS (1992) Use of Propofol (Diprivan) for awake craniotomies: technical note. Surg Neurol 38: 271–272
63. Skirboll SS, Ojemann GA, Berger MS, Lettich E, Winn R (1996) Functional cortex and subcortical white matter located within gliomas. Neurosurgery 38: 678–685
64. Smalley SR, Laws ERJr, O'Fallon JR, Shaw EG, Schray MF (1992) Resection for solitary brain metastasis: role of adjuvant radiation and prognostic variables in 229 patients. J Neurosurg 76: 444–449
65. Soffietti R, Chio A, Giordana MT, Vasario E, Schiffer D (1989) Prognostic factors in well-differentiated cerebral astrocytomas in the adult. Neurosurgery 24: 686–692

66. Strauss C, Romstöck J, Fahlbusch R (1993) Intraoperative mapping of the floor of the IVth ventricle. In Loftus CM, Traynelis VC (eds): Intraoperative Monitoring Techniques in Neurosurgery. McGraw-Hill, New York, pp 213–218
67. Strauss C, Romstöck J, Nimsky C, Fahlbusch R (1993) Intraoperative identification of motor areas of the rhomboid fossa using direct stimulation. J Neurosurg 79: 393–399
68. Taylor MD, Bernstein M (1999) Awake craniotomy with brain mapping as a routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. J Neurosurg 90: 35–41
69. Uematsu S, Lesser R, Fisher RS, Gordon B, Hara K, Krauss GL, Vinig EP, Webber RW (1992) Motor and sensory cortex in humans. Topography studied with chronic subdural stimulation. Neurosurgery 31: 59–72
70. Walsh AR, Schmidt RH, Marsh HT (1992) Cortical mapping and local anaesthetic resection as an aid to surgery of low and intermediate grade gliomas. Br J Neurosurg 6: 119–124
71. Weber JP, Silbergeld DL, Winn HR (1993) Surgical resection of epileptogenic cortex associated with structural lesions. Epilepsy surgery. Neurosurg Clin North Am 4: 327–336
72. Wunderlich G, Knorr U, Herzog H, Kiwit JCW, Freund HJ, Seitz RJ (1998) Precentral glioma location determines the displacement of cortical hand representation. Neurosurgery 42: 18–27
73. Yousry TA, Schmid UD, Jassoy AG, Schmidt D, Eisner WE, Reulen HJ, Reiser MF, Lissner J (1995) Topography of the cortical motor hand area: prospective study with functional MR imaging and direct motor mapping at surgery. Radiology 195: 23–29

Comments

This reviewer fully agrees with the importance of intra-operative mapping of function to conduct the surgical resection of lesions in and around eloquent areas. This should be a standard methodology in the management of such cases. I also agree that this information should be obtained cortically as well as subcortically. None the less functional MRI (fMRI) offers currently precise data for pre-operative identification of function, particularly motor, and therefore has a relevant place in pre-operative planning. A fMRI in a 3D reconstruction is a most valuable guide for the surgeon. Their comment of the use of cold saline for fast resolution of the fits induced by stimulation is interesting.

F. Isamat

The character of this study is said to be prospective and they included all patients with a severe pre-operative deficit and they did not include paediatric cases. They used a train of constant current intermediate frequency (60 Hz) biphasic square waves at an intensity of 0.5 to 16 mA. For identification of motor response an observer was used watching the face and the arm. They especially pointed out that using cortical stimulation at the end of the resection can verify the integrity of the motor tract. In the awake patients they have used a similar technique to map the postcentral sensory area with the patient describing paraesthesias. Language mapping was done by the suppression of speech through stimulation. One of the important findings in their central area lesions was that a majority of the patients had early but transitory worsening of their neurological status (30 with, 27 without). Degree of resection was assessed by postoperative MRI. It is interesting to note that only 51% of the cases had a total resection and 35% had subtotal resection meaning a residual tumour volume up to 10 cc. In their discussion they point out that cases have been described by other authors with permanent worsening of neurological function despite negative mapping and they also point out the difference in the principle of mapping motor tracts versus speech areas demonstrated by direct motor action and the latter demonstrated by inhibition of its function. The other interesting note is that all patients with permanent worsening had high-grade gliomas and that their rate of permanent neurological impairment was relatively low compared to other studies using similar techniques such as the one published by Cedzich *et al.* [1].

J. Schramm

Correspondence: Hugues Duffau, M.D., Service de Neurochirurgie 1, Hôpital de la Salpêtrière, 47 Bd de l'hôpital, 75651 Paris, Cedex 13, France.