Intraoperative subcortical stimulation mapping for hemispheric perirolandic gliomas located within or adjacent to the descending motor pathways: evaluation of morbidity and assessment of functional outcome in 294 patients

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Object. Intraoperative stimulation mapping of subcortical white matter tracts during the resection of gliomas has become a valuable surgical adjunct that is used to reduce morbidity associated with tumor removal. The purpose of this retrospective analysis was to assess the morbidity and functional outcome associated with this method, thus allowing the surgeon to predict the likelihood of causing a temporary or permanent motor deficit.

Methods. In this study, the authors report their experience with intraoperative stimulation mapping to locate subcortical motor pathways in 294 patients who underwent surgery for hemispheric gliomas within or adjacent to the rolandic cortex. Data were collected regarding intraoperative cortical and subcortical stimulation mapping results, along with the patient’s neurological status pre- and postoperatively. For patients in whom an additional motor deficit occurred postoperatively, its evolution was examined.

Of 294 patients, an additional postoperative motor deficit occurred in 60 (20.4%). Of those 60, 23 (38%) recovered to their preoperative baseline status within the 1st postoperative week. Another 12 (20%) recovered from their postoperative motor deficit by the end of the 4th postoperative week, and 11 more recovered to their baseline status by the end of the 3rd postoperative month. Thus, 46 (76.7%) of 60 patients with postoperative motor deficits regained their baseline function within the first 90 days after surgery. The remaining 14 patients (4.8% of the entire study population of 294) had a persistent motor deficit after 3 months. Patients whose subcortical pathways were identified with stimulation mapping were more prone to develop an additional (temporary or permanent) motor deficit than those in whom subcortical pathways could not be identified (27.5% compared with 13.1%, p = 0.003). This was also true when additional (permanent) motor deficits lasted more than 3 months (7.4% when subcortical pathways were found, compared with 2.1% when they were not found; p = 0.041).

Conclusions. In patients with gliomas that are located within or adjacent to the rolandic cortex and, thus, the descending motor tracts, stimulation mapping of subcortical pathways enables the surgeon to identify these descending motor pathways during tumor removal and to achieve an acceptable rate of permanent morbidity in these high-risk functional areas.

Key Words • glioma • intraoperative stimulation mapping • subcortical motor pathway • white matter tract

The prognostic significance of the extent of resection remains a controversial issue in the treatment of hemispheric gliomas.2,12,14 Notwithstanding, in any circumstance in which the surgeon attempts to resect a glioma that is within or adjacent to motor pathways, stimulation mapping can be a reliable method to minimize morbidity related to the tumor resection.1,3,4,6,7,13,18

Preoperatively, functional imaging has enabled surgeons to identify cortical regions that have functional importance as it relates to the glioma volume. Currently, there is no reliable imaging method to identify intact and functional subcortical pathways. Subcortical fiber tracking is a promising new imaging modality that is based on the principle of the anisotropic diffusion of water in axons, otherwise known as diffusion tensor imaging.16 We have started to use this method to visualize descending motor pathways starting from a functional cortical site and extending through the corona radiata, posterior limb of the internal capsule, and the cerebral peduncle. Nevertheless, diffusion tensor imaging tractography may be limited in areas where the tracts pass through the tumor or edema (unpublished data).

For the last 15 years, we have used subcortical stimula-
tion mapping procedures to identify descending subcortical pathways during resection of hemispheric gliomas. The purpose of this study was to describe our method of intraoperative subcortical stimulation mapping, and to define the morbidity profile associated with the use of this modality in a population that consists exclusively of patients with gliomas that are either within or adjacent to the cortical and subcortical motor pathways.

Clinical Material and Methods

Patient Population

The study population consisted of all patients with hemispheric gliomas within or adjacent to the rolandic cortex who underwent surgery in which intraoperative cortical and subcortical stimulation mapping methods were used.

Patients ranged in age from 18 to 79 years (median 46 years), and included 129 women (44%) and 165 men (56%). There were 122 patients (41%) with LGGs, and 172 (56%) had HGGs. Forty-two percent (124 patients) had a preoperative motor deficit (3/5 strength or more, excluding the 99% who had a deficit preoperatively were excluded from this analysis. Hospital records, operative reports, intraoperative mapping worksheets, and follow-up records were reviewed for each patient. The data collected consisted of findings related to intraoperative cortical and subcortical mapping, patients’ pre- and postoperative neurological status, age, sex, and results of tumor histological examinations. All patients with a postoperative additional motor deficit were followed up for at least 3 months postoperatively. This study was conducted with approval from the Committee on Human Research from both institutions.

To assess the factors that may be associated with functional morbidity when using subcortical stimulation mapping methods, we analyzed the relationship of morbidity to intraoperative and tumor histological findings, preoperative neurological deficit, and year of surgery. The latter variable was evaluated to assess whether a surgeon’s experience with this modality had any influence on patients’ functional outcome. For the purpose of this analysis, Grade II astrocytomas, oligoastrocytomas, oligodendrogliomas, and gangliogliomas were grouped as LGGs, whereas anaplastic astrocytomas, glioblastomas multiforme, and Grade III oligoastrocytomas were considered to be HGGs. Tumors were graded according to the World Health Organization classification.15,21 For patients in whom an additional motor deficit was observed postoperatively, we examined the evolution of this deficit over time. Any additional motor deficit that persisted beyond 3 months postoperatively was considered to be permanent for this outcome evaluation. Data regarding the patients’ postoperative neurological status were obtained from hospital charts by using the follow-up examination notes based on the attending neurosurgeon’s and neurooncologist’s evaluations.

The intraoperative procedure used for subcortical stimulation mapping is described in detail elsewhere.1,3 Briefly, a constant-current generator (Ojemann Cortical Stimulator; Radionics, Inc., Burlington, MA) is used to deliver a biphasic square-wave pulse to depolarize the cortical motor neurons or descending axonal pathways. Once the cortical motor region is stimulated and identified, the same current is used to localize descending motor pathways. The current may vary from 2 to 16 mA (60 Hz, 1 msec, single-phase duration), depending on the anesthetic status of the patient. The patient’s body temperature is maintained at 36°C or above. Since 1997, a multichannel electromyography recording method has been used, which results in greater sensitivity in detecting muscle movements.39 This allows the
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Statistical Analysis

We evaluated whether histological findings, presence of a preoperative motor deficit, or a functional site found during subcortical stimulation mapping were predictors of additional motor morbidity (temporary or permanent) by using multivariate logistic regression models that included all three variables. Probability values and ORs presented in this study were calculated from these multivariate analyses.

Results

Intraoperative Findings

Subcortical stimulation mapping was attempted in all patients, and we were able to identify subcortical motor tracts in 149 (51%). During the first few years of this study period, approximately 6% of patients were awake while being surgically treated. Since then, stimulation mapping has been performed under asleep conditions in 99% of patients.

Incidence of Morbidity and its Time Course

There were a total of 60 patients (20.4%) who experienced an additional motor deficit postoperatively. Of these patients, 23 (38.3%) recovered within the 1st postoperative week, and in another 12 (20%) postoperative motor deficit resolved by the end of the 1st postoperative month. Additional motor deficits in 11 (18.3%) of 60 patients resolved by the end of the 3rd postoperative month. In the remaining 14 (23.3%), a permanent deficit, that is, one lasting longer than 3 months, was identified. These 14 patients with additional, permanent motor deficits constitute 4.8% of the entire study population. Of these 14 patients, eight were judged to have a mild neurological deficit, that is, 4/5 strength or better. In three patients the affected muscle groups were able to move against gravity (3/5, moderate deficit), whereas in the other three the neurological deficit was severe, that is, the muscle groups were not able to move against gravity.

Patient Groups According to Intraoperative Findings

Tables 1 and 2 show the intraoperative findings in detail, including cortical and subcortical stimulation mapping results, and the presence of a preoperative neurological deficit as it relates to functional outcome. Stimulation mapping of the motor cortex was performed in the majority of our patient population (276 [94%] of 294), and cortical motor sites were identified in 260 (94% of 276 patients in whom cortical mapping was attempted). Stimulation mapping of the motor cortex was not attempted in 18 patients (12 of whom underwent repeated operations) in whom either there was no cortex overlying the tumor (that is, a resection cavity) or in whom the exposure did not allow cortical mapping (that is, the dura mater was adherent to cortex).

In the remaining 276 patients in whom cortical stimulation mapping was attempted, cortical motor sites were not identifiable in 16, regardless of the current used. In these 16 patients, a motor response to cortical stimulation could not be elicited despite adequate body temperature and a func-
deficit. N = number.

patients, that is, those in whom both cortical and subcortical
deficit was permanent (Table 2). Within this group of pa-
ents (7.6%) of these patients the additional
132 suffered an additional motor deficit (temporary or per-
data were found, identifiable subcortical sites (p = 0.012). For patients
in whom we could not find subcortical pathways by using stimulation mapping, the in-
cidence of additional motor deficits (temporary or perma-
nent) was 14.8% (19 of 128), and for 2.3% (three of 128),
the additional deficit was permanent. Within this group of
patients, that is, when cortical sites were found but no sub-
cortical site was identified, the presence of a preoperative
motor deficit increased the overall incidence of additional post-
operative deficits from 10.7 to 20.8% (p = 0.015), but did not
have a statistically significant effect on the incidence of a
permanent deficit (7.7% for neurologically intact patients
compared with 7.4% for those who had a preoperative de-

Cortical and Subcortical Sites Identified. As shown in Table 2, the two most common scenarios
occurred when both cortical and subcortical sites were identi-
fied (132 patients) and when there were identifiable cortical
sites but subcortical sites were not found (128 patients).
Figure 1 outlines the incidence of additional temporary and
permanent motor deficits based on the intraoperative map-
ping findings along with the preoperative motor status. On
analysis of the 260 patients in whom cortical sites were
found, identifiable subcortical sites (p = 0.012) and a pre-
operative motor deficit (p = 0.015) were factors associated
with a higher incidence of additional postoperative motor
deficits in multivariate analysis.

Risk Factors for Additional Motor Deficits

Table 1 summarizes the incidence of additional tempo-
rary and permanent motor deficits as they relate to intraop-
erative and histopathological findings, and the presence of
a preoperative neurological deficit. Multivariate analysis on
the entire group of 294 patients showed that the presence of
a preoperative motor deficit, along with identification of a
subcortical site with stimulation mapping, were indepen-
dent risk factors for an additional postoperative motor de-
fect. Patients with identifiable subcortical pathways were
more prone to experience an additional (temporary or per-
manent) motor deficit than those in whom subcortical path-
ways could not be identified (27.5% compared with 13.1%,
p = 0.003). This was also true when only additional (per-
manent) motor deficits lasting more than 3 months were
considered (7.4% when subcortical pathways were found
compared with 2.1% when subcortical pathways were not
found; p = 0.041). Patients in whom a motor deficit was
present before surgery were more likely to have an addi-
tional motor deficit postoperatively compared with those
whose motor functions were intact (25.8% compared with
16.5%, p = 0.046). Nevertheless, the presence of a preoper-
ative motor deficit was not a predictor for development of a
permanent postoperative motor deficit.

The odds that an additional postoperative motor deficit
would develop were increased 1.8 times (95% CI 1.03–
3.29) in the presence of a preoperative motor deficit, and 2.6
times (95% CI 1.39–4.69) if a subcortical site was identified
during tumor removal. Multivariate analysis showed that
the relative increase in the odds for one factor, that is, find-
ing a subcortical site or preoperative deficit, did not depend
on the presence or absence of the other factor. In other
words, there was no statistically significant interaction be-
tween these two variables. Thus the OR for a patient in
whom both factors were positive compared with that for a
patient in whom both factors were negative can be estima-
ted by multiplying the two individual OR estimates. There-

Fig. 1. Chart outlining incidence of additional postoperative mo-
tor deficit. N = number.
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fore, these results indicate a 4.7-fold increase in the odds of a new temporary deficit in patients who had a preoperative deficit and in whom a subcortical pathway was found during surgery. For permanent motor deficits, the only statistically significant risk factor was presence of an identifiable subcortical site, which increased the risk 3.8 times (95% CI 1.02–13.81).

Histological findings did not have a statistically significant impact on functional morbidity. Similarly, the year of surgery failed to show any predictive pattern, indicating there is no substantial learning curve for this intraoperative method.

Discussion

The goal of this retrospective analysis was to determine the incidence of a temporary or permanent motor deficit developing postoperatively when the subcortical stimulation mapping modality is used to locate the descending motor pathways. This incidence was assessed in a high-risk population of patients in whom glial tumors were located within the rolandic cortex or directly adjacent to it and its descending subcortical motor pathways. This is the first extensive series of patients evaluated using this modality to determine its effect on postoperative morbidity. In the current literature there is no similar study that specifically addresses this particular issue, that is, postoperative morbidity, according to whether cortical and/or subcortical functional sites were identified with stimulation mapping. There are, however, a limited number of series and case reports, most of which include tumors with various histologies, including nonneoplastic lesions, in which this method has been used. The heterogeneity of these studies in terms of lesion characteristics, without details provided regarding the relationship of morbidity to the intraoperative findings specifically, motivated us to assess our experience over the past 15 years with this stimulation mapping method.

In a recent study, Eisner, et al.,9 presented 10 patients with subcortical lesions in the sensorimotor strip. These patients presented with a histologically mixed group of tumors, including mostly metastatic and nonneoplastic lesions, for which cortical and subcortical stimulation mapping methods were used. Although their case series is not comparable with our study because of the lesion characteristics, five patients who had no preoperative motor deficit remained neurologically intact after surgery. Nevertheless, of the five patients in whom a motor deficit was found preoperatively, four improved within the first 4 postoperative weeks, whereas in the remaining patient the additional motor deficit was permanent. In this earlier study, however, no attempt was made to assess whether an additional motor deficit arose based on whether the subcortical pathways were found. Thus, it is difficult to use the results of Eisner, et al., to predict the likelihood of an additional motor deficit.

Duffau, et al.,6 reported their experience with cortical and subcortical mapping in 60 patients in whom lesions including gliomas, metastatic tumors, and vascular malformations located in “supratentorial brain eloquent areas” were found. Forty-three (71%) of their patients underwent motor mapping after induction of general anesthesia, whereas the remaining patients underwent awake craniotomies. Although the authors identified eloquent areas in all cases, it is not clear in how many patients subcortical sites were identified. Thirty-one patients (52%) had an additional neurological deficit, of which 16 were motor deficits, including nine patients with a supplementary motor area syndrome, which is a reversible dysfunction. An additional deficit resolved within 3 months in all cases except in three patients with HGGs in whom a preoperative deficit was present. In a case report published 1 year later, Duffau7 described the use of subcortical stimulation to locate and map different somatotopic areas of the internal capsule during computer-assisted resection of a cavernoma. The patient in this case suffered mild worsening of the existing hemiparesis, which resolved by the 10th postoperative day. Recently, the same group reported their experience with mapping subcortical motor pathways in 14 patients with LGGs involving the nondominant striatum.8 Additional motor deficits were observed in 10 patients, and resolved in all but one within the first 3 postoperative months. No attempt was made, however, to relate an additional deficit to identification of cortical and subcortical pathways.

In the literature there are also a few studies in which subcortical stimulation mapping of the motor pathways was used as an adjunct to surgery, but these reports do not specifically address the method or the morbidity rate associated with the use of subcortical mapping of the motor pathways.10,17,19

Our detailed analysis of the study population in which subcortical stimulation mapping was used has provided very useful data. First, the subcortical mapping technique is a robust stimulation mapping method for identification of subcortical motor pathways during resection of gliomas. In our experience, this identification was possible in most cases, except when the motor cortex could not be exposed, or when we simply could not identify the motor cortex for various reasons, including possible variations in anesthetic regimens. Notwithstanding, despite not finding a cortical functional site or simply not using the cortical mapping method, we were still able to identify subcortical descending pathways in 50% of these cases. Second, the data provided in this study, based on the intraoperative findings, can be used to predict the likelihood of suffering both an additional and a permanent deficit.

In our experience, when both a cortical and subcortical site was found, regardless of whether a preoperative motor deficit existed, the likelihood of a permanent deficit eventually developing was 7.6%. In contrast, when a subcortical site was not found, despite identification of a cortical site, the likelihood of a permanent deficit developing decreased to approximately 2%. Based on our knowledge of current spread described earlier, it is clear that if subcortical sites are found, the surgeon is either within or very close (that is, 2–3 mm) to the descending motor tracts. This is why we advocate a procedure of routinely alternating tumor resection with stimulation mapping to avoid proceeding too far in the resection without looking for subcortical pathways. This is especially true when the operation takes place within or directly adjacent to the rolandic cortex. It has been suggested that this surgical strategy, that is, continuing resection until a positive response is found, could result in a higher likelihood of a permanent deficit. Indeed, this has been our experience, because pushing the resection close to the subcortical pathways that have been stimulated could result in additional edema or retraction injury to these pathways.
which, although it leads to an increased incidence of permanent morbidity, is often not disabling. Nevertheless, if the subcortical sites are not found by the end of the tumor resection when operating in this region, the surgeon can be relatively certain that the chance of a permanent deficit is only 1.9 or 2.7%, at most, depending on the patient’s motor function.

Another way to interpret this would be to conclude that in the most common scenario, in which both a cortical and subcortical site are found, regardless of the preoperative motor deficit status of the patient, an additional motor deficit can be found in up to 37% of patients temporarily, yet only approximately 7% of patients will eventually have a permanent postoperative motor deficit, which in most cases will not be debilitating. This is based on our knowledge of the stimulating current spread associated with this procedure, indicating that when subcortical pathways are identified during stimulation mapping, the resection margin is either within them or 2 to 3 mm away. This is why we advocate the method of intermittent tumor resection and stimulation mapping in a back-and-forth fashion, especially as the resection gets closer to the motor and subcortical pathways. Thus, when the subcortical pathways are found with stimulation mapping, the surgeon must stop and not resect further, because of the potential injury to these pathways. As it is, we found a 7% permanent morbidity at this point.

The other scenario consists of a situation in which a cortical site is found but the subcortical pathways cannot be identified. This typically indicates a circumstance in which the bipolar electrode is more than 2 to 3 mm away from the motor pathways at any given time during or at the end of the resection. Regardless of the presence of a preoperative motor deficit, the likelihood of causing a permanent motor deficit in this scenario drops to approximately 2%. Certainly, the number of additional motor deficits that are temporary will be higher when a preoperative motor deficit is found, but most importantly, the number of permanent deficits in this setting is certainly quite low.

In situations in which the cortical site cannot be found, the surgeon must be extremely cautious in relying on subcortical mapping alone. In our experience, we were able to salvage the procedure after finding subcortical pathways in 50% of these cases, whether we actually looked for the cortical site or whether we looked for and did not find it. We recommend extreme caution in this setting and if the surgeon is going to use this method, we recommend starting with a very high current of approximately 10 to 12 mA, and proceeding up to 16 mA. The failure to find subcortical pathways in this setting, especially if the anesthetic conditions are ideal, can be relied on in predicting the postoperative outcome, although the numbers in our series were too small for us to predict the likelihood of additional or permanent deficits with any degree of statistical certainty.

In addition to the risk associated with identifying subcortical pathways, performing surgery in a patient with a preoperative motor deficit increased the likelihood of postoperative functional morbidity. We would like to reemphasize that our study group consisted of patients with tumors located in very close proximity to or within the descending motor tracts, which may have contributed to this increased risk. In addition, postoperative new motor deficits may be caused by injury to tiny perforating arteries in some cases, as we have documented on postoperative imaging studies, for example, on diffusion-weighted sequences.

Conclusions

When using stimulation mapping methods to identify subcortical pathways, the surgeon is able to achieve an acceptable risk of permanent motor deficits in this high-risk patient population, which consists of those with gliomas that are within or adjacent to motor tracts. In this setting, if both cortical and subcortical sites are found with stimulation mapping, one can expect a 7.6% rate of permanent motor deficits postoperatively, of which only three (2.3%) of 132 of our patients had 2/5 strength or less. In cases in which subcortical pathways could not be identified but in which the functionally intact status was confirmed by stimulation of the corresponding cortical sites, the incidence of permanent morbidity was 2.3%, of which group no patient had 2/5 function or less. Our results indicate that these methods can be applied in patients whose tumors are located within or adjacent to functional motor pathways, and will result in an acceptable rate of postoperative morbidity that is mostly transient.

References

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Manuscript received May 19, 2003. Accepted in final form October 27, 2003.
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