Optimal treatment of insular tumors remains controversial. Thanks to the pioneering work by Yaşargil et al., we learned that removal of insular tumors was possible with low morbidity. These preliminary reports were followed by several recent publications. From an oncological point of view, the resection rate correlates with the survival rate.

The clinical relevance of intraoperative mapping and monitoring has been demonstrated in various publications. Intraoperative mapping and monitoring involving CMAPs is a valid modality for reducing iatrogenic morbidity during surgery in and around the central region as well as for intracranial aneurysms. Two methods are used for intraoperative mapping and monitoring during surgery in and around the insula. The first is the TCES of the motor cortex. Neuloh et al. have proven that continuous intraoperative mapping and monitoring is a valid indicator of motor pathway function during insular glioma surgery. However, their report, as well as the previous anecdotal reports on monitoring for insular tumor surgery, implies a direct stimulation of the motor cortex allows only monitoring without functional localization of the descending motor pathways.

The second method is using a bipolar stimulus for direct subcortical stimulation. Functional guidance using a bipolar subcortical stimulation has been employed by several groups. It has been described as a useful mapping tool for identifying the deep motor tracts at the medial and dorsal part of insular gliomas but it does not allow monitoring of the function.

The purpose of this study was to establish a protocol in which we could use both modalities, TCES for monitoring and subcortical stimulation for mapping. For this purpose, we modified the monopolar stimulation technique for subcortical stimulation. This was combined with the classic direct cortical stimulation in a protocol. The clinical relevance and the impact on the resection rate were examined.

Methods

Patient Population

Intraoperative neurophysiological monitoring and mapping was performed in 15 patients with insular tumors of the insula. All patients had provided informed consent, and the local ethics committee permitted all examinations. Patients ranged in age from 23 to 61 years.
The presenting symptoms, handedness, results of neurological examination, and Karnofsky Performance Scale status were evaluated for each patient before surgery. Motor function was assessed according to the BMRC scale. The topography of the tumor was analyzed on preoperative MR imaging studies, and tumors were categorized using the classification of Yaşargil. According to this, Type 3 tumors are restricted to the insula or to parts of it (Type 3A) or may include the corresponding opercula (Type 3B). Type 5 tumors involve, in addition to the insula and the opercula, one or both paralimbic orbitofrontal and temporopolar areas, without (Type 5A) or with (Type 5B) parts of the limbic system.

**Surgical Technique**

In cases involving Type 3 and 3A tumors, we used a transsylvian approach. In cases of Type 5 tumors, we utilized a combined transsylvian transfrontal and/or transtemporal technique.

**Intraoperative Mapping and Monitoring**

In all cases, intravenous anesthesia was performed without administering volatile anesthetics. Induction of anesthesia was achieved by a bolus of propofol (1–2 mg/kg) and fentanyl (5–10 µg/kg). Anesthesia was maintained by continuous propofol administration (75–125 µg/kg/h). Intraoperative analgesia maintained with fentanyl (1–2 µg/kg/h). Neuromuscular blocking agents were used only for intubation (rocuronium 0.3–0.4 mg/kg or mivacurium 0.2 mg/kg) but not during surgery. With this setup, neuromuscular blocking was effective for only 15–25 minutes during intubation, and patient positioning as verified by the the train of 4. No further muscle relaxants or drugs with a muscle-relaxing side effect were used in the course of the operation.

The Nicolet Endeavor system (Cardinal Healthcare) was used in all cases for stimulation and recordings. The motor cortex was stimulated by an anodal TCES. For this purpose stimulation electrodes were placed 4 cm bilateral of the vertex. Trains of 5 monopolar, anodal constant-voltage electrical pulses, each of duration 0.3 msec at a frequency of 500 Hz, were applied. Stimulation intensity was adjusted to a slightly suprathreshold level with a maximum of 400 V (Fig. 1).

Subcortical stimulation was performed by a 0.5-mm round electrode embedded in silicon. The electrode (anode) was placed on the insula after surgical exposition or in the tumor resection area. The cathode was placed on the side of the forehead ipsilateral to the stimulation side. For stimulation, we applied trains of 3 monopolar, anodal constant-current electrical pulses, each at duration 0.1 msec at a frequency of 400 Hz. The maximum for stimulation intensity was set at 10 mA. These stimulation parameters were evaluated at a preliminary study at our institution (unpublished data). Using repetitive subcortical stimulation, the motor descending pathways were identified in the internal capsule and the centrum semiovale. The elicitation of CMAPs following 3-mA subcortical stimulation was defined as a critical distance to the pyramidal tract and was set as the resection border. This is an empirical value (Fig. 2).

We recorded CMAPs from the forearm flexor, thenar, and quadriceps muscles contralateral to the side of stimulation. A pair of subdermal needle electrodes was used for recording. Recording filters were set to a low of 100 Hz and a high of 1.5 kHz.

**Data Evaluation**

Monitoring results, intraoperative events, and clinical data were documented. Postoperative MR imaging was performed in all patients.

**Results**

**Patient Population**

Symptoms included a history of seizures in 5 cases, hemiparesis in 3, psychological alterations in 2, speech disturbances in 1, and headaches in 9. There were 9 Type 3 and 6 Type 5 tumors. All 15 patients harbored an intrinsic tumor. Histological examination revealed 9 cases of WHO Grade II, 5 cases of WHO Grade III, and 1 case of glioblastoma multiforme.
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**Stimulation Results**

Following transcranial stimulation, CMAPs were recorded in all cases. The mean stimulation intensity was 363 V (range 269–400 V). Even in cases involving large tumors with mass effect, transcranial stimulation was successful. Hence, in all cases a monitoring parameter was available. Online evaluation and analysis of the CMAPs allowed quantitative monitoring of the motor system.

Monopolar ASCS was successful in 12 of 15 cases. The mean stimulation intensity was 4.9 mA, with a minimum of 3 mA and a maximum of 5.3 mA. The stimulation electrode was placed on the insula or on the dorsomesial border of the tumor, and stimulation was performed. The recorded CMAPs were analyzed in the same manner as those recorded following transcranial stimulation. As tumor dissection proceeded dorsally, stimulation intensity was reduced up to the level of 3 mA. If CMAPs were elicited with 3-mA stimulation, this plane was defined as the resection border nearer to the pyramidal tract. In 3 cases no CMAPs were observed during monopolar subcortical stimulation, even with maximum stimulation intensity 5.3 mA. This was due to the fact that the pyramidal tract was dorsally displaced and the stimulation electrode could not be placed in its vicinity. The low stimulation intensity avoids a mass current spread and hence reduces false-positive results. In these 3 cases transcranial stimulation was successful.

**Unchanged CMAPs**

Based on the experience with direct cortical stimu-

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Unchanged</th>
<th>Reversible Change</th>
<th>Δamp</th>
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<tbody>
<tr>
<td>TCES</td>
<td>10 of 15</td>
<td>5 of 15</td>
<td>80–85%</td>
</tr>
<tr>
<td>ASCS</td>
<td>7 of 12</td>
<td>5 of 15</td>
<td>87–93%</td>
</tr>
</tbody>
</table>

*Δamp = amplitude alteration.*

**Fig. 2.** Flow chart showing the ASCS procedure. PT = pyramidal tract.

**Fig. 3.** Waveform of CMAPs recorded from the thenar muscle after transcranial and after ASCS. The potentials are stable throughout the procedure.

**Reversible CMAP Deterioration**

In 5 cases, reversible significant CMAP changes were recorded (Table 1). These changes were observed both in the transcranial and subcortical recordings. We noted that the CMAP amplitude was reduced between 80 and 85% in the transcranial group and between 87 and 93% in the subcortical group. Changes in the subcortical group were recorded up to 20 seconds earlier than in the transcranial group (Fig. 4). Hence, during subcortical stimulation CMAP changes were greater and detected earlier.

In 2 cases CMAP changes were observed during tumor resection on the dorsomedial aspect. These changes led to definitive cessation of the resection because satisfactory cytoreduction was achieved. In an additional 3 cases, CMAP changes were thought to be due to mechanical vasospasm in the M2 or M3 segment. Recording
of CMAP changes led to the application of papaverine on the medial cerebral artery. Compound muscle action potentials recovered to normal between 30 and 120 seconds following this procedure.

Irreversible CMAP Deterioration

In a larger patient population Neuloh et al. observed irreversible CMAP changes in 5% their cases during insular tumor surgery. In our series all CMAP alterations were reversible. No case of irreversible CMAP change was observed.

Clinical Outcome

Compound muscle action potentials were unchanged in 10 cases following transcranial stimulation and in 7 following subcortical stimulation. There was no clinical deterioration of motor function postoperatively in these cases. One patient had a transient facial paresis, which completely resolved within 72 hours of surgery.

In 5 cases reversible CMAP changes were recorded. In 3 patients the postoperative clinical condition was unchanged. In the other 2 patients a transient deterioration of motor function was observed. Preoperatively these patients had had hemiparesis (BMRC Grade 3/5); postoperatively the paresis was BMRC Grade 2/5. After 1 week, motor function improved to Grade 4/5.

Tumor Removal

Tumor resection was total in 3 cases involving stable transcranial CMAPs and negative subcortical stimulation. Subcortical mapping was used as a functional navigation tool. In 7 cases with stable transcranial and subcortical CMAPs, tumor removal was total in 3 and subtotal in 4. In the latter 4 cases, the resection border was defined according to the 3-mA stimulation plane. In 5 patients reversible CMAPs were recorded. In 2 cases resection was stopped and considered subtotal, and in the other 3, following total recovery of the CMAPs, resection was extended to total (Table 2).

Discussion

Recent work supports the fact that the insula represents an anatomical, cytoarchitectural, and functional interface between the limbic system and the neocortex. Insular tumors are therefore related to eloquent structures, including the opercular speech pathways in the dominant hemisphere, the motor tract in the corona radiata, and the internal capsule in their dorsal apical extension. In addition there is a close anatomical relation between the insula and branches of the medial artery supplying motor areas and pathways. The lateral lenticulostriate arteries course from their entry zone at the anterior perforating

<table>
<thead>
<tr>
<th>Extent of Tumor Removal</th>
<th>Reversible CMAP Changes</th>
<th>Unchanged CMAP &amp; CMAP &gt;3 mA</th>
</tr>
</thead>
<tbody>
<tr>
<td>subtotal</td>
<td>4</td>
<td>2 of 5</td>
</tr>
<tr>
<td>total</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2: Tumor removal based on the ASCS results

Fig. 4. Waveform of significant CMAP changes as the result of vasospasm. The ASCS recordings (thin arrow) were earlier and larger than the TCES recordings (wide arrow). Following papaverine application, transcranial and subcortical stimulation recordings resolved to normal (double arrow).
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substance along the medial tumor border to the dorsal part of the internal capsule; the deep M₃ perforating arteries course along the dorsal and apical parts of the tumor to the corona radiata, and the M₁ and M₅ branches within the sylvian fissure fan out laterally over the insular cortex and the opercula.²²,²³,²⁴,⁵⁵,⁵⁸,⁵⁹ Due to the complex anatomical situation, a higher risk for new deficits, in particular motor deficits, is posed. As a consequence, neurosurgeons still recommend a conservative treatment for insular tumors.⁴⁸

Intraoperative monitoring during insular surgery is mainly performed with the traditional bipolar low-frequency stimulation technique.¹⁴,¹⁵,¹⁷ This method has been described as a useful mapping tool for identifying the deep motor pathways when approaching the dorsomedial tumor border. This is especially valuable with infiltrative growing lesions.¹⁴ The technique of monopolar ASCS, as described here, also allows mapping of the pyramidal tract. The 3-mA stimulation level, as defined in the present series, is an empirical value, and no scientific data exist to prove this. However, we believe that low stimulation intensity allows a more precise stimulation volume, thus allowing a closer approach to the pyramidal tract. However, the exact distance with 3 mA is unclear.

The choice of a monopolar stimulus is based on investigations performed by Hern et al.,²⁴ who examined the direct electrical excitability of pyramidal cells of the motor cortex and was the first author to advocate an anodic stimulation technique. In 1993 Taniguchi et al.⁵³ described a further modification of the monopolar stimulation technique. A high-frequency (300–500 Hz) anodic rectangular pulse was used to record CMAPs during surgery after induction of general anesthesia. The requisite stimulation intensity of 20 mA was markedly below that of low-frequency bipolar stimulation. Five pulses were needed to trigger a CMAP. This count was lower, by a factor of 50–100, than in the previously mentioned studies on bipolar stimulation.²³,²⁴,³⁵,³⁷,²⁰,²¹,²⁸ The monopolar anodic stimulus leads to excitation of the pyramidal cell zone.⁴¹ The high-frequency pulse sequence leads to an accumulation of EPSPs in the motoneurons of the spinal cord. As demonstrated by Landgren et al.,³¹ as well as Day et al.,³² a temporary accumulation of EPSPs is necessary to activate the resting motoneurons even under general anesthesia.⁵³ When a stimulus has been transmitted via the synapse, the so-called EPSPs are registered in the postsynaptic membrane.⁹

The EPSPs indicate the depolarization of the postsynaptic cell, which can last for up to 20 msec.⁹ An action potential is produced as soon as the membrane potential exceeds the threshold value of ~60 mV. Two temporally separate stimuli reaching the synapse produce 2 EPSPs; these can accumulate and thus increase the membrane potential. An action potential is the result of this accumulation.

A series of tests in 9 patients showed that monopolar cortex stimulation provides a simple technique for low-intensity stimulation of the motor cortex.⁵³ Repetitive stimulation could be performed throughout the entire operation. The short repetition time enabled surgical maneuvers to be correlated with changes in the CMAPs.

In 1996 Cedzich et al.⁷ demonstrated the practicability of motor cortex mapping (33 patients) as well as intraoperative monitoring (25 patients). The intraoperative application of this neurophysiological examination technique has failed thus far due to lack of experience. In their study, Cedzich et al. designated anodic monopolar cortex stimulation as a still experimental method and stressed the necessity for further studies.

The method used in the present study for monitoring is the so-called stop-and-go technique. Surgery is stopped when significant CMAP alterations are recorded. If recovery occurs, surgery is continued, whereas with permanent changes the procedure is stopped. Using this approach during spinal cord tumor surgery, several authors reported an improved functional outcome in cases in which it was possible to maintain a D wave.¹²,⁴⁹ Therefore, recovery of CMAPs indicates recovery of the motor tract.

Compared with the bipolar subcortical stimulation, monopolar stimulation provides potentials (CMAPs) and therefore a quantitative analysis of motor function. The clinical value of CMAP monitoring during perinordic surgery has been demonstrated in previous reports.⁷,²⁹,³⁵,³⁶,³⁸,³⁹ The CMAP alterations observed in our study were larger and faster after subcortical stimulation than after transcranial stimulation. An explanation or this observation is the fact that subcortical stimulus is more close to the motor tract, and therefore manipulations and/or hemodynamic changes are more severe around the tract than the motor cortex. In the motor cortex cerebral plasticity mechanisms may play a role compensating a compromise of the motor system. Monopolar cortical stimulation has been proven to be a reliable method for monitoring subcortical pathways. Changes in motor evoked potential latency and amplitude serve as warning signs during surgery and are of prognostic value.²⁹,⁴⁹

This is a new method and further investigation is needed. The use of 3 mA as stimulation border is based on empirical values. The exact distance to the pyramidal tract is, however, unclear. This issue, as well as the question of the subcortical current spread, requires further examination.

Conclusions

The aim of the study was to establish a protocol for both mapping and monitoring during surgery in and around the insula. The protocol presented in this study fulfills these criteria. Both mapping and quantitative monitoring are provided. There was no negative impact on the resection rate, and functional outcome was good. The technique is a useful tool that provides functional mapping and monitoring of the descending motor pathways. Although this is a preliminary report, the results are encouraging and further clinical evaluation of the method should be performed.

Disclaimer

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