MAJOR progress in surgical therapy for brainstem lesions, such as vascular malformations and gliomas, has been achieved within the last decade based on advanced imaging techniques, anatomical investigations, and newly introduced neurophysiological methods. Magnetic resonance (MR) imaging helps differentiate primary brainstem hematoma from hemorrhage due to occult vascular malformations and enables precise localization of lesions. Since the inception of MR imaging, an increasing number of surgical series in which the successful removal of vascular malformations such as cavernous hemangiomas has been documented.7,10 In addition, direct surgical treatment of gliomas has become a major topic based on the MR imaging classification of intrinsic brainstem tumors.3,6,19,20,25,26

The presence of functionally intact brainstem tissue between a lesion and the surface of the brainstem with the risk of additional postoperative morbidity due to the surgical approach17,18,24 illustrates the importance of using anatomical landmarks to achieve surgical access through functionally “silent areas” of the brainstem Lesions that are approached via the rhomboid fossa can cause severe neurological morbidity because of superficially located nuclei and fibers. Optomotoric deficits such as abducens nerve palsy, internuclear ophthalmoplegia, “one and a half” syndrome, and paresis of the facial nerve are seen in cases of pontine lesions, and deficits from the lower cranial nerves are frequently observed in cases of medullary lesions.3,17–19,24 Instances of functional morbidity following surgical access can be caused by the variability of external landmarks, as Lang and coworkers13 pointed out when they conducted a macroscopic investigation of the medullary striae, the most prominent visible structure of the rhomboid fossa. In subsequent microscopic analysis of intrinsic brainstem anatomy morphometric measurements were used to define safe pericollicular entry zones above and below the facial colliculus (Fig. 1 left).22 In cases of space-occupying intrinsic lesions, which displace nuclei and fibers, these morphometric data are of limited value (Fig. 1 right), and the surgeon requires the use of advanced neurophysiological techniques5,16,23,24 to provide safe surgical corridors into the brainstem. The value and limitations of electrical brainstem mapping can only be appreciated on the basis of a

Pericollcular approaches to the rhomboid fossa. Part II. Neurophysiological basis

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Object. The authors describe their technique of electrophysiological mapping to assist pericollicular approaches into the rhomboid fossa.

Methods. Surgical approaches to the rhomboid fossa can be optimized by direct electrical stimulation of superficially located nuclei and fibers. Electrophysiological mapping allows identification of facial nerve fibers, nuclei of the abducens and hypoglossal nerves, motor nucleus of the trigeminal nerve, and the ambiguous nucleus. Stimulation at the surface of the rhomboid fossa performed using the threshold technique allows localization above the area that is located closest to the surface. Simultaneous bilateral electromyographic (EMG) recordings from cranial motor nerves obtained during stimulation document the selectivity of evoked EMG responses. With respect to stimulation parameters and based on morphometric measurements, the site of stimulation can be assumed to be the postsynaptic fibers at the axonal cone. Strict limitation to 10 Hz with a maximum stimulation intensity not exceeding 2 mA can be considered safe. Direct side effects of electrical stimulation were not observed.

Conclusions. Electrical stimulation based on morphometric data obtained on superficial brainstem anatomy defines two safe paramedian supra- and infracollicular approaches to the rhomboid fossa and is particularly helpful in treating intrinsic brainstem lesions that displace normal anatomical structures.

KEY WORDS • brainstem surgery • brain mapping • neurophysiological mapping • threshold technique • rhomboid fossa morphometry • pericollicular approach
Surgical approaches to the rhomboid fossa

Fig. 1. Left: Schematic drawing showing the morphometry of the rhomboid fossa with superficially located motor structures and pericollicular approaches. Roman numerals indicate cranial nerves. Right: Intraoperative photograph showing a rhomboid fossa in which an underlying large pontine cavernous hemangioma distorts normal anatomical structures.

detailed knowledge regarding the neurophysiological background of this method.

Clinical Material and Methods

Patient Population

A total of 50 patients—20 with intraaxial lesions, 20 with lesions infiltrating the brainstem, and 10 with lesions displacing the rhomboid fossa—underwent intraoperative brainstem mapping between 1990 and 1997. The intraaxial lesions mainly consisted of vascular malformations (cavernous hemangiomas in 10 patients, capillary telangiectasia in two patients, hematoma in one patient, and gliomas in seven patients). Ependymomas (11 patients) and primitive neuroectodermal tumors (eight patients) were the most frequently occurring infiltrative lesions, and in one case a plexus papilloma with an infiltrative growth pattern was removed. The group of displacing lesions was rather inhomogeneous; it included hemangioblastoma in one patient, epidermoid tumors in two, cerebellar gliomas in four, lymphomas in one, and metastatic disease in two patients. All lesions were removed via a standard suboccipital midline approach. Electrophysiological and clinical results obtained in a selected number of patients have been previously published.24

The anesthetic regimen was based on total intravenous anesthesia. Following induction with midazolam, nitrous oxide, and a short-acting muscle-relaxing agent (atracurium besylate), anesthesia was maintained with propofol (6–12 mg/kg/hour) and alfentanil (60 μg/kg/hour). Additional muscle-relaxing agents were not administered until the end of the surgical procedure.

Electrical Stimulation

Electrical stimulation was performed using monopolar constant-current/constant-voltage techniques with rectangular monophasic pulses (Pathfinder I; Nicolet Corp., Madison, WI, and NL1; Grass Instrument Co., Quincy, MA). The reference electrode was placed either in the cervical muscles exposed by surgery in the form of a needle electrode or at the nasopharyngeal muscles by using silver ball electrodes. In some early cases, additional bipolar constant-current stimulation was performed using silicone strip electrodes similar to the electrodes used for intradural spinal cord monitoring.23,24 Because these electrodes proved to be too rigid for positioning within the fourth ventricle, since 1996 we have exclusively applied bipolar constant-current stimulation by using a coaxial stimulation probe with a rather planar stimulation area (Neurosign 100; Magstim Com., Whitland, Wales, UK). Stimulation intensity did not exceed 2 mA at 1 V, except in one patient with a hypertensive pontine hemorrhage in whom intensities up to 10 mA were applied. Stimulus duration varied between 100 and 400 μsec. The stimulus rate did not exceed 10 Hz.

Electromyographic Recording

Simultaneous bilateral six- to eight-channel electromyographic (EMG) recordings of cranial nerve muscles (fifth–12th nerves) were performed to document the selectivity of evoked responses (Figs. 2 and 3). For the EMG recordings, monopolar stainless-steel electrodes were placed 5 mm apart in a bipolar recording setup to cover a representative muscle area. Primary interest focused on intraoperative localization of the facial colliculus and the hypoglossal nucleus to identify margins for the supra- and infracollicular approaches into the brainstem, as previously described.23,24 Electrodes for the facial nerve were placed in the orbicular muscles of the mouth and eye and the nasal muscle; those for the nucleus of the abducent nerve were positioned in the vicinity of the lateral rectus muscle within the periorbital tissue. For the 12th cranial nerve nucleus, electrodes were placed in the genioglossal muscle.23,24

With respect to the location of the lesion, additional
nuclei such as the motor nuclei of the trigeminal (musculus masseter) and lower cranial nerves (soft palate and musculus vocalis) were included in the investigation.

Results

In all but one of the 50 patients who had hypertensive hemorrhage, the facial nerve fibers and the nucleus of the hypoglossal nerve could be selectively identified. In intrinsic lesions this included identification on the side of the lesion as well as on the contralateral side. The EMG responses were limited to the side and site of stimulation. Electrical stimulation at the facial colliculus was followed by selective responses of the ipsilateral facial muscles (Fig. 2 left). Because of the complex anatomy of the colliculus, selective responses from sixth cranial nerve could be obtained in approximately 10% of cases. Stimulation of the trigone of the hypoglossal nerve was followed by selective responses of the ipsilateral genioglossal muscle (Fig. 2 right). Other motor areas such as the ambiguous nucleus (Fig. 3 left) and the motor nucleus of the trigeminal nerve (Fig. 3 right) could also be selectively localized.

The application of the threshold technique proved to be extremely useful in obtaining these results (Fig. 4). For identification of facial nerve fibers at the level of the facial colliculus, for example, suprathreshold stimulation with a stimulation intensity of 2 mA was applied, starting 15 mm above the obex (Fig. 4 left). Using suprathreshold stimulation intensities, the EMG responses were not selective. In the presence of continuous stimulation, the probe was slowly moved rostrally until maximum EMG amplitude of the facial muscles could be documented. When that particular area was reached, the electrical threshold was obtained by slowly reducing the stimulation intensity (Fig. 4 right) until no stimulation effect could be observed, thus identifying the area with the shortest distance between the stimulation probe and the facial nerve fibers. Facial nerve fibers come as close as 0.23 mm to the ependyma during the ascending course of the facial nerve medial to the abducent nerve nucleus and lateral to the median sulcus.22 As seen in Fig. 4, the area of maximum stimulus effect corresponds to the morphometrically measured 6.7-mm rostrocaudal extension of the facial colliculus. The average stimulation intensity for the facial nerve fibers within the facial colliculus was 0.25 mA in those patients in whom the lesions were adherent to the brainstem and no incidence of preoperative morbidity was observed, based on a stimulus duration of 200 μsec and constant-current stimulation. In those patients in whom there were preexisting conditions of cranial nerve morbidity, stimulation intensities had to be increased considerably. In those cases, up to 2 mA stimulation intensity was necessary to obtain reproducible EMG responses; in one case (a patient with hypertensive hemorrhage) no response could be recorded.

The same technique was applied for localization of the hypoglossal nucleus (Fig. 2 right). The stimulation probe was placed 15 mm above the obex at the level of Luschka’s foramina and, in the presence of continuous stimulation, the probe was slowly moved caudally until the upper
pole of the nucleus was reached. The upper pole comes as close as 0.55 mm to the surface and again could be reliably identified using the threshold technique. Following identification of landmarks of the infracollicular approach into the brainstem on the unaffected side, the side of the lesion was mapped to anticipate the mass effect and distortion of brainstem anatomy and to define the exact entry zone above or below the facial colliculus. For intrinsic lesions the incision into the rhomboid fossa was exclusively based on the results of the electrical mapping. The two illustrative cases that we report demonstrate the value of electrical mapping because, in both cases, the lesion was located within the suspected area of the colliculus. Brainstem mapping led to an infracollicular approach in one patient (Fig. 5), whereas in the second case the supracollicular approach was used (Fig. 6). In five cases of cavernomas and two cases of endophytic gliomas, the incision was not performed at the site of maximum bulging, but varied accordingly in the cranial or caudal direction. Identification and localization of other nuclei, including those located on the contralateral side, proved helpful for visualization of the pattern of displacement and, therefore, the tumor-growth pattern.

In lesions with infiltrative growth patterns, such as ependymomas and medulloblastomas, the technique proved helpful to achieve both a safe plane of dissection and complete removal of the lesion.

**Infracollicular Approach**

The infracollicular–collicular approach to the brainstem was used in 13 cases. The patients suffered from hemorrhages due to cavernous hemangiomas (seven patients), capillary telangiectasia (one patient), or hypertensive disease (one patient). In four cases a glioma was accessed using the approach that coursed below the facial colliculus and above the hypoglossal trigone. Nearly all cases of additional postoperative morbidity included horizontal gaze palsies (internuclear ophthalmoplegia and one and a half syndrome) and facial nerve paresis. In all cases these deficits were transient. In one case of endo–exophytic glioma, definite deterioration of preexisting lower cranial nerve morbidity was observed, requiring the performance of a tracheotomy and gastrostomy.

**Supracollicular Approach**

The surgical approach above the facial colliculus was used in seven patients: in three cases of cavernous angiomato, one in capillary telangiectasia, and in three of astrocytoma. The facial colliculus served as the caudal border of the approach, and the medullary velum with the fibers of the trochlear nerve was the cranial limit of surgical exposure. Incidences of transient postoperative morbidity were seen in the majority of cases and included horizontal gaze palsies (internuclear ophthalmoplegia and one and a half syndrome), which proved to be permanent in one patient with a glioma. In one case transient paresis of the trochlear nerve was seen.

**Illustrative Cases**

**Case 1**

This 42-year-old man was admitted to the hospital with a history of increasing gait disturbance, diplopia, and numbness on the left side that had lasted several weeks. A
Case 2

This 23-year-old woman was admitted to the hospital with a 6-month history of progressive gait disturbance and diplopia. Neurological examination disclosed right abduc- cent nerve palsy, internuclear ophthalmoplegia, trigeminal hypesthesia, and facial nerve weakness. Furthermore, left hemiparesis including hemihypesthesia was noted. Magnetic resonance imaging revealed diffuse enlargement of the pons and a contrast-enhancing pontine lesion (Fig. 6 left). Angiography revealed pathological vasculariza- tion. Surgery was performed via a suboccipital midline approach. Following exposure of the rhomboid fossa, maximum bulging and discoloration were seen in the upper portion on the paramedian right side. The facial colliculus was identified on both sides by using electrical stimulation. The ascending facial nerve fibers on both sides could be traced using the threshold technique. We chose a paramedian supracollicular approach into the rhomboid fossa and achieved resection of the vascularized tumor portion. After surgery additional bilateral trochlear nerve paresis developed in the patient, which most likely was due to stretching within the medullary velum caused by retractor placement. A deterioration in right facial nerve function was noted. Both symptoms, as well as the patient’s hemiparesis, resolved within months. The preexisting horizontal gaze disturbances persisted. Histological evaluation revealed an anaplastic glioma classified as World Health Organization Grade III. Conventional radiotherapy was performed and no further tumor progression has been observed on control MR imaging during the last 36 months. Postoperative MR imaging (Fig. 6 right) demonstrated, similar to the first case, visualization of the surgical corridor.

Discussion

Surgical treatment of lesions affecting the brainstem has become a major topic of research activity within the last decade. The increasing number of publications demonstrates the growing interest in this delicate surgical field and the parallel good surgical results, especially in well-defined brainstem lesions.1,2,5,7,16,20,25,26

Recent publications have provided descriptions of safe surgical approaches to the rhomboid fossa both above and below the facial colliculus.2,12,22 Morphometric analysis of the facial colliculus and the lower cranial nerve trigones of the rhomboid fossa can provide valuable information to the surgeon.22 However, this information cannot be transferred directly to the surgical field because there is massive distortion of normal brainstem anatomy in the presence of intrinsic lesions (Fig. 1). Brainstem mapping with direct electrical stimulation, which was introduced in 1993,23 can be used to identify superficially located motor nuclei and fibers of the rhomboid fossa during surgery and has become a widely used and accepted technique.2,5,16,20,24 Application of this technique requires a detailed knowl- edge of neurophysiology to optimize surgical approaches and minimize incidences of surgical morbidity in cases in which there are intrinsic lesions and lesions infiltrating the brainstem. Knowledge about possible side effects regarding the cardiovascular system and the exact site of stimulation are of particular interest for clinical application because the stimulation theoretically could be effective at various levels of the motor pathway.

Site of Stimulation

To make this technique clinically useful, it is essential to define the site of stimulation precisely. The collision technique of using high-frequency stimulation to rule out or verify a presynaptic origin of stimulation cannot be applied because of possible side effects regarding the cardiovascular system. The observation that peripheral EMG responses could be obtained with as little stimulation in-
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tensity as 0.1 mA and a stimulation duration of 100 μsec strongly indicates that the peripheral motor neuron is the site of stimulation. These parameters are similar to those given to identify the facial nerve during cerebellopontine angle surgery. They are inadequate for stimulation of the first motor neuron. For direct cortical stimulation of the pyramidal tract, stimulation intensity usually varies between 2 to 5 mA with frequencies higher than 40 to 50 Hz up to 500 Hz when using a stimulation duration ranging between 100 and 400 μsec. Most likely the axonal cone with a threshold 10 times lower than the axon’s threshold represents the presumed site of stimulation. Additional peripheral stimulation directed toward the root exit zones is unlikely because stimulation would include peripheral motor neurons of other cranial nerves. This was excluded by simultaneous bilateral multichannel EMG recordings, which demonstrated selective responses on the side and site of stimulation. The selectivity of responses also excludes diffuse brainstem stimulation. The site can also be directly calculated using the motor threshold for facial nerve fibers within the colliculus and fibers of the nucleus of the hypoglossal nerve. The various threshold values correspond with the distances from the fibers to the surface of the rhomboid fossa. For facial nerve fibers, we know from anatomical studies that the average minimum distance between the fibers and the ependymoma measures 0.23 mm. For the cranial pole of the nucleus of the hypoglossal nerve, this distance was measured to be 0.55 mm. Between threshold intensity (I) and the closest distance (d) of a stimulation probe to axons, a mathematical equation can be calculated:

\[ I = K \times d^2 \]

in which K is a constant for a given unit of microamperes per square millimeter. This K value varies from large axons (30–500 μA/mm²) to small axons (≤ 5000 μA/mm²). These K values, which were derived from animal studies, are applied for spatial stimulation within brain tissue. The calculation is based on monopolar stimulation using monophasic impulses of 200-μsec duration under the condition that the impedance around the stimulation electrodes within the tissue does not vary.

The K value for stimulation of facial nerve fibers in a selected number of cases with lesions displacing the brainstem anatomy, but without infiltrative growth, was calculated to be 4726 μA/mm², based on the measured anatomical distance of 0.23 mm and the intraoperative threshold of 0.25 mA when using a stimulus duration of 200 μsec: K = 250 μA/(0.23 mm²) = 4726 μA/mm².

Based on the K value for the facial nerve, the stimulation intensity necessary to excite hypoglossal nerve fibers can be calculated because the distance of the nucleus surface is known to be 0.55 mm. The theoretical stimulation intensity for hypoglossal nerve fibers can be calculated as being 4726 μA. If 4726 μA/mm² × (0.55 mm²) = 1430 μA.

The measured intensity for the motor threshold of the hypoglossal nerve nucleus was 1.5 mA. These calculations point to the axons of the peripheral motor neuron as the site of intraoperative electrical stimulation. The K values published by Yeomans vary between 30 and 500 μA for large axons and up to 5000 μA for small axons. The human facial nerve axons are large axons, and this contrasts with the K values calculated earlier, which exceed 4000 μA/mm². However, one has to consider that K values based on animal experiments are calculated by spatial stimulation within the tissue and, therefore, under conditions of stable impedance. We have performed surface stimulation. Compared with brain tissue, ependyma and cerebrospinal fluid have a lower impedance. Under these conditions, up to 90% of current spread and, therefore, a reduction in effective stimulation intensity can be expected, which places the K values for facial nerve fibers within the expected range for large axons (JS Yeomans, personal communication, 1994).

Morota, et al., used a high dosage of volatile anesthetic agent without a negative effect. Their clinical observation regarding stimulation results also points to peripheral motor neurons as the site of stimulation because volatile anesthetic agents have a well-defined negative influence on the excitability of the first motor neuron. The influence regarding the excitability of the peripheral motor neuron, in contrast, can be neglected. From these various observations the peripheral axon and, respectively, its initial segment can be assumed to be the site of electrical stimulation.

Side Effects and Safety Aspects of Electrical Stimulation

Particular attention was paid to the possible cardiovascular side effects of electrical stimulation because the parasympathetic dorsal motor nucleus of the vagus nerve is located immediately lateral to the hypoglossal trigone. In one patient with known cardiac arrhythmia, a ventricular tachyarrhythmia was encountered 24 hours after surgery. In another patient with known ventricular arrhythmia, a short asymptomatic course of ventricular extrasystoles was observed immediately following stimulation. The arrhythmia began after stimulation was terminated. Except for these two cases, in which possible side effects were observed, we observed no measurable effects regarding cardiac arrhythmia or blood pressure within the applied range of stimulation intensity below 2 mA, stimulus duration up to 400 μsec, and stimulation frequency limited to 10 Hz.

Possible brain damage as a result of electrical stimulation is mainly caused by an imbalance in the blood-brain barrier (BBB). Damage to the BBB is dependent on the applied charge density (Coulomb [C/cm² × phase]) under the stimulation electrode. From histological evaluations of cortical resections of epileptogenic tissue that had been stimulated prior to resection, we know that up to the maximum applied charge density of 57 μC/cm² × phase, no histological changes could be documented for stimulation lasting several hours. Charge densities in brainstem stimulation stayed well below these values. In those cases in which we used constant-voltage stimulation within the parameters described earlier, the electrode surface of 0.0043 cm² produces a charge density of 0.59 μC/cm² × phase. With constant-current stimulation, which is now being used exclusively, charge densities up to 0.0014 μC/cm² × phase are reached. Limitation of electrical stimulation to 1 V (constant-voltage technique) and, respectively, 2 mA (constant-current technique) certainly has no adverse side effects on the BBB (A Møller, personal communication, 1995). The limitation of stimulus frequency to 10 Hz is based on animal experiments using stereotactically implanted electrodes in the dorsal and rostral areas of the
EMG activity data may provide a reliable monitoring technique during brainstem surgery.2,24

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