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Transcranial Electrocortical Stimulation to Monitor Facial Nerve Motor Function during Cerebellopontine Angle Surgery

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Abbreviation List

APB	–	abductor pollicis brevis muscle
AUC	–	area under the curve
BAEP	–	brainstem auditory evoked potential
CMAP	–	compound muscle action potential
CN	–	cranial nerve
CPA	–	cerebellopontine angle
CSF	–	cerebrospinal fluid
dB	–	decibels
DES	–	direct electrical stimulation
DFP	–	delayed facial palsy
EEG	–	electroencephalography
EMG	–	electromyography
FMEP	–	facial motor evoked potential
FN	–	facial nerve
HB	–	House and Brackmann classification
HL	–	hearing level
Hz	–	Hertz
IAC	–	internal auditory canal
IOFNM	–	intraoperative facial nerve monitoring
ISI	–	interstimulus interval
kOhms	–	kiloohms
mA	–	milliamperes
MEP	–	motor evoked potential
min	–	minute
MRI	–	magnetic resonance imaging
ms	–	milliseconds

µsec	–	microseconds
µV	–	microvolts
REZ	–	root exit zone
ROC	–	receiver operating characteristic
sec	–	seconds
SEP	–	somatosensory evoked potential
TES	–	transcranial electrical stimulation
V	–	volts
VS	–	vestibular schwannoma

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Introduction

"... the human being´s facial expression fascinates me,
because it serves the most basic and bestial pleasure
and participates in the strongest and
most gentle emotion of the spirit."
Charles Bell, 1806 (76)

The artistic representations of facial palsy from the ancient Egyptians, Greeks, Romans and Incas as well as other native cultures in pre-Columbian America can indicate that the history of peripheral facial palsy parallels the history of the human race itself (163). It is worth mentioning that the recognition of the condition came far before the understanding of the anatomy and physiology of the cranial nerves. Contributing to this delay up until the 18th century may have been the prohibition of human dissections and the lack of knowledge regarding fixation techniques for cadavers (186).

The first enumeration of the cranial nerves was initiated by Galen, a physician and anatomist who worked in Rome during the second century (186). Galen described seven pairs of cranial nerves in which the fifth pair was composed of two different nerves, namely the facial nerve and the vestibulocochlear nerve of modern terminology (186). Galen´s description has remained the source of authority concerning human anatomy throughout the Middle Ages (186).

The first medical treatise of facial palsy is attributed to Avicenna (Abu-Ali al Husayn ibn Abdalla Ibn Sina, 980-1037 A.D.) who showed a very advanced knowledge for his time (76;83;163). This is due to his recognition of central and peripheral facial palsy, and his assumptions on the causes and pathophysiology of the condition. Compression following nerve injury or tumor growth or even nerve sectioning was already recognized among the causes of the facial palsy

(83). Avicenna also disserted on its clinical and surgical management and the outcome (83).

By the end of Middle Ages, Galen´s research was surpassed by the printed descriptions and illustrations of human dissections of Andreas Vesalius, from 1537-1543, who is considered the reformer of anatomy (186). Even though Vesalius had maintained Galen´s description of the seven pairs, some figures in his work demonstrate accurate representations of nerves III-VII in modern terminology (186) (Fig. 1).

It was not until 1779 that the cranial nerves were reclassified into 12 pairs by the German anatomist Samuel Thomas Soemmerring in his doctoral dissertation (186) (Fig. 2). This classification also included the nervus intermedius along with the seventh pair (facial nerve) and is essentially still in use today (186). Despite Soemmerring´s description, the facial nerve was only recognized as the motor nerve of the face by Sir Charles Bell in 1821 (76).

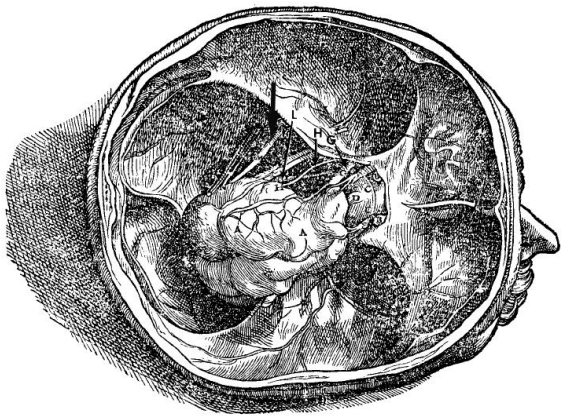

Figure 1. *Upper view of the cranial fossae showing the brainstem and the cranial nerves from Vesalius´ De humanis corporis fabrica (1543, Fig. 14). The facial nerve was already represented but not described according to modern nomenclature (black arrow). Adapted from Shaw (186).*

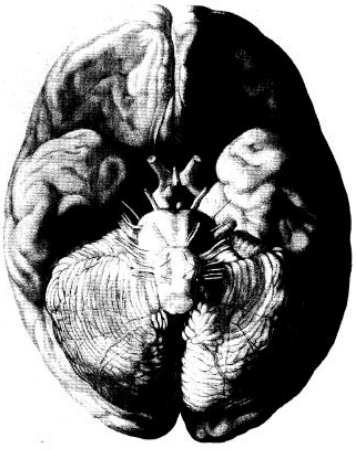

Figure 2. *Illustration of the inferior brain surface from Soemmerring´s Tabula baseos encephali (1799, frontispiece). Adapted from Shaw (186).*

Almost a century passed until the description of the first successful removal of a cerebellopontine angle (CPA) tumor, in which the patient survived (9;89). In 1894, Sir Charles Ballance (1856-1936), a British surgeon, reported on the case of a 49 year-old woman affected by a solid tumor attached to the posterior surface of the petrous bone (9;89). The fifth and seventh nerves were injured at operation leading to postoperative right eye ulceration and the removal of the eye thereafter (9). The patient was still alive 12 years after the surgery maintaining the same neurological status (9) (Figs. 3-7).

At that time, facial palsy was an acceptable sequelae of CPA surgery as stated by Dandy in 1925 (32): “The one outstanding sacrifice of this operation [(total removal of vestibular schwannoma (VS)] is hemifacial paralysis”. Dandy (32) described modifications in the unilateral approach to the CPA originally introduced by Dr. Fedor Krause in 1903 (95) attempting total vestibular schwannoma (VS) removal and also suggesting that it might be possible in the future to preserve the facial nerve (FN) (32). These words sounded somewhat prophetic since 6 years later, Cairns described 3 cases of VS in which the FN was anatomically preserved (22).

Interestingly, Cairns also commented on the spontaneous recovery from facial palsy that followed tumor removal by saying: “These experiences suggest that it may be possible in a certain number of cases to remove an acoustic tumor and its capsule completely without destroying the facial nerve, a procedure that has several advantages over spino-facial or hypoglossalfacial anastomosis. It appears that the facial nerve may be considerably damaged at operation and yet recover if it is left in continuity. In such cases it is advisable to wait some time before doing a spino-facial or hypoglossalfacial anastomosis.”(22). Surprisingly, Cairns already recognized that as early as 1904, Stewart and Holmes reported on a case in which the FN was evidently spared following VS surgery and its function had recovered spontaneously after seven months (22).

Figure 3. *Intraoperative photograph of the first successful surgery in the cerebellopontine angle. Adapted from from Ballance (9) (1907, Some points in the surgery of the brain and its membranes) with permission of the Becker Medical Library, Washington University School of Medicine.*

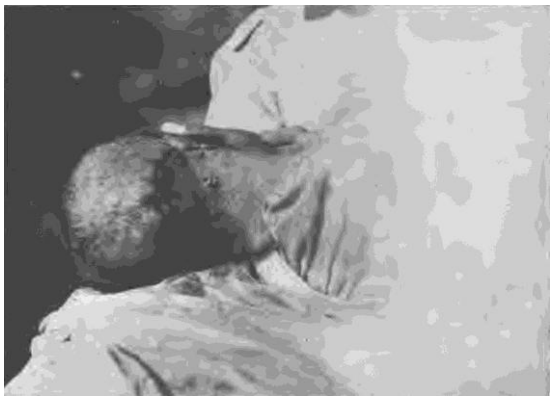

Figure 4. *Intraoperative photograph at the end of the first successful surgery in the cerebellopontine angle. Adapted from Ballance (9) (1907, Some points in the surgery of the brain and its membranes) with permission of the Becker Medical Library, Washington University School of Medicine.*

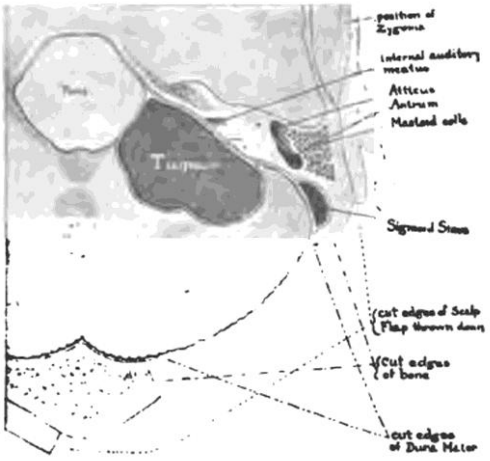

Figure 5. *Schematic drawing of the relationship between the tumor and the posterior fossa structures. Adapted from Ballance (9) (1907, Some points in the surgery of the brain and its membranes) with permission of the Becker Medical Library, Washington University School of Medicine.*

Figure 6. *Photograph of the tumor immediately after resection. Adapted from Ballance (9) (1907, Some points in the surgery of the brain and its membranes) with permission of the Becker Medical Library, Washington University School of Medicine.*

Figure 7. *Photograph of the patient 12 years after surgery. Adapted from Ballance (9) (1907, Some points in the surgery of the brain and its membranes) with permission of the Becker Medical Library, Washington University School of Medicine.*

1 Facial Nerve Injury Following Cerebellopontine Angle Surgeries

Dealing with CPA tumors has developed from almost a death sentence at the beginning of the 20th century (81;89;155;170) to the current concept of functional microsurgery (171). In this interim, several developments regarding radiological diagnosis, the introduction of the operative microscope and microsurgical techniques, advances in the field of neuroanesthesia, as well as intraoperative neuromonitoring were responsible for significant reductions in the morbidity and mortality in patients suffering from CPA tumors (36;38;42;51;52; 54;56;61;71;72;77;80-82;89;98;127;136;138;141;147;155;170;176;192;196;201)

The aims of surgery in the CPA have changed from tumor resection and prolongation of life to the anatomical and functional preservation of the cranial nerves (81;175). This evolution in surgical therapy is precisely illustrated by Moskowitz and Long, who divided the surgical treatment of VS into four distinct phases (138) (Table 1). Although significant advances have been observed in the recent era, FN anatomical preservation during VS surgery is currently around the range of 94% and FN functional preservation is in the low range of 70%.

In addition, FN injury is not exclusively related to VS surgery and may also occur postoperatively in several tumors of the CPA. Meningiomas of the CPA have a common anatomical location and are classified according to their site of tumor origin in relationship to the internal auditory canal (IAC). The tumors may arise anterior to IAC (Group 1), involve the IAC (Group 2), superior (Group 3), inferior (Group 4) or posterior (Group 5) (142). The operative strategies and functional facial and cochlear nerve outcomes are different among the groups (142;203). Immediate postoperative facial paresis can be observed in 13 to 23.7% depending on the tumor location (142). Management of CPA epidermoids has improved during the past 30 years, however postoperative facial weakness still occurs in 5 to 8.3% of patients (167;174). Similarly, trigeminal neurinomas remain challenging entities and their surgical treatment may lead to postoperative facial paralysis in up to 10.7% of cases (173). Therefore, in general, facial weakness is still a complication of major concern in patients undergoing CPA surgery (3;6;36;43;51;56;98;172;199).

***Table 1**. Facial Nerve Outcome following Vestibular Schwannoma Surgery.*

Vestibular Schwannoma	Overall Mortality	Total tumor removal	FN Anatomical Preservation	FN Functional Preservation (grades I/II)
Pioneer Era (1890-1925)	33.9%	NA	NA	NA
Curative Era (1925-1960)	20%	17.9%	8.3%	NA
Magnification Era (1960-1974)	9.2%	83.6%	79.3%	NA
Recent Era (from 1975)	0.75%	93%	94%	72.2%
*Samii and Matthies 1997 (172)**	1.1%	97.9%	93%	64%
*Samii et al. 2006 (169)**	0	98%	98.5%	59%

* with monitoring; FN – facial nerve; NA – not applicable.

1.1 The Impact of Facial Palsy on Quality of Life

"The postoperative paralysis is always a tragedy for the patient and disturbing for the surgeon."

Tos 1992 (208)

Approximately 50% of FN fibers must be injured before weakness is clinically demonstrated (150). The FN contains 7,000 to 11,600 fibers working in unison to bring about the muscle contraction that gives facial expression (30;101;154). In this regard, facial expression plays a significant role in interpersonal communication being of interest from both an evolutionary and a social standpoint (29). Unfortunately, facial palsy has been rarely demonstrated as such an elegant and enigmatic expression as portrayed by Leonardo da Vinci in the *Mona Lisa* painting, in which the enigmatic smile of his model has provoked

generations of observers (2;76) (Fig. 8). Adour believes that the *Mona Lisa* smile represents a piece of topographic anatomy well illustrated by Leonardo da Vinci, a compulsive anatomist, who painted a classic example of contracture in the facial muscles following nerve regeneration after facial palsy (2).

Conversely, facial palsy after tumor removal has accounted for the majority of impairments leading to a significant negative impact on patients´ ability to express emotions and their quality of life (1;29;31;81;141;187;205). Moreover, it has been suggested that long-term sequelae of facial palsy has been underestimated by physicians since patients may experience higher levels of distress in spite of a good technical FN result (4;29;31). In other words, the level of distress may not correlate to the clinical grade of facial palsy giving a less optimistic interpretation of the outcome (4;31). Patients with low self-esteem, young people and women are at a particular risk to suffer postoperatively from higher levels of distress due to facial palsy (31).

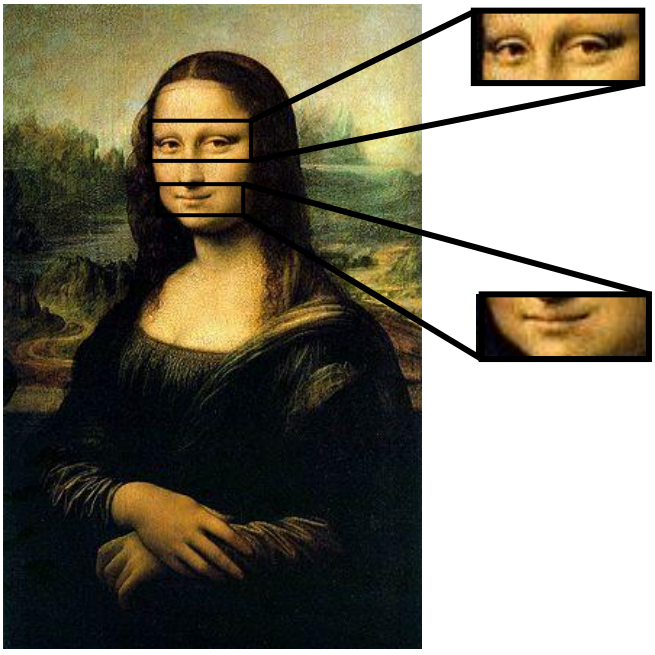

Figure 8. *The reduction of the interpalpebral distance (upper right) and the elevation of the mouth´s corner (lower right) suggest a contracture of the facial muscles following nerve regeneration after Bell´s palsy. The contracture is represented by a deepening of the nasolabial fold that lifts and shortens the upper lip (2). Mona Lisa. Oil on Poplar. Leonardo da Vinci (1503-1506). Musée Du Louvre, Paris.*

1.2 On the Mechanisms of Postoperative Cranial Nerve Deficit

Cranial nerves (CN) are at a particular risk of injury during surgeries in the skull base (128). This may be due to differences in their histological and anatomical structure in comparison to peripheral nerves that make the CN more susceptible to intraoperative injury (128). CN lack an epineurium, a firm perineurium and possess less content of connective tissue (14;82;128;147;184). Additionally, the intracranial portions of the CN harbor the transition zone between peripheral (by Schwann cells) and central myelin (by olygodendrocytes) that is considered the weakest point within the nerve (128). The unique histological structure together with the fact that CN are not subjected to movement leave them particularly vulnerable to surgical stretching, as well as to electrical and mechanical trauma (82;103;104;128;184).

Even though the nerves are often not macroscopically damaged or sectioned during surgery, surgical manipulation frequently leads to transient postoperative functional deficit (128). These manipulations comprise traction, compression, contact with surgical instruments including the suction device, bipolar cautery, exposure to blood and irrigation fluid and even drying as a result of insufficient irrigation (128;184). Interestingly, there is no significant statistical difference among the various types of surgical manipulations, however it seems that suction is an important factor in postoperative facial palsy while cauterization is the least important factor (208). Thus, several pathological mechanisms may account for postoperative CN deficit, namely segmental demyelination, comprised microcirculation, postoperative edema and “synaptic stripping” (128).

Segmental demyelination may induce a transient conduction block with (partial) loss of function (128). Remyelination of the axons proceeds in the following weeks/months leading to complete recovery of function (128). However, segmental demyelination may be accompanied by axonal changes that reveal injuries resulting in wallerian degeneration and consequently impairment in function recovery (128).

Considering that CN lie freely in the cerebrospinal fluid (CSF), their vascularization comes from direct vessels and vessels located on the pia mater (128). In this way, the force of tumor stretching may compromise intraneural microcirculation that in association with the removal of a significant length of the tumor capsule contribute to additional impairment of the blood supply to the nerve (103;104;128). Postoperative CN edema occurs gradually during surgery and may subsequently cause nerve damage due to compression as CN course through the bony canals (128).

Finally, “synaptic stripping” is a phenomenon defined as microglial proliferation as a consequence of nerve trauma. This process begins right after nerve injury and reaches its summit in 4 to 6 days thereby reducing the synaptic contacts with the neuronal bodies ultimately leading to transient functional loss (128). In addition, significant changes are observed in the cell bodies resulting in metabolic changes in the context of nerve regeneration (128).

Postoperative facial palsy may then be a consequence of transient conduction block (neuropraxia) or some degree of axonal degeneration (23;24;30;166). By using electrophysiological studies following mechanical trauma or nerve sectioning, early changes in the distal portion of the motor nerve and muscle are observed (23;24). The distal portion retains its electrical excitability for 2 to 5 days, thereafter axonal degeneration takes place leading to the abolition of excitability and conduction (23;24;47;154) while the motor end-plate maintains its full excitability for 5 to 10 days (23;24). Interestingly, the velocity of complete degeneration in the motor nerve fibers is proportional to the severity of nerve damage so that fast degeneration is observed in neurotmesis whereas slow degeneration is seen in axonotmesis (47).

1.2.1 Postoperative Delayed Facial Palsy

A bimodal distribution of postoperative delayed facial palsy (DFP) has been described for CPA tumors: early onset (within 48 hours) and late onset (72 hours or later) (56). The incidence of DFP has varied from 3.5 to 41% following VS resection (5;6;21;42;50;51;56;65;69;88;98;99;102;127;152;169;179;180; 208;212). This variability is partially due to discrepancies in DFP definition (56) which may best be defined as the spontaneous onset of partial to complete deterioration of the facial function within hours to days postoperatively (51;56;98;99;127;152;169;179; 180;212).

DFP typically occurs 3 to 4 days after surgery, but can also be observed as late as several weeks postoperatively (51;56;99;180). The origin of DFP has not yet been defined, however neural edema (especially within the meatal foramen) as a consequence of vasospasm, ischemia, disturbed microcirculation, venous outflow obstruction, surgical manipulation, iatrogenic injury, fluid shifts, sterile arachnoiditis after CPA surgery or the loss of muscle tone following immediate denervation can be attributed as the causes of DFP (56;99;127;152;179;180). DFP of later onset has a more speculative origin because neural edema and vasospasm are unlikely to account for this phenomenon as late as 30 days postoperatively (56). Late occurrence of facial palsy and its lack of responsiveness to corticoids (51;99;127) or to surgical decompression of the FN within the temporal bone indicate that other mechanisms may be at work (51;179).

Some studies have asserted that the reactivation of latent herpesvirus (herpes-virus simplex and varicella-zoster virus) following surgical stress and surgical manipulation of the facial nerve and its sensory ganglia, is a process that is similar to facial dysfunction after Bell´s palsy (51;99;152). Besides the assumption of a similar pathophysiological mechanism, DFP and Bell´s palsy may also share analogous radiological changes, in which a diffuse magnetic resonance imaging (MRI) enhancement is observed from the distal

intracanalicular segment to the mastoid descending segment of the FN (152). Herpetic reactivation has a high incidence after trigeminal surgery (percutaneous procedures and microvascular decompression) but can also be observed following VS surgery (22). Nonetheless, the cause-effect relationship between herpes reactivation or infection and DFP remains to be proved (56).

2 Intraoperative Facial Nerve Monitoring

2.1 Historical Background

Intraoperative monitoring of the FN is not a new concept *per se* (81) since Dr. Fedor Krause (94), on July 14th 1898, described the use of monopolar FN stimulation during a cochlear nerve section for intractable tinnitus and reported his findings, as follows: "…The divided acusticus was now placed backward, so that it came in contact with the cerebellum. Unipolar faradic irritation of the remaining nerve trunk with the weakest possible current of the induction apparatus resulted in contractions of the right facial region, especially of the orbicularis oculi, as well as of the branches supplying the nose and the mouth. The irritation of the displaced acusticus (using also the very weakest possible current), caused the right shoulder to be elevated twice in succession. The accessorius situated below had undoubtedly been reached by the current, because it was, together with the stump of the acusticus, bathed in liquor that had trickled down…".

With this description, Krause not only reported the first use of FN monitoring but also anticipated the enduring problem of current spread (225). Similar techniques were developed during the following years however Givré and Olivecrona in 1949 (52) introduced a significant advance by employing a special nurse to observe the patient´s face beneath sterile drapes. Givré and Olivecrona (52) even advocated surgery under local anesthesia because facial

function could be assessed throughout the procedure. In addition, they were possibly the first to direct attention to the assessment of postoperative function prediction. Following tumor resection, the function of the FN was tested either by voluntary function or faradic stimulation (52). During the 1960s, Hilger (63), Jako (72) and Parsons (154) devised FN stimulators for parotid and ear surgery. Jako´s device was unique because of a motion detector that was placed inside the patient´s mouth which alerted the surgeon with an audible signal in response to facial movements (72;81). This method has surpassed the first “acoustic” FN monitoring performed by “facial nerve protectors”, in which surgical assistants “shouted” to the surgeon whenever a facial movement was observed [Miehlke 1964, cited by (160)].

The technique of observing the patient´s face for visible contractions remained the state of the art for FN identification until the late 1970s (36;157;225). In 1979, Delgado et al. (36) introduced the use of intraoperative electromyographic (EMG) surface electrodes for FN monitoring during CPA surgeries to improve identification and to facilitate the dissection of the FN. In 1982 Sugita and Kobayashi (199) modified this technique by using a new device which consisted of a pair of accelerometers attached to the orbicularis oculi and oris that converted facial movements into audible sounds through a loudspeaker to provide acoustic feedback to the surgeons. Thereby the surgeons were able to recognize facial responses without the necessity of having a member of the surgical staff observing the patient´s face (199). Sugita and Kobayashi (199) also documented a false-positive error due to an inadvertent stimulation of the trigeminal nerve, in which the patient had the FN sectioned because of the misjudgement. Moller and Jannetta (134;135) introduced the next refinement by developing a system which combined the acoustic monitoring of spontaneous EMG activity and EMG activity in response to electrical stimulation. Thereafter, Prass and Lüders (159;160) correlated and classified the specific patterns of EMG and acoustic activities as the result of surgical manipulations.

2.2 The Impact of Intraoperative Monitoring on the Anatomical and Functional Preservation of the Facial Nerve

For many years, FN function had been evaluated by means of electrical stimulation and monitoring the visible and palpable activity of the facial muscles during surgery in the posterior fossa, temporal bone and parotid gland, as well as monitoring the evoked activity with electrical recordings (61). However, demonstration of the improvement in FN anatomical and functional preservation by using intraoperative FN monitoring (IOFNM) was not assessed until 1987. Harner et al. (61) retrospectively compared 48 monitored patients matched by age, tumor size and most recent year of operation, to unmonitored patients. Similar overall FN anatomical preservation rates were observed, 88% in the monitored group and 79% in the unmonitored group. Nevertheless, differences were most striking when patients were subclassified by tumor size so that patients with large tumors the FN anatomical preservation rates improved from 37% in the unmonitored group to 67% in the monitored group (61). While for small and medium-sized tumors no difference was noted in the immediate postoperative period, although there were more patients affected with total loss of function in the unmonitored group (61).

That study was updated thereafter including 91 patients with the same methodology, in other words, matched with 91 unmonitored patients (60). Again, better outcomes were demonstrated for patients with large-sized tumors, in which the FN anatomical preservation raised from 41% in the unmonitored group to 71% in the monitored group (60). It is worth mentioning that significant improvements in FN function were obtained in the monitored group, especially at 3-month and 1-year follow-ups (60). Harner et al. (60) thereby concluded that IOFNM demonstrated an increased ability to preserve the FN with less postoperative deformity and stated “I don´t think I could convince anybody at our institution with experience to give up monitoring under any circumstances.”

Niparko et al. (147) studied retrospectively 29 monitored and 75 unmonitored patients affected by VS. Testing the results for the subgroups revealed that monitoring was significantly associated with satisfactory facial function 1 year postoperatively for patients harbouring large tumors (> 2 cm), whereas for smaller tumors the better results in the monitored group did not achieve statistical significance. Leonetti et al. (106) investigated the advantages of IOFNM during the infratemporal approach by analyzing 31 unmonitored versus 20 monitored patients (106). Normal postoperative FN function was increased from 70% in the unmonitored patients to 93% in the monitored patients. In addition, none of the monitored patients developed severe facial palsy postoperatively (106;107). In a historical cohort, Hammerschlag and Cohen (59) compared 111 consecutively monitored patients to 207 previously unmonitored patients. The overall rate of complete facial palsy decreased from 14.5 to 3.6% with monitoring.

Dickens and Graham (38) evaluated the postoperative results of 108 patients stratified into three groups, namely: group I had no facial monitoring (38 patients), group II was monitored using a motion type detector system (29 patients), and group III was monitored by means of an EMG system (41 patients). Normal facial function or slight facial dysfunction was encountered in 39% of the patients in the unmonitored group and in 55% of the motion detector group, whereas 87% of the EMG monitored group preserved an excellent facial function postoperatively (38;96). Kwartler et al. (96) retrospectively reviewed the FN function of 155 unmonitored and 89 monitored patients. The monitored large-sized tumor group showed statistically significant better functional results at the immediate postoperative period and at discharge (96). At the long-term follow-up, no statistical difference was noted, although there remained a trend toward better results in the monitored group (96).

The results are sound but should be interpreted with care because of the problematic issue of comparing studies due to the lack of standardization in FN grading and distribution of tumor sizes (38). Moreover, it should be remembered that regardless of the monitoring technique, IOFNM is merely a technical

adjunct that can aid both the experienced and inexperienced surgeon and does not replace surgical skills and experience (14;15;38;72;77;81;98; 154;188;190;199). Nevertheless, monitoring may have a special educational role by refining the surgeons´ technique in order to favor sharp over blunt dissection that is known to produce more EMG activity (81;210), as Kartush (77) stated: "… monitoring appears to be an outstanding teacher which molds the techniques of young surgeons by providing important feedback during dissection. Thus, monitoring reinforces the essence of microsurgical technique…".

Since the NIH Consensus Statement on Acoustic Neuroma (1) explicitly recommended routine use of IOFNM, there have been no formal clinical trials to assess the benefits of surgery with monitoring over surgery without monitoring (224;225). The studies that have emerged thereafter in the literature have maintained the same concepts of retrospective data evaluation, although clear benefits in the quality of the postoperative facial function may be observed in monitored patients, not only in those affected by VS (97;136;141;149;189;195;219), but also in patients suffering from CPA and skull base diseases (103;117;118).

Overall studies indicate that there is an improvement in FN outcome by using IOFNM, especially in large tumors (44;61;74;77;80-82;85;87;103;107;110; 117; 118;132;134;136;141;147;148;159;160;184;193;195;219;228).

Thus, intraoperative neuromonitoring has been established as one of the methods in which modern neurosurgery can improve surgical results while reducing morbidity (77;168), even though a controlled, prospectively and randomized study is still lacking until now (81;178). Such a study is unlikely to be enrolled because most surgeons who have included monitoring in their practice believe that there is indeed a benefit and are reluctant to withdraw intraoperative monitoring from their patients (77;80;81). Furthermore, IOFNM may also improve hearing preservation outcomes because of the likelihood of reducing surgical trauma that may jeopardize both nerves (60;61;77;81).

2.3 The Objectives of Intraoperative Facial Nerve Monitoring

The main purpose of intraoperative monitoring is to make the surgical team aware of the ongoing changes in the neural function thereby permitting modifications in surgical strategies that can ultimately avoid neural damage (77;80). Effective neurophysiologic monitoring requires knowledge of pertinent anatomy and physiology; selection of the appropriate monitoring techniques based on the structures at risk for each surgical procedure; and appropriate interpretation of the evoked responses based upon knowledge of the normal activity (77;81). Thus, the objectives of IOFNM include (77;78;80;147;151;188;189;224;225):

A – Identifying precociously the FN in soft tissue, tumor and bone;

B – Warning the surgeon of an unexpected facial stimulation;

C – Mapping the course of the FN in the temporal bone or tumor by using electrical stimulation;

D – Enhancing neural preservation by reducing mechanical trauma to the FN during rerouting or tumor dissection;

E – Assessing the prognosis of the FN function at the end of tumor removal.

Achieving these goals demands the use of various monitoring techniques that are now available. Standard FN monitoring techniques during CPA and skull base surgery include direct electrical stimulation and free running EMG (204). Alternative FN monitoring techniques have been devised mostly by taking advantage of the antidromic and orthodromic properties of motor nerve excitation after peripheral stimulation (26-28;164;181;213-217). These techniques have the advantage of being used in patients anesthetized with neuromuscular blocking agents and monitoring of the entire nerve with a single electrode (225). Although interesting results have been reported from these studies (26-28;164;181;213-217), the lack of transynaptic conduction, that is,

the absence of the brainstem component, corresponds to the major limitation of antidromic and orthodromic potentials because a complete section of the FN at CPA may be associated with little or no changes in response amplitude (78;156). This is due to the preservation of the aforementioned nerve electrical excitability peripheral to the injury site that takes some days to disappear (23;24;47;154). Moreover, the sensitivity of these techniques to nerve injury is still unclear so far and nerve potentials cannot be converted into audible signals to provide immediate feedback to surgeons (147;225). Nevertheless, further investigations should be encouraged (225).

2.4 Technical Considerations

2.4.1 Types of Stimuli

Electrical stimulation is conventionally performed by applying rectangular pulses delivered by two electrodes, namely the cathode that becomes negative and the one that becomes positive which is called the anode (73). The basic parameters for a rectangular pulse are intensity and pulse duration, measured in milliamperes (mA) and milliseconds (ms), respectively (73). The stimulation of the nerve depends on the amount of charge (coulombs, C) delivered, which is the product of the amount of current (current intensity) and the amount of time of current application (pulse duration) (73;184). In practical means, it is worth noting that for a comparison among studies, not only should the current delivered be considered, but also the pulse duration. In this way, a charge delivered to a nerve using a 0.2 mA stimulation threshold with 50 μsec of pulse duration is equivalent to 0.1 mA when a 100 μsec pulse duration is applied (184).

2.4.2 Types of Stimulators

Two types of stimulators are commercially available, the constant-current and the constant-voltage (73). Constant-current stimulators maintain the current intensity at a desired level, while constant-voltage stimulators maintain a constant voltage between electrodes (73). The strength of the stimulus may then be measured in mA or in volts (V) (154). Thus, the current delivered to the tissues is related directly to the voltage, and inversely to the resistance by Ohm´s law (Amplitude = Voltage/Resistance) (154).

Constant-current stimulators are employed in most neurophysiological studies due to their consistent response (73;134). Moller and Jannetta (134) have described constant-voltage stimulation with the assumption that most of the current applied flows through lower impedance fluids instead of through the nerve. Therefore by using a constant-current device the current intensity should be raised to a higher level to obtain an adequate response (134). In this way, if the fluid is suddenly removed or if the nerve becomes exposed, the higher current then comes in direct contact to the nerve with potentially damaging consequences (134;224;225).

On the other hand, Prass and Lüders (158) have demonstrated no practical advantage of constant-voltage over constant-current stimulation by employing a “flush tip” probe (a stimulation probe that is insulated to the tip) and advocated the use of the constant-current because the amount of current delivered is not affected by the diameter of the stimulation probe. These results were further confirmed by Kartush et al. (82) indicating that constant-current sources can be effectively used with the insulation of the stimulating probes. In addition, stimulus artifacts, especially current shunting, may be minimized when bipolar electrodes are used along with flush-tip insulation probes (82;158).

Additionally, by using constant-voltage stimulators the current delivered changes with tissue resistance and therefore may be erratic and unsuitable for quantitative evaluations and signal averaging (73). Therefore, their use should

be restricted to FN identification during surgeries in the posterior fossa (73). The use of constant-current or constant-voltage stimulators is still a matter of debate thereby future studies, especially experimental, are necessary and should be dedicated to solving this controversy definitively (225).

2.4.3 Types of Stimulation Probes

Even though two electrodes are always necessary to produce electrical stimulation, “monopolar” stimulation is defined in such situations where only one active electrode is in close contact to the stimulated tissue, while the reference electrode is placed far from the target tissue (73;146). Monopolar and bipolar stimulation probes have been used in several studies (225). The current density is better distributed in monopolar probes representing an advantage of this method. This leads to a direct correlation between the stimulus strength and the obtained responses (73). Current spreading is a major problem inducing false-positive responses by causing the activation of any tissue, especially the CN, lying along the current pathway (36;49;62;73;80;82). These responses may be minimized by placing the reference electrodes far from the target tissue, especially in directions not traversed by other nerves, and by using a larger reference electrode in relation to the active electrode (73).

Bipolar stimulation is considered when both electrodes are active and placed in close contact to the stimulated tissue (73;146). The electrodes can be configured side by side, as a bayonet forceps, or concentrically (73). This type of stimulation shows more specificity and precision in localization because it tends to stimulate mainly the tissue under or in between the two electrodes thus reducing the likelihood of current spreading to a distant reference electrode (60-62;73;80;82;225). Moreover, the tip orientation of bipolar electrodes can produce changes in amplitude responses (12;73;82). Interestingly, longitudinal placement of the electrodes over the nerve axis requires one-half to two-thirds of the current intensity that is required when electrodes are positioned

orthogonally or across the nerve axis (73;82). Limitations of bipolar stimulation comprise the complexity of its current distribution and current shunting to cerebrospinal fluid or blood collections leading to false-negative responses (62;73;134). Compared to bipolar probes, monopolar electrodes require a current intensity two to three times higher in order to reach the same responses (82).

The best stimulation protocol is a continuous source of debate (82;184;225). Although Moller and Jannetta (134) have demonstrated some advantages of constant-voltage over constant-current, their study compared monopolar voltage to bipolar current. However, depending on the desired clinical goals, variations of protocols may be necessary to optimize the effect of monitoring (147). Owing to significant differences in the electrical characteristics of monopolar and bipolar probes, some authors recommend concurrent use of both probes based on the specific clinical goals (82). Thus monopolar stimulation can be utilized in tumor mapping when high sensitivity is indispensable, whereas the bipolar configuration is most suitable for CN differentiation within the CPA considering its high specificity and low current requirements (15;78;80;82;132;182;189).

2.4.4 Types and Placement of Recording Electrodes

Surface, subcutaneous needle, monopolar or bipolar intramuscular hook wire electrodes can be used for EMG recording (62;188;224;225). Wire electrodes have the highest impedance and the lowest field of view; the subdermal needles have an intermediate impedance and a large field of view; whereas surface electrodes have the lowest impedance and the largest field of view (182).

Surface electrodes are time-consuming, less specific, susceptible to artifacts and easily displaced during surgery (188;224;225). For these reasons they are considered inadequate for EMG monitoring (62;188). Conversely, hook wire

electrodes, even though advocated by some investigators due to their high sensitivity and specificity for detecting muscular responses (12;62;125;134;160), have no major practical advantage and may be more traumatic to the skin and muscles (225). Therefore, EEG platinum needle electrodes are the most commonly used because of their large uninsulated surface compared to single-fiber EMG electrodes and their ability to identify specific muscle activity anywhere within the target muscle (225).

Initial studies of facial EMG used a single recording channel to monitor both the superior and inferior branches of the FN by placing one electrode of the bipolar configuration in each of the orbicularis oculi and orbicularis oris (134). This range montage, however, is more vulnerable to artifacts, because of the wider separation in between the electrodes, and to impairments in response recognition to direct electrical stimulation (DES) during sustained EMG activity (225). Multichannel recordings have overcome both limitations due to the likelihood increase of having at least one channel free of ongoing EMG activity allowing adequate DES even during EMG irritation (225). In addition, multichannel electrode montage increases the sensitivity of EMG recordings (19;57). It is thus recommended to monitor at least two branches of the FN by using two recording channels (two electrodes of the bipolar configuration for each of the superior and inferior branches of the FN) and other CN (225).

In addition to EMG recordings, devices based on motion detectors of the facial muscles may be useful adjuncts because of the inability of EMG-based techniques for FN monitoring during electrocautery (62;188;210;225). The created artifacts that occur concurrently to cautery jeopardize adequate identification of EMG responses that might indicate FN damage from thermal injury (225). As a result, there is an increased risk of FN injury during this particular surgical step (225). In spite of the several motion detectors (14;72;139;187;190;191;199;210;211;232) and even the video-based systems (45;46;140) that have been developed, EMG recordings remain the most sensitive indicator of FN activation (14;38;46;159;188;191;225). During posterior fossa surgeries, EMG recordings require lower current levels to be

activated and react earlier than an audio alarm (14;38). Furthermore, the elicitation of evoked EMG responses that might correspond to FN injury are detected in the EMG monitor without producing facial movements that sound the audio alarm (14). It should be noted that no device allows adequate monitoring during electrocautery (78).

2.4.5 Anesthesia

FN EMG monitoring can be performed under essentially all types of anesthetic regimens with the exception of neuromuscular blocking agents that might hinder the accuracy of IOFNM by interfering with propagation of potentials which might be incompatible with appropriate EMG monitoring (147;225). Nonetheless, some studies have demonstrated that even under moderate to profound levels of peripheral neuromuscular blockade, it is possible to elicit facial EMG activity either by DES or mechanical manipulation without compromising FN monitoring (18;20;64;105). The assumption is that facial muscles are somehow insensitive to neuromuscular blocking agents (18;20). This phenomenon is not entirely understood, although a different type of innervation (a greater number and size of neuromuscular junctions) and a lower affinity of acetylcholine receptors in the facial muscles to acetylcholine are suggested as potential explanations (18;20).

Further studies in a large patient series should be performed to confirm these findings. Moreover, chronically injured FN, as in the case of CPA diseases, may present a greater sensitivity to lower levels of neuromuscular blockade (18). For now, there is a general belief that even a partial blockade compromises spontaneous and mechanically evoked activities and thus its use should not be recommended for FN monitoring (12;82;225). Short-acting agents, namely succynilcholine, may be administered during tracheal intubation because it is expected to be cleared during the surgical approach returning to normal status before the critical stages of the surgery have been reached (62;80;225).

3 Direct Electrical Stimulation

IOFNM with electrical stimulation has become a widely used technique during CPA surgeries (11). The use of direct electrical stimulation (DES) is very simple in its concept (80). A stimulating probe is used to apply DES over the posterior fossa structures and to generate the compound muscle action potentials (CMAP) that are recorded through paired electrodes placed on the patient´s face in the ipsilateral facial muscles whereas a ground electrode is positioned at the forehead (80) (Fig. 9). The response of the facial muscles is monitored acoustically through a loudspeaker and the magnitude of the muscle contractions is visually observed on the monitor (11;12). It is important to recognize that the stimulus intensity required to evoke CMAPs is higher in injured nerves or nerve roots (64;191). DES may be used as an adjunct during surgical exploration within the anatomical regions traversed by FN providing real-time information about the nerve status (11;53;154). The safety of nerve stimulation has been well established both in animal models (67;68) and clinical practice (15;82;184).

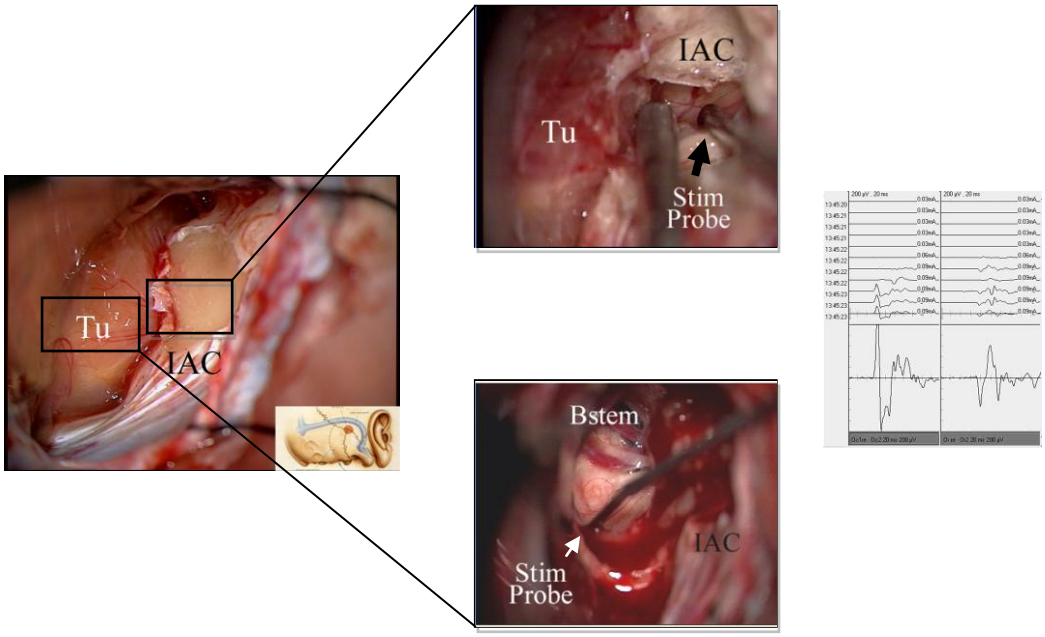

Figure 9. *Mechanisms of direct electrical stimulation. Intraoperative photographs depict the surgical view of a large vestibular schwannoma on the right side (left). The facial nerve can be stimulated during different steps in the surgical procedure by using a stimulation probe in the internal auditory canal (IAC) (upper center) or at the end of tumor resection at the brainstem (lower center). The evoked compound muscle action potentials (CMAP) should be demonstrated on both branches after stimulation (right). Bstem – brainstem; IAC – internal auditory canal; Stim Probe – stimulation probe; Tu – tumor.*

3.1 Intraoperative Use

Tumors arising in the CPA and temporal bone may displace, attenuate or even encase the FN in a way that its identification may be cumbersome (82). In smaller tumors, FN identification and confirmation is straightforward with DES (225). But frequently, especially in larger tumors, the only way to locate the nerve appropriately is by using DES (225). Precise FN location is the first step toward preservation of function (15). Therefore, FN identification is thus the primary utility of DES (53;225) and the most adequate technique for mapping (53;80). Regardless of the stimulation protocol (whether bipolar versus monopolar probes or constant-current versus constant-voltage stimulators), FN

location is determined by using higher charges (usually between 0.3 to 1 V or 0.1 to 3 mA) within the CPA, the temporal bone, as well as the tumor surface (98;125;126;184;188;194;225). Generally, stimulation is more easily obtained when the nerve is located close to the electrode rather than far from the stimulating probe (73) but if the current is too high, monopolar probes will permit current spreading from tissues to FN (188;226;227). Herein, it is important to recognize that by using stimulation intensities of about 0.5 to 0.6 mA, the current spread is dispersed within a maximum of 2 cm from the electrode (226). Furthermore, approximately 1 mA of current is equivalent to 1 mm of bone covering the FN (188;190;191).

Within the posterior fossa, however, a smaller current is usually necessary to stimulate the exposed FN (generally 0.1 to 0.2 mA) (188). Stimulation of the trigeminal motor fibers may produce EMG activity in the facial muscle channels due to considerable crosstalk between channels (14;225). Differentiation can be accomplished by their different waveforms, namely smaller amplitude and shorter latencies observed with trigeminal EMG responses (226). The activation of trigeminal motor fibers typically produces EMG responses in 3 to 4 ms, while facial responses are obtained rather late in 6 to 8 ms (207;225;226). Following nerve identification, the stimulus intensity is reduced to minimize current spreading which may be set at the lowest intensity required to elicit an evoked EMG response (36;126;194). FN stimulation is then performed throughout the surgical procedure to confirm nerve location and integrity (36).

Before tumor resection, the tumor capsule should be stimulated to confirm whether there are any FN fibers in the area to be dissected (36;188;225). If no responses are obtained even when using high charges, then it is assumed that the FN is far from the stimulating area thereby the dissection can proceed more rapidly without risking the FN (82;188;225). This is particularly useful in VS because a posterior position of the FN can be rarely found in approximately 3% of the patients (177;197) even though the nerve typically runs through the anterior superior or anterior middle portion of the tumor capsule in VS (22;177).

In this way, DES helps to avoid sectioning an aberrant course or splayed nerve that may be positioned in the posterior capsule of the tumor (188).

Additional warning of unexpected FN stimulation has gained some interest recently after a description of nerve splitting which may be frequently recognized, especially in medial arising VS (134;197;198). FN splitting occurs in approximately 36% of medial VS and is recognized by selective stimulation (197). In this situation, the FN has two portions, one major branch located on the anterior middle part of the tumor capsule and one minor branch that runs over the cranial tumor pole (197;198). Stimulation of the smaller branch evokes responses exclusively in the orbicularis oris muscle (198). The selectivity of evoked responses gives rise to the assumption of a topographical arrangement of the FN fibers within the CPA (198). Ashram et al. (7), on the other hand, attributed the same electrophysiological results of long-latency, low-amplitude EMG responses recorded only on the orbicularis oris channel to the stimulation of the nervus intermedius. This recognition has the same surgical impact regardless of whether or not this smaller branch is considered the nervus intermedius (198) due to the likely protection of the FN from inadvertent sectioning by indicating that the main trunk of the nerve is located in an entirely different location within the CPA (7;198).

3.2 Function Prediction

After the completion of the tumor removal, the facial function is evaluated (80;188;225). In order to assess postoperative facial function several protocols of FN stimulation were devised using a wide variety of stimulation sources, stimulator electrode designs, placements and types of recording electrodes and IOFNM criteria (69;70;184;225). A detailed description of the published studies of the function prediction of DES is summarized on Table S 6. Intraoperative information based on the results of DES would permit the surgeon to give the patient an immediate assessment with regard to the likely FN function (192).

Additionally, accurate and early prediction of both FN injury and FN recovery may allow adequate planning for the best management including earlier procedures of facial reanimation before significant facial muscle atrophy has developed (8;69;70;87;201). On the other hand, a correct function prediction may also avoid unnecessary surgical procedures while function recovery is still likely (43).

3.2.1 Amplitude of Evoked Compound Muscle Action Potential

The introduction of the absolute amplitude value of the contraction of the facial muscles after tumor removal as a predictor parameter was proposed initially by Harner et al. (60). Thereafter, Beck et al. (11) have quantified the magnitude of muscle contraction in response to 0.05 mA of stimulation at the brainstem. CMAP amplitude is directly proportional to the number of stimulated muscle fibers (184) thereby reflecting the number of intact axons (53;62;227). Interestingly, the absolute CMAP values at the internal auditory canal (IAC) remain relatively constant throughout the procedure but those over the root exit zone (REZ) usually decrease as the surgery proceeds (126;222;226;227). This observation may demonstrate a fairly temporal relationship between progressive nerve damage and surgical manipulation ultimately indicating a loss of conducting axons from intraoperative injury (62;227). The major limitation of this method comprises the wide interindividual variability because of the inconsistency in needle position and the size of the monitored muscles among patients (184). This is reflected by a great threshold variation among the published studies. Some studies consider CMAP amplitude from 100 µV to 500 µV in response to 0.05-0.6 mA of brainstem stimulation as the cut-off value for a compromised postoperative facial function (4;11;145;194;227). Thus, patients demonstrating a reduced amplitude in muscle contractions are correlated to impaired postoperative facial function (11;16;60). Maximal or near-maximal

stimulation would render larger CMAPs, but the risk of electrical injury would be unnecessarily increased (184).

3.2.2 Stimulation Threshold

For activating the FN, the minimal amount of stimulation is usually sought, so that the best conducting fibers respond (184). The stimulus threshold is achieved by finding the electrical threshold necessary to produce an EMG recording. If a response is obtained, this is evidence of an intact anatomical and functional FN (60). The lack of standardization of the techniques and parameters precludes a detailed analysis among published results (184;225). However, there is a trend toward predicting good postoperative function by applying low-threshold stimulation at the brainstem following tumor resection, especially lower than 0.05 to 0.1 mA (19;84;192) or 0.1 V (121), while elevated thresholds of levels as high as 2 to 3 mA (87;191) or 1 to 3 V are commonly associated with severe facial dysfunction (65;225).

3.2.3 Proximal-to-Distal Amplitude Ratio

Together with the introduction of EMG surface electrodes for the accurate recording of evoked responses, Delgado et al. (36) also suggested stimulation at both the IAC and REZ to assess postoperative facial function at the end of tumor resection. As a result, both absolute CMAP amplitudes were used to confirm nerve integrity so that similar amplitudes were correlated to facial weakness with rapid function recovery whereas amplitude reduction between the REZ and IAC was associated with longstanding facial weakness (36). The extent of the axonal damage is therefore estimated by using the relative amplitude ratio (61).

Proximal-to-distal amplitude ratio eliminates the interindividual variability of each response that is found with other electrophysiological techniques of function prediction (201). Therefore, this method is believed to be more accurate than the abovementioned (201). Besides stimulating the FN at distal IAC and REZ the role of DES is extended to the detection and quantification of conduction block (201). Although these findings were not corroborated by Benecke et al. (15), overall studies considering the ratio criteria for predicting the FN outcome indicate that there is indeed an improvement in function prediction when compared to absolute amplitude and stimulation threshold (3;16;53;61;69;201;227).

Proximal-to-distal amplitude ratio greater than 30% is a strong indicator of good to excellent facial function, especially for the long-term (53;69;147;201;227). In addition to EMG recordings, Prass and Lüders (159) have also observed the acoustic responses elicited by stimulation and described that the responses obtained at the porus were sometimes higher than those heard when the brainstem was stimulated. All patients, in which this observation occurred, showed immediate facial palsy (159).

3.2.4 A Comparison of Electrophysiological Methods for Function Prediction

Critical comparative studies of electrophysiological methods for facial function prediction are scarce in the literature. In general, the use of all three electrophysiological methods provides reliable prediction of postoperative FN outcome, as summarized on Table S 6. By analyzing the different methods individually during skull base and CPA surgeries, Magliulo and Zardo (119;120) compared the predictive value of amplitude response, stimulation threshold and proximal-to-distal ratio. Beck´s method (500 µV amplitude of ongoing EMG activity lasting for 30 sec and 500 µV in response to 0.05 mA) failed to predict FN outcome because patients with thresholds greater than 0.05 mA were not

considered (119;120). Silverstein´s method (≤ 0.1 mA), representing the stimulus threshold group, correctly predicted the final facial outcome in 84 to 86.9% of the patients, while the ratio method, that was represented by Berges´ method (R = R´/R´´, in which R´ corresponds to the minimal stimulation intensity at CPA divided by the amplitude response and R´´, the intensity and amplitude at the IAC), rendered 90 to 91.3% correct function prediction (119;120). The limited data and the retrospective study design prevent definite conclusion, nonetheless, it seems that the ratio method provides the best results when used alone (119;120). Sobottka et al. (194), on the other hand, demonstrated that the absolute values of proximal stimulation were better predictors than ratio.

The concurrent use of amplitude response and stimulus threshold, however, increases the ability of function prediction for both early and late postoperative function by reducing the rates of false-positive results when compared to stimulation threshold alone in either a constant-current or constant-voltage stimulation protocol (121;145). Similarly, the association of stimulus threshold and proximal-to-distal ratio was also found to be beneficial, especially in predicting the final outcome for patients affected by moderate to severe postoperative facial dysfunction (69;70). Thus, a combination of methods may provide the best predictive assessment of postoperative facial function (225).

4 Free Running Electromyography

Continuous free running EMG is typically monitored from paired electrodes, which are placed in the muscles innervated by nerves or nerve roots that are considered to be at risk of damage during surgical procedure (64). Actually, the concept of continuous FN monitoring in order to provide immediate feedback to the surgeon was introduced with acoustic devices (72;134;160;187). These techniques were used to detect facial movements in response to FN mechanical trauma during surgical manipulation (15;64;72;134;159;160;187) (Fig. 10).

Accordingly, EMG recordings from several muscles can be monitored concurrently by using a loudspeaker for acoustic feedback and an oscilloscope for visual feedback (Fig. 11) (62;80;189). The most important type of EMG recording during surgery is the neurotonic discharge. These discharges comprise muscle unit potentials activity in response to mechanical or metabolic irritation of the nerve that innervates the monitored muscle (62). Interestingly, it is worth noting that similar to triggered CMAPs, injured motor nerves are less likely to evoke neurotonic discharges following mechanical trauma (64).

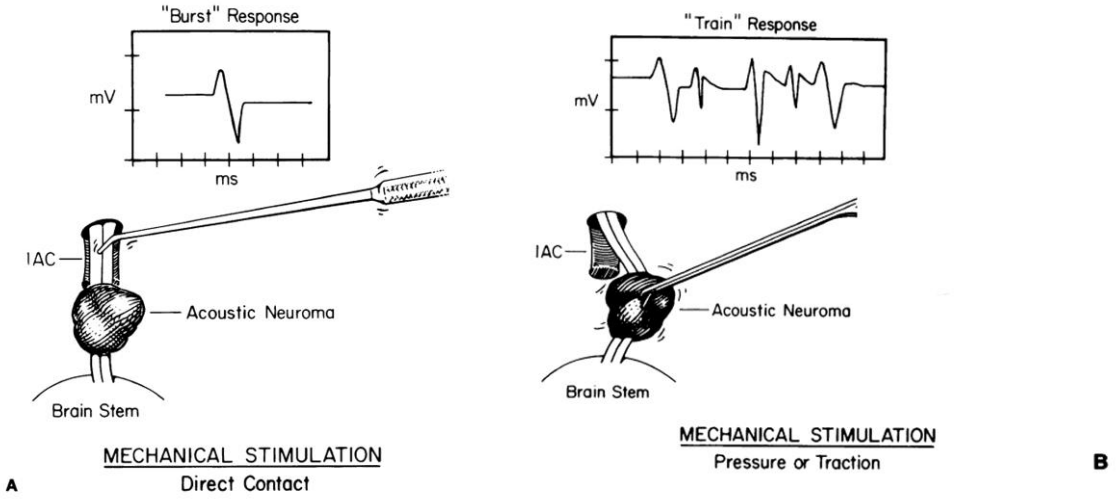

Figure 10. *Mechanisms of continuous EMG recordings in response to surgical maneuvers. The contact of the surgical instruments elicits EMG responses immediately after stimulation (left) while traction produces a delayed response called train activity (right). Adapted from Kartush et al. (78).*

Although FN preservation was improved by using “acoustic” monitoring, interest in analysing the patterns of EMG activity in response to specific surgical manipulation has gained attention only with the studies of Prass and Lüders (159;160). The patterns of EMG activity were then classified into spontaneous and evoked activity (159;160). The evoked activities correspond to the great majority of the documented intraoperative EMG responses that occur as a direct consequence of surgical maneuvres (159;160). DES, mechanical trauma and electrocautery were all related to evoked EMG activities of different amplitudes and waveforms that were further divided into bursts, trains and pulse EMG patterns (160). In addition, the EMG patterns also differed in degree of synchrony, duration and/or temporal relationship with the eliciting events (160).

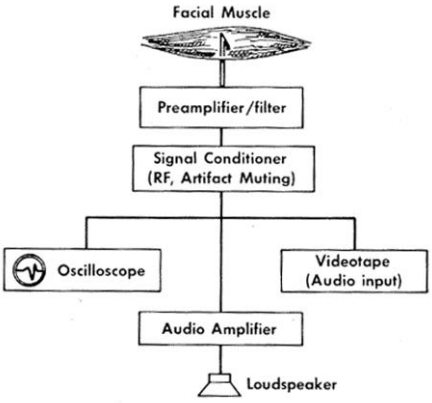

Figure 11. *A scheme of acoustic facial EMG monitoring. Adapted from Prass and Lüders (160).*

The pulse pattern is observed following DES and is easily recognized by its pulsed audible signs in synchrony with the electrical stimulation (160). The burst pattern is the most frequently encountered EMG activity which is characterized by short, relatively synchronous bursts of motor unit potentials that last up to a few hundred milliseconds (160). There is a direct cause and effect relationship between the appearance of the burst activity and the initiating events, in other words the surgical manoeuvres, namely direct mechanical trauma, electrocautery or irrigation (143;159;160). Interestingly neurotonic discharges are less likely to occur following sudden laceration of the nerve (62;78). Bursts probably arise owing to the mechanoreceptor properties or metabolic irritation of the nerve fibers resulting ultimately in the depolarization and elicitation of the action potential (62;160). Thus, burst pattern probably corresponds to a single discharge of multiple FN axons (160). Rapid and high-frequency mechanical trauma may produce EMG bursts of greater density than slower rates of compression (160). The elicitation of burst activity is an indirect sign of a

functional FN because bursts are easily obtained in healthy axons when compared to FN severely compromised by tumor involvement (62;159;160). Therefore, burst patterns of EMG activity are probably due to FN stimulation of several mechanisms and may not necessarily correspond to nerve injury (160). Eventually the burst pattern is followed by sustained periodic activity that lasts up to 30 seconds (160).

Finally, the train pattern is characterized by asynchronous trains of motor unit potentials with a duration of up to several minutes (159;160). Two types of trains were identified that differ in regard to frequency, amplitude, regularity of interval, pattern of build up and decline of motor unit potentials (160). High-frequency trains (50 to 100 Hz) have a typical acoustic quality that resembles an airplane engine which is called the bomber potentials. Low-frequency trains (1 to 50 Hz), on the other hand, render an acoustic signal that is similar to popping popcorn with a lower occurrence than high-frequency trains (160). Train activity is mostly correlated to the surgical traction of the FN, especially when the traction occurs in a lateral-to-medial direction (143;159;160). Interestingly there is a delay from seconds to minutes between the occurrence of the provoking event and the onset of the train activity (160). Similar to the burst pattern, electrocautery, mild nerve trauma and free irrigation may also be associated with episodes of EMG train activity, especially the bomber type, while the release of brain retractors and dissectors leads to a reduction in EMG activity (65;143;160).

Because of onset delay, establishing a direct cause and effect relationship between surgical manipulation and EMG responses is a difficult issue regarding train activity (160). However, the onset delay of train activity in response to lateral-to-medial traction may be explained by the compromise of arterial supply and consequent nerve ischemia (160). This results in the repetitive firing of one or more motor units due to maintenance of the axonal membrane potential above the level of the action potential threshold (160). Train responses are frequently observed in FN severely involved by a tumor which becomes more susceptible to dissection and surgical traction (160). The identification of train

activity may indicate potential or ongoing FN injury (popcorn type) or even significant injury (bomber type) (160).

Even though a variety of audible signals and EMG patterns were described, the studies in the field had remained a continuous source of controversy (Table 3) until the year 2000 when Romstöck et al. (165) provided a detailed analysis of intraoperative EMG patterns with respect to their surgical implications. Romstöck et al. (165) identified five types of spontaneous EMG patterns instead of the three described by Prass and Lüders (159;160). In addition to bursts and spikes, train activity was further subdivided into A, B and C trains (Fig. 12) (165).

Spikes correspond to bi- or triphasic potentials with one large peak (≤ 2,000 µV of amplitude). Bursts are defined as an isolated complex of superimposed spikes arranged in a spindle-like fashion that exhibit several large peaks of up to 5,000 µV and last up to several hundred milliseconds (165). A-train is a unique sinusoidal waveform pattern with a typical high-frequency acoustic signal that always has a sudden onset, an amplitude never exceeding 500 µV, a frequency of 60 to 200 Hz, and a duration of milliseconds to several seconds (165). B-train is a regular or irregular sequence of single spike or burst components (B_S – B spikes or B_B – B bursts) that has a gradual onset and long duration from 500 ms to hours (165). C-train is characterized by a continuous EMG irregular activity (Fig. 13) (165).

Spikes and bursts occur immediately after direct mechanical trauma from surgical instruments near the CN and together with B and C-trains are clinically irrelevant (143;165). Nevertheless, the occurrence of A-trains is associated with FN injury (161;162;165). The A-train EMG pattern is highly suggestive of repetitive discharges that are found in chronic denervation processes and myopathies (165). These discharges are initiated by a spontaneously fibrillating muscle fiber that leads to the activation of several adjacent muscle fibers and the ephatic reactivation of pacemaker fibers (165). Therefore, following nerve injury, the corresponding muscle fibers may become unstable and serve as a pacemaker because they are no longer under neural control (165). The first

occurrence of A-trains can always be correlated with specific surgical maneuvres, especially the dissection of the tumor surface near the brainstem and intrameatal decompression (165).

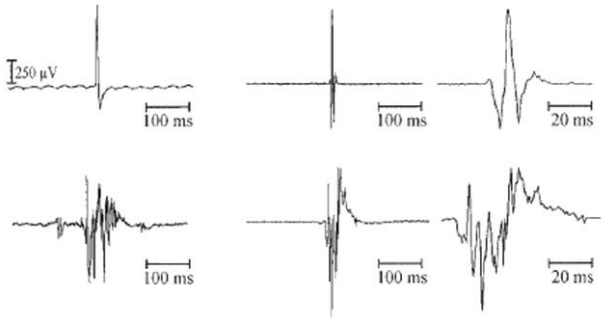

Figure 12. *Electromyographic representations of spikes (upper row) and bursts (lower row). Adapted from Romstöck et al. (165).*

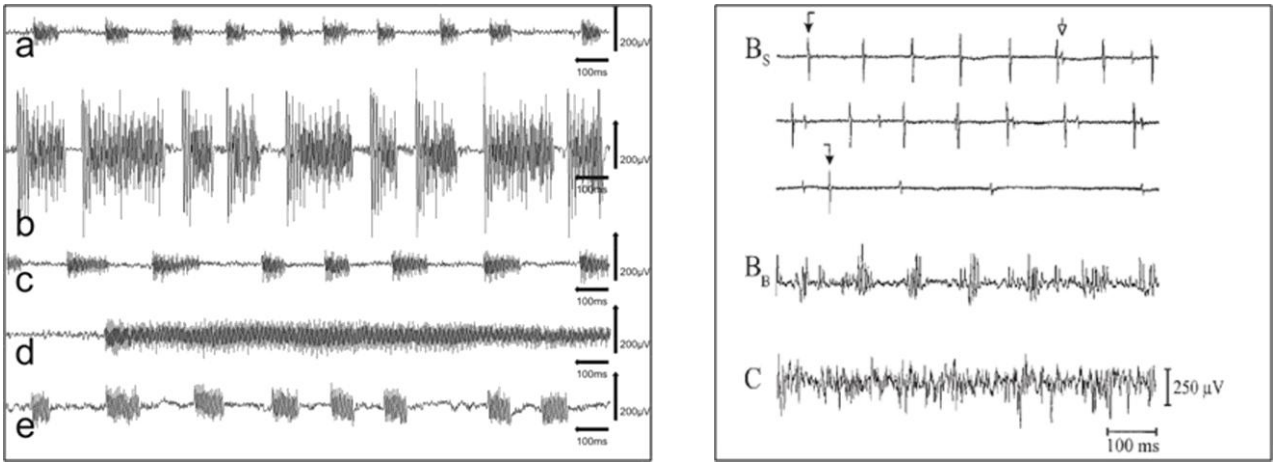

Figure 13. *Electromyographic representations of A-trains (left graphics), B-trains (Bs – B-spikes, Bb – B-bursts) and C-trains (right graphics). Adapted from Romstöck et al. (165) and Prell et al. (162).*

4.1 Intraoperative Use

The main reason fo using free running EMG is to supply the surgical team with immediate information about nerve location and to give continuous feedback on any ongoing activity that could result in nerve injury (60;62;64;172). Because of the apparent absence of delay, EMG activity following mechanical trauma may be valuable for localizing during tumor resection by warning the surgeon about nerve proximity even when the FN has not come into field (61;90;159;160). Additionally, in the absence of neurotonic discharges, the surgery may proceed faster because the FN is expected to be far from the working area (61;86;190). Even though only train activity may indicate nerve injury (159-162;165), any EMG activity may serve as a warning sign of FN manipulation thereby allowing changes in the surgical strategy before irreversible injury has occurred (30;41;55;165). As a result surgical trauma and consequently the risk of FN damage are minimized when continuous feedback of the nerve´s functional status is made available (165).

4.2 Function Prediction

Although there is agreement regarding the usefulness of continuous EMG monitoring for detecting unexpected mechanical trauma (60;62;64;172), its role in facial function prediction is still controversial (53;55;65;90;143;144;215). This may be partially due to the lack of standardization of EMG patterns in published studies and offline analysis of the intraoperative findings (143;144;162;165). Table S7 provides a detailed analysis of the published studies regarding the function prediction of free running EMG.

In previous studies, the intensity and frequency of train activities were found to be correlated to postoperative FN outcome (60;61;103;143;144). Because of this, the presence of high-frequency and high-amplitude trains (143) or even

intensity reduction of the train activity during the final stages of tumor resection were indicative of poor postoperative outcome (103;144). However, the detailed analysis of the EMG patterns indicates that the significance of the EMG potentials is not related to their amplitudes but to the waveform patterns (162;165). As aforementioned, only train activities are related to FN injury, especially A-trains (162;165). Romstöck et al. (165) identified this type of EMG activity in almost all of the patients affected by postoperative facial paresis. A sensitivity of 86% and a specificity of 89% were calculated indicating that A-train occurrence was a highly accurate predictor of postoperative facial paresis (165). In that study, however, a correlation between the number of A-trains and postoperative facial function could not be demonstrated (165). Thereafter, Prell et al. (162) showed that a quantitative EMG parameter, namely the train time, was a reliable indicator of postoperative facial palsy. Interestingly, two time thresholds could be defined, 0.5 sec and 10 sec (162). For patients with normal preoperative function, a train time of less than 0.5 sec is strongly correlated with a good postoperative outcome, whereas the 10 sec time threshold is associated with facial deterioration in patients either with normal preoperative function and those affected with preoperative facial palsy (162). In addition to train time, postoperative complete facial palsy may also be suggested in patients with silent EMG responses, in which no more bursts can be evoked at the end of tumor removal (103;144). This may represent axonal damage because healthy axons are likely to respond to mechanical manipulation (62). The combination of continuous EMG monitoring and DES may improve the prediction of facial function (144), although this has not been established until now (65).

Objectives

Recently, transcranial electrocortical stimulation (TES) has also been used to monitor FN function (3;39;48;168;220;231) because it seems to overcome most of the disadvantages of triggered CMAP and free running EMG (48). However in reports so far, the advent of facial MEP (FMEP) monitoring has been impaired by the low success rate of orbicularis oculi muscle monitoring and the lack of standardized protocol and parameters.

This study was conducted to investigate the success rate of orbicularis oculi and oris muscles MEP (FMEP) for FN monitoring by using a stepwise protocol, in which TES parameters are progressively changed according to the elicitation of the best MEP responses. In other words, the parameters may be better defined with a stepwise protocol so that the stimulation protocol is individually obtained rather than empirically. This might facilitate in the future an adequate comparison among different studies. Besides multichannel monitoring by improving the success rate of orbicularis oculi monitoring would allow for a better outcome prediction because both superior and inferior branches of the FN would be monitored. Moreover, multichannel monitoring could attenuate the impact of artifacts and technical failures by evoking responses in at least one channel.

This study also sought to evaluate the usefulness of FMEP in predicting FN outcome during surgeries at the CPA. At the moment, the criteria applied for intraoperative FMEP monitoring are somehow adapted from limb MEP studies. However, limbs and face or even superior and inferior levels of the face have unique cortical representations that might lead to different MEP responses and interpretations. Therefore an active search for the best threshold levels was provided.

Patients and Methods

1 Patients

FMEPs were recorded intraoperatively from 60 patients undergoing CPA surgery between August, 2006 and August, 2007 at the Department of Neurosurgery, Eberhard Karls University Hospital, Tübingen, Germany. Collected data included patient gender, age, tumor histology, tumor size, FMEP baseline values, FMEP final values, hand MEP baseline values, pre- and postoperative facial motor function, and final-to-baseline FMEP ratios.

2 Methods

Vestibular schwannomas (VS) were classified according to the Hannover classification, as follows: Class T1, purely intrameatal; T2, intra- and extrameatal; T3a, filling the cerebellopontine cistern; T3b, reaching the brainstem; T4a, compressing the brainstem; and T4b, dislocating the brainstem and compressing the fourth ventricle (122-124;170;171). Patients harboring tumors classes T1 and T2 were considered to have small tumors, while those with classes T3 and T4 were considered to have large tumors. For non-VS tumors, the major diameters on the orthogonal planes were used to calculate the tumor-equivalent diameter (*d*), proposed by Sekhar et al. (183) to describe more accurately the tumour diameter of petroclival meningiomas, which is defined as $d = (abc)^{1/3}$. Tumors were considered to be large with a tumor-equivalent diameter ≥ 2.5 cm and small < 2.5 cm. Herein, its use was extended to all histological types to ease comparison between them.

2.1 Anesthetic Protocol and Intraoperative Monitoring

Induction was achieved with thiopental and the subsequent infusion of sufentanil and rocuronium. The maintenance was conducted with continuous infusion of remifentanil and propofol.

Somatosensory evoked potential (SEP), brainstem auditory evoked potential (BAEP) and electromyography (EMG) of the FN were monitored continuously (Endeavor, Viasys Healthcare, Madison, WI, USA) by an experienced electrophysiological team. For large tumors that reached the lower cranial nerves, EMG of the glossopharyngeal, vagus, accessorius and hypoglossal nerves were monitored as well. Direct electrical stimulation of the FN was performed by using a concentric bipolar hand-held stimulation probe being the responses (CMAPs) recorded in the subdermally placed needle electrodes into the ipsilateral orbicularis oculi and orbicularis oris muscles. Continuous EMG and direct electrical stimulation were routinely used for FN identification and assessing the functional status following tumor removal. However, these data were not considered simultaneously for this study.

2.1.1 Somatosensory Evoked Potential (SEP)

SEPs were always used for patient positioning, especially those operated on in a semisitting position, and for large tumors leading to brainstem compression. SEPs were measured after median nerve stimulation by using square-wave electrical pulses with 200 µsec duration and 16-25 mA intensity delivered at 5.1 Hz stimulation rate through surface electrodes placed at the ipsilateral wrist. Recording electrodes were placed in the contralateral parietal area at C3´ or C4´ and FZ according to the International 10-20 EEG System. SEP graphics were obtained by using a 10-250 Hz bandpass filter, 50 ms analysis time and 300 to 500 sweeps.

2.1.2 Brainstem Auditory Evoked Potential (BAEP)

BAEPs were used for assessing hearing function in all patients with preoperative functional hearing. BAEPs were continuously obtained and monitored during the entire surgery through the administration of 100 µsec rectangular pulse click stimulation. Special ear plugs delivered 11.7 pulses per second (11.7 Hz) of 95 dB normal hearing level (HL) in the operative ear. The contralateral ear was masked with white noise of 65 dB HL. Between 500 and 1000 sweeps were averaged requiring 43 sec to 1:26 min to deliver a reliable BAEP graphic. The filters were set within 150 and 1500 Hz. The analysis time was 10 to 15 ms from stimulus onset. Impedance was controlled to lower than 5 kOhms.

2.1.3 Facial Motor Evoked Potential (FMEP)

TES was performed using corkscrew-like electrodes inserted in the scalp and positioned at CZ and C3 or C4 (International 10-20 EEG system) for left or right side stimulation, respectively. The contralateral abductor pollicis brevis (APB) muscle was used as a control to ensure that the FN was not stimulated extracranially. Stimulation was always applied contralaterally to the affected side using 1, 3 or 5 rectangular pulses ranging from 200 to 600V (mean 380 V) with 50 µsec of pulse duration and an interstimulus interval (ISI) of 2 milliseconds (ms) (Fig. 14). Bandpass filters (150-3000 Hz) were used to attain waveforms.

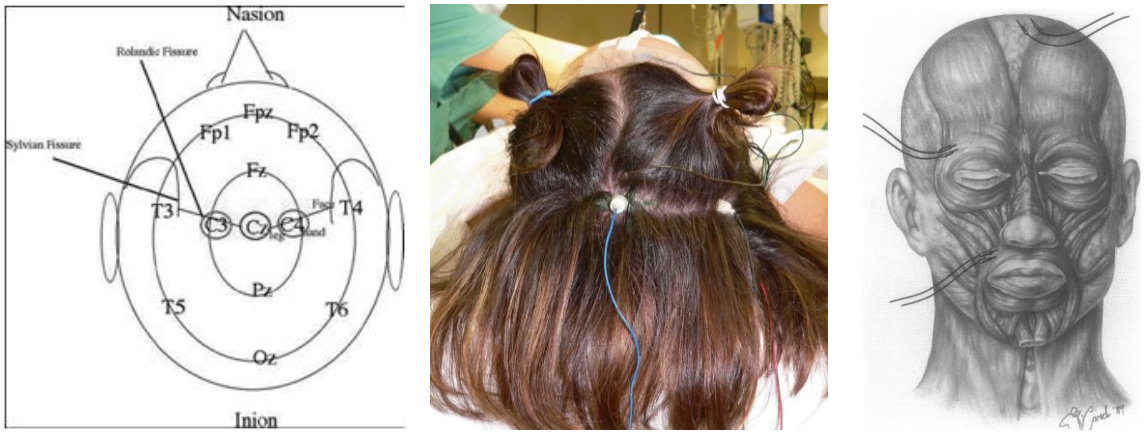

Figure 14. *The positioning of the corkscrew electrodes according to the International 10-20 EEG system (left). The electrodes are placed at C4 and CZ for right side stimulation (center), whereas the responses are obtained in subdermally positioned bipolar electrodes in the orbicularis oculi and oris muscles (right).*

The number of pulses and stimuli intensity was increased according to facial and hand MEP responses. A train of 5 pulses was used only in cases of unsatisfactory response to a train of 3 pulses. In most cases the stimulation parameters were not altered, however, because of the progressive suppression that anesthetic agents have on motor neurons (evoked potential fading) (111;115), some patients had mild increments in voltage intensity to achieve better FMEP responses.

FMEPs were recorded into five surgical steps, namely baseline, dural opening, tumor dissection, tumor resection, and dural closure (final), as well as according to the demand of the surgical team and after neurotonic discharges at EMG. FMEP latency was defined as the time from stimulus onset to the first wave deflection. For this study, longer latencies of more than 10 ms were considered to avoid the misinterpretation of peripheral FN activation (39). FMEP amplitude was defined as the voltage between the maximum positive and the maximum negative peaks of the waveforms. The best amplitude response before dural opening was considered as the baseline value. For patients with a significant increase in the amplitude value at the end of the surgery, the baseline was set at the highest value during tumor approach. Facial potentials were recorded

from paired needles placed in the orbicularis oculi and oris muscles for assessing FN function. FMEPs and CMAPs were obtained from the same electrodes and muscle groups that were used for EMG monitoring.

TES was performed intermittently with BAEPs and SEPs recordings. The surgical team was continuously warned about the incoming stimuli, especially during the microsurgical steps due to undesirable movements as a consequence of transcranial stimulation. TES was mostly achieved by taking advantage of short intervals during changes in surgical instruments or modifications in the microscope position by the surgeon. Due to significant interindividual variability for absolute amplitude FMEP values, a final-to-baseline FMEP ratio was calculated for each patient and correlated to the immediate postoperative FN function examined by the surgical team using the House-Brackmann (HB) classification evaluated at discharge (Table 2) (66).

2.2 Statistical Analysis

The statistical analysis was performed with SPSS 13.0 (SPSS, Inc., Chicago, IL). Nonparametric Spearman correlation coefficients were used to evaluate the correlation between the FMEP ratio and immediate postoperative FN function outcome. Receiver Operating Characteristic (ROC) curves were constructed to determine the best cut-off of orbicularis oculi and oris muscles final-to-baseline ratios and the area under the curves (AUC) were calculated to estimate accuracy. By using different cut-off amplitude ratios, sensitivity and specificity of both muscles were determined. Postoperative HB 1 and 2 were considered satisfactory and HB 3-6 was considered unsatisfactory.

***Table 2**. House and Brackmann Classification. (66)*

Grade	Description	Characteristics
1	Normal	Normal facial function in all areas
2	Mild dysfunction	Gross: Slight weakness noticeable on close inspection; may have slight synkinesis At rest: Normal symmetry and tone Motion: Forehead, moderate to good function Eye: Complete closure Mouth: Slight asymmetry
3	Moderate dysfunction	Gross: Obvious but not disfiguring difference between two sides; noticeable but not severe synkinesis, contracture and/or hemifacial spasm At rest: Normal symmetry and tone Motion: Forehead, slight to moderate function Eye: Complete closure with effort Mouth: Slightly weak with maximum effort
4	Moderately severe dysfunction	Gross: Obvious weakness and/or disfiguring asymmetry At rest: Normal symmetry and tone Motion: Forehead, none Eye: Incomplete closure Mouth: Asymmetrical with maximum effort
5	Severe dysfunction	Gross: Only barely perceptible motion At rest: Asymmetry Motion: Forehead, none Eye: Incomplete closure Mouth: Slight movement
6	Total paralysis	No movement

Results

The majority of patients (n = 38) had surgery for resection of VS followed by petroclival meningioma (n = 8). Tumors were mostly of large size (55%) Preoperatively, normal facial function was documented in almost all except for 7 patients, in whom a slight facial weakness (HB 2) was observed (Table 3). FMEP from the orbicularis oris and oculi muscles could be reliably monitored in 86.7% and 85% of the patients, respectively. Single pulse never rendered hand MEPs and therefore facial muscles responses, when obtained, were interpreted as direct extracranial stimulation unreliable for monitoring. Only when using 3 to 5 train pulses, both contralateral facial and hand MEP could be observed.

Artifacts were occasionally observed in MEP recordings of the orbicularis oculi and orbicularis oris muscles preventing continuous data acquisition (11 of 120 baseline measures). Among the technical failures observed in this study, FMEP could not be obtained from either muscle in three patients. Only one presented a slight facial weakness (HB grade 2) preoperatively. The other six technical failures consisted of short-latency multi-pulse response (< 10 ms) and regarded as peripheral FN stimulation. FMEP amplitude and latency had a wide interindividual variability (complete data are demonstrated on Tables 3 and S8 in supplement). The median latency of orbicularis oculi and oris muscles FMEP were 15.1 and 14.8 ms, respectively, while the absolute amplitude were in the range of 120 µV for both muscles (Table 3). The abductor pollicis brevis MEP that was used as a control response had a median latency of 23.4 ms and approximately 1100 µV of absolute amplitude (Table 3). In eleven patients (18.3%), the stimuli intensity was enhanced with a mean value of 63.5 V (range 20 to 260 V) to achieve better FMEP responses as a consequence of potential fading due to progressive anesthesia (Table S8 in supplement). No complications related to TES were documented. Slight head movements could be observed following stimulation in some patients, however they were not cumbersome for microsurgery.

***Table 3**. Patient demographics.**

Male	25
Female	35
Median Age (yr)	46
range	5 - 71
Diagnosis	
Vestibular Schwannoma	38
Petroclival Meningioma	8
Jugular foramen meningioma	2
Other	12
Preoperative Facial Function	
HB 1	53
HB 2	7
Postoperative Facial Function	
HB 1	37
HB 2	7
HB 3	8
HB 4	4
HB 5	4
HB 6	0
Motor Evoked Potential (median)	
Oculi	
Latency (ms)	15.1
range	10 – 24.5
Amplitude (μV)	110
range	9.95 - 830
Oris	
Latency (ms)	14.8
range	10 – 23.4
Amplitude (μV)	120
range	16.4 - 1400
Hand (APB)	
Latency (ms)	23.4
range	18.8 – 33.1
Amplitude (μV)	1104
range	9.37 - 2000

* APB – *abductor pollicis brevis* muscle; ms – millisecond; μV – microvolt.

Satisfactory postoperative facial function (HB 1 and 2) was achieved in 44 patients (73.3%). No complete postoperative facial palsy (HB 6) was observed due to the routine use of multimodal IOFNM (DES and free running EMG). The immediate postoperative FN function correlated moderately with the FMEP ratio, so that the higher the ratio, the better the FN function for the orbicularis oculi muscle (r = - 0.197, N = 51, *p* = 0.165) and for the orbicularis oris muscle (r = - 0.362, N = 52, *p* = 0.008) (Fig. 15). By calculating the ROC curves of both muscles, we have interestingly found two different cut-off values, 80% FMEP amplitude ratio for the orbicularis oculi muscle and 35% amplitude ratio for the orbicularis oculi muscle. A useful correlation between FN function and FMEP ratio was observed at the cut-off amplitude values of 80, 50 and 35% (Tables 4 and 5). FMEP has a good accuracy as a diagnostic test measured by the AUC for orbicularis oculi (AUC = 0.689 ± 0.092 – standard error; 95% CI = 0.508 – 0.870, *p* = 0.049) and orbicularis oris muscles (AUC = 0.692 ± 0.106 – standard error; 95% CI = 0.485 – 0.899, *p* = 0.039) (Fig. 16).

Frequently, full amplitude preservation (> 100% FMEP final-to-baseline ratio) was documented, however it was not associated with improvements in FN function. Only one patient had postoperative improvement of FN function from HB 2 to HB 1, even though there were no significant changes in the FMEP amplitude ratios (Patient 34, Table S 8). Only one of 30 patients with an 80% or greater final amplitude of the orbicularis oculi muscle had more than two grades of function deterioration. Whereas for the orbicularis oris muscle, only three of 42 patients with final amplitude greater than 35% were affected by more than two grades of facial function deterioration. Marked FMEP reduction in both muscles was observed in only one patient that is demonstrated in Figure 17. Four patients (6.7%) presented FMEP loss at the end of the surgery. All of them suffered facial paresis postoperatively, although in different degrees (HB 3, 1 patient; HB 4, 2 patients; and HB 5, 1 patient) (Fig. 18).

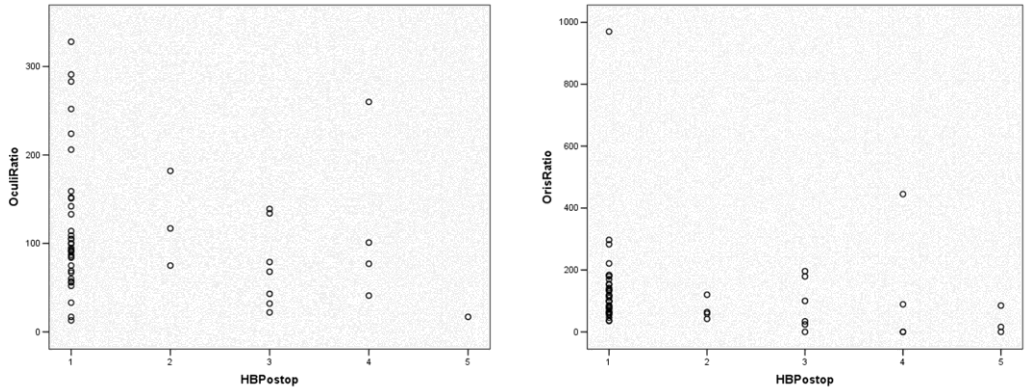

Figure 15. *Correlation between facial motor evoked potential (FMEP) final-to-baseline ratios to immediate postoperative function in the orbicularis oculi (left graph) and orbicularis oris (right graph) muscles. There was a negative correlation between FMEP amplitude and postoperative facial function, in which the greater the ratio, the better the likelihood of a good postoperative outcome (orbicularis oculi, r = - 0.197, N = 51, p = 0.165; orbicularis oris, r = - 0.362, N = 52, p = 0.008).*

Table 4*. Comparison of facial motor evoked potential (FMEP) amplitude ratios with unsatisfactory (HB 3 – 6) postoperative outcome in the orbicularis oculi muscle.*

Cut-off amplitude (%)	Sensitivity (%)	Specificity (%)	*P* value*
80	66.7	71.8	0.037
50	41.7	92.3	0.012
35	25	92.3	0.134

**P* value – Fisher´s Exact Test (2-sided)

***Table 5**. Comparison of facial motor evoked potential (FMEP) amplitude ratios with unsatisfactory (HB 3 – 6) postoperative outcome in the orbicularis oris muscle.*

Cut-off amplitude (%)	Sensitivity (%)	Specificity (%)	*P* value*
80	53.8	69.2	0.187
50	53.8	89.7	0.003
35	53.8	100	0.000

**P* value – Fisher´s Exact Test (2-sided)

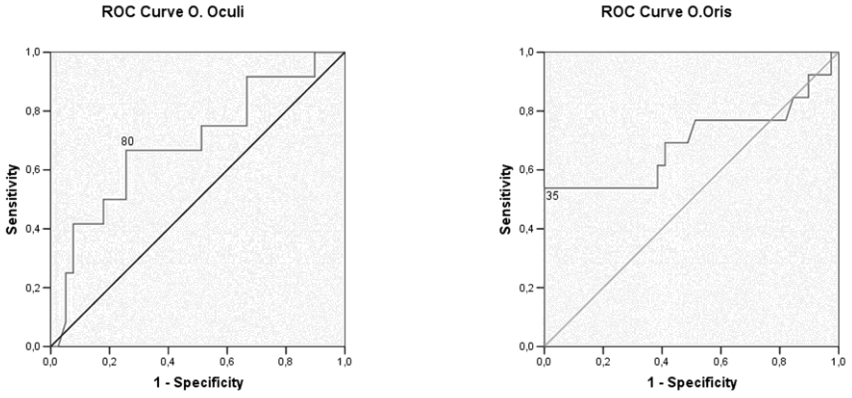

***Figure 16.** Receiver Operating Characteristic (ROC) curves for orbicularis oculi (left graph) and orbicularis oris (right graph) muscles. In a ROC curve the true positive rates (Sensitivity) are plotted in the function of the false positive rates (1 – Specificity) for different cut-off values. Accuracy is calculated by the area under the ROC curve (AUC). For the orbicularis oculi muscle (left graph), the best cut-off amplitude value was 80% (AUC = 0.689 ± 0.092 – standard error; 95% CI = 0.508 – 0.870, p = 0.049). Whereas for the orbicularis oris muscle (right graph), the best cut-off amplitude value was 35% (AUC = 0.692 ± 0.106 – standard error; 95% CI = 0.485 – 0.899, p = 0.039).*

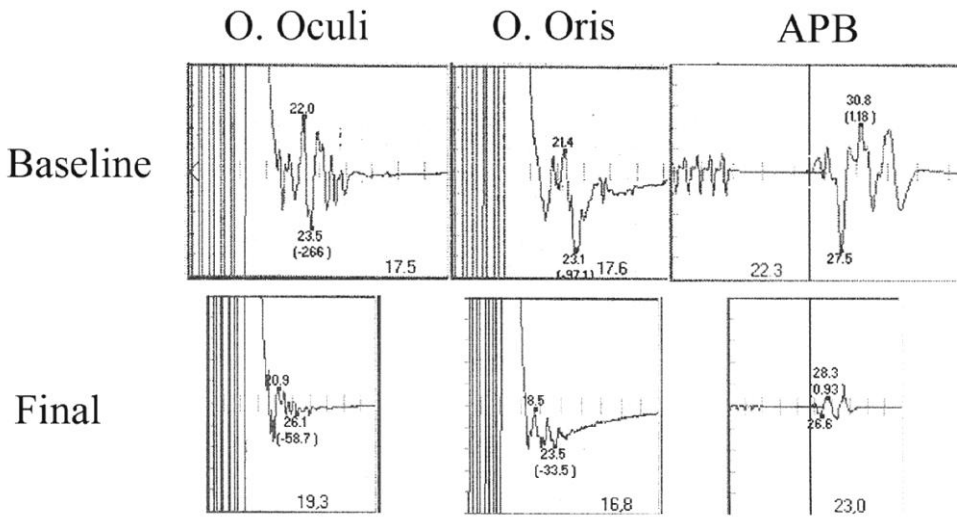

Figure 17. *Intraoperative MEP recordings in patient 14 (Table S 8) harbouring a large vestibular schwannoma (T3 – Hannover Classification) obtained before dural opening (baseline) and at the end of the surgery (final). FMEP ratios of the orbicularis oculi and oris muscles MEP showed a significant amplitude decrease after tumor removal, 22% and 34%, respectively. This patient suffered HB grade 3 facial paresis postoperatively. APB – abductor pollicis brevis muscle. The absolute amplitude values are represented in parentheses (microvolts for the orbicularis oculi and oris muscles and millivolts for APB).*

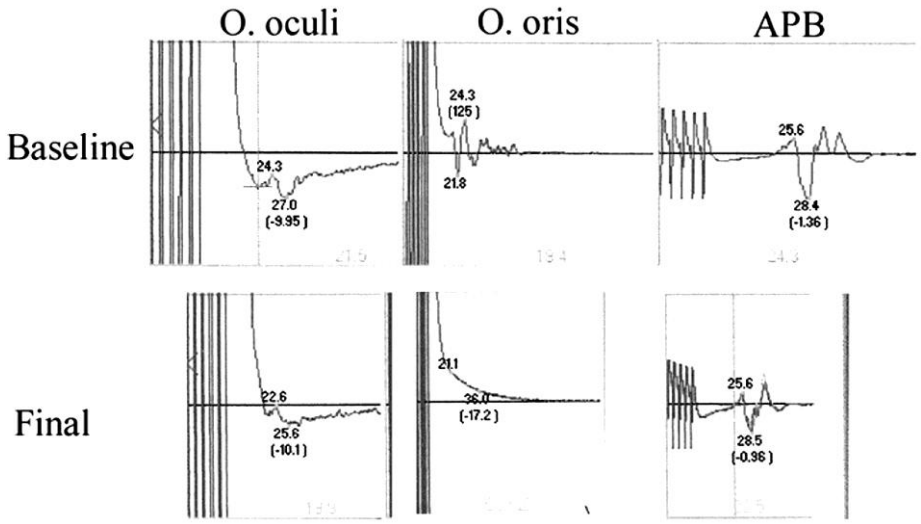

Figure 18. *Intraoperative facial and hand MEP recordings in the patient 11 (Table S 8) affected with a large vestibular schwannoma (T4a – Hannover Classification) obtained at the beginning of the surgery (baseline) and at the end of the surgery (final). Note FMEP loss of the orbicularis oris muscle. This patient developed a HB grade 4 facial paresis postoperatively. APB – abductor pollicis brevis muscle. The absolute amplitude values are represented in parentheses (microvolts for the orbicularis oculi and oris muscles and millivolts for APB).*

Discussion

1. *The Limitations of Standard Intraoperative Facial Nerve Monitoring Techniques*

Even though there is an increasing rate of FN preservation due to the introduction of routine intraoperative FN monitoring (3;145;165;172), facial weakness is still a complication of major concern in patients undergoing CPA surgery (3;172). Triggered CMAP obtained with DES can only be used intermittently and following the identification of the nerve at the brainstem. This is particularly difficult in patients harboring large tumors, in whom the adequate placement of the stimulation probe is disturbed due to the anatomical distortion of the brainstem and late identification of the proximal FN that is inaccessible during most of the surgical procedure (3;48;165;204). Thus, DES is highly dependent on the surgeons´ ability to locate correctly the exit zone of the FN on the brainstem (3). Some studies have demonstrated that proximal FN identification and the recording of the brainstem-to-distal IAC CMAP ratio cannot be performed in 30% to 35% of monitored patients owing to technical reasons, distorted anatomy or surgical approach (3;39). Intermittent use may also be cumbersome and delay the surgical procedure because whenever stimulation is performed, a temporary stoppage in dissection is necessary (225). Therefore, DES may not afford a continuous assessment of the FN function even if this method is available in all cases (39).

Free running EMG relies on neurotonic discharges in response to surgical maneuvres that can indicate injury to the FN (162;165). A major limitation is that special software is necessary for offline analysis. In other words, the train activity, which is accurate in predicting FN function, can only be evaluated quantitatively after surgery (162;165). In addition, free running EMG provides only an approximate correlation between the frequency of the neurotonic discharges and the degree of nerve injury so that neither their presence nor

their absence assures the anatomical and functional integrity of the FN at the completion of tumor resection (62). Moreover, it is also worth noting that sharp transection of the FN may not evoke neurotonic discharges, whereas mechanical stimulation of the distal nerve stump that is still in continuity with the muscle may provoke EMG activities (62;64;78;79). Both situations should be acknowledged because of their significant impact in function prediction when using free running EMG.

2. *The Historical Background and Introduction of Motor Evoked Potential to Facial Nerve Monitoring*

Concurrently to the advances in EMG monitoring, Merton and Morton (130;131) and Merton et al. (129) devised a protocol for obtaining muscle motor evoked potentials (MEP) of the upper and lower limbs through single pulse electrical stimulation of the scalp in healthy subjects. Interestingly, a slight voluntary contraction of the contralateral target muscle (between 10 and 25% of the muscle strength) somehow focuses the stimulus in a way that the motor threshold is markedly reduced, a phenomenon called facilitation (129;133). Spinal epidural recordings in humans have demonstrated that after single pulse TES two types of waves are conducted (17;34). Direct depolarization of the motor cortex results in a large and brief wave, whose latency is compatible with the conduction time of the fast corticospinal tract fibers after vertical fiber depolarization without intervening synapses. This wave is called direct (D) wave (17;34). Following the D wave, several smaller waves are easily recorded corresponding to horizontal fiber depolarization or transsynaptic activation of the motor cortex (17;34). These waves are called indirect (I) waves (17;34). After description, TES has been used in a wide variety of clinical and neurophysiological studies (133). One major problem is that it is relatively painful when used in awake subjects (17;37;108;133).

Besides TES, the human brain can also be stimulated by brief intense magnetic fields. In 1985, Barker et al. (10) described this non-invasive novel method of directly stimulating the motor cortex by using a pulsed magnetic field, in which less discomfort for the patients is produced over the electrical stimulation. The most obvious difference between electrical and magnetic stimulation of the brain is the pain perception in the scalp (17;37;108;133). In addition, TES activates the corticospinal neurons producing a direct stimulation of pyramidal outflow (D wave) followed by collateral activation (I waves), whereas magnetic stimulation activates the corticospinal tract indirectly by producing only I waves (17;108). This explains the shorter latency of MEP after electrical stimulation (17;133). For hand muscle MEP, the latency elicited by TES was 1.8 ms faster than that obtained with magnetic stimulation (133). Exception occurs, however, with the tilting of the magnetic coils that can induce the direct stimulation of the corticospinal tract and result latencies comparable to those obtained after TES (17).

Due to the limitations of SEP and the “wake-up test” for ensuring motor pathway integrity, MEP was then applied to the intraoperative monitoring of the motor function (33;75;108). Nonetheless, there was initially great difficulty in obtaining intraoperative muscle MEP because anesthetized patients are unable to facilitate MEP responses by voluntary contraction of the target muscles, as well as a depression in cortical excitability owing to the use of many anesthetic agents (25;75). Thus, further modifications of the MEP protocol were provided for recording under general anesthesia (75;202). Tanigushi et al. (202) introduced a new protocol in which the MEP responses could be obtained without averaging, thereby providing real-time monitoring. Thereafter, the method of short trains of pulses was described, in which the MEP responses were enhanced following TES in anesthetized patients (75). TES intraoperative MEP monitoring is preferred to magnetic stimulation because the later has particular disadvantages (113;115;116). Heating can be a problem if the coil is used for longer periods, especially when using the first constructed devices (17), and inaccurate positioning of the magnetic coil under the sterile drapes comprise the major disadvantages of intraoperative magnetic stimulation.

MEP has routinely been used to monitor major motor pathways intraoperatively during several neurosurgical procedures (34;39;108;115;168), especially during spinal surgeries (75;91;92;100;229;230). The presence of muscle MEP indicates the preservation of the functional integrity of the motor cortex, the corticospinal tract, the alpha motor neurons, the peripheral nerve and the neuromuscular junction (168).

FMEP obtained by TES of the contralateral face motor cortex has recently been introduced to monitor FN function and may be considered the most promising method in FN monitoring (3;39;48;168;204;220;231). The first reported use of facial MEP (FMEP) was done by Zhou and Kelly in 2001 (231) during brain tumor resections, in which only the orbicularis oris muscle was monitored. Despite the description of the first FMEP use, the predictive value of FMEP was not directly assessed in that study. The evoked responses on the facial channels were analyzed generally together with the limb MEP recordings precluding definitive conclusions about their interpretation (231). Yingling and Gardi (225) have assigned the application of FMEP monitoring as the most significant advance in the field since the advent of EMG monitoring in the late 1970s.

3. Facial Motor Evoked Potential Protocol

FMEP has emerged as an adjunctive tool to the standard intraoperative neurophysiological methods in predicting FN function postoperatively in patients undergoing skull base surgeries (3;39;48). Nonetheless, the advent of FMEP monitoring has been impaired by a low success rate in orbicularis oculi muscle monitoring and the lack of standardized protocol and parameters (Table S9).

Peripheral FN responses are of major concern accounting for most of the technical failures observed in this study. Consequently, longer latency thresholds (> 10 ms) are applied in most of the studies in the field (39;48)

because it has been previously described that the latency of peripheral FN responses with transcranial magnetic stimulation is approximately 4 to 7 ms (40;93;112;153;206;209;221;223), while following TES it ranges from 3 to 7 ms (13;39;153). Besides peripheral FN stimulation, failure in obtaining intraoperative MEP may also be demonstrated in patients affected by preoperative motor dysfunction (25;75;92;92;229-231). Nonetheless, only one of the technical failures observed in this study occurred in a patient who had a slight preoperative facial palsy (HB 2).

Artifacts are a particular problem in FMEP monitoring because of the close proximity of stimulation to the recording sites. Because of this, the artifacts are usually large and may overwrite the FMEP recordings themselves (48). However, by using the progressive protocol, the developed parameters rendered high rates of orbicularis oculi and oris muscle FMEP monitoring that are similar to those obtained with limb MEP, in other words approximately 85% (75;229;230). Interestingly, artifacts are more prone to occur from recordings in the orbicularis oculi muscle. This may be attributed to the large cortical representation of the lower face in comparison to the upper face providing better results for monitoring in the orbicularis oris muscle (48).

In the present study, the absence of contralateral FMEP response to single pulse TES, together with longer latencies, confirm that muscle responses were not extracranially generated (3). Hemispheric electrode montage over C3/C4 and CZ TES allows for the best responses to facial monitoring because of the likelihood reduction of the extracranial stimulation of the targeted contralateral facial muscles (39). Conversely, using a lateral electrode montage, there is an increasing risk that a strong TES may activate the corticospinal tract deep in the brain or even at the foramen magnum's level (168). Thus, it would be feasible to have a corticospinal tract injury above the level of stimulation masked by a misleading preservation of MEP (168). To overcome this possibility, the stimulation intensity should be kept as low as possible (168). By gradually increasing the stimulation intensity, the presented protocol tried to activate superficially the corticospinal tract by working near motor threshold level (200).

The optimal stimulation parameters for the APB and tibialis anterior muscles that provide the lowest motor thresholds are a train of 5 stimuli along with an individual pulse duration of 0.5 ms and an ISI of 4 ms (200). This ISI allows for the complete recovery of each consecutive D wave regardless of TES intensity (34;35;200). Even though APB motor thresholds are lower by using an ISI of 4 ms, there is no statistical significance in comparison to an ISI of 2 ms (200). If so, we could assume that an ISI of 2 to 4 ms is also useful in obtaining complete stimulation recovery for FMEP monitoring.

Since single pulse TES muscle MEP response is suppressed under general anaesthesia (25;168), multipulse TES is required to overcome the anaesthesia-induced suppression (58;75). It is suggested that this effect is the result of the temporal summation of stimuli at the cortical sites (58). So far the number of pulses has not been defined for FMEP monitoring being reported from as low as 1 pulse (220) to a train of 5 pulses (Table 9) (3;39;48;231). However, as we have demonstrated, 3 to 5 pulses provide the best results considering FMEP in accordance with previous studies (3;39;48;231). We believe that the pulse number should be adjusted on an individual basis, as we have presented, rather than according to the needs of the operator or according to the institutional preference (115). Besides, excessive electrical stimulation increases the risk of thermal injury to the brain and scalp (108;115) therefore a lower number of repetitions and frequency of stimulation is recommended and should be kept to the minimum required (17;73).

4. Intraoperative Facial Motor Evoked Potential Monitoring and Facial Nerve Outcome

Pathologic MEP amplitude reductions might be caused by corticospinal tract injury, root or peripheral nerve trauma, stretching, ischemia or pressure (115). Several potentially confounding factors occur during CPA surgery, namely anesthesia, stimuli failure, scalp edema, neuromuscular blockade, and

intracranial air which is of particular interest in patients undergoing surgery in the semisitting position (3;108;115;218;231). Subdural air collections might cause a significant amplitude reduction, especially in SEP monitoring, not related to neurological damage (108;115;218). But excluding the confounding factors, what amount of FMEP reduction should be considered as the warning sign of a definitive motor lesion?

MEP disappearance is the only widely accepted warning sign (115;229;230) that mostly correlates to postoperative motor deficit (3;168;229;230). MEP loss might or might not be preceded by obvious changes in amplitude (115). Given that many but not all injury mechanisms are irreversible, by using a MEP disappearance criteria as the warning sign, intraoperative monitoring more frequently identifies than avoids injury (115). In addition, the recovery of MEP following deterioration or loss without jeopardizing the motor function, which is usually observed during aortic, orthopaedic, or even spinal cord tumor surgeries (91;92;115;137), is seldom reported concerning FMEP (3). Therefore, there is a general concern that MEP loss may be too sensitive and insufficiently specific (115).

Considering the wide variability of FMEP amplitude between patients (3), partly due to alpha motor neuron excitability fluctuations (115), a final-to-baseline amplitude FMEP ratio of 50% was calculated providing excellent results to predict the postoperative FN function (3;39;48). Similar results are described for limb MEP, in which an amplitude reduction of more than 50% should be reported to the surgical team, thereby leading to changes in surgical maneuvres (91;92;137;229-231).

By using ROC curves, we have found a statistical correlation at different cut-off values for both monitored muscles. For the orbicularis oculi muscle, an 80% ratio (20% amplitude decrease) was calculated and for the orbicularis oris muscle, a 35% ratio (65% amplitude decrease) was identified for correlation with the postoperative FN motor function. Nevertheless, monitoring the orbicularis oris muscle FMEP was more consistent leading to stronger statistical results.

One could argue that an 80% FMEP amplitude criterion seems to be too high. However, mild MEP reductions (30%) were used for guidance during intramedullary spinal cord tumor resection leading to surgery stoppage, irrigation with warm saline and the wait for recovery (91;137). Irrigating the wound with warm saline is suggested to have an effect of “washing away” potassium which is basically a blocking agent that is released as a consequence of the surgical manipulation (91). If there is no recovery of the MEP responses in the following minutes, the surgeon may decide for a conservative resection or only a biopsy (91). Using this “preventive” approach, Morota et al. (137) detected MEP reductions greater than 50% in only 15.8% of the patients (all of them had postoperative paraplegia).

Also we have noted, as Dong and co-workers (39), that sensitivity increases with higher cut-off ratios and specificity increases with lower cut-off values. In addition, the 35% amplitude criterion provided sufficient sensitivity and specificity to predict FN deterioration in our series, especially for the orbicularis oris muscle, and in a previous study (39). Thus, we suggest that maintained decrements of FMEP ratio to levels between 80 and 35% during tumor removal should be used as warning signs for altering surgical strategies avoiding permanent motor injury.

Even though FN injury becomes possible following a reduction of more than 50% and more likely, but not certain, after a reduction of more than 65% amplitude (39;168), there still exist some false-positive and false-negative results (3;39;48). Since FMEP is generated by subpopulations of facial nerve axons (39), false-negative results are believed to be caused by minor injuries affecting axons not included in the FMEP that could ultimately lead to mild facial weakness without considerable FMEP changes (48).

On the other hand, gradual muscle MEP amplitude fading could be a potential factor to justify false-positive results during stable anaesthesia without scalp edema (111;115). For lower limb MEP, it is necessary to have a voltage increment of about 11V/h to maintain MEP amplitude levels of more than 50 µV in neurologically intact patients (111). It means that the longer the surgery, the

higher the chance of causing false-positive results due to the increased need of raising stimulation intensity to maintain the same amplitude levels. As an increase in stimuli does not recover pathologic MEP reductions (114), we do not believe that increments of voltage stimuli had interfered with our results. A more gradual evolution is an important differentiation of this phenomenon from a more abrupt pathologic MEP reduction (111;114;137).

Although FMEP reduction is a good predictor of postoperative facial function (3;39), the parameters used so far consider merely the initial and final FMEP amplitude values. Thus, it would be possible to have patients presenting FMEP loss or significant FMEP decrease during certain surgical maneuvres who lately recovered ultimately achieving the end of the surgery at normal FMEP amplitude ratios.

Accordingly, an event-to-baseline FMEP amplitude ratio might reach more significant results in predicting postoperative facial function. Future studies should be dedicated to find more relevant warning signs as “the point of no return” concerning facial motor functions permitting the surgical team to change surgical strategies intraoperatively in order to prevent definitive motor deficit.

Conclusions

Intraoperative neuromonitoring has been established as one of the methods in which modern neurosurgery can improve surgical results while reducing morbidity. Standard intraoperative facial nerve monitoring using both direct electrical stimulation and free running electromyography have significantly contributed to the recent improvements in the surgical results of patients undergoing surgery in the cerebellopontine angle during this century. However, facial nerve injury is still a complication of major concern due to its severe negative impact on the patient´s quality of life. Therefore, additional methods of intraoperative facial nerve monitoring are being devised and their development should be stimulated. In this regard, facial muscle evoked potential has emerged as a significant advance in intraoperative facial nerve monitoring because of the entire assessment of the facial motor pathway from the motor cortex to the neuromuscular junction.

Facial muscle evoked potential can be reliably obtained using TES with 3 to 5 train pulses rendering high rates of successful orbicularis oculi and oris muscles monitoring. Stable intraoperative facial muscle evoked potentials predict a good immediate postoperative outcome for facial nerve function. Moreover, a facial muscle evoked potential final-to-baseline ratio reduction to levels below 80% for the orbicularis oculi muscle and 35% for the orbicularis oris muscle is correlated with postoperative facial weakness. Thus, ratio decreases to levels between 80 and 35% during tumor removal should be used as warning signs for altering the surgical strategies in order to avoid definitive motor injury. Facial muscle evoked potential can be used as an adjunctive tool to standard facial nerve monitoring. However, further refinements of this technique are still necessary in order to minimize artifacts and to make this method even more reliable.

Reference List

1. Acoustic neuroma. NIH Consens Statement 9:1-24, 1991.
2. Adour KK: Mona Lisa syndrome: solving the enigma of the Gioconda smile. Ann Otol Rhinol Laryngol 98:196-199, 1989.
3. Akagami R, Dong CC, Westerberg BD: Localized transcranial electrical motor evoked potentials for monitoring cranial nerves in cranial base surgery. Neurosurgery 57:78-85, 2005.
4. Anderson DE, Leonetti J, Wind JJ, Cribari D, Fahey K: Resection of large vestibular schwannomas: facial nerve preservation in the context of surgical approach and patient-assessed outcome. J Neurosurg 102:643-649, 2005.
5. Arriaga MA, Luxford WM, Atkins JS, Jr., Kwartler JA: Predicting long-term facial nerve outcome after acoustic neuroma surgery. Otolaryngol Head Neck Surg 108:220-224, 1993.
6. Arriaga MA, Luxford WM, Berliner KI: Facial nerve function following middle fossa and translabyrinthine acoustic tumor surgery: a comparison. Am J Otol 15:620-624, 1994.
7. Ashram YA, Jackler RK, Pitts LH, Yingling CD: Intraoperative electrophysiologic identification of the nervus intermedius. Otol Neurotol 26:274-279, 2005.
8. Axon PR, Ramsden RT: Intraoperative electromyography for predicting facial function in vestibular schwannoma surgery. Laryngoscope 109:922-926, 1999.
9. Ballance C: Some Points in the Surgery of the Brain and its Membranes. 1907. London, Macmillian.
10. Barker AT, Jalinous R, Freeston IL: Non-invasive magnetic stimulation of human motor cortex. Lancet 325:1106-1107, 1985.
11. Beck DL, Atkins JS, Jr., Benecke JE, Jr., Brackmann DE: Intraoperative facial nerve monitoring: prognostic aspects during acoustic tumor removal. Otolaryngol Head Neck Surg 104:780-782, 1991.
12. Beck DL, Benecke JE, Jr.: Intraoperative facial nerve monitoring. Technical aspects. Otolaryngol Head Neck Surg 102:270-272, 1990.

13. **Begum T, Ikeda A, Matsuhashi M, Mikuni N, Miyamoto S, Hashimoto N, Nagamine T, Fukuyama H, Shibasaki H: Ipsilateral facial sensory and motor responses to basal fronto-temporal cortical stimulation: evidence suggesting direct activation of cranial nerves. Epilepsy Res 71:216-222, 2006.**

14. **Bendet E, Rosenberg SI, Willcox TO, Gordon M, Silverstein H: Intraoperative facial nerve monitoring: a comparison between electromyography and mechanical-pressure monitoring techniques. Am J Otol 20:793-799, 1999.**

15. **Benecke JE, Jr., Calder HB, Chadwick G: Facial nerve monitoring during acoustic neuroma removal. Laryngoscope 97:697-700, 1987.**

16. **Berges C, Fraysse B, Yardeni E, Rugiu G: Intraoperative facial nerve monitoring in posterior fossa surgery: prognostic value. Skull Base Surg 3:214-216, 1993.**

17. **Beric A: Transcranial electrical and magnetic stimulation. Adv Neurol 63:29-42, 1993.**

18. **Blair EA, Teeple E, Jr., Sutherland RM, Shih T, Chen D: Effect of neuromuscular blockade on facial nerve monitoring. Am J Otol 15:161-167, 1994.**

19. **Bozorg GA, Kalamarides M, Fraysse B, Deguine O, Favre G, Martin C, Mom T, Sterkers O: Comparison between intraoperative observations and electromyographic monitoring data for facial nerve outcome after vestibular schwannoma surgery. Acta Otolaryngol 125:1069-1074, 2005.**

20. **Brauer M, Knuettgen D, Quester R, Doehn M: Electromyographic facial nerve monitoring during resection for acoustic neurinoma under moderate to profound levels of peripheral neuromuscular blockade. Eur J Anaesthesiol 13:612-615, 1996.**

21. **Briggs RJ, Luxford WM, Atkins JS, Jr., Hitselberger WE: Translabyrinthine removal of large acoustic neuromas. Neurosurgery 34:785-790, 1994.**

22. **Cairns H: Acoustic Neurinoma of Right Cerebello-pontine Angle. Complete Removal. Spontaneous Recovery from Post-operative Facial Palsy. Proc R Soc Med 25:7-12, 1931.**

23. **Campbell EDR, Hickey RP, Nixon KH, Richardson AT. Value of Nerve-Excitability Measurements in Prognosis of Facial Palsy. Br J Med 2:7-10, 1962.**

24. **Campbell EDR: A simple prognostic test in facial palsy. J Laryngol 77:462-466, 1963.**

25. **Chen X, Sterio D, Ming X, Para DD, Butusova M, Tong T, Beric A: Success rate of motor evoked potentials for intraoperative neurophysiologic monitoring: effects of age, lesion location, and preoperative neurologic deficits. J Clin Neurophysiol 24:281-285, 2007.**

26. **Colletti V, Fiorino F, Policante Z, Bruni L: Intraoperative monitoring of facial nerve antidromic potentials during acoustic neuroma surgery. Acta Otolaryngol 117:663-669, 1997.**

27. **Colletti V, Fiorino FG: Advances in monitoring of seventh and eighth cranial nerve function during posterior fossa surgery. Am J Otol 19:503-512, 1998.**

28. **Colletti V, Fiorino FG, Policante Z, Bruni L: New perspectives in intraoperative facial nerve monitoring with antidromic potentials. Am J Otol 17:755-762, 1996.**

29. **Coulson SE, O'dwyer NJ, Adams RD, Croxson GR: Expression of emotion and quality of life after facial nerve paralysis. Otol Neurotol 25:1014-1019, 2004.**

30. **Cramer HB, Kartush JM: Testing facial nerve function. Otolaryngol Clin North Am 24:555-570, 1991.**

31. **Cross T, Sheard CE, Garrud P, Nikolopoulos TP, O'Donoghue GM: Impact of facial paralysis on patients with acoustic neuroma. Laryngoscope 110:1539-1542, 2000.**

32. **Dandy W: An Operation for the Total Removal of Cerebellopontine (Acoustic) Tumors. Surg Gynecol Obstet 41:129-148, 1925.**

33. **Deletis V: What does intraoperative monitoring of motor evoked potentials bring to the neurosurgeon? Acta Neurochir (Wien) 147:1015-1017, 2005.**

34. **Deletis V, Shils JL: Neurophysiology in Neurosurgery: A modern intraoperative approach. 2002. San Diego, Academic Press.**

35. **Deletis V, Isgum V, Amassian VE: Neurophysiological mechanisms underlying motor evoked potentials in anesthetized humans. Part 1. Recovery time of corticospinal tract direct waves elicited by pairs of transcranial electrical stimuli. Clin Neurophysiol 112:438-444, 2001.**

36. **Delgado TE, Bucheit WA, Rosenholtz HR, Chrissian S: Intraoperative monitoring of facila muscle evoked responses**

obtained by intracranial stimulation of the facila nerve: a more accurate technique for facial nerve dissection. Neurosurgery 4:418-421, 1979.

37. **Devinsky O: Electrical and magnetic stimulation of the central nervous system. Historical overview. Adv Neurol 63:1-16, 1993.**

38. **Dickins JR, Graham SS: A comparison of facial nerve monitoring systems in cerebellopontine angle surgery. Am J Otol 12:1-6, 1991.**

39. **Dong CC, MacDonald DB, Akagami R, Westerberg B, Alkhani A, Kanaan I, Hassounah M: Intraoperative facial motor evoked potential monitoring with transcranial electrical stimulation during skull base surgery. Clin Neurophysiol 116:588-596, 2005.**

40. **Duckert LG, Hohmann D, DeMeester C: Electrical evaluation of the facial nerve in acoustic neuroma patients: preliminary comparison between transcranial magnetic coil stimulation and electroneurography. Am J Otol 13:113-116, 1992.**

41. **Eisner W, Schmid UD, Reulen HJ, Oeckler R, Olteanu-Nerbe V, Gall C, Kothbauer K: The mapping and continuous monitoring of the intrinsic motor nuclei during brain stem surgery. Neurosurgery 37:255-265, 1995.**

42. **Esses BA, LaRouere MJ, Graham MD: Facial nerve outcome in acoustic tumor surgery. Am J Otol 15:810-812, 1994.**

43. **Fenton JE, Chin RY, Fagan PA, Sterkers O, Sterkers JM: Predictive factors of long-term facial nerve function after vestibular schwannoma surgery. Otol Neurotol 23:388-392, 2002.**

44. **Fenton JE, Chin RY, Shirazi A, Fagan PA: Prediction of postoperative facial nerve function in acoustic neuroma surgery. Clin Otolaryngol Allied Sci 24:483-486, 1999.**

45. **Filipo R, De SE, Bertoli GA: Intraoperative videomonitoring of the facial nerve. Am J Otol 21:119-122, 2000.**

46. **Filipo R, Pichi B, Bertoli GA, De SE: Video-based system for intraoperative facial nerve monitoring: comparison with electromyography. Otol Neurotol 23:594-597, 2002.**

47. **Fisch U: Prognostic value of electrical tests in acute facial paralysis. Am J Otol 5:494-498, 1984.**

48. **Fukuda M, Oishi M, Takao T, Saito A, Fujii Y: Facial nerve motor-evoked potential monitoring during skull base surgery predicts**

facial nerve outcome. J Neurol Neurosurg Psychiatry 79:1066-1070, 2008.

49. Gantz BJ: Intraoperative facial nerve monitoring. Am J Otol Suppl:58-61, 1985.

50. Gardner G, Robertson JH: Facial nerve function in cerebellopontine angle tumor surgery. Am J Otol Suppl:74-79, 1985.

51. Gianoli GJ, Kartush JM: Delayed facial palsy after acoustic neuroma resection: the role of viral reactivation. Am J Otol 17:625-629, 1996.

52. Givre A, Olivecrona H: Surgical experiences with acoustic tumors. J Neurosurg 6:396-407, 1949.

53. Goldbrunner RH, Schlake HP, Milewski C, Tonn JC, Helms J, Roosen K: Quantitative parameters of intraoperative electromyography predict facial nerve outcomes for vestibular schwannoma surgery. Neurosurgery 46:1140-1146, 2000.

54. Gormley WB, Sekhar LN, Wright DC, Kamerer D, Schessel D: Acoustic neuromas: results of current surgical management. Neurosurgery 41:50-58, 1997.

55. Grabb PA, Albright AL, Sclabassi RJ, Pollack IF: Continuous intraoperative electromyographic monitoring of cranial nerves during resection of fourth ventricular tumors in children. J Neurosurg 86:1-4, 1997.

56. Grant GA, Rostomily RR, Kim DK, Mayberg MR, Farrell D, Avellino A, Duckert LG, Gates GA, Winn HR: Delayed facial palsy after resection of vestibular schwannoma. J Neurosurg 97:93-96, 2002.

57. Grayeli AB, Guindi S, Kalamarides M, El GH, Smail M, Rey A, Sterkers O: Four-channel electromyography of the facial nerve in vestibular schwannoma surgery: sensitivity and prognostic value for short-term facial function outcome. Otol Neurotol 26:114-120, 2005.

58. Haghighi SS: Monitoring of motor evoked potentials with high intensity repetitive transcranial electrical stimulation during spinal surgery. J Clin Monit Comput 17:301-308, 2002.

59. Hammerschlag PE, Cohen NL: Intraoperative monitoring of facial nerve function in cerebellopontine angle surgery. Otolaryngol Head Neck Surg 103:681-684, 1990.

60. **Harner SG, Daube JR, Beatty CW, Ebersold MJ: Intraoperative monitoring of the facial nerve. Laryngoscope 98:209-212, 1988.**

61. **Harner SG, Daube JR, Ebersold MJ, Beatty CW: Improved preservation of facial nerve function with use of electrical monitoring during removal of acoustic neuromas. Mayo Clin Proc 62:92-102, 1987.**

62. **Harper CM, Daube JR: Facial nerve electromyography and other cranial nerve monitoring. J Clin Neurophysiol 15:206-216, 1998.**

63. **Hilger JA: Facial nerve stimulator. Trans Am Acad Ophthalmol Otolaryngol 68:74-76, 1964.**

64. **Holland NR: Intraoperative electromyography. J Clin Neurophysiol 19:444-453, 2002.**

65. **Hone SW, Commins DJ, Rames P, Chen JM, Rowed D, McLean A, Nedzelski JM: Prognostic factors in intraoperative facial nerve monitoring for acoustic neuroma. J Otolaryngol 26:374-378, 1997.**

66. **House JW, Brackmann DE: Facial nerve grading system. Otolaryngol Head Neck Surg 93:146-147, 1985.**

67. **Hughes GB, Bottomy MB, Dickins JR, Jackson CG, Sismanis A, Glasscock ME, III: A comparative study of neuropathologic changes following pulsed and direct current stimulation of the mouse sciatic nerve. Am J Otolaryngol 1:378-384, 1980.**

68. **Hughes GB, Bottomy MB, Jackson CG, Glasscock ME, III, Sismanis A: Myelin and axon degeneration following direct current peripheral nerve stimulation: a prospective controlled experimental study. Otolaryngol Head Neck Surg 89:767-775, 1981.**

69. **Isaacson B, Kileny PR, El-Kashlan H, Gadre AK: Intraoperative monitoring and facial nerve outcomes after vestibular schwannoma resection. Otol Neurotol 24:812-817, 2003.**

70. **Isaacson B, Kileny PR, El-Kashlan HK: Prediction of long-term facial nerve outcomes with intraoperative nerve monitoring. Otol Neurotol 26:270-273, 2005.**

71. **Jacob A, Robinson LL, Jr., Bortman JS, Yu L, Dodson EE, Welling DB: Nerve of origin, tumor size, hearing preservation, and facial nerve outcomes in 359 vestibular schwannoma resections at a tertiary care academic center. Laryngoscope 117:2087-2092, 2007.**

72. **Jako GJ: Trans Am Acad Ophthalmol Otolaryngol 69:340-342, 1965.**

73. **Jayakar P: Physiological principles of electrical stimulation. Adv Neurol 63:17-27, 1993.**

74. **Jellinek DA, Tan LC, Symon L: The impact of continuous electrophysiological monitoring on preservation of the facial nerve during acoustic tumour surgery. Br J Neurosurg 5:19-24, 1991.**

75. **Jones SJ, Harrison R, Koh KF, Mendoza N, Crockard HA: Motor evoked potential monitoring during spinal surgery: responses of distal limb muscles to transcranial cortical stimulation with pulse trains. Electroencephalogr Clin Neurophysiol 100:375-383, 1996.**

76. **Jongkees LB: [Notes on the history of facial nerve surgery]. HNO 27:325-333, 1979.**

77. **Kartush JM: Intra-operative monitoring in acoustic neuroma surgery. Neurol Res 20:593-596, 1998.**

78. **Kartush JM: Electroneurography and intraoperative facial monitoring in contemporary neurotology. Otolaryngol Head Neck Surg 101:496-503, 1989.**

79. **Kartush JM, Bouchard KL: Intraoperative facial nerve monitoring. In: Kartush JM, Bouchard KL: Neuromonitoring in Otology and Head and Neck Surgery, pp. 99-100, 1992. New York, Raven Press.**

80. **Kartush JM, LaRouere MJ, Graham MD, Bouchard KR, Audet BV: Intraoperative cranial nerve monitoring during posterior skull base surgery. Skull Base Surg 1:85-92, 1991.**

81. **Kartush JM, Lundy LB: Facial nerve outcome in acoustic neuroma surgery. Otolaryngol Clin North Am 25:623-647, 1992.**

82. **Kartush JM, Niparko JK, Bledsoe SC, Graham MD, Kemink JL: Intraoperative facial nerve monitoring: a comparison of stimulating electrodes. Laryngoscope 95:1536-1540, 1985.**

83. **Kataye S: [Facial paralysis as described by Avicenna]. Ann Otolaryngol Chir Cervicofac 92:79-82, 1975.**

84. **Kawaguchi M, Ohnishi H, Sakamoto T, Shimizu K, Touho H, Monobe T, Karasawa J: Intraoperative electrophysiologic monitoring of cranial motor nerves in skull base surgery. Surg Neurol 43:177-181, 1995.**

85. **Kaylie DM, Gilbert E, Horgan MA, Delashaw JB, McMenomey SO: Acoustic neuroma surgery outcomes. Otol Neurotol 22:686-689, 2001.**

86. **Kinney SE, Prass R: Facial nerve dissection by use of acoustic (loudspeaker) facial EMG monitoring. Otolaryngol Head Neck Surg 95:458-463, 1986.**

87. **Kirkpatrick PJ, Tierney P, Gleeson MJ, Strong AJ: Acoustic tumour volume and the prediction of facial nerve functional outcome from intraoperative monitoring. Br J Neurosurg 7:657-664, 1993.**

88. **Kirkpatrick PJ, Watters G, Strong AJ, Walliker JR, Gleeson MJ: Prediction of facial nerve function after surgery for cerebellopontine angle tumors: use of a facial nerve stimulator and monitor. Skull Base Surg 1:171-176, 1991.**

89. **Koerbel A, Gharabaghi A, Safavi-Abbasi S, Tatagiba M, Samii M: Evolution of vestibular schwannoma surgery: the long journey to current success. Neurosurg Focus 18:e10, 2005.**

90. **Kombos T, Suess O, Kern BC, Funk T, Pietila T, Brock M: Can continuous intraoperative facial electromyography predict facial nerve function following cerebellopontine angle surgery? Neurol Med Chir (Tokyo) 40:501-505, 2000.**

91. **Kothbauer K, Deletis V, Epstein FJ: Intraoperative spinal cord monitoring for intramedullary surgery: an essential adjunct. Pediatr Neurosurg 26:247-254, 1997.**

92. **Kothbauer KF, Deletis V, Epstein FJ: Intraoperative monitoring. Pediatr Neurosurg 29:54-55, 1998.**

93. **Kotterba S, Tegenthoff M, Malin JP: Perioperative lesions of the facial nerve: follow-up investigations using transcranial magnetic stimulation. Eur Arch Otorhinolaryngol 254:140-144, 1997.**

94. **Krause F: Surgery of the Brain and Spinal Cord. vol 2, pp. 737-743, 1912. New York, Rebman Co.**

95. **Krause F: Zur Freilegung der hinteren Felsenbeinfläche und des Kleinhirns. Beitr Klein Chir 37:728-764, 1903.**

96. **Kwartler JA, Luxford WM, Atkins J, Shelton C: Facial nerve monitoring in acoustic tumor surgery. Otolaryngol Head Neck Surg 104:814-817, 1991.**

97. **Lacombe H, Keravel Y, Peynegre R, Eshraghi A: [Value of the monitoring of the facial nerve in the evaluation of facial function in translabyrinthine surgery for acoustic neuroma]. Ann Otolaryngol Chir Cervicofac 111:89-93, 1994.**

98. **Lalwani AK, Butt FY, Jackler RK, Pitts LH, Yingling CD: Facial nerve outcome after acoustic neuroma surgery: a study from the era of cranial nerve monitoring. Otolaryngol Head Neck Surg 111:561-570, 1994.**

99. **Lalwani AK, Butt FY, Jackler RK, Pitts LH, Yingling CD: Delayed onset facial nerve dysfunction following acoustic neuroma surgery. Am J Otol 16:758-764, 1995.**

100. **Lang EW, Chesnut RM, Beutler AS, Kennelly NA, Renaudin JW: The utility of motor-evoked potential monitoring during intramedullary surgery. Anesth Analg 83:1337-1341, 1996.**

101. **Lang J: Anatomy of the brainstem and the lower cranial nerves, vessels, and surrounding structures. Am J Otol Suppl:1-19, 1985.**

102. **Lanman TH, Brackmann DE, Hitselberger WE, Subin B: Report of 190 consecutive cases of large acoustic tumors (vestibular schwannoma) removed via the translabyrinthine approach. J Neurosurg 90:617-623, 1999.**

103. **Lenarz T, Ernst A: Intraoperative facial nerve monitoring in the surgery of cerebellopontine angle tumors: improved preservation of nerve function. ORL J Otorhinolaryngol Relat Spec 56:31-35, 1994.**

104. **Lenarz T, Sachsenheimer W: Prognostic factors for postsurgical hearing and facial nerve function in cases of cerebellopontine angle-tumours. The meaning of brain stem evoked response audiometry (BERA). Acta Neurochir (Wien) 78:21-27, 1985.**

105. **Lennon RL, Hosking MP, Daube JR, Welna JO: Effect of partial neuromuscular blockade on intraoperative electromyography in patients undergoing resection of acoustic neuromas. Anesth Analg 75:729-733, 1992.**

106. **Leonetti JP, Brackmann DE, Prass RL: Improved preservation of facial nerve function in the infratemporal approach to the skull base. Otolaryngol Head Neck Surg 101:74-78, 1989.**

107. **Leonetti JP, Matz GJ, Smith PG, Beck DL: Facial nerve monitoring in otologic surgery: clinical indications and intraoperative technique. Ann Otol Rhinol Laryngol 99:911-918, 1990.**

108. **Levy WJ, Jr.: Clinical experience with motor and cerebellar evoked potential monitoring. Neurosurgery 20:169-182, 1987.**

109. **Lin VY, Houlden D, Bethune A, Nolan M, Pirouzmand F, Rowed D, Nedzelski JM, Chen JM: A novel method in predicting immediate**

postoperative facial nerve function post acoustic neuroma excision. Otol Neurotol 27:1017-1022, 2006.

110. Linden RD, Tator CH, Benedict C, Charles D, Mraz V, Bell I: Electrophysiological monitoring during acoustic neuroma and other posterior fossa surgery. Can J Neurol Sci 15:73-81, 1988.

111. Lyon R, Feiner J, Lieberman JA: Progressive suppression of motor evoked potentials during general anesthesia: the phenomenon of "anesthetic fade". J Neurosurg Anesthesiol 17:13-19, 2005.

112. Maccabee PJ, Amassian VE, Cracco RQ, Cracco JB, Anziska BJ: Intracranial stimulation of facial nerve in humans with the magnetic coil. Electroencephalogr Clin Neurophysiol 70:350-354, 1988.

113. MacDonald DB: Safety of intraoperative transcranial electrical stimulation motor evoked potential monitoring. J Clin Neurophysiol 19:416-429, 2002.

114. MacDonald DB: Intraoperative facial motor evoked potentials? J Neurosurg 106:517-518, 2007.

115. MacDonald DB: Intraoperative motor evoked potential monitoring: overview and update. J Clin Monit Comput 20:347-377, 2006.

116. MacDonald DB, Janusz M: An approach to intraoperative neurophysiologic monitoring of thoracoabdominal aneurysm surgery. J Clin Neurophysiol 19:43-54, 2002.

117. Magliulo G, Petti R, Vingolo GM, Cristofari P, Ronzoni R: Facial nerve monitoring in skull base surgery. J Laryngol Otol 108:557-559, 1994.

118. Magliulo G, Petti R, Vingolo GM, Ronzoni R, Cristofari P: Facial nerve monitoring of skull base and cerebellopontine angle lesions. Eur Arch Otorhinolaryngol Suppl:S314-S315, 1994.

119. Magliulo G, Zardo F: Facial nerve function after cerebellopontine angle surgery and prognostic value of intraoperative facial nerve monitoring: a critical evaluation. Am J Otolaryngol 19:102-106, 1998.

120. Magliulo G, Zardo F: Intra-operative facial nerve monitoring. Its predictive value after skull base surgery. J Laryngol Otol 111:715-718, 1997.

121. Mandpe AH, Mikulec A, Jackler RK, Pitts LH, Yingling CD: Comparison of response amplitude versus stimulation threshold

in predicting early postoperative facial nerve function after acoustic neuroma resection. Am J Otol 19:112-117, 1998.

122. Matthies C, Samii M: Management of vestibular schwannomas (acoustic neuromas): the value of neurophysiology for evaluation and prediction of auditory function in 420 cases. Neurosurgery 40:919-929, 1997.

123. Matthies C, Samii M: Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. Neurosurgery 40:1-9, 1997.

124. Matthies C, Samii M, Krebs S: Management of vestibular schwannomas (acoustic neuromas): radiological features in 202 cases--their value for diagnosis and their predictive importance. Neurosurgery 40:469-481, 1997.

125. Maurer J, Pelster H, Amedee RG, Mann WJ: Intraoperative monitoring of motor cranial nerves in skull base surgery. Skull Base Surg 5:169-175, 1995.

126. Maurer J, Pelster H, Mann W: [Intraoperative monitoring of motor cranial nerves in operations of the neck and cranial base]. Laryngorhinootologie 73:561-567, 1994.

127. Megerian CA, McKenna MJ, Ojemann RG: Delayed facial paralysis after acoustic neuroma surgery: factors influencing recovery. Am J Otol 17:630-633, 1996.

128. Menovsky T, van Overbeeke JJ: On the mechanism of transient postoperative deficit of cranial nerves. Surg Neurol 51:223-226, 1999.

129. Merton PA, Hill DK, Morton HB, Marsden CD: Scope of a technique for electrical stimulation of human brain, spinal cord, and muscle. Lancet 320:597-600, 1982.

130. Merton PA, Morton HB. Electrical Stimulation of Human Motor and Visual Cortex through the Scalp. J Physiol 305:9-10. 1980.

131. Merton PA, Morton HB: Stimulation of the cerebral cortex in the intact human subject. Nature 285:227, 1980.

132. Metson R, Thornton A, Nadol JB, Jr., Fee WE, Jr.: A new design for intraoperative facial nerve monitoring. Otolaryngol Head Neck Surg 98:258-261, 1988.

133. Mills KR, Murray NM, Hess CW: Magnetic and electrical transcranial brain stimulation: physiological mechanisms and clinical applications. Neurosurgery 20:164-168, 1987.

134. **Moller AR, Jannetta PJ: Preservation of facial function during removal of acoustic neuromas. Use of monopolar constant-voltage stimulation and EMG. J Neurosurg 61:757-760, 1984.**

135. **Moller AR, Jannetta PJ: Monitoring of facial nerve function during removal of acoustic tumor. Am J Otol Suppl:27-29, 1985.**

136. **Morikawa M, Tamaki N, Nagashima T, Motooka Y: Long-term results of facial nerve function after acoustic neuroma surgery--clinical benefit of intraoperative facial nerve monitoring. Kobe J Med Sci 46:113-124, 2000.**

137. **Morota N, Deletis V, Constantini S, Kofler M, Cohen H, Epstein FJ: The role of motor evoked potentials during surgery for intramedullary spinal cord tumors. Neurosurgery 41:1327-1336, 1997.**

138. **Moskowitz N, Long DM: Acoustic Neuromas. Historical Review of a Century of Operative Series. Neurosurg Q 1:2-18, 1991.**

139. **Mourier KL, Raggueneau JL, George B, Boissonnet H, Hodes JE, Cophignon J: Intra-operative monitoring of the facial nerve with an air inflated balloon. Technical note. Acta Neurochir (Wien) 117:63-65, 1992.**

140. **Murphy EK: Use of an infrared camera to improve the outcome of facial nerve monitoring. Am J Electroneurodiagnostic Technol 48:38-47, 2008.**

141. **Nabhan A, Ahlhelm F, Reith W, Steudel WI, Schwerdtfeger K: [Function of the facial nerve after operative treatment of acoustic neurinomas. Influence of intraoperative monitoring]. Nervenarzt 76:170-174, 2005.**

142. **Nakamura M, Roser F, Dormiani M, Matthies C, Vorkapic P, Samii M: Facial and cochlear nerve function after surgery of cerebellopontine angle meningiomas. Neurosurgery 57:77-90, 2005.**

143. **Nakao Y, Piccirillo E, Falcioni M, Taibah A, Kobayashi T, Sanna M: Electromyographic evaluation of facial nerve damage in acoustic neuroma surgery. Otol Neurotol 22:554-557, 2001.**

144. **Nakao Y, Piccirillo E, Falcioni M, Taibah A, Russo A, Kobayashi T, Sanna M: Prediction of facial nerve outcome using electromyographic responses in acoustic neuroma surgery. Otol Neurotol 23:93-95, 2002.**

145. **Neff BA, Ting J, Dickinson SL, Welling DB: Facial nerve monitoring parameters as a predictor of postoperative facial nerve**

outcomes after vestibular schwannoma resection. Otol Neurotol 26:728-732, 2005.

146. Nelson KR, Phillips LH: Neurophysiologic monitoring during surgery of peripheral and cranial nerves, and in selective dorsal rhizotomy. Semin Neurol 10:141-149, 1990.

147. Niparko JK, Kileny PR, Kemink JL, Lee HM, Graham MD: Neurophysiologic intraoperative monitoring: II. Facial nerve function. Am J Otol 10:55-61, 1989.

148. Nissen AJ, Sikand A, Curto FS, Welsh JE, Gardi J: Value of intraoperative threshold stimulus in predicting postoperative facial nerve function after acoustic tumor resection. Am J Otol 18:249-251, 1997.

149. Nissen AJ, Sikand A, Welsh JE, Curto FS, Gardi J: A multifactorial analysis of facial nerve results in surgery for cerebellopontine angle tumors. Ear Nose Throat J 76:37-40, 1997.

150. Normand MM, Daube JR: Cranial nerve conduction and needle electromyography in patients with acoustic neuromas: a model of compression neuropathy. Muscle Nerve 17:1401-1406, 1994.

151. Noss RS, Lalwani AK, Yingling CD: Facial nerve monitoring in middle ear and mastoid surgery. Laryngoscope 111:831-836, 2001.

152. Ohata K, Nunta-aree S, Morino M, Tsuyuguchi N, Haque M, Inoue Y, Ogura H, Hakuba A: Aetiology of delayed facial palsy after vestibular schwannoma surgery: clinical data and hypothesis. Acta Neurochir (Wien) 140:913-917, 1998.

153. Ohira T, Shiobara R, Kanzaki J, Toya S: Identification of the exact stimulated site in transcranial magnetic stimulation of the facial nerve. Eur Arch Otorhinolaryngol Suppl:S243-S246, 1994.

154. Parsons RC: Electrical Stimulation of the Facial Nerve. Laryngoscope 76:391-406, 1966.

155. Penzholz H: Development and present state of cerebellopontine angle surgery from the neuro- and otosurgical point of view. Arch Otorhinolaryngol 240:167-174, 1984.

156. Prasad S, Hirsch BE, Kamerer DB, Durrant J, Sekhar LN: Facial nerve function following cerebellopontine angle surgery: prognostic value of electroneurography. Am J Otol 14:326-329, 1993.

157. Prasad S, Hirsch BE, Kamerer DB, Durrant J, Sekhar LN: Facial nerve function following cerebellopontine angle surgery:

prognostic value of intraoperative thresholds. Am J Otol 14:330-333, 1993.

158. Prass R, Luders H: Constant-current versus constant-voltage stimulation. J Neurosurg 62:622-623, 1985.

159. Prass RL, Kinney SE, Hardy RW, Jr., Hahn JF, Luders H: Acoustic (loudspeaker) facial EMG monitoring: II. Use of evoked EMG activity during acoustic neuroma resection. Otolaryngol Head Neck Surg 97:541-551, 1987.

160. Prass RL, Luders H: Acoustic (loudspeaker) facial electromyographic monitoring: Part 1. Evoked electromyographic activity during acoustic neuroma resection. Neurosurgery 19:392-400, 1986.

161. Prell J, Rampp S, Rachinger J, Scheller C, Naraghi R, Strauss C: Spontaneous electromyographic activity during microvascular decompression in trigeminal neuralgia. J Clin Neurophysiol 25:225-232, 2008.

162. Prell J, Rampp S, Romstock J, Fahlbusch R, Strauss C: Train time as a quantitative electromyographic parameter for facial nerve function in patients undergoing surgery for vestibular schwannoma. J Neurosurg 106:826-832, 2007.

163. Resende LA, Weber S: Peripheral facial palsy in the past: contributions from Avicenna, Nicolaus Friedreich and Charles Bell. Arq Neuropsiquiatr 66:765-769, 2008.

164. Richmond IL, Mahla M: Use of antidromic recording to monitor facial nerve function intraoperatively. Neurosurgery 16:458-462, 1985.

165. Romstock J, Strauss C, Fahlbusch R: Continuous electromyography monitoring of motor cranial nerves during cerebellopontine angle surgery. J Neurosurg 93:586-593, 2000.

166. Rosler KM, Jenni WK, Schmid UD, Hess CW: Electrophysiological characterization of pre- and postoperative facial nerve function in patients with acoustic neuroma using electrical and magnetic stimulation techniques. Muscle Nerve 17:183-191, 1994.

167. Safavi-Abbasi S, Di RF, Bambakidis N, Talley MC, Gharabaghi A, Luedemann W, Samii M, Samii A: Has management of epidermoid tumors of the cerebellopontine angle improved? A surgical synopsis of the past and present. Skull Base 18:85-98, 2008.

168. Sala F, Manganotti P, Tramontano V, Bricolo A, Gerosa M: Monitoring of motor pathways during brain stem surgery: what we

have achieved and what we still miss? Neurophysiol Clin 37:399-406, 2007.

169. Samii M, Gerganov V, Samii A: Improved preservation of hearing and facial nerve function in vestibular schwannoma surgery via the retrosigmoid approach in a series of 200 patients. J Neurosurg 105:527-535, 2006.

170. Samii M, Matthies C: Management of 1000 vestibular schwannomas (acoustic neuromas): surgical management and results with an emphasis on complications and how to avoid them. Neurosurgery 40:11-21, 1997.

171. Samii M, Matthies C: Management of 1000 vestibular schwannomas (acoustic neuromas): hearing function in 1000 tumor resections. Neurosurgery 40:248-260, 1997.

172. Samii M, Matthies C: Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve--preservation and restitution of function. Neurosurgery 40:684-694, 1997.

173. Samii M, Migliori MM, Tatagiba M, Babu R: Surgical treatment of trigeminal schwannomas. J Neurosurg 82:711-718, 1995.

174. Samii M, Tatagiba M, Piquer J, Carvalho GA: Surgical treatment of epidermoid cysts of the cerebellopontine angle. J Neurosurg 84:14-19, 1996.

175. Sampath P, Holliday MJ, Brem H, Niparko JK, Long DM: Facial nerve injury in acoustic neuroma (vestibular schwannoma) surgery: etiology and prevention. J Neurosurg 87:60-66, 1997.

176. Sampath P, Long DM: Acoustic Neuroma. In: Winn HR: Youmans Neurological Surgery. pp.1147-1168, 2004. Philadelphia, Saunders.

177. Sampath P, Rini D, Long DM: Microanatomical variations in the cerebellopontine angle associated with vestibular schwannomas (acoustic neuromas): a retrospective study of 1006 consecutive cases. J Neurosurg 92:70-78, 2000.

178. Sargent EW, Beck DL: Facial nerve monitoring. Laryngoscope 105:1017-1018, 1995.

179. Sargent EW, Kartush JM, Graham MD: Meatal facial nerve decompression in acoustic neuroma resection. Am J Otol 16:457-464, 1995.

180. Scheller C, Strauss C, Fahlbusch R, Romstock J: Delayed facial nerve paresis following acoustic neuroma resection and

postoperative vasoactive treatment. Zentralbl Neurochir 65:103-107, 2004.

181. Schmid UD, Sturzenegger M, Ludin HP, Seiler RW, Reulen HJ: Orthodromic (intra/extracranial) neurography to monitor facial nerve function intraoperatively. Neurosurgery 22:945-950, 1988.

182. Sclabassi RJ, Kalia KK, Sekhar L, Jannetta PJ: Assessing brain stem function. Neurosurg Clin N Am 4:415-431, 1993.

183. Sekhar LN, Swamy NK, Jaiswal V, Rubinstein E, Hirsch WE, Jr., Wright DC: Surgical excision of meningiomas involving the clivus: preoperative and intraoperative features as predictors of postoperative functional deterioration. J Neurosurg 81:860-868, 1994.

184. Selesnick SH, Carew JF, Victor JD, Heise CW, Levine J: Predictive value of facial nerve electrophysiologic stimulation thresholds in cerebellopontine-angle surgery. Laryngoscope 106:633-638, 1996.

185. Shamji MF, Schramm DR, Benoit BG: Clinical predictors of facial nerve outcome after translabyrinthine resection of acoustic neuromas. Clin Invest Med 30:E233-E239, 2007.

186. Shaw JP: A history of the enumeration of the cranial nerves by European and British anatomists from the time of Galen to 1895, with comments on nomenclature. Clin Anat 5:466-484, 1992.

187. Silverstein H: Microsurgical instruments and nerve stimulator--monitor for retrolabyrinthine vestibular neurectomy. Otolaryngol Head Neck Surg 94:409-411, 1986.

188. Silverstein H, Rosenberg S: Intraoperative facial nerve monitoring. Otolaryngol Clin North Am 24:709-725, 1991.

189. Silverstein H, Rosenberg SI, Flanzer J, Seidman MD: Intraoperative facial nerve monitoring in acoustic neuroma surgery. Am J Otol 14:524-532, 1993.

190. Silverstein H, Smouha E, Jones R: Routine identification of the facial nerve using electrical stimulation during otological and neurotological surgery. Laryngoscope 98:726-730, 1988.

191. Silverstein H, Smouha EE, Jones R: Routine intraoperative facial nerve monitoring during otologic surgery. Am J Otol 9:269-275, 1988.

192. Silverstein H, Willcox TO Jr, Rosenberg SI, Seidman MD: Prediction of facial nerve function following acoustic neuroma

resection using intraoperative facial nerve stimulation. Laryngoscope 104:539-544, 1994.

193. Sluyter S, Graamans K, Tulleken CA, Van Veelen CW: Analysis of the results obtained in 120 patients with large acoustic neuromas surgically treated via the translabyrinthine-transtentorial approach. J Neurosurg 94:61-66, 2001.

194. Sobottka SB, Schackert G, May SA, Wiegleb M, Reiss G: Intraoperative facial nerve monitoring (IFNM) predicts facial nerve outcome after resection of vestibular schwannoma. Acta Neurochir (Wien) 140:235-242, 1998.

195. Sterkers JM, Morrison GA, Sterkers O, El-Dine MM: Preservation of facial, cochlear, and other nerve functions in acoustic neuroma treatment. Otolaryngol Head Neck Surg 110:146-155, 1994.

196. Sterkers O, Rey A, Kalamarides M, Matheron R, Bouccara D: [Trans-petrous surgery in acoustic neuroma. Value of preoperative audiovestibular and facial investigation in the risk evaluation of facial nerve function]. Ann Otolaryngol Chir Cervicofac 114:176-183, 1997.

197. Strauss C: The facial nerve in medial acoustic neuromas. J Neurosurg 97:1083-1090, 2002.

198. Strauss C, Prell J, Rampp S, Romstock J: Split facial nerve course in vestibular schwannomas. J Neurosurg 105:698-705, 2006.

199. Sugita K, Kobayashi S: Technical and instrumental improvements in the surgical treatment of acoustic neurinomas. J Neurosurg 57:747-752, 1982.

200. Szelenyi A, Kothbauer KF, Deletis V: Transcranial electric stimulation for intraoperative motor evoked potential monitoring: Stimulation parameters and electrode montages. Clin Neurophysiol 118:1586-1595, 2007.

201. Taha JM, Tew JM, Jr., Keith RW: Proximal-to-distal facial amplitude ratios as predictors of facial nerve function after acoustic neuroma excision. J Neurosurg 83:994-998, 1995.

202. Taniguchi M, Cedzich C, Schramm J: Modification of cortical stimulation for motor evoked potentials under general anesthesia: technical description. Neurosurgery 32:219-226, 1993.

203. Tatagiba M, Acioly MA: Retrosigmoid Approach to the Posterior and Middle Fossa. In: Ramina R, Pires Aguiar PH, Tatagiba M: Samii´s Essentials in Neurosurgery. pp.137-154, 2008. Stuttgart, Springer.

204. Tatagiba M, Acioly MA: Vestibular Schwannoma: current state of the art. In: Ramina R, Pires Aguiar PH, Tatagiba M: Samii´s Essentials in Neurosurgery. pp.175-188, 2008. Stuttgart, Springer.

205. Thomsen J, Zander OP, Tos M: Pre- and postoperative facial nerve testing in patients with acoustic neuromas. Acta Otolaryngol 99:239-244, 1985.

206. Tokimura H, Yamagami M, Tokimura Y, Asakura T, Atsuchi M: Transcranial magnetic stimulation excites the root exit zone of the facial nerve. Neurosurgery 32:414-416, 1993.

207. Torrens M, Maw R, Coakham H, Butler S, Morgan H: Facial and acoustic nerve preservation during excision of extracanalicular acoustic neuromas using the suboccipital approach. Br J Neurosurg 8:655-665, 1994.

208. Tos M, Youssef M, Thomsen J, Turgut S: Causes of facial nerve paresis after translabyrinthine surgery for acoustic neuroma. Ann Otol Rhinol Laryngol 101:821-826, 1992.

209. Triggs WJ, Ghacibeh G, Springer U, Bowers D: Lateralized asymmetry of facial motor evoked potentials. Neurology 65:541-544, 2005.

210. Uziel A, Benezech J, Frerebeau P: Intraoperative facial nerve monitoring in posterior fossa acoustic neuroma surgery. Otolaryngol Head Neck Surg 108:126-134, 1993.

211. Uziel A, Benezech J, Frerebeau P, Irolla E, Vidal D: [Peroperative monitoring of the facial nerve in surgery for acoustic neuroma]. Ann Otolaryngol Chir Cervicofac 108:438-445, 1991.

212. Wedekind C, Hildebrandt G, Klug N: A case of delayed loss of facial nerve function after acoustic neuroma surgery. Zentralbl Neurochir 57:163-166, 1996.

213. Wedekind C, Klug N: Nasal muscle F-wave for peri- and intraoperative diagnosis of facial nerve function. Electromyogr Clin Neurophysiol 38:481-490, 1998.

214. Wedekind C, Klug N: Assessment of facial nerve function in acoustic tumor disease by nasal muscle F waves and transcranial magnetic stimulation. Muscle Nerve 23:58-62, 2000.

215. Wedekind C, Klug N: Recording nasal muscle F waves and electromyographic activity of the facial muscles: a comparison of two methods used for intraoperative monitoring of facial nerve function. J Neurosurg 95:974-978, 2001.

216. Wedekind C, Klug N: Facial F wave recording: a novel and effective technique for extra- and intraoperative diagnosis of facial nerve function in acoustic tumor disease. Otolaryngol Head Neck Surg 129:114-120, 2003.

217. Wedekind C, Klug N: F-wave recordings from nasal muscle for intraoperative monitoring of facial nerve function. Zentralbl Neurochir 57:184-189, 1996.

218. Wiedemayer H, Schaefer H, Armbruster W, Miller M, Stolke D: Observations on intraoperative somatosensory evoked potential (SEP) monitoring in the semi-sitting position. Clin Neurophysiol 113:1993-1997, 2002.

219. Wiet RJ, Bauer GP, Stewart D, Zappia JJ: Intraoperative facial nerve monitoring: a description of a unique system. J Laryngol Otol 108:551-556, 1994.

220. Wilkinson MF, Kaufmann AM: Monitoring of facial muscle motor evoked potentials during microvascular decompression for hemifacial spasm: evidence of changes in motor neuron excitability. J Neurosurg 103:64-69, 2005.

221. Wolf SR, Goertzen W, Schneider W: [Transcranial magnetic stimulation of the facial nerve in patients with acoustic neuroma]. HNO 39:482-485, 1991.

222. Wolf SR, Schneider W, Hofmann M, Haid CT, Wigand ME: [Intraoperative monitoring of the facial nerve in transtemporal surgery of acoustic neurinoma]. HNO 41:179-184, 1993.

223. Wolf SR, Strauss C, Schneider W: On the site of transcranial magnetic stimulation of the facial nerve: electrophysiological observations in two patients after transection of the facial nerve during neuroma removal. Neurosurgery 36:346-349, 1995.

224. Yingling CD, Gardi JN: Intraoperative monitoring of facial and cochlear nerves during acoustic neuroma surgery. Otolaryngol Clin North Am 25:413-448, 1992.

225. Yingling CD, Gardi JN: Intraoperative monitoring of facial and cochlear nerves during acoustic neuroma surgery. 1992. Neurosurg Clin N Am 19:289-315, vii, 2008.

226. Yokoyama T, Uemura K, Ryu H: Facial nerve monitoring by monopolar low constant current stimulation during acoustic neurinoma surgery. Surg Neurol 36:12-18, 1991.

227. Yokoyama T, Uemura K, Ryu H, Sugiyama K, Nishizawa S, Shimoyama I, Nozue M: Intraoperative facial nerve monitoring by

monopolar low constant current stimulation and postoperative facial function in acoustic tumor surgery. Eur Arch OtorhinolaryngolS316-S318, 1994.

228. Zeitouni AG, Hammerschlag PE, Cohen NL: Prognostic significance of intraoperative facial nerve stimulus thresholds. Am J Otol 18:494-497, 1997.

229. Zentner J: Motor evoked potential monitoring during neurosurgical operations on the spinal cord. Neurosurg Rev 14:29-36, 1991.

230. Zentner J: Noninvasive motor evoked potential monitoring during neurosurgical operations on the spinal cord. Neurosurgery 24:709-712, 1989.

231. Zhou HH, Kelly PJ: Transcranial electrical motor evoked potential monitoring for brain tumor resection. Neurosurgery 48:1075-1080, 2001.

232. Zini C, Gandolfi A: Facial-nerve and vocal-cord monitoring during otoneurosurgical operations. Arch Otolaryngol Head Neck Surg 113:1291-1293, 1987.

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
Delgado et al. 1979(36)	Retro	14	VS	50	CV	Mono	1, frontalis	IAC, REZ	Absolute CMAP amplitude at both sites (0 to 30 V)	Similar amplitude confirmed gross integrity of FN; Decreased amplitude between IAC and REZ in two cases that had mild and severe facial palsy
Harner et al. 1987(61)	Retro	48	VS	50	CV	Bipo	1, two to four (oculi, oris, mentalis, masseter, or temporalis); 1, surface	IAC, REZ	Relative CMAP amplitudes on both sites (10 to 50 V)	Mild reduction (< 50%), moderate (≥ 50%) or no proximal response was strongly correlated to postoperative facial dysfunction
Harner et al. 1988(60)	Retro	91	VS	50	CV	Bipo	1, oculi or oris, mentalis, masseter, temporalis; 1, surface	IAC, REZ	Any response to stimulation (from 10 V); if the proximal response is low, distal stimulation (IAC) to define extent of lesion	If a response is observed, this means intact FN; Low CMAP response – definite increase in facial weakness
Silverstein et al. 1988 (191)	Retro	301	Ot, VS	200	CC	Mono	NA, oris (motion detector)	REZ	> 0.3 mA stimulation at the end of tumor resection	Facial weakness is expected; If > 3 mA – facial palsy is likely to occur

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Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
Niparko et al. 1989(147)	Retro	29	VS	100	CC	Bipo	NA	IAC, REZ	Equal proximal and distal response at the end of tumor resection	67% - HB I at 1 week; 88% - HB I at 1 year
Beck et al. 1991(11)	Retro	56	VS	100	CC	Mono	1, Oris	REZ	1. 500 µV amplitude of neurotonic discharge (trains) sustained for ≥ 30 sec; 2. 500 µV amplitude of O. oris response using 0.05 mA stimulation at the end of tumor resection.	Four groups of patients: A. < 500 µV EMG and > 500 µV to stimulation; B. > 500 µV EMG and to stimulation; C. < 500 µV EMG and to stimulation; D. > 500 µV EMG and < 500 µV to stimulation. Group A – at 1 week, 97% had HB grade I
Kirkpatrick et al. 1991(88)	Retro	18	CPA	1,000	CC	Bipo	1, Oris	NA	Any response to 0.5-1.0 mA stimulation (up to 5 mA)	Small tumor – 73% had HB I/II at 3 to 43 mo; Large tumor – 43% had HB III/V at 3 to 43 mo
Berges et al. 1993(16)	Retro	43	VS	NA	CC	Mono	2, Oris, Oculi	IAC, REZ	A ratio was calculated by using the minimal stimulation threshold (I) and the induced amplitude EMG response (A) in the CPA (R´= I/A) and IAC (R´´ = I/A); R = R´ / R´´	R < 2 – 90% HB I/II at 10 days; R > 2 – 10% HB I/II at 10 days

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Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
Kirkpatrick et al. 1993(87)	Retro	26	VS	1,000	CC	Both	2, Oculi, Oris	REZ	≤ 2 mA stimulation after tumor resection	67% - HB I/II at 6 to 43 mo
Prasad et al. 1993(157)	Retro	34	CPA	100 to 200	CV	NA	2, Oculi, Oris	REZ	Pre vs. Post tumor resection variation ≤ 0.2 V of proximal stimulation	90% - HB I/II at 2 days; 83% - HB I/II at 1 to 44 mo
Wolf et al. 1993(222)	Pros	25	VS	100	CC	Mono	3, tumor side; 1, opposite side	REZ	1. 500 µV amplitude of neurotonic discharge (trains) sustained for ≥ 30 sec; 2. 500 µV amplitude of muscle response using 0.1 to 0.4 mA stimulation at the end of tumor resection.	Response < 500 µV EMG and > 500 µV to stimulation was correlated to normal facial function in 90% of the patients at 1 day
Lacombe et al. 1994(97)	Retro	62	VS	100	CC	Mono	2, oculi, oris	REZ	Stimulation threshold	≤ 0.1 mA – All HB I/II at 1 mo; Between 0.1 and 0.3 mA – 71.4% HB I/II at 1 mo; > 0.3 mA – 20% HB I/II at 1 mo.
Lalwani et al. 1994(98)	Retro	129	VS	200	CV	Mono	2, Oculi, Oris	REZ	≤ 0.2 V stimulation after tumor resection	Stimulation threshold not correlated with immediate postop; 98% - HB I/II at 1 year; if > 0.2 V – 50% HB I/II

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Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
Lenarz and Ernst 1994(103)	Retro	30	CPA	100	CC	Both	2, Oculi, Oris	NA	Stimulation threshold	Significantly increased in patients with postop facial weakness (0.73 mA) indicating poor outcome and long-lasting nerve damage
Maurer et al. 1994(126)	Retro	35	VS	100	CC	Both	2, Oculi, Oris	REZ	Relative EMG amplitude reduction of more than 50% after tumor resection in comparison to before resection	More frequent poor outcomes in patients with relative amplitude reduction
Silverstein et al. 1994(192)	Retro	44	VS	200	CC	Mono	NA (EMG); Oris (motion detector)	REZ	≤ 0.1 mA stimulation after tumor resection (EMG or motion detector)	95% - HB I/II at ≥ 1 year; If between 0.1 to 0.2 mA – 82% HB I/II
Yokoyama et al. 1994(227)	Retro	52	VS	100	CC	Mono	NA	IAC, REZ	Mean EMG amplitude to stimulation over the REZ (> 100 µV) or percentage of EMG amplitude between REZ and IAC (> 30%) with 0.5-0.6 mA stimulation	Good or excellent outcome at 6 to 24 mo
Maurer et al. 1995(125)	Retro	102	CPA, Skull base	100	CC	Both	2, Oculi, Oris	REZ	Relative EMG amplitude reduction of more than 50% after tumor resection in comparison to before resection	More frequent poor outcomes in patients with relative amplitude reduction

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Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
Taha et al. 1995(201)	Retro	20	VS	100	CC	Mono	2, Oculi, Oris	Distal IAC, REZ	Proximal-to-Distal CMAP amplitude ratio with lowest stimulation intensity (0.05-0.1 mA)	Ratio > 2/3 – all patients with HB III or better at immediate postop and HB I at 14-28 mo; Ratio > 1:3 / < 2:3 – 90% HB III or worse at immediate postop and 100% HB III or better at final follow-up; Ratio < 1/3 – all patients with HB IV or worse at immediate and at final follow-up
Selesnick et al. 1996(184)	Retro	49	CPA	50	CC	Mono	NA, Multich	REZ	≤ 0.1 mA stimulation after tumor resection	90% - HB I/II at 1 year; If between ≤ 0.2 mA – 78% HB I/II
Hone et al. 1997(65)	Pros	27	VS	100	CC	Bipo	2, Frontalis, Oris	REZ	Lowest current to elicit > 250 µV for facial muscle contraction	Stimulus threshold > 0.1 mA – HB > 2 at the immediate postop and 6 mo
Magliulo and Zardo 1997(120)	Retro	23	Skull base	NA	CC	Mono	2, Oculi, Oris	IAC, REZ	1. Ongoing train activity and muscle contraction to stimulation (Beck´s Method - 1991); 2. Ratio between IAC and REZ (Berges´ Method - 1993);	Berges´ and Silverstein´s method showed better sensitivity; Ratio of the evoked amplitude response predicted the facial function

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
									3. Stimulation threshold (Silverstein´s Method -1994).	in 91.3% of the patients at 1 year; Stimulation threshold correctly predicted the facial function in 86.9%; Beck´s method failed to predict postop facial function.
Nissen et al. 1997(148)	Retro	81	VS	NA	CV	Mono	NA	IAC, REZ	Minimal voltage stimulus to elicit an EMG response (Stimulus Threshold)	Median threshold of 0.1 V – HB I/II at 6 mo; Median threshold of 0.725 V – HB III/IV at 6 mo
Zeitouni et al. 1997(228)	Pros	109	VS	NA	CC	Mono	2, Oculi, Oris	REZ	1. Minimal current stimulus to elicit an EMG response (Stimulus Threshold); 2. CMAP amplitude	Intraoperative thresholds significantly associated with immediate and late follow-up – 87% threshold between 0.05 – 0.1 mA (HBI/II 83% at immediate and 91.6% at 1 year); CMAP amplitude failed to predict facial function
Mandpe et al. 1998(121)	Pros	44	VS	NA	CV	Mono	2, Oculi, Oris	IAC, REZ	1. Stimulation Threshold (≤ 0.1V); 2. CMAP amplitude (0.2 V above threshold);	≤ 0.1 V – 74% HB I/II at discharge; CMAP amplitude ≥ 200 µV – 89% HB I/II at discharge;

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
									3. Threshold + CMAP amplitude.	Low threshold + high amplitude – 88% HB I/II at discharge; The use of FN threshold + amplitude is a better predictor than threshold alone.
Magliulo and Zardo 1998(119)	Retro	34	VS	NA	CC	Mono	2, Oculi, Oris	IAC, REZ	1. Ongoing train activity and muscle contraction to stimulation (Beck´s Method - 1991); 2. Ratio between IAC and REZ (Berges´ Method - 1993); 3. Stimulation threshold (Silverstein´s Method -1994).	Ongoing activity < 500 µV and muscle contraction > 500 µV – confirmed an expected favorable outcome at 10 days; Ratio < 2 – 90% HB I/II and R > 2 – 87.5% HB V/VI; ≤ 0.1 mA – 84% HB I/II at 10 days; Berges´s method is more accurate, while Beck´s method is more limited.
Sobottka et al. 1998(194)	Retro/ Pros	60	VS	100	CC	Mono	2, Oculi, Oris	REZ	1. Proximal and distal absolute CMAP amplitude (0.05-0.1 mA); 2. Stimulation threshold; 3. Proximal-to-distal CMAP amplitude ratio.	CMAP amplitude > 800 µV – 94% good or excellent outcome at immediate and 100% at 6 to 18 mo; CMAP amplitude < 300 µV – all severe facial palsy at immediate and long-term

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
										follow-up; < 0.3 mA – 86.4% excellent or good facial function at immediate and 100% long-term; > 0.3 mA – all moderate to severe facial palsy; Amplitude ratio was not found to be more predictive (low specificity).
Axon and Ramsden 1999(8)	Pros	184	VS	200	CC	Bipo	2, Oculi, Oris	Proximal to the site of tumor	Minimal stimulation threshold (0.05 mA)	94% sensitivity in predicting good long-term facial function and 91% PPV
Fenton et al. 1999(44)	Pros	35	VS	100	CC	NA	NA	Medial and lateral to tumor	Minimal stimulation intensity medial and lateral to tumor after tumor resection	Medial minimal stimulation ≤ 0.1 mA – 96% HB I/II at immediate postop; ≥ 0.15 mA – 30% HB I/II, is suggestive of an abnormal facial function.
Goldbrunner et al. 2000(53)	Pros	137	VS	100	CC	Bipo	2, Oculi, Oris	Distal IAC, REZ	Proximal-to-Distal CMAP amplitude ratio with lowest stimulation intensity (0.5 mA)	Ratio > 0.8 - 1.6% risk of severe facial weakness at 6 mo; Ratio < 0.1 – 75% risk of severe facial weakness at 6 mo;

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
										Absolute CMAP amplitude values reached statistical significance only for subgroups (HB IV/V).
Fenton et al. 2002(43)	Pros	67	VS	100	CC	NA	2, Oculi, Oris	Medial to tumor	Minimal stimulation intensity medial and lateral to tumor after tumor resection	0.1 mA – 88% of the patients were correctly predicted to have a favorable initial outcome on the basis of tumor size and stimulation threshold
Isaacson et al. 2003(69)	Retro	229	VS	100	CC	Mono	2, Oculi, Oris	IAC, REZ	1. Stimulus threshold 2. Proximal-to-distal CMAP amplitude ratio;	≤ 0.5 mA – 93.6% HB I/II at 6 mo; Ratio > 0.33 – 97% HB I/II at 6 mo.
Akagami et al. 2005(3)	Pros	71	CPA	NA	NA	NA	2, Oculi, Oris	NA	Proximal-to-distal CMAP amplitude ratio	Independent variable predictive of satisfactory FN outcome
Anderson et al. 2005(4)	Retro	67	VS (> 3cm)	NA	CC	Mono	NA	REZ	Absolute CMAP amplitude > 100 µV in response to as high as 0.4 mA stimulation	93% - HB I/II at final follow-up (6 mo to 1 yr)
Bozorg-Grayeli et al. 2005(19)	Pros (multi)	111	VS	NA	CC	Mono	4, Oculi, Oris, Frontalis,	Fundus, IAC, REZ	Lowest intensity that elicits a response > 100 µV on at least one channel	< 0.05 mA – appeared to improve the prognostic value for predicting

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
							Platysma			immediate postop function; 0.01-0.04 mA - 93% HB I/II at day 8; 0.05-0.3 mA – 85% HB I/II at day 8; > 0.3 mA – 79% HB I/II at day 8.
Grayeli et al. 2005(57)	Pros	89	VS	NA	CC	Mono	4, Oculi, Oris, Frontalis, Platysma	Fundus, IAC, REZ	1. Lowest intensity that elicits a response > 100 µV on at least one channel; 2. Stimulation threshold	0.01-0.04 mA – 90% HB I/II at days 1 and 8; 0.05-0.2 mA – 75% HB I/II at days 1 and 8; > 0.2 mA – 20% HB I/II.
Neff et al. 2005(145)	Pros	74	VS	NA	CC	NA	2, Oculi, Oris	REZ	1. Response amplitude > 240 µV or greater and; 2. Stimulation threshold 0.05 mA or less	One criterium – 85% HB I/II at 1 year; Both criteria – 98% probability of HB I/II at 1 year; Stimulus threshold or response amplitude alone had a lower probability with the same result
Isaacson et al. 2005(70)	Retro	60	VS	100	CC	Mono	2, Oculi, Oris	IAC, REZ	1. Stimulus threshold; 2. Proximal-to-distal CMAP amplitude ratio	Accurate in predicting increased risk of long-term FN dysfunction when used a logistic regression model;

***Table S 6**. Summary of the published studies on the predictive value of Direct Electrical Stimulation (DES).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (CC/CV)	Probe	Channels, Muscle	Stimulation Site	IOFNM criteria	Results
										Score ≥ 0.8 – all patients with final HB III or better; Score < 0.8 – 67% do not regain eye closure.
Lin et al. 2006(109)	Pros	38	VS	200	CC	Bipo	3, Oculi, Oris, Frontalis	REZ	Percentage ratio was calculated by dividing the CMAP response to REZ stimulation (0.05-0.3 mA) by the amplitude of distal ipsilateral transcutaneous maximal stimulus response	CMAP > 50% of the maximum – 93% PPV of HB I/II at immediate postop; CMAP > 20% of the maximum – 81% PPV.
Shamji et al. 2007(185)	Retro	127	VS	NA	NA	NA	NA	NA	Stimulation threshold	< 0.1 mA – predictive of functional nerve preservation

* Bipo – bipolar probe; CC – constant-current; CMAP – compound muscle action potentials; CPA – cerebellopontine angle; CV – constant-voltage; EMG – electromyographic; FN – facial nerve; HB – House and Brackmann classification; IAC – internal auditory canal; IOFNM – intraoperative facial nerve monitoring; mA – milliamperes; mo – months; Mono – monopolar probe; multi – multicenter study; Multich – multichannel; µsec – microseconds; µV – microvolts; NA – not attributable; Ot – otological procedures; PPV – positive predictive value; Pros – prospective; Retro – retrospective; REZ – root exit zone; sec – seconds; V – volts; VS – vestibular schwannoma.

***Table S 7**. Summary of the published studies on the predictive value of Continuous Electromyographic (EMG) monitoring.**

Study	Study design	Number of Patients	Histology	Channels, muscles	IOFNM criteria	Results
Harner et al. 1987(61)	Retro	48	VS	1, two to four (oculi, oris, mentalis, masseter, or temporalis)	Intensity of neurotonic discharge	Severe neurotonic discharges were strongly correlated to postoperative facial dysfunction
Harner et al. 1988(60)	Retro	91	VS	1, oculi or oris, mentalis, masseter, temporalis	Intensity of neurotonic discharge	Predicted the degree of postoperative facial weakness
Lenarz and Ernst 1994(103)	Retro	30	CPA	2, oculi, oris	1. Number of train events; 2. ratio (trains/hour)	Correlated to the postoperative facial function (> 26 trains – HB III or greater); > 5.4 trains/hour – predictive of poorer immediate postoperative function (HB III or greater).
Eisner et al. 1995(41)	Retro	16	Brainstem	1, for both oculi; 1, for both oris	Duration of PSA 1. slight PSA – EMG activity for a few sec; 2. extreme PSA – EMG activity for several hours, similar to trains.	Extreme PSA – permanent postoperative déficit; Any EMG activity – normal function; Constant EMG activity/slight PSA – transient or incomplete palsy.
Grabb et al., 1997(55)	Retro	17	Fourth ventricle	1, for both oculi; 1, for both oris	Facial muscle EMG activity	The presence of irritation activity was associated with postoperative facial weakness
Hone et al. 1997(65)	Pros	27	VS	2, frontalis, oris	1. Number of spontaneous or mechanically induced contractions (> 20); 2. Number and length of trains with repetitive activity (> 199 sec)	74% had more than 20 contractions and 59% had more than 200 sec of train activity; Neither was predictive of postop FN function.

***Table S 7**. Summary of the published studies on the predictive value of Continuous Electromyographic (EMG) monitoring.**

Study	Study design	Number of Patients	Histology	Channels, muscles	IOFNM criteria	Results
Kombos et al. 2000(90)	Pros	60	CPA	2, oculi, oris	Duration of EMG activity 1. single discharges or < 2 min; 2. EMG activity of 2-5 min; 3. EMG activity > 5 min; 4. loss of EMG activity.	< 2 min EMG activity – good immediate and long-term function; 2-5 min EMG activity – 60% good immediate function (93.3% sensitivity and PPV); > 5 min EMG activity (73.3% sensitivity and PPV) – 67% fair and 33% poor immediate function; Loss of EMG – all poor immediate and late function; Burst duration does not necessarily correlate with postop outcome.
Romstöck et al. 2000(165)	Pros	30	CPA	3, oculi, oris, nasalis	Analysis of EMG waveform patterns (spikes, bursts, trains)	Occurrence of A-trains is a reliable predictor of postop facial palsy; Spikes, bursts, B and C-trains were clinically irrelevant.
Nakao et al. 2001(143)	Pros	51	VS	2, oculi, oris; oris (motion detector)	Number, duration, frequency and amplitude of train responses	Train duration (30 sec to 20 min) and number (1 to 14) were not predictors of facial function; High-amplitude (≥ 250 μV) – 85.7% HB V or VI at discharge; No trains – 77.8% facial palsy (HB VI) at discharge; High-frequency (bomber type) – 60% HB V or VI at discharge.
Wedekind and Klug 2001(215)	Pros	33	CPA	2, oculi, oris	Analysis of EMG waveform patterns 1. transient activity that ceases after manipulation stoppage; 2. Ongoing lasting activity that continues w/o	The frequency of the first category was significantly higher in patients with good outcomes at immediate and at 3 mo (Sens 69%, Spec 94%); The frequency of the third category was higher but not significant in patients with

***Table S 7**. Summary of the published studies on the predictive value of Continuous Electromyographic (EMG) monitoring.**

Study	Study design	Number of Patients	Histology	Channels, muscles	IOFNM criteria	Results
					manipulation, amplitude < 200 μV; 3. Ongoing lasting activity > 200 μV.	poor postop outcome (immediate and long-term) (Sens 45%, Spec 89%); Continuous EMG recording does not provide reliable prediction of facial function.
Nakao et al. 2002(144)	Pros	49	VS	2, oculi, oris; oris (motion detector)	Analysis of burst and train patterns 1. irritable pattern; 2. silent pattern; 3. stray pattern (persistent trains up to 20 min); 4. ordinary pattern.	Irritable pattern – 91% HB III or better at discharge and 100% at 1 year; Silent pattern – 82% HB V or VI at discharge and HB III or better at 1 year; Stray pattern – all HB V or VI at discharge and HB III or better at 1 year; Ordinary pattern – 77% HB I/II at discharge and 92.3% HB III or better at 1 year.
Prell et al. 2007(162)	Retro	40	VS	3, oculi, oris, nasalis	A-trains quantitative parameter (train time)	Reliable predictor of immediate and long-term FN outcome; Two thresholds 0.5 sec and 10 sec; 0.5 sec-threshold – train time less than threshold correlates with good postop function; 10 sec-threshold – less than 10 sec was correlated with less deterioration (1 HB grade) and more than 10 sec (2 HB grades or more).

* CMAP – compound muscle action potentials; CPA – cerebellopontine angle; EMG – electromyographic; FN – facial nerve; HB – House and Brackmann classification; IOFNM – intraoperative facial nerve monitoring; min – minutes; mo – months; μV – microvolts; NA – not attributable; PPV – positive predictive value; Pros – prospective; PSA – pathological spontaneous activity; Retro – retrospective; sec – seconds; Sens – sensitivity; Spec – specificity; V – volts; VS – vestibular schwannoma.

***Table S 8**. Correlation between neurophysiological data and postoperative facial nerve outcome.**

No.	Sex	Age (yr)	Diagnosis	Size	Voltage		Final-to-baseline FMEP ratio (%)		Preop HB Grade	Postop HB Grade
					Baseline	Increase	Oculi	Oris		
1	M	33	Bstem Cyst	large	400		100	100	1	1
2	M	5	Medullo	small	300	400	33	77	1	1
3	M	61	VS	small	240	400	43	179	1	3
4	M	15	VS	small	300		182	64	1	2
5	F	56	VS	large	600		NA	0	1	5
6	M	56	Petrocl Mening	large	400		87	221	1	1
7	F	36	VS	large	300	400	139	24	1	3
8	F	67	Petrocl Mening	small	400		105	170	1	1
9	M	63	VS	large	400		100	136	1	1
10	F	47	Petrocl Mening	large	340		17	85	1	5
11	F	29	VS	large	400		101	0	1	4
12	F	7	Chordoma	large	400		NA	99	1	1
13	M	59	Bstem Cavern	small	400		92	99	1	1
14	F	49	VS	large	280		22	34	1	3
15	M	42	VS	small	250		91	80	1	1
16	M	39	Epidermoid	small	270		67	55	1	1
17	M	21	VS	small	280		151	58	1	1
18	F	47	VS	large	200		252	283	1	1
19	F	50	VS	large	400		60	155	1	1
20	M	52	VS	small	300		100	152	1	1
21	F	45	VS	large	400		41	445	1	4
22	M	40	Metastase	small	400		17	64	1	1
23	F	43	VS	large	400		77	89	1	4
24	F	53	VS	large	400		NA	NA	1	2
25	M	71	Petrocl Mening	large	400		260	0	2	4
26	F	35	VS	small	390		291	970	1	1
27	M	28	Cholesteatoma	small	300		57	35	1	1
28	F	66	Petrocl Mening	small	400		93	62	1	1
29	F	49	VS	small	400		224	86	1	1
30	M	43	VS	small	350		85	NA	1	1
31	F	68	VS	large	330		NA	NA	1	2
32	F	47	VS	large	350	400	NA	16	1	5
33	M	35	VS	small	400		133	183	1	1
34	F	58	Petrocl Mening	large	400		52	82	2	1
35	F	29	VS	large	300	356	32	NA	2	3
36	F	58	VS	small	350	400	114	NA	1	1
37	M	47	VS	small	400		142	184	1	1
38	F	62	VS	large	360		283	117	1	1

***Table S 8**. Correlation between neurophysiological data and postoperative facial nerve outcome.**

No.	Sex	Age (yr)	Diagnosis	Size	Voltage		Final-to-baseline FMEP ratio (%)		Preop HB Grade	Postop HB Grade
					Baseline	Increase	Oculi	Oris		
39	F	45	Petrocl Mening	small	326	400	NA	0	1	3
40	M	51	VS	small	400		152	72	1	1
41	M	43	VS	small	400		109	46	1	1
42	F	31	VS	large	400		13	99	1	1
43	F	62	Jugular For	small	400		56	110	1	1
44	M	42	VS	large	352	400	NA	120	2	2
45	F	45	VS	large	400		NA	NA	2	5
46	F	27	Ependymoma	small	400		91	136	1	1
47	M	53	VS	small	400		NA	59	2	2
48	F	40	VS	large	300		79	100	1	3
49	F	69	VS	small	252		206	116	1	1
50	F	39	VS	large	260	284	134	NA	1	3
51	F	49	VS	small	250	280	69	131	1	1
52	M	30	Meningioma	large	250		84	37	1	1
53	F	45	Petrocl Mening	large	300		75	179	1	1
54	M	61	Hemangio	large	300		159	297	1	1
55	F	63	Papilloma	large	260	280	328	142	1	1
56	F	46	Jugular For	large	400		95	119	1	1
57	M	45	Trig Mening	small	300		68	196	1	3
58	F	55	VS	large	380		105	65	1	1
59	M	38	VS	large	380		117	NA	1	2
60	F	46	VS	large	380		75	42	2	2

* Bstem Cavern – brainstem cavernoma; Bstem Cyst – brainstem cyst; F – female; FMEP – facial motor evoked potential; HB – House-Brackmann; Hemangio – hemangioblastoma; Jugular For – jugular foramen meningioma; M – male; Medullo – flocculus medulloblastoma; NA – not applicable; Papilloma – plexus papilloma; Petrocl Mening – petroclival meningioma; Trig Mening – trigeminal meningioma; VS – vestibular schwannoma; yr – years.

***Table S 9**. Summary of the published studies on the predictive value of Facial Motor Evoked Potentials (FMEP).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (Trains/ ISI)	Intensity	Electrode Montage	Channels, Muscles	IOFNM criteria	Results
Zhou and Kelly 2001(231)	Pros	50	Brain tumor	500	5, Freq 0.5 to 2 Hz	40 to 160 mA	1-2 cm anterior to C3 and C4	1, oris	Persistent MEP decrease of > 50%	MEP amplitude reductions were associated with postop motor deficits; The degree of amplitude reduction was correlated with the degree of immediate postop worsening; No mention of facial function.
Dong et al. 2005(39)	Pros	76	Skull base	50/ 500	3 to 4, ISI 1 or 2 ms	100 to 400 V	1 cm anterior to C3/C4 and CZ (M3/M4-MZ)	1, oris	Final-to-baseline MEP ratio	Significant immediate postop facial deficits predicted 50% ratio - Sens 100%, Spec 88%; 35% ratio - Sens 91%, Spec 97%; 0% ratio (loss) - Sens 64%, Spec 100%; FMEP loss accounted for all patients who developed complete facial palsy postop.

***Table S 9**. Summary of the published studies on the predictive value of Facial Motor Evoked Potentials (FMEP).**

Study	Study design	Number of Patients	Histology	Pulse (µsec)	Stimulus Protocol (Trains/ ISI)	Intensity	Electrode Montage	Channels, Muscles	IOFNM criteria	Results
Akagami et al. 2005(3)	Pros	71	Skull base	50	3 to 5, ISI 1 to 3 ms	200 to 400 V	C3/C4 and CZ	1, oris	Final-to-baseline MEP ratio	A 50% final-to-baseline ratio predicted immediate HB I/II facial function
Fukuda et al. 2008(48)	Retro	26	Skull base	NA	5, ISI 1 ms	180 to 550 V	C3/C4 and CZ	2, oculi, oris	Final-to-baseline MEP ratio	A 50% threshold consistently predicted immediate HB I/II facial function and palsy of both muscles
Present Study 2009	Retro	60	CPA	50	3 or 5, ISI 2 ms	200 to 600 V	C3/C4 and CZ	2, oculi, oris	Final-to-baseline MEP ratio	Immediate postoperative facial function correlated significantly with the FMEP ratio in the orbicularis oculi muscle at 80% amplitude ratio and orbicularis oris muscle at 35% ratio; FMEP loss was always related to postoperative facial paresis

* cm – centimeter; CPA – cerebellopontine angle; EMG – electromyographic; FN – facial nerve; FMEP – facial motor evoked potential; HB – House and Brackmann classification; Hz – hertz; IOFNM – intraoperative facial nerve monitoring; ISI – interstimulus interval; mA – milliamperes; MEP – motor evoked potential; ms – milliseconds; µsec – microseconds; NA – not attributable; Pros – prospective; Retro – retrospective; sec – seconds; Sens – sensitivity; Spec – specificity; V – volts; VS – vestibular schwannoma.

Abstract

Objective: This study was conducted to investigate the success rate of the orbicularis oculi and oris muscles motor evoked potentials (FMEP) for facial nerve function monitoring by using a stepwise protocol and to evaluate its usefulness in predicting facial nerve outcome during cerebellopontine angle (CPA) surgeries.

Methods: FMEPs were recorded intraoperatively from 60 patients undergoing CPA surgery. Transcranial electrocortical stimulation (TES) was performed using corkscrew electrodes positioned at a hemispheric montage (C3/C4 and CZ). The contralateral abductor pollicis brevis muscle was used as the control response. Stimulation was always applied contralaterally to the affected side using 1, 3 or 5 rectangular pulses ranging from 200 to 600V with 50 microseconds of pulse duration and an interstimulus interval (ISI) of 2 miliseconds (ms). Facial potentials were recorded from needles placed in the orbicularis oculi and oris muscles.

Results: FMEP from the orbicularis oris and oculi muscles could be reliably monitored in 86.7% and 85% of the patients, respectively. The immediate postoperative facial function correlated significantly with the FMEP ratio in the orbicularis oculi muscle at 80% amplitude ratio ($p = 0.037$) and orbicularis oris muscle at 35% ratio ($p = 0.000$). FMEP loss was always related to postoperative facial paresis, although in different degrees.

Conclusions: FMEPs can be obtained reliably using TES with 3 to 5 train pulses. Stable intraoperative FMEPs can predict a good postoperative outcome of facial function. However, further refinements of this technique are still necessary in order to minimize artifacts and to make this method even more reliable.

Zusammenfassung

Titel: Zur elektrophysiologischen Ableitung der Funktion des Nervus fazialis bei Operationen am Kleinhirnbrückenwinkel mittels transkranieller Elektrostimulation

Ziel: Diese Studie untersucht bei chirurgischen Eingriffen am Kleinhirnbrückenwinkel, bei denen der Nervus facialis anatomisch und funktionell gefährdet ist, die Durchführbarkeit des Facialis-Monitoring und dessen prognostischen Wert für das postoperative Ergebnis mittels elektrophysiologischer Ableitung motorisch evozierter Potenziale (MEP) des Musculus orbicularis oculi und Musculus orbicularis oris (FMEP).

Methoden: Bei 60 mikrochirurgischen Eingriffen am Kleinhirnbrückenwinkel wurden intraoperative FMEPs abgeleitet. Eine transkranielle Elektrostimulation (TES) wurde mit Corkscrew-Elektroden an den Positionen C3, C4 und CZ nach gängiger hemisphärischer Montage durchgeführt. Der kontralaterale Musculus abductor pollicis brevis wurde als Kontrollantwort verwendet. Die Stimulation erfolgte immer kontralateral der betroffenen Seite. FMEPs wurden von Nadeln registriert, die in den M. orbicularis oculi und den M. orbicularis oris gelegt waren. Dazu wurden 1, 3 oder 5 Rechteckimpulse im Intervall von 200 V bis 600 V mit einer Impulsdauer von 50 Mikrosekunden und eines Zwischenstimulus-Intervalls von 2 Millisekunden verwendet.

Ergebnisse: In 86.7% der Fälle konnte ein FMEP des M. orbicularis oris und in 85 % der Fälle ein FMEP des M. orbicularis oculi zuverlässig abgeleitet werden. Die unmittelbare postoperative Funktion des Nervus facialis korrelierte signifikant mit den Werten der FMEPs: 80% der Amplitudenrate bei dem M. orbicularis oculi ($p = 0.037$) 35% der Amplitudenrate bei dem M. orbicularis oris ($p = 0.000$). Ein FMEP-Verlust war immer mit postoperativen Fazialisparesen in verschiedenen Schweregraden verbunden.

Schlussfolgerungen: FMEPs können zuverlässig abgeleitet werden, indem TES mit 3 bis 5 Train-Pulsen verwendet werden. Stabile intraoperative FMEPs haben eine Voraussagekraft für ein gutes postoperatives Ergebnis des N. facialis. Eine weitere Verfeinerung der Technik wird jedoch in Zukunft noch notwendig sein, um Artefakte zu minimieren und diese Methode als zuverlässiges intraoperatives Monitoring sich etablieren zu lassen.

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