Facial nerve motor evoked potentials during skull base surgery to monitor facial nerve function using the threshold-level method

Sarnthein, J ; Hejrati, N ; Neidert, M C ; Huber, A M ; Krayenbühl, N

Facial nerve motor-evoked potentials during skull base surgery to monitor facial nerve function by the "threshold-level" method

Johannes Sarnthein[1,3], PhD; Nader Hejrati[1],cand med; Marian C. Neidert[1], MD; Alexander Huber[2], MD; Niklaus Krayenbühl[1], MD

[1] Klinik für Neurochirurgie, UniversitätsSpital Zürich, Switzerland

[2] Klinik für Ohren-, Nasen-, Hals- und Gesichtschirurgie, UniversitätsSpital Zürich

[3] Center for Integrative Human Physiology, Universität Zürich, Switzerland

Corresponding author:

PD Dr. Johannes Sarnthein

Klinik für Neurochirurgie, UniversitätsSpital Zürich,

8091 Zürich, Switzerland

johannes.sarnthein@usz.ch

Tel +41 44 255 5672

Fax +41 44 255 4399

Figures: 6

Tables: 2

Words in abstract: 280

Words in text: 3050

ABSTRACT

Object: During surgeries that put the facial nerve (FN) at risk of injury, FN function can be continuously monitored by transcranial FN motor evoked potentials (FNMEPs) in FN target muscles. Despite their advantages, FNMEPs are not yet widely used. While most authors use a 50% reduction of FNMEP response amplitudes as a warning criterion, our approach was to keep the response amplitude constant by increasing the stimulation intensity and to establish a warning criterion based on the "threshold-level" method.

Methods: We included 34 consecutives procedures involving 33 adult patients (median age 47 years) where FNMEPs were monitored. A threshold increase >20mA for eliciting FNMEPs in the most reliable FN target muscle was considered a prediction of reduced postoperative FN function and subsequently a warning was issued to the surgeon. Pre-and early postoperative function was documented using the House-Brackmann (HB) grading system.

Results: FNMEP monitoring was feasible in all 34 surgeries in at least one FN target muscle. The mentalis muscle yielded best results. HB grade deteriorated in 17/34 patients (50%). The warning criterion was reached in 18/34 patients (53%), which predicted an 83% risk of HB deterioration. Sensitivity amounted to 88% (CI 64%-99%) and specificity to 82% (CI 57%-96%). FNMEP deterioration and deteriorated HB grade showed a high degree of association (p<0.001). The impact of FNMEP monitoring on surgical strategy is exemplified in one illustrative case.

Conclusions: In surgeries that put the facial nerve at risk, the intraoperative increase in FNMEP stimulation threshold was closely correlated to postoperative facial nerve dysfunction. FNMEP monitoring is a valid indicator of FN function in skull base surgery. It should be used as an adjunct to direct electrical FN stimulation and continuous EMG monitoring of FN target muscles.

1. INTRODUCTION

Microneurosurgery of the skull base, especially of the cerebellopontine angle, still carries a significant risk to impair facial nerve (FN) function. Among the technical measures to preserve FN function, intraoperative neuromonitoring (IONM) has become mandatory and is constantly being advanced.[3] During surgery, IONM serves to communicate impending nerve damage to the surgeon and to predict postoperative neurological state. As a standard method of IONM, direct electrical stimulation (DES) of the FN serves to elicit compound muscle potentials recorded from FN target muscles. DES is used to identify the FN in the surgical field, to map its course, and for intermittent testing of FN function. As another standard method, free-running electromyography (EMG) of FN target muscles provides a continuous feedback of FN activity.

More recently, FN motor evoked potentials (FNMEPs) have been introduced.[4,7] FNMEPs allow to activate the motor pathway proximal of the surgical field by transcranial electric stimulation (TES) of the motor cortex and to record responses in FN target muscles. With this technique FN function can be monitored continuously. Despite this advantage, FNMEP has not yet become a standard tool of IONM, possibly due artifacts in the signals and uncertainties in the interpretation of the results. We have therefore tested several electrode types to record FNMEPs. Most authors use the decrease in FNMEP response amplitude as warning criterion.[1-4,8,12] However, FNMEP responses have inherent variability and are hard to quantify. Also, high FNMEP stimulation intensity is needed to achieve maximal FNMEP response already at baseline so that subsequent response deterioration can be assessed. Inspired by promising findings in IONM of motor function during surgery at the level of the spine,[5] the cortex,[17] the brainstem,[16] and the FN,[9] we propose here to monitor the increase of the stimulation threshold needed to elicit FNMEPs in order communicate with the surgeon and to predict postoperative FN function.

2. PATIENTS AND METHODS

2.1. Patient selection

We included all adult consecutive patients from August 2011 to December 2012 who underwent surgical procedures within the cerebellopontine angle with intraoperative neuromonitoring of FN function. Collection of personal patient data and scientific workup was approved by the institutional ethics review board (Kantonale Ethikkommission KEK-ZH 2012-0212). The selection criterion resulted in a series of 34 surgical procedures in 33 patients (21 female, median age 47y, range 20-84y). Patient characteristics are listed in Table 1.

2.2. Pathology

Table 1 shows the list of patients' pathology. Twenty-two patients were operated on vestibular schwannoma, 4 on meningioma, 4 on a trigeminal neuralgia and 4 patients had other pathologies (PICA aneurysm, brainstem cavernoma, medulloblastoma and tuberculoma).

2.3. Neurological assessment

FN function was scored according to the House Brackmann (HB) Grading System (range 1–6; grade 1: normal facial muscle function, grade 6: total palsy).[10] Preoperative scores and postoperative scores at the first postoperative day were taken from patient records.

2.4. Anesthesia management

Following the standard protocol for neurosurgical interventions, anesthesia was induced with intravenous application of the sedative drug Propofol (4 to 8 mg/kg/min), the opioid analgesic Remifentanil (1–2 μg/kg/min) and the skeletal muscle relaxant Atracurium (0.5 mg/kg). After intubation, the neuromuscular blocking drug, Atracurium, was omitted because of its interference with electrophysiological monitoring and mapping.

2.5. Neurophysiological monitoring technique

Intraoperative neurophysiological monitoring was performed using the ISIS system (www.inomed.com). Free-running EMG was recorded from FN target

muscles. DES for precise localization of the FN in the surgical field was initiated with 0.2 mA at large distance from the FN and reduced to a minimal current of 0.05 mA as long as the FN was well identified. TES for FNMEP was performed using a constant current stimulator with maximal stimulator output 220 mA. Limb motor evoked potential (MEP) and FNMEP responses were amplified and filtered (100-3000 Hz) before display.

2.6. Sites for recording of muscle activity

Among FN target muscles, we recorded responses from the muscles orbicularis oculi, nasalis, orbicularis oris, and mentalis. Depending on the requirements of the surgery, in some patients only a subset of FN target muscles was recorded. Thenar muscles served as target muscles to monitor upper extremity MEP responses.

2.7. Electrodes for recording of muscle activity

Thenar muscle MEP responses were recorded with pairs of non-insulated straight needle electrodes placed under the skin (stainless steel, 0.4 x 12 mm Neuroline Twisted pair, www.ambu.com), typically overlying the target muscle belly. Impedance was typically below 5 kΩ. These electrodes were also used for FN target muscles.

In an attempt to optimize recording of muscle activity, we also tested two other electrode types. Compared to straight needles, hook needle electrodes (stainless steel, 0.35 x 12 mm, www.SPESmedica.com) intrude into the skin only for a shorter depth. We hypothesized that the shorter depth would increase specificity for muscle activity while still being easy to handle. Impedance was typically below 5 kΩ. As a third electrode type, we tested wire electrodes (stainless steel, 0.11 mm diameter, recording area 0.002 mm², www.SPESmedica.com) that record activity very specific to the target muscle since only a very small area is exposed from insulation, which results in high impedance (typically above 50 kΩ).

2.8. Transcranial electric stimulation

TES current was delivered through 2 corkscrew electrodes (www.sgm.hr) placed at electrode sites C3/C4 *vs.* Cz. While the montage C3 *vs.* C4 is optimal for low MEP stimulation thresholds for the upper extremities,[18] we chose stimulation

against Cz to reduce neck movements disturbing to the surgeon. A bite block was placed in the mouth to prevent bite injuries of the tongue resulting from motor stimulation of the jaw.

TES was performed by applying rectangular pulses. To reduce the stimulation artefact in recordings, the pulse shape was symmetrically biphasic with positive and negative deflections during the pulse width. Only the phase of anodal current was considered in the calculation of the effective charge that was delivered to the patient. The width of the anodal phase ranged between 0.2ms and 0.5ms and was typically 0.4ms.

TES pulses were applied in trains of 3 to 6 pulses for FNMEP and MEP. While an interstimulus interval (ISI) of 4ms is optimal for limb MEP,[18] we used ISI = 2ms to widen the interval between the TES artefact in the signal traces and the FNMEP response.

To distinguish between corticobulbar and peripheral stimulation,[20] we added a control pulse either 20ms before or 40ms after the pulse train. Parameters were chosen such that for at least one FN target muscle the TES pulse train elicited a response but the control pulse did not.

2.9. Determination of MEP stimulation threshold

The baseline FNMEP stimulation threshold was determined before skin incision. To obtain the baseline MEP threshold we started by a fixed pattern of stimulus intensity at 30mA, and then increased by 5mA increments until one of the target muscles responded reliably to stimulation. At least 2 seconds elapsed from one stimulus train to another. An evoked FNMEP response as low as 20 μV with appropriate response latency qualified as reliable FNMEP response,[6,16] although responses were typically >100 μV. The testing was repeated continuously and at short intervals when FN function was assumed to be at risk.

2.10. Electrophysiological data analysis

Whenever reduced FNMEP amplitude responses were observed, technical failures were ruled out primarily, and anesthesia parameters were checked. Secondarily the number of stimulating pulses and subsequently the FNMEP stimulation intensity were elevated with the aim to obtain constant FNMEP response amplitude. At higher stimulus intensity, disturbing muscle reactions necessitated

precise synchronization of FNMEPs with surgical requirements. Gradually progressive threshold elevations were attributed to anesthetic fade[11] and the baseline FNMEP threshold was adjusted.[6,16] Rapid threshold elevations were analyzed in the context of the surgical manipulations and were considered possibly pathological. FNMEPs were considered deteriorated and the surgical team was notified whenever the FNMEP intensity threshold had to be elevated by >20 mA. Data analysis focused on those FN target muscles with the most salient FNMEP responses and in which corticobulbar - as opposed to peripheral - stimulation was most clearly evident.

2.11. Statistical analysis

Statistical analyses were performed with custom scripts in Matlab R2010a (www.Mathworks.com). For ratios, the 95% confidence intervals (CI) were obtained on the basis of the binomial distribution. Distributions were compared by non-parametric testing. Statistical significance was established as $p<0.05$.

The outcomes of FNMEP and neurological examinations were dichotomized for statistical treatment in contingency tables with the chi^2 test. A contingency table contains the elements true positive (TP), true negative (TN), false positive (FP) and false negative (FN). Derivations of these are the sensitivity or true positive rate $TPR = TP/(TP+FN)$, the false positive rate $FPR=FP/(FP+TN)$, the accuracy $ACC=(TP+TN)/(TP+TN+FP+FN)$), the specificity $1-FPR$, the negative predictive value $NPV = TN/(TN+FN)$, and the positive predictive value $PPV = TP/(TP+FP)$.

3. RESULTS

3.1. Representative FNMEP responses

Figure 1 shows representative traces recorded from FN target muscles in patient 26 at baseline. The control pulse was delivered 20ms before the train of 5 pulses. None of the muscles responded to the control pulse, which excludes peripheral stimulation for the chosen set of stimulation parameters. The train of 5 pulses elicits a response in all muscles. The response latency exceeds 20ms for thenar muscles. FN target muscles show a variety of response latencies and the

responses are polyphasic to a varying degree. The variability of responses may be related to the modification of FN anatomy in the presence of the lesion.

Impedances were below 5 kΩ for straight and hook needles and around 100 kΩ for the wire electrode. The recording from the wire electrode stands out as it is contaminated with 50 Hz line hum. The low signal-to-noise ratio made it difficult to interpret the results of FNMEPs, the free-running EMG, and the localization of the FN by DES in the surgical field. The wire electrode was therefore only applied in a limited number of cases.

3.2. FNMEP threshold increase is correlated with postoperative HB grade

Figure 2 shows ΔI_{th}, the increase of FNMEP stimulation threshold, with respect to the postoperative HB grade. Depicted is the value of ΔI_{th} for the FN target muscle that corresponded most reliably to FNMEPs. Under physiological considerations, stimulation intensity should be depicted as charge. From a practical point of view, the current delivered is readily available from our IONM monitoring device. We therefore depict the increase of stimulation current. The postoperative HB grade and the increase in current needed to elicit FNMEPs was correlated with rho=0.62 (p<0.001 Spearman).

3.3. Intraoperative warnings are associated with HB grade deterioration

Pre- and early postoperative HB grades of all patients are listed in **Table 1**. HB grade deteriorated in 17/34 patients (50%, CI 32%-68%). During the course of surgery, the threshold to elicit FNMEP responses increased by $\Delta I_{th} > 20$ mA in 18/34 (53%, CI 35%-70%) and a warning was issued to the surgical team (**Table 1**).

Of all N=34 cases, TN=14 had no warning and no HB deterioration; TP=15 patients had FNMEP warnings and HB deterioration; FP=3 had warnings but no new deficit; FN=2 had no warning but a new deficit. Thus, FNMEP deterioration to the warning criterion predicts an 83% risk of HB deterioration (PPV, CI 59%-96%). With 14 true negative cases out of all 16 negative cases, the NPV was 88% (CI 62%-98%). In 17 cases HB deteriorated and a warning had been issued in 15 of them (sensitivity 88%, CI 64%-100%). In 17 cases HB remained unchanged and in 14 of these FNMEPs remained stable (specificity 82%, CI 57%-96%). For all patients, the occurrence of deteriorated FNMEPs and deteriorated HB grade showed a high degree of association (p<0.001, chi² test).

3.4. Effects of varying the warning criterion

In **Figure 3** the receiver operating characteristic (ROC) curve shows the predictive power of FNMEPs as the warning criterion was varied. The numbers denote the points on the curve where the warning criterion ΔI_{th} was at 20mA and at 15mA, respectively. The area under the curve is AUC=0.80.

Concerning surgical outcome the Positive Predictive Value (PPV) is of particular importance. **Figure 4** shows the derivations of the contingency table as a function of the warning criterion, i.e. the increase in stimulation threshold ΔI_{th}. With increasing threshold a maximal accuracy in prediction is achieved for $\Delta I_{th} = 20$mA. With the warning criterion at 20mA, the fact of issuing a warning was associated with a risk of PPV=83% of postoperative deterioration of FN function.

3.5. Stimulation parameters, FN target muscles and recording electrode types

Median stimulation threshold to elicit FNMEP responses at baseline was 75 mA, which corresponds to a pulse with charge 26 µC. The threshold was higher than the MEP threshold to elicit responses at the thenar muscle (median 63 mA, 22 µC) in 25 of 30 patients (83%, p<0.001, sign test).

Monitoring FNMEPs was feasible in all 34 procedures in at least one FN target muscle. Not all muscles were monitored in all patients.

We obtained reliable results in 15/30 (50%) recordings at the orbicularis oculi muscle, in 6/25 (24%) recordings at the nasalis muscle, in 33/48 (69%) recordings at the orbicularis oris muscle and in 45/52 (87%) recordings at the mentalis muscle. The mentalis yielded the best result among all FN target muscles. The rates for different electrode types are presented in **Table 2.** Contrary to our initial expectation, straight needle electrodes produced the best results.

3.6. Illustrative case where FNMEP recording influenced the surgical strategy

A 38 year old male patient (HB = I) presented with a vestibular schwannoma of diameter 30 mm (patient **21**). At a later stage of surgery, DES of the FN proximal to the surgical field did not elicit muscle responses. Based solely on this finding, one could have assessed FN function to be lost and decided for a surgical strategy of rapid radical tumor resection. However, FNMEPs could still be elicited **(Figure 5)**, albeit only in the mentalis muscle and at highly elevated stimulation threshold of 90

mA (baseline 60 mA). This advanced the interpretation that the loss of DES response might have been due to anatomical changes induced by the tumor. Therefore the surgeon decided for less radical tumor resection. Postoperative evaluation revealed only moderately severe FN dysfunction (HB = IV). In this case, the presence of FNMEP recordings – as opposed to DES alone – contributed to preservation of FN function.

4. DISCUSSION

4.1. The "threshold-level" method for FNMEP interpretation

MEPs are a well-established component of intraoperative neurophysiological monitoring of cortico-spinal tract function.[13] More recently, the indication for MEP monitoring has been extended to also monitor the function of the corticobulbar tract, in particular FN function.[4,7] Most authors consider a reduction of FNMEP response amplitude of more than 50% as warning criterion[1-4,7,8,12] as widely accepted for MEPs in supratentorial surgery.[15,19] The "threshold-level" method has first been proposed for monitoring spinal cord function.[5] There is one report of FNMEP threshold monitoring in the literature.[9] We report here a series of surgeries where FNMEPs were analyzed by the "threshold-level" method to monitor FN function intraoperatively. With this approach we obtained a sensitivity of 88% and a specificity of 82%, which is in the range of values reported by other authors.[2,4,7,8] With the warning criterion at 20mA, an intraoperative warning was associated with a risk of PPV=83% (CI 59%-96%) of postoperative deterioration of FN function. A high NPV of 88% (CI 62%-98%) indicates that the absence of an intraoperative warning predicts good postoperative facial nerve function.

4.2. Clinical value of FNMEP monitoring

The clinical value of FNMEP monitoring is twofold. On one hand, DES proximal to the lesion may fail to produce responses in FN target muscles, as shown in our case description **(Figure 5)**. Then the fact that FNMEPs can be elicited indicates that FN function is not totally lost. Based on this information the surgeon has refrained from aggressive tumor resection and FN function could be preserved.

The increase in stimulation threshold ΔI_{th} on the other hand, informs the surgeon about possible postoperative deterioration of FN function if a warning criterion is reached. The criterion adopted in our study was motivated by values

published for surgeries at the level of the spine,[5] the cortex,[17] and the brainstem.[16] This criterion lead to a warning issued in 18/34 surgical interventions (53%). However, one has to bear in mind that the 3 instances of warnings without ensuing HB deterioration cannot strictly qualify as "false positive cases" since action was taken intraoperatively with the aim to prevent paresis.

There is a tradeoff between sensitivity and specificity as shown by the ROC in **Figure 3**. We found the highest accuracy ACC = 85% (CI 69%-95%) for ΔI_{th} = 20mA, which was associated with PPV=83%. This PPV may be considered high, since a warning predicts an 83% chance of reduced postoperative FN function. With lower ΔI_{th} as a criterion, warnings are issued earlier and are associated with a lower chance of reduced postoperative FN function. In general, more sensitive warning criteria have been shown to trigger surgical re-evaluation earlier.[6,14] If we reduce ΔI_{th} to 15mA, PPV is reduced to 80%, which is only a small effect (**Figure 4**). To achieve a substantial reduction to PPV=62%, the warning criterion must be lowered to 10mA. This in turn reduces specificity to 41%, which may jeopardize the credibility of FNMEP monitoring. Furthermore, most patients in our series showed only a mild deterioration of FN function when looking at changes in HB grades. Based on long-term studies in the literature we expect an improvement of FN function at later follow-up visits.[1,8,12] Regarding changes of intraoperative surgical strategy, a simple algorithm based on FNMEPs cannot be defined. Considering conflicts between postoperative facial nerve function and completeness of tumor resection, surgical management decisions should also depend on patient individual factors such as tumor entity (malignant vs. benign), patient age, and individual tolerance of facial nerve deficits.

For future surgeries we propose to not simply issue a warning to the surgeon, but to inform in a more detailed way based on the findings of this study. The threshold increase ΔI_{th} is reported together with the PPV, i.e. the associated risk for any deterioration of postoperative FN function (**Figure 4**). In addition, the degree of deterioration can be estimated from the amount of threshold increase (**Figure 2**).

4.2. Advantages of the "threshold-level" method

Warning criteria based on FNMEP response amplitude have some drawbacks. First, there is inherent variability in the amplitude of the muscle responses; FNMEP responses are often polyphasic and extended over time so that they are difficult to

quantify. Second, high FNMEP stimulation intensity is needed to achieve maximal FNMEP response already at baseline so that subsequent response deterioration can be assessed. High MEP stimulation intensity may cause movements such as neck twitches, which are disturbing to the surgical procedure.

As a different approach, the "threshold-level" method operates with lower FNMEP stimulation intensity at onset. This approach aims to keep the response amplitude constant throughout surgery by adapting the FNMEP stimulation intensity. It has been suggested that in an event of deterioration of corticospinal tract function, this method may provide a warning earlier.[6]

As a further simplification, we focused our analysis on the FN target muscle that gave the most reliable response (mentalis muscle in 87%). In our opinion this approach is feasible since fibers of all muscle branches are running in close topographical relation within the compact FN course in the CPA. In contrast to procedures that involve the peripheral branches of the facial nerve, it seems unlikely that FN injuries during CPA procedures involve only a subset of facial nerve muscles. As expected from studies that show a high correlation between different branches of the FN,[2,8] the analysis of the best responding muscle was representative and useful for prediction of postoperative FN function as defined by the HB grading system.

4.3. Distinguishing between corticobulbar and peripheral stimulation

The main value of FNMEPs is to activate the corticobulbar tract proximal to the surgical field and to record responses of FN target muscles in order to monitor the function of the tract (**Figure 6**). Due to the proximity between the stimulating electrodes and the FN target muscles, peripheral stimulation may also occur. Several criteria have been proposed to distinguish between corticobulbar and peripheral stimulation.[2-4,7-9,12]

Ideally, a corticobulbar FNMEP response should occur after a latency of about 10ms and it should be polyphasic. Furthermore, it has been claimed that a corticobulbar response requires stimulation by a train of several pulses and response to a single pulse is due to peripheral stimulation.[7,20] In the double train approach we have therefore added a train consisting of a single control pulse to the train of 3 to 6 pulses, which was intended to evoke FNMEP responses. Only if a response to the control pulse was absent, the response to the train was qualified to be a corticobulbar FNMEP.

5. CONCLUSIONS

In surgeries that put the facial nerve at risk, the intraoperative increase in stimulation threshold was closely correlated to postoperative facial nerve dysfunction. A threshold increase >20mA predicted an 83% risk for deterioration of HB grade. FNMEP monitoring is a valid indicator of postoperative FN function in skull base surgery. It should be used as an adjunct to direct electrical FN stimulation and continuous EMG monitoring of FN target muscles.

6. DISCLOSURE

7. ACKNOWLEDGEMENT

8. REFERENCES

1.   Acioly MA, Gharabaghi A, Liebsch M, Carvalho CH, Aguiar PH, Tatagiba M: Quantitative parameters of facial motor evoked potential during vestibular schwannoma surgery predict postoperative facial nerve function. **Acta Neurochir (Wien) 153:**1169-1179, 2011
2.   Acioly MA, Liebsch M, Carvalho CH, Gharabaghi A, Tatagiba M: Transcranial Electrocortical Stimulation to Monitor the Facial Nerve Motor Function During Cerebellopontine Angle Surgery. **Neurosurgery 66:**ONS354-ONS361, 2010
3.   Acioly MA, Liebsch M, de Aguiar PH, Tatagiba M: Facial Nerve Monitoring During Cerebellopontine Angle and Skull Base Tumor Surgery: A Systematic Review from Description to Current Success on Function Prediction. **World Neurosurg**, 2011

4. Akagami R, Dong CC, Westerberg BD: Localized transcranial electrical motor evoked potentials for monitoring cranial nerves in cranial base surgery. **Neurosurgery 57:**78-85; discussion 78-85, 2005

5. Calancie B, Harris W, Brindle GF, Green BA, Landy HJ: Threshold-level repetitive transcranial electrical stimulation for intraoperative monitoring of central motor conduction. **Journal of Neurosurgery 95:**161-168, 2001

6. Calancie B, Molano MR: Alarm criteria for motor-evoked potentials: what's wrong with the "presence-or-absence" approach? **Spine 33:**406-414, 2008

7. Dong CCJ, Macdonald DB, Akagami R, Westerberg B, Alkhani A, Kanaan I, et al: Intraoperative facial motor evoked potential monitoring with transcranial electrical stimulation during skull base surgery. **Clin Neurophysiol 116:**588-596, 2005

8. Fukuda M, Oishi M, Takao T, Saito A, Fujii Y: Facial nerve motor-evoked potential monitoring during skull base surgery predicts facial nerve outcome. **Journal of Neurology Neurosurgery and Psychiatry 79:**1066-1070, 2008

9. Goto T, Muraoka H, Kodama K, Hara Y, Yako T, Hongo K: Intraoperative Monitoring of Motor Evoked Potential for the Facial Nerve Using a Cranial Peg-Screw Electrode and a "Threshold-level" Stimulation Method. **Skull Base-an Interdisciplinary Approach 20:**429-433, 2010

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

11. 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

12. Matthies C, Raslan F, Schweitzer T, Hagen R, Roosen K, Reiners K: Facial motor evoked potentials in cerebellopontine angle surgery: technique, pitfalls and predictive value. **Clin Neurol Neurosurg 113:**872-879, 2011

13. Mendiratta A, Emerson RG: Transcranial electrical MEP with muscle recording, in Nuwer MR (ed): **Intraoperative Monitoring of Neural Function.** Amsterdam: Elsevier, 2008, Vol 8, pp 260-272

14. Neuloh G, Bogucki J, Schramm J: Intraoperative preservation of corticospinal function in the brainstem. **J Neurol Neurosurg Psychiatry 80:**417-422, 2009

15. Neuloh G, Pechstein U, Cedzich C, Schramm J: Motor evoked potential monitoring with supratentorial surgery. **Neurosurgery 54:**1061-1070; discussion 1070-1062, 2004

16. Sarnthein J, Bozinov O, Melone AG, Bertalanffy H: Motor-evoked potentials (MEP) during brainstem surgery to preserve corticospinal function. **Acta Neurochir (Wien) 153:**1753-1759, 2011

17. Szelenyi A, Hattingen E, Weidauer S, Seifert V, Ziemann U: Intraoperative motor evoked potential alteration in intracranial tumor surgery and its relation to signal alteration in postoperative magnetic resonance imaging. **Neurosurgery 67:**302-313, 2010

18. 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

19. Szelenyi A, Langer D, Kothbauer K, De Camargo AB, Flamm ES, Deletis V: Monitoring of muscle motor evoked potentials during cerebral aneurysm surgery: intraoperative changes and postoperative outcome. **J Neurosurg 105:**675-681, 2006

20. Ulkatan S, Deletis V, Fernandez-Conejero I: Central or peripheral activations of the facial nerve? **J Neurosurg 106:**519-520; author reply 520, 2007

8. FIGURE LEGENDS

Figure 1. Representative FNMEP and MEP responses. The traces were recorded in patient 26 at baseline. Visible at -20ms is the artefact of the TES control pulse, which does not elicit muscle activity. The TES train of 5 pulses elicits polyphasic responses at various latencies. Pulses were biphasic and the width of the anodal phase was 0.25ms. Signals recorded from hook needle electrodes are labeled "hook"; the signal from the wire electrode is labeled "wire"; all other signals were recorded from straight needle electrodes.

Figure 2. FNMEP threshold increase is correlated with postoperative HB grade. Shown is ΔI, the intraoperative increase in FNMEP threshold for the FN target muscle that corresponded most reliably, as a function of postoperative HB grade (Spearman's correlation rho=0.62, p<0.001). The oblique line represents a linear fit to the data. The dotted line at 20mA indicates the threshold level at which a warning was issued to the surgical team. Warnings were issued in 18/34 surgeries (53%).

Figure 3. Receiver operating characteristic (ROC) curve. Depicted are sensitivity and specificity of FNMEP as the warning criterion is varied. The numbers denote the points on the curve where ΔI_{th} was set to 20mA and 15mA, respectively. The area under the curve is AUC=0.80.

Figure 4. Derivations of the contingency table as a function of the warning criterion. With increasing threshold ΔI_{th} a maximal accuracy in prediction is achieved for ΔI_{th}=20mA. Lowering ΔI_{th} increases sensitivity at the expense of specificity.

Figure 5. Persisting FNMEPs in the absence of FN responses to direct FN stimulation. Mentalis FNMEP at the end of surgery in patient 21, 1min time interval between traces. The stimulation artefact of a TES train of 6 pulses is seen at -40ms (biphasic pulses, anodal phase width 0.5ms). The train elicits a polyphasic FNMEP response in the mentalis muscle. The control pulse at 0ms does not elicit muscle activity.

Figure 6. Activation of the corticobulbar tract *vs.* peripheral stimulation of FN target muscles. During activation of the corticobulbar tract, anodal stimulation of the motor cortex (red arrow) elicits activation of lower motor neurons in the FN nucleus of the brainstem, from where FN target muscles are activated. As a confounder, peripheral stimulation (yellow arrows) may also activate FN target
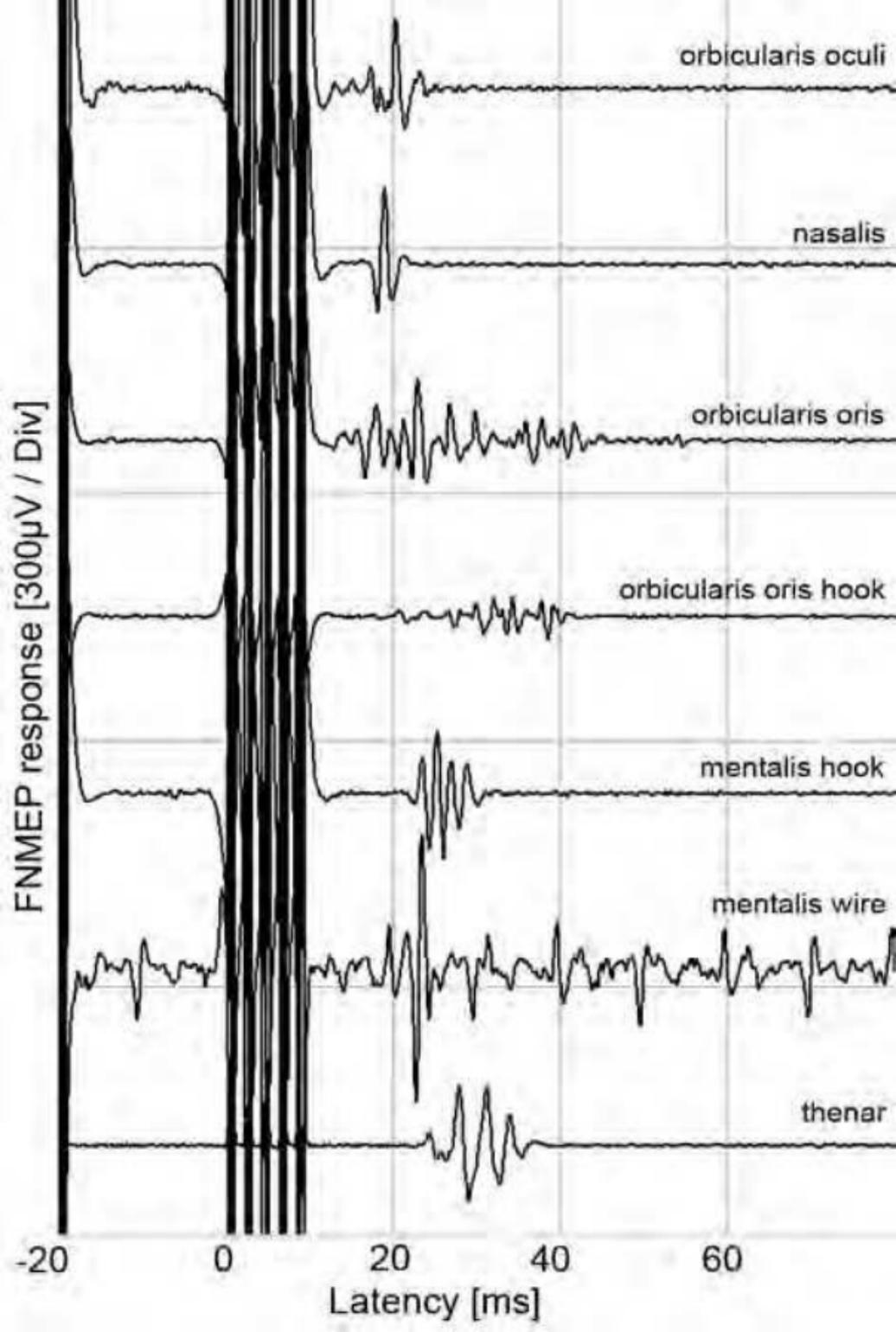
15

muscles, albeit at shorter latencies and already in response to single stimulation pulses.
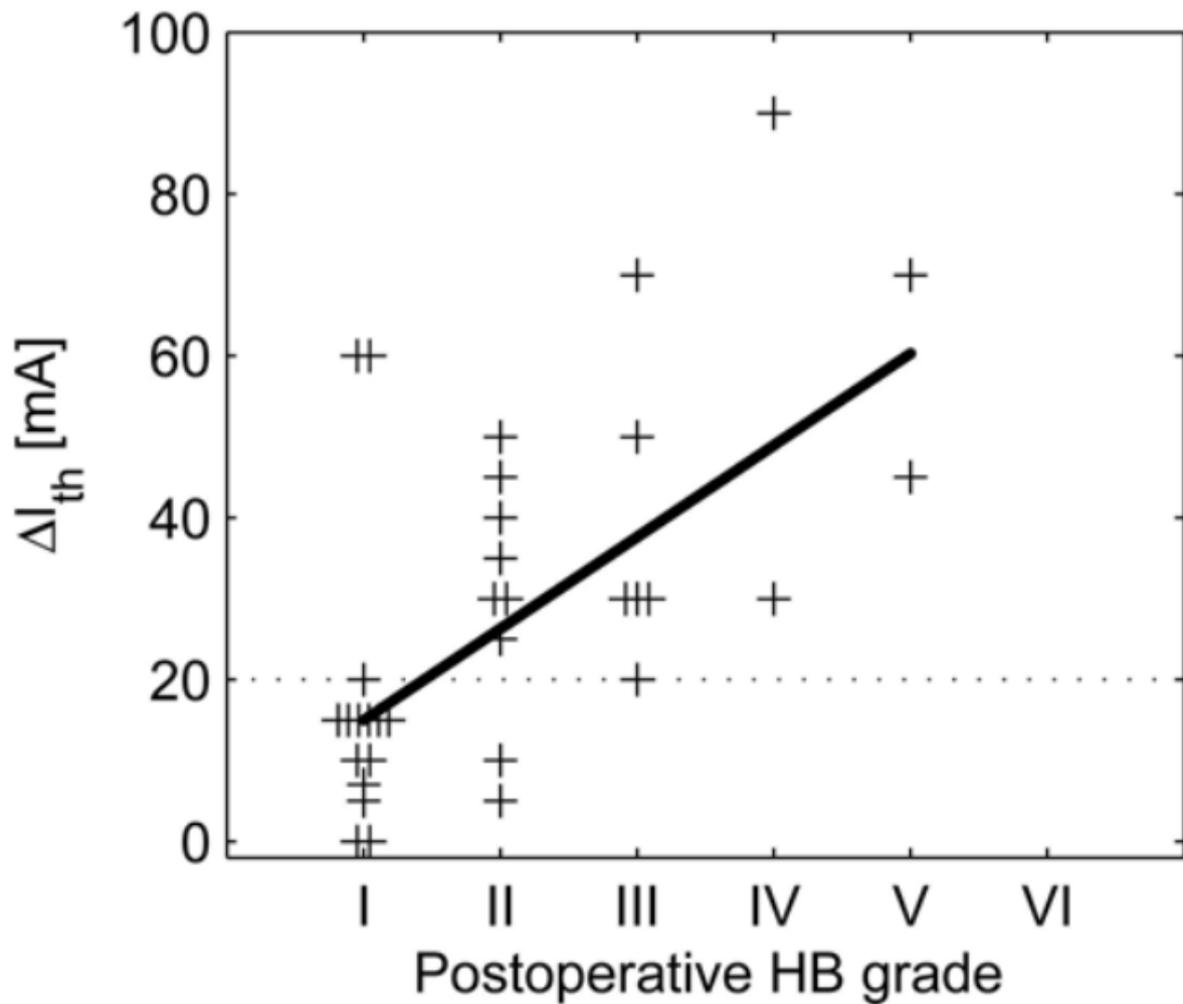
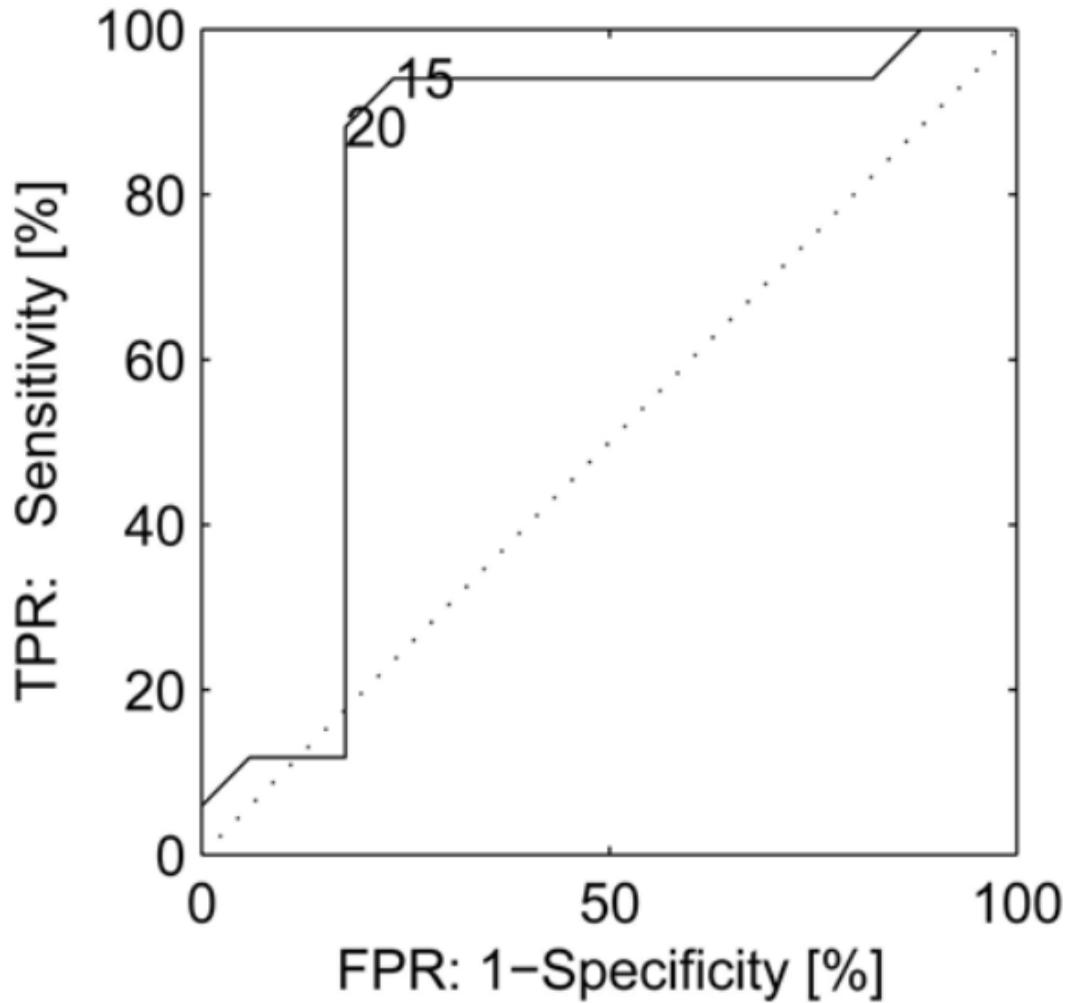**Table 1: Patient characteristics;** vs vestibular schwannoma; mn menignioma; tn trigeminal neuralgia

No	Sex	Age	Pathology	HB pre	HB post	HB deterioration	FNMEP pre [mA]	FNMEP post [mA]	FNMEP increase >20mA
1	M	20	vs	I	I	0	110	110	0
2	F	37	tn	I	I	0	140	140	0
3	M	54	vs	I	I	0	75	80	0
4	M	67	vs	I	II	1	135	140	0
5	F	56	vs	I	I	0	85	92	0
6	M	36	vs	I	I	0	100	110	0
7	F	70	vs	II	II	0	90	100	0
8	F	46	tn	I	I	0	60	70	0
9	M	69	vs	I	I	0	185	200	0
10	F	64	AVM with associated PICA aneurysm	I	I	0	75	90	0
11	F	82	tn	I	I	0	75	90	0
12	F	46	mn	I	I	0	45	60	0
13	M	33	mn	I	I	0	80	95	0
14	F	67	tn	I	I	0	65	80	0
15	F	43	vs	I	III	1	55	75	0
16	F	47	vs	I	I	0	60	80	0
17	F	47	mn	I	II	1	135	160	1
18	F	31	vs	I	II	1	80	110	1
19	M	52	mn	I	III	1	65	95	1
20	F	49	vs	I	III	1	65	95	1
21	M	38	vs	I	III	1	60	90	1
22	F	48	vs	I	II	1	80	110	1
23	F	46	vs	I	IV	1	80	110	1
24	F	58	vs	I	II	1	50	85	1
25	F	21	vs	I	II	1	100	140	1
26	F	72	vs	I	V	1	40	85	1
27	M	43	vs	I	II	1	65	110	1
28	F	46	vs	I	III	1	100	150	1
29	F	30	tuberculoma	I	II	1	60	110	1
30	M	21	medulloblastoma	I	I	0	80	140	1
31	F	84	vs	I	I	0	90	150	1
32	M	37	brain stem cavernoma	VI	V	0	80	150	1
33	M	40	vs	I	III	1	90	160	1
34	M	58	vs	I	VI	1	60	150	1

Table 2: Comparison of EMG-electrode types

Muscle	Electrode type	Successful recordings	
orbicularis oculi	straight needle	15/30	(50%)
nasalis	straight needle	6/25	(24%)
orbicularis oris	straight needle	22/31	(71%)
	hook needle	11/17	(65%)
mentalis	straight needle	23/25	**(92%)**
	hook needle	22/27	(81%)
	wire	3/5	(60%)

Figure: Plot of ΔI_{th} [mA] versus Postoperative HB grade (I–VI).