Transcranial motor-evoked potentials of laryngeal muscles for intraoperative neuromonitoring of the vagus nerve during thyroid surgery

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Vagus nerve · Motor-evoked potential · Electromyographic endotracheal tube · Transcranial electrical stimulation · Recurrent laryngeal nerve palsy

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Abstract

Purpose

The aim of this study was to elucidate normative features of vagal motor-evoked potentials (MEPs) induced by transcranial electrical stimulation (TES) and to determine the influence of functional decline of the recurrent laryngeal nerve (RLN) on vagal MEPs during thyroid surgery.

Methods

A total of 54 patients undergoing elective thyroid surgery under general anesthesia were enrolled in this study. Vagal MEPs induced by TES were measured from the vocal cord using one of two types of electrodes (wire type or wide and flat type) mounted on an endotracheal tube. We investigated the effects of stimulation intensity and train pulse number on vagal MEP amplitude, the time course of vagal MEP amplitude during surgery, and the effects of functional decline of the RLN on vagal MEPs.

Results

The success rate of vagal MEP monitoring with wide- and flat-type electrodes was significantly higher than that with wire-type electrodes. Reliable vagal MEPs were obtained at a stimulation intensity of approximately 300 V with 3 or more pulses in 91% of the patients without preoperative RLN palsy (RLNP), and the amplitude was augmented with increasing stimulation intensity and train pulse number. Vagal MEP amplitude decreased during thyroid surgery and then partially recovered at the end of surgery. Vagal MEP amplitude recorded from the electrode ipsilateral to preoperative RLNP was significantly lower than that on the contralateral intact side.

Conclusion

Vagal MEPs induced by TES can be obtained with a high success rate during thyroid surgery and would reflect functional status of the RLN.

Introduction

Motor-evoked potential (MEP) monitoring is an established practice option for surgery with a risk of motor injury in the brain and spinal cord [1]. Recent studies have demonstrated that the functions of cranial nerves such as the facial and vagus nerves can also be monitored using MEPs elicited by transcranial electrical stimulation (TES) during skull base surgery [2–5]. MEP monitoring by TES is an effective method for providing real-time information on integrity of the facial and vagal pathways and for predicting their postoperative functions.

Patients with dysfunction of the vagus nerve present with dysphagia, hoarseness, and/or dyspnea because the efferent motor fibers of the vagus nerve supply all of the striated muscles of the larynx and pharynx [6]. In order to record electromyography (EMG) activities for monitoring the vagus nerve during surgery, needle or hook-wire electrodes were previously inserted into the posterior pharyngeal wall, soft palate, and vocalis muscles [7, 8]. Electromyographic endotracheal tubes (EMG tubes) equipped with a pair of recording electrodes to make direct contact with the vocal cords have recently been developed for evaluating the function of the recurrent laryngeal nerve (RLN) during thyroid surgery. EMG tubes, which are easy to use and are less invasive than needle electrodes, are becoming popular for monitoring the function of not only the RLN during thyroid surgery but also the vagus nerve during skull base surgery [4, 5, 9, 10].

A nerve monitoring system with EMG tubes in which EMG evoked by direct electrical stimulation of the RLN in the surgical field can be monitored for thyroid surgery is now commercially available

(NIM-Response® 3.0 system, Medtronic Japan Co., Ltd., Tokyo, Japan). However, MEP monitoring of the vagus nerve (vagal MEP) with TES by using an EMG tube has not yet been systematically investigated in detail, although the method has been clinically applied during skull base surgery [2–5]. In addition, it has remained unclear how surgical injury of the peripheral vagus nerve and RLN affect vagal MEPs recorded from the vocal cord [1, 4].

The aim of this study was to (1) elucidate normative features of vagal MEPs recorded by using an EMG tube and (2) evaluate the effects of injury of the vagus nerve and RLN on vagal MEPs in patients undergoing thyroid surgery with a risk of injury of the nerves. The results of this study should be useful for establishing normative vagal MEPs and should contribute to the expansion of intraoperative vagal MEP monitoring to not only skull base surgery but also thyroid surgery.

Methods

Patients

The protocol of the present study was approved by the Institutional Ethics Committee of Shinshu University School of Medicine, Matsumoto, Japan (document number: 2151). The study was then registered with the University Hospital Medical Information Network (UMIN) in Japan, number UMIN000025714. The study was carried out in an operating theater at Shinshu University Hospital, Matsumoto, Japan from January 2017 to December 2017. Written informed consent was obtained from all patients before enrollment in the study. The present study was performed as a non-randomized prospective trial. Patients with American Society of Anesthesiologists physical status I or II who were scheduled for elective thyroid surgery under general anesthesia were included in this study. Both patients with and those without a history of thyroid surgery were included in this study. Preoperative recurrent laryngeal nerve palsy (RLNP) was diagnosed by description of resection of the RLN in the previous operative record and by evident hoarseness of the voice.

Anesthesia

An electrocardiogram, noninvasive blood pressure, percutaneous oxygen saturation, expiratory carbon dioxide partial pressure ($ETCO_2$), body temperature and bispectral index (BIS) were recorded during general anesthesia. Anesthesia was induced with target-controlled propofol infusion set at an effect-site concentration of 3 μg/ml and fentanyl at 100 μg. Rocuronium (0.6 mg/kg) was used as a muscle relaxant to facilitate endotracheal intubation. There are two types of commercially available EMG tubes: wire electrodes type [NIM™ EMG Endotracheal Tube (NIM-Tube), Medtronic Japan Co., Ltd., Tokyo, Japan] and flat and wide electrodes type [NIM TriVantage EMG Tube® (NIMTV-Tube), Medtronic Japan Co., Ltd., Tokyo, Japan]. The former electrode endotracheal tube (NIM-Tube) was used from January 2017 to March 2017 and the latter tube (NIMTV-Tube) was used from March 2017 to December 2017. EMG tubes with inner diameters of 8.0 mm and 7.0 mm were used for male and female patients, respectively, according to the patient's tracheal width on a preoperative chest X-ray. If deviation or stenosis of the trachea caused by growth of the thyroid tumor was observed in the chest X-ray or computed tomography scan, EMG tubes with inner diameters of 7.0 mm and 6.0 mm were used for male and female patients, respectively. The trachea was intubated by using a McGRATH® MAC video laryngoscope (Aircraft Medical Ltd., Edinburgh, UK) to confirm placement of the EMG tube in the proper positional relationship between the electrodes and vocal cords.

Anesthesia was maintained with propofol (effect-site concentration set at 2.0–3.5 μg/ml), remifentanil (0.1–0.25 μg/kg/min) and fentanyl. After tracheal intubation, 4 mg/kg of sugamadex was administered and recovery from the muscle relaxant was confirmed by using acceleromyography (TOF-Watch®; Nihon Kohden Ltd., Tokyo, Japan) of the adductor pollicis muscle. No additional muscle relaxant was administered in the subsequent study period.

Conditions for measurement of vagal MEPs

Corkscrew electrodes for TES (Unique Medical Co., Ltd., Tokyo, Japan) were placed on the scalp at C3 and C4 or Cz according to the international 10–20 system of electrode placement. Constant voltage stimuli consisting of 1 to 5 monophasic rectangular pulses with a pulse duration of 50 μs and an interstimulus interval of 0.95 ms were generated with a SEN-4100 stimulator (Nihon Kohden Ltd., Tokyo, Japan) based on the method of Ito et al. [4]. Vagal MEPs elicited by TES at C3/C4 or at C3/Cz were measured in a preliminary study to clarify the relationship between the stimulation site and amplitude of vagal MEPs. In the subsequent research, stimulation electrodes were placed at C3 and C4. The anode and cathode were switched according to the hemisphere stimulated because a monophasic waveform was used in this study. Vagal MEPs were recorded from the vocal cords by using electrodes on the EMG tube. EMG signals were amplified (Neuropack MEB-2312; Nihon Kohden Ltd., Tokyo, Japan) and filtered (200–3000 Hz). Amplitude of the vagal MEP was defined as the peak-to-peak distance in μV. The onset latency was defined as the time at which the source waveform deviated from the baseline at approximately 10 ms after TES [11].

Study protocol

When using NIM-tube, the stimulation intensity selected was 300 V with a train of 5 pulses. When using NIMTV-Tube, vagal MEPs were measured according to the following protocol. First, we investigated the relationship between stimulation intensity and vagal MEP amplitude. Stimulation intensities were selected to be between 100 and 400 V with an increment of 50 V and with a train of 5 pulses. We also investigated the relationship between train pulse number and vagal MEP amplitude. Vagal MEPs were evoked with changes in the train pulse numbers from 1 to 5 at a constant voltage that could produce a vagal MEP amplitude of 150–200 μV in each patient with a train of 5 pulses. Next, vagal MEPs evoked by the defined voltage in each patient with a train of 5 pulses as mentioned above were recorded before starting surgery, after exposing the thyroid gland, after removal of the thyroid gland, before closure, and immediately after surgery. In this study, a reliable vagal MEP was defined as follows: (1) onset latency of vagal MEP being between 10 and 13 ms based on the results of a previous study in which the onset latency of vagal MEP was investigated [11, 12] and (2) significant amplitude larger than approximately 200 μV from the baseline being detected. Successful monitoring with EMG tubes was defined as vagal MEP being able to be measured stably throughout the thyroid surgery. MEPs from laryngeal muscles were also monitored by direct stimulation of the RLN in the surgical field using the NIM-Response® 3.0 system to identify the RLN or ensure the integrity of the RLN. When an intact RLN was directly stimulated by the probe, the system created a beep sound and a signal alert on the monitor to warn us in an all-or-none fashion.

Statistical analysis

Data are expressed as means ± standard deviations, percentage or numbers. Statistical data analysis was conducted using GraphPad Prism 6 (GraphPad Software, San Diego, California, U.S.A.). We used unpaired and paired Student’s t-tests, one-way analysis of variance, post hoc Dunnett's test and the chi square test. $p < 0.05$ was considered statistically significant.

Results

A total of 54 patients were enrolled in this study. Demographic characteristics and intraoperative parameters including data monitored with two types of EMG tubes are shown in **Table 1.** Interim analysis after 30 patients (NIM-Tube n = 15, NIMTV-Tube n = 15) had been enrolled showed that the successful rate of vagal MEP monitoring with NIMTV-Tube was significantly higher than that with NIM-tube (p = 0.02) when vagal MEPs were elicited by TES at C3/C4. NIMTV-Tube was used for vagal MEP monitoring in the subsequent study period. Final analysis showed that the successful rate of vagal MEP monitoring with NIMTV-Tube was significantly higher than that with NIM-Tube (p = 0.02) as shown in **Table 2.** There were no significant differences between the two groups in types of diseases and types of surgery performed. All surgeries in this study were performed by experienced attending surgeons. The mean baseline vagal MEP amplitude at a stimulation intensity of 300 V with NIM-Tube and with NIMTV-Tube were 289 ± 157 μV (n = 9) and 253 ± 192 μV (n = 36) respectively, with no significant difference in amplitude (p = 0.25). However, NIMTV-Tube was better than NIM-Tube for stable recordings of vagal MEPs throughout the thyroid surgery. There were 5 patients with preoperative unilateral RLNP caused by previous thyroid surgery. Baseline vagal MEPs were obtained in 31 of 34 patients without preoperative RLNP. Vagal MEPs could not be identified clearly in 3 patients because large EMGs probably derived from muscle responses in the temporal and mandibular regions masked them.

In the initial 8 patients of the study after the interim analysis, corkscrew electrodes were placed at positions C3, C4 and Cz to evoke vagal MEPs. **Figure 1** shows vagal MEPs elicited by TES at C3/Cz and at C3/C4. Vagal MEP amplitude gradually increased with increasing stimulation intensity. There were no significant differences between left and right vagal MEPs when the anode was placed at C3 and the cathode was placed at Cz or C4. Vagal MEP amplitude elicited by TES at C3/C4 (anode/cathode) were significantly higher than those at C3/Cz (anode/cathode) at stimulus intensity from 200 to 350 V ($p < 0.05$). In the subsequent study, vagal MEPs were elicited by TES at C3/C4.

Figure 2 shows the relationship between stimulation intensity and vagal MEP amplitude in responses to TES with a train of 5 pulses. Vagal MEP amplitude gradually increased with increasing stimulation intensity. **Figure 3** shows the relationship between train pulse number and vagal MEP amplitude. Vagal MEP amplitude gradually increased with increasing train pulse number. Three or more pulses per train were required to evoke reliable vagal MEPs. Mean onset latencies of vagal MEPs were 10.39 ± 0.77 ms on the right side and 10.47 ± 0.71 ms on the left side. This difference did not reach statistical significance ($p = 0.83$). The mean stimulation intensity that could produce a vagal MEP amplitude of 200 μV was 295 ± 51 V ($n = 31$).

Figure 4 shows the time course of vagal MEP amplitude changes during thyroid surgery in patients ($n = 39$) without preoperative RLNP and without intraoperative transection of the RLN. Vagal MEP amplitude decreased to 67 ± 36% of the baseline during thyroid surgery and then showed a moderate recovery trend at the end of surgery, although no signal alerts were displayed on the NIM-Response® 3.0 system and there were no patients who suffered from evident RLNP in the postoperative round.

Bilateral vagal MEPs could be measured in 4 of the 5 patients with preoperative unilateral RLNP. Vagal MEP amplitude measured from the electrode ipsilateral to the RLNP increased with increasing stimulation intensity and train pulse number (**Figure 5 and Figure 6**). It should be noted that vagal MEP amplitude on the ipsilateral injury side was significantly lower than that on the contralateral intact side at stimulation intensities of 350 and 400 V and at train pulse numbers of 4 and 5.

Resection of the RLN was performed intraoperatively in only 1 patient in the current study. We present an illustrative case demonstrating intraoperative sudden deterioration of vagal MEP amplitude in a 61-year-old male patient without preoperative RLNP. Vagal MEPs on both sides were obtained before surgery in the patient. After the left RLN had been identified and then resected because of cancer invasion in the left RLN, vagal MEP amplitude markedly decreased on the left side but not on the right side (**Figure 7**). The next day, the patient developed voice hoarseness. Postoperative laryngoscopy revealed left vocal cord paralysis.

Throughout the current study period, mean blood pressure was kept above 60 mmHg. The BIS values were in the range of 40–60 until the end of surgery. Ventilation was adjusted to maintain $ETCO_2$ at 35–40 mmHg and body temperature was maintained at 36.0–37.5℃.

Discussion

The major findings of this study were as follows: (1) vagal MEPs using NIMTV-Tube could be reliably monitored in approximately 91% of the patients, (2) vagal MEP amplitude decreased during thyroid surgery, and (3) functional loss of the RLN resulted in decreased vagal MEP amplitude.

The results of this study, in which two types of commercially available EMG tubes were used, showed that the success rate of obtaining reliable vagal MEPs with NIMTV-Tube was significantly higher than that with NIM-Tube ($p = 0.02$). The randomized controlled trial was not conducted to compare the success rate of vagal MEP recording between the NIMTV-Tube and NIM-Tube groups. In a clinical setting, we have used NIM-Tube for intraoperative neuromonitoring for the RLN since 2012. In other words, we were accustomed to use it at the start of this study. Thus, it is unlikely that the difference in progress of learning how to use it resulted in the difference in success rate between the two groups. There were no significant differences in patient characteristics, types of disease, types of surgery performed, methods for evaluation of vagal MEPs and members of the surgical team between the two groups. Taken together, we presumed that the bias produced by nonrandomized research designs was minimal. Therefore, the difference in success rate of vagal MEP recording might be at least in part due to the difference in the types of electrode mounted on the endotracheal tubes. Nonetheless, there were no significant differences in vagal MEP amplitude at baseline between the two EMG tubes. The results indicated that both of the EMG tubes can monitor vagal MEPs but that NIMTV-Tube is better than NIM-Tube for stable recordings of vagal MEPs during surgery.

Monitor dysfunction by using NIM-Tube has been reported at rates ranging from 5% to 20% [13, 14]. Malposition and malrotation of the EMG tube are the main causes of monitor dysfunction. Contact between the electrodes and vocal cords must be maintained for high-quality recording. Tube malposition easily decreases EMG amplitude from the vocal cords [15]. Patients undergoing thyroidectomy are generally positioned with the neck extended to facilitate exposure of the neck after induction of general anesthesia. We measured vagal MEPs after the neck extension in this study. Therefore, we presumed that neck extension aggravated the contact of EMG tube electrodes with the vocal cords, resulting in failure of recording. In addition, surgical manipulation may affect contact between the electrodes and vocal cords. The contact area of wire electrodes mounted on NIM-Tube is small compared with that of flat and wide electrodes mounted on NIMTV-Tube. Thus, it is likely that malposition and malrotation of NIM-Tube easily result in poor contact between the electrodes and vocal cords.

Myogenic MEPs in the limbs elicited by TES at C3/Cz are mainly unilateral responses [1]. In contrast, there was no significant difference between left and right vagal MEPs when the anode was placed at C3 and the cathode was placed at Cz (**Figure 1**), indicating the bilateral corticobulbar pathway activation to the laryngeal motoneurons. The results are consistent with the results of a previous study confirming the bilateral nature of corticobulbar pathway projections for laryngeal muscles [12]. Vagal MEP amplitudes elicited by TES at C3/C4 (anode/cathode) were significantly higher than those at C3/Cz (anode/cathode) at stimulus intensities from 200 to 350 V. TES at C3/C4 promotes deeper current penetration than that at C3/Cz [1]. Therefore, TES at C3/C4 may produce a large amplitude of vagal

MEPs.

The basic mechanism of muscle MEP generation is temporal and spatial summation of excitatory postsynaptic potentials in lower motor neurons. In general, the amplitude of MEP increases with increasing stimulation intensity and train pulse number [1]. Adding pulses and increasing stimulation intensity augmented vagal MEP amplitude, and the onset latency was 10–13 ms, indicating that the waveforms observed in this study were muscle MEPs and not stimulus artifacts or the results of direct vagus nerve stimulation, consistent with a previous study [16]. Based on our results, we presume that at least 3 pulses per train are necessary to evoke reliable vagal MEPs. However, the total stimulus duration should be less than 10 ms because of the short onset latency of vagal MEPs. An onset latency of 10–13 ms was consistent with that in previous studies [11, 12]. The onset latency on the left side tended to be longer than that on the right side, but the difference did not reach statistical significance. Thus, the elongated course of the left RLN had little impact on the onset latency of vagal MEPs. TES generates muscle contraction not only in the larynx but also in other parts of the body. A previous study showed that NIMTV-Tube can be used to assess activity in only the vocal cord muscles, not the posterior cricoarytenoid muscle a little distant from the electrodes [17], indicating that the electrodes mounted on NIMTV-Tube cannot detect compound action potential in muscles distant from them. Thus, it is unlikely that vagal MEPs recorded in the present study were derived from contraction of the muscles distant from the electrodes mounted on the endotracheal tube. In addition, we demonstrated that resection of the RLN resulted in reduction of vagal MEP amplitude (**Figure 6** and **Figure 7**). These results also suggest that vagal MEPs are at least in part derived from contraction of the muscles innervated by the RLN.

Paresis and paralysis of the RLN can be caused by excessive traction, thermal injury, crush injury by forceps, clamps or retractors, and transection [10]. Traction is recognized as the most common cause of injury to the RLN [18]. An experimental study showed that stretch injury of a peripheral nerve for a short time causes prolonged reduction of compound action potentials of the nerve according to the intensity of stretch [19]. In the present study, vagal MEP amplitude significantly decreased during thyroid surgery and tended to recover at the end of surgery. It is possible that the decrease in vagal MEP amplitude observed during thyroid surgery was due to transient and reversible functional decline of the RLN caused by the thyroid surgery procedure. In other words, the slight decrease in vagal MEP amplitude may be caused by subclinical injury of the nerve. The finding that intraoperative resection of the RLN caused a marked decrease in vagal MEP amplitude as shown in **Figure 7-a** supports this notion.

Vagal MEP amplitude from the ipsilateral side of RLN injury in patients with preoperative unilateral RLN injury was significantly lower than that from the contralateral healthy side, suggesting that vagal MEP amplitude reflects ipsilateral RLN function. However, it should be noted that vagal MEP amplitude was very small but that vagal MEP was still present in patients with preoperative RLNP as shown in **Figure 6**. The RLNs supply all of the intrinsic muscles of the larynx except for the cricothyroid muscle. The cricothyroid muscle is innervated by the external branch of the superior laryngeal nerve (EBSLN), a branch of the vagus nerve. Selective direct stimulation of the EBSLN produces EMG response recorded with EMG tubes in 70-80% of patients [20]. Therefore, it is likely that vagal MEPs can be produced through the EBSLN even if RLN function is completely lost.

In previous studies, direct stimulation of the vagus nerve or nucleus was used to evoke laryngeal muscle response during skull base surgery [8, 21]. This method requires identification of the nerve or the nucleus at the brainstem. To overcome that disadvantage, vagal MEPs elicited by TES have been introduced for intraoperative monitoring of the vagus nerve [4]. We demonstrated that reliable vagal MEPs could be obtained at a stimulus intensity of approximately 300 V with 3 or more pulses per train. These results will be useful for obtaining reproducible vagal MEPs and providing proper interpretation of the MEPs.

We showed that vagal MEP amplitude changed depending on the functional status of the RLN, indicating the possibility that measurement of vagal MEPs allows determination of the functional state of the RLN during thyroid surgery. RLNP is one of the most serious complications of thyroid surgery. Compound action potentials from the EMG tube in response to direct stimulation of the RLN have been commonly measured during thyroid surgery [17, 22]. However, visual nerve identification remains the gold standard of RLN management because the direct stimulation method does not decrease nerve injuries compared with visualization alone [23–25]. A stimulating probe instrument is placed on or near the nerve, resulting in the generation of a true stimulus-triggered EMG response. This method has two benefits: to verify the functional integrity of the RLN during surgery and to aid the surgeon in RLN localization [9]. However, the presence of a muscle response does not guarantee preservation of postoperative function because contraction of the target muscles may be evoked via part of the nerve distal to the site of damage, and subtle functional changes of the RLN cannot be detected [26]. In addition, Thomusch et al. [27] reported that stimulation of the vagus nerve was a significantly better predictor of postoperative dysfunction than was direct stimulation of the RLN. These results suggest that stimulating a neural pathway distant from the surgical site is one of the potentially effective techniques for evaluating integrity in the entire neural pathway. Vagal MEPs elicited by TES may enable evaluation of the integrity of the vagal pathway without identification of the nerves during thyroid surgery, not in an all-or-none fashion. A slight decrease in vagal MEP amplitude might be a warning criterion. Further studies are necessary to verify the clinical utility of vagal MEPs for preventing RLNP.

Conclusion

In conclusion, vagal MEPs could be successfully obtained in approximately 91% of the patients at a stimulation intensity of 300 V with 3 or more pulses per train. Vagal MEP amplitude changed depending on the functional status of the RLN. Our findings suggest that vagal MEP monitoring contributes to evaluation of the functional status of the RLN during thyroid surgery.

Conflict of Interest

The present research was supported solely by hospital and department sources. None of the authors have any financial interests in products related to this study.

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Figure legends

Figure 1. Relationship between stimulation site and amplitude of transcranial electrical stimulation-induced motor-evoked potentials from the left or right laryngeal muscles (vagal MEPs). There was no significant difference between right laryngeal and left laryngeal vagal MEPs when the anode was placed at C3 and the cathode was placed at Cz. Right vagal MEP amplitudes elicited by TES at C3/C4 (anode/cathode) were significantly higher than those at C3/Cz at stimulus intensities from 200 to 350 V. Data are expressed as means ± SDs (n = 8) *p < 0.05, C3/Cz stimulation versus C3/C4 stimulation for right laryngeal muscles

Figure 2. Relationship between amplitude of transcranial electrical stimulation-induced motor-evoked potentials from the laryngeal muscles (vagal MEPs) and stimulation intensity in patients without preoperative recurrent laryngeal nerve palsy. (**a**) Representative waveforms of vagal MEPs at stimulation intensities of 100, 150, 200, 250, 300, 350 and 400 V. (**b**) Mean amplitudes of vagal MEPs at the above intensities. Data are expressed as means ± SDs (n = 31)

Figure 3. Relationship between amplitude of transcranial electrical stimulation-induced motor-evoked potentials from the laryngeal muscles (vagal MEPs) and train pulse number in patients without preoperative recurrent laryngeal nerve palsy. (**a**) Representative waveforms of vagal MEPs with changes in the train pulse number from 1 to 5 at an intensity that could produce a vagal MEP amplitude of 150–200 μV in each patient. (**b**) Mean amplitudes of vagal MEPs. Data are expressed as means ± SDs (n = 31)

Figure 4. Intraoperative time course of transcranial electrical stimulation-induced motor-evoked

potentials from the laryngeal muscles (vagal MEPs) during thyroid surgery (n = 39). A: before starting surgery, B: after exposing the thyroid gland, C: removal of the thyroid gland, D: before closure, E: just after surgery. Data are expressed as percent of baseline (means ± SDs). *p < 0.05 versus baseline control before starting surgery

Figure 5. Representative waveforms of transcranial electrical stimulation-induced motor-evoked potentials from the laryngeal muscles (vagal MEPs) in a patient with preoperative unilateral recurrent laryngeal nerve palsy. Vagal MEPs were measured on both the normal and paralytic sides. (**a**) Relationship between stimulation intensity and vagal MEPs with a train of 5 pulses. (**b**) Relationship between train pulse number and vagal MEPs at a stimulation intensity of 350 V

Figure 6. Comparison of transcranial electrical stimulation-induced motor-evoked potentials from the laryngeal muscles (vagal MEPs) between the paralytic and normal sides in patients with preoperative unilateral recurrent laryngeal nerve palsy. (**a**) Stimulation intensity- and (**b**) train pulse number- (mean stimulation intensity of 300 ± 71 V) dependent changes of vagal MEPs (n = 4). Data are expressed as means ± SDs. *p < 0.05, normal side versus paralytic side

Figure 7. Representative waveforms of transcranial electrical stimulation-induced motor-evoked potentials from the laryngeal muscles (vagal MEPs) during thyroid surgery in a patient with intraoperative resection of the recurrent laryngeal nerve (RLN). Resection of the RLN resulted in sudden deterioration of vagal MEP amplitude only on the resected side (arrow). Vagal MEPs recorded from (**a**) resected side and (**b**) unresected side electrodes during thyroid surgery. A: before starting surgery, B: after

exposing the thyroid gland, C: during thyroid surgery and before resection of the RLN, D: after resection of the RLN

Table 1 Demographic characteristics and intraoperative parameters

Female / Male	40 / 14
Age (years)	56 ± 16
Body weight (kg)	59 ± 9
Height (cm)	158 ± 7
Type of disease	
Thyroid cancer	48
Goiter	6
Type of surgery	
Total thyroidectomy	28
Subtotal thyroidectomy	23
Lymph node dissection	3
Intraoperative data	
Surgery time (min)	277 ± 133
Anesthesia time (min)	342 ± 141
Blood loss (ml)	95 ± 94

Values are means ± SDs or numbers

Table 2 Demographic characteristics and surgical data of patients in two groups

	NIM™ EMG Tube (n = 15)	NIM TriVantage EMG Tube® (n = 39)	p value
Type of disease			0.17
Thyroid cancer	100% (15)	85% (33)	
Goiter	0% (0)	15% (6)	
Type of surgery			0.07
Total thyroidectomy	33% (5)	59% (23)	
Subtotal thyroidectomy	67% (10)	33% (13)	
Lymph node dissection	0% (0)	8% (3)	
Success rate of recordings			
Success rate	60%	91%	0.02*

Data are expressed as percentage (n). *p *v*alue < 0.05

Figure 1

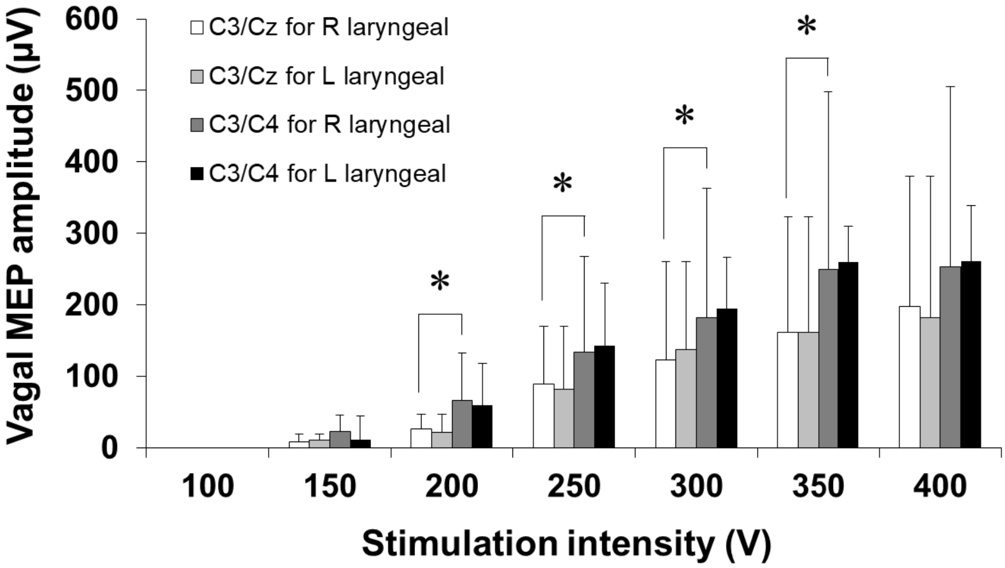

Vagal MEP amplitude (μV)
600
500
400
300
200
100
0
C3/Cz for R laryngeal
C3/Cz for L laryngeal
C3/C4 for R laryngeal
C3/C4 for L laryngeal
*
*
*
*
*
100
150
200
250
300
350
400
Stimulation intensity (V)

Figure 2

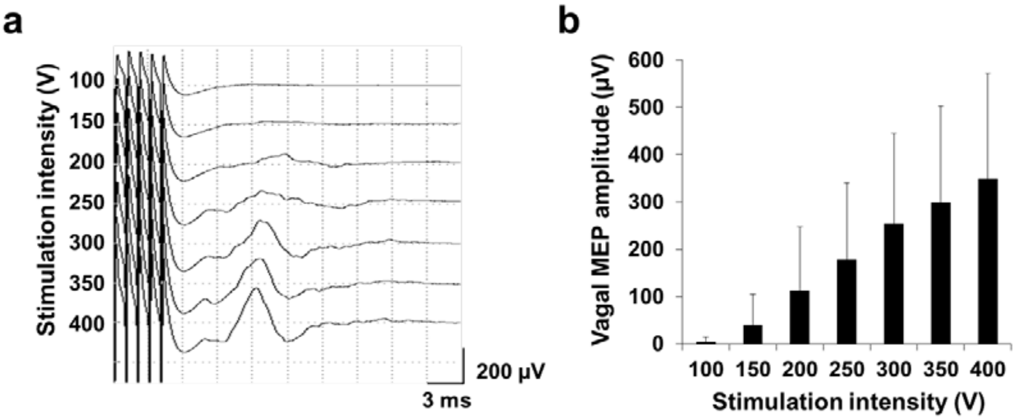

a
Stimulation intensity (V)
100
150
200
250
300
350
400
200 μV
3 ms
b
Vagal MEP amplitude (μV)
600
500
400
300
200
100
0
100 150 200 250 300 350 400
Stimulation intensity (V)

Figure 3

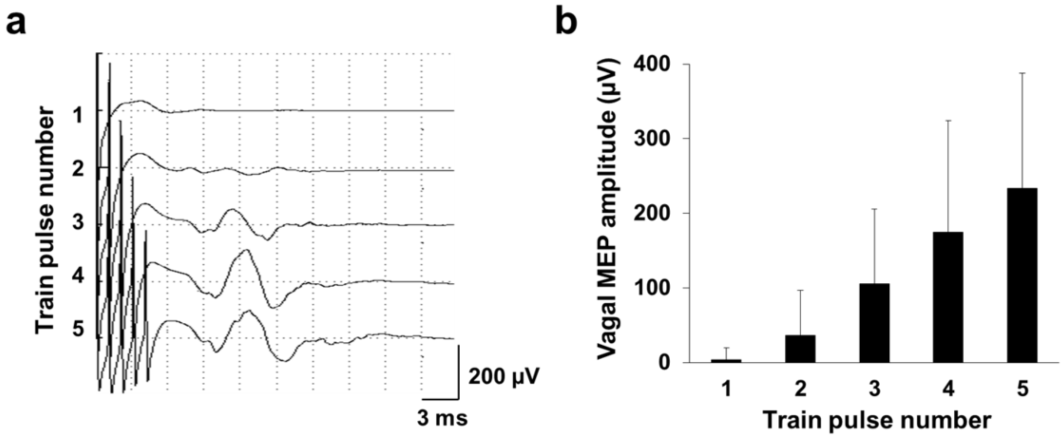

a
Train pulse number
1
2
3
4
5
200 μV
3 ms
b
Vagal MEP amplitude (μV)
400
300
200
100
0
1
2
3
4
5
Train pulse number

Figure 4

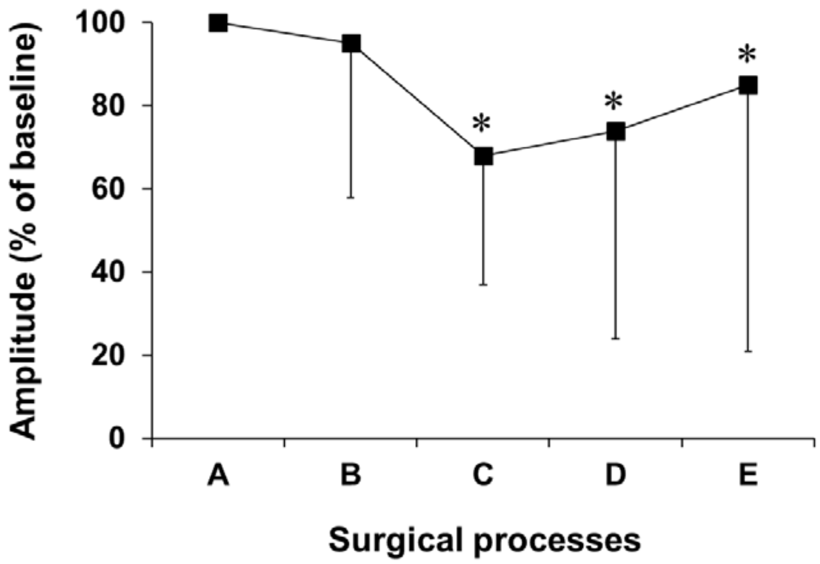

Amplitude (% of baseline)
100
80
60
40
20
0
*
*
*
A
B
C
D
E
Surgical processes

Figure 5

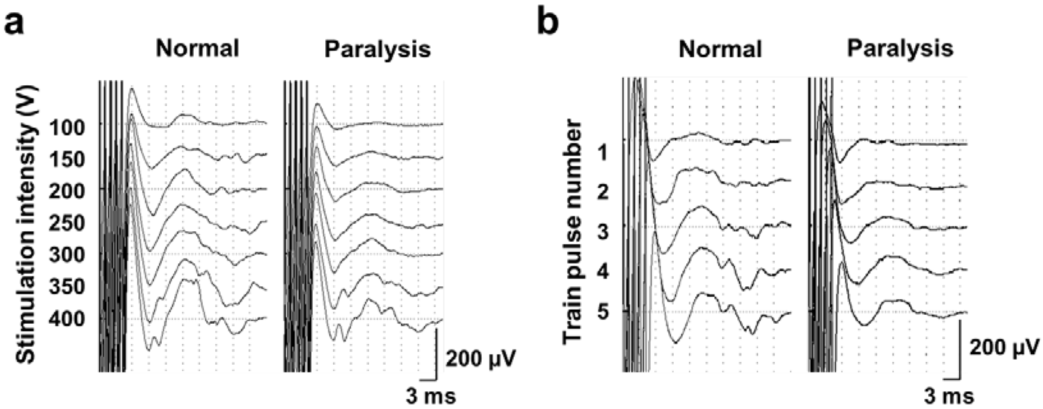

a
Normal
Paralysis
Stimulation intensity (V)
100
150
200
250
300
350
400
200 µV
3 ms
b
Normal
Paralysis
Train pulse number
1
2
3
4
5
200 µV
3 ms

Figure 6

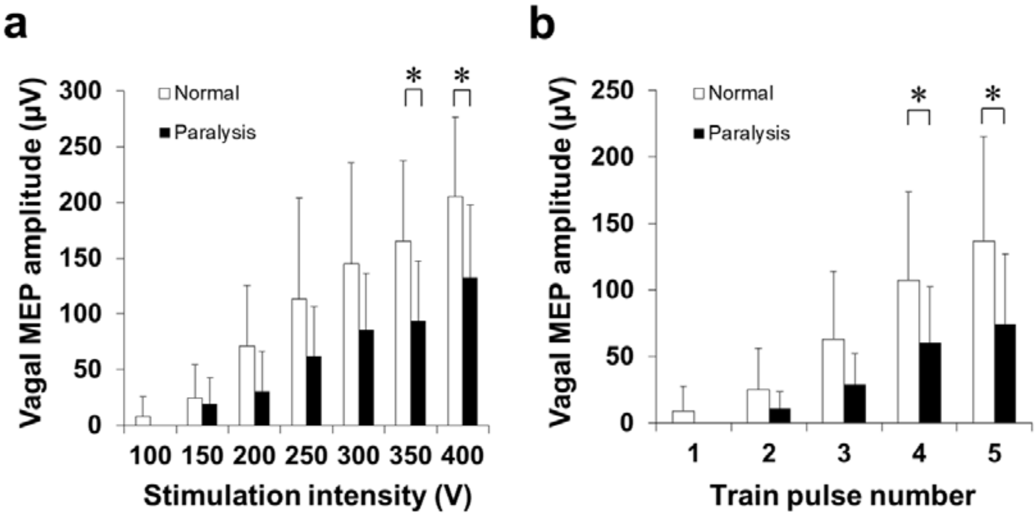
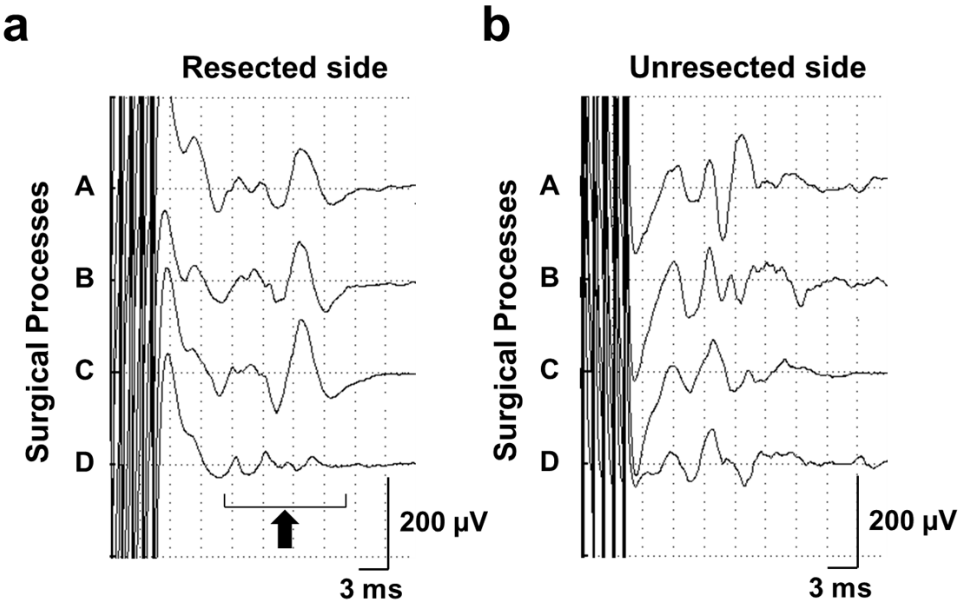

a
Vagal MEP amplitude (μV)
300
250
200
150
100
50
0
Normal
Paralysis
*
*
100 150 200 250 300 350 400
Stimulation intensity (V)
b
Vagal MEP amplitude (μV)
250
200
150
100
50
0
Normal
Paralysis
*
*
1
2
3
4
5
Train pulse number

Figure 7


a
Resected side
Surgical Processes
A
B
C
D
200 µV
3 ms
b
Unresected side
Surgical Processes
A
B
C
D
200 µV
3 ms