Resection of lesions located in or around the brainstem has a high potential for postoperative complications, such as hemiparesis, ataxia, facial palsy, or dysphagia. Dysphagia, one of the most serious complications, can result from the intraoperative damage of the corticobulbar tract, brainstem nuclei, or lower CNs. The sudden onset of unilateral or bilateral vagus nerve dysfunction leads to dysphagia and aspiration pneumonia.1,2,25

The vagus nerve has been monitored using electrodes endoscopically or laryngoscopically placed in the vocal fold, percutaneously placed transcricothyroid electrodes, or surface electrodes on an endotracheal tube.8,15,26 Using these methods, the vagus nerve was directly stimulated to confirm its integrity. Thus, it was impossible to prevent damage to the vagus nerve before exposing the nerve. The presence of muscle responses during surgery does not always indicate preservation of postoperative vagus function.16,17 In addition, monitoring function in this way is particularly difficult in patients harboring large tumors.1,21

For preservation of swallowing function, continuous monitoring of not only vagal rootlets but also of the endotracheal tube electrode recording was a safe and effective method to provide continuous real-time information on the integrity of both the supranuclear and infranuclear vagal pathway. This method is useful to prevent intraoperative injury of the brainstem corticobulbar tract or the vagal rootlets and to avoid the postoperative dysphagia that is often associated with brainstem or skull base surgeries.

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corticobulbar tract of the vagus pathway is needed. Although monitoring the MEPs from the vocal muscle by transcranial or direct motor cortical stimulation has been reported, recording required direct needle insertion into the vocal cord. Here, we present a method for intraoperative monitoring of vagus nerve function using endotracheal tube surface electrodes with transcranial electrical stimulation, and we report the resulting postoperative swallowing function.

Methods

Patient Population

Between April 2009 and June 2010, 15 consecutive patients ranging in age from 19 to 69 years (mean 49.5 years) underwent resection of tumors around the brainstem at Fukushima Medical University (Table 1). Among these patients, 3 suffered from swallowing disturbance before surgery due to vagus nerve palsy, 2 with petroclival meningioma and 1 with jugular foramen schwannoma. The trial protocol was reviewed and approved by the local independent ethics committee. Informed consent was obtained from all patients or their legal representatives before enrollment in the study.

Recording Electrodes

The recording method adopted for this research was based on the method reported by Mikuni et al. Electromyography signals from the vocal cords were recorded using an endotracheal tube (Xomed, Medtronic, Inc.) fitted with 4 stainless steel wire electrodes (2 pairs, each positioned on the right and left sides). To contact the vocal cords, the electrodes were exposed for only a short distance slightly superior to the cuff. On intubation, the endotracheal tube was placed by an anesthesiologist so that the bilateral vocal cords were symmetrically in contact with the paired electrodes.

Transcranial Electrical Stimulation

Corkscrew electrodes were placed subdermally on the scalp at C3 and C4 according to the International 10-20 System for electrode placement. The anode and cathode were switched according to the hemisphere stimulated. A 5-pulse monopolar anodal electrical stimulus was applied. The frequency of the train pulse was 1000 Hz, and the duration of each single pulse was 0.05 msec. Intraoperatively, the motor cortex was stimulated using a voltage 20% above the threshold level.

Although both sides of the motor cortex were stimulated during surgery, the stimulation side was chosen from the side of the main tumor location. In patients with lesions located in or around the midbrain and/or pons, the ipsilateral side of the lesion was stimulated transcranially. In patients with lesions located in or around the medulla oblongata and/or vagus nerve rootlets, the contralateral side of the lesion was stimulated.

Anesthesia

Anesthesia was induced with a bolus injection of propofol (1.5–2.0 mg/kg) and fentanyl (2 mg/kg) and was maintained by the continuous infusion of propofol (6–10 mg/kg/hr). Additional fentanyl (2 mg/kg) was injected every 60 minutes. Before tracheal intubation, all patients received a vecuronium bromide bolus injection (0.1 mg/kg) followed by drip infusion (0.07–0.15 mg/kg/hr) to maintain a stable level of neuromuscular blockade. The muscle relaxation level was monitored by recording the compound muscle action potentials of the abductor pollicis muscles or by observing accelerated thumb movement after electrical stimulation of the ulnar nerve. For that purpose, we used 2-Hz train-of-4 electrical stimulations of the ulnar nerve and measured the acceleration of thumb movement with an acceleration transducer. The train-of-4 ratio, [(acceleration by the fourth stimulation/acceleration by the first stimulation) × 100] was maintained between 1% and 15%.

Motor Evoked Potential Recording

Motor evoked potential monitoring was started after the train-of-4 ratio became stable. Stimulation-elicited compound muscle action potentials were recorded repetitively during surgical procedures. The filter settings were 50–100 Hz (low bandpass) and 2 kHz (high bandpass). The operator received a warning when an MEP disappeared or its amplitude decreased to less than 50% of the control level in 3 consecutive recordings (a few seconds after initiation of the change). To monitor the corticospinal tract, compound muscle action potentials were recorded from the contralateral thenar muscles with a pair of subcutaneous stainless steel needle electrodes (CN 10669; Unique Medical Co. Ltd.). Each change in MEP recording was assessed by a clinical laboratory technologist.

Functional Grade of Swallowing

Swallowing was assessed clinically using criteria adapted from the following reported protocol. Grade 1, independent swallowing (normal swallowing for all food consistencies or difficulty during the oral to pharyngeal phases with spontaneous compensation and cleaning of residual food with no signs of tracheal aspiration and/or laryngeal penetration); Grade 2, mild dysphagia (slight aspiration of liquids with cough reflex); Grade 3, moderate dysphagia (aspiration for 2 or more food consistencies with or without cough reflex, good compensation during postural maneuvers); and Grade 4, severe dysphagia (aspiration for 2 or more food consistencies with or without cough reflex, no compensation during postural maneuvers, indication for enteral feeding). Swallowing assessment was performed before surgery and 3 days, 1 week, and 4 weeks after surgery.

Results

Motor Evoked Potentials of the Vagus Nerve

Compound muscle action potentials from the vocalis muscle were assessed intraoperatively in all patients, except for the left side of 1 patient (Case 1) who had left vagus nerve palsy before surgery. Baseline MEPs were obtained with the threshold of transcranial electrical stimulation ranging from 140 to 230 V (mean 168 ± 36 V [± SD]). The latency of compound muscle action poten-
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Diagnosis</th>
<th>Affected Brainstem or Vagal Rootlets</th>
<th>Surgical Approach</th>
<th>Tumor Resection</th>
<th>Side of Transcranial Stimulation</th>
<th>MEP Amplitude†</th>
<th>Tumor Dissection–Induced MEP Changes</th>
<th>Functional Grade of Swallowing</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Contralateral Thalamus Muscle</td>
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<td>1</td>
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<td>transcondylar fossa</td>
<td>partial</td>
<td>rt</td>
<td>consistent</td>
<td>ND</td>
<td>consistent</td>
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<tr>
<td>2</td>
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<td>MB, pons, MO</td>
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<td>partial</td>
<td>lt</td>
<td>permanent &lt;50%</td>
<td>permanent &lt;50%</td>
<td>transient 10%</td>
</tr>
<tr>
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<td>pons</td>
<td>lat suboccipital</td>
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<td>lt</td>
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<td>permanent &lt;50%</td>
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<tr>
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<td>MB, pons, MO</td>
<td>combined petrosal</td>
<td>partial</td>
<td>lt</td>
<td>permanent &lt;50%</td>
<td>consistent</td>
<td>from pons</td>
</tr>
<tr>
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<td>MO, vagal rootlets</td>
<td>lat suboccipital</td>
<td>partial</td>
<td>lt</td>
<td>permanent &lt;50%</td>
<td>consistent</td>
<td>from pons</td>
</tr>
<tr>
<td>6</td>
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<td>MB, pons, MO</td>
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<td>total</td>
<td>rt</td>
<td>permanent 0%</td>
<td>permanent &lt;50%</td>
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</tr>
<tr>
<td>7</td>
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<td>pons, MO</td>
<td>lat suboccipital</td>
<td>partial</td>
<td>rt</td>
<td>transient 0%</td>
<td>consistent</td>
<td>from pons</td>
</tr>
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<td>rt clival chordoma</td>
<td>MB, pons</td>
<td>posterior petrosal</td>
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<td>lt</td>
<td>transient 0%</td>
<td>consistent</td>
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<td>lt</td>
<td>consistent</td>
<td>consistent</td>
<td>transient 5%</td>
</tr>
<tr>
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<td>pons</td>
<td>lat suboccipital</td>
<td>total</td>
<td>rt</td>
<td>consistent</td>
<td>consistent</td>
<td>consistent</td>
</tr>
<tr>
<td>11</td>
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<td>pons</td>
<td>lat suboccipital</td>
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<td>rt</td>
<td>consistent</td>
<td>consistent</td>
<td>consistent</td>
</tr>
<tr>
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<td>pons</td>
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<tr>
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<td>pons, MO</td>
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<td>total</td>
<td>lt</td>
<td>consistent</td>
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<td>consistent</td>
</tr>
<tr>
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<td>MO, vagal rootlets</td>
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<td>lt</td>
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<td>consistent</td>
</tr>
<tr>
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<td>pons</td>
<td>suboccipital</td>
<td>total</td>
<td>rt</td>
<td>consistent</td>
<td>consistent</td>
<td>consistent</td>
</tr>
</tbody>
</table>

* MB = midbrain; MO = medulla oblongata; ND = not determined.
† “Consistent” indicates a consistent MEP amplitude greater than 50% of control level.
The amplitude of control MEPs at the start of surgery ranged from 20 to 600 μV (mean 118.5 ± 115.2 μV). No complications associated with the placement of the endotracheal tube electrodes on the vocal cord were observed. There were no signs of abnormal changes in heart rate or arterial blood pressure during MEP recording.

**Motor Evoked Potential Findings and Postoperative Swallowing Function**

In 1 patient with left jugular foramen schwannoma (Case 1), left vagal MEPs were not obtained (Table 1). Therefore, it was impossible to evaluate the postoperative swallowing function from the MEP findings in this case. In 7 patients (Cases 2–8), the MEP amplitude transiently deteriorated to less than 50% of the control level on the right side. In Cases 2, 3, 4, and 6, MEPs of both sides deteriorated when menigiomas compressing the brainstem were dissected from the pons or basilar artery. In Case 5, with right jugular foramen schwannoma, right vagal MEPs decreased when the tumor was dissected from the vagal rootlets, while left MEPs showed no change. These 5 patients had postoperative dysphagia, which gradually improved. At 4 weeks after surgery, 2 patients still had Grade 2 and 3 dysphagia.

In 2 patients (Cases 7 and 8), vagal MEPs of 1 side transiently disappeared when the tumors were dissected from the brainstem or the vagal rootlets. The MEP amplitude in these patients returned to greater than 50% of the control level during surgery. After surgery, both patients had dysphagia of functional Grade 3 or 4 but recovered to Grade 1 at 4 weeks.

In 7 patients (Cases 9–15), the MEP amplitude was consistent, maintaining more than 50% of the control level throughout the operative procedures. After surgery, all 7 patients were neurologically intact with functional swallowing (Grade 1).

**Illustrative Cases**

**Case 3: Evaluation of the Corticobulbar Tract**

This 19-year-old woman was referred to us with left-sided facial palsy and hearing loss. Magnetic resonance imaging demonstrated a tumor mass in the left CPA that was strongly compressing the brainstem and cerebellum with brain edema (Fig. 1A). The tumor was subtotally resected via a right lateral suboccipital approach (Fig. 1B). At that time, the right vagal MEP response from the left motor cortex stimulation also deteriorated. After tumor resection, the MEP amplitude recovered to greater than 50% of the control level. Postoperatively, swallowing function deteriorated to Grade 4 and recovered within 4 weeks. During the second operation, the remnant tumor was totally resected via a craniofacial approach.

**Discussion**

The significance of intraoperative motor function monitoring using transcranial electrical stimulation of the motor cortex on aneurysm or tumor surgeries has been reported.11,13,14,18 Stimulation-elicited compound muscle potentials were recorded from thenar, abductor pollicis, flexor carpi radialis, and anterior tibial muscles or corresponding muscles for spinal lesions to monitor the corticospinal motor pathway. Recent studies have demonstrated that facial nerve function can be monitored using MEPs by transcranial stimulation.1,4,6,22,28,30 In the present study, we have demonstrated that intraoperative compound electromyographic activity from the vocalis muscle was successfully monitored using surface electrodes on an endotracheal tube by transcranial electrical stimulation of the motor cortex. The vagal MEPs were used to monitor the vagus nerve pathway from the corticobulbar tract to the vagus nerve rootlets.

Previously reported techniques for monitoring the function of the vagus nerve recounted clinical problems with electrode placements or stimulation methods. Placement of the electrodes required invasive or complicated procedures, including insertion of a needle electrode through percutaneous puncture or by surgical exposure of the cricothyroid ligament, laryngoscopic placement of a postcricoid surface paddle-style electrode, or laryngoscopic insertion of a needle electrode into the vocal cord.11,15,26 Continuous observation of the vocal cord movement required consistent placement of a laryngoscope and direct inspection when the vagus nerve nucleus was directly stimulated through the floor of the fourth ventricle.27 The observer might not correctly identify the discrete movements of the vocal cord elicited by the stimulation.

In previous reports, the vagus nerve or nucleus was directly stimulated.3,10,17,24 Mikuni et al.10 successfully used endotracheal tube electrodes to monitor the activity of the vagus nerve by direct stimulation. Since direct stimulation methods require identification of the nerve or the nucleus at the brainstem, these procedures cannot provide continuous real-time monitoring before or during resection of the
Intraoperative monitoring of vagal MEPs

lesion. Direct stimulation is particularly difficult in patients harboring large tumors. In addition, the presence of muscle response during surgery does not always indicate preservation of the postoperative function because part of the nerve distal to the damage may transmit signals to the target muscles. The simple method presented here can evaluate the functional integrity of the vagal pathway from the corticobulbar tract, nucleus of the vagus, vagal rootlet, and laryngeal nerve without interruption.

Recent studies have demonstrated that MEPs by transcranial stimulation have been used to evaluate the corticonuclear tract in the CNs, such as facial nerve function. Deletis et al. also reported a method for monitoring MEPs from the vocal muscles by using hook wire electrodes for transcranial or direct cortical electrical stimulation. Our method using transcranial stimulation made it possible to monitor the corticobulbar tract continuously and to detect functional damage of the tract during surgery. One side of the transcranial stimulation induced bilateral vagal MEPs since the motor neurons directly innervate the bilateral nucleus ambiguus. Therefore, damage at the level of the supranuclear corticobulbar tract induced deterioration of bilateral vagal MEPs, whereas the damage at the level of the infranuclear pathway, such as the nucleus ambiguus or vagal nerve rootlets, induced unilateral deterioration.

In the present study, MEPs of the hand were also monitored. In 7 patients without deterioration of vagal MEPs, results of vagal and hand MEPs were compatible. Six patients showed no change and 1 showed transient deterioration in MEPs of the hand. In Cases 1 and 5, MEPs of the hand did not change since the tumor mainly affected the vagal rootlets. In another 6 patients with transient or permanent deterioration of vagal MEPs, results of vagal and hand MEPs were not equivalent. Deterioration of vagal and hand MEPs probably implies damage in different areas of the brainstem since tumors compressing the brainstem could shift and fan the corticobulbar and corticospinal motor fibers. Surgical maneuvers to dissect tumors from the brainstem may directly damage the nuclei or motor fibers in addition to causing the vascular injuries. Further analysis of cases is required to clarify the clinical value of the discrepancies in corticobulbar and corticospinal MEPs. Vagal MEPs by transcranial electrical stimulation could be an additional important monitoring method for tumors compressing the brainstem.

Damage to the corticobulbar tract can have a significant effect on the swallowing mechanism. Several clinical reports have indicated that corticobulbar dysfunction, especially from cerebrovascular disorders, may result in dysphagia. The incidence of dysphagia in conscious patients after stroke has been reported to range from less than 30% to more than 50%. Accurate continuous monitoring of both supranuclear and infranuclear parts of the vagus nerve pathway is of great value for brainstem or skull base surgeries since the monitoring can contribute to assessments of the intraoperative damage of the brainstem and/or the vagus nerve and to prevent postoperative

Fig. 1. Case 3. Evaluation of the corticobulbar tract. A: Preoperative MRI study demonstrating a tumor in the left CPA, which strongly compresses the brainstem and cerebellum. B: Postoperative MRI study demonstrating subtotal removal of the tumor. C: Vagal MEP recordings from bilateral electrodes on an endotracheal tube. During dissection of the tumor from the brainstem, MEP amplitudes on both sides deteriorated and persisted after tumor resection. D: Illustration demonstrating the damaged site (X) of the vagal pathway.
dysphagia. However, previously available intraoperative techniques were insufficient to provide reliable prognostic data of postoperative swallowing function.\(^2\) In this study, we demonstrated that the stable MEP activities from the vocalis muscle during surgery predicted a good outcome of postoperative swallowing function. We also showed that transient deterioration of vagal MEPs may imply postoperative transient difficulty in swallowing, and patients with permanent deterioration of vagal MEPs might have permanent dysphagia.

The present study has some limitations. Besides the vagal MEP preservation, the swallowing function requires the integrity of the afferent pathway as well as other CNs such as the trigeminal, facial, and glossopharyngeal nerves. Therefore, comprehensive evaluation of swallowing function should be performed, including assessment of intraoperative monitoring of other CNs.

Another limitation is that a warning criterion of vagal MEP deterioration has not been established in the present study. For brainstem surgery, a 22\%–50\% reduction in MEP response amplitude has been proposed as a warning criterion.\(^{12,19,23}\) In the present study, we proposed a 50\% reduction in MEP amplitude as a warning criterion. When the MEPs disappeared, the surgeon received the warning immediately. When the MEP amplitude decreased to less than 50\% of the control level, the surgeon received the warning, usually after 3 consecutive recordings, requiring a few seconds. Our results of postoperative swallowing function suggested that the warning criteria are sufficient. Further studies of intraoperative vagal MEP monitoring with a larger number of patients are needed to establish a warning criterion for vagal MEP monitoring and to prevent the postoperative dysphagia after brainstem surgery.

**Conclusions**

Motor evoked potential monitoring of the vagus nerve elicited by transcranial electrical stimulation of the motor cortex and recorded using endotracheal tube electrodes was a safe and effective method providing stable responses and real-time information on the integrity of both the supranuclear and infranuclear vagal pathway. Our findings suggest that vagal MEP monitoring could contribute to preventing intraoperative injury of the brainstem corticobulbar tract or the vagal rootlets and to avoid the postoperative swallowing dysfunction in patients undergoing brainstem or skull base surgeries.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
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Author contributions to the study and manuscript preparation include the following. Conception and design: Ito. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Ito, Ichikawa, Itakura, Saito. Critically revising the article: all authors. Review and submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ito. Supervision: Sakuma, Saito.

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