Contralateral and ipsilateral corticobulbar motor evoked potentials elicited by magnetic and electrical stimulation of primary motor cortices for laryngeal muscles

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Introduction

Previous studies have shown that bilateral corticobulbar motor evoked potentials (CoMEPs) could be elicited from a single side of the laryngeal muscles by electrical and magnetic stimulation of the primary motor cortices (M1) for laryngeal representation (Ertekin et al., 2001; Khedr and Aref, 2002; Rödel et al., 2004; Deletis et al., 2008, 2009). Systematic evaluation of the cortical excitability of contralateral and ipsilateral corticobulbar projections to laryngeal muscles was not performed.

In the present study, we applied **navigated transcranial magnetic stimulation (nTMS)** generating modified patterned nTMS protocol (Rogić et al., 2014) to the M1 for the laryngeal muscle representation of the left and right hemispheres, and recorded contralateral (left-hemisphere stimulation) and ipsilateral (right-hemisphere stimulation) CoMEPs from the right cricothyroid muscle in the group of healthy subjects. In the group of patients undergoing craniotomy, CoMEPs were recorded from bilateral cricothyroid muscles by applying **transcranial electrical stimulation (TES)** over C3/Cz and C4/Cz.

Objective

The objective of this study was to evaluate the excitability of contralateral and ipsilateral corticobulbar pathways, using the methodologies of nTMS and TES.

Methodology

Healthy subjects and patients

In **11 healthy subjects**, the primary motor cortex (M1) for laryngeal muscles was mapped with **nTMS in both hemispheres** and the CoMEPs were recorded from the right cricothyroid muscle.
In **15 patients undergoing left craniotomy**, CoMEPs were obtained from cricothyroid muscles bilaterally, using **TES over C3/Cz and C4/Cz**.

nTMS mapping and procedure – healthy subjects

- A single nTMS stimuli was used to map M1 for hand muscle (abducor pollicis brevis muscle, APB), and a modified patterned nTMS protocol (Rogić et al., 2014) was used for mapping of the M1 for the cricothyroid muscle in both hemispheres. Mapping of the M1 for the APB muscle was performed to determine the resting motor threshold.

- In order to elicit CoMEPs from the cricothyroid muscle, a visual object naming task was used. The script was written for the Presentation program (Neurobehavioral Systems, Albany, CA, USA), which sent the trigger for the onset of magnetic stimulation.

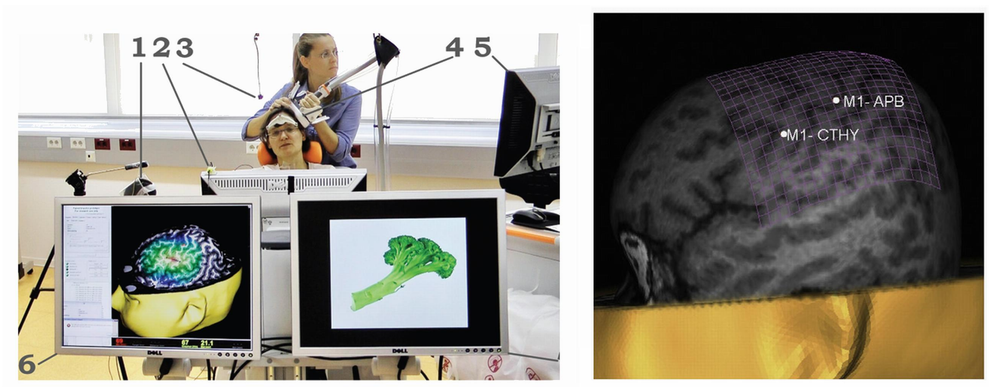

Fig 1. nTMS mapping in healthy subjects. Left: Subject during a visual object-naming task with the examiner holding the coil on the dominant hemisphere. 1 = microphone connected to electromyography amplifier, 2 = monitor with the visual object presented to the subject with the attached photo sensor for picture onset registration, 3 = microphone connected to the video camera, 4 = magnetic coil for nTMS, 5 = monitor with MRI for precise determination of stimulation site, 6 = cloned monitor 5 for video shooting, and 7 = cloned monitor 2 for video shooting. **Right**: cortical locations of M1 for hand and laryngeal muscle shown for the left hemisphere. CTHY=cricothyroid muscle

TES and procedure – patients

- Electrical stimuli were delivered through corkscrew electrodes using the 10/20 international EEG system montage: C3/Cz for the left- and C4/Cz for the right-hemisphere stimulation. Short train of stimuli protocol (Deletis et al., 2011) was used, consisting of three to five stimuli of 0.5 ms duration each, separated by a 2–4 ms interstimulus interval, with a train repetition rate of 2 Hz and a maximum intensity of up to 120 mA.

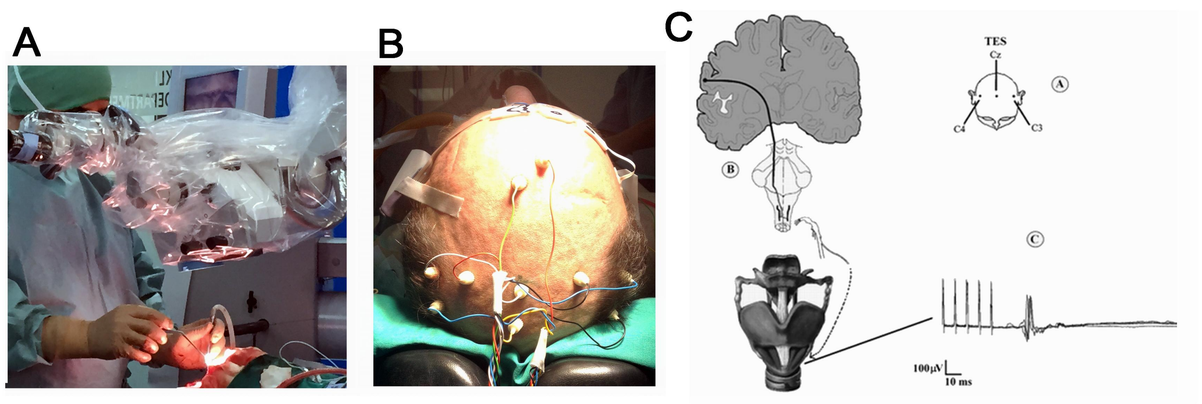

Fig 2. Intraoperative TES mapping in patients. A: Neurosurgeon during tumor operation in Clincal Medical Centre "Sisters of Mercy" Zagreb**. B: TES montage for M1 stimulation and montage for recording of somatosensory evoked potentials.. C:** Schematic of stimulation and recording. (A) Montage over the scalp for transcranially elicited CoMEPs from cricothyroid muscle. (B) Schematics of the primary motor cortex, corticobulbar pathways, vagal nucleus, vagal nerve, and superior laryngeal nerve with cricothyroid muscles. (C) Superposition of four single CoMEPs from cricothyroid muscle after TES of the M1 for the laryngeal muscles.

Recording of CoMEPs from laryngeal muscles

CoMEP responses were recorded by hook-wire electrode consisting of a 27-gauge needle and 76 μm wire (Deletis et al., 2011). Methodology for insertion of electrode is described by Hirano and Ohala (1969) and Deletis et al. (2011).

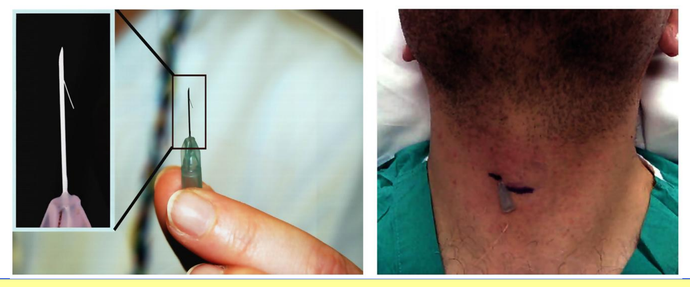

Fig 3. Hook-wire electrode and skin mark indicating position of the cricothyroid muscle with the needle inserted.

Results

► In five out of 11 healthy subjects, both contralateral and ipsilateral CoMEPs were recorded from the right cricothyroid muscle. The latency of contralateral CoMEP was 11.75 ± 2.07 ms and amplitude 288.86 ± 209.14 μV, while the latency of ipsilateral CoMEPs was 11.75 ± 1.98 ms and amplitude 144.50 ± 85.30 μV.

► In eight out of 15 patients, contralateral and ipsilateral CoMEPs were elicited with TES over C3/Cz, while in five out of 15 patients contralateral and ipsilateral CoMEPs were elicited with TES over C4/Cz. For the C3/Cz TES, the contralateral CoMEP amplitude was 334.42 ± 101.54 μV with the latency of 13.27 ± 1.87 ms, while the ipsilateral CoMEPs amplitude was 180.83 ± 103.67 μV with the latency of 13.74 ± 2.53 ms. For the C4/Cz TES, contralateral CoMEPs were recorded with the amplitude of 341.22 ± 81.98 μV and latency of 13.76 ± 2.53 ms, while ipsilateral CoMEPs were recorded with the amplitude of 154.76 ± 54.28 μV and latency of 14.58 ± 3.04 ms .

► **Overal result: Contralateral CoMEP amplitude responses were significantly larger compared to ipsilateral CoMEP amplitudes in both groups.**

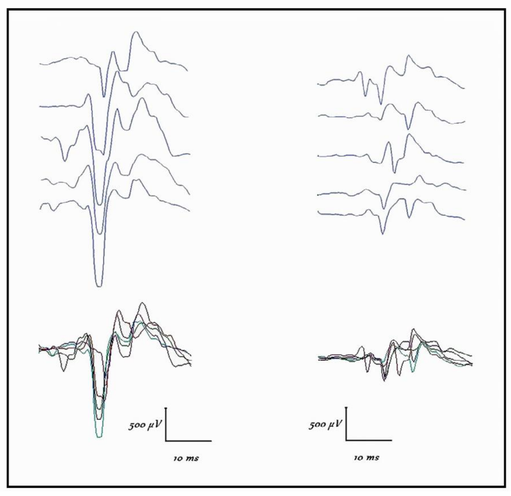

Fig 4. Shematic view of contralateral (left side of the figure) and ipsilateral (right side of the figure) CoMEP responses from the right cricothyroid muscle elicited by nTMS of the left hemisphere for inducing contralateral CoMEPs and right hemisphere for inducing ipsilateral CoMEPs.. Repeatability and superimposed CoMEP responses are presented.

Conclusions

We obtained significantly larger amplitude responses of contralateral CoMEPs from cricothyroid muscles compared to ipsilateral CoMEP amplitude using nTMS in healthy subjects and TES in patients. This confirms the bilateral nature of corticobulbar pathway projections for laryngeal muscles, with contralateral domination.

Significance

The results of the bilateral nature of corticobulbar projections to the laryngeal muscles will influence decision-making for optimal recording of CoMEPs with regard to the lesion site during preoperative and intraoperative mapping of M1 for laryngeal muscle representation.
The findings are also of particular importance in the light of pathophysiological studies aimed at understanding the mechanisms of motor speech disorders (such as stuttering, cluttering, dysarthria or tick disorder) as well as for studying cortical excitability in patients with sleep apnea.

References

Ertekin et al. **Clin Neurophysiol 2001**;112:86–94; **Espadaler** et al. **Clin Neurophysiol 2012**;123:2205–11; **Hirano and Ohala. JSLHR 1969**:362–73.; **Khedr and Aref. Eur J Neurol 2002**;9:259–67.; **Deletis** et al. **Riv Med 2008**;14:159–65.; **Deletis** et al. **Clin Neurophysiol 2009**;120(2):336–41.; **Deletis** et al. **Clin Neurophysiol 2011**;122(9):1883–9.; **Rödel** et al. **Laryngoscope 2004**;114:918–22.; **Rogić** et al. **J Neurosurg 2014**;120(5):1033–41.; **Rogić Vidaković** et al. **Clinical Neurophysiology 2015**; 126(8); 1570-1577.; **Ulkatan** et al. **J Neurosurg 2007**;106:519–20.