Influence of repeated oral and maxillofacial region movement to central nervous system and motor learning at stomatognathic system

（口腔顎顔面領域における反復運動が中枢神経系および顎口腔系の運動学習へ及ぼす影響）

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I. Abstract:

[Objective]

The aim of this study was to examine the effect of a combination of a repetitive tooth bite training (TBT) and a repetitive tongue lift training (TLT) on corticomotor excitability of the tongue and jaw muscles as assessed by transcranial magnetic stimulation (TMS). In addition, the purpose of this study was to investigate the effect of 3 weeks of TLT on suprahyoid muscle activities and tongue pressure during tongue lift movement in healthy participants.

[Materials and methods]

Study 1: Sixteen healthy individuals participated in three kinds of training tasks consisting of 41-min TBT, 41-min TLT, and 82-min TBT+TLT. Motor-evoked potentials (MEP) from the tongue muscle, masseter muscle, and first dorsal interosseous muscle were measured before and after the training tasks.

Study 2: Eight healthy participants performed a standardized 58 min of TLT consisting of three series for 3 weeks (5 consecutive days / week). Tongue pressure and electromyogram activity (EMG) from suprahyoid muscles were recorded during TLT at Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3. During TLT, in the first and third series, all participants performed tongue lift movement (at 10, 20, and 40% of maximum voluntary contraction (MVC)) without visual feedback. During second series, all participants performed tongue lift movement with visual feedback of the force level.

[Results]

Study 1: The amplitude of tongue MEPs after training with TLT and TLT+TBT, and masseter MEPs after training with TBT and TLT+TBT, were significantly higher than before training ($P<0.05$). Tongue MEPs and masseter MEPs were significantly higher after TLT+TBT than after TBT or TLT ($P<0.05$).

Study 2: The tongue pressures during 100% MVC at Day-1 in Week-3, and Day-5 in Week-3 were significantly higher than the tongue pressure during 100% MVC at Day-1 in Week-1 as baseline ($P < 0.05$). Coefficients of determination (CDs) of the target force level–tongue pressure, which were used to evaluate the accuracy of performance, at Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3 were significantly higher than that at Day-1 in Week-1 ($P < 0.05$). However, there were no significant differences in relative ratios of root mean square of EMG amplitude on the first series among any of the measurement points in each force level.

[Conclusion]

These results suggest that a task combining both jaw and tongue movement training is associated with a greater degree of neuroplasticity in the corticomotor control of jaw and tongue muscles than either task alone. In addition, that long-term of TLT with day off (assuming of weekend) improved not only accuracy of the performance to reach target force level, but also the maximum tongue pressure without the alternation of suprahyoid muscles activities in healthy subjects. These findings may affect rehabilitation of complex sensorimotor functions, including jaw and tongue muscle tissue, in patients suffering from orofacial sensorimotor dysfunction and stroke patients with dysphagia.

II. Introduction

Animal and human studies have both convincingly shown that cortical control of the jaw and tongue muscles allows for fine regulation and accurate coordination of jaw and tongue movements needed to execute fast and highly complex oral sensorimotor tasks, respectively[1-5]. The motor cortex in animals indeed plays a significant role in the fine control of jaw and tongue movements such as those associated with tongue protrusion and the semi-automatic movements associated with chewing and swallowing[6-11]. Like corticomotor control of other muscles in the body, this corticomotor control of jaw and tongue musculature is also subject to neuroplastic changes. Neuroplasticity has a role in several functions, including the capability to adapt to changes in the environment and to store information in memory associated with learning[12]. For example, training of a coordinated movement involving several muscles and joints requires an activity-dependent coupling of cortical networks[13]. In addition, training rapidly and transiently establishes a change in the cortical network representing the thumb, which encodes kinematic details of the practiced movement[14].

In the case of the corticomotor control of orofacial sensorimotor functions, several animal studies have demonstrated neuroplasticity in the motor cortex related to learning of novel sensorimotor functions in the orofacial region, and to tooth loss and other dental manipulations[5, 10, 11, 15, 16]. In addition, previous studies in humans have shown that the specific plasticity of corticomotor pathways could be established after a series of repetitive motor tasks such as jaw [17-19] or tongue movements[20-25]. Although some studies have investigated the effects of short-term training in jaw or tongue movements on corticomotor excitability related to the control of the jaw and tongue, no study has yet investigated the effect of combined training (e.g. jaw and tongue movements) on plasticity of corticomotor pathways in the same participants. Since in daily life humans perform multiple orofacial sensorimotor tasks that involves both jaw and tongue muscles, it is essential to investigate the effects of combined orofacial sensorimotor tasks on the corticomotor excitability related to the control of jaw and tongue movements.

There are isolated activation areas in the dorsal aspects of the human sensorimotor cortex whose anatomical locations are at the border between the motor cortex related to tongue motor control and jaw motor control[26]. Closely approximating and often overlapping motor cortical sites representing both tongue and jaw muscles have been demonstrated in animals[6, 7, 16, 27-29]. Our previous human studies have investigated the effects of repetitive tongue lift movements on corticomotor excitability related to the control of the jaw and tongue muscles and have suggested that repetitive tongue lift movements trigger neuroplasticity in the corticomotor representation not only of the tongue musculature but also of jaw-closing muscles[25]. However, to our knowledge, no studies have addressed the effects of combinations of repetitive tongue and jaw movements on corticomotor excitability related to the jaw and tongue musculatures. To understand better how jaw and tongue sensorimotor control is effected and to provide a neuroscientific underpinning for the establishment of rehabilitation programs for patients suffering from orofacial sensorimotor dysfunctions, it is important to clarify the possible interrelationships in corticomotor excitability related to the control of both jaw and tongue sensorimotor functions.

Tongue pressure (TP) during tongue lift movements has an important role during swallowing. To polish up the diagnosis and therapy for patients with swallowing disorders, it is essential to clarify the mechanism of control about TP during tongue lift movements in human. Past studies investigate the role of tongue lift movement during swallowing in humans. TP measurement during the tongue lift movement has an important role as clinical signs of dysphagic tongue movements[30]. Utanohara et al. demonstrated the negative correlation between maximum tongue pressure (MTP) during the tongue lift movement and aging[31]. Tsuga et al. showed that there was a significant difference in MTP between elderly participants with frail and healthy participants[32]. MTP of amyotrophic lateral sclerosis patients during the tongue lift movement were significantly lower than that of healthy participants[33]. Since these studies shows that MTP during the tongue lift movement is one of useful tools to evaluate the function of swallowing, tongue lift movement may have the potential to establish the rehabilitation program for patients with swallowing dysfunction. Final aim of our project is to establish the rehabilitation program using tongue lift movement for the stroke patients with swallowing dysfunction based on evidence from experimental data. To make the evidence about the rehabilitation program using tongue lift movement, we have previously demonstrated that repeated tongue lift training (TLT) for five continuous days or 58 min of TLT within one day can trigger neuroplastic changes in the motor cortex related to the tongue muscles in central nervous system in healthy participants[25]. We also investigated the effect of TLT for 5 continuous days on suprahyoid muscle activities and TP in healthy participants and suggested that accuracy of performance was improved without affecting MTP[34]. However, orofacial motor task as rehabilitation for the stroke patients with swallowing dysfunction will be performed for a long term. To apply our experimental data to the clinical situation, it is essential to investigate the effect of long-term tongue lift movements as rehabilitation for TP and muscle activities related to swallowing. The hypothesis of the present study was that long term of repeated tongue lift movement would improve not only the accuracy of performance but also MTP in healthy participants.

Therefore, the aim of this study was to examine the effect of a combination of a repetitive tooth bite training (TBT) and a repetitive tongue lift training (TLT) on corticomotor excitability of the tongue and jaw muscles as assessed by transcranial magnetic stimulation (TMS). In addition, the purpose of this study was to investigate the effect of 3 weeks of TLT on suprahyoid muscle activities and TP during tongue lift movement in healthy participants.

III. Materials and methods

Study 1: Combination of jaw and tongue movement training influences neuroplasticity of corticomotor pathways in humans

Sixteen healthy volunteers (7 men and 9 women) in the age range of 19–29 years (mean age ± standard deviation (SD); 22.9 ± 2.8 years) participated in the study. Before the experiment, participants were informed about the experimental procedures and informed consent was obtained from all participants. The ethics committee, Region Midtjylland, Denmark, approved the project based on the guidelines set forth in the Declaration of Helsinki II. Exclusion criteria were medical or psychological problems, epilepsy, metal implants in the head, a pacemaker, an implanted drug pump, and pregnancy. The three training tasks were performed on separate days in a randomized order. To avoid any carry-over effects, an interval of at least 1 week was set between each of the training tasks. The training tasks consisted of 41 min of TBT, 41 min of TLT, and 82 min of TBT+TLT. TBT and TLT were based on our previous experimental design[18, 25, 32]. Bite force during the TBT and tongue pressure during the TLT were measured by a tongue pressure measurement system (JMS Co., Hiroshima, Japan)[36]. Participants kept a tongue pressure probe on their anterior teeth or lips and their left hand during TBT and TLT, respectively.

In training for each task, participants performed 5 s of maximum biting on the anterior teeth three times before and after the TBT, 5 s of maximum tongue lifting three times before and after the TLT, or both tasks before TBT+TLT. Each task training consisted of three series, and one series consisted of one force level (5 kPa or 10 kPa). During the first and third series, participants were instructed to perform the different force levels without visual feedback. During the second series, participants were instructed to perform the different force levels with visual feedback of the target force level, calculated from the tongue pressure measurement system on the monitor. In each series, participants alternately performed a 30-s rest block and a 30-s task block during a 360 s period. In the task block, participants alternately performed a 5-s rest block and a 5-s task block with auditory signal (Figure 1).

During training for each task, the EMG activities from the left masseter muscle (LM), the right masseter muscle (RM), the left suprahyoid muscles (LS), and the right suprahyoid muscles (RS) were recorded. The EMG signals were amplified 5,000 times (Disa Electronik, Disa 15C01, Skovlunde, Denmark) and filtered in the bandwidth 10 Hz to 1 kHz for offline analysis.

The measurements of motor-evoked potentials (MEPs) evoked by TMS from each participant were carried out in six sessions: (1) before TBT, (2) 5 min after TBT, (3) before TLT, (4) 5 min after TLT, (5) before TBT+TLT, and (6) 5 min after TBT+TLT (Figure 1). During the measurements of MEPs evoked by TMS, EMG activities were recorded from the RM, right tongue muscle (RT), and right first dorsal interosseous (FDI: as an internal control). During the masseter MEPs measurements, participants kept a special biting device between the anterior teeth[18, 35] in order to secure constant pre-activation level of the masseter muscles, which is required for TMS to elicit a MEP[18, 37, 38]. During the tongue MEPs and FDI MEPs measurements, all participants were instructed to keep the tongue and the hand in a natural and relaxed position. The EMG signals were recorded, bandpass-filtered (10 Hz to 5 kHz), and stored on a Viking EMG apparatus (Viasys Healthcare, Madison, WI, USA) during the measurements of TMS-evoked MEPs. The TMS was delivered using a a Magstim 200 stimulator (Magstim Co., Whitland, Dyfed, UK) with a focal figure-eight coil. To standardize the anatomical locations in accordance with the 10-20 system of electrode placement, participants wore a flexible cap on their head where a coordinate system with a 1-cm location was drawn. The coil of the stimulator positioned 45 degrees from the sagittal plane, so that the induced current flowed in a plane perpendicular to the scalp sites [20-22, 39]. The scalp sites at which EMG responses were evoked in the tongue, masseter, or FDI muscles were determined according to the lowest stimulus strength. The(MT) of each muscle were measured and defined as the minimum stimulus intensity that produced 5 out of 10 clearly discernible MEPs from the background EMG activity in the muscle[18, 21, 22]. Onset latency was measured from the averaged MEPs from the non-rectified signal[21, 22].

To assess the MEPs, stimulus-response curves and motor cortex mapping were calculated from the MEP signals as previously described[19, 25]. Stimulus-response curves consisted of 90%, 100%, 120%, and 160% MT. Twelve TMS–MEPs were elicited at each intensity with an inter-stimulus interval of 10–15 s. For motor cortex mapping, eight TMS stimuli at 120% MT at each grid were applied to the sites over the scalp identified on a snugly fitting and flexible cap marked with the 1×1 cm^2 grid in an anterior-posterior and lateral-medial coordinate system[40]. The sites over the scalp covered 5 cm from the vertex and 5 cm anterior and posterior to the interaural line (a total of 25 grids). The anterior-posterior grid lines relate to the vertex (Cz) in accordance with 10-20 system of electrode placement. The first grid to be stimulated was always the center of the “hot spot”. Then the TMS coil was moved anteriorly and subsequently posteriorly at increasing and decreasing latitudes. The motor cortex areas (cm^2) calculated from MEPs having amplitudes greater than 5 μV (tongue), 10 μV (masseter), and 50 μV (FDI) were determined on the 1×1 cm^2 grid. The center of gravity (COG) was calculated according to Ridding et al[41].All data are presented as mean values and standard errors of the mean (SEM). EMG root mean square (RMS) values for each muscle (masseter and suprahyoid muscles) during each motor task were analyzed using two-way repeated measures analysis of variance (ANOVA) with three series (first, second, and third series) and side (left and right) as factors. Actual force values of the two force levels in the three series of TBT and TLT and the coefficient of variations (CVs) calculated from EMG RMS values and actual force values in the three series during TBT and TLT were analyzed with one-way repeated measures ANOVA. EMG RMS values and actual force values during maximum voluntary contraction (MVC) between before and after training tasks of TBT and TLT were analyzed with a paired *t*-test. The MT of the masseter, tongue, and FDI MEPs and onset latencies of the masseter, tongue, and FDI MEPs at the MT at each session in each training task were analyzed with one-way repeated measures ANOVA. The MEP amplitudes of the masseter, tongue, and FDI MEPs were analyzed using three-way ANOVA with stimulus intensity (90% MT, 100% MT, 120% MT, and 160% MT), training (TBT, TLT, and TBT+TLT) and time (before and after training) as factors. MEP areas of the masseter, tongue, and FDI MEPs were analyzed using two-way ANOVA with training (TBT, TLT, and TBT+TLT) and time (before and after training) as factors. The COG measures and MEP areas were analyzed using one-way ANOVA.When appropriate, the ANOVAs were followed by post hoc Tukey tests to compensate for multiple comparisons. P values less than 0.05 were considered significant. All tests were carried out using STATISTICA (StatSoft Inc., OK, USA). Sample size was calculated using G-Power software analysis assuming an ANOVA and a significant level of 0.05. A sample size of sixteen participants achieves 80% power to detect a difference in terms of effect size of 0.17.

Study 2: Long-term tongue lift training effects on tongue function

The study involved 8 healthy individuals (4 women, 4 men; mean (± standard error of the mean) age, 28.2 ± 2.1yr) with normal stomatognathic function. All participants reported no medical, physical or psychological problems. Informed consent was obtained from all participants before the start of the experiment. The Institutional Ethics Committee approved the study (EC14-019), and the guidelines set out by the Declaration of Helsinki were followed.

During the TLT, a TP measurement system (JMS Co., Hiroshima, Japan)[36] was used to measure TP according to our previous study[34]. Participants sat upright and relaxed in a dental chair with the head supported by a headrest, and they kept a TP probe on their tongue and their right hand during TLT. All participants performed a standardized 58 min of TLT consisting of three series for 3 weeks (5 consecutive days / week). In each day, participants performed a maximum tongue lift movement to determine the 100% maximum voluntary contraction (MVC) before the TLT (defined as MTP during tongue lift movement). In the first and third series, participants received no visual feedback but were simply instructed to target different force levels. During the second series, muscle activity level via the TP measurement system data was displayed on a monitor for visual feedback to participants. One series consisted of three measurements (10, 20, and 40% MVC), and one measurement consisted of one force level (10, 20, or 40% MVC). During all measurements, participants alternated between a 30-s rest-block and a 30-s task-block for 360 s. In the task-block, participants alternated between a 5-s rest-block and a 5-s task-block, at a given auditory signal. To avoid tongue muscle fatigue, a 30-s rest period was allowed between each series.

The TP from the TP measurement system were recorded during all tasks at Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3 (Figure 2). TP during each task was also calculated for each 5 s period for all participants. To evaluate the accuracy of the performance on each day, the coefficient of determination (CDs) of the target force level–TP curve were calculated from the first and third series on the measurement points. Electromyogram (EMG) of the left suprahyoid (LS) and right suprahyoid (RS) muscles was recorded using disposable bipolar surface electrodes (NM319Y; Nihon Kohden, Tokyo, Japan) at Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3. EMG activity during each task was initially quantified by calculating the root mean square (RMS) of EMG amplitude in each 5-s period from LS and RS. Relative ratios of RMS of EMG amplitude in each force level on each first series were calculated.

All data was presented as mean values and standard errors of the means. MTP during tongue lift movement was analyzed with one-way analysis of variance (ANOVA) among the measurement point. CDs of the target force level–TP curve was analyzed with two-way ANOVA with series (the first and third series) and measurement points (Day-1 in Week 1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3) as repeated measures. As suprahyoid muscles activities, relative ratios of RMS of EMG amplitude in each force level on the first series were analyzed with one-way ANOVA among the measurement point. Values of $P < 0.05$ were considered significant.

IV. Results

Study 1: Combination of jaw and tongue movement training influences neuroplasticity of corticomotor pathways in humans

1. Performance of the TBT, TLT, and TBT+TLT

Figure 3A-D shows comparisons of EMG RMS values between each series in each muscle for each training task. EMG RMS values during each motor task were not significantly dependent on series and side (Figure 3A-D). Figure 3E-H shows comparisons of EMG RMS values and actual forces during maximum voluntary contraction before and after TBT or TLT. There were no significant differences in EMG RMS values and actual forces during MVC between before and after the training for any task (Figure 3E-H).

2. Motor-evoked potential recordings

The MTs of the masseter were significantly lower after TBT than before TBT ($P < 0.005$). The MTs of the tongue were significantly lower after TLT than before TLT ($P < 0.05$). In

TBT+TLT, the MTs of the masseter and tongue were significantly lower after TBT+TLT than before TBT+TLT ($P < 0.005$). The MTs of the FDI were not significantly different between before and after training in each task. The onset latencies of the masseter MEPs, tongue MEPs, and the FDI MEPs were not significantly different between before and after training in each training task.

3. Stimulus-response curves

The tongue MEPs were significantly dependent on stimulus intensity ($F_{3, 135} = 2.60$, $P < 0.001$) and on time ($F_{1, 45} = 1.38$, $P < 0.001$) but not on training ($F_{2, 45} = 29.1$, $P = 0.065$). In TLT, there were significantly higher tongue MEPs after the training task at 160% MT stimulus intensity than before the training task ($P < 0.001$) (Figure 4A). In TBT+TLT, there were significantly higher tongue MEPs after the training task at 120% MT and 160% MT stimulus intensity than before the training ($P < 0.001$) (Figure 4C). The masseter MEPs were significantly dependent on stimulus intensity ($F_{3, 135} = 3,92$, $P < 0.001$), on training ($F_{1, 45} = 48.2$, $P < 0.05$), and on time ($F_{2, 45} = 2.35$, $P < 0.001$) (Figure 5B and C). In TBT, there was significantly higher masseter MEPs after the training at 120% MT and 160% MT stimulus intensity than before the training task ($P < 0.001$) (Figure 5B). In TBT+TLT, there were significantly higher masseter MEPs after the training task at 120% MT and 160% MT stimulus intensity than before the training task ($P < 0.001$) (Figure 5C). The FDI MEPs were significantly dependent on stimulus intensity ($F_{3, 135} = 3.66$, $P < 0.001$), but they were not significantly dependent on training ($F_{1, 45} = 0.01$, $P = 0.990$) and on time ($F_{2, 45} = 0,05$, $P = 0.817$) (Figure 6).

Figure 7 shows comparisons of masseter MEPs, tongue MEPs, and FDI MEPs after the training task among TBT, TLT, and TBT+TLT. The tongue MEPs in TBT+TLT at 120% MT and 160% MT stimulus intensity were significantly higher than in TBT at 120% MT and 160%

MT stimulus intensity ($P < 0.001$), and in TLT at 160% MT stimulus intensity ($P < 0.05$) (Figure 7A). The masseter MEPs were significantly higher in TBT+TLT at 120% MT and 160% MT stimulus intensity than in TLT at 120% MT and 160% MT stimulus intensity ($P < 0.001$) and in TBT at 160% MT stimulus intensity ($P < 0.05$) (Figure 7B). The FDI MEPs were not significantly dependent on training task ($P = 0.979$) (Figure 7C).

4. Motor cortex areas

Tongue MEP areas were significantly dependent on training ($F_{2,90} = 3.80$, $P < 0.05$) and on time ($F_{1,90} = 46.7$, $P < 0.001$). In TLT and TBT+TLT, there were significantly larger motor cortex areas from which TMS evoked tongue MEPs by 120% MT after the training task (21.8 ± 3.7 mm^2 and 23.8 ± 2.0 mm^2, respectively) than before the training task (16.7 ± 3.9 mm^2 and 17.6 ± 2.6 mm^2, respectively) ($P < 0.001$). These tongue MEP areas were significantly higher after TBT+TLT (23.8 ± 2.0 mm^2) than after TLT (21.8 ± 3.7 mm^2) ($P < 0.05$) and after TBT (19.9 ± 3.4 mm^2) ($P < 0.001$) (Figure 8). Masseter MEP areas were significantly dependent on training ($F_{2,90} = 3.03$, $P < 0.05$), and on time ($F_{1,90} = 50.7$, $P < 0.001$). In TBT and TBT+TLT, there were significantly larger motor cortex areas from which TMS evoked masseter MEPs by 120% MT after the training task (21.8 ± 2.9 mm^2 and 23.9 ± 1.6 mm^2, respectively) than before the training task (16.6 ± 3.1 mm^2 and 16.4 ± 4.0 mm^2, respectively) ($P < 0.001$). The masseter MEP motor cortex maps were significantly higher after TBT+TLT (23.9 ± 1.6 mm^2) than after TBT (19.8 ± 4.8 mm^2) ($P < 0.05$) and after TLT (19.9 ± 3.4 mm^2) ($P < 0.001$) (Figure 9). FDI MEP areas were not significantly dependent on training ($F_{2,90} = 0.31$, $P = 0.732$) and on time ($F_{1,90} = 0.01$, $P = 0.981$). (Figure 10). There were no significant changes among sessions for any of the COG outcomes (Table 1).

Study 2: Long-term tongue lift training effects on tongue function

Figure 11 shows the comparison of MTP during tongue lift movement among the measurement point. MTP during tongue lift movement at Day-1 in Week-3, and Day-5 in Week-3 were significantly higher than that at Day-1 in Week 1 ($P < 0.05$). Figure 12 shows the comparisons of first and third series on CD of the target force level–TP at among the measurement point. CDs of the target force level–TP curve were significantly dependent on the series (the first and third series) and measurement points (Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3) ($P < 0.01$). Post-hoc testing demonstrated that CDs of the target force level–TP at Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3 were significantly higher than that at Day-1 in Week-1 ($P < 0.05$).

In suprahyoid muscles activities, Figure 13 shows the comparisons of relative ratios of RMS of EMG amplitude calculated recorded from LS and RS in each force level on the first series. There were no significant differences in relative ratios of RMS EMG amplitude on first series among any of the measurement points in each force level.

V. Discussion

Study 1: Combination of jaw and tongue movement training influences neuroplasticity of corticomotor pathways in humans

Previous studies of the cortical excitability of the limb motor cortex [12-14, 42-48] and orofacial motor cortex[1-5, 20-25] have revealed cortical neuroplasticity associated with training humans in a sensorimotor task. The present TMS study has demonstrated for the first time that a training task combining both jaw and tongue movements was associated with a greater excitability and area of the motor representation of jaw and tongue musculature in the motor cortex than a simple training task alone. These alterations are consistent with a larger degree of neuroplasticity in the corticomotor control of theses muscles in the combined task paradigm. In addition, this TMS study demonstrated that a short-term repetitive and standardized bite training on anterior teeth triggered neuroplastic changes in the corticomotor control of jaw-closing muscles and a short-term repeated and standardized TLT triggered neuroplastic changes in the corticomotor control of tongue muscles.

In the jaw sensorimotor task, the performance of a repetitive 1 hour tooth clenching / biting tasks on 5 continuous days can trigger neuroplastic changes in in the corticomotor control of the jaw musculature[18]. Zhang et al. investigated the effect of short-term (1 hour) sensorimotor training of the jaw muscles on corticomotor pathways, and their findings suggested that the short-term training task induced signs of neuroplastic changes in the corticomotor pathways related to the masseter muscle[19]. The present study applied a similar experimental design (e.g. short-term TBT) and demonstrated that the MT of the masseter MEP after the training task at 160% MT stimulus intensity were significantly higher than before the training task, whereas the MT of the tongue and FDI MEPs did not change after the training task in TBT. Moreover, in TBT, there was a significantly larger motor cortex area from which TMS could evoke masseter MEPs after the training task compared to before the task, whereas the tongue motor cortex area and FDI motor cortex area were not significantly different after the TBT. In addition, the present study demonstrated that there were no significant changes between before and 5 min after training for any of the COG outcomes of masseter MEPs. The present results suggest that a short-term TBT can indeed trigger neuroplastic changes in excitability of the corticomotor control of the masseter muscle. On the other hand, our previous study investigating the effect of TLT over 5 consecutive days on the excitability of the corticomotor representation of the human tongue and jaw musculature suggested that 5-day repeated TLT can trigger neuroplasticity reflected in sustained increased excitability of the corticomotor representation of not only the tongue muscles, but also the masseter muscles[25]. However, the present results show that the MT of tongue MEPs and the tongue motor area were not significantly different between before the TBT and after the TBT; this finding suggests that a short-term jaw sensorimotor task in contrast to a 5-day repetitive jaw sensorimotor task cannot trigger neuroplastic changes of the tongue motor representations in the human motor cortex. Additional studies are needed to investigate further the effects of a short-term jaw sensorimotor task on the excitability of the corticomotor control of both the jaw and tongue musculature.

Previous TMS studies have demonstrated that neuroplastic changes in the corticomotor excitability specifically related to tongue motor control can be induced when human participants learn to perform tongue-protrusion tasks [21-23], complex tongue tasks[24], and TLT[25]. The present findings are consistent with the specificity suggested by these previous studies since we found that short-term TLT also can trigger neuroplastic changes reflected in increased excitability of the corticomotor control of tongue musculature but not of jaw musculature. Furthermore, in investigating the effect of a combined training task involving both jaw and tongue movements on the excitability of the corticomotor control of the tongue and jaw musculature, the present study showed that the tongue MEPs at 120% MT and 160% MT stimulus intensity were significantly higher in TBT+TLT than in TBT. In addition, the masseter MEPs at 120% MT and 160% MT stimulus intensity were significantly higher in TBT+TLT than in TLT, and in TBT at 160% MT stimulus intensity, and the tongue areas in the motor cortex after TBT+TLT were significantly higher than after TLT and after TBT. These novel findings suggest that a combined sensorimotor task involving both jaw and tongue muscles may be associated with a larger degree of neuroplasticity in the corticomotor control of these muscles than either task alone. The combined task also may have clinical utility in patients who are suffering from impairment of sensorimotor functions involving the jaw and tongue muscles, such as chewing or swallowing impairment. In swallowing for example a combination of sensory stimuli (pharyngeal electrical stimulation and cold oral stimulation) combined with swallowing has recently been shown to enhance motor cortex excitability and suggested to be of potential clinical usefulness in dysphagic patients[49]. Also relevant to our findings is a study by Svensson et al. showing that the tongue protrusion task is associated with neuroplasticity of corticomotor excitability related to the tongue musculature after one hour of tongue training[21,22]. Boudreau et al. demonstrated that bi-directional tongue training and multi-directional tongue training differentially altered the excitability of the tongue motor cortex[50]. Furthermore, Lu et al. have demonstrated that a single bout of low-level tooth clenching activity (10 N) for 1 h following the same protocol used for the tongue task training studies failed to evoke any signs of neuroplasticity related to the control of the masseter muscle[17]. These studies suggest that neuroplasticity in the motor cortex may depend on the duration, direction, and force level of the specific sensorimotor task, and point to the need to further investigate the minimum level of jaw and tongue motor tasks training parameters that may lead to neuroplasticity of corticomotor excitability related to the jaw and tongue musculature.

A methodological limitation of our study was that the enhanced neuroplastic effects of the combined task involving both jaw and tongue movements (TLT+TBT), compared to the TLT or TBT alone, were not at least in part due to the longer duration of the TLT+TBT training. An additional group of either a 41-minute TLT + TBT or a 82-minute TBT and TBT would have been optimal, and could be incorporated into future studies to address further the effects on corticomotor pathways of combined tongue and jaw tasks. It should also be noted that although some studies have tested for neuroplasticity after the training has ceased[21,22], the present study did not perform follow-up TMS measurements. Thus, to clarify further the neuroplastic effects of a combined task involving both jaw and tongue movements, further investigations are warranted to define the effects as well as possible carry-over neuroplastic effects of a long-term task combining both jaw and tongue movements. Such information might also be useful clinically to improve oral rehabilitation paradigms for patients with dysphasia or dysmasesis.

Study 2: Long-term tongue lift training effects on tongue function

In the present study, our results demonstrated that when human continuously perform 58 min of TLT for 5 continuous days / week, the accuracy of performance about TLT was significantly improved after 1 week, and TP during 100% MVC was significantly increased after 2 weeks. On the other hands, there were no significant differences in suprahyoid muscles activities during TLT within 3 weeks.

Our previous study showed that a 5 consecutive days of TLT improved not MTP but the accuracy of performance about tongue lift in healthy participants[34]. In addition, 5 consecutive days of TLT can trigger neuroplastic changes in motor cortex related to tongue muscles[25]. These findings just suggested neuroplasticity in the motor cortex related to tongue movements in central nervous system occurred faster than improvement of MTP in peripheral system[25, 34]. On the other hands, our present results demonstrate that TP during 100% MVC at Day-1 in Week-3, and Day-5 in Week-3 were significantly higher than that at Day-1 in Week-1. Our present results suggest that repeated TLT has some potential to improve not only neuroplastic change in central nervous system but also MTP in peripheral system in healthy participants. Further studies applying the patients with dysphasia will be needed to clarify the control mechanism of tongue lift to establish the rehabilitation program for swallowing. To evaluate the accuracy of the target force level about TLT, we analyzed CDs calculated from TP. Our previous study investigated the effect of 5 continuous days of TLT as same as the present study paradigm and showed that the CDs of TP in the fifth day become significantly lower than in the baseline in the first day[34]. Since experimental design in the present study set 5 consecutive days / week for TLT, 2 days / week set as day off (assuming of weekend). Our present results also demonstrated that CDs of the target force level-TP in the first series on Day-1 in Week-2 were significantly higher than that at Day-1 in Week-1. In addition, Kim et al. also investigated the effect of tongue-to-palate resistance training for 4 weeks (5 days / week) on tongue muscle activity and oropharyngeal swallowing function and demonstrated that the effectiveness of the training in increasing tongue muscle activity and improving the function of swallowing in dysphagia patients[51]. Our results suggest that an adequate rest does not affect improvement of the performance of TLT.

In jaw movements as orofacial motor task, a past study investigated the effect of jaw movement task for 10 weeks on masticatory muscle activities recorded by EMG, and showed that masticatory muscle activities were significantly lower after 10 weeks than before training when the participants perform the same bite force, which may be due to motor adaptations[52]. Our previous results also demonstrated that effect of tooth clenching training for masticatory muscle activities and demonstrated that tooth clenching training significantly improve the accuracy of the performance within 5 days[18,34]. These findings suggests that training paradigm of jaw movements may improve accuracy of performance to reach target force level. On the other hands, our previous study showed although accuracy of the performance of TP was improved by TLT, suprahyoid muscle activities were not significantly changed within 5 days. Although our present study applied long-term TLT for 3 weeks, there were no significant differences in suprahyoid muscles activities within 3 weeks. Our present results suggest that although repeated orofacial motor task can improve the performance due to motor learning, mechanism of motor adaptation related muscle activities during orofacial motor task may be difference between jaw and tongue movements. However, since suprahyoid muscles activities measuring by surface EMG did not evaluate the pure muscle activities during tongue motor task as a technological limitation, this limitation may influence the no significant differences in suprahyoid muscles activities on each measurement point. Further studies are needed to investigate the motor learning of muscle activity related to swallowing.

VI. Conclusion

These results suggest that a task combining both jaw and tongue movement training is associated with a greater degree of neuroplasticity in the corticomotor control of jaw and tongue muscles than either task alone. In addition, that long-term of TLT with day off (assuming of weekend) improved not only accuracy of the performance to reach target force level, but also the maximum tongue pressure without the alternation of suprahyoid muscles activities in healthy subjects. These findings may affect rehabilitation of complex sensorimotor functions, including jaw and tongue muscle tissue, in patients suffering from orofacial sensorimotor dysfunction and patients with dysphagia.

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Tables and Figures

Table 1. Center of gravity measures from the cortical motor maps of the tongue, masseter and first dorsal interosseous (FDI) muscles.

			COG measure (cm)	
	Measurement point		**Ant-Post**	**Lat-Med**
	Tongue	**before training**	**3.1 ± 0.1**	**8.0 ± 0.1**
		after training	**3.1 ± 0.1**	**8.0 ± 0.1**
TLT	**Masseter**	**before training**	**4.1 ± 0.1**	**9.0 ± 0.1**
		after training	**4.0 ± 0.1**	**9.0 ± 0.1**
	FDI	**before training**	**1.3 ± 0.3**	**6.1 ± 0.2**
		after training	**1.3 ± 0.2**	**6.0 ± 0.2**
	Tongue	**before training**	**3.1 ± 0.2**	**8.0 ± 0.1**
		after training	**3.1 ± 0.1**	**8.1 ± 0.3**
TBT	**Masseter**	**before training**	**4.0 ± 0.2**	**9.1 ± 0.1**
		after training	**4.1 ± 0.2**	**9.1 ± 0.1**
	FDI	**before training**	**1.3 ± 0.3**	**6.0 ± 0.2**
		after training	**1.3 ± 0.3**	**6.0 ± 0.2**
	Tongue	**before training**	**3.1 ± 0.1**	**8.0 ± 0.2**
		after training	**3.0 ± 0.1**	**8.1 ± 0.3**
TLT+TBT	**Masseter**	**before training**	**4.0 ± 0.1**	**9.0 ± 0.1**
		after training	**4.1 ± 0.2**	**9.1 ± 0.1**
	FDI	**before training**	**1.3 ± 0.3**	**5.9 ± 0.3**
		after training	**1.3 ± 0.3**	**6.1 ± 0.2**

Mean ± SE. Ant- Post; anterior-posterior, Lat-Med; lateral-medial.

TLT; tongue lift training, TBT; teeth bite training, FDI; first dorsal interosseous.

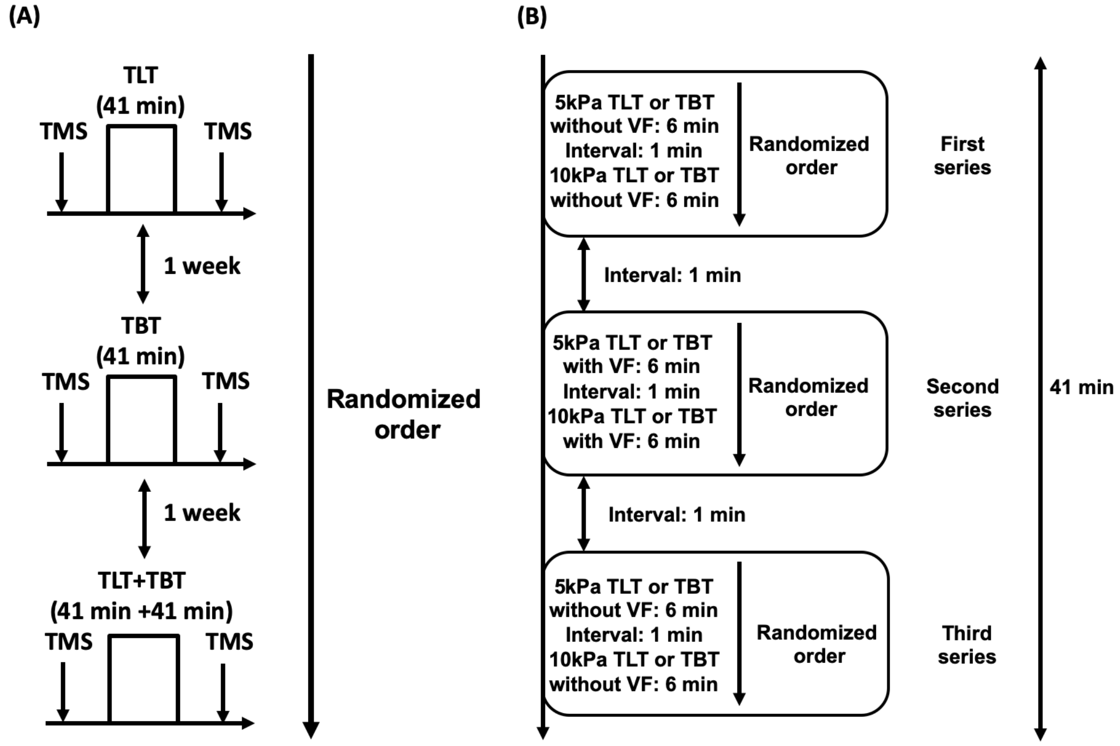


Figure 1. Overview of study design (A) and TBT or TLT (B).

TBT; tooth bite training, TLT; tongue lift training, VS; visual feedback,

TMS; Transcranial magnetic stimulation, MVC; maximum voluntary contraction.

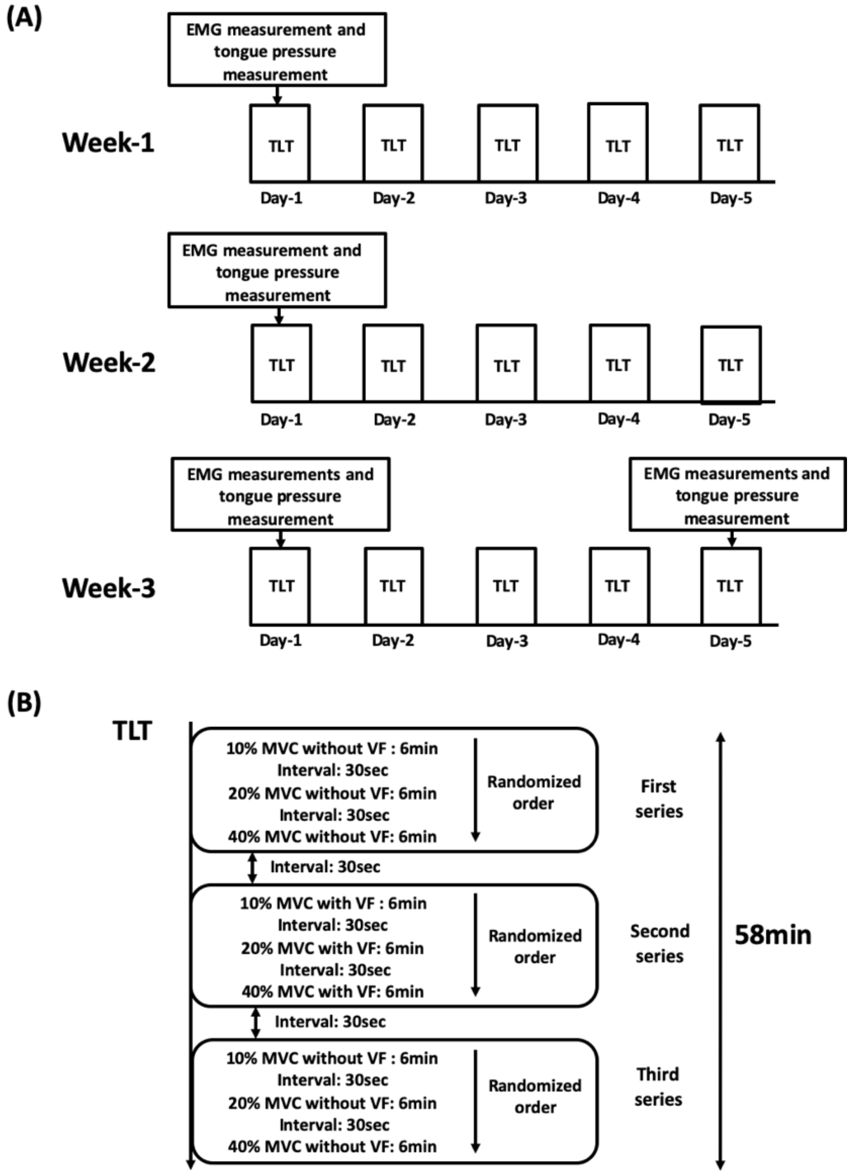


Figure 2. Overview of experimental protocol (A) and Overview of tongue lift training (B)

Abbreviations

EMG; electromyogram, TLT; tongue lift training, VF; visual feedback.

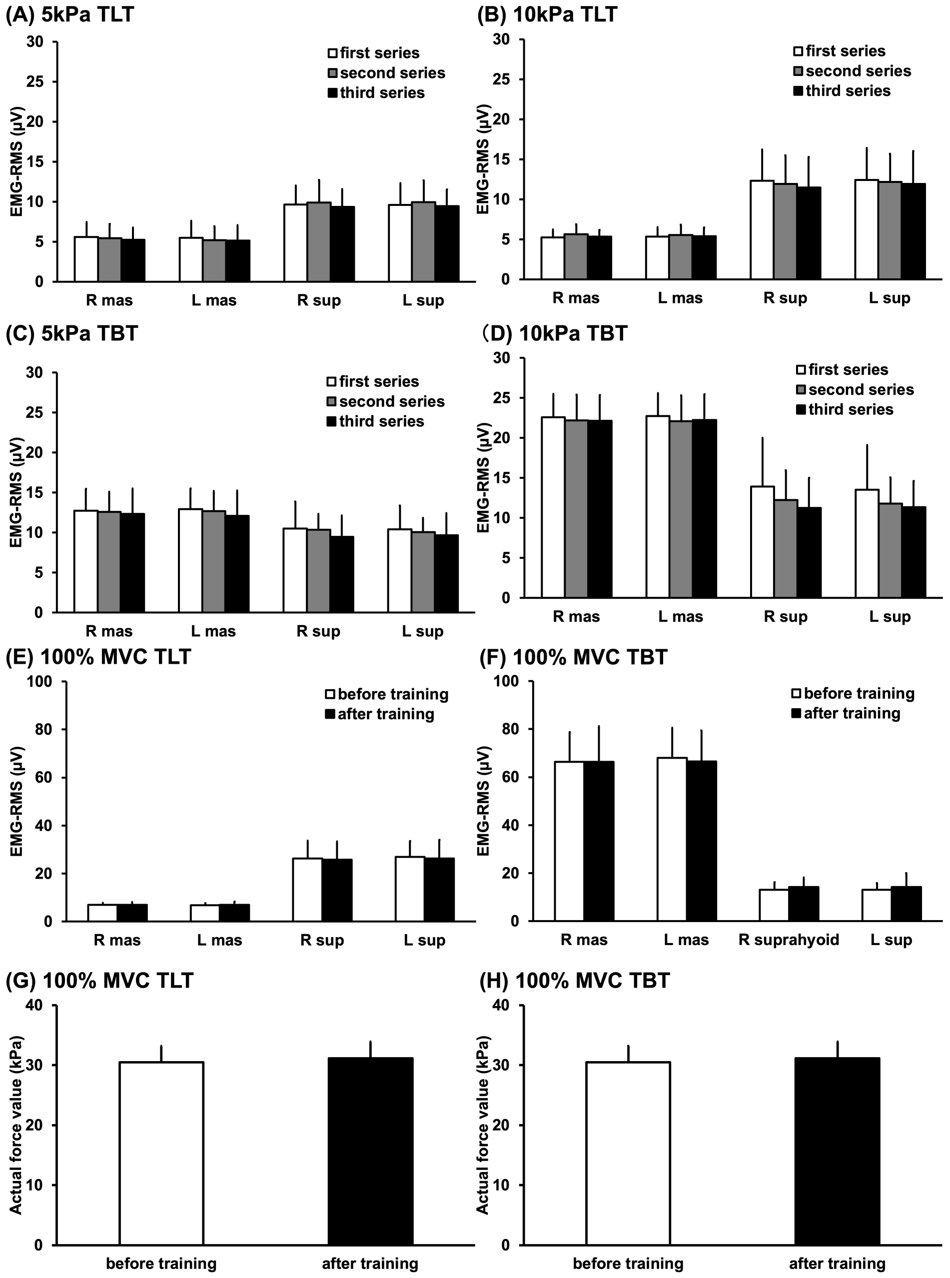


Figure 3. Comparison of EMG RMS values between each series in each muscle with 5 kPa TLT (A), 10 kPa TLT (B), 5 kPa TBT (C), and 10 kPa TBT (D), and EMG RMS values and actual forces during MVC between before and after TLT (E, G) or TBT (F, H). Error bar; Mean ± SE.

EMG-RMS; electromyographic root mean square, TLT; tongue lift training, TBT; tooth bite training, MVC; maximum voluntary contraction.

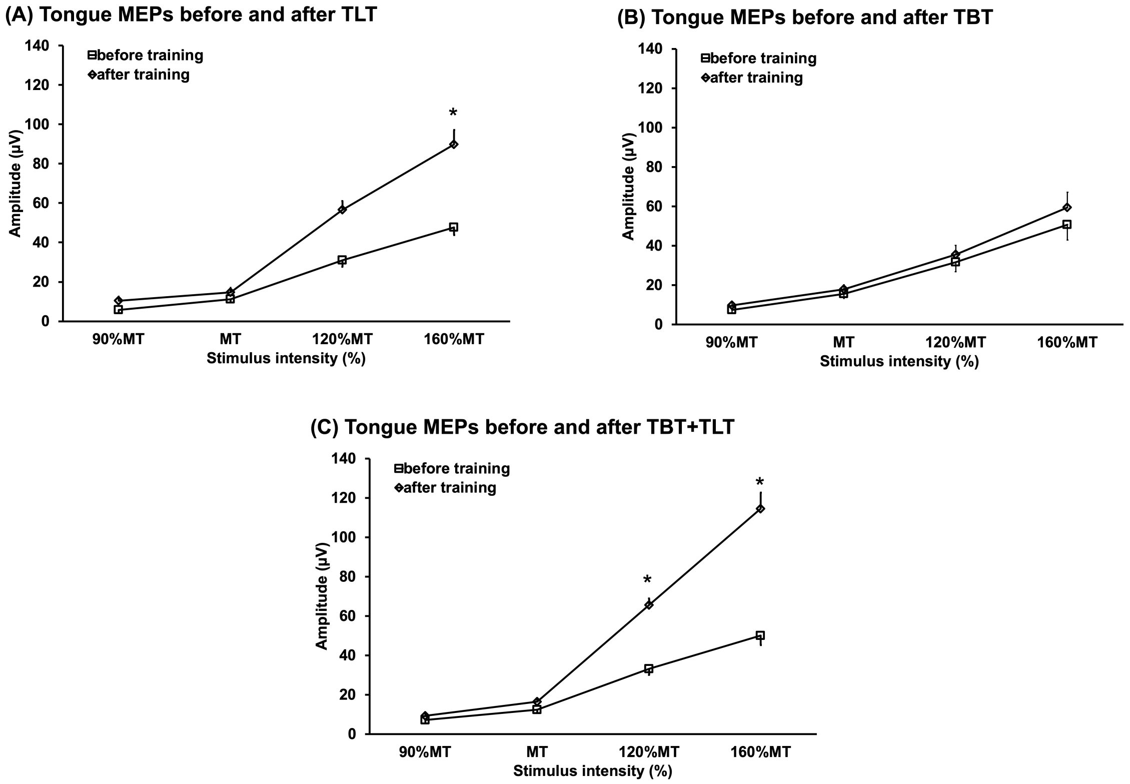
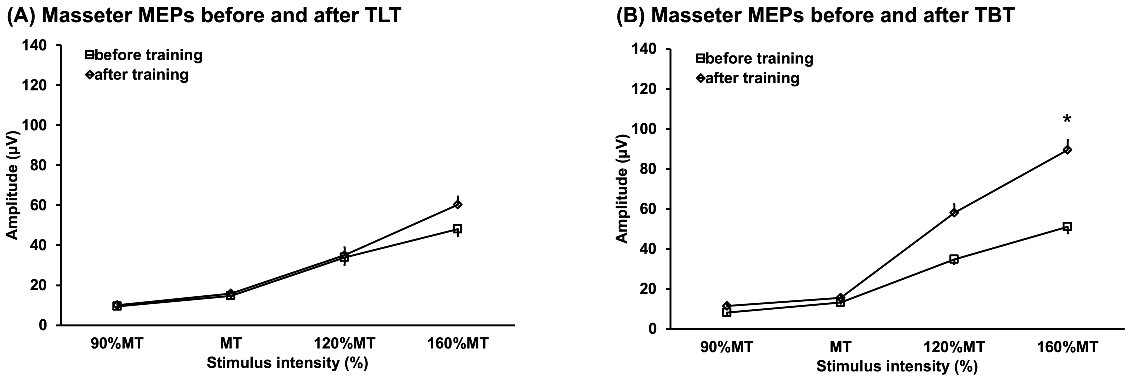


Figure 4. Stimulus-response curves obtained by TMS of the tongue area of the motor cortex in TLT (A), TBT (B), and TBT+TLT (C).

*Significantly higher after training than before training ($P < 0.001$). Error bar; Mean ± SE.

TMS; transcranial magnetic stimulation, MEP; motor-evoked potential, TLT; tongue lift training, TBT; tooth bite training, MT; motor threshold.



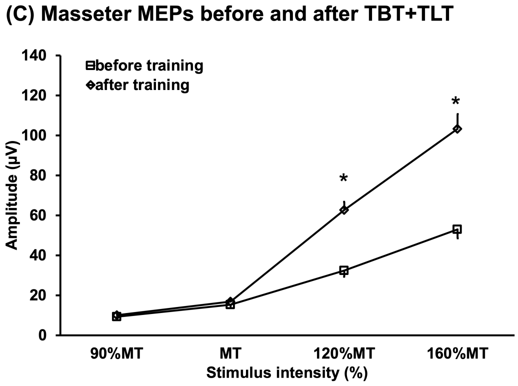


Figure 5. Stimulus-response curves obtained by TMS of the masseter area of the motor cortex in TLT (A), TBT (B), and TBT+TLT (C).

*Significantly higher after training than before training ($P < 0.001$). Error bar; Mean ± SE.

TMS; transcranial magnetic stimulation, MEP; motor-evoked potential, TLT; tongue lift training, TBT; tooth bite training, MT; motor threshold.

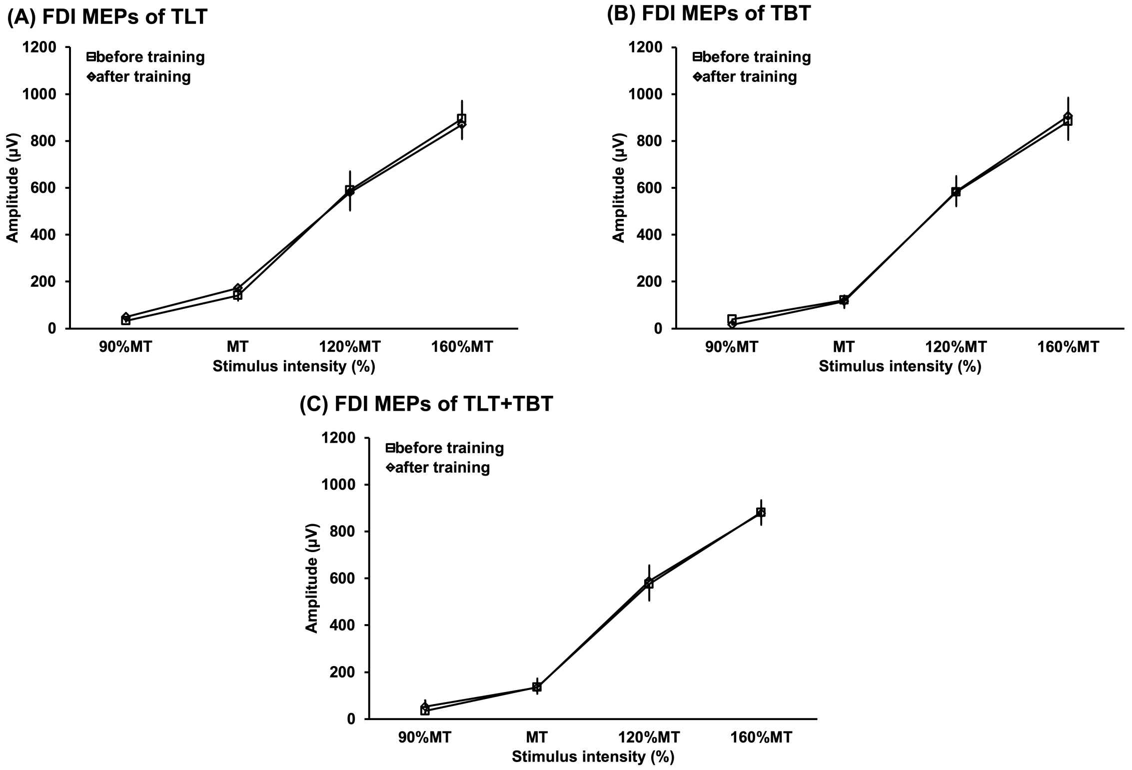


Figure 6. Stimulus-response curves obtained by TMS of the FDI area of the motor cortex in TLT (A), TBT (B), and TBT+TLT (C).

Error bar; Mean ± SE.

TMS; transcranial magnetic stimulation, MEP; motor-evoked potential,

FDI; first dorsal interosseous, TLT; tongue lift training, TBT; tooth bite training, MT; motor threshold.

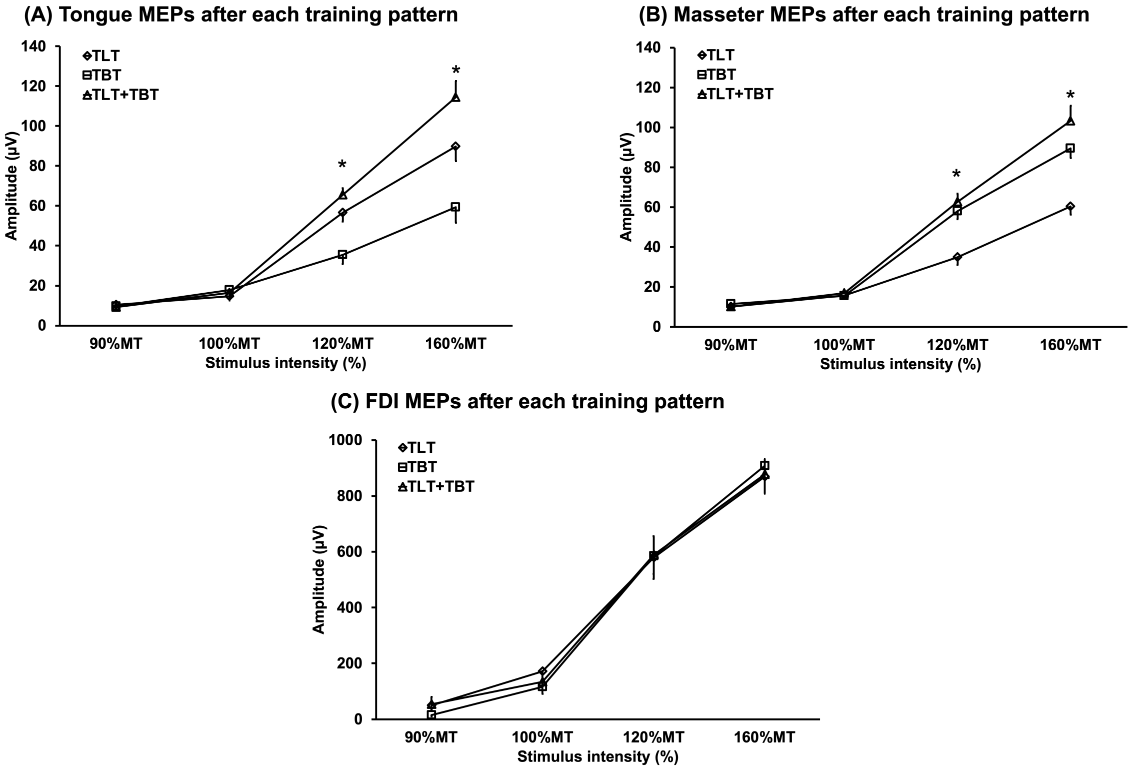


Figure 7. Comparisons of masseter MEPs, tongue MEPs, and FDI MEPs after trainings among TBT, TLT, and TBT+TLT.

*Significantly higher tongue MEPs at TLT+TBT with 120% MT and 160% MT stimulus intensity than with TBT ($P < 0.001$), and with 160% MT stimulus intensity than with TLT ($P < 0.05$) (A). *Significantly higher masseter MEPs at TLT+TBT with 120% MT and 160% MT stimulus than with TLT ($P < 0.001$), and with 160% MT stimulus intensity than with TBT ($P < 0.05$) (B). Error bar; Mean ± SE.

TMS; transcranial magnetic stimulation, MEP; motor-evoked potential,

FDI; first dorsal interosseous, TLT; tongue lift training, TBT; tooth bite training, MT; motor threshold.

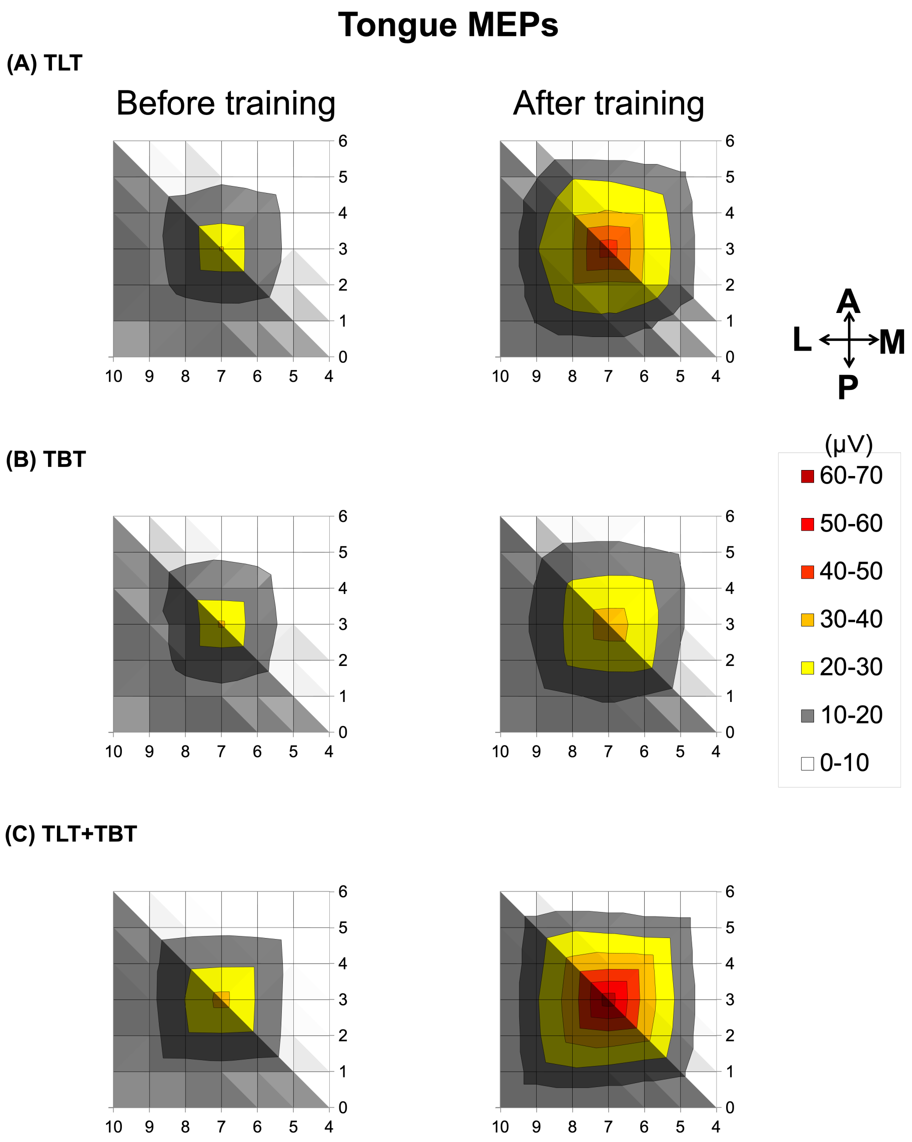


Figure 8. Motor cortex maps of the tongue area in TLT (A), TBT (B), and TBT+TLT (C) generated in 16 participants (mean amplitudes) by TMS of multiple scalp sites arranged in a 1 × 1-cm^2 grid. Arrows indicate directions (A; anterior, L; lateral, M; medial, P; posterior). The value zero on the y-axis corresponds to the Cz line (interaural line).

FDI; first dorsal interosseous, TLT; tongue lift training, TMS; transcranial magnetic stimulation, Cz, vertex. MEP; motor-evoked potential, TMS; transcranial magnetic stimulation, TLT; tongue lift training, TBT; tooth bite training; Cz, vertex.

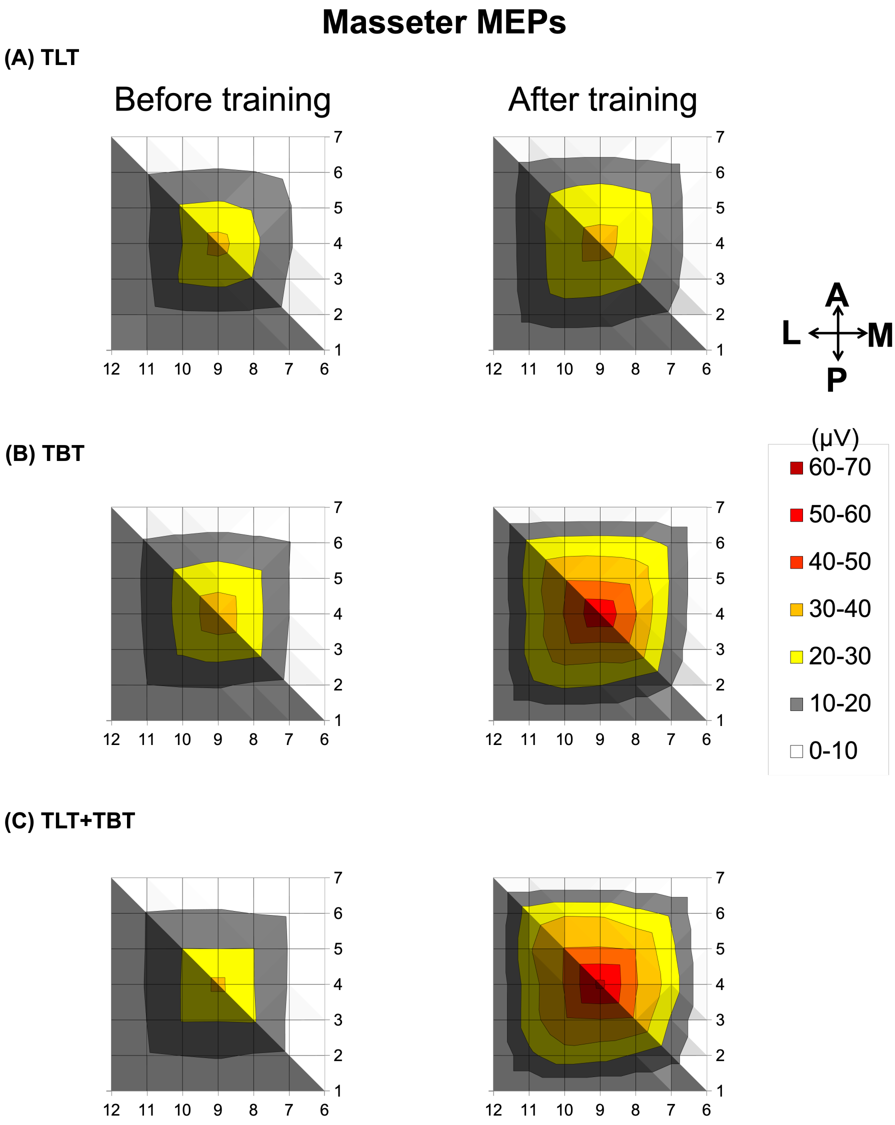
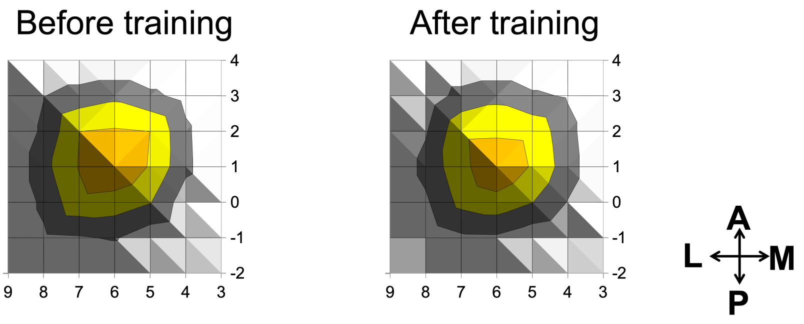


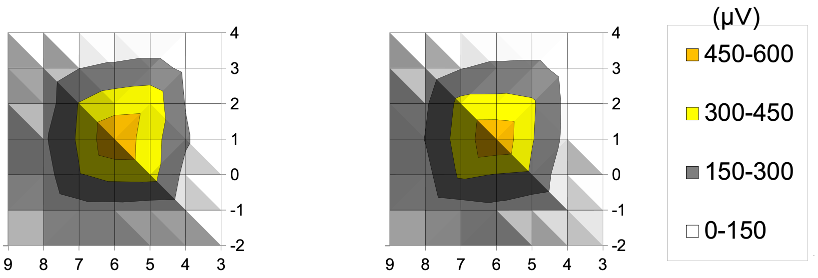
Figure 9. Motor cortex map of the masseter area in TLT (A), TBT (B), and TBT+TLT (C) generated in 16 participants (mean amplitudes) by TMS of multiple scalp sites arranged in a 1 × 1-cm^2 grid. Arrows indicate directions (A, anterior; L, lateral; M, medial; P, posterior). MEP; motor-evoked potential, TMS; transcranial magnetic stimulation, TLT; tongue lift training, TBT; tooth bite training, Cz, vertex.

FDI MEPs

(A) TLT



(B) TBT



(C) TLT+TBT

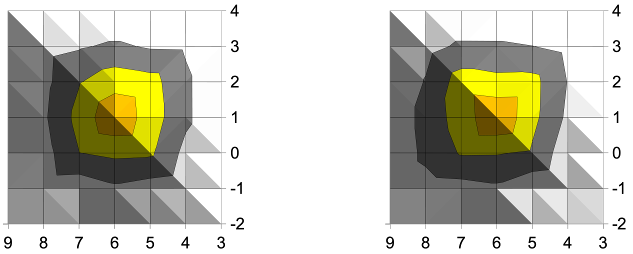


Figure 10. FDI motor cortex maps in TLT (A), TBT (B), and TBT+TLT (C) generated in 16 participants (mean amplitudes) by TMS of multiple scalp sites arranged in a 1 × 1-cm^2 grid. Arrows indicate directions (A, anterior; L, lateral; M, medial; P, posterior).

FDI; first dorsal interosseous, MEP; motor-evoked potential, TMS; transcranial magnetic stimulation, TLT; tongue lift training, TBT; tooth bite training, Cz, vertex.

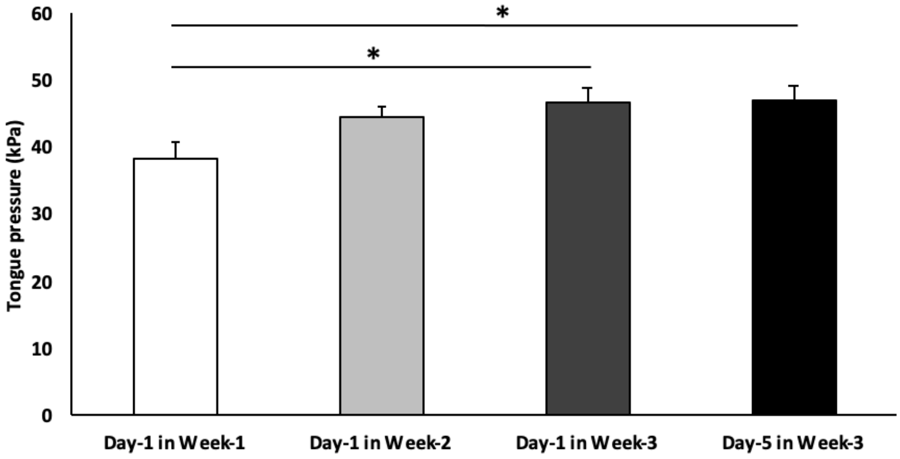


Figure 11. Comparison of the maximum tongue pressure during tongue lift movement among Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3.

* indicates significantly higher than at Day 1 in week 1 ($P < 0.05$). Error bar; Mean ± SE.

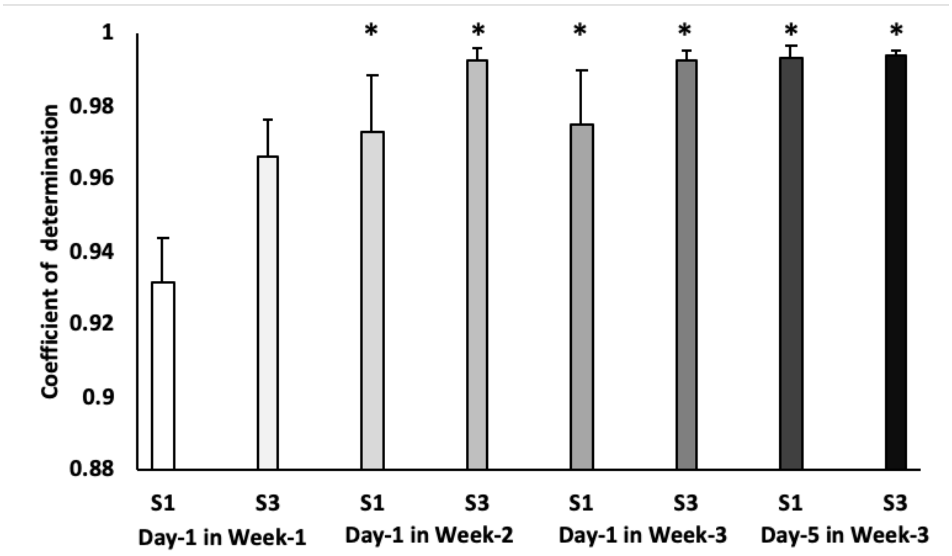


Figure 12. Comparison of the first and third series on coefficients of determinations (CDs) of the target force level–tongue pressure among Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3.

* indicates significantly higher than at Day-1 in Week-1 ($P < 0.05$). Error bar; Mean ± SE.

Abbreviations: S1; first series, S2; second series, S3; third series

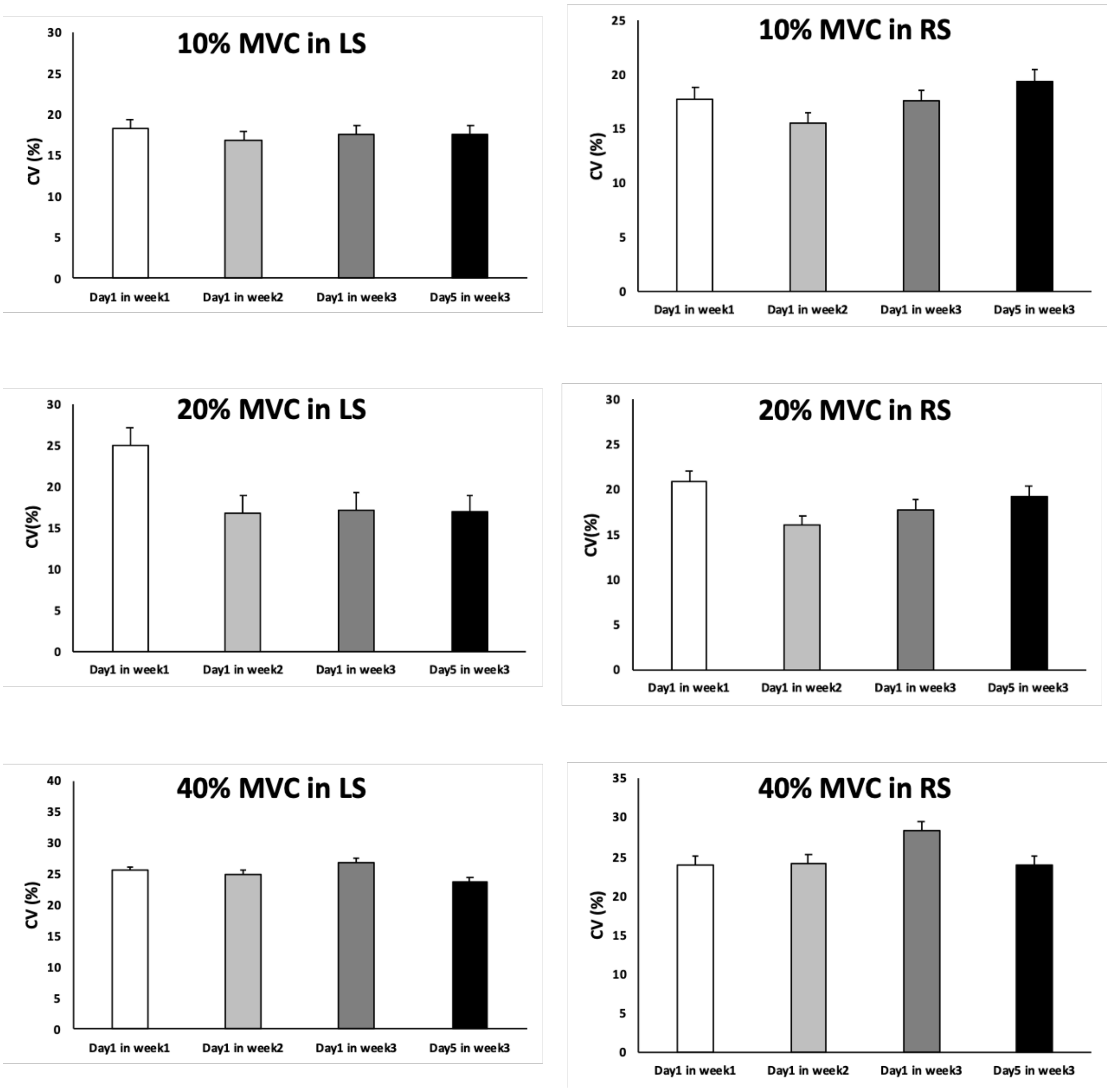


Figure 13. Comparison of relative ratios of root-mean-square of electromyogram (RMS EMG) amplitude among Day-1 in Week-1, Day-1 in Week-2, Day-1 in Week-3, and Day-5 in Week-3 on 10 % maximum voluntary contraction (MVC) in LS (A), 10 % MVC in RS (B), 20 % MVC in LS (C), 20 % MVC in RS (D), 40 % MVC in LS (E), and 40 % MVC in RS (F).

Error bar; Mean ± SE.

Abbreviations: MVC; maximum voluntary contraction, S1; first series, S2; second series, S3; third series, LS; left suprahyoid muscle, RS; right suprahyoid muscle.