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RESEARCH ARTICLE

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Plasticity in corticomotor control of the human tongue musculature induced by tongue-task training

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Abstract Transcranial magnetic stimulation (TMS) has been used to assess characteristics of the corticomotor control of the jaw muscles, but less is known about the cortical control of the human tongue and its modification by training. The aim of the present study was to determine the effect of training humans in a novel tongue-protrusion task for 1 week on corticomotor excitability as assessed by changes in electromyographic activity elicited in the tongue musculature by TMS, and in the tongue cortical motor map revealed by TMS. Eleven healthy subjects participated. Stimulus–response curves were generated from the motor evoked potentials (MEPs) recorded in the tongue musculature and, from the first dorsal interosseos (FDI) muscle as a control, at three time periods: at baseline, immediately after the 1-week training period, and at 2-weeks follow-up. In addition, the corticomotor representations of the tongue and FDI muscles were mapped on a 1×1 cm scalp grid. The tongue-training task required each subject to protrude the tongue onto a force transducer placed in front of the subject, and consisted of a relax–protrude–hold–relax cycle lasting 12.5 s with 1 N as the target at the hold phase. The subjects repeated this task for 60 min every day for 1 week. All subjects reported moderate levels of fatigue in the tongue during the first training day; however, these subjective reports decreased during the week (ANOVA $P<0.001$), and the subjects showed a progressive increase in their ability to perform the task successfully ($P<0.001$). The threshold for evoking MEPs by TMS in the tongue musculature was significantly decreased after the last training day compared with baseline and the 2-weeks follow-up ($P<0.001$). The amplitude of the MEPs in the tongue musculature was significantly increased at higher intensities of TMS after the last training day but returned to baseline values at the 2-weeks follow-up ($P=0.005$). No significant effect of the training on MEPs in the FDI was observed ($P=0.493$). Analysis of the corticomotor topographic maps revealed a significant ($P<0.05$) increase in excitability and, hence, the cortical area from which TMS could evoke MEPs in the tongue, although the center of gravity representation for the tongue or FDI muscles remained stable. The present findings suggest that a specific and reversible plasticity of the corticomotor excitability related to tongue muscle control can be induced when humans learn to perform successfully a novel tongue task.

Keywords Trigeminal physiology · Transcranial magnetic stimulation · Tongue · Motor learning · Plasticity

Introduction

The control and rapid coordination of tongue movements is essential for a number of complex orofacial behaviors such as swallowing, mastication, respiration, speech, licking, gaping, coughing, gagging and vomiting (Dubner et al. 1978; Lowe 1981; Sawczuk and Mosier 2001). The brain stem and central pattern generators participate in the neural control network of tongue movements (Lund 1991; Sawczuk and Mosier 2001) but a series of electrophysiological studies in awake monkeys have clearly documented a prominent role of the primary face motor cortex

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(MI) including the tongue MI for the fine control of tongue movements such as those associated with tongue protrusion and the semiautomatic movements of chewing and swallowing (Murray et al. 1991; Murray and Sessle 1992a, 1992b, 1992c; Martin et al. 1997, 1999; Yao et al. 2002a). Thus, intracortical microstimulation (ICMS) of the face MI and lateral pericentral cortex has been shown to generate twitch responses as well as more complex movements of the tongue, and extracellular recordings in these cortical regions demonstrate differentiated neuronal firing patterns during voluntary and semiautomatic tongue movements (e.g., Murray and Sessle 1992a; Martin et al. 1997, 1999; Yao et al. 2002a). Furthermore, reversible inactivation of the face MI by cooling markedly impairs the monkey's ability to carry out these tongue movements (Murray et al. 1991; Yamamura et al. 2002). Consistent with the monkey studies, functional brain imaging studies in humans have revealed that tongue movement and contraction is associated with significant activity in the sensorimotor cortex, as well as in supplementary motor area, operculum, insula, and several subcortical regions (Corfield et al. 1999; Martin et al. 2001).

Transcranial magnetic stimulation (TMS) has been used extensively in humans to assess the corticomotor pathways in limb muscles (Rothwell 1997; Abbruzzese and Trompetto 2002), although relatively few studies have examined the control of the jaw muscles (Benecke et al. 1988; Cruccu et al. 1989; Macaluso et al. 1990; McMillan et al. 1998a, 1998b, 2001; Gooden et al. 1999; Nordstrom et al. 1999; Romaniello et al. 2000) or the tongue musculature (Muellbacher et al. 1994, 1998, 2001; Meyer et al. 1997; Katayama et al. 2001; Fadiga et al. 2002; Rodel et al. 2003). An interesting aspect of the corticomotor control is the demonstration of facilitation of the TMS-induced motor evoked potentials (MEPs), for example in small intrinsic hand muscles such as the first dorsal interosseos (FDI) muscle following repeated stimulation of the peripheral nerves (Stefan et al. 2000; Ridding et al. 2000, 2001; McKay et al. 2002). Furthermore, motor-point stimulation of the FDI muscle paired with TMS of the human motor cortex is associated with expansion of the area of scalp from which responses in the FDI muscle can be elicited (McKay et al. 2002). Training tasks and motor learning have indeed been shown to influence the corticomotor projections in several different muscle groups (Karni et al. 1995; Elbert et al. 1995; Byl et al. 1996; Remple et al. 2001). Motor skills can operationally be defined as the process by which movements, produced either alone or in a sequence, come to be performed effortlessly through repeated practice (Ungerleider et al. 2002). Learning of sequential finger movements is associated with a slowly evolving (over the course of weeks) reorganization within MI as revealed by functional magnetic resonance imaging (fMRI) scans of a more extensive representation of the movements. Furthermore, more rapid changes (over the course of days) occur in cerebellum, striatum and other motor related cortical areas (Ungerleider et al. 2002).

There have, however, been no detailed studies in primates of learning-associated plasticity of the cortical control of the tongue musculature or, specifically, the effects of motor task training on MEPs in the tongue. Therefore, the aim of the present study was to apply a novel tongue-protrusion task, which has been used extensively in studies on corticomotor control in monkeys (Murray et al. 1991; Murray and Sessle 1992b; Martin et al. 1997), in a motor learning paradigm in humans and to test its effect on the corticomotor excitability assessed by changes in the cortically evoked electromyographic (EMG) activity elicited in the tongue musculature by TMS, and in the tongue cortical motor map revealed by TMS.

Materials and methods

Subjects

The study was carried out in 11 healthy volunteers (5 women and 6 men, all right-handed) aged 21–29 years (mean ±SD 24.5±2.4 years). The subjects reported no medical, physical or psychological problems. Informed consent was obtained in accordance with the guidelines of the Helsinki Declaration. The study was carried out in Orofacial Pain Laboratory at the Center for Sensory-Motor Interaction, Aalborg University, with the approval of the Local Ethics Committee.

Recording of motor evoked potentials

The subjects sat upright and relaxed in a dental chair with the head supported by a headrest. EMG activity was recorded from the right side of the tongue dorsum and the right FDI muscles. In three of the subjects, bilateral EMG recordings were obtained from the tongue dorsum and from the right perioral facial muscles (2 cm lateral from the corner of the mouth). Disposable self-adhesive silver chloride electrodes (Type 9013S0211; Medtronic, Minneapolis, MN, USA) were placed on the dorsal surface of the relaxed tongue (2–3 mm from midline, 10 mm from tongue tip) with an inter-electrode distance of 2 cm. Disposable surface electrodes (Type 720-01 K; Medicotest, Oelstykke, Denmark) were placed over the FDI (muscle belly—caput metatarsale I). The EMG signals were amplified, filtered (20 Hz–1 kHz), sampled at 4 kHz (Counterpoint MK2; Dantec, Skovlunde, Denmark) and stored on disk for offline analysis. A total of 300 ms of EMG activity was recorded (with 100 ms pre-stimulus activity and 200 ms of post-stimulus activity).

Transcranial magnetic stimuli (MagLite-r25, Dantec; peak magnetic field 1.9 T) were delivered with a 5 cm diameter figure-of-eight coil to the left side of the scalp. The coil of the stimulator was oriented 45° obliquely to the sagittal midline so that the induced current flowed in a plane perpendicular to the estimated alignment of the central sulcus. Three markings on the coil helped to identify the position in relation to the scalp sites. The scalp sites at which EMG responses were evoked in the tongue or FDI muscles at the lowest stimulus strength were determined. The motor threshold was measured in the relaxed muscles with the use of a descending and ascending method, and was defined as the minimum stimulus intensity that produced five discrete MEPs clearly discernible from the background EMG activity (tongue MEP >5 μV and FDI MEP >50 μV).

The MEPs were assessed by two methods: stimulus–response curves (e.g., Devanne et al. 1997; Ridding and Rothwell 1997), and motor cortex mapping (e.g., Wilson et al. 1993; McMillan et al. 1998a, 1998b). Stimulus–response curves were constructed in steps of 10% of stimulator output, from below the motor threshold to the maximum stimulator output. Twelve stimuli were presented at each

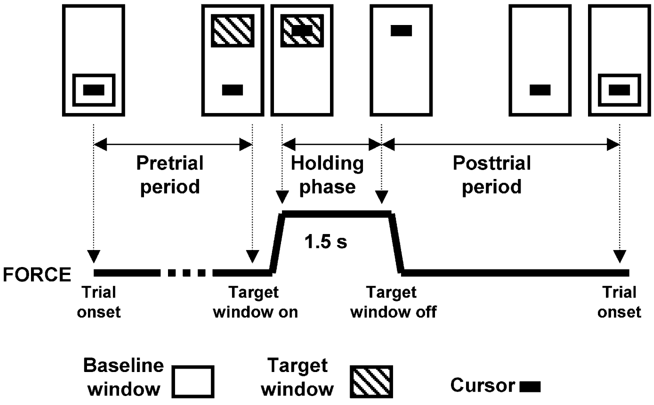

Fig. 1 Schematic presentation of the tongue-protrusion task. The subjects were given visual feedback of the force signal when the tongue was protruded onto a force transducer. A computer program controlled the timing of the baseline and target windows. The hold phase was maintained for 1.5 s and corresponded to 1 N

stimulus level with an inter-stimulus interval of 10–15 s. For motor cortex mapping, magnetic stimuli were delivered at the sites over the scalp identified by a snugly fitting, flexible cap marked with 1×1 cm grids in an anterior–posterior and lateral–medial coordinate system (Wilson et al. 1993). The anterior–posterior grid lines were related to the vertex (Cz) in accordance with the 10–20 electroencephalographic (EEG) electrode placement system. The stimulator output was set at 20% above the motor threshold, and 12 stimuli were delivered to each site. The grid was stimulated in a regular pattern, beginning at the center of the motor representation, and then moving anterior then posterior at increasing and decreasing latitudes (sites typically covered 7 cm from the vertex, and 4 cm anterior and posterior to the inter-aural line corresponding to at least 56 grids). The areas (cm^2) of the tongue and FDI maps with MEP amplitudes greater than 5 μV and 100 μV, respectively, were determined on the 1×1 cm grid. Furthermore, the center of gravity (COG) was determined according to the description of Ridding et al. (2000): $X=\Sigma a_i X_i/\Sigma a_i$, where a_i is the amplitude at the scalp site whose coordinate is X_i. In a similar way the Y-coordinate was determined.

Tongue-protrusion task

The subjects performed a tongue-protrusion task in the laboratory for 7 consecutive days, which was based on the tasks described in monkey studies (Murray et al. 1991). They were seated upright in a comfortable dental chair. The subject was asked to protrude the tongue onto a force transducer that was affixed rigidly to a beam on the chair in front of the subject; the force plate was located in the midline, 2 cm anterior to the most anterior portion of the upper lip. A horizontal beam to secure a constant distance to the force transducer supported the forehead. The transducer output controlled the vertical position of a cursor on a computer monitor located in front of the subject. During each tongue-protrusion trial, a computer-controlled baseline window appeared initially at the bottom of the computer screen and, after a pretrial period, it was displaced instantaneously to a pre-set target-window level (equivalent to a force of 1.0 N) on the computer screen (Fig. 1). The subjects were asked to move the cursor into the target window and then hold the cursor within the target window for a specific minimum holding phase. The following periods were defined for the tongue protrusion task: a 10-s pretrial period during which the baseline window remained at the bottom of the screen and the subject sat relaxed in the chair; a dynamic phase (ramp), which was the period from the onset of the rise of the cursor from the bottom of the screen to the moment that the cursor entered the target window; a holding phase, which was the period from entry of the cursor into the target window to the end of the 1.5-s holding phase. A successful tongue protrusion trial was defined by the following criteria: the cursor remained within the baseline window during the 10-s pretrial period; the cursor exited the baseline window within 1 s of target window appearance; and the cursor remained within the target window for the specified minimum holding phase (1.5 s). The performance success rate was determined as the number of successful protrusion trials relative to the total number of protrusion trials performed during the 60 min training period each day.

Subjective sensations evoked by the tongue-task training

After each session of the tongue-protrusion task training (every day for 7 days), the subjects were asked to score the intensity of fatigue and to give a description of their sensations in the tongue. Muscle fatigue was scored on a 0–7 categorical scale: 0 none at all, 1 very weak, 2 weak, 3 moderate, 4 somewhat strong, 5 strong, 6 very strong, 7 very strong, maximal.

Experimental protocol

The stimulus–response curves and motor cortex mapping were performed on three separate sessions: (1) baseline, (2) 30 min after the training session on the seventh day of tongue-task training (post-training), and (3) 2 weeks after the end of the tongue-task training (2-weeks follow-up). The recording procedure was the same in the three sessions. The onset latency and peak-to-peak amplitude were measured on the non-rectified, averaged MEPs.

Statistical analyses

The performance success rates were compared with repeated measures one-way analysis of variance (ANOVA), and the fatigue scores were analyzed with repeated measures ANOVAs for ranks. The MEP amplitudes were analyzed with two-way ANOVAs with stimulus intensity (% of maximum output) and session (baseline, post-training, and 2-weeks follow-up). COG measures and MEP areas were analyzed with one-way ANOVAs. When appropriate the ANOVAs were followed by post hoc Tukey tests to compensate for multiple comparisons. All data are presented as mean values and standard errors of mean (SEM). The level of significance was set at $P<0.05$.

Results

Task performance and subjective sensations

The subjects considered the tongue-protrusion task a novel experience, and one that required considerable learning. Indeed, on the first day they only reached a mean success rate of 25.3±3.3% in their performance of the task (Fig. 2A). During the training there was a gradual improvement in their success rate, and by the end of the 7-day training period they had reached on average a success rate of 39.5±4.0%, which was significantly higher than the earlier success rates ($F=5.261$, $P<0.001$; Tukey $P<0.001$).

At baseline none of the subjects had any tongue complaints. The tongue-protrusion task was initially associated with a strong sensation of fatigue (Fig. 2B). The fatigue scores, however, decreased significantly during the course of the 7 days ($F=10.535$, $P<0.001$)

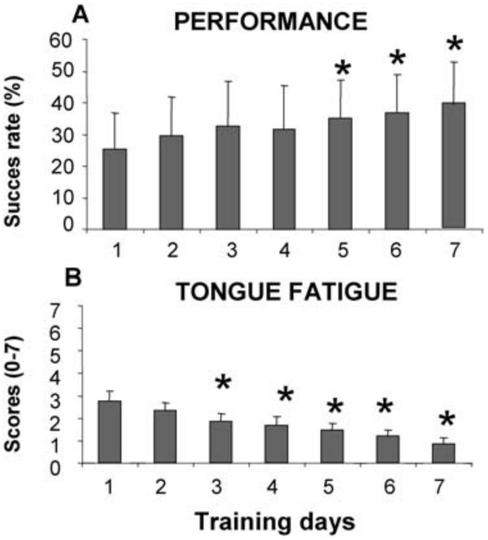

Fig. 2A,B Assessment of performance success rates (**A**), and subjective sensations of fatigue in the tongue (**B**) during the 7 days with the repeated tongue-protrusion task. *Significantly different compared with day 1 values (Tukey *P*<0.05)

with significantly lower scores from day 3 to day 7 compared with day 1 scores (Tukey *P*<0.033). Some subjects also reported a sensation of "a bigger tongue" or "difficulties with pronunciation" during the first training sessions.

Motor evoked potential recordings

MEPs in the right tongue musculature could be evoked by stimulation of discrete areas of the left scalp, approximately 2–3 cm anterior to the Cz and 7–8 cm lateral to the mid-sagittal plan. The MEPs in the FDI were evoked by stimulation of the scalp close to the Cz line and about 6 cm lateral to the mid-sagittal plan. In accordance with previous reports (Meyer et al. 1997), it was possible with the tongue surface electrodes to record low-amplitude MEPs on both the right and left side of the tongue dorsum when the left tongue motor cortex was stimulated (Fig. 3). For the three tested subjects, the ipsilateral MEPs were similar to the contralateral MEPs with respect to latency and amplitude (Fig. 3). Thus, only MEPs from the contralateral (right side) tongue were measured for the stimulus–response curves and motor cortex mapping studies. Furthermore, stimulation of the tongue motor cortex was not associated with any detectable MEPs in the perioral facial or FDI muscles (Fig. 3). Stimulation of the appropriate site of the left hand motor cortex evoked high-amplitude MEPs in the right FDI muscle, but no EMG responses from the tongue or perioral facial muscles (Fig. 3).

The motor thresholds for the tongue MEPs among the three sessions were significantly different (*F*=15.077, *P*<0.001), with the lowest motor thresholds in the post-training session (44.4±0.8%) compared with the baseline (51.7±1.6%) and the 2-weeks follow-up (51.2±1.2%) (Tukey *P*<0.003). There were no significant differences among the motor threshold in the FDI muscle at baseline (45.5±1.3%), in the post-training session (46.4±1.2%) and at the 2-weeks follow-up (45.6±1.7%) (*F*=0.827, *P*=0.452).

The onset latency of the tongue MEPs was significantly influenced by stimulus intensity (*F*=3.276, *P*=0.005), and was significantly shorter at maximum stimulus intensity (7.7±0.2 ms) when compared with the latency at motor threshold (8.0±0.1 ms). The onset latency of the MEPs in the FDI also depended on stimulus intensity (*F*=29.324, *P*<0.001), with significantly faster onsets at maximum stimulus intensity (20.6±0.5 ms) compared with the latency at motor threshold (22.5±0.4 ms). The onset latencies of the MEPs in the tongue or FDI muscles did not differ among the sessions.

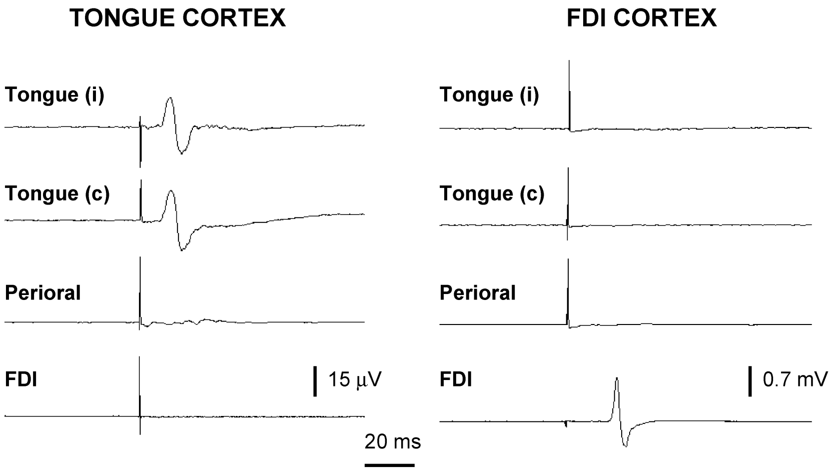

Fig. 3 Averaged traces (12 sweeps) from a single subject with transcranial magnetic stimulation of the left tongue motor cortex and first dorsal interosseos (FDI) motor cortex. Motor evoked potentials were recorded from the right (*c* contralateral) and left side (*i* ipsilateral) of the tongue musculature, right perioral facial and right FDI muscles

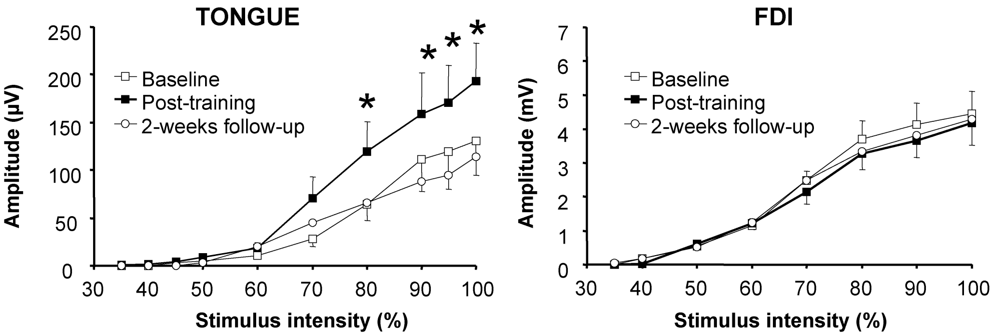

Fig. 4 Stimulus–response curves obtained from transcranial magnetic stimulation of the tongue motor cortex and first dorsal interosseos (FDI) motor cortex in 11 subjects (means ±SEM). Stimulus intensity is expressed in percentage of maximum output. *Significantly higher compared with values of the baseline and 2-weeks follow-up sessions (Tukey *P*<0.05)

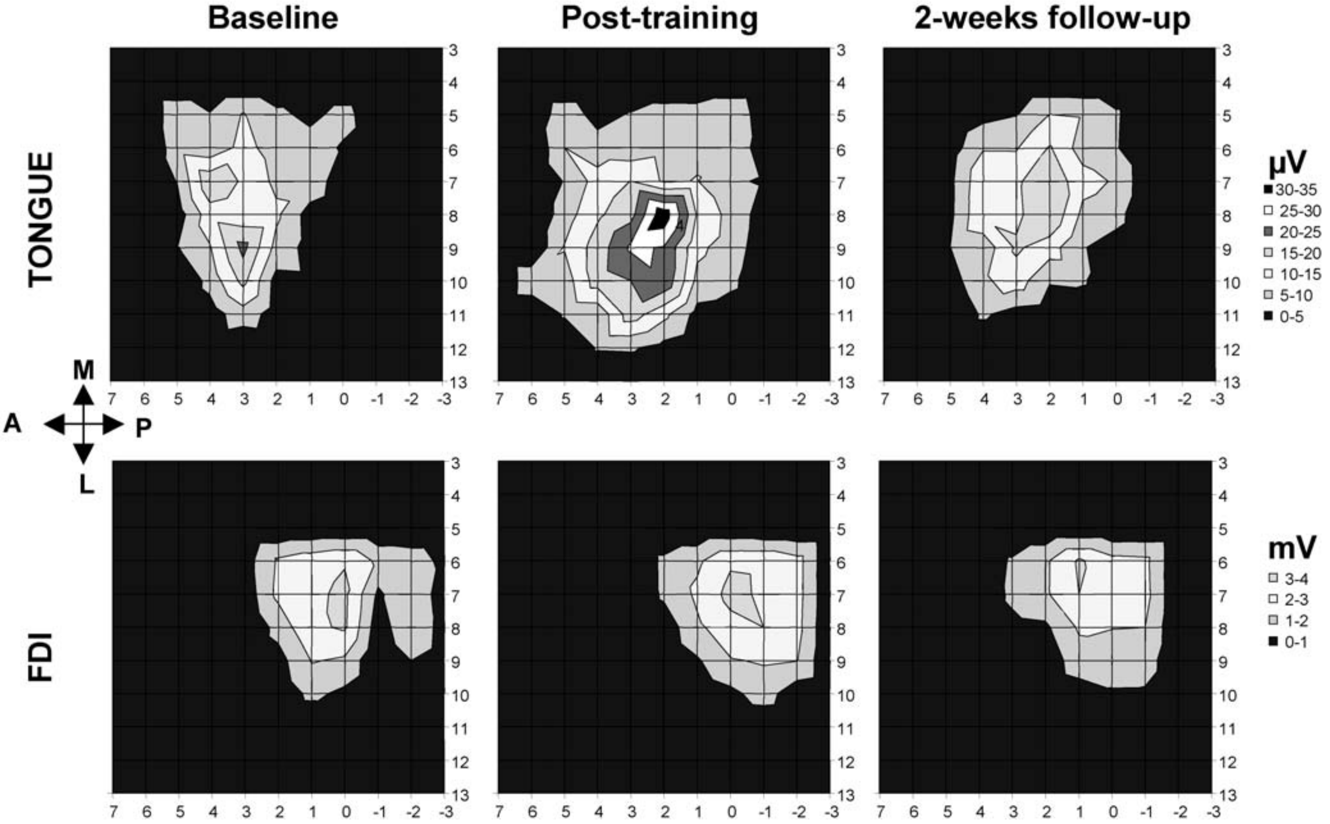

Fig. 5 Tongue and first dorsal interosseos (FDI) cortical motor maps generated in 11 subjects (mean amplitudes) by transcranial magnetic stimulation of multiple scalp sites arranged in a 1×1 cm grid. *Arrows* indicate directions (*A* anterior, *P* posterior, *M* medial, *L* lateral). Zero on the *X*-axis corresponds to the Cz line (interaural line)

Stimulus–response curves

The tongue MEPs were significantly dependent on stimulus intensity (*F*=8.661, *P*<0.001) and on experimental session (*F*=7.135, *P*=0.005), with a significant interaction between these factors (*F*=4.167, *P*<0.001). Post-hoc tests demonstrated significantly higher tongue MEPs in the post-training session at 80% stimulus intensity and above when compared with the baseline and the 2-weeks follow-up session (Tukey *P*<0.05) (Fig. 4).

An additional analysis was performed to adjust for the lower motor threshold (mean difference 7.3%) in the post-training session, which could have shifted the entire stimulus–response curve to the left. However, when the MEPs in the contralateral tongue musculature were adjusted for a 10% shift in motor threshold, the post-training session was still associated with significantly higher tongue MEPs at stimulus intensities above 90% (Tukey *P*<0.044).

Table 1 Center of gravity measures from the tongue and the first dorsal interosseos (FDI) cortical motor maps

Site	Session	Center of gravity measures (cm)		
		Anterior–posterior	Medial–lateral	Length
Tongue	Baseline	2.2±0.4	7.4±0.2	7.8±0.3
	Post-training	2.3±0.3	7.8±0.3	8.2±0.2
	2-weeks follow-up	2.3±0.2	7.6±0.2	7.9±0.2
FDI	Baseline	0.5±0.2	6.3±0.1	6.4±0.1
	Post-training	0.3±0.2	6.1±0.2	6.2±0.2
	2-weeks follow-up	0.8±0.2	6.1±0.1	6.2±0.1

The MEPs in the FDI muscles were significantly influenced by stimulus intensity (ANOVA F=33.937, P<0.001) but not by experimental session (F=0.733, P=0.493), and there was no significant interaction between the factors (F=0.622, P=0.843) (Fig. 4).

Cortical motor maps

The tongue cortical motor maps (MEP amplitude >5 μV) were significantly different among the three sessions (F=4.104, P=0.032), with significantly larger areas in the post-training session (21.5±2.4 cm^2) compared with the baseline (15.0±2.2 cm^2; Tukey P<0.033) but not the 2-week follow-up (16.5±2.5 cm^2; Tukey P=0.112) (Fig. 5). In contrast, the FDI cortical maps (MEP amplitude >100 μV) were not significantly different between the sessions (F=0.594, P=0.562) (mean areas 10.9±1.6 cm^2).

The center of gravity analysis revealed no significant differences among the three sessions in the anterior–posterior (F=0.218, P=0.806) or medial–lateral (F=2.877, P=0.08) coordinates or the length of the vector (F=2.906, P=0.078) for the tongue MEPs (Table 1). There was no difference in the anterior-posterior (F=2.27, P=0.129), medial-lateral (F=2.652, P=0.095) or length of the vector (F=2.137, P=0.144) for the MEPs in the FDI muscle (Table 1).

Discussion

These findings represent the first documentation of plasticity in the corticomotor control of the human tongue musculature associated with the learning of a novel orofacial task. We have shown that the acquisition of this new orofacial motor skill over a 7-day period of training in a tongue-protrusion task resulted in significant changes in the motor threshold and amplitude of MEPs elicited by TMS in the tongue musculature. Furthermore, the MEP changes in the tongue musculature were associated with a significant expansion of the cortical area related to the tongue-evoked responses. These plastic changes were also reversible since the cortical and MEP parameters had returned to baseline levels by 2 weeks after the tongue-training task had ceased. In addition, the changes appeared to be specific for the tongue musculature since there was no evidence from the cortical and MEP parameters for the FDI muscle of plasticity associated with the acquisition of the learned tongue behavior.

Tongue-task training

Although humans utilize the tongue in a variety of orofacial motor paradigms (Dubner et al. 1978; Lowe 1981; Sawczuk and Mosier 2001), the study utilized a task that reflected a novel tongue motor behavior for humans. There was a gradual and significant improvement in the performance success rate as the subjects in the study learned the task over the 7-day training period, despite some muscle fatigue during task performance. This symptom, however, progressively decreased over the course of the training, and is unlikely to have accounted for the plasticity since the changes in MEPs and the cortical motor map were documented 30 min after the time when the subjects had scored their fatigue in the post-training session. The plastic changes associated with the learning of the orofacial motor task appear to be specific to the tongue since they were not accompanied by comparable changes in the FDI muscle, suggesting that they do not reflect a generalized plasticity in corticomotor pathways.

Plasticity in motor control

It is noteworthy that the changes in orofacial motor behavior are consistent with data of many recent studies applying several different experimental techniques to the corticomotor control of limb movements. These studies documented a remarkable plasticity of MI, which they characterized as a dynamic construct that is modeled in a use-dependent manner by behaviorally significant experiences such as those, and which might be associated with motor skill learning. Firstly, recent positron emission tomography (PET) and especially fMRI studies in humans have revealed multiple representation of a movement in limb MI (Grafton et al. 1992, 2002; Elbert et al. 1995; Karni et al. 1995; Sanes et al. 1995; Byl et al. 1996; Pearce et al. 2000; Remple et al. 2001), consistent with ICMS findings that limb MI (e.g., Kwan et al. 1978; Sessle and Wiesendanger 1982) and the face MI (e.g., Huang et al. 1988; Waters et al. 1990; Murray and Sessle 1992a) of awake monkeys show multiple sites or “nests” or “efferent zones” that represent a particular movement, and that may reflect the diversity of functional contingencies with which that movement is involved. Secondly, plasticity in limb MI organizational features has indeed been revealed in primates (including humans) and in subprimates as a consequence of focal blockade or ICMS of MI or peripheral sensory or motor nerve manipulation, and also in association with motor learning (Nudo et al. 1990, 1996; Keller et al. 1996; Donoghue 1997; Buonomano and Merzenich 1998; Sanes and Donoghue 2000; Schieber 2001). From PET and fMRI studies, it has been reported for example that learning of a skilled digit movement results in an expansion of the PET- or fMRI-defined primate MI representing hand movements, and that these changes may persist for days or months depending on the training parameters (Seitz et al. 1990; Jenkins et al. 1994; Karni et al. 1995). Those studies also noted that the emergence of this altered MI representation may correspond in time with a human subject's attainment of maximum performance in the trained manual task, raising the possibility that motor practice induces recruitment of additional MI units into a network representing specifically the trained task, and that the network may constitute a site for the long-term memory of the task. Furthermore, TMS studies also have demonstrated that training of particular forelimb movements can result in an enhanced representation in MI of the muscles engaged in the task; these plastic changes may occur within a single training session or over a longer period of time needed to acquire the motor skill (Pascual-Leone et al. 1994; Classen et al. 1998). In studies using ICMS in animals, progressive expansion of limb MI motor representations can occur after monkeys are trained in digit or forearm tasks, suggesting that a neurophysiological correlate of a motor skill resides in MI after skill acquisition, and that the size of a motor representation in MI may be related to motor skill (Nudo et al. 1996).

Plasticity in tongue corticomotor control

Our MEP findings are consistent with recent data on the latency and stimulus–response functions of the MEPs elicited by TMS in the tongue musculature (Muellbacher et al. 1994, 1998, 2001; Meyer et al. 1997; Katayama et al. 2001; Fadiga et al. 2002; Rodel et al. 2003), although the amplitudes of the MEPs were smaller than those reported previously. This difference in amplitude could be explained by the slight contraction of the tongue musculature used in most other studies to obtain good contact between the dorsum of the tongue and the EMG electrodes applied to a spoon-shaped intraoral device. A slight activation of most cranial muscles is known to facilitate the amplitudes of the MEPs (e.g., Cruccu et al. 1989). However, small amplitude MEPs have also previously been recorded from the relaxed tongue musculature (e.g., Meyer et al. 1997). In the present study, we applied surface EMG electrodes directly to the dorsum of the tongue and asked the subjects to keep the tongue in a relaxed position, and this accordingly was associated with a very low level of EMG activity.

In addition to the TMS studies on tongue MEPs in humans, other findings bearing on our data come from primate studies using surface electrical stimulation, ICMS, or reversible or irreversible (i.e., ablation) cortical inactivation. These studies have revealed that the lateral part of area 4, and area 6, may be related to the initiation and control of orofacial movements. For example, ICMS evokes elemental orofacial movements such as tongue protrusion only from the face MI, whereas semiautomatic movements such as chewing and swallowing can be evoked from the face MI as well as the more lateral cortical masticatory area, and inactivation of the face MI or these more lateral regions may disrupt these movements (Clark and Luschei 1974; Luschei and Goodwin 1975; Larson et al. 1980; Huang et al. 1988; Martin et al. 1999; Murray and Sessle 1992a; Narita et al. 2002; Yamamura et al. 2002). The ICMS data also revealed the limited representation of jaw-closing, as opposed to tongue and face movements, consistent with findings that reversible bilateral cold block of the face MI (Murray et al. 1991) may markedly disturb the animal's ability to perform a trained tongue protrusive task, as opposed to a biting task. These findings underscore the importance of the face MI, the area stimulated by TMS in the present study, in the fine motor control of especially tongue movements; this is also borne out by single neuron recordings in awake monkeys, which have documented that many face MI neurons preferentially show activity related to tongue movements during performance of the tongue-protrusion task or during the semiautomatic movements of chewing and swallowing (Murray and Sessle 1992b, 1992c; Sessle et al. 1995; Martin et al. 1997; Yao et al. 2002a, 2002b).

However, until the present study, there had been no study of the possible plasticity of the orofacial motor control in humans. This topic has also received virtually no attention in the non-human primate, although there are clinical and animal behavioral reports attesting to the plasticity or progressive return of function of face sensorimotor cortex following cortical disruption or trauma to peripheral tissues (Luschei and Goodwin 1975; Larson et al. 1980; Martin and Sessle 1993; Hamdy et al. 1996; Yamamura et al. 2002), and several studies have documented plasticity of this region in subprimates, especially after manipulation of peripheral tissues or nerves (Nudo et al. 1990, 1996; Keller et al. 1996; Donoghue 1997; Buonomano and Merzenich 1998; Sanes and Donoghue 2000; Scheiber 2001; Chen et al. 2002). Our present findings, nonetheless, gain support from recent preliminary data pointing to plasticity of the face MI in awake monkeys trained in a tongue-protrusion task analogous to that used in the present study (Yao et al. 2002c; Sessle and Yao 2003). The ICMS-defined orofacial motor representations and neuronal activity patterns within the face MI were determined before and after the monkeys learned this orofacial behavior. Consistent with findings in limb MI (see above) and with the present findings in humans, it was found that the proportion of loci in tongue MI from which tongue protrusion could be evoked by ICMS was significantly higher than that before training. Moreover, before the tongue-training task, only one-quarter of the face MI neurons showed tongue-protrusion-related activity, whereas three-quarters of those recorded after training had tongue-protrusion-related activity. These preliminary data are indicative of neuroplasticity of the face MI, and provide additional evidence for a role for MI in orofacial motor learning in primates.

The change in the tongue cortical motor maps in our analysis was significant and specific to the tongue area, and is consistent with findings in limb MI (see above). The center of gravity technique may have a lower spatial resolution than imaging techniques such as fMRI, and it was not able to capture a significant shift in the tongue cortical motor maps, although there was on average a 4 mm lateral shift for the representation of the tongue in the post-training session (Table 1). However, it is conceivable that the change might have been even greater if we had tested for cortical plasticity in the first 1–2 days during the subjects' acquisition of the motor skill rather than several days after the motor skill training had started. There is evidence in the limb motor plasticity literature that repetition of a learned motor behavior may indeed be associated with a return to or below baseline values as participants continue to practice the learned behavior, although there are also published data that are not fully in accord with this view (Grafton et al. 1992; Pascual-Leone et al. 1994; Karni et al. 1995; Sanes and Donoghue 2000).

Finally, the present observations of plasticity in the corticomotor control of human tongue musculature could be related to aspects of strength training rather than motor skill learning. However, Remple et al. (2001) demonstrated in rats that a progressive increase in performance success rates, but not an increase in strength, was associated with significant increases in the motor cortex representation of forelimb movements. Moreover, it is unlikely that the present tongue-protrusion task would have any influence on the strength since the target force was only 1 N, which represents 3–18% of the maximal tongue force production (Sha et al. 2000; Blumen et al. 2002).

Significance of plasticity in tongue motor control

The present findings in humans and the preliminary data in monkeys of the plasticity of the corticomotor control of orofacial movements, together with the considerable literature already available of plasticity of the cortical control of limb movements (see above), suggest that the face MI represents a crucial element in these effects. The acquisition of a new orofacial motor skill, such as that which occurred as a result of the training in the novel tongue-protrusion task used in the present study, is associated with a facilitation of the corticomotor drive to the tongue musculature, and may be the result of plastic changes occurring in the tongue motor map in MI. The tongue cortical motor maps expanded after the human subjects had been trained in the tongue task for 7 days, and the monkey data also point to changes occurring at the MI neuronal level. Thus, it seems very likely that MI plastic changes mediate, at least in part, the acquisition of the learned orofacial motor behavior, and that the face MI represents a dynamic and adaptive construct that is crucial to the learning of new motor skills. These motor skills can range from relatively simple movements such as tongue protrusion to more complex motor skills in which tongue movements play an important role, e.g., the learning of masticatory skills, including the ability to use the tongue to help continuously to reposition a food bolus between the teeth for the appropriate breakdown of the bolus to a suitable size for swallowing.

Future research directions

Our findings point to several fruitful areas of research. Future studies could test specifically for cortical plasticity related to the acquisition of the more complex masticatory motor skills noted above, and also for its potential role in the recovery of function, e.g., associated with masticatory and speech impairment following a cortical lesion or as a consequence of trauma to peripheral orofacial tissues. For example, tongue MEPs have been shown to provide important information in the assessment of corticolingual pathways following stroke, or in neurodegenerative disorders like amyotrophic lateral sclerosis (e.g., Urban et al. 1997, 1999, 2001). The role of sensory inputs in the acquisition of orofacial motor skills and associated cortical plasticity also needs investigation since many face MI neurons receive orofacial sensory inputs (Kubota 1976; Murray and Sessle 1992b, 1992c; Martin et al. 1997; Yao et al. 2002a, 2002b), and these inputs may be important, indeed perhaps crucial, during motor learning. Moreover, the TMS technique used in the present study does not allow for a precise delineation of the actual cortical, or subcortical, regions involved in the plastic changes during the learning of the new motor skill (Siebner and Rothwell 2003), and our use of surface recording of tongue MEPs does not provide any definition of the actual tongue muscle(s) associated with the plastic changes. Thus, future experiments might also be directed toward examining plasticity related to specific tongue muscles by the use of intramuscular lingual recordings in association with TMS and other techniques providing greater resolution (multi-channel EEG, fMRI, PET). These experiments might be designed to test for plasticity at several time periods or, in association with a longer training period, to ascertain more definitively the onset and duration of improvement in motor performance in relation to plastic changes in the corticomotor control of the tongue musculature.

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