

RESEARCH ARTICLE

Sensory Processing

Theta-burst stimulation over primary somatosensory cortex modulates the tactile acuity of the tongue

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Abstract

Emerging studies in humans have established the modulatory effects of repetitive transcranial magnetic stimulation (rTMS) over primary somatosensory cortex (S1) on somatosensory cortex activity and perception. However, to date, research in this area has primarily focused on the hand and fingers, leaving a gap in our understanding of the modulatory effects of rTMS on somatosensory perception of the orofacial system and speech articulators. The present study aimed to examine the effects of different types of theta-burst stimulation (TBS)—continuous TBS (cTBS), intermittent TBS (iTBS), or sham—over the tongue representation of left S1 on tactile acuity of the tongue. In a repeated-measures design, 15 volunteers participated in four separate sessions, where cTBS, iTBS, sham, or no stimulation was applied over the tongue representation of left S1. Effects of TBS were measured on both temporal and spatial perceptual acuity of the tongue using a custom vibrotactile stimulator. Results showed that cTBS significantly impaired spatial amplitude threshold at the time window of 16–30 min after stimulation, whereas iTBS improved it at the same time window. The effect of iTBS, however, was smaller than cTBS. In contrast, neither cTBS nor iTBS had any effect on the temporal discrimination threshold. The current study establishes the validity of using TBS to modulate somatosensory perception of the orofacial system. Directly modifying somatosensation in the orofacial system has the potential to benefit clinical populations with abnormal tactile acuity, improve our understanding of the role of sensory systems in speech production, and enhance speech motor learning and rehabilitation.

NEW & NOTEWORTHY The current study examines the effects of different types of theta-burst stimulation (TBS) [continuous TBS (cTBS), intermittent TBS (iTBS), sham] over the tongue representation of left primary somatosensory cortex (S1). Results show that the spatial acuity of the tongue can be impaired or improved by cTBS or iTBS, respectively. Directly modifying somatosensation in the orofacial system can benefit clinical populations with abnormal tactile acuity, advance our understanding of sensory systems in speech production, and improve speech motor learning and rehabilitation.

orofacial system; primary somatosensory cortex; somatosensory perception; speech production; transcranial magnetic stimulation (TMS)

INTRODUCTION

Somatosensory input is essential for motor control. If somatosensory input is not properly processed both before and during movement, the resulting motor output exhibits abnormalities and/or inaccuracies (1, 2). Growing evidence indicates impairments in somatosensory function are a major contributor to the motor dysfunction commonly observed in

neurologic injury or disorders such as Parkinson's disease, cerebral palsy, dystonia, and ataxia (3–6).

Primary somatosensory cortex (S1) plays a crucial role in somatosensory processing, and, importantly, has demonstrated a high capacity for plastic change (7). Changes in response properties of S1 neurons and local excitatory/inhibitory circuitry in S1 have been observed in animals in response to manipulation of sensory experience (8, 9) and repetitive



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intracortical microstimulation (10, 11). In humans, emerging studies have used forms of repetitive transcranial magnetic stimulation (rTMS) as a tool to investigate somatosensory perception (for review, see Ref. 12). A low-frequency rTMS train (1 Hz or below) is able to reduce cortical excitability of somatosensory cortex and hence diminish tactile and proprioceptive acuity (e.g., see Refs. 13 and 14). In contrast, high-frequency rTMS (5 Hz or above) increases the excitability of S1 and usually results in an improvement of somatosensory perception (e.g., see Refs. 15 and 16).

More recently, theta-burst stimulation (TBS) has gained popularity as a method to alter cortical excitability. Compared with traditional rTMS approaches, TBS offers a unique opportunity to induce powerful and long-lasting effects to the stimulated cortical areas with a much shorter stimulation time (less than 1 min) and lower stimulation intensity. TBS can be applied intermittently (iTBS) or continuously (cTBS). Intermittent TBS (bursts of 3 pulses at 50 Hz for 2 s, repeated every 10 s for a total of 190 s, 600 pulses) tends to increase cortical excitability and induce long-term potentiation (LTP) in targeted neural circuits, whereas continuous TBS (bursts of 3 pulses at 50 Hz at a rate of 5 Hz for 40 s, 600 pulses in total) tends to decrease cortical excitability and induce long-term depression (LTD) in targeted circuits (17). TBS over S1 has been shown to facilitate (iTBS) and inhibit (cTBS) somatosensory cortex activity and somatosensory perception (e.g., see Refs. 18–20). For example, significant improvements in both tactile spatial and temporal acuity were observed in the contralateral (but not ipsilateral) index finger for up to 30 min after the end of the iTBS train over S1 (19, 21). In contrast, cTBS over left S1 significantly increased temporal and spatial amplitude discrimination thresholds in the hand for up to 18 min (20).

Previous studies in this area have predominantly centered on the hand and fingers, resulting in a dearth of understanding of the modulatory effects of rTMS on the orofacial system and speech articulators. Orofacial somatosensation plays an important role in speech-motor learning (22–24), and recent computational simulation work suggests somatosensory input is as important for accurate speech production as it is for limb and posture control (25). TMS has the potential to both enhance and impair all aspects of orofacial somatosensation, an improvement over existing methods like anesthesia, which can only block tactile sensation. Thus, modulating somatosensory activity and perception of the orofacial system and speech articulators with TBS has promise both in basic science work to improve our understanding of the role of sensory systems in speech production and, potentially, to modulate speech motor learning and rehabilitation, especially for people with speech motor disorders. The present study aimed to examine the effects of different types of theta-burst stimulation (cTBS, iTBS, sham) over the tongue representation of left S1 on the tactile acuity of the tongue. The left hemisphere was selected as the site for stimulation given its frequent use as the target site in hand TBS studies (e.g., see Refs. 19, 20, and 26) and its crucial role in speech production.

METHOD

Subjects

Seventeen right-handed adult individuals were recruited. All participants reported no hearing problems and no

personal or family history of seizures or other neurological disorders. Participants provided written informed consent and were compensated monetarily for their participation. The Institutional Review Board of the University of Wisconsin–Madison approved the experimental protocol.

We based our expected effect size on a previous study showing that cTBS over the left S1 significantly impaired somatosensory acuity of the hand (Cohen's $d = 0.93$, $N = 16$, post hoc Tukey's test, 3–7 min after the cTBS train, $P = 0.001$) (20). We conservatively estimated an effect size of 0.8 considering that the effect on the tongue might be weaker, and determined that even at 80% power, a sample size of 14 would be sufficient to detect significant ($\alpha = 5\%$) acuity changes (G*Power 3.1, Ref. 27).

One participant withdrew after finishing the first visit for reasons unrelated to the study. One participant was excluded because we failed to localize their tongue representation in the motor cortex, as no clear tongue motor-evoked potentials (MEPs) could be observed under safe maximum TMS intensity. In total, data from 15 participants (8/7 females/males, 18–48 yr, mean 25.3 ± 8.5) were further analyzed.

Experimental Procedure

The current study used a within-subject design. Each participant completed four sessions in which they underwent the same behavioral procedure (see Fig. 1). There was at least 1 wk between each session. During the first three visits, participants received cTBS, iTBS, or sham stimulation over the left S1. The order of visits was pseudorandomized to ensure that it was counterbalanced across all participants. The fourth (control) visit involved only behavioral tasks without any brain stimulation.

The timeline of each visit is depicted in Fig. 1A. Spatial amplitude discrimination threshold (SDT, ~80 s/block) and temporal discrimination threshold (TDT, ~100 s/block) tasks were used to measure spatial and temporal tactile acuity of the tongue, respectively (Fig. 1D; see *Task and Stimuli* for more detailed task information). Participants first completed a brief training to familiarize them with each task. Once the performance criteria of the training trials were met (five consecutive correct responses), baseline (pre-TBS) tests began. Baseline tests consisted of three blocks of each task, with the tasks alternating. A 1-min break was given after each block. When the baseline tests were completed, participants received single-pulse TMS to localize S1 and determine the active motor threshold. TBS was delivered following a 20-min break to allow the somatosensory cortex to recover from any potential disruption related to single-pulse TMS. Finally, post-TBS tests were performed every 5 min for 45 min following stimulation: participants completed 10 blocks of each task (SDT and TDT), alternating between the tasks with a 1-min break in between each task.

Task and Stimuli

A custom vibrotactile stimulator (Cortical Metrics, Fig. 1C) was used to measure both the temporal discrimination threshold and spatial amplitude discrimination threshold of the tongue. A similar device has previously been used to measure the temporal and spatial amplitude acuity of the hand (20, 28, 29). The device consists of two plastic circular

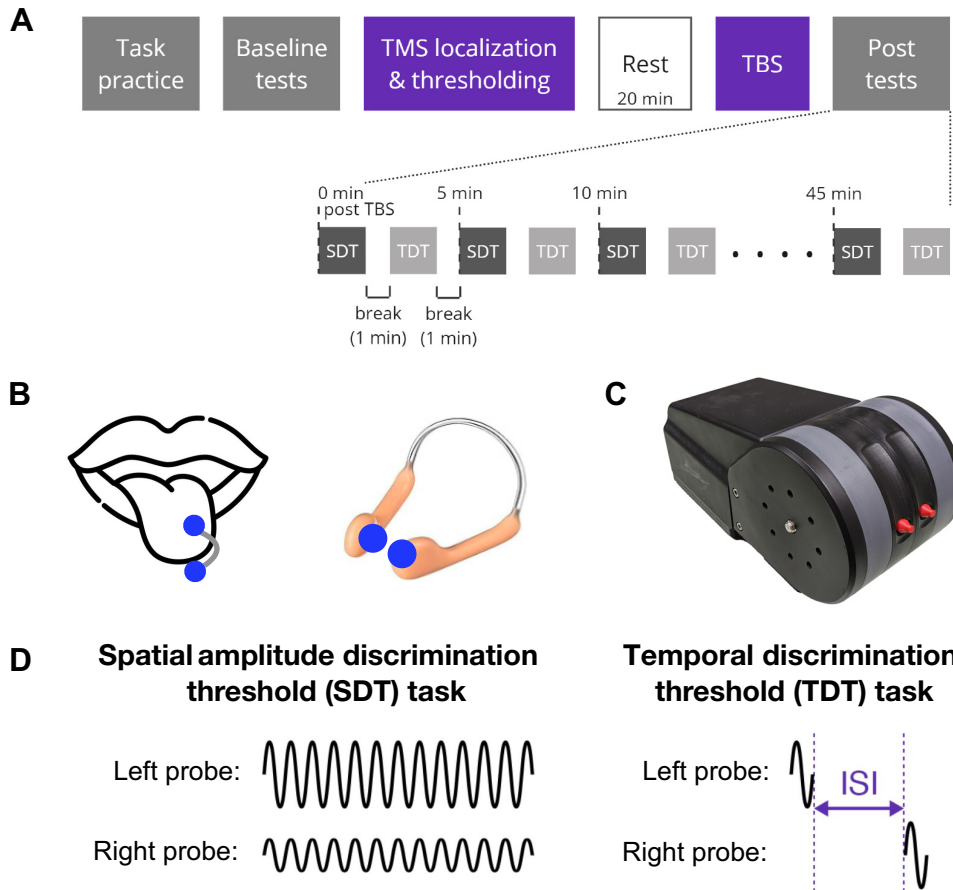


Figure 1. Experimental procedure. **A:** timeline of each visit. During each visit, participants received a different type of theta-burst stimulation (TBS) [continuous (cTBS), intermittent (iTBS), or sham] or no stimulation (control). Spatial amplitude discrimination threshold (SDT, dark gray) and temporal discrimination threshold (TDT, light gray) were estimated before stimulation (baseline tests) and every 5 min for 45 min following stimulation (post tests). **B:** electromyography (EMG) recording from the tongue. To record EMG activity from the tongue muscles, two disposable EEG cup electrodes (blue) were mounted to a swimming nose clip, which was placed on the right side of the tongue blade (electrodes placed on dorsal and ventral surfaces). **C:** somatosensory stimuli. A custom vibrotactile stimulator was used to deliver tactile stimuli while participants positioned their tongue on the two probes (red). **D:** somatosensory acuity tasks. *Left:* spatial amplitude discrimination threshold task, in which participants were asked to determine which probe vibrated more intensely. *Right:* temporal discrimination threshold task, in which participants were asked to determine which probe vibrated first. ISI, interstimulus interval.

(3-mm diameter) probes located on the surface of a rotatory cylindrical disk. The distance between the two probes was set at ~ 2.4 cm to ensure participants could feel both probes, one on each side of the tongue.

During both tasks, participants were seated comfortably in a chair in front of the vibrotactile stimulator, which was placed on a height-adjustable stand set to a comfortable position. Participants positioned their tongues on the two probes (using the same tongue position in each session) and were instructed to try to maintain even pressure against both probes. During the 1-min break between tasks, participants were able to relax their tongues. They were instructed to reposition their tongue on the probes to get ready for the task at least 10 s before the next block (a countdown timer was shown on a computer monitor). Earplugs were provided to minimize the auditory cues resulting from the vibrating probes.

Spatial amplitude discrimination threshold task.

Each block of the SDT task consisted of 15 trials, with each block yielding a unique measurement of the participants' discrimination threshold. For each trial, the two probes were vibrated simultaneously at 25 Hz for a duration of 500 ms (Fig. 1D, left). Participants were instructed to report which probe vibrated more intensely by clicking a computer mouse (left click = left probe is more intense, right click = right probe is more intense). The amplitude difference of vibration between the two probes was set at 100 μ m for the first trial of

each block and was subsequently varied with a step size of 20 μ m. A 1-down 1-up rule was followed for the first five trials and then adjusted to a 2-down 1-up rule for the rest of the trials (i.e., two correct responses decreased the amplitude difference by 20 μ m while one incorrect response increased the amplitude difference by 20 μ m). The amplitude of one probe (standard probe) remained constant at 200 μ m throughout all trials. The location of the standard and test was randomized on a trial-by-trial basis. The intertrial interval (ITI) was set at 4 s. The perceptual SDT for each block of the task was calculated as the average of the amplitude difference in the last five trials (20, 30, 31).

Temporal discrimination threshold task.

Each block of the TDT task consisted of 21 trials, with each block yielding a unique measurement of the participants' discrimination threshold. For each trial, the two probes were vibrated at 25 Hz for 40 ms at an amplitude of 300 μ m (Fig. 1D, right). The interstimulus interval (ISI) between the first and second vibrating probe was set at 150 ms for the first trial of each block and was subsequently varied following a 1-down 1-up rule, with a step size of 15%. Participants were instructed to identify which probe vibrated first and respond as quickly as possible by making a mouse click (left click = left probe vibrated first, right click = right probe vibrated first) with their right hand. The first vibrating probe (left or right) was randomized on a trial-by-trial basis. The ITI was set at 3 s. The perceptual TDT for each block of the task was

calculated as the average ISI measured from the last five trials (20, 28, 32, 33).

Electromyography Recording

Electromyography (EMG) was recorded using a BrainSight built-in 2-channel EMG device. To record EMG activity from the tongue muscles, two disposable EEG cup electrodes were mounted to a swimming nose clip, which was placed on the right side of the tongue blade (Fig. 1B, electrodes placed on dorsal and ventral surfaces) (34, 35). The ground electrode was placed on the forehead for tongue EMG recordings.

TMS and Neuronavigation

TMS was delivered using Magstim 200 (single pulse) and Magstim Super Rapid Plus (TBS) stimulators with a D702 70-mm figure-of-eight coil (Magstim Company Ltd., UK). A BrainSight neuronavigation system (Rogue Research, Montreal, QC, Canada) was used to digitally register an MNI template brain (BrainSight default) with the TMS coil.

After baseline testing, single-pulse TMS (monophasic, Magstim 200) was used to localize the tongue representation in the left primary motor cortex (M1 hotspot), following a similar procedure as previously described (35). The coil was placed tangential to the skull, aiming to induce a current flow from posterior to anterior under the junction of the two wings of the figure-of-eight coil. The coil's position was adjusted until robust tongue MEPs were consistently observed. After localization, biphasic single-pulse TMS (Magstim Super Rapid) was applied over the M1 hotspot to determine the active motor threshold, the minimum intensity at which TMS elicited MEPs with an amplitude of at least 200 μ V on at least 5 of 10 pulses when the tongue muscle was contracted at 20%–30% of the maximum. Participants were trained to maintain the target level of muscle contraction using EMG feedback from the electrodes placed on the tongue, displayed visually on a computer monitor. The M1 hotspot of each participant was then marked on an MNI average head model using BrainSight Neuronavigation. For S1, we initially positioned the TMS coil 2 cm posterior to the M1 hotspot on the cortical surface, a common method for localizing hand S1 (see Ref. 12 for a review). If single-pulse TMS over this region elicited MEPs from the tongue muscles, the coil was moved posteriorly until tongue MEPs were no longer elicited. The M1 hotspot, S1 location, and active motor threshold were determined for each of the three TMS visits following the same procedure. The averaged coordinates of stimulated sites on the MNI template brain were $-49, -24, 48$ for the cTBS session, $-48, -23, 48$ for the iTBS session, and $-49, -24, 47$ for the sham session, respectively.

To avoid any potential effect induced by single-pulse TMS, TBS was applied following a 20-min break after localization. Participants received cTBS (bursts of 3 pulses at 50 Hz at a rate of 5 Hz for 40 s, 600 pulses in total), iTBS (bursts of 3 pulses at 50 Hz for 2 s, repeated every 10 s for a total of 190 s, 600 pulses), or sham stimulation over the tongue representation of left S1 at 80% of active motor threshold. The coil's positioning and orientation (with the handle oriented 45° from the midline) were visually monitored throughout the whole stimulation. For sham stimulation, the coil was

placed over S1 and rotated 90°, with the coil handle pointing vertically upward while still maintaining contact with the scalp.

Data Analysis

For both TDT and SDT, we defined the baseline threshold for each participant as the average of the discrimination thresholds estimated from the last two blocks of the baseline tests. We omitted the first block from the average because some participants showed large changes in thresholds from the first to the second block, likely due to increased familiarization. Threshold estimates were stable by the second baseline block, indicated by a lack of difference for either task between the second and third baseline blocks (paired *t* test, $P > 0.05$ in all sessions). Baseline thresholds for each task across sessions (cTBS, iTBS, sham, and control) were compared using repeated-measures ANOVAs. During post-TBS tests, discrimination thresholds were binned into three time windows (0–15 min, 16–30 min, and 30+ min after stimulation). We first assessed the significance of threshold changes in each task using paired-sample *t* tests with a significance level of $\alpha = 0.05$, comparing the thresholds in each of the three post-TBS time windows against baseline threshold. No adjustment for multiple *t* tests was applied due to the exploratory nature of this analysis. Discrimination thresholds during post-TBS tests were then normalized by dividing them by the baseline thresholds on a session-specific basis. To compare changes in thresholds across sessions, a single repeated-measures ANOVA was conducted for each task (SDT, TDT) using baseline-normalized thresholds with sessions (cTBS, iTBS, sham, and control) and time windows (0–15, 16–30, 30+ min) as independent variables. In the event of an interaction, follow-up post hoc comparisons at each time window were conducted using repeated-measures ANOVA across sessions. Further post hoc pairwise comparisons between sessions at a particular time window (one-tailed *t* tests with Bonferroni correction, given our prior hypothesis regarding the effects of different stimulations) were conducted only in the event of a significant main effect of this follow-up ANOVA.

All statistical analyses were performed in R (R Core Team). Repeated-measures ANOVAs and *t* tests were performed with the *rstatix* package (36). Partial eta squared (η^2) and Cohen's *d* were calculated for repeated-measures ANOVAs and *t* tests, respectively, to determine effect size for statistically significant effects.

RESULTS

The mean active motor thresholds (% stimulator output) for each stimulation were 38.3 ± 5.9 (cTBS), 38.7 ± 7.4 (iTBS), and 37.7 ± 5.9 (sham). There was no significant difference in active motor thresholds across the three stimulation sessions ($F_{2,28} = 1.25$, $P = 0.302$).

Spatial Amplitude Discrimination Threshold Task

The mean spatial amplitude discrimination thresholds during the baseline phase were 34.1 ± 20.9 μ m (cTBS), 43.8 ± 16.9 μ m (iTBS), 37.9 ± 16.6 μ m (sham), and 40.9 ± 21.8 μ m (no stimulation control), with no significant difference in SDT across sessions ($F_{3,42} = 1.31$, $P = 0.283$, see Supplemental

Fig. S1; all Supplemental materials are available at <https://osf.io/v4thu/>). To further evaluate the reliability of the SDT task, the intraclass correlation coefficient (ICC, using average measures) was calculated based on a two-way mixed-effects model. The across-session ICC for baseline SDT was estimated to be 0.78, suggesting good reliability of the spatial amplitude discrimination task (37).

Stimulation with cTBS significantly impaired spatial amplitude discrimination threshold at the time window of 16–30 min after stimulation ($+20.08 \mu\text{m}$, $t_{14} = 2.73$, $P = 0.016$, $d = 0.7$), whereas iTBS improved it at the same time window ($-8.07 \mu\text{m}$, $t_{14} = 2.16$, $P = 0.049$, $d = 0.56$) (Fig. 2A). The suppression and enhancement effects induced by cTBS and iTBS persisted numerically past 30 min after stimulation, though these effects did not reach statistical significance at this later time window (cTBS: $+18.1 \mu\text{m}$, $t_{14} = 1.87$, $P = 0.082$, $d = 0.48$; iTBS: $-6.63 \mu\text{m}$, $t_{14} = 1.8$, $P = 0.093$, $d = 0.47$). No significant change was observed at any post-TBS time window during the sham or control (no stimulation) sessions ($P > 0.13$ in all cases). Comparing between sessions (cTBS, iTBS, sham, and control) revealed a significant interaction between session and time ($F_{6,84} = 2.64$, $P = 0.021$, partial $\eta^2 = 0.16$). Follow-up ANOVAs at each time window showed that there were significant differences between sessions only at the time window of 16–30 min after stimulation ($F_{3,42} = 6.98$, $P < 0.001$, partial $\eta^2 = 0.33$; other $P > 0.05$). Post hoc tests revealed that the baseline-normalized thresholds after cTBS were significantly higher than those after control ($t_{14} = 3.22$, $P = 0.037$, $d = 0.83$), but there was no significant difference between cTBS and sham ($t_{14} = 2.51$, $P = 0.149$). The baseline-normalized thresholds after iTBS, however, showed only marginally significant differences (after Bonferroni correction) when compared with the sham session ($t_{14} = 2.28$, $P = 0.191$) and showed no significant difference when compared with the control session ($t_{14} = 0.61$, $P = 1$).

Group-averaged trial-by-trial spatial amplitude discrimination performance for each session is shown in Fig. 3A. Performance across all time windows (baseline, 0–15 min, 16–30 min, and 30 min after stimulation) for all four sessions reached a plateau around trial 9 of 15, which is similar to previous experiments that measured spatial amplitude acuity of the hand (20). The effects of cTBS and iTBS on SDT occurred when performance had already reached the plateau.

Temporal Discrimination Threshold Task

The mean temporal discrimination thresholds during the baseline phase were 37.3 ± 20.8 ms (cTBS), 37.6 ± 20.3 ms (iTBS), 37 ± 21.4 ms (sham), and 42.4 ± 27.7 ms (no stimulation control), with no significant difference in TDT across sessions ($F_{3,42} = 0.34$, $P = 0.795$, Supplemental Fig. S2). The across-session ICC for baseline TDT was estimated to be 0.77, suggesting good reliability of the temporal discrimination task (37).

In contrast to the effects of cTBS and iTBS on SDT, neither cTBS nor iTBS had effects on TDT (Fig. 2B). No significant change was observed during any session ($P > 0.13$ in all cases). The baseline-normalized thresholds did not differ significantly between sessions at any post-TBS time window. Group-averaged trial-by-trial temporal discrimination performance for each session is shown in Fig. 3B. Performance across all time windows (baseline, 0–15 min, 16–30 min, and 30 min after stimulation) for all sessions reached a plateau around trial 17 of 21.

DISCUSSION

The current study establishes the capacity of TBS over the tongue representation in S1 to modulate tactile perception of the tongue. Specifically, cTBS was found to impair spatial amplitude discrimination, whereas iTBS enhanced it. The maximal effects did not occur until 16–30 min after the end of TBS. In contrast to the modulatory effects on spatial discrimination, neither cTBS nor iTBS influenced temporal discrimination. TBS thus presents a new way to modulate somatosensation in the orofacial system.

It is noted that the effect of iTBS on tongue spatial acuity was smaller than cTBS ($+20.08 \mu\text{m}$, Cohen's $d = 0.7$ vs. $-8.07 \mu\text{m}$, Cohen's $d = 0.56$). Moreover, although the threshold changes induced by iTBS did differ from the baseline phase, they did not show significant differences when directly compared with control sessions (sham or no stimulation). This is consistent with previous TBS studies on the hand showing that the effect of iTBS over S1 tends to be less robust and stable than that of cTBS (12). This may be because the effects of cTBS and iTBS arise through distinct cellular mechanisms. A previous study found that somatosensory-evoked potentials (SEPs) and high-frequency oscillations

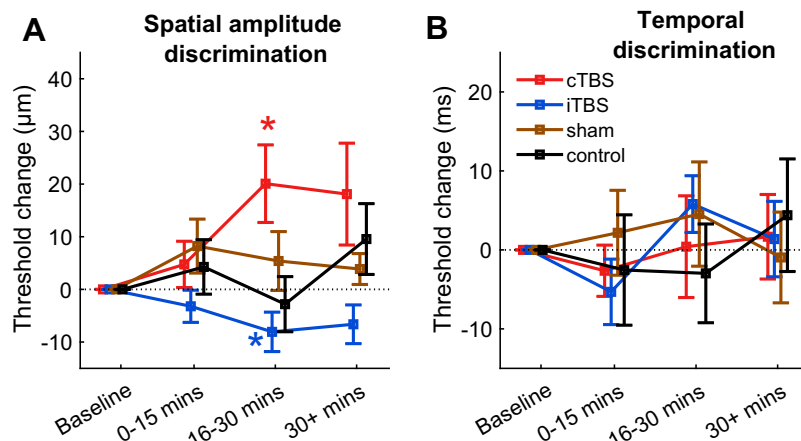


Figure 2. A: spatial amplitude discrimination thresholds (SDT). B: temporal discrimination thresholds (TDT). Threshold changes in the baseline, 0–15 min, 16–30 min, and 30 min after stimulation are shown for different groups. Error bars show standard error, and *a significant change ($P < 0.05$) from baseline. cTBS, continuous theta-burst stimulation; iTBS, intermittent theta-burst stimulation.

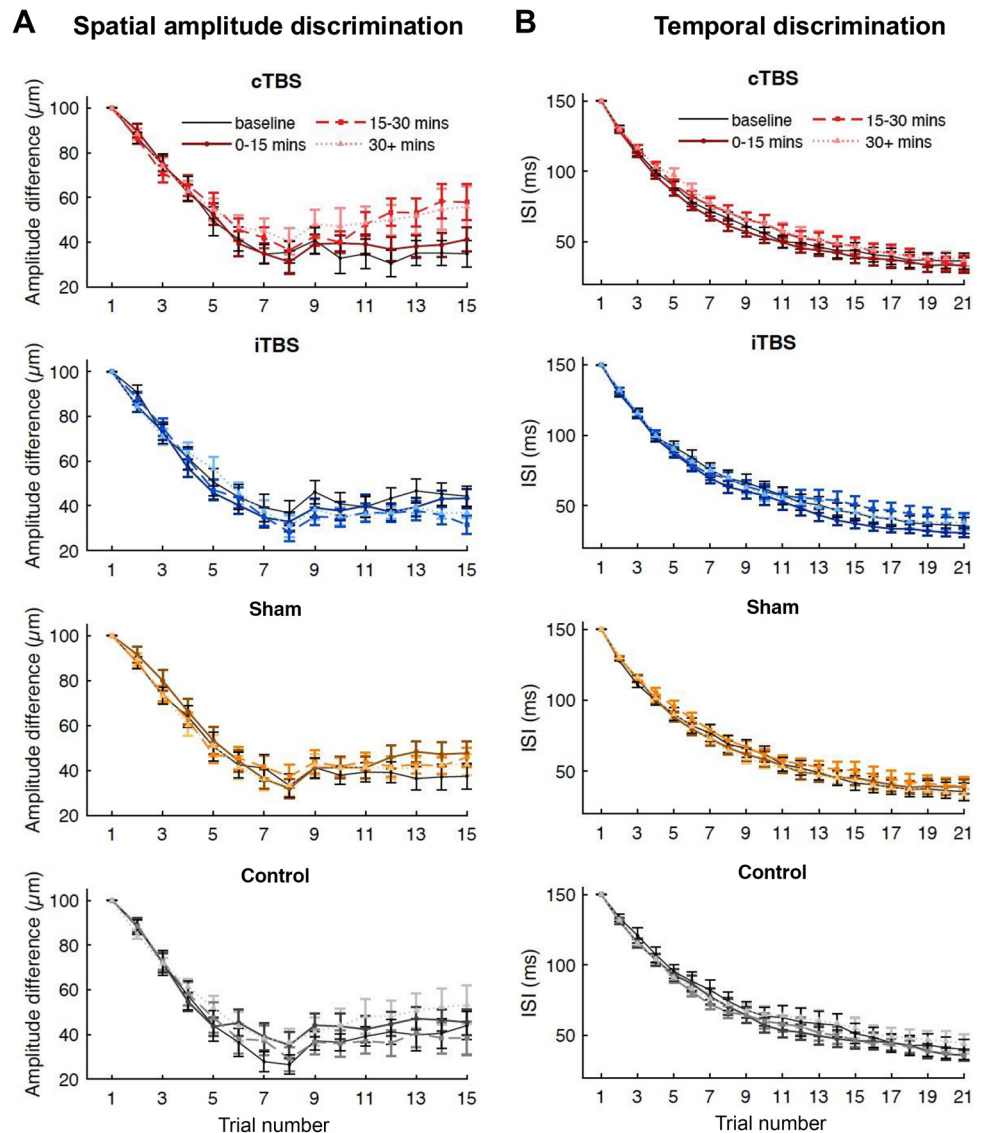


Figure 3. Group-averaged spatial amplitude discrimination performance (A) and temporal discrimination performance (B) for each trial, averaged across blocks within each time window. Lighter colors indicate data from later time windows. Error bars show standard error. cTBS, continuous theta-burst stimulation; iTBS, intermittent theta-burst stimulation.

(HFOs) were differently modulated by cTBS and iTBS: iTBS facilitated SEPs without changes in HFOs whereas cTBS modulated HFOs without changes in SEPs (38). Late HFOs (i.e., HFOs occurring after the N20 peak in an SEP) have been associated with the activity of inhibitory GABAergic interneurons in the superficial cortical layers (39–41). Therefore, it is possible that cTBS influences tongue acuity by modulating the excitability of GABAergic inhibitory interneurons, particularly those involved in generating the late HFOs within the superficial layers of S1, whereas iTBS does not. However, the exact mechanisms that underlie the effects of TBS on S1/S2 excitability are not fully understood. Future studies are needed to clarify the neurophysiological effects of cTBS and iTBS over S1 and their relationship with behavioral performance.

Interestingly, the maximal modulatory effect did not appear immediately following TBS. Instead, significant increases and reductions of SDT were observed from 16 to 30 min following cTBS and iTBS, respectively. This is in line with a previous study (38), showing both cTBS and iTBS over S1 caused changes in the excitability of intracortical circuits, as measured

by SEPs and HFOs, but these effects were only observed 15–30 min after TBS. Similar time-dependent effects were also observed in a study in which cTBS was applied over the lip representation of M1: discrimination of lip-articulated speech sounds was impaired between 20 and 35 min after cTBS, but not immediately after cTBS (<20 min) (42). A previous study using cTBS applied to the hand representation in S1, however, showed that SDT on the hand was impaired immediately after the application of cTBS and persisted for up to 18 min (20). Such differences could potentially relate to the specialized functions and neural organization of hand and speech articulatory representations in M1 and S1. Compared with the hand representation, speech articulatory representations are typically smaller and often positioned more medially and deeper within the cortex. Thus, it is possible that the process of inducing and solidifying synaptic changes in articulatory representations may require a longer time than in the hand representation. Alternatively, the inconsistency between the hand-S1 study and this study may have resulted from the fact that responses to TMS can vary largely across individuals and differences in methodology (see Ref. 12 for a review).

In contrast to the modulatory effects of S1-TBS on spatial amplitude discrimination of the tongue, neither cTBS nor iTBS over left S1 influenced temporal discrimination. We see two potential (nonexclusive) explanations for this result. First, the lack of change in TDT may be caused by the compensatory involvement of other cortical areas, which could offset the S1 excitability changes induced by TBS. Unlike spatial amplitude discrimination, temporal discrimination has been found to engage multiple cortical areas, including the secondary somatosensory cortex (43, 44), anterior cingulate, and supplementary motor areas (45, 46). Moreover, growing evidence suggests that the superior temporal gyrus, prefrontal, and parietal cortices might play an important role in tactile temporal perception (47, 48). Experimentally, mixed results have been reported from studies investigating the effects of TBS over S1 on temporal acuity of the hand. Lee et al. (28) observed no changes in temporal acuity after applying cTBS over S1, whereas other studies found significant impairment following cTBS (20) and improvement following iTBS (21). Second, even though participants were given earplugs to minimize the auditory cues resulting from the vibrating probes, it is possible that participants might have still been able to hear the individual probes (asynchronously) vibrating. The use of these additional auditory temporal cues may have obscured TBS-induced effects on somatosensory temporal acuity during the temporal discrimination task. As such, this null result should be interpreted cautiously. Further work that completely blocks auditory cues could help clarify whether the lack of effects of TBS on temporal discrimination of the tongue observed in the current study was due to participants relying on auditory cues to compensate for the impaired temporal discrimination or whether temporal discrimination is truly unaffected by TBS stimulation of S1.

In the current study, the left hemisphere was chosen as the stimulation site because of its dominant role in speech production. However, the tongue is bilaterally represented in the cortex, with both hemispheres processing somatosensory information from both sides of the tongue (49). Indeed, previous studies have reported neural activation in both contralateral and ipsilateral S1 in response to somatosensory stimulation of the tongue (for a review, see Ref. 50). It is thus possible that differences between the present study and previous work in the hand, which is primarily represented in the contralateral hemisphere of the brain, may result from this difference in laterality. Broadly, we expect that TMS applied to the analogous location in the right hemisphere would have similar effects on tactile perception. However, there is evidence suggesting that the right S1 might be more dominant during certain somatosensory processing tasks (51). It is thus possible that the different effects of left S1 stimulation on temporal and spatial somatosensory perception of the tongue observed in the current study may result from such hemispheric specialization. Precise spatial somatosensory perception may require the involvement of both the left and right S1, whereas temporal somatosensory perception may be more lateralized, with possible dominance of the right hemisphere. Future research investigating the effects of right S1 stimulation on temporal and spatial somatosensory perception of the tongue is needed to further clarify this point. Moreover, it would be worthwhile for future research

to explore the effects of bilateral stimulation of S1 to potentially induce a more robust modulatory effect.

Another factor that could influence the interpretation of the current study is the method used to target the tongue representation of S1. Systematic reviews have revealed that when MRI is not available, the most common method used to localize S1-hand involves positioning the coil 2 cm posterior to the M1 representation of hand muscles (12, 52). In the present study, we followed the common method used in the hand studies: tongue representation of S1 was localized by moving 2 cm posterior from M1-tongue. However, recent work showed that instead of 2 cm posterior from M1-hand, S1-hand is close to the C3/C4 electroencephalography (EEG) electrode locations on the scalp, or ~2 cm lateral and 0.5 cm posterior to the M1-hand (53). Moreover, these estimates, whether 2 cm posterior or 2 cm lateral and 0.5 cm posterior to the M1-hand, may not be accurate for individual participants; the range of scalp locations across participants can vary by as much as 3–4 cm in each direction for each location. Therefore, nearby regions like the secondary somatosensory cortex and sensory association areas may also have been affected. The effects observed in the current study might be the result of combined influence from multiple somatosensory areas.

The current study used a custom vibrotactile stimulator to measure both the temporal discrimination threshold and spatial amplitude discrimination threshold of the tongue. Task-specific parameters mostly followed those used in a previous hand study using a similar stimulator (20), with a few adjustments made to accommodate the unique attributes of the tongue. In contrast to the hand study, where participants were able to rest their hands on the stimulator, participants in our study were required to continuously protrude their tongue to maintain contact with the two probes without the option to rest during the task. To prevent participant fatigue, we aimed to 1) restrict each block to a maximum of 1 min, leading to a total of 15 trials per block for the SDT task and 21 trials for the TDT task, and 2) provide a 1-min break between blocks during which participants were able to relax their tongue. Consequently, the 1-down 1-up rule was applied for the first five trials, as opposed to the first 10 trials used in the hand study, and the 2-down 1-up rule was applied for the rest of the trials. For the TDT task, several participants in a pilot study found the starting ISI used in the hand study (60 ms) to be challenging when applied to the tongue. We thus increased the starting ISI to 150 ms and, to achieve a faster convergence within the limited number of trials, changed the step size to 15% (ranging between 22.5 ms and ~2 ms) instead of a fixed step size of 5 ms. We believe that this new step size can more effectively capture changes in ISI across a broader range. Our tasks with the task-specific adaptive methods and parameters were demonstrated to be both efficient and reliable: participants' performances reached a plateau during the last five trials in each block, similar to what was observed in the hand study (Fig. 3). Moreover, the high intraclass correlation coefficient (ICC) across sessions suggests the measurements are consistent and reproducible across different testing sessions.

The present study establishes the validity of using neuro-modulatory techniques to modulate somatosensation in the orofacial system. Importantly, applying TBS over S1 has the potential to affect all types of orofacial somatosensation,

including proprioceptive signals. Due to the inability to block proprioception of the tongue using anesthetics (52, 53), a lingering question in the field of speech motor control is the impact of a complete loss of proprioception on speech (25). Using TMS to modulate somatosensation in the orofacial system may serve as an improvement over previous attempts to decrease somatosensory acuity through the use of topical anesthetics (54, 55), which affect only tactile sensitivity. In addition, using TMS to modulate orofacial somatosensation can also benefit clinical populations with abnormal tactile acuity, such as patients with Parkinson's disease (56). Therefore, directly modifying somatosensation of the human orofacial system can provide valuable insights into the role of sensory systems in speech production, and has the potential to improve tactile acuity and speech production in both healthy and clinical populations.

DATA AVAILABILITY

Data will be made available upon reasonable request.

SUPPLEMENTAL MATERIAL

Supplemental Figs. S1 and S2: <https://osf.io/v4thu/>.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

D.-L.T., M.T., C.A.N., and B.P. conceived and designed research; D.-L.T. performed experiments; D.-L.T. analyzed data; D.-L.T., C.A.N., and B.P. interpreted results of experiments; D.-L.T. prepared figures; D.-L.T. drafted manuscript; D.-L.T., C.A.N., and B.P. edited and revised manuscript; M.T., C.A.N., and B.P. approved final version of manuscript.

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