

# Neurorehabilitation and Neural Repair

<http://nnr.sagepub.com/>

---

## Differential Effects of Neuromuscular Electrical Stimulation Parameters on Submental Motor-Evoked Potentials

Sebastian H. Doeltgen, John Dalrymple-Alford, Michael C. Ridding and Maggie-Lee Huckabee

*Neurorehabil Neural Repair* 2010 24: 519 originally published online 12 March 2010

DOI: 10.1177/1545968309360417

The online version of this article can be found at:

<http://nnr.sagepub.com/content/24/6/519>

---

Published by:



<http://www.sagepublications.com>

On behalf of:



[American Society of Neurorehabilitation](http://www.asnr.org)

**Additional services and information for *Neurorehabilitation and Neural Repair* can be found at:**

**Email Alerts:** <http://nnr.sagepub.com/cgi/alerts>

**Subscriptions:** <http://nnr.sagepub.com/subscriptions>

**Reprints:** <http://www.sagepub.com/journalsReprints.nav>

**Permissions:** <http://www.sagepub.com/journalsPermissions.nav>

**Citations:** <http://nnr.sagepub.com/content/24/6/519.refs.html>

# Differential Effects of Neuromuscular Electrical Stimulation Parameters on Submental Motor-Evoked Potentials

Neurorehabilitation and  
Neural Repair  
24(6) 519–527  
© The Author(s) 2010  
Reprints and permission: <http://www.sagepub.com/journalsPermissions.nav>  
DOI: 10.1177/1545968309360417  
<http://nnr.sagepub.com>  


Sebastian H. Doeltgen, PhD,<sup>1,2</sup> John Dalrymple-Alford, PhD,<sup>1,2</sup>  
Michael C. Ridding, PhD,<sup>3</sup> and Maggie-Lee Huckabee, PhD<sup>1,2</sup>

## Abstract

**Background.** Neuromuscular electrical stimulation (NMES) of the muscles underlying the pharynx and faucial pillars affects the excitability of corticobulbar projections in a frequency- and duration-specific manner. The anterior hyomandibular (submental) muscles are primary targets for the clinical application of NMES to improve disordered swallowing, but the optimal NMES parameters for this application are unknown. **Objective.** To determine the influence of NMES parameters on the excitability of corticobulbar projections to the submental musculature. **Methods.** Transcranial magnetic stimulation (TMS) was used in event-related protocols, triggered by either volitional contraction of the submental muscles or pharyngeal swallowing, to assess corticobulbar excitability prior to, immediately following, and 30, 60, and 90 minutes post-NMES in 25 healthy volunteers. In the first 2 experiments, 4 stimulus frequencies (5, 20, 40, and 80 Hz) and 3 NMES dosages, manipulated through stimulus train durations or number of repetitions, were evaluated. The optimal excitatory NMES triggered by volitional swallowing (event-related NMES) was then replicated in a new sample and contrasted with non-event-related NMES (either discrete events or continuously for 1 hour). **Results.** It was found that 80Hz NMES increased motor-evoked potential (MEP) amplitude at 30 minutes and 60 minutes poststimulation only after 60 repetitions of 4-s event-related NMES trains. Non-event-related and continuous NMES did not affect MEP amplitudes. No changes in MEP onset latencies were observed. **Conclusions.** Changes in corticobulbar excitability induced by NMES of the submental muscle group are frequency and dose dependent and only occur after NMES triggered by volitional swallowing. Underlying neural mechanisms are discussed.

## Keywords

neuromuscular electrical stimulation, deglutition, motor control, motor-evoked potential, transcranial magnetic stimulation

## Introduction

Neuromuscular electrical stimulation (NMES) of the anterior hyomandibular (submental) and laryngeal musculature has become an increasingly popular treatment modality for patients with swallowing disorders.<sup>1</sup> However, the precise effects of this treatment on oropharyngeal swallowing biomechanics and safety remain unclear. Improved swallowing function has been documented,<sup>2,3</sup> but other studies have reported unchanged electromyographic activity of the stimulated muscles<sup>4,5</sup> or descent of the thyolaryngeal complex during stimulation in healthy volunteers<sup>6</sup> and individuals with disordered swallowing.<sup>7</sup> These discrepancies may in part relate to the different treatment protocols used across studies because stimulation parameters and the types of NMES administered (event-related or non-event-related) differed.

In fact, prior research on other muscles involved in swallowing has documented that NMES affects the excitability of corticobulbar motor projections to the pharyngeal<sup>8</sup> and faucial pillar muscles<sup>9</sup> in a frequency- and duration-specific manner. What is important is that changes in corticobulbar excitability were positively related to swallowing function

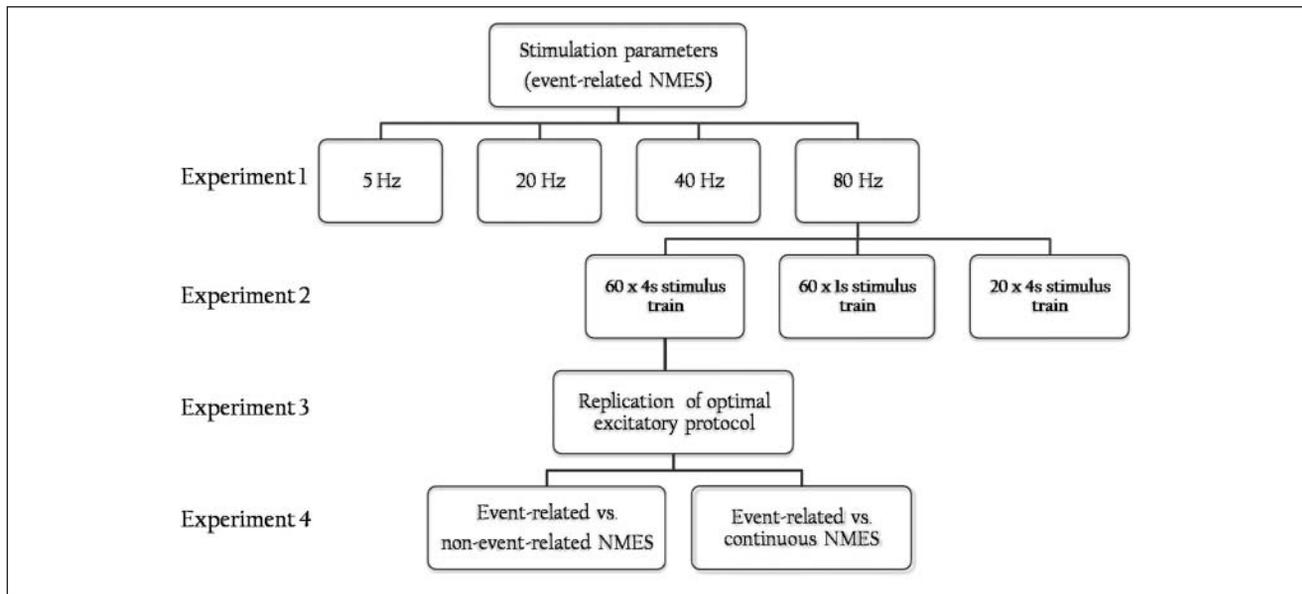
<sup>1</sup>University of Canterbury, Christchurch, New Zealand

<sup>2</sup>Van der Veer Institute for Parkinson's and Brain Research, Christchurch, New Zealand

<sup>3</sup>The Robinson Institute, School of Paediatrics and Reproductive Health, University of Adelaide, Adelaide, Australia

### Corresponding Author:

Sebastian H. Doeltgen, Swallowing Rehabilitation Research Laboratory, Van der Veer Institute for Parkinson's and Brain Research, 66 Stewart Street, Christchurch, New Zealand  
Email: [sebastian.doeltgen@adelaide.edu.au](mailto:sebastian.doeltgen@adelaide.edu.au)



**Figure 1.** Overview of experimental sequence: the effect of neuromuscular electrical stimulation (NMES) frequency on corticobulbar excitability was evaluated first (experiment 1), followed by an evaluation of NMES dose (varied by number of stimulus train repetitions or stimulus train length; experiment 2). The optimal excitatory protocol was then replicated (experiment 3), and the effects induced by event-related and non-event-related NMES protocols were compared (experiment 4)

in both studies,<sup>8,9</sup> indicating a relationship between underlying neural substrates and biomechanical events during swallowing. Specifically, the amplitude of motor-evoked potentials (MEPs) induced by transcranial magnetic stimulation (TMS) to the motor cortex increased after 5-Hz NMES and decreased after 20- and 40-Hz NMES of the muscles underlying the pharyngeal mucosa compared with prestimulation baseline.<sup>8</sup> Maximal changes were induced by 10 minutes of non-event-related NMES, whereas NMES of 5 minutes or 20 minutes duration produced smaller posttreatment changes. However, excitatory and inhibitory stimulation parameters appear to differ as a function of site of stimulation. For example, 0.2-Hz NMES facilitated and 5-Hz NMES inhibited MEPs recorded from the musculature underlying the faucial pillars.<sup>9</sup>

Based on these previous findings, it is likely that different muscles, or groups of muscles, involved in swallowing will have specific optimal stimulation parameters. Furthermore, NMES administered during execution of a purposeful motor task (event-related NMES) may be superior to NMES administered when the target muscle is at rest (non-event-related NMES).<sup>10</sup> However, a beneficial effect of time-locked endogenous and exogenous neuromuscular excitation has not been conclusively evaluated in swallowing rehabilitation. The present study provides a systematic examination of different NMES protocols on the excitability of the corticobulbar projection to the submental muscle group. These muscles represent a vital component of the pharyngeal phase of swallowing<sup>11</sup> and are a common target for the clinical

application of NMES in swallowing rehabilitation.<sup>1,2,4-7</sup> Four experiments (Figure 1) examined NMES effects of stimulation frequency and dose, replication of optimal parameters in a second sample, and a comparison of event-related and non-event-related NMES procedures.

## Methods

### Participants

A total of 14 young healthy adults were initially screened for inclusion into experiments 1 and 2. Of these, 4 were excluded because no discernible MEPs could be recorded during the volitional contraction condition. Therefore, 10 young, healthy adults (mean age, 27.5 years; standard deviation, 2.9 years; 7 women; 7 right handed<sup>12</sup>) participated in the examination of stimulus frequency and dose parameters in 2 event-related NMES paradigms. For experiments 3 and 4, 15 healthy participants (mean age, 27.1 years; standard deviation, 7.1 years; 14 right handed<sup>13</sup>) of 19 initially screened were examined to replicate the effects of optimal stimulation parameters identified with the first sample and to assess the relative influence of non-event-related protocols. The study was approved by the appropriate Human Ethics Review Committee and all participants gave fully informed consent. They had no medical history or current symptoms of dysphagia and reported no neurological impairment and no drug use that would potentially affect their swallowing or neurological function.

### Electrode Placement

Participants were seated in a comfortable chair. Two surface electrodes (neonatal solid gel electrodes, BRS-50K, blue sensor) were mounted on the undersurface of the chin, recording electrical activity from the collective submental muscle group: left and right anterior belly of digastric, portions of the left and right mylohyoid and left and right geniohyoid. Electrode placement was standardized by placing the anterior electrode first, with its anterior edge located directly behind the inner bony edge of the mandible and the lateral edges overlapping 1 cm on either side of midline. The second electrode was placed posteriorly with a gap of 5 mm between electrodes. The submental electrodes were used to apply NMES and to record MEPs at baseline and at several assessments poststimulation.

In addition, 2 surface electrodes were mounted to the skin overlying the left thyrohyoid muscle, with the uppermost electrode positioned 2 cm lateral to midline over the superior aspect of the thyroid cartilage and the lower electrode positioned 1 cm inferior to the upper electrode. The thyrohyoid electrodes were used to trigger electrical stimulation during the event-related NMES protocols. A ground electrode was mounted over the bony mandibular prominence at the base of the vertical ramus.

### Triggering of NMES

Event-related submental NMES was triggered throughout by activity from the thyrohyoid electrodes because the onset of laryngeal elevation during swallowing is more closely related to the onset of thyrohyoid activity than to the onset of mylohyoid activity,<sup>4</sup> which is a central component of the submental musculature. Triggering event-related NMES from thyrohyoid sEMG activity ensured that NMES was applied in the functional context of laryngeal elevation during the pharyngeal phase of the swallow. The trigger threshold was determined for each participant and set at a level of 75% of the mean maximum thyrohyoid sEMG activity (in  $\mu\text{V}$ ) of 10 noneffortful saliva swallows. This value was chosen as it ensured that event-related NMES was applied during the muscle activation at the onset of the pharyngeal phase of the volitional swallow. Non-event-related NMES, in contrast, was triggered by a computerized external trigger when the submental musculature was at rest and not from swallowing-related thyrohyoid sEMG.

### Triggering of MEP Outcome Measurement

To assess corticobulbar excitability in a functionally relevant context, MEPs were recorded during 2 submental muscle activation conditions: voluntary contraction and contraction associated with the reflexive, pharyngeal phase of a volitional swallow. TMS was triggered from submental sEMG,

with the threshold set to 75% of the individual's mean maximum submental sEMG activity of 10 noneffortful saliva swallows that were performed with minimized voluntary oral movements. All trigger thresholds were identified at the beginning of each of the data acquisition sessions. For volitional swallowing, participants were instructed to "swallow your saliva." Participants were instructed to limit any volitional, oral preparatory movements, in particular tongue movements, during this condition. For the volitional submental contraction condition, they were instructed to "contract the muscles under your chin as if stifling a yawn."<sup>13</sup> Visual feedback about the degree of muscle contraction was provided to participants by means of online submental sEMG. They were asked to match the degree of submental muscle activity during volitional contraction to the degree of submental muscle contraction displayed during swallowing. They practiced the volitional contraction condition, alternating between swallows and contractions, for approximately 5 minutes prior to data collection.

In addition to the objective of assessing corticobulbar excitability during performance of swallowing-related motor tasks, pilot work also revealed that motor responses in the submental musculature at rest could not be elicited reliably. This observation is consistent with studies of other facial muscles, which have reported preactivation to be necessary for reliable MEP detection.<sup>14</sup>

Corticobulbar excitability was assessed using focal TMS of the submental motor cortex using a figure-of-8 coil with an outer wing diameter of 70 mm and a maximum output of 2.2 Tesla (2nd Generation Double 70 mm Coil, 3190-00, Magstim Company Ltd, Whitland, Wales, UK). The optimal scalp locations for evoking submental MEPs from both hemispheres were identified. Data were recorded from the hemisphere from which the largest MEPs could be evoked. TMS intensity for further MEP testing was set to the value at which 50% of the maximal MEP amplitude was recorded. These procedures have been documented to produce reliable MEPs recorded during volitional swallowing.<sup>13</sup>

Prior to NMES, MEP baseline measures were obtained from each participant. In counterbalanced order, 15 submental MEPs were elicited by volitional and swallowing-related contraction of the submental muscles and recorded for offline analysis. TMS was triggered automatically when the preset submental sEMG threshold was reached. The same triggering threshold was used for eliciting MEPs during the volitional swallowing and the volitional muscle contraction conditions, ensuring that MEPs were evoked at a matched sEMG level during both conditions. Subsequent to the NMES treatment period, 15 MEPs were evoked during each of the muscle contraction conditions and recorded for offline analysis. Further counterbalanced sets of 15 MEPs for each condition were recorded at 30, 60, and 90 minutes posttreatment, as reported previously.<sup>8,9</sup>

### Experiment 1: Stimulation Frequency of Event-Related NMES

Event-related NMES treatment consisted of 60 repetitions of 4-s stimulus trains that were triggered approximately every 10 s from thyrohyoid activity during volitional swallows. Submental stimulation consisted of a square-wave pulse (duration 200  $\mu$ s), and the intensity was set to 75% of the individual's pain threshold. Across 4 sessions, the variable of frequency (5, 20, 40, or 80 Hz) was randomly assigned and all other parameters held constant.

### Experiment 2: Stimulation Dose of Event-Related NMES

The frequency of NMES was set to the 80 Hz identified as optimal for inducing short-term facilitation of MEP amplitude in experiment 1. Two counterbalanced sessions used event-related NMES either with fewer stimulus trains (20 instead of 60 stimulus trains) or shorter stimulus trains (1 instead of 4 s).

### Experiment 3: Replication in a New Sample

To assess the reproducibility of the results of event-related NMES across different participant populations,<sup>14</sup> we replicated the 80-Hz event-related NMES paradigm in a different participant cohort using methods identical to those in experiment 1.

### Experiment 4: Event-Related NMES Protocol Versus 2 Non-Event-Related NMES Protocols

For the first non-event-related protocol, sixty 80-Hz stimulus trains of 4 s duration (200  $\mu$ s pulse width) were administered every 10 s at an intensity of 75% of the individual's pain threshold. Non-event-related NMES was triggered by an automated trigger system and not from swallowing-related thyrohyoid activity.

For the second non-event-related protocol, NMES was administered continuously for 1 hour, again at an intensity of 75% of the individual's pain threshold and at a stimulus frequency of 80 Hz.

### Data Analysis

Statistical analyses were performed on the averaged percentage change from prestimulation baseline for the average of 15 MEPs at each posttreatment recording (5, 30, 60, and 90 minutes posttreatment). Repeated-measures analyses of variance (ANOVAs) were performed to examine the effects of the independent variables tested in each experiment across time. Separate follow-up 1-way ANOVAs were performed for significant main effects and interactions, a statistical

approach previously reported in the literature.<sup>15</sup> All analyses were undertaken separately for amplitude and latency measures recorded during each of the 2 muscle contraction conditions.

## Results

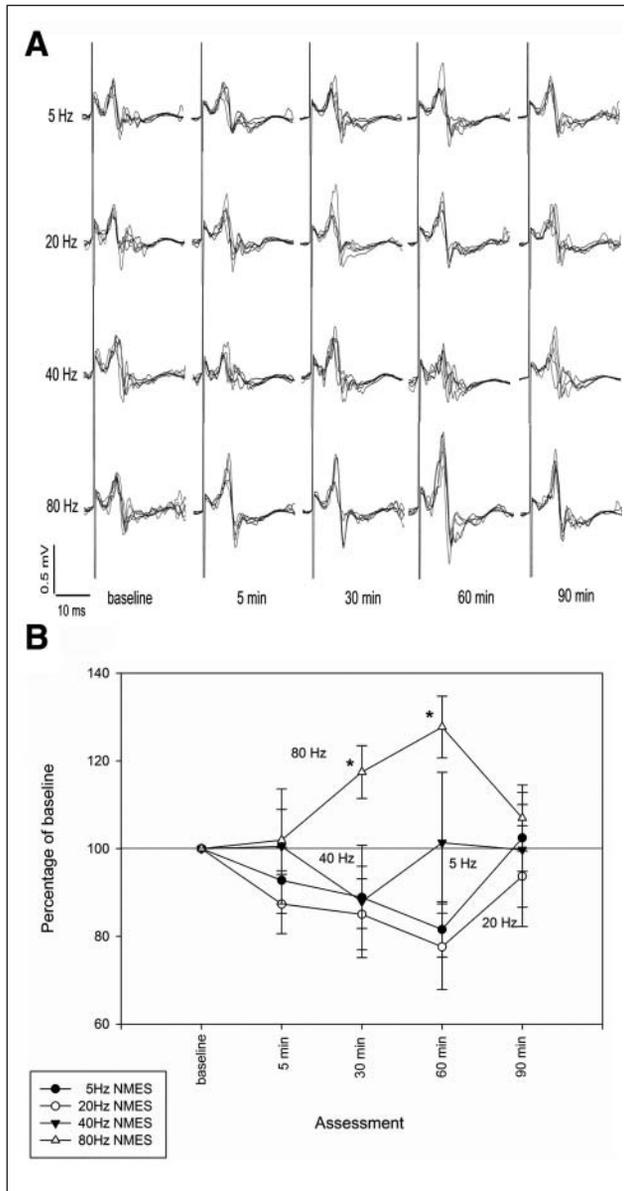
### MEP Amplitude During Pharyngeal Swallowing Condition (Experiments 1 to 4)

No discernible MEPs could be recorded during the pharyngeal swallowing condition in 2 of the 10 participants of experiments 1 and 2, and 5 of the 15 participants of experiments 3 and 4. In those who did display MEPs during the pharyngeal swallowing condition, none of the evaluated NMES treatment protocols affected MEP amplitudes when MEPs were recorded during this muscle preactivation condition ( $P > .2$ ). Therefore, only the effects of the various NMES paradigms on MEPs recorded during the volitional contraction condition are presented in detail below.

### MEP Amplitude During Volitional Contraction Condition

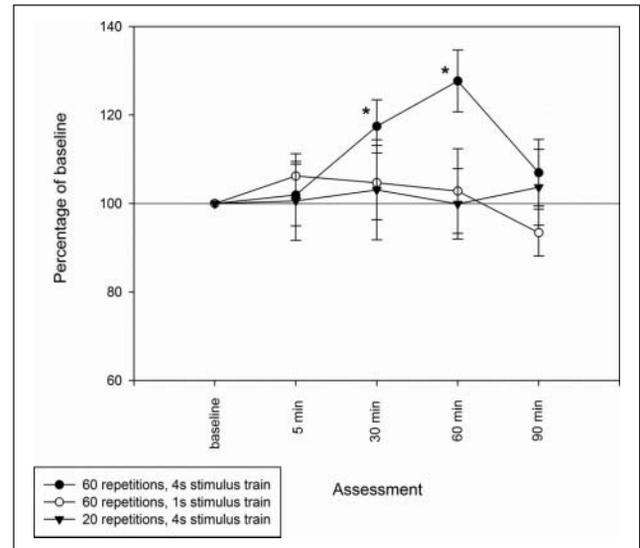
*Experiment 1: stimulus frequency of event-related NMES.* Relative to prestimulation baseline, there was a mean increase in MEP amplitude after 80-Hz NMES and a mean decrease in MEP amplitude after 5- and 20-Hz NMES. Repeated-measures ANOVA of the MEP amplitude data using the within-participant variables of frequency (5, 20, 40, and 80 Hz) and time (5, 30, 60, and 90 minutes posttreatment) revealed a significant Frequency  $\times$  Time interaction [ $F(9, 81) = 2.6$ ;  $P = .011$ ]. Separate 1-way ANOVAs with the within-participant factor of time were performed for each frequency to further assess the time course of the treatment-induced effects. There were no significant changes across time for the 5-, 20-, and 40-Hz frequencies ( $P > .057$ ). A significant time effect was confirmed only for the 80-Hz NMES [ $F(3, 27) = 6.1$ ;  $P = .001$ ]. One-sample comparisons relative to baseline for the 80-Hz condition revealed a significant increase at 30 minutes ( $P = .017$ ; effect size,  $d = 1.30$ ) and 60 minutes posttreatment ( $P = .003$ ;  $d = 1.76$ ; Figure 2).

*Experiment 2: stimulation dose of event-related NMES.* A repeated-measures ANOVA of the MEP amplitude data of all 3 doses of 80-Hz NMES (60 repetitions of 4-s stimuli, 60 repetitions of 1-s stimuli, and 20 repetitions of 4-s stimuli) showed a significant interaction of dose type and time [dose type:  $F(2, 18) = 0.811$ ,  $P = .46$ ; time:  $F(3, 27) = 2.5$ ,  $P = .08$ ; interaction:  $F(6, 54) = 2.69$ ,  $P = .023$ ; Figure 3]. No significant time effects were found for either of the 2 lower-dose protocols (60 repetitions of 1-s stimuli and 20 repetitions of 4-s stimuli) unlike that shown by the dose type reported in experiment 1 (60 repetitions of 4-s stimuli).



**Figure 2.** Neuromuscular electrical stimulation (NMES) stimulus frequency: effect of NMES stimulus frequency on motor-evoked potential (MEP) amplitude recorded during volitional submental muscle preactivation. (A) First 5 MEPs of each assessment of each frequency from 1 representative participant. (B) Relative change from baseline (group mean and standard error of the mean of MEP amplitude of 10 participants)<sup>a</sup> <sup>a</sup> \* $P < .05$  versus baseline.

**Experiment 3: replication of 80-Hz event-related NMES protocol.** For the second cohort, 1-way repeated-measures ANOVA revealed a significant effect of time [ $F(3, 42) = 3.58$ ;  $P = .021$ ], with a significant increase of MEP amplitude from pretreatment baseline at 60 minutes [ $t(14) = 2.64$ ,  $P = .02$ ;  $d = 0.98$ ]. As treatment protocols were identical for the 2 participant cohorts, data of both groups were pooled.

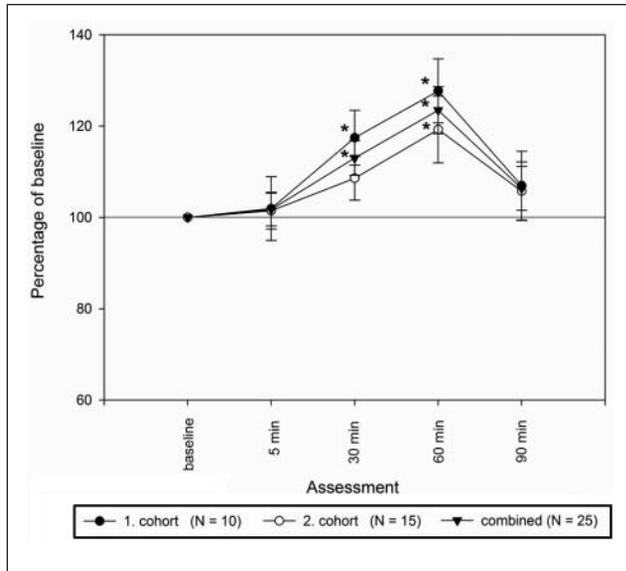


**Figure 3.** Neuromuscular electrical stimulation (NMES) dose: effect of NMES dose on motor-evoked potential (MEP) amplitude recorded during volitional submental muscle preactivation (group mean and standard error of the mean of 10 participants)<sup>a</sup> <sup>a</sup>Significant changes only occurred after 60 repetitions of 80-Hz NMES trains of 4-s duration. \* $P < .05$  versus baseline.

One-way ANOVA of the combined MEP amplitude data recorded during volitional contraction revealed a significant effect of time [ $F(3, 72) = 9.22$ ;  $P < .001$ ]. One-sample comparisons demonstrated a significant increase from pretreatment baseline at 30 minutes [ $t(24) = 3.2$ ,  $P = .004$ ;  $d = 0.906$ ] and 60 minutes [ $t(24) = 4.37$ ,  $P < .001$ ;  $d = 1.24$ ; Figure 4].

**Experiments 4: comparison of 80-Hz event-related NMES to two 80-Hz non-event-related NMES protocols.** Unlike the event-related protocol, the 2 non-event-related protocols produced no discernible change in MEP amplitude post-stimulation. However, the repeated-measures ANOVA of the MEP amplitude data of all 3 types of 80-Hz NMES protocols (event-related, non-event-related and 1-hour continuous NMES) showed no significant main effects or interactions [type of stimulation:  $F(2, 28) = 0.88$ ,  $P = .42$ ; time:  $F(3, 42) = 2.1$ ,  $P = .12$ ; interaction:  $F(6, 84) = 1.13$ ,  $P = .35$ ; Figure 5].

The lack of a significant interaction was likely the result of a change occurring in only 1 condition and only at the 60-minute poststimulation assessment. Given the prior evidence from experiments 1 to 3 and replication of the effect of 80-Hz event-related NMES in a second participant cohort at 60 minutes poststimulation specifically, a 1-way ANOVA with planned comparison of changes in MEP amplitudes at this time point was performed between the event-related NMES and 2 non-event-related NMES protocols. This comparison confirmed a significant difference between the 3 conditions at 60 minutes poststimulation [ $F(1, 42) = 4.81$ ;



**Figure 4.** The 80-Hz neuromuscular electrical stimulation (NMES) replication study: replication of the 80-Hz NMES protocol—effects on motor-evoked potential (MEP) amplitude recorded during volitional submental muscle preactivation (group mean and standard error of the mean of 10 participants [cohort 1], 15 participants [cohort 2], and both cohorts combined [25 participants])<sup>a</sup>  
<sup>a</sup>\* $P < .05$  versus baseline.

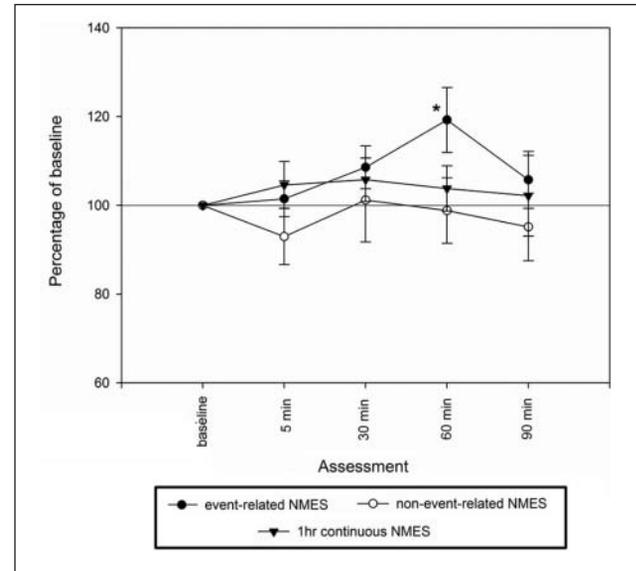
$P = .034$ ]. One-sample  $t$  tests comparing MEP amplitudes at 60 minutes to prestimulation baselines revealed a significant increase only after event-related NMES [ $t(14) = 2.64$ ,  $P = .02$ ;  $d = 0.98$ ].

### MEP Onset Latency During Swallowing and Contraction Conditions (Experiments 1 to 5)

MEP onset latencies were not affected by any of the NMES treatment protocols evaluated in the present experiments ( $P > .05$ ), regardless of whether MEPs were recorded during the volitional contraction or the volitional swallowing conditions.

## Discussion

The major findings of this study are that (1) there are lasting, frequency-specific effects of event-related NMES on submental MEP amplitude and (2) these effects are observed only in MEPs evoked during volitional contraction and not those evoked during the reflexive pharyngeal phase of volitional swallowing. Additionally, the largest significant changes in MEP amplitude occurred at 60 minutes postintervention. The excitatory effect observed after 80-Hz NMES was replicated in a second participant cohort, thereby, demonstrating robustness of research outcomes.



**Figure 5.** Effects of neuromuscular electrical stimulation (NMES) event-context: effect on motor-evoked potential (MEP) amplitude, recorded during volitional muscle preactivation, in response to 80-Hz NMES trials administered in an event-related context (swallowing triggered), a non-event-related context (at rest), and continuously for 1 hour (group mean and standard error of the mean of 15 participants)<sup>a</sup>  
<sup>a</sup>Significant changes from prestimulation baseline only occurred after event-related NMES. \* $P < .05$  versus baseline.

Also, significant changes in MEP amplitude were only observed after event-related NMES and not after non-event-related NMES, even when the latter was administered continuously for 1 hour.

The results of this study are in agreement with previous research that has documented frequency-specific changes in MEP amplitude in response to NMES of muscles innervated by corticobulbar neural networks.<sup>8,9</sup> However, unlike previous research, we recorded MEP outcome measures in the functional context of volitional and reflexive muscle contraction. This allows interpretation of the frequency-specific effects of NMES on corticobulbar excitability during performance of these motor tasks.

The frequency specificity of the induced effects and the time course over which these effects evolved lend some support to the hypothesis that mechanisms similar to long-term potentiation might underlie the observed changes. Specifically, long-term potentiation results from coincident excitation of presynaptic and postsynaptic cells has been shown to occur after high-frequency stimulation of nerve cells *in vitro*.<sup>16</sup> In humans, time courses comparable with those documented here have been reported after altered peripheral input to the cranial muscles,<sup>8,9,17</sup> hand muscles,<sup>18,19</sup> and arm muscles.<sup>20</sup> It is worth mentioning that the decrease in MEP amplitude observed after 5-Hz NMES (Figure 2) approached statistical significance ( $P = .057$ ) at

an observed power of 0.657. This inhibition of MEPs might reflect long-term depression-like changes of synaptic strength at lower stimulation frequencies.

In principle, the effects induced by event-related NMES are similar to those reported in the context of paired associative stimulation. In this technique, coincident or mismatched activation of cortical motor neurons by afferent input (produced via a peripheral nerve stimulus) and a transcranial magnetic stimulus is thought to be the driving mechanism for the lasting modulation of induced cortical excitability.<sup>18</sup> Similarly, during event-related NMES, afferent sensory input (produced by the NMES-induced muscle contraction) was paired with endogenous excitation of submental motor neurons by the swallowing motor command, a protocol that led to changes in motor cortical excitability in the current study. When NMES-induced sensory input was not paired with endogenous muscle contraction during non-event-related NMES, lasting changes in corticobulbar excitability were not seen. Even when non-event-related NMES was administered at a high dose for 1 hour, no changes in corticobulbar excitability were observed. In the context of reports that increased pharyngeal MEP amplitudes are related to increased swallowing function in individuals with dysphagia,<sup>8</sup> one might argue that clinically, peripheral sensorimotor stimulation administered in a functional context, which was the only protocol found to increase submental MEP amplitude at 60 minutes after stimulation, may be more effective in inducing functional changes in swallowing behavior than sensorimotor stimulation at rest. Indeed, clinical studies have shown no effects of non-event-related NMES on the myoelectric activity in the submental musculature of 10 healthy participants after ten 1-hour treatment sessions.<sup>5</sup> Similarly, postintervention swallowing function did not differ between 2 groups of 8 individuals with dysphagia, of whom 1 group received an experimental treatment session of 10 minutes of electrical faucial pillar stimulation and the other received sham stimulation.<sup>21</sup> Other studies have reported improved ratings of swallowing function in individuals with dysphagia after varying numbers of non-event-related NMES treatment sessions of 1 hour<sup>2</sup> or 30 minutes duration,<sup>22</sup> although debate exists around the methodological designs of these studies.<sup>23</sup> The present study has documented changes in the excitability of corticobulbar motor projections to the submental musculature after event-related NMES; however, the clinical implications of these results are limited until a rehabilitative useful relationship to improved swallowing function in patients with dysphagia can be shown.

The finding that non-event-related NMES did not induce changes in cortical plasticity is in contrast to findings in previous studies, which have reported changes in MEP amplitude after 10 minutes of non-event-related NMES of the musculature underlying the pharyngeal<sup>8</sup> or faucial pillar<sup>9</sup> mucosa. The reasons for this are unclear. It is possible that

differences in the innervation patterns and histochemical compositions of the tested muscles contribute to this discrepancy. It has also been demonstrated that there exists a window of optimal stimulus duration for non-event-related pharyngeal NMES (10 minutes), outside of which no changes in corticobulbar excitability were observed.<sup>8</sup> Although effective when applied in an event-related context, short trains of non-event-related submental NMES, as administered in the present study, may not be sufficient for altering the excitability of corticobulbar projections. On the other hand, 1 hour of continuous NMES may exceed what is optimally required to facilitate corticobulbar excitability. Future research is warranted to identify whether non-event-related NMES administered to the submental musculature at different dosages yields neurophysiological benefits.

Changes in corticobulbar excitability after pharyngeal or oral non-event-related NMES are linked to changes in swallowing function.<sup>8,9</sup> One might therefore expect that MEPs recorded during swallowing would also be affected by NMES. This was not found to be the case. The differential effects of NMES indicate that different neural networks may be involved in the motor control of the muscle contraction conditions tested in these experiments and that only those networks activated during volitional contraction are affected by NMES. For example, voluntary contraction is generally thought to recruit mainly excitatory neuronal circuits in the primary motor cortex, whereas recent research suggests that during swallowing, inhibitory circuits might instead be crucially involved.<sup>16</sup> It is also known that the reflexive muscle contractions associated with the pharyngeal phase of swallowing are under substantial control of brainstem pattern generators,<sup>24</sup> which may have reciprocal effects on the excitability of neural networks in the motor cortex. Teasing apart the relative contributions of different neural networks to the execution of volitional and reflexive motor components of swallowing and their response to peripheral NMES will be an important objective of future investigations.

In agreement with the initial hypothesis, MEP facilitation after 80-Hz NMES only occurred at the highest dose of NMES evaluated. This is likely because of an overall greater level of sensorimotor stimulation, and further research will need to evaluate whether these effects can be enhanced by administering more stimulus train repetitions or longer stimulus trains.

Although not specifically examined in these experiments, previous research using peripheral electrical stimulation suggests that the changes in corticobulbar excitability documented in the present experiment originate at a cortical level. For example, changes in the amplitude of pharyngeal MEPs in response to pharyngeal electrical stimulation were greatest in MEPs recorded from the dominant hemisphere.<sup>8</sup> Additionally, an electrical stimulation study of the pharyngeal muscles<sup>25</sup> has demonstrated changes in the motor responses to TMS over M1 in the absence of changes

in brainstem reflexes. This observation is consistent with stimulation-induced changes in MEPs of small hand muscles<sup>19</sup> that occurred without changes in spinal motoneuron excitability.

The present experiments provide evidence that sensorimotor stimulation, through swallowing-triggered NMES to the submental musculature, can induce plastic changes in the primary motor cortex. These changes in corticobulbar excitability are dependent on the NMES parameters used. What is important, however, is that the neurophysiological effects induced by this intervention remain to be linked to functional changes in swallowing performance. An evaluation of clinical relevance will be an essential prerequisite before any of the documented results can support the use of NMES in swallowing rehabilitation. This is of particular importance as previous research has demonstrated that the excitability of corticobulbar projections to the oral and pharyngeal musculature is linked to swallowing performance.<sup>8,9</sup> The observation that MEPs recorded during volitional contraction but not the pharyngeal phase of volitional swallowing were affected by NMES suggests that differences exist in the neural networks governing the motor execution of these tasks. These networks may be affected differentially by NMES. Similarly, it is conceivable that various forms of insult to the central nervous system affect the neural networks involved in swallowing, within and outside the primary sensorimotor area, in different ways. Further research is therefore needed to identify which pathological presentations of swallowing function can be best improved with NMES.

### Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

### Funding

This work was supported by a small project grant of the Neurological Foundation of New Zealand (Grant Number 0415-SPG).

### References

1. Carnaby-Mann GD, Crary MA. Examining the evidence on neuromuscular electrical stimulation for swallowing. *Arch Otolaryngol Head Neck Surg.* 2007;133:564-571.
2. Freed ML, Freed L, Chatburn RL, Christian M. Electrical stimulation for swallowing disorders caused by stroke. *Respir Care.* 2001;46:466-474.
3. Leelamanit V, Limsakul C, Geater A. Synchronized electrical stimulation in treating pharyngeal dysphagia. *Laryngoscope.* 2002;112:2204-2210.
4. Burnett TA, Mann EA, Stoklosa JB, Ludlow CL. Self-triggered electrical stimulation during swallowing. *J Neurophysiol.* 2005;94:4011-4018.
5. Suiter DM, Leder SB, Ruark JL. Effects of neuromuscular electrical stimulation on submental muscle activity. *Dysphagia.* 2006;21:50-60.
6. Humbert IA, Poletto CJ, Saxon KG, et al. The effect of surface electrical stimulation on hyo-laryngeal movement in normal individuals at rest and during swallowing. *J Appl Physiol.* 2006;101:1657-1663.
7. Ludlow CL, Humbert I, Saxon K, Poletto C, Sonies B, Crujido L. Effects of surface electrical stimulation both at rest and during swallowing in chronic pharyngeal dysphagia. *Dysphagia.* 2007;22:1-10.
8. Fraser C, Power M, Hamdy S, et al. Driving plasticity in the human adult motor cortex is associated with improved motor function after brain injury. *Neuron.* 2002;34:831-840.
9. Power M, Fraser C, Hobson A, et al. Changes in pharyngeal corticobulbar excitability and swallowing behavior after oral stimulation. *Am J Physiol Gastrointest Liver Physiol.* 2004;286:45-50.
10. DeKroon JR, Ijzermann MJ, Chae J, Lankhorst GJ, Zilvold G. Relation between stimulation characteristics and clinical outcome in studies using electrical stimulation to improve motor control of the upper extremity in stroke. *J Rehabil Med.* 2005;37:65-74.
11. Logemann JA. *Evaluation and Treatment of Swallowing Disorders.* 2nd ed. Austin, TX: Pro-Ed; 1997.
12. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologica.* 1971;9:97-113.
13. Doeltgen SH, Ridding MC, O'Beirne GA, Dalrymple-Alford J, Huckabee ML. Test-retest reliability of motor evoked potentials (MEPs) at the submental muscle group during volitional swallowing. *J Neurosci Methods.* 2009;178:134-137.
14. Macaluso GM, Pavesi G, Bonanni M, Mancina D, Gennari P. Motor-evoked potentials in masseter muscle by electrical and magnetic stimulation in intact alert man. *Arch Oral Biol.* 1990;35:623-628.
15. Mistry S, Verin E, Singh S, et al. Unilateral suppression of pharyngeal motor cortex to repetitive transcranial magnetic stimulation reveals functional asymmetry in the hemispheric projections to human swallowing. *J Physiol.* 2007;585:525-538.
16. Bliss TVP, Gardner-Mewin AR. Long-lasting potentiation of synaptic transmission in the dentate area of the unanaesthetized rabbit following stimulation of the perforant path. *J Physiol.* 1973;232:357-374.
17. Hamdy S, Aziz Q, Rothwell JC, Hobson A, Thompson DG. Sensorimotor modulation of human cortical swallowing pathways. *J Physiol.* 1998;506:857-866.
18. Stefan K, Kunesch E, Cohen LG, Benecke R, Classen J. Induction of plasticity in the human motor cortex by paired associative stimulation. *Brain.* 2000;123:572-584.
19. Ridding MC, Brouwer B, Miles TS, Pitcher JB, Thompson PD. Changes in muscle responses to stimulation of the motor cortex induced by peripheral nerve stimulation in human subjects. *Exp Brain Res.* 2000;131:135-143.
20. Ziemann U, Corwell B, Cohen LG. Modulation of plasticity in human motor cortex after forearm ischemic nerve block. *J Neurosci.* 1998;18:1115-1123.

21. Power ML, Fraser CH, Hobson A, et al. Evaluating oral stimulation as a treatment for dysphagia after stroke. *Dysphagia*. 2006;21:49-55.
22. Blumenfeld L, Hahn Y, LePage A, Leonard R, Belafsky PC. Transcutaneous electrical stimulation versus traditional dysphagia therapy: a nonconcurrent cohort study. *Otolaryngol Head Neck Surg*. 2006;135:754-757.
23. Logemann JA. The effects of Vitalstim on clinical and research thinking in dysphagia. *Dysphagia*. 2007;22:11-12.
24. Jean A. Brain stem control of swallowing: neuronal network and cellular mechanisms. *Physiol Rev*. 2001;81:929-961.
25. Hamdy S, Rothwell JC, Aziz Q, Singh KD, Thompson DG. Long-term reorganization of human motor cortex driven by short-term sensory stimulation. *Nat Neurosci*. 1998;1:64-68.