ORIGINAL ARTICLE

Effects of Submental Neuromuscular Electrical Stimulation on Pharyngeal Pressure Generation

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Objective: To investigate the immediate and late effects of submental event-related neuromuscular electrical stimulation (NMES) on pharyngeal pressure generation during noneffortful and effortful saliva swallows.

Design: Before-after trial.

Setting: Swallowing rehabilitation research laboratory.

Participants: Sex-matched (N=20) healthy research volunteers.

Interventions: Participants received 80Hz NMES of 4-second duration to floor of mouth muscles that was time-locked to 60 volitional saliva swallows.

Main Outcome Measures: Manometry measures of peak pressures and duration of pressure events in the oropharynx, hypopharynx, and the upper esophageal sphincter (UES) were derived during execution of noneffortful and effortful saliva swallows. Measures were taken at baseline, during stimulation, and at 5-, 30-, and 60-minutes poststimulation.

Results: Baseline pharyngeal and UES pressures did not differ between stimulated and nonstimulated swallows. At 5- and 30-minutes poststimulation, peak pressure decreased at the hypopharyngeal and at the UES sensor during noneffortful swallows. The effect lasted up to an hour only in the hypopharynx. No changes in duration of pressure events were observed.

Conclusions: Using this treatment paradigm, decreased peak amplitude in the hypopharynx up to an hour after treatment indicates a potential risk of decreased bolus flow associated with NMES. On the other hand, decreased UES relaxation pressure may facilitate bolus transit into the esophagus.

Key Words: Deglutition; Electric stimulation; Rehabilitation.

NEUROMUSCULAR ELECTRICAL stimulation (NMES) is an established rehabilitative approach in the field of physiotherapy to assist the recovery of motor function.[1,2] In the past decade, NMES has increasingly been applied to swallowing rehabilitation in order to aid in the recovery of impaired swallowing function. The application of electric stimulation in a group of patients with dysphagia was first reported in 1997[3] and has experienced increased use since 2002, with the introduction of a commercially available device with preset stimulation parameters.[4]

Despite the application of NMES in clinical practice, there is conflicting scientific evidence to support the development of guidelines for patient-specific intervention approaches. Reports of efficacy of electric stimulation in the rehabilitation of swallowing disorders are controversial and have been the subject of several reviews.[5-8] In addition, there persists a lack of knowledge regarding its specific effects on the neurophysiology and biomechanics underlying swallowing.[5,9]

Prior research in swallowing rehabilitation has demonstrated that NMES induces neuromodulatory effects and that these effects are highly dependent on stimulation parameters, such as frequency, stimulus duration, or stimulus intensity.[10-13] For instance, NMES induces changes in the excitability of descending corticobulbar motor projections to the pharyngeal[10,11] and submental muscle groups,[13] reflected in changes in motor evoked potential (MEP) amplitude. The direction of the induced effects is highly dependent on the stimulus frequency, whereas the magnitude of effects has been reported to depend on the stimulation dose.[10] Research has shown that changes induced in corticobulbar motor representation can be functionally relevant, with 1 study documenting an associated reduction in aspiration.[10] Other studies found potential for NMES induced adverse effects on swallowing biomechanics by introducing descent of the hyolaryngeal complex.[14-16]

It is not yet known if experimentally induced neural changes in the motor representation of the submental muscle group influences swallowing function. Prior research by our group[13] provided a systematic examination of the neuromodulatory effects of different NMES protocols to the submental muscle group. Electric stimulation was applied during execution of swallowing events, thus providing event-related stimulation (EREstim). In accordance with previous findings in the pharyngeal musculature,[10] the largest changes in MEP amplitude,

List of Abbreviations

CPG	central pattern generator
EREstim	event-related stimulation
ICC	intraclass correlation coefficient
LTD	long-term depression
LTP	long-term potentiation
MEP	motor evoked potential
NMES	neuromuscular electrical stimulation
RM-ANOVA	repeated-measures analysis of variance
UES	upper esophageal sphincter

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a measure of corticobulbar excitability, occurred at 60 minutes poststimulation. It was suggested that mechanisms similar to long-term potentiation (LTP) and long-term depression (LTD) might underlie the observed changes. Interestingly, low frequencies of stimulation (5 and 20Hz) resulted in an inhibition of MEP amplitude, whereas the reported facilitation of neural transmission was only seen for 80Hz of stimulation.

We investigated if the facilitory effects of NMES on MEP amplitude, as described in the protocol by Doeltgen et al,[13] are accompanied by biomechanical changes in swallowing function. Both immediate and longer-term effects were explored to provide information about peripheral and central changes, respectively. We hypothesized that 80Hz NMES administered to the submental muscle group would affect pharyngeal and upper esophageal sphincter (UES) pressure generation, albeit in different ways. First, we anticipated immediate effects of submental NMES on UES pressure generation. We hypothesized that facilitory NMES, when paired with pharyngeal swallowing, would result in an immediate increase in the contractile strength[17] of submental muscles during stimulated swallowing, consequently resulting in greater anterior pull on the hyolaryngeal complex and consequent decreased UES nadir pressure.

Regarding pharyngeal pressure generation, we anticipated no immediate pharyngeal effects of stimulation, because the targeted submental muscles do not directly contribute to pharyngeal pressure generation. However, we hypothesized that functional changes of those structures can be driven by changes at a central motor control level. As such, we aimed to target the central nervous system via application of EREstim to the peripheral nervous system. We therefore hypothesized that increased pharyngeal pressure would occur 60 minutes poststimulation as a functional manifestation of the overall neural facilitation documented previously.[13] Swallowing is generally described as a synergistic sensorimotor response,[18,19] with the central pattern generators (CPGs) located at the brainstem level distributing commands to functionally distinct muscles for well coordinated swallowing. Effortful swallowing has been found to result in increased pharyngeal pressure generation,[20] presumably through cortical modulation of the brainstem motor response. Similarly, we hypothesized that increased excitability of cortical pathways resulting from NMES would produce a similar pharyngeal effect in the poststimulation period.

METHODS

Participants

Twenty-seven young healthy subjects (mean age ± SD, 23.7±3.9y; mean age women, 21.6y; mean age men, 25y) were recruited to the project. None reported any swallowing problems. Five participants were excluded due to failed calibration of the manometry catheter and another 2 due to intolerance of pharyngeal catheter placement used in manometry. Thus, data from 20 sex-matched participants were included in the analysis.

Procedures

The research took place in a university-affiliated swallowing rehabilitation research laboratory. Ethics approval was obtained from the appropriate regional health and disability ethics committee and informed consent was obtained from all research participants prior to initiating data collection. Each participant was seated comfortably in an upright position throughout data collection.

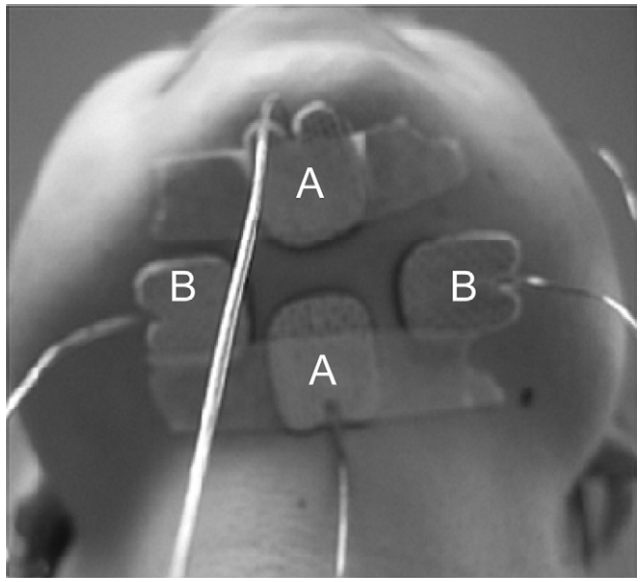

Fig 1. Electrode placement. Abbreviations: A, NMES electrodes; B, EMG (trigger) electrodes, electromyographic (trigger) electrodes.

Experimental Protocol

Electrode placement. After cleaning the skin surface with an alcohol prep, 2 surface electrodes[a] were positioned at midline over the submental muscle group (anterior belly of digastric, mylohyoid, and geniohyoid). A 5-mm distance was maintained between the electrodes. A ground electrode was mounted over the bony prominence overlying the base of the vertical ramus of the mandible. Lateral to the electrodes used for delivering NMES, 2 additional electrodes were used to trigger NMES during the event-related treatment sessions (fig 1). By placing surface electrodes for electric stimulation over the submental muscles only, the activated anterior belly of the digastric, mylohyoid, and geniohyoid muscles were anticipated to pull the hyoid bone upward, accompanied by a rise of the entire laryngeal complex, without concurrent reinforcement of counteracting infrahyoid muscles during the EREstim episodes. This electrode placement was consistent with that evaluated previously,[13] which was seen to result in corticobulbar facilitation. All electrodes were connected to an amplifier (Dual Bio Amp, ML 135[b]) and a recording system (Powerlab 8/30, ML 870[b]). Data were acquired at a sampling rate of 10kHz, with high pass filtering of 10Hz.

Placement of manometry catheter. A thin manometry catheter (Model CT/S3+emg, 2.1mm in diameter[c]) with 3 solid-state unidirectional, posteriorly orientated sensors was placed transnasally into the pharynx and esophagus. The proximal sensor was placed at the base of the tongue and the midpharyngeal sensor was placed approximately even with the laryngeal additus. The distal sensor was placed within the UES. Correct catheter placement was obtained using a pull-through technique until the most distal sensor was situated just proximal to the high-pressure zone of the UES at rest, as indicated by the presence of a typical M wave in the third sensor during swallowing.[21]

Baseline recordings. Before acquisition of baseline measures, each subject was given a demonstration and directions regarding the performance of noneffortful (saliva) swallows and effortful (saliva) swallows and was allowed to practice these tasks using pharyngeal manometric waveforms for

visual feedback. Each subject was then asked to complete another 10 repetitions of noneffortful swallows and effortful swallows without visualization to represent baseline data. The 2 tasks were counterbalanced across participants.

EREstim protocol. The protocol for application of NMES is identical to that which was previously reported by Doeltgen,[13] and on which this study is based. Participants received NMES to floor of mouth muscles at a frequency of 80Hz and stimulus duration of 4 seconds that was time-locked to 60 noneffortful, volitional swallows.[13] The threshold for triggering EREstim was set at 75% of the mean amplitude of 10 noneffortful baseline swallows. Thus, during all research tasks, EREstim was triggered as participants executed a pharyngeal swallow and the recorded surface electromyographic activity exceeded the previously defined amplitude threshold. Each research participant was prompted to complete the 60 stimulated saliva swallows at intervals of 1 swallow per 30 seconds. The level of stimulation intensity was set at 75% of the maximum tolerated threshold. In order to define the maximum tolerated intensity for each individual, intensity was gradually increased in increments of 2mA, and participants were allowed time to accommodate to each level of stimulation. Increases were discontinued when participants indicated that they would not tolerate a further increase in intensity. For men, the mean stimulus intensity was 18±4.7mA, for women, the mean stimulus intensity was 17.12±3.0mA.

Outcome measurements. Outcome data consisted of 2 measures: (1) peak manometric pressure and (2) manometric pressure duration. Peak manometric pressure was defined as the greatest pharyngeal pressure identified at sensors 1 and 2 and the lowest UES relaxation pressure at sensor 3. Duration of pressure was defined as the time between onset and offset of the swallowing-related pressure change at sensor 1 and sensor 2, and the time between the 2 high pressure peaks surrounding the drop in UES pressure at sensor 3. In addition, the latency between peak pressure in sensor 1 and sensor 2 was investigated (fig 2). Manometric data were collected during the first 10 stimulated swallows. Data were also collected before NMES (baseline), as well as 5-, 30-, and 60-minutes poststimulation during 10 repetitions of both noneffortful and effortful swallows to determine potential stimulation induced effects (fig 3).

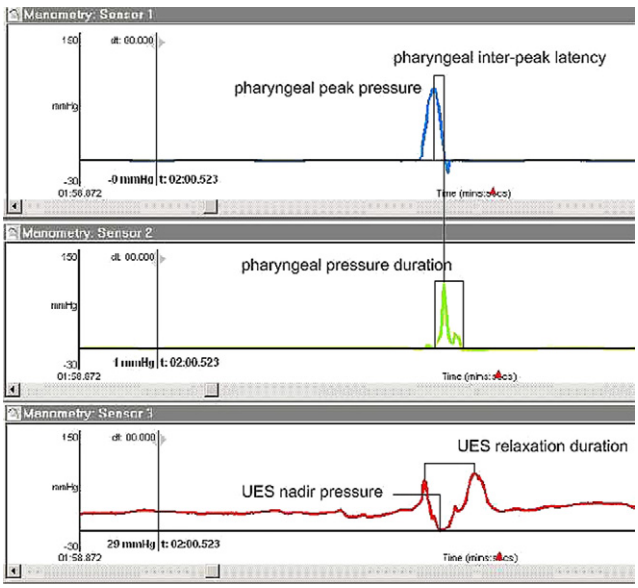

Fig 2. Manometry profiles with indicated outcome measures.

Statistical Analysis and Data Preparation

Two main analyses were performed to investigate the effects of stimulation on pressure measures: (1) during stimulation and (2) across the poststimulation assessment period.

Immediate effects during stimulation. Main effects were calculated for sensor (oropharynx and hypopharynx) and condition (control swallow, stimulated swallows) on averaged data. For UES data, the effect of condition (control swallow, stimulated swallow) was established.

Longer-term effects of EREstim protocol. Main effects were calculated for sensor (oropharynx and hypopharynx, or UES), swallow type (effortful, noneffortful), and time (baseline, 5-, 30-, and 60-min poststimulation). Pressure data obtained from sensors 1 and 2 were analyzed as separated variables in the same general linear model repeated-measures analysis of variance (RM-ANOVA), whereas data obtained from sensor 3 were analyzed in a separate RM-ANOVA. This approach is justified because sensors 1 and 2 represent positive pressure generation, whereas data obtained from sensor 3, due to a drop in UES pressure, are seen to reflect subatmospheric pressure events.[22] Incorporating all in a single analysis would result in an obligatory sensor effect that reflects the inherent nature of the data rather than an experimental result.

A priori significance level was set at $P<.05$. The sphericity assumption for repeated measures was tested using a Mauchly test, and when this assumption was not met the Greenhouse-Geisser correction was applied. Intrarater and interrater reliability of 20% of the data were tested using an intraclass correlation coefficient (ICC). Sets of 4 randomized subjects were reanalyzed and compared with the original data.

Trial effects. Before statistical analysis, RM-ANOVA was used to evaluate potential trial effects. Preliminary statistical analyses revealed that there was a significant trial effect ($F_{5,82}=2.67$, $P=.032$) in the analysis of immediate effects of EREstim on peak pharyngeal pressure. The interaction between condition, trial, and sensor was also significant ($F_{9,162}=2.79$, $P=.005$) in this analysis. A post hoc paired t test showed that the pressure generation of trial 1 at sensor 1 during EREstim differed significantly from peak pressure generation of trial 2 ($t_{19}=-2.82$, $P=.011$) and trial 3 ($t_{19}=-3.47$, $P=.003$). This was thought to be linked to a confounding surprise effect, as indicated by a wincing behavior of the participants when first exposed to stimulation during swallowing. Therefore, the data of all first stimulated swallows were discarded and excluded from the average. There were no significant trial effects for all nonstimulated swallows; therefore, all 10 trials were included in the averages of these swallows.

RESULTS

Intrarater and interrater reliability. Intra- and interrater reliability were considered high for all measurements with an ICC for intrarater reliability for peak and nadir manometry amplitudes of .996 and an ICC of .959 for pressure duration. Interrater reliability was also high with an ICC ranging from .963 for peak and nadir manometry amplitudes to .884 for duration of pressure generation measurements.

Immediate Effects of Stimulation

Peak pharyngeal and esophageal pressure. Analysis revealed no main effects of either condition ($F_{1,19}=.01$, $P=.98$) or sensor ($F_{1,19}=1.45$, $P=.243$) (fig 4) on pharyngeal peak pressures when baseline measures were compared with stimu-

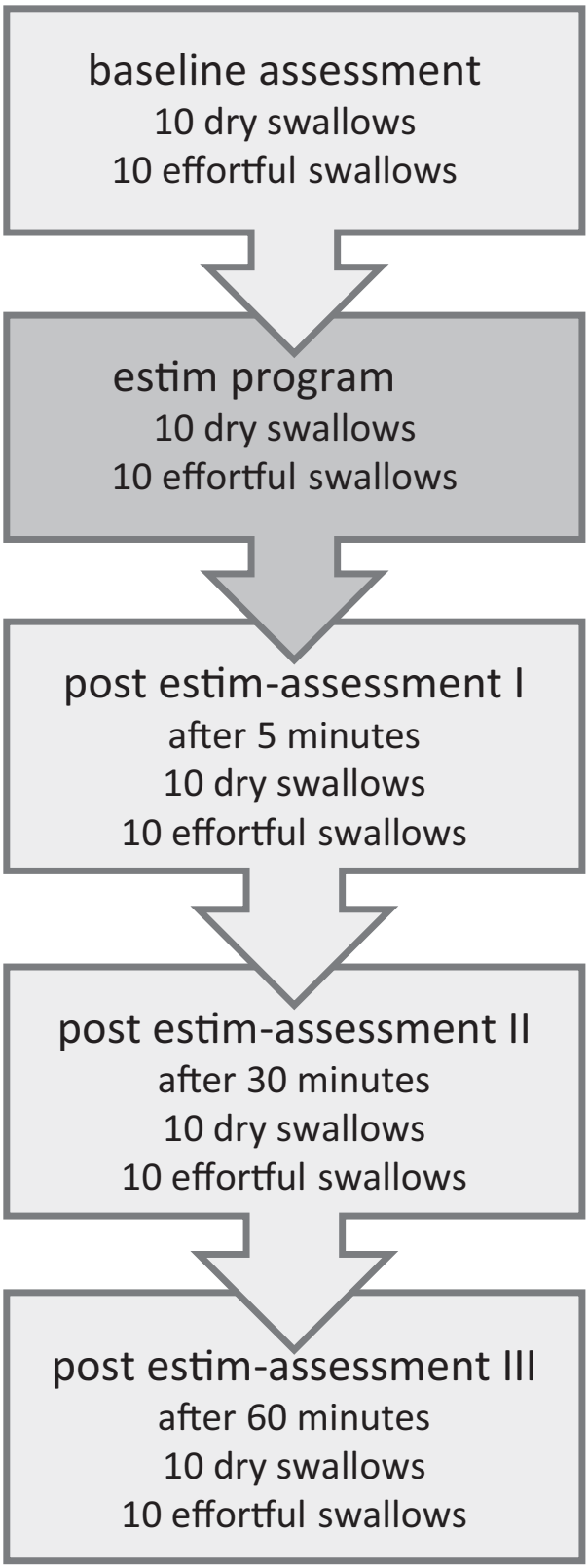

Fig 3. Outline of treatment session with data collection. Abbreviation: Estim, Electrical stimulation.

lated swallows. There was likewise no difference in nadir pressure at sensor 3 between stimulated swallows and nonstimulated swallows ($F_{1,19}$=1.18, P=.291) (see fig 4).

Pharyngeal and esophageal pressure duration. Within the pharynx (sensors 1 and 2), stimulated swallows did not affect pressure durations ($F_{1,19}$=.69, P=.416) or peak-to-peak duration ($F_{1,19}$=.13, P=.721) compared with nonstimulated swallows. For UES opening duration, there was also no significant change of pressure duration ($F_{1,19}$=1.4, P=.251).

Longer-Term Effects of EREstim Protocol

Peak pharyngeal and esophageal pressure. Three-way RM-ANOVA revealed a significant main effect of swallow type (noneffortful, effortful) ($F_{1,19}$=26.34, P<.001) in the pharynx and in the UES ($F_{1,19}$=9.29, P=.007). Subsequently, swallowing types were analyzed separately.

For the noneffortful swallowing condition, there was a significant main effect of time ($F_{3,57}$=3.36, P=.025) in the pharynx, as well as a significant sensor by time interaction ($F_{3,57}$=3.48, P=.041). Separate post hoc t tests for each sensor revealed that pressure was reduced compared with baseline only in sensor 2 at 5 minutes (t_{19}=2.16, P=.044), 30 minutes (t_{19}=2.79, P=.012), and 60 minutes (t_{19}=3.37, P=.003) after stimulation (fig 5A). With Bonferroni correction for 6 comparisons (2 sensors at 3 timepoints), these P values change to P=.264, P=.072, and P=.018, respectively. At the level of the UES, there was a significant main effect of time ($F_{3,57}$=2.87, P=.044). Post hoc comparisons revealed a significant decrease in UES nadir pressure between baseline and 5 minutes (t_{19}=2.09, P=.05) and 30 minutes (t_{19}=2.3, P=.033), but not at 60 minutes (t_{19}=1.58, P=.129) poststimulation. With Bonferroni correction for 3 comparisons (3 timepoints), these P values change to P=.150, P=.099, and P=.387, respectively. Please see table 1 for mean difference values, confidence intervals, and Cohen d effect sizes for all post hoc comparisons.

For the effortful swallowing condition, there were no significant main effects or interactions at any level of the pharynx or the UES (fig 5B). Across all assessment times, effortful swallows consistently generated greater peak pharyngeal pressures and lower UES pressures than noneffortful swallows.

Pharyngeal and esophageal pressure duration. As for the peak pharyngeal pressure measures, 3-way RM-ANOVA re-

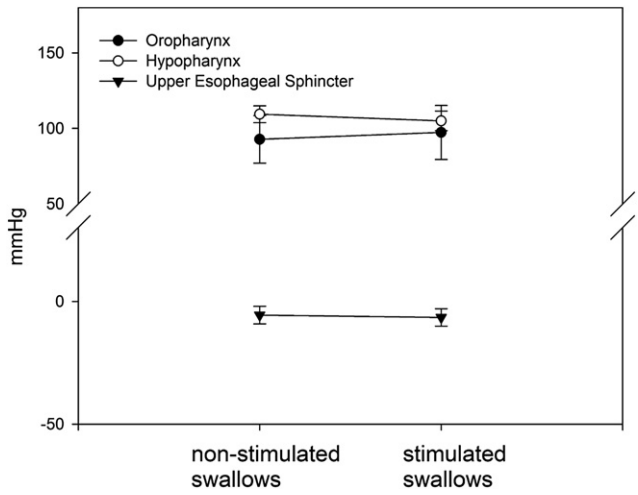

Fig 4. Immediate effects of EREstim on pharyngeal pressure generation.

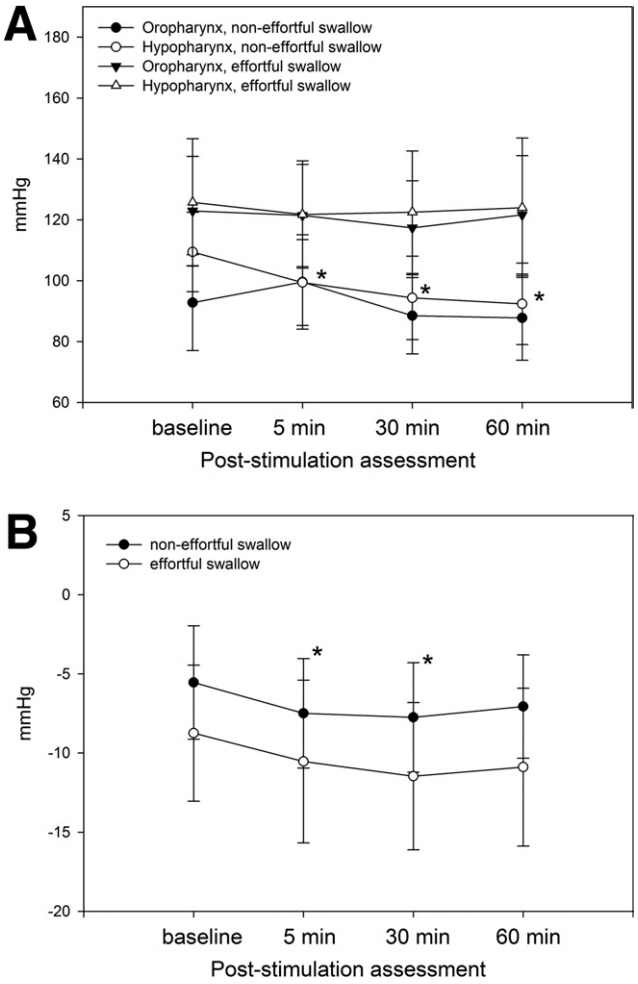

Fig 5. (A) Longer-term effects of EREstim on pharyngeal pressure generation. (B) Longer-term effects of EREstim on UES relaxation pressure. *Statistically significant differences compared to baseline measures.

vealed a significant main effect of swallow type (noneffortful, effortful) ($F_{1,19}$=40.89, P<.001). Subsequently, both swallowing types were therefore analyzed separately. During the noneffortful swallowing condition, pharyngeal and UES pressure durations did not change across the poststimulation assessments (pharynx: $F_{3,57}$=1.61, P=.197; UES: $F_{3,57}$=2.285, P=.088).

During the effortful swallowing condition, there was also no significant main effect of time ($F_{2,44}$=2.72, P=.07) in the pharyngeal sensors, but a significant time by sensor interaction ($F_{3,57}$=3.46, P=.022). UES relaxation duration was not significantly influenced in the effortful swallowing condition ($F_{3,57}$=1.13, P=.344). The duration between peak pharyngeal pressures (peak sensor 1 to peak sensor 2) also did not vary across the poststimulation assessment period (control swallows: $F_{3,57}$=1.16, P=.324; effortful swallows: $F_{3,57}$=.59, P=.627).

DISCUSSION

This study investigated the immediate and longer-term effects of NMES applied to the submental muscle group on pressure generation in the oropharynx, hypopharynx, and UES during saliva and effortful swallows. The main findings were that during stimulated swallowing, the amplitude of pharyngeal and esophageal pressure generation did not differ compared with nonstimulated control swallowing. In the poststimulation period, when using Bonferroni adjustment to correct for multiple comparisons, there was a decrease in pharyngeal pressure at 60 minutes poststimulation only for the noneffortful swallowing condition.

However, when Bonferroni correction is not applied, EREstim led to decreased pharyngeal pressure during noneffortful swallowing at 30 and 60 minutes and decreased UES nadir pressure at 5- and 30-minutes poststimulation. Peak pharyngeal pressure during effortful swallowing was not affected by EREstim either during or poststimulation. No changes in the duration of pressure events were observed for either swallowing condition. Effortful swallowing produced an overall greater pharyngeal pressure and lower UES relaxation pressure than noneffortful swallowing.

Although correcting for multiple comparisons using the Bonferroni method is historically recommended to avoid type I errors, application of this method to these data is inappropriate for several reasons. The Bonferroni method of correction provides an overly conservative estimate and is considered invalid when there is a lack of independence between comparisons, as in the case of post hoc testing for repeated measures across time.[23] More recent commentary on statistical approaches suggests a more pragmatic approach of evaluating confidence intervals and effect size as a means of identifying patterns of change in data and spurious significant findings.[24,25] Table 1 represents the confidence intervals surrounding the mean difference between *t* tests comparisons and the related Cohen *d*. For all significant comparisons, the confidence interval does not include zero. Importantly, for all significant comparisons, the Cohen *d* values range from .242 (considered a small effect) to .565 (considered a moderate effect).[26] Additionally, the pattern of biomechanical change follows a similar, but inverted, trajectory of change as MEP amplitudes in the study of Doeltgen,[13] using the same stimulation protocols. This would indicate that the significant findings identified through the multiple post hoc comparisons are indeed true findings and do not represent type I error. Finally, as the data suggest a potential contraindication of this treatment protocol, the risk of a type I error is strongly preferred over a type II error. It is much better to err on the side of identifying an adverse clinical consequence than failing to identify the consequence when it exists. Therefore, we consider the finding of decreased pharyngeal pressure during noneffortful swallowing at 30- and 60-minutes poststimulation and decreased UES nadir pressure at 5- and 30-minutes poststimulation a valid and important result of this study.

Immediate effects of stimulation. The broadly expected impact of NMES in swallowing rehabilitation is increased contraction in muscles that are responsible for safe and efficient pharyngeal swallowing because of increased, albeit not necessarily physiologic, recruitment of motor units by NMES. As the submental muscles, which play a critical role in UES opening, were targeted for stimulation, we anticipated that UES nadir pressure would decrease during EREstim. Yet, the data did not confirm this hypothesis. There were no immediate changes in UES nadir pressure during stimulated swallows, which suggests that hyolaryngeal elevation was not significantly altered during NMES.

For the rehabilitation of swallowing disorders the absence of immediate effects on swallowing function implies that NMES assisted swallowing is not better than normal swallowing, and these data therefore suggest that NMES may not be an effective

Table 1: Mean Differences, 95% Confidence Intervals, *P* Values, and Effect Sizes of Post Hoc Comparisons of Noneffortful Swallowing Data

Sensor	Post Hoc Comparison	Mean Difference	95% Confidence Interval		*P*	Cohen *d*
			Upper	Lower		
Oropharynx	Baseline and 5-min poststimulation	−6.800	−16.321	2.721	.151	−.20
	Baseline and 30-min poststimulation	4.305	−6.302	14.912	.406	.13
	Baseline and 60-min poststimulation	5.020	−7.543	17.583	.413	−.015
Hypopharynx	Baseline and 5-min poststimulation	10.040	.316	19.764	.044	.324
	Baseline and 30-min poststimulation	15.075	3.764	26.386	.012	.493
	Baseline and 60-min poststimulation	17.045	6.472	27.619	.003	.565
UES	Baseline and 5-min poststimulation	1.945	.002	3.888	.050	.242
	Baseline and 30-min poststimulation	2.204	.199	4.208	.033	.272
	Baseline and 60-min poststimulation	1.520	−.484	3.524	.129	.194

compensatory technique. However, considering the population of young, healthy participants used in this study, it is unclear how the same stimulation program would affect an impaired swallowing system. Immediate biomechanical effects of stimulation in a group of patients with chronic dysphagia after stroke are reported in a study of Ludlow et al,[14] who found a significant lowering of the hyoid bone when stimulating submental and laryngeal regions at rest. However, when electric stimulation at motor level intensity was applied during swallowing, there were no immediate significant consequences to performance and safety of swallowing as evaluated using videofluoroscopic analysis. These findings are consistent with the absence of pharyngeal pressure changes during stimulation in the present study. Yet, the absence of immediate alterations on muscle performance does not exhaustively describe the effectiveness or noneffectiveness of a treatment protocol.

Although this specific NMES paradigm did not affect pharyngeal pressure generation during stimulation in healthy individuals, the same paradigm has previously been shown to induce a lasting increase in corticobulbar excitability[13] at 30 and 60 minutes after stimulation. Therefore, we tested whether changes in corticobulbar excitability at these timepoints are functionally relevant for swallowing. In fact, similar functional changes have been reported to occur in the hand musculature after peripheral electric stimulation.[27]

Longer-term effects of EREstim protocol. As hypothesized, we detected changes in pharyngeal peak and UES nadir pressure in the poststimulation period. The NMES paradigm on which this study was based was previously found to produce statistically significant increases in MEP amplitude at 30- and 60-minutes poststimulation. An inverted trend was observed in our biomechanical data, with a significant decrease of pressure at 5-, 30-, and 60-minutes poststimulation in the hypopharynx and at 5- and 30-minutes poststimulation in the UES during noneffortful swallows. No significant changes of peak pressure were seen in the oropharynx. In the absence of significant immediate pressure changes, the observed time dependency of the effects might be explained by the highly complex and synergistic organization of swallowing, which is heavily but not exclusively controlled by a CPG situated in the brainstem.[18,19,28-30] Thus, the effects that manifested in an altered functional performance are assumed to be centrally driven.

Accumulating reports of stimulation-induced and time-dependent neuromodulatory treatment effects suggest that the observed after-effects on motor cortical excitability may be related to phenomena such as LTP and LTD.[10,11,13] Changes in synaptic strength at 30- and 60-minutes postintervention are reported in related research investigating LTP and LTD.[31-34] The observed time course of the effects on pharyngeal pressure generation corresponds to previous findings,[13] which provided the foundation for this study. However, the direction of the change in pharyngeal pressure was different from what we had expected. Whereas Doeltgen[13] report facilitated corticobulbar excitability, the present data document that hypopharyngeal peak and UES nadir pressures were significantly reduced.

After the previously proposed explanation of underlying neuromodulatory processes, the unexpected changes in pressure generation might be related to LTD-like mechanisms. Remarkably, Doeltgen[13] found changes in MEP amplitude during volitional contraction of submental muscles but not during the pharyngeal phase of swallowing. Because any time-delayed changes in pharyngeal pressure in swallowing seen after submental EREstim have to be considered as indirect or generalized effects, it could be considered that these changes may have originated at a lower motoneuron level. Those findings resemble the outcome of a study by You et al.[35] The authors found that high-frequency peripheral stimulation of 100Hz led to significant LTD on the spinal withdrawal reflex in rats. After conducting a transection of the spinal cord, they located the source of neuromodulation at the lower motoneuron level. Thus, it could be hypothesized that the 80Hz used for stimulation in the current study was excitatory for cortically elicited MEPs in voluntary contractions of submental muscles,[13] but behaved differently on neuronal transmission during volitional swallowing. In the context of the underlying neuronal framework, the observed stimulation-induced pharyngeal pressure changes in swallowing might be attributed to either increased inhibition in cortical excitability or the modified output of brainstem swallowing CPGs.

More recent research was able to show that the induction of neural LTP-/LTD-like changes is also found at brainstem level,[36,37] providing further support for the CPG as a potential platform of modulation for the swallowing system. Increased relaxation of the UES during swallowing therefore could be explained by an increased inhibitory output to the rostral branch of the superior laryngeal nerve via the swallowing CPG. In this context, it would also be important to further investigate the role of the submental area as a relevant receptive field for the modulation and manipulation of swallowing at different intensities of stimulation, as was previously emphasized by Power et al.[12]

Interestingly, it has previously been shown that pharyngeal electric stimulation resulted in an increase in the size of the pharyngeal cortical motor representation, whereas the size of the esophageal motor representation decreased after stimulation.[38] The present data cannot identify whether an increase in the submental motor representation, as previously shown[13] using the same stimulation parameters, occurred at the expense

of the pharyngeal motor representation. However, if this was the case, it may be that decreased pharyngeal excitability resulted in decreased pharyngeal pressure generation.

Effortful swallows were included to maximize the anticipated stimulation-induced functional effects, by increasing volitional modulation of swallowing and consequently increasing contraction force of muscles by an enhanced recruitment of motor units.[17,39] However, NMES did not significantly alter the peak pressure in effortful swallows. Hypothetically, one could argue that increased volitional effort in swallowing overrides the potentially adverse effects of NMES. Thus, increased facilitory drive from enhanced volitional control during effortful swallowing may compensate for the inhibitory changes induced by NMES.

Alternatively, declining peak pressures observed in the pharynx may be an expression of fatigue. However, it seems perplexing that effortful swallowing, which should require higher metabolic demands, did not present any obvious symptoms of fatigue.[40] Additionally, prior research evaluating the potential effects of repeated volitional swallowing that would potentially produce fatigue[41] and prolonged catheter placement in the pharynx[11,41] found no significant effects on neural transmission, as measured by MEPs.

The absence of changes in duration of pressure events remains unexplained; however, with regard to future rehabilitative interventions, the independence of those measures might be important to consider. In our case the unchanged duration of the UES opening time might indicate that there is not an enlarged upward hyoid movement responsible for the decrease of pressure in the UES but a centrally modified swallowing pattern.

Study Limitations

This research was limited to evaluating specific biomechanical features of swallowing in mostly young, healthy participants and did not extend to evaluate older controls or patients with swallowing impairment. As such, we did not directly evaluate the overall safety of swallowing with other measures, such as videofluoroscopy, as was done by Humbert et al.[15] Extension of the study population and validation of manometric changes using imaging techniques would be of great value in future studies for translating results to a patient population.

In addition, inclusion of a sham control group, which did not receive active stimulation, would provide insight into whether the act of repeated swallowing alone induces significant changes in swallowing biomechanics. We propose that in the present study, 60 repetitive saliva swallows at intervals of 1 swallow per 30 seconds was not sufficient to induce significant changes in swallowing biomechanics. This proposition is supported by a recent study by Macrae et al,[42] which did not find significant pressure changes within sessions of repeated swallows using the same manometry catheter as we did in the present study. In addition, Al-Toubi et al[41] examined corticobulbar excitability by recording MEP measures before and at several timepoints after 60 volitional saliva swallows. The authors did not find any significant effects on the excitability of corticobulbar projections to the submental musculature. By assuming that those corticobulbar projections reflect use-dependent pathways of swallowing, we argue that there is evidence that 60 volitional saliva swallows do not induce biomechanical or neurophysiologic changes in swallowing. We cannot, however, rule out that 60 stimulated swallows have no effect on voluntary adaptation of swallowing rather than neural adaptation of behavior.

Although the present study was designed to examine if previously documented changes in corticobulbar excitability[13] translated into changes in swallowing biomechanics, inclusion of a control group stimulated at a sensory level would provide additional information about the impact of EREstim to the submental area.

CONCLUSIONS

This study sought to evaluate the biomechanical adaptations in swallowing associated with a previously evaluated treatment paradigm using EREstim,[13] which produced an excitatory effect on neural transmission. Unexpectedly, we found a reduction in hypopharyngeal pressure at 5-, 30-, and 60-minutes poststimulation. These biomechanical findings suggest that this stimulation program could potentially lead to swallowing that is considered less safe. The observed decrease in UES relaxation pressure at 5- and-30 minutes poststimulation could potentially facilitate bolus transfer into the esophagus as the resistance at the UES is less pronounced and might be linked to an increased hyolaryngeal elevation.

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Suppliers

a. BRS-50K; Ambu A/S, Baltorpbakken 13, DK-2750 Ballerup, Denmark.
b. ADInstruments, Unit 6, 4 Gladstone Rd, Castle Hill, NSW 2154, Australia.
c. Medical Measurements Inc, 6 Linden St, Hackensack, NJ 07601.