Changes in pharyngeal corticobulbar excitability and swallowing behavior after oral stimulation

M. Power,1 C. Fraser,1 A. Hobson,1 J. C. Rothwell,2 S. Mistry,1 D. A. Nicholson,3 D. G. Thompson,1 and S. Hamdy1

Departments of 1GI Science and 2Radiology, University of Manchester, Hope Hospital, Salford M6 8HD; and 3Sobell Department of Neurophysiology, Institute of Neurology, London WC1N 3BG, United Kingdom

Submitted 12 March 2003; accepted in final form 18 August 2003

Power, M., C. Fraser, A. Hobson, J. C. Rothwell, S. Mistry, D. A. Nicholson, D. G. Thompson, and S. Hamdy. Changes in pharyngeal corticobulbar excitability and swallowing behavior after oral stimulation. Am J Physiol Gastrointest Liver Physiol 286: G45–G50, 2004. First published August 28, 2003; 10.1152/ajpgi.00114.2003.—Faucial pillar (FP) stimulation is commonly used in swallowing rehabilitation, yet its physiological basis remains uncertain. We investigated the effects of intraoral FP stimulation on human corticobulbar excitability and swallowing behavior, to explore the possibility of a central mechanism for functional change. In 10 healthy subjects, corticobulbar projections to pharynx were investigated with transcranial magnetic stimulation, via intraluminal electrodes, before and up to 1 h after 10 min of electrical FP stimulation with three frequencies (0.2, 1, and 5 Hz) or sham and peripheral (median nerve) stimulation. In a second study, swallowing behavior was assessed with videofluoroscopy before and after FP stimulation. FP stimulation at 5 Hz inhibited the corticobulbar projection (−14 ± 6%, P < 0.02) and lengthened swallow response time (+114 ± 24%, P = 0.02). By comparison, FP stimulation at 0.2 Hz facilitated this projection (+60 ± 28%, P < 0.04), without enhancing swallowing behavior. Neither 1-Hz, sham, nor median nerve stimulation altered excitability. Thus changes in corticobulbar excitability to FP stimulation are frequency dependent with implications for the treatment for neurogenic swallowing dysfunction.

cortical plasticity; deglutition; faucial pillars; oropharynx; transcranial magnetic stimulation; videofluoroscopy

NORMAL SWALLOWING IS A COMPLEX neuromuscular activity that is constantly modulated by peripheral (sensory) feedback (8). Impairments of sensation have, for example, been implicated in aspiration after stroke (2, 6, 17) and are known to result in dysphagia and/or aspiration when induced by oropharyngeal anesthesia in healthy subjects (22). Indeed, it was nearly a century ago that sensory stimulation was first advocated as a method for improving swallowing (26). Since then, stimulation of the more accessible parts of the oropharynx has been promoted as a potential treatment for dysphagia, albeit with questionable evidence for efficacy.

The anterior faucial pillars (FP) are bilaterally located on the oral side of the velum and form part of the soft palate, comprising mainly the palatoglossus muscles (8, 20), which insert into the tongue base and function to pull the tongue up and back, constrict the pillars, and lower the velum. Sensory innervation of FP is via the maxillary branch of the trigeminal nerve and the glossopharyngeal nerve, whereas motor innervation is from the pharyngeal branch of the vagus nerve. FP stimulation has now become commonly employed to treat swallowing disorders, although data to support its use in neurogenic dysphagia are controversial and unsupported by randomized controlled trials (5, 20, 25, 29). FP stimulation is given to the patient at the bedside, either by mechanical stroking or with the application of a cold probe. However, both approaches are difficult to quantify or standardize, and there is great variability across the swallowing therapy profession as to how to precisely apply these techniques, because, despite its enthusiastic use, no prescriptive guidelines for FP therapy have been produced (5). Moreover, the neurophysiological mechanisms that might drive improvement in swallowing function after FP stimulation remain unknown.

In previous studies with transcranial magnetic stimulation (TMS), we have described the normal pattern of projections from human motor cortex to swallowing musculature. Pharyngeal and esophageal motor representation is bilaterally organized, but displays interhemispheric asymmetry with functional hemispheric dominance, independent of handedness (13). After unilateral hemispheric stroke, one-third of patients develop oropharyngeal dysphagia, almost certainly as a consequence of damage to the dominant swallowing hemisphere (10), putting them at risk of aspiration pneumonia and malnutrition (19, 30). Swallowing in most patients usually recovers slowly over several weeks and is functionally associated with reorganization of swallowing motor areas in the cortex of the undamaged, previously nondominant hemisphere (12). We have also shown that electrical stimulation of the pharynx produces long-lasting changes in swallowing motor cortical excitability that are virtually identical to changes noted within the unaffected hemisphere during recovery from dysphagic stroke (9, 14). This effect is frequency specific (5 Hz being optimal) and, importantly, is associated with short-term improvement in swallowing function, indicating a role for stimulus-induced excitability changes as therapy after cerebral injury (9). Thus changes in the corticopharyngeal motor projection detectable by TMS appear to be closely associated with swallowing function and its recovery.

Because little is known about which characteristics of FP stimulation might be important in changing swallowing or whether FP stimulation produces changes in the corticobulbar pathway, similar to those produced by pharyngeal stimulation, we sought to determine whether FP stimulation in healthy adults 1) induces change in swallowing motor cortex; 2) shows a frequency and site-dependent effect; and 3) produces change...
in swallowing behavior. Our hypothesis, based on our pharyngeal stimulation data, was that high-frequency (5 Hz) but not low-frequency (1 or 0.2 Hz) FP stimulation would induce excitatory changes in the corticobulbar projection to pharynx and modify swallowing performance.

METHODS

Participants

We studied 10 healthy adult volunteers (8 men, mean age 40 yr, range 26–55 yr) recruited from the local community. All subjects were screened before recruitment and excluded if there was any evidence of previous swallowing difficulty, medical illness, or neuromodulating medication. All gave informed, written consent before the study, which was previously approved by the Salford and Trafford Health Authority Ethics Committee.

Electrophysiological Techniques

Cortical stimulation. Cortical stimulation was performed by using a magnetic stimulator (Magstim 200, MAGSTIM, Whittington, Dyfed, UK) connected to a 70-mm outer diameter figure-of-eight coil, placed over the regions of interest on the scalp (13, 14). With the use of this configuration, the maximal magnetic field generated by the stimulator is 2.2 T.

Electromyogram responses. Electromyogram (EMG) responses were detected from the pharynx by using a single pair of bipolar platinum ring electrodes (interelectrode distance = 1 cm), built into a 3-mm-diameter intraluminal catheter (Gaeltec, Dunvegan, Isle of Skye, UK). One single solid-state strain-gauge transducer (Gaeltec) was also incorporated into the catheter, between the electrode pair, which enabled manometric positioning of the catheter within the pharyngeal lumen. The electrode pair was connected to a preamplifier (CED 1902, Cambridge Electronic Design, Cambridge, UK) with filter settings of 5 Hz to 2 kHz. Response signals were then collected through a laboratory interface (CED 1401 plus) at a sampling rate of 4–8 kHz.

Electrical stimulation of the FP. Electrical stimulation of the FP was performed by using a finger-mounted electrode assembly (St Mark’s glove electrode, model 13L40, Dantec, Skovlunde, Denmark). The stimulation electrode pair was positioned over the tip of the finger and inserted intraorally to touch the FP being analyzed by using frame-by-frame analysis. Data were stored on digital cassette tape (Panasonic UK, Bracknell, Berkshire, UK). Subjects were studied in the standing position, and barium sulphate liquid was prepared to manufacturer’s recommendations for thin liquid (60% wt/vol) (EZ-HD, E-Z-EM, London, UK). The volume of barium was measured and placed into a Kapitek beaker (Kapitek, Slough, UK) ready for drinking. Before measurements began, a 3-ml bolus of barium liquid was used to familiarize the subjects with the taste. Screening was then commenced by using a 10-ml bolus, and all subjects were instructed to retain the full volume in their mouth until commanded to swallow. Images were subsequently acquired without magnification until the bolus had traveled below the upper margin of the thoracic esophagus. Images were taken in the lateral view, according to previously described protocols (12, 20), with the anatomic markers for imaging being the lips anteriorly, the cervical spine posteriorly, the nasopharynx superiorly, and the upper margin of the thoracic esophagus inferiorly. Total screening time was kept <80 s (range 42–73 s) in all cases, giving a radiation dose of <0.3 mSv.

Five measures of swallowing were chosen: 1) to evaluate the flow of the bolus through the mouth (oral transit time); 2) to evaluate the flow of the bolus through the pharynx (pharyngeal transit time); 3) to examine swallow onset [swallow response time (SRT)]; 4) to examine duration of airway closure (airway closure duration); and 5) to examine upper esophageal sphincter opening (cricopharyngeal opening time). All measures were temporally referenced to a standard “trigger point,” defined conventionally as the point at which the ramus of the mandible crosses the tongue base (20).

Oral transit time was defined as the interval in seconds between the first frame showing backward motion of the tail of the bolus and the first frame showing the arrival of the head of the bolus at the trigger point.

Pharyngeal transit time was defined as the interval in seconds between the first frame showing the arrival of the bolus head at the trigger point to the last frame to show the tail of the bolus passing through the cricopharyngeal sphincter.

SRT was defined as the interval in seconds between the first frame showing the bolus head at trigger point to the first frame showing upward excursion of the larynx.

Airway closure duration was defined as the interval in seconds between the first frame showing the bolus head at trigger point to the first frame showing disappearance of the tail of the bolus through the cricopharyngeal sphincter.

Experimental Protocols

Protocol 1: Corticobulbar excitability and FP stimulation. For each study, the volunteer sat comfortably in a chair, and the pharyngeal stimulation was performed by using Ag–AgCl cup electrodes placed over the median nerve at the wrist (28). The stimulation electrode pair was positioned over the median nerve contralateral to whichever hemisphere was being magnetically stimulated. The electrodes were connected to an electrical stimulator (model DS7; Digitimer) via a trigger generator (Neurolog System, Digitimer), which delivered stimuli (0.2-ms pulse width, 280 V) at a frequency of 2 Hz (28), by using a set intensity of 75% maximum tolerated sensation as determined by the method and formula described above and for a 10-min duration.
goesophageal EMG catheter was inserted transnasally or transorally, depending on subject preference. The catheter position was then adjusted manually, so the pharyngeal electrodes were 3 cm above the upper esophageal sphincter.

The cranial vertex was then marked on the scalp, and the optimal site for magnetic stimulation of the pharyngeal motor area was determined by discharging the 70-mm figure-of-eight coil over multiple scalp positions over both hemispheres by using suprathreshold stimulus intensities. The site evoking the largest pharyngeal EMG response for the pharynx was then identified and marked on the scalp. A series of cortical stimulations over this position was then performed, commencing at a subthreshold intensity and increasing by 5% stimulator output steps until a threshold intensity was found that evoked pharyngeal EMG responses of >20 \(\mu V\) on at least 5 of 10 consecutive trials. Repeated stimulations were then carried out at intensities of 95, 100, 105, 110, 115, and 120% threshold in randomized order. Ten stimuli were delivered at each intensity, with an interval of 5 s between each stimulation.

After baseline measures, FP electrical stimulation was applied for 10 min at a frequency of either 5, 1, or 0.2 Hz, at 75% of the maximum tolerated intensity or sham stimulation, where the FP electrode made contact but no current was applied, with the order in which these conditions were applied being prerandomized. The number of swallows during FP stimulation was also recorded. After stimulation (or sham), the electrode was removed from the mouth, and cortical stimulation was performed immediately, at 30 min and at 1 h, by using an identical protocol to that used for the baseline measures. As an additional somatic control, the effect of median nerve stimulation at 2 Hz was also studied on a separate occasion with similar recordings being measured.

Protocol 2: Swallowing behavior and FP stimulation. On a separate day to protocol 1, each subject received a baseline videofluoroscopy exam, comprising six consecutive swallows, each with a 10-ml bolus. Thereafter, FP stimulation [using only frequencies (5 and 0.2 Hz) shown to induced changes in corticobulbar excitability] or sham was performed, with the subject seated in a manner identical to that in protocol 1. The videofluoroscopy examination was then repeated immediately after stimulation, at 30 min and at 1 h, by using an identical experimental protocol.

Data Analysis

With the stimulus-response plot TMS data, the mean values of the cortically evoked EMG responses across all intensities were combined to produce a grand mean value for each interval for each individual. These grand mean values were compared before and after FP stimulation by using the general linear model repeated-measures ANOVA in SPSS. A Greenhouse-Geisser correction for degrees of freedom was applied when required. TMS values were expressed in terms of percent change compared with baseline and shown (data and figures) as means ± SE, unless otherwise stated. Only significant main effects and interactions are reported. Swallowing behavior data were compared by using repeated-measures ANOVA with the Friedman test. FP sensory thresholds and number of visible swallows during stimulation were compared by using the Wilcoxon signed-rank test. TMS and videofluoroscopy data were correlated by using a simple linear regression analysis.

RESULTS

For both protocols, FP stimulation was well tolerated. Subjects described FP stimulation as a “sharp buzzing” felt around the soft palate or base of the tongue. No subjects experienced any retching or vomiting during stimulation. In addition, there were no reports of gagging sensation during stimulation, although, on introduction of the FP electrode into the oral cavity, some subjects described a mild urge to gag, which settled immediately. The mean stimulation currents used to achieve 75% of the maximum tolerated intensity in FP were 8.4 ± 1.5, 10.1 ± 1.3, and 11.7 ± 2.8 mA after 5, 1, and 0.2 Hz, respectively, being greater for the lower frequencies (\(P < 0.05\) vs. 5 Hz). The mean stimulation current for median nerve stimulation was 2.8 ± 0.3 mA. Over the 10 min of FP stimulation, there was no difference in number of swallows induced by 5 Hz (12 ± 2), 1 Hz (15 ± 5), 0.2 Hz (14 ± 3), or sham stimulation (9 ± 3).

Corticobulbar Excitability

The mean stimulation intensity used for cortical stimulation across studies was 1.8 ± 0.1 T. In all subjects, cortical stimulation evoked reproducible triphasic pharyngeal responses with a mean latency of 7.8 ± 0.4 ms. Across studies, the mean baseline pharyngeal amplitude was 64 ± 10 \(\mu V\).

The effects of FP stimulation on the size of the corticobulbar pharyngeal projection are shown in Figs. 1 and 2. Figure 1 shows some typical EMG responses before and after FP stimulation at 5 and 0.2 Hz; Fig. 2 plots the average poststimulus effect over 60 min, normalized to the prestimulus values in all subjects for each condition. There was no nonspecific effect of time on the TMS response [2-factor ANOVA, \(F(3, 67) = 0.59, P = 0.600\)]. However, changing the condition (frequency) of stimulation had a dramatic effect on the TMS response, indicated by a significant time \(\times\) frequency interaction: [2-factor ANOVA, \(F(10, 67) = 1.93, P < 0.05\)].

Stimulation at 5 Hz decreased excitability, as determined by smaller response amplitude [1-way ANOVA, \(F(3, 27) = 4.01, P < 0.02\)], whereas stimulation at 0.2 Hz increased excitability [\(F(3, 27) = 3.39, P < 0.04\)]. Post hoc \(t\)-test analysis showed that 0.2-Hz stimulation had a later effect, and this was maximal at 60 min after the end of stimulation \((P < 0.01)\), whereas the 5-Hz effect was maximal at 30 min \((P < 0.05)\). After 5-Hz stimulation, both 1-Hz and sham FP stimulation and median nerve stimulation had no effect on corticobulbar excitability. FP stimulation, across all conditions, had no effect on response latency.

Swallowing Behavior

The effects of FP stimulation on swallowing function as measured with videofluoroscopy are shown in Table 1. Only those frequencies that changed excitability (and sham) were studied.

After 5-Hz stimulation, the SRT showed a profound lengthening with a maximal change of 114% at 30 min poststimulation \((P < 0.01)\). This change coincided with the maximal inhibition of the corticobulbar pathway observed with TMS. Other swallowing measures were unaffected by 5-Hz stimulation.

After 0.2-Hz stimulation, all swallowing measures remained unaffected across the 60 min. Similarly, sham stimulation had no effect on any swallowing measures.

Relationship Between Corticobulbar Excitability and Swallowing Behavior

To explore the association between the effects of FP stimulation on cortical excitability and on swallowing behavior, a simple linear regression was performed across subjects for each time interval after 5-Hz FP stimulation, the only frequency that also induced changes in swallowing function.
Variables chosen were the percent change in pharyngeal response to TMS and change of SRT (poststimulation SRT – prestimulation SRT) on videofluoroscopy. At 30 min, a strong negative correlation was found [correlation coefficient \( r = -0.831; r^2 = 0.691 \); 95% CI for \( r \) (Fisher’s z transformed) = \(-0.974 \) to \(-0.208 \); two-sided \( P = 0.021 \)]. By contrast, no consistent correlation was found immediately after stimulation [correlation coefficient \( r = -0.320; r^2 = 0.103 \)] or at 60 min [correlation coefficient \( r = 0.324; r^2 = 0.105 \)].

**DISCUSSION**

This study has shown that, depending on the frequency of input, the excitability of corticobulbar projections can be altered by sensory conditioning of a region of the mouth (FP) proximal from the muscle of interest (pharynx). Furthermore, whereas the present experiments explored only a subset of the total possible range of parameters, even within those, we found that it was possible to reverse the effect from facilitation to inhibition by changes in frequency. Indeed, contrary to our hypothesis, 5-Hz stimulation produced inhibitory changes in the corticobulbar projections, which were associated with detrimental changes to healthy swallowing behavior. The implication is that the pattern of stimulation is an important parameter in producing “plastic” changes in corticobulbar excitability and must be borne in mind when developing strategies to promote recovery after injury.

**Table 1. Effects of faucial pillar stimulation on mean swallowing measures**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Pre</th>
<th>Immediate</th>
<th>Post 30 min</th>
<th>Post 60 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTT</td>
<td>0.38±0.05</td>
<td>0.50±0.12</td>
<td>0.56±0.10</td>
<td>0.47±0.09</td>
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<tr>
<td>SRT</td>
<td>-0.32±0.09</td>
<td>-0.37±0.14</td>
<td>-0.41±0.15</td>
<td>-0.36±0.10</td>
</tr>
<tr>
<td>PTT</td>
<td>0.72±0.04</td>
<td>0.71±0.05</td>
<td>0.73±0.05</td>
<td>0.75±0.04</td>
</tr>
<tr>
<td>AC</td>
<td>0.87±0.21</td>
<td>0.82±0.16</td>
<td>0.91±0.17</td>
<td>0.87±0.20</td>
</tr>
<tr>
<td>CPO</td>
<td>0.52±0.02</td>
<td>0.53±0.03</td>
<td>0.53±0.02</td>
<td>0.53±0.02</td>
</tr>
<tr>
<td>5 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTT</td>
<td>0.32±0.04</td>
<td>0.35±0.06</td>
<td>0.30±0.05</td>
<td>0.32±0.04</td>
</tr>
<tr>
<td>SRT</td>
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<td>-0.07±0.10*</td>
<td>0.06±0.15†</td>
<td>-0.04±0.05*</td>
</tr>
<tr>
<td>PTT</td>
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<td>0.82±0.05</td>
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<tr>
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<td>0.62±0.02</td>
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<td>0.58±0.02</td>
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<tr>
<td>Sham</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTT</td>
<td>0.27±0.02</td>
<td>0.29±0.06</td>
<td>0.25±0.01</td>
<td>0.30±0.07</td>
</tr>
<tr>
<td>SRT</td>
<td>-0.34±0.16</td>
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<tr>
<td>CPO</td>
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<td>0.60±0.04</td>
<td>0.61±0.05</td>
<td>0.59±0.04</td>
</tr>
</tbody>
</table>

Values are means ± SE in S. Pre, before stimulation; Immediate, stimulation performed immediately; Post, after stimulation; OTT, oral transit time; SRT, swallow response time; PTT, pharyngeal transit time; AC, airway closure duration; CPO, criopharyngeal opening time. * \( P < 0.05 \) and † \( P < 0.01 \), repeated-measures ANOVA.

Fig. 1. The cortically evoked pharyngeal electromyogram responses in 1 individual are shown at suprathreshold (110%) intensity, before and after 5-Hz (A) and 0.2-Hz (B) faucial pillars (FP) stimulation. Ten responses are superimposed for each time point. The cortical stimulus (arrow) was applied at 0 ms. It can be seen that 5-Hz stimulation decreases the pharyngeal response amplitudes. By contrast, 0.2-Hz stimulation increases the pharyngeal response amplitudes.

Fig. 2. Grand group mean %change (±SE) in pharyngeal response amplitude after faucial pillar stimulation at 5 Hz (●), 0.2 Hz (○), 1 Hz (★), and sham (▲) and after median nerve stimulation (×). It can be seen that 5 Hz is inhibitory, whereas 0.2 Hz is excitatory. Both effects are delayed, being greatest at 30 and 60 min, respectively (* \( P < 0.05 \), ** \( P < 0.01 \), post hoc t-tests). By comparison, 1 Hz, sham, and median nerve stimulation had no effect.
These findings raise a number of important questions that need to be addressed. For example, why should FP stimulation show such a frequency-dependent effect? Furthermore, is FP stimulation a relevant receptive field for the elicitation and/or modulation of swallowing? To answer the first question, we need to consider the role of sensory input in swallowing. Swallowing is a complex activity that is highly dependent on sensory feedback (15, 16, 24), with this being conveyed by cranial nerves V, IX, and X. This input displays extensive brain stem convergence, with trigeminal (and vagal) afferent fibers terminating within the trigeminal spinal nuclei and nucleus of the tractus solitarius (NTS) of the dorsal region of the brain stem swallowing center (3, 15). In previous human swallowing studies of sensory conditioning, pharyngeal stimulation can produce long-term changes in motor cortical excitability: a 10-min period of stimulation increased pharyngeal cortical excitability for at least 30 min after the input, but was not associated with changes in brain stem excitability (9, 14). By contrast, a reduction in human oropharyngeal sensation, by local anesthesia (22) or afferent nerve damage (21), can disrupt the normal pattern of volitionally initiated swallowing. Thus oropharyngeal sensation is a powerful modulator of swallowing, both centrally and peripherally (1, 7).

In the case of FP stimulation, it is likely that inputs from the innervating trigeminal and glossopharyngeal nerves ascend to cortex, via the NTS, and trigeminal spinal nucleus, and thereby influence cortical function (4). With respect to the effects of stimulation frequency on excitability, it is well recognized, in animals, that repetitive stimulation of afferent swallowing pathways can exert both excitatory and inhibitory actions on the firing pattern of cortical swallowing neurons (23, 31, 23). In rabbits, for example, pontine stimulation can excite cortical neurons at low intensities (and frequencies), which become inhibited at higher strengths (32). It is therefore plausible that in our study, FP stimulation at 5 Hz resulted in an activation of inhibitory circuits in cortex for pharynx, but, at a lower frequency, may have favored excitation. The former may be a consequence of the strengths of input, with higher frequencies producing a more intense stimulus, which may have been perceived as more noxious. Indeed, recent human studies of pharyngeal stimulation found differential effects on the TMS-evoked pharyngeal responses when high and low frequencies were applied (9). A similar phenomenon may be occurring in the case of FP stimulation. Whether noxious oral stimulation might cause vagal excitation, which is also recognized to inhibit cortical excitability (11), is less clear. There was no retching, nausea, or vomiting during the study. However, subclinical vagal stimulation may have been present, and this may have influenced the results.

Of interest, this effect appears to resemble the much briefer sequence of synaptic events that occur in the central pattern generator during the buccopharyngeal phase of swallowing, i.e., excitation of buccal neurons and inhibition of pharyngoesophageal neurons (15, 24), both being dependent on the site of swallowing afferent input. Thus (5-Hz) FP stimulation may be inducing some of its effects by virtue of the fact that the site of input is proximal to the pharynx, with the expectation that there would be (distal) inhibition of the pharynx given its location relative to FP.

With respect to the second question of the relevance of FP as a trigger for swallowing, many workers have argued that the receptive fields directly relevant to elicitation of the swallow do not include FP (2, 5, 27). Indeed, Pouderoux et al. (27) found that swallowing never took place when the infused bolus (of contrast) remained within the velopharynx and only occurred when it had spilled over or progressed to the pyriform sinuses. The implication from these data is that FP has little direct relevance to the elicitation of swallowing and may, in fact, be part of a “holding” area for food accumulation before swallowing. In this circumstance, it may be preferential to inhibit the pharyngeal swallow while intraoral transfer of foods takes place. In support of this contention, we found no increase in elicited swallows to electrical FP stimulation at any of the frequencies applied compared with sham. This could be interpreted as indicating that the FP region has weak projections to NTS and other brain stem (and cortical) swallowing areas. This notion is in keeping with the neurophysiology of swallowing, because both trigeminal and glossopharyngeal nerve stimulation are relatively poor at evoking swallowing, compared with superior laryngeal nerve stimulation (15, 16, 18, 24).

With regard to the behavioral effects of FP stimulation on swallowing, it is noteworthy that, whereas modest inhibition of the corticobulbar pathway produced a clear (detrimental) slowing of the SRT, facilitation of the pathway had no effect, at least in healthy subjects. The fact that FP stimulation can delay SRT implies that oral stimuli can inhibit swallowing circuitry, either directly or possibly as a consequence of stimulus spread to other swallowing areas, including the pyriform sinuses, where the afferent swallowing projections are stronger (24). Moreover, this detrimental effect has implications for how FP stimulation is performed in patients because, depending on its application, there may be a risk of doing more harm than good (9): the use of FP stimulation in the treatment of swallowing disorders remains a contentious issue (29). In this light, future controlled studies of low- and high-frequency FP stimulation in dysphagic stroke may help to establish the functional relevance of stimulus-induced modulation of the corticobulbar pathway.

In conclusion, we have shown that human oral stimulation of the FP displays a frequency-specific effect on altering healthy corticobulbar excitability, and that inhibition of this pathway is associated with detrimental changes to swallowing behavior. These observations provide guidance in determining the role of therapeutic oral stimulation, which will have relevance in the management of patients with neurogenic dysphagia.

ACKNOWLEDGMENTS

The authors thank L. Slobodian and J. Bradshaw, Department of Radiology, for invaluable assistance with videofluoroscopy.

GRANTS

M. Power was an Medical Research Council (MRC) Clinical Training Fellow. S. Hamdy is an MRC Clinician Scientist. A. Hobson was funded by the Lord Dowding Trust for Humane Research.

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