Features of Cortically Evoked Swallowing in the Awake Primate (Macaca fascicularis)

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INTRODUCTION

Swallowing is a complex sensorimotor function requiring the precisely coordinated, bilateral activation of a large number of respiratory and alimentary muscles. Consistent with the complexity of the swallowing motor sequence, the neural control of swallowing is multidimensional in nature, involving peripheral afferent inputs arising from the oropharynx, an integrative medullary network, muscles innervated by several bulbar and cervical nerves, and descending inputs from higher cortical and subcortical centers to both the brainstem network and the bulb and cervical motor nuclei (Carpenter 1989; Doty 1968; Dubner et al. 1978; Miller 1982; Sessle and Henry 1989).

Despite an emphasis in the literature on the importance of the brain stem network in the triggering and sequencing of the neuromuscular events associated with swallowing, there is a growing body of evidence pointing to the likelihood that cortical mechanisms play a central role in the initiation and regulation of swallowing. Reports of swallowing deficits in humans after hemispheric stroke (Daniels and Foundas 1997; Hamdy et al. 1996, Meadows 1973; Robbins and Levine 1988), cortical ablation studies in animal models (Larson et al. 1980; Lund and Lamarre 1974; Luschei and Goodwin 1975; Sumi 1972), cortical stimulation studies (Car 1970; Hamdy et al. 1996; Miller and Bowman 1977; Penfield and Rasmussen 1950), neuroanatomic tracing studies (Kuypers 1958a,b), and neuronal recording studies examining the activity patterns and properties of “swallow-related” cortical neurons (Martin and Sessle 1993; Martin et al. 1997; Murray and Sessle 1990) have suggested that the lateral pericentral cortex, the anterolateral frontal cortex, the frontal and parietal opercula, and the insula mediate swallowing as well as a number of related functions such as sucking, mastication, and salivation. Nevertheless, although these cortical regions have been implicated in the initiation and modulation of swallowing, as well as in the integration of swallowing within the complex array of sensorimotor functions involving the upper alimentary and respiratory systems, the output organization of the cortical swallowing representation has not been documented. In particular, there have been no detailed studies of the topography and characteristics of cortically evoked swallowing in the awake primate. Because previous investigations of cortically evoked swallowing have employed surface stimulation with macro-electrodes in anesthetized preparations (Car 1970; Miller and...
current understanding of the organization and characteristics of evoked swallowing is limited in such investigations by the possibility of altered central neural excitability associated with the use of anesthesia, extensive current spread, and the difficulty in stimulating areas buried deep within the cortical sulci, particularly the central sulcus along which substantial portions of the face primary motor and somatosensory cortices are found (Huang et al. 1989a,b; Lin et al. 1994; Murray and Sessle 1992; Murray et al. 1991).

The development of intracortical microstimulation (ICMS) has provided a means of stimulating a localized cortical region in the awake animal in attempts to gain insights into the functional organization of the “excitable” cortex (Asanuma 1981). In our previous studies, we have applied this technique in defining the output organization of the primate face primary motor cortex (face-MI) (Huang et al. 1989b; Murray and Sessle 1992) and the cortical masticatory area (CMA) (Huang et al. 1989a). The present study represents the first attempt to define the output features of the “cortical swallowing representation” with the use of ICMS applied within the lateral sensorimotor cortex of the awake monkey. We also have combined this technique with cortical cold block (Narita et al. 1995; Sessle et al. 1995b) and single cortical neuronal recordings (Martin et al. 1997), and these data have been reported separately. Our objectives in the present study were to define the topographical organization of cortically evoked swallowing, to examine the relations between ICMS stimulus parameters and features of cortically induced swallowing, and to compare the patterns of swallowing evoked from different cortical regions with patterns of naturally occurring swallowing.

Some of these data have been briefly reported (Martin et al. 1993; Sessle et al. 1995a).

METHODS

The experiments were performed on two adult female monkeys (Macaca fascicularis; H7, H8; weight 2.5–3.1 kg) that were cared for according to the Guiding Principles of the American Physiological Society and the guidelines of the Canada Council for Animal Care (Guide to the Care and Use of Experimental Animals, vols. I & II). Many of the methods have been described in detail (Huang et al. 1988; Murray and Sessle 1992), and so only a brief account of the methods employed will be given here. The animals were studied during an ongoing investigation of the cortical swallowing area/CMA and MI that lasted 11 mo in monkey H7 and 13 mo in monkey H8. Each monkey first was trained to sit quietly in a primate chair and accept small amounts of fruit juice and food. When the monkey was fully trained, a headcap of dental acrylic was fixed to the skull under general anesthesia (pentobarbital sodium, 25 mg/kg iv) to stabilize the head during ICMS trials. When the monkey had adapted to the headcap, the monkey again was anesthetized and a stainless steel chamber (25-mm diam) was implanted over the lateral extent of the central sulcus along which subcortical sites where such ICMS intensities could be applied without exceeding the upper ICMS intensity limit of 60 μA. In addition, in some of the microelectrode penetrations used for the ICMS studies, the microelectrode also was used to record the activity of single cortical neurons (e.g., Huang et al. 1988; Murray and Sessle 1992); these data for MI neurons have been reported separately (Martin et al. 1997).

Data analysis

The orofacial movements induced by ICMS were verified and assessed by direct visual observations by two investigators and by analysis of the EMG recordings. Multiple channels of selected signals (EMG recordings, stimulus) were digitized (EMG activity full-wave rectified and smoothed; bandwidth 30–1,000 Hz, time constant 32 ms, sampling rate/channel: EMG 3,125/s, stimulus event data 200/s) with the Cambridge Electronics 1401 data acquisition board and Spike2 analysis package.

Swallowing was identified on the basis of a characteristic EMG profile in GG and the laryngeal muscle (in monkey H7, CT; in monkey H8, TH). In addition, swallowing was confirmed by direct visual observation of the monkey during the experimental session and by

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reviewing videotaped recordings of the monkey’s behavior for evidence of a prominent and rapid elevation and subsequent descent of the larynx that is characteristic of swallowing. Swallow onset was defined as the point at which the level of GG EMG activity associated with the swallow exceeded, for \( \geq 200 \) ms, 2 SD of the mean GG EMG activity that occurred during a period before ICMS delivery during which the monkey was at rest. Swallow offset was defined as the time at which the swallow-related CT burst fell to <2 SD of the mean EMG activity in CT during the same rest period. Swallow duration was defined as the period from swallow onset to offset. Swallow latency was defined as the duration between the onset of ICMS (C/S) and the swallow onset (see preceding text). Two measures of EMG magnitude were computed: total area under the swallow-related GG EMG curve (i.e., from swallow onset to offset), and mean GG EMG amplitude between swallow onset and offset.

To compare patterns of evoked swallowing with patterns of naturally occurring swallowing and to further characterize swallowing evoked from different cortical areas, the EMG burst durations in the GG, MASS, and CT, and the GG-CT and MASS-GG EMG onset latencies were compared statistically for 30 swallows that occurred as monkey H7 masticated and swallowed a raisin and sucked and swallowed fruit juice, and \( \geq 15 \) swallows evoked from each of face-MI, principal part of CMA (CMAp), and the cortical region ventral to CMAp. A one-way ANOVA and post hoc Tukey comparisons were used; an alpha of \( P = 0.05 \) was considered significant.

As a means of examining the association between ICMS intensity and swallow-related EMG characteristics, swallow latency, swallow duration, mean GG EMG amplitude and area under the GG EMG curve were computed and plotted for swallows evoked at threshold and at suprathreshold intensities (ranging from 1.3 to 6 times threshold) for selected intracortical sites.

Electrolytic lesions (DC, 10—20 \( \mu A \), 10 s) were placed at selected intracortical sites. The animals then were anesthetized deeply with pentobarbital (30 mg/kg iv) and perfused through the heart with heparin-saline followed by 10% buffered formalin. Histological reconstruction of the cortex was carried out after the termination of the experiments by procedures similar to those previously described (Huang et al. 1988). Stimulation sites were reconstructed according to the intracortical depth of ICMS, the location of electrolytic lesions, and the coordinates of microelectrode tracks.

**RESULTS**

**Topographic distribution and general features of evoked swallowing**

The responsive cortex was divided operationally into four major cortical regions on the basis of anatomic location, the presence or absence of ICMS-evoked twitch responses, and the properties of afferent inputs to neurons in different cortical regions (identified in separate experiments using single neuron recordings). These four regions were the primary face motor cortex (MI; see METHODS), the primary face somatosensory cortex (SI), the CMAp corresponding to Brodmann’s area 6, and an area of cortex ventral to CMAp, \( \geq 5 \) mm deep in relation to the cortical surface. On the basis of its functional and cytoarchitectonic features (e.g., Jones and Burton 1976; Roberts and Akert 1963; Vogt and Vogt 1919), SI may extend anterolaterally into the region classically considered to be CMA. However, for the present study, SI was defined operationally as the explored region that was caudal to the central sulcus and the imaginary line drawn as the continuation of the central sulcus toward the Sylvian sulcus; CMAp was defined as the precentral region lateral to MI and rostral to SI. ICMS exploration of SI was much more limited than that of MI or

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**TABLE 1. Number of intracortical sites where swallow was evoked by ICMS in monkey H7**

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>Left</th>
<th>Right</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orificial motor sites where swallowing was evoked by ICMS (C/S)</td>
<td>63/499 (13)</td>
<td>207/570 (36)</td>
<td></td>
</tr>
<tr>
<td>Orificial motor site where swallowing only was evoked by C/S</td>
<td>15/499 (3)</td>
<td>29/570 (5)</td>
<td></td>
</tr>
<tr>
<td>C/S evoked swallow sites where T/S evoked muscle twitch</td>
<td>14/63 (22)</td>
<td>35/207 (17)</td>
<td></td>
</tr>
<tr>
<td>C/S evoked swallow sites located 5 mm deep to cortical surface</td>
<td>18/63 (29)</td>
<td>13/207 (6)</td>
<td></td>
</tr>
<tr>
<td>C/S evoked swallow sites where C/S also evoked other motor responses</td>
<td>53/63 (84)</td>
<td>189/207 (91)</td>
<td></td>
</tr>
</tbody>
</table>

Percentages are in parentheses. * Sites where short train stimulus (T/S) evoked orofacial muscle twitch and/or continuous stimulus (C/S) evoked orofacial movement. † C/S-evoked swallowing, unaccompanied by other orofacial movements, at a minimum of one intracortical microstimulation (ICMS) intensity. ‡ T/S-evoked responses included facial, tongue, jaw, and supraglottic twitch. § C/S-evoked responses included rhythmic jaw movements (RJMs), tongue protrusion, licking, jaw opening, and lip smacking.

CMA because the position of the stainless steel chamber was relatively rostral in relation to SI.

The topographic distribution of ICMS-evoked swallowing initially was explored in monkey H8 to determine the overall location and extent of the swallowing representation. In total, ICMS was applied at >500 intracortical sites along 43 microelectrode penetrations in the left and right pericentral regions. Swallowing was evoked by C/S at \( \sim 10\% \) of sites along penetrations located within a 4 \( \times \) 5 mm area of the pericentral cortex that included CMA and the most lateral extent of face-MI. Stimulation at sites within the surface cortex (i.e., \(<5 \) mm deep from the cortical surface) as well as in deeper areas (5–8 mm below surface) evoked swallowing. Swallowing could not be evoked by T/S.

In monkey H7, a more detailed analysis of ICMS-evoked swallowing was performed. Orofacial motor responses were elicited by ICMS (e.g., orofacial muscle twitch evoked by T/S, and/or orofacial movement evoked by C/S) at a total of 1,069 sites along 150 microelectrode penetrations in the right and left pericentral cortices. The pattern of evoked motor responses was consistent with our earlier finding of a multiple, nested arrangement of orofacial motor responses in face-MI with an extensive representation of facial and tongue muscle responses in face-MI but a relatively limited representation of jaw muscles (Huang et al. 1988; Murray and Sessle 1992).

Of the 1,069 sites where orofacial motor responses were evoked by ICMS in monkey H7, swallowing was evoked by C/S at 270 intracortical sites (i.e., 25%). In contrast, swallowing was not induced by T/S at any site within monkey H8 (as in monkey H8). The proportion of orofacial motor sites where swallowing was evoked by C/S was greater for the right hemisphere, compared with the left hemisphere, by a factor of almost three (see Table 1). In the right hemisphere, microelectrode penetrations sites where swallowing was evoked were located within a 10 \( \times \) 7.5 mm area on the cortical surface whereas, in the left hemisphere, these penetrations were located within a 10 \( \times \) 5 mm area. The lowest thresholds for evoking swallowing were 5 \( \mu A \) in the right hemisphere and 8 \( \mu A \) in the left hemisphere; \( \sim 63\% \) of the evoked swallows were induced at C/S currents \( \leq 30 \mu A \).
Of the 270 sites where swallowing was evoked, a substantial proportion were sites where T/S evoked twitch responses of the facial, tongue, jaw, or suprathyroid musculature, indicating that these sites were within the ICMS-defined face-MI (see Table 1 and Figs. 1 and 2). However, the vast majority of sites where swallowing was evoked were not twitch sites, indicating that they were located outside of the ICMS-defined face-MI; these sites were immediately anterior, lateral, and/or caudal to face-MI and, based on histological reconstruction, were located within both face-SI and the more rostral region corresponding to CMA. Furthermore whereas most sites where swallowing was evoked by C/S were located within the surface cortex (i.e., <5 mm deep in relation to the cortical surface), some sites were located in deeper areas (i.e., between 5 and 8 mm deep with respect to the cortical surface; Fig. 1). In both hemispheres, microelectrode penetrations along which deep swallowing sites were found were located primarily within the rostral portions of the swallowing representations, immediately anterior and lateral to face-MI (see Fig. 1).

Of the 270 sites where swallowing was evoked by C/S ICMS, C/S also evoked other motor responses at the majority of sites (Table 1). These other evoked responses included RJMs, tongue protrusion, licking, jaw opening, and lip smacking. In some cases, these other motor responses were observed in association with swallowing on all trials across all ICMS parameters employed at a given intracortical site. In other cases, across multiple applications of ICMS representing a range of C/S currents, swallowing and these other orofacial motor responses were evoked individually on some trials (i.e., either swallowing or another behavior was evoked) and in combination within a single movement sequence on other trials (see below), suggesting differential thresholds for swallowing and other orofacial behaviors at a given intracortical site.

Of the total of 270 sites where swallowing was evoked, swallowing ONLY (i.e., swallowing unaccompanied by other orofacial movements) was evoked at 44 (16%) of the sites. Sites where swallowing ONLY was evoked generally were located along penetrations within the rostral portion of the swal-
lowing representation in both hemispheres (see Fig. 3). Whereas the proportion of all orofacial motor sites where swallowing was evoked was greater for the right than the left hemisphere, the proportion of swallowing sites where swallow only was elicited was greater for the left hemisphere (see Table 2). Furthermore in both hemispheres, the proportions of swallow only sites that were located $\leq 5$ mm deep with respect to the cortical surface were substantially greater than those located within the surface cortex (see Table 2).

Other evoked movements

Of the 1,069 sites where orofacial motor responses were evoked by ICMS in monkey H7, RJMs were evoked at 194 (18%) sites located within an area that included the lateral region of face-MI, face-SI, the more lateral CMAp, and the region $\geq 5$ mm deep to the cortical surface (see Fig. 4). This area overlapped and extended beyond the evoked swallowing representation in both hemispheres. RJMs were evoked both in isolation and in association with swallowing at different intracortical sites. Furthermore at some sites, RJMs were elicited in isolation at some ICMS currents but were accompanied by swallowing at other ICMS currents (see preceding text).

Swallowing features in face-MI

In total, 18% (i.e., 49/270) of the sites where swallowing was evoked were located within the ICMS-defined face-MI with a somewhat greater proportion in the left than the right hemisphere (see Table 1 and Fig. 5A). Furthermore all twitch sites where swallowing was evoked were located $<5$ mm deep to the cortical surface, confirming that the swallowing representation within MI is located within the surface cortex bilaterally. The lowest threshold for evoking swallowing within MI was 7 $\mu$A. Within MI, ICMS evoked swallow only at 22% (i.e., 11/49) of sites in both hemispheres (see Table 2). These
sites were located along a single penetration in the left hemisphere and along three separate penetrations in the right hemisphere and were within the most lateral regions of the face-MI. Indeed in the right hemisphere, these sites were located within a noncontiguous region of face-MI, lateral to the tongue-MI representation. T/S ICMS evoked submental/suprahyoid twitch at all swallow ONLY MI sites, at thresholds as low as 10 mA.

At the majority (i.e., 38/49) of the MI swallowing sites, however, swallowing was evoked in association with other orofacial movements. That is, swallowing occurred after evoked RJMs at 17/49 MI sites, after lip smacking at 8/49 MI sites, and in association with various complex sequences of tongue movements, lip pursing, and jaw opening at 13/49 MI sites at thresholds as low as 10 μA. At MI sites where swallowing was evoked in association with other orofacial movements, T/S evoked a variety of responses including tongue retraction, tongue protrusion, lateral tongue deviation, and chin twitch. Those MI sites where swallowing was accompanied by other movements were located within the most lateral portion of face-MI, particularly in the left hemisphere (see Fig. 3).

Swallowing features in CMAp

In total, 65% of the sites where swallowing was evoked were located within the surface cortex, outside of and immediately anterior and lateral to the ICMS-defined face MI (see Fig. 1). This region corresponds to the CMAp as defined by Huang et al. (1989a). Swallow ONLY was evoked at ~10% of these nontwitch sites in each hemisphere (see Table 2). The lowest threshold for evoking swallowing was 5 μA. At the majority of sites, swallowing was evoked after a series of RJMs or, somewhat less frequently, after other orofacial movements including jaw opening, smacking, tongue protrusion, and/or lip protrusion.

Swallowing features in deep cortex

Of the 270 intracortical sites where swallowing was evoked, 11% were located ≥5 mm deep to the cortical surface (see Fig. 5B). Furthermore the proportion of deep intracortical sites where swallowing was evoked was substantially greater in the left than the right hemisphere (see Table 1). The lowest thres-
old for evoking swallowing within this deep region was 10 \mu A in both hemispheres. Of the deep sites where swallowing was elicited, swallow ONLY was evoked at 50 and 46% of deep sites in the left and right hemispheres, respectively, in contrast to swallowing sites within MI and CMAp where a substantially lower proportion were swallow ONLY sites (see Table 2). At the remaining deep intracortical sites, swallowing was elicited in association with various orofacial movements including tongue protrusion, jaw opening, lip protrusion, sucking, smacking, and RJMs. T/S did not evoke any orofacial muscle twitch at any deep intracortical site.

Swallowing features in face-SI

Intracortical sites within face-SI where swallowing was evoked accounted for 5% of the total number of swallow sites. In contrast to face-MI, CMAp, and the deep cortical area, swallow ONLY was never evoked within face-SI and swallowing typically occurred after RJMs. The lowest ICMS current that evoked swallowing within face-SI was 20 \mu A.

Swallow-related EMG parameters

Comparisons of EMG patterns of evoked and naturally occurring swallowing are summarized in Fig. 6. [Because the natural juice swallow produced statistically significantly shorter burst durations in both GG and CT than the natural raisin swallow (\textit{t}-test, \textit{P} < 0.05), both the natural juice and raisin swallows were included in subsequent comparisons with evoked swallowing. There was no clear EMG burst in MASS associated with the natural juice swallow, however.]

EMG patterns of cortically evoked and naturally occurring swallowing showed some clear similarities. Most notably, both the GG and MASS EMG onsets preceded the CT EMG onset for all of the evoked and naturally occurring swallows analyzed. Nonetheless there were some differences in the EMG patterns. ANOVA indicated a statistically significant main effect of type of swallow (e.g., natural juice swallow, natural raisin swallow, swallow evoked from MI, swallow evoked from CMA, or swallow evoked from the deep cortical region) on swallow-related EMG burst duration for GG (\(F = 17.02, \text{df} = 4, \text{P} < 0.0001\)), MASS (\(F = 5.26, \text{df} = 3, \text{P} = 0.03\)), and CT (\(F = 18.59, \text{df} = 4, \text{P} < 0.0001\)). Post hoc comparisons indicated that swallowing evoked from the deep cortical area, ventral to CMAp, was characterized by statistically significantly longer EMG bursts in GG (\(q = 3.93, P < 0.00652\)), and CT (\(q = 3.93, P < 0.00652\)) than the natural juice swallow and, for GG (\(q = 3.93, P < 0.00652\)) and MASS (\(q = 3.74, P < 0.0105\)), the natural raisin swallow also. Furthermore swallowing evoked from the deep area was associated with significantly longer bursts in GG and CT than swallowing evoked from any other cortical region examined and also a significantly longer burst in MASS than swallowing evoked from face-MI. In contrast, swallowing evoked from face-MI was characterized by a shorter CT burst duration than that.
associated with the natural raisin swallow ($q = 3.93$, $P < 0.00652$) and swallowing evoked from all other cortical areas. ANOVA also indicated a main effect of type of swallow on the latency of GG to CT EMG onset ($F = 6.93$, $df = 4$, $P < 0.0001$) and the latency of MASS to GG EMG onset ($F = 3.06$, $df = 3$, $P = 0.035$). Post hoc comparisons indicated that swallowing evoked from face-MI was characterized by significantly longer GG-CT and MASS-GG EMG latencies than the natural swallows. Furthermore swallowing evoked from face-MI had a significantly longer GG-CT latency than swallowing evoked from the deep cortical area and a significantly longer MASS-GG latency than that evoked from the area corresponding to CMAp.

The effects of varying ICMS current on evoked swallow-related GG EMG activity was examined quantitatively for $14\%$ of the $270$ swallowing sites in monkey $H7$. Increases in ICMS intensity were associated with increases in GG EMG amplitude for $65\%$ of the sites examined; this effect was seen both for total area under the swallow-related GG EMG curve and for mean amplitude of the swallow-related GG EMG burst. In addition, $59\%$ of the sites studied show decreases in evoked swallow-related GG EMG latency with increases in ICMS intensity (see Fig. 7A). The mean swallow-related GG EMG latency for sites where this latency effect was found was somewhat less than the mean latency at sites that did not show a consistent modulation of latency with changes in ICMS intensity (i.e., mean latency for sites showing latency effect was $2.36 \pm 1.06$ s compared with mean latency of $3.00$ s for sites not showing the effect). Of the $37$ sites examined quantitatively, $12$ were located within the ICMS-defined MI, $16$ in CMAp and $9$ were deep sites (see preceding text). Of the MI sites, $75\%$ showed increases in swallow-related GG EMG magnitude with increases in ICMS intensity and $66\%$ showed decreases in GG EMG latency. The mean GG EMG latency at threshold for MI sites was $2.17 \pm 1.06$ (SD) s, whereas the shortest suprathreshold latency was $0.44$ s. For sites within CMAp, increases in ICMS intensity were associated with increases in GG EMG magnitude and decreases in GG EMG latency for $56$ and $44\%$ of the sites, respectively. The mean GG EMG latency at threshold for CMAp sites was greater than that for MI sites (i.e., $2.86 \pm 1.59$ s). The shortest evoked swallow-related GG EMG latency was $0.34$ s. At deep sites, swallow-related GG EMG amplitude was increased and latency de-

FIG. 6. Schematic diagram indicating durations and relative timing onsets of swallow-related electromyographic (EMG) activities in genioglossus (GG), masseter (MASS), and cricothyroid (CT) muscles during natural swallowing of raisin (A), natural swallowing of juice (B), swallow evoked by intracortical microstimulation applied to face-MI (C), swallow evoked from the cortical masticatory area (CMAp) (D), and swallow evoked from deep cortical area (E), $>5$ mm deep to the cortical surface for monkey $H7$. EMG activities have been aligned to the onset of activity in GG across the $5$ swallow conditions shown; Solid bars indicate mean swallow-related EMG burst durations, and narrow bars indicate $\pm$ SD.

FIG. 7. Stimulus-response curves indicating effects of varying intensity of C/S ICMS on the latency of the onset of swallow-related genioglossus EMG. Each line denotes a single ICMS site in monkey $H7$. Stimulation intensity is expressed as a function of movement threshold (T), au., arbitrary units.
Swallowing can be evoked by ICMS delivered to sites within the lateral pericentral cerebral cortex in both hemispheres of the awake monkey. Furthermore, swallowing was evoked from a number of distinct cortical regions: the lateral region of face-MI, the lateral face-SI, the area immediately lateral and/or anterior to face-MI, corresponding to the CMA (Huang et al. 1989a), and a deep cortical area, ventral to CMA, localized to the underlying white matter and the inner face of the frontal operculum. Swallow only was evoked at some intracortical sites, particularly within the rostral portion of the swallowing representation in the deep cortical area and, to a lesser extent, within the most lateral aspect of face-MI. At the majority of intracortical sites, however, swallowing was evoked in association with other orofacial motor behaviors. Indeed, the cortical representations of swallowing and RJMs were overlapped extensively. This study also has shown that the EMG profiles of cortically evoked and naturally occurring swallowing, while similar, are characterized by certain temporal differences, as are swallows evoked from different cortical regions. Furthermore, changes in ICMS intensity modulated both the latency and the magnitude of cortically evoked swallow-related EMG activity. These findings indicate that swallowing in the primate is represented within a number of spatially and cytoarchitectonically distinct cortical foci including face-MI, face-SI, CMA, and the frontal operculum. Our findings are consistent with the view that these cortical foci participate fundamentally and perhaps differentially in the initiation and modulation of swallowing in the primate, as well as in the integration of the swallow within the complex masticatory sequence. The present ICMS findings also have confirmed earlier documentation by ourselves and others of the multiple nested organization of the orofacial musculature in face-MI and the extensive representation of tongue and facial muscles in face-MI compared with the limited representation of jaw muscles (see Huang et al. 1988, 1989b; Murray and Sessle 1992). They also have confirmed that masticatory-like movements can be elicited by ICMS applied not only to sites within CMA but also to sites within face-MI and face-SI (Huang et al. 1989a).

Swallowing representation within lateral sensorimotor cortex

Previous studies have shown that repetitive surface electrical stimulation of restricted regions of the anterolateral frontal and lateral pericentral cortex can evoke swallowing in a number of species, including humans (Car 1970; Miller and Bowman 1977; Penfield and Rasmussen 1950; Sumi 1969; Woolsey et al. 1952). This evoked swallowing frequently may be accompanied by rhythmic jaw movements elicited from more widespread cortical areas (Huang et al. 1989a; Penfield and Rasmussen 1950; Lund and Lamarre 1974; Liu et al. 1993). For example, Miller and Bowman (1977) reported that swallowing alone, or swallowing preceded by several chewing-like movements, can be evoked in the monkey by trains of repetitive electrical stimulation of >2 s, applied to the caudal and lateral surface of the precentral cortex lateral to MI, including Brodmann’s areas 44, 3, 1, and 6. However, the present finding that swallowing was elicited from sites within the ICMS-defined face-MI, as well as from sites within the CMA, face-SI, and the frontal operculum, supports the view that a more extensive cortical representation, including MI, is involved in the sensorimotor control of swallowing. This finding is in keeping with our earlier data showing that C/S ICMS applied both within face-MI and lateral to face-MI can evoke other types of semi-automatic movements in the awake monkey (Huang et al. 1989a). It also is consistent with our previous finding that single neurons within the ICMS-defined tongue-MI show swallow-related activity (Martin et al. 1995, 1997), as do neurons in the CMA (Sessle et al. 1995a). It is noteworthy that swallowing was not evoked by T/S ICMS at any intracortical sites within the present study. This finding confirms early work suggesting that the temporal summation of multiple inputs is required to trigger the bulbar swallowing center (Jean and Car 1979; Miller 1982). On the basis of evidence that the corticofugal swallowing pathway is direct from the cortex to the mesencephalon and becomes polysynaptic between the mesencephalon and the medulla (Car 1973), temporal summation could occur at multiple points along this polysynaptic route.

Although the involvement of the CMA in swallowing may not be unexpected in view of earlier reports of CMA neurons showing activity related to ingestive behavior (Lund and Lamarre 1974), the apparent involvement of face-MI requires some comment. Face-MI, like limb-MI, is believed to superimpose a set of specific motor synergies on subcortical circuits controlling the basic organization of muscle activities. In the case of swallowing and mastication, the literature points to the importance of brain stem pattern generators in their temporal sequencing. On the basis of findings by Hoffman and Luschei (1980) that most biting task-related MI neurons may not exhibit a strong relation with chewing, Evarts (1986) indeed concluded that MI plays a major role in the control of operantly conditioned movements (e.g., biting task) but only a minor role in semiautomatic movements involving the same muscles. Our present data indicating that ICMS applied to face-MI can evoke both swallowing and mastication challenge this conclusion. These findings, together with our previous documentation that some tongue-MI neurons exhibit firing related both to a trained orofacial motor task and to swallowing or chewing (Martin et al. 1997; D. Yao, K. Yamamura, N. Narita, G. M. Murray, and B. J. Sessle, unpublished data) and that cold block of face-MI, as well as CMA/swallow cortex, may interfere with swallowing and chewing-related movements (Narita et al. 1995, 1999; Sessle et al. 1995b), suggest a more fundamental role for face-MI in the control of these semiautomatic movements.

Swallow only versus swallow associated with other oral movements

One of the major findings of the present study was that swallow only was evoked at some sites. Indeed C/S ICMS at intensities as low as 15 μA produced series of as many as three forceful swallowing responses at some intracortical sites. Although swallowing occurring within or at the end of a masticatory sequence, or preceded by other movements, may occur...
as a consequence of these associated orofacial movements, the elicitation of swallowing only after ICMS may be more directly related to the effects of ICMS per se. In this vein, our finding that swallow only was elicited at some intracortical sites in both hemispheres may suggest that these intracortical sites represent “primary” cortical foci for the control of swallowing.

Swallowing evoked from multiple different regions

Our findings that swallowing can be evoked by C/S ICMS applied to four functionally and cytoarchitectonically distinct cortical regions are consistent with our previous finding that RJMs are evoked by ICMS applied to these same four cortical regions (Huang et al. 1989a). Moreover our documentation of differences in the properties of swallows evoked from these four regions is also consistent with our earlier work, which showed that differences in the RJM patterns evoked from different cortical regions. The swallows evoked from face-MI, face-SI, CMAp, and the deep cortical area tended to differ in terms of the oral movement sequence within which the swallows occurred. For example, swallowing only was evoked primarily from the rostral part of the swallowing representation, whereas swallowing in association with mastication typically was evoked more caudally. This finding contrasts with that of Miller and Bowman (1977) who reported that combined masticatory and swallow-related movements were elicited primarily from the region anterior to the monkey’s subcentral dimple, whereas swallowing alone was more frequently elicited posterior to the dimple. In considering this discrepancy, it is noteworthy that many of the swallow only sites found in the present investigation were located in the deep cortical area, ventral to the CMAp, consistent with our previous findings for evoked mastication (Huang et al. 1989a). The surface stimulation technique used by Miller and Bowman (1977) would have limited effectiveness in evoking swallowing from deep cortical sites. Their use of anesthesia also may explain the difference between their data and the present findings based on awake monkeys. In addition to the finding that swallow only sites were located rostrally within the swallowing representation, the proportions of swallow only sites were different for the different cortical regions. That is, swallow only was evoked at a substantially greater proportion of sites within the deep cortical region than within any other cortical areas examined. Indeed, swallow only was not evoked at any site within face-SI. This finding of a relative predominance of swallow only sites within the deep cortical region suggests the possibility that this deep area, which corresponds to the white matter and frontal operculum underlying the rostral aspect of the CMAp, represents a cortical region of specialized function in relation to the control of swallow-related oropharyngeal movements.

It is noteworthy that swallow only also was evoked from a number of intracortical sites located within a noncontiguous region of face-MI, lateral to the main face-MI representation as well as at some sites within the most lateral region of the main face-MI representation. Interestingly, T/S ICMS evoked, at low threshold, submental/suprahypoid twitch at all these swallow only sites within face-MI, whereas T/S ICMS evoked a variety of orofacial twitch responses at face-MI sites where swallowing was evoked in association with other orofacial movements. Given that ICMS evoked swallowing at thresholds as low as 7 μA at these sites, this region of face-MI may play a role in driving motoneurons innervating the submental/suprahypoid muscles such as the geniohyoid, mylohyoid, anterior belly of the diaphragm and the hyoglossus, many of which are activated during the “leading complex” or earliest phase of the buccopharyngeal swallow (Carpenter 1989; Doty 1968; Dubner et al. 1978; Miller 1982). It is possible that this lateral region of face-MI where swallow only was evoked plays a role in initiating the swallow through the activation of these early muscle activities in the swallow. Although submental/suprahypoid EMG activity was not examined in the present study, future studies combining single neuron recordings from this region and ICMS or spike triggered averaging would be useful in detailing the output properties of neurons at these intracortical sites in relation to swallowing. Our finding that swallow only, submental/suprahypoid twitch sites were lateral within face-MI, whereas face-MI sites where swallow was evoked with other orofacial movements were generally located more medially also suggests that there may be functionally distinct regions within face-MI in relation to the control of swallowing with the lateral region being a “primary” area and that the more medial region involved is other aspects of swallowing control. This view is supported by our recent single neuron study, which showed that neurons within tongue-MI neurons show several distinct swallow-related firing patterns (Martin et al. 1997).

In the other cortical regions, swallowing was more frequently, or always, accompanied by other orofacial movements, most commonly RJMs. It is well established that swallowing and mastication are highly integrated (Lund and Enomoto 1993), swallowing occurring at particular points within the masticatory motor sequence (McFarland and Lund 1995) and CMAp and face-SI may be involved in regulating this coordination.

Swallows evoked from face-MI, face-SI, CMAp, and the deep area also showed certain statistically significant differences in the temporal patterns of the swallow-related EMG profiles. In particular, swallowing evoked from the deep area was characterized by significantly longer burst durations than swallows evoked from other areas and from naturally occurring swallowing, whereas swallowing evoked from face-MI tended to have shorter CT durations. Differences in the relative timing of muscle activities also were found in that MI-evoked swallows had longer intramuscle EMG onset latencies than those evoked from other areas. These findings, combined with our finding of differences in the proportions of swallow only sites across cortical regions, implies that these multiple cortical foci may participate differentially in regulation of swallowing in the primate. It also suggests that modulations of the swallowing motor sequence associated with changes in behavioral context (e.g., swallowing after sucking vs. after mastication) (Kempainen et al. 1993) or different bolus characteristics such as volume, consistency, temperature, or taste (Bisch et al. 1994; Dantas 1990; Lazarus et al. 1993; Logemann et al. 1995) may be mediated through the activation of different regions of the cortical swallowing representation.

ICMS properties and swallow-related EMG patterns

The present finding that increases in ICMS intensity were associated with alterations in the magnitude and latency of swallow-related EMG activity in GG provides further evidence
that the cerebral cortex plays a role in modulating the swallow. This finding is of interest in relation to reports that human subjects are able to modify aspects of the oropharyngeal swallow voluntarily (Kahrilas et al. 1991) and in light of studies indicating that dysphagia secondary to hemispheric stroke is characterized frequently by a delay in the initiation of the pharyngeal phase of swallowing and weakness of swallow-related pharyngeal activity (Robbins and Levine 1988). Our finding suggests that such voluntary and stroke-related alterations in swallowing function may arise, in part, because of damage to the cortical foci that we have shown are involved in the initiation and modulation of the swallowing synergy.

**Bilateral cortical swallowing representation**

Hamdy et al. (1996) recently have reported that individual muscle groups active in swallowing, including oral and pharyngeal muscles, are bilaterally but asymmetrically represented in the human motor and premotor cortex based on transcranial magnetic stimulation mapping. Our finding that swallowing was evoked by ICMS in both hemispheres of both monkeys is consistent with this finding of bilateral oropharyngeal muscle representation. However, although we did document a larger proportion of orofacial sites where swallowing was evoked in the right, compared with the left hemisphere, the proportion of swallow only sites was greater for the left than the right hemisphere, as was the proportion of deep sites. Therefore it would be premature to propose an asymmetry of the cortical swallowing representation in the primate based on our present findings. Although our findings do not support a strong asymmetry, they do raise the possibility of a functional interaction between the two descending corticofugal pathways such that unilateral damage could interfere with normal corticofugal mechanisms despite bilateral cortical representation.

**Involvement of face-SI**

It also should be noted that cortical dysfunction, associated with naturally occurring or experimental lesions or inactivation, may result in swallowing impairment not only from interruption to corticobulbar output pathways such as those from the precentral gyrus but also possibly from interference with the neural circuitry mediating the processing of afferent inputs from the oral cavity, upper respiratory tract, and esophagus. The likelihood that such afferent information plays an important role in swallowing is underscored by our finding that swallowing was evoked by ICMS applied to face-SI. The potential importance of this cortical region in swallowing is suggested further by neuroanatomic and neurophysiologic evidence indicating that the precentral cortex receives prominent somatosensory inputs, both directly via thalamocortical fibers and indirectly via the somatosensory cortex (Dubner et al. 1978; Huang et al. 1989b; Jones 1987; Murray and Sessle 1992) and that stimulation of nerves supplying laryngeal or pharyngeal mucosa gives rise to evoked potentials in a restricted region of the ipsilateral frontoorbital cortex (Car 1977; Sumi 1972). This reinforces the view that these ascending sensory inputs may be used by swallow-related areas of the cortex in initiating or guiding deglutition and that some dysfunctional states may involve damage to the circuitry carrying or processing these inputs. Indeed because some neurons within the lateral precentral cortex receive orofacial mechanosensitive afferent inputs, it is possible that sensory inputs to these neurons play a role in guiding both trained and semiautomatic movements. Nonetheless, we cannot yet rule out the possibility that orofacial inputs generated during a masticatory or swallow-related movement may be responsible for the movement-related activity of MI or CMA neurons. This does seem unlikely, however, because not all movement-related MI or CMA neurons have detectable orofacial inputs, because orofacial inputs to most neurons in face-SI, which is a major source of afferent input to MI, are “gated out” immediately preceding and during motor performance in awake monkeys (Lin and Sessle 1994), and because the movement-related activity of most face-MI neurons is not influenced by cold block of the ipsilateral face-SI (D. Yao, K. Yamamura, N. Narita, G. M. Murray, and B. J. Sessle, unpublished results).

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