Neuronal Activity Patterns in Primate Primary Motor Cortex Related to Trained or Semiautomatic Jaw and Tongue Movements

DONGYUAN YAO, KENSUKE YAMAMURA, NORIYUKI NARITA, RUTH E. MARTIN, GREGORY M. MURRAY, AND BARRY J. SESSLE
Faculty of Dentistry, University of Toronto, Toronto, Ontario M5G 1G6, Canada

Received 3 July 2001; accepted in final form 19 December 2001

Yao, Dongyuan, Kensuke Yamamura, Noriyuki Narita, Ruth E. Martin, Gregory M. Murray, and Barry J. Sessle. Neuronal activity patterns in primate primary motor cortex related to trained or semiautomatic jaw and tongue movements. J Neurophysiol 87: 2531–2541, 2002; 10.1152/jn.00543.2001. The present study was undertaken to determine the firing patterns and the mechanoreceptive field (RF) properties of neurons within the face primary motor cortex (face-MI) in relation to chewing and other orofacial movements in the awake monkey. Of a total of 107 face-MI neurons recorded, 73 of 74 tested had activity related to chewing and 47 of 66 neurons tested showed activity related to a trained tongue task. Of the 73 chewing-related neurons, 52 (71.2%) showed clear rhythmic activity during rhythmic chewing. A total of 32 (43.8%) also showed significant alterations in activity in relation to the swallowing of a solid food (apple) bolus. Many of the chewing-related neurons (81.8% of 55 tested) had an orofacial RF, which for most was on the tongue dorsum. Tongue protrusion was evoked by intracortical microstimulation (ICMS) at most (63.6%) of the recording sites where neurons fired during the rhythmic jaw-opening phase, whereas tongue retraction was evoked by ICMS at most (66.7%) sites at which the neurons firing during the rhythmic jaw-closing phase were recorded. Of the 47 task-related neurons, 21 of 22 (95.5%) examined also showed chewing-related activity and 29 (61.7%) demonstrated significant alteration in activity in relation to the swallowing of a juice reward. There were no significant differences in the peak firing frequency among neuronal activities related to chewing, swallowing, or the task. These findings provide further evidence that face-MI may play an important role not only in trained orofacial movements but also in chewing as well as swallowing, including the control of tongue and jaw movements that occur during the masticatory sequence.

INTRODUCTION

Recent studies conducted in our laboratory have suggested that face primary motor cortex (face-MI) plays an important role in the initiation and control of primate tongue and facial movements with only a minor role in the control of jaw-closing movements. Murray et al. (1991) showed that reversible inactivation by cooling of the monkey’s face-MI, including tongue-MI, significantly reduced the successful performance of a trained tongue-protrusion task but had little effect on a biting task. Consistent with this, the activity patterns of single neurons recorded at tongue-MI sites were found to be related to a trained tongue-protrusion task but not to a trained biting task (Murray and Sessle 1992b,c). Finally, intracortical microstimulation (ICMS) within face-MI evoked orofacial twitch-like movements that were dominated by movements of the tongue or facial muscles (Huang et al. 1988; Martin et al. 1997; Murray and Sessle 1992a).

Whereas such findings reinforce the view that face-MI plays an integral role in the control of voluntary tongue movements, the extent to which face-MI also regulates semiautomatic tongue movements, such as those produced during mastication and swallowing, remains unclear. However, several lines of evidence now point to the possibility that face-MI and adjacent regions of the lateral pericentral cortex play a prominent role in semiautomatic movements. For example, bilateral ablation of the face area of the primate precentral cortex, including Brodmann’s areas 4 and 6 (Larson et al. 1980; Luschei and Goodwin 1975), and of the more laterally located cortical masticatory area (CMA) (Lund and Lamarre 1974) can result in masticatory deficits. Our recent studies have also shown that reversible inactivation by cooling of the lateral pericentral cortex reduces the incidence of chewing and swallowing after chewing, and alters swallow- and chewing-related electromyographic (EMG) patterns in awake monkeys (Narita et al. 1999, 2002). This is consistent with earlier studies by Sumi (1972) showing that reversible inactivation or unilateral or bilateral ablation of the anterolateral frontal cortex may suppress chewing and swallowing elicited by electrical stimulation of the pons in anesthetized rabbits. Recent brain imaging studies in humans have demonstrated swallow-related bilateral activation within Brodmann’s areas 3, 4, and 6, and several other cortical areas (Hamdy et al. 1999; Martin et al. 2001). Repetitive electrical stimulation of regions of the anterolateral frontal and lateral pericentral cortex evokes chewing-like rhythmic jaw movements and/or swallowing in a number of species, including primates (Car 1970; Huang et al. 1989b; Martin and Sessle 1993; Martin et al. 1999; Miller and Bowman 1977; Penfield and Rasmussen 1950; Sumi 1969). Single-neuron recording studies in monkeys have shown that some neurons within the lateral precentral cortex, including Brodmann’s areas 4 and 6, and the CMA, exhibit activity patterns related to the orofacial movements executed during ingestion, licking, food transport, chewing, and/or swallowing (Hoffman and Luschei 1980; Kubota and Niki 1971; Lund and Lamarre 1974; Luschei et al. 1971; Martin et al. 1995, 1997; Murray and Sessle 1992b). Thus overlapping cortical regions have been implicated in...
chewing and a number of related ingestive and alimentary functions such as swallowing.

Given the previous findings of Murray et al. (1991) and Murray and Sessle (1992b,c) suggesting a prominent role for face-MI in voluntary tongue movements, an investigation of face-MI neurons in relation to chewing and swallowing as well as voluntary tongue movements would afford the opportunity to clarify and compare the role of this cortical region in semiautomatic versus voluntary motor behaviors. Tongue movements are critical to several components of chewing and swallowing including food intake, bolus formation, bolus transport through the oral cavity, and bolus propulsion through the pharynx (for review, see Cunningham et al. 1991; Miller 1982; Sawczuk and Mosier 2001). Therefore the aims of the present study were to determine whether neurons within the ICMS-defined face-MI significantly alter their firing rates in relation to chewing; whether face-MI neurons that exhibit chewing-related activity patterns also significantly alter their firing rates in relation to swallowing and during a voluntary, trained tongue-protrusion task; the ICMS effects at face-MI sites where neurons exhibiting chewing-related firing patterns are found; and the mechanoreceptive field (RF) properties of face-MI neurons exhibiting firing patterns related to chewing.

Some of the data have been briefly reported in abstract form (Yamamura et al. 1998).

**METHODS**

**Animal preparation and task training**

The study was carried out in two female monkeys (Macaca fascicularis, 3–3.5 kg) in accordance with the guiding principles of the American Physiological Society and the Canadian Council for Animal Care. The experimental protocols were approved by the University of Toronto Animal Care Committee. Because the methods have been described in detail (Lin et al. 1993; Martin et al. 1997, 1999; Murray and Sessle 1992a,b; Murray et al. 1991), only a brief description follows.

A head cap of dental acrylic was fixed to the skull under full surgical and aseptic procedures (induction: atropine, 0.05 mg/kg; acepromazine, 0.05 mg/kg; and ketamine HCl, 10 mg/kg; 2:1 N₂O/O₂, with 3.0% halothane: maintenance: 0.5% halothane; with 3.0% halothane; and ketamine HCl, 10 mg/kg; 2:1 N₂O/O₂). (Lin et al. 1993; Martin et al. 1997, 1999; Murray and Sessle 1992a,b). A longer pulse ICMS train [3 s-train, 0.2-ms pulses at 50 Hz, ±0.6 μA (continuous stimulus; C/S)] was not systematically applied but was occasionally used in some penetrations to evoke semiautomatic movements at ±500-μm intervals to a depth of 8–10 mm (Huang et al. 1989b; Martin et al. 1999).

**Data analysis**

After the animal had finished one chewing sequence, the next food bolus was similarly delivered within the next 4–10 s. A minimum of 7 successful task trials or 10 masticatory trials were carried out. EMG recordings were made simultaneously with the single-neuron recordings; vertical and horizontal jaw movements were also recorded with a photoelectric transducer that measured the displacement of a light source attached to the monkey’s chin by the previously implanted magnet. Some neurons also were tested for a RF by applying light tactile stimuli with hand-held probes and firm nonnoxious mechanical stimuli to the skin of the face and to the oral cavity (Murray and Sessle 1992a,b); no systematic identification of deep RFs was carried out.

**Intracortical microstimulation and neuronal recording**

After the monkey was trained, face-MI was identified and mapped for evoked orofacial twitch-like movements by applying ICMS [±30 μA, 35-ms train of 12 cathodal pulses, each pulse 0.2 ms, 333 Hz (short-train stimulus, T7/S)] during daily transdural microelectrode penetrations of the precentral cortex as previously detailed (e.g., Murray and Sessle 1992a; Martin et al. 1997, 1999). These MI mappings took 2–3 wk. A longer pulse ICMS train [3 s-train, 0.2-ms pulses at 50 Hz, ±60 μA (continuous stimulus; C/S)] was not systematically applied but was occasionally used in some penetrations to evoke semiautomatic movements at ±500-μm intervals to a depth of 8–10 mm (Huang et al. 1989b; Martin et al. 1999).

Extraocular recordings were made with glass-coated tungsten electrodes (Z = 0.5–2 MΩ at 1 kHz) in the daily sessions from both hemispheres of each monkey to examine the activity of single neurons at ICMS-defined sites within face-MI (Huang et al. 1988; Martin et al. 1997; Murray and Sessle 1992a,b) during chewing and swallowing of standardized amounts of fruit (apple, 10 × 6 × 6 mm) and during the trained tongue-protrusion task. Each food bolus was placed on an applicator stick and was delivered to the animal by the experimenter. After the animal had finished one chewing sequence, the next food bolus was similarly delivered within the next 4–10 s. A minimum of 7 successful task trials or 10 masticatory trials were carried out. EMG recordings were made simultaneously with the single-neuron recordings; vertical and horizontal jaw movements were also recorded with a photoelectric transducer that measured the displacement of a light source attached to the monkey’s chin by the previously implanted magnet. Some neurons also were tested for a RF by applying light tactile stimuli with hand-held probes and firm nonnoxious mechanical stimuli to the skin of the face and to the oral cavity (Murray and Sessle 1992a,b); no systematic identification of deep RFs was carried out.

**Data analysis**

After the animal had finished one chewing sequence, the next food bolus was similarly delivered within the next 4–10 s. A minimum of 7 successful task trials or 10 masticatory trials were carried out. EMG recordings were made simultaneously with the single-neuron recordings; vertical and horizontal jaw movements were also recorded with a photoelectric transducer that measured the displacement of a light source attached to the monkey’s chin by the previously implanted magnet. Some neurons also were tested for a RF by applying light tactile stimuli with hand-held probes and firm nonnoxious mechanical stimuli to the skin of the face and to the oral cavity (Murray and Sessle 1992a,b); no systematic identification of deep RFs was carried out.
considered to be task related only if the neuronal firing frequency during the task period was statistically significantly different from that during the PTP of the same task (paired t-test; \( P < 0.05 \)) and if the onset of neuronal activity occurred within 580 ms of the onset of GG activity associated with the tongue-protrusion task (i.e., in effect, the onset of neuronal activity had to occur by the beginning of the holding phase of the task).

For data analysis of chewing-related neuronal activity, the total masticatory period of each masticatory trial was defined as the period from the onset of the AD activity associated with mouth opening to obtain the test food to the onset of the GG activity associated with swallowing (Fig. 1). Each masticatory period was further divided into a food-preparatory phase, rhythmic-chewing phase, and pre-swallowing phase. The food-preparatory phase was defined as the period from the onset of the first AD burst as the animal opened its mouth to obtain food to the end of this burst (initial jaw opening) plus the period from the end of the AD burst to the start of rhythmic chewing (food transportation). During this phase, there were no clear rhythmic cycles as occurred in rhythmic chewing and in the pre-swallowing phase (see Fig. 1 and following text). The rhythmic-chewing phase was defined as the period from the end of the food-preparatory phase to the end of MA activity related to the rhythmic chewing. Each cycle during the rhythmic-chewing phase actually had three component phases, namely an opening phase, a fast-closing (FC), and a slow-closing (SC) phase; the FC and SC phases were collectively termed the jaw-closing phase. Because the monkeys chewed unilaterally, the jaw usually moved during the FC phase to the working side (the side where the foodstuff was placed between the molars and chewed). The SC phase began with peak deceleration of the jaw. The pre-swallowing phase was defined as the period from the end of the rhythmic chewing to the onset of GG activity related with swallowing. The pre-swallowing phase was characterized by clear GG activity with minimal MA activity, larger lateral jaw movements, and wider cycles. Swallowing following mastication was characterized by no jaw movement, a longer GG duration than that during the rhythmic-chewing phase, and synchronization of GG, MA, and AD activity (see Fig. 1).

Digitized data related to initial jaw opening and/or food transportation before the start of the rhythmic-chewing phase were analyzed by aligning a minimum of 10 masticatory trials to the peak activity in the AD muscle related to the initial jaw opening or the point of maximum jaw closing during the food-preparatory phase. The activity of single neurons was also aligned for a minimum of 20 rhythmic-chewing cycles to the point of maximum jaw opening or peak activity in AD muscle during the rhythmic-chewing phase. Neurons were considered to be chewing-related only if the neuronal firing frequency during at least one of the three masticatory phases (see preceding text) was statistically significantly different from that during the prechewing period of the same masticatory trial (1-way ANOVA with repeated measures; \( P < 0.05 \)). The neurons were considered to be related to firing during the rhythmic jaw-opening or -closing phase if the rhythmical neuronal burst occurred, respectively, during the jaw-opening phase of each chewing cycle during GG and AD activity or occurred during the early part of jaw closing before the onset or during MA activity.

A swallow-related neuronal activity pattern was defined as a significant alteration of neuronal firing rate, relative to that during the PTP (see definition preceding text), during the 50-ms interval immediately before the GG activity defining swallow onset, the swallow (i.e., the interval between the GG activity defining swallow onset and offset), or both the 50-ms interval and the swallow (Martin et al. 1997). For each neuron, a one-way ANOVA with repeated measures and post hoc comparisons (Duncan’s multiple range test) were performed to determine whether the average rates of neuronal activity during these three intervals were significantly different.

The peak firing frequency of the neurons during the rhythmic jaw-opening phase was compared with that of the neurons during the

![Fig. 1](http://jn.physiology.org/). A masticatory sequence of chewing a standardized piece of apple by the awake monkey. A: 3 basic masticatory phases: food-preparatory phase, rhythmic-chewing phase, and pre-swallowing phase (see text for definition). B: the further subdivision of the food-preparatory phase: initial jaw opening and food transportation. Ver, vertical movement of the mandible; Hor, horizontal movement of the mandible; MA, rectified and low-pass filtered electromyogram (EMG) activity in the masseter muscle; GG, rectified and low-pass filtered EMG activity in the genioglossus muscle; AD, rectified and low-pass filtered EMG activity in the anterior digastric muscle.
rhythmic jaw-closing phase (Student’s $t$-test, $P > 0.05$). For the neurons showing both task- and chewing-related excitation, one-way ANOVA with repeated measures and post hoc comparisons (Duncan’s multiple range test) were performed to compare the peak firing frequencies during the task and during the food-preparatory phase, the rhythmic-chewing phase and the pre-swallowing phase. For the neurons showing swallow-related excitation, comparable analyses were performed to compare the peak firing frequency during each of the three chewing phases and the swallowing of the solid bolus; the peak firing frequency during the task with that during the swallowing of the juice reward following the task (paired $t$-test); and the peak firing frequency during the swallowing of the solid bolus following the chewing with that during the swallowing of the juice reward following the task (paired $t$-test). $P < 0.05$ was considered statistically significant. Values are expressed as means ± SD.

**Histological procedures**

The histological methods were similar to those previously described (e.g., Huang et al. 1989b; Murray et al. 1991). Briefly, in each hemisphere and just before the animal was killed, electrolytic lesions (10–20 $\mu$A cathodal current for 10–15 s) were made with glass-coated tungsten electrodes were placed at selected intracortical sites or at the bottom of electrode tracks. At other selected intracortical sites, electrolytic lesions (30–50 $\mu$A anodal current for 30 s) were made with epoxyxilite-coated stainless-steel electrodes. Immediately prior to perfusion, four electrodes were placed in the cortex outside the area that had been investigated. These electrodes aided orientation of the block of cortical tissue so that sections could be prepared parallel to the electrode penetrations. Then the animal was deeply anesthetized with pentobarbital sodium (30 mg/kg iv) and perfused thorough the heart with heparin-saline followed by 2.0% potassium ferricyanide in 10.0% buffered formalin. The block of cortical tissue was stored in 10.0% buffered formalin. The histological procedures were similar to those previously described (e.g., Figs. 2 and 3 show the spatial distribution within face-MI of both monkeys. Not all of these neurons showing both task- and chewing-related excitation, one-way ANOVA with repeated measures and post hoc comparisons (Duncan’s multiple range test) were performed to compare the peak firing frequencies during the task and during the food-preparatory phase, the rhythmic-chewing phase and the pre-swallowing phase. For the neurons showing swallow-related excitation, comparable analyses were performed to compare the peak firing frequency during each of the three chewing phases and the swallowing of the solid bolus; the peak firing frequency during the task with that during the swallowing of the juice reward following the task (paired $t$-test); and the peak firing frequency during the swallowing of the solid bolus following the chewing with that during the swallowing of the juice reward following the task (paired $t$-test). $P < 0.05$ was considered statistically significant. Values are expressed as means ± SD.

**RESULTS**

**General features of the face-MI neurons**

The activity of a total of 107 neurons was recorded from the ICMS-defined face-MI of both monkeys. Not all of these neurons were examined during both chewing/swallowing (C/S) and tongue task/swallowing (T/S) performance. Details of orofacial motor responses to T/S and C/S ICMS delivered to sites along microelectrode penetrations within lateral pericentral cerebral cortex have been published elsewhere (Martin et al. 1999). Figures 2 and 3 show the spatial distribution within face-MI of penetration tracks within which chewing-related neurons were recorded and face-MI neuronal RFs delineated. Of the 107 neurons, 41 neurons were tested for chewing-related activity only, 33 neurons were tested for both chewing and task-related activity, and the remaining 33 neurons were tested only for tongue task-related activity. All neurons that showed chewing-related activity and/or tongue-protrusion task-related activity were also examined for swallow-related activity.

Of 73 chewing-related neurons, 55 were tested for afferent input. An orofacial RF was found in 45 (81.8%) of these neurons. For 38 (84.4%) of these 45 neurons, the RF was on the superior tongue surface (e.g., Fig. 3); the remaining neurons had a RF on the lip, face or intraoral mucosa. One neuron with an inhibitory RF on the tongue surface was also found. Of the 66 neurons examined during the tongue task, 44 were tested for an orofacial sensory input, and an orofacial RF could be delineated in 30 (68.2%). In 23 (76.7%) of these 30 neurons, the RF was on the superior tongue surface; the remaining neurons had a RF on the lip or oral mucosa.

**Chewing-related neuronal activity patterns during food-preparatory and rhythmic-chewing phases**

Four main patterns of chewing-related activity could be distinguished (see Figs. 4–8) while the monkey masticated the solid food bolus. The majority of neurons ($n = 52$, i.e., 71.2%) showed a clear rhythmicity during the rhythmic-chewing phase (e.g., Figs. 4 and 5). However, 10 neurons (13.7%) had increased activity only when the monkey’s mouth initially opened to obtain food or just before rhythmic chewing (Fig. 6), 7 neurons (9.6%) fired tonically throughout the total masticatory period (Fig. 7), while 4 (5.5%) showed decreased activity (Fig. 8) during this period. Three (4.1%) of the 73 neurons showing chewing-related activity also fired between 366 ± 169 ms, mean ± SD) the initial jaw opening to obtain food. In 24 (46.2%) neurons that showed rhythmic activity, each phasic burst occurred during the jaw-opening phase of each chewing cycle (Fig. 4). The majority ($n = 20$, i.e., 83.3%) of these 24 neurons that fired during the jaw-opening phase of each chew-
ing cycle also increased their firing during the food-preparatory phase, with 5 (20.8%) showing neuronal activity only during initial jaw opening, 3 (12.5%) showing only food-transportation-related activity, and 12 (50.0%) showing both initial jaw opening and food-transportation-related activity. In the remaining 28 (53.8%) neurons showing rhythmic activity, the phasic burst occurred during the early part of jaw closing before or after the onset of MA activity. The majority \( (n = 24, \text{i.e., } 85.7\%) \) of these 28 neurons that fired during the jaw-closing phase also increased their firing during the food-preparatory phase (Fig. 5), with 3 (10.7%) firing only during the initial jaw opening, 14 (50.0%) only during the food transportation, and 7 (25.0%) during both the initial jaw opening and food transportation.

A variety of orofacial movements could be evoked by T/S ICMS applied at the neuronal recording sites (Table 1, Fig. 3). Whereas tongue protrusion was evoked by ICMS at most of the loci (63.6%) showing rhythmic neuronal activity during the rhythmic jaw-opening phase, tongue retraction was evoked by T/S ICMS at most (66.7%) loci from which neurons firing during the rhythmic jaw-closing phase were recorded (Table 1).

The maximum jaw opening occurred after \( (58 \pm 7 \text{ ms}, n = 20) \) the corresponding peak activity in the AD muscle (Fig. 9).

Analysis of the peak neuronal activity in 44 of the 52 rhythmically firing neurons revealed that the peak firing frequency of the neurons showing activity during the rhythmic jaw-opening phase \( (71 \pm 37 \text{ Hz}, n = 21) \) was not significantly (Student’s \( t \)-test, \( P > 0.05 \)) different from that of the neurons showing activity during the rhythmic jaw-closing phase \( (62 \pm 36 \text{ Hz}, n = 23) \). Further, analysis of the intervals between the peak neuronal activity in these neurons and the corresponding peak activity in the AD muscle revealed that the peak activity of the neurons firing during the jaw-opening phase occurred before \( (32 \pm 43 \text{ ms}, n = 21) \) the corresponding peak activity in each rhythmic burst in the AD muscle and that the peak firing of the neurons firing during the jaw-closing phase occurred well after \( (112 \pm 53 \text{ ms}, n = 23) \) the peak of the AD activity (Fig. 9).

**FIG. 3.** Examples of face-MI neuronal mechanoreceptive fields (RFs) at microelectrode penetration sites where chewing-related neurons were recorded in 3 parasagittal sections within face-MI of the left hemisphere of the monkey shown in Fig. 2. Histological sections A–C correspond to planes shown in Fig. 2. Arrowheads indicate directions of ICMS-evoked tongue movement shown along the penetration tracks. ○ ICMS-evoked jaw movement. Facial figurines indicate the RFs of the neurons recorded at sites within the ICMS-defined face-MI.

**FIG. 4.** An example of a “rhythmic firing” neuron that fired during the rhythmic jaw-opening phase. \( A \): an example of the neuron’s activity in relation to a single masticatory trial. \( B \): the neuron’s activity in relation to 11 masticatory trials aligned to the point of maximum jaw closing (vertical line in the figure) during the food-preparatory phase. The traces showing movements of the mandible and the EMG activity of the MA, GG, and AD muscles are derived from averaged data. \( C \): the neuron’s phasic activity in relation to 33 rhythmic-chewing cycles aligned to the point of maximum jaw opening (vertical line in the figure) during the rhythmic-chewing phase, but shown in prolonged time scale. \( D \): the neuron’s swallow-related activity by aligning 7 chewing trials to the point of the GG-defined swallow onset (the vertical line shown in \( D \)). Inset: the orofacial RF of the neuron and the tongue movement direction (arrow) evoked by ICMS (threshold T for movement, 30 \( \mu \text{A} \)) applied at the neuronal recording. Note the rhythmic bursts coincident with the onset of GG and AD activity that preceded the opening movement of the jaw.
During the food-preparatory phase, the peak of the neuronal activity during the initial jaw opening of the neurons firing during the rhythmic jaw-opening phase occurred before (95 ± 175 ms, n = 14) the peak of the initial jaw-opening-related AD activity and that of the neurons firing during the rhythmic jaw-closing phase also occurred before this initial peak (17 ± 25 ms, n = 10). In contrast, the peak food-transportation-related activity of the neurons firing during the rhythmic jaw-opening phase and that of the neurons firing during the rhythmic jaw-closing phase occurred well after (314 ± 151 ms, n = 17; 436 ± 160 ms, n = 13, respectively) the peak of the initial jaw-opening-related AD activity.

For those neurons showing only activity during the food-preparatory phase, the peak of neuronal activity during the initial jaw opening occurred long before (456 ± 1033 ms, n = 8) the peak of the initial jaw-opening-related AD activity, while the peak of the food-transportation-related activity occurred well after (640 ± 139 ms, n = 5) this peak. The peak of the food-transportation-related activity of the neurons showing only food-preparation-related activity occurred significantly later (1-way ANOVA, P < 0.05) than that of the neurons firing during the rhythmic jaw-opening or -closing phase; there was no significant difference in other parameters between these neurons.

Pre-swallow and swallow-related neuronal activity patterns

Consistent with the description by Martin et al. (1997), 32 (43.8%) of the 73 neurons showing chewing-related activity also fired during the pre-swallowing phase and in addition displayed swallow-related activity (i.e., during the 50-ms interval preceding the onset of swallow of the solid food bolus and/or during the interval between the GG-defined swallow onset and offset; see Figs. 4 and 5); 23 (31.5%) fired during the pre-swallowing phase only (Table 2).

Of the 32 neurons that showed significant alterations of activity in relation to swallowing, 5 (15.6%) showed a significant alteration of firing during the 50-ms interval preceding swallow onset activity, 13 (40.6%) showed a significant alteration of firing during the swallow, and 14 (43.8%) during both.

Task-related neuronal activity patterns

Of the 66 neurons examined for task-related activity, 47 (71.2%) showed activity related to the tongue-protrusion task. Similar to previous findings (Murray and Sessle 1992b), four patterns of activity were found. A tonic firing throughout the task was documented in 29 (61.7%) neurons, 3 (6.4%) had phasic-off-tonic activity, 5 (10.6%) phasic firing, and 10 (21.3%) depressed activity associated with the task. In addition, three of these neurons increased firing before (321 ± 143 ms) the onset of GG activity associated with the animal’s initiation of tongue protrusion.

A total of 22 of these task-related neurons was also tested for chewing-related activity, which was documented in 21 (Table 3, Figs. 4–6). Of the 21 neurons, 16 (76.2%) showed both task- and chewing-related increase in neuronal activity, 4 (19.0%) showed task-related inhibition and chewing-related excitation,
and 1 (4.8%) showed both task- and chewing-related inhibition of neuronal activity. For the 16 neurons showing both task- and chewing-related activity, statistical analysis (1-way ANOVA with repeated measures and post hoc Duncan’s multiple range test) showed there was no significantly difference between the peak firing frequencies during the task (82 ± 30 Hz) and during the food-preparatory phase (96 ± 45 Hz) or rhythmic-chewing phase (60 ± 34 Hz); however, peak firing frequency during the pre-swallowing phase (50 ± 35 Hz) was significantly lower \((P < 0.05)\) than that during the task.

Of the 66 neurons examined for task-related activity, 39 (59.1%) showed activity alteration in relation to the swallowing of a task juice reward during the 50-ms interval preceding the swallow onset and/or during the GG-defined swallow onset and offset (see Table 3). Of the 47 neurons showing task-related activity, 29 (61.7%) demonstrated activity alteration during the 50-ms interval preceding swallow onset and/or during the GG-defined swallow onset and offset.

Of the 21 neurons showing both task- and chewing-related activity, 11 (52.4%) showed swallow-related excitation, and 2 (9.5%) showed swallow-related inhibition of neuronal activity. For these 11 neurons showing swallow-related excitation, there were no significant differences (1-way ANOVA with repeated measures, \(P > 0.05\)) between the peak firing frequencies during the three chewing phases (99 ± 36, 70 ± 49, 65 ± 34 Hz for the food-preparatory phase, the rhythmic-chewing phase, and the pre-swallowing phase, respectively), but there was a significant decrease in firing frequency during the pre-swallowing phase compared to the task activity.

![Figure 6](file-url)  
**FIG. 6.** An example of a “food-preparation-related” neuron. The neuron showed a discharge burst as the animal opened its mouth and protruded its tongue to take the food-stuff. **A:** an example of the neuron’s activity in relation to a single masticatory trial. **B:** the neuron’s activity in relation to 10 masticatory trials aligned to the point of maximum jaw closing (vertical line in the figure) during the food-preparatory phase. **C:** an example of the neuron’s activity in relation to a tongue-protrusion task trial. **D:** the neuron’s task-related activity by aligning 12 task trials to the force onset (the vertical line in D). Inset: the neuron’s RF and ICMS-evoked tongue movement.

![Figure 7](file-url)  
**FIG. 7.** An example of a “tonic excitation” neuron. The neuron was tonically active before and after the masticatory phase but manifested an increase in its tonic firing throughout the masticatory period. **A:** an example of the neuron’s activity in relation to a single masticatory trial. **B:** the neuron’s activity in relation to 10 masticatory trials aligned to the point of AD onset (vertical line) related to initial jaw opening. Inset: the neuron’s RF and ICMS-evoked tongue movement.
phase, and the pre-swallowing phase, respectively) and during the swallowing of the solid bolus following the chewing (63 ± 42 Hz); similarly, there were no significant differences (paired t-test, P > 0.05) between the peak firing frequencies during the task (68 ± 42 Hz) and during the swallowing of the juice reward following the task (101 ± 92 Hz). In addition, the peak firing frequency during the swallowing of the solid bolus following the chewing (63 ± 42 Hz) was not significantly different (paired t-test, P > 0.05) from that during the swallowing of the juice reward following the task (101 ± 92 Hz).

**DISCUSSION**

The present study has shown that many neurons within face-MI alter their firing rates during chewing and swallowing as well as in relation to a trained tongue movement. Semiautomatic movements are generally considered to be generated and modulated primarily by the “central pattern generators” at the spinal and bulbar levels (e.g., see Donoghue and Sanes 1994; Dubner et al. 1978; Lemon et al. 1998; Nakamura and Katakura 1995) in contrast to voluntary body movements, which have generally been considered to be dependent on supraspinal and suprabulbar structures, including the motor cortex. Together with our previous observations (Huang et al. 1989a; Martin et al. 1999; Sessle et al. 1995) that long-train ICMS within the primate lateral face-MI can evoke rhythmic jaw movements and swallowing and that many face-MI neurons show swallow-related activity (Martin et al. 1997), the present findings suggest that face-MI plays an important role not only in the control of voluntary movements, such as trained tongue protrusion and tongue movement during food preparation, but also in semiautomatic movements such as chewing and swallowing.

The observations of the mecanosensitive afferent input to face-MI in the present study are consistent with our previous findings (Martin et al. 1997; Murray and Sessle 1992a) in terms of the proportion of recorded neurons with an identified orofacial RF and the location of the RFs within the orofacial region. In particular, the present study has confirmed that face-MI receives substantial sensory inputs from intraoral sites, in particular the tongue dorsum, and has provided more support for the notion that oral mecanosensitive inputs are important in the regulation of orofacial movements. The view is also supported by previous studies showing that cooling of face SI, a source of input to face-MI, impairs tongue-task performance (Lin et al. 1993) and rhythmic jaw and tongue movements and EMG activity associated with chewing (Lin et al. 1998). Studies of limb sensorimotor cortex have indicated that the movement-related activity of many MI neurons may not be simply reflecting reafferentation (for review, see Asanuma 1989; Georgopoulos 1994; Marple-Horvat and Armstrong 1999; Nelson 1996; Wise 1993). This view is supported by findings that not all face-MI neurons with movement-related activity have a detectable sensory input, that some MI neurons fire in advance of the EMG-defined movement onset, and that immediately preceding and during orofacial movements, there is a gating of

**TABLE 1. Relationship between pattern of chewing-related face-MI neuronal activity and movement evoked by ICMS applied at the neuronal recording site**

<table>
<thead>
<tr>
<th>Movement Evoked by ICMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Chewing-Related Neurons</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>Rhythmic firing</td>
</tr>
<tr>
<td>During the jaw-closing phase</td>
</tr>
<tr>
<td>During the jaw-opening phase</td>
</tr>
<tr>
<td>Food preparation-related</td>
</tr>
<tr>
<td>Tonic excitation</td>
</tr>
<tr>
<td>Tonic depression</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. MI, primary motor cortex. * Both tongue protrusion and jaw closing were evoked at the same tongue task/swallowing (T/S) intracortical microstimulation (ICMS) threshold intensity at one location in which a jaw closing-related neuron was recorded.
orofacial somatosensory afferent inputs to face-MI (Yamamura et al. 1999), or to SI (Lin and Sessle 1994), which is a major source of input to face-MI (see Dubner et al. 1978; Huang et. al. 1989b; Jones 1986; Murray and Sessle 1992a).

Our data revealing that substantial numbers of MI neurons display chewing-related activity are consistent with earlier findings in face-MI (Kubota and Niki 1971; Luschel et al. 1971). However, we have documented four major patterns of activity. These different patterns are similar to data reported earlier in face-MI by Kubota and Niki (1971) although these authors did not describe any neuronal activity patterns characteristic of those MI neurons that we found with increased activity only during the food-preparatory phase or with decreased activity. The various patterns of chewing-related activity of MI neurons may reflect their involvement in the jaw movements and especially the tongue movements occurring during different phases of mastication because most MI neurons in this study were recorded from the ICMS-defined tongue-MI region.

In the case of the food-preparatory phase, the animal opens its mouth and protrudes its tongue to take and to transport a food bolus to the occlusal surfaces of the teeth. The current studies have revealed that the majority of face-MI neurons, including those showing an increase in activity only during the food-preparatory phase as well as most of the rhythmically firing neurons, are active during the initial jaw opening and/or food transportation of the food-preparatory phase. These findings are consistent with our recent observations of marked tongue- and jaw-movement deficits during the food-preparatory phase caused by bilateral cold block-induced inactivation of the monkey’s face-MI (Yao et al. 2000; Yamamura et al. 2002). Although they could initiate mastication during face-MI cold block, the monkeys had considerable difficulty in taking a piece of the test food into the oral cavity and frequently dropped the food and also had difficulty in manipulating and transporting the food to the occlusal table. These deficits were associated with a significant prolongation of the food-preparatory phase and significant changes in the temporal relationships of the AD and GG activities during the initial jaw opening and food transportation and as a large increase in the cycle duration during food transportation; the duration and amplitude of these EMG activities were also changed during cold block. Thus face-MI may play a crucial role in coordinating the complex tongue and jaw movements that are required to ingest, transport, and place the foodstuff on the occlusal table and keep the foodstuff on the working side in order for the breakdown of the foodstuff. It is likely that face-MI, given its large representation of the muscles of facial expression (Huang et al. 1988; McGuinness et al. 1980; Sessle and Wiesendanger 1982), also coordinates those facial muscles contributing to the ingestion and manipulation of the foodstuff, but the present investigation did not study these muscles.

During the rhythmic-chewing phase, tongue protrusion occurs during the jaw-opening phase, whereas tongue retraction is a feature of the jaw-closing phase. Most neurons altered their activity during the rhythmic-chewing phase. Our recent studies have shown that bilateral cold block-induced inactivation of face-MI produces relatively more subtle changes during the rhythmic-chewing phase than during the food-preparatory phase (Yao et al. 2000; Yamamura et al. 2002), which is consistent with the effects of bilateral cortical ablation on mastication (Larson et al. 1980). For example, face-MI cold block did not produce any significant changes in duration of the rhythmic-chewing phase, cycle duration, or the temporal relationship between the AD and GG activities. However, cold block did cause a significant change in the amplitude and/or the duration of AD, GG, and MA activity, which is consistent with the observations of a decrease in jaw-opening movements.

**TABLE 2. Chewing-related face-MI neurons also showing pre-swallow and/or swallow-related activity**

<table>
<thead>
<tr>
<th>Type of Chewing-Related Neurons</th>
<th>Number of Neurons Showing Pre-swallow and Swallow-related Activity (No. of Neurons)</th>
<th>Number of Neurons Showing only Pre-swallow-related Activity (No. of Neurons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythmic firing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the jaw-closing phase</td>
<td>16 (50.0)</td>
<td>11 (47.8)</td>
</tr>
<tr>
<td>During the jaw-opening phase</td>
<td>9 (28.1)</td>
<td>10 (43.5)</td>
</tr>
<tr>
<td>Food preparation-related</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Tonic excitation</td>
<td>3 (9.4)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>Tonic depression</td>
<td>4 (12.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>32 (100.0)</td>
<td>23 (100.0)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.
during mastication after cortical ablation (Larson et al. 1980). Together with these previous findings, the current data suggest that the duration and amplitude of masticatory-related EMG activities during the rhythmic-chewing phase may be modulated by the face-MI while the basic timing of these EMG activities may be more dependent on other cortical areas (e.g., CMA) (Narita et al. 1999, 2002) or the brain stem central pattern generators (Dubner et al. 1978; Lund 1991; Luschei et al. 1981; Nakamura and Kataoka 1995).

After the monkey carried out a series of rhythmic jaw-opening and closing as well as tongue-protrusion and retraction movements during the rhythmic-chewing phase, it moved the masticated food bolus to the pharyngeal region in preparation for swallowing. We found that the majority of face-MI neurons also altered their activity during this pre-swallow phase, and some of them also showed swallow-related activity. This is consistent with our recent observations of a tongue deficit in the monkey’s manipulation of the food bolus into the pharyngeal region during face-MI cold block, as reflected in an elongation of the pre-swallowing phase time after the end of the rhythmic-chewing phase (Yao et al. 2000; Yamamura et al. 2002). These findings suggest that face-MI plays a very important role in manipulating and positioning the food bolus to an appropriate position to swallow.

As noted in the preceding text, we found some neurons altered their firing during a particular phase (e.g., the food-preparatory phase, or the rhythmic-chewing phase) and a small group of neurons altered their activity throughout the whole masticatory period. These various patterns of chewing-related activity may reflect different types of MI neurons (e.g., corticocortical association neurons, cortical interneurons, and corticobulbar projection neurons) involved in responding to movement-generatedafferent inputs, in initiating and regulating tongue and jaw movements, or in some other form of chewing-related sensorimotor integration. Some MI neurons changed their activity during the interval immediately preceding the EMG-defined chewing onset, that is, in advance of chewing. Thus it is probable that these neurons may play a role in driving tongue or jaw motor units in chewing rather than their activity being, for example, simply a reflection of movement-generated reafference (see preceding text). Some of the early firing MI neurons and other chewing-related MI neurons were also activated during the chewing itself, and so these neurons may initiate or drive motor units later in the chewing synergy. These different neuronal firing patterns may be related to differences in the duration and relative timing of chewing-related EMG bursts across the changing chewing conditions as the foodstuff is triturated. In addition, our present studies have also shown that ICMS at most loci showing neuronal activity during the rhythmic jaw-opening phase produced tongue protrusion, whereas tongue retraction was evoked by ICMS at most loci from which the neurons firing during the rhythmic jaw-closing phase were recorded. This suggests that face-MI might also play an important role in coordinating tongue and jaw movements to prevent damage of the tongue during chewing.

The view is further supported by findings (Huang et al. 1988; Murray and Sessle 1992a) that, in some MI loci, tongue protrusion and jaw-opening movements, or tongue-retraction and jaw-closing movements, can be simultaneously evoked at threshold by the same ICMS stimulus intensity.

Our present studies have demonstrated that some face-MI neurons may show activity not only in relation to chewing or the tongue-protrusion task but also in relation to the semiautomatic movement of swallow. This is consistent with our earlier report that many task-related neurons in face-MI also show activity in relation to swallowing (Martin et al. 1997). Furthermore, there were no significant differences in the peak firing frequency between neuronal activities related to chewing, swallowing or the task. This suggests that some MI neurons may be equally involved and important in both voluntary and semiautomatic movements. An additional implication of these findings is that the activity of these face-MI neurons in chewing, tongue protrusion, and swallowing reflects the need for a close neuronal integration in the control of these various motor activities. This is supported by our previous findings that jaw and tongue movements can often be evoked by ICMS at the same loci within MI and that there is an extensive overlap of swallow cortex and CMA defined by long-train ICMS in the awake monkey (Huang et al. 1988; 1989b; Martin et al. 1999; Murray and Sessle 1992a). On the other hand, we also noticed that chewing-related face-MI neurons that only showed food-preparation-related activity did not exhibit any pre-swallow or swallow-related activity. This finding could suggest that orofacial movements during the food-preparatory phase might be specific to this behavior and are not incorporated into the movement sequence of swallowing.

We thank Drs. C. Y. Chiang, J. O. Dostrovsky, R. Dubner, H. C. Kwan, and W. A. MacKay for reviewing earlier drafts of the manuscripts and/or advice throughout the study. We are grateful to Dr. Y. Zhang for help in analyzing some data and for thoughtful suggestions. We are also thankful to D. Lindsay, S. Carter, and K. MacLeod for technical assistance, F. Yuen for secretarial service, and Dr. Y. Yamada for generously providing the magnets. D. Yao was the recipient of a Canadian Institutes of Health Research (CIHR) Studentship. This research was supported by CIHR Grant MT-4918 to B. J. Sessle and by Ontario Ministry of Health Career Scientist Award and Natural Sciences and Research Council of Canada Grant OGPO-171208 to R. E. Martin. B. J. Sessle is the holder of a Canada Research Chair.

Present addresses: K. Yamamura, Dept. of Oral Biological Science, Niigata University Graduate School of Medical and Dental Sciences, 2-5274 Gakkochi Dori, Niigata 951-8514, Japan; N. Narita, Faculty of Dentistry at Mastudo, Niho University, 2-870-1 Sakaecho-Nishi, Mastudo, Chiba 271, Japan; R. E. Martin, Faculty of Health Sciences, University of Western Ontario, London, Ontario N6G 1H1, Canada; G. M. Murray, Faculty of Dentistry, University of Sydney, Sydney, New South Wales 2010, Australia.

REFERENCES


HUANG CS, HIRABA H, MURRAY GM, AND SESSLE BJ. Topographical distribution and functional properties of cortically induced rhythmic jaw move-

J Neurophysiol • VOL. 87 • MAY 2002 • www.jn.org