PROPERTIES OF NEURONES IN PRIMATE FACE MOTOR CORTEX IN RELATION TO OROFACIAL MOVEMENTS AND INFLUENCE OF FACE PRIMARY SOMATOSENSORY CORTEX

By

Dongyuan Yao

A thesis submitted in conformity with the requirements for the Degree of Doctor of Philosophy, Faculty of Dentistry, in the University of Toronto

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ABSTRACT

There is little information of the sensorimotor cortical mechanisms controlling semi-automatic orofacial movements and the role of sensory inputs to the motor cortex (MI) during orofacial movements. An electrophysiological investigation was conducted in the unanaesthetised monkey to study (a) the activity patterns of single neurones recorded in face MI during orofacial movements, (b) the effects of reversible cold block of ipsilateral face primary somatosensory cortex (SI) on the orofacial movements and related activity of face MI neurones, and (c) modulation of somatosensory responses of face MI neurones evoked by orofacial stimuli during chewing.

Face MI neurones exhibited a variety of neuronal activity patterns during chewing as well as a trained tongue-protrusion task. Most of the chewing-related neurones showed activity associated with rhythmic jaw movements or food preparatory movements. Some of the neurones showing the task- and/or chewing-related activity also showed significant alterations in activity in relation to swallowing.

Unilateral cold block of SI had little effect on the performance of the orofacial movements or on task and chewing and/or swallowing-related activity of most face MI neurones. These data suggest that movement-induced reafferentation via the ipsilateral face SI
may not be a significant factor in accounting for the activity of most face MI neurones related to orofacial movements.

A diminution of orofacial-evoked neuronal responses was a general feature of face MI during chewing. This suppression appeared dependent in part on an intact ipsilateral face SI in only a small portion of neurones tested during cold block of SI. These data support the view that the gain of somatosensory afferent inputs to MI can be adjusted to compensate for the increased sensory input produced during or as a result of movements but ipsilateral face SI may play a minor role in this mechanism.

These findings indicate that face MI may play an important role in the control of not only voluntary but also semi-automatic orofacial movements and that ipsilateral face SI may have only a limited role in influencing MI neuronal activity.
ACKNOWLEDGEMENTS

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<th>Description</th>
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<tbody>
<tr>
<td>AD</td>
<td>anterior digastric muscle</td>
</tr>
<tr>
<td>arc</td>
<td>arcuate sulcus</td>
</tr>
<tr>
<td>cen</td>
<td>central sulcus</td>
</tr>
<tr>
<td>CMA</td>
<td>cortical masticatory area</td>
</tr>
<tr>
<td>CMN</td>
<td>corticomotoneuronal neurone</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>C/S</td>
<td>long-train (continuous) stimulus</td>
</tr>
<tr>
<td>DCN</td>
<td>dorsal column nuclei</td>
</tr>
<tr>
<td>EMG</td>
<td>electromyography</td>
</tr>
<tr>
<td>fMRI</td>
<td>functional magnetic resonance imaging</td>
</tr>
<tr>
<td>GABA</td>
<td>y-aminobutyric acid</td>
</tr>
<tr>
<td>GG</td>
<td>genioglossus muscle</td>
</tr>
<tr>
<td>ICMS</td>
<td>intracortical microstimulation</td>
</tr>
<tr>
<td>MA</td>
<td>masseter muscle</td>
</tr>
<tr>
<td>MI</td>
<td>primary motor cortex</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>Po</td>
<td>posterior nucleus of thalamus</td>
</tr>
<tr>
<td>PT</td>
<td>pyramidal tract</td>
</tr>
<tr>
<td>PTN</td>
<td>pyramidal tract neurone</td>
</tr>
<tr>
<td>PTP</td>
<td>pre-trial period</td>
</tr>
<tr>
<td>RF</td>
<td>mechanoreceptive field</td>
</tr>
<tr>
<td>RJM</td>
<td>rhythmical jaw movement</td>
</tr>
<tr>
<td>SI</td>
<td>primary somatosensory cortex</td>
</tr>
<tr>
<td>SII</td>
<td>second somatosensory cortex</td>
</tr>
<tr>
<td>SMA</td>
<td>supplementary motor areas</td>
</tr>
<tr>
<td>T/S</td>
<td>short-train stimulus</td>
</tr>
<tr>
<td>VB</td>
<td>ventrobasal complex of thalamus</td>
</tr>
<tr>
<td>VL</td>
<td>ventralis lateralis of thalamus</td>
</tr>
<tr>
<td>VLo</td>
<td>ventralis lateralis pars oralis of thalamus</td>
</tr>
<tr>
<td>Vme</td>
<td>mescephalic trigeminal nucleus</td>
</tr>
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</table>
Vmo: trigeminal motor nucleus
VPL: ventral posterolateral nucleus of thalamus
VPLo: ventralis posterior lateralis pars oralis of thalamus
VPM: ventral posteromedial nucleus of thalamus
VPO: ventroposterior oralis of thalamus
CHAPTER I. ROLE OF PRIMARY SOMATOSENSORY CORTEX AND OROFACIAL SENSORY INPUTS TO PRIMARY MOTOR CORTEX OF THE PRIMATE IN OROFACIAL MOVEMENTS: REVIEW OF THE LITERATURE

I. INTRODUCTION: WHY STUDY THE ROLE OF PRIMARY SOMATOSENSORY AND PRIMARY MOTOR CORTEX IN RELATION TO MOVEMENT?

The role of the cerebral cortex in the control of motor function has long been a subject of clinical and experimental studies. As early as 1870, Fritsch and Hitzig found that electrical stimulation of the dog's cerebral cortex elicits movements of the contralateral body musculature. After more than a century of investigation, the importance of sensorimotor integration in the cerebral cortex in forelimb motor control has been addressed extensively, whereas comparatively little information is available of cortical mechanisms contributing to the sensorimotor integration of orofacial movement.

The primary motor cortex (MI) of the primate is defined as that single contiguous region located within and immediately rostral to the central sulcus from which twitch-like movements can be readily evoked by low-intensity intracortical microstimulation (ICMS; 200 µs at 333 Hz for 35 ms, ≤ 30 µA). The extent of MI cortex has been considered to be approximately coincident with Brodmann's cytoarchitectonic area 4 (1909), which is characterized by a thick, agranular cortex with large pyramidal cells in layer V. The involvement of MI in the control of movements and some of the underlying mechanisms has been demonstrated by (1) surface stimulation (for review, see Woolsey 1952), (2) ICMS (for review, see Asanuma 1981a,b; Humphrey 1986), (3) cooling (for review, see Brooks 1983), or ablation studies (for review, see Kuypers 1981), (4) single-neurone recording (for review, see Wise 1993; Georgopoulos 1994), and (5) functional imaging as revealed in magnetic resonance (fMRI) (for review, see
Le Bihan and Karni 1995; Le Bihan et al. 1995) and positron emission tomography (PET) studies (for review, see Ashe and Ugurbil 1994; Picard and Strick 1996).

The primary somatosensory cortex (SI) consists of Brodmann’s (1909) area 3a, 3b, 1, and 2 located in the postcentral gyrus, and is the cortical area of the primate that receives a major and rather direct somatic afferent inflow and that play a role in somatic sensibility (Mountcastle 1984). However, the SI may also play an important role in movement control. The view is based on evidence derived by (1) SI stimulation (for review, see Woolsey 1958), (2) cooling or ablation in animals or damage of SI in humans (for review, see Asanuma 1981, 1989; Freund 1987), (3) neuronal recording (for review, see Nelson 1996), (4) functional imaging (for review, see Mueller et al. 1997), and (5) anatomical tracing of reciprocal connections (for review, see Jones 1986).

In spite of our improved understanding of the role of face MI and SI in the control of orofacial movements, there is only limited information of possible integration between SI and MI in the generation and control of orofacial movement. Studies in limb cortex have suggested that limb SI cortex may be involved in motor control by descending modulation as well as by interactions with MI since SI as well as MI corticofugal outputs can modulate afferent inputs that may influence movement (for review, see Jones 1986; Murray et al. 1999).

This chapter will first outline movement-related modulation of afferent transmission. Then, since most of our understanding of the mechanisms of orofacial movement control comes from analogies with the extensive literature related to forelimb movement control, it will describe general features of the role of forelimb MI and SI in forelimb movement control, followed by a outline of our current understanding of the properties and role of face MI and SI. Because more detailed information is generally available of the primate sensorimotor cortex and since the non-human primate was used as the experimental animal in the present studies, this review
will concentrate on features of the primate sensorimotor cortex. However, reference will be made to investigations involving other animal models when the results of these experiments are relevant or are important from a comparative point of view.

II. MOVEMENT-RELATED MODULATION OF OROFACIALafferent TRANSMISSION

II.1 CORTICOFOGAL EFFECTS ON OROFACIAL REFLEXES

SI cortex seems to be involved in motor control by descending modulation as well as by interaction with other cortical areas such as MI. Both SI and MI provide corticofugal outputs that can modulate afferent input (Jones 1986; Chapman et al. 1987; Willis 1988). Most investigations of cortical effects on orofacial reflexes have focused on the effects of cortical stimulation on jaw reflexes. For example, electrical surface stimulation of dorsolateral cerebral cortex (SI or MI) modulates spontaneous or reflex-induced masseter and digastric activity in the tranquilized squirrel monkey (Chase et al. 1973); inhibition of masseter (latency 4-5 ms) followed by digastric facilitation (latency 8-10 ms) occurs with either MI or SI stimulation.

A variety of studies in subprimates have also demonstrated that orbital or SI cortical stimulation exerts predominantly facilitatory effects on digastric and mainly inhibitory influences on masseter reflex or motoneuronal activity (e.g., Sessle 1977; Olsson and Landgren 1980; Chiang et al. 1990).

II.2 CORTICOFOGAL EFFECTS ON SINGLE SOMATOSENSORY NEURONES

Electrophysiological investigations have demonstrated two general modulatory phenomena: afferent inhibition and corticocofugal modulation. Virtually all these studies in trigeminal somatosensory system have been carried out in subprimates. Mechanoreceptive
excitatory input to neurones in the trigeminal brainstem complex, the ventral posteromedial nucleus of the thalamus (VPM) or face SI can be inhibited by mechanical or electrical stimulation of surrounding orofacial regions (e.g., Darian-Smith and Yokota 1966b; Sessle and Dubner 1971; Sessle et al. 1981; Soja et al. 1999; for review, see Dubner et al. 1978). The occurrence of afferent inhibition raises the possibility that part of the movement-related modulation in trigeminal somatosensory pathways to the cortex (see below) may come from the inhibitory effects induced by afferents activated by moving orofacial tissues.

Several studies have employed electrical stimuli of face SI or MI to assess the role of cortical inputs in the processing of tactile inputs in the trigeminal brainstem complex and thalamus. Electrical stimulation of cortex produces both pre- and post-synaptic modulation in the trigeminal brainstem complex and VPM, resulting in excitatory and inhibitory effects upon trigeminal brainstem and VPM neurones (Darian-Smith and Yokota 1966a, b; Dubner and Sessle 1971; Sessle and Dubner 1971; Sessle et al. 1981; Woolston et al. 1983; for reviews, see Towe 1973; Dubner et al. 1978). Corticofugal projections to the brainstem have been suggested to play an important role in the modulation of somatosensory responses during orofacial movements. It is believed that cortico-trigeminal or cortico-thalamic inputs may reduce the noise level in sensory pathways and increase the signal-to-noise ratio in critical pathways (Dubner et al. 1978).

Several studies suggest a reciprocal feedback loop between trigeminal brainstem nuclei and face SI (Dubner and Sessle 1971; Woolston et al. 1983; Welker et al. 1988). For example, Woolston et al. (1983) recorded effects of electrical stimulation of sensorimotor cortex in rats on the responses of neurones in trigeminal subnucleus interpolaris to mechanical stimulation of vibrissae and they observed both inhibitory and excitatory effects. Responses evoked by peripheral mechanical stimulation are enhanced when whisker deflection is preceded by
stimulation of cortical areas responsive to the same whiskers (36% of total sample of 45 cells) and suppressed only if trigeminal subnucleus interpolaris cells whose mechanoreceptive field (RF) does not overlap with that of the cortical stimulation site (18% of sample). It has been suggested that these effects are most reliable in projection neurones because only 2 of 13 cells with single whisker RFs (i.e. most likely local circuit neurones) (Jacquin et al. 1989) are modulated by cortical stimulation. Furthermore, Jacquin et al. (1990) compared the response properties of 536 subnucleus interpolaris neurones after acute or chronic SI ablation to those of 385 neurones in normal rats and found that cortical ablation significantly increases the size of RFs, the number of the neurones expressing convergence of vibrissae and guard-hairs, and the number of neurones unresponsive to mechanical orofacial stimuli. They suggested a significant cortico-trigeminal projection exists in the rat and contributes to the control of RF size, receptor convergence, and base-line responsiveness in a significant number of low-threshold trigeminal subnucleus interpolaris neurones. However, they did not describe the methodology for defining SI and the possibility exists that part of MI was involved in the ablation that they carried out.

II.3. MOVEMENT-RELATED MODULATION OF SOMATOSENSORY-EVOKED POTENTIALS AND PSYCHOPHYSICAL MEASURES

There are numerous studies demonstrating a suppression of evoked potentials in the medial lemniscus, VPL and SI during digit or forelimb movements in humans (e.g., Rushton et al. 1981; Cohen and Star 1987), monkeys (e.g., Dyhre-Poulsen 1978; Chapman et al. 1988; Jiang et al. 1990b; Courtemanche et al. 1997) and subprimates (e.g., Shin and Chapin 1990); the origin of this modulation may be both peripheral and central.
Psychophysical studies have also shown that the threshold for detecting cutaneous stimuli rises when the stimulated area was actively moved and that this change can precede the onset of movement (e.g., Angel and Malenka 1982; Angel et al. 1985; Chapman et al. 1987). However, Chapman et al. (1987) showed that while the discrimination and perception of suprathreshold stimuli were not altered during the movement, the detection thresholds were increased, in the same subject, during movement of the stimulated arm. To date, there appear to be no studies investigating the effects of orofacial movements on evoked potentials in face SI, although movement effects on responses of single neurones in face SI have been described (see below). Owall and Moller (1974) have tested the ability of humans to detect objects between their teeth during conscious biting and chewing. On average, the tactile threshold during chewing (0.91 mm) was much larger than (sixty times) during conscious biting (0.015 mm). This suggests that somatosensory responses may have been modulated during the movement. However, other factors may have confounded the data, e.g. adaptation of periodontal ligament mechanoreceptors (tooth displacement recovers only 50% after each chewing stroke).

II.4. STUDIES OF SINGLE NEURONES DURING MOVEMENT

Modulation of responses to afferent stimulation during orofacial movements has been demonstrated at three levels of the trigeminal system: trigeminal brainstem sensory nuclei (e.g., Olsson et al. 1986), VPM (e.g., McClean et al. 1990) and face SI (Lin and Sessle 1994).

During cortically induced chewing, somatosensory responses of neurones in the rostral trigeminal sensory nuclei of anaesthetized rabbits are selectively modulated. Jaw reflex responses to low-threshold inputs are suppressed while reflex protective responses to noxious stimuli are phasically facilitated (Lund et al. 1981; Lund and Rossignol 1981; Lund and
Olsson 1983; Olsson et al. 1986). These studies suggest that suppression of low-threshold afferent inputs prevents disruption of jaw closure during mastication by a reflex response to these sensory inputs generated by normal movements; in contrast, facilitation of high-threshold responses (e.g. jaw-opening reflex) in the jaw-closing and occlusal phases of mastication may serve to protect the mouth and tongue from injury.

Although the modulation of sensory transmission through interneurons close to the trigeminal motor nucleus appears to depend on the type of sensory input that they receive, this is not a general rule applied to all components of the trigeminal brainstem complex. For example, neurones in the caudal trigeminal brainstem complex (the medullary dorsal horn) that received noxious input were not phasically modulated; most were tonically inhibited during fictive mastication (Kim et al. 1986). Although some of the tonic inhibition appeared to be related to the fictive mastication, much of the tonic inhibition was strongly related to the period of cortical stimulation and thus may have involved direct descending corticofugal pathways.

McClean et al. (1990) have shown that human VPM neurones with a lip or tongue RF are consistently active when these structures are involved in the production of speech sounds. The magnitudes of these responses are similar to those elicited by experimentally applied mechanical stimuli, suggesting that speech-induced somatosensory inputs may not be controlled at the thalamic level.

Lin and Sessle (1994) first documented that somatosensory responses of face SI neurones are modulated during trained orofacial movements. They found that for face SI neurones tested during both force dynamic and holding phases of task period, the evoked activity (i.e., the number of evoked spikes in 50 ms after the onset of stimulation) was decreased in at least one of the two phases for the majority (90%) of 31 neurones studied during a tongue-protrusion
task and 61% of 23 studied during a biting task. No neurones tested showed a clear facilitation of evoked activity during the task period of either task. It was suggested that some of the neurones in face SI with direct corticofugal projection to the brainstem (e.g., Kuypers 1981; Sirisko and Sessle 1983; for review, see Darian-Smith 1973; Dubner et al. 1978; Kuypers 1981; Bushnell et al. 1987) might be concerned with the modulation of somatosensory responses during movements and may explain the somatotopically organized and movement-specific modulation of the low-threshold somatosensory responses of face SI neurones during tongue-protrusion and jaw movements. These corticofugal activities may modulate the somatosensory responses in such a way as to adjust the gain of somatosensory inputs evoked during movements or generated by the movements, and thus maintain the sensorimotor system's sensitivity to the externally applied disturbance (Lin and Sessle 1994; for review, see Sessle et al. 1999). Similarly, Hiraba et al. (1997) showed somatosensory responses of face SI neurones are modulated during masticatory movements.

These findings indicate that sensory transmission is modulated during orofacial movements. The modulation appears not to be generalized or nonspecific but to be dependent on the location of a neurone's RF and type of movement performed.

III. ROLE OF PRIMARY MOTOR CORTEX IN OROFACIAL MOVEMENTS

IIIA. ORGANIZATIONAL FEATURES OF PRIMARY MOTOR CORTEX

IIIA1. CYTOARCHITECTONIC ORGANIZATION AND TOPOGRAPHIC REPRESENTATION

MI has been divided into six layers, labeled laminae I-VI, based on its cytoarchitectonic features. Although MI lacks a prominent layer IV, granular neurones still may be sparsely distributed in the adjacent cytoarchitectonic layers (Sloper 1973; Leichnetz 1986). The MI can
be distinguished to some extent from other areas by its cytoarchitectonic features and natural markers. The rostral border of MI is located on the convexity of the precentral gyrus where area 4 gradually merges with area 6 without any obvious difference in cell size or cytoarchitectonic structure. The caudal border of MI lies deep in the central sulcus, adjacent to area 3a. The boundary between area 3a and 4 can be distinguished by the appearance of clusters of large Betz cells in area 4, the absence of a thicker and more densely packed granular layer in area 4, the sudden disappearance of the sharp demarcation between layer VI and white matter in area 4 whereas the border between gray and white matter is very clear-cut for the entire somatosensory cortex, and a thicker cortical layer in area 4 compared with area 3a (e.g., Jones et al. 1978; Wiesendanger and Miles 1982). The large Betz cells are located predominantly in the upper part of the central sulcus and sparsely scattered anteriorly and laterally. The face region of area 4 tapers rostrally and laterally and becomes almost indistinguishable from area 6α (Vogt and Vogt 1919). Laterally, the Betz cells are not uniformly dispersed and do not reach the enormous size of those in the leg and arm MI (Walker and Green 1938). Medially, area 4 extends to the superior bank of the cingulate sulcus where it has no obvious cytoarchitectonic difference with the adjacent area 6 (Wise and Tanji 1981; Tanji and Kurata 1982; Mitz and Wise 1987).

The physiological definition of MI has largely been based on a framework of knowledge established by early surface stimulation investigation (e.g., Penfield and Boldrey 1937; Woolsey et al. 1952) and later by ICMS studies (e.g., Asanuma and Sakata 1967). However, there are well recognized limitations of surface stimulation including the difficulty of determining current spread and the inability to map regions within the depths of the cortex (e.g., central sulcus region). In contrast, the technique of ICMS, which was introduced by Asanuma and Sakata (1967), allows for the delivery of much smaller currents within the
depths of the cortex, and to more localized regions. Indeed, the technique has afforded a means for more precise definition of output or efferent zones from MI (e.g., Kwan et al. 1978; Humphrey 1986; Lemon et al. 1986). Nevertheless, there are some inherent problems in the mapping of MI with ICMS. ICMS can activate single pyramidal tract neurones (PTNs) directly and trans-synaptically. Whereas the trans-synaptic spread of excitation that results from single intracortical shocks is probably restricted by the local organization of synaptic input (Asanuma and Rosen, 1973), repetitive stimuli probably recruit much larger numbers of PTNs, some of which may lie at some distance from the stimulating electrode (i.e. 600 μm for short-train ICMS of 50 μA in lamina V) (Asanuma and Rosen 1973). Indirect activation of pyramidal tract neurones by electrical stimuli means that to some extent the resulting motor effect reflects the organization of pyramidal tract neurones, rather than the output of the PTNs themselves and places new emphasis on the need for studies on the input pathways to MI. The recurrent axon collaterals of PTNs extend as far as 1.0 mm (Jankowska et al. 1975a; DeFelipa et al. 1986) and are as equally excitable as their cell bodies (Asanuma et al. 1976). ICMS also excites interneurones and their axons or other passing axons exerting excitation or inhibition on the PTNs (Phillips and Porter 1977). The stimulation threshold for the initial segment of the axon is lower than that for the soma (Gustafsson and Jankowska 1976). Landau et al (1965) also indicated that the thresholds for activating the pyramidal tract (PT) are lower in the white matter than in the gray matter. Also, excessive ICMS currents can produce noxious effects to the brain (Asanuma and Arnold 1975).

Penfield and Boldrey (1937) provided the first unique evidence for functional localization in the human cortex. They summarized the general pattern of localization in the well-known "homunculus" diagram delineating the organization of the human cortex. One of the striking features of this map is the overwhelming representation of the upper lip, lower lip and tongue.
Salivation and complex movements, such as mastication and vocalization, also can be induced in the area lateral to the representation of the lip and tongue. Woolsey et al (1952) demonstrated the effects of cortical surface stimulation as “motor face charts” (for details, see section IIIB.1.1).

A prominent organizational characteristic of the motor cortex appears to be the existence of multiple but discrete efferent microzones (Wiesendanger 1986) which control single muscles or simple muscle synergies (e.g., Asanuma 1981a, b; Huang et al. 1988). These cortical output zones are heavily overlapped (e.g., Andersen et al. 1975; Kwan et al. 1978). The functional significance of this organization may be that it facilitates the selection of functionally significant clusters of output zones in the production of movement by afferents to motor cortex (Kwan et al. 1978; Humphrey 1986). The multiply represented efferent zones would allow the elemental movement to be used in association with other elemental movements in the production of different complex movement patterns.

Like those neurones in visual cortex (Hubal and Wiesel 1972), auditory cortex (Imig and Brugge 1978), and somatosensory cortex (Jones and Wise 1977), the neurones in motor cortex with common physiological properties appear to extend vertically through all layers of the cortex in narrow columns approximately 500 μm wide (Mountcastle 1957). However, the column-like clusters in cortex, so far as they can be identified anatomically, appear as short strip-like configurations rather than circumscribed columns (Jones 1981, 1983).

IIIA.2 SOMATOSENSORY PATHWAYS TO THE PRIMARY MOTOR CORTEX

Somatosensory inputs reach MI through three major sources: 1) specific thalamic nuclei, including ventralis lateralis (VL) (Olszewski, 1952), ventralis posterior lateralis pars oralis (VPLo) (Strick 1975; Kievit and Kuypers 1977; Jones et al. 1979; Tracey et al. 1980;
Asanuma et al. 1983a, b, c; Leichnetz 1986), and ventralis lateralis pars oralis (VLo) (Holsapple et al. 1991; Shindo et al. 1995), 2) corticocortical association fibres of the ipsilateral hemisphere (Pandya and Kuypers 1969; Muakkassa and Strick 1979; Leichnetz 1986; Porter 1997), and 3) commissural fibres via the corpus callosum (Jones and Wise 1977; Jones et al. 1977; Gould et al. 1986; Leichnetz 1986).

The thalamocortical fibres project densely to layer III (Sloper 1973; Jones 1975a, b; Jones and Burtons and Burton 1976; Asanuma et al 1983a, b, c). The corticocortical and commissural fibres terminate in layer IV and in all supragranular layers (Goldman-Rakic and Nauta 1977; Jones and Wise 1977; Godschalk et al. 1984; Leichnetz 1986; Barbas and Pandya 1987). Thus, all major afferent fibre systems projecting to MI terminate primarily in the granular and supragranular layers (Jones et al. 1975, 1979; Porter 1981). The significance of the segregation of these input sources (i.e. thalamus, contralateral and ipsilateral cortex) is uncertain.

The VPM is a major site of termination of orofacial sensory information relayed from the brain stem, and third-order neurones in this region project to sensorimotor cortical areas. Current evidence (e.g., Zarzecki 1989; Kaneko et al. 1994; Caria et al. 1997; for review, see Jones 1986; Porter 1990) suggests that low-threshold mechanoreceptive sensory input to MI is conveyed both via indirect projections from the primary SI, and also via direct thalamic projections (Jones 1986).

Neuronal recordings within MI have revealed a prominent representation of sensory input (e.g., Evarts 1973; Lemon et al. 1976, 1981a, Wong et al. 1978; Fetz et al. 1980; Tanji and Wise 1981; Cheney and Fetz 1984; Huang et al. 1989a; Murray and Sessle 1992a; Martin et al. 1997). For example, Huang et al. (1989a) found most face MI neurones (69% of 526) in awake monkeys (Macaca fascicularis) were activated by light tactile orofacial stimulation,
especially of the perioral area, and few neurones responded to deep orofacial stimuli. Although contralateral afferent inputs predominated, 21% of the neurones received ipsilateral or bilateral orofacial input. They also found that most MI neurones (81%) received afferent input from an orofacial area which has a close spatial match with the area within in which movement could be evoked by ICMS applied to neuronal recording site. Similarly, Martin et al (1997) examined 79 tongue MI neurones and found 53 (67%) showed an orofacial RF; 17% had ipsilateral, 28% contralateral, and 55% bilateral afferent inputs. In the primary limb MI, most studies (Lemon and Porter 1976; Lemon et al 1976; Wong et al. 1978; Fetz et al. 1980; Lemon 1981a, b; Strick and Preston 1982b; Izraeli and Porter 1993) agree that deep inputs project to a substantial number of limb MI neurones (varying from 30% to 92%). For example, Wong et al. (1978) showed 65% of 728 limb MI neurones received peripheral input, and that of these input-driven neurones, 18% respond to cutaneous input, 73% to joint input, and 9% to both. This prominent deep input to limb MI contrasts with the evidence for a relatively minor deep input to face MI.

IIIA.3 CORTICOCORTICAL CONNECTIONS BETWEEN PRIMARY MOTOR CORTEX AND OTHER CORTICAL AREAS

Physiological studies have demonstrated the connectivity between MI and other cortical areas (for review, see Jones 1986). The principal inputs to MI are from areas 1 and 2 of SI and the anterior part of area 5; area 4 returns corticocortical fibres to all these three areas as well as area 3a but has no direct connection at all with area 3b. Area 3b projects anteriorly to area 3a but not area 4. Area 5 receives projections from areas 1 and 2 and projects anterior to area 4 (Strick and Kim 1978; Zarzecki et al. 1978; Jones and Porter 1980; Porter 1997). Although the presence of a projection from area 3a to MI has been controversial, it is now clear that such
a projection exists (Phillips et al. 1971; Zarzecki et al. 1978; Ghosh et al. 1987; Porter 1991; Avendano et al. 1992; Izraeli and Porter 1995). SII has been proposed as an alternate pathway for the peripheral input to MI (Tanji and Wise 1981; Jones 1982). Godschalk et al. (1990) showed that most retrogradely labeled cells were found in the SII and posterior parietal cortex (area 7b) after HRP injection into the MI of the monkey, and neurones in the SII and area 7b could be antidromically activated by stimulation in the MI. Area 6, including the premotor and supplementary motor areas (SMA), also has reciprocal connections with the MI (Pandya and Vignolo 1971; Barbas and Pandya 1987). In addition, MI also receives afferents from the orbital cortex (area 12), insular cortex, frontoparietal operculum (including the deep part of the cortical masticatory area), rostral division of the cingulate motor area, and the cingulate motor area on the ventral bank (Tokuno et al. 1997).

Although there is a wealth of anatomic studies, not much is known about the functional role of individual afferent inputs to the MI e.g. what information is provided by each corticocortical and thalamocortical pathway in relation to the actual performance of a motor behaviour. Previous studies have shown a role for the connections between the SMA and MI (Tanji and Kurata 1985) or MI and the thalamus (Nambu et al. 1991). Although the number of identified neurones was small, and the latter study only investigated a simple motor task of phasic lever-lifting, their studies indicated that SMA input to MI is important in developing a preparatory type of activity in MI, and the thalamus (VPLo) provides substantial inputs to MI in movement execution. Recently, Aizawa and Tanji (1994) studied the responsiveness of neurones in the MI of monkeys (Macaca Fuscata) to electrical stimulation of SMA, SI, and the ventral subnucleus of the thalamus (VPLo) with chronically implanted electrodes. All neurones examined were characterized by their relation to a motor task performed by the animals. Movement-related neurones (active immediately before and during reaching
movements) were activated by thalamic, SI and SMA stimulation or by any combination of those stimuli. More than half of the movement-related neurones, which were activated exclusively by either thalamic or SMA stimulation, exhibited an activity onset that was earlier than that observed in the earliest muscles. Their findings further indicated that the SMA input to MI is important in developing a preparatory type of activity in MI, whereas the thalamus (VPLo) provides substantial inputs in movement execution. By contrast, most movement-related neurones that responded only to SI stimulation were late in the onset of their movement-related activity, which suggests the information conveyed by this SI-MI corticocortical input is not crucial in the early phase of movement-related activity in MI. Previous studies reporting on movement-related activity in MI are consistent with this view (Inase et al. 1989; Wannier et al. 1991).

III.A.4 SUBCORTICAL PROJECTIONS FROM PRIMARY MOTOR CORTEX

MI sends projections to a variety of subcortical structures, such as the striatum, red nucleus, pontine nuclei, the thalamic nuclei, brain stem, and spinal dorsal and ventral horns (Porter 1981; Wiesendanger 1986).

It is well documented that the axons of PTNs may influence the activities of both α- and γ-motoneurones, either via connections with interneurones or (in the case of corticomotoneuronal neurones, CMNs) via direct corrections with motoneurones (e.g., Clough et al. 1971; Mortimer and Akert 1961). Numerous anatomical (e.g., Liu and Chambers 1964; Kuypers 1981; Lawrence et al. 1985), electrophysiological (e.g., Woolsey et al. 1952; Bernhard et al. 1953; Preston and Whitlock 1961; Landgren et al. 1962a, b; Clough et al. 1968; Jankowska et al. 1975b), and behavioural (e.g., Leyton and Sherrington 1917; Lawrence and Kuypers 1968a; Passingham et al. 1983; Nudo et al. 1988) investigations have indicated a
powerful influence of these PTNs, particularly the CMNs, on the \( \alpha \)-motoneurones controlling distal movements and suggest that the MI is particularly important for the fine control of distal movements. However, the extent of these PTNs' role in the fine control of distal movement varies. For example, the pioneering studies by Tower (cat: 1935; monkey: 1940) indicated that the deficit in motor function was minute in the cat and much more discrete in the monkey after chronic disruption of the pyramidal tract (PT); these results have been confirmed in cat (e.g., Asanuma et al. 1981) and monkey (e.g., Lawrence and Kuypers 1968).

In addition to powerful influence on motoneurons, some projections from motor cortex may be involved, as pointed out above, in the control of movement by modulating afferent input through sensory nuclei. Some studies have shown that somatosensory responses in dorsal column nuclei (DCN) and thalamus can be inhibited by ICMS in topographically related regions of MI; moreover, the threshold for detecting cutaneous stimuli may rise when the stimulated area is actively moved (Chapman et al. 1987; Feine et al. 1990).

III.B. GENERAL FEATURES OF PRIMARY MOTOR CORTEX IN RELATION TO THE CONTROL OF MOVEMENTS

III.B.1 ROLE OF PRIMARY MOTOR CORTEX IN THE CONTROL OF MOVEMENTS

III.B.1.1 STIMULATION OF PRIMARY MOTOR CORTEX

The representation of movements within contralateral precentral cortex was first systematically mapped by Leyton and Sherrington (1917). The pictorial summary of their experiments shows an orderly representation of movements elicited in different parts of their body by cortical stimulation. Current knowledge about somatotopic localization in MI is mainly based on a series of extensive surface mapping experiments by Woolsey and his co-investigators (Woolsey et al., 1952, 1953; Woolsey 1958, 1964) to define the precise
localization of the body parts in the MI (also see section IIIA. 1). Using 60 Hz a.c. electrical stimulation of the cortical surface, they reconstructed their results in "motor figurine charts" and "simiunculi" form (Woolsey et al. 1952; Woolsey, 1964). They found a complete and continuous body representation on the precentral gyrus, extending from the posterior bank of the arcuate sulcus anteriorly to the anterior bank of the central sulcus, and from the cingulate sulcus medially to the anterior subcentral sulcus and lower threshold current for induction of movement within the cortical regions representing the thumb, toe and orofacial areas. A striking feature of these maps is the overwhelming representation of the distal extremities and orofacial area. The orofacial representation extended from the depth of the central posteriorly to the vertical limb of arcuate sulcus anteriorly, and from the horizontal limb of the arcuate sulcus medially to the anterior subcentral sulcus laterally. Despite the extensive overlap for each muscle, the orofacial region revealed by the surface stimulation was represented in the cortex as a face area enclosing rostrally, medially, and caudally a central area of tongue. They also noted that foci for different muscles are not discrete entities as in a mosaic, rather there is very extensive overlap in the cortical motor patterns.

Investigations into the fine structures of this map argue strongly against a purely somatotopic representation of muscles in the motor cortex output and provide some clues as to how the cortical output controls the different subsets of muscles that are used in all but the simplest voluntary movements. The new findings have been revealed by careful use of ICMS in conscious (Kwan et al. 1978; Cheney and Fetz 1985; Humphrey 1986; Huang et al. 1988; Aizawa et al. 1990) or sedated animals (Sessle and Wiesendanger 1982; Strick and Preston 1982a), and the use of "spike-triggered averaging", a sophisticated method of examining the cortical output that completely avoids the disruptive effects of electrical upon the brain (Fetz and Cheney 1980; Lemon et al. 1987). Electrical stimulation cannot mimic but does disrupt the
progress of voluntary movement. Spike-triggered averaging, however, shows that clusters of output neurones facilitate the same muscle, and each muscle may be represented many times over in the cortex. The overlapping representations of different muscles may subserve the control of complex muscle synergies that underlie voluntary movement (for review, see Lemon 1988).

The evidence that the section of the PT causes profound changes in the motor map (e.g., Mitz and Humphrey 1986), and that electrical stimulation elicits relative simple movements, suggests that this functional map is more complex than the output map itself since there are other important maps with area 4: this includes an input map of afferents arriving over cortico-cortical and subcortical pathways (e.g., direct somatosensory feedback from the moving limb, which may select intracortical circuits that can influence the cortical outputs to construct the complex pattern of muscular activity underlying voluntary movements) (for review, see Lemon 1988).

IIIB.1.2 LESIONS OF PRIMARY MOTOR CORTEX

To elucidate the function of a particular structure within the CNS, lesion techniques have been used in many studies (e.g., Asanuma and Arissian 1984; Dursteler and Wurtz 1988). However, the data obtained from lesion experiments should be interpreted with caution since there are several limitations that should be kept in mind. Incomplete destruction of the structure, removal of excessive tissue, postoperative oedema and infections, postoperative recovery and plasticity of function may confound interpretation (Wiesendanger, 1981b). Indeed, Glassman (1978) has suggested that "brain lesions do not show you what the region in question does, but rather what the rest of the whole complex brain does without the part in question".
In humans, damage of the MI or corticospinal tracts produces a profound and lasting deficit in the ability to individuate movements, which constitutes a major functional impairment for patients (Penfield 1954; LaPlane et al. 1977). Although a patient with such a lesion may recover the ability to flex and extend all the fingers together, the ability to move fingers individually remains permanently deficient, rendering the patient unable to button buttons, tie shoelaces, or use many everyday utensils.

In monkeys, experimental lesions of the motor cortex or corticospinal tract produce a deficit of individuated finger movements resembling that seen in humans (Lawrence and Kuypers 1968a, b; Hepp-Reymond et al. 1972, 1974). After these lesions are made, monkeys rapidly recover the use of their fingers in walking and climbing. However, fine digital skill does not return even after several years (Lawrence and Kuypers 1968a, b). This subtle but nevertheless important motor deficit was first observed with PT lesions by Tower (1940). She concluded that one of the major roles of the corticospinal tract is to control discrete digital skill. Similar phenomena have been observed in subprimates (for review, see Armstrong 1986) with PT lesions. More electrophysiological and anatomical evidence has suggested that CMNs may confer the capacity to perform skilled finger movements (e.g., see Bernhard et al. 1953; Preston and Whitlock 1961; Fetz and Cheney 1980; Lawrence et al. 1985; Buys et al. 1986; Lemon et al. 1986; Wise and Donoghue 1986). Hoffinan and Strick (1995) have also provided evidence that lesion of the arm area of MI causes marked changes in the kinematics and the pattern of muscle activity of step-tracking movements of the wrist. These various data suggest that the PT and MI are required for refined modulation of basic locomotor central pattern generating circuits, resident at the subcortical level, and that the MI may function to superimpose more refined synergies onto basic locomotor circuits to allow accommodation of these circuits to more demanding conditions. Single-neurone recordings from the MI of awake cats have shown that marked changes in motor
cortex neuronal firing rates tended to occur only when the cat was required to negotiate obstacles (Armstrong 1986; Drew 1988).

The nature of the deficiencies following PT lesions suggests that the PT and the MI provide flexibility (e.g., see Beck and Chambers 1970), speed and agility (e.g., see Hepp-Reymond and Wiesendanger 1972), fractionation of movement (e.g., see Lawrence and Kuypers 1968a; Buys et al. 1986), precise spatiotemporal pattern of muscle activity (Hoffman and Strick 1995), power of muscular contraction (e.g., see Beck and Chambers 1970), and tailoring of subcortically generated synergies to more stringent environmental conditions (e.g., see Armstrong 1986). With regard to the latter, MI may modulate the relative degree of phasing between subcortical structures, their relative amplitudes and may contribute to the adaptability of subcortical circuits by fairly direct control over individual alpha motoneurones.

IIIB.1.3 SINGLE-NEURONE RECORDING DURING VOLUNTARY MOVEMENTS

The technique of extracellular single-neurone recording in awake animals allows a study of relation between the activity patterns of single neurones and identified movement parameters, and has provided important insights into the function of the cerebral cortex. Nevertheless, some limitations of this technique need to be borne in mind. Firstly, the sampling bias is almost always toward the largest cells. Secondly, the nature of the neurones under study is not clear, that is, whether it is a local interneurone or a neurone projecting to other areas of the brain. In addition, subthreshold changes and hyperpolarization of membrane potential which may affect the excitability of neurones are usually undetected by extracellular recordings. Furthermore, although single-neurone recordings may show a correlation of neuronal activity with a behaviour, other techniques must be applied to demonstrate the functional significance of these activities.
IIIB.1.3.1 Neuronal Activities in Relation to Different Parameters of Voluntary Movements

Many studies have attempted to correlate the firing rates of single neurones with various measures of the movement including force, rate of change of force, position, direction, velocity, and acceleration (e.g., Evarts 1981; Stein 1982; Georgopoulos 1988; Georgopoulos et al. 1992; Scott and Kalaska 1997; for review, see Wise 1993; Donoghue and Sanes 1994; Georgopoulos 1994). This section will focus only on the relationship of the firing rates of single neurones with force, rate of change of force, direction of movement to elucidate the principles of MI in the control of the parameters of voluntary movements. Due to the complexity of neural network from the single neurones to final movement, no definitive statement, however, can be made whether the movement variables are controlled by MI. Voluntary movements require more than one neurone in MI for their generation (e.g., Humphrey et al. 1970; Roland et al. 1982; Blasdel and Salama 1986; Georgopoulos 1988), and many corticospinal neurones terminate on interneuronal networks (e.g., Lundberg 1979) that can influence the relationship between cortical neuronal firing and movement. Furthermore, the requirement for activity in a particular neurone may change as a movement unfolds (Kwan et al. 1988), or may be markedly different for two slightly different movements (e.g., Muir and Lemon 1983) or under different behavioural conditions (e.g., Fetz and Finocchio 1975).

Several studies have demonstrated definite relations with force (e.g., Humphrey et al. 1970; Thach 1978; Cheney and Fetz 1980) while others found no such relation (e.g., Schmidt et al. 1975) or only a weak relation (e.g., Evarts 1969; Muir and Lemon 1983; Picard and Smith 1992), while yet another study (Humphrey et al. 1970) suggested that correlations with force could be improved by mathematical manipulations of the activities of several single neurones that were recorded simultaneously. However, the studies by Picard and Smith (1992) suggested a more important role of somatosensory inputs to MI than that of object weight per
se associated with the grip force during the periods of grasping, lifting and holding an object with a hand. These suggest the modulation of motor cortical activity with object texture, especially for neurones with cutaneous RFs, appears largely dissociated from the forces generated by the hand and may be more related to peripheral rather than to central processing. The somatosensory feedback generated during the task probably contributed to the regulation of prehensile force by exerting a texture-dependent modulation of excitable of elements with the motor cortical network.

Similar attempts have been made to identify a relation between rate of force change and neuronal firing rate and a correlation has been found to exist in most studies (e.g., Conrad et al. 1977; Evarts 1968; Humphrey et al. 1970; Smith et al. 1975; Cheney and Fetz 1980; but see Schmidt et al. 1975). Neuronal activities of the MI have been also correlated with the direction of a movement. Earlier studies (e.g. Georgopoulos et al. 1982; Schwartz et al. 1988; Kalaska et al. 1989; Richle and Requin 1989) confirmed that the direction of limb movement markedly affects motor cortical activity. Cortical cells show a preferential direction of limb movement associated with the greatest activity (Georgopoulos et al. 1982; 1992). The broad tuning of individual MI neurones to movement direction coupled with their firing rate variability (Lee et al. 1998) and MI neuronal interactions improved population coding of limb movement direction (Maynard et al. 1999). Evidence also suggests that motor cortical neurone discharge is influenced by arm posture. Caminiti et al. (1990, 1991) found that cells in MI altered their directional tuning as a function of the starting arm position for reaching movements along parallel hand paths in different parts of the workspace. In a complementary study, Scott and Kalaska (1995, 1997) reported that the activity of many MI cells was altered when monkeys made reaching movements along the similar handpaths while holding the arm in two different orientations. Sergio and Kalaska (1997) further demonstrated that the directional tuning of
MI proximal-arm-related cell activity is not constant with the direction of force exerted at the hand.

However, some controversies remain. Firstly, there is some evidence that many cells in MI reflect the direction of visual cue rather than the direction of limb force (Martin and Ghez 1985; Alexander et al. 1990). Secondly, in addition to showing a correlation to the movement direction, the discharge of cells in MI (Evarts 1968; Evarts et al. 1969; Cheney and Fetz 1980; Fu et al. 1993) shows a correlation with other kinetic or kinematic variations, such as force. Thirdly, there is evidence (Mussa-Ivaldi 1988) that the sum of activation vectors over a whole population of cells would be colinear with hand movement direction regardless of the process that is responsible for the tuning characteristics of the individual cells. A demonstration of spatial tuning in any neuronal structure does not necessarily imply that the resident neurones encode the planning of multi-joint arm movements in terms of direction. Fourthly, since MI appears to be organized in terms of multiply represented output zones each of which is associated with a characteristic functional subunit of movement, then graded or weighted combinations of these different functional efferent zone subunits should produce the desired direction of arm movement in space (e.g., see Murphy et al. 1978), and presumably, any desired voluntary movement of the body, including distal movements.

The above review suggests that complex relations might exist between cortical neuronal firing rate and movement parameters. Furthermore, Fromm (1983) and Bauswein et al. (1991), for example, have found a pronounced effect of changes in torque on the sensitivity of a neurone to position, and Donchin et al. (1998) found most neurones in the forelimb MI showed activity specific to bimanual coordination, which is strikingly different from the activity of the same neurones during unimanual movements. From the above it appears that MI is not concerned with any particular parameter or parameters of movement, such as force,
velocity, acceleration, or even direction. These parameters are only partial descriptors of the totality of the movement being performed; furthermore, they are all poor indicators of the various torques (e.g., interaction, coriolis), directions, velocities, and accelerations that occur within the moving body. However, under the appropriate conditions (i.e., stereotyped trained tasks such as precise force applications under, say, isometric conditions), or by the use of appropriate analysis procedures (e.g. vectorial weighting and combination), it appears possible to demonstrate relations between one or more of these parameters and MI neuronal firing rates. However, the relations are not simple but appear to vary depending on task conditions, and, in fact, complex interactions appear to exist between some of the different movement parameters. Perhaps a better model is to view motor cortex as a structure that, in light of peripheral anatomical constraints, encodes the appropriate levels of muscle activity in a specific set of muscle synergies that are required for a particular movement.

IIIB.1.3.2 Timing of Onset of Neuronal Activity in Relation to Onset of Voluntary Movement-
Central and Peripheral Inputs

Several studies of the onset times of motor cortex neuronal activity in relation to movement onset have shown a wide range of recruitment times, typically extending over several hundred milliseconds (e.g., Porter and Lewis 1975; Smith et al. 1975; Thach 1978; Cheney and Fetz 1980; Fetz et al. 1980; Murphy et al. 1985; Lecas et al. 1986; Schwartz et al. 1988). In contrast to a late onset of activity change in SI neurones in relation to force increase, MI neurones showed a significant earlier change (Hepp-Reymond et al. 1989). In a population of CMNs, Cheney and Fetz (1980) found a broad distribution of onset times, with most extending up to 120 ms before their target muscles; a few CMNs fired as early as 400 ms prior to onset of target muscle electromyography (EMG) (see also Smith et al. 1975). Mushiake et al. (1991) have shown that
most MI neurones exhibit similar activity during pre-movement and movement periods, regardless of whether the sequential motor task was visually guided or internally determined.

Some data have emphasized the role of corticoperipheral loop circuits during voluntary movements. Those neurones that fire in advance of EMG activity evidence of the commencement of movement, particularly those identified as CMNs, are the best candidates for drivers of the movement. Favorov et al. (1988) found that neurones in the motor (10%) and the sensory cortices (5%) started to discharge far ahead of the actual movement of the hand and that changes in firing during pre-movement was also due to sensory inputs. Some of the discharges were accompanied by an increase of the tone of the target muscle. Section of the dorsal column abolished these discharges, perhaps due to loss of internal feedback information, not likely due to decreased excitability of the MI, resulting from elimination of the sensory input, since it has been shown that elimination of the sensory input does not decrease the excitability of the MI (Asanuma and Arissian 1984). Similarly, those neurones that showed changes in firing after movement onset could also drive the movement but at least part of their activity might be related to reafference (see Wolpaw 1980a, b). During unrestrained forelimb reaching movements, Murphy et al. (1985) showed that neurones from the ICMS-defined proximal forelimb region became active about 60 ms earlier than neurones from the ICMS-defined distal forelimb region; this pattern reflected the proximal-to-distal pattern of activation seen in the forelimb EMG activity patterns. This finding fulfilled a prediction of their “nested zone” model of motor cortex organization, that is, that cellular aggregates, categorized by ICMS into different proximal or distal forelimb zones, should fire in a fashion that corresponds to the sequential activation of muscles at the limb during voluntary movement. The classes of CMNs that resembled the phasic-tonic pattern or the phasic-ramp pattern, tended to fire earlier than the neurones that exhibited a tonic or static discharge without an initial phasic component (Smith et al. 1975; Cheney and Fetz 1980).
IIIC. GENERAL FEATURES OF PRIMARY FACE MOTOR CORTEX IN RELATION TO THE CONTROL OF OROFACIAL MOVEMENTS

IIIC.1 CONTROL OF VOLUNTARY OROFACIAL MOVEMENTS

The role of different parts of the central nervous system (CNS) in the coordination of the various orofacial muscles is either not known or not well understood, partially due to the difficulty of studying orofacial movements compared with those of limb movements since most orofacial movements, such as speech, licking, swallowing, chewing, biting, sucking, and facial expression, involve complex activities in the muscles of the face, jaw, and tongue (e.g., see Dubner et al. 1978; Thexton 1984) and, for their proper execution, many of these activities require bilateral synchronous activation of the same orofacial musculatures, a feature that differs from most limb movements. However, some insights into the role of the face MI in the control of orofacial movements have been provided by surface stimulation (Walker and Green 1938; Woolsey et al. 1952), ICMS (Clark and Luschei 1974; McGuinness et al. 1980; Gould et al. 1986; Huang et al. 1988, 1989a; Murray and Sessle 1992a), lesioning (Green and Walker 1938; Luschei and Goodwin 1975; Larson et al. 1980), anatomical tracing (Kuypers 1958b), and single-neurone recording (Kubota and Niki 1971; Luschei et al. 1971; Hoffman and Luschei 1980; Sirisko and Sessle 1983; Huang et al. 1988, 1989a; Murray and Sessle 1992a, b, c; Martin et al. 1997) techniques. These studies have implicated an important role for face MI in the control of orofacial movements.

Data from a number of studies suggest that the face MI is less concerned with the motor control of jaw-closing movements than with the motor control of face, tongue, or jaw opening movements (Walker and Green 1938; Woolsey et al. 1952; Clark and Luschei 1974; McGuinness et al. 1980; Huang et al. 1988; Murray and Sessle 1992a). However, some studies (Luschei et al. 1971, 1975; Hoffman and Luschei 1980; Larson et al. 1980) have
reported an important role for face MI in jaw closing movements. Most orofacial movements involve a complex interplay and coordination among the various face, jaw, and tongue musculatures, and the data (see below) have described heavily overlapped representations for the face, jaw (mainly jaw opening), and tongue muscles within the face MI (Huang et al. 1988, 1989a; Murray et al. 1991); this organizational feature may provide part of the basis for the complex coordination characteristic of orofacial movements.

There is also good evidence for a prominent sensory input to the face MI (Kubota and Niki 1971; Hoffman and Luschei 1980; Sirisko and Sessle 1983; Huang et al. 1988, 1989a; Murray and Sessle 1992a; Martin et al. 1997; see below) and, analogous to findings in the limb MI, a close spatial relationship has been recently identified between sensory input and ICMS-defined motor output for many single neurones within face MI (Huang et al. 1989a; Murray and Sessle 1992a). Sensory inputs to the face MI may play a similar role in the control of movement as hypothesized above. In addition, there is some limited evidence that single neurones within lateral precentral cortex alter their firing rates in association with trained jaw or untrained tongue movements (Kubota and Niki 1971; Luschei et al. 1971; Lund and Lamarre 1974; Hoffman and Luschei 1980; Murray and Sessle 1992a; Martin et al. 1997), and some of these neurones appear to be in receipt of sensory information from the orofacial area.

IIIC.2 ROLE OF PRIMARY FACE MOTOR CORTEX IN THE CONTROL OF OROFACIAL MOVEMENTS

IIIC.2.1 STIMULATION OF PRIMARY FACE MOTOR CORTEX

Many studies have used surface stimulation or ICMS to stimulate the face MI. Surface stimulation of the precentral gyrus of monkeys evokes excitation of the jaw-opening muscles and mainly inhibition of the jaw-closing muscles and rhythmical jaw movements could be
induced from the lateral part of the precentral gyrus (Sherrington 1906). However, the most important contribution of surface stimulation of face MI to our understanding of MI was that it provided us the functional location of the face MI or "motor figurine charts" (see section IIIB.1.1). Since almost half of the MI face area occurs in the depth of the rostral bank of the central sulcus (Woolsey et al. 1952; McGuinness et al. 1980), complete mapping of the MI face area with surface stimulation would be difficult.

The ICMS technique, however, has provided us many important aspects of the face MI in motor control. With this technique (0.2 ms pulses at 200 Hz for 175-200 ms, 100 μA or 200 μA), Clark and Luschei (1974) first identified the excitability of the MI jaw area in the lightly tranquilized monkeys and found jaw opening was more frequently evoked (84%) than jaw closing. However, the stimulation current and the duration of train pulses were far from desirable for limiting current spread and decreasing the noxious effect (Asanuma and Arnold 1975).

McGuinness et al. (1980) found that multiple representations of individual muscles were observed in several noncontiguous foci. The most frequently evoked movement involved the zygomaticus major muscle. They also reported that facial muscle representations were clustered into a rostral zone and a caudal zone in the precentral gyrus, with the tongue representation located between and along the lateral extent of these two zones. However, no EMG recordings were carried out to confirm the evoked muscle movements, and the topographical representation of the jaw muscles was not related to those of the face and tongue muscles. Moreover, because of the relatively few penetrations made in the MI face area, the extent of MI, especially at the medial border, was difficult to delineate from this study.

Sessle and Wiesendanger (1982) found that ICMS thresholds needed to evoke face, jaw and tongue movements were as low as those required for evoking hand movements. The
anterior and posterior borders of the MI face area were delineated by penetrations in which no movement was evoked by ICMS (≤30 μA).

Gould et al. (1986) found that the topographical organization of face MI (defined by ICMS at a depth of 1800 μm) was better described as a mosaic of regions, each region representing movement of a localized part of the body. Within each cortical region, there were multiple representations of individual muscle movements. Their results were not completely consistent with previous findings that MI could be conceptualized as a single somatotopic representation (Woolsey et al. 1952; Woolsey 1958, 1964), dual rostral and caudal representations (McGuinness et al. 1980; Strick and Preston 1982a) or a horseshoe-shaped organization (Kwan et al. 1978; Sessle and Wiesendanger 1982). In addition, detailed descriptions of tongue and jaw movements and the possible bilateral representation of orofacial muscles were not reported in this study.

Using short train of ICMS (200 μs pluses at 333 Hz for 35 ms, ≤ 30 μA), Huang et al. (1988) have confirmed the general pattern of orofacial representation in the monkey MI revealed by surface stimulation (see section IIIB.1.1) and found bilateral orofacial representation exists in the monkey’s MI. They have also found clear evidence for multiple representation of a particular muscle, thus supporting the notion that multiple, yet discrete, efferent microzones represent an essential organizational principle of the MI. Between the digit and face representations, Aizawa et al. (1990) have identified a subregion in the monkey’s MI that is characterized by its relationship to bilateral or ipsilateral hand movements.

Murray and Sessle (1992a) have confirmed the general organizational features of the face MI that have been described in previous studies (see above), but they documented in detail the organizational features for tongue MI. They found that tongue movements were well
represented. A variety of tongue movements could be evoked by ICMS at tongue MI sites and were categorized in protrusion, retrusion, laterally directed, and other types of tongue movement. Low-threshold (i.e. \( \leq 5 \mu A \)) ICMS-defined tongue MI sites were considered to represent an "efferent zone". A close spatial match was found between ICMS-defined output and superficial somatosensory afferent input for tongue MI. The types of movements evoked by ICMS at jaw MI sites principally involved jaw opening, and to a much lesser extent, jaw closing; some of these movements exhibited horizontally directed vector components to the movement. A greater proportion of neurones within jaw MI than tongue MI received a deep input or an input from afferents supplying periodontal tissues. The representations for face, jaw, and tongue movements were overlapped.

The ICMS studies in the MI face area have revealed many features of cortical organization comparable to that found in the MI limb area. However, most orofacial movements require a bilateral coordination of face, jaw and tongue muscles which distinguish it from the unilateral or alternating pattern of activity commonly occurring in limb muscles. Bilateral and/or ipsilateral orofacial representation in the MI has been reported in several previous studies (Walker and Green 1938; Lauer 1952; Woolsey et al. 1952; Sinsko 1984) and certainly support notion of the cortical integration of unilateral or bilateral activities of the numerous face, jaw and tongue muscles.

The application of ICMS within MI as well as cortical masticatory area (CMA) and SI can also evoke different patterns of masticatory-like jaw movements and swallowing in awake monkeys (Huang et al. 1989b; Martin and Sessle 1993; Martin et al. 1999). The cortically induced movements can be differentiated in the frontal plane into ipsilateral-, vertical-, and contralateral-directed movements, which are associated with different patterns of masticatory muscle EMG activity (Huang et al. 1989b). Swallowing as well as chewing can be evoked by ICMS in each
hemisphere from most of CMA, immediately anterior and/or lateral to face SI and MI but overlapping their most lateral regions (Martin et al. 1999); a few sites are several mm deep to the “classical” CMA, in a region that appears to correspond to the CMA “deep” region from which masticatory-like movements can be evoked (Huang et al. 1989b). The EMG patterns of evoked swallows show some significant differences between these three different regions but are generally similar to natural swallows, consistent with earlier findings for the evoked masticatory-like movements (Huang et al. 1989b).

These ICMS data thus support a role for the primate lateral pericentral cortex, including face MI and SI, in the initiation and/or regulation of swallowing as well as mastication, and are consistent with the view that these spatially and cytoarchitectonically distinct cortical regions may participate fundamentally but perhaps differentially in the initiation and modulation of primate swallowing and mastication as well as in integrating swallowing within the complex masticatory sequence (Huang et al. 1989b; Martin et al. 1999).

III.C.2.2 LESIONS OF PRIMARY FACE MOTOR CORTEX

In humans with damage involving the orofacial representations of the precentral gyrus or PT, the so-called “pseudobulbar palsy”, the clinical condition consists of weakness and spasticity of the bulbar muscles and is associated with dysarthria and dysphagia (Walton 1977). The tongue may appear somewhat smaller than normal on account of spasticity, but is not wrinkled and does not exhibit fasciculations; the jaw-jerk, palatal, and pharyngeal reflexes are exaggerated (Walton 1977).

These observations have been confirmed and elaborated by animal studies. These lesion studies have emphasized a particular importance for the face MI in the control of the facial and the tongue movements. For example, experimental induced lesions in the face MI in the
chimpanzee produced a contralateral hemiparesis involving the lower facial muscles and tongue (Leyton and Sherrington 1917). Green and Walker (1938) observed that the unilateral extirpation of area 4 produced a more severe and longer lasting contralateral paresis of the lower facial muscles and tongue than that induced by ablations of the lower part of area 6. Interestingly, mastication was little affected by these cortical lesions.

The studies by Kirzinger and Jürgens (1982) showed that more extensive, and bilateral, lesions in areas 44, 6b, 4, 3, 1, and 2 in four squirrel monkeys, caused similar deficits to those observed by Green and Walker (1938), although the deficits tended to be more severe, and this may be a reflection of the more extensive cortical lesions. After recovery, all four animals exhibited paresis of lips, tongue, and masticatory muscles, and the animals were unable to feed themselves. Swallowing was impossible and no tongue movements could be performed even if food was placed in the mouth. However, grasping and locomotion were normal.

The above review has suggested an important role for the area 4 region of lateral precentral cortex in the control of face and tongue movements. But its role in biting movements is unclear. Green and Walker (1938) reported that monkeys with lateral precentral lesions exhibited vigorous and unimpaired jaw closing with the masseter muscles contracting strongly, and there was increased resistance to opening the jaw. These data suggested that there was an enhancement of biting following lateral precentral lesions. Luschei and Goodwin (1975) have tested the effects of cortical ablation (various regions of lateral precentral or postcentral gyri) on a trained biting task in monkeys and found that immediately after total bilateral ablation of the MI face area, the monkeys could not perform the biting task except for some repetitive forceful biting. These monkeys could again generate powerful phasic bites with the same or slightly longer reaction time after several months of retraining although they were not able to maintain the low, steady force required during the initial phase of the biting task.
However, it should be noted that the MI areas representing the jaw muscles are smaller than those representing the face and tongue muscles and are usually widely scattered in the precentral gyrus (Woolsey et al., 1952; McGuinness et al., 1980; Gould et al., 1986; Huang et al., 1989b; Murray et al., 1992a). Thus, the ablations carried out by Luschei and Goodwin (1975) would likely have interfered more with face and tongue movements than with jaw movements, but interference with face and tongue movements was not reported in their study. Coordination of face, jaw and tongue muscles might be more important than jaw muscles alone in tasks which require the maintenance of a steady biting force.

Larson et al. (1980) examined the effects of ablation of the lateral precentral cortex on chewing in two monkeys and found that only bilateral lesions, which included the MI face area, produced a permanent deficit in the chewing patterns. Bilateral ablations of the far-lateral precentral cortex alone only transiently disturbed the chewing movement, but eventually the chewing pattern became normal within 49 days after ablation. After extensive bilateral ablation of the precentral cortex including both the MI face area and the far-lateral precentral cortex, tongue movements and voluntary chewing were severely disrupted. Chewing could only be induced when food was placed between the monkeys’ molars. Although the rate of chewing was unaffected by this extensive ablation, the amplitude of chewing movements was much reduced in the vertical and horizontal dimensions. They concluded that the MI face area was probably involved in the coordination of orofacial muscles to allow for a normal, efficient mastication and they suspected that the subcortical pattern generator was inadequate to produce coordinated, efficient tongue movements required for mastication and was not autonomous unless it was activated from central or peripheral inputs. Since the exact boundary of the cortical area(s) which control chewing movements had not yet been determined, the area and extent of cortical ablation
which was necessary to perturb chewing movements were difficult to assess with the level of knowledge available at the time.

IIIC.2.3 LOCAL REVERSIBLE COOLING OF PRIMARY FACE MOTOR CORTEX

Compared with cortical ablation, cooling can produce repeated, brief, local, reversible dysfunction of neuronal tissue without the compensatory neuronal reorganization that occurs after permanent lesions (see Murray et al. 1991). With cooling of neuronal tissue, neuronal excitability initially increases and then decreases. Transdural cooling results in a rapid and powerful reduction of evoked and spontaneous activity directly beneath the thermode when the temperature has decreased to 28 °C. Benita and Conde (1972) provided evidence that cooling of fibre tracts to temperatures between 20 °C and 10 °C resulted in minimal conduction disturbances, and that it was necessary to cool fibre tracts to 0 °C to block conduction completely. In addition, synaptic transmission began to be disrupted at neuronal temperatures below 20 °C, and to resume as soon as rewarming was commenced (Benita and Conde 1972; Campeau and Davis 1989). This evidence suggests that cooling blocks synapses. Failure of synaptic transmission is presumably due to alterations in the membrane permeabilities for specific ions, such as Na⁺, K⁺, and Ca²⁺. If freezing is avoided, the effects of cooling appear to be completely reversible. To assess meaningfully the extent of the cooling inactivation, each cooling device, or thermode, has to be calibrated by constructing isotherms for the tissue being cooled (Brooks 1983). A limitation of the technique is imprecise knowledge of the exact extent of inactivated brain. The rapidity with which recovery occurs following cooling (Benita and Conde 1972; Campeau and Davis 1989) argues for synaptic block and not other factors, such as spreading depression (Leão 1972), as the likely consequences of brain cooling (Brooks 1983).
Cooling of MI has been used in a few earlier studies to test the effects on limb movements. Cooling of primate forelimb MI appears to produce a rapid and reversible inactivation of cortex that manifests as a functional impairment of motor activities such as the dramatic contralateral limb deficit (Trendelenburg 1911) and an increase in reaction time for the wrist movement (Sasaki and Gemba 1985).

Murray et al. (1991) tested the effects of reversible inactivation of ICMS-defined face MI in two monkeys that were trained to perform both a tongue-protrusion task and a biting task. During bilateral cooling of the thermodes on the dura overlying the face MI, there was a significant reduction in the success rates for the performance of the tongue-protrusion task in comparison with control series of trials (i.e., pre-cool and post-cool) in which the thermodes were kept at 37°C. Quantitative analyses of force and EMG activity showed that the principal deficit was an inability of each monkey to exert sufficient force with its tongue for a sufficient length of time onto the tongue-protrusion task transducer; this deficit was paralleled by a reduction in the level of activity in the genioglossus, and digastric EMG activity. At 4 minutes after commencement of rewarming, task performance had returned to control, pre-cool levels. This depressant effect on the tongue-protrusion task was reproducible on different days, but identical cooling conditions in the same monkeys did not significantly affect the success rates for the performance of the biting task. However, there was a slight but significant reduction for one of the monkeys in the rate of force application during the initial force dynamic phase of the biting task.

The same effects on success rates of the tongue-protrusion task and biting task were found when the same cooling experiment was carried out with the thermodes placed directly on the pia overlying face MI. Unilateral cooling of face MI through the pia did not result in a significant reduction in success rates for the performance of the tongue-protrusion task in comparison with
the control series of trials. These findings are consistent with evidence that primate MI have an extensive representation for the tongue, and face movements and only a very small representation for jaw-closing movements. These data suggest that face MI plays a critical role in the generation of tongue, and facial movements, but is less important in the generation of jaw-closing movements.

Narita et al. (1995, 1999) have shown that bilateral cold block of pericentral cortex markedly affected the ability of monkeys to carry out mastication and swallowing. Significant changes also occurred in mastication and swallow-related EMG activity patterns. These findings provide evidence that the face MI is very important in the control of tongue movements during mastication and that the lateral pericentral cortex also plays a critical role in the initiation and regulation of mastication and swallowing in the primate.

III.2.4 SINGLE-NEURONE RECORDINGS DURING OROFACIAL MOVEMENTS

III.2.4.1 Introduction

Only a limited number of studies have addressed the activities of single neurones within the face MI of awake monkeys performing orofacial movements. Studies of primate face MI have used trained tasks involving biting (Luschei et al. 1971; Hoffman and Luschei 1980; Murray et al. 1991; Murray and Sessle 1992b, c) and tongue protrusion (Murray et al. 1991; Murray and Sessle 1992b, c). One study, presumably of face MI (Kubota and Niki 1971), and another of CMA (Lund and Lamarre 1974), recorded neuronal activity patterns during more "natural" movements such as mastication and spontaneous orofacial movements. Current evidence indicates that there is only a small representation for jaw closing within primate face MI (Clark and Luschei 1974; Gould et al. 1986; Huang et al. 1988; Murray and Sessle 1992a; Woolsey et al. 1952). Studies using ICMS (Gould et al. 1986; Huang et al. 1988, 1989a) or
single-neurone recordings of afferent inputs (Huang et al. 1989a) have demonstrated an extensive representation within the primate face MI for tongue and facial muscles, and studies employing trained tongue or biting tasks have shown a prominent activity for single face MI neurones (Murray and Sessle 1992b,c; Martin et al. 1997).

IIIC.2.4.2 Single-Neurone Recordings during Orofacial Movements

Although several limitations exist (see below), single-neurone recordings have been made in face MI during semiautomatic movements and trained behaviours in many studies and provide a basis for understanding the role of face MI in control of orofacial movements.

Kubota and Niki (1971) recorded mastication-related neuronal activities of 77 single neurones within the lateral precentral cortex of awake monkeys (Macaca fuscata). Of these neurones, the activities of 36 were related mainly to closing movements (jaw closer neurones), 38 to opening movements (jaw opener neurones), and 3 were non-specific. They further classified these jaw closer neurones as three subtypes: type 1 neurones (27/36), which fired mainly during the early phase of the closing movement; type 2 neurones (7/36), which fired mainly during the later phase of the closing movement; and intermediate neurones (2/36), which fired throughout the closing phase. Similarly, they classified jaw opener neurones as type 1 neurones (10/38), which fired mainly during the early phase of the jaw opening movement, and intermediate opener neurones (28/38), which increased their firing rates throughout the opening phase. Although they identified some of their neurones as PTNs, they did not report that they attempted to identify any neurones on the basis of RF properties or ICMS-evoked effects. The latter gives a much clearer idea of the particular efferent zone to which a particular neurone may be related. Therefore it is possible that they were, in fact, not recording from face MI. Rather, they may have been recording from a premotor cortical
region or even from the CMA (see Huang et al. 1989b); major contributions to the PT come not only from MI but also from cortex rostral and caudal to MI (Brodal 1981), and lateral to MI. Furthermore, even if Kubota and Niki (1971) were recording within the ICMS-defined face MI it is possible that, in light of the detailed documentation of the extensive representation of the face, jaw, and tongue musculatures within face MI (Gould et al. 1986; Huang et al. 1988, 1989a; Murray and Sessle 1992a; Woolsey et al. 1952), some of the neurones which were observed to modulate their activities during jaw opening or jaw closing movements, could have been specifically concerned with face or tongue motor activities that would likely have occurred in association with the various jaw movements studied by Kubota and Niki.

Other studies have involved single-neurone recordings in face MI during trained behaviours. Luschei et al. (1971) studied single-neurone activity in the precentral face area of the primary MI in five monkeys. Three main types (i.e. "early-on", "early-off", "late-on") of biting task-related neurones could be identified based on their firing rate in relation to the jaw movement. However, most of the neurones recorded by Luschei et al. (1971) were in anatomical area 6 rather than area 4, although from their map and in light of current evidence (see Huang et al. 1988, 1989a), it would appear that at least some of the neurones were recorded within ICMS-defined face MI. A very diverse pattern of activity was noted during the post-task ingestion period for these "early-on" and "early-off" neurones. Some units appeared to be unaffected by the ingestion movement, while others fired in low-frequency bursts that were in phase with the ingestion movements. The only "typical" pattern observed was for neurones to be silent during the first or second ingestion movement and then to begin firing in rhythmical bursts during subsequent movements. Luschei et al. (1971) also noted that
many neurones modulated their responses during ingestion movements but did not exhibit any relation with the biting task.

Hoffman and Luschei (1980) recorded single-neuronal activity within MI during the biting task at a number of different biting force levels, and they observed similar firing patterns of neuronal activity to those described by Luschei et al. (1971). They also found the discharge rates of some biting task-related MI neurones could be modulated during certain phases of the chewing cycle (i.e. closing and/or opening phase). These data of Hoffman and Luschei (1980) pointed to “a greater role for motor cortex in controlling an operantly conditioned movement and to a lesser role for motor cortex in an instinctive movement using the same muscles” (Evarts 1981, 1986), and in accordance with the concept that MI is less concerned with automatic than with learned movements (Phillips and Porter 1977). This latter concept may be true; however, the data of Hoffman and Luschei (1980) may not support this concept due to the unknown targets of the MI neurones, differences in modulation of sensory responsiveness (e.g., see Lund and Olsson 1983; Chapin and Woodward 1986) and patterns of temporalis and masseter EMG activity under the operantly and semiautomatic jaw movement conditions (Hylander and Johnson 1985). Therefore, it is possible that a particular subset of face motor cortical neurones might exhibit afferent contributions to the control of automatic or learned jaw movements.

Murray and Sessle (1992b) found there was a significantly higher proportion of neurones in tongue MI that were related to the tongue-protrusion than to the biting task and the proportion of neurones in jaw MI that were related to the biting task was higher than to the tongue-protrusion task and the proportion of biting task-related neurones at ICMS-defined jaw-closing sites was higher than that at jaw-opening sites. Furthermore, for those neurons at face MI sites, there was no significant difference between the proportion of neurones related to the tongue-protrusion task
and the proportion of neurones related to the biting task; most of neurones that were recorded at face MI sites did not alter their firing rates during either task.

Murray and Sessle (1992c) also found that some neurones within ICMS-defined face MI exhibited directional relations; that is, the change in firing rate between the pre-trial period and the task period for the tongue-protrusion task was significantly different for each neurone depending on the direction in which the activity of the neurone was studied. These data provided evidence that the different ICMS-defined tongue MI sites may be efferent zones that drive particular elemental components of tongue movement in a weighted manner and thereby effect the appropriate changes in tongue-protrusion task. Tongue MI may be involved in the generation of other tongue movements in a similar fashion.

Similarly, Martin et al. (1995, 1997) found that some neurones within ICMS-defined tongue MI showed significant alterations of activity in relation to the swallowing of a juice reward and/or mastication in addition to significant modulations of firing in association with performance of the trained tongue-protrusion task. These findings suggest that the region of cortex involved in swallowing includes MI and that tongue MI may play a role in the regulation of semiautomatic tongue movements, in addition to trained motor behaviors. Swallow-related tongue MI neurones exhibited a variety of swallow-related activity patterns and were distributed throughout the ICMS-defined tongue MI at sites where ICMS evoked a variety of types of tongue movements. These findings are consistent the view that multiple efferent zones for the production of tongue movements are activated in swallowing. Many swallow-related tongue MI neurones had an orofacial RF, particularly on the tongue dorsum, supporting the view that afferent inputs may be involved in regulation of the swallowing synergy.

The review above suggests that different efferent zones may be recruited in close temporal relations during the biting or tongue-protrusion task. Furthermore, at these spatially distinct
efferent zones, and even those zones from which ICMS elicited the same tongue movement, neurones were recorded that exhibited different patterns of neuronal activity and different peripheral origin of mechanosensitive input; the latter came principally from superficial mechanoreceptors in the tongue dorsum. Thus it appears that different efferent tongue MI zones might be deployed differentially, in terms of magnitude and pattern of neuronal activity, to produce the appropriate change in tongue shape and position required to perform the tongue-protrusion task.

IV. ROLE OF PRIMARY SOMATOSENSORY CORTEX IN OROFACIAL MOVEMENTS
IVA. ORGANIZATIONAL FEATURES OF PRIMARY SOMATOSENSORY CORTEX
IVA.1 CYTOARCHITECTONIC ORGANIZATION AND TOPOGRAPHIC REPRESENTATION

By the use of the evoked potential technique, Woolsey and his colleagues (Marshall et al. 1937; Woolsey 1947; Woolsey et al. 1942, 1979; for review, see Woolsey 1958) noted that the contralateral body surface is represented in SI of monkeys with the tail most medial and the tongue most lateral. They also found that SI of monkeys includes the four strip-like architectonic fields in the postcentral gyrus of Brodmann (1909) and the Vogts (1919), i.e., areas 3a, 3b, 1, and 2. Similarly, the representation of the orofacial region in awake monkeys was found immediately lateral to that of the hand, and there was a clear somatotopic pattern of organisation within face SI: the periorbital or nose region was located most medially, then followed laterally in sequence the representation of the upper lip, lower lip, and intraoral area in the face SI (Huang et al. 1989b; Lin et al. 1994a).

The boundary of areas 4, 3a, 3b, 1, 2, and 5 can be identified by examining cell distributions according to established cytoarchitectonic criteria (Felleman et al. 1983; Pons
and Kaas 1986; Ghosh et al. 1987). The criteria summarized by Widenser and Cheney (1997) are as follows: 1) area 4/3a boundary: the appearance of an attenuated layer IV, sharpening the boundary between grey and white matter, and the loss of large Betz cells; 2) area 3a to 3b: the appearance of a cell-free layer V in 3b, increased density of layers II through IV with a uniform cell population, and maximum narrowing of the grey matter at the corner of the postcentral gyrus where it begins to flatten out; 3) area 3b to 1: appearance of laminated cells arranged in a distinct radial organization, a decrease in density of the middle cortical layers II and V, and less densely stained layer IV and VI in area 1; 4) area 1 to 2: an increase in cortical thickness in area 2, the appearance of large pyramidal cells in layers III and V, and the appearance of less densely stained layers IV and VI in area 2; and 5) area 2 to 5: appearance of less densely and thinner layers IV and VI in area 5, an increase in the clarity of lamination in area 5, and a decrease in the thickness as well as the number of pyramidal cell of layer III.

The possible functional meaning of the cytoarchitectural differentiation of SI has been demonstrated by showing that areas 3b and 1 receive inputs principally from cutaneous receptors, and areas 3a and 2 receive inputs principally from muscle and joints receptors (Mountcastle and Powell 1959a, b). A strong and sequential outflow of connections has been demonstrated from areas 3a and 3b to areas 1 and 2 which are interconnected with the motor areas (Vogt and Pandya 1977; Jones et al. 1978). Furthermore, it was proposed that columnar organization represents the basis of the functional organization of SI (for review, see Mountcastle 1984); neurones in the same column have been suggested to have the same RF and the same modality properties. Investigations in unanaesthetized monkeys (Favorov and Whitsel 1988a,b) suggest that the topographic organization in the forelimb SI of Macaca fascicularis should be regarded as a mosaic of discrete units-segregates (similar to Mountcastle’s column); however, the neurones in the same “segregate” demonstrate a great
variation in the location and size of the RF; nevertheless, a small skin area appears to be common to RFs of all neurones in the segregate.

With the high resolution multiunit recording technique introduced by Welker (1971), Paul et al. (1972) discovered an individual, complete representation of the hand in each of areas 3b and 1 in monkeys. The series of studies in anaesthetized monkeys also have suggested an individual, complete representation of body surface in each of areas 3b, 1 and 2 and at least a partial representation in area 3a in monkeys (Merzenich et al. 1978, 1987; Kaas et al. 1979; Nelson et al. 1980; Pons et al. 1985; Stryker et al. 1987). This individual complete representation in each cytoarchitectonic area has not been supported by another series of studies in awake monkeys (e.g., Dreyer et al. 1975; McKenna et al. 1982). The discrepancy between these two series of studies appears to be due to the effects of anesthetics and the mapping techniques used (Duncan et al. 1982; Favorov and Whitsel 1988a,b).

Several studies have investigated representation of the head and face in SI in awake (e.g. Dreyer et al. 1975) and anaesthetized monkeys (e.g., Sur et al. 1982; Pons et al. 1985; Cusick et al. 1986). For example, Dreyer et al. (1975) observed that a mirror-symmetric topographic organization in face SI exists about the boundary between areas 3 and 1, that a single region in the periphery is represented several times in widely separated locations in face SI, and that neurones belonging to different submodality classes are segregated, i.e., cutaneous inputs mainly in area 3b and 1 and deep inputs mainly in areas 3a and 2.

Cusick et al. (1986) have also explored the representations of the face, teeth and oral cavity in areas 3b and 1 of SI in five anaesthetized squirrel monkeys. With multiunit recordings, typically at depths of 800-1200 μm from the brain surface, they found a complete, topographically organized representations in area 3b, and a separate representation in area 1 which was organized roughly in parallel to that in area 3b. The two representations adjoin
along the midline representation of scalp, nose, and lips, and the border between areas 3b and 1 signals mirror reversals in the topographic organization, i.e., reversals in receptive field sequences across the border. In addition, there was evidence for remarkable individual variability in the representation of the lips in area 3b.

Sirisko and Sessle (1983) and Huang et al. (1989a) observed that many neurones in area 3a of monkey receive a low-threshold afferent input from jaw, facial, and tongue muscles, and that neurones with cutaneous or intraoral afferent inputs predominate in areas 3b and 1 of the awake monkey (Dreyer et al. 1975; Huang et al. 1989a).

Lin et al. (1994a) found that nearly all of the face SI neurones responded to light tactile stimulation, and most of them received contralateral input (78%) and showed a rapidly adapting response to tactile stimulation (82%). There was no significant difference in the ratio of slowly adapting to rapidly adapting neurones in areas 1 and 3b.

IVA.2 SOMATOSENSORY PATHWAYS TO THE PRIMARY SOMATOSENSORY CORTEX

Sensory information accesses to SI through either ascending somatosensory pathways or transcortical connections (see section IVA.3). Ascending pathways to somatosensory cortex include spinothalamic and spinocervical tracts, as well as the dorsal column-medial lemniscal system (e.g., Dreyer et al. 1974; for review, see Mountcastle 1984, Willis and Coggeshall 1991). The dorsal column system has long been regarded as the principal pathway of the spinal cord serving the more complex aspects of mechanoreceptive sensibility, including the sensory guidance of movements (Mountcastle 1984). The DCN which project to the ventral posterolateral nucleus of thalamus (VPL) via the medial lemniscal pathway receive inputs directly from ipsilateral dorsal root ganglion cells as well as from second-order neurones
located in the dorsal horn of the spinal cord (e.g., Dreyer et al. 1974; Ellis and Rustioni 1981; for reviews, see Mountcastle 1984; Willis and Coggeshall 1991). Inputs from muscle proprioceptors in the forelimb are processed in laminae IV-VII and IX neurones in the spinal cord which project to the cuneate nucleus and then to the contralateral thalamus; for the hindlimb, inputs are relayed through Clarke’s column and reach the contralateral thalamus after synapses in nucleus z; the spinothalamic tract may also transmit some proprioceptive information (for review, see Willis and Coggeshall 1991). Dykes et al. (1986) have shown injections of HRP into area 3a of SI labeled neurones in a rostral and dorsal cap of the ventroposterior thalamus ( termed as ventroposterior oralis, VPO). Injections into the forelimb portion of area 3b labeled neurones in the VPL. Inputs from deep structures were consistently located in the VPO nucleus and cutaneous inputs activated neurones in the VPL. The existence of functionally distinct subdivisions within the somatosensory nuclei of the thalamus suggested a parallel processing and relay of somatosensory information at this level of this somatosensory pathway. Each cytoarchitectonic area of SI received parallel inputs from adjacent parts of the thalamus (Whitsel et al. 1978; Jones et al. 1979; Cusick et al. 1985) and complex patterns of reciprocal “feedback” projections exist among these areas.

The ascending pathways to the CNS that transmit sensory information from low-threshold orofacial mechanoreceptors have been described in detail (Darian-Smith 1966, 1973; Dubner et al. 1978; see also Matsushita et al. 1982; Jones et al. 1986a,b; Rausell and Jones 1991a,b). Briefly, most orofacial mechanoreceptive primary afferents have their somata within the trigeminal ganglion, and terminate centrally within trigeminal spinal or main sensory nuclei of the brainstem except for jaw muscle spindle afferents and some periodontal afferents that have somata located in the trigeminal mesencephalic nucleus. Second-order neurones project to the VPM and ventrobasal complex (VB), which relay non-noxious and nociceptive sensory
information to SI and SII (Simone et al. 1993; Havton and Ohara 1993; Vahle-Hinz et al. 1994). On the basis of staining for cytochrome oxidase, Rausell and Jones (1991a) have divided VPM in monkeys into a lightly stained matrix domain and an intensely stained rod domain which extends antero-posteriorly through the full extent of the nucleus. With retrograde and anterograde tracing techniques, Rausell and Jones (1991b) found that the rod and matrix compartments have different patterns of input and output connections: the relay neurones in the rod domain receive their inputs from the main sensory nucleus and project to the middle layers of face SI; the relay neurones in the matrix domain receive their inputs from the caudal nucleus of the trigeminal spinal complex and project to the superficial layers (I and II) of face SI.

Muscle afferents from jaw and tongue muscles terminate on trigeminal motoneurons or a variety of bulbar interneurones (e.g., see Nazruddin et al. 1989; Nishimori et al. 1986; Shigenaga et al. 1988). Furthermore, Dessem et al. (1997) showed that the major projection areas of jaw-muscle afferents were the trigeminal motor nucleus (Vmo), regions dorsal to Vmo, reticular formation, spinal trigeminal nucleus, superior cerebellar peduncle, and mesencephalic trigeminal nucleus (Vme). Based on their sensitivity during stretching of the jaw muscles and/or their silencing or not during the release phase of muscle stretch, jaw-muscle spindle afferents were classified as primary-like (high sensitivity during stretching) or secondary-like. Primary-like spindle afferents projected most strongly to the Vmo, while secondary-like spindle afferents projected most strongly to the region dorsal to the Vmo. Luo and Dessem (1996) have provided anatomical evidence for recurrent feedback between jaw-muscle spindle afferents within Vme. The projection of jaw-muscle spindle afferents to the caudal brainstem region may play a significant role in masticatory muscle stretch reflexes and in the integration of trigeminal proprioceptive information and its transmission to higher
centers (Luo and Dessem 1995) and there is evidence that some of this proprioceptive information projects through the VPM to reach face SI (e.g., Bowman 1971; Dreyer et al. 1975; Sirisko and Sessle 1983; Huang et al. 1988).

IVA.3 CORTICORTICAL CONNECTIONS BETWEEN PRIMARY SOMATOSENSORY CORTEX AND OTHER CORTEX AREAS

SI receives from and sends fibers to many cortical areas including MI (also see section IIIA.3). Connectivity between SI and other cortical areas, and between the fields of SI has been demonstrated with ablation-degeneration techniques (Jones and Powell 1969a,b, 1970; Vogt and Pandya 1977) and anterograde (autoradiographic) and retrograde (HRP) labeling methods (Jones et al. 1978) in the monkey (for review, see Jones 1986). Area 3a receives muscle afferent input (Phillips et al. 1971) and projects to area 2, as well as to MI. Area 2 receives both deep and tactile input and may function as an integration center for somatosensory information arriving from both corticocortical and thalamocortical routes (Iwamura and Tanaka 1978; Iwamura et al. 1980; Pons and Kaas 1986). The SMA and premotor area, the neurones of which lead area 4 neurones in the initiation of movement, receive inputs from areas 1, 2, 5, and 4. There are also interconnections between SI and SII (Manzoni et al. 1990; Barbaresi et al. 1995). Corticostriatal projections from SI have also been demonstrated in primates (Jones et al. 1977; Künzie 1977; Flaherty and Graybiel 1991; for review, see Jones 1986).

There is also connectivity between the fields of SI (see section IVA.1). The differential somatosensory deficits, after ablation of different areas of SI, confirm this sequential outflow of connections (Randolph and Semmes 1974; Iwamura and Tanaka 1991; Porter and Izraeli 1993). Ultimately, it is this total pattern of feedforward and feedback interconnections and
parallel ascending inputs which contribute to the SI neuronal activity observed during movement. The different patterns of connection for each cytoarchitectonic area may relate to the functional differences between the different areas of SI.

IVA.4 CORTICOFUGAL PROJECTIONS FROM PRIMARY SOMATOSENSORY CORTEX

The SI sends fibres not only to a variety of cortical regions (see section IVA.3), but also to subcortical areas. However, differences between MI and SI projections exist: CMN projections are mainly derived from the precentral gyrus and cortical projections to the trigeminal brainstem sensory complex and spinal dorsal horn are mainly derived from postcentral gyrus (for review, see Kuyper 1981; Wiesendanger 1981). The sensorimotor corticofugal projections have been showed at trigeminal brainstem complex (Darian-Smith 1966; Dubner et al. 1978), VPL, VPM, and DCN levels in several species (rat: Valverde 1962, 1966; Wise and Jones 1977; Bourassa et al. 1995; cat: Chambers and Liu 1957; Kuypers and Tuerk 1964; Gordon and Miller 1969; Weisberg and Rustioni 1979; monkeys: Kuypers 1958b, 1965; Weisberg and Rustioni 1977); MI neurones project to the ventrolateral zone surrounding the cuneate nucleus which relays proprioceptive information from the periphery in the cat (Rosen and Sjolund 1973; Dykes et al. 1982), and SI neurones project upon the core of the cuneate nucleus proper which receives primarily cutaneous input from the distal forelimb (Weisberg and Rustioni 1977, 1979; Cheema et al., 1983, 1985). The VPL appears to receive inputs from SI while MI projects more to the ventrolateral nucleus (for review, see Jones 1986). Studies in the rat have shown that cells of the entire upper part of layer VI and majority of lower part of layer IV of cortical barrel fields project to the VPM (Bourassa et al. 1995). In addition, about half of the pyramidal tract neurones in primate are located in all four areas of SI and in area 5 of the parietal cortex (Russel and DeMyer 1961; Murray and Coulter 1981). However, differences between MI and SI projections exist:
corticomotoneuronal projections are mainly derived from the precentral gyrus and cortical projections to the trigeminal brainstem sensory complex and spinal dorsal horn are derived mainly from the postcentral gyrus (for review, see Kuypers 1981; Wiesendanger 1981). These anatomical arrangements have provided a substrate for movement-related modulation of somatosensory transmission which has been demonstrated in neurophysiological recording studies in the anaesthetized and awake animals as well as in psychophysical and evoked potential studies in human subjects.

IVB. GENERAL FEATURES OF PRIMARY SOMATOSENSORY CORTEX IN RELATION TO THE CONTROL OF MOVEMENTS

IVB.1 ROLE OF PRIMARY SOMATOSENSORY CORTEX IN THE CONTROL OF MOVEMENTS

IVB.1.1 STIMULATION OF PRIMARY SOMATOSENSORY CORTEX

Surface stimulation of SI can elicit movements which are somatotopically represented as a mirror image of the MI motor map (Penfield and Rasmussen 1950; Woolsey et al. 1953, 1979; Woolsey 1958). The evoked movements cannot be abolished after ablation of either MI or SMA (Woolsey et al. 1953), suggesting existence of a functional linkage to motoneurons that is not dependent upon precentral cortex. However, Short-train ICMS (200-μs pulses at 333 Hz for 35 ms, ≤30μA) of SI is ineffective in evoking any short-latency muscle twitch in awake monkeys (Rosen and Asanuma 1972, Kwan et al. 1978; Sessle and Wiesendanger 1982). As stated in section IVA.4, SI areas contain large numbers of corticospinal neurones (Coulter et al. 1976; Coulter and Jones 1977; Sessle and Wiesendanger 1982; Toyoshima and Sakai 1982; Bentivoglio and Rustoni 1986; Galea and Darian-Smith 1994). Many of these neurones terminate in the spinal cord dorsal horn and seem to influence transmission of sensory
information to higher levels (Fetz 1968; Cheema et al. 1984b). Labeling studies have shown that some SI neurones terminate in laminate V, VI, and VII of the spinal cord (Cheema et al. 1984a; Ralston and Ralston 1985; Casale and Light 1991). The dendrites of motoneurons can extend well beyond the boundaries of the motor nuclei, raising the possibility that some SI corticospinal neurones could terminate directly on the dendrites of motoneurons (Rose and Richmond 1981; Keirstead and Rose 1983; Liang et al. 1991). Of course, the possibility of non-monosynaptic effects on motoneurons from SI corticospinal neurones also exists. Widener and Cheney (1997) have shown single-pulse ICMS produced effects at all corticomotoneuronal cell sites in MI but at only 14% of SI sites. The large fraction of SI effects that was inhibitory represented yet another marked difference between corticomotoneuronal cell sites in MI and SI sites (25% vs 93%).

IVB.1.2 LESIONS OF PRIMARY SOMATOSENSORY CORTEX

In humans, damage or excision of SI leads initially to a complete anaesthesia and motor dysfunction that resemble those disturbances accompanying peripheral deafferentation; these recede but leave the patient with dystonia, an inability to maintain steady postures or forces, and ataxia (for review, see Freund, 1987). Removal of the postcentral gyrus does not produce paralysis but does result in loss of the sense of movement and the sense of position in space in the extremities contralateral to the lesioned cortex (Penfield and Rasmussen 1950); the defect is maximum in the distal parts of the limbs and incomplete at the shoulder and hip. In fact, clumsiness in using the contralateral hand, especially fingers, is the general finding of the studies involving ablation or reversible inactivation of the primate forelimb SI (Tatton et al. 1975; Asanuma and Arissian 1984; Hikosaka et al. 1985; Iwamura and Tanaka 1991) and clinical neurological observations (Roland 1987; Pause et al. 1989; for review, see Freund
Patients may use imagery to compensate for lack of sensory inputs to compare with motor commands when they are deafferented as a result of somatosensory cortex damage (Aglioti et al. 1996). Deafferented patients use visual cues to update their reference about current limb position (Gordon and Soechting 1995); without visual cues, performance suffers. It has been suggested that patients cannot generate corrective signals resulting from the comparison of afferent and efferent signals (Bard et al. 1995; Gordon et al. 1995; Aglioti et al. 1996).

The use of experimentally induced SI lesions in animals has verified the data in patients with damage in SI. Several studies have shown severe, long-lasting and localized deficits on a variety of manual discrimination tasks after removal of the hand area in SI (Ruch et al. 1938; Randolph and Semmes 1974; Iwamura and Tanaka 1991; for review, see Freund 1987). Excision of area 3 of SI results in a general deficit, whereas excision of area 1 or 2 of SI produces a selective effect apparent only on more difficult “form”, “texture”, or “angle” discrimination tasks. These data suggest area 3 is the initial and principle target for the afferent projections from VPL of the thalamus and is concerned with all types of somatosensory information; then it projects to areas 1 and 2 which are concerned especially with texture or shape.

After surgical ablation of forelimb SI (Lawrence and Hopkins 1976; Asanuma and Arissian 1984), the behaviour of monkeys in a cage shows no difference from that before the operation; however, the monkeys can no longer use the fingers properly to pick up food pellets from a small hole in a test device or show excessive movements of the other three fingers during removal of food with the index finger and thumb. The clumsiness disappears rapidly after a week although the usage of the fingers is still a little clumsier than normal. Studies by (Zainos et al. 1997) have found that monkeys lose their ability to categorize the speed of
moving tactile stimuli for more than 60 days after removal of the SI although the animals still can detect the stimuli.

Possible functions of the motor output linkage from SI are not well understood. Earlier studies (Asanuma et al. 1979; 1980) showed that surface potentials in MI evoked by peripheral nerve stimulation are diminished, but not abolished, following SI ablations. There is no difference between response latencies to activation of high-threshold cutaneous fibres in both SI and MI (Asanuma et al. 1979). Studies by Brinkman et al. (1985) showed that cooling of area 2 did not reduce the responses of area 4 cells to passive joint movements, nor did it alter the over-all pattern of activity of these cells during self-initiated lever pulling while that could still be performed. Cooling of area 2 did cause a significant increase in background cellular discharge in area 4 while the animal was at rest. Afferent impulses which were generated by passive joint movement and which had been shown to influence cells in area 4 of the conscious monkey at short latencies were probably not transmitted through cortico-cortical connections from area 2. These findings indicate that there are parallel inputs to MI and SI and the clumsiness of forelimb movement caused by cold block of area 2 may be due to cold block-induced inactivation of corticofugal effects from SI on subcortical centres involved in somatosensory transmission. Recent studies by Izraeli and Porter (1993) suggest area 2 input to MI may modulate such input from other sources (e.g. from thalamus). Indeed, some individual MI cells receive convergent input from both thalamus and SI (Kosar et al. 1985; Zarzecki 1991). Injection of muscimol [γ-aminobutyric acid (GABA) agonist] in selective finger areas of SI in the awake monkeys produced a striking yet reversible dysfunction of fingers which included various symptoms depending on the site of injection, i.e., the monkey was unable to detect a piece of food but revealed no obvious deficit in the pattern of finger movements after injections in areas 3b or 1; yet loss of finger coordination which disabled the
monkey from picking up a small piece of food from a small hole was noted after injections in area 2 (Hikosaka et al. 1985). These data suggest that different areas of SI have novel functions and also that area 2 plays a crucial role in the control of fine finger movements for manipulating objects.

The SI has been suggested to play an important role in acquisition of motor skills. Sakamoto et al. (1989) trained three cats to pick up a small piece of food from a rotating beaker. In these cats, the training period necessary for acquisition of the motor skill for the forelimb contralateral to a SI lesion (areas 1, 2, and a part of 5) was significantly longer than for the forelimb ipsilateral to the lesioned cortex. Lesions of the same areas after training did not impair the learned motor skill although the cats did have trouble to reach the beaker accurately. It has been postulated that the inputs from the periphery to SI and the inputs from the lesioned SI to MI participate in learning motor skills. Physiological studies also support this notion by showing that tetanic stimulation of area 2 causes a long-lasting facilitation of the excitatory postsynaptic responses of target neurones in MI (Sakamoto et al. 1987; Keller et al. 1990; Caria et al. 1997). On the other hand, rapid, repetitive, highly stereotypic movements applied in a learning context can actively degrade cortical representations of sensory information guiding fine movements (Byl et al. 1996).

The SI may compensate for the motor function after inactivation of MI. Sasaki and Gemba (1985) supported this notion by showing that cooling of the monkey's forelimb MI resulted in only paresis of the wrist muscles and enhanced the pre-movement field potential in forelimb SI, which is consistent with the observation that SI cortical stimulation can evoke contralateral movement after MI ablation (Woolsey et al. 1953); in contrast, simultaneous cooling of forelimb MI and SI resulted in paralysis of wrist muscles and the monkey stopped lifting a lever within a few minutes of cooling.
The above data suggest that the deficit observed after the SI lesion is mainly an incoordination of movement which may be due to deficient sensorimotor integration instead of deficits in the generation of movement; SI may participate in learning of new motor skills and may partially compensate for the motor function after MI lesions.

IVB.1.3 SINGLE-NEURONE RECORDING DURING VOLUNTARY MOVEMENTS

In view of the importance of sensory input in motor control, abundant connections between SI and MI and other motor cortical areas and corticofugal projections from SI (see section IVA.4), it is natural to think that certain SI neurones may play a role in the guidance of movements. The following will review the role of SI in motor control elucidated by the single-neurone recording technique.

The fact that the discharge of some SI neurones precedes the onset of movement (e.g., Nelson et al. 1991; Cohen et al. 1994) and the pattern of discharge in some cases closely resembles that the MI neurones suggested that SI could receive the central command for initiation of movement and execution of movement that are then transmitted to MI. However, recent studies have not provided a consensus of SI neuronal firing preceding movement (see below). Unambiguous interpretation of the complex afferent inputs relies on an evaluation in conjunction with copies of the efferent motor signals. Evarts and other investigators have suggested that the connection between SI and MI serves as a transcortical reflex in the guidance of movement (for review, see Evarts 1986), whereas Favorov et al (1988) have suggested instead that the sensory inputs from SI change the excitability of the cortical efferent columns in MI by circulating impulses between the columns and the periphery and that this connection is important for motor learning (for review, see Asanuma 1989; Asanuma and Pavilides 1997).
IVB.1.3.1 Neuronal Activities in Relation to Different Parameters of Voluntary Movements

Relatively fewer studies have investigated the correlation between SI neuronal discharges and features of voluntary movement behaviour. Nevertheless, several studies have suggested that SI and MI may use similar codes that simplify the transformation of information between the movement representations in these two areas.

Jennings et al. (1983) suggested that the activity of the neuronal populations in areas 2 and 3a is sufficient to provide a unique signal of the steady-state position of the forelimb and the force exerted by the forelimb recording SI neurones in monkeys, which were trained to hold the forearm at different pronation-supination postures and to exert different directions and magnitudes of steady torque. In a subsequent study, Evarts et al. (1983) also observed a population of MI neurones with activity related to the position of the forelimb and strongly related to small changes of force. Of particular interest, Fromm and Evarts (1982) showed that PTNs of SI, in accordance with PTNs of MI, show reflex responses to afferent stimuli occurring during the monkey’s performance of a forearm pronation-supination task and that their discharge frequency varies as a function of the strength of muscular contraction. Burbaud et al (1991) studied the neuronal discharge of neurones of areas 2 and 4 in awake monkeys during fast arm movements. They observed that 41% of area 2 and 52% of area 4 neurones show reciprocal activity during the two reciprocal directions of the forearm movement (flexion or extension), and 31% of area 2 and 24% of area 4 neurones have activity related to movement velocity.

The studies by Wannier et al. (1986, 1991) and Hepp-Reymond et al. (1989) indicated that SI neurones have activity related to force regulation during a precision grip task by awake monkeys. There is a similarity between SI and MI in the existence of similar discharge patterns and a linear relation between the firing rate and isometric force; however, differences
exist between SI and MI in the different proportions of neuronal activity patterns, in a late onset of activity change in SI neurones and a larger range of firing rate-force slopes in SI neurones (Hepp-Reymond et al. 1989; Wannier et al. 1986, 1991). The studies by Tremblay et al. (1996) also indicated 22% of texture-related cells are sensitive to contact force. For some of these cells, however, discharge also covaries with speed of contact surface presentation.

Many studies (for review, see Georgopoulos 1995) have pointed out that the primate forelimb MI and posterior parietal cortex appear capable of encoding the direction of an arm reaching movement in space (see section IIIB.1.3.1). Similar observations have made for SI. Cohen et al. (1994) and Ruiz et al. (1995) have presented evidence that activity of group of monkey SI neurones can represent the direction of moving tactile stimuli. The magnitude of the population vector varies with stimulus speed. Cohen et al. (1994) have also provided that SI neurones with forelimb tactile RFs may show “proprioceptive-like” activity during visually cued active movements, even when direct contact of the RFs with external surfaces is avoided. These data suggest that there are dynamically maintained internal representations of sensory environment that are necessary for high-order processing. Prud’Homme and Kalaska (1994) recorded 254 forelimb SI neurones in six monkeys trained to make active arm movements in eight directions away from a central starting position; more than 80% of the neurones showed broad continuous directional tuning resembling the properties of arm-related neurones in motor and parietal cortex in similar task conditions (e.g., Georgopoulos et al. 1982; Kalaska et al. 1983). They also applied external loads to the arm in different directions, which produced changes in muscle activity without altering the hand path or joint angle changes of the arm during the movement the activity of majority of 93 of SI neurones responding to inputs from peripheral proprioceptors was significantly altered by the load. Prud’homme et al. (1994) observed active arm movements evoked directionally tuned tactile and “deep” activity in area
3b and 1, in particular in the deeper cortical laminae that are the source of the descending output pathways from SI. These data suggest that information about both movement kinematics and movement dynamics are represented in SI as well as MI.

Recently, Riehle and Requin (1995) recorded single-neuronal activity in primate premotor cortex, MI, parietal cortex, and SI and suggested that these regions are activated sequentially as behaviours progress from planning to initiation to execution. Interestingly, about half of the neurones in parietal cortex and SI had activity changes related to impending movements during the time between the issuance of the movement cue and the start of the movement.

IVB.1.3.2 Timing of Onset of Neuronal Activity in Relation to Onset of Voluntary Movement—Central and Peripheral Inputs

Anatomical evidence suggests that the feedforward and feedback interconnections between SI and other cortical areas and the parallel ascending inputs contribute to the SI neuronal activity observed during movements. However, it is difficult to distinguish between centrally originating activity and re-afferent activity of SI neurones. This pre-movement activity has been observed in forelimb SI (e.g., Soso and Fetz 1980; Fromm and Evarts 1982; Nelson 1987; Nelson et al. 1991; Cohen et al. 1994) where it has been suggested to be of central origin and may provide for corticofugal modulation of somatosensory inputs prior to and during movements (for review, see Wiesendanger 1981; Chapin 1987); however, the pre-movement activity in SI might also reflect a state of readiness to receive an input (re-afferent) that has not yet arrived or a state of readiness to make a movement, i.e., "the perceptual set" or "motor set" proposed by Evarts and his colleagues (1984).

Bioulac and Lamarre (1979) and Favorov et al. (1988) showed pre-movement activity in forelimb SI and MI neurones in monkeys, both studies suggested that the activity was mainly
peripheral in origin because they could abolish the activity by deafferentation or dorsal column sections. Under some conditions, however, a few SI neurones are active before a measurable limb displacement, and it is unlikely that there is a central source for task-related activity change (Prud'Homme et al. 1994). Under these conditions, the activity of area 3b, which receive sparse precentral connections, is generally larger that in area 1, although areas 3b and 1 receive similar thalamic input. The activity may indicate that area 1 neurones are more likely than area 3b neurones to be suppressed by motor commands issued before movements are made (for review, see Nelson 1996). However, Bioulac and Lamarre (1979) could not completely rule out the existence of internal feedback or of corollary discharges because these inputs may not have been strong enough to overcome the dramatic suppression of the excitability level of SI neurones, suggested by the weakened spontaneous activity, after deafferentation. Although most of their recordings were obtained three to four weeks after deafferentation when the neurone's spontaneous activity had increased, they did not consider the possibility that the motor program may have reorganized so that the corollary discharges/efference copy or corticofugal modulation may not have been necessary because no afferent inputs were expected by the motor centres. This again emphasizes that interpretation of data from lesion experiments may be complicated by the lesion-induced plasticity changes in the CNS.

Although Evarts (1974) had failed to detect SI neuronal discharge prior to EMG onset of a forelimb movement, Fromm and Evarts (1982) subsequently recorded from identified PTNs in SI of monkeys performing a pronation-supination task and demonstrated that these neurones exhibited activity prior to the earliest EMG onset associated with movement. Evarts and Fromm (1981) also suggested that the existence of such pre-movement activity might also depend on the location of neurones recorded and the type of tasks the monkey performed, i.e.,
pre-movement activity in SI might be less likely to be detected in a reaction-time abrupt ballistic movement. Inase (1989) also showed in monkeys that few SI neurones were active prior to a simple key-press digital movement. Wannier et al. (1986, 1991) also suggested that few SI neurones were active prior to a precise grip movement by monkeys, which was consistent with the results of Aizawa and Tanji (1994), who showed that MI neurones activated only by SI stimulation and not by others exhibited later onsets of movement-related activity. Lebedev and Nelson (1995) noted there were rhythmically firing (20-50 Hz) neurones in monkey SI and postulated that rhythmically firing neurones might tonically inhibit rapidly adapting neurones and release them from the inhibition at go-cue onset and prior to voluntary movements. Nelson (1988) showed that pre-movement activity changes that led muscle activation commonly were of different magnitude depending on the modality of the triggering stimulus. However, Wannier et al. (1986, 1991) related the onset of neuronal activity to the change of grip force from a low level to higher level instead of from rest to movement which may explain the discrepancy between their data and others which have shown the presence of pre-movement activity (e.g., Soso and Fetz 1980; Fromm and Evarts 1982; Nelson 1987; Nelson et al. 1991). Nevertheless, the inability to detect pre-movement neuronal activity does not necessarily mean that SI neuronal discharges during the movement are mainly peripheral in origin.

IVC. GENERAL FEATURES OF PRIMARY FACE SOMATOSENSORY CORTEX IN RELATION TO THE CONTROL OF OROFACIAL MOVEMENTS

IVC.1 ROLE OF PRIMARY FACE SOMATOSENSORY CORTEX IN THE CONTROL OF OROFACIAL MOVEMENTS

IVC.1.1 STIMULATION OF PRIMARY FACE SOMATOSENSORY CORTEX
In parallel with the face MI studies showing that surface electrical stimulation can evoke activity of facial, tongue, and jaw-opening musculatures in primates (Penfield and Rasmussen 1950; Walker and Green 1938; Woolsey et al. 1952), surface electrical stimulation over face SI in humans can evoke tongue, lip, and jaw movements (Penfield and Rasmussen 1950; Woolsey 1958; Picard and Olivier 1983). These studies also showed that the tongue is extensively represented over the lateral postcentral gyrus, i.e. the sensation of actual tongue movement, with or without any tongue movement, can be evoked at many sites over the postcentral gyrus (Penfield and Rasmussen 1950; Picard and Olivier 1983).

Although short-train ICMS (200-μs pulses at 333 Hz for 35 ms, ≤30 μA) of face SI is ineffective in evoking any short-latency muscle twitch in monkeys, long-train ICMS (200-μs pulses at 50 Hz for 3 s, ≤60 μA) can evoke tetanic contraction of orofacial muscles and rhythmical jaw movements (RJMs, Huang et al. 1989b) and swallowing (Martin et al. 1999). Studies in anaesthetized subprimates have also suggested that RJMs can be induced from SI regions receiving peri- and intraoral inputs (Morimoto and Kawamura 1973; Lund et al. 1984; Lund and Enomoto 1988). The administration of ketamine (10 mg/kg i.m.) to reduce the animal’s consciousness or the local infiltration of anaesthetics into the RF of neurones in ICMS sites cannot prevent the elicitation of the rhythmic jaw movements, although the thresholds for RJMs do increase after administration of ketamine (Huang et al. 1989b). This suggests the elicitation of the rhythmic jaw movements by ICMS is not due to the peripheral input.

These data suggest that face SI may play an important role in orofacial motor control. Several single-neurone recording and cortical ablation studies have been conducted in relation to chewing or licking movements or voluntary tongue movements (Lin et al. 1993; 1994a) have confirmed the role of the face SI in the control of orofacial movements.
IVC.1.2 LESIONS OF PRIMARY FACE SOMATOSENSORY CORTEX

Although Penfield and Rasmussen (1950) demonstrated that movements of the tongue, lip, or jaw and vocalization or arrest of speech can be evoked by surface stimulation over the human lateral postcentral gyrus, only deficits in sensory discrimination were reported (on the contralateral side of the face and the tongue) after ablation of the lateral central gyrus and no mention was made of any gross motor deficit. However, several studies have demonstrated subtle motor deficits after face SI ablation. For example, Luschei and Goodwin (1975) reported the performance of the biting task was "essentially" normal in the first post-lesion test in one monkey with a bilateral postcentral gyrus lesion. However, they did not explain what they meant by "essentially" normal and did not report any such relevant data in detail.

Kirzinger and Jürgens (1982) made more extensive and bilateral lesions of areas 44, 6b, 4, 3, 1, and 2 in four squirrel monkeys (see also section IIIC.2.2). Immediately after the surgery, all four animals could not feed themselves and swallowing was impossible. The monkeys grasped the food, and pressed it against their lips with the mouth closed; no tongue movement or swallowing occurred if the food was put in the mouth by the experimenters. They observed that swallowing recovered in three days for all the monkeys and unaided feeding recovered four days after the surgery in two monkeys and after seven days in one monkey, but one monkey did not regain this ability within the experiment period (22 post-operative days).

The above review has highlighted the deficiency of knowledge from face SI ablation studies of the role of face SI in orofacial movement control. The above-mentioned studies did not define the cortical regions removed with any method other than anatomical landmarks and most of the ablations included more than the lateral postcentral gyrus. Ablation of CMA in rabbits or monkeys (Luschei and Goodwin 1975; Larson et al. 1980; Enomoto et al. 1987; Inoue 1989) may have included part of the face SI due to the extension of SI onto the
precentral gyrus at the lateral limit of the central sulcus in monkeys (Vogt and Vogt 1919; Jones and Burton 1976), and there is no clear demarcation between face SI and CMA in monkeys and rabbits (Lund et al. 1984; Huang et al. 1989b). The possible involvement of other cortical areas prevents any implication from these studies as to the role of face SI in the control of the orofacial movements studied to date. Also, the inherent problems of ablation studies within the CNS (see section IIIB.1.2) should be kept in mind.

IVC.1.3 LOCAL REVERSIBLE COOLING OF PRIMARY FACE SOMATOSENSORY CORTEX

Bilateral cold block of face SI has been carried out and has provided clearer insights than the experiments with lesions. Face SI cold block disrupts trained orofacial motor behaviour by the monkey, and preferentially disturbs the animal’s performance of a tongue-protrusion task as opposed to a biting task (Lin et al. 1993). Detailed analyses of force and EMG activity showed that the principal deficit produced by bilateral face SI cold block is a reduction in the monkey’s ability to maintain a steady tongue protrusive force in the force-holding period during each trial and to exert a consistent force across different tongue-protrusion trials (see Lin et al. 1993). Bilateral face SI cold block does not significantly affect successful performance of the biting task, consistent with an earlier study reporting that performance of a biting task was normal in one monkey with bilateral cortical lesions limited to the postcentral gyrus (Luschei and Goodwin 1975). However, cooling affects the monkey’s ability to maintain a steady force in the holding period during each bite trial and to exert a consistent bite force across different trials. Unilateral face SI cold block does not significantly affect successful performance of either the biting task or tongue-protrusion task, which may be due to bilateral representations in face SI (Lin et al. 1993).
The differences between face SI and MI (see above) in the effects on tongue motor behaviour of bilateral cooling of each of these regions (e.g. reversible inactivation of face MI by cooling affects the monkey’s ability to exert enough tongue-protrusive force to maintain the required force, whereas bilateral cooling of SI mainly influences its ability to maintain a steady tongue-protrusion force during each trial and to exert a consistent force between different trials), suggest that face MI is important in the generation and fine control of voluntary tongue movements while face SI is important especially in the fine control of these movements. The finding (Lin et al. 1993) of a cold block-induced increase in the variation with which tongue-protrusive force can be maintained by the monkey indicates that the effect of bilateral cooling of face SI on performance of the tongue-protrusion task is likely due to an impairment in sensorimotor integration and in the fine control of force maintenance, and to a lesser extent in the generation of adequate force with the tongue. These data are consistent with findings that digital tactile inputs to the cortex are important in precision grip tasks to adjust the ratio between grip force and load force and that grip force regulation is impaired under digital cutaneous anaesthesia (e.g. Johansson et al. 1992) and with clinical neurological observations that patients with cortical lesions in the postcentral gyrus frequently have deficient digital force control (Pause et al. 1989).

The findings that bilateral face SI cold block preferentially disturbs tongue task as opposed to biting task performance are consistent with single neuronal data. The activity of most SI neurones with a tongue RF (79% of 56) or with a lip RF (60% of 93) was significantly altered during the tongue-protrusion task (Lin et al. 94a,b). The population of face SI neurons related to the tongue-protrusion task is significantly larger than (25%) related to the biting task, thus establishing a neuronal correlate for the findings that bilateral cold block of face SI results in a marked impairment in the performance of the tongue-protrusion task but only minor effects on
the biting task (see above). These data also provide additional evidence indicating an important role for face SI in operantly conditioned orofacial movements.

Similarly, bilateral face SI cold block impaired RJMs and EMG activity associated with mastication and increase the total mastication time (Lin et al. 1998). This was due principally to an increase in the oral transport time (i.e. time for manipulation of bolus after chewing and before swallowing). With chewing time, cooling resulted in a significant increase in anterior digastric muscle duration, a significant delay in the onset of masseter EMG activity, and a significant increase in the variance of geniglossus EMG duration. These data suggest that the face SI play an important role in semiautomatic movements.

The above findings suggest the face SI is involved in the control of semiautomatic movements and the trained orofacial motor behaviours. However, whether the effects of cold block of SI on tongue-protrusion task are due to the block of the sensory input to the MI and other cortical motor areas or due to cold block-induced inactivation of corticofugal effects from SI on subcortical centers involved in somatosensory transmission remains unknown.

IVC.1.4 SINGLE-NEURONE RECORDING DURING VOLUNTARY MOVEMENTS

IVC.1.4.1 Introduction

In the single-neurone recording studies of primate face MI, with the exception of those of Murray and Sessle (1992b,c), who defined the face MI or CMA with ICMS, a problem with most of the studies in the lateral precentral is that no definition was made of the site of neuronal recording other than from anatomical landmarks. Some neurones in the penetration tracks close to the central sulcus in these studies may have indeed recorded activity in face SI, e.g. Lund and Lamarre (1974) recorded single-neurone activity in the lower precentral and superior temporal gyrus in monkeys making voluntary and semiautomatic rhythmic
movements, but their recordings may have included activity from some face SI neurones because rhythmic jaw movements can be evoked from face SI and overlap and no clear demarcation exists between CMA and face SI (Huang et al. 1989b).

Superficial orofacial mechanosensitive inputs have been shown to be a dominant feature of neurones in face SI (see section IVA.1). Superficial mechanoreceptive sensory inputs appear to play an important role in the control of orofacial movements during speech (for review, see Abbs and Cole 1982; Smith 1992). Microneurographic recordings from human infraorbital nerve have shown that many primary afferents with a cutaneous or mucosal RF fire during speech and mastication (Johansson et al. 1988a,b; Nordin and Hagbarth 1989; Nordin and Thomander 1989); microelectrode recordings of somatosensory neurones in the human thalamus have also shown that neurones with a lip or tongue RF are consistently active during the production of speech sounds (McCLean et al. 1990). Appenteng et al. (1982a,b) also reported that many hair afferents and some skin and mucosal afferents in anesthetized rabbits are activated by imposed displacement of the jaw or stimulus-evoked chewing. Therefore, it is conceivable that afferent inputs to face SI may also play a role in orofacial movement control and that these neurones may be active during orofacial movements.

IVC.1.4.2 Single-Neurone Recordings during Orofacial Movements

Yamamoto et al. (1988) investigated the responsiveness of 90 neurones in the somatosensory cortex and gustatory areas during licking and chewing in freely moving rats. These neurones were classified as: “mechanosensitive” (22%), “movement-related”(30%), “taste” (39%), “temperature” (2%), “anticipation” (4%), and “attention” (2%) neurones. For example, mechanosensitive neurones showed rhythmic activity in different phases of the licking cycle, depending on the location of their RF in the orofacial region. Movement-related
neurones changed their activity tonically during licking and chewing; however, their RF could not be identified. They suggested that these neurones with different functions are well organized anatomically within the cortex, and may subserve cortical neural mechanisms involving integration of orolingual sensory inputs, perception of taste, and control of ingestive behaviour. Although Yamamoto et al. (1988) suggested that the neurones recorded were located in the oro-lingual somatosensory and taste areas, it is unclear whether all the neurones were in these areas. First, the position of the electrodes were located according to stereotaxic coordinates and by monitoring activity evoked by passive jaw movements, mechanical stimulation of the oral region by a brush and by anodal current stimulation of the tongue surface (criteria which cannot really differentiate the overlapping SI and MI in rats (e.g., see Sapienza et al. 1981; Wise and Donoghue 1986). Second, the locations in the cortex of only 56 of 90 units were histologically identified. Third, the location of an orofacial RF could only be identified in the "mechanosensitive" neurones and some "taste" neurones.

Lin et al. (1994a) recorded 116 neurones from face SI in the monkey and found most of these neurones during tongue-protrusion and biting tasks exhibited a preferential relation to the tongue-protrusion task as distinct from the biting task, and none showed task-related activity during the biting task only. Some face SI neurones (27% of 101) showed a significant change in firing rate up to 130 ms before a significant change in genioglossus EMG activity associated with the tongue protrusion task. They also noted some SI neurones fire preferentially with a certain direction of tongue-protrusion (Lin et al. 1994b). Furthermore, Lin and Sessle (1994) also found that the trained orofacial movements modulated somatosensory responses of the face SI neurones (see section II.4.).

The studies by Hiraba et al. (1997) investigated face SI neuronal activity during mastication in eight awake cats. 52% (362/699) of the neurones showed activity related some
aspects of mastication and were considered as mastication-related neurones (MRNs). The MRNs were divided into three types by their activity pattern: the rhythmical type, showing rhythmical bursts in pace with the masticatory rhythm; the sustained type, showing a sustained firing during the period of taking food and the transient type, showing intense discharges coincidence with biting hard food. The MRNs had RFs in the perioral, tongue, periodontal and mandibular regions. The activities of mandibular transient MRNs, tongue rhythmical MRNs and periodontal transient MRNs were correlated with food texture, whereas perioral rhythmical MRNs, perioral sustained MRNs and tongue sustained MRNs were not. Both facial and intraoral MRNs were scattered throughout the facial and intraoral projection areas in SI. These findings provide evidence that orofacial SI monitors masticatory movements for food ingestion. The authors did not apparently consider the possibility that some of the activity may be related to corticofugal modulation of the central pattern generator for mastication or somatosensory transmission during mastication.

The ablation, surface stimulation and ICMS studies reviewed above suggest face SI may play a role in orofacial movement control. In addition, single neurone recordings of behaving monkeys have shown that, during trained orofacial movements, activity patterns of SI as well as MI neurones may correlate with various parameters of movements. While a variety of different neuronal activity patterns in face MI suggest their involvement in control of tongue and jaw movements and face MI neurones have been shown capable of encoding directions of tongue movement, comparable data are also available for face SI. Analogous findings in limb SI (see section IVB.1) have led to the suggestion that the activity of limb SI neurones may be involved, on one hand, in the sensory guidance or control of voluntary movements; on the other hand, the pre-movement activity of forelimb SI neurones suggests that some SI neuronal activity may be central in origin and may be involved in the corticofugal control of somatosensory responses prior
to and during the movement. Corollary discharge or efference copy theory suggests that the afferent signals elicited by movements are operated upon in conjunction with the motor command which informs the analyzing centres (e.g., SI) that the sensory signals are self-generated rather than externally generated. Indeed, numerous studies have shown that somatosensory responses can be modulated during movements and that SI may have the ability to shape the movement-related activity during movement. Thus, SI may transmit somatosensory information important in the control of voluntary movement and also be involved in the learning of motor tasks.

V. STATEMENT OF THE PROBLEM AND AIMS OF THE STUDY

The above literature review demonstrates the relatively extensive body of knowledge of the importance of the forelimb SI in the control of voluntary forelimb movements and the growing understanding of the role of face MI in the control of voluntary orofacial movements. While studies considering the role of face SI in the control of voluntary orofacial movements are very limited, some insights have been provided in the limited number of studies that have applied single-neurone recording and cortical stimulation and ablation techniques to investigate the role of face SI in orofacial movements. Nevertheless, current data lack information about how face MI uses peripheral sensory information and many details of involvement of face SI in motor control remain unclear.

The activity of limb SI neurones may be involved in the sensory guidance or control of voluntary movements; on the other hand, the pre-movement activity of forelimb SI neurones suggests that some SI neuronal activity may be involved in the corticofugal control of somatosensory responses prior to and during the movement. Earlier studies have indicated that there are parallel inputs to MI and SI and impairment of forelimb movement caused by cold block of SI may be due to cold block-induced inactivation of corticofugal effects from SI on subcortical
centers involved in somatosensory transmission. While a variety of neuronal activity patterns in face MI suggest their involvement in control of tongue and jaw movements and face MI neurones have been shown capable of encoding directions of tongue movement, comparable data are also available for face SI. Indeed, recent data suggest that face MI and SI may have some role in semi-automatic movements such as mastication and swallowing, but questions remain, such as what is the exact role of face MI in the control of mastication? Do the neurones showing tongue task-related activity also show chewing-related activity? Furthermore, as outlined above, most face MI neurones receive an orofacial mechanosensitive afferent input and both face SI and MI play an important role in the control orofacial movements. These findings raise the question: whether face SI could conceivably contribute to motor control by relaying its orofacial afferent inputs to face MI and thereby influence both the responsiveness to orofacial stimuli and the movement-related activity of face MI neurones. Does the role of face MI in the control of tongue and chewing movements depend on the functional integrity of face SI? Many studies have shown that SI has the ability to shape the movement-related activity during movement. For example, Lin and Sessle (1994) have shown orofacial movements modulate the evoked somatosensory responses of face SI neurones. Is it possible that, as suggested for limb MI, afferent inputs to face MI are modulated during orofacial movements so that only selected inputs useful in guiding the movement or in adapting the movement to an altered orofacial environment gain access to MI? Does face SI contribute this modulation?

In view of these unresolved matters, the present study was initiated with the following aims: to test 1) whether face MI neurones show chewing-related activity as well as activity in other orofacial movements and to define the features of the chewing-related activity; 2) whether ipsilateral face SI cold block could affect chewing and tongue-protrusion task as well as face MI neuronal activity related to chewing or tongue task; 3) whether chewing modulates
the evoked somatosensory responses of face MI neurones; and 4) whether ipsilateral face SI
cold block can also affect face MI neuronal activity evoked by orofacial stimulation.
INTRODUCTION

Recent studies conducted in our laboratory have suggested that face MI plays an important role in the generation and control of tongue and facial movements with only a minor role in the control of jaw-closing movements (Murray and Sessle 1992b,c; Murray et al. 1991). Specifically, Murray et al. (1991) showed that reversible inactivation by cooling of the primate face motor cortex, including tongue MI, significantly reduced the successful performance of a trained tongue-protrusion task by monkeys and showed little effects on a biting task. Consistent with this finding, single neurones located at tongue MI sites exhibited activity patterns that were related to a trained tongue-protrusion task but not a trained biting task (Murray and Sessle 1992b,c).

Whereas face MI has been implicated in the control of voluntary tongue movements, the extent to which face MI also plays a role in the regulation of semiautomatic tongue movements, such as those produced during mastication, remains unclear. However, there are several lines of evidence from approaches utilising cortical inactivation or ablation, stimulation, and recording of single neuronal activity that point to the possibility that the lateral pericentral cerebral cortex may play a prominent role in chewing. For example, bilateral ablation of the face area of the primate precentral cortex, including Brodmann’s areas 4 and 6 (Luschei and Goodwin 1975; Larson et al. 1980), and of the more laterally located CMA (Lund and Lamarre 1974) has been reported to give rise to masticatory deficits. Recent studies from our laboratory have shown that reversible inactivation by cooling of the lateral
pericentral cortex results in a reduction of the incidence of swallowing after chewing as well as alterations in swallow and chewing-related EMG patterns in awake monkeys (Narita et al. 1999; Sessle et al. 1995b). 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 elicited by electrical stimulation of the pons in the anaesthetised rabbit and with the recent PET study in human by Hamdy et al. (1999) demonstrating increased regional cerebral blood flow within bilateral Brodmann’s areas 3, 4 and 6 and several other cortical areas during swallowing.

Cortical stimulation studies also have pointed to a prominent role for the lateral pericentral cerebral cortex in mastication and swallowing. Repetitive electrical stimulation of regions of the anterolateral frontal and lateral pericentral cortex has been shown to evoke chewing-like rhythmic jaw movement and/or swallowing in a number of species, including man (Penfield and Rasmussen 1950; Car 1970; Miller and Bowman 1977; Martin et al. 1993, 1999; Huang et al. 1989b). These evoked rhythmic chewing-like movements are frequently followed by swallowing. However, rhythmic chewing-like movements also can be elicited from more widespread cortical areas (Sumi 1969; Lund and Lamarre 1974; Huang et al. 1989b; Martin et al. 1999).

Single neurone recording studies in monkeys have shown that some neurones 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, mastication, and/or swallowing (Kubota and Niki 1971; Luschei et al. 1971; Lund and Lamarre 1974; Hoffman and Luschei 1980; Murray and Sessle 1992b). For example, Kubota and Niki (1971) reported that 74 of 77 neurones recorded in the lateral precentral
cortex of awake monkey exhibited phasic alterations of firing in association with rhythmical jaw-opening or closing movements. Martin et al. (1995, 1997) also reported some neurones within ICMS-defined tongue MI showed significant alterations of activity in relation to chewing and the swallowing of a juice reward and/or mastication.

Taken together, these studies implicate overlapping regions of the cerebral cortex in chewing and in a number of related ingestive and alimentary functions such as swallowing. We chose to examine specifically the role of face MI in chewing and swallowing for several reasons. First, previous studies from our laboratory showed that the activities of some face MI neurones appear to be modulated during ingestive movements and that chewing-like rhythmic movements and swallowing can be evoked by ICMS of face MI in awake monkeys (Huang et al. 1989b; Martin et al. 1993, 1995, 1997; 1999; Sessle et al. 1995a) and chewing and swallowing may be disrupted by cold block of the ICMS-defined face MI or swallow cortex, including the lateral portion of tongue MI (Sessle et al. 1995b; Narita et al. 1999). Second, given the previous findings of Murray et al. (1991) and Murray and Sessle (1992b,c) suggesting a prominent role for tongue MI in voluntary tongue movements, an investigation of tongue MI in chewing and swallowing would afford the opportunity to clarify and compare the role of this cortical region in semiautomatic versus voluntary motor behaviours. Thirdly, 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 Miller 1982; Cunningham et al. 1991). As such, a fuller account of the neural mechanisms mediating chewing and swallow-related tongue movements is essential to a comprehensive understanding of chewing and swallowing.

Therefore the aims of the present study were: 1) to determine whether neurones within
the ICMS-defined face MI significantly alter their firing rates in relation to mastication; 2) to determine whether face MI neurones that exhibit mastication-related activity patterns also significantly alter their firing rates during the swallowing events following mastication and a voluntary, trained tongue-protrusion task; 3) to determine the ICMS effects at face MI sites where neurones exhibiting mastication-related firing patterns are found and to relate these ICMS effects to the chewing-related neuronal firing patterns observed, and 4) to determine the RF properties of tongue MI neurones exhibiting firing patterns related to mastication.

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

METHODS

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. Since the methods have been described in detail (Murray et al. 1991; Murray and Sessle 1992a, b; Lin et al. 1993; Martin et al. 1997;), 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% halothane; maintenance: 0.5-1.5% halothane). The head cap supported a stainless-steel cylinder (25 mm in diameter) that was implanted over the exposed dura covering the lateral pericentral cortex. Electrodes (36-40 gauge, single-stranded, Teflon-coated stainless steel: Cooner Wire, Chatsworth, CA) were placed unilaterally in the genioglossus (GG), masseter (MA), and anterior digastric (AD) muscles to record chronically their EMG activity. After the animal recovered from the surgery, it was trained in a tongue-
protrusion task. The tongue task was the same as that previously described in detail by Murray et al. (1991), Murray and Sessle (1992b) and Martin et al. (1997). Briefly, the task required the monkey to protrude its tongue onto a force transducer that was affixed in front of the monkey rigidly to a beam on the primate chair in which the monkey sat. The transducer output controlled the vertical position of a cursor on a computer monitor also located in front of the monkey. For each tongue-protrusion trial, a computer-controlled baseline window appeared initially at the bottom of the computer screen and, after a pre-trial period (PTP), was displaced instantaneously to a preset target-window level (equivalent to a force of 1.0 N) on the computer screen. This was the cue for the monkey to protrude its tongue symmetrically toward a conical force plate attached to the transducer and located in the midline, 2 mm anterior to the most anterior portion of the upper lip, with its center level with the vermillion border of the upper lip. The monkey had to move the cursor into the target window and then hold the cursor within the window for a specified minimum holding phase (usually 0.3-0.5 s).

The following tongue-task periods were defined: a PTP during which the baseline window remained at the bottom of the screen; a dynamic phase, representing the period from the onset of significant rise in GG EMG activity to the moment that the cursor entered the target window; a holding phase, which was the period from entry of the cursor into the target window to the end of the 0.3- to 0.5-s holding phase; the task period, which was defined as the period composed of both the dynamic and holding phases. A successful tongue-protrusion trial was one that met the following criteria: the cursor remained within the baseline window during the 1- to 1.5-s PTP; the cursor exited the baseline window within 3 s of target window appearance; and the cursor remained within the window for the specified minimum holding phase. A successful trial was rewarded at the termination of the holding phase with 0.4 ml of
fruit juice delivered automatically to the monkey through a tube that opened at the apex of the force plate. “Unsuccessful” trials were not rewarded.

After the monkey was trained, the face MI was next identified and mapped for evoked orofacial twitch-like movements by applying ICMS \( \leq 30 \, \mu A, \, 35\text{-ms train of 12 cathodal pulses, each pulse 0.2 ms}, \, 333 \, \text{Hz (short-train stimulus, T/S)} \) during daily transdural microelectrode penetrations of the precentral cortex, as previously detailed (e.g. Murray and Sessle 1992a; Martin et al. 1997). These MI mappings took 2-3 weeks. A longer pulse ICMS train \( [3 \, \text{s-train, 0.2-ms pluses at 50 Hz,} \leq 60 \, \mu A \, \text{(continuous stimulus; C/S)}] \) was applied to evoke semi-automatic movements at \( \leq 500\text{-\mu m} \) intervals along each microelectrode penetration to a depth of 8-10 mm (Huang et al. 1989b; Martin et al. 1999).

Extracellular recordings were made with glass-coated tungsten electrodes \( (Z = 0.5-2 \, \Omega \, \text{at 1 kHz}) \) in the daily sessions from two hemispheres of both monkeys to examine the activity of single neurones at ICMS-defined sites within the ipsilateral face MI (Huang et al. 1988; Murray and Sessle 1992a, b; Martin et al. 1997) during chewing of standardised amounts of fruit (apple, \( 10 \times 6 \times 6 \, \text{mm} \)) and during the trained tongue-protrusion task. Neurones were searched for that showed chewing and/or tongue protrusive-related activity. EMG recordings were made simultaneously with single neurone 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. A minimum of 7 successful task trials or 10 masticatory trials were carried out. Some neurones also were tested for a RF by applying light tactile stimuli with hand-held probes and firm non-noxious mechanical stimuli to the skin of the face and to the oral cavity (Murray and Sessle 1992a, b).

Force, EMG, and neuronal spike data were digitised (EMG activity full-wave rectified
and smoothed, time constant 20 ms; sampling rate/channel: force 200/s, EMG 3125/s, neuronal spike event data 200/s) with the Cambridge Electronics 1401 data acquisition system and Spike2 analysis package. As previously described (Martin et al. 1997; Murray and Sessle 1992a, b), digitised data related to the tongue task were analysed by aligning trials to the onset of the significant increase in GG EMG activity after target window appearance. The onset of a significant increase in EMG activity was defined as the point in each trial at which the analog signal exceeded two standard deviations (SD) of the mean level of EMG activity during the PTP for the trial for > 200 ms. Neurons were 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 EMG 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 EMG activity associated with mouth opening to obtain the test food to the onset of the GG EMG activity associated with swallowing. 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 onset of the first AD EMG burst as the animal opened its mouth to obtain food to the end of this EMG burst (initial jaw opening) plus the period from this latter time point to the start of rhythmic chewing (food transportation). The rhythmic chewing phase was defined as the period from the end of the food preparatory phase to the end of MA EMG activity related to the rhythmic chewing. The pre-swallowing phase was defined
as the period from the end of the rhythmic chewing to the onset GG EMG activity related with swallowing.

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

A neurone was considered as swallow-related only if there was a significant alteration of neuronal firing rate, relative to the neuronal activity during the PTP (see definition above), during the 50-ms interval immediately before the GG activity defined swallow onset, the swallow (i.e. the interval between the GG activity defined swallow onset and offset (Martin et al. 1997) or both the 50-ms interval and the swallow. For each neurone, a repeated measure analysis of variance 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 neuronal firing frequency associated with liquid-swallow
following successful performances was compared with that associated with solid bolus-swallow following chewing (paired t-test). \( P < 0.05 \) was considered statistically significant. Values were expressed as mean ± SD.

**Histological Procedures**

These were similar to those previously described (e.g. Huang et al. 1989b; Murray et al. 1991). Briefly, in each hemisphere and just before sacrifice of the animal, electrolytic lesions (10-20 μA cathodal current for 10-15 s) with glass-coated tungsten electrodes were placed at selected intracortical sites or at the bottom of electrode tracks. In other selected intracortical sites, electrokytic lesions (30-50 μA anodal current for 30 s) were achieved with epoxylite-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 anaesthetised with pentobarbital sodium (30 mg/kg i.v.) and perfused thorough the heart with heparin-saline followed by 2% potassium ferricyanide in 10% buffered formalin. The block of cortical tissue was stored in 2% potassium ferrocyanide in 10% buffered formalin for 2 weeks and serial paraffin sections (20 μm thick) were prepared and stained, and the locations of intracortical lesion sites were assessed; these sites were then correlated with the borders of the different cytoarachitectonic areas (see Jones et al. 1978; Sessle and Wiesendanger 1982).

**RESULTS**

*EMG Activity Patterns Associated With the Masticatory Sequence*
The masticatory sequence (Fig. II-1) was the whole set of movements from ingestion to swallow. It was made up of a food preparatory phase, rhythmic chewing phase, and pre-swallowing phase. Each food preparatory phase contained an initial jaw-opening phase and a food transportation phase. During the masticatory sequence, the food was gathered during the initial jaw opening phase, moved backward to the molars during the food transportation phase, then broken down during the rhythmic chewing phase and prepared for swallowing during the pre-swallowing phase.

Once food was ingested, the monkey used 3 basic types of cycles that differed in shape, duration, and number of phases to prepare for swallowing. One of these basic types of cycles in the rhythmic chewing phase was similar to the type II cycles described by Schwartz et al. (1989) in the rabbit. Briefly, the cycles during the rhythmic chewing phase had three phases, namely opening phase, fast closing (FC), slow closing (SC) phase. Since the monkeys chewed unilaterally, the jaw usually moved to the working side (the side, in which foodstuff existed between the molars) during FC. SC began with peak of deceleration of jaw, which was more obvious during chewing hard food. Pre-swallowing phase was characterised by very active GG, little MA EMG activity, larger lateral movement and wider cycles. However, there were not clear 5 phases in the cycles: FC, SC, O1 (a brief but rapid early opening), O2 (a pause), and O3 (final rapid opening phase), as noted by Schwartz et al. (1989) in the rabbit. During the food preparatory phase, there were no clear rhythmic cycles as occurred in rhythmic chewing and in the pre-swallowing phase.

As previously described (Martin et al. 1997), swallowing following mastication was characterised by no jaw movement, a larger and longer GG EMG duration than that during the rhythmic chewing phase, and synchronisation of GG, MA, and AD activity.
General Features of the Face MI Neurones

The activity of a total of 107 neurones was recorded from the ICMS-defined face MI of both monkeys. Not all of these neurones were examined during both chewing/swallowing and tongue task/swallowing performance. Figures II-2, II-3, and II-4 show orofacial motor responses to T/S and C/S ICMS delivered to sites along microelectrode penetrations within lateral pericentral cerebral cortex, and the spatial distribution within face MI of penetration tracks within which chewing-related neurones were recorded and face MI neuronal RFs were delineated. Of the 107 neurones, 41 neurones were tested for only chewing-related activity, 32 neurones were tested for both chewing and task-related activity, and the remaining 34 neurones were tested only for tongue task-related activity. All neurones that showed chewing-related activity and/or tongue-protrusion task-related activity were also examined for swallowing-related activity.

Of 73 chewing-related neurones (Table II-1), 55 were tested for afferent input. An orofacial RF was found in 45 (81%) of these neurones. For 38 of these 45 neurones, the RF was on the superior tongue surface (e.g., Fig. II-4); the remaining neurones had a RF on the lip, face or intraoral mucosa (Table II-2). One neurone with an inhibitory RF on the tongue surface was also found. Of the 66 neurones examined during the tongue task, 44 were tested for an orofacial sensory input, and an orofacial RF could be delineated in 30 (69%). In 23 of these 30 neurones, the RF was on the superior tongue surface; the remaining neurones had a RF on the lip and oral mucosa.

Chewing-related Neuronal Activity Patterns During Food Preparatory and Rhythmic Chewing Phase
Four main patterns of chewing-related activity could be distinguished (see Figs. II-5-II-9, Table II-1). The majority of neurones (n = 52, i.e. 71%) showed a clear rhythmicity during the rhythmic chewing phase (e.g. Figs. II-5 and II-6) but 10 neurones (14%) had increased activity only when the monkey’s mouth initially opened to obtain food or just before rhythmic chewing (Fig. II-7), 7 (10%) fired tonically throughout the total masticatory period (Fig. II-8), and 4 (5%) had a decrease in activity (Fig. II-9) during this period (Table II-1); 3 of the 73 neurones showing these patterns also fired before (366 ± 169 ms) the initial jaw-opening to obtain food. In 24 (46%) neurones that showed rhythmical activity, each rhythmical burst occurred during the jaw-opening phase of each chewing cycle (Fig. II-6). In the remaining 28 (54%) neurones the rhythmic burst occurred during the early part of jaw closing before the onset or during MA EMG activity (Fig. II-10); 44 (85%) of the neurones showing rhythmical activity also increased their firing during initial jaw opening and/or food transportation (Table II-3, Fig. II-11). Whereas 14 (50%) jaw closing-related neurones showed only food transportation-related activity, 12 (50%) jaw opening-related neurones showed both initial jaw opening and food transportation-related activity. 3 (11%) of the jaw closing-related neurones showed only initial jaw opening-related activity and 7 (25%) of the jaw closing-related neurones showed both initial jaw opening and food transportation-related activity (Table II-3). A variety of orofacial movements could be evoked by ICMS applied at the neuronal recording sites (Table II-4, Figs. II-2 and II-4). Whereas tongue protrusion was evoked by ICMS at most of the loci (64%) showing rhythmic jaw opening-related neuronal activity, tongue retraction was evoked by ICMS at most (67%) loci from which the jaw closing-related neurones were recorded (Table II-4).

The maximum jaw-opening occurred after (58 ± 7 ms, n = 20) the corresponding peak
EMG activity in the AD muscle. Further analysis of 44 of those 52 neurones with chewing-related rhythmicity revealed that the peak activity of the jaw opening-related neurones occurred before (32 ± 43 ms, n = 21) the corresponding peak EMG activity in each rhythmic burst in the AD while the peak firing of jaw closing-related neurones was later (112 ± 53 ms, n = 23) than the peak of the AD EMG activity. The majority of these jaw opening-related neurones showed peak activity in the late part of jaw opening, and most of the jaw closing-related neurones showed peak activity in the early part of jaw closing (Fig. II-10). The peak firing frequency of the jaw opening-related neurones (71 ± 37 Hz, n = 21) was not significantly different from that of the jaw closing-related neurones (62 ± 36 Hz, n = 23). During the food preparatory phase, the peak of the initial jaw opening-related activity (87 ± 24 Hz, n = 14) of the jaw opening-related neurones occurred before (97 ± 175 ms, n = 14) the peak of the initial jaw opening-related AD EMG activity, and that of the jaw closing-related neurones (69 ± 29 Hz, n = 10) also occurred before (17 ± 250 ms, n = 10) this initial peak. In contrast, the peak food transportation-related activity (90 ± 31 Hz, n = 13) of the jaw opening-related neurones and that of the jaw closing-related neurones (69 ± 36 Hz, n = 17) occurred after (435 ± 160 ms, n = 13; 314 ± 151 ms, n = 17, respectively) the initial jaw opening-related peak AD EMG activity.

For those neurones showing only activity during the food preparatory phase, the peak of the initial jaw opening-related neuronal activity (94 ± 85 Hz, n = 8) occurred before (456 ± 1033 ms, n = 8) the peak of the initial jaw opening-related AD EMG activity while the peak of
the food transportation-related activity (73 ± 35 Hz, n = 5) occurred (640 ± 139 ms, n = 5) after
this peak. The peak of the food transportation-related activity of the neurones showing only
food preparation-related activity occurred significantly (P < 0.05, one-way ANOVA) later than
that of jaw opening-related or closing-related neurones showing also rhythmic activity; there
was no significant difference in other parameters between these neurones.

Pre-swallow and Swallow-related Neuronal Activity Patterns

Consistent with the description by Martin et al. (1997), 32 of those 73 neurones
showing chewing-related activity also showed jaw movement-related activity during the pre-
swallow phase and neuronal activity alteration during the 50-ms interval preceding swallow
onset and/or during the GG-defined swallow onset and offset and 23 showed only jaw
movement-related activity during the pre-swallow phase. Of the 24 rhythmic jaw opening-
related neurones, 8 showed both pre-swallow related activity and neuronal activity alteration
during the 50-ms interval preceding swallow onset and/or during the GG-defined swallow
onset and offset and 12 showed only pre-swallow jaw-movement related activity. Of the 28
rhythmic jaw opening-related neurones, 16 showed both pre-swallow related activity and
neuronal activity alteration during the 50-ms interval preceding swallow onset or/and during
the GG-defined swallow onset and offset and 11 showed only pre-swallow jaw movement-
related activity. Of the 7 neurones showing tonic excitation during mastication, 3 showed both
pre-swallow related activity and neuronal activity alteration during the 50-ms interval
preceding swallow onset or/and during the GG-defined swallow onset and offset and 2 showed
only pre-swallow jaw movement-related activity. Of the 4 neurones showing depressed activity
during chewing, all showed pre-swallow related activity and neuronal activity alteration during
the 50-ms interval preceding swallow onset or/and during the GG-defined swallow onset and offset. However, none of the 10 food preparation-related neurones showed any pre-swallow or swallow-related alteration in activity.

Of the 32 neurones that showed significant alterations of activity in relation to swallow, 5 showed a significant alteration of firing during the 50-ms interval preceding swallow onset activity and 13 showed a significant alteration of firing during the swallow and 14 during both.

Task-related Neuronal Activity Patterns

Of the 66 neurones examined for task-related activity, 47 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 neurones (62%), 3 (6%) had phasic-off-tonic activity, 5 (11%) phasic firing, and 10 (21%) depressed activity associated with the task; in addition, 3 of these neurones increased firing before (321 ± 143 ms) the onset of GG EMG activity associated with the animal’s initiation of tongue protrusion.

Of the 66 neurones examined for task-related activity, 39 (59%) showed activity alteration during the 50-ms interval preceding swallow onset or/and during the GG-defined swallow onset and offset. Of the 39 neurones that showed significant alterations of activity in relation to swallow, 4 showed a significant alteration of firing during the 50-ms interval preceding swallow onset activity and 22 showed a significant alteration of firing during the swallow and 13 during both. Of the 47 neurones showing task-related activity, 29 (62%) demonstrated activity alteration during the 50-ms interval preceding swallow onset or/and during the GG-defined swallow onset and offset.
A total of 22 of these task-related neurones was also tested for chewing-related activity which was documented in 21 of them. Of these 21 neurones showing both task and chewing-related activity, 3 (15%) showed rhythmic jaw opening-related activity, 10 (47%) showed rhythmic jaw closing-related activity, 5 (23%) showed activity related to food preparation, 2 (10%) showed tonic firing during chewing, and 1 (5%) showed depressed activity during chewing. Of the 21 neurones, 16 showed both task and chewing-related increase in neuronal activity, 4 showed task-related inhibition and chewing-related excitation, and 1 showed both task and chewing-related inhibition of neuronal activity. In the 16 task and chewing-related neurones, the peak firing frequency was $82 \pm 30, 96 \pm 45, 60 \pm 45, 51 \pm 34$ Hz for the task, the food preparation phase, rhythmic chewing phase and pre-swallowing phase during chewing, respectively. There was no significantly difference (one-way ANOVA with repeated measures) between the peak firing frequencies during the task and during chewing except that the peak firing frequency during the pre-swallowing phase was lower than that during the task.

In the 4 neurones showing task-related depression and chewing-related excitation, the peak firing frequency was $27 \pm 24, 75 \pm 15, 89 \pm 66, 69 \pm 48$ Hz for the task, the food preparation phase, rhythmic chewing phase and pre-swallowing phase during chewing, respectively. Although there was a tendency that the peak firing frequencies during chewing to be higher than those during task, there was no significant difference (one-way ANOVA with repeated measures) between the peak firing frequencies during the task and during chewing.

Of the 21 neurones showing both task and chewing-related activity, 11 showed swallow-related excitation and 2 showed swallow-related inhibition of neuronal activity. For these 11 neurones showing swallow-related excitation, the peak neuronal firing frequency associated with liquid-swallow following successful task performances ($101 \pm 92$ Hz) was not
significantly different (paired t-test, $P>0.05$) from that associated with solid bolus-swallow following chewing ($60 \pm 34$ Hz).

DISCUSSION

The present study has demonstrated that many face MI neurones that altered their firing rates in relation to a voluntary movement, in the form of the trained tongue protrusion and tongue movement during the food preparation phase of mastication, also showed modulated activity in relation to chewing and swallowing; many of these neurones also displayed swallow-related activity. The chewing and swallow-related neurones exhibited a variety of activity patterns. Many received orofacial afferent inputs especially from the superior tongue surface and they were recorded at sites where ICMS evoked a variety of types of tongue movement. Tongue protrusion was evoked by ICMS at most of the loci (64%) showing jaw opening-related rhythmic neuronal activity, whereas tongue retraction was evoked by ICMS at most (67%) loci from which the jaw-closing related neurones were recorded. The present study has also confirmed the previous observations in our laboratory (Huang et al. 1989a; Martin et al. 1999; Sessle et al. 1995a) that long train ICMS within the primate lateral tongue MI can evoke rhythmic jaw movements. These findings suggest that the 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.

Involvement of Motor Cortex in Chewing

Classically, voluntary movements of the body are considered to be controlled by
supraspinal and suprabulbar structures, including the motor cortex in particular, whereas semiautomatic movements are thought to be generated and regulated primarily at the spinal and bulbar levels. In the case of chewing, much of the circuitry for the control of chewing-related movements is thought to be located within “the chewing centre” in the brainstem (for review, see Dubner et al. 1978; Luschei and Goldberg 1981; Lund 1991; Nakamura and Katakura 1995). Although there is mounting evidence for an involvement of the brainstem in chewing and swallowing, there has been relatively little emphasis on the contribution of motor cortex to the initiation and regulation of chewing.

Our findings of movement-related activity patterns in face MI neurones recorded at sites from which ICMS evokes tongue movements, are consistent with earlier reports that show activity related to a trained tongue task or chewing (e.g., Kubota and Niki 1971; Luschei et al. 1971; Kubota 1976; Hoffman and Luschei 1980; Murray and Sessle 1992b). Taken together with our earlier neuronal and ICMS data, they are also consistent with the view that multiple, discrete efferent zones exist for the production of elemental tongue movements and for tongue movements associated with semi-automatic movements such as chewing. Thus, the combined activation of different efferent zones could contribute to the neural framework required for the complexity of tongue movements in orofacial motor behaviours and to the need for close neuronal integration for control of these behaviours.

Furthermore, our data revealing that substantial numbers of MI neurones display chewing-related activity add further evidence in support of the view, based on the effects of disruption or ICMS of face MI and earlier recordings of chewing-related activity in face MI (Penfield and Rasmussen 1950; Kubota and Niki 1971; Luschei et al. 1971; Luschei and Goodwin 1975; Huang et al. 1989b), that face MI plays an important role not only in the
control of voluntary movements such as trained tongue protrusion, but also in semi-automatic movements (see Sessle et al. 1995a). The chewing-related activity of the face MI neurones revealed 4 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 the small number of MI neurones that we found showing increased activity only during the food preparatory phase or showing decreased activity. The findings suggest that the various types of chewing-related activity may reflect different types of cortical neurones (for example, corticobulbar projection neurones, cortical interneurones, and corticocortical association neurones) involved in driving chewing-related movements or in responding to movement-evoked afferent inputs or in some other form of sensorimotor integration related to chewing. In addition to the neurones which only showed an increase in activity during food preparation phase, the majority of rhythmic jaw movement-related MI neurones also showed food preparation-related activity (Table II-3). The findings are consistent with our observations of a marked tongue movement deficit during the food preparation phase caused by bilateral inactivation of face MI by cooling (unpublished observation). Some MI neurones showed altered activity only during the interval immediately preceding the EMG-defined chewing onset, that is, in advance of chewing. Thus it is likely that these neurones may be involved in driving tongue motor units in chewing rather than their activity being, for example, simply a reflection of movement-generated reafference (see below). It is possible that these early firing MI neurones could be involved in the cortical initiation of chewing, including the driving of specific muscles. Nonetheless, other chewing-related MI neurones were activated during the chewing itself, and so, these neurones may initiate or drive motor units later in the chewing synergy. These different neuronal firing
patterns may have been related to differences in the duration and relative timing of chewing-related EMG bursts across the changing chewing conditions as the foodstuff was tritured. In addition, our present studies have also shown that ICMS at most loci showing rhythmic jaw-opening related neuronal activity produced tongue protrusion whereas tongue retraction was evoked by ICMS at most loci from which jaw-closing related neurones were recorded (see Table II-4). This suggests face MI might play an important role in coordination of the tongue and jaw movement to prevent damage of the tongue during chewing.

Our present studies have demonstrated that some tongue MI neurones may show activity not only in relation to chewing or the tongue-protrusion task but also in relation to the semi-automatic movement of swallow. One possible interpretation for this finding is the tongue movements involved in chewing and tongue protrusion are not specific to these behaviours, but rather are also incorporated into the movement sequence of swallowing. Thus a given tongue MI neurone may be activated during both activities because the same movement subunit of the motor cortex is recruited. The population of activated tongue MI neurones presumably would be distinct, however, underlying the distinct tongue movement sequences seen in, for example, swallowing, licking, and chewing (Dubner et al. 1978; Hiiemae and Crompton 1985; The Benton and MaGarrick 1988, 1989). Another interpretation is that the activity of these tongue MI neurones in both swallowing and chewing reflects the needs for a close neuronal integration of the control of these various motor activities. Our findings are also consistent with the other studies (Huang et al. 1989b; Martin et al. 1999) showing an extensive overlap of swallow cortex and CMA defined by long train ICMS in the awake monkey. On other hand, we also noticed that tongue neurones which only showed food preparation-relation activity did not exhibit any pre-swallow or swallow-related activity. The
possible interpretation of this finding is that tongue movements during the food preparation phase are specific to this behaviour, not being incorporated into the movement sequence of swallowing.

*Contribution of Somatosensory Inputs*

The data describing the mechanoreceptive afferent input to tongue MI in the present study are consistent with the previous findings in our laboratory (Murray and Sessle 1992a; Martin et al. 1997) in terms of the portion of recorded neurones with an orofacial identified RF and the location of the RFs. The present study confirmed that tongue MI receives substantial sensory inputs from intraoral sites, in particular the tongue dorsum. Our finding that the majority of tongue protrusion, chewing and swallow-related neurones had a RF on the tongue dorsum is consistent with the notion that oral mechanoreceptive inputs are important in the regulation of orofacial movement. For example, such sensory inputs may be very important for preventing damage of the tongue during chewing by modulating tongue movement during the rhythmic chewing phase. The view is supported by recent studies by Lin et al. (1998) showing an increase in the pre-swallowing phase duration and a significant increase in the variance of GG EMG duration during bilateral inactivation of the monkey’s face SI which is a source of input to face MI. Similarly, afferent input is suggested to play an important role in swallowing by the findings that certain aspects of the swallow, e.g. the amplitude and velocity of tongue movement, can be modulated by bolus characteristics (Halmet 1989; Martin 1991; Kahrilas et al. 1993). It is nonetheless unclear the extent to which this afferent-induced modulation is dependent upon sensorimotor cortex as opposed to brainstem circuits.

Also still uncertain is the extent to which movement-related activity of MI is of central
origin or reflects sensory inputs from the periphery. Data from the limb sensorimotor cortex have revealed that the movement-related activity of many limb MI neurones is not a reflection of reafferentation although there is also some contrary evidence (for review, see Asanuma 1989; Wise 1993; Georgopoulous 1994; Nelson 1996). Our data are also in accord with the view that reafferentation is not a major factor accounting for the movement-related activity of MI neurones, although we cannot exclude in these experiments the possibility that this activity may be a reflection, at least in part, of peripherally evoked orofacial afferent inputs accessing face MI by routes other than through the ipsilateral face SI e.g. other ipsilateral cortical areas, ipsilateral posterior thalamus, contralateral sensorimotor cortex (e.g. Aizawa and Tanji 1994; Jones 1986; Kaneko et al. 1994; Nelson 1996). Nevertheless, there are several other lines of evidence indicating that the MI movement-related activity patterns in most MI neurones might not simply be due to reafference via SI or other peripheral input pathways to MI. First, not all task or chewing- or swallow-related MI neurones had a detectable RF from which orofacial excitatory inputs could have been activated during orofacial movements. Second, as discussed above, some MI neurones fired in advance of the EMG-defined movement onset, and so it is unlikely that these activity patterns were exclusively due to reafference. Third, other studies in our laboratory have demonstrated a gating of orofacial somatosensory afferent inputs to face SI neurones immediately preceding and during the monkey’s performance of the tongue-protrusion task (Lin and Sessle 1994). Fourth, our studies have provided direct evidence that a gating of orofacial somatosensory afferent inputs to face MI neurones may occur during the monkey’s performance of chewing (see Chapter IV). Thus it is likely that some orofacial inputs to face MI may indeed be suppressed, given that face SI is a major source of input to face MI (see Dubner et al. 1978; Jones 1986; Huang et al. 1989b; Murray and Sessle 1992a).
It is possible that, as suggested for limb MI, afferent inputs to face MI are modulated during orofacial movements so that only selected inputs useful in guiding the movement or in adapting the movement to an altered orofacial environment gain access to MI. All these lines of evidence support the contention that movement-related activity patterns of most face MI neurones might not simply reflect a result of reafference arising from the movement performed. Chapters III and IV provide additional findings bearing on these matters.
<table>
<thead>
<tr>
<th>Type of Chewing-Related Neurones</th>
<th>Number of Neurones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonic Excitation</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Tonic Depression</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Food Preparation-Related</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Rhythmic Firing</td>
<td></td>
</tr>
<tr>
<td>Jaw Closing-Related</td>
<td>28 (38%)</td>
</tr>
<tr>
<td>Jaw Opening-Related</td>
<td>24 (33%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>73 (100%)</strong></td>
</tr>
<tr>
<td>Type of Chewing-Related Neurones</td>
<td>Tongue Surface</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Tonic Excitation (n=6)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Food Preparation-Related (n=8)</td>
<td>6 (75%)</td>
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<tr>
<td>Tonic Depression (n=4)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Rhythmic Firing</td>
<td></td>
</tr>
<tr>
<td>Jaw Closing-Related (n=20)</td>
<td>14 (70%)</td>
</tr>
<tr>
<td>Jaw Opening-Related (n=17)</td>
<td>11 (65%)</td>
</tr>
<tr>
<td>Total (n=55)</td>
<td>38 (69%)</td>
</tr>
<tr>
<td>Type of Chewing-Related Neurones</td>
<td>Food Preparation-Related (n=10)</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td></td>
<td>Showing Only Initial Jaw Opening-Related Activity</td>
</tr>
<tr>
<td></td>
<td>4(40%)</td>
</tr>
<tr>
<td></td>
<td>3(11%)</td>
</tr>
<tr>
<td></td>
<td>5(21%)</td>
</tr>
</tbody>
</table>
Table II-4. 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>Type of Chewing-Related neurones</th>
<th>Movement Evoked by ICMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tongue Protrusion</td>
</tr>
<tr>
<td>Tonic Excitation (n=6)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Food Preparation-Related (n=10)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Tonic Depression (n=4)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Rhythmic Firing</td>
<td></td>
</tr>
<tr>
<td>Jaw Closing-Related (n=24)</td>
<td>3*(13%)</td>
</tr>
<tr>
<td>Jaw Opening-Related (n=22)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td>Total (n=66)</td>
<td>22 (33%)</td>
</tr>
</tbody>
</table>

* Both jaw closing and tongue protrusion were evoked at the same ICMS threshold stimuli at one location in which a jaw closing-related neurone was recorded.
FIGURE LEGENDS

Figure II-1. A masticatory sequence of chewing a standardised piece of apple by the awake monkey. A shows three basic masticatory phases: food preparatory phase, rhythmic chewing phase, pre-swallowing phase (see text for definition). B shows the further subdivision of food preparatory phase: initial jaw opening and food transportation phase. In this and subsequent Figures, Ver: Vertical movement of the mandible, Hor: Horizontal movement of the mandible, MA: Rectified EMG activity in the masseter muscle. GG: Rectified EMG activity in the genioglossus muscle, AD: Rectified EMG activity in the anterior digastric muscle.

Figure II-2. Details of orofacial motor responses to ICMS (T/S or C/S) delivered to sites along microelectrode penetrations within right lateral pericentral cerebral cortex of one monkey. Parasagittal histological sections A and B corresponding to planes A and B shown in the inset. Planes A and B are separated by ~2 mm. Each ICMS site is represented by, with the responses to C/S denoted in upper case, and the responses to T/S in lower case characters to the right of each ICMS site. Evoked movement thresholds are indicated to the left of the corresponding ICMS sites. Note that C/S ICMS applied to the postcentral gyrus evoked a number of movements including lip, jaw, and tongue movements in addition to swallow and rhythmic jaw movements; these were not twitch movements (from Martin et al. 1999).

Figure II-3. Spatial distribution, within face MI of the left hemisphere of another monkey of penetration tracks in three parasagittal sections within which neurones were found to be chewing-related. cen: central sulcus. arc: arcuate sulcus. Continuous line on the left encloses
stimulation/recording sites from which orofacial movements could be evoked by ICMS; camera lucida drawings of parasagittal histological sections corresponding to planes “a”, “b”, and “c” are shown on the right. Electrode penetration tracks in each plane have been superimposed on the corresponding histological sections and the chewing-related neurones recorded at each site are indicated according to their pattern of activity. → in each section indicates an electrolytic lesion made in a track adjacent to the one in which the neurones were recorded. Plane a indicates 3 neurones recorded in 2 tracks, plane b shows 23 neurones recorded in 5 tracks, and plane c indicates 3 neurones recorded in 2 tracks. Note that of the 29 chewing-related neurones shown in this Figure, 48% also had swallowing-related activity; 7 of the 29 neurones were also tested for task-related activity and 43% of the 7 neurones showed the task-related activity.

Figure II-4. Examples of face MI neuronal RFs at microelectrode penetration sites where chewing-related neurones were recorded in three parasagittal sections within face MI of the left hemisphere of the monkey shown in Figure II-3. Histological sections a, b, and c correspond to planes a, b, and c shown in Figure II-3. Arrowheads indicate directions of ICMS-evoked tongue movement shown along the penetration tracks. O indicates ICMS-evoked jaw movement. Facial figurines indicate the RFs of the neurones recorded at sites within ICMS-defined face MI.

Figure II-5. An example of a “rhythmic firing” neurone which could be classified as “jaw opening-related”. A shows an example of the neurone’s activity in relation to a single masticatory trial. B shows the neurone’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, AD muscles are derived from averaged data. C shows the neurone’s activity in relation to 22 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. The orofacial RF of the neurone and the tongue movement direction (arrow) evoked by ICMS (threshold T for movement, 20 μA) applied at the neuronal recording site are illustrated to the right. Note the rhythmic bursts coincident with the onset of GG and AD activity that preceded the opening movement of the jaw.

Figure II-6. An example of a “rhythmic firing” neurone which could be classified as “jaw closing-related”. A shows an example of the neurone’s activity in relation to a single masticatory trial. B shows the neurone’s activity in relation to 12 masticatory trials aligned to the point of maximum jaw closing (vertical line in the figure) during the food preparatory phase. C shows the neurone’s activity in relation to 24 rhythmic chewing cycles aligned to the point of maximum jaw opening (vertical line in the Figure) during the rhythmic chewing phase. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right. Rhythmic jaw closing-related bursts occurred preceding the onset of MA activity and the jaw closing movements.

Figure II-7. An example of a “food preparation-related” neurone. The neurone showed a discharge burst as the animal opened its mouth and protruded its tongue to take the foodstuff. A shows an example of the neurone’s activity in relation to a single masticatory trial. B shows
the neurone’s activity in relation to 12 masticatory trials aligned to the point of AD onset (vertical line) related to initial jaw opening. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right.

Figure II-8. An example of a “tonic excitation” neurone. The neurone was tonically active before and after the masticatory phase but manifested an increase in its tonic firing throughout the masticatory period. A shows an example of the neurone’s activity in relation to a single masticatory trial. B shows the neurone’s activity in relation to 10 masticatory trials aligned to the point of AD onset (vertical line) related to initial jaw opening. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right.

Figure II-9. An example of a “tonic depression” neurone. The neurone showed some tonic activity before and after the masticatory period but during this period its firing was markedly reduced. A shows an example of the neurone’s activity in relation to a single masticatory trial. B shows the neurone’s activity in relation to 10 masticatory trials aligned to the point of AD onset (vertical line) related to initial jaw opening. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right.

Figure II-10. Distribution of peak rhythmic neuronal activity in relation to peak AD activity. The peak of AD activity is indicated by time 0. The arrow indicates the time of maximum jaw opening.
Figure II-11. An example of a neurone which showed both initial jaw opening and food transportation-related activity. A shows an example of the neurone's activity in relation to a single masticatory trial. B shows the neurone's activity in relation to 11 masticatory trials aligned to the point of maximum jaw closing (arrowhead in the bottom of Figure) during the food preparatory phase. The neurone's RF and ICMS-evoked tongue movement are depicted to the right.
Figure II-1
Figure II-2
Figure II-3

- Jaw opening-related
- Jaw closing-related
- Tonic excitation
- Tonic depression
Figure II-4

- Tongue retrusion
- Tongue protrusion
- Tongue ipsi-lateral
- Tongue contra-lateral
- Jaw closing

1mm
Figure II-10

- Jaw opening-related neurones
- Jaw closing-related neurones
**Figure II-11**

(A) Graph showing various data waves labeled Ver, Hor, MA, GG, AD, with annotations indicating open and left right.

(B) Graph with annotations for initial jaw opening and food transportation, showing data waves with a scale of 0.2 s and 5 imp (10 ms bins), and a notation for T = 30 μA.
CHAPTER III. EFFECTS OF REVERSIBLE COLD BLOCK OF FACE PRIMARY SOMATOSENSORY CORTEX ON OROFACIAL MOVEMENTS AND RELATED FACE PRIMARY MOTOR CORTEX NEURONAL ACTIVITY

INTRODUCTION

The primary somatosensory cerebral cortex is considered to play important roles in sensorimotor integration and control. This view stems from numerous studies of limb SI that have shown that stimulation or lesions of limb SI induces, respectively, movements or motor deficits in humans and experimental animals, that the activity patterns of SI neurones may correlate with one or more parameters of limb movement, that there are abundant interconnections between SI and other cortical areas involved in motor control such as the primary motor cortex, and that SI exerts corticofugal influences on movement and on somatosensory transmission during movement (for review, see Jones 1986; Freund 1987; Asanuma 1989; Chapman 1994; Keller 1996; Nelson 1996). Similarly for primate face SI, it has been shown that chewing and other movements may be evoked from face SI (Huang et al. 1989b) and that bilateral cold block-induced inactivation of face SI also disrupts both chewing and trained orofacial motor behaviour in monkeys (Lin et al. 1993, 1998). Moreover, many neurones in face SI show activity related to a trained orofacial motor task or chewing in monkeys (Lin et al. 1994; Murray et al. 1999) and cats (Hiraba et al. 1997). Since we and others have also documented in monkeys that many face MI neurones have an orofacial RF and that activity related to performance of the task or chewing is also a characteristic of face MI neurones (Luschei et al. 1971; Kubota 1976; Hoffman and Luschei 1980; Murray and
Sessle 1992b; Martin et al. 1997), the possibility arises from the above-mentioned studies that this MI neuronal activity may be a reflection of movement-generated orofacial afferent inputs projecting to MI via face SI. Therefore, the aim of the present study was to use reversible cold block of face SI to determine if task, chewing, and swallow-related neuronal activity recorded in face MI is dependent on the functional integrity of the ipsilateral face SI and to compare the effects of unilateral cold block of SI on task and chewing performance with those of bilateral cold block of SI.

Some of the data have been briefly reported in abstract form (Yao et al. 1996, 1997, 1998).

METHODS

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. Each monkey was trained to perform a tongue-protrusion task. Single-neurone recordings were made from face MI in each monkey to test the effects of ipsilateral cold block of face SI on their activity in relation to the tongue-protrusion task, mastication and swallowing. Since many of the methods have been described in detail (see Chapter II, and Lin et al. 1993; Murray et al. 1991; Murray & Sessle 1992a, b; Martin et al. 1997), only a brief description follows.

Training and Surgical Procedures

Each monkey was seated comfortably in a primate chair and was trained to accept light
tactile mechanical stimulation of the facial skin and most of the oral cavity without any appreciable orofacial movements. The monkey was also trained to allow the investigator to open and close its jaw and to rest the jaw lightly on a custom-made interoccusal block while the tactile stimulation of the intraoral tissue was carried out.

Details of the initial training sessions and surgical placement of a head cap for stabilising the head painlessly during the training and experimental sessions have been previously described (Murray et al. 1991; Lin et al. 1993a). The tongue task has been described in the previous chapter. Briefly, the tongue-protrusion task required the monkey to protrude its tongue symmetrically out the mouth towards a small force plate attached to a force transducer. A target window appeared after PTP (randomly varied between 1.0 and 1.5 s) at a pre-set target level (equivalent of a force of 1.0 N), and this was the cue for the monkey to protrude the tongue towards the force-plate, to move the cursor into the target window, and to hold the cursor there for a minimum of 0.3 s. In addition to the PTP, the following periods were also defined for the task (for detail descriptions, see Murray et al. 1991; Lin et al. 1993): a force-on reaction time period, a force dynamic phase, a force holding phase, and a reward delivery phase. The task period was defined as the period composed of both the dynamic and holding phases. A successful tongue-protrusion trial was one that met the following criteria: the cursor remained within the baseline window during the 1- to 1.5-s PTP; the cursor exited the baseline window within 3 s of target window appearance; and the cursor remained within the window for the specified minimum holding phase.

Surgical procedures for implantation of two stainless steel cylinders (25 mm in diameter) over the exposed dura covering the lateral pericentral cortex, or for unilateral insertion of EMG
electrodes to the orofacial muscles have also been described in the previous chapter. The presence of the stainless-steel cylinders allowed for the daily penetration of the face MI cortex in each hemisphere with a glass-coated tungsten microelectrode (0.5-2 MΩ at 1 kHz) and placement of a thermode over the dura covering face SI. To monitor the EMG activity associated with the task and mastication, electrodes (36-40 gauge, single-stranded, Teflon-coated stainless steel: Cooner Wire, Chatsworth, CA) were placed in left GG, MA, and AD muscles to record chronically their EMG activity.

Neuronal Recordings and Cold Block of Face SI

After training, the face MI was next 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) during daily transdural microelectrode penetrations of the precentral cortex, as previously detailed (e.g., Murray and Sessle 1992a; Martin et al. 1997). In addition, the orofacial representations within the ipsilateral face SI were mapped by defining the RF of single neurones (Lin et al. 1993). These MI and SI mappings took 2-3 weeks. Then in daily sessions, a thermode (2.5 x 7.5 mm dimensions) was placed lightly on the dura over the lateral half of the face SI, that is over the cortical somatosensory representations for the tongue and other intraoral regions and part of the perioral area. In some sessions, a second thermode was also lightly placed on the dura over the lateral half of the contralateral face SI in addition to ipsilateral face SI.

Transdural microelectrode recordings were made to examine the activity of single neurones at ICMS-defined sites within the ipsilateral face MI (Huang et al. 1988; Martin et al.
1997; Murray and Sessle 1992a, b) during chewing of standardised amounts of fruit (apple, 10 x 6 x 6 mm) and during the trained tongue-protrusion task. Neurones that showed chewing and/or tongue protrusion-related activity were studied in detail. EMG recordings and visual observation of swallowing incidences were made simultaneously with single neurone 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. Some neurones also were tested for a RF by applying light tactile stimuli with hand-held probes and firm non-noxious mechanical stimuli to the skin of the face and to the oral cavity (Murray and Sessle 1992a, b; Martin et al. 1997). Then, while the alcohol-water solutions maintained the thermode temperature at 37 °C during the pre-cool period, a pre-cool control sequence of task trials or masticatory trials was carried out. Then the thermode was cooled to 2-4 °C, and 4 min later a sequence of test was conducted over 5-6 min. After the last trial, the thermode was rewarmed to 37 °C, and 4 min later, a final series of trials constituted the post-cool control period. A minimum of 7 successful task trials or 10 masticatory trials were carried out in each condition (i.e. pre-cool, cool, post-cool). This chapter does not describe the effect of SI cold block on the neuronal orofacial RF properties; this is the subject of the next chapter of this thesis. Isotherms and SI neuronal recordings were carried out to confirm the effectiveness of cooling for inactivation of the cortex beneath the cooling block and to confirm that cooling did not significantly affect adjacent cortical regions such as the face MI (see Figs. III-1 and III-2). Consistent with previous findings (Lin et al. 1993; Murray et al. 1991), Figure III-1 shows cortical inactivation abolished spontaneous and evoked single neurone activity by mechanical stimulation within the cortex beneath the thermode and these effects were
reversible. The current data have confirmed the observations by Lin et al. (1993) and Murray et al. (1991) that thermod cooling blocks synaptic transmission within a considerable portion of the lateral half of the SI, and that the activity of the face MI is not directly affected by cooling the face SI.

Details of construction of isotherms were described by Murray et al. (1991) and Lin et al. (1993). Briefly, at the final terminal experiment in one monkey under general anaesthesia (induction: ketamine HCl 20 mg, 2:1 N₂O/O₂ with 3% halothane, maintenance: 0.5-1.5% halothane), isotherms (see Brooks 1983) were constructed from measurements of temperature at 0.0-, 1.0-, 2.0- and 3.0-mm depths along tracks within nearby forelimb postcentral cortex; the tracks were spaced at 0.5 and 1.0 mm distance from and parallel to the edge of a cooled thermode (2-4 °C) that was placed in contact with dura after the chamber and soft tissue over the exposed dura were removed. We also measured the temperature of the cortical surface directly under a cooled thermode (2-4 °C). Forelimb postcentral cortex was chosen because we wished to minimise the possibility of damage to, and thereby difficulty in histological reconstruction of, the face sensorimotor cortex. Temperature was monitored with a thermocouple inserted into a 21-gauge needle, and, from the temperatures recorded at these cortical sites, isotherms were generated (see Figure 2).

Force, EMG, and neuronal spike data were digitised (EMG activity full-wave rectified and smoothed, time constant 20 ms; sampling rate/channel: force 200/s, EMG 3125/s, neuronal spike event data 200/s) with the Cambridge Electronics 1401 data acquisition system and Spike2 analysis package.
Data Analysis

Tongue-protrusion Task

Success rates were defined as the ratio of the number of successful trials to the total number of task trials. For each sequence of trials, any trials that exhibited evidence of an anticipatory reaction by the monkey, i.e. a significant increase in EMG activity sooner than 180 ms after the appearance of the target window, were excluded from further analysis. The Chi-square test was used to test for significant differences ($P < 0.05$) in success rates between different periods.

As described in the previous chapter, digitised EMG, force and neuronal data related to the tongue task were analysed by aligning trials to the onset of the significant increase in GG EMG activity after target window appearance. The onset of a significant increase in EMG activity was defined as the point in each trial at which the analogue signal exceeded two standard deviations of the mean level of EMG activity during the PTP for the trial for $> 200$ ms.

In order to evaluate any changes during unilateral cold block of face SI in the performance of the task which might not be detected by simple comparison of the success rates, more detailed analyses were performed on the force and EMG signals as described by Murray et al. (1991) and Lin et al. (1993). Briefly, five parameters from the force signals were analysed: the maximum force during the task; the mean force during the force holding phase for the period from 200 ms after force-on to the end of the force-holding phase; the average force slope (i.e. mean rate of change of force) during the force dynamic phase; force-on reaction time (from target window on to the onset force deflection) and force variation during
the holding phase (i.e., fluctuation of holding force, calculated as the ratio of the standard deviation of the force to the mean force for the period from 200 ms after force-on to the end of the force-holding phase). EMG activity during task trials was assessed in terms of the area under the rectified and smoothed EMG signal of GG activity for the 1-s period after force-on and presented as amplitude (A/D units) x time (s). A value expressed in "A/D units" is the digital representation of the amplitude of the rectified and smoothed EMG signal. Tests of statistical significance involved one-way ANOVA.

*Chewing and Swallowing*

The total masticatory period of each masticatory trial was defined as the period from the onset of the AD EMG activity associated with mouth opening to obtain the test food to the onset of the GG EMG activity associated with swallowing. 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 onset of the first AD EMG burst as the animal opened its mouth to obtain food to the end of this EMG burst (initial jaw opening) plus the period from this latter time point to the start of rhythmic chewing (food transportation). The rhythmic chewing phase was defined as the period from the end of the food preparatory phase to the end of MA EMG activity related to the rhythmic chewing. The pre-swallowing phase was defined as the period from the end of the rhythmic chewing to the onset of GG EMG activity related with swallowing. The duration of the total masticatory period, the food preparatory phase, rhythmic chewing phase, and the pre-swallowing phase was termed the total masticatory time (TMT), preparatory phase time (PPT), rhythmic chewing
phase time (RCPT), and pre-swallowing phase time (PSPT), respectively.

In order to evaluate any changes during unilateral or bilateral cold block of face SI in the performance of the chewing which might not be detected by simple comparison of TMT and chewing phase durations (e.g. PPT, RCPT and PSPT), more detailed analyses were performed on EMG signals as described by Lin et al. (1998). Analyses of EMG activity during the rhythmic chewing phase, pre-swallowing phase and swallowing involved assessment of the mean amplitude, peak amplitude duration of the rectified and smoothed EMG activity from the MA, AD, and GG muscles and their temporal onset. The cycles during the food preparation phase were omitted as they contained irregular movements.

Swallowing was identified on the basis of characteristic EMG profiles in GG muscle and confirmed by direct visual observation of prominent and rapid elevation and subsequent descent of the larynx characteristic of swallowing (Martin et al. 1997, 1999). Briefly, swallowing onset for both task- or chewing-related swallowing was defined as the point at which the level of GG EMG activity associated with swallowing exceeded, for ≥ 200 ms, 2 SD of the mean GG EMG activity that occurred during the PTP. Swallow offset was defined differently for task- and chewing-related swallowing since task-related swallowing was followed by a lick during the juice reward phase immediately after each successful task trial. This swallow-lick sequence was associated with a prolonged, double-peaked EMG burst in GG. Therefore, for task-related swallowing, swallow offset was determined by subtracting the mean lick duration (the average duration of the first two licks that occurred immediately after delivery of the juice reward at the end of the tongue-protrusion task) from the time at which the swallow-lick-related GG burst fell below 2 SD of the mean GG EMG activity that occurred
during the PTP. Chewing-related swallow offset was defined as the time at which the swallow-related GG burst fell to < 2 SD of the mean GG EMG activity during the PTP. In order to evaluate any changes during unilateral or bilateral cold block of face SI on the performance of the swallowing which might not be detected by simple comparison of the incidences, more detailed analyses were performed on the duration, mean and maximum amplitude of GG, AD, and MA EMG signals.

Orofacial Movement-related Neuronal Activities

In accordance with Murray and Sessle (1992b) and Martin et al. (1997), neurones were considered to be task related only if the neuronal firing frequency during the task period was 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 EMG 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).

The details of data analysis of chewing- and swallowing-related neuronal activity have been described in the previous chapter. Briefly, digitised data related to initial jaw opening and/or food transportation before the start of the rhythmic chewing phase were analysed in relation to 10 masticatory trials aligned to the point of maximum jaw closing during the food preparatory phase or peak EMG activity in the AD muscle associated with the initial jaw-opening. The activity of single neurones was also aligned for a minimum of 20 rhythmic chewing cycles and 10 pre-swallowing cycles to the point of maximum jaw opening or peak EMG activity in the AD muscle during the rhythmic chewing or pre-swallowing phase.
Neurones were considered to be chewing-related only if the neuronal firing frequency during at least one of the three masticatory phases (see above) was statistically significantly different from that during the pre-chewing period of the same masticatory trial (one-way ANOVA with repeated measures, $P < 0.05$). The neurones were considered to be related only to jaw opening or closing if the rhythmical neuronal burst occurred, respectively, during the jaw-opening phase of each chewing cycle during GG and AD EMG activity or occurred during the early part of jaw-closing before the onset or during MA EMG activity. A swallow-related neuronal activity pattern was defined as a significant alteration of neuronal firing rate, relative to that during the PTP, during the 50-ms interval immediately preceding swallow onset, or during the swallow itself (i.e. the interval between swallow onset and offset), or during both the 50-ms interval and the swallow. For each neurone, one-way ANOVA and post-hoc comparisons (Student’s Newman-Keuls test; $P < 0.05$ considered statistically significant) were performed to determine whether the average rates of neuronal activity during pre-cool, cool and post-cool periods were significantly different. Values were expressed as mean $\pm$ S.D.

*Histological Procedures* (see Chapter II)

RESULTS

*Extent of Cold Block of Face SI*

The cortical region covered by the thermode in both monkeys was characterised by single neurones that responded to light tactile stimulation of localised parts of orofacial region including the tongue, and lip. The rostral margin of the thermode near its medial aspect was 1
mm caudal to the ICMS-defined MI and central sulcus. In accordance with the previous study (Murray et al. 1991), the current neuronal study in face SI has shown that cooling with the thermode markedly and reversibly abolishes the activity of neurones directly beneath the thermode (see Fig. III-1) and the isotherm study finding predict that face SI cold block does not affect the activity of the neurones recorded ≥ 1mm beyond the boundary of the thermode (see below).

Figure III-2 shows that the cortical temperature measured at a 0.5 mm distance from and parallel to the edge of a cooled thermode (2-4 °C) and at 0.0, 1.0-, 2.0- and 3.0 mm depths along tracks within forelimb SI was 14, 23.6, 25.8, 26.8°C, respectively. The cortical temperature at a 1.0 mm distance from and parallel to the edge of a cooled thermode and at 0.0, 1.0-, 2.0- and 3.0 mm depths along tracks within forelimb SI was 30, 27.2, 28.4, 30.9°C, respectively. The cortical temperature measured at the point directly beneath a cooled thermode and on the surface of forelimb SI was 9°C. The rectal temperature of the animal was 33.5 °C when the cortical temperatures were measured. These data suggest that the cortical temperature at ≥ 1mm beyond the boundary of the thermode was little decreased.

**Effects of Cold Block of Face SI on Chewing and Swallowing**

Effects of unilateral and bilateral cold block of face SI on chewing and swallowing following mastication were tested in one of the monkeys. In accordance with the findings of Lin et al. (1998), bilateral cold block of face SI resulted in an impairment in the monkey’s ability to masticate the solid food bolus. Bilateral cold block of face SI caused a significant prolongation of the pre-swallowing phase (i.e. from the end of rhythmic chewing phase to the
GG onset related to swallow) but did not affect the TMT (PPT + RCPT + PSPT), PPT, or RCPT (Fig. III-3). Further analysis of the pre-swallowing phase showed that the cycle duration (time from maximum jaw opening to the next maximum jaw opening) did not change (Fig. III-4); this suggests the prolongation of the pre-swallowing phase was due to an increase in the cycle numbers during bilateral cold block of face SI. This might suggest bilateral cold block of face SI has caused an impairment in orofacial movements in the pre-swallowing phase and has induced a significant delay in the onset of swallowing.

Although no change could be identified in rhythmic chewing phase or rhythmic chewing cycle duration during bilateral cold block of face SI, cooling-induced changes in chewing EMG activity were apparent. Bilateral cold block induced a significant increase in duration of AD activity (ANOVA, $P < 0.001$) compared with pre-cool and post-cool conditions (see Fig. III-5). Bilateral cold block also induced a significant decrease in mean amplitude of AD activity during the rhythmic chewing phase in one session and induced a significant increase in mean and peak amplitude of MA activity in another session. The data suggest that bilateral cooling of face SI results in an alteration in timing of muscle activity during rhythmic chewing. Therefore, we analysed the temporal relations between the EMG activity of these three muscles during pre-cool, cool and post cool conditions. Cooling resulted in a significant delay (ANOVA, $P < 0.001$) in the onset time of MA EMG activity (Fig. III-6).

In contrast, during the pre-swallowing phase, bilateral cooling of face SI did not result in an alteration in timing of muscle activity (Fig. III-6), although bilateral cold block did induce a significant increase in mean and peak amplitude of MA activity in this phase during the session that bilateral cold block of face SI also induced a significant increase in mean and peak
amplitude of MA activity during the rhythmic chewing phase (see above). Bilateral cold block of face SI did not affect chewing-related swallow EMG activity of these three muscles and their temporal relations.

Similar to the effects of bilateral cold block of face SI, unilateral cold block of face SI did not affect the TMT, PPT, RCPT but did cause a significant prolongation of the pre-swallowing phase (Fig. III-3). Further analysis of the pre-swallowing phase showed that the cycle duration (time from maximum jaw opening to the next maximum jaw opening) (Fig. III-4) and duration of AD, GG, MA EMG activity was significantly prolonged (Fig. III-5). Nevertheless, unilateral cold block of face SI did not cause any significant change in EMG activity during the rhythmic chewing phase (see Figs. III-5 and III-6).

Swallow regularly occurred when the animals ingested the liquid or solid bolus after it had been masticated. Neither unilateral nor bilateral cold block of SI significantly reduced the occurrence of swallowing or modified the EMG parameters of swallowing behaviour associated with mastication of the bolus (see Figs. III-5 and III-6).

**Effects of Cold Block of Face SI on Tongue-Protrusion Task**

In contrast to the significant decrease in success rates of the tongue-protrusion task during bilateral cold block of face SI (Lin et al. 1993), no significant effect was observed on the monkeys' ability to perform the task during unilateral cooling of face SI (see Fig. III-7). Detailed data analysis revealed that the reaction time, the mean of maximum force and mean force and the mean force variation were also unaffected (Table III-1). GG EMG parameters during the task were also not affected by cooling (i.e., in one monkey, 30.65 ± 13.99 A/D
units. n=32, ANOVA, *P* > 0.05) compared with those in the pre-cool (32.68 ± 16.48, n=44) and post-cool conditions (32.9 ± 15.09, n=43). However, a significant decrease in the rate of force change during the dynamic phase in one monkey was noted and there was a tendency to decrease in the rate of force change in the other monkey during the cooling condition although there was not statistically significant difference compared with the control conditions (see Table III-1).

*Effects of Cold Block of Face SI on Face MI Neuronal Activities*

The activity of a total of 73 neurones was recorded from the ICMS-defined face MI of both monkeys. Of the 73 neurones, 45 neurones were tested for the effects of cold block on chewing-related activity, 13 neurones were tested for the effects of cold block on both chewing and task-related activity, and the remaining 15 neurones were tested for the effects of cold block on only tongue task-related activity. The general properties of these neurones have been described in chapter II of this thesis.

Of 58 chewing-related neurones, the majority (76%) of neurones showed no significant change in chewing-related activity during SI cold block compared to pre-cool and post-cool trials (Table III-2, Figs. III-8 and III-9). Nonetheless, cold block induced a decrease in activity in 11 of the neurones (see Figs. III-10 and III-11) and an increase in chewing-related activity in 3 (Table III-2). There was no clear indication that SI cold block preferably affected neurones showing any one of the 4 main patterns of chewing-related activity. Cold block did not produce any apparent effects on the swallow-related neuronal activity following chewing.

Similarly, for the task-related activity, there was no significant change in the task-related
activity of the majority (71%) of the neurones tested (n = 28) during cold block of SI (see Table III-2 and Fig. III-12). A cold block-induced decrease in activity was seen in 8 neurones (Fig. III-13); 3 of these 8 neurones were also tested for cold block effects on their chewing-related activity, and 2 of the 3 neurones showed cold block-induced depression. Cold block did not show any effects on the swallow-related neuronal activity in relation to swallow of a juice reward.

The spontaneous activity of 73 neurones was also examined, and cold block of SI again did not affect the majority of the neurones (72.5%). Cold block produced a decrease in spontaneous firing in 15 neurones and an increase in 5 neurones. There was also a decrease in task-related activity in 4 and a decrease in chewing-related activity in 8 of the 15 neurones showing cold block-induced depression of spontaneous activity.

DISCUSSION

This chapter has provided a detailed description of the effects of inactivation of SI by cooling on orofacial movements (i.e. tongue protrusion and chewing) and related face MI neuronal activity. We have provided evidence supporting the view that MI is involved in the control of both voluntary and semi-automatic movements such as chewing, and that face SI may contribute to the modulation of mastication, and we have provided new data that the movement-related activity of most face MI neurones may not depend on the functional integrity of the ipsilateral face SI. We found that unilateral inactivation of the face SI by cold block had little effect on performance of chewing, swallowing, and the tongue-protrusion task and that many face MI neurones show chewing and/or task-related activity that for most
neurones is not affected by ipsilateral cold block of face SI. The face MI neurones show swallowing-related activity that for all neurones tested is not affected by ipsilateral cold block of face SI. These data support the view that while both these cortical regions may be involved in the control of semi-automatic as well as trained orofacial motor behaviour, the movement-related activity of most face MI may not depend on the functional integrity of the ipsilateral face SI.

**Extent of Cortical Cooling**

We have previously provided evidence and detailed arguments that cortical cooling disturbs synaptic transmission beneath the cortical thermode so that the cold block effects can be attributed to a disruption in the synaptic transmission within the ICMS-defined face SI (see Lin et al. 1993, 1998; Murray et al. 1991). Unlike the previous studies (see Murray et al. 1991; Lin et al. 1993, 1998), we kept the dura intact when the cortical temperatures were measured to ensure that the cooling conditions were similar to those when we tested the effects of face SI on MI neuronal activities. The current study has provided evidence that cold block of face SI is effective and reversible in abolishing face SI neuronal activity underneath the thermode (Fig. III-1) and that there is very little change in temperature 1.0 mm distance from the cooled thermode (Fig. III-2), which is consistent with the report (Murray et al. 1991) that cooling did not affect the peripherally evoked activity of single MI neurones recorded 1.0 mm normal to the side of the thermode and at depth of 0.5 mm. This also indicates that it is unlikely that the observed effects of cold block of face SI on the orofacial movements and related MI neuronal activity were direct effects of cooling on the adjacent cortical area. Cold block might not have
directly affected area 3a of face SI, but the projection from area 3a to the MI would likely have been affected because cortical neurones in area 3a have indirect connections with MI in monkeys, via areas 1 and 2 (Jones et al. 1978; for review, see Jones 1986) which would have been affected by the cooling. However, we might not have affected the cortico-bulbar projections from area 3a which have profound and complex modulating effects on jaw-closing and jaw-opening reflex (e.g. Sessle 1977; Olsson and Landgren 1980).

**Effects of SI Cold Block on the Tongue-Protrusion Task**

In contrast to bilateral cold block of face SI, unilateral cold block of face SI did not reduce success rates for the performance of the tongue-protrusion task. A possible reason for our negative finding is that the tongue may have been somewhat affected during the unilateral cooling, but the monkey was still able to perform the task at the control level of success rates. This is consistent with the studies reporting that some SI neurones have ipsilateral or bilateral orofacial representations and bilateral projections to the brainstem (see Lin et al. 1994a). In parallel with the finding that success rates for the performance of the task were not affected during unilateral cold block of SI, the reaction time, the maximum force, mean force, mean force variation, and GG activities were also unaffected. However, unilateral cold block of SI did induce a significant decrease in the rate of force change during the dynamic phase in one monkey and a trend to decrease in another monkey (see Table III-1). These data suggest, as for the bilateral cold block of face SI (Lin et al. 1993), that the fine movement was affected in one monkey during the unilateral cold block of face SI but the extent of deficit was not severe enough to cause a failure of the performance of the task.
Effects of Cold block of SI on Chewing and Swallowing

In a previous study, Huang et al. (1989b) have reported there is an extensive region of pericentral cortex devoted to the representation of rhythmic jaw movements. Four regions were identified, one being face SI. Although a brainstem central pattern generator is undoubtedly crucial for the generation of the basic rhythm of mastication (for review, see Dubner et al. 1978; Luschei and Goldberg 1981; Lund 1991; Nakamura and Katakura 1995), there is evidence that these different cortical regions (i.e. face MI, SI, the principle part of the CMA, and a deep part of CMA located in the inferior face of the operculum) play a role in the production or control of the different patterns of chewing. The current study has provided evidence that bilateral cold block of face SI does not prevent chewing from occurring, but rather results in subtle changes to certain aspects of mastication, consistent with findings of Lin et al (1998). We have shown bilateral cold block of SI caused a significant increase in the PSPT, increase in the duration of AD activity, and delays in the onset of MA activity during the rhythmic chewing phase. In addition, our present data indicate that the increase in the pre-swallowing phase time during cold block of SI may be due to an increase in chewing cycle number, not due to an increase in cycle duration. This might result, at least in part, from the bilateral loss of orofacial sensation needed to manipulate the food bolus. The thermodes used for reversible cold block of SI covered the lateral part of the face SI which contains the cortical representations for the tongue and other intraoral regions and part of perioral area. It was considered adequate to cover this lateral part of face SI to test for SI cold block effects on chewing, as this is the only SI region from which rhythmic jaw movements can be evoked by ICMS (Huang et al. 1989b). As a consequence, more cycles of orofacial movements would be
required to move the food bolus to the appropriate site in order to initiate swallowing, the change in the PSPT and AD, MA, and GG duration induced by unilateral cold block of SI may be due to an increase in cycle duration although the rhythmicity of chewing movements may be unchanged, suggesting that this feature of chewing is susceptible to disruption of sensory inputs to and outputs from unilateral SI. The animals might have had difficulty in manipulating the bolus towards the oropharynx before swallowing and it is likely that the cause of the deficit was due to impaired tongue movement. These findings are similar to those of Lin et al. (1998) and consistent with those of previous investigations (Lin et al. 1993, 1994a,b; Lin and Sessle 1994) that the face SI plays an important role in the fine control of voluntary movements. They suggest that face SI plays an important role in the control of orofacial movements (e.g. tongue movement) to form and position the food bolus during the pre-swallowing phase and inactivation of SI by cooling can delay the occurrence.

While, as noted above, it is possible that the impairment in mastication during cold block of SI may have been related to some disturbance in sensory perception from intraoral regions, at least part of the reason likely relates to the demonstrated role of the lateral face SI in modulation of the central pattern generator for mastication (Huang et al. 1989b; Lin et al. 1998). The modulatory effects of cooling the face SI could then reflect disruption of known pathways from the SI to adjacent cortical regions or from the SI to the subcortical regions such as the central pattern generator brainstem (for review, see Dubner et al. 1978; Kuypers 1981; Luschei and Goldberg 1981).

The effects on chewing of cold block of face SI appear to be more subtle than the effects of cold block of the lateral pericentral cortex from which rhythmic jaw movements can be
evoked by ICMS (Narita et al. 1995, 1999). Recently, we have also shown reversible cold block of specifically face MI mainly causes a dramatic prolongation of food preparation and pre-swallowing phases and the animals have difficulty in transporting the foodstuff to initiate chewing or swallowing (unpublished observation). Our observations support the view that these different cortical regions may be differentially involved in the selection or control of movement patterns during semi-automatic orofacial movements (Huang et al. 1989b).

Properties of Orofacial Movement-related Face MI Neuronal Activities

Consistent with previous findings (e.g. Murray and Sessle 1992a, Martin et al. 1997), a particular feature of face MI revealed in the present study was the presence of an orofacial afferent input to the majority of recorded neurones from superficial mechanoreceptors. These findings contrast with the prominent representation of deep input to limb motor cortical neurones (Wong et al. 1978; Fetz et al. 1980; Asanuma 1981). Superficial mechanoreceptive afferent input appears to play an important role in the control of orofacial movements such as during speech (e.g., Abbs and Cole 1982), chewing (Lin et al. 1998; Hiraba 1999) and performance of tongue protrusion (Lin et al. 1993).

This study has shown that there are many neurones with the ICMS-defined face area of the MI that alter their firing during orofacial movements such as the tongue-protrusion task, chewing and swallowing. This finding is in accord with previous findings within lateral precentral cortex of single neurone activity in relation to orofacial movements (e.g., Kubota and Niki 1971; Luschei et al. 1971; Kubota 1976; Hoffman and Luschei 1980; Murray and Sessle 1992b; Martin et al. 1997) and also is consistent with our current knowledge of the
behavioural relations of neuronal activity within forelimb MI (e.g., see Evarts 1981; Lemon 1988). Together with the earlier face MI neuronal and ICMS data (e.g., Murray and Sessle 1992a, b; Martin et al. 1997), the present data also reveal that multiple, discrete efferent zones exist for the production of elemental tongue movements and for tongue movements associated with semi-automatic movements such as chewing and swallowing. Thus, the combined activation of different efferent zones could contribute to the neural framework required for the complexity of tongue movements in orofacial motor behaviours and to the need for close neuronal integration for control of these behaviours.

Our data also support the view that face MI plays an important role not only in the control of voluntary movements such as trained tongue protrusion, but also in semi-automatic movements (see Sessle et al. 1995a). Consistent with the effects of disruption or ICMS of face MI and earlier findings of chewing or swallowing-related activity in face MI (Penfield and Rasmussen 1950; Kubota and Niki 1971; Luschei et al. 1971; Luschei and Goodwin 1975; Huang et al. 1989b; Martin et al. 1997, 1999), the data have shown that substantial numbers of MI neurones display chewing and/or swallowing-related activity. The findings suggest that, consistent with the findings of different swallowing-related activity patterns in face MI in the current and previous studies (Martin et al. 1997), the various types of chewing and/or swallowing-related activity may reflect different types of cortical neurones involved in driving chewing- and/or swallowing-related movements or in responding to movement-evoked afferent inputs or in some other form of sensorimotor integration related to chewing or swallowing. As argued in the previous chapter, these different neuronal firing patterns may be related to differences in the duration and relative timing of chewing-related bursts of muscle
activity across the changing chewing conditions as the foodstuff is triturated.

**Effects of Inactivation of Face SI on Face MI Neuronal Activity**

Approximately one-quarter of the face MI neurones showed a change in task or chewing-related activity during cold block of the ipsilateral face SI; this change was mainly reflected as a decrease in movement-related activity. This finding suggests that the movement-related activity of some MI neurones may reflect a tonic facilitatory input from the ipsilateral SI to MI or a reafferentation by excitatory orofacial sensory inputs relaying through SI to MI and phasically evoked by the task or chewing movements. A small proportion of neurones also showed a cold block-induced change in spontaneous activity and again this was mainly reflected as a decrease in activity. Some MI neurones manifested a cold block-induced increase in spontaneous or movement-related activity, and although their numbers were very small, this does suggest that part of the SI influence on MI neuronal activity may be depressive as well as facilitatory. Inhibitory as well as excitatory influences from limb SI on limb MI neurones have previously described (see Brinkman et al. 1985; Asauma 1989; Zarzecki 1989; Izraeli and Porter 1993; Widener and Cheney 1997).

Nonetheless, the majority of face-MI neurones showed no significant change in their task or chewing-related activity and all face MI neurones showed no significant change in swallowing-related activity during SI cold block, indicating that the movement-related activity of most face MI neurones may not be dependent on the functional integrity of the ipsilateral face SI. This is consistent with our observations that the face SI does not contribute to the responses of most face MI neurones evoked from the neuronal RF (see Chapter IV) and with
data from the limb sensorimotor cortex revealing that the movement-related activity of many limb MI neurones is not a reflection of reafferentation, although there is also some contrary evidence (for review, see Asanuma 1989; Wise 1993; Georgopoulos 1994; Nelson 1996). Our data are also in accord with the view that reafferentation is not a major factor accounting for the movement-related activity of MI neurones, although we cannot exclude in these experiments the possibility that this activity may be a reflection, at least in part, of peripherally evoked orofacial afferents inputs accessing face MI by routes other than through the ipsilateral face SI e.g. other ipsilateral cortical areas, ipsilateral posterior thalamus, contralateral sensorimotor cortex (e.g., Jones 1986; Aizawa and Tanji 1994; Kaneko et al. 1994; Nelson 1996). Nevertheless, as well as our present data of the effects of SI cold block, there are several other lines of evidence indicating that the movement-related activity patterns of most MI neurones are not simply a result of reafference via SI or other peripheral input pathways to MI, as argued in the previous chapter.

We have shown that unilateral face SI cold block only affected task-related activity in a minority of face MI neurones and had little effect on the awake monkey's performance of the tongue-protrusion task. The limited effect of unilateral SI cold block on task-related MI neuronal activity may not be the likely explanation for the marked disruptive effects that bilateral cold block of primate face SI has on tongue-task performance (Lin et al. 1993). Previous studies (Murray et al. 1991; Lin et al. 1993) also support this notion by demonstration of the differences between face SI and MI in the effects of cooling these regions on the tongue-protrusion task. In view of the critical role that face MI plays in tongue-task performance (Murray et al. 1991) and the limited effect of unilateral SI cold block on task-related MI
neuronal activity documented in the present study, cold block-induced loss of sensation in the orofacial region and inactivation of corticofugal effects from SI on subcortical centres involved in somatosensory transmission and motor control appear to be likely explanations for the marked disruptive effects that bilateral cold block of primate face SI has on tongue-task performance (Lin et al. 1993) and the limited effects that unilateral cold block has on tongue-task performance.

In the case of the disruptive effects on chewing of bilateral SI cold block vis-à-vis the restricted influence we documented here of unilateral SI cold block on MI chewing-related activity, cold block-induced loss of sensation in the orofacial regions and disruption of corticofugal effects from primate face SI on subcortical regions, such as the brainstem ‘chewing centre’ (Dubner et al. 1978; Luschei and Goldberg 1981; Lund 1991), must again be considered as a likely explanation. However, in this case, there is also the possibility that the disruptive effects on chewing might conceivably be due in part to the SI cold block affecting SI projections to chewing-related neurones that also can be found in the more lateral ‘cortical masticatory area’ and that may project to these subcortical regions (Lund and Lamarre 1974; Luschei and Goldberg 1981; Sessle et al. 1995a).
Table III-1. Effects of Unilateral Cold Block of SI on Tongue-Protrusion Task Parameters

<table>
<thead>
<tr>
<th></th>
<th>Max force (N)</th>
<th>Mean force(N)</th>
<th>Mean force variation</th>
<th>Force Slope(N/s)</th>
<th>Reaction time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monkey 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-cool (n=81)</td>
<td>1.18 ± 0.07</td>
<td>1.06 ± 0.06</td>
<td>7.41 ± 3.34%</td>
<td>1.63 ± 0.53</td>
<td>763 ± 589</td>
</tr>
<tr>
<td>Cool (n=49)</td>
<td>1.15 ± 0.79</td>
<td>1.04 ± 0.06</td>
<td>7.58 ± 3.43%</td>
<td>1.46 ± 0.55</td>
<td>732 ± 513</td>
</tr>
<tr>
<td>Post-cool (n=114)</td>
<td>1.18 ± 0.78</td>
<td>1.06 ± 0.59</td>
<td>7.33 ± 3.18%</td>
<td>1.67 ± 0.71</td>
<td>945 ± 687</td>
</tr>
<tr>
<td>( P )</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Monkey 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-cool (n=44)</td>
<td>1.34 ± 0.16</td>
<td>1.09 ± 0.13</td>
<td>15.00 ± 7.89%</td>
<td>2.59 ± 1.25</td>
<td>1155 ± 928</td>
</tr>
<tr>
<td>Cool (n=32)</td>
<td>1.26 ± 0.14</td>
<td>1.03 ± 0.10</td>
<td>14.00 ± 7.66%</td>
<td>2.08 ± 0.78</td>
<td>1459 ± 1078</td>
</tr>
<tr>
<td>Post-cool (n=43)</td>
<td>1.29 ± 0.15</td>
<td>1.09 ± 0.12</td>
<td>12.30 ± 7.41%</td>
<td>2.78 ± 1.01</td>
<td>1423 ± 1142</td>
</tr>
<tr>
<td>( P )</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table III-2. Effects of Reversible Cold Block of Unilateral Face SI on Ipsilateral Chewing or Task-Related Face MI Neuronal Activity

<table>
<thead>
<tr>
<th>Type of Chewing-Related Neurones</th>
<th>Increase</th>
<th>Decrease</th>
<th>No Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonic Excitation (n=6)</td>
<td>1 (17%)</td>
<td>1 (17%)</td>
<td>4 (66%)</td>
</tr>
<tr>
<td>Food Preparation-Related (n=8)</td>
<td>0 (0%)</td>
<td>3 (38%)</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>Tonic Depression (n=3)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>Rhythmic Firing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaw Closing-Related (n=22)</td>
<td>1 (5%)</td>
<td>4 (18%)</td>
<td>17 (77%)</td>
</tr>
<tr>
<td>Jaw Opening-Related (n=19)</td>
<td>1 (5%)</td>
<td>3 (16%)</td>
<td>15 (79%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Task-Related Neurones</th>
<th>Increase</th>
<th>Decrease</th>
<th>No Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonic Excitation (n=17)</td>
<td>0 (0%)</td>
<td>6 (35%)</td>
<td>11 (65%)</td>
</tr>
<tr>
<td>Phasic-Off-Tonic (n=2)</td>
<td>0 (0%)</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Phasic Excitation (n=6)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>Tonic Depression (n=3)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>2 (67%)</td>
</tr>
</tbody>
</table>
FIGURE LEGENDS

Figure III-1. Response of a face SI neurone to mechanical stimulation with a cotton applicator to touch its receptive field before, during, and after SI cold block. The recording site was underneath the thermode (approximate depth 0.6 mm). T = Touch.

Figure III-2. The temperatures in forelimb SI when temperature of the thermode on the dura over forelimb SI was 2-4°C.

Figure III-3. Effects of bilateral (A) and unilateral (B) cold block of face SI on mastication. TMT=total mastication time; PPT=preparatory phase time; RCPT=rhythmic chewing phase time; PSPT=pre-swallowing phase time. Both bilateral and unilateral cold block significantly elongated PSPT and did not significantly change PPT, RCPT, and TMT. ** indicates $P<0.01$ and *** indicates $P<0.001$ (ANOVA).

Figure III-4. Effects of bilateral (A) and unilateral (B) cold block of SI on cycle duration during the rhythmic chewing phase and pre-swallowing phase of mastication. Unilateral cold block significantly ($P<0.01$, ANOVA) elongated cycle duration during the pre-swallowing phase.

Figure III-5. Effects of bilateral (A, B, C) and unilateral (D, E, F) cold block of SI on duration of EMG activities during the rhythmic chewing phase, pre-swallowing phase and swallow. In this and subsequent Figures, MA: Rectified EMG activity in the masseter muscle, GG: Rectified EMG activity in the genioglossus muscle, AD: Rectified EMG activity in the
anterior digastric muscle. The durations are illustrated from top to bottom for those during the rhythmic chewing phase, pre-swallowing phase and swallowing, and for each are shown prior to cortical block (pre-cool), during cold block (cool) and post-cool. Note that bilateral cold block of SI was associated with statistically significant and reversible prolongation of AD burst duration during the rhythmic chewing phase and that unilateral cold block of SI caused a statistically significant and reversible prolongation of AD, GG, MA burst duration during the pre-swallowing phase. *, **, and *** indicate P<0.05, P<0.01 and P<0.001, respectively.

Figure III-6. Effects of bilateral (left) and unilateral (right) cold block of SI on the time relationships of the onset of EMG activities during the rhythmic chewing phase, pre-swallowing phase and swallowing. The onsets of EMG activity of GG and MA are aligned relative to the onset (time = 0.0 s) of EMG activity in AD muscle. Phase relationships are illustrated from top to bottom for those during the rhythmic chewing phase, pre-swallowing phase and swallowing, and for each are shown prior to cortical block (pre-cool), during cold block (cool) and post-cool. Note that bilateral cold block of SI was associated with statistically significant and reversible delay in the onset of MA muscle EMG activity during the rhythmic chewing phase. The data are expressed as mean ± S.D. and sample size varies from 34 to 65 for rhythmic chewing phase, from 17 to 47 for rhythmic chewing phase and from 8 to 13 for swallowing. *** indicates P<0.001.

Figure III-7. Success rates (%) for performance of tongue-protrusion task for pre-cool, cool, and post-cool conditions during unilateral cooling of face SI. There was no significant different in the success rates under the cool condition in comparison with those under the pre-cool and post-cool conditions (Chi-square test, P>0.05).
Figure III-8. Example of effects of reversible unilateral cold block of face SI on jaw opening-related activity of ipsilateral face MI neurone. For each of the 3 conditions (pre-cool, cool, post-cool), the Figure illustrates from top to the bottom the neuronal activity (bin size 10 ms) during 42 rhythmic chewing cycles carried out by the awake monkey, the rectified and averaged EMG activity of the AD and MA muscles during the trials. No RF was found for this neurone. ICMS-evoked tongue movement is depicted to the right. Note that cold block produced no clear change in neuronal activity during cooling.

Figure III-9. Example of effects of reversible unilateral cold block of face SI on jaw closing-related activity of ipsilateral face MI neurone. For each of the 3 conditions (pre-cool, cool, post-cool), the Figure illustrates from top to the bottom the neuronal activity (bin size 10 ms) during 20 rhythmic chewing cycles carried out by the awake monkey, the rectified and averaged EMG activity of the AD and MA muscles during the trials. The neurone's RF and ICMS-evoked tongue movement are depicted to the right. Note that cold block produced no clear change in neuronal activity during cooling.

Figure III-10. Example of effect of reversible unilateral cold block of face SI on jaw opening-related activity of ipsilateral face MI neurone. The Figure is arranged as for Figure III-8, but note in this case that cold block reversibly depressed the jaw opening-related activity of the neurone.

Figure III-11. Example of effect of reversible unilateral cold block of face SI on jaw closing-related activity of ipsilateral face MI neurone. The Figure is arranged as for Figure III-9, but
note in this case that cold block reversibly depressed the jaw closing-related activity of the neurone.

Figure III-12. Example of effects of reversible unilateral cold block of face SI on tongue task-related activity of ipsilateral face MI neurone. For each of the 3 conditions (pre-cool, cool, post-cool), the Figure illustrates from top to the bottom the neuronal activity (bin size 100 ms) during 7 successful performances of the tongue-protrusion task carried out by the awake monkey, the rectified and averaged EMG activity of the GG muscle during the trials and the averaged protrusive force developed during these trials. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right. Arrowheads indicate the onset of the tongue protrusive force. Note that cold block produced no clear change in neuronal activity during cooling.

Figure III-13. Example of effect of reversible unilateral cold block of face SI on the tongue task-related activity of ipsilateral face MI neurone. The neurone’s RF and ICMS-evoked tongue movement are depicted to the right. The Figure is arranged as for Figure III-12, but note in this case that cold block reversibly depressed the task-related activity of the neurone.
Figure III-1
Figure III-2

- - - 0.5 mm from the edge of the thermode
- - 1.0 mm from the edge of the thermode
- - Directly underneath the thermode
- - Rectal temperature
Figure III-3
Figure III-4
Figure III-6
Figure III-7
Figure III-10

Post-cool

Cool

Pre-cool

MA (A/D units)  AD (A/D units)  No. of Spikes

T=30 µA

0.25 s
MA (A/D units) | AD (A/D units) | No. of Spikes
---|---|---
Pre-cool
Cool
Post-cool

Figure III-11

T=20 µA
INTRODUCTION

The previous chapters and earlier findings in our laboratory have suggested that face MI plays an important role in the control of orofacial movements during semi-automatic movements such as chewing and swallowing in awake monkeys (Martin et al. 1997) as well as trained tongue movements (Murray et al. 1991; Murray and Sessle 1992a). Somatosensory inputs to face MI may be involved in this control since many neurones of primate face MI receive a somatopically arranged somatosensory input that is dominated by orofacial tactile inputs (Huang et al. 1989a; Murray and Sessle 1992b; Martin et al. 1997). The primate limb MI also receives a somatopically organized somatosensory input involving tactile and proprioceptive afferents (e.g. see Strick and Preston 1978; Asanuma et al. 1979, 1980, Lemon 1979; Marple-Horvat and Armstrong 1999).

Somatosensory inputs can reach MI through three major sources: 1) specific thalamic nuclei, including VL (Olszewski, 1952; Kang et al. 1999), VPLo (Strick 1975; Kievit and Kuypers 1977; Jones et al. 1979; Tracey et al. 1980; Asanuma et al. 1983a, b, c; Leichnetz 1986), and VLo (Holsapple et al. 1991; Shindo et al. 1995), 2) commissural fibres via the corpus callosum (Jones and Wise 1977; Jones et al. 1977; Gould et al. 1986; Leichnetz 1986), and 3) corticocortical association fibres of the ipsilateral hemisphere (Pandya and Kuypers 1969; Muakkassa and Strick 1979; Leichnetz 1986; Porter 1997). There is indeed anatomical and electrophysiological evidence of abundant connections and interaction between limb SI and MI...
(e.g., Ghosh and Porter 1988; Jones et al. 1978; Vogt and Pandya 1977; Zarzecki 1989; Porter et al. 1990). Although to the best of our knowledge there are no anatomical studies addressing the issue of interconnections between face SI and MI, previous studies in our laboratory (Murray et al. 1991; Murray and Sessle 1992a,b,c; Lin et al. 1993, 1994a,b) have demonstrated (a) similar differential effects, induced by cold-block of either face SI or MI, on trained tongue-protrusion and biting behaviours, (b) similar preferential SI and MI neuronal activity related to the tongue-protrusion task, (c) a similar variety of neuronal activity patterns in SI and MI during the task, and (d) many neurones in SI and MI that similarly exhibit a single preferred direction of firing and a systematic change in firing rate with changes in tongue-protrusion direction. Furthermore, we have shown that chewing and/or task-related activity of some face MI neurones is dependent upon an intact ipsilateral face SI (see Chapter III). The above-mentioned evidence raises the possibility that functional interconnections exist between face SI and MI and that some SI neuronal activity may be used for modulating face MI neurones during orofacial movements.

The movement-related activity of face SI neurones during orofacial movements may originate from MI or other motor centres, i.e., "corollary discharge" or "efference copy" (for review, see Evarts 1971; Matthews 1988; McCloskey 1981). This theory suggests that the afferent signals elicited by movements are operated upon in conjunction with the motor command which informs the analysing centres (e.g., SI) that the sensory signals are self-generated rather than externally generated (Matthews 1988). Several studies have demonstrated modulation of somatosensory inputs to limb SI (e.g., Chapman et al. 1988; Jiang et al. 1990, 1991a; Shin et al. 1994) and face SI during movement (Lin and Sessle 1994; Fanselow and Nicolelis 1999). There is also evidence that responses of MI neurones to electrical cutaneous stimulation during locomotion are modulated (e.g., Palmer et al. 1985) although there is not any
analogous study on modulation of responses of face MI neurones during orofacial movements. The existence of corticofugal projections (for review, see Kuypers 1981) from SI that can modulate sensory relay neurones in thalamus, brainstem, or spinal cord (for review, see Dubner et al. 1978; Wiesendanger 1981; Bushnell et al. 1987; Chapin 1987) suggests that the role of face SI may involve the corticofugal modulation of ascending somatosensory inputs and reflex activity during movements (for review, see Dubner et al. 1978; Wiesendanger 1981; Bushnell 1987; Chapin 1987). In view of the reciprocal projections between SI and MI (Jones et al. 1978; Vogt and Pandya 1977; Porter 1997) and the role of face SI in subcortical modulation, face SI may also contribute to the modulation of sensory transmission to face MI neurones.

Because of the common features outlined above of face MI and face SI and the abundant connections that exist between SI and MI, the aims of this study were to test: 1) whether somatosensory inputs to face MI neurones are modulated during chewing, and 2) whether the responses of face MI neurones evoked by orofacial stimulation and any modulation of MI neuronal activity during chewing are dependent upon an intact SI.

Some of the data have been briefly reported in abstract form (Yamamura et al. 1999; Yao et al. 1999).

METHODS

This investigation used three monkeys (*Macaca fascicularis*, weight 3-3.5 kg) that were cared for according to the Guiding Principles of the American Physiological Society and the Guidelines of the Canadian Council for Animal Care (Guide to the Care and Use of Experimental Animals, Vol. I, 2nd edition, 1993). Single-neurone recordings were made from the face MI to characterise the activity of neurones evoked by peripheral orofacial stimulation and to investigate
the modulation of the responses of face MI neurones to peripheral stimulation during chewing and to test whether the evoked response in face MI and any modulation is dependent on an intact ipsilateral face SI. Many of the methods have been reported previously (see Murray and Sessle 1992a,b,c; Lin and Sessle 1994); therefore, only a brief outline will be given here, and the following will instead concentrate on those aspects not previously reported in detail.

Surgical Procedures

The monkey was seated comfortably in a primate chair and trained to accept light tactile mechanical stimuli without any appreciable orofacial movements (Lin et al. 1994a). After the initial training, 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% halothane; maintenance: 0.5-1.5% halothane). The head cap supported a stainless-steel cylinder (25 mm in diameter) that was implanted over the exposed dura covering the lateral pericentral cortex. Electrodes (36-40 gauge, single-stranded, Teflon-coated stainless steel: Cooner Wire, Chatsworth, CA) were placed unilaterally in the GG, AD and MA muscles to record chronically their EMG activity. A strong magnet (3.0 mm in diameter and 3.0 mm in length, provided by Dr. Yamada at Niigata University, Japan) was implanted under the chin for attachment of a light source for monitoring jaw movements. A silastic cuff with stainless-steel stimulating electrodes (Hoffer and Loeb 1980) was also implanted on each lingual nerve after placement of the second stainless-steel cylinder.

Electrophysiological Recordings
EMG activity was recorded from GG, AD, and MA muscles, and jaw movement was monitored in the vertical and lateral axes by a photoelectric transducer that measured the displacement of a light source attached to the monkey's chin. Transdural microelectrode penetrations were made in the face MI for extracellular single-neurone recordings as previously described (Murray and Sessle 1992a,b,c; Martin et al. 1997). Face MI neuronal activity was recorded with glass-coated tungsten electrodes ($Z = 0.5-2$ MΩ at 1 kHz) and was monitored on oscilloscopes and a loudspeaker. To isolate the activity of a single-neurone from other neurones throughout the recordings, we repeatedly compared neuronal spikes (polarity, amplitude, and shape) with previously stored trace of the neurone's spike on a digital oscilloscope. After recording, we used CED Spike2 analysis program (CED, Cambridge, UK) to match the templates. Only neurones with a tongue RF, i.e. neurones that received mechanoreceptive afferent inputs from the tongue were searched for studying. Electrical stimulation (1 Hz, 200-μs duration) was applied to the contralateral and/or ipsilateral lingual nerve via the implanted cuff electrode to evoke a neuronal response. The threshold of stimulus intensity ($T$) needed to evoke neuronal activity and the response latency were determined. The response latency of face MI neurones was arbitrarily divided into two groups: $a \leq 8.0$ ms and $a > 8.0$ ms group since Lin and Sessle (1994) described that the response latency of face SI neurones in awake monkey to peripheral stimulation was $9.2 \pm 2.3$ ms (mean ± SD, range: 6.0-14.0 ms). It is unlikely that sensory input can transmit from SI to MI if the response latency of face MI neurones to the lingual nerve stimulation is shorter than or equal to 8.0 ms. The threshold of stimulus intensity required to induce short-latency (8.0-10.0 ms) reflex activity by lingual nerve stimulation in AD and GG muscles was also determined in each session.
During data acquisition in initial studies, electrical stimulus intensities of 1, 1.2, 2T were applied to select an appropriate stimulus intensity for further studies. An electrical stimulus intensity of 1.2T for each neurone was used to test for the modulation of the neurone’s evoked activity during chewing. For each chewing cycle, only one stimulus was applied at a single time interval during the jaw-opening phase or jaw-closing phase. Stimuli were applied as a control when there was not any detectable voluntary jaw movements.

With the thermode temperature maintained at 37 °C, a pre-cool control sequence of trials of stimulation of the lingual nerve (1.2T), mastication, and stimulation of the lingual nerve (1.2T) during chewing were carried out. Then the thermode was cooled to 2-4 °C, and 4 min later a sequence of test trials was conducted over 5-6 min. After the last trial, the thermode was rewarmed to 37 °C, and 4 min later, a final series of trials constituted the post-cool control period. Isotherms and recordings were carried out to confirm the effectiveness of cooling for inactivating the cortex beneath the cooling block and to confirm that cooling did not significantly affect adjacent cortical regions such as the face MI (see Chapter III for details). As shown by our previous studies, 5-6 min is ample time for cortical inactivation since within 4 min, evoked and spontaneous single neurone activity within the cortex beneath the thermode could be abolished (Murray et al. 1991; Lin et al. 1993). Previous studies (Murray et al. 1991; Lin et al. 1993) have provided evidence that thermode cooling blocks synaptic transmission within a considerable portion of the lateral half of the SI, and that the activity of the face is not directly affected by cooling the face SI.

For some face MI neurones, the mechanical threshold and the size of the RF were tested with von Frey filaments before, during, and after cold block of ipsilateral face SI. Noxious stimuli were never used.
Acute Experiments

Acute experiments were also conducted on two of the monkeys under halothane anaesthesia. Electrical stimulation was applied to the orofacial RF of ipsilateral face MI neurones and their spontaneous and electrically evoked (200-μs duration, 1 Hz) neuronal activity was recorded during the pre-cool, cool and post-cool conditions.

Data Analysis

For all the experiments in the awake monkey, the EMG activities from GG, AD, and MA muscles, single neuronal activity, stimulus pulse, and jaw movements were recorded on the computer hard drive. The data then were replayed after the experiment and the EMG signals were digitised and full-wave rectified and smoothed (time-constant: 20 ms; sampling rate/channel: 200 /s).

A peri-event time histogram for the neuronal activity during the chewing in the absence of stimulation was constructed by aligning a minimum of 10 trials at the maximum jaw opening point during the rhythmic chewing phase. A neurone was considered to be chewing-related according to the criteria described in Chapter III.

A poststimulus time histogram (PSTH) aligned to stimulus applied to the lingual nerve at the jaw-opening or jaw-closing phase also was constructed. The duration of the evoked response was defined as the period from the onset of a significant increase in neuronal activity evoked by the stimulation (the point at which the neuronal firing frequency exceeded two standard deviations of the mean level of neuronal activity during the pre-trial period) to the offset of the evoked response (the point at which the neuronal firing frequency fell below two standard deviations of the mean level of neuronal activity during the PTP). Because the
neuronal activity following a stimulus could be a combination of stimulus-evoked activity and chewing-related activity, the number of evoked spikes was calculated from the number of spikes in the period of evoked responses (see above) minus the mean baseline spike number in the corresponding period of trials without stimulation. To evaluate statistically the change of evoked neuronal activity in different phases of the chewing, an analysis of variance and contrast tests were applied to compare the evoked neuronal activity during the jaw-opening and jaw-closing phase with that during the PTP. For comparison between pooled data from all neurones, the mean evoked activity during different phases of the chewing was normalised for each neurone and presented as the percent of the control evoked neuronal activity (during the PTP). Other statistical analyses have been described in the previous chapters.

*Histological Procedures* (see Chapter II)

**RESULTS**

**General Features of the Neurones Recorded**

A total population of 48 face MI neurones were recorded and the activity of 37 face MI neurones was examined during chewing. Of these 48 neurones, 37 had a contralateral RF, 10 had a bilateral and/or ipsilateral RF. Of these 37 neurones tested during chewing, 34 showed chewing-related activity: 6 fired throughout the chewing phase, 1 decreased firing during chewing, 3 showed food preparation-related activity, 12 showed jaw opening-related activity, and 12 showed jaw closing-related activity. Tongue movements were evoked by ICMS (≤ 30 μA) at all 48 recording sites. A total population of 29 MI neurones were also recorded in the
anaesthetised monkeys. Of these neurones, 24 had a tongue RF and 5 had a face RF. Tongue or face movements were evoked by ICMS (≤ 30 μA) at the recording sites.

Features of Evoked Neuronal Activities

The 48 tongue MI neurones were tested with electrical stimulation of the lingual nerve (1.2T). Of these neurones, 17 neurones could be activated at a latency equal to or less than 8.0 ms (6.0 ± 1.2, mean ± SD; range from 4.0 to 8.0 ms), and the evoked response in 31 neurones had a latency longer than 8.0 ms (16.6 ± 5.6; range from 9.0 to 28.0 ms). In addition, 8 neurones also had a second longer-latency response (32.9 ± 18.5; range from 10.0 to 69.0 ms). Figure IV-1 demonstrates these 3 types of responses. Since the evoked latency could be decreased as the stimulation intensity was increased (see Fig. IV-2), all latencies of evoked responses reported are those evoked by stimuli at 1.2T. The presence of a second response also appeared to depend on stimulation intensity. Figure IV-2 shows an example of responses evoked by stimulation of the lingual nerve at intensities of 1T, 1.2T, and 2T. The neurone showed a second longer-latency response at higher stimulation intensities. In contrast, Figure IV-3 demonstrates a neurone showing a second shorter-latency response with the higher stimulation intensity (2T).

Similarly, 24 tongue and 5 face MI neurones were tested with electrical stimulation of their orofacial RF in the anaesthetised monkeys. Of the 24 tongue MI neurones, 2 neurones had a response latency shorter than 8.0 ms, and 22.0 neurones had a latency longer than 8 ms (33.3 ± 17.3, mean ± SD; range from 9.0 to 61.0 ms); 1 neurone also had a second longer-latency response (71.0 ms). All 5 face MI neurones had a latency longer than 8 ms (29.2 ± 10.7, mean ± SD; range from 17.0 to 45.0 ms) and no neurone with a second longer-latency
response was found. There was no significant difference ($P > 0.05$, Student's t-test) between the latencies (> 8.0 ms) of responses evoked from the tongue RFs and from the face RFs.

Modulation of the Evoked Activity During Chewing

Of 30 face MI neurones tested for the chewing-related modulation of evoked responses, 4 showed a tonic firing throughout chewing trials, 3 increased firing only during food preparation phase, 11 fired during rhythmic jaw-opening phase and 11 fired during rhythmic jaw-closing phase and 1 did not show any chewing-related activity (see Table IV-1). Chewing-related modulation of evoked neuronal activity was found in 29 of the 30 neurones. During chewing, the evoked neuronal activity of the majority 25 of the 30 (83.3%) neurones was decreased during both jaw-opening and jaw-closing phases. The evoked second longer-latency responses of 2 neurones were also suppressed during the jaw-opening and jaw-closing phase although the evoked first short-latency responses in the same neurones were not changed during either chewing phase. The evoked responses of 1 neurone were decreased only during the jaw-closing phase. In contrast, there was only 1 neurone showing a significant increase in the evoked neuronal activity during chewing.

Table IV-2 summarises the relationship between the chewing-related activity and modulation of activity evoked by stimulation of the lingual nerve in the 30 neurones. The modulation occurred in all 20 neurones with an evoked response latency longer than 8.0 ms during jaw-closing phase (21.1 ± 26.4% of the control, mean ± SD) and also occurred in 19 of the 20 neurones during the jaw-opening phase (12.6 ± 18.3% of the control). Figure IV-4 shows an example of chewing-induced suppression of lingual nerve-evoked neuronal activity in a chewing-related neurone. Further analysis of this neurone showed the modulation occurred
during the whole period of the chewing cycle but not during the period of 0-50 ms after the maximum jaw opening (Fig. IV-5). Suppression of lingual nerve-evoked neuronal activity was observed in 6 of 10 neurones with an evoked response latency shorter than 8.0 ms, during both jaw-opening (28.4 ± 31.2% of the control) and jaw-closing (35.1 ± 32.4% of the control) phases. Similarly, suppression of the second longer-latency response also occurred in 5 of 6 neurones during both jaw-opening (4.2 ± 55.2% of the control) and jaw-closing (-41.6 ± 114.2% of the control) phases. Moreover, enhancement of lingual nerve-evoked neuronal activity was also observed in 1 neurone with a short and a second longer-latency response, during both jaw-opening and jaw-closing phases. There was not any significant difference in the extent of modulation of evoked responses between jaw-opening and jaw-closing phases and between different type of chewing-related neurones. There was also modulation of evoked responses in the 1 neurone tested that had no clear chewing-related activities. Figure IV-6 shows an example of chewing-induced suppression of lingual nerve-evoked neuronal activity in a chewing-nonrelated neurone. This suggests that a decrease in evoked neuronal activity during movement cannot be simply explained by occlusion of evoked responses with a neurone’s movement-related activity.

Effects of Cold Block of Ipsilateral Face SI on Face MI Neuronal Activity, RF properties and Chewing-related Modulation

The evoked activity of most MI neurones (73.3% of 30 neurones tested) was not affected by cold block of ipsilateral face SI. Similarly, spontaneous activity of most MI neurones (83.3% of 30 neurones tested) was not changed by cold block of ipsilateral SI; spontaneous activity was decreased in 3 and increased in 2. SI cold block did not appear to affect the short-
latency (≤ 8 ms) responses of 7 neurones tested but did suppress long-latency responses in 7 (Fig. IV-7) and increase these responses in 1 of 25 neurones tested. Interestingly, in 2 neurones, SI cold block did not affect the short-latency (≤ 8 ms) responses but did suppress the second longer-latency responses.

The mechanical threshold of the RF of 30 face MI neurones was tested before, during and after ipsilateral SI cold block. The mechanical threshold was 3.8 ± 0.5 g (mean ± SD) and SI cold block caused an increase in the threshold in only 3 and decrease in only 1 face MI neurone. SI cold block also showed a significant increase in the RF size of 1 neurone (one-way ANOVA with repeated measures).

Similarly, during acute experiments, the evoked activity and spontaneous activity of most MI neurones was not affected by cold block of ipsilateral SI. Of 29 neurones tested during SI cold block, spontaneous activity was decreased in 10 and increased in 1. SI cold block did not appear to affect the short-latency (≤ 8 ms) responses of 2 neurones tested but did suppress long-latency responses 6 of 27 neurones tested (Fig. IV-8).

SI cold block affected the chewing-related suppression of evoked activity in only 6 of 19 neurones tested (Fig. IV-9a-c). Of these 6 neurones, SI cold block influenced the chewing-related suppression of evoked activity in 4 neurones during only either the jaw-opening phase or jaw-closing phase, but not during both phases. Of these 4 neurones, SI cold block attenuated the chewing-related suppression of evoked activity in 1 neurone during the jaw-opening phase and in another 1 neurone during the jaw-closing phase, and enhanced the chewing-related suppression of evoked activity in another neurone during the jaw-opening phase and in the fourth neurone during the jaw-closing phase. In the remaining 2 neurones, SI cold block influenced the chewing-related suppression of evoked activity during both the jaw-
opening and jaw-closing phases. SI cold block attenuated the chewing-related suppression of evoked activity in 1 neurone and enhanced in the other neurone (see Fig. IV-9a-c). Cold block of ipsilateral face SI did not affect the chewing-related suppression of short-latency evoked activity ($\leq 8.0$ ms) in any of the 3 neurones tested. In 1 neurone with both a short- and longer-latency response, cold block influenced the chewing-induced suppression of longer-latency response but not the shorter-latency response (see Fig. IV-9a-c).

DISCUSSION

The present study has demonstrated that the majority of face MI neurones with a tongue RF show a suppression of neuronal activity during chewing and some of the movement-induced modulation of MI evoked neuronal activity is dependent on an intact face SI. To the best of our knowledge, the study is the first to document modulation of somatosensory responses of face MI neurones during orofacial movements and the partial involvement of ipsilateral face SI in this modulation. These findings are consistent with observations that peripheral evoked activity in forelimb MI neurones is decreased during forelimb movement in awake cats (Palmer et al. 1985; Marple-Horvat and Armstrong 1999). They are also in accord with observations in medial lemniscus, VPL and SI that the amplitude of evoked potentials or the evoked neuronal activity decreases during digit or forelimb movements (e.g., see Chapin 1987; Chapman et al. 1988; Jiang et al. 1990b; Shin et al. 1994). Further, they are also consistent with observations in VPM, and face SI that evoked neuronal activities decrease during orofacial movements (Lin and Sessle 1994; Fanselow and Nicolelis 1999).

_Characteristics of Evoked Activity_
The primate limb MI receives a somatotopically organized short-latency somatosensory input from tactile and proprioceptive afferents (e.g., Strick and Preston 1978; Asanuma et al. 1979, 1980; Lemon 1979; Marple-Horvat and Armstrong 1999). For example, Lemon (1979) reported that shortest latency was 6.0 ms for a tap delivered to biceps muscle. Similarly, Marple-Horvat and Armstrong (1999) observed the onset latency of limb MI neuronal responses to stimulation of the superficial radial and ulnar nerves was 6.0 ms. In the present study, we have found that 35% of 48 face MI neurones tested had a very short-latency (≤8.0 ms, range 4.0-8.0 ms) response, and 65% of 48 neurones had a latency longer than 8.0 ms (range: 9.0-28.0 ms); a small proportion of neurones also had a second longer-latency response. However, whether there were one or two evoked responses might depend on the stimulation intensity (see Figs IV-2 and IV-3). However, Huang et al. (1989a) reported the onset latency of face MI neuronal responses to mechanical stimulation of the RF was 14.7 ± 2.8 ms, with a range of 10.0-24.0 ms and did not observed any shorter latency (≤8.0 ms) responses. The difference between the present data and Huang et al’s may be due to the different methodology they used from what we used in the current study.

There are three basic possibilities concerning how trigeminal activity could be transferred to MI neurones: 1) through specific thalamic nuclei, including ventralis lateralis (VL); 2) through corticocortical association fibres of the ipsilateral hemisphere (Pandya and Kuypers 1969; Muakkassa and Strick 1979; Leichnetz 1986), and 3) through commissural fibres via the corpus callosum. The direct thalamic input to MI originates mainly from VL (Olszewski, 1952; Donoghue et al. 1979; Herkenham 1980) and also from posterior nucleus of thalamus (Po) and VPLo (e.g., Lemon and van der Burg 1979). However, it is unlikely that the short-latency sensory information is transmitted through VL and/or Po since latencies of evoked
responses in these sites appeared to be too long (an average of 35.1 and 19.0 ms, respectively) (Diamond et al. 1992; Farkas et al. 1999). Nevertheless, Lemon and van der Burg (1979) have demonstrated that VPLo relays short-latency (6.6 ± 2.2 ms, mean ± SD, most of the onset latency range 4-9 ms) sensory information to limb MI. Our data showing somatosensory inputs to the face MI with latencies as short as 4.0 ms strongly support a direct thalamic input to face MI, and this is supported by the short latency of evoked response in the monkey’s VPM (e.g., Tremblay et al. 1993). Studies in the rat (Nicolelis and Chapin 1994; Nicolelis et al. 1994; Fanselow and Nicolelis 1999) and cat (see Darian-Smith 1966; Dubner et al. 1978) have also demonstrated that VPM neurones may exhibit peripherally evoked responses with similarly short latencies. Although we are unaware of any anatomical studies addressing the connection between primate face MI and VPM, Shin and Chapin (1990b) have reported that some VPM neurones respond to stimulation of the MI in the rat. Whether the short-latency responses in face MI is mediated through VPM needs further investigation.

The short-latency responses in the face MI is unlikely to be mediated by pathways between face MI and SI. This view is based on our data showing that cold block of face SI did not significantly alter short-latency responses (i.e. ≤ 8 ms) in face MI. The observations by Lin and Sessle (1994) that the mean onset latency of the electrically evoked neuronal activity in primate face SI was 9.2 ± 2.3 ms (mean ± SD) also support this notion. They would also rule out the possible involvement in such short-latency responses of transmission of sensory information to the face MI through commissural fibres via the corpus callosum. Nevertheless, in view of these features and connections that exist between SI and MI (e.g., see Asanuma et al. 1981; Porter 1997), face SI may be involved in some of the longer responses evoked by electrical stimulation since cold block of SI did alter longer-latencies (> 8.0 ms) responses.
This is consistent with data showing the latency of activation (11.20 ± 3.09 ms, mean ± SD) by peripheral stimulation (Farkas et al. 1999) of face MI neurones and with reports that ablation of the somatosensory cortex reduced the size of evoked potentials in MI (Asanuma et al. 1980; Farkas et al. 1999). Our finding is also in accord with observations of the influence of SI on limb MI activity (Zarzecki 1989; Caria et al. 1997).

Modulation of Evoked Activity During Chewing

Modulation of somatosensory responses during orofacial movements has been shown in studies observing suppression of excitability of trigeminothalamic neurones and brainstem interneurones during masticatory movements induced by cortical stimulation (e.g., Kim et al. 1986; Olsson et al. 1986) and modulation of somatosensory responses of face SI neurones has also been demonstrated during orofacial movements (Lin and Sessle 1994; Fanselow and Nicolelis 1999). In the current study, we found a diminution of short-latency (≤ 8.0 ms) and longer-latency (>8.0 ms) evoked neuronal activity to be a general feature of somatosensory responses evoked in face MI neurones. Although the data are consistent with those observed in limb MI (Lemon 1979; Palmer et al. 1985; Marple-Horvat and Armstrong 1999), our data further suggest that differences may exist between the jaw-opening phase and jaw-closing phase in some cells (e.g., Fig.IV-5). This is consistent with the report that many of the responses in the cat limb MI to cutaneous stimulation exhibit an increase during the swing phase of the step and a decline to a minimum during the beginning of the next stance phase (Palmer et al. 1985). This is also in accord with the observations by Chapin and Woodward (1982) of neurones showing phasic facilitation just before the footfall event, but suppression during all other phases. During chewing, the majority of the face MI neurones showed a
suppression of evoked activity. The nonsignificant difference in the pattern and magnitude of modulation between chewing-related and chewing-nonrelated neurones during chewing is consistent with analogous observations in face SI (Lin and Sessle 1994) during tongue-protrusion and biting tasks.

It is noteworthy that one jaw opening-related neurone showed a significant increase of evoked activity of both short and longer components during both jaw-opening and jaw-closing phase. This was not a result of higher stimulation intensity since other cells with even higher thresholds showed a suppression during chewing. These findings do not support the observation of Jiang et al. (1991) of nonspecific and widespread suppression of forelimb SI evoked activity before and during rapid elbow movements of monkeys. However, Lin and Sessle (1994) reported that 2 of the 7 task-related neurones in face SI showed a significant increase during the time period 200-300 ms before the EMG onset of GG activity associated with the tongue-protrusion task.

Location and Origin of the Modulation

Movement-related somatosensory modulation has been demonstrated during limb movements at different levels of the lemniscal system (e.g., Chapin 1987; Chapman et al. 1988; Jiang et al. 1990b, 1991; Wiesendanger 1981). The origin of this modulation has been suggested to both peripheral and central. Several studies have suggested the peripheral inputs play an important role in the modulation of somatosensory afferent inputs (e.g., Rushton et al. 1981; Schmidt et al. 1990a,b). In contrast, many studies suggest that it is central in origin. Indeed, it has been shown that somatosensory responses in DCN, thalamus, and limb SI can be inhibited by ICMS in limb MI (e.g., Jiang et al. 1990a; Shin and Chapin 1990a) or limb SI
(e.g., Shin and Chapin 1990b) and the threshold for detecting cutaneous stimuli may rise when the stimulated area is actively moved (e.g., Chapman et al. 1987; Feine et al. 1990). There exist MI corticofugal output pathways capable of modulating efference copy have evolved whereby central commands for movement are considered to modulate incoming sensory information, with MI a critical element in these mechanisms. Similar observations have been found to exist at different levels of the trigeminal lemniscal system (e.g., Lin and Sessle 1994; Faselower and Nicolelis 1999). The documentation (Lin and Sessle 1994) that 50% of the face SI neurones show a suppression of evoked activity before the EMG activity onset associated with the tongue-protrusion movements also supports the evidence that at least part of the modulation of somatosensory afferent inputs during orofacial movements may be central in origin.

As noted above, previous data have shown that the responses of the limb MI neurones to peripheral electrical stimulation during limb movements may be modulated in cat (Palmer et al. 1985; Marple-Horvat and Armstrong 1999) and in monkey (Lemon 1979). Our data have shown that the responses of the majority of face MI neurones to electrical stimulation of the lingual nerve during chewing are also modulated. Several studies have demonstrated that surface stimulation in face SI or MI can produce a somatotopically organised modulation of orofacial reflexes, the presynaptic excitability of trigeminal primary afferents, the excitability of trigeminal motoneurones and brainstem sensory relay neurones and interneurones, and the excitability of VPM neurones (for review, see Darian-Smith 1973; Dubner et al. 1978; Bushnell et al. 1987). These data raise the possibility that somatotopically organised corticofugal projections to the brainstem and thalamus may play an important role in the modulation of somatosensory responses that we have documented in face MI during chewing.
However, there is also another possibility that the projections from face SI to face MI contribute to the modulation of face MI neuronal activity evoked by peripheral stimulation during chewing. It is known that the primate MI receives some of its sensory information via pathway from the somatosensory cortex (see above). Such pathways may transmit movement phase-related sensory inputs to face MI. Indeed, we found that reversible cold block of ipsilateral face SI influenced the chewing-related suppression of long-latency evoked activity (> 8.0 ms) in 6 of 19 neurones tested. However, we did not find that face SI cold block affected the chewing-related suppression of short-latency evoked activity (≤ 8.0 ms), although only 3 neurones were tested. In 1 neurone with both a short- and longer-latency response, cold block influenced the chewing-induced suppression of longer-latency responses but not short-latency responses (see Figs IV-9a-c).

Thus, both face SI projections to the brainstem and thalamus and projections to face MI may contribute the modulation of the somatosensory responses that we have documented in face MI during chewing. However, considering that not all chewing-induced modulation of face MI neuronal activities were affected by inactivation of ipsilateral SI plus the existence of connections between face MI and other cortical areas, we cannot rule out the possibility that other cortical areas may also contribute to the modulation.

Possible Mechanisms and Functional Significance

We have provided evidence to suggest that the modulation of low-threshold somatosensory responses in face MI during chewing is not generalised or nonspecific. First, not all neurones with a tongue RF showed modulation of evoked responses. Second, there is evidence that evoked neuronal activity of some neurones was modulated in a specific jaw
movement phase (e.g., jaw-closing phase) (see Table IV-2) or modulated at specific time intervals (see Fig. IV-5). The diminution of evoked neuronal activity during chewing in the current study cannot be explained by "occlusion" or "saturation" of the somatosensory pathway during the movement because this diminution of evoked neuronal activity can occur in chewing-nonrelated neurones and in the phase that does not show any chewing-related activity. Part of the modulation phenomena might be explained by the interaction of the evoked neuronal activity with kinaesthetic feedback as described by Lin and Sessle (1994) for face SI and by central mechanisms regulating the excitability of the afferent paths from orofacial mechanoreceptors to face MI (see below).

The diminution of the evoked neuronal activity during chewing documented in the present study suggests that the motor centres can adjust the gain of transmitting elements in the somatosensory afferent pathways to compensate for the increased sensory input produced during or as a result of movement (e.g. Chapin 1987; Mackay and Crammond 1989; Lin and Sessle 1994). Indeed, a so-called homeostatic rule of sensory regulation (Mackay and Crammond 1989) indicates that sensory responsiveness of part of the cerebral cortex may be reduced in proportion to the total instantaneous afferent input to that cortical region. Our data are also consistent with the theory of corollary discharge and efference copy that is thought to modulate the transmission of sensory information (for review, see McCloskey 1981); concepts of corollary discharge and efference copy have evolved whereby central command for movement are considered to modulate incoming sensory information, with MI a critical element in these mechanisms. There exist MI corticofugal output pathways capable of modulating somatosensory inputs (for review, see Jones 1986; Willis 1988). Similar studies in the trigeminal sensorimotor system have demonstrated that the face MI can modulate orofacial
reflexes, the presynaptic excitability of trigeminal primary afferents, the excitability of trigeminal brainstem sensory relay neurones and interneurones, and the excitability of VPM neurones (for review, see Darian-Smith 1973; Dubner et al. 1978; Bushnell et al. 1987). Although we are unaware of any study showing that the modulation of face SI neuronal activity was inhibited by ICMS in face MI, the modulation of limb SI neuronal activity inhibited by ICMS in limb MI has been reported (e.g., Jiang et al. 1990a). These corticofugal activities may modulate the somatosensory responses in such a way as to adjust the gain of somatosensory inputs evoked during the movements or generated by the movements and thus maintain the sensorimotor system's sensitivity to externally applied disturbances. In addition, the present data suggest that face SI may not only be involved in the corticofugal modulation of somatosensory inputs (see Lin and Sessle 1994), but also responsible for the modulation of evoked responses in some face MI neurones. This modulatory effect of face SI on face MI might be used for accurate positioning and fine control of orofacial movements.
Table IV-1. Summary of Face MI Activity Evoked by Stimulation of the Lingual Nerve

<table>
<thead>
<tr>
<th>No. of Neurones with Evoked Activity</th>
<th>First Response</th>
<th>Second Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>latency ≤ 8 ms</td>
<td>&gt;8 ms</td>
</tr>
<tr>
<td>Tonic Excitation (n=4)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Food Preparation-Related (n=3)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Rhythmic Firing: Jaw Opening-Related (n=11)</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Jaw Closing-Related (n=11)</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Chewing-nonrelated Neurones (n=1)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total (n=30)</td>
<td>10</td>
<td>20</td>
</tr>
</tbody>
</table>
Table IV-2. Summary of Modulation of Face MI Activity Evoked by Stimulation of the Lingual Nerve During Chewing

<table>
<thead>
<tr>
<th>Type of Chewing-Related Neurones</th>
<th>( \text{Modulation of Evoked Activity (% of control)} )</th>
<th>( \text{First Response} )</th>
<th>( \text{Second Response} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \text{Latency} \leq 8 \text{ ms} )</td>
<td>( &gt;8 \text{ ms} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td>( \text{JO} )</td>
<td>( \text{JC} )</td>
<td>( \text{JO} )</td>
</tr>
<tr>
<td>Tonic Excitation (( n=4 ))</td>
<td>4.2% (( n=1 ))</td>
<td>-3.7% (( n=1 ))</td>
<td>24.4 ± 39.5% (( n=3 ))</td>
</tr>
<tr>
<td>Food Preparation-Related (( n=3 ))</td>
<td>NM (( n=1 ))</td>
<td>NM (( n=1 ))</td>
<td>7.6 ± 10.8% (( n=2 ))</td>
</tr>
<tr>
<td>Jaw Opening-Related (( n=11^* ))</td>
<td>33.0 ± 30.8% (( n=3 ), NM(( n=2 ))</td>
<td>42.3 ± 37.1% (( n=3 ), NM(( n=2 ))</td>
<td>7.8 ± 9.7% (( n=4 ), NM(( n=1 ))</td>
</tr>
<tr>
<td>Jaw Closing-Related (( n=11 ))</td>
<td>33.7 ± 47.7% (( n=2 ))</td>
<td>43.8 ± 26.7% (( n=2 ))</td>
<td>19.9 ± 23.2% (( n=9 ))</td>
</tr>
<tr>
<td>Chewing-nonrelated Neurones (( n=1 ))</td>
<td></td>
<td>5% (( n=1 ))</td>
<td>10% (( n=1 ))</td>
</tr>
</tbody>
</table>

\( \text{NM} = \text{no modulation, JO = jaw-opening phase, JC = jaw-closing phase.} \) \( ^* \text{includes a neurone, whose lingual nerve stimulation evoked activity was enhanced during chewing that is not listed in this table.} \)
FIGURE LEGENDS

Figure IV-1. An example of MI neuronal activity evoked by stimulation of contralateral lingual nerve. Top trace of each panel represents a single trial with 1.2 T of stimulation intensity. The PSTH was built from 47 trials in neurone A, 30 in neurone B, and 69 in neurone C, and arrowheads represent the onset of stimulation. The RF of each neurone was arranged to the right. Note the shortest latency was 22.0, 4.0 and 7.0 ms for neurone A, B, C, respectively. Neurone C also had a second and longer-latency (69.0 ms) response.

Figure IV-2. An example of relationship of stimulation intensities of contralateral lingual nerve and MI neuronal evoked activities. The inserted single trace in panel A, B and C represents a single trial with 1, 1.2, and 2 T of stimulation intensity, respectively. Each PSTH was built from 34 trials. Note the latency of the evoked response by 1 T stimulation (A) was longer than that by 1.2 (B), and 2 T (C) stimulation, and a second longer-latency response occurred with 1.2 and 2 T stimulation.

Figure IV-3. Another example of relationship of stimulation intensities of contralateral lingual nerve and MI neuronal evoked activities. This Figure is arranged as for Figure IV-2. Each PSTH was built from 23 trials and arrowheads represent the onset of stimulation. The RF of each neurone was arranged to the right. Note the latency of the evoked response by 1 T stimulation (A) was longer than that by 1.2 (B), and 2 T (C) stimulation, and a second shorter-latency response occurred with 2 T stimulation.
Figure IV-4. Modulation of MI neuronal response evoked by stimulation of the contralateral lingual nerve during chewing. This neurone showed a significant change in firing rate during jaw-closing phase. All trials were aligned to the start of the stimulus indicated by arrowheads and each PSTH was built from 30 trials. PSTH A: stimulation of the lingual nerve (1.27) when the animal was wakeful but quiet and no orofacial movement was detected. PSTH B: stimulation of the lingual nerve (1.27) when the jaw was opening. PSTH C: stimulation of the lingual nerve (1.27) when the jaw was closing. D: plot shows the chewing-related activity (O) as well as evoked activity plus chewing-related activity (●). E: number of evoked spikes in 50 ms (■, see Methods) calculated by subtracting value (O) from value (●) for the PTP, jaw-opening phase, and jaw-closing phase for chewing. Vertical bars, 1 SD of the mean number of spikes indicated; the evoked activity value is significantly different from PTP value (* $P < 0.05$).

Figure IV-5. Further analysis of modulation of MI evoked activity of chewing-related neurone reported in Figure IV-4, during chewing. Top shows (i) the mean number of spikes in 50-ms period for trials without stimulation of the contralateral lingual nerve (O) and (ii) the mean number of spikes in 50-ms periods after the onset of evoked response (●) during each time period indicated. Bottom shows for each time period the mean number of evoked spikes in 50-ms periods (■) calculated by subtracting value (i) from value (ii). Time 0 represents the maximum jaw-opening during chewing. Vertical bars: 1 SD of the mean number of spikes. *** $P < 0.001$.

Figure IV-6. Modulation of MI neuronal response evoked by stimulation of the contralateral lingual nerve during chewing. This neurone did not show a significant change in firing rate
during chewing. All trials were aligned to the start of the stimulus indicated by arrowheads and each PSTH was built from 20 trials. PSTH A: stimulation of the lingual nerve (1.27) when the animal was quite and no orofacial movement was detected. PSTH B: stimulation of the lingual nerve (1.27) when the jaw was opening. PSTH C: stimulation of the lingual nerve (1.27) when the jaw was closing. D: plot shows the chewing-related activity (O) as well as evoked activity plus chewing-related activity (●). E: number of evoked spikes in 16 ms (◼, see Methods) calculated for the PTP, jaw-opening phase, and jaw-closing phase for chewing. Vertical bars: 1 SD of the mean number of spikes indicated; the evoked activity value is significantly different from PTP value (* P< 0.05).

Figure IV-7. An example of MI neuronal activity evoked by stimulation of the ipsilateral (A) or contralateral (B) lingual nerve. The RF of neurone A and B was located on the ipsilateral (A) or contralateral (B) anterior tongue dorsal surface (see face figurines). All trials were aligned to the start of the stimulus indicated by arrowheads. Each PSTH of neurone A was built from 30 trials and that of neurone B was constructed from 40 trials. Note that cold block of face SI was associated with a decrease in the evoked MI neuronal activity in neurone B, but not in neurone A compared with pre-cool and post-cool conditions.

Figure IV-8. An example of MI neuronal activity evoked from the neurone’s RF in the anaesthetised monkey. This Figure was arranged as for Figure IV-7. The RF of neurone A and B was located on the contralateral anterior tongue dorsal surface (see face figurines). Each PSTH of neurone A was built from 25 trials and that of neurone B was constructed from 34 trials, and the bin width in all PSTHs was 2 ms. Note that cold block of face SI was associated
with a decrease in the evoked MI neuronal activity in neurone B, but such a decrease was not readily apparent in neurone A compared with pre-cool and post-cool conditions.

Figure IV-9a-c. Effects of cold block of face SI on chewing-induced modulation of MI neuronal response evoked by stimulation of the contralateral lingual nerve. Figure IV-9a. PSTHs for the evoked response during pre-cool, cool, and post-cool conditions. All trials were aligned to the start of the stimulus indicated by arrowheads and each PSTH was built from 15 trials. Arrowheads represent the onset of stimulation. Figure IV-9b. Quantitative analysis of the neurone reported in Figure IV-9a. The plots show (i) the mean number of spikes in 6-ms or 48-ms periods for trials without stimulation (○) and (ii) the mean number of spikes in 6-ms periods for the first or in 48-ms periods for the second component of the evoked response after the onset of the corresponding component for the evoked responses (●) during each time period indicated. Figure IV-9c. Further analysis of the neurone reported in Figure IV-9a-b. The plots show for each time period the mean number of evoked spikes in 6-ms (left) or 48-ms periods calculated by subtracting value (i) from value (ii) in Figure IV-9b. Note the evoked responses had a short and longer component and SI cold block significantly depressed a second longer-latency response. Also note the first component of the evoked response was not significantly affected and movement-induced modulation of the second component of the evoked response disappeared during SI cold block. * $P < 0.05$
Figure IV-1

A

B

C

No. of Spikes

No. of Spikes

No. of Spikes

Contra-lateral

Contra-lateral

Contra-lateral

0.25 mV

0.25 mV

0.25 mV

20 ms
Figure IV-3
Figure IV-5

(A) No. of Spikes

(B) No. of Evoked Spikes
Figure IV-7
Figure IV-9a
Figure IV-9b
CHAPTER V. GENERAL DISCUSSION AND CONCLUSIONS

The MI, as well as SI, have been shown to be crucial in sensorimotor integration and control. Previous studies (Murray et al. 1991; Murray and Sessle 1992a,b,c; Lin et al. 1993, 1994a,b) have demonstrated (a) similar differential effects, induced by cold block of face SI or MI, on the tongue-protrusion and biting tasks, (b) similar SI and MI neuronal activity preferentially related to the tongue-protrusion task, (c) the existence of a variety of similar activity patterns in SI and MI during the task, and (d) many neurones in SI and MI that exhibit a single preferred direction of firing and a systematic change in firing rate with changes in tongue-protrusion direction. The findings outlined above raise the question whether face SI could conceivably contribute to motor control by relaying its orofacial afferent inputs to face MI and thereby influence both the responsiveness to orofacial stimuli and the movement-related activity of face MI neurones. In view of the above electrophysiological evidence and abundant connections and integration between SI and MI (e.g., Pandya 1977; Jones et al. 1978; Ghosh and Porter 1988; Vogt and Zarzecki 1989; Porter et al. 1990; Porter 1997), the general aim of this study was to clarify the role of sensory inputs via face SI to primate face MI and to determine how these areas contribute to sensorimotor integration and control of orofacial movements.

The specific aims of the present study were to test 1) whether face MI neurones show chewing-related activity as well as activity in other orofacial movements and to define the features of the chewing-related activity; 2) whether ipsilateral face SI cold block could affect chewing and tongue-protrusion task as well as face MI neuronal activity related to chewing or tongue task; 3) whether chewing modulates the evoked somatosensory responses of face MI neurones; and 4) whether ipsilateral face SI cold block can also affect face MI neuronal
activity evoked by orofacial stimulation. The investigation that involved the techniques of reversible, cooling-induced inactivation of face SI and single-neurone recordings in face MI was carried out and successfully addressed all the specific aims of this thesis. It has provided original and fundamental data relevant to our understanding of cortical control of orofacial movements.

We have confirmed the general functional features of face MI neurones in relation to the task and swallowing that has been reported in previous studies (Murray and Sessle 1992b; Martin et al. 1997) and have documented in detail the functional properties of face MI neurones in relation to chewing. These data are also consistent with the view that multiple, discrete efferent zones exist for the production of elemental tongue movements and for tongue movements associated with semi-automatic movements such as chewing. Thus, the combined activation of different efferent zones could contribute to the neural framework required for the complexity of tongue movements in orofacial motor behaviours and to the need for close neuronal integration for control of these behaviours. Furthermore, our data revealing that substantial numbers of MI neurones display chewing- and/or swallowing-related activity add further evidence in support of the view, based on the effects of disruption or ICMS of face MI and earlier recordings of chewing-and/or swallowing-related activity in face MI (Penfield and Rasmussen 1950; Kubota and Niki 1971; Luschei et al. 1971; Luschei and Goodwin 1975; Huang et al. 1989b; Martin et al. 1997), that face MI plays an important role not only in the control of voluntary movements such as trained tongue protrusion, but also in semi-automatic movements (see Sessle et al. 1995a).

The chewing-related activity of the face MI neurones has revealed 4 major patterns of activity. The findings suggest that the various types of chewing-related activity may reflect
different types of cortical neurones (for example, corticobulbar projection neurones, cortical interneurones, and corticocortical association neurones) involved in driving chewing-related movements or in responding to movement-evoked afferent inputs or in some other form of sensorimotor integration related to chewing. In addition to the neurones which only showed an increase in activity during food preparation phase, the majority of rhythmic jaw movement-related MI neurones also showed the food preparation-related activity. The findings are consistent with the tongue movement deficit during the food preparation phase caused by bilateral inactivation of face MI by cooling (unpublished observation). Some MI neurones showed altered activity only during the interval immediately preceding the EMG-defined chewing onset, that is, in advance of chewing. Thus it is likely that these neurones may be involved in driving tongue motor units in chewing rather than their activity being, for example, simply a reflection of movement-generated reafference (see below). It is possible that these early firing MI neurones could be involved in the cortical initiation of chewing, including the driving of specific muscles. Nonetheless, other chewing-related MI neurones were activated during the chewing itself, and so these neurones may initiate or drive motor units later in the chewing synergy. These different neuronal firing patterns may have been related to differences in the duration and relative timing of chewing-related EMG bursts across the changing chewing conditions as the foodstuff was trituated.

The thesis has also demonstrated that some tongue MI neurones show activity in relation to tongue-protrusion task as well as chewing and/or swallowing. One possible interpretation of this finding is the tongue movements involved in chewing and tongue protrusion are not specific to these behaviours but rather are also incorporated into the movement sequence of swallowing. Thus a given tongue MI neurone may be activated during
both activities because the same movement subunit of the motor cortex is recruited. The population of activated tongue MI neurones presumably would be distinct, however, underlying the distinct tongue movement sequences seen in, for example, swallowing, licking, and chewing (Dubner et al. 1978; Hiiemae and Crompton 1985; Texton and MaGarrick 1988, 1989). Another interpretation is that the activity of these tongue MI neurones in both swallowing and chewing reflects the needs for a close neuronal integration of control of these various motor activities. Our findings are also consistent with the earlier studies (Huang et al. 1989b; Martin et al. 1999) showing an extensive overlap of swallow cortex and CMA defined by long train ICMS in the awake monkey. On the other hand, we also noticed that tongue MI neurones showing food preparation-relation activity did not exhibit any pre-swallow or swallow-related activity. The possible interpretation of this finding is that tongue movements during food preparation phase are specific to this behaviour, not being incorporated into the movement sequence of swallowing.

Face SI could conceivably contribute to motor control by relaying its orofacial afferent inputs to face MI and thereby influence the movement-related activity of face MI neurones. In the next phase of the study, an attempt was made to determine whether the activity of face MI neurones related to a trained tongue-protrusion task or chewing and swallowing was dependent on the functional integrity of the ipsilateral face SI and whether inactivation of face SI affects orofacial movements. The study revealed that both the task- and chewing-related activity of most face MI neurones and the swallowing-related activity of all face MI neurones tested was independent of the functional integrity of the ipsilateral face SI. Similarly, unilateral cold block of SI had limited effects on the performance of the task or chewing and no effects on swallowing. Approximately one-quarter of the face MI neurones also did show a change in
task or chewing-related activity during cold block of ipsilateral face SI; this change was mainly reflected as a decrease in movement-related activity. This finding suggests that the movement-related activity of some MI neurones may reflect a tonic facilitatory input from the ipsilateral face SI to face MI or a reaффerentation by excitatory orofacial sensory inputs relaying through SI to MI and phasically evoked by the task or chewing movements. A small proportion of neurones also showed a cold block-induced change in spontaneous activity and again this was mainly reflected as a decrease in activity. Some MI neurones manifested a cold block-induced increase in spontaneous or movement-related activity, and although their numbers were very small, this does suggest that part of the SI influence on MI neuronal activity may be depressive as well as facilitatory.

The majority of face MI neurones, however, showed no significant change in the movement-related activity during SI cold block. This indicates that the movement-related activity of most face MI neurones may not be dependent on the functional integrity of the ipsilateral face SI, consistent with limb sensorimotor cortex data revealing that sensory inputs to most limb MI neurones have been suppressed during the limb movements (Lemon 1979; Palmer 1985) and the movement-related activity of many limb MI neurones is not a reflection of reaффerentation (although there is also some contrary evidence) (Evarts 1986; Asanuma 1989). Our findings are also in accord with the view that reaффerentation might not be a major factor accounting for the movement-related activity of MI neurones, although we cannot exclude in these experiments the possibility that this activity may be a reflection, at least in part, of peripherally evoked orofacial afferent inputs accessing face MI by routes other than through the ipsilateral face SI e.g. other ipsilateral cortical areas, ipsilateral posterior thalamus, contralateral sensorimotor cortex. Nevertheless, in addition to our data of the effects of SI cold
block outlined above, there are several other lines of evidence indicating that the MI movement-related activity patterns in most face MI neurones might not simply be due to reafferentation via face SI or other peripheral input pathways to MI. First, not all task-, swallowing- or chewing-related face MI neurones have a detectable RF from which orofacial excitatory inputs could have been activated during orofacial movements. Second, as noted above, some MI neurones fire in advance of the EMG-defined movement onset, and so it is unlikely that these activity patterns are exclusively due to reafferentation. Third, other studies in our laboratory have demonstrated that a gating of orofacial somatosensory afferent inputs to face SI neurones immediately preceding and during the monkey’s performance of the tongue-protrusion task (see Lin and Sessle 1994). Fourth, our studies have provided direct evidence that a gating of orofacial somatosensory afferent inputs to face MI neurones happens during the monkey’s performance of chewing (see Chapter IV). These various lines of evidence support the view that movement-related activity patterns of most face MI neurones might not simply reflect a result of reafferentation arising from the movement performed.

The limited effects of unilateral face SI cold block on ipsilateral task- or chewing-related activity in face MI neurones would appear to explain the limited effects of unilateral face SI cold block on the awake monkey’s performance of the tongue-protrusion task or chewing. Since the ipsilateral SI is a major source of afferent input to MI from peripheral tissues projecting to the cortex, these findings also suggest that movement-induced reafferentation via the ipsilateral face SI may not be a significant factor in accounting for the activity of most face MI neurones related to both trained movements and semi-automatic movements such as chewing and swallowing. In view of the critical role that face MI plays in tongue-task performance (Murray et al. 1991) and the limited effect of unilateral SI cold block on task-
related MI neuronal activity documented in the present study, cold block-induced inactivation of corticofugal effects from SI on subcortical centres involved in somatosensory transmission and motor control appears to be the likely explanation for the marked disruptive effects that bilateral cold block of primate face SI has on tongue-task performance (Lin et al. 1993). In the case of the disruptive effects on chewing of bilateral SI cold block (Lin et al. 1998) vis-à-vis the restricted influence we document here of unilateral SI cold block on MI chewing-related activity, cold block-induced disruption of corticofugal effects from primate chewing-related activity, cold block-induced disruption of corticofugal effects from primate face SI on subcortical regions, such as the brainstem ‘chewing centre’ (Dubner et al. 1978; Luschei and Goldberg 1981; Lund 1991; Nakamura and Katakura 1995), must again be considered as a likely explanation. However, in this case, there is also the possibility that the disruptive effects on chewing might conceivably be due in part to the SI cold block affecting chewing-related neurones that also can be found in the more lateral ‘cortical masticatory area’ and that may project to these subcortical regions (Lund and Lamarre 1974; Luschei and Goldberg 1981; Sessle et al. 1995a).

As discussed above and suggested for limb MI, it is possible afferent inputs to face MI are modulated during orofacial movements so that only selected inputs useful in guiding the movement or in adapting the movement to an altered orofacial environment gain access to MI. Modulation of orofacial somatosensory responses during movements has been demonstrated in studies showing decreased excitability of trigeminothalamic neurones and brainstem interneurones with a skin or mucosa RF during masticatory movements induced by cortical stimulation (e.g., Kim et al. 1986; Olsson et al. 1986) and modulation of somatosensory responses of face SI neurones has also been demonstrated during orofacial movements (Lin and Sessle 1994; Fanselow and Nicolelis 1999). However, the modulation of somatosensory
responses of face MI neurones had not been demonstrated during orofacial movements until the present study. Most single neurones in the face MI were found to alter their firing rate during chewing and although the data suggest that some of this movement-related activity in the face MI might conceivably come from re-afferent inputs from the moving orofacial structures, arguments were proposed in favour of the view that orofacial inputs may be modulated during the orofacial movements. In view of the reciprocal projections between SI and MI (Vogt and Pandya 1977; Jones et al. 1978; Porter 1997) and the role of face SI on modulation of subcortical inputs, face SI may also contribute to the modulation of sensory transmission to face MI neurones.

Therefore, the last part of this study was to investigate the possible modulation of evoked orofacial somatosensory responses of face MI neurones during chewing and the possible of involvement of face SI in this modulation and in evoking the responses of face MI neurones. In the present study, we have found that about one-third of the face MI neurones tested had a very short-latency (≤ 8.0 ms) response evoked by stimulation of lingual nerve, and the remaining face MI neurones tested had a latency longer than 8.0 ms; some also had a second longer-latency response. The short-latency responses (≤ 8.0 ms) point to a direct pathway to face MI. This is consistent with the data showing SI cold block did not appear to affect the short-latency (≤ 8.0 ms) although SI cold block did affect long-latency responses in a small portion of these neurones tested. During acute experiments, the evoked activity and spontaneous activity of most MI neurones also was not affected by cold block of ipsilateral SI. These various findings are consistent with the findings that SI cold block did not affect the orofacial movement-related activity of most of face MI neurones tested.

A diminution of evoked neuronal activity was found to be a general feature of somatosensory responses of primate face MI neurones during chewing. While the data are
consistent with those observed in forelimb SI (Chapin and Woodward 1982a,b; Jiang et al. 1991), face SI (Lin and Sessle 1994; Fanselow and Nicolelis 1999) and limb MI (Lemon 1979; Palmer et al. 1985; Marple-Horvat and Armstrong 1999), our data further suggest a movement specificity in the suppression of somatosensory responses in MI neurones. Also, the data showed there was no significant difference in the pattern and magnitude of modulation between chewing-related and chewing-nonrelated neurones during chewing, which is consistent with analogous observations in face SI (Lin and Sessle 1994) during tongue-protrusion and biting tasks.

Evidence has also been provided that the diminution of evoked neuronal activity during the orofacial movement cannot be explained by "occlusion" or "saturation" of the somatosensory pathway during the movement because this diminution of evoked neuronal activity can occur in chewing-nonrelated neurones and can occur in the phase that does not show any chewing-related activity. Part of the modulation phenomena might be explained by the interaction of the evoked neuronal activity with kinaesthetic feedback as described by Lin and Sessle (1994) for face SI.

Movement-related somatosensory modulation has been demonstrated during limb movements at different levels of the lemniscal system (e.g., Wiesendanger 1981; Chapin 1987; Chapman et al. 1988; Jiang et al. 1990b, 1991). The origin of this modulation has been suggested to both peripheral and central. Several studies have suggested the peripheral inputs play an important role in the modulation of somatosensory afferent inputs (e.g., Rushton et al. 1981; Schmidt et al. 1990). In contrast, many studies suggest that it is central in origin. Indeed, it has been shown that somatosensory responses in dorsal column nuclei, thalamus, and limb SI can be inhibited by ICMS in limb MI (e.g., Jiang et al. 1990a; Shin and Chapin 1990a) or
limb SI (e.g., Shin and Chapin 1990b); moreover, the threshold for detecting cutaneous stimuli may rise when the stimulated area is actively moved (e.g., Chapman et al. 1987; Feine et al. 1990), and there exist MI corticofugal output pathways capable of modulating somatosensory inputs. Similarly, modulation of orofacial somatosensory responses during movements has also suggested that it is central in origin (e.g., Kim et al. 1986; Olsson et al. 1986; Lin and Sessle 1994; Fanselow and Nicolelis 1999).

Several studies have demonstrated that surface stimulation in face SI or MI can produce a somatotopically organised modulation of orofacial reflexes, the presynaptic excitability of trigeminal primary afferents, the excitability of trigeminal motoneurones and brainstem sensory relay neurones and interneurones, and the excitability of VPM neurones (for review, see Darian-Smith 1966, 1973; Dubner et al. 1978; Bushnell et al. 1987;). These data raise the possibility that somatotopically organised corticofugal projection to the brainstem and thalamus may play an important role in the modulation of somatosensory responses that we have documented in the face MI during chewing. There is also another possibility that projections from face SI contribute to the modulation of face MI neuronal activity evoked by peripheral stimulation during chewing. It is known that the primate MI receives some of its sensory information via the somatosensory cortex (see above). Such pathways may transmit movement phase-related sensory input to the MI. However, considering that not all chewing-induced modulation of face MI neuronal activities were affected by inactivation of ipsilateral SI and the existence of the connections between face MI and other cortical areas, we cannot rule out the possibility that other cortical areas may also contribute to the modulation.

The present data are in accord with the view that the motor centres can adjust the gain of transmitting elements in the somatosensory afferent pathway to compensate for the increased
sensory input produced during or as a result of the movement (e.g., see Wall 1975; Chapin 1987, MacKay and Crammond 1989; Lin and Sessle 1994; Fanselow and Nicolelis 1999; Marple-Horvat and Armstrong 1999). The data are also consistent with the theory of corollary discharge and efference copy that is thought to modulate the transmission of sensory information (for review, see McCloskey 1981); concepts of corollary discharge and efference copy have evolved whereby central command for movement are considered to modulate incoming sensory information, with MI a critical elements in these mechanisms. There exist MI corticofugal output pathways capable of modulating somatosensory inputs (for reviews, see Jones 1986; Willis 1988). Similar studies in the trigeminal sensorimotor system have also demonstrated that the face MI can modulate orofacial reflexes and excitability of neurones at different levels of the trigeminal lemniscal system (for review, see Darian-Smith 1973; Dubner et al. 1978; Bushnell et al. 1987). Although we are unaware of any study showing that the modulation of face SI neuronal activity can be inhibited by ICMS in face MI, modulation of limb SI neuronal activity inhibited by ICMS in limb MI has been reported (e.g., Jiang et al. 1990a). This corticofugal activity may modulate the somatosensory responses in such a way as to adjust the gain of somatosensory inputs evoked during the movements or generated by the movements and thus maintain the sensorimotor system's sensitivity to externally applied disturbances.

Our present data further suggest that face SI is not only involved in the corticofugal modulation of somatosensory inputs (see Lin and Sessle 1994) but is also responsible for the modulation of evoked response in some face MI neurones. This modulatory effect of face SI on face MI might be used for accurate positioning and fine control of orofacial movements.
Final comments and future directions

Our data revealing that substantial numbers of MI neurones display chewing-related activity add further that face MI plays an important role not only in the control of voluntary movements such as trained tongue protrusion, but also in semi-automatic movements. Taken together with the earlier neuronal and ICMS data, our data are also consistent with the view that multiple, discrete efferent zones exist for the production of elemental tongue movements and for tongue movements associated with semi-automatic movements such as chewing. Thus, the combined activation of different efferent zones could contribute to the neural framework required for the complexity of tongue movements in orofacial motor behaviours and to the need for close neuronal integration for control of these behaviours.

The cold-block study revealed that both the orofacial movement-related and spontaneous activity of most face MI neurones was independent of the functional integrity of the ipsilateral face SI and the movement-related activity of a small portion of MI neurones may reflect a tonic facilitatory input from the ipsilateral face SI to face MI or a reafferentation by excitatory orofacial sensory inputs relaying through SI to MI and phasically evoked by the task or chewing movements. The findings also suggest that reafferentation may not be a major factor accounting for the movement-related activity of MI neurones. However, we cannot exclude in these experiments the possibility that this activity may be a reflection, at least in part, of peripherally evoked orofacial afferents inputs accessing face MI by routes other than through the ipsilateral face SI (e.g. other ipsilateral cortical areas, ipsilateral posterior thalamus, contralateral sensorimotor cortex); this might be tested in the future by cold block or local anaesthetic block of these regions as well as peripheral local anaesthetic block of afferent inputs. Indeed, the somatosensory responses in most of face MI neurones are modulated during
chewing. This suggests that the face MI may have the ability to shape movement-related activity during the movement. Thus, face MI appears to be capable of modulating somatosensory inputs to MI and may adjust the gain of somatosensory inputs evoked during the movements or generated by the movements and thus maintain the sensorimotor system’s sensitivity to externally applied disturbances. Our findings could be extended in future studies that investigate the possible mechanisms for this modulation (i.e. through efference copy from face MI) by testing the effects of cold block or local anaesthetic block of face MI on the peripherally evoked neuronal responses in SI, VPM or trigeminal sensory complex during orofacial movements.

Chewing or swallow-related neuronal activity has been documented in face MI and several activity patterns defined, but there has been no systematic studies of these properties in SI or CMA/swallow cortex (except for some chewing-related neurones described in CMA (e.g., Lund and Lamarre 1974). Such approaches are needed in order to clarify whether similar or different patterns of semi-automatic movement-related activity patterns occur in MI, SI and CMA/swallow cortex and thereby provide further insights into the different roles that these three regions may play in semi-automatic movements.

This study, in conjunction with recent studies in face MI, has also provided evidence which has suggested an important role of face sensorimotor cortex not only in the generation and control of voluntary orofacial movements, but also in the generation and control of semi-automatic orofacial movements. The present study suggests future experiments to extend our findings. For example, the localized injections of local anaesthetics or more specific neurotransmitter analogues, such as a GABA agonist (e.g., muscimol) while chewing or swallowing is being performed would provide additional tests in orofacial semi-automatic
movement control. We predict that specific deficits in tongue and jaw movement would result that would reflect the nature of the movement that could be evoked by ICMS from the site of neuronal recording. An analogous approach could be applied to the other cortical areas (e.g., CMA, SI) noted above and implicated in semi-automatic movements, and testing for the dependency of their properties on other cortical areas through the use of cold block, local anaesthetic injections, etc.

This study has also provided evidence that short-latency responses (≤ 8.0 ms) can be evoked in face MI and that cold block of ipsilateral SI does not affect such short-latency responses. These findings suggest that such short-latency responses might involve a more direct pathway to MI (e.g., via thalamus). To test this hypothesis, future experiments could inject anatomical tracers into the MI of the monkey to provide anatomical evidence whether there are connections between face MI and SI, and between face MI and thalamus nuclei such as VPM. To test the role of a possible direct pathway from thalamus to the face MI, inactivation of thalamus (i.e. VPM) by cold block or local anaesthetic injection could be carried out to test whether MI neuronal activity is affected.

Our present study involved tongue-task training. This training may have caused plasticity in MI and other cortical orofacial regions that are associated with learning of the motor skill. Recent PET and fMRI studies have reported that learning of a skilled digit movement results in an expansion of the PET or fMRI-defined primate MI representing hand movements and that these changes may persist for days or months depending on the training parameters (e.g. Seitz et al. 1990; Jenkins et al. 1994; Kami et al. 1995). Transcranial magnetic stimulation studies also report that training of particular forelimb movements can result in an enhanced representation in MI of the muscles engaged in the task (e.g., Pascual-Leone et al. 1994;
Classen et al. 1998) and studies using ICMS also reveal progressive changes in limb MI motor representations after monkeys are trained in digit or forearm tasks (Nudo et al. 1996), prompting Nudo et al to conclude that a neurophysiological correlate of a motor skill resides in MI after skill acquisition and that the size of a motor representation in MI may be related to motor skill. MI plasticity has also been revealed as a consequence of focal blockade or ICMS of MI, or peripheral sensory or motor nerve manipulation in primates including humans, and in subprimates (e.g. Nudo et al. 1990; Keller et al. 1996; Donoghue 1997; Buonomoto and Merzenich 1998).

There are as yet no analogous studies in face MI and other cortical orofacial areas. Future experiments can extend our current study to test if learning of a novel orofacial motor behaviour is associated with changes in the neuronal properties and ICMS features in face MI, SI and CMA/swallow cortex. These studies in awake primates will give new insights into the cortical mechanisms underlying orofacial sensorimotor control, particularly of semi-automatic orofacial movements, and provide important initial steps in determining the neuroplastic and adaptive characteristics of the sensorimotor cortex required for the acquisition of orofacial motor skills and memory. Clarification of the roles of the different cortical regions in orofacial motor control and their plasticity and adaptative characteristics with changes in sensory inputs or learning also has clinical significance in view of the limited scientific underpinning of current therapeutic approaches (see Goldstein 1990; Martin and Sessle 1993) to manage and retrain patients suffering from speech and ingestive impairment after cortical damage or peripheral lesions.
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