Mastication and its Control by the Brain Stem

J. P. Lund

Department de Stomatologie and Centre de Recherche en Sciences Neurologiques, Ds24, Pav. Prine, Université de Montréal, CP 6128, Succ A, Montréal, Canada H3C 3J7.

ABSTRACT: This review describes the patterns of mandibular movements that make up the whole sequence from ingestion to swallowing food, including the basic types of cycles and their phases. The roles of epithelial, periodontal, articular, and muscular receptors in the control of the movements are discussed. This is followed by a summary of our knowledge of the brain stem neurons that generate the basic pattern of mastication. It is suggested that the production of the rhythm, and of the opener and closer motoneuron bursts, are independent processes that are carried out by different groups of cells. After commenting on the relevant properties of the trigeminal and hypoglossal motoneurons, and of internurons on the cortico-bulbar and reflex pathways, the way in which the pattern generating neurons modify sensory feedback is discussed.

KEY WORDS: motor control, central pattern generation, mastication, brain stem, motoneurons, reflexes, sensory afferents, interneurons, deafferentation, paralysis.

I. INTRODUCTION

Mastication is the first stage of digestion in most mammals. It is an intermittent rhythmic act in which the tongue, facial, and jaw muscles act in coordination to position the food between the teeth, cut it up, and then prepare it for swallowing. During the course of evolution, the mammalian jaws and dentitions have evolved in several directions from their reptillian prototype in order to take maximum advantage of the various classes of food that exist. Now there are several general groups of animals with distinct types of masticatory systems. For example, carnivores are adapted to shear meat into pieces and swallow them with little chewing, while herbivores are specialized for the almost continuous grinding of fibrous food. Although the movements that a cow uses to chew its cud are obviously different from those of a dog crunching up bones, there appear to be some features that are the same in all mammals that chew, and this suggests that the fundamental mechanisms of control are common to all.

II. PATTERNS OF MOVEMENT

The determination of the basic features of mastication depends on adequate descriptions of the patterns of movement and muscle activity, and on comparisons between species. Good descriptions of mastication can be found for the opossum, cat, rat, hamster, and rabbit, but it is unfortunate that there are no comparable descriptions of human mastication that include the sequential changes in the form of the masticatory cycle and in the patterns of muscle activity.

We lack a common terminology, and this makes the interpretation of data from different laboratories and from different species difficult. Since no system of classification is in general use, I will use one that was developed from work.
on the rabbit, and that in turn is based in large part on that of Hiiemae. This system has three advantages: (1) it describes the whole process of mastication from ingestion to swallowing, (2) it is simple, and (3) it is analogous to the terminology used for locomotion, so that comparisons between the two motor systems are easier to make. Descriptions of the various terminologies that have been proposed can be found in Hiiemae and Schwartz et al. Although it has been said that the pattern of mastication is stereotyped, there is, in fact, a great deal of variability between cycles within the same series of movements (Figure 1), between foods, and between individual subjects. We should not ignore this characteristic, nor try too hard to describe mastication in terms of an average cycle or typical envelope that contains most movements. Uncoving the relationships between the different variables helps us to understand the system that controls the movements. As will be seen, the evidence suggests that sensory inputs to the brain stem cause most of the variability by modifying a regular centrally generated pattern.

A. Masticatory Sequence

The masticatory sequence (Figure 2) is the whole set of movements from ingestion to swal-

FIGURE 1. Two-dimensional frontal view of the movement of the mandible of an adult female subject chewing dried beefstick. These data were recorded with a model 5 kinesiograph. (Stohlter, C. S., unpublished work.)
FIGURE 2. A masticatory sequence from an awake rabbit. The head was fixed during the recording of movements of the mandible with a photodiode system. A piece of rabbit chow was put into the mouth (left), transported to the molar teeth during the preparatory series, chewed during the reduction series, and prepared for swallowing (preswallowing series). Swallowing occurred during the THY burst. Cycles 4 to 6, 11 to 13, and 25 to 27 appear in Figure 3, while all the cycles of the preparatory and preswallowing series and 5 reduction series trials marked with the horizontal bars were used for Figure 4. Abbreviations: VERT, LAT, A-P-vertical, lateral, and anterior-posterior movements of a small light attached to the mandibular symphysis; RDIG-, LDIG-, RDMA-, LDMA-, RPTE-, THY-electromyograms from the right (R) and left (L) digastric, deep masseter, medial pterygoid, and thyrohyoid muscles, respectively. (From Schwartz, G., Enomoto, S., Valliquette, C., and Lund, J. P., J. Neurophysiol., 62, 273, 1989. With permission.)

1. Preparatory Series

There is great inter-species variability in the way in which food is gathered and broken into chewable pieces. Most herbivores crop leaves, rodents, and lagomorphs (rabbits and hares) gnaw, while other species cut meat into pieces or break the shells of insects. Afterward, the food is moved to the posterior teeth by the tongue, aided in some animals by tossing of the head. Movements of the head are not of much importance in rabbits. They move the food backward during a short series of type I cycles that have only two phases, fast closing (FC) and opening (O) (Figure 3). There is usually little lateral movement during closure (Figure 4A) or electromyographic activity (EMG) in the jaw-closing muscles, but the digastrics (jaw-opening muscles) are very active (Figure 2). This series comes
FIGURE 3. Examples of the three main types of masticatory cycle from the sequence shown in Figure 2, showing the phases and the automatic detection of the start and end of the EMG bursts. (A) Type I cycle in which O and FC are indicated. Note the low level of closer muscle EMG activity in FC, the irregularity of the closer muscle bursts in the first type II cycle, as well as the intermittent digastric activity in the first half of SC. (B) Type II cycles later in the series. The closer bursts are less irregular, and there is little activity in the digastrics during SC. (C) Type III cycles illustrating the pause between closer and opener activity during O1 and O2. (From Schwartz, G., Enomoto, S., Valliquette, C., and Lund, J. P., J. Neurophysiol., 62, 273, 1989. With permission.)
FIGURE 4. Two-dimensional frontal views of mandibular movements in the rabbit from the sequence shown in Figure 2. Type I (A), type II (B), and type III cycles (C) are shown. The arrows give the direction of movement. (From Schwartz, G., Enomoto, S., Valiquette, C., and Lund, J. P., J. Neurophysiol., 62, 273, 1989. With permission.)
to an abrupt end as the posterior teeth begin to reduce the food (Figures 2 and 3).

2. Reduction Series

Most of the breakdown of the food occurs in this series of movements, which is the part of the masticatory sequence that is the best described in many papers. The movements of the reduction series are often called chewing cycles: we call them type II. Type II cycles have three phases in rabbits and in many other species, including man. As well as O and FC, there is a slow closing phase (SC, Figure 3B). The digastric burst begins at or soon after the end of the closer burst and gradually increases in amplitude. The opening movement is smooth and fast in rabbits (Figures 3B and 4B), man, and macaques, but in many other species there are two or three opening phases in the typical cycle of the reduction series. In the rabbit, this type of three-phase opening movement occurs mainly in the preswallowing series.

Since most animals chew unilaterally, the jaw usually moves to the working side during FC (Figure 4B). SC begins with the peak of deceleration that is caused when the teeth engage the food (Figure 3b). The jaw-closing muscles are not very active during FC, but there is a rapid increase in EMG activity within a few milliseconds of the start of SC, and the activity continues to rise during the first half of the phase. As the lower jaw moves medially during SC (Figure 4B), the food is ground between the upper and lower molars. For obvious reasons, this phase is called the power stroke. The vertical amplitude of the movements gradually falls during the reduction series as the size of the food particles gets smaller, and this continues during the preswallowing series.

3. Preswallowing Series

A period of preswallowing behavior has been defined in rabbits, cats, and opossums, and probably occurs in other species. As Figure 3C shows, the type III cycles that compose the series have 5 phases: FC, SC, and three opening phases: a brief but rapid early opening phase (O), a pause (O), and final rapid opening phase (O). Jaw-closer EMG activity ends prior to O, but the digastric burst does not begin until the start of O in rabbits; this suggests that the movement in O occurs passively.

B. Relationship between Phase and Cycle Length

It has been known for several years that the length of all phases do not necessarily vary equally when the duration of the masticatory cycle changes. For instance, Hiemae and Thexton et al. showed that cycle duration of cats is best correlated with the duration of early opening (O and O), while Morimoto et al. concluded that the duration of opening and of SC were both important determinants of cycle length in the rabbit. The situation was clarified by Schwartz et al., who showed that relationship between the duration of the cycle and its constituent phases depends on cycle type.

Type I cycles are the shortest, FC and O durations are about equal, and variations in the length of both have an equivalent effect on cycle duration. In turn, the length of the two phases is determined by the duration of the digastric burst. The dependence of FC on digastric activity probably occurs because the major jaw-closing muscles are almost inactive. Elastic recoil is the major force that closes the jaw, and the strength of this will depend on the length of the stretched closer muscles.

Type II cycles are intermediate in duration, longer than type I, but shorter than type III. Although O is still an important contributor, variations in FC duration are uncorrelated with cycle duration. Most of the temporal variability in the cycle is due to changes in the SC phase. A similar relationship was found in humans chewing gum. In rabbits, the duration of SC is governed by the length of the bursts in the jaw-closing muscles, particularly those on the working side.

Type III cycles are the longest, but this is not due to a lengthening of the bursts in either jaw-opening or -closing muscles; it is caused by a pause between the end of the closer burst and digastric burst (Figure 1). Most of the variation
in type III cycle duration is accounted for by changes in the length of this pause, which in turn controls O$_2$ duration.\textsuperscript{9}

**C. Effect of Food**

Differences in the type, number, and size of food pieces appear to influence almost all the parameters of mastication. The length of the masticatory sequence is short for soft foods and long for those that are hard or tough.\textsuperscript{5,37} Average duration of the cycles in monkeys, cats, and rabbits increase with the size and/or toughness of food.\textsuperscript{5,13,37} It is probable, though not proven, that this is due to the lengthening of SC. Masseter activity during SC is greater when rabbits eat chow than when they chew carrot, which are softer,\textsuperscript{37} and the duration and amplitude of masseteric bursts of humans are greater for hard chewing gum than for soft.\textsuperscript{38} The frontal two-dimensional profiles of human masticatory cycles tend to have a wider and more pronounced SC when chewing tough rather than soft foods.\textsuperscript{17}

**D. Summary**

The evidence from the analysis of the masticatory movements suggests that the control of mastication is dependent in large part on sensory feedback. There is no other way to explain the coordination of the tongue, lips, and jaws to move the food around, the effects of different foodstuffs on the pattern of movement, or the abrupt changes from cycle to cycle.

**III. ANIMAL MODELS**

Animal models are necessary to study the neural mechanisms controlling the movements of mastication in detail. These were of two basic types: awake animals chewing on food, and anesthetized or decerebrate preparations in which jaw movements are induced by some type of stimulus.

**A. Behaving Animals**

Unrestrained, awake preparations have been used for some studies of masticatory control in cats and rabbits.\textsuperscript{39-41} A considerable amount of information has also been derived from chronic experiments of awake monkeys whose head movements were restricted during the recording sessions. These experiments have been particularly useful for studies of the behavior of neurons in the sensorimotor areas of the cerebral cortex.\textsuperscript{52-46} This topic will not be discussed here, but a review of these papers can be found in Luschei and Goldberg\textsuperscript{14} and Lund and Enomoto.\textsuperscript{11}

**B. Other Preparations**

Three types of stimulus have been used to induce mastication in conscious and unconscious animals: mechanical, pharmacological, and electrical. The latter is most common and has usually been applied to the sensorimotor cortex.

**1. Electrical Stimulation of CNS**

It has been known for more than 100 years that electrical stimulation of the sensorimotor cortex of many species evokes rhythmic movements of the jaws.\textsuperscript{47} In order to evoke these, the cortex or its output pathway, the cortico-bulbar tracts, must be repetitively stimulated at a minimum of 6 to 10 Hz, but 40 to 60 Hz is the optimum range.\textsuperscript{48-51} The region from which these movements can be produced became known as the cortical masticatory area. It lies below the primary motor cortex in the most inferior part of the precentral gyrus of humans and monkeys, and in the orbital gyrus in cats.\textsuperscript{44,52-58} The various functions of the cerebral cortex are not as differentiated in lower species, and in animals like rabbits and guinea pigs the masticatory area overlies parts of the face area of the primary motor and sensory cortical areas.\textsuperscript{59,60} New data from Huang et al.\textsuperscript{46} show that there may also be an overlap of functions in the monkey. They report
that rhythmic jaw movements can be evoked by repetitive intracortical microstimulation from many sites in the primary motor and sensory face areas, as well as from the traditional masticatory area.

Most studies of the brain stem circuits that are fundamental to mastication have used cats, rabbits, or guinea pigs. These models were chosen because the movements produced by electrical stimulation look very natural. Ferrier was the first to report that stimulation of the cortex of guinea pigs and rabbits evokes movements that looked like mastication, and his findings have been confirmed many times. Furthermore, the patterns of masticatory movements change with the site of stimulation within the masticatory area. Bremer found that three basic patterns of masticatory movements that he saw occurring naturally in the rabbit, gnawing, vertical mastication, and ruminatory or milling movements, were represented in adjacent parts of the cortex. Lund et al. confirmed most of Bremer's findings, but they were not able to evoke gnawing movements in anesthetized animals. They showed that the masticatory cycles produced by stimulation of the most anterior part of the cortical region are similar in form to the type I cycles of natural chewing. Like type I cycles, they have only two phases and the digastric muscles are very active, while the jaw-closer muscles are not. Type II cycles are evoked by stimulation of the posterolateral part of the masticatory area. After several seconds of constant stimulation, the cycle time begins to get longer, opening becomes slower, and eventually these type II cycles change to type III.

The pattern of mastication also depends on the site of stimulation of the cat's masticatory area, the orbital gyrus, and, in addition, rhythmic lapping, licking, and retching can be evoked from adjacent sites. Three types of masticatory movements can be elicited from distinct sites in the cortex of monkeys.

Mastication can also be activated by stimulation of the basal ganglia, lateral hypothalamus, parts of the amygdala and midbrain reticular formation.

2. Sensory Stimulation

Decerebrate animals can chew. This was first shown by Bazett and Penfield, who fed precollicular decerebrate cats by putting food at the back of their mouths. Bremer showed that mastication in decerebrate rabbits could be caused by touching or rubbing the mucosa or the teeth, and that the type of pattern changed from gnawing to rumination when the site of stimulation was moved to the back of the mouth. Furthermore, lightly anesthetized animals will chew on objects placed in the mouth, or in response to tonic pressure applied to the hard palate.

Thexton et al. have found recently that a high-frequency digastric rhythm (10 to 18 Hz) can be elicited by electrical stimulation of the lip of decerebrate rabbit pups.

3. Pharmacological Stimulation

Spontaneously occurring periods of rhythmic movement of the jaws occur when certain anesthetics are given, and the pattern in guinea pigs under ketamine has been described. These movements are similar to type I masticatory cycles in that they have only two phases, little lateral movement and little activity in the jaw-closing muscles.

A different type of rhythmical jaw movement in guinea pigs is caused by injections of the dopamine agonist, apomorphine. In these movements, the jaw swings widely to the side during opening and back during closing. This activity is thought to originate in the striatum and to be transmitted to the brain stem via the superior colliculus. Hashimoto et al. suggest that there may be another relay on this pathway in the mesencephalic reticular formation.

IV. SENSORY FEEDBACK

In order to understand the contribution of sensory feedback in the control of mastication, the first requirement is a description of the signals
sent to the brain stem during the movements. It is important to know which types of primary afferents are tonically, phasically, or occasionally active, and if possible what causes them to fire. With this knowledge, it is possible to propose functions for those that are active. A detailed review of this topic was published recently by Rossignol et al., so only a brief summary of the firing patterns of the different classes of receptors during mastication will be given here. The "average" pattern of firing of some of them are shown schematically in Figure 5.

A. Epithelial Mechanoreceptor Afferents

Primary afferents from skin, hair, and mucosal receptors have been recorded in the mandibular division of the Gasserian (V) ganglion of anesthetized rabbits. About 60% of hair afferents were excited during mastication, and they tended to fire throughout the cycle. However, their firing frequency was modulated during the cycle and was found to be proportional to the velocity of movement in all directions. Some hair afferents that innervated the lower lip were excited if the lips touched together, or if they touched "food" (simulated in these experiments by a rubber tube).

Most skin afferents were not active during mastication. The only ones that fired regularly and phasically when nothing touched the skin had receptive fields close to the corner of the mouth, which is the part of the face where the greatest stretching of the skin occurs during jaw movements. Some skin afferents that had fields on the lower lip did fire during movement, but only when their receptive fields were touched by the tube or by the upper lip. Mucosal afferents with fields on the lip and elsewhere in the mouth behaved similarly. When the rubber tube was in contact with the receptive field, bursts of activity were generated during jaw closure (Figure 5).

B. Periodontal Afferents

Most mechanosensitive periodontal primary afferents innervate only one root and are sensitive to the force or rate of change of force applied to the crown of the tooth. Two populations have been identified: the first have their cell bodies in the V ganglion, while the axons of the second group travel through the ganglion and sensory root to join cell bodies that are in the trigeminal mesencephalic nucleus (n V mes). Most receptors innervated by n. V mes. neurons are in the apical regions of the periodontal ligament, and these tend to be more slowly adapting than the receptors in the coronal portion that are innervated by cells in the ganglion (see Byers and Dong for details).

As one expects, these receptors are activated by biting and mastication. Larson et al. found that the firing frequency of periodontal afferents recorded in n. V mes. of awake monkeys is proportional to biting force. Appenteng et al. showed that most V ganglion periodontal afferents from molar teeth are rapidly adapting, and that they fire a short burst at the start of SC during mastication on a rubber tube. Slowly adapting receptors predominate around the incisor teeth and may be active throughout SC. They increase their firing frequency as the pressure increases on the teeth. Most natural foods are not smoothly compressible like a rubber tube, so rapidly adapting receptors can be expected to fire bursts during SC each time the tooth vibrates under the impact of the food (Figure 5).

C. Temporomandibular Joint Afferents

Very little is known about the properties of temporomandibular joint (TMJ) receptors and even less about their activity during mastication. Injections of horseradish peroxidase (HRP) into the TMJ space of cats labeled cell bodies in the mandibular division of the V ganglion, and Lund and Matthews recorded from neurons in the same part of the ganglion that appeared to innervate the joint capsule of rabbits. The afferents were not active when the jaw was at rest, but almost all discharged when the jaw was moved by hand within its normal range of movement. Some coded displacement, others coded velocity, and each seemed to respond best to movements that stretched the part of the capsule in which their receptors could be excited by probing. The few that could be tested were shown to fire similarly during mastication.
D. Muscle Afferents

1. Spindle Afferents

The cell bodies of the jaw muscle spindle primary and secondary afferents are in n. V mes., which makes it possible to record from them with microelectrodes in awake animals. Data have been gathered from monkeys during several behaviors; voluntarily controlled biting, voluntary tracking, and mastication, and from cats that were eating and lapping.

Spindle afferents are very active during voluntary biting. They reach discharge rates of 300 Hz during the dynamic phase of the task, fire at lower but constant rates while force is maintained, and again more rapidly as they are stretched during jaw opening. These afferents...
are also active during lapping and again fire most during opening. Larson et al.\textsuperscript{91,92} recorded from n. V mes. afferents during biting and subdivided them into primaries and secondaries on the basis of their response to stretch. Units with high stretch sensitivity (presumed to be primaries) behaved like the spindle afferents described by Lund et al.,\textsuperscript{96} while afferents with low sensitivity (secondaries) were only active during lapping. However, when Goodwin and Luscher\textsuperscript{99} studied the behavior of monkey spindle afferents during mastication, they were unable to distinguish primary and secondary afferents on the basis of stretch sensitivity. They found that spindle afferents showed a wide variety of patterns of activity during mastication, ranging from those that were only excited during jaw opening to those that fired strongly during SC and must therefore have been responding to fusimotor drive. Some of the latter had large dynamic responses at the start of jaw opening, which does suggest that they were primary afferents. If brittle food like monkey chow was eaten, the jaw-closing muscles were often rapidly unloaded when the teeth broke through, silencing the spindle afferents and causing a silent period in the jaw closer EMG (Figure 5). Taylor and Cody\textsuperscript{39} and Cody et al.\textsuperscript{40} divided the n. V mes. afferents that they recorded in awake cats into two categories according to their firing frequency during jaw opening. They proposed that those with high rate of activity were primaries and those with low activity were secondaries. This classification received support from other experiments on lightly anesthetized cats in which succinylcholine was injected into the bloodstream. This substance increases the dynamic sensitivity of spindle primary endings to stretch.\textsuperscript{101,102} Neurons in the secondary ending group tended to be active at all phases of the movement cycle and their firing frequency was often proportional to the degree of jaw opening; they were therefore most active (80 to 200 Hz) at the end of opening. Afferents in the primary group showed some length sensitivity, but their velocity sensitivity predominated: they fired short bursts at frequencies of up to 600 Hz at the start of opening. Both groups could be very active during SC, particularly when the food was tough.

2. Golgi Tendon Organs and Other Afferents

Golgi tendon organs have been identified in the jaw muscles of kittens, in the area of the attachment of the deep masseter muscle to the zygomatic arch and in the temporalis tendon.\textsuperscript{103} These receptors are in the series with the muscle fibers and their firing frequency is an indicator of muscle tension. Unfortunately, very little is known of their activity during mastication. Five afferents recorded in the V ganglion of the anesthetized rabbit by Lund and Matthews\textsuperscript{94,95} were tentatively identified as coming from tendon organs because they were excited by probing either the medial pterygoid, masseter muscle, or the temporalis tendon, and during a local twitch contraction. They were excited also by manually stretching the muscle and during contraction of the muscle during mastication.

Other neurons that were tentatively identified as tendon organs were found in n. V mes. by Larson et al.\textsuperscript{97} Like the units recorded from the ganglion, these increased their firing frequency during jaw closure. It was suggested that they were tendon organ afferents because their instantaneous firing frequency was modulated in a sawtooth fashion, which Larson et al. believed to be due to the rapid changes in tension brought about by the intermittent contraction of a single motor unit inserting into the receptor. Appenteng and Prochazka\textsuperscript{104} have shown subsequently that tendon organ afferents from ankle extensor muscles do not fire in such a manner. Only IA afferents do this, which suggests that the units classified as tendon organs by Larson et al. may have been a subpopulation of spindle primary afferents.

A few "spindle like" afferents were recorded in the V ganglion by Lund and Matthews.\textsuperscript{94,95} Like the tendon organ afferents, these were excited by probing a muscle, but they were inhibited instead of being excited during the twitch caused by local electrical stimulation. Their firing frequency increased during manual stretch and they showed no dynamic sensitivity. When the cortex was stimulated to cause mastication, they fired only during opening when the mouth...
was empty, but they did become active during closure when a rubber tube was put between the teeth. Because of their sensory responses and the small amplitude of the extracellular action potential, it was suggested that the "spindle-like" units could be Group III muscle afferents.

Although pain afferents from muscles and other orofacial tissues must become tonically or phasically active in many pathological conditions, no studies of this type appear to have been published. The best that can be done at the moment is an extrapolation based on data from other muscle groups.105

E. Summary

Most types of low threshold mechanoreceptors are phasically stimulated at the start of or during SC. The notable exceptions are muscle spindle afferents, which, although very active during SC, also fire strongly during jaw opening. These data show that the CNS receives several types of feedback signals that it can use to control the jaw-closer muscles during the most critical phase of mastication.

V. REMOVAL OF AFFERENT INPUTS

Another way to study the role of sensory inputs in motor programming that has proven to be very useful is to remove some of all of them. One can then discover which features of the total motor program have been changed or lost. There are two basic ways of doing this: blockage of transmission in sensory nerves, or the prevention of movement by paralysis.

A. Selective Deafferentation

Schaerer et al.106 injected local anesthetic to block intraoral and TMJ receptors of human subjects. This did not stop mastication, but, since no quantitative analysis was done, we do not know if the mandibular movements were changed. However, it was noted that the subjects had difficulty manipulating the food bolus and keeping it between the teeth. Inoue et al.37 performed extensive orofacial denervations in rabbits by cutting the maxillary and the inferior alveolar nerves. These rabbits would not eat when they recovered from surgery, but they did so when food was placed in the mouth. However, the masticatory sequence was lengthened, the movements were more irregular, vertical and horizontal amplitudes fell, and jaw-closer muscle activity seemed to have been reduced. It appears that these deficits are mainly due to removal of intraoral afferents traveling in the nerves, because Inoue et al.37 found that sectioning only the cutaneous branches had little effect. Goodwin and Luschei107 found that monkeys preferred to chew on the contralateral side when one n. V mes. was lesioned to remove all feedback from muscle spindles, as well as some from periodontal afferents. When both nuclei were destroyed, monkeys again chewed on either side and the frequency and timing of the muscle bursts seemed to be unchanged. This shows conclusively that neither muscle spindle afferents nor n. V mes. periodontal afferents are essential to mastication. However, there is other evidence that n. V mes. lesions do reduce the size of the jaw-closer muscle bursts under some circumstances. This will be discussed in Section VI.B.2.

B. Paralysis: the Fictive Pattern

All movement, and thus all somatosensory feedback, is topped by a chemical blockade of the neuromuscular junction. Meanwhile, the motor output of the central nervous system (CNS) can be analyzed by recording the discharge of whole motor nerves or of motoneurons. Experiments like these were first done to find out if the rhythm of mastication was generated within some part of the CNS or by the alternation of reciprocal reflexes. The conclusion was that many of the features of mastication could be generated within the brain stem. Dellow and Lund51 showed conclusively that the isolated brain stem had the ability to generate the basic features of mastication. They cut the spinal cord of paralyzed decerebrate animals and severed the branchial and cervical nerves to remove all somatic afferent inputs. Furthermore, they were able to show that
the rhythmical masticatory pattern was not due to signals generated by the vascular or respiratory systems. Organized rhythmical motor patterns that remain in the absence of movement are described as “fictive movements”, and the groups of neurons that produce them are known as central pattern generators (CPG). It is generally accepted that circuits of this type control many purposeful rhythmical motor patterns in all classes of animals (e.g., respiration, locomotion, feeding, flying, and swimming). Usually fictive jaw movements have been produced by electrical stimulation of the cortex or other parts of the CNS, although the patterns caused by ketamine and by sensory stimulation of the mouth have also been studied. A comparison of the pattern of activity in the motor nerves and in the muscles before paralysis helps us to determine how much of the total behavior is centrally generated and what features depend on sensory feedback.

The fictive pattern of mastication retains several features of the EMG pattern evoked before paralysis. When the fictive pattern is caused by stimulation of the cortical output, mylohyoid nerve activity gradually builds up into the first burst of the sequence, just as in mastication, and this coincides with inhibition of masseter nerve activity. The masseter burst follows and activity then alternates in the two nerves throughout the rest of the sequence. There are also two groups of antagonistic hypoglossal motoneurons, one that fires during jaw opening (tongue protrusion) and the other during closing (retraction); this alternating activity continues after paralysis, and it coincides with inhibition of masseter nerve activity. The masseter burst follows and activity then alternates in the two nerves throughout the rest of the sequence.

C. Summary

The rhythmical activation of the various muscle groups involved in mastication is generated by a CPG in the brain stem. Sensory feedback, particularly from intraoral mechanoreceptors, modifies the basic pattern and is particularly important for the proper coordination of tongue, lips, and jaws.

VI. ACTIVATION OF AFFERENTS

Knowing the pattern of activity of the several classes of primary afferents, one can suggest which groups participate in controlling a particular phase or parameter of the movements. More information can be acquired by selectively stimulating each one.

A. Tonic Stimulation

In Section III.B.2 (animal models) it was reported that tonic stimulation of periodontal and mucosal afferents can initiate mastication and fictive mastication in decerebrate or lightly anesthetized animals. Sometimes this type of sensory stimulation has to be coupled with subthreshold electrical stimulation of the CNS of rabbits to be effective. It has been reported that activation of muscle spindle afferents by tonic stretch of the jaw-closing muscles of cats does not normally initiate fictive mastication, but that it does make a subthreshold cortical stimulus effective. Furthermore, the duration of the masticatory cycle and the fictive cycle are similarly affected by changes in the stimulus parameters. In the rabbit, the frequency of movements evoked by a constant level of cortical stimulation with the mouth empty is not changed by paralysis, although it does fall by about 10% in the cat.

Although we lack the detailed comparisons of the timing of the motoneuron bursts to the various muscles and compartments within muscles that have been done in other systems, some differences have been found in the real and fictive patterns that suggest the general roles that sensory afferents play in mastication. First, and most important, when the electrical stimulus is supra-threshold and constant, the fictive pattern is very regular, in contrast to the natural situation, particularly when tough or brittle foods are being chewed. Second, the firing frequency of jaw-closer motoneurons is much less in fictive mastication; this will be discussed again in Sections VI and VII.
during spontaneous rhythmical jaw movements in guinea pigs anesthetized with ketamine; however, there was no change in the cycle frequency, even though the masseter burst was longer.

Tonic pressure on the maxillary incisor of rabbits causes the lateral jaw reflex, in which the mandible swings to the contralateral side by the coordinated action of several muscles or parts of muscles on the two sides. The same stimulus given during the vertical type of cortically induced mastication causes the jaw to swing to the contralateral side during FC and back to the midline in SC, i.e., changes type I cycles to type II. On the other hand, mastication stops if the pressure on the teeth is too strong, perhaps because the stimulus has become noxious. Even when tonic noxious stimuli are given far from the mouth, they are capable of inhibiting mastication. For instance, strong pinching of the forepaws or distention of the rectum can stop cortically induced mastication in rabbits.

**B. Phasic Stimulation**

It has become apparent from work on many rhythmical systems, including mastication, that the reflex effects of sensory afferents and their actions on the CPG can change dramatically from one phase of the movement to another. As one might imagine, the details vary between groups of receptors.

1. **Epithelial Afferents**

   a. **Modulation of the Jaw-Opening Reflex**

   The jaw-opening reflex (JOR) can be elicited by phasic mechanical stimulation of low-threshold mechanoreceptor afferents in the lips or oral mucosa and by electrical stimulation of V nerve branches. In all animals studied except man, the jaw-closing muscles are inhibited and the digastric muscles are activated at short latency. The responses are bilateral and probably disynaptic on both sides. The jaw-closing motoneurons are inhibited in humans, but the digastrics are not excited, at least not at a similar short latency. Dessem et al. have recently suggested that only closer muscle inhibition is caused by low-threshold mechanoreceptor afferents, and that high-threshold afferents, perhaps even nociceptors, must be stimulated before the digastric motoneurons are excited. However, there are several reasons to think that digastric motoneurons receive excitatory inputs from low-threshold afferents, but that these were not strong enough to cause the motoneurons to fire in the anesthetized cat.

   The first study of the interactions between reflexes and the central rhythm of mastication were carried out by Chase and McGinty. They evoked the digastric jaw-opening reflex by stimulation of the inferior alveolar nerve of awake cats and measured its amplitude at rest and during cortically driven mastication. They reported that the reflex was facilitated during jaw opening and inhibited during closure. Other experiments on awake cats and anesthetized rabbits have shown that the modulation of the digastric response changes with the strength of stimulation. When the stimulus is weak and probably innocuous, the reflex behaves as described by Chase and McGinty (Figure 6). However, there is really no facilitation of the reflex input to the digastric motoneurons during jaw opening, because when the effect of the rhythmical excitatory drive is subtracted, the excitatory effect of the stimulus is seen to be reduced at all phases of the cycle. This pattern changes if higher threshold afferents are recruited. When the stimulus intensity is raised above 1.5 × reflex threshold, phasic facilitation does occur, but during jaw closure, not during the jaw-opening phase (Figure 6). At the same time, the strong stimulus inhibits jaw-closer muscle activity and sometimes even abolishes most of the closer muscle burst.

   The modulation of this reflex was shown to be a property of the CPG when it was found that a similar modulation of digastric nerve activity occurs during fictive mastication. Furthermore, it was argued that the cyclical changes in the digastric responses to the higher intensity stimulation must be due to an action of the CPG on interneurons, and not simply to fluctuations in motoneuron membrane potential, because the biggest responses were out of phase with the EMG burst (Figure 6). I will come back to this in Section VII.
FIGURE 6. The input from the CPG to motoneurons during a type II cycle is shown first. The digastric membrane potential is at about its resting level during FC and most of SC. A large slow potential occurs during O and the neuron fires repetitively at a high frequency. The masseter motoneurons are similarly depolarized during FC and SC, but are strongly hyperpolarized during O. Below is a diagram of the modulation of the jaw-opening reflex. On the left is shown the control digastric responses with the jaw at rest (control). The amplitude of the test response to low-intensity stimulation (<1.5 X threshold) is normally less than control during mastication, particularly during FC and SC. In contrast, the responses to higher intensity stimulation are greatest in SC. Finally, there is a representation of the change in excitability of neurons that receive low- and high-threshold sensory that appears to take place during mastication. The first are inhibited at all phases, while the excitability of the second is low in FC and O and high in SC. (Adapted from Lund, J. P. and Olsson, K. A., TINS, 6, 458, 1983.)
b. Modulation of the Masticatory Pattern

Low-intensity intraoral stimulation has little effect on the duration of the masticatory cycle in rabbits. However, when a stimulus of higher intensity occurs early in closure, the cycle is shortened because of the reduction of the closer muscle bursts, but if the stimulus arrives during jaw opening the cycle is lengthened. Similarly, weak electrical stimuli given to the interdental gingiva of the maxilla of human volunteers had little effect on cycle time, while painful stimuli were effective. The most consistent change was a lengthening of the cycle when the painful stimulus occurred during jaw closure.

2. Periodontal Afferents

a. Modulation of the Jaw-Opening Reflex

The jaw-opening reflex can also be caused by hard taps to the teeth. A pattern of response like the JOR can occur during SC when rabbits are eating hard foods: the closer muscles are transiently inhibited and the digastrics are briefly excited. This pattern seems to be caused by sudden increases in the resistance to jaw closure. It is often seen in the first cycle of the reduction series, but is much rarer in later cycles (Figures 2 and 3). Although the JOR could disappear because the food gets softer, there is evidence that it is actively suppressed after the first type II cycle. Lavigne et al. studied cortically driven mastication in anesthetized rabbits with the mouth empty and also when a steel ball on a rod was thrust between the molar teeth of one side. They found that a JOR often occurred in the first cycle in which the ball was introduced, but was absent in subsequent cycles, although, of course, the steel got no softer.

b. Modulation of the Masticatory Pattern

The most interesting finding from the study of Lavigne et al. was that, with the exception of the first cycle, the duration and amplitude of the jaw-closer muscle burst went up dramatically during SC when the ball was between the teeth. In addition, SC and the cycle were significantly longer, and the mandible swung further toward the contralateral side during SC. There was no significant effects on the digastic burst. Most of these results have been confirmed by Morimoto et al., who placed plastic strips between the teeth. They showed that the increase in muscle activity was proportional to the thickness of the strips. In both experiments, sectioning or anesthetizing nerves carrying the periodontal afferents abolished most, but not all, of the effects of obstructing jaw closure. These experiments provide strong evidence that action of periodontal inputs on the jaw-closer muscle burst changes from inhibition to excitation at the transition from the preparatory to the reduction series of movements.

3. Muscle Spindle Afferents

When food or an artificial substance stops or slows movement during SC, muscle spindle afferents as well as periodontal afferents are stimulated (Figure 5). It has long been thought that the spindle afferents stimulated in this way should increase jaw-closer motoneuron activity, and this was confirmed by Morimoto et al. They found that lesions of n. V mes. abolished the residual effect of placing plastic strips between the teeth during cortically evoked mastication in rabbits without periodontal afferents.

When brittle food is eaten, periodontal and muscle spindle primary afferents are alternately unloaded and loaded each time the food fractures. This probably accounts for the fractionation of the closer muscle EMG during SC into alternating silent periods and bursts shown diagrammatically in Figure 5.

As far as I know, the only study of the effects of phasically stimulating muscle spindle inputs during all parts of the masticatory cycle was carried out in awake cats by Chase and McGinty. They electrically stimulated n. V mes. to excite spindle afferents (and inevitably some periodontal afferents) and recorded the resulting H reflex in the masseter muscle. During mastication, the H reflex was facilitated during jaw closure and inhibited during opening.
C. Summary

Certain types of tonic afferent input can initiate mastication and probably contribute to the general drive that keeps the movements going. Some phasic inputs are phase promoting, that is, they enhance the activity of the agonist muscles. This is very important during SC, when muscle spindle afferents and periodontal pressoreceptors provide positive feedback to the jaw-closing muscles. Others have the potential to inhibit muscle activity or to terminate a phase. If these are normally activated by movement, their influence must be counteracted by the CPG. If they are high threshold and are only occasionally activated, their effects may be enhanced to provide added protection.

VII. BRAIN STEM ELEMENTS

The brain stem is the only part of the central nervous system that is essential for mastication, because decerebrate animals (see above) and animals without a cerebellum or spinal cord can chew. Our knowledge of different groups of brain stem neurons that participate in the control of mastication will now be summarized. The major components and connections that will be discussed are shown diagrammatically in Figure 7. An excellent review of trigeminal interneurons can be consulted by those who want more information.

A. Central Pattern Generator

The cortex exerts its action on the brain stem CPG via the corticobulbar tracts, and the projection is mainly contralateral. The mesencephalic RF also projects contralaterally to the CPG through a nonpyramidal pathway.

CPGs vary from simple circuits containing a few neurons, like those that control many invertebrate activities, to the complex systems that generate mammalian motor rhythms. Feldman et al. have shown why it is probable that the two major components of pattern of respiration, the rhythm or timing (determining the length of the cycle and the frequency of repetition), and the motoneuron bursts (the duration and pattern of firing of the different motoneuron pools) are generated in separate stages by different groups of brain stem neurons. The evidence that suggests that this model is also applicable to mastication.

1. Rhythm Generation

The rhythm of mastication seems to be produced by groups of cells in the medial bulbar reticular formation (RF) between n. V. mot and the inferior olive. There are three pieces of evidence in favor of this statement. First, anatomical and electrophysiological studies have shown that neurons in the medial nuclei of the medullary RF receive direct projections, predominantly contralateral, from the masticatory area of the cerebral cortex. Second, lesioning or surgically isolating the medial RF abolishes mastication, even when the lateral parvo cellular reticular nuclei are intact. Finally, neurons in the medial RF become rhythmically active during fictive mastication.

When a cut is made to the base of the brain along the midline of the caudal medulla, the rhythm is abolished on the side ipsilateral to the stimulation site in the cortex, but not on the contralateral side. This shows that there are two rhythm generators that can function independently, that each is mainly controlled by the contralateral cortex, and that they are usually coordinated by axons that cross to the other side (Figure 7).

Even when the interstimulus intervals of the train of cortical shocks are randomly ordered, the rhythm generator is capable of producing a regular fictive pattern. It seems to do this by the sequential activation of several groups of neurons (Figure 7). Corticobulbar stimulation excites neurons in and above the dorsal part of n. reticularis paragigantocellularis (PGC) and it is possible that the types of sensory stimuli that elicit mastication may excite the same neurons. Er microbioc et al. mapped responses to pressure on the teeth and mucosa throughout the brain stem RF. Mechanical thresholds were quite low, and most neurons adapted slowly. It is interesting that, although the predominant response of neurons recorded in the mesencephalon and rostral pons was inhibition, several neurons that appeared to be in or near PGC were excited.
PGC neurons do not fire rhythmically when the cortex is stimulated, but they do appear to induce rhythmical firing in neurons in and just above the rostral part of n. reticularis gigantocellularis (GCo), and these, in turn, may entrain a more caudal group of gigantocellularis neurons (GCc) (Figure 7).

In contrast to some other CPGs, we know very little about the synaptic processes of masticatory rhythm generation, except that glycine is not an essential transmitter. The frequency of cortically driven mastication is not altered significantly by the glycine antagonist, strychnine, or by methysergide, a serotonin (5HT) H2 receptor antagonist. However, 5HT should not be dismissed as a putative transmitter before antagonists to the H1 receptors have been tried.

Nakamura and co-workers have suggested that the neurons of the medial RF control the trigeminal motoneurons directly. This implies that not only the rhythm, but also the parameters of the motoneuron bursts are encoded by the neurons of GCc, and there is some evidence to support this proposition. Stimulation of medial nuclei excites digastric motoneurons and inhibits mas-
seteric motoneurons at very short latency, and medial RF neurons can be antidromically activated by stimulation of n. V mot. On the other hand, anatomical studies have not provided much evidence that medial reticular areas have a strong monosynaptic projection to V motoneurons, suggesting that the rhythm generators act mainly via other groups of premotor neurons close to n. V mot. This point of view has been expressed in several papers from the group at UCLA.

2. Burst Generation

Horseradish peroxidase (HRP) is captured by the presynaptic terminals and transported back to the cell body, where it can be revealed by histochemical methods. When HRP was injected into the trigeminal motor nucleus to label premotor neurons, very few of these turned out to be in or adjacent to GC. Many labeled somata were found in the border zone surrounding n. V mot. that was called regio h by Meesen and Olszewski. The dorsal zone of regio h is usually known as the supratrigeminal nucleus (n. V sup.) and lateral zone as the intertrigeminal nucleus (n. V int.). Other groups of labeled neurons lay in the dorsal parts of the Vth main sensory nucleus (n. V princ.) and the most rostral division of nucleus oralis (n. V oral.τ). Some labeled cells were found in the lateral parvocellular RF medial to nucleus interpolaris, and there was a small compact group of cells just lateral to n XII mot. With the exception of this last group and n. V princ., all the regions were labeled bilaterally.

Since cuts made just behind n. V mot. that isolate the lateral RF do not change mastication, it is probable that only the premotor neurons close to n. V mot. form the burst generators shown in Figure 7. There is now strong evidence that some of the neurons in this area participate in pattern generation. Donga et al. recorded from cells in n. V sup., n. V int. and n. V oral.τ in anesthetized and paralyzed rabbits, and found that there were neurons in each nucleus that fired rhythmical bursts in phase with the fictive rhythm induced by cortical stimulation. They showed that some of these were premotor neurons by antidromically activating them from the contralateral n. V mot.

For the sake of simplicity, we will only discuss the formation of the opener and closer muscle bursts, although the control process must also include a way of combining the various motoneuron pools to produce the more complex patterns. To explain alternating opening and closure, intracellular recordings from motoneurons (see later) show that three processes are necessary:

1. Inhibition of closer motoneurons during opening
2. Generation of the opener burst
3. Generation of the closer burst

Opener motoneurons are not inhibited during closure.

a. Inhibition of Closer Motoneurons

Inhibition of jaw-closer muscle activity occurs before the digastric becomes active in the first opening movement of a series and has a lower cortical threshold than the opener burst. This means that it cannot be initiated by reciprocal inhibition. In any case, it is improbable that trigeminal opener motoneurons reciprocally inhibit their antagonists even when they are active, because there is little evidence that any form of recurrent inhibition occurs in V or XII motoneurons. In the spinal cord, these processes depend on the activation of Ia inhibitory interneurons and Renshaw cells by recurrent collaterals, which until recently had never been seen leaving V, VII, and XII motoneuron axons. However, Moore and Appenteng have recently published drawings of 4 HRP-filled rat jaw-closer motoneurons that do appear to show axon collaterals. It must now be determined if this is more than a chance finding.

In the model of the brain stem circuits, the inhibition of closer motoneurons comes from a group of inhibitory premotor interneurons that form one of the components of the burst generators (Figure 7). Although these have not been positively identified, it is possible that some of these are in n. V sup. High-threshold inputs terminate the closer muscle bursts and some of these neurons are excited by strong stimulation of several trigeminal nerve branches. It was postulated...
that neurons in this nucleus mediate disynaptic inhibition of jaw-closer motoneurons during the jaw-opening reflex\textsuperscript{117,160,161} even before it was known that neurons in the nucleus project to n. V mot. on both sides.\textsuperscript{149,162,163} Kamogawa et al.\textsuperscript{164} recently filled commisural (contralaterally projecting) neurons in n. V sup. with HRP and were able to show that the same neurons also had axon collaterals to the ipsilateral n. V mot. The terminal branches of the axons appeared to arborize among closer motoneurons.

b. Generation of Opener Bursts

The only group of interneurons that is definitively known to project to the digastric motoneuron pool are in n. V oral.\textsuperscript{11} Olsson and Westberg\textsuperscript{165} identified this ipsilateral projection by antidromic stimulation. These premotor neurons received excitatory inputs from low-threshold lingual, inferior alveolar nerve afferents, and from high-threshold muscle afferents. Most contralaterally projecting n. V oral. premotor neurons recorded by Donga and Lund\textsuperscript{166} had similar inputs and were not phasically active during fictive mastication; however, some did fire bursts during the opening phase. This supports the suggestion that many of the interneurons involved in the jaw-opening reflex are normally outside the burst generator.\textsuperscript{120,139,165}

The rhythmic excitatory drive to digastric motoneurons is facilitated by L-glutamate, N-methyl-D-aspartate (NMDA), noradrenaline, and 5HT and blocked by the iontophoretic application of AVP (d-2-amino-5-phosphovalerate), which is a specific antagonist of the NMDA receptor.\textsuperscript{167} The latter is an important finding because it has been found that slow rhythmic EPSPs generated by some other CPGs are caused by the release of excitatory amino acids (glutamate or aspartate) that activate NMDA receptors in motoneurons. This is followed by the opening of voltage-sensitive Na\textsuperscript{+} channels and it is the resulting Na\textsuperscript{+} current that completes the depolarization. Repolarization is very slow during the plateau potential that underlies the motoneuron burst.\textsuperscript{114}

c. Generation of Closer Bursts

Although it has usually been assumed that n. V sup. neurons inhibit closer motoneurons, many of them are excited by sensory inputs that promote the closer muscle burst. Branches leave the axons of N. V mes. spindle afferents and terminate in n. V sup.,\textsuperscript{154,168,169} where they excite many neurons.\textsuperscript{168-170} Although the three reports differ in the percentage of neurons that received input from more than one muscle, all found that a considerable number could be excited by probing both the masseter and the temporalis muscles. Jerge\textsuperscript{170} reported that pressure on the teeth or gingivae activated units in the caudal parts of the nucleus, and that a few had convergent inputs for spindles and oral mechanoreceptors.

Appenteng et al.\textsuperscript{171} used spike-triggered averaging in anesthetized rats to show that interneurons just caudal to n. V mot. make monosynaptic excitatory connections within the masseter motoneuron pool. Some of these interneurons are also excited by periodontal and muscle spindle afferents. Noxious inputs suppress the closer burst (see earlier) and also inhibit these neurons.

The boundaries of the burst generators may be continuously expanding and contracting, depending on circumstances and the complexity of the movements.\textsuperscript{79} Imagine an interneuron that receives a rhythmic drive from the rhythm generator. As long as this is not strong enough to make it fire, it is not a part of a burst generator, but if the rhythmic drive increases, if it receives a convergent excitatory input from higher centers or has a peripheral receptive field, it may begin to fire rhythmically. It is then contributing to the drive potential that underlies the burst.

B. Control of Motoneurons by the CPG

Although trigeminal (V), facial (VII), and hypoglossal (XII) motoneurons are all important in the control of mastication, the facial motoneurons have not been studied during mastication. Unless otherwise stated, the data come from V motoneurons.
There are two basic types of motoneurons. The first, the fusimotor (gamma) motoneurons, have the smaller cell bodies, narrower axons, conduct more slowly, and innervate the contractile portions of the intrafusal fibers within the muscle spindles. The other motoneurons (alpha) innervate extrafusal muscle fibers and therefore directly control the contraction of the muscle. The original studies of alpha and gamma motoneurons showed that they have conduction velocities in the approximate range of 50 to 120 m/s and 10 to 50 m/s, respectively, in the cat hindlimb.\textsuperscript{174} Beta motoneurons that innervate both intra- and extra-fusal fibers are common in some muscles,\textsuperscript{175} and a small number have recently been found to occur in rat masseter.\textsuperscript{176} Trigeminal motoneurons are not easily separated by their physical properties. The diameters of cat motoneuron axons are unimodally distributed between 1 and 16 |\textmu|m\textsuperscript{177} and motoneuron cell body diameters do not form two populations in the rabbit,\textsuperscript{178} although they appear to do so in rats.\textsuperscript{179} However, Sessle\textsuperscript{180} was able to define two populations in the cat on the basis of different responses to various stimuli and he estimated that alpha motoneurons conduct at between 26 to 72 m/s and gammas at 16 to 36 m/s.

\textbf{1. Alpha Motoneurons}

Intracellular recordings from motoneurons during fictive mastication of guinea pigs and cats show that the rhythmic bursts of activity of V and XII motoneurons are caused by large amplitude slow potentials. Digastric motoneurons fire in bursts of 150 to 250 ms in duration that contain up to 30 spikes, and the instantaneous frequency can be as high as 250 Hz. These spikes are superimposed on rhythmic depolarizing shifts that drop to about the level of the resting membrane potential between the bursts, but they are not hyperpolarized (Figure 6).\textsuperscript{59,68,181} The pattern of activity in XII motoneurons is similar,\textsuperscript{64} but closer motoneurons behave very differently. The most striking features of the intracellular records from masseter motoneurons are the large, slow hyperpolarizing potentials during the phase of digastric activity (opening). These are probably inhibitory postsynaptic potentials (IPSPs) generated at synapses on or close to the cell soma because they are easily reversed by Cl\textsuperscript{-} injections through the intracellular electrodes.\textsuperscript{58,108}

The rhythmic IPSPs are one of the mechanisms that counteract excitation caused when muscle spindles are stretched during the contraction of antagonist muscles.\textsuperscript{182-184} Spindles are plentiful in certain parts of the jaw-closing muscles, but neither the digastrics nor the muscles of the tongue of nonprimates contain many.\textsuperscript{185} This may be the reason that the rhythmic IPSPs are not seen in digastic and XII motoneurons.

The slow depolarizing potentials that alternate with the IPSPs are often too small in amplitude to cause the masseter motoneurons to fire.\textsuperscript{68,181} However, they seem to be much more active in the paralized preparation, particularly when something is put between the teeth to increase the activity of periodontal and muscle spindle afferents.\textsuperscript{36} It is well known that many regions of the cerebral cortex, including the motor cortex, project disynaptically to the motoneurons\textsuperscript{163,186} and that synaptic potentials of short duration often follow each cortical shock at short latency. Prominent stimulus-linked EPSPs occur in digastric motoneurons and IPSPs in masseter motoneurons and the amplitude if these potentials are strongly modulated during the masticatory cycle.\textsuperscript{59,108,146} This has led to the hypothesis that slow drive potentials are simply an aggregate of these short-latency potentials.\textsuperscript{59,108,146} This is an interesting proposition, but other evidence suggests that the two processes are independent. First, EMG bursts do not always contain significant amounts of activity that are linked to the cortical shocks.\textsuperscript{60} Second, there is evidence that the synaptic mechanisms of the two types of potential are different. Enomoto et al.\textsuperscript{142} have shown that the short-latency IPSPs are probably caused by the release of glycine by inhibitory interneurons excited by cortical afferents, because strychnine, a glycine antagonist, blocks these potentials. Strychnine also increases the amplitude of the short-latency bursts in the digastic muscle.\textsuperscript{141} However, the slow IPSPs are not blocked by strychnine, suggesting that they are transmitted by synapses from other interneurons that do not use glycine as a neurotransmitter. Furthermore, the
rhythmic drive potentials of digastric motoneurons seem to depend on NMDA receptors, while cortical short-latency EPSPs do not. 167 It seems probable, then, that the slow potentials represent the fundamental output of the burst generators when they are being driven only by the rhythm generator, and that these potentials are normally modified by sensory feedback and by inputs from higher centers of the CNS (Figure 7).

2. Gamma Motoneurons

Gamma motoneurons have been classified into subtypes according to their action on the muscle spindle. The main division is into static and dynamic fusimotor neurons: when dynamic gamma motoneurons fire, they increase the sensitivity of the spindle primary endings (IA afferents) to the rate of change of muscle length (velocity sensitivity), while the main effect of static gammas is to make secondary endings (Group II afferents) more length sensitive. 174 There have been no reports of intracellular recording from trigeminal gamma motoneurons, but Taylor and co-workers have recorded the activity of axons dissected from the masseter nerve of anesthetized cats and identified fusimotor neurons by several tests. 100–102 They found that fusimotor neurons were often tonically active when the jaw was in its postural position. Just before rhythmic jaw movements began, one group increased their discharge rate, which then remained relatively constant throughout the whole series of movements. The authors suggested that these were dynamic fusimotor neurons. Another group that were phasically excited during jaw closure were thought to be static fusimotor neurons. The effect of this activity on the pattern of firing of spindle afferents was discussed in Section IV.D.1. 146

It has also been reported that gamma motoneurons are very active during voluntary biting in monkeys. 96 Their activity increases at the same time or even before that of alpha motoneurons, they fire while force is maintained and stop just before it is released. Larson et al. 91,92 suggest that the gamma motoneurons active during biting are of the dynamic rather than the static type. However, this is based on their classification of spindle afferents by their responses to stretch, which may not be a reliable test (see Section IV.D.1). It is becoming well accepted that the relative balance of static and dynamic sensitivity of the muscle spindle receptors is tailored to a particular movement pattern, 79,100 but this is just one of the ways in which the CPG controls afferent feedback.

C. Control of Interneurons and Primary Afferents by the CPG

It is clear that one of the functions of CPGs is to adjust the gain of reflexes, to suppress those that are unnecessary, and to facilitate those that enhance motor performance. 79 They do this through the fusimotor system, and by their direct action on the alpha motoneurons (e.g., slow IPSPs), but there is a lot of evidence that they alter transmission from the primary afferents to interneurons, as well as modulate the interneurons themselves.

Several experiments have shown that the excitability of jaw reflex interneurons and primary afferent terminals is controlled during mastication. In addition, the sensory detection threshold rises during movement, 187,188 and there is some evidence that our perception of oral stimuli is changed during mastication. 189

1. Neurons with Cortical Inputs

The possibility that the CPG modulates cortico-bulbar interneurons has already been mentioned. Neuroanatomical studies have shown that most parts of the brain stem that contain the labeled V premotor neurons also receive inputs from the sensorimotor cortex. These include n. V prin., n. V oral T, n. V sup., and n. V int. and lateral reticular areas medial to the spinal nucleus. 138,146,190–195 Neurons in all these areas can be excited by cortical stimulation. 73,131,163,166,196–200

It has already been noted that the amplitude of EPSPs in digastic motoneurons and the IPSPs in masseter motoneurons that follow cortical stimuli are cyclically modulated. 59,108,146 Much of the variation in amplitude probably occurs be-
cause of changes in motoneuron membrane properties induced by the slow potentials, but the premotor neurons are also controlled. Olsson et al.73,163 have shown that the responses of many n. V prin., n. V int., and n. V oral r neurons to cortical shocks are generally reduced during mastication (Figure 6). Many of these neurons also receive excitatory low-threshold orofacial inputs.

2. Neurons with Low-Threshold Orofacial Inputs

The digastric jaw-opening reflex response to low-threshold inputs is inhibited during all phases of mastication (Section VLB). The data gathered during intracellular recording show that this is unlikely to be due to postsynaptic inhibition of the motoneurons by the CPG, because even during jaw closure digastric motoneurons are not hyperpolarized (Figure 6). This led Lund and Olsson201 to postulate that the interneurons on this reflex arc must be tonically inhibited by the CPG (Figure 7). Although Olsson et al.73,163 did not identify interneurons, the fact that the responses of low-threshold neurons recorded in n. V prin., n. V int., and n. V oral r to peripheral stimulation was reduced in all phases of mastication indicates that the hypothesis is probably correct.

Included among the inhibited neurons were some in n. V prin. and oral. r that projected to the ventrobasal thalamus,73,160 and most neurons in the nucleus caudalis with low-threshold receptive fields are tonically inhibited during fictive mastication.202 A general reduction in the responsiveness of second-order neurons with low-threshold mechanoreceptive fields may be the reason for a rise in the sensory detection threshold during movement.203

3. Neurons with High-Threshold Orofacial Inputs

Although it is necessary to suppress reflex responses to low-threshold orofacial mechanoreceptors so that the jaw closure can take place, it is still necessary to protect the mouth against damage during mastication. This seems to be done by enhancing the response to high-threshold afferents during closure. Although digastric motoneurons are more sensitive to high-intensity stimulation of the IA nerve (>1.5 × threshold) during the closing phases of mastication and fictive mastication than at rest,120,126 this cannot be explained by the postsynaptic events in the motoneurons (Figure 6). To account for this phase modulation, Lund and Olsson201 postulated that the CPG increases the excitability of the high-threshold interneurons during closure. This hypothesis was supported by the results of Olsson et al.,73 who recorded from neurons in n. V int. that had thresholds of >1.5 × the reflex threshold. In several cases, the probability firing to IA stimulation rose and the latency of the spikes decreased during closure (Figure 7).

4. Primary Afferents

The modulation of the amplitude of the low-threshold jaw-opening reflex during mastication seems to be due, at least in part, to changes in the presynaptic terminals of the primary afferents. Kurosawa et al.204 used Wall’s technique to show that inferior alveolar nerve cutaneous afferent terminals in n. V oral are hyperpolarized during the jaw-opening phase and depolarized during the closing phase of fictive mastication. This would result in enhanced synaptic transmission during opening and decreased transmission during closure. Decreased release of an excitatory transmitter can explain the reduction in the firing of postsynaptic neurons (and in the digastric response) during closure, but if there is increased release during opening the CPG must be counteracting this by postsynaptic inhibition of the relay cells, since their excitability tends to be lowest during this phase.73

The CPG has at least two ways of controlling muscle spindle primary afferents during mastication. The first is through the fusimotor system (see Section VLB). The second seems to occur by a synaptic action of the CPG on n. V mes. (Figure 7). Kolta et al.205 caused n. V mes. spindle afferents to fire tonically by holding the mouth open and found that approximately 40% of these were modulated during fictive mastication. In almost all cases, this effect was a rhythmical in-
hition: the action potentials coming from the periphery failed to enter the cell body of these pseudo-monopolar cells during the jaw-opening phase. It seems plausible that this occurs because the neuron is phasically hyperpolarized. Nomura and Mizuno\textsuperscript{206} showed that 40\% of n. V mes. spindle afferents have dendritic processes, and synapses on neurons in the nucleus have been seen in several species.\textsuperscript{207-210} Some of these synapses contain adenosine deaminase and come from neurons in the hypothalamus and periaqueductal grey matter.\textsuperscript{211,212} However, it is unlikely that these neurons are responsible for the phasic inhibition during opening because adenosine acts slowly and is usually classified as a modulator rather than a classic synaptic transmitter.\textsuperscript{213} There are also axonal varicosities in contact with the cell bodies or proximal axon n. V mes. neurons that contain encephalin, substance P, serotonin, or immunologically similar substances.\textsuperscript{214} When these substances are applied microiontophoretically to n. V mes. neurons, neither encephalin nor substance P changes the firing rate,\textsuperscript{215} but there is some preliminary evidence that serotonin is inhibitory.\textsuperscript{216} The somas or axon hillocks of some n. V mes. neurons are connected together by gap junctions\textsuperscript{207,208} that provide electrotonic coupling.\textsuperscript{217} If rhythmical inhibition causes action potentials to fail in the stem axon, this would prevent the generation of an action potential in a coupled cell, thereby reducing the excitatory input to jaw-closer motoneurons. In addition, it is likely that the hyperpolarization causes the axon potentials to fail before they enter the branches of the stem axon to n. V sup. Inhibition of spindle afferent cell bodies could thereby inhibit the strong disynaptic stretch reflex\textsuperscript{218} during jaw opening.

D. Summary

The central pattern of mastication seems to be generated in two stages: the rhythm by neurons in the midline reticular formation and the bursts by premotor neurons near the motor nuclei. The burst generators excite the opener alpha motoneurons and inhibit the closers during the opening phase, but during the closer burst the opener motoneurons are not inhibited. Dynamic gamma motoneurons are tonically active during mastication, while static gammas are excited during closure. The CPG also modulates primary afferents and interneurons in order to suppress unwanted reflexes and to favor those that enhance motor performance.

VIII. CONCLUSIONS

The basic features of mastication can be programmed by the brain stem in the absence of sensory inputs, but such movements would be highly inefficient and even dangerous to the organism. Sensory feedback from a variety of intraoral, joint, and muscle receptors interact with the central control system at several levels to adapt the program to the characteristics of the food. This is the source of the variability in the pattern of mastication.

REFERENCES

10. Lavigne, G., Kim, J. S., Valiquette, C., and Lund, J. P., Evidence that periodontal pressure receptors pro-


52. Beevor, C. E. and Horsley, V., A further minute analysis by electrical stimulation of the so-called motor region (facial area) of the cortex cerebri in the monkey (Macacus sinicus), Phil. Trans. R. Soc. B., 185, 39, 1894.
73. Olsson, K. A., Sasamoto, K., and Lund, J. P.,


Lund, J. P. and Rossignol, S., Modulation of the amplitude of the digastric jaw opening reflex during the masticatory cycle, Neuroscience, 6, 95, 1981.


Sherrington, C. S., Reflexes elicitable in the cat from pinna, vibrissae and jaws, J. Physiol., 51, 404, 1917.


186. Nakamura, Y., Nozaki, S., and Kikuchi, M., Possible inhibitory neurons in the bulbar reticular for-


197. Limanskii, Y. P. and Gura, E. V., Corticofugal influences on neurons of the main trigeminal sensory nucleus, Translated from Neurofiziologiya, 1, 47, 1969.


213. Schubert, P., Modulation of synaptically evolved


