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# Experiments On The Neural Control Of Rhythmical Mastication

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**EXPERIMENTS ON THE NEURAL CONTROL  
OF  
RHYTHMICAL MASTICATION**

by

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**Submitted in partial fulfillment  
of the requirements for the degree of  
Doctor of Philosophy**

**Faculty of Graduate Studies  
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**London, Canada**

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ABSTRACT

Rhythmical mastication was produced by electrical stimulation through bipolar electrodes of suprabulbar structures, in anesthetized and decerebrate rabbits, and in conscious rabbits previously implanted with electrodes under anesthesia. The most frequently used stimulation sites were within the corticobulbar tracts and putamen. Inflation of a 5 ml balloon within the mouth of anesthetized or decerebrate rabbits could also evoke mastication, and the central and peripheral masticatory stimuli were shown to summate. Paw-pinching or rectal distention inhibited the masticatory movements produced by CNS stimulation. Pressure on the labial or lingual surface of an upper incisor tooth activated a contralateral jaw movement reflex which also modified or inhibited the centrally-induced mastication. In the latter reflex, the zygomatic-mandibular and anterior temporal muscles of the side opposite the stimulated tooth were the principle movers of the mandible into its lateral posture. Repetitive electrical stimulation of the mucosa surrounding the tooth would elicit a similar reflex, which was shown to be polysynaptic.

In phase with the patterned masticatory movements, bursts of multineuronal activity were recorded from the mylohyoid and masseteric muscle branches of the trigeminal nerve, and from the hypoglossal nerve and nucleus. Reciprocal activity occurred in the nerves to the above jaw-opening and jaw-closing muscles. The pattern of neural activity during electrical stimulation was unchanged by muscle paralysis. These bursts were found to recur regularly within the XII nucleus at a maximum rate per animal which varied from 2.4-4.5

bursts/sec, even when the electrical stimulus pulses were delivered at a random frequency. Transection of the XII, XI, X, IX, VII and V cranial nerves, the I and II cervical nerves and the spinal cord did not prevent the appearance of the rhythm. Masticatory patterning was likewise independent of cardiac or respiratory timing information.

It was concluded that rhythmical mastication is controlled by a brain-stem pattern generator, activated from higher centers or from the mouth, which is responsive to peripheral or central modulation, but which does not depend on external timing information for its basic cyclical output.

## INTRODUCTION

Every living organism must obtain energy from its external environment to survive. In the animal kingdom, this need has been met by the evolution of a specialized organ, the mouth, whose primary task is the ingestion of food. It has also been said to play a critical role in the evolution of the brain (Young 1963, 1968). The evolution of teeth increased the efficiency of ingestion and mastication, while the acquisition of jaws constituted a major step in the development of vertebrates, the importance of which "can hardly be overestimated" (Colbert, 1955). Smith (1953) expressed the concept in the following statement: "Without the predatory power of jaws and teeth and the possibility of swift and accurate pursuit of prey ..... there would have been no centralization of the nervous system such as ultimately produced the brain, and the earth would never have known the phenomenon of consciousness, at least of an order superior to that of the lobster, scorpion or butterfly."

In general, amongst those animals with jaws and teeth, the basic method of preparing food for swallowing and digestion is similar. This most successful method of mastication is in essence a rhythmic opening and closing of the jaws, which gradually reduces the size of food particles by crushing them between the teeth. During this process, saliva is mixed amongst the food to assist digestion and, by its lubricating action, to allow the food bolus to be swallowed.

Superimposed on the basic rhythmical opening and closing movements of the mandible are forward, backward and lateral movements; these occur before, during, and after tooth contact (Anderson, 1968). The relative importance of these accessory movements is largely determined by dietary factors. During mastication, the tongue, cheek and lip muscles must also act in concert to keep the food between the teeth and to prevent injury to themselves. Thus there must be co-ordination of activity in the motor nerves supplying these structures: the V, VII and XII cranial nerves, and probably also the XI cranial and the upper cervical nerves.

Rhythmical mastication can be studied in a limited fashion by the observation of animals during feeding. Fortunately, it is possible to produce masticatory movements on demand under experimental conditions in the following manner. Repetitive electrical stimulation of the motor cortex and of subcortical structures in animals, particularly rabbits, has been shown by many workers to evoke rhythmical co-ordinated jaw and tongue movements which resemble normal mastication. Their work will be reported in detail in the following historical review.

Most investigators of masticatory control have, however, studied the jaw and tongue reflexes on the assumption that these reveal the neurological basis of rhythmical mastication. The classic paper by Sherrington (1917) was the first of these. Sherrington showed that mechanical and electrical stimuli applied to the gum bordering the upper and lower teeth or the front part of the

hard palate evoked jaw opening in the decerebrate cat. This jaw-opening reflex was then sharply followed by active closure, initiated by stretch of the elevator muscles. The latter response is generally termed the jaw-jerk reflex. Modification of the amplitude of these reflex responses occurs under many circumstances. Facilitation and inhibition of the jaw-opening and jaw-jerk reflexes by other concurrent neural events have been studied by a large number of investigators, beginning with Cherbouliez and Laugier (1926). In contrast, when the present experiments were begun in order to study the effects of oral, general somatic and visceral stimuli on mastication, only Miller and Sherrington (1916) and Brémer (1923) had reported similar studies.

Miller and Sherrington (1916) showed that rhythmical swallowing movements could be produced in decerebrate cats both by stimulation of the inferior fovea of the IVth ventricle or by squirting water into the pharynx. These two stimuli could summate to increase the frequency of swallowing. In a similar way, Brémer (1923) found that it was possible to obtain masticatory movements when a previously subliminal electrical stimulus was applied to the motor cortex immediately after the cessation of rhythmical masticatory movements secondary to rubbing the buccal commissures.

The mechanism by which the brain produces repetitive mastication is controversial. Sherrington (1917) and Creed, Denny-Brown, Eccles, Liddell and Sherrington (1932) pointed out that biting into food tends to initiate the jaw-opening reflex, which in turn activates and alternates with the jaw-jerk reflex "so long as there is something biteable between the jaws". These conclusions were

used by Rioch (1934) to formulate a theory explaining how electrical stimulation of the motor cortex could produce rhythmic mastication: this theory was extended to include voluntary control. She suggested that the masticatory area of the cortex acts directly upon the trigeminal motor nucleus to excite the jaw-opening motoneurons and inhibit the jaw closers. Jaw opening would thus occur, stretching the jaw closing muscles; which would in turn excite the jaw-jerk reflex. As soon as the jaw was raised, opening would occur again and the cycle could then be repeated as long as the jaw-opening motoneurons were tonically activated from above. Food between the teeth would additionally reinforce the jaw-opening phase. This theory of peripheral patterning of mastication has been generally accepted (Kawamura, 1963, 1967; Jerge, 1964; Kidokoro, Kubota, Shuto and Sumino, 1968a; Anderson, 1968; Chase and McGinty, 1970a), although Magoun, Ranson and Fisher (1933) suggested that stimulation of suprabulbar sites activated a rhythmic brain-stem center controlling mastication.

In 1961 Bullock commented that the mechanism by which patterned motor activity was produced by a nervous system is "one of the core questions of general neurology", but one which had received little direct attention. As with the specific case of mastication, patterning was at that time generally believed to be achieved through reflex chains (Bullock, 1961; Gray, 1950); but subsequently, evidence has been steadily accumulating that many rhythmic motor patterns in invertebrate species arise within the central nervous system and are not dependent on external timing (Wilson, 1961; Wyman, 1965; Miller, 1965; Wiersma and Ikeda,

1964; Horridge, 1968; Hoy and Wilson, 1969). Indeed, Horridge has gone so far as to state that in lower animals, "centrally controlled sequences of motor impulses and central inhibition of motoneurons to antagonistic muscles are the general rule".

However, evidence for similar control in the vertebrate is not as striking. The pattern of respiratory activity is not basically dependent on proprioceptive feedback (Adrian and Buytendijk, 1931; Hukuhara and Okada, 1956; Wang, Ngai and Frumin, 1957), but the patterning of locomotion and swimming is still supposed by some to take place in the periphery (Riss, 1969; Eyzaguirre, 1969), although recent evidence favours a central origin (Viala and Buser, 1965; 1969a,b).

The present series of experiments began as an investigation of the effects of various peripheral stimuli on rhythmical masticatory movements produced during stimulation of the corticobulbar projections and limbic areas in the anesthetized rabbit. The latter areas, also stimulated by Kawamura and Tsukamoto (1960a,b) and Schärer, Kasahara and Kawamura (1967), were not productive, except when examined with the chronic implantation of electrodes, when stimulation could be carried out without the influence of anesthetic agents. As a species comparison, similar studies were also begun in the anesthetized cat. However, rhythmical mandibular movements were infrequently elicited and it soon became evident that the rabbit was the more suitable animal for this type of research. Later studies were continued exclusively in this species. During the investigation of rabbits, a previously undescribed jaw reflex

was discovered and further investigation of this reflex forms the second part of the thesis.

In view of the increasing evidence, as mentioned above, that many motor patterns arise within the central nervous system in invertebrates, it seemed opportune to re-investigate, in the mammal, the generally accepted theory of peripheral control of rhythmical mastication, with the hypothesis that this activity is also basically patterned within the brain.



### HISTORICAL REVIEW

This review will consider the following topics:

- A. The jaw-opening reflex
- B. The jaw-jerk reflex
- C. The effects of interactive stimuli on the above reflexes
- D. Rhythmical mastication evoked by stimulation of the cerebral cortex
- E. Cortico-bulbar masticatory pathways
- F. Pathological and experimental lesions
- G. Rhythmical mastication of non-cortical origin
- H. Summary.

Although this thesis is primarily concerned with the control of rhythmical mastication, it was thought appropriate to include papers dealing with the jaw-opening and jaw-jerk reflexes in this review because of their importance to the peripheral theory of masticatory patterning of Rioch (1934).

#### A. Jaw-opening reflex.

In addition to the receptive field described by Sherrington (1917) for this reflex (gums, teeth and hard palate), jaw opening can also be produced by stimulation of the surface of the tongue (Cardot and Laugier, 1922; Harrison and Corbin, 1941; Hoffman and Tönnies, 1948; Kawamura and Fujimoto, 1958). For experimental purposes, the reflex is most often evoked by electrical stimulation of the lingual, superior dental or inferior dental branches of the trigeminus (Blier and Kleitman, 1930; Pfaffmann, 1939; King, Minz and Unna, 1955; Hugelin and Dumont, 1961; Kubota, Kidokoro and Suzuki, 1968; Chase and McGinty, 1970a,b). The effects on the amplitude of the reflex and the postsynaptic potentials recorded from the trigeminal motoneurons in response to stimulation of the aforementioned nerves are comparable in all

respects (Kidokoro et al, 1968a). After separation of the mandible into two halves by cutting through the symphysis, Sherrington (1917) found that the reflex was predominantly unilateral. This was confirmed by Kawamura and Fujimoto (1958).

The jaw-opening reflex arc is now known to be polysynaptic, with one or two interneurons connecting the primary afferent fiber to the digastric motoneurons (Hugelin and Dumont, 1961; Kidokoro et al, 1968a). The posterior belly of the digastric, which is innervated by the facial nerve, is also activated (Cardot and Laugier, 1923; Tournade, Calleja and Calleja, 1940a). Associated with reflex jaw-opening is a corresponding inhibition of the antagonistic jaw-closers: the medial pterygoid, temporalis and masseter muscles (Sherrington, 1917; Schoen, 1931; Hoffman and Tönnies, 1948; Goldberg and Nakamura, 1968; Kidokoro et al, 1968a).

#### B. Jaw-jerk reflex.

The jaw-jerk reflex is a myotatic reflex which is activated by stretch of the muscle spindles in the jaw-closing muscles (McIntyre, 1951). In contrast to the jaw-opening reflex, only muscles on the ipsilateral side are activated (Harrison and Corbin, 1941; Hufschmidt and Spuler, 1962). Primary cell bodies of the afferent fibers are located in the trigeminal mesencephalic nucleus (Allen, 1919; Thelander, 1924; Rioch and Lambert, 1934; Harrison and Corbin, 1941; Szentagothai, 1948; Jerge, 1963a) and make monosynaptic excitatory connections with jaw-closing motoneurons (McIntyre, 1951; Hugelin and Bonvallet, 1956; Nakamura,

Goldberg and Clemente, 1967; Sauerland, Knauss, Nakamura and Clemente, 1967; Kubota et al, 1968). However, although Kawamura suggested that concurrent reciprocal inhibition of jaw-opening motoneurons occurs (Kawamura and Fujimoto, 1958; Kawamura, 1963), this has now been shown to be untrue (Kidokoro et al, 1968a).

C. The effects of interactive stimuli on the jaw-opening and jaw-jerk reflexes.

A large number of papers has been published on the effects of previous or concurrent stimuli on the amplitude of either of these two reflex jaw movements or on the "mass" electrical activity in the appropriate efferent nerves. These are presented in chronological order in Table I. In summary of these studies, three general types of interactive stimuli were used:

- (a) Segmental - electrical stimulation of lingual, inferior dental, vagus or hypoglossal nerves,
- (b) Reticular - direct electrical stimulation of the reticular formation or indirect alterations in its level of activity by peripheral stimuli or humoral changes,
- (c) Electrical stimulation of the orbital gyrus.

Stimulation of the orbital gyrus initiates facilitation and inhibition of trigeminal motoneurons through both the segmental and reticular levels. Approximately 10 msec after a single stimulus pulse, the jaw-opening reflex is facilitated, while the jaw-jerk reflex is inhibited (Chase and McGinty, 1970a,b), probably through interneurons in the supratrigeminal nucleus. A later phase of jaw-jerk

suppression occurs by activation of the medullary inhibitory area (Sauerland, Nakamura and Clemente, 1967).

The encéphale isolé preparation has been extensively used in the investigation of the reticular activating system (RAS) because the partially-isolated brain does not show rapid fluctuations in the level of arousal (Hugelin and Dumont, 1961). However, because the spinal cord is severed in this preparation, it was necessary to investigate the modulation of motor activity by the RAS at the brain-stem level. Changes in the amplitude of the jaw-opening and jaw-jerk reflexes, which are homologues of the spinal flexor and myotatic reflexes (Sherrington, 1917) were employed for this purpose.

During the passage from deep sleep to the awake state, the motoneurons are initially most responsive to segmental stimuli, then reticular and, finally, the cortical effects predominate (Dell, 1963). The effect of many interactive stimuli on the jaw reflexes therefore depends on both the resting level of reticular activity and the changes in that level brought about by the stimulus.

#### D. Rhythmical mastication evoked by stimulation of the cerebral cortex.

The surface of the cerebral cortex was first shown to be electrically excitable by Fritsch and Hitzig (1870) who were less concerned about mundane motor activities than in finding the seat of consciousness. However, they did find that the cerebral cortex of the dog was divisible into an area anterior to the coronal sulcus, where one could produce movements of the opposite side of

the body upon stimulation, and the rest of the cerebrum which was electrically inexcitable. The rostral motor area was further divisible into subunits where stimulation evoked movements of distinct parts of the body. Among these subdivisions Fritsch and Hitzig included an "area facialis". "Tetanization" of the brain in this region, which lay on the ascending limb of the coronal gyrus, gave facial aftermovements of a trembling character. Rhythmical masticatory or lapping movements were not described.

Ferrier (1873; 1886) carried out similar experiments to confirm that the cortex was electrically excitable, in the hope of providing support for the views of Hughlings Jackson (1873) that movements were anatomically represented within the brain. Ferrier's experiments are reviewed and discussed in his text-book, "The Brain" (1886). Extensive mapping of the cortices of a variety of animals, including the macaque, dog, cat, rabbit, guinea pig and rat, uncovered areas where stimulation was followed by single or repetitive movements of the face and mouth. The repetitive movements in the rabbit, guinea pig and rat were described as a "frequently repeated chumping and munching action of the jaws".

Most of the subsequent experiments primarily dealing with mastication or the allied rhythmical activity of lapping were carried out in the rabbit or cat. These will be discussed in the second section below. For the moment, I will review the results obtained from other species.

(1) Man, apes, monkeys, dogs and lower mammals:

Delineation of the cortical masticatory area. Beevor and Horsley (1894) were the first to study the motor cortex of monkeys by electrical stimulation. In the macaque, they produced rhythmical mastication by stimulation of an area at the foot of the precentral gyrus. Two short reports on the cerebral cortex of the orang, gorilla and chimpanzee delivered to the Royal Society of London by Grünbaum and Sherrington (1901; 1904), caused later workers "to accept that the motor cortex was a well-localized zone" (Weed and Langworthy, 1926), which extended along the whole length of the precentral convolution and sulcus centralis. At the inferior extremity, bounded below by the sylvian sulcus, Grünbaum and Sherrington described a masticatory area somewhat smaller in extent than the corresponding region outlined by Beevor and Horsley. Their findings were confirmed by Vogt and Vogt (1907) and Walker and Green (1938) in a variety of monkeys and primates. Mastication did not occur by spread of current to the classical motor area (Area 4) because it could still be evoked after ablation of this part of the cortex (Walker and Green, 1938). They inferred from cytoarchitectural studies of the human cortex that stimulation of the corresponding region of the human cortical Area 6 $\beta$  would also produce mastication (Vogt and Vogt, 1926). This was shown to be true by Foerster (1931; 1936), who carried out systematic stimulation of the human cortex during surgery.

Area 6 $\beta$  was not considered to be truly motor by Penfield and Boldrey (1937), who did not describe rhythmical movements of

either the tongue or jaws. However, this apparent disagreement may only be a difference in interpretation, as recognized by the latter authors who stated that "we have eliminated all convulsive movements, whether tonic or clonic. The criterion of an epileptiform seizure is that the phenomena produced by stimulation continue and may advance after withdrawal of the electrode." This definition includes masticatory movements which generally continue after the stimulus is removed.

Penfield and Jasper (1954) stated that "mastication", which they took to include smacking of the lips, chewing and swallowing, was an incomplete act when elicited from the human rolandic cortex. These complex movements did appear, however, during stimulation of the temporal lobe or deep within the sylvian fissure.

Cortical representation of mastication has also been demonstrated from analogous areas in the dog (Smith, 1938; Babkin and Van Buren, 1951), sheep (Maracci, 1877; Zeehan, 1899; Simpson and King, 1911), guinea pig (Ferrier, 1886; Langlois, 1889; Tarchanoff, 1878; Rioch, 1934), hedgehog (Mann, 1896) and opossum (Rogers, 1924).

Description of the movements and related responses. In man, monkeys and apes, chewing, licking, swallowing and grinding movements were seen during stimulation (Beever and Horsley, 1894; Grindbaum and Sherrington, 1901; 1904; Vogt and Vogt, 1907; 1919; Foerster, 1931, 1936). Beever and Horsley described the observed chewing movements in the following words: "... the lower jaw begins to execute a series of rhythmical movements of grinding the teeth. To describe

the movement in detail; the mouth is opened, the lower jaw depressed and carried towards the same side, and then the mouth is closed by raising the lower jaw; directly the teeth are separated the tongue is advanced, and is retracted immediately before the teeth come together again; this latter movement of the tongue is thus dependent on and co-incident with the action of the lower jaw". In no other area of the cortex did a continuous galvanic current produce either rhythmical movements or motor effects which also outlasted the stimulus (Foerster, 1931). Epileptic convulsions originating from area 6 $\beta$  began with the same types of movements as were seen during stimulation.

Smith (1938) and Babkin and Van Buren (1951) described a variety of activities concerned with the ingestion of food during stimulation of the anterior composite gyrus of the dog. Mastication with synchronous tongue movements, respiratory inhibition, salivation, swallowing, oesophageal contraction and inhibition of gastric antral motility were the typical responses. Stimulating just below the sigmoid gyrus, the jaw movements were peculiar in that, although opening and closing recurred rhythmically, the lower jaw was never seen to close beyond 45 degrees. Moving away from the sigmoid gyrus along the anterior composite gyrus, movements with the appearance of normal mastication were then encountered during stimulation, while below this region was found another type of unusual masticatory activity. The movements were again rhythmical, but this time the mandible did not fall below 45 degrees. When the whole masticatory area was removed and the white matter



stimulated, the responses appeared unchanged.

The movements of the mandible which Maracchi (1877) witnessed in the sheep were extremely noisy and resembled exactly the act of rumination. A very interesting observation made by Simpson and King (1911) was that lambs would suck when the area corresponding to the face, mouth and tongue area in the adult was stimulated and that the sucking was accompanied by synchronous tail wagging.

(2) Cat and rabbit:

Delineation of the cortical masticatory area. Although Mann (1896) was able to produce rhythmical movements of the jaws during stimulation of the rabbit and hedgehog cortex he was unable to do so in the cat. However, many other subsequent studies have shown that a cortical masticatory area does exist in this animal (Economo, 1902; Sherrington, 1905; Brémer, 1923; Magoun et al, 1933; Ward and Clark, 1935; Smith, 1938; Bailey and Sweet, 1940; Carol, 1942; Hess, Akert and McDonald, 1952; Kawamura and Adachi, 1960; Kawamura, 1963; Chase, McGinty and Serman, 1968a; Chase and McGinty, 1970a). This area occupies the orbital gyrus and presylvian sulcus and would appear to be analagous with the regions already described as subserving mastication in monkeys, man and dogs. There is a similarity in the cytoarchitecture of the region and the wide variety of effects produced by electrical stimulation in a variety of species (Smith, 1938).

The cortical masticatory area of the rabbit, by far the most popular animal for the study of rhythmical mastication, occupies a similar region to that of the guinea pig (Ferrier, 1886; Rioch, 1934) and covers a much greater proportion of the motor strip than the corresponding region in higher animals. Extending ventrally

to the rhinal fissure, its boundaries have been delineated by the following authors: Furstner (1875), Ferrier (1886), Gad (1891), Réthi (1893), Carpenter (1895), Economo (1902), Miller (1920), Brémer (1923), Rioch (1934), Kawamura and Tsukamoto (1960a), Kawamura, Tsukamoto and Miyoshi (1961), Schärer, Kasahara and Kawamura (1967), and most recently by Sumi, (1969). Destruction of one hemisphere does not change the responsiveness of the remaining cortical masticatory area to electrical stimulation (Réthi, 1893).

Description of the movements and related responses. Brémer (1923) wrote that excitation of the cortical masticatory centers of the cat and rabbit reproduced exactly the types of reflex mastication seen in both species. This analogy of the cortical and reflex responses was particularly evident in the rabbit, in which all the observed masticatory movements were rhythmic. In that animal, both the cortical and buccal reflexogenic zones, representing the different types of mastication, changed from the front to the rear in the following order: munching or nibbling, vertical mastication, and "rumination". Rioch (1934) was unable to confirm Brémer's findings. However, two cortical zones representing vertical mastication and movements apparently analagous to Brémer's "rumination" were outlined by Réthi (1893), Kawamura et al (1961), and Schärer et al (1967). Tooth contact was observed by the last-named authors to occur during "rumination", but not during vertical mastication.

Brémer (1923) emphasized the complexity of mastication, "un ensemble de mouvements coordonnés des mâchoires, des lèvres, des joues et de la langue. Les muscles qui réalisent ces mouvements

sont innervés par les V, VII et XII paires de nerfs crâniens."

At low stimulus frequencies, only single contractions of the jaws with each stimulus pulse were observed by Rioch (1934), Kawamura and Tsukamoto (1960a) and Tsukamoto (1963a). When stimuli of approximately 10Hz or of greater frequency were used only rhythmic chewing movements occurred (also reported by Sumi, 1969), which often continued for several seconds after the stimulus was terminated. Above the threshold stimulus frequency, the rate of chewing increased with the frequency of stimulation to reach a maximum rate of 5.75 strokes/sec at approximately 200 Hz (Kawamura and Tsukamoto, 1960a). The maximum rate of chewing observed by Rioch (3.2 strokes/sec) and Sumi (approximately 4.0/sec) are closer to the natural frequency of mastication (3.5-4.0/sec) observed when rabbits chew carrots (Kawamura and Tsukamoto, 1960a).

The latency between the start of stimulation and the appearance of the first masticatory movements was very variable. Sumi (1969) reported values ranging from 40 sec at low stimulation frequencies to 200 msec when the frequency exceeded 20 Hz, which is in approximate agreement with those quoted by Rioch (1934) and by Kawamura and Tsukamoto (1960a).

Brémer (1923) found that it was possible to obtain a cortical masticatory response to a subliminal stimulus, applied immediately after a buccal stimulus which had provoked reflex mastication. Cortically-induced mastication can also be inhibited by stimulation of the superior laryngeal nerve or lingual nerve (Sumi, 1969, 1970b). Stimulation of the ventral caudate nucleus may inhibit

masticatory movements induced by cortical stimulation (Tsukamoto, 1963c).

Mastication, which can be evoked by stimulation of either hemisphere, was shown to be a bilateral act in the rabbit by Miller (1920). He divided the mandible at the symphysis and the soft tissues of the floor of the mouth as far back as the angle of the jaw. The muscles of both sides functioned synchronously and in harmony during unilateral stimulation. Simultaneous stimulation of the right and left cortical masticatory areas was carried out by Schärer et al (1967) and Sumi (1969). Schärer et al reported "no changes in the predominantly vertical 'cortical chewing pattern' with extensive tongue movements and with no tooth contacts". Conversely, Sumi found that the motor responses were enhanced by bilateral stimulation and the facilitation was unaltered after splitting the corpus callosum.

Recently Sumi (1970a) has endeavoured to gain further insight into the mechanism of co-ordination of both mastication and swallowing by analysing the patterns of activity recorded from single hypoglossal motor fibers during stimulation of the cortex. He found that most fibers discharged bursts of impulses in phase with rhythmic chewing, the majority being concurrent with jaw closing. Among these, some units also fired after each stimulus pulse while others did not. The remaining units either discharged regularly with each stimulus or sporadically, showing no tendency to follow the rhythm of chewing. Paralysis with gallamine triethiodide did not alter the pattern of discharge.

E. Cortico-bulbar masticatory pathways.

The first attempts to trace motor pathways down from the cortex to the brain-stem motor nuclei in the rabbit were made by Gad (1891), but he was unable to find any subcortical structures which yielded masticatory movements during stimulation. Réthi (1893) and Economo (1902) could trace infracortical pathways for swallowing and chewing through the lower part of the internal capsule by serially sectioning the brain in a coronal plane and stimulating the cut surface. Stimulation of the cerebral peduncles, however, caused only tonic contraction of the masseters. Réthi therefore postulated that a co-ordinating center for mastication and swallowing lay in the region of the optic thalamus where "willing stimulation" from the cortex evokes the combined movements of eating.

Economo also tried to trace the pathways by histological means. After he had obtained masticatory movements from one hemisphere, he extirpated the small area of grey matter beneath the electrodes. Three weeks afterwards the rabbits were sacrificed and the Marchi method was employed to trace the degenerating tracts. Fibers could be seen running in the ipsilateral internal capsule into the cerebral peduncle where they divided into a dorsal and a ventral stream. The dorsal stream appeared to terminate in the ventral nucleus of the thalamus while the ventral group continued in the peduncle, eventually passing dorsally into the substantia nigra. Only by removing larger pieces of cortex could degeneration be traced into the pyramids. Economo therefore concluded that the intercalary center for the normal act of eating postulated by Réthi actually lay in the rostral half of the substantia nigra and was

closely connected with the V, VII, X and XII cranial nerves. This conclusion was reached independently by von Bechterew (1909) after he had found that swallowing and chewing occurred during stimulation of the lateral part of this region.

Hayashi (1952), who stimulated the cortex with both electrical pulses and nicotine, found that the evoked masticatory movements were abolished by removal of the homolateral thalamus. He therefore deduced that the pathways relayed in this structure, before crossing the midline to a masticatory executing center located in the substantia nigra. The right and left masticatory centers were assumed to be interconnected. It appears to the reviewer that the reason for the loss of mastication after removal of the thalamus was probably due to damage to the internal capsule, although Hirayama (1943) also reported that the corticofugal fibers synapsed in the ipsilateral thalamus in the dog. From there fibers were presumed to pass into the midbrain, decussate, and travel to the contralateral trigeminal motor nucleus. Another structure named as a possible intercalary center in the descending masticatory projection in the rabbit was the subthalamus (Kawamura and Tsukamoto, 1960b). Fibers leaving this structure were supposed to decussate in the midbrain before reaching the V motor nucleus (Tsukamoto, 1963a).

The bulk of the evidence, however, shows that these corticobulbar pathways pass directly into the brain-stem, where they connect, via interneurons, with the branchial motoneurons of both sides. Miller (1920) was the first to suggest that a prebulbar co-ordinating center was unnecessary. He found that both rhythmical mastication

and deglutition could be elicited by stimulation of the infracortical tracts as far caudally as the mammillary bodies. This was confirmed by Rioch (1934) in rabbits and guinea pigs. Below this level, stimulation yielded only tonic jaw closure, as found by Réthi (1893) and other proponents of prebulbar co-ordinating centers. Miller showed that the observed closure was a consequence of spread of current to the mandibular nerve at the point of its emergence from the skull. Furthermore, he quoted a personal communication from Sherrington, who suggested that the fibers concerned in the evocation of mastication and swallowing left the cerebral peduncles on their way to the motor nuclei. Due to their dispersion, the fibers would be more difficult to excite. This view was later supported by Brémer (1923).

Corticofugal pathways for rhythmical lapping were traced to an even lower level in the cat by use of the Horsley-Clark technique (Magoun et al, 1933). Lapping had a wider cortical representation than chewing in this animal and was the only rhythmical oral activity encountered below the level of the cortex itself. The most caudal point at which stimulation could produce rhythmical lapping lay in the caudal pons, on the dorsolateral surface of the cortical fibers immediately rostral to the formation of the pyramids. To prove beyond doubt that the substantia nigra was not an intercalary center for lapping, and, by inference, for mastication, Magoun et al stimulated this structure three to six weeks after removal of the jaw motor area, when all relevant corticofugal fibers should have degenerated. No lapping or masticatory movements were seen.



Andersson, Kitchell and Persson (1958) suggested that an area medial to the tractus solitarius, stimulation of which produced ruminal and masticatory activity in goats, "might be a locus for the central co-ordination of all mechanisms involved in rumination". They did recognize that the rhythmical mastication might be due to direct stimulation of parts of the nucleus of the tractus solitarius or its afferent fibers which could normally be activated by the regurgitation of the ruminal contents. In this regard, Bailey and Brémer (1938) have reported masticatory activity during stimulation of the central end of the cut vagus of the cat.

#### F. Pathological and experimental lesions.

The observation of human anencephalics and animals deprived of various portions of the brain has led a number of people to conclude that the structures above the brain-stem are not necessary for the co-ordination of mastication and the closely-related act of sucking. Ferrier (1886) was the first to show that young medullary animals will suck if a nipple is placed between their lips. He also reported that human bulbo-spinal anencephalics suck and swallow normally on the breast. Monnier and Willi (1947) confirmed these findings in the human, and a number of reports have extended Ferrier's observations on experimentally prepared animals.

Bazett and Penfield (1922) decerebrated cats above the pons. These animals, which lived up to three weeks after the operation, not only swallowed but chewed their food or stomach tube if it was inserted into the back of the mouth. Chewing can also be provoked in the decerebrate cat and rabbit by rubbing the mucosa



of the buccal commissures (Brémer, 1923).

Although medullary animals will exhibit chewing in response to tactile stimulation, Brémer stated that the thalamus appears indispensable for the restoration of effective mastication in the decorticate cat and rabbit. Perhaps he did not allow a sufficient time for recovery, because Rothman (1910) found that mesencephalic dogs gradually recover the ability to eat spontaneously. Certainly, decorticate dogs and cats are capable of chewing, lapping and swallowing after their muzzles are placed in their food (Zeliony, 1913; Dusser de Barenne, 1920; Hambourger, 1937). If the olfactory tracts and pyriform lobes are left intact, these animals can smell out and ingest their food unaided. Green and Walker (1938) and Karplus and Kreidl (1914) found that monkeys will chew food and in some cases eat unassisted after bilateral ablation of the motor face area or even of the whole cortex. Schaltenbrand and Cobb (1931) found that both striate and thalamic cats ate spontaneously. Sniffing, biting, chewing, licking and swallowing were observed in cats recovering from removal of the neocortex and additional portions of the forebrain by Bard and Rioch (1937) and Rioch and Brenner (1938).

Gad (1891) concluded that mastication and swallowing of food are pure reflex acts mediated through the brain-stem, but that the cortex is necessary for the formation of the food bolus and for pushing it back into the oropharynx. This hypothesis is supported by the observation that, following bilateral section of the cerebral peduncles, monkeys had difficulty in chewing and more obviously in moving the bolus back into the pharynx (Bucy, Ladli

and Ehrlich, 1966).

G. Rhythmical mastication of non-cortical origin.

Even if Gad's conclusions are accepted, "it is clear that the basal olfactory areas, together with the associated ventral portion of the striatum and lower centers with which they are connected, namely, the hypothalamus, subthalamus and reticular substance of the brain-stem, are capable of elaborate feeding reactions of a highly complicated type" (Bard and Rioch, 1937). Pathways must therefore converge upon a bulbar co-ordinator not only from the corticobulbar system, but also from the older subcortical structures. This was shown experimentally by Schaltenbrand and Cobb (1931). After completing their aforementioned observations on chronic decorticate cats, they stimulated the exposed surface of the brain at the time of sacrifice and obtained licking, chewing, salivation and whisker movements from the anterior commissure. In similar preparations, Rioch and Brenner (1938) obtained comparable movements while stimulating the olfactory tubercle and pyriform lobe.

(1) Thalamus and adjacent areas. Réthi (1893) briefly recorded that mastication could be observed during stimulation of the optic thalamus of rabbits, and Sachs (1909) made confirmatory observations in the rhesus monkey. His more precise techniques localized the productive sites to the anterior third of the ventro-lateral nucleus. However, Sachs was careful to state that his results were not evidence for special thalamic centers for automatic or rhythmic movements.

The extensive work of Hess and his associates on the

functions of the diencephalon, summarized in English by Gloor (1954) and by Hess (1957), was carried out on cats implanted with chronic stimulating electrodes. Cats licked, snapped or chewed 4-5 times per second when sites in the thalamic radiations, medial part of the ventral thalamic nucleus, and backwards along the pathway of the trigeminal lemniscus towards the midbrain were stimulated (Hess, 1940; Hess and Magnus, 1943; Magnus, 1945; Hess et al, 1952; Hess, 1957). Corresponding stimulation points were found further forward in the bed of the stria terminalis (Hess, 1957). Licking and chewing often occurred together or in alternation. Stimulation of adjacent regions of the thalamus and the septum gave rise to protective movements of the mouth and tongue, as though the animal were trying to rid itself of an annoying foreign body ("hair-in-the-mouth" response).

(2) Hypothalamus. Hess and Magnus (1943) and Magnus (1945) also found that licking and chewing could be evoked from a number of sites in the lateral hypothalamus, as did Larsson (1954) in his study of hypothalamic organization of mechanisms regulating the food intake of goats. These sites lay dorsally close to the descending fornix and caudally in the middle and ventral parts of the hypothalamus. Mastication could occur alone or in combination with hyperphagia, as was also reported in the cat by Delgado and Anand (1953) and Anand and Dua (1955), leading Larsson to the following conclusion. "It thus seems probable that the structures in the hypothalamus regulating food intake also exert influence on the masticatory and licking movements in co-ordinating these motor functions to be a part of the manifestation of hunger."

Hess and Magnus (1943) and Magnus and Lammers (1956) considered the septum, anterior commissure, bed of the stria terminalis and hypothalamus to be part of an old rhinencephalic system for mastication, or perhaps for oral sensation. By contrast, they postulated that the thalamic regions which produced licking and chewing were part of the thalamocortical projection system, particularly from the trigeminal nerve (Magnus, 1945; Hess et al, 1953; Magnus and Lammers, 1956).

(3) Amygdaloid complex. Schärer et al (1967) have reported that the rhythmical jaw movements obtained by stimulation of the lateral hypothalamus in rabbits could be differentiated from similar movements obtained during stimulation of the lateral amygdaloid nucleus. Although in both cases the jaw movements were characterized by a chewing stroke with large lateral movements, regular tooth contact was only recorded during amygdaloid stimulation. Tooth contacts occurred solely on the side contralateral to the stimulation sites.

There are many other reports of rhythmical mastication and lapping being produced by stimulation of the amygdaloid complex and allied areas (Takahashi, 1951; McLean and Delgado, 1953; Anand and Dua, 1955). Kaada (1951) observed rhythmic, well-coordinated chewing movements (1.0-1.2/sec) when stimulating points within the rostral piriform cortex, again mainly in the periamygdaloid region, and within the amygdala of cats, dogs and monkeys. This response, which only appeared after a long latency varying from 5-15 seconds, continued as long as the stimulus persisted (up to 2 minutes) and frequently longer (Kaada, 1951; Gastaut, 1952; Ugin and Kaada, 1960).

The majority of sites within the amygdala itself were located in the rostral regions. In the cat, the basal nucleus was the most productive, with scattered points in the lateral and central nuclei (Kaada, Andersen and Jansen, 1954; Magnus and Lammers, 1956; Usin and Kaada, 1960). Kawamura and Tsukamoto (1960a) and Tsukamoto (1963a) recorded masticatory movements at the rate of 3.5-4.0/sec while stimulating the lateral amygdaloid nucleus in rabbits. Licking and chewing, in conjunction with swallowing and retching were frequently obtained from the same electrode. Active points for salivation approximately coincided with those for licking and chewing (Gastaut, Vigouroux, Corriol and Badier, 1951; Sano, 1958; and Magnus and Lammers, 1956).

Chewing, swallowing and licking during stimulation of the amygdala could still be obtained after bilateral ablation of the cortex lateral to the rhinal fissure (Kaada, 1951; Baldwin, Frost and Wood, 1956; Kawamura and Tsukamoto, 1960a), while unilateral ablation of the lateral amygdala did not alter the responses obtained by stimulating the homolateral jaw motor area (Kawamura and Tsukamoto, 1960a). These findings indicate that the amygdaloid areas act independently of the motor cortex. Magnus and Lammers (1956), however, postulated a close functional relationship between these two regions.

Gastaut (1953) proposed the existence of two rhinencephalic systems. The first comprises the orbital gyrus, the olfactoseptal and piriformo-amygdaloid formations and their mesodiencephalic projections. Its functions include the protection and utilization of the oral cavity and also the organization of complex activities of a sexual and food-gathering nature. The

second system, comprising limbic cortex, hippocampo-mamillo-thalamic formations and their meso-diencephalic connections, is concerned with emotion. Gastaut did not believe that these structures constitute a true motor system. Conversely, Wood et al (1958) suggest that the amygdala has separate motor centers for jaw opening (basal medial nucleus) and for jaw closure (lateral nucleus) which would necessarily act together to co-ordinate such functions as chewing.

Movements of the face and jaws during stimulation of the mesial amygdala were seen in human patients and in chronically implanted macaques (Baldwin, Frost and Wood, 1954). The monkeys, but not the humans, were observed to chew. However, Jasper and Rasmussen (1958) report that masticatory movements, which are always associated with impaired responsiveness, confusion or amnesia, can be produced by stimulation of the human amygdaloid or periamygdaloid areas, inferior insula and adjacent cortex. Penfield and Jasper (1954) suggest that masticatory movements seen in certain types of epilepsy originate in the region of the amygdala.

It was concluded by Kawamura and Tsukamoto (1960b) and by Tsukamoto (1963b) that the masticatory pathway from the lateral amygdala and lateral hypothalamus in the rabbit to the V motor nucleus passed through the dorsal part of the mesencephalic reticular formation. They assumed that the cortical jaw motor area is predominantly concerned with regulating jaw opening while the amygdala regulates jaw closing.

#### H. Summary.

Although in the past attention has been mainly directed

to the elucidation of the role of the cortex and limbic structures in feeding and feeding automatisms it is evident that the brain-stem, including the motor nuclei and primary connections of the cranial nerves, is the level most directly concerned with ingestion. The basic patterns are probably reflex in nature, requiring integrated activity of those cranial nerves which take part in such feeding responses as chewing, salivation and swallowing, and also in the rejection of unacceptable objects (Brobeck, 1960). Food would serve as a stimulus for these reflexes.

The nature of these "basic patterns" remains unknown. Are they performed by a chain of reflexes, as Br mer (1923) supposed, each stage of ingestion being triggered by the sensations arising during the completion of a prior phase, or is the whole of the pattern laid down within the central nervous system and released by a triggering stimulus? Perhaps the true mechanism is a combination of centrally-encoded motor patterns modified by sensations. In the experiments about to be described, one part of the feeding act, the masticatory phase, was investigated, to see how it could be influenced by peripheral stimuli, and whether it was patterned within the brain or in the periphery.

TABLE I

Summary of experiments on the Jaw-Opening (J.O.) and Jaw-Jerk (M.R.) reflexes.

Date	Authors	Preparation	Summary and Conclusions
1917	Sherrington	Decereb. cats	Described J.O. and M.R. and noted tendency for these reflexes to give rhythmical mastication.
1922	Cardot, Laugier	Anesth. dogs	Threshold current giving J.O. varies directly with level of anesthesia.
1923	Cardot, Laugier	Not stated	Afferents for J.O. in lingual nerve, efferents in mylohyoid V and digastric VII.
1923	Brocq-Rousseu et al	Anesth. horses, cats, rabbits	Advised use of J.O. as test for depth of anesthesia in humans.
1926	Cherbouliez, Laugier	Anesth. dogs	Stimulation of peripheral X. Resulting cerebral anemia first ↑, then ↓ J.O.
1930	Blier, Kleitman	Ditto	Stimulation of central sciatic or X, distention of rectum or stimulation of viscera; ↓ J.O. Cerebral anemia had no effect.
1939	Bonvallet, Mins	Anesth. or decereb. dogs	Summation occurs when J.O. elicited by stimulation of gingival and lingual nerves. Moderate stimulation of sciatic; ↑ J.O. Strong sciatic stimulation; ↓ J.O.
1940 a,b	Tournade et al	Dogs	Moderate stimulation of sciatic; ↑ J.O. Strong sciatic stimulation; ↓ J.O. Stim. of central X; ↓ J.O. J.O. ↑ during inspiration.
1941	Harrison, Corbin	Decereb. dogs	Lesions of the mesencephalic V root disrupted ipsilateral M.R. arc, but not J.O.



Date	Authors	Preparation	Summary and Conclusions
1955	King et al	Anesth. cats	Stimulation of (1) central sciatic; ↓ J.O. (2) medio-dorsal bulbar RF; ↑ J.O., ↓ patella reflex (3) rostral RF; ↓ J.O., ↑ patella reflex. Concluded that flexors and extensors oppositely influenced by RF.
1955	Hugelin	Paralysed cats	Stimulation of mesencephalic RF, or ↑ PCO <sub>2</sub> or ↑ adrenaline; ↓ J.O. while ↑ digastric motoneurone excitability. Concluded that general motor facilitation occurs, but non-essential local reflexes blocked.
1956	Hugelin, Bonvallet	Cats encéphale isolé	M.R. are monosynaptic.
1957	Hugelin, a,b,c Bonvallet	Ditto	Stimulation of mesencephalic RF; ↓ J.O., ↑ M.R. Reticular effects rapidly suppressed by cortex as arousal occurs.
1958	Hugelin, Bonvallet	Ditto	Stimulation of medial or cubital nerves. Degree of facilitation varies inversely with level of cortical arousal.
1958	Kawamura, Fujimoto	Anesth. or decereb. cats and dogs.	J.O. ↑ during inspiration. J.O. response in contralateral digastric ↓ ipsilateral.
1961	Blom, Skoglund	Anesth. cats	During the first 600-800 msec of repetitive sciatic stimulation, J.O. ↓ .
1961	Hugelin	Cats encéphale isolé	Stimulation of mesencephalic RF; ↓ J.O., ↑ M.R., ↑ digastric response to stimulation of motor cortex or chorda tympani nerve. Concluded that the level of RAS activity determines the type of motor activity.
1961	Hugelin, Dumont	Ditto	Stimulation of mesencephalic RF; ↓ J.O., ↑ M.R., ↑ excitability of digastric and masseteric motoneurons. Concluded ↓ J.O. at level of first relay.

Date	Authors	Preparation	Summary and Conclusions
1963	Chapot et al	Ditto	Inspiration; ↓ M.R. Expiration, ↓ PCO <sub>2</sub> ; ↑ M.R.
1963	Dell	Review	During sleep or rest, pain activates polysynaptic flexor reflexes (e.g. J.O.). On waking, RAS ↓ of flexor reflexes and ↑ antigravity reflexes (e.g. M.R.). Further arousal produces ↑ of cortico-motor discharges and general depression of all reflexes.
1963	Hugelin, Cohen	Review	All the individual changes seen after activation of RAS by central or peripheral stimuli are part of a general arousal. The RAS is subject to cortical inhibitory control.
1964	Chapot et al	Not stated	Stimulation of n. supratrigeminalis or lingual nerve; ↓ M.R. ↓ PCO <sub>2</sub> or ↓ temperature; ↑ M.R. Suggested that n. supratrigeminalis receives inputs from Golgi tendon organs and group II fibers from jaw-closing muscles.
1965	Stoika et al	Not stated	Repetitive stimulation of large afferent fibers of aortic nerve gives sleep and ↑ M.R., ↑ J.O.
1966	Chapot et al	Cats encéphale isolé	Temperature ↓ ; M.R. ↑ due to ↑ size of action potential PCO <sub>2</sub> ↓ ; M.R. ↑ due to ↑ in excitability.
1966	Sauerland et al	Paralysed cats	Stimulation of the orbital cortex; ↓ M.R.
1967	Goldberg	Ditto	Stimulation of lingual nerve; ↓ M.R. Concurrent IPSPs recorded in masseteric motoneurons. Effects mediated through area in the brain stem.
1967	Nakamura et al	Cats encéphale isolé	Repetitive stimulation of orbital cortex; ↓ M.R. only during first sec.
1967	Puizillot, Sayadi	Cats sectioned above thalamus and below medulla	Repetitive stimulation of central X; ↑ M.R. and sleep.

Date	Authors	Preparation	Summary and Conclusions
1967 a	Sauerland, et al	Paralysed cats	Stimulation of the orbital cortex (1) when the EEG is synchronized causes non-reciprocal ↓ of spinal reflexes and M.R. (2) when EEG is desynchronized causes ↓ of anti-gravity reflexes including M.R. and ↑ of flexors.
1967 b	Sauerland et al	Cats encéphale isolé	Direct bilateral projections from orbital cortex to pontine facilitatory area and medullary inhibitory area. Stimulation of the orbital cortex after medulla transected below V motor n; ↑ M.R.
1968 a	Chase et al	Freely- moving cats	15 msec latency from stimulation of orbital cortex to ↓ M.R. During rhythmical mastication evoked by repetitive cortical stimulation, ↑ M.R. in closing phase, ↓ M.R. in opening phase.
1968 b	Chase et al	Ditto	Gradual ↓ M.R. as animal passed from alert state to active sleep.
1968	Chase, Nakamura	Cats encéphale isolé	Stimulation of central vagus (1) single pulse; ↓ M.R. (2) repetitive pulses; ↑ M.R.
1968	Enomoto et al	Freely- moving cats	High intensity stimulation of V mesencephalic n. to evoke M.R. activates inhibitory neurones in n. supratrigeminalis causing ↓ M.R.
1968	Goldberg, Nakamura	Decerebrate cats, sectioned below medulla	Stimulation of lingual nerve; bilateral ↓ in M.R. - Early IPSP in masseteric motoneurones via disynaptic path through n. supra-trigeminalis. Late IPSP via polysynaptic path.
1968	Kawamura	Anesth. dogs	Inflammation of the receptive field lowers threshold for J.O.

Date	Authors	Preparation	Summary and Conclusions
1968 a,b	Kidekoro et al	Anesth. cats	Stimulation of inferior dental nerve; ↓ M.R. Early disynaptic IPSP via n. supratrigeminalis. Late polysynaptic IPSP. No reciprocal inhibitory connections between jaw-closing and jaw-opening motoneurons. No inhibition of antagonists by jaw muscle afferents.
1968	Kubota et al	Decereb. cats	Stimulation of superficial radial nerve; ↓ J.O., ↓ M.R. Similar of lumbar flexor and extensor reflexes. IPSPs in masseteric and lumbar motoneurons; ↓ lumbar reflexes dependent on intact medulla.
1969	Chase, Clemente	Freely- moving cats	Sleep; ↑ J.O. highest in quiet sleep.
1969	Sauerland, Misuno	Paralysed cats	Stimulation of orbital cortex induces two phases of ↓ M.R. (1) short latency IPSP (2) long latency PAD.
1970 a	Chase, McGinty	Freely- moving cats	Stimulation of orbital cortex (1) ↑ J.O., ↓ M.R. after latency of 8-20 msec (2) ↓ J.O., ↑ M.R. for a further 60 msec. During mastication evoked by repetitive stimulation, ↑ J.O. in opening phase, ↑ M.R. in closing phase.
1970 b	Chase, McGinty	Ditto	Stimulation of orbital cortex ↓ M.R. and activates digastric motoneurons after latency of 15 msec.
1970 a,b	Chase et al	Cats, encéphale isolé	Stimulation of central X; (1) ↑ M.R., ↑ J.O. for 5 msec (2) ↓ M.R., ↓ J.O. for 35 msec (3) ↑ M.R., ↓ J.O. for 50 msec. Effects caused by stimulation of cardiovascular afferents.
1970	Nakamura et al	Not stated	Stimulation of XII; ↓ M.R. bilaterally. Not abolished by pontomedullary section.

EXPERIMENTAL METHODSGENERAL METHODS

Experiments involving stimulation of the central nervous system, or activation of a lateral jaw movement reflex, were performed on a total of 110 male New Zealand albino rabbits (body weight 2.3-5.2 kg) and, for a species comparison, on 7 male cats (body weight 2.7-4.1 kg). Among the 71 rabbits which yielded results, 32 were anesthetized with urethane (1.6 mg/kg I.V.) and 8 with chloralose (50 mg/kg I.V.). Twenty-five were decerebrated at a precollicular level, 5 having been initially anesthetized with ether and 20 with thiopental sodium (average dose 3.0 mg/kg). Light methoxyfluorane anesthesia was maintained subsequent to decerebration to reduce spontaneous movements. Six rabbits were anesthetized with sodium pentobarbital (30 mg/kg I.V.) to enable electrodes to be chronically implanted, and the animals were afterwards allowed to recover. Five of the 7 cats gave experimental results: 3 were anesthetized with urethane (1.6 mg/kg I.P.) and 2 with sodium pentobarbital (30 mg/kg I.P.).

During the acute experiments, core temperature was monitored by a rectal thermometer inserted 5 cm beyond the anus, and maintained at  $38 \pm 1^{\circ}$  C in the rabbit and at  $37 \pm 1^{\circ}$  C in the cat by means of a heating blanket. After tracheostomy and tracheal intubation each rabbit was fitted into a stereotaxic instrument (D. Kopf Industries) and the inferior walls of the auditory canals were fractured to allow standard rat ear bars to be inserted in the horizontal plane. With each animal placed in this instrument, the

snout was fixed to an adjustable support that allowed free access to the mouth. The cats were placed in the stereotaxic apparatus in the normal manner.

In those acute experiments (Ia, Ic and II) which included stimulation of the central nervous system, the cerebral cortical surface was exposed and covered with a layer of paraffin oil which had been warmed to 38°C. Stainless steel concentric bipolar electrodes (In Vivo Metric Systems NE100, pole separation 0.5 mm, tip resistance 5-10 K ohms in .9% saline) were then inserted into a variety of subcortical structures using the co-ordinates of the atlas of Sawyer, Everett and Green (1954) for the rabbit, and of Snider and Neimer (1961) for the cat.

At the termination of all experiments involving cerebral stimulation, the brains were perfused with 0.9% saline solution, followed by 10% buffered formalin. Each brain was then cut into blocks by lowering a knife in the coronal plane, in front of and behind the electrode tracks. The blocks were later removed and stored in 10% buffered formalin. Following fixation, sections 50 $\mu$  thick were cut parallel to the electrode tracks, using a modification of the freezing technique of Marshall (1940) and stained with cresyl violet and/or luxol fast blue. The actual position of stimulation points was later calculated from the stereotaxic co-ordinates by measuring from the base of the electrode tracks. In some instances the iron deposition and staining technique of Green (1962) was used to mark stimulation points. Post-mortem examination of the plane of decerebration was done in 14 instances. These general methods were used where applicable in the following experiments.

EXPERIMENT I: Afferent influences on jaw rhythms.Group a. Anesthetized and decerebrate rabbits.

This group included 11 animals anesthetized with urethane, 8 with chloralose and 5 decerebrates, all of which gave rhythmical masticatory movements in response to cerebral stimulation. After stimulation of the corticobulbar tracks in 4 of the decerebrate rabbits had been shown to elicit mastication, the cerebellum was removed.

Electrical stimulation. Ten to thirty second trains of mono or biphasic square-wave electrical pulses of 1 msec duration were delivered at a frequency of 40 Hz by a Grass stimulator (S4) and stimulus isolation unit (SIU 4678). At each stimulation site, a threshold stimulus voltage (T1) for the production of rhythmical mastication was found. This varied between 0.6 and 30 V.

Interactive stimulation. To test for sensory interactions during the induced jaw movements, three types of stimuli were separately utilized. These were: (1) paw-pinching to the point of withdrawal; (2) rapid rectal distention with the bulb of a 5 ml Foley catheter; and (3) moderately heavy backward pressure on the labial surfaces of the upper incisor teeth. A fourth type of interposed stimulation came from the sudden distention of a 5 ml Foley bulb between the dorsum of the tongue and the hard palate: this was coupled with ongoing subthreshold stimulation of central sites previously established as capable of invoking the jaw rhythm.

Recording. Vertical movements of the mandible were transduced to current flow changes between an electrode attached and moving with the mandible and a stationary electrode at the bottom of a saline

bath (Figure 1). These changes were then recorded on a Beckman Type R. Dynagraph. This transducer was not checked for linearity and the record was used solely as an indicator of the vertical direction and the frequency of jaw movements.

Group b. Free-moving rabbits.

The 6 rabbits anesthetized with sodium pentobarbital were immobilized in a standard rabbit stereotaxic head-holder (D. Kopf Industries) and twisted nichrome bipolar electrodes, tip separation 0.5 mm were then implanted in up to 8 subcortical sites/animal. After the electrodes had been secured to the skull with screws and self-curing methyl methacrylate resin, the animals were removed from the head-holder.

Electrical stimulation procedures and parameters similar to those previously described were used before the animal regained consciousness, in the awake animals which had recovered from the effects of surgery (several days to weeks after operation) and during terminal anesthesia. Mandibular movements were recorded either as integrated E.M.G. changes in masseter muscle activity or by a type TF10C Grass force-displacement transducer attached by a thread to the lower incisors. Interactive stimuli were not used.

Group c. Anesthetized cats.

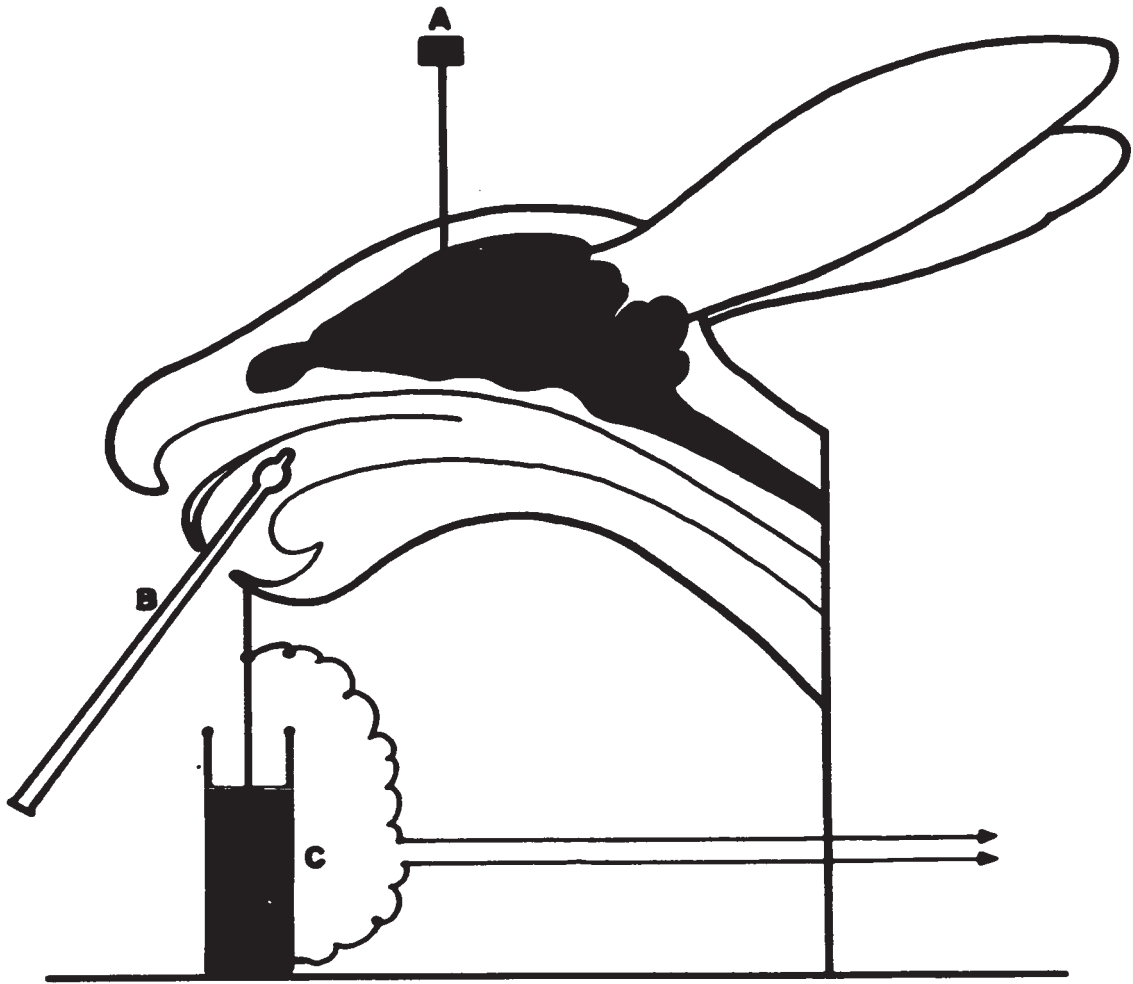
In the experiments performed on the 5 cats which make up this group, the procedures for electrical stimulation and recording were the same as those described for the rabbits of Group a. Interactive stimuli were not used.



FIGURE 1.

Diagrammatic representation of stimulation and recording procedures  
in Experiment I, Group a.

- A - central stimulating electrode within the rabbit's brain,
- B - Foley catheter in the approximate position within the mouth at which the balloon was inflated (6 cm from the incisal edge),
- C - saline-filled transducer, connected to a Beckman 9853 strain gauge coupler.



EXPERIMENT II: Masticatory patterning.

All twenty-one rabbits were anesthetized with urethane and initially prepared as described in the general method.

Surgical preparation. In six animals in which recordings were to be made from the trigeminal nerve, the zygomatic arch and superficial belly of the masseter muscle were removed on one side to reveal the masseteric nerve. The mylohyoid nerve was exposed by removing the remainder of the masseter, the ascending ramus and angle of the mandible.

In another 6 rabbits, the hypoglossal nerve was identified in the neck as it crossed the hyoglossus muscle and prepared for recording by dissecting it free from the surrounding fascia.

All nerves were cut as far distally as possible, and surrounded by pools of warmed paraffin oil formed by suturing a copper ring to the wound edge.

Nine additional rabbits were prepared for recording from the hypoglossal nucleus in the following manner. An occipital craniotomy and removal of the arch of the atlas were followed by severing of the spinal cord at the level of C2. Nerves C1, C2, XII, XI, X, IX and VII were cut bilaterally and the exposed surface of the medulla covered with 2% agar in Ringer-Locke solution. Bilateral parietal craniotomy and removal of the occipital poles of the cerebrum provided access to the trigeminal nerves, which were exposed by removing bone from the base of the tentorium. These nerves were then severed. Arterial blood pressure was continuously recorded and maintained when necessary at the level prevailing before section of the spinal cord with an intravenous infusion of methoxamine hydrochloride in 10% dextrose saline.

In all twenty-one animals, gallamine triethiodide (Flaxedil, 5 mg/Kg.hr I.V.) was administered either before recording was commenced or after data had been gathered in the unparalysed state. Animals were then respired by a positive pressure respirator at a volume and frequency sufficient to maintain the end-tidal CO<sub>2</sub> concentration, measured by a Beckman CO<sub>2</sub> Analyser, at about 4.5%.

Electrical stimulation. Rhythmical masticatory movements and bursts of neuronal activity in the branches of the trigeminal nerve, hypoglossal nerve and nucleus were evoked by electrical stimulation of the putamen or of the corticobulbar pathways from their point of origin down to the level of the pons. All records of activity in the branches of the trigeminal nerve were made while using 10 sec trains of stimulation of 40 Hz, 1 msec pulse duration and a voltage of 1.5 times threshold.

The effect of the various input parameters described below on the frequency of masticatory discharges was calculated from records of hypoglossal nerve and nucleus activity. Trains were generally of 10 sec duration although longer trains were sometimes necessary because, at stimulation frequencies below 20 Hz, mastication did not always commence within the first 10 sec of stimulation. Pulses were always of 1 msec duration. Threshold voltages for the production of rhythmical activity (T<sub>1</sub>) were found for each stimulation point, using a constant frequency stimulus of 40 Hz. Voltages 1.5, 2 and 3 times this value (T<sub>1.5</sub>, T<sub>2</sub>, T<sub>3</sub>) were employed for subsequent stimulation trials. The trains of constant frequency stimulation (5-500 Hz) were delivered by a Grass S4 stimulator and isolation unit.

A train of stimulus pulses of constant frequency could theoretically be the source of timing for a rhythmical motor output. This timing information was therefore eliminated by using stimulation of random frequency. Trains of pulses of constant voltage and duration were obtained by amplifying the output of an Electra Model 63 White Noise Generator, and using this signal to trigger the stimulator. The average frequency of stimulation was varied between 4.2 and 680 Hz by adjusting the amplifier gain or the frequency control of the stimulator.

Interval histograms of sample stimulus trains were exponential in form (Figure 2), although there were a greater number of short intervals than predicted for an ideal random process. However, the mean of the distribution approximately equalled the standard deviation (e.g. at an average stimulation frequency of 52.4 Hz, the mean interval between pulses being 19.1 msec, the standard deviation was  $\pm 20.7$  msec). Each stimulus train was therefore accepted as a random process.

Using both methods of stimulation, multiple trials separated by 40 sec intervals were carried out both before and after paralysis. In 5 paralysed animals, the respirator was turned off during some periods of random frequency stimulation to see if the removal of this rhythmic input abolished the regular masticatory discharges.

Interactive stimulation. In six of the 21 animals, a balloon was inflated in the mouth, with and without simultaneous central stimulation, whilst recording from the hypoglossal nerve, or from the hypoglossal nucleus before cutting the trigeminal nerve. During

centrally evoked rhythmical masticatory discharges, the paws were heavily pinched, before sectioning of the cord.

Recording. Discharges were recorded from the hypoglossal nerve trunk and the branches of the trigeminal nerve by silver wire bipolar electrodes, and from the hypoglossal nucleus by fine concentric bipolar electrodes, shaft diameter 0.25 mm and tip separation 0.5 mm (In Vivo Metric Systems SNE100). Each recording electrode was connected serially to a Grass P15 preamplifier, a Type 2A63 plug-in amplifier of a Tektronix 565 oscilloscope and an Ampex 4-channel tape recorder. The stimulus train and the femoral arterial blood pressure or ECG were also recorded on tape. Tapes were later replayed for analysis or photography.

Data analysis. The neural recordings from the hypoglossal nerve and nucleus were integrated by a Beckman Type R dynagraph. A single point in time to represent each burst of multineuronal activity was drawn by hand on the paper record when the level of activity exceeded an arbitrary threshold (see Figure 3). Intervals between bursts of activity could then be measured and subjected to some of the statistical analyses developed for the treatment of point processes. First, graphs were drawn of the relationship between the frequency of stimulation and the frequency of the resulting masticatory discharges. Second, autocorrelelograms were used to show that the bursts of neural activity recurred at regularly spaced intervals in time during random frequency stimulation. Cross-correlations with the ECG or arterial pulse train were done in 6 rabbits to see if the

occurrence of bursts was statistically dependent on the heart beat. These latter two types of analyses were done by hand using the methods described by Gerstein and Kiang (1960) and Perkel, Gerstein and Moore (1967). Effects of paralysis or variations in the voltage of stimulation on the frequency of bursts of multi-neuronal activity were analysed by the Friedman Two-Way Analysis of Variance. The correlation between the frequency of bursts and the stimulation frequency was done by the Spearman Rank Correlation method. Non-parametric analyses were used in these cases because the data were not drawn from a population having a normal distribution.

The areas under the integrated neurogram curves of single bursts were expressed as the weight of the cut-out paper records (see Figure 3) and compared before and after paralysis. Since the frequency of stimulation and frequency of discharge affected the area of the curve, records made before and after paralysis were compared by a paired t test after equalization of these variables.

FIGURE 2.

Histograms of stimulation trains.

- A - interval histogram of a pulse train of average frequency 70.9 Hz.  
Horizontal scale, 6.25 msec/division; vertical scale, 25 counts/  
division.
- B - time histogram of a similar pulse train, average frequency 71 Hz.  
Horizontal scale, 12.5 msec/division; vertical scale, 25 counts/  
division.
- C - time histogram of a regular pulse train of frequency 71 Hz using  
the same scale as B. The contrast between these regularly recur-  
ring events and the random occurrence of pulses in B is obvious.

All records run from right to left.



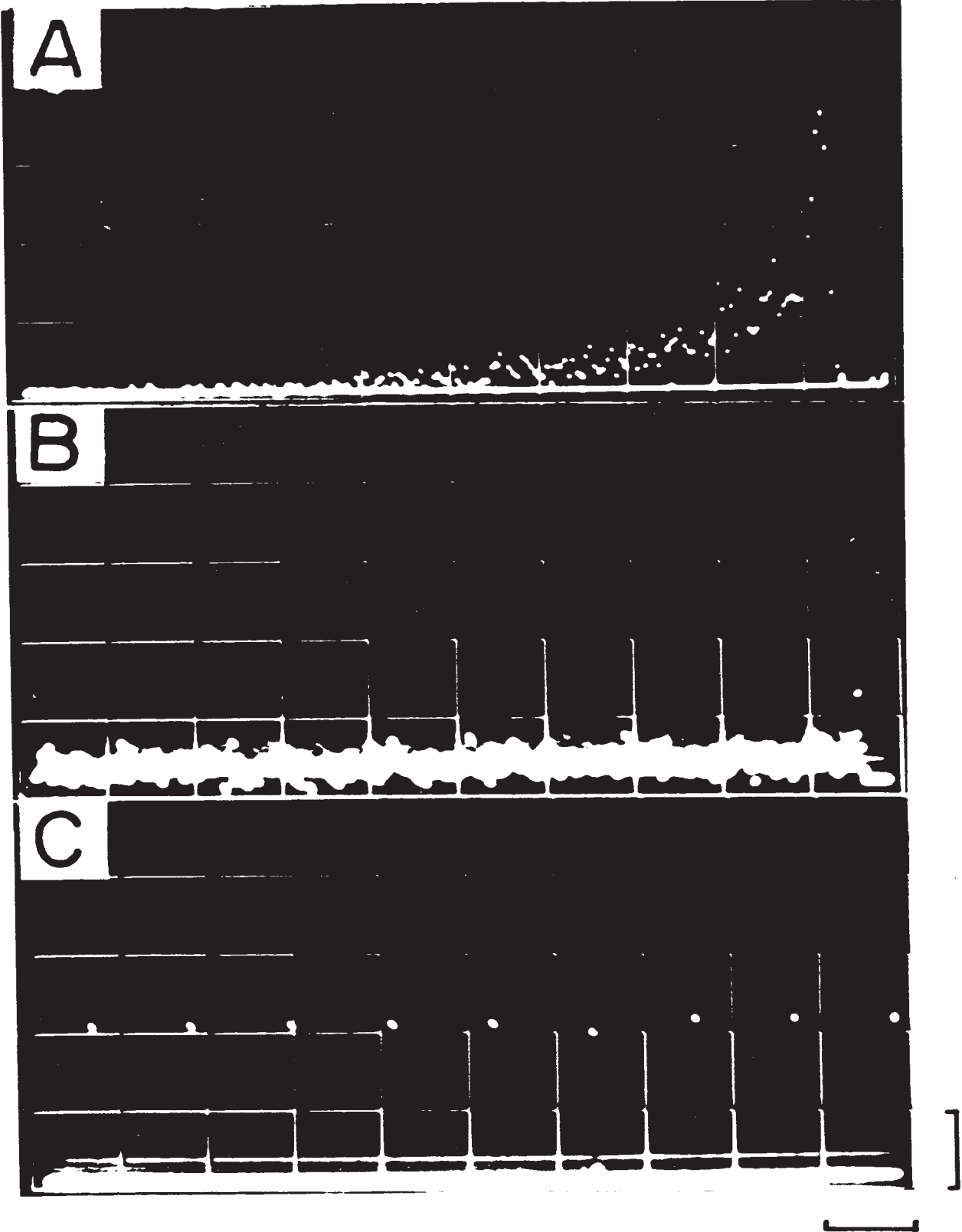


FIGURE 3.

Conversion of integrated neurograms to a point process.

Tracing from a polygraph recording on curvilinear paper.

A - discharge from XII nucleus during stimulation of the internal capsule in an anesthetized paralyzed rabbit, integrated in B and reduced to a point process, C.

D - time, calibration 0.2 secs.

↓ - start of stimulation (40 Hz, T1.5, 1 msec).

The shaded area under the curve was cut out and weighed. The area occupied by each burst could then be compared with similar recordings made before paralysis.



EXPERIMENT III: Lateral jaw movement reflex.

A total number of 20 decerebrate rabbits was used. As a preliminary study, two rabbits were decerebrated at a precollicular level and allowed to recover from the anesthesia. Fluid balance and body temperature were maintained for a period of 50 hours and the lateral jaw movement reflex in response to maxillary incisor pressure was then recorded on a kymograph via a string attached to the lower incisors.

The remaining 18 decerebrate rabbits were used in the main series of acute experiments. The left eye, lacrimal glands and periorbital fat were removed to give access to the deep muscles of mastication and the infraorbital nerve. The latter could be cut when necessary as it passed across the floor of the orbital cavity.

Stimulation procedures. Both mechanical and electrical stimuli were used to elicit muscular reflex activity before and after section of the infraorbital nerve. Pressure was applied separately to all surfaces of the maxillary central incisors and to the surrounding attached gingiva and palatal mucosa of the 18 rabbits through a short rod, circular in cross-section (cross-sectional diameter 1.27 mm). The rod was attached to a Grass force-displacement transducer (TF 10C) held in the experimenter's hand. This stimulus was applied both in the presence of and the absence of a 100 g or 200 g load hanging freely from the mandibular incisors.

Trains of electrical pulses, (1-30 Hz, 6-15 v, and 1 or 2 msec duration) supplied by a Grass stimulator (S4) and isolation unit (SIU 4678), were also applied to the anterior oral and labial mucosa of 8 of the rabbits through bipolar platinum wire electrodes (tip separation 2 mm).

EMG Recording. In 12 rabbits, concentric bipolar electrodes were inserted into each left superficial masseter, zygomatico-mandibular, anterior temporal, external pterygoid and digastric muscles. These muscles are named in accordance with the terminology of Fox (1965). Recordings were made from one or two of the above muscles in the remaining 6 animals.

Visual observations of jaw movements were made during mechanical and electrical stimulation of the reflexogenic zone: EMG activity was viewed on a Tektronix oscilloscope (565) or integrated and recorded on a Grass polygraph. In the former instance the traces were photographed by a Grass kymograph camera. When the electrical stimuli were used, the records were stored simultaneously on magnetic tape (Ampex SP 300) and later replayed for analysis.

## RESULTS

Amongst the 39 rabbits which did not yield results, the most common cause of failure was shock or irreversable brain damage suffered during attempts to sever the cranial nerves within the skull. This problem was finally overcome with increasing practice, by maintaining the blood pressure as near as possible to its preoperative level with infusions of methoxamine hydrochloride in 10% dextrose saline and by abandoning attempts to sever the VIII nerve. This nerve leaves the brain-stem under the cover of the flocculus, which in the rabbit lies in a bony canal lateral to the rest of the cerebellum. Attempts to retract or remove the flocculus led to massive, uncontrollable hemorrhage. Other animals were either too deeply anesthetized to be responsive to stimulation or died by damage inflicted during decerebration or during electrode placement.

### EXPERIMENT I: Afferent influences on jaw rhythms.

#### Group a. Anesthetized and decerebrate rabbits.

More than 1000 subcortical points were stimulated from the anterior border of the putamen back to the middle of the medulla, but excluding most of the thalamus. Rhythmical movements of the mandible were obtained from 87 loci, situated in the following structures: cortico-bulbar tracts from the subcortical white matter down to the pyramids (30), putamen (27), external capsule (9), anterior commissure (6), globus pallidus (4), lateral hypothalamus (4), mesencephalic reticular formation (3), substantia nigra (2), and reticular thalamus (2). These sites are shown in Figure 4.

A study of all anatomical structures from which jaw movements

could be produced was not attempted. Attention was directed particularly towards the interactive effects of central stimulation and other simultaneous stimuli.

A latent period of from 0.2 to 13.6 msec separated the start of suprathreshold stimulation from the first of the rhythmical mandibular movements, which began with a lowering of the mandible from its rest position. Rhythmical opening and closing movements then followed, at a frequency of from 1.0 to 5.0/sec. The tongue was protruded between the teeth during jaw opening and retracted at the start of closure. The average frequency of movement recorded when stimulating various sites is shown in Table II. The influence of stimulus parameters on the frequency of mastication is considered in Experiment II. Removal of the cerebellum in 4 decerebrates did not abolish the masticatory movements (Figure 5).

A single opening-closing cycle usually followed the cessation of central stimulation, but after-chewing was observed for up to 4 seconds in lightly anesthetized preparations. Deep anesthesia completely abolished the movements.

#### Effects of peripheral stimuli (Summarized in Table II).

Distention of an oral balloon. In 7 lightly anesthetized rabbits, distention of the oral balloon alone caused rhythmical chewing movements similar to those produced by central stimulation. Deepening the anesthesia abolished this response. However, when distention was now coupled with subthreshold stimulation of sites capable of producing rhythmic jaw movements, the chewing reappeared (Figure 6).

Tooth pressure. Firm pressure applied perpendicular to the labial surface of an upper incisor tooth caused a swing of the mandible to the contralateral side, with no noticeable change in vertical position. This posture was maintained until the pressure was removed. (In Experiment III this reflex will be described in detail). When light pressure was applied during stimulated masticatory movements, wide lateral excursions preceded each opening stroke. Increased force completely inhibited the rhythmical movements, but these returned following release of the pressure (Figure 7).

Paw-pinching and rectal distension. Pinching of the paws was also consistently inhibitory (Figure 7). It was observed that more pressure had to be applied to the hindpaws than the forepaws to produce complete inhibition. Following removal of a stimulus which had produced complete inhibition, the rate of jaw movements was often enhanced. Partial inhibition was obtained during rectal distension with a Foley catheter.

Group b. Free-moving rabbits.

Twenty-nine chronic electrodes were implanted in 6 animals. Rhythmical masticatory movements were obtained from stimulation of 2 sites in the lateral amygdaloid nucleus, 3 in the subthalamus, and from single sites in the putamen, anterior commissure and mesencephalic reticular formation (Figure 4). A recording made whilst stimulating the lateral amygdala is shown in Figure 8. Results are summarized in Table III.

The frequency of chewing (2.0-5.5 strokes/sec) was greater than that found in the same rabbits when anesthetized. For



example, in 1 animal, light anesthesia (pentobarbital, 20 mg/Kg) reduced the frequency of movements elicited by stimulation of the anterior commissure from 4.7 to 1.4 strokes/sec. The attainment of a surgical level of anesthesia completely abolished the response to stimulation of the lateral amygdala.

Stimulation of the subthalamic nucleus caused one rabbit to approach the edge of the cage. It then began mouthing and chewing at the wall. Turning of the head to the right, and chewing of the fur on the rear right paw, were seen during stimulation of the point situated in the right mesencephalic reticular formation dorso-lateral to the red nucleus.

In one animal, chewing movements were seen to continue for 18 seconds after stimulation of the lateral amygdala had ceased.

#### Group c. Anesthetized cats.

Three hundred points were stimulated, mainly within the amygdala, hypothalamus, subthalamus and mesencephalic reticular formation. True rhythmical movements of the mandible were infrequently seen. When present they more closely resembled rhythmical lapping (1-2 strokes/sec) than mastication (Figure 8). Initial jaw opening was followed by tongue protrusion far beyond the lips, tongue curling, retrusion and finally, jaw closure. This type of movement was obtained from two sites in the subthalamus, and from a solitary site in the lateral habenula nucleus (Figure 9). Salivation accompanied movements except when stimulating the habenula. Swallowing occurred approximately every five seconds.

during stimulation of four sites in the central and basal amygdaloid nuclei. The oral movements recorded were not due solely to the increased salivation because stimulation of many sites throughout the hypothalamus and amygdala caused a flow of saliva without concomitant jaw movements.

TABLE II

## Effects of peripheral stimuli on rhythmical mastication.

Stimulation site (N)	Latency range (secs)	Mean masticatory frequency and range (strokes/sec)	Facilitation by oral balloon (n/N)	Paw-pinching (n/N)	Inhibition Incisal pressure (n/N)	Rectal distention (n/N)
Putamen (11)	0.2-13.6	2.8 1.5-5.0	38/49	8/8	1/1	8/13
Cortico-bulbar tracts (19)	0.2-9.0	3.0 1.6-4.0	37/49	41/47	30/37	4/6
Reticular Formation (3)	1.1-4.0	3.0 1.0-3.4	18/23	8/9	8/15	2/5
Substantia nigra (2)	5.2-11.1	2.4 1.7-2.6	15/21	9/9	12/13	1/1
Lateral hypothalamus (3)	0.2-2.5	3.1 1.0-4.0	8/10	-	-	1/1
TOTAL N=38			n/N=116/151	n/N=66/73	n/N=51/66	n/N=16/26

Results from 20 rabbits are tabulated. The average number of movements/sec were calculated from trials in which suprathreshold stimulus parameters were employed.

N - number of stimulation points

n/N - number of facilitatory interactions/number of attempted interactions

n/n - number of inhibitory interactions/number of attempted interactions

TABLE III

Summary of results obtained in rabbits implanted with chronic stimulating electrodes

Stimulation site (N)	Latency range (secs)	Mean masticatory frequency and range	
		Unanesthetized	Anesthetized
Lateral amygdala (2)	0.85-7.6	4.5 n=12 3.5-5.5	no response n=6
Subthalamus (3)	0.75-8.5	3.7 n=24 2.0-5.5	no response n=6
Putamen (1)	0.5 -8.2	4.7 n=8 4.0-5.0	1.6 n=6 1.0-2.0
Anterior commissure (1)	1.25-5.5	4.7 n=6 3.7-5.2	1.4 n=7 1.0-2.1
Mesencephalic reticular formation (1)	Animal turned to ipsilateral side and nibbled at hind-paw. Latency and rate not calculated.	n=12	no response n=8

Results from 6 rabbits are shown. These were calculated from trials in which supra-threshold stimulus parameters were employed. The same stimulation parameters were used during anesthesia (pentobarbital 20 mg/kg).

FIGURE 4.

Map of stimulation sites giving mastication in the rabbit.

Sites within the rabbit brain, projected onto a sagittal plane, from which rhythmical mastication was evoked in Experiment I, groups a (•) and c (x). Drawn from the atlas of Monnier and Gangloff (1961).

- C - internal capsule
- P - putamen
- A - anterior commissure
- E - external capsule
- G - globus pallidus
- M - lateral amygdala
- L - lateral hypothalamus
- R - reticular areas of thalamus  
and midbrain
- S - substantia nigra
- T - cortico-bulbar tracts
- V - V motor nucleus
- D - D - approximate plane of decere-  
bration in 9 animals of Group a

Calibration - 3 mm.

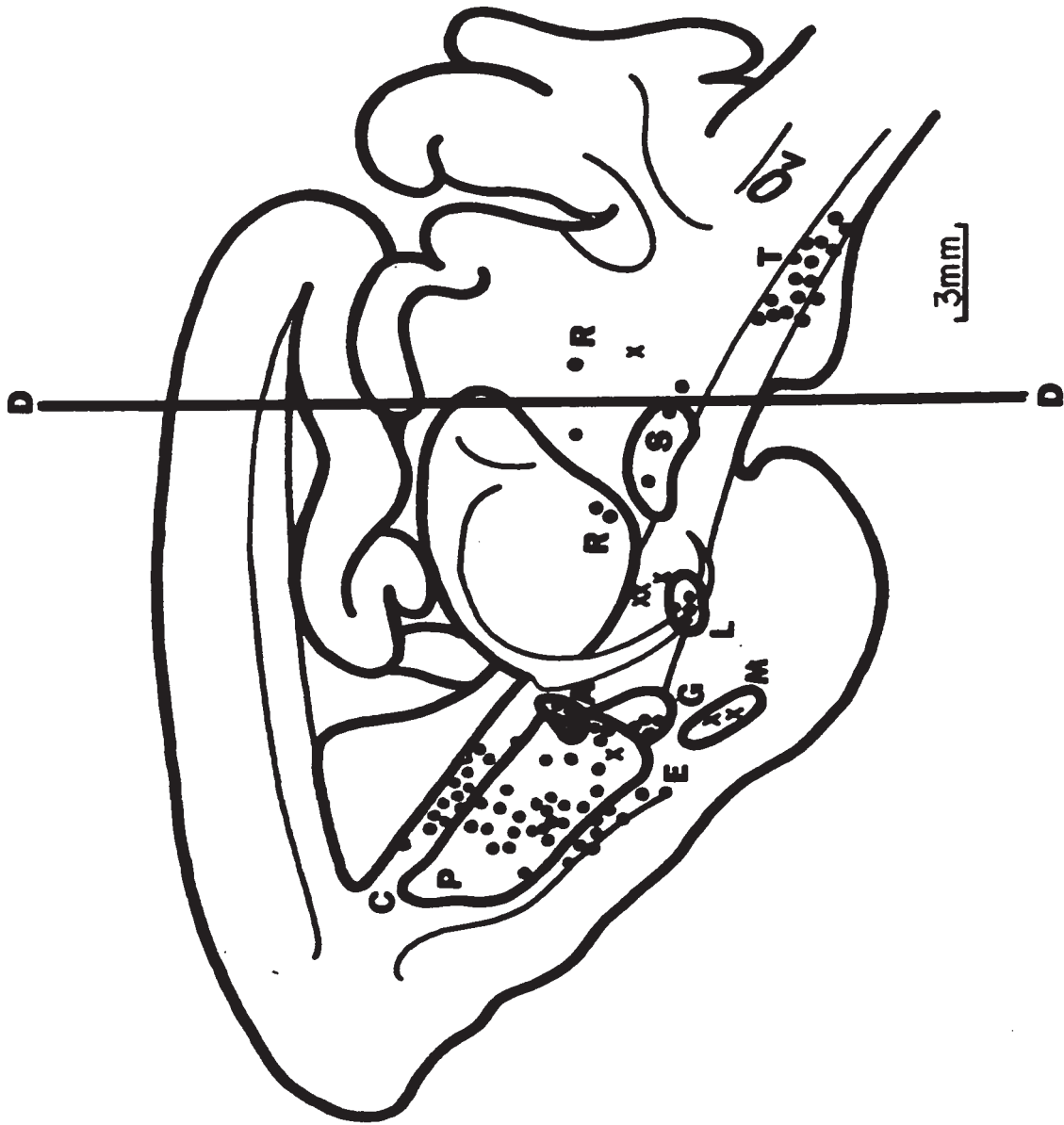


FIGURE 5.

Mastication after removal of the cerebellum.

Tracing of recordings made before (A) and after (B) removal of the cerebellum in a decerebrate rabbit whilst stimulating a point in the caudal region of the substantia nigra. Stimulus parameters 6 V, 1 msec, 40 Hz. The arrows mark the beginning and end of stimulation.

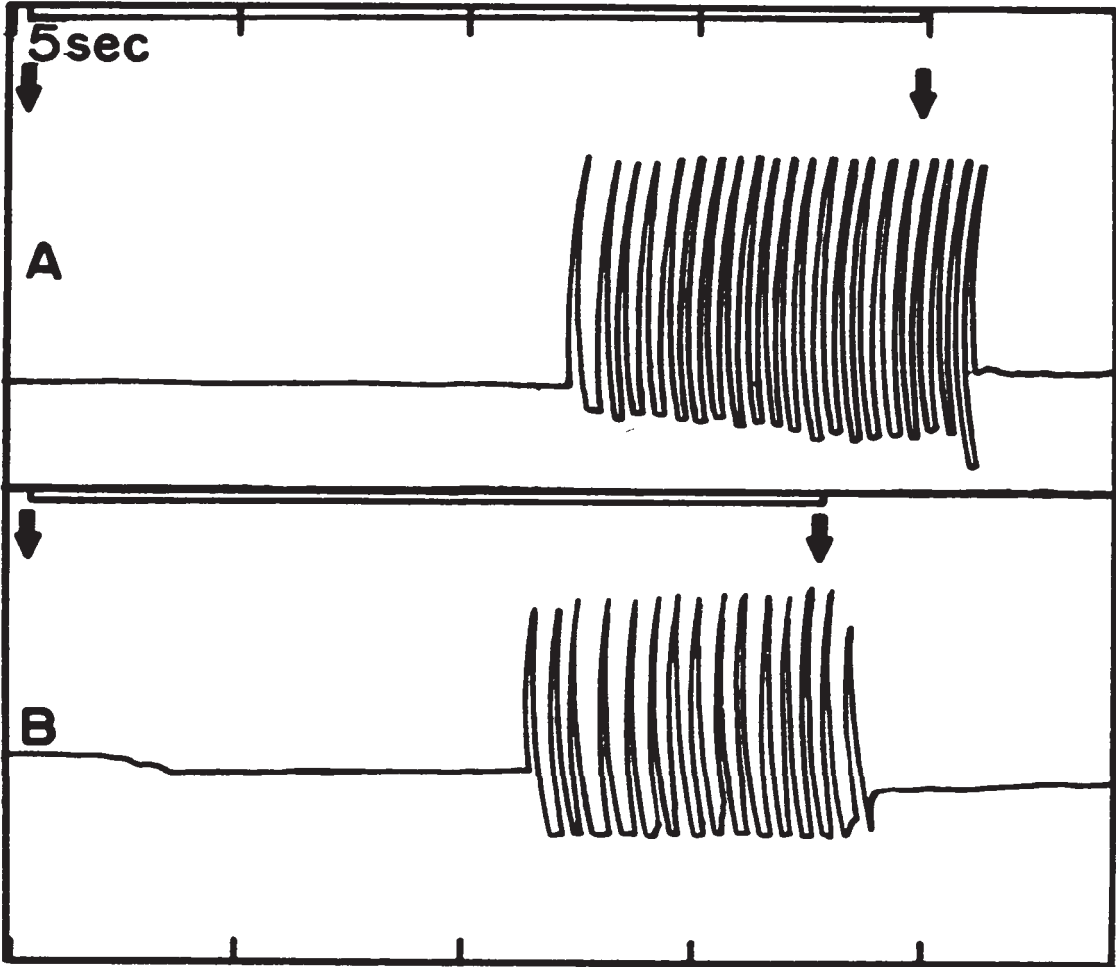




FIGURE 6.

Summation of oral and central stimulation.

Tracing from a polygraph record.

M - record of jaw movement in the vertical plane (opening downwards). With earlier suprathreshold stimulation (not shown) the rate of opening-closing cycles was 2.5-3.0/sec

The filled arrows delineate two intervals of subthreshold stimulation (4 V, 1 msec, 40 Hz) of a point within the putamen of an anesthetized rabbit which had previously given rhythmical jaw movements using a higher stimulus voltage. Putting a Foley catheter in the mouth (1) and its partial inflation (2) had no effect in the absence of central stimulation. When coupled with subthreshold central stimulation, the inflation (3) induced rhythmical jaw movements. There was cessation of these on deflation (4) and a short recurrence with the irritation of catheter removal (5). Other central stimulation sites gave similar results (Table II).

R - record of respiratory movements.

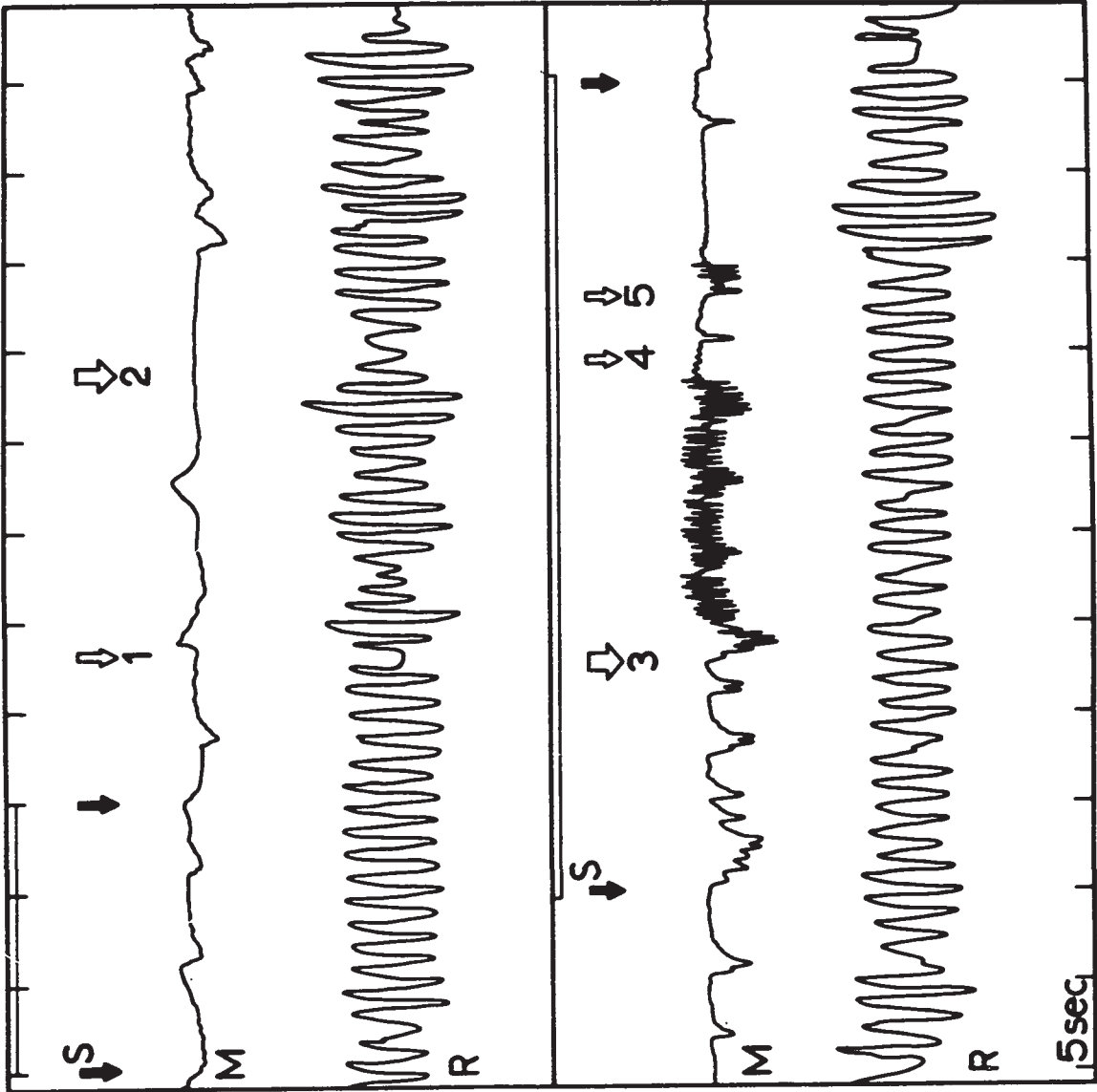


FIGURE 7.

Inhibition of rhythmical mastication.

Tracings from polygraphic records.

- A - Rectal distention from inflation of a Foley catheter bulb (unfilled arrows) produced a temporary and partial inhibition of rhythmical jaw movements evoked by putamen stimulation (8 V, 1 msec, 40 Hz), between the filled arrows.
- B - Paw-pinching in the period between the unfilled arrows was inhibitory to an on-going rhythm produced by stimulation of the globus pallidus (6.5 V, 1 msec, 40 Hz).
- C - The jaw rhythm recorded during stimulation of the cortico-bulbar tracts in the pons (6 V, 1 msec, 40 Hz) was inhibited by heavy pressure first applied to the labial surface of the upper left central incisor ( $\perp$ ). After release of pressure and resumption of chewing, the labial surface of the upper right central incisor ( $\perp$ ) was pressed.

Similar interactions were obtained during stimulation of the other central structures shown in Figure 4 and Table II.

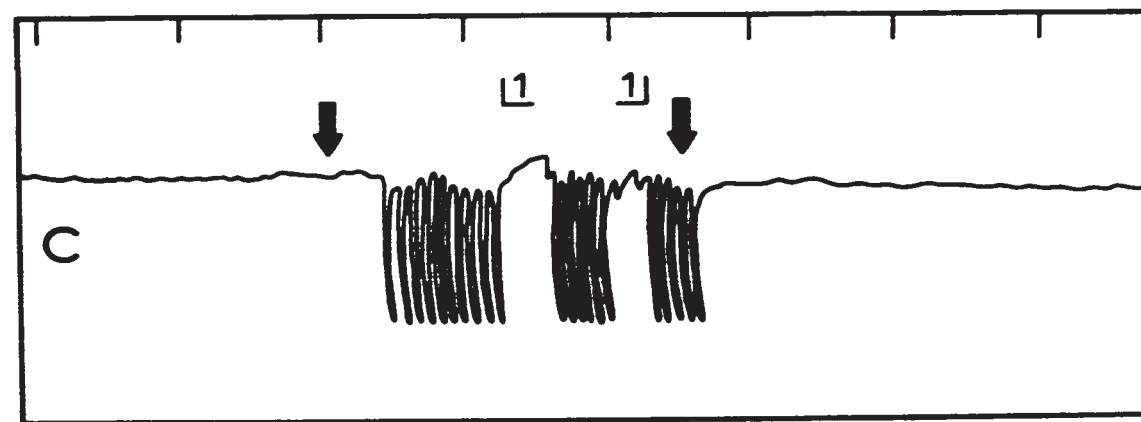
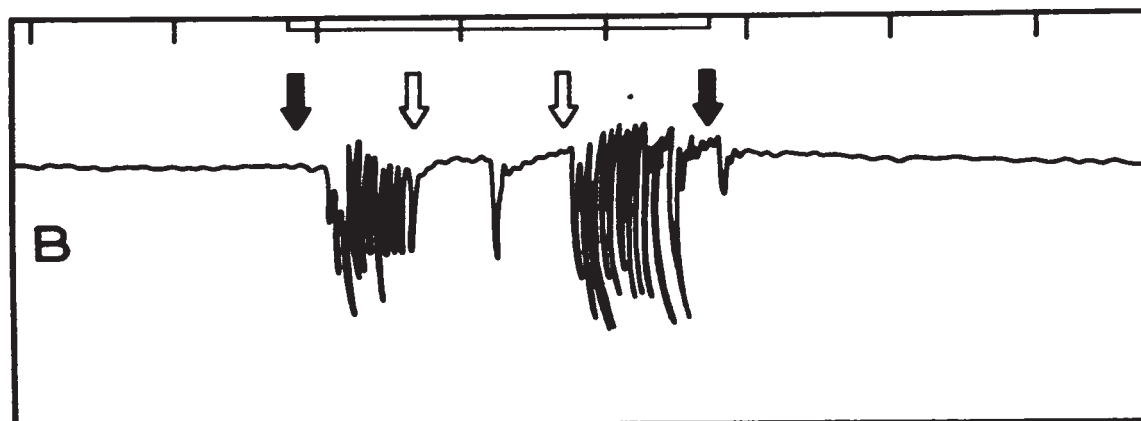
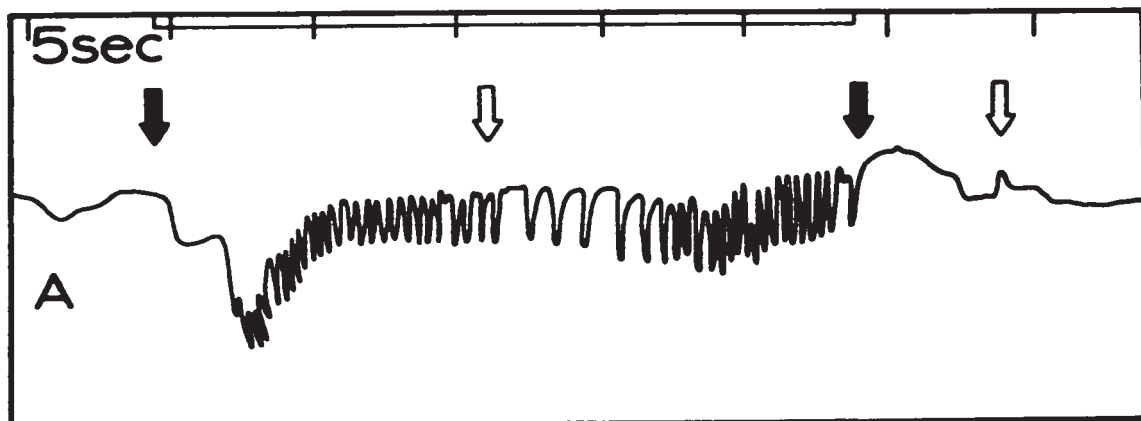


FIGURE 8.

Mastication recorded from an unanesthetized rabbit and lapping in  
an anesthetized cat.

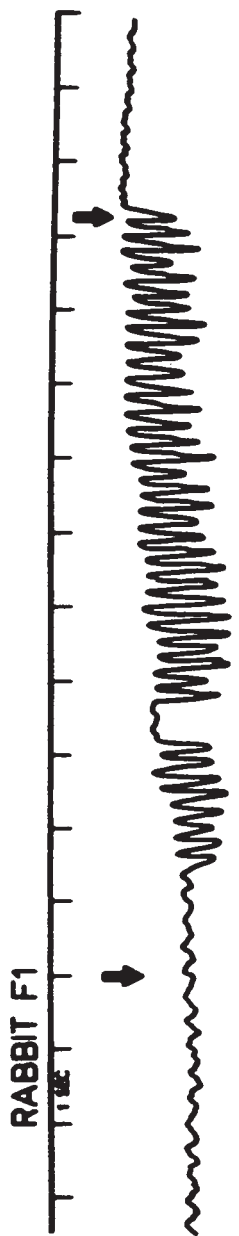
Tracing of polygraph records.

M - masticatory movements recorded from a strain gauge transducer  
whilst stimulating the lateral amygdala (10 V, 1 msec, 40 Hz)  
in an unanesthetized rabbit implanted with chronic electrodes.

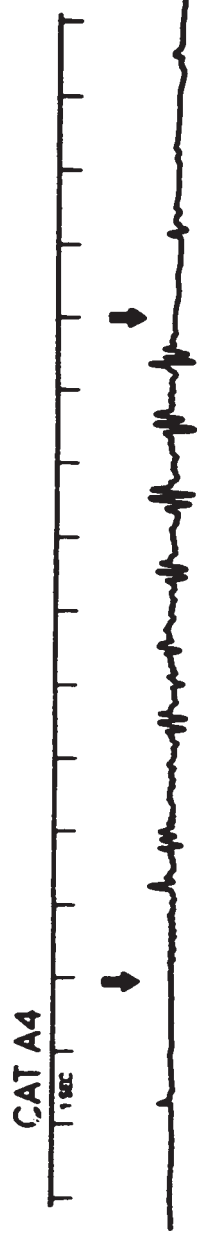
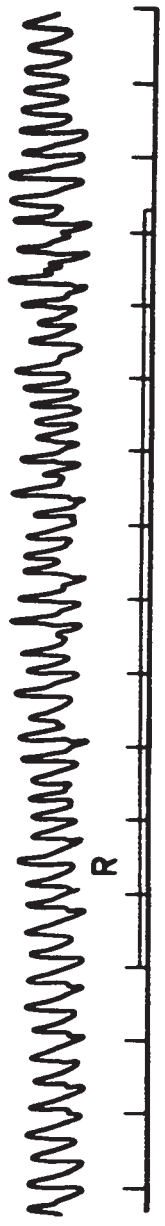
R - respiration.

L - lapping movements evoked by stimulation of the subthalamic  
nucleus (11 V, 2.5 msec, 20 Hz) in an anesthetized cat and  
recorded via a strain gauge transducer.

Stimulation occurred between the filled arrows.



M



L

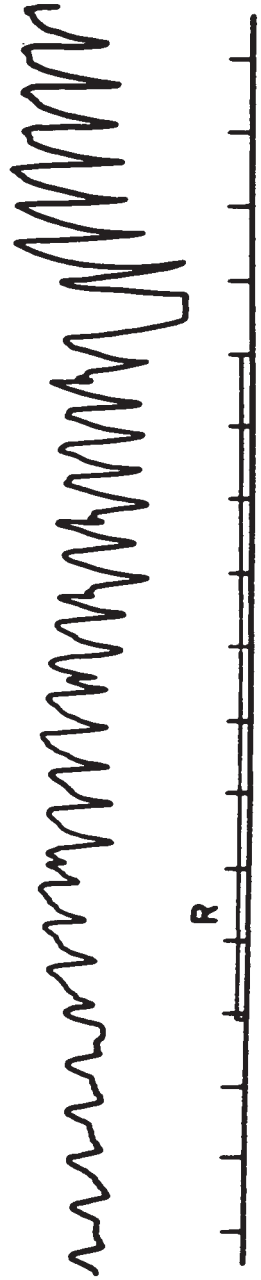
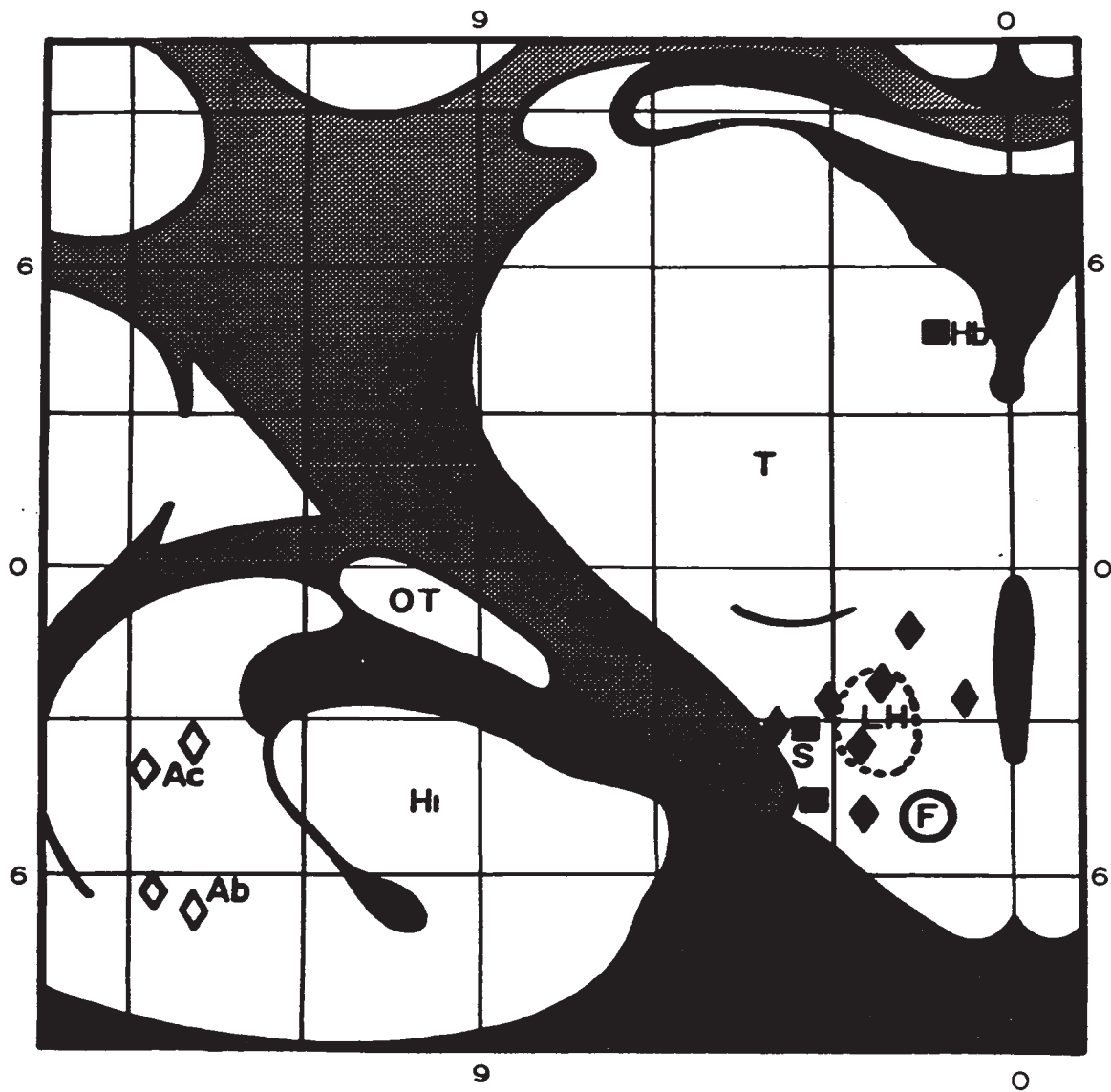


FIGURE 9.

Map of stimulation sites giving lapping in the cat.

A composite drawing incorporating sections A8-A10.5 from the stereotaxic atlas of Snider and Neimer (1961) showing stimulation points from which oral responses were evoked in 5 cats.

- Hb - habenula
- T - thalamus
- OT - optic tract
- LH - lateral hypothalamus
- S - subthalamus
- F - fornix
- Hi - hippocampus
- Ac - central amygdaloid nucleus
- Ab - basal amygdaloid nucleus
- - lapping
- ◇ - swallowing
- ◆ - salivation.





EXPERIMENT II: Masticatory Patterning

During ipsi- or contra-lateral CNS stimulation, bursts of activity which were in phase with the observed masticatory movements were recorded from masseteric and mylohyoid branches of the trigeminal nerve and from the hypoglossal nerve or nucleus. Jaw opening was always the first movement observed. Usually one or two chewing movements and discharge bursts followed the cessation of stimulation, although sometimes the masticatory activity was lost before the end of the stimulus train.

Recordings were made from the trigeminal nerve in 6 rabbits. Activity in the masseteric nerve was associated with jaw closing, and in the mylohyoid it was synchronous with jaw opening. Bursts of activity still occurred during 47 stimulation trials after the animals had been paralysed with gallamine triethiodide (Figure 10). When recording from the two branches of the mandibular nerve, activity was always seen initially in the neurogram recorded from the mylohyoid nerve after a latency of between 0.34 and 2.4 sec. Discharges recurred alternately in these nerves to jaw-opening and jaw-closing muscles throughout the period of activity. Recordings of regular bursts of neural activity were similarly made from the hypoglossal nerve and nucleus after paralysis (Figure 10).

It was noted that, after bilaterally sectioning the cranial nerves V and XII, the perioral muscles innervated by the facial nerves still contracted rhythmically during stimulation of the central site previously giving mastication. All visible

evoked movements were then abolished by sectioning the facial nerves.

The following results are all taken from records from the hypoglossal nerve and nucleus. Bursts of activity began in these structures after a minimum latency of 80 msec from the beginning of stimulation.

Relationship between the stimulation (input) frequency and the discharge (output) frequency. The effect of changes in input frequency on the output frequency is summarized in Table IV and illustrated for both regular and random frequencies in Figures 11 and 12. A threshold input frequency, which at T1.5 varied from animal to animal between 9 and 21 Hz, had to be exceeded before a low frequency output was observed. The output (bursts/sec) then rose with increases in the input frequency up to an input frequency designated L, which ranged from 18-30 Hz at T1.5. Increase in the input frequency beyond the value H (80-400 Hz, T1.5) resulted in a decrease in output frequency. Between L and H the output frequency showed little variation from trial to trial, which resulted in the generally low value of the SEM, or with variations in the input frequency ( $N=94$ ,  $r_s=.13$ ,  $t=1.26$ ,  $P>.20$ ). The mean output frequency between L and H was therefore called the limiting discharge frequency (L.D.F.). This varied from animal to animal between 2.4 and 4.5 bursts/sec at T1.5.

The effect of increasing the voltage of stimulation in 5 series of trials summarized in Table IV was, firstly, to lower the values of both the threshold input frequency and L, and to

raise the value of H. Secondly, the output frequency was raised over the whole input frequency range ( $N=65$ ,  $\chi^2_r = 69.1$ ,  $df=2$ ,  $P<.001$ ): in particular, L.D.F. was increased ( $N=5$ ,  $\chi^2_r = 11$ ,  $df=2$ ,  $P<.01$ ).

Effect of random frequency stimulation in paralysed animals on the regularity of the output. As previously stated, the stimulus trains were found to be approximately random, and incapable of providing the animal with timing information. In contrast, the output recorded from the hypoglossal nerve (5 rabbits) or from the hypoglossal nucleus (9 rabbits), still consisted of regular bursts of activity, as illustrated in Figure 13. This conclusion, based on the visual appearance of 261 trials, was verified in 73 autocorrelation analyses which always showed sharply defined peaks at regular intervals in time. The autocorrelation analyses of the records in Figure 13 are shown in Figure 14.

In 12 of the 45 cross-correlation analyses, there were no intervals following each QRS complex during which bursts of neural activity tended to occur (e.g. Figure 14A), which would indicate independence between the two events. However, the other 33 cross-correlation histograms exhibited peaks (Figure 14B, 14C). As these peaks varied in phase and magnitude in the same animal from sample to sample and disappeared when a number of trials were added together (Figure 15), it is suggested that these two regular processes have no cause and effect relationship. Turning off the respirator did not abolish the discharge pattern.

Comparison before and after paralysis. When multiple stimulus trials were run at T1.5 in 5 rabbits, both before and 15 minutes

after the administration of the first dose of gallamine, no differences could be seen in the input/output relationship (Table IV and Figure 16). Paralysis did not significantly affect the input/output frequency relationship ( $N=51, \chi^2_r = 0, df=1, P>.99$ ) over the whole range or change the value of the L.D.F. ( $N=6, \chi^2_r = 0, df=1, P>.99$ ). The area under the integrated curve, as expressed by the weight of the cut-out record was not significantly affected by paralysis ( $N=30, t=.3715, df=29, P>.20$ ).

Effects of peripheral stimuli. As in unparalysed animals, distention of an oral balloon could cause rhythmical hypoglossal discharges in 6 rabbits of a similar frequency (2.2-3.6 bursts/sec) to those evoked by electrical stimulation (Figure 17), and in 12 of 15 trials, these two inputs were shown to summate (Figure 18). Again, the masticatory activity could be inhibited by heavy paw-pinching in 15 of 18 trials. Masticatory bursts during oral stimulation were periodically interrupted by larger bursts which, from records made before paralysis, were known to be associated with swallowing.

TABLE IV

Summary of results obtained from recordings of XII nerve and nucleus activity.

Rabbit	Constant frequency stimulation				Random frequency stimulation				Stim- lation series		
	Threshold frequency (Hz)	Latency (msec)	L(Hz)	H(Hz)	L.D.F. +S.E.M. (bursts/ sec)	Threshold frequency (Hz)	Latency (msec)	L(Hz)		H(Hz)	L.D.F. +S.E.M. (bursts/ sec)
80n	10	280-780	20-25	> 200	3.2±.09	-	-	-	-	-	T1.5a
	-	340-1650	< 30	> 100	2.9±.19	-	360-1430	< 20	> 80	3.0±.25	T1.5p
82n	20	200-1700	25-30	> 200	2.8±.09	-	270-610	< 20	80-100	2.6±.21	T1.5a
	-	410-1020	< 20	> 80	2.9±.11	-	130-970	< 20	> 80	2.6±.10	T1.5p
83n	18	660-5250	20	100-150	3.4±.09	-	1640-3860	< 20	> 100	3.7±.15	T1.5p
85N	-	700-750	-	-	3.7±.17	-	-	-	-	-	T1.5a
88N	-	80-980	< 20	150-200	3.6±.09	-	410-1240	< 20	> 100	3.2±.11	T1.5p
98N	-	-	-	-	-	-	1020-1740	< 25	> 80	2.4±.07	T1.5p
99n	10	80-2140	18	200	3.2±.04	-	-	-	-	-	T1.5a
	12	120-3920	18	200	3.1±.06	-	250-1950	< 20	> 80	3.2±.08	T1.5p
100n	-	-	-	-	-	-	820-2260	< 25	> 100	3.0±.04	T1.5a
	16	680-2060	25-30	100-120	2.4±.29	-	820-2240	< 25	> 100	3.1±.08	T1.5p
101n	18	100-2120	20-25	170-200	3.9±.07	14-21	210-1960	28-30	130-150	4.2±.05	T1.5p
	10	120-660	15-20	170-200	4.5±.06	11-14.5	220-1440	20-28	210-260	4.2±.04	T2p
	8	80-860	8-10	170-200	4.2±.04	11-14.5	180-1720	20-28	360-400	4.5±.05	T3p

Rabbit	Constant frequency stimulation				Random frequency stimulation				Stimu- lation series		
	Threshold frequency (Hz)	Latency (msec)	L(Hz)	H(Hz)	L.D.F. ±S.E.M. (bursts/ sec)	Threshold frequency (Hz)	Latency (msec)	L(Hz)		H(Hz)	L.D.F. ±S.E.M. (bursts/ sec)
102N	-	-	-	-	-	-	80-960	-	-	2.9±.10	T1.5p
103N	<12	280-1320	19	150-200	4.0±.08	-	-	-	-	-	T1.5a T1.5p
104N	-	200-2260	19	150-200	4.2±.10	-	-	-	-	-	T1.5p
105N	-	200-900	-	-	3.5±.00	-	250-1150	-	-	3.8±.08	T1.5p
106N	-	-	-	-	-	-	300-900	-	-	3.3±.25	T1.5p
	-	-	-	-	-	-	350-1150	-	-	3.7±.09	T2p
	-	-	-	-	-	-	300-1050	-	-	4.1±.10	T3p
	-	-	-	-	-	9	80-760	30	300-400	4.0±.05	T1.5p
	-	-	-	-	-	6	200-720	25-30	300-400	4.2±.09	T2p
	-	-	-	-	-	8	110-1710	15-20	400-450	4.4±.04	T3p

N - recording from XII nucleus

n - recording from XII nerve

L - input frequency at which output reaches L.D.F.

H - input frequency above which output falls below L.D.F.

L.D.F. - limiting discharge frequency

T1.5a - trials run before paralysis at a voltage 1.5 x threshold

T1.5p - trials run after paralysis at a voltage 1.5 x threshold.

FIGURE 10.

Rhythmical masticatory discharges recorded from V and XII nerves  
and the XII nucleus in 3 paralysed rabbits.

Stimulation sites: A - Subcortical white matter, 30 V,  
B - pedunculus cerebri, 9.9 V,  
C - internal capsule, 12 V.

The frequency of stimulation was 40 Hz and the pulse duration 1 msec.

Calibrations, 200 V and 1 sec.

ma - masseteric nerve

m - mylohyoid nerve

h - hypoglossal nerve

H - hypoglossal nucleus

s - stimulus

e - ECG

↓ - marks point where the level of  
activity appears depressed below  
baseline during firing of the  
nerve to the antagonistic muscle.

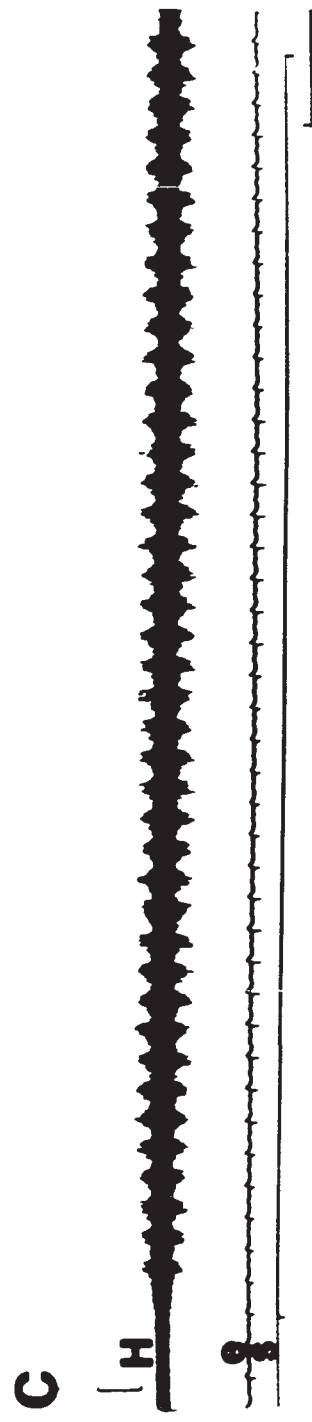
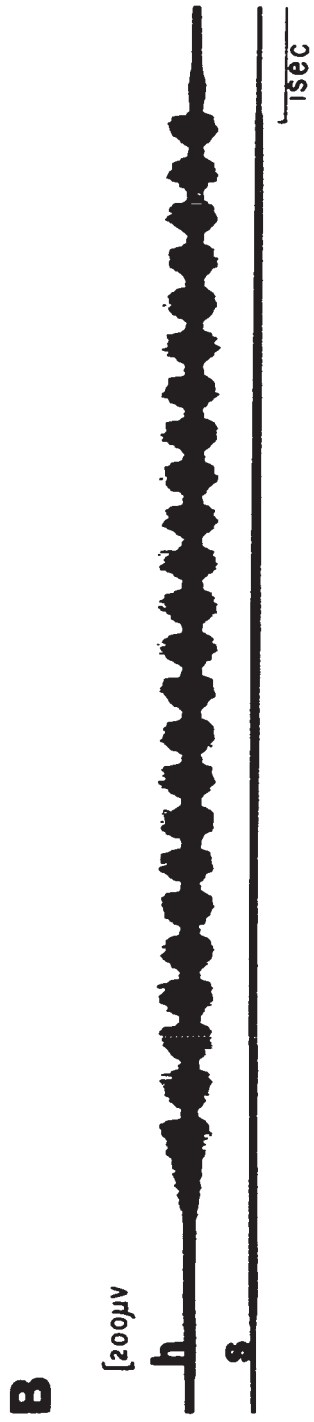
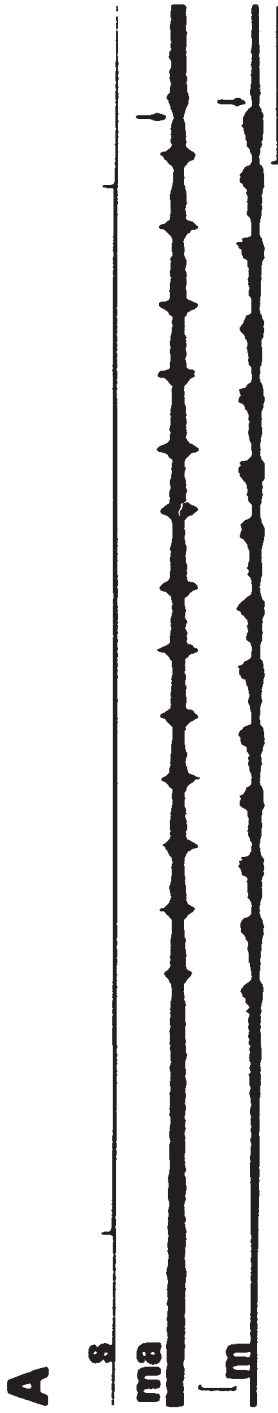




FIGURE 11.

Input/output relationship: constant frequency stimulation.

Semilog plot of the relationship between the stimulation frequency, using regular trains of monophasic pulses and the rate of occurrence of bursts of neural activity. The stimulus was delivered to the internal capsule. Three stimulus strengths were used: T1, 5, 13.5 V (●); T2, 18 V (○); T3, 27 V, (x).

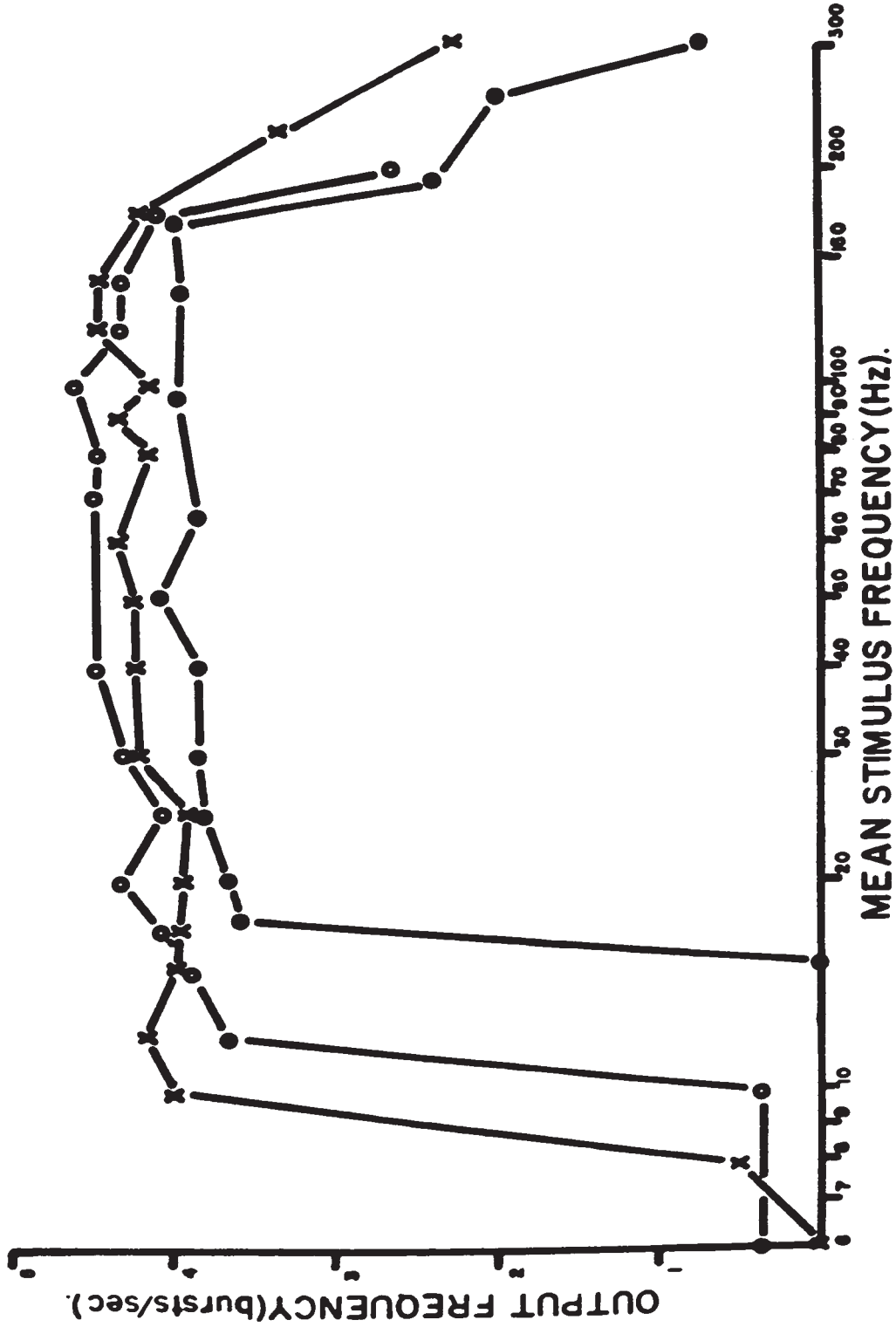


FIGURE 12.

Input/output relationship: random frequency stimulation.

Semilog plot of the relationship between the average stimulation frequency using random trains of monophasic pulses and the rate of occurrence of bursts of neural activity. The stimulus was delivered to the internal capsule but not at the same locus as in Figure 11, which was compiled using data from the same animal. The three stimulus voltages used were T1, 1.5, 6.75 V (•); T2, 9 V (o); T3, 13.5 V (x).

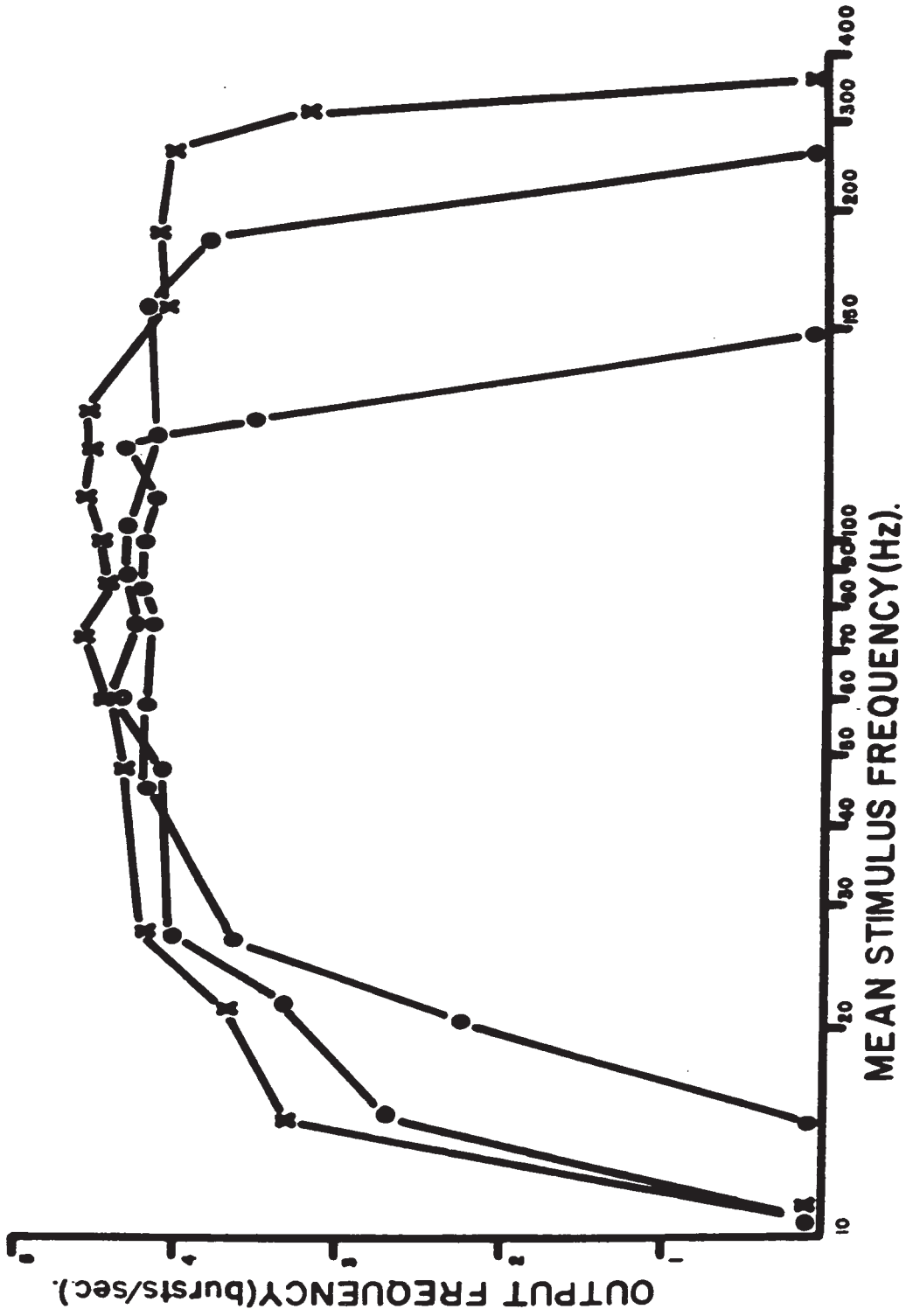


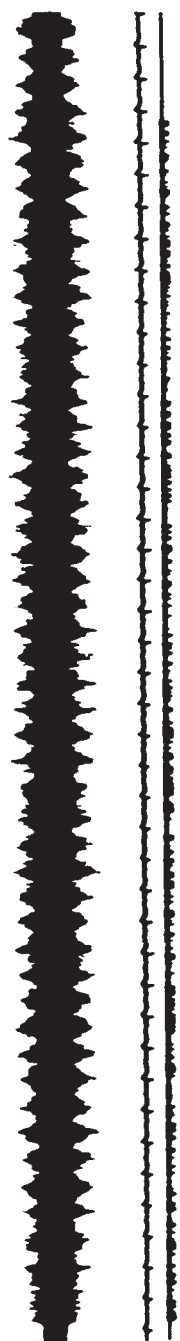
FIGURE 13

Rhythmical masticatory discharges recorded during random frequency stimulation.

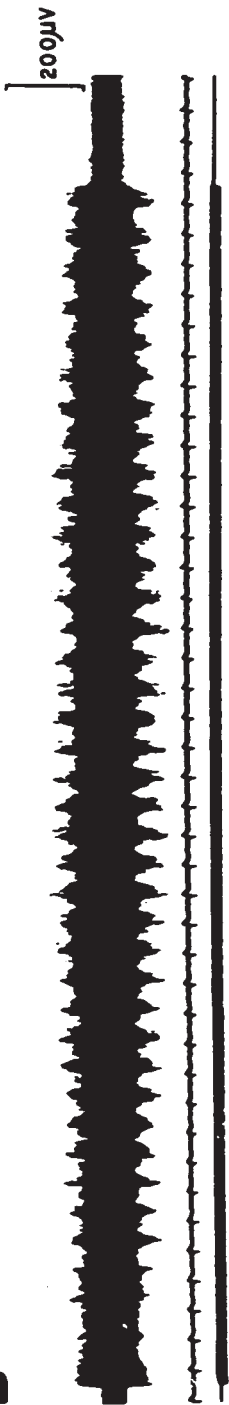
Recordings from the hypoglossal nucleus after nerves C1, C2, XII, XI, X, IX, VII and V and the spinal cord had been cut, made during monopolar monophasic stimulation of the internal capsule in one paralysed rabbit. The respirator was turned off for the period of stimulation. All three recordings were obtained from the same animal.

- A - T3 (24 V), average frequency 152 Hz,
  - B - T2 (16 V), average frequency 285 Hz,
  - C - T1.5 (12 V), average frequency 221 Hz,
  - e - ECG,
  - s - stimulus,
- Calibrations, 200  $\mu$ V and 1 sec.

**A**



**B**



**C**

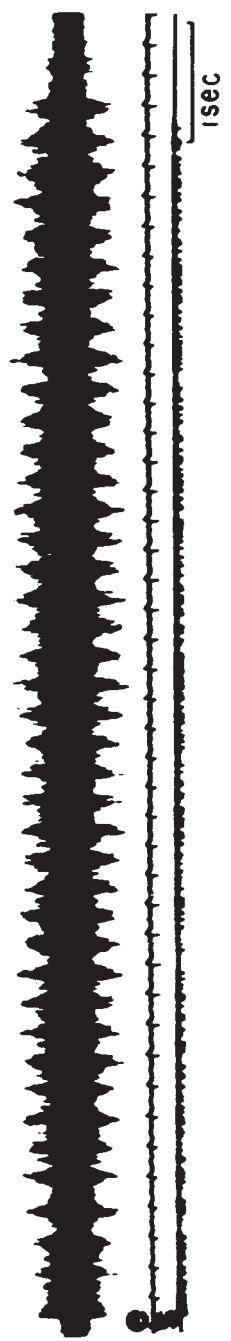


FIGURE 14.

Auto- and cross-correlation histograms.

Analyses of neurograms shown in Figure 13 calculated for the 5 secs of stimulation time in which the neural pattern was most regular. The cross-correlation histograms between heart beats and the following bursts of neural activity are shown beneath the auto-correlation histograms of the integrated neurograms. The interval between events is plotted on the abscissa. Both analyses were continued for 1 sec following the initial event. Note that in the same animal, various phase relationships were encountered in the cross-correlation histograms.

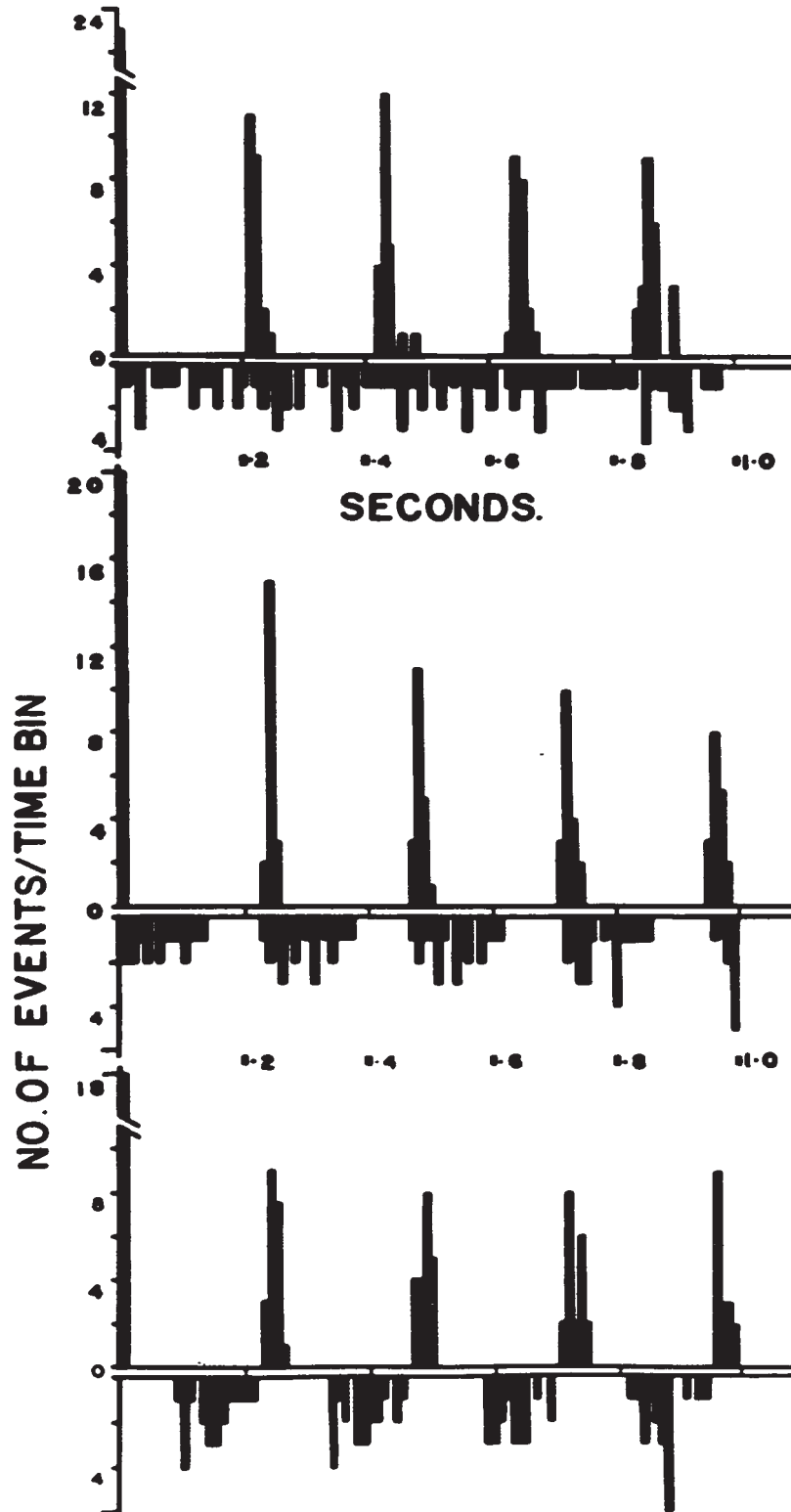




FIGURE 15.

Cross-correlation histograms of multiple stimulation trials.

Cross-correlation analyses between each heart beat and the bursts of neural activity which occurred in the following second were taken from XII nucleus recordings made in two rabbits. The interval between events is plotted on the abscissa. In the upper analysis, the results from the 3 cross-correlation analyses in Figure 14 were pooled with 3 more analyses derived from the same rabbit. The lower analysis was compiled from 8 stimulation trials in a separate animal.

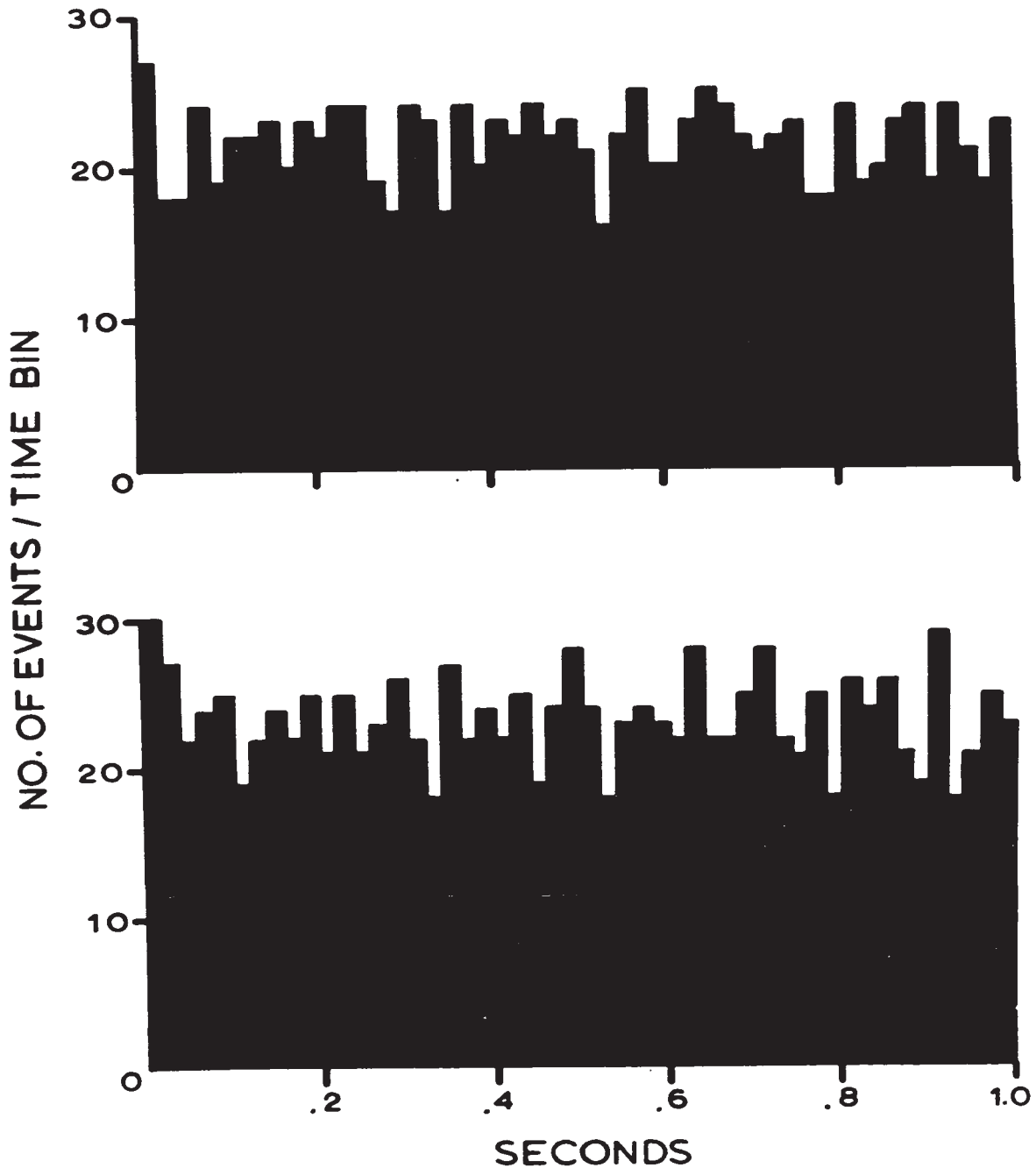
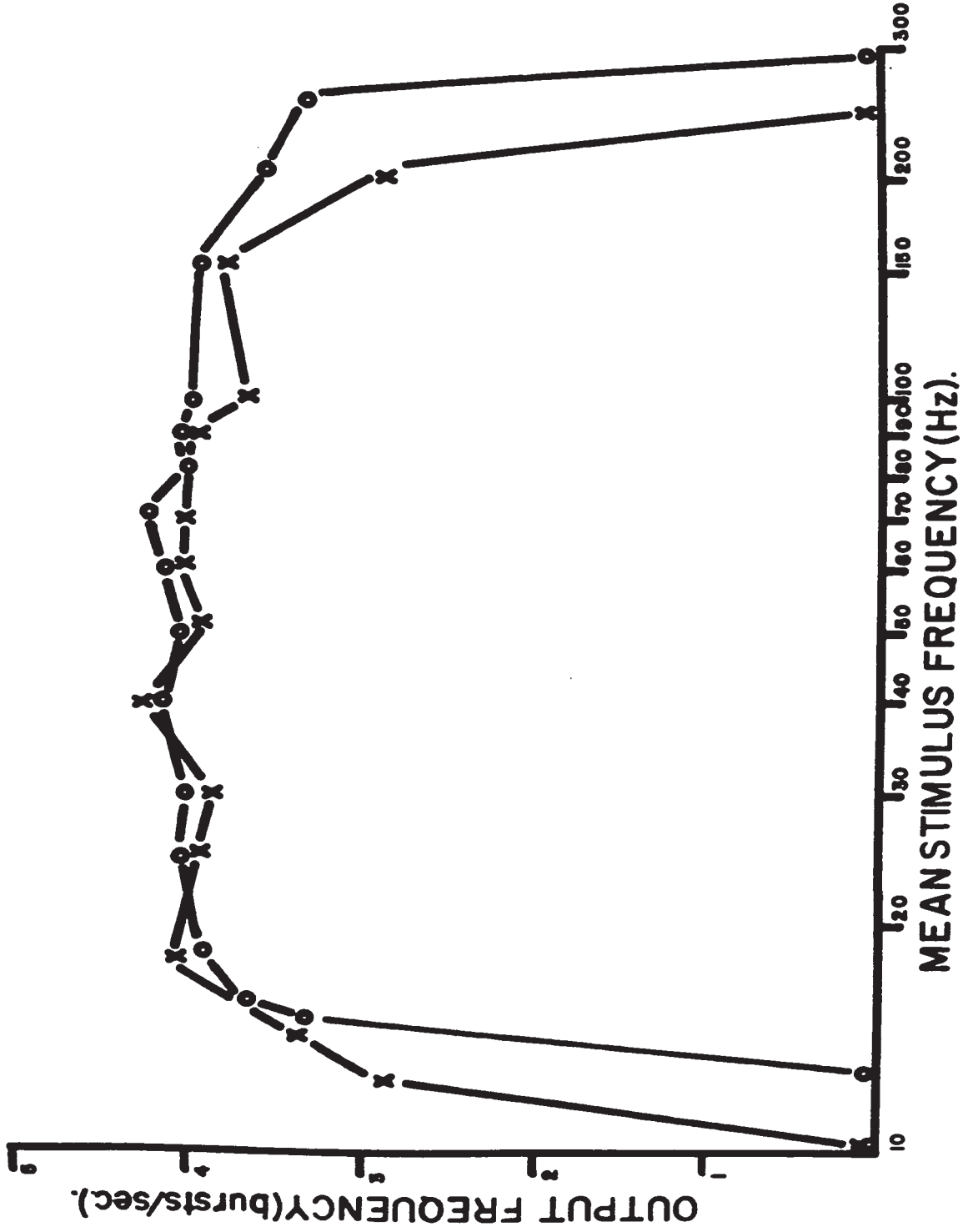


FIGURE 16.

Input/output relationship: effect of paralysis.

Semilog plot of the relationship between the average stimulation frequency and the output bursts recorded from the XII nucleus before (o) and after (x) paralysis with gallamine. The sub-cortical white matter was stimulated with random trains of monophasic pulses at a voltage 1.5 times threshold (10.5 V).



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FIGURE 17.

Rhythmical masticatory discharges in response to oral stimulation.

Three recordings from the hypoglossal nucleus of 2 paralysed rabbits: B and C are taken from the same animal. Rhythmical masticatory discharges, which were interrupted by longer-lasting swallowing activity, occurred in response to inflation of a Foley catheter between the tongue and hard palate (not marked).

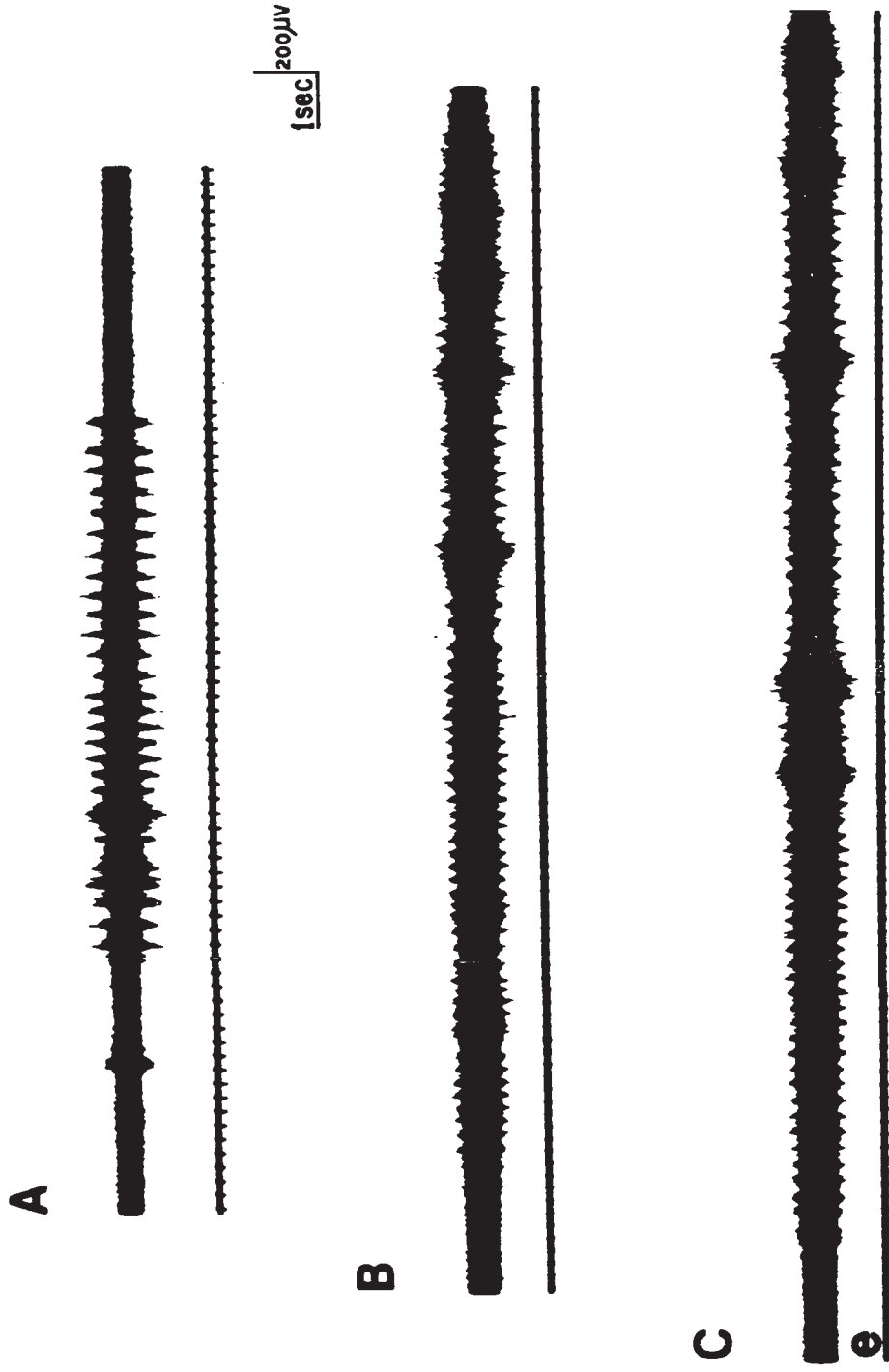


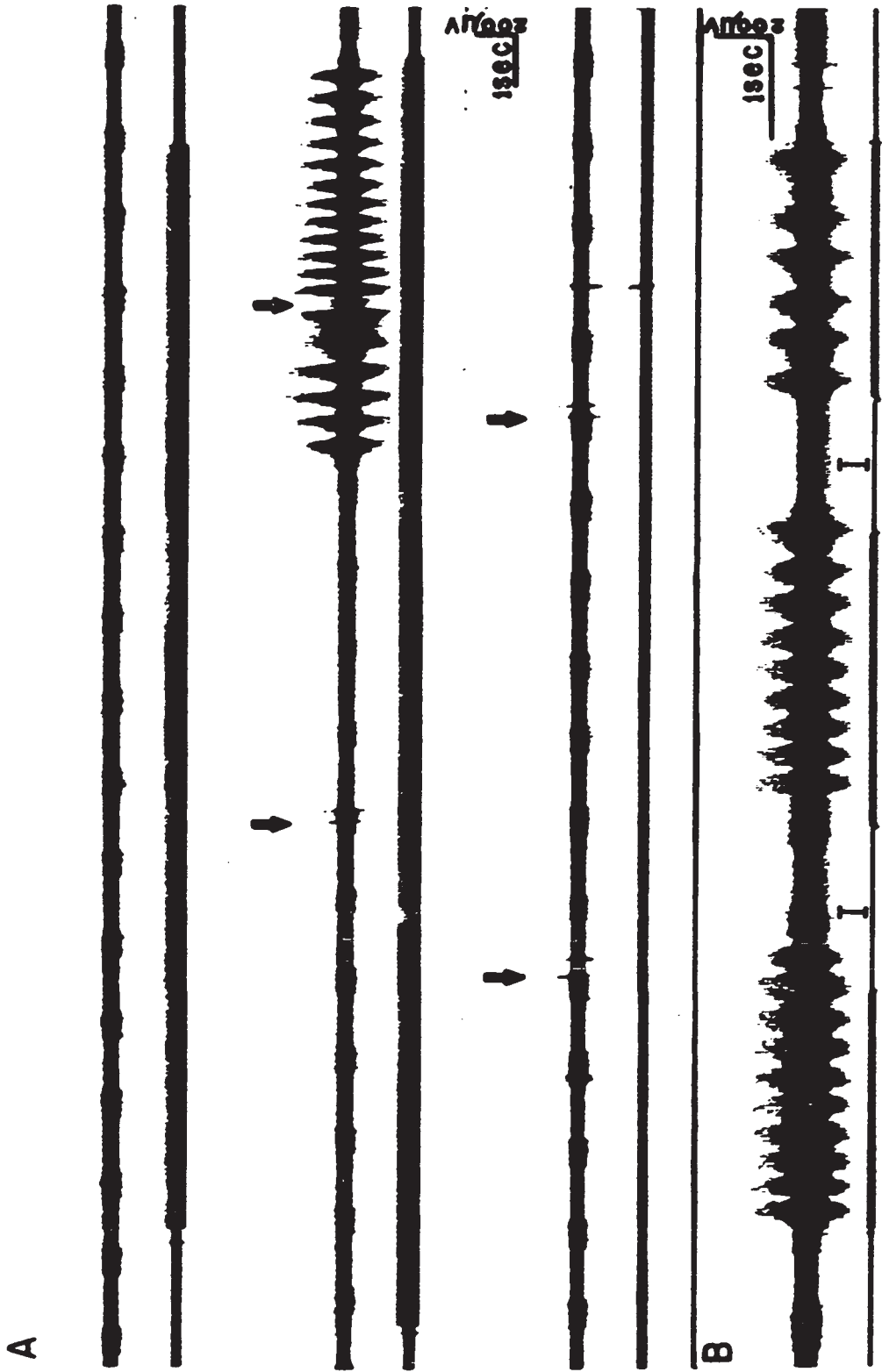
FIGURE 18.

Summation of oral and central masticatory stimuli in paralysed rabbits.

A - In the top trace the subcortical white matter was stimulated at an intensity insufficient to cause a masticatory discharge (9.5 V, 1 msec, 40 Hz). In the middle trace, this was accompanied by inflation of an oral Foley catheter between the arrows. The two inputs summated, whereas stimulation by the balloon alone was ineffective (lower trace).

B - Inhibition of masticatory discharges by paw-pinching (I) (marked by grounding the stimulus record) whilst stimulating the putamen (7 V, 1 msec, 40 Hz). Stimulation did not cease during the period of pinching (the stimulation artifact is still visible in the neural recording).

The small-amplitude rhythmical fluctuations in the baseline were also seen before paralysis, when they were in time with the respiratory movements.





EXPERIMENT III: Lateral jaw movement reflex.

Pressure applied to the labial or lingual surface of a maxillary central incisor produced, in all 20 decerebrate rabbits, a brisk movement of the mandible to the contralateral side, with little or no movement in the vertical direction (Figure 19). It remained in this position for a period of 2 to 10 secs if the pressure was maintained; thereafter the jaw would slowly return to the midline despite the continuation of stimulation. The return began sooner when the stimulus was applied to the lingual surface or incisal edge than when applied to the labial surface; this was perhaps in part due to the difficulty in maintaining a pressure from within the mouth. Mesial or distal tooth surface application was ineffective, so too was pressure applied to any part of the second incisors, gingiva or palate.

Direct and integrated electromyograms recorded from the left masticatory muscles during pressure application to the right central incisor are shown in Figure 20. The zygomatico-mandibular and anterior temporal muscles always showed the highest levels of activity and maintained them for the longest period of time. The responses of the other three muscles were more variable. At the beginning of the reflex the external pterygoid always fired, while the digastric muscle showed either no activity or a phasic activity at the start of stimulation. The superficial masseter showed no response at the beginning of pressure stimulation, but activity was later seen whilst the mandible remained in contralateral deviation or when the stimulus was released. This post-stimulus

activity, which often persisted in the superficial masseter for many secs, was sometimes seen to be rhythmical and to be accompanied by chewing movements.

When the stimulus was rapidly released an occasional "off" response was seen in the external pterygoid, zygomatico-mandibular, and anterior temporal muscles. This response could occur even though EMG activity and the mandible had returned to their resting positions.

A pressure of at least 300 g rapidly applied was necessary to elicit the reflex. By increasing the pressure, the level of EMG activity could be increased, reaching a maximum at a load of 7 kg. Large loads applied slowly did not evoke any reflex activity (Figure 21). A sharp, heavy tap evoked only the jaw-opening reflex through activation of the digastric muscle.

When the appropriate stimulus was applied to the maxillary left incisor, the mandible moved to the right, and EMG activity on the left side was confined to the external pterygoid muscle (Figure 20). When this procedure was repeated with a 100 g weight attached to the mandibular incisors, the consequent tonic activity in the superficial masseter and anterior temporal muscles was inhibited by ipsilateral incisal pressure (Figure 22). If the load was increased, an inhibition of tonic activity could also be observed in the zygomatico-mandibular muscle.

Section of the infraorbital nerve within the orbital cavity of 3 rabbits abolished the reflex and the pattern of mus-

cular activity previously evoked by pressure stimulation of the ipsilateral incisor. Section more peripherally at the point of nerve entry into the infraorbital foramen, before its union with the anterior superior alveolar nerves, did not abolish the response.

A similar reflex was elicited in 8 rabbits by electrical stimulation of the gingiva surrounding a central incisor or of the adjacent palatal mucosa of the same side. Stimulus parameters of 30 Hz, 6-15 V, and 1 msec duration were found to be adequate. Upon application, the jaw first jerked open and then moved to the contralateral side, closing as it did so. Meanwhile, activity was recorded in 5 animals in the ipsilateral digastric muscle 7.2-9.0 msec (Table V) from the beginning of the first stimulus pulse; thereafter, the amplitude of the response diminished and was finally lost. Evoked activity commenced in the zygomatico-mandibular EMG after an 78-220 msec delay (2-6 pulses) from the start of the stimulus train. This then followed each stimulus pulse with a latency of 9.0-16.0 msec (Figure 23). The amplitude and complexity of this wave form rose to a maximum, and then gradually decreased; but activity was still present in these muscles after the digastric had ceased to fire.

The following factors lead to the conclusion that we were, in fact, evoking two reflexes: the jaw-opening reflex activation of the digastric, and a lateral jaw movement reflex. There was independence shown in the relevant firing patterns during electrical stimulation (Figure 23). The stimulus voltage threshold for digastric activity was less than the minimum threshold neces-

sary to cause lateral deviation. When isolated pulses or trains of less than 7 Hz were used, only digastric EMG activity with jaw opening occurred and the mandible did not swing to the contralateral side. Finally, digastric activity was often absent when the lateral reflex was evoked by pressure.

TABLE V

Summary of results obtained from EMG recordings during the lateral jaw movement reflex evoked by

electrical stimulation.

Rabbit	Digastric latency range (msec)	Zygomatiko-mandibular	
		Initial delay range (msec)	Latency range (msec)
5	7.4-9.0	82.5-130	9.2-13.0
11	7.2-9.0	80.0-200	9.0-16.0
13	7.4-8.4	78.0-160	9.0-11.2
16	7.2-8.4	80.0-200	9.0-16.0
18	7.5-9.0	78.0-220	9.0-13.0

99

The initial delay is the period of time between the start of the first stimulus pulse and the beginning of the EMG response. The latency is the period between later stimulus pulses and the following EMG response. These two periods are identical in the digastric recordings. Stimulus parameters used were 30 Hz, 6-15 V, 1 msec.

FIGURE 19.

Lateral jaw movement reflex in an unanesthetized rabbit.

Showing contralateral displacement of the mandible during the application of firm labial pressure to the upper incisor teeth of an unanesthetized decerebrate rabbit 50 hours after operation. The illustration is a tracing of a recording made on an ink-writing kymograph via a lever attached by a string to the lower incisors. No concurrent vertical movements of the mandible were observed. Pressure was applied between the two sets of arrows to l (upper left central incisor) and to l (upper right central incisor). A movement of the mandible to the right is in the direction of the arrow.

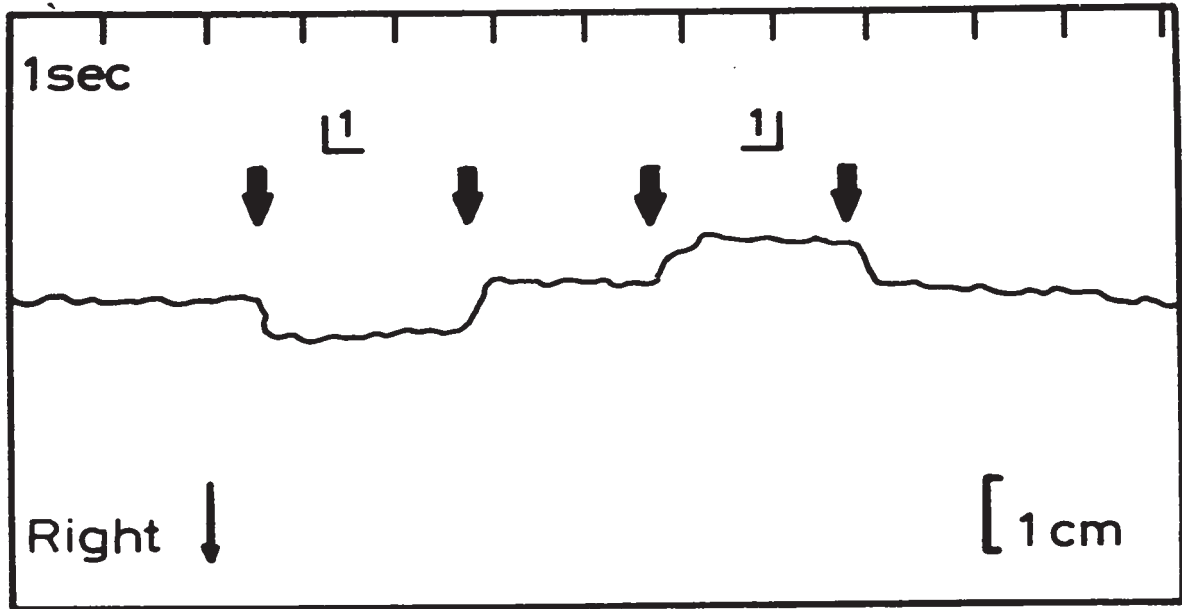


FIGURE 20.

Integrated and direct EMG recordings during contra- and ipsilateral  
central incisor pressure

A, integrated and B, direct EMG recordings during the lateral jaw movement reflex, taken from the following muscles of the right side:

P - external pterygoid

M - superficial masseter

D - digastric

T - anterior temporal

Z - zygomatico-mandibular

S - record from the pressure applicator.

In A, pressure was applied to the labial surface of the upper left central incisor (C) and then to the upper right central incisor (I). At L, pressure was applied to the lingual surface of the upper left central with a blunt probe. The final integrated trial shows an example of "off" activity upon removal of the stimulus. In B, while recording EMG activity directly on paper film, pressure was applied to the upper left central incisor (C) and to the upper right central incisor (I).



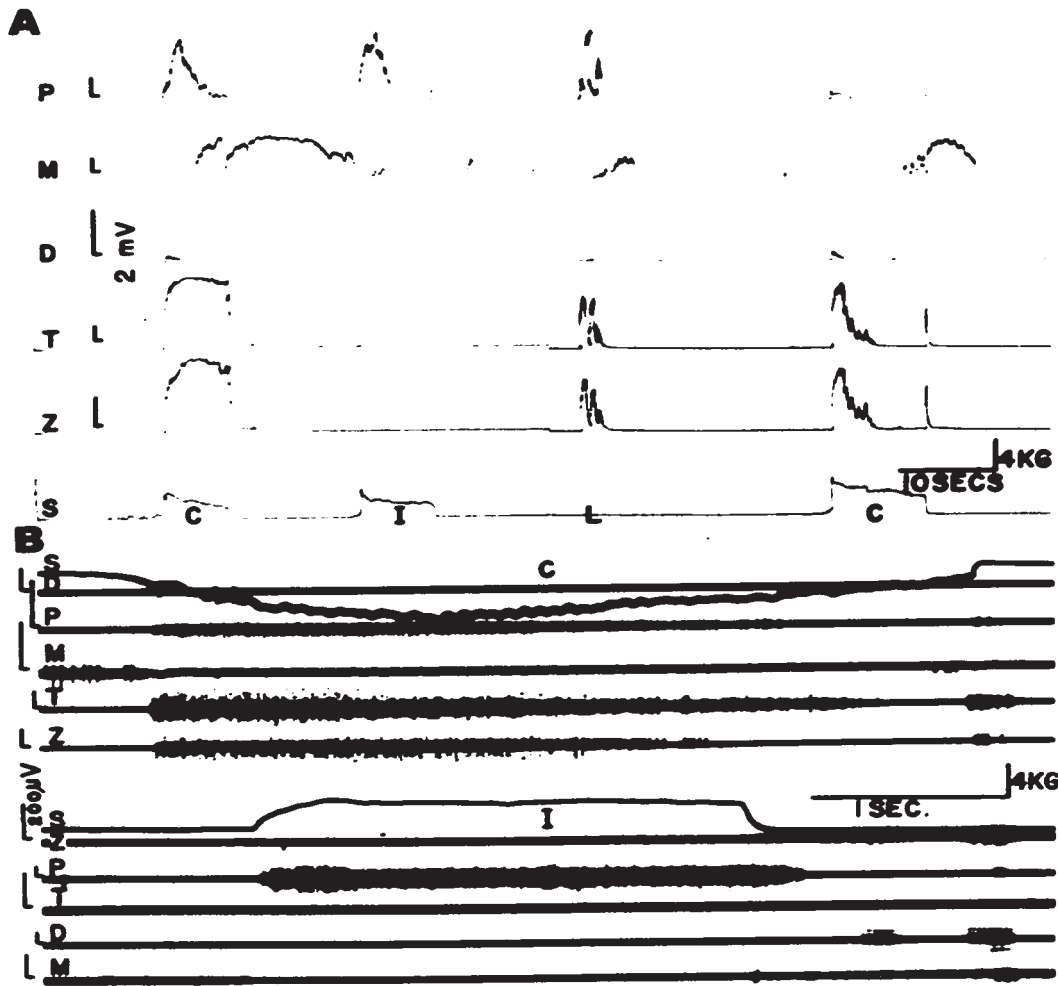


FIGURE 21.

Integrated EMG response to slow pressure application.

Pressure rapidly applied to the labial surface evoked the lateral jaw movement reflex with its accompanying EMG activity (C<sub>1</sub> and C<sub>3</sub>). When the stimulus was applied slowly (C<sub>2</sub>), only a small "off" response was observed. The reflex response was often depressed for up to 60 secs after removal of the labial pressure stimulus, but pressure on the lingual surface (L) restored the excitability. Lingual pressure was therefore used in this instance to equalize conditions between trials.

- P - external pterygoid
- M - superficial masseter
- D - digastric
- T - anterior temporal
- Z - zygomatico-mandibular
- S - record from pressure applicator.

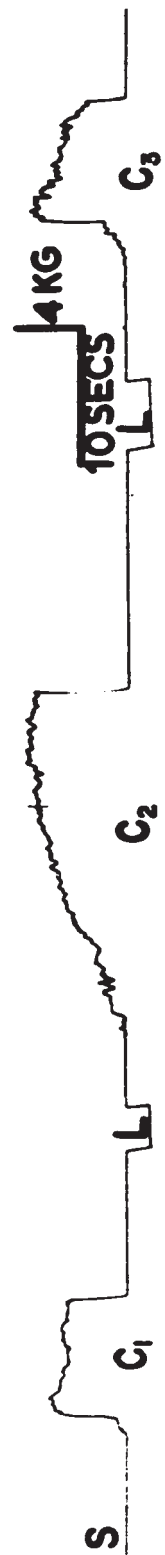
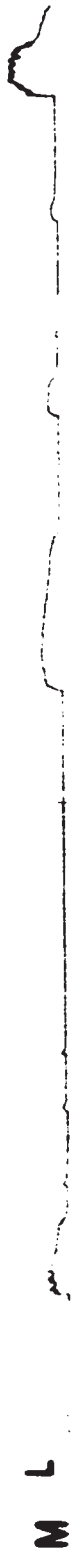


FIGURE 22.

Inhibition of background activity during ipsilateral incisor stimulation.

At the arrow, 100 g was hung from the lower incisors. Inhibition of tonic activity during ipsilateral incisor pressure (I) can be seen in the anterior temporal muscle (T). Inhibition of background activity in the zygomatico-mandibular muscle could be seen if the load on the mandible was increased to 200 g prior to Z<sub>1</sub>. Note that the lateral pterygoid (P) fired during contralateral (C) and ipsilateral pressure and that inhibition occurred in the superficial masseter (M) during both ipsi- and contralateral stimulation.

P - external pterygoid

M - superficial masseter

D - digastric

T - anterior temporal

Z - zygomatico-mandibular

S - record from pressure applicator.

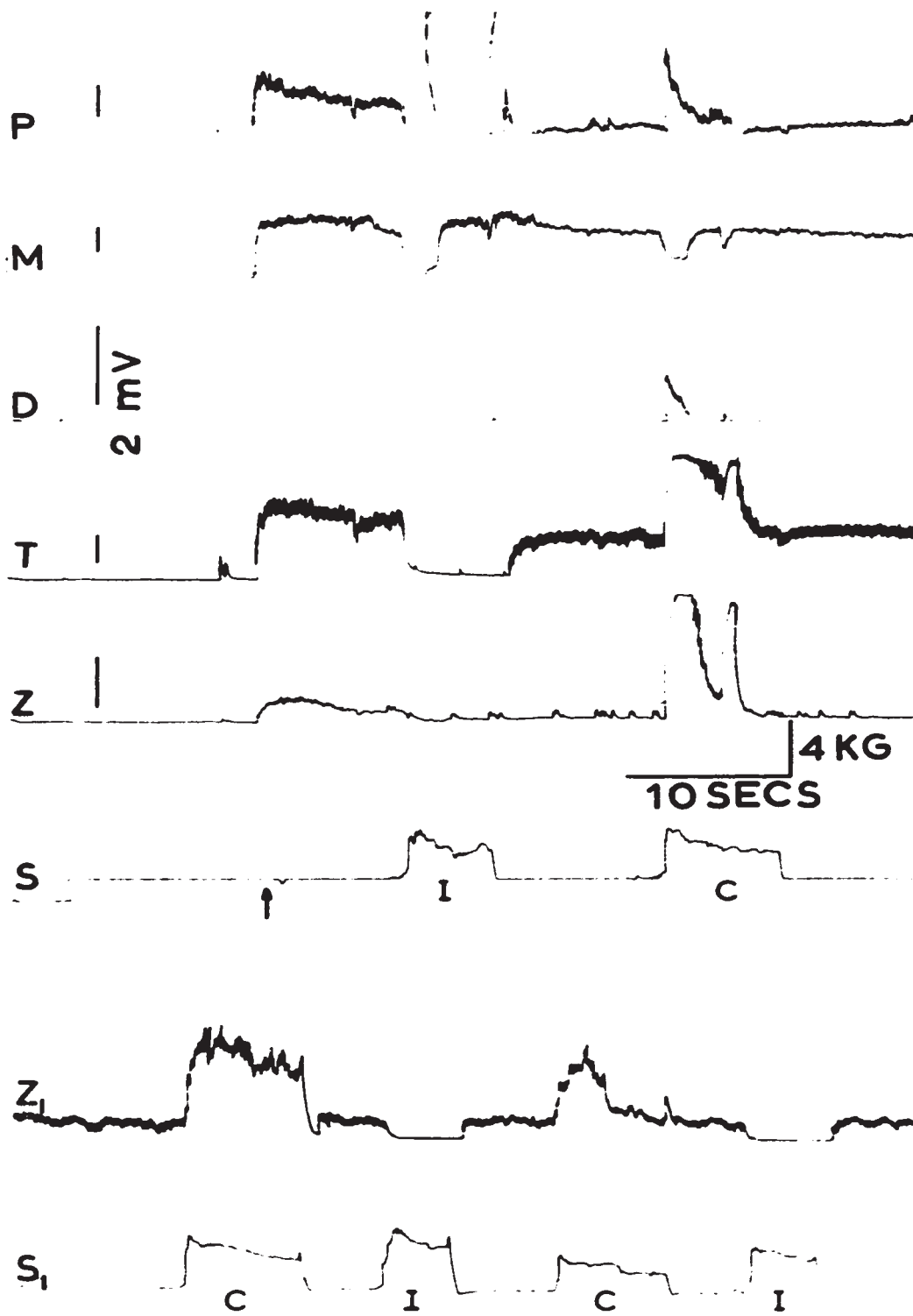


FIGURE 23.

Activation of the lateral jaw movement reflex by electrical stimulation.

Direct EMG recordings from the right side during electrical stimulation of the left hard palate.

Top record (6 V, 30 Hz, 2 msec): Digastric activity began 7.2

msec after the first pulse. The accompanying deflection seen in recording from the zygomatico-mandibular muscle is probably a movement artifact. True EMG activity was first seen in the Z record approximately 118 msec after the start of the train.

Middle record (6 V, 30 Hz, 2 msec): The digastric fired after the first stimulus pulse but not again until late in the recording. Once the zygomatico-mandibular began to fire, activity increased in this muscle.

Bottom record (6 V, 5 Hz, 2 msec): Only the digastric is active.

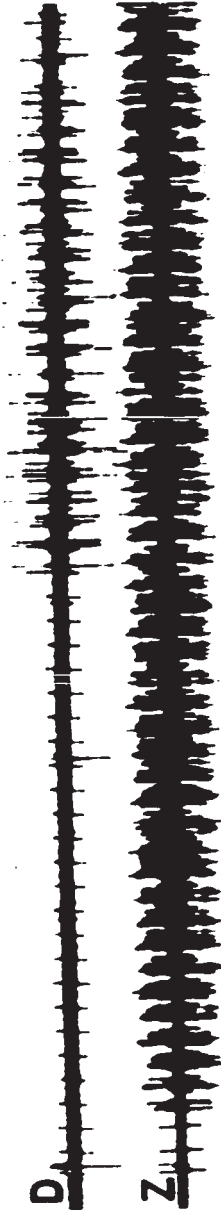
(•) - stimulus pulse

D - digastric

Z - zygomatico-mandibular.



500μV  
50 mSECS



500μV  
200mSECS

### DISCUSSION

Rhythmical mandibular movements have been produced by electrical stimulation of a large number of sites within the central nervous system of the rabbit. Since the movements meet the criteria set out by Gloor (1960), namely those of absence of frequency following, latency, post-stimulatory continuation, and ineffectual loci, it may be concluded that this phenomenon is truly of central neural origin. These criteria are similarly fulfilled by the bursts of neuronal activity before and after paralysis. To these properties can be added interaction, either facilitatory or inhibitory, with another simultaneous neurophysiological process. The described interactions appear to be of significance in normal functional mastication.

#### Evidence for central pattern generation of rhythmic mastication.

Proof that the central nervous system alone can generate the pattern of neuronal activity which results in rhythmical mastication demands that all timing information supplied by proprioceptors in the oro-facial region be removed. This was presumably accomplished in the present study by paralyzing the animals with a dose of gallamine triethiodide which has been shown to block both intrafusal and extrafusal muscle fiber activity in the cat (Carli, Dietschiff and Pompeiano, 1967). Rhythmic masticatory discharges in response to stimulation were not abolished, confirming the findings of Sumi (1970a). There is the possibility that some intrafusal fibers remained active long after the extrafusal fibers had been



paralysed (Granit, Homma and Matthews, 1959). Sumi did not eliminate this possibility, nor did he remove timing information of rhythmic inputs of vascular or respiratory origin.

In the present study, severing branchial and cervical nerves and the spinal cord did not prevent regular masticatory discharges from occurring in the hypoglossal nucleus. Thus, afferent inputs from unblocked intrafusal fibers, peripheral respiratory or vascular mechanoreceptors could not have been responsible for the rhythmic masticatory output.

The major source of external timing information available to the central nervous system in Sumi's preparation came from the regular trains of electrical pulses which he used to produce the rhythmical effects. Egger and Wyman (1969) have demonstrated that the rhythmic stepping seen by Sherrington (1913) in the deafferented hind limbs of cats was, in fact, an artifact caused by patterning in the electrical stimulus used to provoke the movements. In the present experiments, this cannot be the explanation for the rhythmical bursts of activity observed in those 271 trials where the stimulus was of random frequency.

Finally, timing information could conceivably be supplied by the pulsation of vessels within the brain or by fluctuations in intracerebral pressure during the respiratory cycle. A stimulus which can cause a rise in blood pressure and stronger pulsations may lead to excitation of neurones (Perl and Whitlock, 1961). Werner and Mountcastle (1963) suggested that such oscillatory mechanical irritation may have been the cause of regularity in the

discharge pattern of some thalamic neurones. They rejected this hypothesis because no frequency dependence could be demonstrated between neural discharge patterns and events in the cardiac or respiratory cycles. Similarly, it does not appear that such mechanical factors are of any importance in the patterning of mastication. In the present studies, the discharges persisted in the partly deafferented preparation when the respirator was turned off. Perkel, Gerstein and Moore (1967) showed that independent pace-makers of nearly the same frequency, simulated by a computer, exhibit peaks in the cross-correlation histogram, the magnitude and phases of which vary from sample to sample. Similarly the apparent dependence of the neural discharges on events in the cardiac cycle shown in certain of the cross-correlation analyses probably arises by chance, particularly as the peaks disappeared with increasing sample size. The masticatory rhythm does not, therefore, appear to be timed by the cardiac rhythm or respiratory movements.

Evidence for direct activation of  $\alpha$  motoneurones during rhythmical mastication.

Hunt (1951) was the first to discover that during reflex muscular contractions, the  $\gamma$  motoneurones may discharge before the  $\alpha$  motoneurones, leading to the speculation that some voluntary movements were also initiated by  $\gamma$  activation of the muscle spindles and subsequent firing of the  $\alpha$  motoneurones by Ia afferent fibers (Eldred, Granit and Merton, 1953; Merton, 1953; Granit, 1955, 1958). While this general servoloop hypothesis could apply to the control of mastication, as has been suggested by Murphy (1967), Davey and

Taylor (1966) and Taylor and Davey (1968), the following facts suggest that the motoneurons are directly excited, both by descending pathways and from the oral cavity.

Muscle spindles are a necessary part of the servoloop, but it is doubtful if they are present in tongues of subprimates (Sherrington, 1894; Boyd, 1937, 1941; Carleton, 1937; Weddell, Harman, Lambley and Young, 1940; Cooper, 1953). Similarly, the mylohyoid and digastric muscles, which open the jaw, are probably spindle-free in the rabbit, guinea pig and cat (Willems, 1911; Allen, 1919; Thelander, 1923; Szentagothai, 1949; Kidokoro et al, 1968a). However, if muscle spindles do exist in these muscles, and if activation of these spindles by the  $\gamma$  motoneurons is necessary to provoke  $\alpha$  motoneuron firing, high doses of paralyzing agents should reduce the amplitude of the integrated neurogram. Then, spindle activation would no longer occur and the  $\alpha$  motoneurons would be silent. Since the hypoglossal nerve and mylohyoid nerve, which supply the above muscles show large bursts of rhythmical masticatory activity which are unchanged in size by paralysis, it is most likely that the  $\alpha$  motoneurons are being directly excited.

#### Cortical and non-cortical masticatory areas.

Although central sites from which it is possible to evoke masticatory movements by electrical stimulation were shown in the historical review to be very widespread, they can be broadly classified into three categories:

- (1) Motor cortex, basal ganglia and their bulbar projections.

Into this group could also be placed the trigeminocortical projection pathways (Magnum, 1945).

It is probable that stimulation of the putamen, globus pallidus, substantia nigra and subthalamic nucleus in fact activates cortico-fugal fibers in passage, or coursing around, these structures (Magoun et al, 1933). However, the peculiar behavior seen in one rabbit of this present series in response to chronic stimulation of the subthalamus, suggests that the masticatory movements in this case were actually a part of a complicated behavioral pattern.

(2) Limbic Structures.

Our results confirm Kawamura and Tsukamoto's (1960a) finding that, in the rabbit, masticatory movements arise from stimulation of the lateral amygdala and lateral hypothalamus. We were unable to produce these movements from the amygdala in rabbits considered to be surgically anesthetized, which is the probable reason why this structure was unresponsive when stimulated in Experiment I, Group a.

(3) Reticular structures.

Whether efferent pathways capable of activating mastication originate in these regions, or are in passage, is difficult to assess. Kawamura and Tsukamoto (1960b) consider that amygdalo-hypothalamic masticatory pathways and the cortico-bulbar projections pass respectively through the dorsal and ventral regions of the mesencephalic reticular formation which Lyon, Halpern and Mintz (1968) include in two separate feeding systems. Alternatively, the movements may occur as a consequence of cortical activation via ascending trigeminal pathways which pass through the reticular formation (Kerr, Haugen and Melzack, 1955).

The finding that lapping was the only type of rhythical consummatory movement occurring in response to stimulation of sub-cortical structures in the cat agrees with the results obtained by Magoun et al (1933). However, stimulation of the thalamic region from which is also obtained lapping will, on occasion, evoke mastication (Hess, Akert and McDonald, 1952). These workers consider that the oral movements arise secondary to activation of trigemino-thalamo-cortical projection pathways.

It is interesting to note that many areas within the above three groups are additionally implicated in the control of consummatory behavior. Delgado and Anand (1953), Morrison and Mayer (1957), Montemurro and Stevenson (1957), Robinson and Mishkin (1968) and Lyon et al (1968), for example, have stimulated or lesioned such central areas and influenced eating and drinking activity.

The relative contributions made by alterations in motivation and in motor control in the production of the observed changes are difficult to assess. Lyon et al (1958) and Wyrwicka and Chase (1970) suggested that aphagia produced by lesions of the hypothalamus and mesencephalon may be due to disruption of ascending oral sensory pathways or descending motor components controlling feeding activity. Adipsia may have a similar origin. The involvement of the hypothalamus in both the regulation of food intake and in co-ordinating mastication and licking "to be a part of the manifestation of hunger" was postulated by Larsson (1954).

However, as shown in the present experiments and in earlier work outlined in the historical review, no areas other than the brain-

stem appear to be necessary for the production of rhythmical, coordinated masticatory movements.

Location of the pattern generator.

Cortico-fugal fibers do not synapse directly on the cranial motoneurons in subprimate species (Cajal, 1909; Walberg, 1957; Szentagothai and Rajkovits, 1958; Kuypers, 1958; Haartsen, 1962; Valverde, 1962). Instead, they have been reported to terminate in the following adjacent structures: the main sensory and spinal trigeminal nuclei, nucleus supratrigeminalis and the dorso-lateral parvocellular region of the reticular formation. In the rabbit, these projections are mainly contralateral (Haartsen, 1962).

Only three anatomical studies (Kuypers, 1958; Kawana and Kusama, 1964; Mizuno, Sauerland and Clemente, 1968) have attempted to trace degenerating fibers into the brain-stem from lesions confined solely to the orbital cortex, which includes the masticatory area. Preterminal degeneration was found bilaterally in the spinal trigeminal nucleus of cats and was most pronounced in the interpolar nuclei, caudal parts of the oral nuclei and rostral regions of the caudal nuclei. Kawana and Kusama (1964) described projections to the reticular formation medial to the main sensory and spinal V nuclei. Direct connections were also seen to those regions of the reticular formation known to influence somatic and visceral activity and which probably mediate the widespread motor inhibition and autonomic responses which result from electrical stimulation of the orbital gyrus (Smith, 1938; Bailey and Sweet, 1940; Hess et al, 1952; Sauerland et al, 1967a; Sauerland, Nakamura and Clemente, 1967; Nakamura et al, 1967).

When considering amygdalo-fugal masticatory pathways, we have many choices, but little evidence. The route favored, but not proved, by Kawamura and Tsukamoto (1960b) passed to the lateral hypothalamus, proceeded into the dorsal part of the midbrain reticular formation and, by intrareticular pathways, to the cranial motor nuclei.

As lapping movements were evoked from the habenula in one cat in the present study, it may be that an amygdalo-habenular projection, via either the stria terminalis or the amygdalo-habenula tracts, carries consummatory information. Crosby, Humphrey and Lauer (1962) stated that the habenula is a way station for olfactory and other inputs to motor centers. They suggested that impulses could then travel to the dorsal tegmental nucleus, either by way of the habenulo-tegmental tract or via the habenulo-peduncular tract, interpeduncular nucleus and pedunculo-tegmental tract. Fibers from the dorsal tegmental nucleus join the dorsal longitudinal fasciculus, which was stated by Crosby to "end in the motor nuclei of the trigeminal, the facial and probably the hypoglossal nerves and in the nucleus ambiguus, providing for co-operative action of the striated muscle in feeding". However, Zyo, Omukai and Ban (1962) and Valverde (1961) reported no such definite connections in the rabbit, although they did show projections into the central grey and more lateral regions of the reticular formation adjacent to the trigeminal complex.

Several anatomical and electro-physiological considerations point to the spinal trigeminal nucleus or the reticular formation in its immediate vicinity as the site of masticatory pattern generation. This suggestion was made by Kuypers (1958). Firstly,

this region is the rostral end of a column of cells which contains the interneurons on the cortico-spinal pathways, formed in the spinal cord by the so-called "intermediate zone" (Szentagothai-Schimert, 1941; Lloyd, 1941; Nyberg-Hansen and Brodal, 1963). These internuncial cells are also proprioceptors on the spinal reflex pathways (Lundberg and Voorhoeve, 1962; Horn, Phillips and Porter, 1962; Stewart and Preston, 1967). Interneurons with similar properties were described by Porter (1967) in the brain-stem. He showed that spinal trigeminal or adjacent reticular neurons transmit both cortical and peripheral information to the hypoglossal motor nucleus. Although Porter only studied responses to single pulse or short train stimulation, cortical and oral masticatory stimuli could perhaps converge at this interneuronal level. The spinal trigeminal nucleus is additionally equipped to co-ordinate the complex masticatory movements through its efferent connections with the motor V, VII and XII nuclei (Cajal, 1909; Woodburne, 1936; Green, De Groot and Sutin, 1957; Stewart and King, 1963).

There are other, although less specific, reasons for suggesting, as did Cajal (1909), that the internuncials controlling mastication lie in the reticular formation medial to the trigeminal complex. As previously stated, this area receives projections from the cortical masticatory areas, from more medial reticular regions receiving cortical projections (Valverde, 1961; 1966) and from the sensory trigeminal nuclei (Lorente de Nó, 1933; Woodburne, 1936; Hernandez-Peon and Hagbarth, 1955; Torvik, 1956; Stewart and King, 1963; Valverde, 1966). Neurons of this region



project to the cranial motor nuclei (Cajal, 1909; Lorente de Nó, 1933; Valverde, 1962). It may be that the direct cortical projections to the trigeminal nuclei are not predominantly motor, but instead are concerned with the modulation of sensory transmission. Connections of this type have been demonstrated by Darian-Smith and Yokota (1966), Schende and King (1967), Hepp-Reymond and Wiesendanger (1969) and Sauerland and Mizuno (1969).

While it appears reasonable to assume from the above evidence that the cells of the masticatory pattern generator lie in the lateral regions of the brain-stem, their exact position is uncertain. Microelectrode recording in these regions during mastication produced by stimulating prebulbar sites should resolve this problem.

#### A preliminary model of the pattern generator.

A simple model can be proposed in which both the short latency trigeminal and hypoglossal responses, and the long latency response of rhythmical mastication secondary to cortical stimulation, are mediated through common interneurons. Jaw-opening motoneurons discharge 15 msec after single shocks to the cortical masticatory area (Kawanura and Tsukamoto, 1960a; Goldberg and Nakanura, 1968; Chase and McGinty, 1960a) and to trigeminal sensory nerves (Kidokoro et al, 1968). Porter (1967) and Sumi (1960a) identified single hypoglossal neurons which discharged 5-15 msec after each cortical shock; these cells are connected to both cortico-bulbar and lingual nerve inputs by interneurons in or near the spinal trigeminal nucleus. It has been demonstrated in the present study

that both corticobulbar and oral stimulation will activate rhythmic mastication. Bursts of neuronal activity occurred during repetitive CNS stimulation only after a latent period of more than 80 msec. This activity was observed in both the trigeminal and hypoglossal systems. One could suggest that during the relatively long period that precedes the first burst of masticatory activity the responses to each single stimulation pulse are gradually changed into a rhythmic output as neurones of the pattern generator become coupled together.

There is evidence, nevertheless, that the masticatory pattern is not formed by the interneurones in the fast corticobulbar pathway. During repetitive stimulation, most hypoglossal motoneurones continued to fire after each stimulus pulse and also in bursts in time with each chewing cycle, while another group of hypoglossal motoneurones discharged repetitively only in time with mastication (Sumi, 1960a). There are two alternative explanations for these facts. Either the hypoglossal motoneurones are themselves capable of elaborating the masticatory pattern, or, secondly, there are two groups of cortico-hypoglossal interneurones. One group would be responsible for the discrete, short-latency discharge and the other would generate the masticatory pattern. Neither the hypoglossal nor the trigeminal motoneurones appear to have the properties necessary for pattern generation. Strong excitatory or inhibitory coupling is needed to account for the regular appearance of synchronized bursts in many neurones (Wilson and Waldron, 1968). The motoneurones probably do not have the collaterals required for this activity (Cajal, 1909; Lorente de Nó,

1933; 1947) and they are not synaptically activated during antidromic stimulation of adjacent cells (Porter, 1965; Kidekoro et al, 1968a). Electrotonic coupling has been found among spinal motoneurons and in the mesencephalic trigeminal nucleus (Nelson, 1966; Baker and Llinás, 1970). Unless strong electrotonic transmission can be demonstrated in the V and XII motor nuclei, coupling must be accomplished by higher-order neurons.

Thus, the evidence indicates that the pattern of mastication is generated amongst a pool of interneurons at the bulbar level. Some possible models of this pattern generator are illustrated in Figure 24. Activation of this structure would occur during repetitive stimulation of the CNS sites already referred to (page 113) and during stimulation of the mouth by a food bolus.

FIGURE 24.

Possible models of the masticatory pattern generator.

A - fast cortico-bulbar pathways and connections mediating the jaw-opening and jaw-jerk reflexes.

B - theoretical masticatory pathways involving a brain-stem pattern generator receiving cortical (C) and oral (Bu) inputs. Motoneurons may receive both A and B.

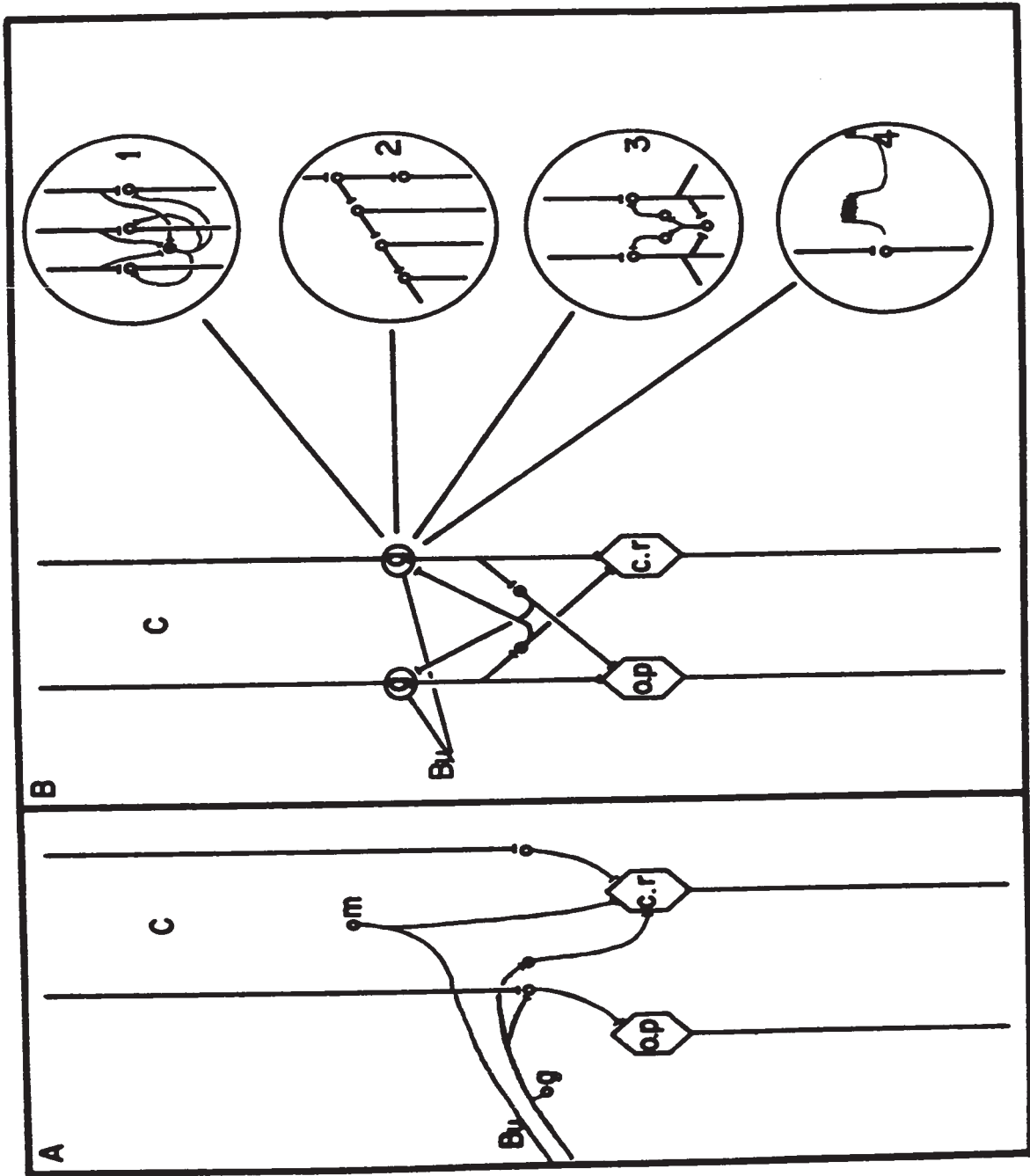
The insets show possible pattern generator interneuronal assemblies.

1. Negative internal coupling. Upon release from internal inhibition, all cells are in a state of increased excitability and are fired together by the descending fibers. This type of pattern generator may be responsible for rhythmical thalamo-cortical discharges (Andersen and Eccles, 1961; Andersen, Eccles and Sears, 1964; Andersen and Rudjford, 1964).

2. and 3. Positive internal coupling. Positive synaptic coupling between interneurons would place the motoneurons under continuous heavy excitatory bombardment. The bursts would be timed by reciprocal inhibition at the motoneuronal and/or interneuronal levels. Some of the proposed models of the locust flight system are of this variety (Wilson and Waldron, 1968).

4. Reciprocally connected neurons firing on release from inhibition. Bursts may be generated by cells which are capable of discharging at high frequency for 100 msec or more. Hippocampal pyramidal cells have been shown to discharge in this manner either during excitation or on rebound from inhibition (Kandel and Spencer, 1961).

- 
- g - trigeminal ganglion. Site of cell bodies of afferent neurones involved in the jaw-opening reflex.
  - n - mesencephalic trigeminal nucleus. Site of cell bodies of muscle spindle afferents for jaw-jerk reflex.
  - o.p - motoneurones of jaw-opening and tongue-protruding muscles.
  - c.r - motoneurones of jaw-closing and tongue-retracting muscles.
  - Ⓢ - interneurones forming the pattern generator.
    - o - cell bodies of excitatory interneurones.
    - e - cell bodies of inhibitory interneurones.



Properties of the pattern generator.

The analysis of latencies from the integrated neurogram necessarily gives only an approximate measure of the delay between the start of stimulation and the beginning of the masticatory discharge. However, the minimum recorded latency of about 80 msec is of the same order as those demonstrated by Sumi (1970) for single fibers.

It is possible that the long latency which precedes the first masticatory discharge is artifactual. Electrical stimulation activated a large number of surrounding cells or fibers which do not necessarily have the same properties. As many of these cells could have opposing functions (e.g. Biszi, 1969) the result could be a distortion or even complete failure of the "naturally occurring" output (Marchiafava, 1968). Considerable time could be lost before a particular output pattern emerges from the interneuronal pool receiving conflicting information.

Nevertheless, physiological delays of a magnitude similar to those found in the present study have been reported. Everts (1966) observed that, in monkeys making conditioned hand movements, spikes in pyramidal tract neurones preceded the resultant EMG activity by 50-100 msec. He also found, as in Experiment I, Group a, that recordable movements began at least 200 msec after the pyramidal discharges commenced. This additional time was due partly to delays in his mechanical recording system.

Therefore, it is probable that the pre-discharge latency represents the time necessary for coupling amongst the interneurons

of the pattern generator to produce a synchronized output. Whether this synchronization occurs as a result of positive or negative internal coupling (Figure 23: parts 1, 2 and 3), with or without external inhibition (Figure 23: part 4), is a problem for future investigation.

Similarly, any explanation of the input-output relationships are speculative. One may suggest that the initial increase in output with input represents recruitment of members of the pattern generator pool, until a stable output is reached that is not responsive to increased presynaptic activity. The fall of the output with high-frequency stimulation, is, however, probably a consequence of high-frequency presynaptic depolarization blockade (Krnjevic and Miledi, 1959).

The poststimulation aftermovements and discharges may occur because of reverberation within the pattern generator or, as has been suggested by McIntyre, Mark and Steiner (1956), prolonged transmitter action.

In contrast with certain other known central pattern generators for flight and locomotion in insects (Wilson and Wyman, 1965; Hoy and Wilson, 1969), the addition of proprioceptive feedback during unobstructed movements does not affect the transfer characteristics of the system, which again emphasizes the fundamental independence of the central mechanism.

#### Interactions.

The augmentory and inhibitory effects of peripheral stimuli on evoked jaw rhythms were unaffected by decerebration and removal of the cerebellum. These interactions are not, therefore, dependent on ascending-descending loops involving centers



above the mesencephalon.

As stated in the previous section, it is likely that summation of prebulbar inputs and ascending inputs from the mouth, which at higher intensities are both capable of producing rhythmical mastication, takes place at the level of the interneurons forming the pattern generator. If summation occurred at the motoneurone level, then two independent pattern generators would need to be involved, an unnecessarily complex arrangement.

The inhibition of rhythmical movements during paw-pinching and rectal distention is probably part of a widespread alteration of neuronal excitability. Running movements evoked by stimulation of the posterior hypothalamus can be abolished by pinching any part of the body (Ectors, Brookers and Gerard, 1938). Reflexes are also affected. Blier and Kleitman (1930) found that repetitive stimulation of the sciatic nerve completely abolished the jaw-opening reflex, while rectal distention was partly inhibitory. A similar difference in the degree of inhibition of rhythmical jaw movements by forepaw pinching and rectal distention was seen in the present study. Other reports set out in Table I similarly stated that concurrent sciatic stimulation inhibited the jaw-opening reflex.

There is much evidence that this inhibition of motor activity is brought about through the reticular formation. As a generalization, direct electrical stimulation of this diffuse structure mimics the non-specific effects of somatic and visceral afferent stimulation (King, Minz and Unna, 1955; Hugelin, 1955; Hugelin and Cohen, 1963; Beritov, 1968). While there is some compartmentaliza-

tion of the reticular formation into medullary inhibitory and pontine facilitatory areas (Magoun, 1944; Magoun and Rhines, 1946; Rhines and Magoun, 1946), Sauerland, Nakamura and Clemente (1967) infer from their results that when afferents to both these regions are stimulated, the inhibitory influences prevail over mono- and polysynaptic reflexes at all levels of the CNS.

Inhibition of mastication during paw-pinching may occur by postsynaptic inhibition of the trigeminal and hypoglossal motoneurons. Kubota et al (1968) found, in the cat, that stimulation of the superficial radial nerve suppressed both flexor and extensor reflexes, along the whole length of the neuraxis. This depression of reflexes was produced, at least partially, at the level of the final common pathway, for they recorded concurrent IPSPs in lumbar flexor and extensor motoneurons and in the motoneurons of the jaw-closing muscles. As with the inhibition of rhythmical mastication, the prepontine regions and cerebellum were not necessary for the generation of this inhibition. However, the brain-stem was needed for the depression of lumbar reflexes, and by inference the suppression of jaw reflexes and rhythmical mastication.

Suppression of mastication may also occur by inhibition of interneurons or by presynaptic depolarization. It is known that spinal interneurons mediating both cortically-originating and segmental responses are subjected to reticular inhibitory control (Marchiafava, 1968). Low frequency stimulation of the bulbar inhibitory area which was too weak to cause presynaptic inhibition of primary afferents, or postsynaptic potentials in motoneurons,

inhibited interneurons capable of exciting flexor efferents (Engbert, Lundberg and Ryall, 1965). Extensor interneurons are subjected to similar reticular inhibition (Helmqvist and Lundberg, 1961). It is also possible that presynaptic inhibition of interneurone axons, as suggested by Engberg et al (1965), could contribute to the inhibition of mastication.

Sometimes the first few masticatory cycles following the removal of the inhibitory stimulus occurred at a faster rate than was observed before inhibition. For reasons which were previously stated, it appears that the motoneurons receive an input which has already been patterned into reciprocal bursts by other elements within the brain-stem. Therefore, while the motoneuronal excitability may be raised during the period immediately following an IPSP (Coombs, Curtis and Eccles, 1959), perhaps increasing the number of spikes/burst, it can hardly be expected to change the frequency at which the bursts are generated. This "rebound facilitation" of the masticatory frequency is therefore indirect evidence that at least part of the inhibition must take place at the level of the intercalated neurons forming the masticatory pattern generator.

While Granit and Kaada (1952) postulated that reticular inhibition of  $\gamma$  motoneurons could be an indirect mechanism for the suppression of activity in  $\alpha$  motoneurons, inhibition of masticatory discharges was produced in the present study by paw-pinching after probable opening of the  $\gamma$  loop by paralysis. Therefore, the abolition of mastication could not be solely the result of a

decrease in spindle excitability. It would therefore seem that the suppression of mastication by paw-pinching and rectal distention is mediated by the brain-stem reticular formation. Inhibition of both the pattern generator and the motoneurons probably occurs.

Although activation of the lateral jaw movement reflex could also interrupt the rhythmical masticatory cycle via a general reticular mechanism, a more selective action would seem probable. Biting one's tongue during a closing phase of rhythmical chewing results in reflex jaw opening by inhibition of jaw-closing motoneurons and activation of the depressors. In a similar way, activation of those neurons which swing the jaw to the contralateral side and inhibition of their antagonists could modify the masticatory movements or abolish them completely. Sumi (1969, 1970b) similarly showed that the swallowing and jaw-opening reflexes can interrupt cortically evoked chewing. Reflexes such as these appear to be able to prevent expression of the rhythmic drive by a recruitment of motoneurons for more basic activities.

#### Lateral jaw movement reflex.

This reflex has not previously been described in the literature. The initiators of the lateral jaw movement reflex in response to pressure applied to the crown of an incisor tooth appear to be periodontal pressor receptors innervated by sensory fibers travelling in the superior alveolar nerves. It is uncertain whether the electrical trains used to evoke the response act by stimulation of gingival and palatal afferent endings. Pressure and touch stimulation of these same areas was ineffective,

suggesting that the electrical stimulus spread to the fibers emanating from the periodontal pressoreceptors.

Periodontal pressoreceptor activity has been recorded by a number of authors in the superior and inferior alveolar nerves of dogs and cats (Pfaffman, 1939; Corbin and Harrison, 1940; Yamada, Sakada, Murata and Ueyama, 1961; Matthews, 1965; Hannam, 1969) and in the inferior alveolar nerve of the rabbit (Ness, 1954). In all studies, single units could be characterized as fast-adapting, slow-adapting or spontaneously active. Certain properties of these receptors appear to be relevant to the present discussion. They are all direction specific, as in the present reflex, which could not be provoked by mesial and distal pressure. Slow pressure application is a relatively ineffective stimulus for these receptors, as it proved to be for elicitation of lateral jaw movement. The slowly adapting fibers continue to fire at high rates relative to their initial peak frequency for many minutes during the application of continuous pressure, and would supply the tonic afferent activity necessary to maintain the jaw in its lateral posture.

Although the threshold pressure necessary to excite these receptors was only 2-100 g (Pfaffman, 1939), Ness (1954) found that the highest frequencies of discharge occurred at heavier pressures (1000-4000 g), which are greater than the threshold necessary to elicit the lateral jaw movement reflex.

Fast-adapting fibers sometimes show an "off" response following removal of the pressure applicator (Ness, 1954), which may provide a peripheral explanation for the "off" activity seen

in certain of our records.

The pathways from the periodontal receptors to the ipsilateral and contralateral motoneurons concerned in this reflex cannot be definitely established. Corbin and Harrison (1940) recorded action potentials in the caudal half of the trigeminal mesencephalic nucleus, presumable from primary afferent neurones, in response to blunt pressure stimulation of the homolateral teeth and hard palate. However, although destruction of this nucleus in cats abolished the jaw-jerk response of the same side, it had no effect on the jaw-opening reflex elicited by pressure on the teeth or anterior part of the hard palate (Harrison and Corbin, 1941). Also, as the cell bodies of primary afferent fibers connected to the slowly-adapting type of periodontal receptors lie in the trigeminal ganglion, while the mesencephalic nucleus contains only faster-adapting units (Beaudreau and Jerge, 1968; Jerge, 1963a), which would be less effective in maintaining the lateral jaw movement reflex, it would seem that the afferent limb of the present reflex has its primary neurones in the trigeminal ganglion.

Second-order neurones firing during pressure application to the teeth have been identified in the main sensory nucleus and in the rostral part of the spinal trigeminal complex (Kruger and Michel, 1961; Eisenman, Landgren and Novin, 1963; Kawamura and Nishiyama, 1966). Receptive fields were always restricted to the ipsilateral side. Most units were activated from single teeth, were direction specific and were slowly adapting (Kawamura and Nishiyama, 1966), but some received inputs from several teeth.

Cells exhibiting similar responses, many of which additionally responded to jaw opening, have been found in the nucleus supratrigeminalis (Eisenman et al, 1963; Jerge, 1963b). Jerge re-emphasized Torvik's earlier speculation (Torvik, 1956) that this small nucleus, strategically placed between the main sensory and trigeminal motor nuclei, contained interneurons participating in trigeminal reflex pathways which Lorente de N6 (1933) had drawn from histological material. Kidokoro et al (1968b) recently showed that these neurons inhibit jaw-closing motoneurons during the jaw-opening reflex. They may act in the lateral jaw movement reflex to inhibit the ipsilateral superficial masseter, anterior temporal and zygomatico-mandibular muscles.

The long delay from the beginning of the stimulus train until the first activity was recorded in the contralateral muscles, together with the latency of 9-16 msec between each pulse and the resulting activity, indicated that the pathway from the primary sensory neurons to the motoneurons is complex. It is, of course, possible that each burst of activity was evoked by a stimulus pulse further back in the train. Hugelin and Dumont (1961) suggested that the jaw-opening reflex contained a minimum of three synapses; while Kidokoro et al (1968a) calculated that a disynaptic linkage would account for the minimum central delay which they observed. If we assume that the minimum delay between a peripheral stimulus pulse and the beginning of digastric activity (7.2 msec) represents a disynaptic linkage, there would appear to be at the very least two extra synapses in the fastest pathway to the

zygomatico-mandibular and anterior temporal muscles. This pathway probably reaches the contralateral motor nucleus via crossed trigemino-reticular pathways similar to those originally described by Cajal (1909).

The pattern of activity recorded during activation of the reflex is in agreement with that expected on purely anatomical grounds. The zygomatico-mandibular and anterior temporal muscles are considered to be primarily elevators and retractors of the mandible (Fox, 1965), and their unilateral activation would tend to draw the mandible to the same side. The external pterygoids appear to act as stabilizers of the rotating condyles and would be expected to be active on both sides. The superficial masseter, which is a protruder of the jaw in the rabbit, returns the mandible to its midline resting position as the activity in the prime movers fades.

Rhythmical side-to-side ruminatory movements of the mandible have been evoked in rabbits by rubbing the buccal mucosa or electrically stimulating the posterior regions of the cortical masticatory area (Brömer, 1923). The only non-rhythmic, apparently reflex, lateral movement of the jaw previously described is the corneo-mandibular reflex of von Solder (1902). He regarded this as an example of a purely trigeminally-mediated reflex movement of the mandible to the opposite side, provoked by touching the cornea. Trömer (1918) also accepted the reflex nature of these movements, which would thus far appear to be closely allied with the reflex responses to incisal pressure. However, it is more probable (Kaplan, 1903; Ornsteen, 1935; Wartenberg, 1948) that the corneo-mandibular reflex is in fact a synkinesia, which accompanies strong, reflex closure of the stimulated eye. It can



be elicited by forceful voluntary closure of the eye, but not by stimulation of the cornea through the closed lid.

Although the stimuli used by Sherrington (1917) and by subsequent investigators (Brémer, 1923; Harrison and Corbin, 1941; Hannam and Matthews, 1969) to evoke the jaw-opening reflex in the cat were similar to the stimuli used in the present study, none of them reported observations of lateral mandibular movements. We were also unable to reproduce this lateral movement in anesthetized or decerebrate cats. This is undoubtedly another instance of a species difference. Carnivores do not utilize lateral mandibular movements during the preparation of food; indeed, such movements are precluded by the anatomy of the temporo-mandibular joints and the interlocking canine and carnassial teeth of these animals. Conversely, it is essential for the lagomorph to move its mandible laterally to bring its teeth into a working relationship, as the mandibular arch is much narrower than the maxillary (Mayer, 1969). The temporomandibular joints are constructed to allow this. The lateral jaw movement reflex in the rabbit could act to protect the periodontal membrane from heavy biting pressure while the sliding movement of the lower teeth along the incisal edge of the teeth may also aid in the incision of food.

SUMMARY OF EXPERIMENTAL RESULTSEXPERIMENT I.

- (1) Rhythmical oral movements were produced by repetitive electrical stimulation of cortico-bulbar pathways and of limbic and reticular structures in anesthetized and decerebrate rabbits, in rabbits implanted with chronic electrodes, and in anesthetized cats.
- (2) The frequency of movements in rabbits (1.0-5.0/sec) resembled that of normal chewing, whilst in cats only lapping (1-2/sec) could be elicited. This species difference is probably a reflection of anatomical and dietary dissimilarities.
- (3) Distention of a balloon in the mouth could also cause rhythmical mandibular movements in anesthetized and decerebrate rabbits, and this oral input would summate with the central stimulus.
- (4) Paw-pinching, heavy pressure on an incisor tooth and distention of a balloon inside the rectum inhibited evoked masticatory movements.
- (5) When light pressure was applied to the labial or lingual surface of a central maxillary incisor tooth during mastication, wide lateral excursions to the contralateral side preceded each opening stroke.
- (6) Neither precollicular decerebration nor removal of the cerebellum altered the above responses.

EXPERIMENT II.

- (1) Bursts of multineuronal activity were recorded from branches of the trigeminal motor and hypoglossal nerves and the hypo-

glossal nucleus of anesthetized rabbits, and these were in phase with the observed masticatory movements. Discharges occurred alternately in nerves to jaw-opening and jaw-closing muscles. The latency from the beginning of stimulation of the cortico-bulbar pathways to the beginning of the first burst varied from 80 msec to more than 10 secs.

- (2) Increasing the frequency of stimulation increased the frequency of bursts of activity recorded from hypoglossal motoneurons until an output of 2.4-4.5 bursts/sec was reached at 8-30 Hz. As the stimulus frequency continued to increase, the output did not change until the stimulus frequency exceeded a value which varied from 80-450 Hz. The frequency of burst discharges then declined. This relationship was not altered by paralysis.
- (3) Distention of the oral balloon was still effective after paralysis. Paw-pinching was inhibitory.
- (4) Regularly recurring bursts of activity were evoked in the hypoglossal nucleus by random frequency stimulation after severing the XII, XI, X, IX, VII and V cranial nerves, the I and II cervical nerves, and the spinal cord of paralysed rabbits.
- (5) Mechanical deformation of the brain of vascular or respiratory origin was discounted as the origin of the rhythm, which was therefore attributed to a brain-stem pattern generator. The interneurons forming this structure are thought to lie in the spinal V nucleus or adjacent regions of the reticular formation.

EXPERIMENT III.

- (1) A pressure of at least 300 g, applied to the labial or lingual surface of the upper central incisor teeth, activated a lateral jaw movement reflex in decerebrate rabbits.
- (2) The contralateral posture of the mandible could be maintained for up to 10 seconds if heavy pressure was continuously applied to the tooth.
- (3) The zygomatico-mandibular and anterior temporal muscles of the contralateral side had the highest levels of maintained EMG activity. The external pterygoids of both sides fired at the start of stimulation. Other muscles on the same side as the applied stimulus were inhibited.
- (4) Section of the infraorbital nerve above, but not below its union with the anterior superior alveolar nerves abolished the reflex response when pressing on the ipsilateral incisor.
- (5) A similar reflex could be elicited by electrical stimulation of the pericoronal incisal gingiva, or adjacent palatal mucosa, if the stimulus frequency was greater than 7 Hz.
- (6) At 30 Hz, reflex activity began in the contralateral zygomatico-mandibular and anterior temporal muscles after an initial latency of 78-220 msec and thereafter followed each pulse with a latency of 9-16 msec. Delays of these magnitudes suggest that the reflex pathway is multisynaptic.

CONCLUSIONS

It is concluded that rhythmical mastication is controlled by a brain-stem pattern generator which can be activated by inputs from higher centers or from the mouth itself, but which is not dependent on external timing information for the production of a cyclic output. Noxious peripheral stimulation inhibits the pattern generator as part of a general effect mediated by the reticular formation.

The jaw-opening, and jaw jerk reflexes are not the basic neurological units of pattern generation, but instead act respectively to protect the oral soft tissues, the periodontal membrane, and to maintain mandibular posture. The lateral jaw movement reflex, herein first described, may act to protect the periodontal membrane and, in addition, assist in incision and repositioning of food. During chewing, these three reflexes can act to modify the basic central masticatory pattern.

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