Inhibition of a Monosynaptic Reflex by Electrical Stimulation of the Basal Forebrain or the Orbital Gyrus in the Cat

The brain stem as the extension of the spinal cord into the brain has anatomical and functional characteristics similar to both the spinal cord and the brain. In its reflexive functions the brain stem acts in a manner similar to the spinal cord, whereas in its regulatory functions it behaves more like the brain. When one considers monosynaptic reflex arcs, attention is usually drawn to spinal levels. From degeneration studies in 1948, however, SZENTAGOTHAI[1] described a monosynaptic reflex among the central pathways of the cranial nerves involving only brain stem structures. Sensory neurons within the mesencephalic nucleus and tract of the trigeminal nerve are the afferent limb of this monosynaptic reflex. The central axons of these mesencephalic nucleus nerve cells send reflex collaterals to the motor ganglion cells in the trigeminal motor nucleus. These latter cells are the efferent limb of this monosynaptic arc which has been called the masseteric reflex by HUGELIN and BONVALLET[2], who established the monosynaptic nature of the reflex in adult cats through electrical stimulation and recording experiments.

A series of experimental projects carried out in this laboratory over the past 7 years has lent support to an hypothesis suggesting that certain forebrain structures bear a direct relationship to the brain mechanisms responsible for both the onset of sleep and of behavioral inhibition[3–6]. Cortical EEG synchronization, behavioral inhibition and sleep have been induced through electrical stimulation of a basal forebrain-preoptic region in the cat and monkey and anatomical pathways have been suggested by our physiological experiments which associate this area with the orbitofrontal cortex, septum, hippocampus, midline thalamus and mesencephalic reticular formation[7]. It was subsequently of interest to determine whether stimulation of this forebrain system, capable of inducing so complex a response as sleep, would influence other more specific neurophysiological mechanisms as well. This communication deals with the results of such investigations utilizing the masseteric reflex as a test response.

When stimulating electrodes are placed in the mesencephalic nucleus of V and recording electrodes placed in the masseteric branch of the mandibular nerve, low voltage stimulation will give rise to a two-component peripheral nerve response (Figure 1). The first component is an antidromic volley mediated directly by axons of the sensory neurons of the mesencephalic nucleus while the second component is the orthodromic monosynaptic reflex potential through motoneurons in the motor nucleus of V. Axon collateral fibers from the mesencephalic neurons act as the presynaptic elements of this reflex, while motor neurons are the postsynaptic elements. It should be noted in Figure 1 that the antidromic volley remains relatively stable in amplitude, while the reflex potential varies in amplitude in the expected manner.

Operations were performed under general ether anesthesia on adult cats weighing 2.5–4.0 kg. Exposure of the masseteric nerve was achieved by freeing the edges of the masseter muscle. Bipolar peripheral nerve recording electrodes were then used to monitor activity along this nerve trunk. The cerebral cortex was exposed by craniotomy, and subcortical electrodes were placed through stereotaxic procedures. All wound edges and pressure points were infiltrated thoroughly with a local anesthetic, xylocaine, and a muscular relaxant, Flaxedil, was administered. The masseteric reflex was subsequently established by inserting a concentric bipolar stimulating electrode at a 45° angle behind the bony tentorium and into the mesencephalic nucleus of the trigeminal nerve. The reflex was visualized oscilloscopically, while stimuli were delivered from Grass S4 stimulators through appropriate isolation units.

The masseteric reflex was most consistently observed when the angled stimulating electrodes were placed in the site corresponding to stereotaxic coordinates P3, L2, H-1 to H-3. The average latency of the antidromic volley (conduction along the sensory axons from the mesencephalic Vth nucleus to point of recording on the masseteric nerve) was 1.2 msec. The amplitude of this potential remained consistent in a given preparation, although its size varied in different animals. This is in contrast to the variable amplitude of the monosynaptic reflex volley. The peak latency of the monosynaptic reflex varied from 1.8–3.8 msec with an average of 2.15 msec.

The reflex was elicited repeatedly by gated stimuli delivered to the mesencephalic Vth nucleus at the rate of 1/sec. The interaction effects upon this reflex of stimulation of cortical and subcortical sites were then studied. Consistent inhibition of the masseteric reflex was observed with stimulation of anterior lateral preoptic and basal forebrain subcortical sites (Figure 2B) and of a discrete cortical area localized in the orbital gyrus (Figure 2D). It was also noted that inhibition of the reflex was often accompanied by a slight increase in the amplitude of the antidromic volley, possibly an indication of presynaptic inhibition. Inhibition was best observed when biphasic pulses were delivered at a frequency of 75/sec and a duration of 0.45 msec with 4–6 V. Other frequencies

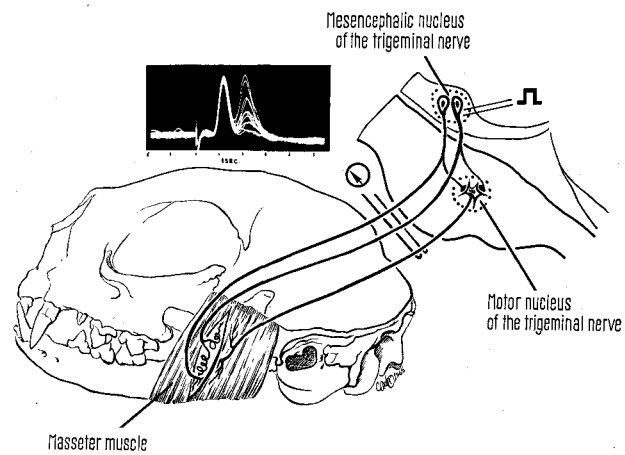

Fig. 1. Diagrammatic representation indicating the anatomical elements comprising the masseteric reflex. Stimuli were delivered to cells in the mesencephalic nucleus and recordings were made on the masseteric nerve. The 2-component response at the upper left is composed of an initial antidromic potential and a secondary reflex potential.

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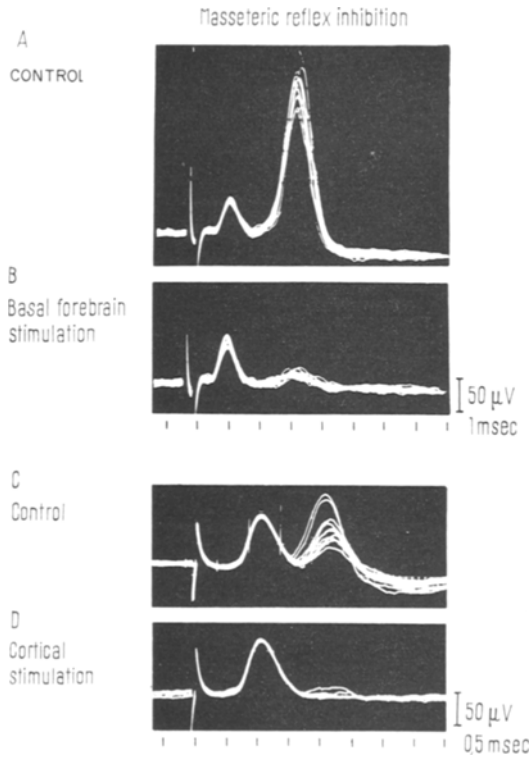

Fig. 2. The control masseteric reflex is illustrated in A and C. Following the artifact, can be observed first the antidromic volley and then the reflex volley as recorded along the masseteric nerve. In B an almost complete inhibition of the reflexive response is observed during the stimulation of the ipsilateral preoptic area, while D shows an even more pronounced effect during stimulation of the ipsilateral orbital gyrus.

were either less effective or ineffective at these sites, and stimulation of different sites resulted in other effects to be described more completely elsewhere.

These findings support an hypothesis developed from our former work which has indicated the existence of a forebrain inhibitory system involving cortical, basal forebrain and limbic structures which descend to reticular areas of the mid- and hindbrain. Stimulation at the rostral end of this system (basal forebrain or orbital gyri) resulted in suppression of motor behavior and the induction of sleep. Inhibition of the masseteric monosynaptic reflex points to the fact that this suppression can be reflected in the most basic of neurophysiological mechanisms as well. This particular finding is especially relevant since relaxation of the antigravity muscles resulting in opening of the mouth in the unsupported lower jaw is usually a behavioral correlate of the initial stages of sleep.

Zusammenfassung. Der monosynaptische Reflex des Nervus massetericus, durch elektrische Reizung des Nucleus mesencephalicus des Trigeminus hervorgerufen und vom Nervus massetericus abgeleitet, konnte durch Reizung bestimmt umschriebener Gebiete des präoptischen basalen Telencephalons oder durch Reizung des Gyrus orbital im Katzen-Cortex effektiv gehemmt werden. Entsprechende Reizung der gleichen Hirngebiete führt zur Synchronisation des Elektrocorticogramms und ruft Schlaf hervor.

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Connective Tissue Degradation and Distensibility Characteristics of the Non-Living Heart

It is well known that the myocardium is infiltrated by a considerable amount of connective tissue. Although collagenous fibers predominate, the myocardium also contains elastic and reticular fibers[1]. These non-muscular components of heart tissue are arranged in such a way as to provide a matrical superstructure upon which the muscular, nervous, and vascular components are arranged. To what extent the connective tissue fibers contribute to the static (much less dynamic) properties of the heart is largely unknown.

Methods. Left ventricular distensibility was compared in 4 groups of rabbit hearts: (1) control, (2) treated with collagenase, (3) treated with elastase, and (4) treated with trypsin.

The protocol for all experiments was as follows: (1) As much fluid as possible was withdrawn from the left ventricle and pressure at this 'zero' volume was recorded. (2) Continuous pressure records were obtained while infusing physiological saline into the left ventricle at a rate of 4.12 ml/min until the pressure reached 40–50 mm Hg. (3) The pump was then reversed and withdrawal was continued at the same rate as infusion. (The hydrostatic level of the saline bath was maintained constant throughout both infusion and withdrawal.) This constituted the first pressure-volume (P-V) curve and it was always obtained within 10 min after isolation of the hearts. (4) After 60 min time lapse (when stiffening was maximal) the second P-V curve was obtained. (5) Immediately after the second P-V curve was obtained, the hearts were stretched one time with the same volume of fluid that was used to obtain the first P-V curve and then the third P-V curve was obtained. (6) The hearts were then incubated for 90 min at 36.5 °C in a solution which contained either collagenase, elastase, trypsin, or buffered physiological saline (pH 7.1, phosphate buffer). The enzymes were obtained from the Nutritional Biochemical Co., Cleveland, Ohio, USA; their concentrations were: collagenase 1.5 mg/ml (pH 7.1, phosphate buffer), elastase 0.4 mg/ml (pH 8.8, carbonate buffer), and trypsin 2 mg/ml (pH 7.95, phosphate buffer). The left ventricular chamber and the coronary circulation were perfused with the solution. The hearts were then immersed in the digestion mixture.

[1] R. H. Licata, in *Cardiology* (Ed. A. A. Luisada, McGraw-Hill, New York, N.Y., USA) vol. 1, p. 61 (1959).