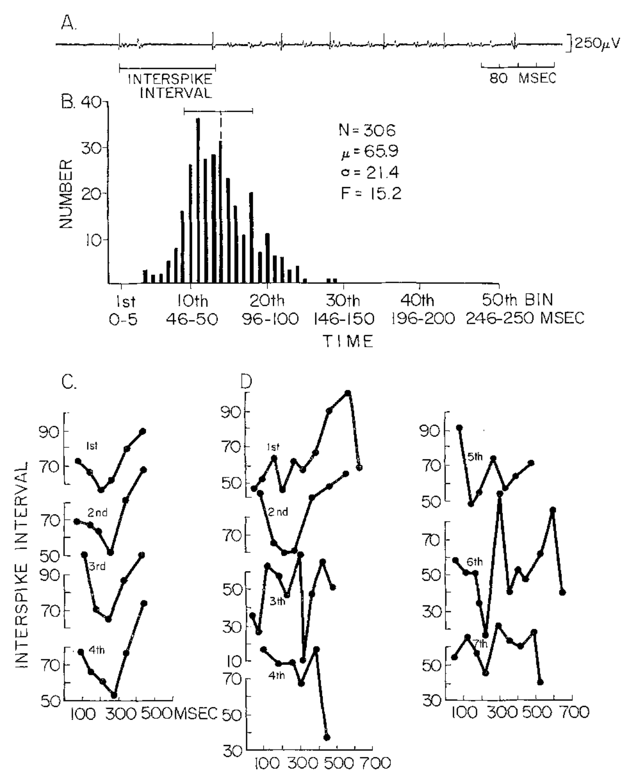
Interspike Interval Patterning in Recurrent Nerve Fibre Activity During Respiration

Previous reports have indicated that respiratory excitation of spinal motoneurons to the intercostal and diaphragm muscles is the caudal segment of the rostro-caudal axis of respiratory control which includes synaptic excitation of some cranial motor nuclei[1–9]. Electromyographic and neurographic analysis of muscles and nerves to the tongue and laryngeal musculature indicate the genioglossus (tongue protruder)[10–13] and laryngeal abductor muscle[4,6,7] are activated during inspiration. The properties of cranial motor nuclei do differ from that of the spinal cord by the relative lack of recurrent collaterals within the cranial motoneuron pool[14], and, in most, the absence of a gamma motoneuron-muscle spindle proprioceptive control[15]. The respiratory control provides a natural synaptic drive of specific brain stem motoneurons to further understand properties of the recruitment and synaptic driving of individual motoneurons within a given cranial nucleus.

Studies of activity patterning of single motor units of the genioglossus muscle innervated by the XII cranial nerve, indicate the smallest motor units are tonically active in inter-inspiratory phases and are recruited before the larger units are recruited in the maximum activity[10,16].



Interspike interval activity of recurrent nerve fibres during respiration. A) Example of respiratory activity recorded from the recurrent nerve of several fibres with various amplitudes. B) First order histogram indicating mean (μ) and standard deviation (σ) of distribution of interspike intervals of largest unit in (A). Frequency (F) is the reciprocal of the mean. C) Time plots of 4 successive inspiratory phases in which the interspike intervals of the largest unit in (A) are plotted against successive time. Notice the consistent pattern of unit discharge during normal respiration. D) Time plots of 7 successive respiratory phases for the same recurrent nerve unit as in (C) but during stimulation of the glossopharyngeal nerve to evoke swallowing.

Interspike interval analysis indicates that in successive inspiratory phases, a given genioglossus motor unit does not respond with a constant frequency but continually presents a non-repeated pattern[11,16].

However, analysis extended to motoneurons of another cranial motor nucleus active in respiration, the nucleus ambiguus, indicates that these motor fibres can respond in both non-consistent and repeated patterned responses. Instead of recording single motor units to the laryngeal adductor and abductor muscles, the recurrent nerve innervating the musculature was cut at its most peripheral extent and dissected into smaller filaments in which only a few motor fibres were recorded by bipolar electrodes (Figure A). The recurrent nerve contains a unimodal distribution with a sharp peak at 10–12 μ[17]. Respiratory pattern of nerve fibres was studied in 32 adult cats anesthesized with urethane or nembutal anesthesia. Respiration was monitored by EMG electrodes in intercostal and genioglossus muscles and a pneumatic cuff around the chest. Data was permanantly stored on FM tape and analyzed with assistence of time-interval histogram programs on the small laboratory computer (PDP-8L).

Most of the motor fibres of the recurrent nerve are periodically active during inspiratory phases (animal breathing ambient air) with average frequencies ranging from 13–25/sec and the mean interspike intervals for the different units ranging from 45–72 msec. First order interspike interval distributions indicated normal curves for the individual units (Figure B). In all of the units studied during inspiration ($N = 69$), a consistent repeated interspike interval pattern is evident. One of several patterns is shown in Figure C in which the unit steadily increases its frequency of firing reaching a peak level, and then slows its frequency to a level less than its initial firing rate.

The respiratory control of single cranial motoneurons (as based on single motor unit studies) can vary in terms of duration and rate when respiration interacts with other reflexes[10,16]. When repeated swallows occur, respiration slows or apnea results. After several swallows, respiration returns with motoneurons more active and individual motor units doubling their activity. The repeated pattern of the recurrent nerve fibre activity appears in both pre- and post-swallow periods of respiration but during the alternation of swallowing and inspiration, when sensory

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stimuli of the laryngo-pharyngeal region is presented, the fibre activity demonstrates a non-repeated pattern in successive respiratory phases. Figure D indicates the pattern of the same unit as in C but during stimulation of the central end of the cut glossopharyngeal nerve to evoke swallowing. This non-repeated pattern resembles the activity of most inframandibular single motor units active during swallowing or that of the genioglossus motor units active in both inspiration and swallowing[11].

These results suggest that the motoneurons of the nucleus ambiguus, activated by the brain stem respiratory interneurons, can be synaptically excited in a semi-stereotyped sequence. Such synaptic excitation is not evident in cranial motoneuron activity in swallowing, and is lost with the interaction of sensory stimuli from the primary nerve (in the cat) evoking swallowing with the synaptic drive of the respiratory pathway on motoneurons innervating the laryngeal musculature.

Résumé. L'interaction des données sensorielles pharyngiennes provenant du nerf glossopharyngien et des influences synaptiques respiratoires du tronc cérébral sur les motoneurones crâniens du noyau ambigu, indique que la caractéristique de décharge répétée des fibres motrices du nerf récurrent durant la respiration devient non-stéréotypée durant l'alternance de la déglutition et de l'inspiration.

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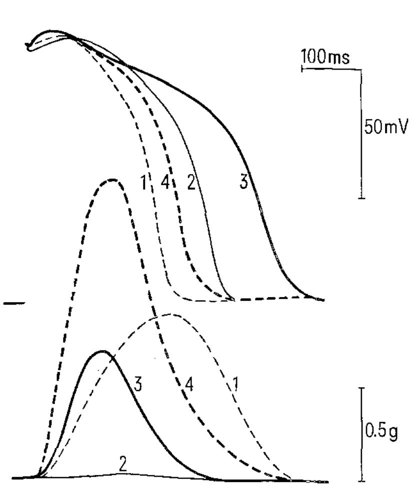
Effect of Epinephrine on the Duration of Action Potential of Papillary Muscles

The duration of cardiac action potentials (AP), namely ventricular, is variable within a relatively broad range of values. It generally abbreviates under those influences, which at constant muscle length increase the rate of tension development; at increased Ca concentration in the medium, at increased frequency of stimulation, during adaptation to rapidly decreased temperature and after artificially prolonged depolarization in sucrose gap experiments[1]. It has been postulated that the abbreviation of AP might reflect a feed-back effect of increased intracellular Ca concentration, which is the common denominator of the above inotropic interventions. The effect of epinephrine, however, does not match this scheme. It increases the Ca influx[2,3] and rate of Ca movements across the sarcotubular membranes[4]; accordingly it exerts a strong positive inotropic effect but is without an appreciable influence on the AP duration[5]. The present experiments were undertaken to explain this discrepancy.

Material and method. The experiments were performed on 8 papillary muscles of cats and confirmed on 22 papillary muscles of guinea-pigs, and on 5 dog trabeculae from the right ventricle. The animals were sacrificed under the urethane anesthesia, hearts were rapidly removed and the preparation was placed into oxygenated Tyrode solution (Na 149 mM; K 5.4 mM; Ca 1.8 mM; Cl 145 mM). The temperature was held constant at 31 °C. Preparations were stimulated at 4 sec intervals unless otherwise stated. Isometric contractions (electromechanical transducer RCA 5734) and transmembrane potentials (glass microelectrodes of 5–15 MΩ) were recorded from oscilloscope tracings. Epinephrine was administered in concentration 6×10^{-6} M. Preparations in which epinephrine elicited spontaneous activity were discarded.

Results and discussion. Under control conditions, epinephrine caused a marked positive inotropic effect and only insignificant changes of AP duration, measured at any level of repolarization. However, if the rate of stimulation was decreased to 7.5 or 4/min, epinephrine always tended slightly to prolong the AP. On the other hand, at stimulation frequency of 60 or 90/min, a small shortening of AP usually followed. Shortening of AP due to epinephrine was also observed in high-Ca Tyrode (5.4 mM) and prolongation in low-Ca Tyrode (0.6 mM).

The bulk of experiments were performed under electromechanical uncoupling in Ca-free Tyrode (Figure). Epinephrine unambiguously and markedly prolongs AP duration under these conditions. The effect is well marked after 1 min of exposure and usually reaches peak value after 2 min. The extent of this change individually varies



Transmembrane action potentials (upper traces) and corresponding isometric contractions (lower traces) redrawn from a representative experiment on cat papillary muscle. Stimulation frequency 30 min, temperature 31 °C. 1. Control in normal Tyrode solution; 2. after 20 min in Ca-free Tyrode; 3. 1 min after addition of 10^{-6} M epinephrine to Ca-free Tyrode; 4. 1 min after subsequent addition of 1.8 mM Ca.

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