charge carriers[7,11,12]. Mn^{++} has usually been regarded to be impermeant and it has been used as an inhibitor of Ca conductance. Antagonistic action of Mn^{++} to the Ca, Sr and Ba action potentials has been demonstrated in guinea-pig's atria, when it was used in low concentrations (0.15–1 m*M*)[6]. In the present study, action potentials with overshoot were elicited under Na-free and Ca-free conditions in the prsence of 2–95 m*M* Mn^{++}. The relatively close agreement between the experimental points and the theoretical slope for a Mn electrode (30 mV/decade at 30 °C) in Figure 2 is consistent with the view that Mn^{++} conductance is large during the peak of the overshoot. Because of the occurrence of Mn action potential and of Mn slow inward current[5] in guinea-pig's ventricular muscle and similar action potentials elicited in frog heart (Dr. D. Ellis, personal communication), membrane permeability to Mn^{++} is hardly negligible in cardiac muscle.

Summary. The membrane potential in guinea-pig's papillary muscles from right ventricle was recorded by glass microelectrodes and stimulation was effected by current pulses applied through a sucrose-gap. Action potentials with overshoot were recorded in the solution lacking Na^+ and Ca^{++} but containing 2–95 m*M* Mn^{++}. The overshoot was inecease with the increased of $[Mn^{++}]_o$ by about 30 mV/decade. Similar Mn^{++}-dependent action potentials were also obtained in Na-free solution containing 0.6 m*M* Ca^{++}. The results indicate that Mn inward current is sufficient to generate action potentials in cardiac muscle.

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Chemical Excitability of Axons: Excitatory and Inhibitory Effects of Putative Neurotransmitters and Modulators on Frog Sciatic Nerves

According to a widely accepted view, neurons and other excitable cells contain two fundamentally different types of electrogenic membranes: chemically-excitable (and usually electrically-inexcitable) synaptic membranes, and electrically-excitable axonal membranes[1]. Most theories of drug action regard synapses as the target for neurotropic drugs, thus assuming explicitly or implicitly that the electrically-excitable membrane of axons is chemically-inexcitable. Although local ionic currents[2] rather than chemical mediators such as acetylcholine[3] appear to be responsible for the propagation of action potentials, drug interaction studies on isolated sciatic nerves[4] have provided experimental evidence for the presence in axonal membranes of specific receptors for acetylcholine, L-epinephrine, histamine and serotonin. We have recently shown (in non-anesthetized, gallamine-paralyzed rabbits)[5,6] that the microiontophoretic administration of acetylcholine, tryptamin, norepinephrine and other putative neurotransmitters to corpus callosum fibres can elicit or inhibit the occurrence of action potentials. Since few if any synapses have been observed in the corpus callosum, these results suggest that axonal membranes may be chemically excitable. We have tested this hypothesis in isolated sciatic nerves (*Rana pipiens* and *Rana catesbeiana*) bathed in a modified Ringer's solution (NaCl 112 m*M*; KCl 3.5 m*M*; $CaCl_2$ 1.8 m*M*; PO_4H_2K/NaOH buffer, pH 7, 0.07 m*M*; dextrose 11 m*M*).

A 5 barrel micropipette system was placed into a desheathed portion of the nerve. A 4.8 *M* NaCl barrel was used for extracellular recording of multiple unit activity; 3 other barrels were used for the microiontophoretic administration (ejecting and holding currents: 5–20 nA) of drugs (0.5 *M*, ph 5) (acetylcholine, norepinephrine, dopamine, 2-phenylethylamine, tryptamine, histamine). A 3 *M* NaCl barrel was used as output for an automatic current balancing system[7] and also to test for current artifacts. We have often recorded spontaneous firing of nerve, suggesting that the preparation was not in a truly physiological state. At most sites, the firing rate was not modified by the administration (5 sec to 3 min) of synaptic activating drugs (0.5 *M*). However, we found units whose rate of firing was modified by these agents. These sites appeared to be highly localized because minor displacements of the electrode rendered the drug ineffective. Acetylcholine (Figure 1) often induced firing. Norepinephrine, 2-phenylethylamine and tryptamine either induced firing or inhibited spontaneous firing, depending on the site. The most common response to histamine administration was a brief period of firing followed by inhibition. In many instances, the effects of acetylcholine (Figure 1), histamine, or norepinephrine outlasted for sec or even min the ejecting current. Different units showed different patterns of response to the drug tested. The effects of most drugs at a given site were usually reproducible, but tachyphylaxis was observed with 2-phenylethylamine, histamine and acetylcholine. Comparing dopamine, norepinephrine, 2-phenylethylamine and tryptamine on the same units, several instances were found in which one amine was excitatory, another inhibitory, and another without effect. Figure 2 shows one example of units in which dopamine (but not norepinephrine) decreased the rate of firing. Whenever norepinephrine and 2-phenylethylamine exerted opposite effects, inhibition usually dominated.

These on-going experiments raise interesting possibilities, but it would be premature to conclude that the drugs tested are able to elicit action potentials in axonal membranes. The results obtained might be due to the artificial experimental conditions of our in vitro set-up

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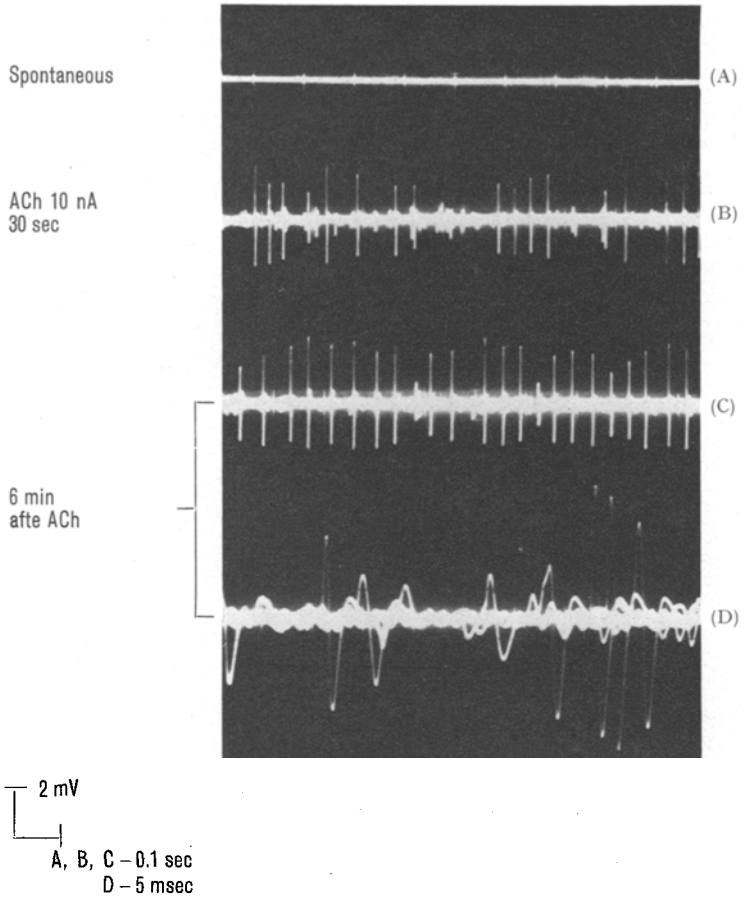

Fig. 1. Drug-induced firing in isolated frog sciatic nerve. The microiontophorectic administration of acetylcholine (10 nA for 30 sec) induced firing (B) in a previously quiescent preparation (A). The acetylcholine-induced firing persisted for more than 6 min after termination of the ejecting current (C). D) shows the spikes at an expanded time scale.

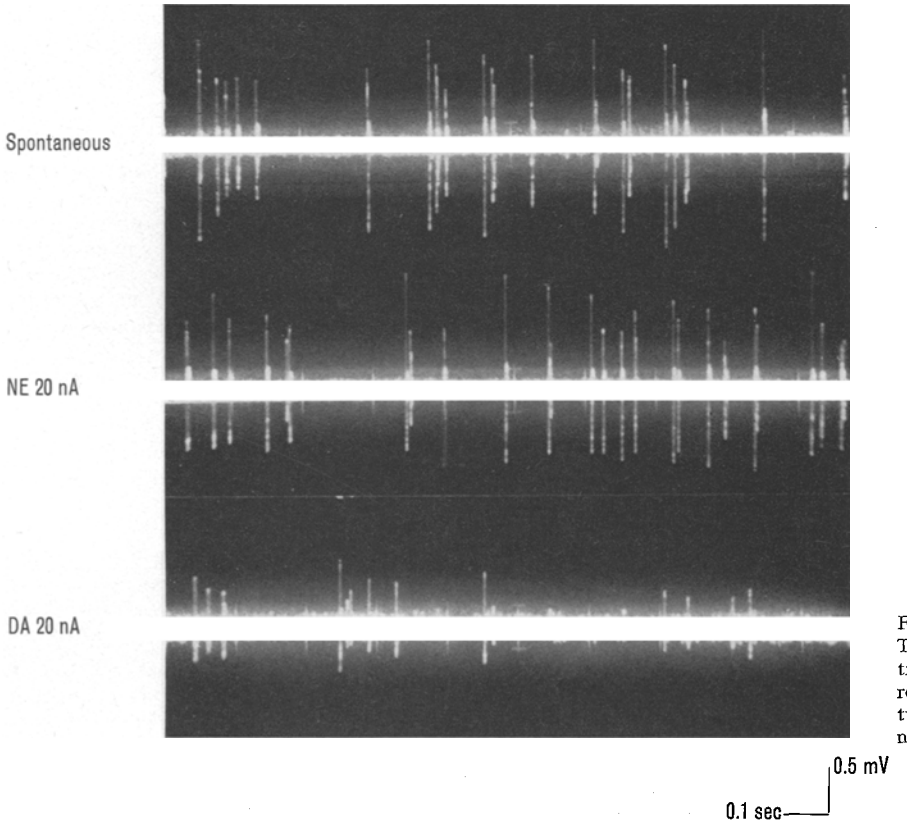

Fig. 2. Selectivity of drug effects. The microiontophoretic administration of dopamine (DA) for 1 min reduced the frequency and amplitude of the spikes whereas that of norepinephrine (NE) did not.

such as pH or drug-induced sensitization to current effects (it is possible that drugs alter the threshold of nerve fibres to the excitatory or inhibitory effects of the ejecting currents).

These results obtained with microiontophoretic drug administration contrast with the paucity of axonal effects induced by these drugs when added to the bathing solution. This may be explained by the development of tachyphylaxis, as observed in the present experiments. There are however scattered reports demonstrating in vitro and in vivo axonal effects of acetylcholine[4-6,8-10], catecholamines[4,6,11,12], histamine[4,13,14], and serotonin[4,15]. The axonal receptors for neuroamines display specificity, stereospecificity, and selective blockade by specific blockers[4].

The functional significance of drug sensitive axonal receptors is at present unclear. They may be devoid of function, or they may serve as a target for the action of diffusible neuromodulators (e.g. 2-phenylethylamine) and of exogenous drugs.

Summary. The microiontophoretic administration of putative neuromodulators (acetylcholine, norepinephrine, dopamine, 2-phenylethylamine, tryptamine, histamine) triggered firing or inhibited on-going activity in isolated frog sciatic nerves.

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The Anterior Cranial Gustatory Pathway in Fish

It has long been known that the lips of fish are supplied by cranial nerves V (trigeminal) and VII (facial), and that taste buds on the lips or barbels are innervated by the latter[1,2]. Recent investigations on the peripheral neural response of fish seem to support the innervation of taste buds by the VIIth nerve[3-5]. Yet, investigations with higher vertebrates suggest that the trigeminus is also involved in the transmission of taste messages[6,7]. Little attention, however, seems to have been given to the functional difference between the trigeminal and facial nerves in fish[8].

In this paper, an attempt was made to throw light on the gustatory neural pathway of fish from the lips to the

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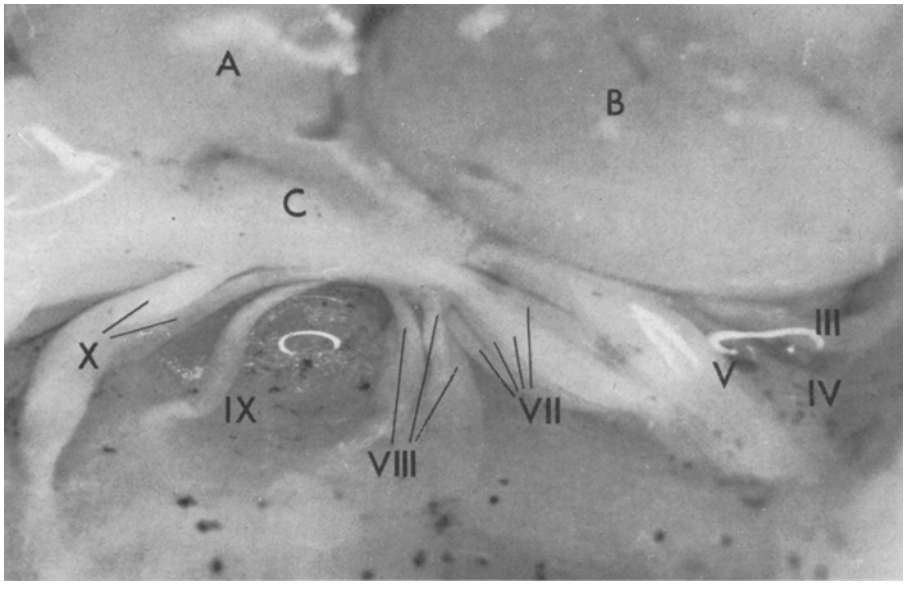

Fig. 1a) Lateral view of the brain and cranial nerves of the puffer. A, cerebellum; B, midbrain; C, medulla oblongata; III, oculomotor nerve; IV, trochlear nerve; V, trigeminal nerve; VII, facial nerve; VIII, vestibular nerve; IX, glossopharyngeal nerve; X, vagus nerve.