It is concluded that in Heidenhain pouches pentagastrin does antagonize secretin-stimulated pepsin but secretin and methacholine do not antagonize one another.

Summary. Secretin-stimulated pepsin secretion from Heidenhain pouches was significantly depressed by concomitant pentagastrin. Pentagastrin by itself was without effect on pouch pepsin. Methacholine, on the other hand, did not antagonize secretin-stimulated pouch pepsin.

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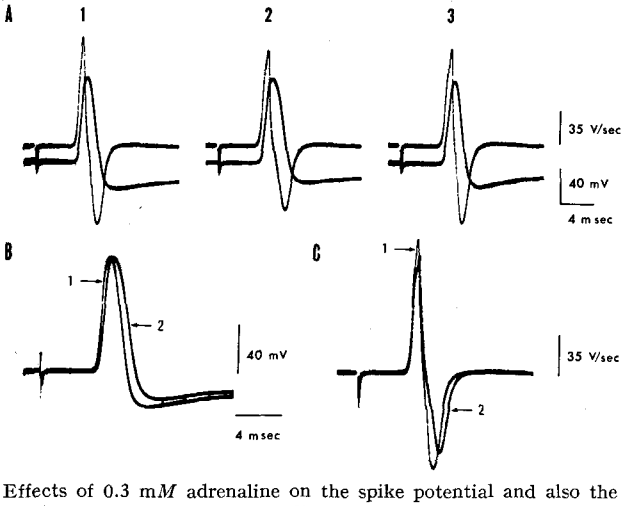
The Direct Action of Adrenaline on the Action Potentials of Bullfrog's (*Rana catesbeiana*) Sympathetic Ganglion Cells

Catecholamines play their roles as chemical transmitters at neuromuscular or interneuronal junctions. It is generally believed that catecholamines released from catecholaminergic neurones act on their target muscle or nerve cells and thereby regulate the excitability (or the resting membrane potential) of these cells. In the case of cardiac muscles, however, catecholamines are able to regulate not only the resting membrane potential but also the shape of the action potential by increasing the plateau amplitude[1,2]. The main effect of catecholamines on the action potential has been explained by an increase of the slow inward current, presumably carried by both calcium and sodium ions[1,2]. Another possible effect of catecholamines was the decrease of potassium conductance[2]. Such direct controls, by catecholamine, of the processes involved in generation of action potentials have not been observed in the nervous system. The present work, however, demonstrated that a catecholamine is indeed able to control directly the generation of action potentials of target nerve cells at interneuronal junctions.



Effects of 0.3 m*M* adrenaline on the spike potential and also the maximum rates of rise and fall of spike potentials in bullfrog's sympathetic ganglion cell. A) Suppression of the peak amplitude of the after-hyperpolarization of action potential and of the maximum rates of rise and fall in the presence of adrenaline. Upper recordings show the maximum rates of rise and fall of action potentials. Lower recordings are action potentials which were produced by applying antidromic stimulations to postganglionic nerve fibres at an interval of 2 sec. These records were taken before (1), 5 min after (2) an application of adrenaline and record 3 was taken 6 min after its withdrawal. B) Action potentials of records 1 and 2 in A) were superimposed in order to clarify the action of adrenaline. Number 1 and 2 are records 1 and 2 in A), respectively. A suppression of the peak amplitude of after-hyperpolarization and a prolongation of the duration of the action potential are clearly seen in 2. C) The maximum rates of rise and fall of action potentials taken from records 1 and 2 in A) were superimposed in order to clarify the effect of adrenaline. Number 1 and 2 are records 1 and 2 in A), respectively. Suppressions of both maximum rates of rise and fall are clearly demonstrated in 2.

The bullfrog's (*Rana catesbeiana*) sympathetic ganglion cells were used throughout. The intracellular recording technique of action potentials are essentially similar to that described elsewhere[3]. The ionic composition of Ringer's solution are as follows: NaCl 112 m*M*, KCl 2 m*M*, $CaCl_2$ 1.8 m*M* and $NaHCO_3$ 2.4 m*M*. Adrenaline bitartrate was used at the concentration of 0.3 m*M* throughout. The experiment was carried out at room temperature (20–23 °C).

When adrenaline was added to perfusate (Ringer's solution), the resting membrane potential of ganglion cells showed no change or slight depolarization, which never exceeded 5 mV, depending on individual cells. Changes in the membrane resistance (input-resistance) of ganglion cell observed in the presence of adrenaline were not detectable even when the membrane was depolarized. In the case of the depolarized membrane by the action of adrenaline, a slight increase of membrane resistance, however, was observed when the membrane potential was fixed at original resting potential level by anodal current. These results indicated that the membrane resistance tended to increase under the effect of adrenaline.

The effect of adrenaline on action potentials was tested by using ganglion cells of which resting membrane potentials showed no depolarization in the presence of adrenaline. Action potentials of these cells were generated by applying repeated antidromic stimulation to postganglionic nerves at intervals of 2 sec. These action potentials produced before, during and after an application of adrenaline were compared with each other, in order to examine the effect of adrenaline and its reversibility. A most significant effect of adrenaline on the action potential was found to be a decrease of the peak amplitude of after-hyperpolarization of action potential, and a maximum rate of fall and also a prolongation of the duration of action potential. These changes were often

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observed without appreciable changes in the amplitude of spike potentials. The other change in action potentials was a decrease of the maximum rate of rise of spike potentials; this change was observed even when the spike peak amplitude was not changed. When an application of adrenaline was sustained, the amplitude of spike potentials was depressed and other changes were also enhanced. All these changes caused by adrenaline were reversible. An example of these experimental results is shown in the Figure.

FATT and KATZ[4] demonstrated that the peak amplitude of an action potential, recorded from the end-plate region of frog skeletal muscle fibres, was suppressed during the activation of the end-plate by transmitter through the shunting effect of ACh on the end-plate membrane. If adrenaline had a similar effect on the synaptic membrane of ganglion cells, the suppression of action potentials observed in the present experiment could be explained in this way. The present results, however, showed that the membrane resistance at resting potential level never decreased but rather tended to increase. Thus, the possibility that the action potential was depressed as a result of the action of adrenaline on the synaptic membrane can be discarded.

The fact that the peak amplitude of after-hyperpolarization and the maximum rate of fall were markedly and reversibly decreased, and also the duration of action potential was prolonged in the presence of adrenaline, clearly demonstrated the decrease in K^+ conductance during the generation of action potential. Similarly, a decrease in the spike potential, particularly the decrease in the maximum rate of rise indicated that the increase in Na^+ conductance responsible for the initiation of spike potentials was also depressed reversibly by the direct action of adrenaline.

It is known that adrenaline might be one of the transmitters which act to depolarize the synaptic membrane of ganglion cells[5]. What is the relation between the action of adrenaline on the synaptic membrane and that on the membrane from where the action potential is actually generated? This question is now under investigation by further experiments. In any case, it can be stressed that the present experimental results indicated that adrenaline is able to control directly the Na^+ and K^+ conductance changes responsible for generation of action potential. Further experiments are needed to study the influence of the action of adrenaline on the Ca^{++} movement during the generation of action potential.

Zusammenfassung. Die direkte Wirkung von Adrenalin auf das Aktionspotential wurde an sympathischen Ganglionzellen des Ochsenfrosches *Rana catesbeiana* studiert. Die Veränderung im Aktionspotential ist reversibel und die Zunahme der Na- und K-Leitfähigkeit wird direkt durch Adrenalin kontrolliert.

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Excitation of Acid and Pepsin Secretion by Cholecystokinin-Pancreozymin in Pavlov and Heidenhain Pouches of the Rat

Cholecystokinin-pancreozymin (CCK-PZ) has the C-terminal tetra peptide sequence in common with gastrin, a peptide sequence that displays all the physiological properties of the parent gastrin molecule[1]. CCK-PZ has been reported to stimulate acid secretion in all species so far studied but its secretory potency seems to be less than that of gastrin[2–7]. The object of previous studies from this laboratory was to determine the gastric secretory response to feeding in conscious rats provided with different pouch preparations and to examine the individual components operating during this kind of natural excitation of the gastric mucosa[8–10]. These studies have mainly concerned the action of gastrin and the vagus nerve per se and the interaction between these two stimuli. The purpose of the present study was to ascertain the role of the vagus nerve for the sensitivity of the acid and pepsin secreting cells to CCK-PZ stimulation. This hormone is likely to take part in the secretory response to feeding, since CCK-PZ is released into the circulation on ingestion of a meal[11,12].

Materials and methods. Female rats of the Sprague-Dawley strain, weighing about 250 g, were prepared with Heidenhain pouches according to Alphin and Lin[13], and Pavlov pouches as described by SVENSSON[8]. The experiments were performed on unanaesthetized rats fasted for 18 h, kept in Bollman cages: the gastric juice was collected in 30 min samples by a perfusion technique[8] and analyzed for HCl by titration against 0.1 *M* NaOH with phenol red as an indicator. The pepsin output was determined by a slight modification of the method of HUNT[14] and expressed in µg, in terms of the activity of a commercial crystalline preparation of pepsin (lot 95 B-1270, Sigma Chemical Co.). Cholecystokinin-pancreozymin (CCK-PZ)[15] was infused via a polyethylene tube inserted in a tail vein, the tube being connected to a motor-driven syringe. Each dose of CCK-PZ was infused for 90 min in stepwise increasing doses until no further significant increase in secretion occurred. The acid and pepsin outputs were calculated from the mean of the last two 30-min periods at each dose.

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