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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*Results.* The dose-response curves for acid and pepsin were established in the dose range 0.03125/2 — 2 μg/h in 6 Pavlov and 6 Heidenhain pouch rats. In the Heidenhain pouches, interdigestive acid secretion was 1.5 ± 0.31 (S.E. of the mean) μeq/30 min, and in the Pavlov pouches 38.8 ± 4.83 μeq/30 min. On infusing CCK-PZ in doses giving maximal responses, the acid secretion rose to 71.7 ± 3.89 μeq/30 min in the Heidenhain pouches and to 95.0 ± 11.41 μeq/30 min in the Pavlov pouches. To make the dose-response curves for the 2 pouch preparations comparable, the interdigestive acid secretion was deducted from the response obtained on stimulation. The maximal response in the individual pouches was referred to as 100%. The Pavlov pouch was more sensitive to CCK-PZ than the Heidenhain pouch (Figure 1). Infusion of supramaximal doses of CCK-PZ was followed by decrease in the secretory rate. Secretion with 2 μg/h was 63.8 ± 6.97 μeq/30 min in the Pavlov pouches, and 43.4 ± 4.72 μeq/30 min with 4 μg/h of CCK-PZ in the Heidenhain pouches.

The interdigestive pepsin secretion was 115 ± 12.7 μg/30 min in the Heidenhain pouches, and 365 ± 36.9 μg/30 min in the Pavlov pouches. CCK-PZ stimulated pepsin secretion in both pouch preparations with a peak of 347 ± 16.0 μg/30 min with 0.25 μg/h in the Heidenhain pouches and 531 ± 52.7 μg/30 min with 0.5 μg/h in the Pavlov pouches, whereafter pepsin secretion declined (Figure 2).

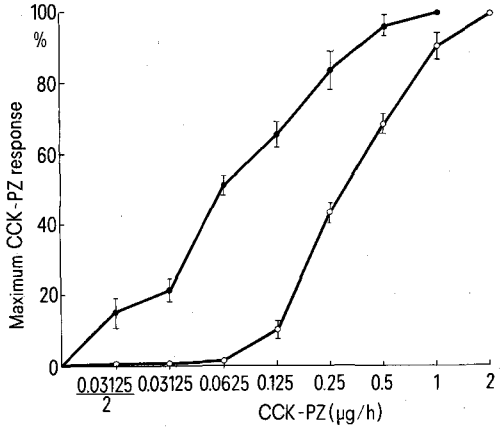


Fig. 1. Acid secretory responses to i.v. infusion of CCK-PZ in rats provided with a Pavlov pouch (●) or a Heidenhain pouch (○). The acid responses are expressed as % of the maximal response to CCK-PZ after deduction of the interdigestive secretion. The mean and S.E. of the mean are calculated from 1 determination in each of 6 rats.

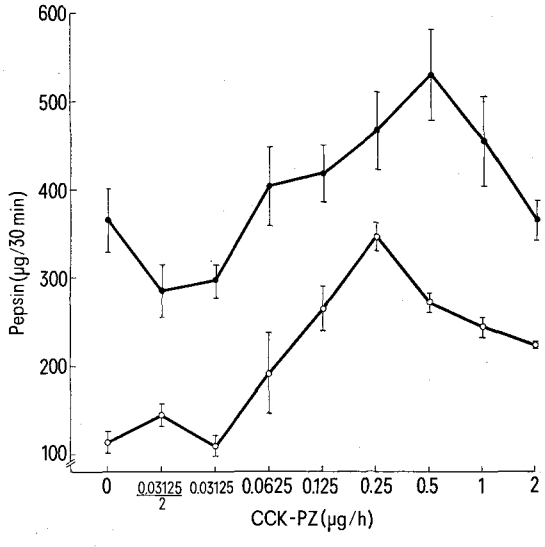


Fig. 2. Pepsin secretory responses in 6 Pavlov (●) or 6 Heidenhain (○) pouch rats in response to i.v. infusion of CCK-PZ. The mean and S.E. of the mean are given.

*Discussion.* The present results demonstrate that CCK-PZ is an effective stimulant of acid secretion in the rat Pavlov and Heidenhain pouch. Furthermore, the vagus nerve facilitates the acid stimulatory potency of CCK-PZ in a similar way as has previously been shown for histamine and gastrin[8,9].

Another similarity between the effect of CCK-PZ and gastrin has been disclosed in the rat, i.e. the property to increase the mobilization of gastric mucosal histamine[16,17]. In addition, the acid secretory response to CCK-PZ can be completely abolished by histamin $H_2$-receptor blockade[17], indicating an implication of gastric mucosal histamine in the mode of action also of CCK-PZ.

In spite of these similarities between CCK-PZ and gastrin, and of the fact that also CCK-PZ is released upon feeding, the significance of this hormone for the gastric secretory response to a meal is still unknown. It should, however, be mentioned that a role for CCK-PZ has been suggested in the dog to sustain the postprandial acid secretion after antrectomy[18]. In the rat, by contrast, the acid response to food is substantially reduced after antrectomy[19].

CCK-PZ has been reported to stimulate pepsin secretion in innervated cat and dog stomach preparations; in the denervated dog stomach, and in man, the reported results are inconsistent[20–23]. In the rat, CCK-PZ exerts a considerable pepsigogue effect in both stomach preparations. On the other hand, gastrin and histamine stimulated pepsin secretion only in the denervated pouch preparation[8,9]. It should, however, be noted that the denervated peptic cells appeared more responsive to CCK-PZ than the innervated ones[24].

*Zusammenfassung.* Nachweis, dass CCK-PZ die Sekretion von Salzsäure und Pepsin in Pavlov- und Heidenhain-Sekretbeuteln stimuliert. Die vagal innervierten Parietalzellen erwiesen sich als empfindlicher für CCK-PZ als die denervierten, während die denervierten Pepsinzellen empfindlicher waren als die innervierten.

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