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NEURAL CONTROL OF SALIVARY MYOEPITHELIAL CELLS

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SUMMARY

1. The pressures in the ducts of the submaxillary, parotid and sublingual glands were recorded in cats under chloralose anaesthesia. A single stimulus applied to the parasympathetic glandular nerve caused a pressure rise, the size of which increased with the initial pressure. This response was abolished by a small dose of atropine.

2. The effect was not due to salivary secretion, since the single stimulus caused salivation only exceptionally. Repetitive stimulation at frequencies too low to evoke secretion could produce summated pressure responses.

3. The single stimulus applied to the chorda tympani was found to cause vasodilatation in the submaxillary gland. This was abolished by a small dose of atropine, together with the pressure rise in the duct. However, repetitive stimulation still caused marked vasodilatation but no pressure response. It was therefore inferred that the pressure rise obtained before atropine was not due to vasodilatation in the gland.

4. It is concluded that the myoepithelial cells of the salivary glands are supplied with a parasympathetic motor innervation which can cause them to contract.

5. Sympathetic stimulation caused no pressure rise when a single stimulus was given but only when repetitive stimulation was used at a frequency approaching that required for secretion.

INTRODUCTION

The nerves of the salivary glands have long been thought to contain not only secretory and vasomotor fibres, but also motor fibres supplying the myoepithelial cells. Schiff (1867) and Gruenhagen (1868) assumed that sympathetic fibres acted on some contractile tissue in the glands, and Unna (1881) suggested that this tissue might be the myoepithelial 'basket cells' described in the parotid gland of the cat by Krause (1865) (quoted by Tamarin, 1966). Experimental evidence to support the view that impulses in the sympathetic nerve may cause a compression in the salivary

glands and expulsion of saliva was brought forward by Eckhard (1869), Mathews (1898), Anrep (1922), Kay (1954, 1955), Coats, Denton, Goding & Wright (1956), Langley & Smith (1959), Travill & Hill (1963) and particularly by Babkin and his co-workers (see Babkin, 1950). In most of these investigations, the conclusion that the sympathetic nerve carries motor fibres was based on experiments showing that sympathetic stimulation caused a flow of saliva especially when the duct system had been filled previously by secretion or by an injection of fluid into the salivary duct. In some glands, such as the parotid of the sheep, the motor response was supposed to be the sole effect of sympathetic stimulation apart from the vascular one. In others secretion also was assumed to occur on sympathetic stimulation, complicating the interpretation of the observations. Nevertheless, the existence of sympathetic motor fibres to the myoepithelial cells of salivary glands is commonly recognized.

A few investigators have concluded that the parasympathetic nerves of the glands carry motor fibres, but this opinion does not seem to be generally accepted. Holzlöhner (1931) and Holzlöhner & Cammann (1934) recorded the rate of salivary flow from the submaxillary gland of the dog using a hot-wire method. On stimulation of the chorda tympani a polyphasic 'tachogram' was obtained, and one component of the curve was attributed to expulsion of saliva from the duct system. However, Maltesos & Weigmann (1939) considered that this curve was polyphasic because the nerve was stimulated at such a high frequency that neuroglandular fatigue occurred—Wedensky inhibition has been demonstrated in submaxillary glands (Wedensky, 1892). Kuntz & Richins (1946), using silver staining in conjunction with denervation studies, concluded that the myoepithelial cells of salivary glands receive parasympathetic fibres only; but when one considers the findings from more refined techniques (see Garrett, 1966*a*, *b*) it is doubtful whether their interpretations were fully justified. Yoshimura, Inoue & Imai (1962) considered that their electron micrographs of submaxillary glands of dogs, after pilocarpine administration, showed contracted myoepithelial cells and they assumed that the cells were supplied by parasympathetic fibres. On the other hand, Travill & Hill (1963), using an enzyme histochemical method as a marker for cell morphology, were of the opinion that adrenaline, but not pilocarpine, contracted myoepithelial cells in the submaxillary gland of mice.

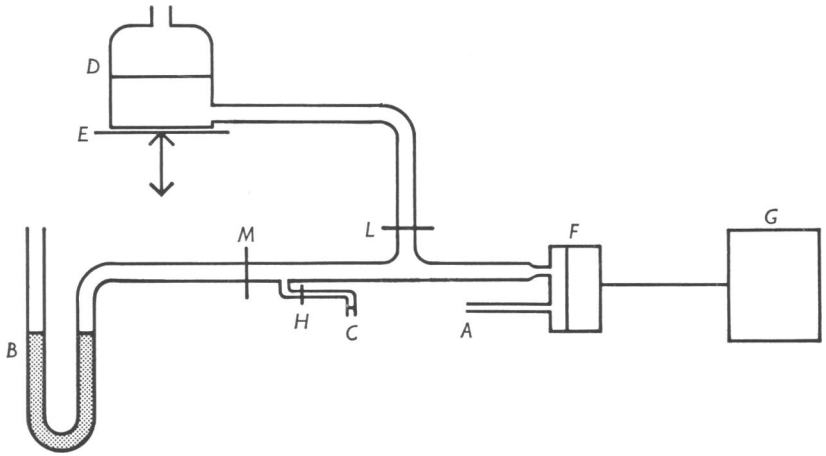
Recent electron microscopical studies have shown that myoepithelial cells in the salivary glands of the cat receive a plentiful *en passant* type of innervation (Garrett, 1966*a*) and denervation studies indicate that some of these nerves are parasympathetic (Garrett, 1966*b*).

In the present experiments pressure rises were recorded in the salivary ducts of cats during electrical stimulation of the sympathetic and para-

sympathetic nerves. Attempts were made to separate the motor, secretory and vascular effects of nerve stimulation. An attempt has also been made to study the effects of nerve stimulation or the intravenous injection of pilocarpine on the electron microscopical appearances of myoepithelial cells.

METHODS

Seventeen cats of both sexes, weighing 3–4 kg, were used. The cats were anaesthetized with chloralose (about 80 mg/kg intravenously after induction with ether). The salivary ducts were exposed and cannulated using glass or polythene cannulae. Text-figure 1 shows the pressure recording system. The cannula was connected via tube *A* to a system consisting of a mercury manometer *B*, an open glass tube *C* placed at the same level as the gland investigated, a pressure bottle *D* containing NaCl solution (0·9 g/100 ml.) on an adjustable



Text-fig. 1. Pressure recording system. *A*, tube connected to salivary cannula; *B*, mercury manometer; *C*, outflow tube to study secretion; *D*, pressure bottle; *E*, table movable in vertical direction; *F*; transducer; *G*, polygraph; *H*, *L* and *M*, clamps.

table *E*, and a strain gauge transducer *F* (Ether Engineering Ltd, Type BP, 15 Mk. 2) operating one channel of a four-channel polygraph *G* (Mingograf 81, Elema-Schönander). The salivary cannula and the polythene tubings connecting it with the pressure bottle and the manometers were filled with saline solution. The equipment made it possible to study either pressures in the gland in a closed system or flow of saliva in an open system. In the former case, after clamping at *H*, a suitable pressure was applied, using the pressure bottle, and the pressure was read on the mercury manometer. The tubings were then clamped at *L* and *M*, and the effect of nerve stimulation or drug injection on the transducer was recorded. To study flow of saliva clamp *H* was removed and clamp *L* opened for a moment to fill the glass tube *C* with saline solution, either only partly, or fully; flow of saliva from the gland on, for example, nerve stimulation could then be observed as movement of the meniscus in the tube, when the flow was very slow, or as drops falling from the opening of the tube.

The chorda-lingual or auriculotemporal nerve (Burgen's method, 1964) or the sympathetic trunk was exposed and cut, and the peripheral stump was stimulated electrically by

single stimuli or repetitively, usually at low frequencies. Square wave pulses of supramaximal strength (6–10 V) and a duration of 2 msec were used.

To study the flow of blood through the submaxillary gland the external jugular vein was cannulated after ligation of all branches, except the main one from the gland, and intravenous injection of heparin. The blood from the gland passed a photo-tube counter which operated an ordinate recorder writing on a smoked drum, and was returned to the cat at intervals by way of a cannula in a femoral vein.

Five cats were used in the electron microscopical studies; the first three cats were taken at the end of duct pressure experiments and two additional animals were studied. In each of the animals both chorda-lingual nerves and cervical sympathetic trunks were sectioned before the final investigation. In the first three animals the submaxillary glands were fixed by a bilateral carotid perfusion of 1·5 % glutaraldehyde, pH 7·4, during stimulation of the chorda-lingual, on one side only, at 10/sec. The unstimulated gland was used as a control. In the third of these experiments the stimulation of the nerve was performed after a closed injection of 200 μg of eserine sulphate down the duct of the test gland. The glands were removed, finely transected, immersed in the fixative at 0–4° C for 1½ hr, washed in phosphate buffered sucrose at 0–4° C overnight and further treated with buffered osmium tetroxide (1 g/100 ml.) at 0–4° C for 1 hr before subsequent embedding in Araldite. In the last two cats control tissue was taken from one gland before stimulation and immediately divided into two; one part was fixed in glutaraldehyde and further treated as above, the other part was fixed only in the 1 % osmium tetroxide mixture for 2 hr before embedding in Araldite. An intravenous injection of pilocarpine was then made; one cat was given 0·5 mg/kg, the other 1·0 mg/kg. When the secretion was flowing profusely tissue was taken from the other test gland and immediately fixed in glutaraldehyde or osmium tetroxide alone and treated similarly to the control tissues. Ultra-thin sections were viewed in an E.M. 6B (AEI) electron microscope after staining with lead (Reynolds, 1963).

RESULTS

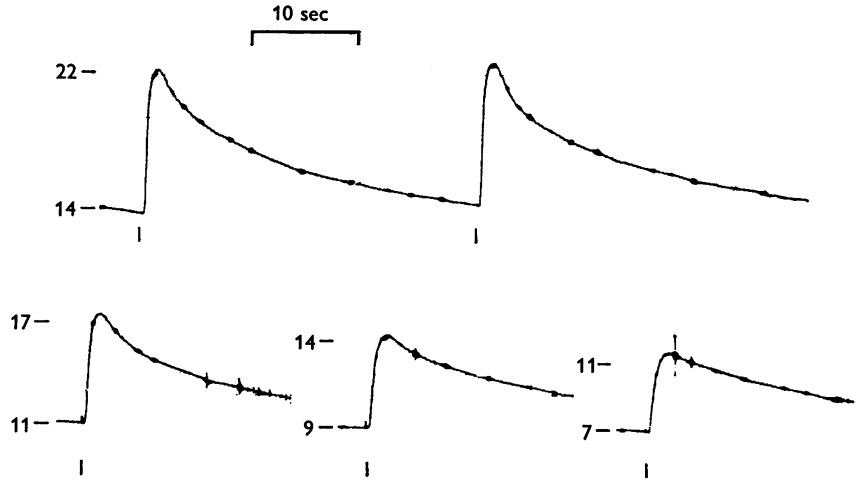
Pressure changes on nerve stimulation

It should be noted that after the introduction of a head of pressure and closure of the system, the pressure tended to decrease slowly in the absence of any stimulation. The slope of this decrease was variable but was only very gradual when the pressure was about 15 mm Hg or less. Observations were made on fifteen submaxillary, four sublingual and three parotid glands.

Submaxillary glands

Parasympathetic stimulation. The classical work by Ludwig (1851) showed that secretion evoked by chorda stimulation can induce a high pressure in a salivary duct connected to a manometer. The first problem of the present investigation, therefore, was to find out whether nerve stimulation can cause a change in pressure which is not accompanied by, or due to, secretion. This proved possible in the case of the parasympathetic innervation when it was found that pressure increases occurred at stimulation frequencies which were too low to cause secretion. When flow of saliva was studied in the open system single stimuli applied to the

chorda-lingual nerve caused secretion in only one submaxillary gland out of the fifteen investigated. In the remaining glands the lowest frequencies causing secretion were 0·5 stimuli/min (1 cat), 1/min (1), 2/min (2), 6/min (5), 12/min (3) and 30/min (2). When the nerve was stimulated at rates below the secretory threshold a pressure rise could invariably be recorded in the closed system. Each stimulus always caused a rise in pressure, which started after a latency of less than 0·5 sec, rapidly reached a maximum and gradually decreased. Further stimuli applied when the pressure had returned to its original level caused identical responses; except that when the preparation had rested for some time the first response was often somewhat smaller than the subsequent ones. It seems reasonable to attribute these rises in pressure to contractions of myoepithelial cells, since these responses could be obtained at stimulation rates which were usually far below those required for secretion.



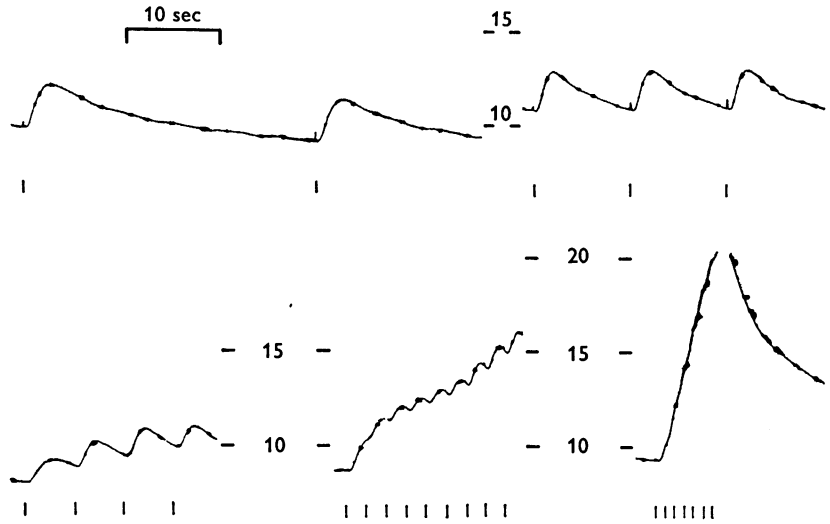
Text-fig. 2. Submaxillary gland. Chorda stimulation at 2/min. Upper records: reproducible effect at similar initial pressures. Lower records: effects of lowering the initial pressure. Horizontal mark: 10 sec. Vertical marks: stimuli applied. The figures give pressures in mm Hg.

The magnitude of the pressure change was dependent on the initial pressure in the system. In the upper part of Text-fig. 2 two responses to single stimuli are shown. Starting from a level of about 14 mm Hg the pressure rose each time to about 22 mm Hg. Below this the effect of lowering the initial pressure is shown. It can be seen that the size of the response increases with the pressure. In eight glands, in which a series of pressures was tried, maximal responses were obtained at initial pressures of 12–27 mm Hg, and the responses varied between 3 and 13 mm Hg

(Table 1). When the basic pressures were further raised the responses were first maintained but at high pressures, for instance above 30 mm Hg, they became smaller. Occasionally very small responses were obtained in the beginning of an experiment. It was then found favourable to increase the pressure to a level of 20–30 mm Hg for a few minutes, then to lower it to the desired level; alternatively, the duct system could be filled in advance by eliciting secretion for a brief period.

TABLE 1. Maximal pressure responses (mm Hg) recorded in submaxillary ducts on application of single stimuli to the chorda

Exp. no. ...	1	2	3	4	5	6	7	8
Initial pressure	16	18	18	18	14	16	27	12
Response	13	7	5	12	9	3	7	5



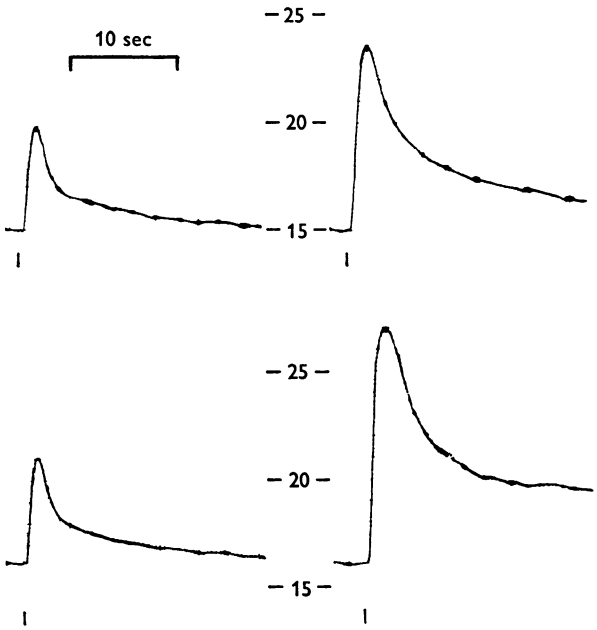
Text-fig. 3. Submaxillary gland. Chorda stimulation at increasing frequencies: 2/min, 6/min, 12/min, 30/min, 60/min. Marks as in Text-fig. 2.

Effects which could be attributed to contractions of myoepithelial cells were ordinarily not seen in the open system. In two glands, however, a very small forward movement of the meniscus in the outflow tube could be observed following each stimulus even when the rate of stimulation was extremely low; the meniscus each time then withdrew to its original position.

When the rate of stimulation was increased, so as not to allow sufficient time for the pressure to return to the base level, summation of the responses seemed to occur. This is illustrated in Text-fig. 3. Separate responses were still obtained at stimulation frequencies of 6 stimuli/min.

At a rate of 12/min, when no secretion had been seen in the open system, the responses started to merge and the general pressure rose. At 30/min a secretory stimulation rate was reached, and the curve rose steeply. Pressure rises corresponding to the stimuli could still be discerned but it could not be decided whether increased rate of secretion at each stimulus now contributed to the individual small rises. At 60/min a fairly smooth, steeply rising curve was obtained.

Eserine sulphate, 0·1 mg/kg intravenously, was found to increase the pressure responses to parasympathetic stimulation, as shown in Text-fig. 4. Before eserine the single stimulus applied to the chorda-lingual nerve



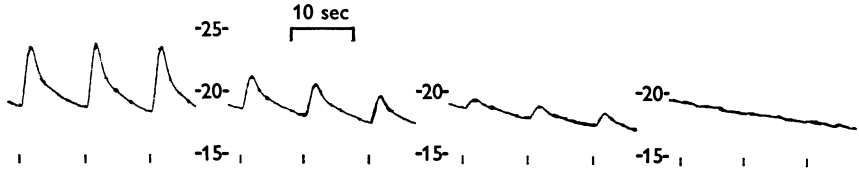
Text-fig. 4. Submaxillary gland. Single stimuli applied to the chorda, at two slightly different pressure levels, before (left) and after 0·1 mg eserine sulphate/kg intravenously (right). The upper right record was 15 min, the lower right about 25 min after eserine. Marks as in Text-fig. 2.

caused a rise of about 5 mm Hg, and 15 min after injection of eserine the response from the same initial pressure was 8·5 mm Hg; later it was as large as 11 mm Hg. Responses of this magnitude had never been obtained in this experiment before eserine, and since it was found that after eserine the single stimulus caused secretion it seems likely that the large responses were in part due to secretion.

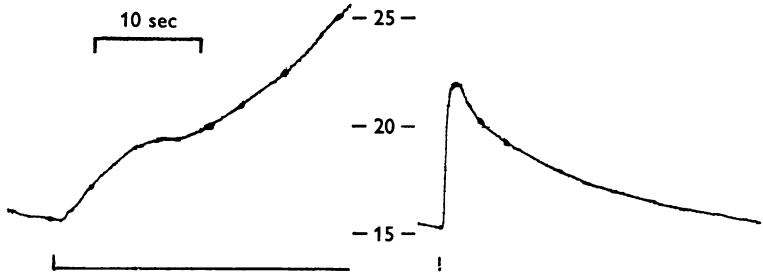
Very small doses of atropine sulphate, 10 μg/kg intravenously, were found to reduce markedly the pressure responses to chorda stimulation.

In Text-fig. 5 this dose was given twice, and the pressure rises were greatly diminished. After an additional dose of 20 μg/kg the responses to the single stimuli were abolished. In Text-fig. 5 small cyclic variations in the base pressure occurred; this was seen in some but not in most experiments.

Sympathetic stimulation. Pressure rises in response to single stimuli applied to the sympathetic trunk were never obtained. Repetitive stimulation was needed to raise the pressure, and the frequency causing this effect was usually of the same order as that required for secretion.



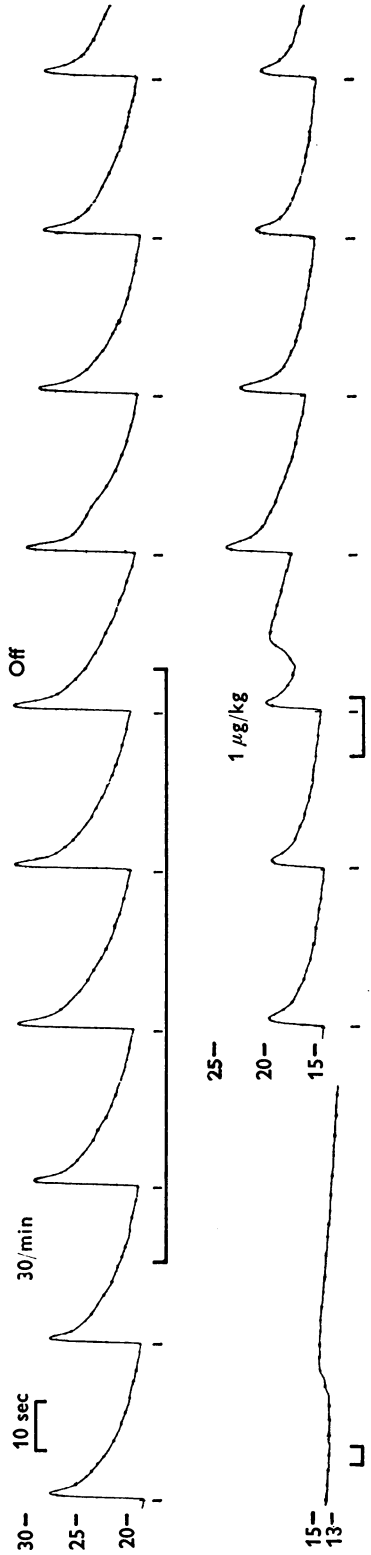
Text-fig. 5. Submaxillary gland. Chorda stimulation at 6/min. Between the sections of the tracing there are intervals of about 5 min. In the beginning of these atropine sulphate was injected intravenously, 10 μg/kg in the two first intervals and 20 μg/kg in the third interval. Marks as in Text-fig. 2.



Text-fig. 6. Submaxillary gland. Stimulation of the sympathetic trunk at 30/min (left record) for the period marked underneath caused a two-phase pressure rise. For comparison the effect of a single chorda stimulus is shown to the right.

Observations of the type shown in Text-fig. 6 might suggest that some contraction of the myoepithelial cells took place during repetitive sympathetic stimulation. In this cat the stimulation rate 120/min seemed near threshold for secretion; once no secretion was elicited, later on, a trace of saliva was produced late during a stimulation period. In the closed system the pressure started to rise after stimulation for about 1 sec (after 2 or 3 stimuli) and reached a maximum; the curve then showed a secondary rise. It may be that the first effect was due to myoepithelial contraction, the second to secretion.

The observations of Text-fig. 7 were made on the gland in which a single stimulus applied to the chorda had a perceptible secretory effect, but the



Text-fig. 7. Submaxillary gland. Upper record: pressure responses to chorda stimulation at 2/min and (for the period marked by the horizontal mark) additional sympathetic stimulation at 30/min. Lower record: intravenous injection of 1 μg adrenaline/kg made twice (at the marks), first alone, then during chorda stimulation.

pressure rises obtained were no doubt mainly due to contraction and not secretion. Additional sympathetic stimulation at 30/min markedly increased the pressure responses to chorda stimulation. Sympathetic stimulation alone did not increase the pressure, and in the open system even 120/min was devoid of secretory effect. The increase in the pressure responses to chorda stimulation which was caused by sympathetic stimulation at 30/min did not appear to be due to 'augmented secretion', for additional sympathetic stimulation did not increase the secretory chorda effect in the open system; in fact, it decreased it slightly, probably because of vasoconstriction. Similarly, adrenaline (1 μg/kg intravenously) increased the pressure responses to chorda stimulation, but no secretion was seen in the open system with this dose of adrenaline; it did not augment the secretory chorda effect and it did have a very small pressure-raising effect of its own. These observations possibly lend some support to the view that the myoepithelial cells can be contracted by adrenergic sympathetic nerves.

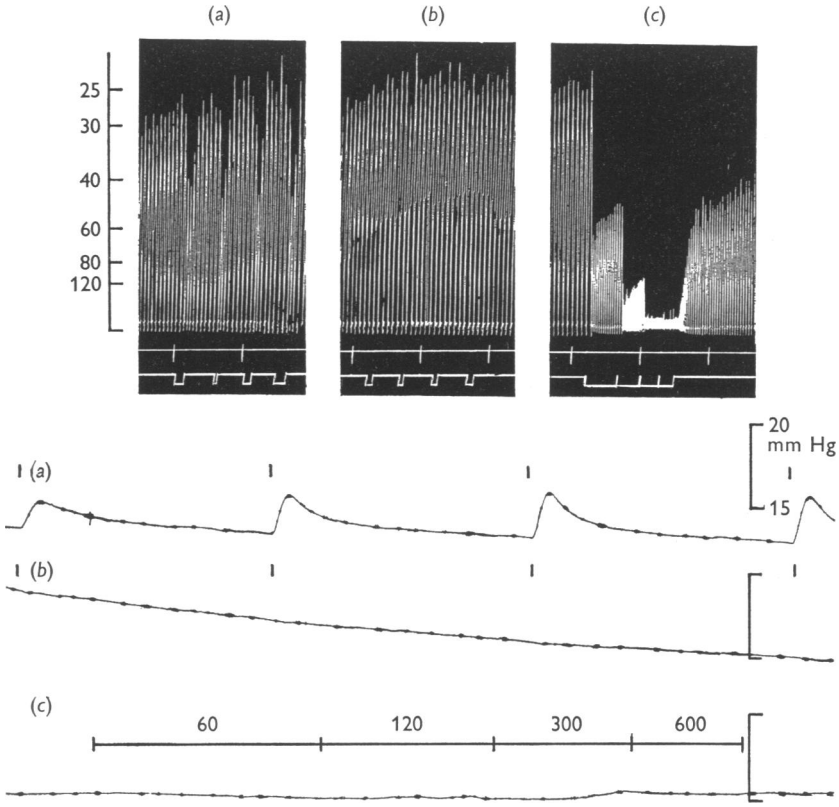
Pressure responses and glandular blood flow. Stimulation of the nerves of the submaxillary gland causes vascular effects; therefore it was necessary to test whether the pressure rises described above were due to sudden changes in blood content of the gland. In three experiments, which yielded similar results, pressure in the duct system and blood flow through the gland were recorded simultaneously. Results from one of the experiments are shown in Text-fig. 8. Single stimuli applied to the chorda-lingual nerve at intervals of 30 sec caused a marked vasodilatation and a pressure rise in the duct system for each stimulus. Atropine sulphate (50 μg/kg intravenously) quickly abolished the vascular and duct pressure responses to single stimuli but with stimulation at 60 and 120/min an increasing vasodilatation occurred without any pressure effect being elicited. At 300/min the vasodilatation was very great, and the pressure started to rise slowly to a level much lower than that produced by single stimuli before atropine. Some small secretion might have occurred at this rate; but at 600/min there was no further rise in pressure.

About 1 hr after injection of atropine some recovery of the vasodilator responses could be seen; even single stimuli caused a small vasodilatation, but no change of pressure in the ducts. Frequencies of 60/min produced a very marked vasodilatation but still no pressure response.

When the sympathetic trunk was stimulated at a low rate, e.g. 2/min, a small vasoconstriction was obtained for each stimulus. Even stimulation at rates which produced very marked vasoconstriction was without pressure effect as long as secretion was not elicited.

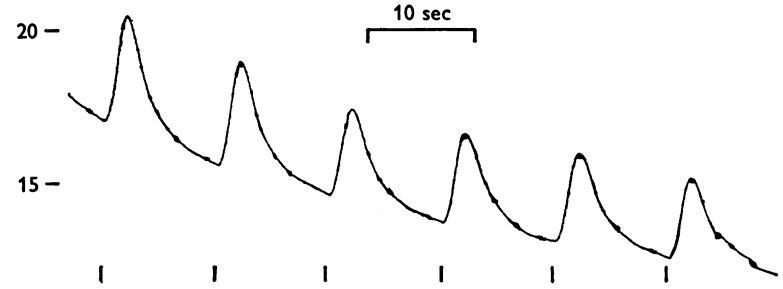
Sublingual and parotid glands

Essentially similar duct pressure results were obtained as in the submaxillary glands. Sympathetic stimulation at increasing frequency caused no rise in pressure in the duct system until secretion was evoked. Parasympathetic stimulation at a rate too low to cause secretion produced a pressure rise for each single stimulus. The pressure responses attained, however, were always smaller than those seen in the submaxillary gland. The highest value reached in a parotid gland was 3·5 mm Hg; a sub-

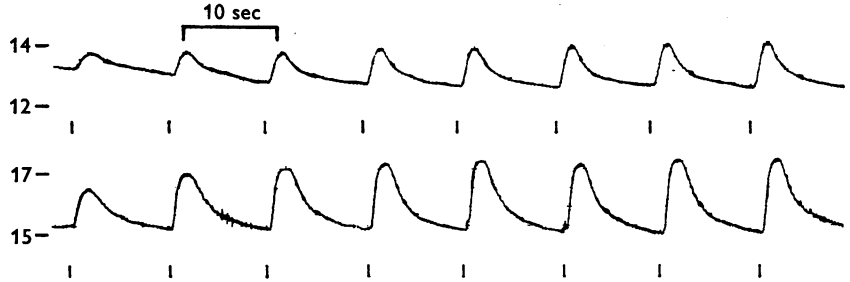


Text-fig. 8. Submaxillary gland. Three sections of a kymograph tracing showing blood flow through the gland (drops/min) and, underneath, the three corresponding polygraph records of the pressure in the duct system. Below blood flow in the kymograph tracing is shown time in min and signal to mark stimulation of the chorda. Four chorda stimuli at intervals of 30 sec are first shown to produce vasodilatation and duct pressure rises (*a*). Repeated 4 min after 50 μg atropine sulphate/kg intravenously they produced neither vascular nor duct pressure responses (*b*). Chorda stimulation at 60/min, 120/min, 300/min and 600/min caused marked vasodilatation but had no, or only very small pressure effect in the ducts (*c*).

maxillary gland of the same cat produced a maximal rise of 7 mm Hg. Text-fig. 9 shows pressure responses in this parotid gland at different initial pressures when the auriculotemporal nerve was stimulated at a rate of 6/min. Secretion was not obtained until the rate had been increased to 120/min. In one sublingual gland a rise of 2·5 mm Hg was noted; the maximum of the corresponding submaxillary gland was 9 mm Hg. In the



Text-fig. 9. Parotid gland. Stimulation of the auriculotemporal nerve at 6/min. Marks as in Text-fig. 2. The pressure was continuously falling and the responses to nerve stimulation decreased correspondingly.



Text-fig. 10. Sublingual gland. Two periods of chorda stimulation at 6/min and two different levels of initial pressure. Marks as in Text-fig. 2.

sublingual gland a gradual increase could often be seen in the responses to chorda-lingual stimulation even at frequencies which did not induce a frank secretion; this was probably due to the continuous filling of the duct system because of the spontaneous secretion characteristic of this gland (Emmelin, 1953). Such an effect at two different pressure levels is demonstrated in Text-fig. 10.

Structural changes in the myoepithelial cells after stimulation

The assessment of the electron microscopical appearances of myoepithelial cells, for evidence of contraction or not, has proved to be much more difficult than anticipated. There are no fixed points from which to

judge any change. Indentation of a parenchymal surface cannot be taken as a definite indication of contraction, for myoepithelial cells are seen at the bifurcations between intercalary ducts and acini and between branchings of acini, thus it is not possible to be certain that what one is seeing in straight electron micrographs is not part of such a bifurcation. Many indentations of acinar cells have been seen in every control gland (as in Pl. 1*B*).

Other features such as the appearances of the myofilaments or the corrugations on the outer surfaces of the cells have been closely scrutinized. A bulging outwards on the basal sides of myoepithelial cells (as in Pl. 1*A*) was not uncommon and may possibly be evidence of relaxation. General assessment in the lower ranges of magnification seems to provide most information. This was always easier with tissues fixed only in osmium tetroxide, probably due to the fact that there is less general staining than after glutaraldehyde and thus more contrast between the cells.

No pattern of difference was detectable between the myoepithelial cells in the test and control glands from the three cats in which the tissues had been fixed during chorda-lingual stimulation on one side. In the two cats from which tissues were fixed before or during pilocarpine stimulation outward bulgings of the myoepithelial cells were less evident in the test gland than in the control gland but apart from this no pattern of difference could be detected.

Although a continuous stimulation was applied to the test glands in an attempt to keep the myoepithelial cells in a state of contraction while being fixed, there is no evidence that these cells are capable of maintaining a contraction and, even if they can, there is no guarantee that the fixatives used were capable of keeping them in a contracted state. Absence of positive evidence of contraction from electron microscopical assessment of ultra-thin sections does not necessarily imply that there were no structural differences between the myoepithelial cells in the test and control tissues but it is envisaged that three-dimensional models from serial sections would be necessary to settle this.

DISCUSSION

The present observations indicate that stimulation of the parasympathetic nerves to the three main salivary glands of the cat excites contractile elements in the glands so causing the pressure to rise in the duct system. This motor activation can be separated from the secretory and the vasodilator activities of the parasympathetic glandular nerves. Secretion also causes a big rise in the pressure when the salivary ducts are connected to a closed system. But in order to elicit secretion repeated stimuli, sometimes as frequent as 30/min, are required, whereas a pressure rise is regularly

obtained by a single stimulus applied to the parasympathetic nerve. The secretory thresholds described here are slightly lower than those found by Beznák & Farkas (1937); among eleven submaxillary glands studied, only one responded with secretion from a single stimulus and the most common secretory threshold was 48/min.

Somewhat surprisingly it was found that single stimuli to the parasympathetic nerve caused a marked vasodilatation and even more surprisingly that this response was very sensitive to atropine. Ever since the days of Heidenhain (1872) the view has been generally held that the vasodilator response is much more resistant to atropine than the secretory response, but in the present study the vasodilator response to single stimuli had an atropine sensitivity almost as large as that of the duct pressure response elicited by single stimuli and the secretory response evoked by a moderate rate of repetitive stimulation. The possibility that the increases in duct pressure, occurring in the absence of secretion, were the mechanical effects of vasodilatation in the gland had to be considered since single stimuli caused both a vasodilatation and a duct pressure rise and both effects were abolished by a small dose of atropine. However, after atropine it was found that repetitive stimulation produced a very marked vasodilatation without a trace of pressure rise in the ducts and so the above possibility became untenable. That such a dilatation can be obtained without any concomitant secretion, after atropine, is in agreement with the work of Heidenhain (1872). The fact that atropine abolishes both the contractile effect and vasodilatation in response to single stimuli, whereas after repetitive firing vasodilatation can be induced although the contractile effect remains absent, seems to suggest that some difference in atropine sensitivity between the two effectors does exist. Alternatively, it may indicate that the mechanism responsible for vasodilatation in the two cases is not the same, but this problem is beyond the scope of the present investigation.

The finding that the pronounced vasoconstriction, elicited by sympathetic stimulation, did not affect the pressure in the duct system adds further support to the view that the duct pressure responses to single parasympathetic stimuli were not caused by vascular effects.

No pressure rises were noticed after single stimuli applied to the sympathetic nerves, and on the whole any motor effects of sympathetic stimulation seemed difficult to separate from secretion. Earlier investigations (summarized by Babkin, 1950, and Emmelin, 1967) have, however, produced more convincing evidence than the present one of the existence of specific motor fibres in the sympathetic nerves of salivary glands. It is possible that repetitive firing is needed to activate the contractile cells by way of the sympathetic nerves. If this be so then the contractile elements

of the salivary glands would be another example of synergism and not antagonism between the two divisions of the autonomic nervous system; this is true for at least some secretory cells also, but not for the vessels.

The contractile structures of the salivary glands are generally assumed to be the myoepithelial cells (see Babkin, 1950; Tandler, 1965; Tamarin, 1966). Electron microscopical investigations by Garrett (1966*a*, *b*) showed that these cells are well supplied with nerves, some of which are probably cholinergic. The present work indicates that such nerves have an excitatory action on the myoepithelial cells.

The present investigation gives no information about the normal function of myoepithelial cells and one can only speculate about it. If a parasympathetic axon supplies both myoepithelial and secretory cells along its course, as seems possible from electron microscopical studies (Garrett, 1966*a*, *b*), and if one considers that a single stimulus will contract the myoepithelial cells but that multiple stimuli are necessary for secretion, then it would appear that the myoepithelial cells are contracted before a parasympathetic secretion. This could be in order to expel pre-existing saliva, to reduce the duct volume or alternatively to act as a support for the underlying structures against a distension which the secretion might otherwise induce. On the other hand, if the motor and secretory axons are separate then there may be elective expression of saliva when required. The experiments show at any rate, that motor effects can be separated from secretory effects in the salivary glands. In this respect the salivary glands resemble the mammary glands, in which oxytocin is known to produce ejection of milk but not secretion.

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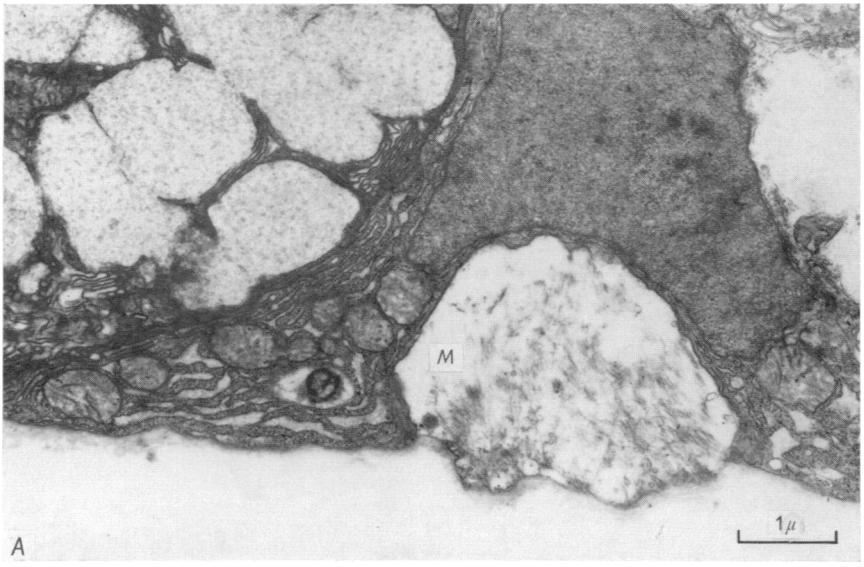
EXPLANATION OF PLATE

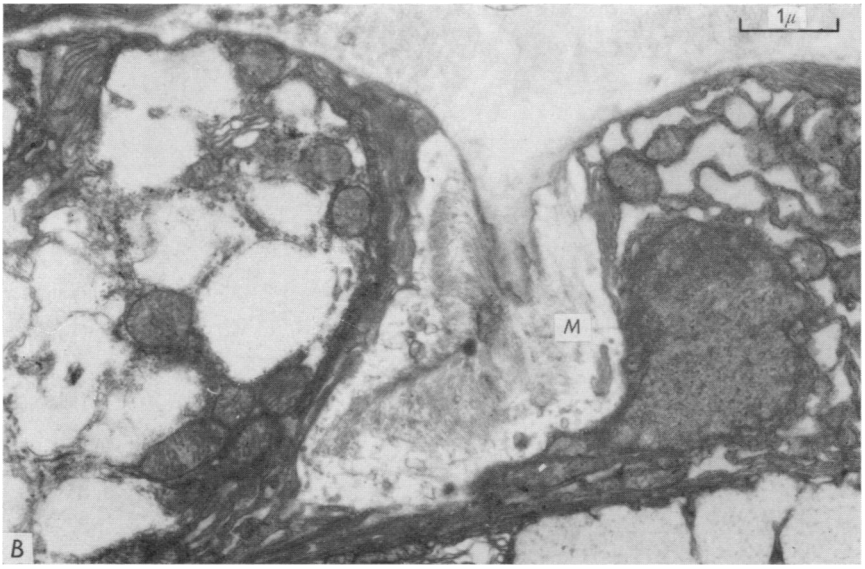
PLATE 1

Electron micrographs of a normal, control, unstimulated, submaxillary gland of a cat, fixed by osmium tetroxide.

A. A myoepithelial cell process (*M*) with its basal surface bulging outwards. This may be due to relaxation.

B. A myoepithelial cell process (*M*) from the same gland, indenting an acinus. This could easily be taken as an indication of contraction.





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