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FURTHER OBSERVATIONS ON THE SECRETION BY THE SUBMAXILLARY GLAND OF THE CAT FOLLOWING SYMPATHETIC STIMULATION.

By J. SECKER.

(*From the Physiological Department, University of Durham College of Medicine, Newcastle-upon-Tyne.*)

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In an earlier publication [Secker, 1934*a*] observations were recorded from which the conclusion was drawn that the sympathetic mechanism controlling secretion of saliva by the submaxillary gland in the cat was cholinergic.

The principal points in the evidence may be summarized thus:

(1) Saliva secreted in response to stimulation of the cervical sympathetic nerve or to injected adrenaline resembled the saliva secreted in response to chorda stimulation in containing a powerful depressor substance [Secker, 1934*b*]. This depressor substance is inactivated by boiling the saliva with dilute alkali or by previous administration of atropine. After atropine, the depression of the blood-pressure is replaced by a rise in pressure.

(2) Eserine potentiates, and atropine annuls, the secretory response to either stimulus.

Feldberg and Guimarãis [1935] have confirmed the presence of the depressor substance in saliva, but show that in several respects it does not behave as acetylcholine when more critical tests are applied. They conclude that the depressor substance does not correspond in its properties with any chemically identified depressant. Further investigations into the properties of the depressor substance in saliva lead me to the conclusion that while this substance has certain properties in common with acetylcholine it cannot be identified with that ester of choline.

These workers also criticize the interpretation given for the observed effects of eserine and atropine and state that their observations give no support to my suggestion that the sympathetic supply of the salivary gland is in any sense cholinergic. They state that eserine, even in moderate

doses, often produces a spontaneous salivary secretion of the "parasympathetic" type and that when eserine has not this delayed effect by itself, it usually has no significant effect on the secretory response to sympathetic stimulation.

The present communication records further observations in support of my suggestion. The method used in the experiments was that described in the earlier paper [Secker, 1934*a*], except that in certain of the experiments salivary secretion was measured as rate of flow along a 1-mm. tube instead of by the method of drop recording.

Stimulation of the cervical sympathetic nerve. I have recorded the fact that there is a wide variation in the sensitivity of the submaxillary gland in cats to faradization of the sympathetic nerve. In no experiment has the response approached in magnitude that following stimulation of the chorda and in several experiments electrical stimulation has failed to evoke any secretion. But administration of eserine salicylate (0·3 mg./kg.), has not in any of the present series of experiments resulted in a spontaneous secretion of saliva. In all experiments an interval of 15–20 min. was allowed before the nerve was stimulated. Further, the secretion in response to stimulation of the sympathetic ceased within 1 min. of the cessation of the stimulus.

In Table I the results of a group of experiments are given as salivary flow in mm. along a 1-mm. tube following faradization of the nerve for 15 sec., commencing from a position of rest of at least 2 min. duration, recorded in 15 sec. intervals.

TABLE I. Salivary flow due to stimulation of the cervical sympathetic nerve.

Cat No.	Before eserine	After eserine
44	0, 4, 2, 1, 0 (7)	6, 7, 4, 1, 0 (18)
45	0, 1, 0 (1)	9, 4, 2, 0 (15)
47	3, 1, 0 (4)	43, 7, 1, 0 (51)
50	0, 0 (0)	8, 0 (8)
52	20, 11, 6, 2 (39)	39, 18, 3, 1, 1 (62)

Stimulation by adrenaline. In these experiments (Table II) the usual procedure of drop recording was carried out and the response in each case is to 0·15 mg. adrenaline injected into the femoral vein.

TABLE II. Salivary flow due to injected adrenaline.

Cat No.	27	34	37	38	39	40	55	59	63	70	71	72	75
Before eserine	1	2	6	0	2	5	3	4	2	5	5	2	8
After eserine	5	6	9	3	14	12	12	6	5	13	8	6	11

The results recorded in Tables I and II show a definite potentiation by eserine of the secretory response to stimulation of the cervical

sympathetic nerve or to adrenaline. The potentiation gradually diminishes with repeated stimulation or repeated doses of adrenaline, the falling off being more rapid in response to nerve stimulation. The decline of the potentiation due to eserine is shown in the following experiment in which adrenaline was given repeatedly at intervals of 10 min. before and after eserine. The figures represent salivary flow recorded in drops:

Before eserine: 18, 19.

After eserine: 30, 31, 28, 26, 25, 24.

These records of new experiments confirm my previous findings and are not in agreement with the statements of Feldberg and Guimarāis, or of Cattell, Wolff and Clark [1934], that eserine has no significant effect on the secretory response to sympathetic stimulation.

The effect of variations in blood-pressure. Eserine causes a fall in arterial blood-pressure and even after an interval of 15–20 min. the pressure commonly fails to return to its original level. It is suggested by Feldberg and Guimarāis that this fall in blood-pressure may mask the secretory action of eserine, and then the small rise of pressure caused by sympathetic stimulation may unmask it again and so stimulate a potentiation of the secretory response to sympathetic impulses. Feldberg and Guimarāis state that "under such conditions a small rise of pressure caused by an injection of saline may start a secretion; and an apparent potentiation of the secretion following a powerfully pressor dose of adrenaline cannot be accorded the significance which Secker attributes to it".

That this is not the true explanation of the results obtained seems evident from the examination of records of long experiments in which the pressure is continually varying from different causes, yet no secretion occurs unless a definite stimulus is applied. Many of my records show the increased secretion on stimulation of the nerve without any appreciable pressor accompaniment to the secretion, and the injection of normal saline solution, commonly accompanied by a slight pressor effect, does not provoke any secretion.

Fig. 1, part of a record obtained after the injection of eserine, illustrates these points. At each of the points *A* and *B* 2 c.c. saline were injected, the rise in pressure at *A* being due to the washing in of a small amount of adrenaline remaining in the cannula. At *C*, 0·5 c.c. saliva in 3 c.c. saline and at *D*, 2 c.c. saline were injected. During the resulting low pressure the sympathetic nerve was stimulated in the interval *E*–*F* and secretion occurred. The secretion ceased while the pressure was still below the level shown at the beginning of the record. The sensitivity of

the sympathetic nerve in this particular experiment was so low that no secretion was obtained on electrical stimulation.

In support of their suggestion that the results obtained may be due to unmasking of the secretory action of eserine, Feldberg and Guimarāis note that the opposite gland may secrete on stimulation of one cervical sympathetic nerve in an eserinized animal. This observation cannot be accepted in support of their suggestion since it has been demonstrated by Babkin, Alley and Stavraky [1932] that stimulation of one chorda tympani nerve causes secretion by the contralateral gland. The probable explanation in both cases is that some chemical agent has been liberated and transported by the blood stream.

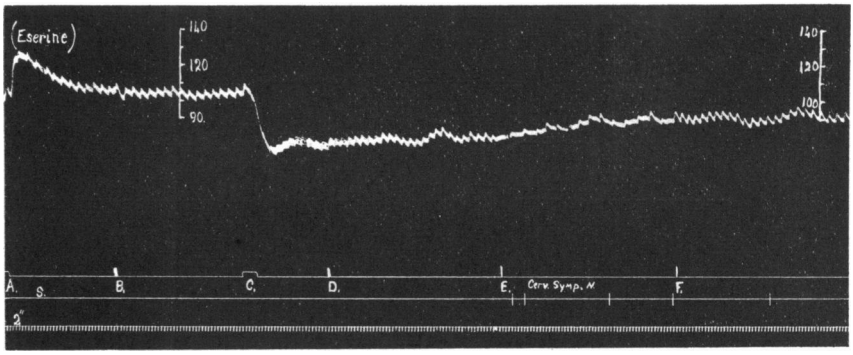

Fig. 1. Salivary secretion after eserine in relation to changes in blood-pressure. For description see text. In this and subsequent tracings S = salivary flow in drops. Time record in 2 sec. intervals.

The action of atropine. In the previous paper it was shown that atropine abolishes the secretory response to sympathetic stimulation. There is an error in the statement of the dose of atropine used in those experiments [Secker, 1934*a*, p. 295], the dose given was 20 mg. to a 3-kg. cat and not 20 mg./kg. as stated.

Feldberg and Guimarāis report that atropine in the small dose sufficient to abolish a strong secretory response to chorda stimulation causes at most a slight diminution of a much weaker sympathetic effect. This is true, but the sympathetic effect is nevertheless abolished by somewhat larger doses. In the present series of experiments the doses of atropine employed have been much smaller than in the previous series; usually a dose of 1 mg. has been repeated until the effect of sympathetic stimulation has been annulled. The amount of atropine required per kg. has varied in different cats, but in every case the dose required has been

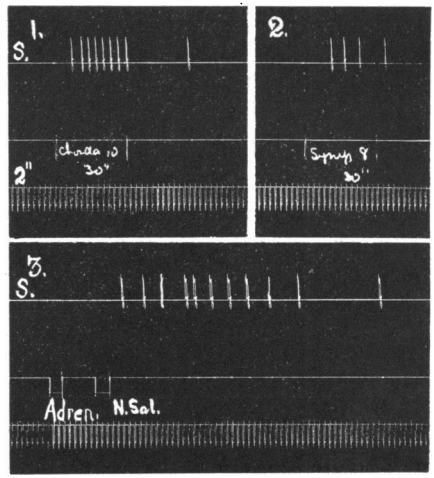

Fig. 2. Salivary secretion. 1, stimulation of chorda. 2, stimulation of cervical sympathetic nerve. 3, injection of 0·15 mg. adrenaline.

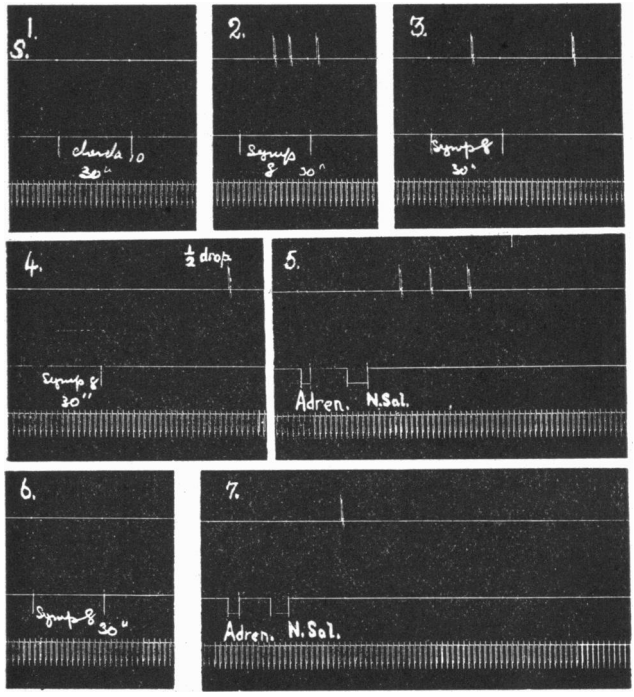

Fig. 3. Salivary secretion after increasing doses of atropine. For description see text.

considerably in excess of that needed to abolish the effects of stimulation of the chorda. As the dose of atropine is increased there is a graded diminution of the secretory response to stimulation of the cervical sympathetic nerve or to injected adrenaline until complete paralysis has occurred. The result of one experiment of this type (cat. 81, 3 kg.) is given in Figs. 2 and 3. The secretory responses to (1) stimulation of the chorda; (2) stimulation of the cervical sympathetic nerve; (3) intravenous injection of 0·15 mg. adrenaline are shown in Fig. 2. The effect of increasing doses of atropine on these responses is shown in Fig. 3. Tracing (1) shows the effect of 1 mg. atropine sulphate on the result of stimulation of the chorda. Tracings (2, 3, 4 and 6) show the effect of sympathetic stimulation after 1, 2, 5 and 11 mg. of atropine respectively. Tracings 5 and 7 show the effect of 0·15 mg. adrenaline after 6 and 11 mg. of atropine. In this experiment it was necessary to give 15 mg. of atropine sulphate (5 mg./kg.) before complete annulment of the secretory response to adrenaline was obtained.

Relationship between secretory and pressor responses. As the secretion is gradually paralysed with increasing doses of atropine there is no corresponding diminution of the slight pressor effect following stimulation of the nerve or of the pressor effect of the adrenaline. It is interesting to note that in certain experiments, particularly when chloralose was used as the anæsthetic, a pressor effect has resulted from stimulation of the nerve even when no secretion has occurred no matter what strength of electrical stimulus was used. This fact is interesting in view of the work of Cattell, Wolff and Clark [1934], these workers having recorded the contractions of the denervated nictitating membrane in cats during sympathetic stimulation of the contralateral submaxillary gland. Fig. 4 shows the pressor effect of stimulation of the sympathetic nerve unaccompanied by secretion in a cat untreated with any drug other than the anæsthetic (chloralose).

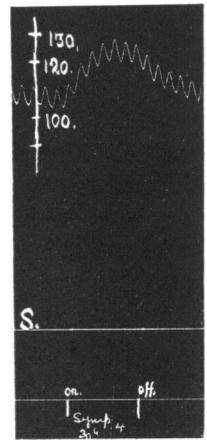

Fig. 4. Pressor effect following stimulation of cervical sympathetic nerve. Note absence of salivary flow.

Summary.

1. Further observations of the potentiating effect of eserine on the secretory response by the salivary gland to sympathetic nerve stimulation and to injected adrenaline are recorded, confirming previous findings.

2. The increased secretory response is shown to be independent of pressor changes.

3. The annulment of the secretory response by atropine necessitates the use of larger doses than those required to annul the effect of chorda stimulation.

I wish to express my thanks to Prof. Burns for his continued interest in the progress of this work. I have also to acknowledge, with thanks, that the expenses of this work were defrayed by a grant from the Medical Research Council.

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