THE EFFECT OF PRESSURE WITHIN THE SUBMANDIBULAR GLAND ON THE GLANDULAR BLOOD CIRCULATION

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As indicated in our previous papers^{1,2,3)}, there are baro-receptors in the submandibular gland of the dog which respond to pressure change within the gland. The impulses from the baro-receptors are transmitted through the afferent fibers in the chorda tympanic nerve. However, the physiologic role of these pressure afferents from the gland is still unknown.

In the present experiment, the electro-salivogram and venous blood flow of the submandibular gland while increasing the pressure within the gland were recorded in order to evaluate the physiologic function of these afferents.

METHODS

Sixteen mongrel adult dogs were used in this experiment. The animals were anesthetized with Nembutal-soda (30 mg/Kg, intravenously). A schematic outline of the experimental procedure is shown in FIG. 1 and 2.

A polyethylene tube of 0.8 mm in diameter was inserted into the excretory duct of the submandibular gland. Prior to the actual experiment, the tube and excretory duct of the gland were filled with saliva by electrical stimulation of the chorda tympanic nerve. Air bubbles in the tube were removed through a T-shaped stopcock. A tube filled with 0.9% saline solution was connected to an electric manometer via the T-shaped stopcock to measure the pressure within the gland. Back-pressure was applied to the duct by a small rubber bulb, and the pressure curve was recorded on a pen-writing oscillograph.

For measurement of the blood-flow from the gland, all branches of the internal maxillary vein were ligated except the branch from the submandibular gland. After injection of Heparin Novo (500 units/Kg) into the vein, a small polyethylene tube with 1 mm diameter was inserted into the internal maxillary vein. Venous blood drops from the cannula were recorded through an electronic drop-counter by the pen-writing oscillograph.

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For the record of the electro-salivogram a Ag-AgCl₂ wire electrode (0.5 mm in diameter) was inserted into the duct about 2.0 cm through the T-shaped tube as illustrated in FIG. 2. Another Ag-AgCl₂ plate electrode was placed on the surface of the glandular body.

RESULTS

A. *Effect of back-pressure on blood-flow of the gland.* Blood out-flow of the glandular branch of the internal maxillary vein in the dog ranged from 4 to

FIG. 1. Schematic diagram of recording apparatus of glandular blood flow. A, Amplifier; B, Bulb; C, Cannula; D, Duct of submandibular gland; Dr, Drop counter; M, Manometer; R, Recorder; S, Submandibular gland; T, Transducer; V₁, V. jugularis ext.; V₂, V. maxill. ext.; V₃, V. maxill. int.; V₄, V. auricularis magna; V₅, Vena from the submandibular gland.

FIG. 2. Schematic diagram of apparatus recording electrogram. A, Amplifier; B, Bulb; D, Duct of the submandibular gland; E, Electrode; M, Manometer; R, Recorder; S, Submandibular gland; T, Transducer.

44 drops per minute in the resting state of the hcmolateral submandibular gland. These rates corresponded to 0.05-0.33 grams of blood per minute per gram gland weight, and the mean value was 0.21 grams per minute per gram gland weight (g/min/g gland) as indicated in TABLE 1.

When a back-pressure above 40 mmHg was applied to the submandibular gland, the venous blood-flow from the gland was 1.5-2 times as much as at the resting state. This blood-flow increasing response was obtained in seven among the nine examined dogs. The individual threshold of this response was 40 to 60 mmHg. A typical sample record of the blood-flow increasing response is shown in FIG. 3. The upper trace in the figure is a record of drops of blood and the lower is the curve of the pressure applied to the gland. In this case, blood-flow was 0.5 drops/sec. (0.9 g/min/g gland) at the resting

TABLE 1. Venous blood flow rate of the resting submandibular gland.

Dog No.	Sex	B. W. (Kg)	side	Drops/min	blood (g)/min/g'and (g)
2	F	6.8	right	30	0.29
9	F	5.5	left	36	0.33
10	M	7.5	right	44	0.33
11	F	8.5	right	36	0.25
12	F	6.5	right	14	0.18
13	F	5.0	right	14	0.13
14	F	7.5	right	4	0.05
			left	7	0.08
15	M	7.0	right	14	0.23
16	F	5.2	right	9	0.15
			left	18	0.26

FIG. 3. Increase of venous blood outflow of the submandibular gland elicited by back-pressure in the duct.

state. When the back-pressure given to the gland was kept at 45 mmHg level for 30 seconds, the glandular blood-flow was increased from 0.5 drops/sec. to 1 drop/sec. (1.8 g/min/g gland). The latency of the response was about 10

FIG. 4. Increased response of ipsilateral glandular blood flow. Back-pressure applied only to the left gland; Blood flow increased only in the left side.

FIG. 5. Effects of dissection of sympathetic and chorda tympanic nerve on blood flow increasing response. A, Control; B, After dissection of the cervical sympathetic nerve; C, After dissection of the chorda tympanic nerve.

seconds. After release of the pressure application to the gland, the blood-flow gradually decreased and returned to the control level within about 20 seconds.

When the pressure application to the gland was repeated, the amount of the blood-flow increasing response gradually diminished after several trials and even disappeared in some cases. However, this blood-flow accelerating response of the gland was induced only in the ipsilateral submandibular gland. As shown in FIG. 4, the blood-flow of the right submandibular gland was not accelerated by pressure application to the left glandular duct, although the blood flow-rate of the left submandibular gland was increased from 8 to 12 drops/min. This fact suggests that the blood-flow accelerating response to the pressure increase in the gland is not a systemic reaction but a local response only in the stimulated gland.

To estimate whether this response is induced by a neural reflex or by a humoral factor like bradykinin, the effects of dissection of the cervical sympathetic nerve and of the submandibular branch of the chorda tympanic nerve on the blood-flow accelerating response of the gland were studied. As shown in FIG. 5, the blood-flow accelerating response of the ipsilateral submandibular gland was not disturbed at all even after dissection of the cervical sympathetic nerve. However, after successive dissection of the submandibular branch of the chorda tympanic nerve, the venous blood out-flow acceleration was com-

FIG. 6. Resting potential and electrosalivogram of the submandibular gland. A, Resting potential; B, Response induced by electrical stimulation of the chorda tympanic nerve; C, Effect of back-pressure applied to the duct.

pletely abolished. These facts imply that the nerve fibers in the chorda tympani might play a part in regard to the blood-flow accelerating response.

B. *Effect of back-pressure on the electro-salivogram.* An electro-salivogram of the submandibular gland was recorded under back-pressure application to the duct in seven dogs. The resting potentials of the submandibular glands ranged from -30 mV to $+10$ mV. In the electro-salivogram, as shown in FIG. 6, an upward deflection of the curve means an increase in positivity of the glandular inside to the glandular surface. The resting potential of the sample record was $+6$ mV (FIG. 6, A), and typical electro-salivographic activity during salivation induced by electrical stimulation of the chorda tympanic nerve is shown in FIG. 6, B. However, the application of 40 mmHg back-pressure to the gland during 30 seconds induced only about 2 mV of negative deflection of the electrogram, and after release of the pressure stimulus a positive deflection of about 2 mV was observed (FIG. 6, C).

DISCUSSION

The blood-flow rate of the submandibular gland of the dog has been reported by several workers⁴⁻⁸. CLAUDE BERNARD⁴ revealed that the gland of the dog in its resting condition received 3-4 ml of blood in a minute. An almost similar value was reported by LANGLEY⁵. However, according to BABKIN⁶ the blood-flow of the resting gland was 1.5 ml per minue in the non-anesthetized dog. ANREP and CANNAN⁷ also described that the venous out-flow of the submandibular gland was 1.44 ml/min in the dog.

ANOCHIN, GOLDBERG and SAMARINA⁸ reported that the character of the anesthetics used in the experiment might strongly affect the volume of blood-flow from the gland and that the mean value was 1.16 ml/min in ether anesthesia. Since the blood-flow of the gland is altered by the character of anesthetics, narcotic condition, blood pressure and weight of the gland, the glandular blood-flow rate must be calculated by ml/min/gland weight (g). According to ANOCHIN et al.⁸, the venous out-flow from the resting submandibular gland of the dog was 0.13-0.37 ml/min/g (mean value was 0.27 ml/min/g). These values coincide well with our present data ranging from 0.05 to 0.33 g/min/g. (0.21 g/min/g). However, the blood flow rate was somewhat different between the right and left gland. This might be attributed to a difference of the venous distribution in the glands and to a slight difference in the surgical manipulation for the insertion of the cannula into the vein.

In 1936, GALPERIN⁹ found that the salivary secretion elicited by pilocarpine injection was affected through the blocking of the chorda tympanic nerve with a 0.2% novocain application, and he suggested that the normal innervated gland might be regulated by the impulses from the intero-ceptive receptors

within the gland. HAJYOTIN¹⁰⁾ also reported that when CO₂ gas or nicotine was added to the perfusing solution of the gland, the blood pressure and respiration was reflectorily changed, and he speculated that this reflex was elicited by excitation of intero-ceptive receptors in the gland. Besides the above described reflexes, our present results reveal that an increase of pressure within the submandibular gland also produces a blood-flow increasing response of the gland.

This response localized only in the stimulated gland, and it was abolished after dissection of the ipsilateral chorda tympanic nerve. Therefore, this blood-flow increasing response is a real reflex and is induced by an increase of pressure within the gland.

KAWAMURA and FUNAKOSHI^{12,3)} have detected the physiological evidence of the existence of baro-receptors in the submandibular gland of the dog, and they indicated that the afferent impulses from the receptors were transmitted through the chorda tympanic nerve. Therefore, the blood-flow increasing response described in the present experiments may refer to the baro-receptors in the gland.

CLAUDE BERNARD⁴⁾ found that vasodilation of the submandibular gland was produced together with salivary secretion by electrical stimulation of the chorda tympanic nerve, and it is widely believed that both secretory and vasodilator nerve fibers are contained in the chorda tympanic nerve.

On the other hand, HILTON and LEWIS^{11,12)} reported that vasodilation in the submandibular gland elicited by chorda tympanic stimulation was attributed to the "stable vasodilator material" which was released from the secretory cells in the gland, and they concluded that there were no vasodilator fibers in the nerves to the submandibular gland. Contrary to their findings, recently BHOOLA, MORLEY, SCHACHTER and SMAJE¹³⁾ pointed out that the latency and pattern of vasodilation produced by chorda tympanic stimulation or application of acetylcholine differed from that of vasodilation induced by bradykinin in saliva, and they postulated that their results well support the view for true vasodilator nerve fibers in the chorda tympanic nerve. The blood-flow increasing response indicated in our present experiment had a longer latency and prolonged after-effect. We, therefore, assume that this effect is due to a slow effective vasodilator material like bradykinin.

These facts suggest that increasing the pressure in the submandibular gland might stimulate the baro-receptors in the gland. The afferent impulses from the receptors are transmitted to the reflex center in some part of the bulb through the chorda tympanic nerve. The efferent impulses to the gland facilitate the release of some vasodilator chemical material from the glandular cells to increase the glandular blood-flow. Since the electro-salivogram during this response was not facilitated, this blood-flow increasing response has no direct effect on the secretory process of the cells, but might be important for

the recovery process of the secretory cells after excitation.

SUMMARY

In the present experiment, the physiologic role of the baro-receptive information from the submandibular gland was studied in the dog. Back-pressure was applied to the unilateral submandibular duct of the anesthetized dog. The pressure-curve and venous out-flow from the submandibular gland and the electro-salivogram of the gland were recorded simultaneously.

Venous out-flow from the gland was distinctly increased by a back-pressure application of 40-60 mmHg to the duct of the gland. However, the electro-salivogram was not distinctly affected by this procedure. This blood-flow increasing response was elicited only in the ipsilateral gland and not in the contralateral side. The blood-flow increasing response was completely abolished by dissection of the ipsilateral chorda tympanica nerve, but not by dissection of the cervical sympathetic nerve to the gland.

The present results imply that baro-receptors in the submandibular gland of the dog play some important physiologic role in regulating the blood supply of the gland, and also suggest that the response has a possibility to promote the recovery process of the activated cells.

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