THE "MEMORY" OF SALIVARY GLAND CELLS

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In experiments on dogs with a chronic fistual of the submandibular salivary gland intravenous or subcutaneous injection of pilocarpine at intervals of a few days was accompanied by a gradual increase in the volume of saliva, reaching a maximum after 5 injections. Retention of the "trace" of the action of pilocarpine was observed also in experiments on a dog with vago-sympathetic anastomosis and subsequent parasympathetic denervation of the gland.

KEY WORDS: salivary gland; pilocarpine; trace reaction; denervation of the gland; vago-sympathetic anastomosis.

The content of various substances in pilocarpine-induced saliva was determined in previous experiments [6] on dogs with a chronic fistual of the submandibular salivary gland under various conditions of its innervation. No importance at that time was attached to the fact that in order to obtain the required secretion background it was necessary to increase the dose initially and later to reduce it. It could be postulated, however, that a "trace" of previous injection of pilocarpine remained in the cells of the gland.

The object of this investigation was to study the characteristics of the response of the gland cells to repeated injections of pilocarpine.

EXPERIMENTAL METHOD

Experiments were carried out on 4 dogs with a chronic fistual of the submandibular (and sublingual) salivary gland. In one of these dogs (No. 4) a vago-sympathetic anastomosis was formed beforehand on the side of the exteriorized gland duct. The preganglionic fibers of the vagus nerve after this operation grew toward the cells of the superior cervical sympathetic ganglion, as was proved by subcutaenous injection of apomorphine (salivation, despite injection of atropine, ocular signs) [5, 6]. The operation of parasympathetic denervation of the gland was then performed. However, reliable data on the effect of repeated injections of pilocarpine could be obtained only after the state of increased excitability of the gland cells had become established at a constant level after the parasympathetic denervation. The level of excitability of the gland was determined by its repsonse to apomorphine. The drug was injected in doses including 3 or 4 acts of vomiting. It was assumed that the impulse activity reaching the gland via the anastomosis (no atropine was injected) was approximately the same. As was expected, the secretion of saliva gradually increased, and after 40-50 days it was established at an almost constant level. Only then (53 days after denervation) were the experiments begun on the dog with injection of pilocarpine. Pilocarpine hydrochloride (0.25% solution) was injected intravenously into dogs Nos. 1, 2, and 4 and initially subcutaneously into dog No. 3, followed by an intravenous injection 65 days later. The volume of saliva was measured every 3 min starting from the time of injection of pilocarpine and continuing for 36 min.

EXPERIMENTAL RESULTS AND DISCUSSION

As Table 1 shows, the volume of saliva secreted in response to injection of pilocarpine increased by 57 and 65% respectively in dogs Nos. 1 and 2 by the time of the 5th injection. Having reached a maximum the volume of saliva then fell a little. Similar results were obtained with dog No. 3. The increase in the

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TABLE 1. Dynamics of Saliva Secretion during Repeated Intravenous Injections of Pilocarpine

Parameters	Dog No. 1, weight 17.5 kg, dose 0.14 mg/kg						Dog No. 2, weight 15.2 kg, dose 0.08 mg/kg				
	experiments						experiments				
	1	2	3	4	5	6	1	3	4	5	7
Intervals between injections (in days)	—	5	4	4	5	6	—	4	4	4	6
Volume of saliva during whole expt. (in ml)	23,0	29,0	29,9	31,4	36,1	30,7	15,2	15,7	19,2	25,2	21,7
Increase in vol. (in %)				36,5	57,0				30,0	65,7	
Volume of saliva in first portion (in ml)	5,0	4,1	3,0	4,4	5,1	3,6	2,7	3,6	4,4	4,8	6,4

TABLE 2. Dynamics of Secretion of Saliva during Repeated Intravenous Injections of Pilocarpine after Denervation of the Gland (vagosympathetic anastomosis followed by parasympathetic denervation; dog No. 4, weight 9.2 kg, dose 0.135 mg/kg)

Parameters	Experiments					
	1	2	3	4	5	6
Intervals between injections (in days)	—	2	3	4	4	4
Volume of saliva during whole expt. (in ml)	18,6	21,1	23,8	21,1	20,7	21,7
Increase in volume (in %)			27,9			
Volume of saliva in first portion (in ml)	3,6	4,2	4,2	4,1	4,1	4,0

volume of saliva observed during repeated injections of pilocarpine could be the result of the accumulation of this drug. Special series of experiments, however, do not confirm this hypothesis of the cumulative properties of pilocarpine. The writers observed earlier that biscuits induce a larger secretion of saliva against the background of previous pilocarpine secretion [6]. It might be expected that feeding a dog with biscuits on the day after injection of pilocarpine should be accompanied (if any pilocarpine still remained in the animal) by increased production of saliva, but this was not observed. Next, after a series of experiments in which pilocarpine was injected at intervals of a few days, it was injected on two successive days. If the pilocarpine had accumulated, it would have induced a greater increase in production of saliva, but this also was not observed.

In the experiments on dog No. 4 with vago-sympathetic anastomosis followed by parasympathetic denervation (Table 2) results similar to those described above were obtained. It will be remembered that after parasympathetic denervation the excitability of the gland cells increases in accordance with the law of increased sensitivity of denervation structures, and for this reason the experiments began after the level of excitability had become stabilized (see the Experimental Method section). The experiments on dog No. 4 showed that changes in the reactivity of the gland cells in response to repeated injections of pilocarpine could take place irrespective of its effect on the cholinergic structures of the brain. Presumably other gland structures can also preserve "traces" of the action of pilocarpine.

These experiments suggest that in response to injection of pilocarpine "traces" of the biochemical changes induced by it may be preserved in the cells of the salivary gland. Gland cells responding to the first injection of pilocarpine as to a novel stimulus become capable of "recognizing" pilocarpine and "remembering" that they have previously been subjected to its influence. Repeated effects thus give rise to a more marked response of the gland.

The possibility of "trace" formation in various tissues of lower and higher organisms is well-known in physiology. They include posttetanic potentiation, the postexcitation decrement, presynaptic inhibition [2, 3, 8], the formation of connections resembling those of conditioned reflexes, and "training" of the most primitive objects [9, 10]. The possible role of changes in RNA in "memorizing" is shown by experiments on planarians and also on rats and mice [1, 4, 7].

If the development of memory is an evolutionary process, "remembering" is presumably a feature to some extent of other cells of both lower and higher organisms. An example of this is the ability of the salivary gland cells to "remember" information brought via the blood stream following the injection of pilocarpine.

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