REACTIONS OF THE DECENTRALIZED AND DENERVATED (PRE- AND POSTGANGLIONIC) HUMAN PAROTID GLAND TO REFLEX STIMULATION, PILOCARPINE, PROSERINE AND ATROPINE

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During the investigation of the secretion of saliva in patients with lesions at various levels in the central and peripheral nervous systems, we discovered several types of reaction to cholinergic (cholinomimetic and cholinolytic) and anticholinesterase (proserine) agents, and also to unconditioned reflex stimulation.

METHOD

We used Krasnogorskii-Yushchenko salivary irrigating capsules. Reflex salivation was studied by means of the application of 30 ml of 0.5% citric acid (at the rate of 10 ml per minute). The pilocarpine secretion was elicited by the subcutaneous injection of 0.5 ml of 1% pilocarpine, and the proserine secretion by the injection of 0.5-1.2 ml of a 0.05-0.1% solution of proserine. Atropine was injected subcutaneously in doses of from 0.3 to 1.2 ml of a 0.1% solution.

RESULTS

1. Decentralization (cortical) of the parotid gland arises in hemiplegias of central origin. Since 1933 we have investigated about 2000 such cases. On the side of the paralysis there is an increase in the reflex, pilocarpine and proserine secretions as a result of the freeing of the bulbar center and humoral automatism from the restraining influence of the cerebral hemisphers* (Fig. 1).

On the side of the lesion, on the other hand, a fall in the reflex, pilocarpine and proserine secretion of saliva takes place. After decentralization of the gland, atropine preserves its cholinolytic function, blocking the reflex and humoral secretion of both glands. However, since on the side of the paralysis there is an increase in both humoral and reflex secretion, its asymmetry is preserved after atropine too, although atropine depresses to a slightly greater degree the secretion of the gland on the same side as the lesion (Table 1).

2. Bulbar, nuclear decentralization arises in the presence of lesions situated in the region of the pons and medulla, when there is depression or suppression of the function of the salivatory centers (over 100 such patients investigated), together with an increase in the pilocarpine and proserine secretion (humoral automatism). Atropine depresses the secretion of both glands but does not correct the asymmetry (Table 2).

Strictly speaking, in nuclear lesions it is not decentralization of the gland which occurs, but denervation, due to interruption of the peripheral neuron or, more correctly, the nucleus of this neuron. In the paralysis

* In contrast to man, after decortication of one hemisphere in animals there is no asymmetry of secretion to humoral stimuli (E. A. Asratyan [1], T. M. Mal'tseva, and I. K. Zhmakin [4]). This fact shows that in man the opposite hemisphere fulfils a restraining function in relation to the humoral secretion of the contralateral gland.

TABLE 1

Patient A., Age 52 yr. Right-Sided Hemiparesis after Thrombosis of the Left Middle Cerebral Artery

Date of investigation	Character of secretion	Volume of secretion (in ml)	
		on the same side as the lesion	on the side of the paralysis
1959			
11/V	Reflex secretion	7.0	13.9
12/VIII	Spontaneous secretion during 15 minutes	1.0	2.5
	Secretion to proserine (1.2 ml of 0.05% solution)	10.0	15.0
19/VIII	Secretion to injection of pilocarpine (0.5 ml of a 1% solution)	25.2	30.4
21/VIII	Secretion to injection of atropine (0.5 ml of a 0.1% solution) with pilocarpine (0.5 ml of a 1% solution)	6.0	8.2

TABLE 2

Patient G., Age 50 yr. Thrombosis of the Right Posterior Cerebellar Artery (Wallenberg-Zakharenlo Syndrome)

Date of investigation	Character of secretion	Volume of secretion (in ml)	
		on the same side as the lesion	on the opposite side
1959			
21/VII	Spontaneous secretion	0.0	0.0
21/VII	Reflex secretion	2.1	4.8
18/VIII	Secretion to proserine (1.5 ml of a 0.05% solution)	2.7	1.4
20/VIII	Secretion to pilocarpine (0.5 ml of a 1% solution)	8.2	5.6
26/VIII	Secretion to injection of atropine (0.5 ml of a 0.1% solution) with pilocarpine (0.5 ml of a 1% solution)	2.3	1.7

TABLE 3

Patient B., Age 31 yr. Trauma to the Base of the Skull, Fracture of the Pyramid on the Left Side. Postganglionic Denervation

Date of investigation	Character of secretion	Volume of secretion (in ml)	
		on the same side as the lesion	on the intact side
1947			
18/VI	Spontaneous secretion	0.0	0.0
	Reflex secretion	0.0	3.5
24/VI	Secretion to pilocarpine (0.5 ml of a 1% solution)	9.1	7.4
17/IX	Secreation to injection of atropine (1.0 ml of 0.1% solution) with pilocarpine (0.5 ml)	262.6	3.0
1948			
15/V	Secretion to injection of atropine (1.0 ml of a 0.1% solution)	236.6	2.0
29/VI	Secretion to injection of proserine (1 ml of a 1% solution)	1.5	4.2

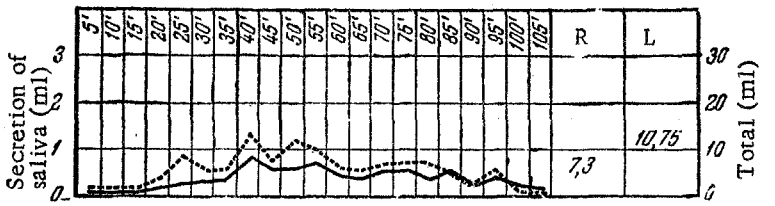

Fig. 1. Changes in secretion of saliva under the influence of injection of 0.5 c.c. of pilocarpine. ——— Secretion on the right; . . . . . secretion on the left. Patient Ol'kh-aya N. I.

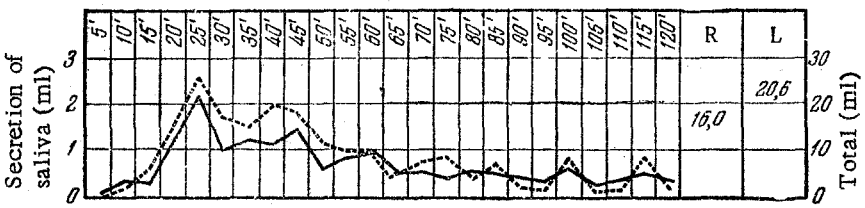

Fig. 2. Changes in the secretion of saliva under the influence of injection of 0.5 ml of 1% pilocarpine and 0.75 ml of proserine in a dilution of 1:1000. ——— Secretion on the right; . . . . . secretion on the left.

alternans of Millard-Gubler, Foville, Raymond-Cestan and Babinski-Nageotte (5 or more patients in each group were investigated), with lesions of the salivatory nuclei and their tracts, we have a combination of types 1 and 2, i.e., decentralization on the side of the paralysis and denervation on the side of the lesion. The pilocarpine secretion in these cases was increased on the side of denervation (Fig. 2).

3. Preganglionic denervation arises after interruption of the gustatory-secretory arc in an area beginning with the salvatory nucleus and the emerging roots of the glossopharyngeal nerve, then forming the tympanic plexus, and continuing further in the form of the nerve of Jacobson and the lesser superficial petrosal nerve to the otic ganglion. Denervation usually arises after a fracture of the base of the skull and of the pyramid of the temporal bone. Because of the interruption of the reflex arc, reflex secretion is absent or diminished, but later the humoral, pilocarpine secretion of saliva is increased. The proserine secretion is preserved as a result of the integrity of the postganglionic neuron. Atropine preserves its function of inhibitor of the secretory process, without affecting the character of the symmetry. Fourteen patients were investigated.

4. Postganglionic denervation also occurs after fracture of the base of the skull and of the pyramid of the temporal bone at the entry to the fallopian aqueduct, but in those cases in which, as a result of the extent of the trauma, the otic ganglion is also affected and the integrity of both the preganglionic and the postganglionic neuron is disturbed at the level of the otic ganglion – the secretory branch of the auriculotemporal nerve. Reflex salivation is suppressed, the secretion to pilocarpine is increased and that to proserine is diminished, and an atropine paradox develops, i.e., an extraordinarily intensive and prolonged secretion of saliva from the denervated gland in response to atropine (Table 3). Seven patients were tested.

We give below a scheme of the relationships appearing in all forms of denervation and decentralization (Table 4).

This scheme may be used for the differential diagnosis of the level of a lesion, especially with damage to the pre- and postganglionic neurons, for an indication of any distinctive clinical signs of these lesions is to be found in the literature.

In conclusion we may dwell on the role of proserine as an indicator in the determination of the level of denervation. Whereas pilocarpine reveals the presence of humoral automatism in all forms of decentralization and denervation, proserine reacts selectively depending on the integrity or disturbance of the pre- and postganglionic neurons, namely by producing an optimal secretory effect with a lesion of the preganglionic neuron and a less marked effect with a lesion of the postganglionic neuron. Proserine thus acts as an indicator of a disturbance

TABLE 4

Reaction Types of the Decentralized and Denervated Parotid Gland in Man

Serial No.	Types of reaction	Reflex secretion		Pilocarpine secretion		Proserine secretion		Reaction to atropine	
		on the side of the lesion	on the opposite side	on the side of the lesion	on the opposite side	on the side of the lesion	on the opposite side	on the side of the lesion	on the opposite side
1	Decentralization (cerebral hemispheres)	Decreased	Increased	Decreased	Increased	Decreased	Increased	Preserved	
2	Bulbar nuclear decentralization	Sharply decreased	Normal or decreased	Increased	Normal	Increased	Normal	Preserved	
3	Preganglionic denervation	Depressed	Normal	Increased	Normal	Uniform		Preserved	
4	Postganglionic denervation	Absent	Normal	Increased	Normal	Decreased	Increased	Atropine paradox	Preserved

Note. In decentralization (1) the opposite side is termed the side of paralysis.

Fig. 3. Changes in the secretion of saliva under the influence of injection of 0.5 ml of 1% pilocarpine. ——— intact gland; . . . . denervated gland. Patient Ves-ov P. K., age 52 yr.

of the most distal nerve formations, namely, the mechanisms of transmission from the nerve to the effector appratus. Pilocarpine-proserine dissociation is thus a characteristic sign of a disturbance of neuroglandular synaptic transmission. Pilocarpine-proserine dissociation is absent in decentralization and in nuclear and preganglionic denervation.

Postganglionic denervation is also accompanied by an atropine paradox.

Extreme degress of denervation of the parotid gland are thus characterized by suppression of proserine secretion and the presence of an extraordinarily intensive atropine secretion (proserine-atropine dissociation).

It must be considered that proserine has the presynaptic membrane (i.e.,the acetylcholine depot) as its point of application. Pilocarpine preserves its cholinomimetic properties in all forms of denervation. Its point of application is the receptive substance of the gland cells themselves. Since in normal conditions atropine blocks synaptic transmission but at the same time does not prevent the secretion of acetylcholine, i.e., does not block the presynaptic membrane, its point of application must be the postsynaptic structure. When this structure is destroyed, from being a paralyzer of saliva secretion, atropine becomes a stimulator. This part of the chemoreceptive substance of the postsynaptic membrane must be recognized, in contrast to a cholinopositive structure, reacting invariably to both pilocarpine and to atropine (after denervation) by a secretory effect, as a cholinonegative, cholinolytic structure (S. L. Levin [5]).

The development of this accessory cholinonegative structure in the process of evolution is the basis of the differential reaction to cholinergic antagonists.

It should be pointed out that G. Grundfest [2] concludes that the chemoreceptive postsynaptic structure consists of two parts – exciting and inhibiting.

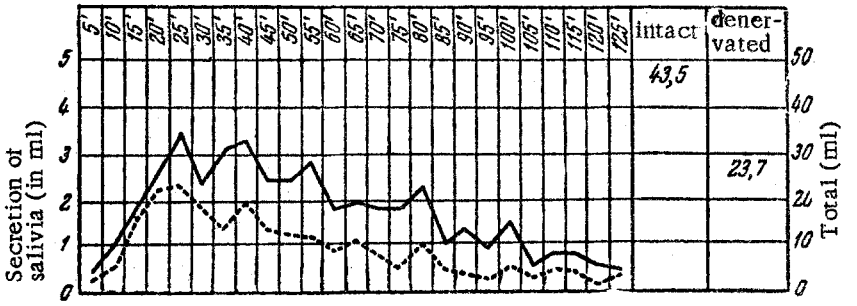

Fig. 4. Changes in the secretion of saliva under the influence of the simultaneous injection of 0.5 ml of 1% pilocarpine and 0.75 ml of 1% proserine. —— intact gland; denervated gland. Patient Ves-ov P. K., age 52 yr.

This supports our concept of the dual function of the postsynaptic formations.

We may thus consider from the foregoing remarks that the points of application of pharmacological agents in relation to the synaptic structures may be arranged in the following order: 1) proserine (presynaptic membrane), 2) atropine (postsynaptic structure) and 3) pilocarpine (acetylcholine) – the chemoreceptive part of the postsynaptic structure, in direct contact with the gland cells.

When the postganglionic neuron is intact, atropine, by interacting with the cholinonegative structure of the postsynaptic chemoreceptive system, produces a block of the secretory cells. When the cholinonegative structure is suppressed after postganglionic denervation, atropine comes into direct contact with the "exposed" cholinopositive (cholinomimetic) structure, producing a violent and extremely powerful cholinomimetic effect.

SUMMARY

The characteristic signs of decentralization (cortico-hemispheric and nucleo-bulbar) and denervation (pre- and postganglionic) of the human parotid gland are presented. These signs may be used for differential diagnosis. The significance of proserine and atropine as indicators of pre- and postganglionic denervation (proserine-atropine dissociation, atropine paradox) was demonstrated. The author illustrates the dual character of chemoreceptive postsynaptic transmission, namely, the presence of cholinopositive (cholinomimetic) phylogenetically older, and cholinonegative (cholinolytic, inhibitory) phylogenetically younger structures. Various special points of application of proserin, atropine, pilocarpine (acetylcholine) are given (within the range of the pre- and postsynaptic transmission).

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