THE EFFECT OF AUTONOMIC STIMULATORS ON CELL DIVISION IN THE CORNEAL EPITHELIUM

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In recent years much research has been carried out on the relationship between mitotic activity and the state of the nervous system. As a result of this research, many facts have been obtained which point to the importance of the central nervous system in the regulation of cell division [1,2,4,7,9,10,11, etc]. So far as the influence of the autonomic division of the nervous system on the process of formation of cells by mitosis is concerned, it is only recently that work on this problem has begun [1,3,5, etc].

In the present research, we investigated the mitotic activity in the corneal epithelium in different functional states of the autonomic nervous system. Changes in the tone of the autonomic nervous system were brought about by administration of various autonomotropic drugs.

METHODS

As a sympatheticomimetic drug we used adrenalin, and to lower the tone of the sympathetic nervous system, we used ergotin, which lowers the sensitivity of the animal to adrenalin. In order to study the influence of the parasympathetic tropic drugs on mitotic activity we used prostigmin, which promotes the accumulation of acetylcholine in the tissues; as a result of this, the tone of the parasympathetic nervous system is raised. As a cholinolytic drug we used atropine. All these various autonomotropic drugs were injected subcutaneously 1-3 hours before decapitation of the animal, in a dose of 0.1 mg/kg body weight, apart from atropine, which was injected in a dose of 0.6 mg/kg body weight.

Experiments were carried out on sexually mature white mice (males) of about the same age. The animals were decapitated always at the same time of day – 12 hr, 30 min. Total preparations of the cornea were obtained and stained with Carazi's hematoxylin. When the dividing cells were being counted, we took into consideration all the stages of cell division. As an index of mitotic activity, we adopted the number of mitoses in the whole cornea, multiplied by 100 and divided by the number of fields of vision. The figures obtained were treated statistically.

For the experiments we used 125 animals. In 65 of these we studied the influence of sympatheticotropic substances, including experiments with adrenalin on 40 mice (20 experimental and 20 control) and experiments with ergotin and 25 animals (15 experimental and 10 control). As regards the study of the influence of the parasympatheticotorpic drugs on the mitotic activity of the corneal epithelium, in experiments on 20 mice the parasympathetic nervous system was stimulated (12 experimental and 8 control animals) and in experiments on 40 animals the influence of the parasympathetic nervous system was depressed (25 experimental and 15 control animals).

RESULTS

According to our findings, in the experiments in which adrenalin was given, a depression of mitotic activity was observed; this was shown by a sharp reduction in the early stages of division in the corneas of the experimental mice. On the average, the decrease in the number of mitoses by comparison with the controls was 67% (Table 1).

It must be mentioned that these figures are in complete agreement with the results of several workers [6, 8, etc.], who have studied the effect of adrenalin on mitosis.

In the experiments in which the sympathetic nervous system was depresed, we obtained quite different results. As is shown by the figures given in Table 1, the injection of ergotin not only did not depress mitotic activity but, on the contrary, it resulted in an increase in the number of mitoses in the corneas of the experimental mice; this increase on the average amounted to 39%. The increase in the absolute number of mitoses in the corneas of the experimental mice was mainly due to the early phases of division – the prophase and metaphase – and it may thus be considered that in the experiments in which the tone of the sympathetic nervous system was lowered, the mitotic activity was increased. Consequently, according to the results obtained in the experiments with administration of sympatheticotropic drugs, an increase in the tone of the

TABLE 1 Experiments in which Sympatheticotropic Drugs were Injected

Experimental series	Subgroup	Number of animals (n)	Mean number of mitoses, M	Difference between C and E: in absolute units $(M_E - M_C)$	Difference between C and E: in % $\frac{(ME - MC)}{MC} \cdot 100\%$	Criterion of significance of the difference between the arithmetic means, $t = \frac{(M_E - M_C)}{\sqrt{m_o^2 + m_c^2}}$
I (adrenalin)	Control(C)	20	64	43	67	16.9
	Exp. (E)	20	21			
II (ergotin)	Control(C)	10	70	27	39	6.43
	Exp. (E)	15	97			

TABLE 2 Experiments in which Parasympatheticotropic Drugs were Injected

Experimental series	Subgroup	Number of animals (n)	Mean number of mitoses, M	Difference between C and E: in absolute units $(M_E - M_C)$	Difference between C and E: in % $\frac{(ME - MC) \cdot 100\%}{MC}$	Criterion of significance of the difference between the arithmetic means, $t = \frac{(M_E - M_C)}{\sqrt{m_o^2 + m_c^2}}$
III (prostigmin)	Control (C)	8	70	22	31	5.52
	Exp. (E)	12	92			
IV (atropine)	Control (C)	15	77	19	25	3.78
	Exp. (E)	25	58			

sympathetic nervous system in the body, brought about by injections of adrenalin, caused a depression of mitotic activity, but a temporary depression of the influence of the sympathetic nervous system (by injection of ergotin) resulted in the stimulation of mitotic activity. It may hence by concluded that the sympathtic nervous system evidently exerts an inhibitory influence on the process of cell division.

The study of the influence of the parasympathetic nervous system in the regulation of cell division was the object of the next 2 series of experiments. In one of these, in response to the injection of prostigmin, an increase in mitotic activity was observed in the experimental mice – on the average by 31% (Table 2).

In the experiments in which atropine was injected, on the other hand, the total number of mitoses was reduced (on the average by 25%), and there was also a fall in the number of early phases of mitosis.

When comparing the results obtained in the different series of experiments, it should be noted that during exclusion of the sympathetic nervous system and during excitation of the parasympathetic nervous system analogous changes were observed in the corneal epithelium: the number of cells undergoing mitosis was increased. During an elevation of the tone of the sympathetic nervous system, as during lowering of the tone of the parasympathetic nervous system, on the other hand, there was a depression of mitotic activity.

These findings are evidence that, firstly, the level of mitotic activity of the corneal epithelium depends on the functional state of the autonomic division of the nervous system; the sympathetic nervous system inhibits the process of cell division and the parasympathetic nervous system has a stimulatory effect on this process, i.e., in the regulation of mitotic activity they behave as antagonists.

SUMMARY

The paper deals with investigations of the mitotic activity in the corneal epithelium of white mice in different functional states of the autonomic nervous system. The latter was attained by the injection of the following autonomotropic substances: adrenalin, ergotin, prostigmin and atropine. Upon injection of adrenalin and atropine the mitotic activity level dropped, whereas the administration of ergotin and prostigmin increased the mitotic activity. The data obtained testify to the fact that the sympathetic nervous system exerts an inhibitory influence on the mitotic activity of the corneal epithelium, while the parasympathetic nervous system has a stimulating action.

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