

THE EFFECT OF DRUG-INDUCED SLEEP ON THE MITOTIC ACTIVITY OF THE CORNEAL EPITHELIUM OF WHITE MICE

S. Ya. Zalkind

From the Moscow Research Institute for Antipoliomyelitis Preparations

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It may be considered firmly established that the state of the nervous system has an essential influence on the mitotic regime of the body. We have shown that excitation of the nervous system, caused by a moderately painful stimulus, leads to a temporary fall in the mitotic activity of the corneal epithelium [1].

The question naturally arose of the influence on the mitotic regime of the opposite state — lowering of the excitation of the nervous system caused by the use of substances leading the animal into a state of artificial, or drug-induced sleep.

The performance of investigations along such lines is all the more justified by the fact that there are indications in the literature [2] that drug-induced sleep has a favorable effect on the course of tissue regeneration. It has been found that the use of small doses and microdoses of a number of narcotics has a stimulating action on the healing of skin wounds in rats, and that under these circumstances the proliferative process begins sooner than in control animals.

We investigated the effect of artificial sleep of short duration, induced by the subcutaneous injection of sodium amytal, on the mitotic activity of the corneal epithelium.

EXPERIMENTAL METHOD

White mice (weighing 14–16 g) were given subcutaneous injections of 0.6 ml of a 0.4% solution of sodium amytal. After 15 minutes they fell asleep. While they were asleep, 3 hours after the injection, the animals were killed by rapid decapitation, and the cornea, with the rest of the eye, was fixed in a mixture of 70° alcohol with 5% acetic acid. Animals of the control group, which received injections of 0.6 ml of physiological saline, were killed at the same time. The subsequent treatment, preparation of total specimens of the cornea and the method of counting mitoses were described in our previous paper [1]. The mitoses were counted in the whole area of the cornea, but the mitotic coefficient was derived from consideration of 100 fields of vision. At the same time as the mitoses were counted the phase coefficient — the ratio between the number of prophase + metaphases to the number of anaphases + telophases — was determined.

EXPERIMENTAL RESULTS

The results obtained are shown in summarized form in the table, which was compiled on the basis of 7 animals in each group (100 fields of vision in each case).

As may be seen from the figures in the table, drug-induced sleep of three hours' duration caused a sharp increase in the number of mitoses in the mice (by 104%). The phase coefficient, which for the control animals was equal to 1.2, rose in the experimental animals to 1.88, which indicated the considerable predominance of early phases of mitosis (prophase and metaphase), i.e., an increase in the number of cells embarking on the process of cell division.

These findings suggest that drug-induced sleep caused stimulation of mitotic activity. In these circumstances sleep had an effect which was directly opposite to that observed in response to excitation of the nervous system caused by painful stimulation [1].

Changes in the Mitotic Activity of the Corneal Epithelium of White Mice under the Influence of Drug-Induced Sleep

Control				Experiment			
prophases 79.8	metaphases 147	anaphases 88.8	telophases 99.4	prophases 205	metaphases 227	anaphases 177.6	telophases 126.7
Sum - 415				Sum - 847			
Phase coefficient $\frac{P + M}{A + T} = 1.2$				Phase coefficient $\frac{P + M}{A + T} = 1.88$			

It is still too early to give an exhaustive explanation of our findings. There are indications in the literature that the use of drug-induced sleep also leads to considerable changes in the metabolism of the body.

It has been shown by the use of labeled methionine that, during drug-induced sleep, an increase takes place in the intensity of incorporation of amino acids in the serum proteins and in a number of organs — the liver, adrenals and cardiac muscle [3].

Controlled experiments revealed that the narcotic drugs themselves (sodium amytal, urethane with veronal) in the doses used did not cause metabolic changes, which were thus associated with the narcotic state itself [4].

From our point of view it was of particular importance that during drug-induced sleep in rabbits a fall was observed in the blood sugar and in increase in the glycogen content of the muscles and liver [5]. The results of this investigation were interesting because, according to Bullough's findings [6, 7], these changes in carbohydrate metabolism were characteristic of an increase in the mitotic activity of the epidermis of the ear in mice.

It is possible, however, that there is a somewhat different explanation of our findings. It may be postulated that the weakening of the influence of the nervous system, as found in the state of artificial sleep, directly or indirectly (possibly by means of a change in the adrenal regime of the body) leads to weakening of the normally present depressing influence of the nervous system on mitotic activity.

Thus although the mechanism of the stimulation which we observed in the mitotic activity of the corneal epithelium cannot yet be regarded as finally explained, the results of physiological and biochemical investigations of the influence of drug-induced sleep on the body are in substantial agreement with our findings.*

SUMMARY

The author studied the effect of drug-induced sleep of short duration on the mitotic activity corneal epithelium (0.6 ml of 0.4% sodium amytal solution). The number of mitoses rose by 10% after 3 hours' sleep. The phasic coefficient rose in the experimental rats up to 1.88%.

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* This paper was already prepared for publication when we learned of the address by L. V. Sokolova: "The influence of drug-induced sleep on mitotic activity in the body". Conference of Young Scientific Workers of the Institute of Experimental Biology of the AMN SSSR, p. 17, 1958.

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