EFFECT OF PILOCARPINE ON THE ELECTRORETINOGRAM OF COLD-BLOODED ANIMALS

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After application of 1% and 0.5% pilocarpine solutions to the isolated frog retina, all components of the electroretinogram (ERG) disappeared completely. Gradual recovery of the ERG was observed only after perfusion of the retina with Ringer-Locke solution not containing pilocarpine for 5-10 min. The inhibitory action of pilocarpine in experiments on the isolated retina was due, evidently, not only to disturbance of respiration of the retina, but also to a marked disturbance of transmission of nervous excitation in its synapses.

Investigations of the action of pilocarpine when instilled into the conjunctival sac have revealed various effects of the drug on the blood vessels of the eye [5]. Experiments [1, 2, 6, 7] show that myopic substances, including pilocarpine, disturb the course of oxidation-reduction and metabolic processes in the lens, iris, and aqueous humor of the eye. However, the effects of pilocarpine on the electroretinogram (ERG), which in the opinion of most investigators [3, 4] reflects the activity of both receptor and horizontal cells (the *a* wave) and of bipolar cells (the b wave) have so far remained virtually unstudied.

To obtain a more definite idea of the effect of pilocarpine on the ERG, the action of different doses of the drug on the isolated frog retina was studied.

EXPERIMENTAL METHOD

The method used to attack this problem was to record the ERG of the isolated retina of cold-blooded animals while perfused with Ringer-Locke solution. Not more than 7-10 min elapsed between enucleation of the eye and the beginning of retinal perfusion. The light-adapted retina or isolated eye was placed in a screened chamber. Experiments were carried out in the following order: after the original ERG had been recorded (illumination of the retina at 5 lx was used as photic stimulus) the perfusion fluid was replaced by 1% pilocarpine solution, after which this was again replaced by perfusion with the ordinary solution and the ERG was again recorded. The pilocarpine solution was made up in Ringer-Locke solution. Photic stimulation was applied at intervals of 3-4 min. Changes taking place in the ERG was estimated from the amplitude of the b and d waves. The height of elevation of the b and d waves was measured in microvolts by reference to a preliminary calibration chart.

EXPERIMENTAL RESULTS

Consistent results were obtained in all experiments. The ERG of the isolated frog retina in response to photic stimulation was of the usual classical shape. In response to application of 1% and 0.5% pilocarpine solutions to the retina, all components of the ERG disappeared after 1 min. After "rinsing" (perfusion) of the retina with Ringer-Locke solution not containing pilocarpine for 5-10 min, a gradual recovery of all components of the ERG was observed. However, in the first minutes of recovery the d wave of the ERG was considerably higher than initially, whereas the b wave still remained below the initial level. These

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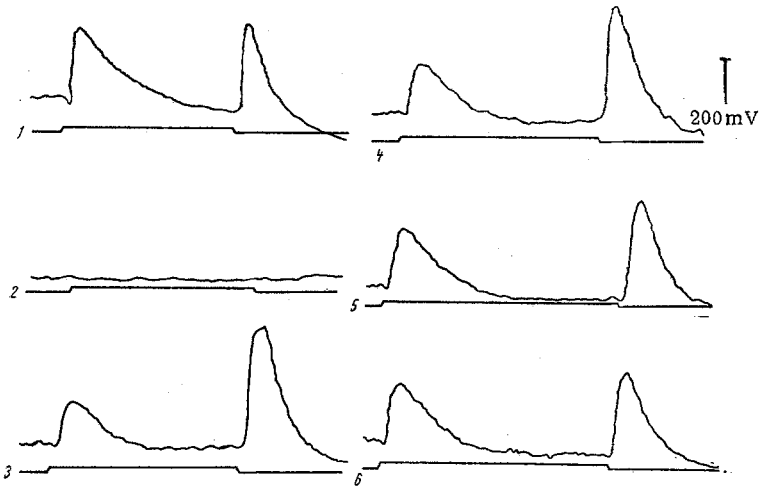

Fig. 1. Changes in ERG of isolated frog retina before (1) and 1 min after its perfusion with 0.5% pilocarpine solution (2), and 3 (3), 5 (4), 8 (5), and 10 (6) min after stimulation (during perfusion with Ringer-Locke solution).

TABLE 1. Changes in Amplitude (in μV) of ERG Waves During the Action of Various Doses of Pilocarpine on the Retina and Eyeball of Cold-Blooded Animals

Time of investigation	1%			0,5%			0,25%			0,1%			0,01%			0,001%		
	wave																	
	a	*b*	*d*	*a*	*b*	*d*	*a*	*b*	*d*	*a*	*b*	*d*	*a*	*b*	*d*	*a*	*b*	*d*
Background	56	244	212	75	428	370	63	369	150	75	444	175	72	518	218	75	431	238
1 min	50	163	100	56	313	213	56	237	88	63	263	50	50	363	100	63	339	163
2 "	44	163	75	56	313	188	50	213	81	56	187	100	50	350	163	63	313	125
3 "	44	175	75	63	350	137	56	200	69	63	163	88	44	288	138	63	325	113

observations showed that with an increase in amplitude of the b wave, the amplitude of the d wave gradually decreased, and by the end of 8-10 min both waves had regained their initial values and the ERG its usual form (Fig. 1).

A decrease in amplitude of the ERG wave was observed not only during the action of large doses of pilocarpine on the isolated retina, but also after instillation of one or two drops of (0.25, 0.1, 0.01, and 0.001%) pilocarpine solution to the vitreous humor of the isolated eye. In these experiments (Table 1), all components of the ERG were simultaneously reduced 2-3 min after application of the pilocarpine. No recovery of the ERG could be observed, for under the conditions of the experiment on the isolated eye it is extremely difficult to remove the pilocarpine. The electrical activity of the retina is closely related to metabolism in its tissues. A decrease in amplitude of the ERG occurs when retinal function is depressed, and restoration of the original ERG is evidence of recovery of retinal function. Changes in the b wave during perfusion of the isolated retina cannot be attributed entirely to deficient oxygenation, for from beginning to end of the experiment the retina was kept in Ringer-Locke solution without the addition of any further oxygen. Despite the hypoxia which undoubtedly existed under those conditions the ERG remained virtually unchanged for 1 h. The inhibitory action of pilocarpine in the experiments on the isolated retina can therefore be explained, not so much by a disturbance of respiration of the retinal tissues as by a marked disturbance of the transmission of nervous excitation in the retinal synapses.

Analysis of the components of the ERG by Granit's method shows that the negative component PIII recovers its function more rapidly than the positive component PII, thus giving the d wave its high amplitude in the initial period of recovery. The subsequent decrease in the d wave can be attributed to gradual recovery of the PII process.

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