ROLE OF NORADRENERGIC TERMINALS OF THE RAT BRAIN IN PASSIVE-AVOIDANCE CONDITIONING

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Changes in the noradrenalin concentration in noradrenergic terminals were studied by a fluorescence-histochemical method in pars ventralis nuclei interstitialis striae terminalis, nucleus septi lateralis, and nucleus preopticus medialis in rats during passive-avoidance conditioning. In preliminarily trained animals the simple reproduction of the conditioned-reflex response (without electrical stimulation of the skin) led to a decrease in the noradrenalin concentration in all structures studied. The results indicate a role in the noradrenergic system of the brain in the reproduction of the passive-avoidance conditioned reflex.

KEY WORDS: conditioned passive-avoidance reflex; noradrenalin; noradrenergic terminals; brain nuclei.

Biochemical and pharmacological investigations have demonstrated the role of noradrenergic brain structures in the reproduction of conditioned reflexes [8, 10, 13, 14]. However, to prove the role of particular neurons in the function of memory trace recall, histochemical methods must be used to detect noradrenalin in the brain structures. The writers are aware of only one investigation in which a luminescence-histochemical method was used to show that virtually all noradrenergic terminals of the brain are activated during reproduction of a conditioned active-avoidance response [6]. However, the conditions of that experiment did not rule out the possibility of an effect of nonspecific loading and muscular work, which themselves could lead to a decrease in the noradrenalin concentration in the brain [7]. The substance used in that investigation to block catecholamine synthesis (α-methyl-p-tyrosine) considerably lowers the level of reproduction of conditioned-reflex responses. The authors cited likewise did not estimate the noradrenalin content in the brain structures quantitatively.

In the present investigation quantitative changes in the noradrenalin concentration were studied in the noradrenergic terminals of nucleus septi lateralis (n.s.l.), par ventralis nuclei interstitialis striae terminalis (n.i.s.t.), and nucleus preopticus medialis (n.p.m.) during reproduction of a conditioned passive-avoidance reflex after blocking noradrenalin synthesis with the substance disulfiram, which itself does not affect the level of reproduction of defensive responses [12-14]. Disulfiram was used because when noradrenalin synthesis is blocked the abolition of presynaptic influences is retarded, whereas increased unit activity accelerates the exhaustion of reserves of the mediator in noradrenergic terminals [1-3, 5].

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-250 g were put through one training session in the apparatus of Jarvik and Kopp [9] by the method of Miller and Springer [11]. The animals received an intraperitoneal injection of disulfiram in a dose of 200 mg/kg body weight in a solution of α-methylcellulose 5-6 h after the end of the training procedure. Testing was carried out 12 h after the injection of disulfiram and continued for 5 min. The animals were then decapitated. The required areas of the brain were excised and treated by the method of Falck and Owman [4]. Noradrenalin was determined quantitatively in histological sections by

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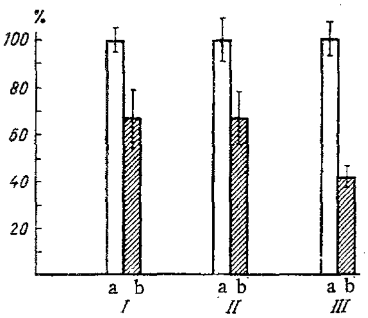

Fig. 1. Changes in noradrenalin concentration in rat brain nuclei during reproduction of conditioned passive-avoidance reflex. Ordinate, noradrenalin concentration (in %): I) change in noradrenalin concentration in terminals of n.i.s.t.; II) change in noradrenalin concentration in terminals of n.s.l.; III) change in noradrenalin concentration in terminals of n.p.m.; a) control; b) experiment.

fluorometry. The intensity of fluorescence of the noradrenergic terminals in the nuclei studied in the control animals 12 h after injection of 200 mg/kg disulfiram was taken as 100%. The significance of differences in the mean values was assessed by Student's criterion.

EXPERIMENTAL RESULTS

The largest number of noradrenergic terminals and maximal fluorescence in both the control and the experimental series were found in n.i.s.t.

In the trained animals reproduction of the conditioned passive-avoidance reflex alone (without electrical stimulation of the skin) led to a decrease ($P < 0.01$) in the noradrenalin concentration in all structures tested (Fig. 1). This decrease in n.s.l. and n.i.s.t. amounted to 33%, but in n.p.m. it was 59%.

About 30% of all the trained animals did not reproduce the conditioned passive-avoidance reflex on testing. In these animals the change in noradrenalin concentration in n.s.l. and n.p.m. was much less marked, and in n.i.s.t. there was in general no difference fron the control.

Animals which were kept in the chamber initially for 5-6 h before the injection of disulfiram and for 12 h thereafter were used as an additional control. No significant difference in the noradrenalin concentration compared with normal concentrations was observed in these rats (not receiving electric-shock reinforcement).

To verify whether the decrease in noradrenalin concentration was the result of the direct action of electrical stimulation, a special series of experiments was carried out. Training and injection of disulfiram followed the pattern described above. The animals were killed with no additional testing 17 h after training. In these experiments also, no significant change in the noradrenalin concentration compared with the control likewise was found.

Quantitative estimation of the noradrenalin concentration thus indicates a role of the noradrenergic brain system in the reproduction of a conditioned passive-avoidance reflex. The results also reveal the participation of certain brain nuclei in these processes.

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