COMPARATIVE EFFECT OF SEROTONIN, INJECTED INTO THE DORSAL HIPPOCAMPUS, ON CONDITIONAL PASSIVE AND ACTIVE AVOIDANCE REFLEXES IN RATS

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Data on the role of the neurochormone serotonin (5-HT) in memory and conditioned reflexes are to some degree highly contradictory, as is also the case with views on the function of this amine. According to some workers [2], differences in the character of action of 5-HT on memory and learning processes when its concentration in the brain rises is due to the emotional quality of the unconditional stimulus, whereas according to others [3] effects of 5-HT depend on the complexity of the reflex formed. There is evidence in the literature that the action of 5-HT on memory processes depends on the properties of the conditional stimuli (CS), which determine the specific character and strategy of the conditioned-reflex responses [4, 7]. We are concerned with the properties of conditioned stimuli that determine the character of achievement of the final unconditioned goal: orientation of behavior in the direction of the conditioned stimuli themselves (the property of sensory reinforcement) or merely the triggering of unconditioned-reflex activity already prepared (the triggering property). One of the main brain structures responsible for the action of 5-HT on behavior is the hippocampus [6], the important role of which in memory and learning processes is not now disputed [1, 5].

The aim of this investigation was to study the effect of 5-HT injected in microdoses directly into the dorsal hippocampus on retention and recall of conditioned reflexes formed to the predominantly reinforcing properties of spatial-situational stimuli and to the predominently triggering properties of a phasic stimulus. Conditioned passive and active avoidance of reflexes (CPAR and CAAR, respectively) were used as models of the corresponding conditioned reflexes.

EXPERIMENTAL METHODS

Experiments were carried out on 37 male albino rats weighing 250-300 g into whose dorsal hippocampus directing cannulas had been introduced beforehand bilaterally at coordinates of AP 3, L 1.5, H 1.5. In the model of CPAR the animals were taught not to go from the illuminated safe compartment into the dark compartment of the apparatus, where they received two painful electric shocks (1.5-2 mA) through the metal grid floor. In the model of CAAR the animals were taught to jump upon a "safety" platform on presentation of the phasic photic conditioned stimulus (CS), reinforced by electric shocks (5 mA), applied through the metal floor of the chamber to the limbs. The criterion of learning of the CAAR was 8-10 conditioned-reflex jumps during 10 presentations of CR without painful punishment. The animals were divided into two groups: Control rats received an injection of a microdose of isotonic NaCl solution, the experimental animals an injection of 5-HT solution 8-10 min before testing of the CPAR and CAAR. 5-HT (serotonin creatinine-sulfate, from Sigma, USA) was diluted in physiological saline to pH 7.2 and injected into the hippocampus in a volume of 0.6-1.0 µl. The data were subjected to statistical analysis by the U and F tests. At the end of the experiment the animals' brains were investigated histologically to determine the exact locations of the cannulas and sites of injection of the neurohormone into the hippocampus.

RESULTS

The effect of 5-HT on retention and recall of the CPAR was studied 24 h after formation of the reflex. The animals were placed in the illuminated compartment of the apparatus and the length of their stay in the safe compartment during 300 sec was recorded.

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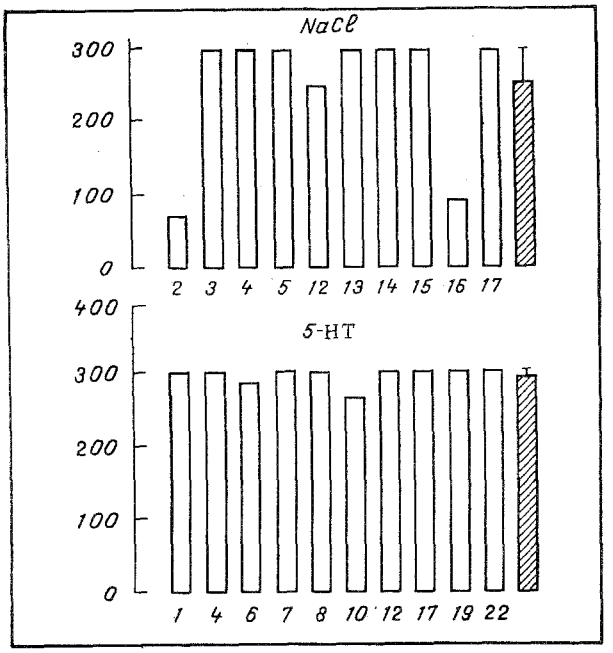

Fig. 1. Effect of 5-HT, injected into dorsal hippocampus, on retention of CPAR. Ordinate, length of animals' stay in illuminated compartment of apparatus (in sec). Shaded columns represent mean duration of CPAR retention for whole group of animals. Numbers beneath columns are serial numbers of rats.

The experiments showed that after microinjection of NaCl solution into the dorsal hippocampus of the control animals (10 rats) retention of CPAR averaged 251 ± 58.8 sec (Fig. 1). Bilateral intrahippocampal injection of 5-HT in a dose of 2 μg into the experimental animals (10 rats) lengthened the time of the rats' stay in the safe compartment: 259 ± 6.73 sec ($P < 0.05$), and this was accompanied by a great reduction in scatter of the data $F (58/6) = 5.35$ ($P < 0.01$, Fig. 1).

In this series of experiments 5-HT, injected into the hippocampus, thus lengthened the retention time of memory traces of passive avoidance. However, the action of 5-HT was of a different character when CAAR was tested. Retention and recall of CAAR were tested after the formation of this reflex by determining the rate of acute extinction, as revealed by the latent period of conditioned responses to the first 10 presentations of CS, and the number of interstimulus responses (Fig. 2). The criterion of complete extinction was five successive absences of conditioned responses to CS.

As the experiments showed, after microinjection of NaCl solution into the control animals (nine rats) complete extinction of CAAR took place during 140 presentations of CS (Fig. 2b). The animals accomplished 55 ± 2.05 correct conditioned-reflex jumps on to the "safety" platforms.

After injection of 5-HT bilaterally into the dorsal hippocampus in a dose of 2 μg into the experimental animals (eight rats) extinction of CAAR took place significantly more rapidly ($P < 0.01$). Under the influence of 5-HT the animals accomplished 8.1 ± 1.16 correct conditioned-reflex jumps on to the platform. Complete extinction took place after 30 presentations of CS (Fig. 2b). 5-HT considerably lengthened the latent period of active avoidance during the first 10 presentations of CS, to 12.6 ± 2.59 sec. The latent period in the control group was 7.4 ± 3.58 sec (Fig. 2c). Application of reminding electric shocks during extinction of the reflex, against the background of the action of 5-HT, did not change the extinction pattern. In most animals the fear response was intensified during the shocks. They fell into a state of cataplexy. Meanwhile, on the 2nd day of the experiment, one reminding shock after injection of 5-HT completely restored this reflex, whereas repeated extinction did not differ from the time course of extinction in the control animals.

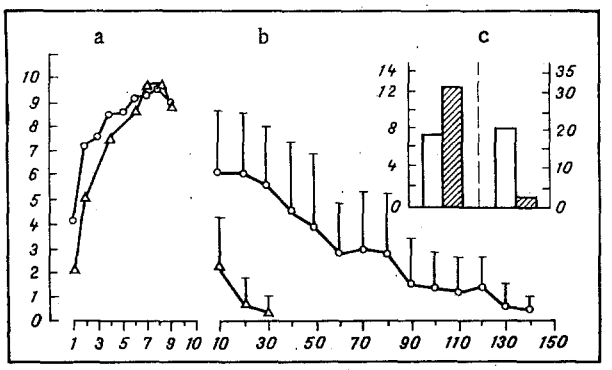

Fig. 2. Effect of 5-HT injected into dorsal hippocampus on time course of extinction and latent period during first 10 tests, and interstimulus responses of CAAR. Ordinate, in a and b, number of correct conditioned responses in 10 presentations of CS: a) learning (days of experiments shown on abscissa); b) extinction (number of presentations of CS shown along abscissa); c) ordinate on left gives latent period (in sec), ordinate on right shows interstimulus responses during period of extinction. Empty circles and unshaded columns, NaCl solution; empty triangles and shaded columns, 5-HT solution.

These data show that 5-HT did not lead to destruction of the temporary connection of CAAR, but probably inhibited its recall.

Thus on the one hand intrahippocampal injection of 5-HT prolongs retention of CPAR formed to the predominantly reinforcing properties of spatial-situational stimuli, and on the other hand, it inhibits recall of CAAR formed to the predominantly triggering properties of a phasic conditioned stimulus. Dependence of the effects of 5-HT on memory processes on the properties of the conditioned stimuli have also been investigated by other workers [4, 7].

It can be concluded from the results that it is important to take into account the properties of the CS when studying the function of monoamines and, in particular, of 5-HT, for at least those of its effects which are mediated through the hippocampal formation.

Participation of the hippocampus in the mechanism of spatial-situational memory [5] is well known. It can be tentatively suggested that the hippocampal 5-HT is responsible for the updating of spatial-situational memory and for strengthening of the reinforcing properties of conditioned stimuli which, in the CPAR situation, leads to prolongation of this type of defensive reflex. In the CAAR situation, updating of spatial-situational reflexes caused by 5-HT probably interfered with performance of the conditioned triggering reflex, and this was manifested in its inhibition and more rapid extinction.

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