TYPE I 5-HT RECEPTORS IN RATS WITH AMNESIA

G. F. Molodtsova and R. Yu. Il'yuchenok

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Amnesia is considered to be due to a disturbance of recall of the memory trace, not its disappearance [2, 12, 16]. There is also evidence which suggests that the serotoninergic system of the brain plays an important role in the formation and recall of the memory tract [1, 4, 5, 7, 10, 13]. However, despite the many studies of the effect of serotonin (5-HT) on conditioned reactions, the role of the serotoninergic system in memory trace recall remains unexplained. The role of 5-HT receptors, through which the mediator acts on the postsynaptic membrane, in processes of memory trace recall and its disturbances in amnesias have virtually not been investigated.

In this investigation to evaluate the role of 5-HT in mechanisms of memory trace recall, the functioning of type I 5-HT (5-HT_1) receptors, with high affinity for 5-HT [15], was investigated on models of "psychogenic" amnesia.

EXPERIMENTAL METHOD

Male Wistar rats weighing 180-200 g were used. A conditioned passive avoidance reflex was formed by the use of a single electrodermal reinforcement (current 1 mA, duration 2 sec) in an apparatus consisting of two compartments — lit (safe) and dark (dangerous), by the usual method [9]. The latent period (LP) of moving into the dark compartment of the apparatus was recorded. The conditioned reflex was considered to be formed if LP of the change of compartment during testing of the animals after 24 h was not less than 180 sec. Rats put into the apparatus but not receiving electrodermal stimulation served as the control. "Psychogenic" amnesia was induced by keeping the animal for 5 min in the dangerous compartment of the apparatus immediately before electrodermal reinforcement on the day of training [17]. The animals were decapitated 24 h after testing, the brain was removed, and the amygdala, the central gray matter of the midbrain, and the hippocampus and frontal cortex were excised in the cold. Specific binding of 5-HT_1 receptors was determined by the radioligand method [13] in the membrane fraction of the corresponding brain structures, which were obtained by centrifugation of brain homogenate for 20 min at 20,000g. The residue was washed in 50 mM Tris-HCl buffer, pH 7.4, and incubated for 10 min at 37°C to remove endogenous 5-HT, after which it was recentrifuged for 20 min at 20,000g. ^{3}H-Serotonin (specific activity 21.8 Ci/mmole, "Amersham International") was used as the radioligand. The samples containing the tissue suspension and ^{3}H-serotonin were incubated for 10 min at 37°C in 50 mM Tris-HCl, pH 7.4, containing 4 mM $CaCl_2$, 5.7 mM ascorbic acid, and 10 μM pargyline. Nonspecific binding was determined with 1 μM unlabeled 5-HT. Bound radioactivity was determined on a "Delta-300" liquid scintillation counter, with 55% efficiency, and expressed in femtomoles/mg protein. Protein in the samples was determined by Lowry's method [11]. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Specific binding of serotonin was found to be depressed in the trained rats, recalling the conditioned passive avoidance reflex [Table 1]. The training procedure itself and testing of untrained animals had no effect on receptor binding of 5-HT. Changes were found only in animals with recall of the conditioned reflex. Specific binding of ^{3}H-5-HT in rats with "psychogenic" amnesia was not depressed during testing the reflex, and it did not differ from binding

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TABLE 1. Specific Binding of ^{3}H-5-HT (2.5 nM) by Membranes of Various Brain Structures in Rats Recalling Conditioned Passive Avoidance Reflex (CPAR) and in Animals with "Psychogenic" Amnesia (in fmoles/mg protein; M ± m)

Group of animals	Brain structure			
	amygdala	central gray matter	frontal cortex	hippocampus
Control	66,5±2,6 (9)	80,6±5,4 (6)	50,0±3,9 (10)	98,6±7,4 (7)
Recalling CPAR	48,6±5,1* (9)	55,0±3,9* (3)	54,1±4,2 (8)	93,0±8,9 (11)
With amnesia	67,2±6,6 (10)	75,2±6,3 (8)	54,3±1,9 (10)	92,2±9,5 (7)

Legend. *$p < 0.01$ compared with control; number of experiments given in parentheses.

in the control animals. Thus in animals trained but with induction of amnesia, receptor binding of 5-HT in the amygdala and central gray matter was enhanced compared with that in rats recalling the conditioned passive avoidance reflex ($p < 0.05$).

There is evidence in the literature that 5-HT$_1$ receptors are located on the postsynaptic membrane of the neuron. It can therefore be suggested that the reduction of serotonin binding by 5-HT$_1$ receptors, discovered in these experiments, weakens the activity of the serotoninergic system of the amygdala and central gray matter. The ascending serotininergic system is known to inhibit neuronal activity in the amygdala [6]. The fact that changes in function of 5-HT$_1$ receptors are observed only in the amygdala and central gray matter, and not in the hippocampus and frontal cortex, is evidently connected with the important role of these structures as formations of the emotiogenic regulatory system of memory [3]. The amygdala and central gray matter take part in the primary evaluation of information reaching the brain, and in the selection of signals for subsequent recall. It can be tentatively suggested that weakening of receptor binding of 5-HT is accompanied by activation of neurons of the amygdala and central gray matter in the process of memory trace recall. Since no attempt has been made to study changes in memort trace recall during blockage of 5-HT$_1$ receptors, our observations on a decrease in the number of functioning 5-HT receptors during recall and the absence of this effect in animals with amnesia can be compared only with the known facts that preservation of skills of various types of conditioned behavior is stronger when the brain 5-HT level is lowered [4, 5, 14]. The absence of any weakening of functional activity of 5-HT$_1$ receptors in animals with amnesia may be one element of the mechanism of memory trace recall in amnesia or may be a result of it.

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