EFFECT OF CHANGING THE BRAIN SEROTONIN AND NORADRENALIN LEVELS ON TRAINING TO EMOTIONALLY DIFFERENT REINFORCEMENT IN RATS

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The effect of precursors of serotonin (5-HT) and noradrenalin (NA) on learning in animals with emotionally different reinforcement was studied. 5-Hydroxytryptophan (5-HTP), in a dose of 10 mg/kg, facilitates training of rats to food reinforcement but impairs learning to nociceptive reinforcement. D,L-Dopa (20 mg/kg) facilitates training to nociceptive reinforcement but has no significant effect on training to food reinforcement. The effect of the precursors on the character of distribution of 5-HT and NA in the brain structures of the trained animals also was determined by the biological significance of the reinforcement used in training.

KEY WORDS: training; emotions; serotonin; noradrenalin.

Differences in the changes in brain serotonin (5-HT) and noradrenalin (NA) levels in animals during training, depending on the biological significance of the reinforcing stimulus, were discovered by the writers previously [1]. The facts obtained are in harmony with the view that the brain serotoninergic system is the neurochemical substrate for emotionally positive reinforcement and the noradrenergic system the substrate for emotionally negative reinforcement [2, 3].

The present investigation is devoted to a comparative analysis of differences in training of animals to emotionally different reinforcement after deliberate changes in the brain 5-HT and NA levels.

EXPERIMENTAL METHOD

Two series of experiments were carried out on 143 male Wistar rats. In series I the effect of the serotonin precursor, 5-hydroxytryptophan (5-HTP; 10 mg/kg intraperitoneally, daily, 1 h before the experiment) and in series II the effect of the noradrenalin precursor, dihydroxyphenylalanine (D,L-dopa; 20 mg/kg intraperitoneally, daily, 1 h before the experiment) on the speed of training of rats was compared with its speed in control animals receiving an equal volume of physiological saline. The effect of each substance was studied in conjunction with training to emotionally positive and emotionally negative reinforcement. The model of training to emotionally negative reinforcement was the conditioned active avoidance reflex to painful punishment (CAAR), and that to emotionally positive reinforcement was the reflex alternate visits to the sources of food on the right and left sides [5]. As soon as the animal reached the criterion of training, experiments were carried out to extinguish the reflexes produced, i.e., to test their stability under conditions of removal of the nociceptive or food reinforcement. At the end of the experiments the concentrations of both amines were analyzed biochemically [6] in various parts of the brain (cortex, hypothalamus, caudal portion of the brain stem) on a Hitachi spectrofluorometer. The experimental data were subjected to statistical analysis on the Mir-2 computer [4].

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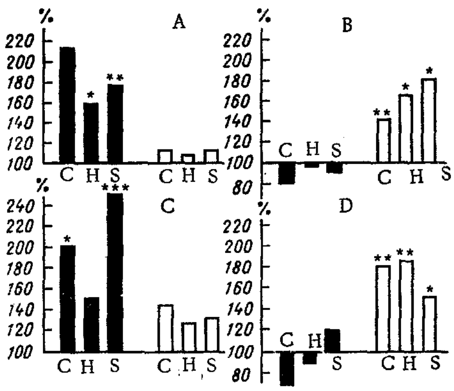

Fig. 1. Changes in 5-HT and NA levels in various brain structures in rats following administration of precursors of their synthesis. Brain level in trained animals receiving injections of physiological saline taken as 100%. Black columns represent 5-HT, white columns NA. A, B) Training to emotionally positive reinforcement; C, C) to emotionally negative reinforcement. A, C) After injection of 5-HTP; B, D) of D, L-dopa. C) Cortex, H) hypothalamus, S) caudal region of brain stem. Statistical significance of differences compared with control: *) P < 0.05, **) P < 0.01, ***) P < 0.001.

EXPERIMENTAL RESULTS AND DISCUSSION

Investigation of the learning process in animals in experiments with food reinforcement after administration of 5-HTP showed considerable facilitation of formation of the consecutive alternate visiting reflex, as shown by its earlier appearance and consolidation. The experimental animals also showed increased stability of the reflex to extinction compared with the control (Table 1). Different results were obtained in experiments to train the animals to nociceptive reinforcement. Under these conditions administration of 5-HTP led to impairment of formation of the CAAR: It was consolidated later and extinction developed just as easily as in the control animals.

The results of the biochemical investigation showed that the 5-HT concentration in the brain of animals receiving 5-HTP was 1.5-2.5 times higher (Fig. 1). During training to food reinforcement the greatest increase in the 5-HT level was found in the neocortex, whereas during training to nociceptive reinforcement the greatest increase in the 5-HT level was found in the caudal region of the brain stem. The NA level was practically unchanged in the animals during training to food reinforcement, but during training in a defensive situation it rose, the highest level being observed in the neocortex.

Investigation of differences in training the animals in experiments with food reinforcement after administration of small doses of D,L-dopa showed that its effect is directed differently on training and on retention of the skill. Despite the fact that the experimental rats, on reaching the criterion of training, required to make rather fewer visits than the control rats, the stability and resistance of the reflex formed in them were lower than the control. By contrast, in the experiments with nociceptive reinforcement administration of D,L-dopa considerably facilitated CAAR formation and increased the stability of the reflex when formed.

The results of the biochemical tests showed that prolonged administration of D,L-dopa led to an increase in the brain NA level by 1.5-1.9 times in both forms of training. In animals trained in the alternating visit reflex the concentration of this amine was highest in the caudal region of the brain stem, whereas during the formation of CAAR in the rats the largest increase in NA concentration was found in the hypothalamus and neocortex. The 5-HT level in the brain showed a tendency to fall after administration of D,L-dopa, especially in the neocortex.

The results of this investigation thus indicate that the effects of 5-HTP and of D,L-dopa on the training of animals depend on the character of the reinforcement used. The fact that the character of the distribution of 5-HT and NA in different brain structures after administration of the precursors of these amines depends on the biological significance of the reinforcement used in training is particularly interesting. For instance, administration of the same dose of 5-HTP during training to food reinforcement led to maximal increase in the

TABLE 1. Effect of 5-HTP and D,L-Dopa on Training of Rats with Emotionally Positive and Emotionally Negative Reinforcement

Experimental conditions	Training to emotionally positive reinforcement			Training to emotionally negative reinforcement		
	number of rats	speed of formation of alternate visit reflex	retention of skill during extinction, %	number of rats	speed of formation of CAAR	retention of skill during extinction, %
Control	28	87,1±10,9	64	34	62,8±22,5	15
5-HTP (10 mg/kg)	21	49,0±7,5‡	73	12	75,0±17,2*	15
Dopa (20 mg/kg)	13	64,6±19,2	52	8	37,5±15,6†	50

*P < 0.05.
†P < 0.01.
‡P < 0.001.

5-HT concentration in the neocortex, whereas during training to nociceptive reinforcement the maximum was found in the caudal region of the brain stem. Administration of D,L-dopa, on the other hand, gave a maximal increase in the NA level in the cortex during CAAR formation but in the brain stem during the formation of the alternate visit reflex.

To assess the physiological significance of these facts it can be postulated that the predominant elevation of the 5-HT and NA levels in the cortex is evidence of active functioning of the corresponding brain structures, whereas the selective increase in their concentration in the brain stem points to a decrease in the functional activity of these structures. From this standpoint the results can be interpreted as confirmation of the hypothesis that the serotoninergic system of the brain is the leading component in training to emotionally positive reinforcement and the noradrenalinergic system plays the leading role in training to emotionally negative reinforcement [2, 3].

LITERATURE CITED

1. N. L. Vekshina and T. P. Semenova, Byull. Éksp. Biol. Med., No. 11, 1285 (1976).
2. E. A. Gromova, in: Structural and Functional Bases of Memory Mechanisms [in Russian], Moscow (1976), pp. 1-17.
3. E. A. Gromova and T. P. Semenova, in: Mechanisms of Modulation of Memory [in Russian], Leningrad (1976), pp. 174-177.
4. E. V. Gubler and A. A. Genkin, The Use of Criteria on Nonparametric Statistics to Assess Differences between Two Groups of Observations in Mediobiological Research [in Russian], Moscow (1969), p. 21.
5. T. P. Semenova, Zh. Vyssh. Nerv. Deyat., No. 6, 1322 (1976).
6. A. S. Welch and B. L. Welch, Anal. Biochem., 30, 161 (1969).