CHARACTER OF CENTRAL SEROTONIN-SENSITIVE STRUCTURES RESPONSIBLE FOR THE DEPRIMING EFFECT OF 5-HYDROXYTRYPTOPHAN ON THE ALARM REACTION IN CATS

L. F. Glushko and A. P. Gilev

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Intraperitoneal injection of 5-hydroxytryptophan in a dose of 50 mg/kg depresses the conditioned-reflex alarm reaction in cats. Benzacine* (1 mg/kg, intravenously) also has a marked blocking effect on this reaction. Serotonin antagonists of the M- (octadine, 4 mg/kg, intravenously) and the D- (mexamine†, 2 mg/kg, intravenously) type abolish the depriming effect of 5-hydroxytryptophan on the alarm reaction without changing the corresponding effect of benzacine.

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In the modern view nervous structures responsible for emotional activity are the limbic system and hypothalamus [1, 5, 15], characterized by a high serotonin content [14] and by the presence of specific serotonin-sensitive neurons [11]. It is also known that serotonin has a blocking effect on behavioral reactions involving the participation of a negative emotional component [3, 8, 12].

With these considerations in mind it was decided to investigate the role of central serotonin-sensitive structures in the manifestation of the negative emotional alarm reaction in cats.

EXPERIMENTAL METHOD

Experiments were carried out on cats of both sexes weighing 1.5-3 kg. The alarm reaction was produced by the method described by Il'yuchenok and Eliseeva [6]. The intensity of the alarm reaction was assessed by a four-point system: 1 point – pressing in the ears, 2 points – closing the eyes, 3 points – drawing in the head, 4 points – curling up into a ball.

To excite the central serotonin-sensitive structures, 5-hydroxytryptophan (5-HTP) was used; this compound readily penetrates into the brain and is converted by decarboxylation into serotonin [16]. To assess the specificity of the action of 5-HTP on central serotonin-sensitive structures, the effects of selective serotonin antagonists of the M- (morphine, octadine) and D- (mexamine†) types on the action of benzacine* and 5-HTP [4, 14] were studied.

The experiments were carried out in autumn and winter. Doses and methods of administration of the drugs are shown in Table 1.

EXPERIMENTAL RESULTS

As Table 1 shows, 30 min after injection of 5-HTP the intensity of the conditioned-reflex alarm reaction diminished, and after 1 h this reaction was completely blocked. The action of 5-HTP persisted for at least 2 h. Since in these experiments the development of 5-HTP effects correlated in time with an increase in the serotonin concentration in the brain [9, 10], it can be concluded that 5-HTP has a depriming effect on the alarm reaction through the influence of endogenous serotonin.

*2-Dimethylaminoethyl ester of benzilic acid hydrochloride.
†5-Methoxytryptamine hydrochloride.

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TABLE 1. Effect of Some Pharmacological Agents on Alarm Reaction in Cats (mean data using a four-point system)

Time (in min)	5-HTP (50 mg/kg, intraperitoneally)	Benzacine (1 mg/kg, intravenously	Mexamine (2 mg/kg, intravenously)	Morphine (2 mg/kg, intravenously)	Octadine (4 mg/kg intravenously)	Against background of mexamine		Against background of morphine		Against background of octadine	
						5-HTP	benzacine	5-HTP	benzacine	5-HTP	benzacine
Initial background	10	10	10	10	10	10	10		9,6	10	10
	(10)	(8)	(3)	(6)	(5)	(3)	(6)	(6)	(6)	(5)	(5)
30	7,6	6,9	10	10	10	10	0	8,6	4,3	8,4	0
	(10)	(8)	(3)	(6)	(5)	(3)	(3)	(6)	(6)	(5)	(5)
60	0	1,5	10	9	10	9,6	0	9,1	4,6	9,4	0
	(10)	(8)	(3)	(6)	(5)	(3)	(3)	(6)	(6)	(5)	(5)
90	0	0,6	10	9,3	10	9	0	9,3	4,1	9,8	0
	(10)	(8)	(3)	(6)	(5)	(2)	(3)	(6)	(6)	(5)	(5)
120	0	0,8	10	9,6	10	10	0	9,6	3,5	10	0
	(10)	(8)	(3)	(6)	(5)	(2)	(3)	(6)	(6)	(5)	(5)

Note. 1) Number of experiments given in parentheses; 2) antagonists injected immediately after mexamine and morphine.

In the opinion of a number of investigators [2, 6], cholinergic structures also participate in the mechanism of negative emotional reactions. It was therefore necessary to determine whether the action of 5-HTP on the alarm reaction is specific. The effect of selective antagonists of M-(morphine, octadine) and D-(mexamine) types on the action of 5-HTP and benzacine was therefore compared. Benzacine was chosen because it belongs to the group of central cholinolytics which, like 5-HTP, have a depriming effect on conditioned-reflex alarm reactions in cats [6]. The experiments showed that benzacine inhibits this reaction. For example, 30 min after injection of benzacine the alarm reaction was clearly diminished (Table 1), and after 90 min it was almost totally blocked. The effect of this drug persisted for 2 h.

It was also shown that M- and D- antagonists of serotonin themselves do not modify the alarm reaction, although two of them (octadine and mexamine) definitely inhibited the depriming action of 5-HTP, without influencing the corresponding action of benzacine. So far as morphine is concerned, it practically completely blocked the action of 5-HTP on the alarm reaction and somewhat reduced the reaction to benzacine.

Both M- (octadine) and D- (mexamine) serotonin antagonists thus selectively depress only the effect of 5-HTP. This suggests that the depriming effect of 5-HTP on the alarm reaction is specific and takes place through interaction between endogenous serotonin and central serotonin-sensitive structures.

It is difficult to imagine that only one mediator is involved in so complex and many-sided a reaction as alarm. Besides acetylcholine, it is probable that serotonin also participates in the regulation of negative emotional reactions. Excitation of cholinergic structures is known to strengthen the alarm reaction [6], whereas activation of serotonin-sensitive structures is accompanied by depression of this reaction. It can be assumed that a functional system responsible for exhibition of the negatively emotional alarm reaction possesses a series of different mediators performing different physiological functions. Acetylcholine evidently plays the role of an activating, and serotonin that of an inhibiting agent. This agrees with Brodie's hypothesis [7] that serotonin is a mediator of the trophotropic system of the hypothalamus, the basis on which negative emotions, as indicated above, are formed.

So far as characteristics of central serotonin-sensitive structures involved in the passive defensive alarm reaction are concerned, depression of the 5-HTP effect by M- and D- serotonin antagonists suggests that these central serotonin-sensitive structures belong to a special type of receptors which differs from the peripheral and are characteristic of the central nervous system.

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