ROLE OF NEUROCHEMICAL MECHANISMS OF THE MEDIAL NUCLEUS RAPHE IN ANXIETY STATES FORMED BY EXPOSURE TO VARIOUS AVERSIVE FACTORS

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Facts obtained in recent years have shown that the medical nuclei raphe are the morphological and functional substrate of the system regulating anxiety states. In fact, their electrocoagulation facilitates avoidance conditioning to pain [6] and enhances the effects of aversive brain stimulation [9] and increases the number of punishable responses [11]. GABA-ergic control of the latter in a conflict situation and its participation in the mechanism of the anxiolytic effects of chlordiazepoxide have been suggested, for chemical stimulation of the nuclei raphe by these substances increases the frequency of the operant food-getting response, reinforced by nociceptive stimulation [10]. Besides GABA, mediator functions in the nuclei raphe also are performed by catecholamines, serotonin (5-HT), and glutamic acid [4, 7, 8], but their role in the genesis of anxiety states induced by various aversive procedures has not been studied.

The situation described above motivated investigations in which dopamine (DA), 5-HT, GABA, and glutamic acid (L-GA) were injected directly into the medial nucleus raphe (MNR) so that their functional roles in different experimental anxiety states could be evaluated.

EXPERIMENTAL METHOD

Experiments were carried out on 18 mature male rats weighing 250-310 g in which an anxiety state was assessed by tests of avoidance of an illuminated space and of a threatening situation, described in detail previously [3]. Solutions of DA, GABA, L-GA (10 μg), and 5-HT (serotonin creatinine sulfate, 20 μg) were injected by means of a microinjection system in a volume of 1 μl with the aid of chemical electrodes, implanted under ether anesthesia into MNR at stereotaxic coordinates [1] (AP 6.5, L 0, H 7.5), and the inborn avoidance reflex (AR) to an illuminated space and AR of "spectator" rats observing the illuminated compartment while the five "victim:" rats used in the experimental series were subjected to nociceptive stimulation (the threatening situation avoidance test) were investigated.

The animals were placed in the experimental situation 5 min after microinjection of the test substances, and by means of a special device mounted on decatrons [3] the time spent by the animals in the illuminated compartment, the number of crossings of boundaries between squares on the floor while the animals remained in the illuminated compartment (motor activity), and the intensity of motivation of the animals' stay in the dark compartment (I) were recorded. The last factor was determined in conventional units [3] as the ratio of the total effort of the animal, developed on the platform of the dark compartment (U) to the time spent by the animal on it (t) and to body weight of the rat (m), and calculated as a parameter of mechanisms controlling the rats' instinctive preference for darkness [12].

In control experiments 1 μl of 0.9% NaCl solution was applied to MNR of the rats. The result was subjected to statistical analysis by the usual methods. After completion of the experiments the animals were killed under ether anesthesia. The position of the chemical electrodes in the brain was verified morphologically.

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TABLE 1. Effect of Monoamines and Amino Acids Injected into MNR on Anxiety States in Tests of Avoidance of an Illuminated Area (numerator) and a Threatening Situation (denominator; $M \pm m$; $n = 5$)

Preparation	Dose, μg	Duration of stay of rats in illuminated compartment, sec	Motor activity (number of times of crossing boundaries between squares in illuminated compartment)	Intensity of motivation of preference of rats for dark compartment (I; conventional units)
NaCl (0.9% solution)	—	3,0±0,88 / 1,8±1,04	5,2±1,04 / 5,2±1,04	0,55±0,09 / 0,53±0,09
DA	10	3,2±1,04 / 2,6±1,4	6,0±0,87 / 6,0±0,87	0,48±0,05 / 0,49±0,06
5-HT	20	4,6±1,5* / 4,4±1,88*	6,0±0,87 / 6,0±0,87	0,50±0,07 / 0,50±0,02
GABA	10	4,8±1,04* / 2,6±1,42	6,4±1,12 / 5,8±1,04	0,57±0,14 / 0,44±0,1
L-GA	10	3,2±1,6 / 2,2±1,6	5,8±0,96 / 5,8±1,04	0,49±0,09 / 0,51±0,1

Legend. *$p \leq 0.05$ compared with control.

EXPERIMENTAL RESULTS

The morphological investigations showed that in all the experiments the monoamines and amino acids acted on those neuronal structures of MNR whose chemical stimulation, by the neurotransmitters used, revealed their differing roles in anxiety states formed by aversive procedures differing in their biological significance. The results of these experiments are given in Table 1. Significantly, in the control investigations and in the threatening situation avoidance test, the duration of stay of the rats in the illuminated compartment was shorter ($p < 0.05$) than the corresponding parameter in the illuminated space avoidance test. Thus two experimentally modeled anxiety states differed essentially in the biological significance of the aversive procedure. In fact, AR of the illuminated space was based on a motivation of fear [3, 12]. The nociceptive response of the "victim" rat, accompanied by vocalization, by running around the chamber, and by micturition and defecation, transformed this motivation in the "spectator" rats into a state of zoosocial negative emotional stress [2, 3]. It will be clear from Table 1 that chemical stimulation of PMR by DA and L-GA did not change the rats' motor activity, did not affect their motivation for staying in the dark compartment, and had no significant effect on the duration of their stay in the illuminated chamber, during the realization of anxiety states formed by motivations of both fear and negative zoosocial stress. Meanwhile, while not influencing the effector motor mechanisms, GABA and 5-HT, injected locally into MNR, significantly increased the duration of the rats' stay in the illuminated compartment in the illuminated space avoidance test. This antiaversive effect is evidence that if the dominant motivation is fear, the neurochemical matrix of anxiety states at the MNR level includes, not dopamine- or glutamatergic, but 5-HT- and GABA-ergic components. This conclusion correlates with the established fact that the anxiolytic action of the serotoninomimetic buspirone and its analogs is blocked by destruction of the nuclei raphe [4].

Conversely, in anxiety formed by aversive action of different biological significance (the threatening situation test), the GABA-ergic mechanisms of MNR were functionally unimportant, and only 5-HT demonstrated an antiaversive effect. This was not due to the presence of a motor deficit of the tested behavior or weakening of mechanisms controlling the rats' instinct for preferring darkness. This conclusion is supported by the fact that local application of GABA to MNR does not affect the parameters of avoidance of a threatening situation, but application of 5-HT lengthens the duration of stay of the "spectator" rats in the illuminated compartment during nociceptive stimulation of "victim" rats, without changing the motor activity or the intensity of motivation of the rats to stay in the dark compartment (Table 1).

It can be concluded from these findings that the neurochemical matrix of anxiety, formed on the basis of negative zoosocial emotional-stress reactions, includes, not GABA-ergic but serotoninergic components of synaptic relays at the MNR level. This conclusion is a weighty argument in support of recent suggestions that 5-HT-ergic "punishment" systems may take part in the regulation of anxiety and may be the morphological and functional substrate for the anxiolytic action of tranquilizers [4, 5].

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ROLE OF THE LIGAMENT OF TREITZ IN REGULATING SOLID FOOD EVACUATION FROM THE DUODENUM

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Since the discovery by Treitz of a supporting muscle of the duodenum, most attention has been paid to the study of its morphology and anatomy [4, 10, 15, 16], whereas its functional role remains unclear. It has been suggested that the ligament of Treitz (LT), as a component of the duodenojejunal junction, is an active regulator of the propulsive ability of the duodenum [2, 10]. However, there have been no direct investigations whose results could characterize, quantitatively and qualitatively, the functional role of LT as a regulator of the evacuatory function of the duodenum. Besides its theoretical interest, this problem also is of great practical importance because of the widespread use of the operation of division of LT in modern surgery for the treatment of duodenostasis [4].

The aim of this investigation was to study the effect of division of LT on the duration and time course of evacuation of solid food from the duodenum.

EXPERIMENTAL METHOD

Chronic experiments were conducted on three dogs with two fistulas: duodenal (5 cm distally to the pyloric sphincter) and intestinal (3 cm distally to LT). The animals were investigated before and during 6 months after division of LT. The experiments were carried out over a period of 6 h after the dogs had been fed a diet (100 g bread + 25 g milk) to which 600 black spheres 1 mm in diameter, made of edible rubber, were added as a comparison substance. To assess evacuation from the duodenum, 30 min after feeding and during excretion of the spheres from the intestinal fistula, 50 red spheres were injected into the duodenum by means of a special plunger. The number of black spheres reflected the general dynamics of evacuation

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