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Hemispheric Peculiarities of Serotonin Involvement in the Processing of Relevant and Irrelevant Information in Mice

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Stimulus-dependent hemispheric-regional changes are found in the activity of the serotoninergic system. Determination of stimulus novelty is provided by a decrease of serotonin and its metabolite content in the frontal cortex of the left hemisphere as well as in the striatum without the effect of lateralization. Presentation of an extinct stimulus is attended by a serotonin increase in the hippocampus of the left hemisphere and in the amygdaloid complex of both hemispheres.

Key Words: *serotonin; 5-hydroxyindoleacetic acid; brain asymmetry; orienting reaction*

At the present time there is strong evidence of the existence of biochemical brain asymmetry in animals. The data mainly concern catecholamines [5,11,14], while much less is known about serotonin [4], even though its involvement in cognitive functions and behavior has been demonstrated repeatedly. Specifically, stimulation of or damage to the nuclei of the midbrain suture enhances or disturbs, respectively, the process of habituation to information presented repeatedly [1,3,7,12,13].

In addition, the interaction found in various behavior tests [10] between biochemical asymmetry and spatial preference behavior implies that neurotransmitter asymmetry is more than an accidental phenomenon, but rather is a brain characteristic which may play an important role in the central organization of behavior. Studies taking account of such interaction would make a valuable contribution to the concept of neurochemical mechanisms of cognitive function. The promise of such investigations, on the one hand, and the scant evidence of serotoninergic lateralization, on the other, prompted us to perform this study, the aim of which was to reveal the laterality of serotoninergic activity and the peculiarities of its manifestation in brain structures in response to the presentation of relevant and irrelevant information.

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MATERIALS AND METHODS

Experiments were carried out on 32 female Wistar rats weighing 180-200 g. The behavioral procedure of habituation of the orienting reaction performed in a Jarvik and Kopp chamber [8] was essentially similar to the earlier described [1] stage of preliminary exposure to a situational stimulus preceding the elaboration of the conditioned passive avoidance re-

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sponse. The scheme consisted of 20 presentations of the experimental chamber (4 times a day for 3 min during 5 days). In the first and last tests the latency of passage was recorded as well as the duration of the stay in the dark compartment. One of the conditions of this technique - the placing of the animal in the illuminated compartment with its tail facing the opening into the dark compartment - was used in the present experiment to obtain data on behavioral asymmetry by recording the side chosen for the starting turn in every test. The percentage preference was calculated according to a known formula [5]:

$$\frac{\textit{right side-left side}}{\textit{right side+left side}} \times 100\%.$$

The stimulus was presented only one time (exploration of the experimental chamber for 1 min) to half of the animals making up a separate group. For biochemical analysis all the animals were decapitated immediately after the behavior test, the brain was promptly removed, and the frontal cortex, striatum, amygdaloid complex, and hippocampus of the left and right hemispheres were isolated in the cold. The activity of the serotoninergic system was assessed according to the content of serotonin and its metabolite 5-hydroxyindoleacetic acid (5-HIAA) using the fluorimetric method [6]. The results were processed by the Student *t* test.

RESULTS

The data of the behavioral experiment showed a decrease of the orienting-exploratory activity in animals by the 20th presentation of the experimental chamber. This was evidenced by a shortening of the mean latency of passage into the dark compartment from 14

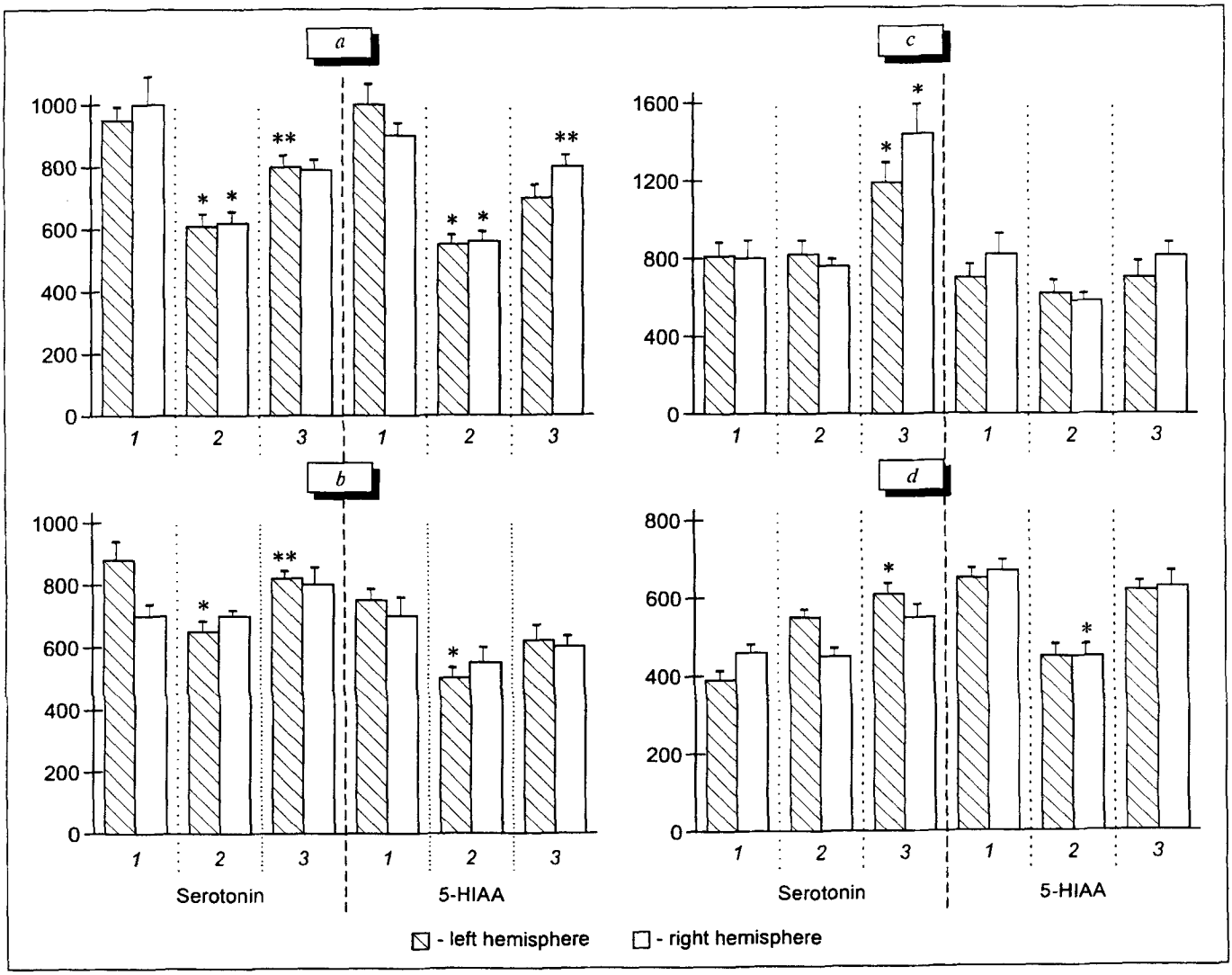

Fig. 1. Content of serotonin and 5-HIAA (ng/g tissue) in the striatum (*a*), frontal cortex (*b*), amygdaloid complex (*c*), and hippocampus (*d*) in the left and right hemispheres of rats under conditions of new and extinct stimulus perception ($n=6$). *1*) intact control; 2) one-time and *3*) multiple presentations of stimulus. $p<0.05$: *compared to intact control, **related to group *2*.

to 3 sec and a prolongation of the stay in there from 152 to 180 sec. The results of calculation of the percentage side preference for the turn attest to behavioral asymmetry, expressed in a 73.6% preference for a right turn.

The data on serotonin and its metabolite 5-HIAA in the brain structures are depicted in Fig. 1. Marked changes in the level of serotonin and its metabolite in the striatum, frontal cortex, and hippocampus were found when the intact group (*1*) was compared with the group in which the new stimulus was presented one time (*2*). In the striatum (Fig. 1, *a, 2*) the serotonin and 5-HIAA content is decreased in both the left ($p<0.02$ and $p<0.01$, respectively) and right ($p<0.05$ and $p<0.01$) hemisphere. The same effect was noted in the frontal cortex (Fig. 1, *b, 2*) of the left hemisphere ($p<0.02$ and $p<0.001$). In the hippocampus (Fig. 1, *d, 2*) a 5-HIAA decrease ($p<0.01$) was revealed in the right hemisphere, while in the left the diminution of the metabolite was insignificant ($p=0.07$). As for the amygdaloid complex, there were no changes in serotonin metabolism in response to the one-time presentation of the stimulus (Fig. 1, *c, 2*).

An opposite process, namely, an increase of the content of serotonin and its metabolite, was found for extinction of the stimulus significance in all brain structures and was assessed in comparison both with the intact group and with experimental group 2. In the striatum (Fig. 1, *a, 3*) there was a reliable increase in serotonin content in the left hemisphere ($p<0.05$) and of 5-HIAA in the right ($p<0.02$), while in the frontal cortex (Fig. 1, *b, 3*) serotonin elevation was found in the left hemisphere ($p<0.002$) only as related to group *2*. However, in comparison with the intact control the alterations revealed in these structures were leveled ($p>0.05$). In the amygdaloid complex (Fig. 1, *c, 3*) the serotonin content rose both in the left ($p<0.05$) and in the right ($p<0.02$) hemisphere when compared to group *2* but, in contrast to the preceding structures, it exceeded the serotonin content in the intact control ($p<0.02$). In the hippocampus (Fig. 1, *d, 3*) a serotonin increase was noted only in the left hemisphere in comparison with group *1* ($p<0.05$).

The effect of more marked alterations of serotoninergic activity in the left hemisphere may be related to the behavior lateralization observed in most of the animals tested.

Thus, there is a clear hemispheric-regional specificity of serotoninergic system involvement in the processing of relevant and irrelevant information. The serotoninergic substrate of the frontal cortex and striatum participates in the response to fresh information (a drop of the level of serotonin and its metabolite), in this case lateralization of the effect (left hemisphere) being noted in the frontal cortex only. The hippocampus and amygdaloid complex play an active role in estimating the irrelevance of the extinguished stimulus, and a unilateral serotonin increase occurs in the former (left hemisphere) and a bilateral increase in the latter. In experiments on males it was previously shown that the stage of preliminary exposure to a conditioned stimulus was followed by a significant serotonin decrease in the amygdaloid complex compared to the intact control [2]. According to our data, in the same structure in females the serotonin content rose in response to presentation of the extinct stimulus. This fact may be of interest in view of the sexual differences in modes of information processing, which are probably based on different neurochemical mechanisms.

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