PHYSIOLOGY

Individual and Typological Behavioral Characteristics of CBA/CaLac Mice

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Individual characteristics of higher nervous activity were studied in CBA/CaLac mice. The animals were divided into groups by the parameters of drinking response conditioning in a complex spatial environment. As distinct from bad learners, good learners exhibited higher orientation and exploratory activity in the open field, rapid adaptation, and low ability to retain the responses. Changes in conditioned reflex activity during neuroses were more pronounced in good learners.

Key Words: *individual and typological characteristics; conditioned reflex activity; behavior; CBA/CaLac mice*

Much recent attention is paid to the problem of individual resistance to psychoemotional stress. A considerable body of evidence show that inherited resistance to emotional stress differs in humans and animals. The resistance to psychoemotional stress (somatic manifestations) is closely related to individual and typological characteristics of the nervous system [3, 13,15]. It is important to evaluate the specific features of higher nervous activity that determine the development, course, and outcome of various diseases.

Here we studied individual and typological behavioral characteristics of CBA/CaLac mice.

MATERIALS AND METHODS

Experiments were performed on 650 female CBA/CaLac mice (class I conventional strain) weighing 20-22 g and obtained from the nursery of the Department of Experimental Biomedical Modeling (Institute of Pharmacology).

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Inbred mice were divided into groups according to the results of drinking response conditioning in complex spatial environment (T-maze with 3 arms) [10,12]. The animals had free access to water and food over 7 days of the post-training rest period. Further experimental manipulations were performed after this period.

Psychophysiological characteristics of mice were evaluated by their behavioral activity. Orientation and exploratory activity was studied in an open field [5]. The test parameters were recorded over the 1st minute and next 2 minutes; the latency of the first visit to the center of the open field was estimated. Non-associative learning task was performed for 4 days to study the reaction of adaptation to the open field [5]. Learning and memory were investigated during passive avoidance conditioning [5]; conditioned drinking response was tested after 21 days [5]. One week after typing, the animals were subjected to experimental stress. Retention of the conditioned drinking response was tested in the T-maze 21 days after stress. Drinking bowls were removed 24 h before retention testing. Conflict situation and paradoxical sleep deprivation served as the models of neuroses [6].

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The results were analyzed by nonparametric Mann—Whitney test. K-mean cluster analysis was applied to test the hypothesis on the existence of phenotypic groups in the general population of CBA/CaLac mice.

RESULTS

Cluster analysis of the results obtained during drinking response conditioning revealed high variability of T-maze behavior. According to K-mean cluster analysis, the total sampling of CBA/CaLac mice was divided into 4 subgroups (clusters). The main criteria for cluster differences were time of attaining the drinking bowl, number of errors, and vertical activity. The mean time of attaining the drinking bowl in animals of cluster 4 was 1 min, freezing time was 2 sec; the animals made on average 6 errors and 5 rearing postures and did not display neurotic reactions, grooming episodes, and defecations. The animals of this group were considered as good learners. Cluster 1 mice significantly differed from good learners by higher vertical activity (by 3.6 times), number of errors (by 2.8 times), time of attaining the drinking bowl (by 2.3 times), immobility period (by 10 times), frequency of neurotic excesses (by 8 times), and displacement activity (grooming episodes, by 5 times; and defecation rate, by 6 times). The animals of this group were considered as bad learners. The mice that were intermediate between good and bad learners entered clusters 2 and 3. The main parameters of these animals (number of errors, time of attaining the drinking bowl, immobility period, and vertical activity) differed from those of group 1 and 4 mice. Our experiment was designed to study the mice with extreme behavioral characteristics. Therefore, the animals demonstrating intermediate T-maze behavior between good and bad learners were excluded from further experiments.

On day 21 after drinking response conditioning, good learners demonstrated worse performance compared to that during typing: the number of errors increased by 2.2 times, time of attaining the drinking bowl increased by 2.4 times, immobility period increased by 26 times, frequency of grooming episodes increased by 6 times, and neurotic reactions appeared. In bad learners, parameters of conditioned reflex activity improved. Analysis of behavioral reactions showed that good learners exhibited active behavioral pattern and increased emotional reactivity. These specific features probably contributed to rapid acquisition of the conditioned response and high irritability during testing. Bad learners were characterized by slower learning and lower irritability during testing, *i.e.* exhibited passive behavioral pattern. Similar observations were described elsewhere [8]: the rats well trained in an alternative maze were attributed to the group of excitable animals; bad learners entered the group of behaviorally inert (depressed) animals.

No differences were revealed in orientation and exploratory behavior of good and bad learners over the 1st minute of open-field testing. However, total locomotor activity of good learners increased by 3.5 times during the next 2 minutes ($p<0.05$). It was associated with an increase in hole behavior and, to a lesser extent, horizontal activity. Locomotor activity of good learners in the open field was much higher compared to bad learners. Experi-

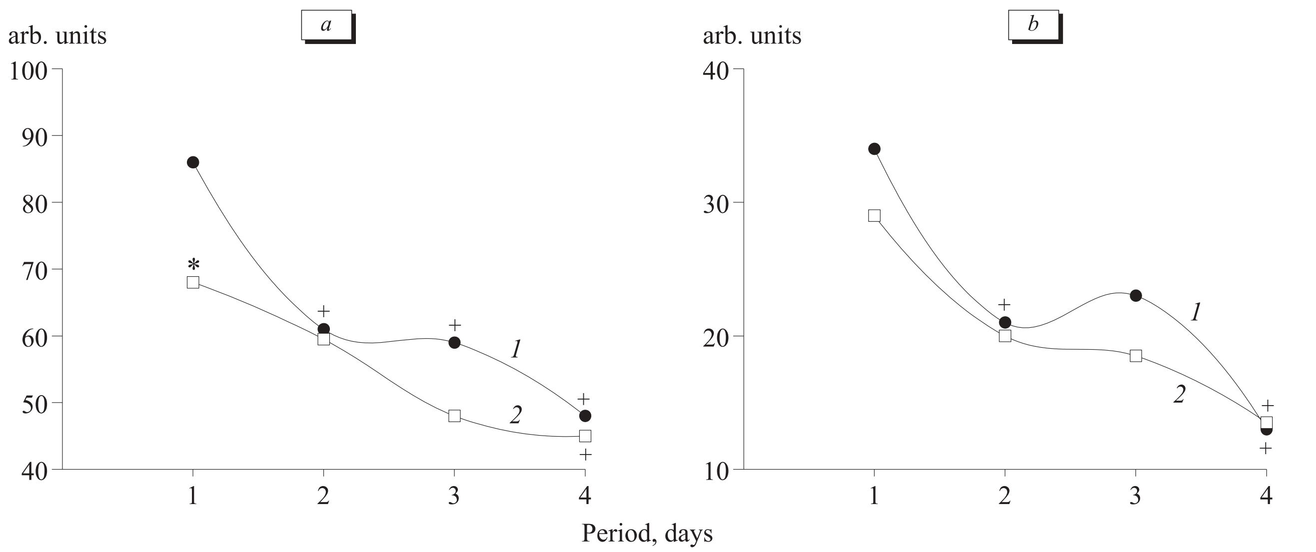

Fig. 1. Orientation and exploratory behavior of male CBA-CaLac mice during adaptation to the open field. *1*) good learners; *2*) bad learners. Total locomotor activity (*a*) and hole response (*b*). $p<0.05$: *compared to good learners; +compared to day 1.

mental mice significantly differed by the rate of adaptation to the open field. Orientation and exploratory activity decreased most rapidly in good learners. Behavioral activity underwent less pronounced changes in bad learners. Intergroup differences were more significant over the last 2 minutes of testing. Total locomotor activity of good learners significantly decreased on day 2 (to 65.3%, $p \leq 0.01$). These changes were related to a decrease in horizontal activity (to 63%, $p \leq 0.05$) and hole response (to 55.2%, $p \leq 0.05$). Total locomotor activity of bad learners decreased only on day 4 (to 63.5%, $p \leq 0.05$), which was mainly associated with a decrease in horizontal activity (to 67%, $p \leq 0.05$) and hole response (to 45%, $p \leq 0.001$, Fig. 1). Rapid extinction of exploratory activity during repeated testing in the open field is a measure of emotional instability and increased emotional reactivity of animals [2].

Intergroup differences were found in the behavior of mice during passive avoidance conditioning. Good learners were characterized by lower latency of entrance into the dark compartment compared to bad learners (36.4±4.4 and 54.0±5.4, respectively, $p \leq 0.05$). However, only small intergroup differences were revealed in passive avoidance retention.

Evaluation of the effect of stress on conditioned activity showed that conflict situation had a negative impact on retention of drinking response in good learners (T-maze test). On day 21 after the conflict situation, parameters of conditioned activity in these animals were much higher than before exposure. Differences were revealed in vertical activity (by 8 times, $p \leq 0.05$), number of errors (by 7 times, $p \leq 0.05$), time of attaining the drinking bowl (by 9 times, $p \leq 0.05$), immobility period (by 90 times, $p \leq 0.05$), frequency of grooming episodes, and defecation rate (by 18 times, $p \leq 0.05$, Fig. 2). These changes were accompanied by the appearance of neurotic excesses. It should be emphasized that no neurotic reactions were found in good learners under control conditions. Testing of conditioned drinking response in bad learners after conflict situation revealed a significant increase in the number of neurotic reactions (by 3 times, $p \leq 0.05$) and time of attaining the drinking bowl. Similar results were obtained in the study of conditioned reflex in outbred rats divided by acquisition of a conditioned drinking response in a T-maze: more pronounced changes after conflict situation were revealed in good learners [10,12]. Impaired drinking response performance in the T-maze in good learners was probably related to high emotional activity and disturbed mechanisms of drinking response conditioning.

Conditioned reflex activity of good and bad learners in the T-maze remained practically unchanged after paradoxical sleep deprivation. Changes in test parameters were comparable to those in intact animals.

Thus, our experiments showed the existence of individual and typological differences in higher nervous activity of CBA/CaLac mice. As distinct from bad learners, good learners are characterized by high exploratory motivation. Only high emotionality of these mice decelerates adaptive response and impairs passive avoidance conditioning. These specific features are not observed during T-maze learning in preadapted animal. The severity of changes in conditioned activity after conflict

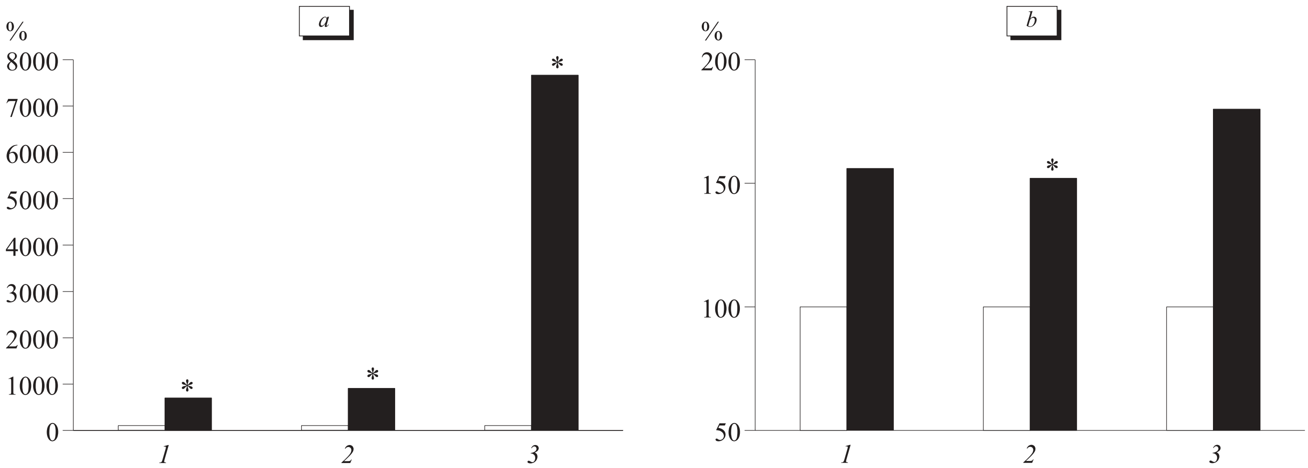

Fig. 2. Conditioned drinking response in male CBA-CaLac mice in a complex spatial environment on day 21 after the conflict situation. Ordinate: % of the values obtained during typing (100%). *a*) good learners; *b*) bad learners. Number of errors during the search for the drinking bowl (*1*); time of attaining the drinking bowl (*2*); and immobility time (*3*). Light bars, parameters during typing; dark bars, parameters during response testing on day 21 after conflict situation. *$p<0.05$ compared to parameters obtained during typing.

situation is mainly determined by emotional reactivity of animals. High emotional reactivity of good learners explains the fact that subjective perception of paradoxical sleep deprivation and conflict situation in these animals led to significant changes in the blood system [9,11]. When discussing the differences in behavioral activity of CBA/CaLac mice, we should emphasize that CBA, CBA/Lac, and C57Bl/6 mice are divided into groups of behaviorally aggressive and submissive specimens under conditions of sensory contact [1,7]. By the level of horizontal activity, C57Bl/6 mice are divided into highly active and low active specimens [14]. Apart from behavioral differences within the strains, differences were revealed in the genomic dose of active ribosomal genes of inbred AKR/J, CBA/Lac, and 101/H mice [4].

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