GENETICS

Differences in the Training Capacity of 101/H and CBA Mice in a Water Labyrinth (Modified Morris' Test)

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The rate of formation of the habit of search for submerged platform was studied by the modified Morris' test in 101/H and CBA mice. The former strain was trained slower than the latter; in addition, 101/H mice of different sexes differed by the time of latent periods of searching for the platform. The results are interpreted as a manifestation of genetically determined disorders of training and/or memory in 101/H mice.

Key Words: *Morris' test; training; memory; 101/H and CBA mice*

The formation of spatial notions in rodents is assessed from the viewpoint of contribution to it of brain structures responsible for memory and cognitive capacity in these animals and, probably, in man. One approach to analysis of spatial training is the use of genetically homogeneous animals with a certain trait [9-11]. Previously, we showed that 101/H mice with unstable genome and excision DNA repair defect are characterized by peculiar behavior: low exploratory activity, high emotional reactivity, abnormal locomotions presenting as "backward movements," opisthotonos induced by barbiturates, and increased sensitivity to sound [1-3]. In this study we compare the behavior of 101/H and CBA mice in a modified Morris water labyrinth. In contrast to the "classical" protocol of the test, when the animals are let into water from different sides of the basin [8], we let them out from the same initial position. The behavior of 101/H mice was abnormal, and we deemed that this simplified variant of spatial task to find a goal is adequate to decreased adaptive potential of these animals.

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MATERIALS AND METHODS

Experiments were carried out in 101/HY (101/H) (13 males and 15 females) and CBA/Lac/Sto (CBA) (20 males and 18 females) mice aged 2.5-3.5 months. An animal was let into a 60×50×40 cm basin (26°C) with a platform 6 cm in diameter, 1 cm submerged below the water level; the animal was to find the platform and climb it in no more than 60 sec. The distance from the initial position of the animal to the platform was 45 cm. The initial orientation of mice toward the platform was always the same. The water was opaque (with milk), so that the platform was not seen. Before testing, each mouse was put into the basin without platform for 1 min. Objects in the room and the experimentator figure served as check points for the animals. The trajectory of mouse movement in the water and time needed to find the platform (latent period, LP) were recorded in each test. Each mouse was tested 12 times for 3 days at 1-h intervals between the tests. If a mouse failed to find the platform within 1 min, the experimentator

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put it on the platform and left there for 60 sec. The data were statistically processed using Student's test and ANOVA unifactorial dispersion analysis.

RESULTS

Figure 1 shows that LP of platform finding was notably longer in 101/H mice than in CBA mice. Significant differences in LP were observed between males ($F_{1/1180}$=195.8, p<0.001) and females ($F_{1/1125}$= 45.14, p<0.001). Unlike CBA mice, 101/H animals showed sex-related significant differences: LP of females were shorter than of males ($F_{1/1047}$=21.7, p<0.001).

Figure 2 shows the mean time needed to find the unseen platform on days 1, 2, and 3 of experiment. In 101/H males and females the LP decreased only on day 2, whereas in CBA mice, LP was still decreasing, that is, training was going on, on day 3 in comparison with day 2.

Thus, in different strains of mice with different capacity to find a submerged platform a defect of this capacity was detected in 101/H mice. Despite the simplification, this modification of the test implies that the animal is capable to form at least a simple spatial notion. It should be based on the capacity to operate with information on the external check points and on the probable localization of the goal and to relating it with one's own position. A similar, although less expressed training defect, was revealed in DBA/2 mice in the same simplified Morris' test [9]. Slow training of 101/H mice cannot be explained by their slow moving in the water due to their locomotion defect [1,2], because the trajectories of CBA and 101/H mice movements in the basin varied. A typical trajectory of CBA mice, particularly at the last stages of experiment, was a virtually straight line from the place of start to the platform, whereas 101/H mice as a rule swam rather chaotically and their LP was longer. In 10-15% of tests 101/H mice either failed to climb the platform they found (although the habit was acquired) or, once climbing it, rapidly jumped off and went on swimming. Similar results were observed in Morris's water labyrinth in

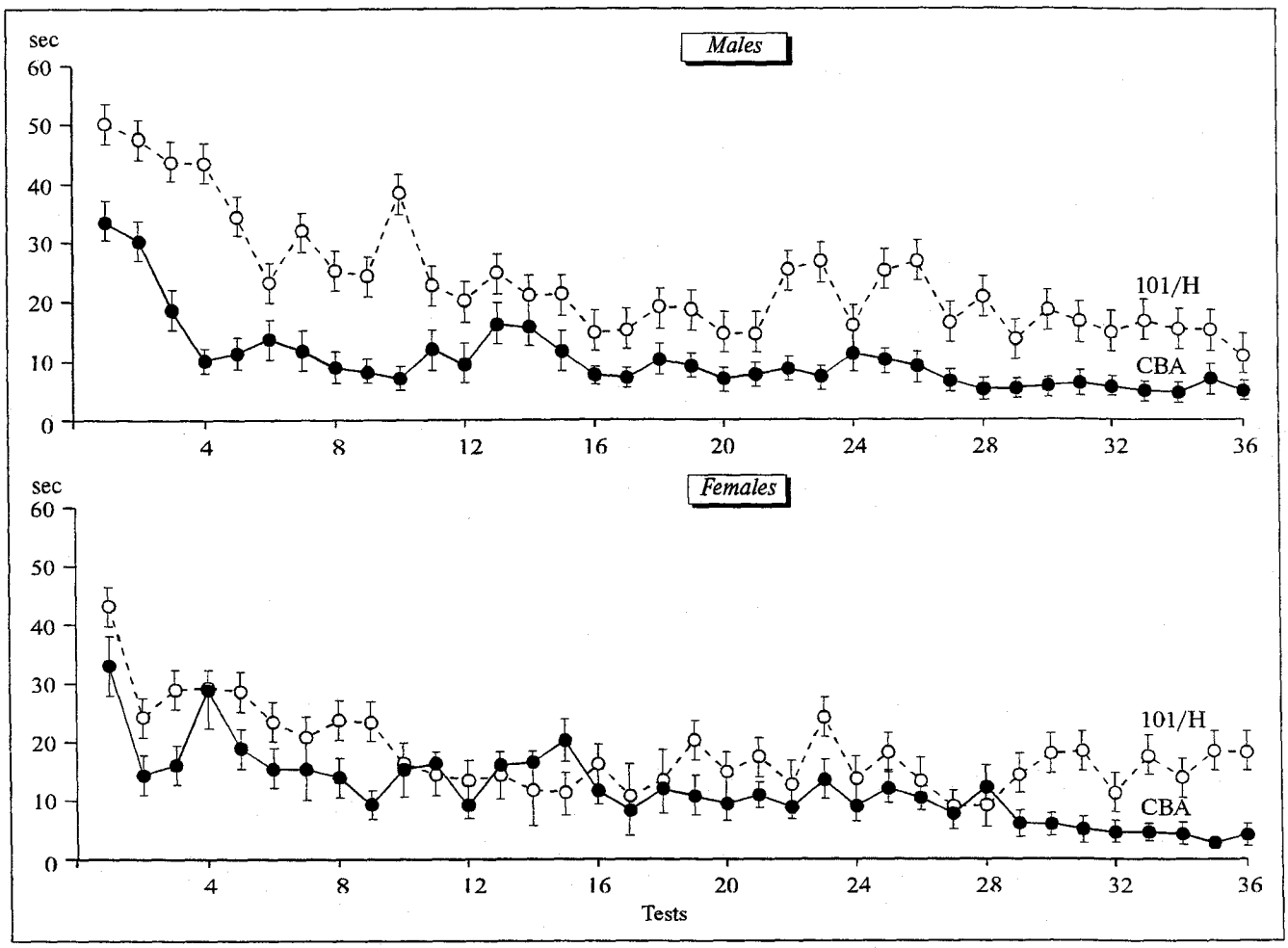

Fig. 1. Time course of latent period of finding the unseen platform by 101/H and CBA mice during 3 days of training.

tests with rats exposed to ethanol and morphine [6,7], which was regarded as impaired motivation. Neurological abnormalities are clearly seen in 101/H mice [2,3], and therefore, abnormal motivation processes can be responsible for their slow training.

Sex differences in the duration of LP in 101/H mice can be explained by differences in the hormone status. However, other tests revealed sex differences in this strain, too [1,3], which indicates that other factors are responsible for sex differences in the training capacity of animals of this genotype.

The intactness and normal function of the hippocampus are obligatory conditions for good results in Morris' test [4,8,9]. A correlation between genetic variability of the area of the layer of infra- and intrapyramidal mossy fibers (dentate fascicle granular cell axons) of the hippocampal CA3 field and efficacy of forming the habit of finding the platform in aqueous Morris' labyrinth have been demonstrated [10]. A decrease in the content or activity of some neurotransmitters, mainly in the glutamate- and/or cholinergic systems, also deteriorates spatial training of mammals [7]. Specific features of brain structure of 101/H mice are deranged stratification of the hippocampal CA3 field and structure of its suprapyramidal zone [3]. These abnormalities can deteriorate the training capacity of this mouse strain, affecting the processes of training and storage of spatial information.

Our findings permit us to hypothesize that training defect of 101/H mice in the spatial test reflects the genetically determined features of their central nervous system. 101/H mice can be a convenient model for studies of drug and genetic correction of some human diseases associated with age and neurodegenerative processes [5].

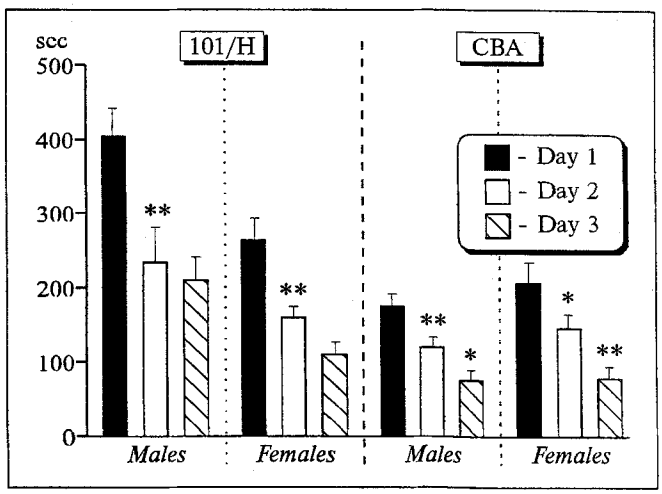

Fig. 2. Mean duration of latent period in different days of the test. *$p<0.05$, **$p<0.01$ *vs.* the previous day of experiment.

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