# PHYSIOLOGY

# Development of Amnesia in Different Mouse Strains

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We studied passive avoidance retrieval after amnestic stimulation (arrest in unsafe section of the experimental setup) in C57Bl/6J, BALB/c, CBA/Lac, AKR/J, DBA/2J, C3H/HeJ, and ASC/Icg mice. We demonstrated resistance to amnestic stimulation in mice with high predisposition to freezing reaction (ASC/Icg) and memory deficit in other mouse strains.

**Key Words**: *memory; amnesia; depression; different mice strains*

Analysis of the effects of amnestic stimulation is a common approach for investigation of memory formation mechanisms [7,9]. However, the dependence of amnesia development on individual status of experimental animals is still poorly studied. We previously discovered resistance to "psychogenic" amnestic stimulation in aggressive mice (behavioral stereotype was formed in a model of long-term agonistic relationships) and monoamine oxidase A knock-out mice with impulsive aggression [2,5,10].

In clinical practice, more pronounced sensitivity to amnestic stimulations in patients with symptoms of depression was noted [8]. However, there are only few studies on experimental animal models of depression-like conditions. We showed memory retrieval deficit during amnesia in mice with learned hopelessness and in submissive individuals [3,5]. At the same time, is not clear how "psychogenic" amnestic stimulus affects memory in the model of genetically determined depression in ASC/Icg mice with high predisposition to freezing reaction (catalepsy). ASC/Icg mice are characterized by reduced motor activity in the open field test, increased immobility in Porsolt test and tail suspension test, and by disorders in extinction of passive avoidance reaction [1,4,6].

Here we analysed the effect of "psychogenic" amnestic stimulation, animal arrest in a dark section of experimental chamber immediately after painful stimulation on the day of passive avoidance training on memory retrieval in different mouse strains.

## MATERIALS AND METHODS

Experiments were carried on 3-3.5-month-old male mice of C57Bl/6J (C57), BALB/c (BALB), CBA/Lac (CBA), AKR/J (AKR), DBA/2J (DBA), C3H/HeJ (C3H), and ASC/Icg (ASC) strains weighting 22-27 g, obtained from the vivarium of Institute of Cytology and Genetics, Siberian Division of the Russian Academy of Sciences and Tomsk nursery. ASC mice (19th generation of breeding for predisposition to catalepsy) were selected from backcross mice from breeding CBA (cataleptic strain) and AKR (resistant to catalepsy) mice [1]. The animals were kept under standard conditions with free access to water and food. Experiments were performed with observation of humanitarian principles in accordance with Regulations for Studies using Experimental Animals (Addendum to Order of the Ministry of Health of the USSR No. 755, December 08.1977) and approved by the Biomedical Ethical

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Passive avoidance training was carried out using conventional protocol of single training in an experimental dark/light chamber. On the day of training, the mouse was placed in the light compartment with the tail towards the aperture and mouse transition to the dark compartment was followed by electrocutaneous stimulus (0.5 mA current, 2 sec duration).

Animal arrest in the dark compartment of the experimental chamber for 5 min immediately after painful stimulation served as the amnestic stimulation. Passive avoidance performance was tested on days 1-9 after learning, the latency of transition into the dark compartment was recorded. The maximum testing time prescribed by the experimental procedure was 180 sec.

The data were processed statistically out using two-way dispersion analysis ANOVA (where the group was the first factor and testing time was the second factor) with subsequent prearranged assessment of differences by the LSD method.

## RESULTS

Figure 1 shows changes in transition latency during continuous testing of passive avoidance performance after single training followed by amnestic stimulation in ASC, CBA, and AKR mice. Data analysis showed significance of group ($F_{2,1}$=13.99, $p$=0.0001) and time factors ($F_{6,26}$=5.44, $p$<0.0001) and their interaction ($F_{12,23}$=3.57, $p$=0.0001). Clear-cut interstrain differences in amnesia development were revealed. In AKR mice, the mean transition latency on all days of testing does not significantly differ from those before passive avoidance training (day 0), which suggests that arrest in the dark compartment on the day of learning completely blocked retrieval of the conditioned reaction. ASC were resistant to the amnestic influence; this resistance persisted throughout the testing period. Repeated intergroup comparisons of transition latency revealed a significant increase of this parameter ($p$<0.05) in ASC mice compared to parental strains CBA and AKR. A tendency to anti-amnestic effect in CBA mice observed 1 day after learning ($p$=0.08) should be noted.

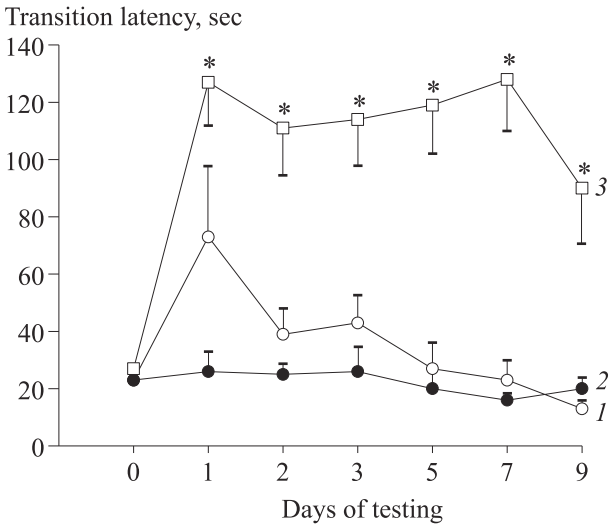


**Fig. 1.** Amnesia development in CBA/Lac (*1*), AKR/J (*2*), and ASC/Icg (*3*) mice. 0: day of training with amnestic influence. *$p$<0.05 compared to *1* and *2*.

In C57, BALB, DBA and C3H mice, arrest in unsafe compartment blocked passive reaction performance, *i.e.* induced amnesia (Table 1). No spontaneous recovery of the retrieval of memory trace was observed during repeated presentation of the learning situation, *i.e.* "psychogenic amnesia" was resistant to the effects of environmental stimuli remaining the procedure of aversive stimulation.

The resistance to the amnestic influence in ASC mice characterized by high level of predisposition to catalepsy, can be explained by preserved capacity to assess the dark compartment as an unsafe signal and, as a consequence, representation of association between memory trace about punishment during learning and aversive context cues in the apparatus during testing. A possible mechanism of amnesia development after arrest in unsafe compartment is forced extinction of the fear reaction [5,

**TABLE 1.** Transition Latency during Amnesia in Different Mouse Strains ($M$±$m$)

| Group | Days of testing | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 5 | 7 | 9 |
| C57 ($n$=10) | 22±2 | 35±3 | 27±2 | 27±2 | 23±3 | 22±3 | 24±4 |
| BALB ($n$=12) | 23±4 | 28±5 | 19±3 | 20±2 | 27±4 | 26±4 | 22±4 |
| DBA ($n$=10) | 19±2 | 33±5 | 31±5 | 30±4 | 19±2 | 20±4 | 17±3 |
| C3H ($n$=7) | 18±2 | 33±6 | 28±7 | 31±7 | 23±7 | 17±5 | 17±3 |

7,9]. In ASC mice, this extinction does not occur, probably due to hypersensitivity of these animals to aversive stimulation, which is seen from high value of startle amplitude after acoustic stimulation [6].

Thus, analysis of individual peculiarities of amnesia formation in different mouse strains showed resistance to amnestic effect in ASC mice with high level of predisposition to freezing reaction.

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