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Long-Term Spatial Memory Retrieval at Different Times Following Formation in Single Session Training in Rats

S. V. Solntseva, Z. I. Storozheva, and V. P. Nikitin

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The dynamics of retrieval of spatial memory formed in single-day training in rats was studied at different terms after training. Good learners, *i.e.* rats successfully learned to find the hidden platform in the Morris water maze after single-day training session, demonstrated spontaneous improvement of maze performance on day 5 after training in comparison with that in 24 h after training. Poor learners (maze performance during learning session did not differ from random level) demonstrated spontaneous improvement of maze performance by day 20 after training. These findings attest to the existence of multiple mechanisms of memory trace transformation at delayed terms after training.

Key Words: *rats; spatial memory; prolonged consolidation; retrieval; latent training*

According to modern concepts, consolidation of long-term memory takes place during certain time period after training (within 24 h) [3,9] followed by extinction of the formed memory or its long-term storage [7,12]. It becomes more evident that the formation of long-term memory is not completed after its consolidation during training [2,8,12]. Some authors hypothesize the existence of a so-called "lingering consolidation", that proceeds permanently during a long period after the learning [4]. Moreover, one may assume that accessibility of memory trace may change with the time elapsed after training [14]. However, studies dealing with memory trace transformation at delayed terms after training are mainly focused on reconsolidation, *i.e.* on the effects of reminder impairment on memory trace stability [1,5]. On the other hand, most investigators studying the consolidation processes employ passive defense models, where memory is formed during a single training session [1,8,14], while protracted consolidation dynamics of more complex skills, particularly spatial skill, remains virtually unstudied.

The objective of the study was to examine dynamics of representation of spatial memory, formed in rats in one training day, at different times of training.

MATERIALS AND METHODS

The experiments were carried out on adult male Wistar rats (n=25, body weight 280-350 g) obtained from Stolbovaya nursery. Before the experiment, the rats were adapted to vivarium conditions for 2 weeks. During adaptation and experiment, the animals were housed in cages (4 animals per cage) with free access to food and water at 21±1°C and 12 daylight cycle. All experiments were conducted in accordance with humanity principles stated in Directive of European Union (Directive 86/609/EC).

Spatial training was carried out in a water maze presented by a round pool 160 cm in diameter and 60 cm high with gray inner surface; the pool was filled with water up to 40 cm (23±2°C). Position of transparent Plexiglas platform, 9 cm in diameter and placed 2 cm lower than water surface, as well as positions of spatial cues in experimental room were constant.

Spatial memory has been formed in a single day. During training, the animals were put into water 4 times from 2 different points (two trials from each

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P. K. Anokhin Institute of Normal Physiology, Russian Academy of Medical Sciences, Moscow, Russia. ***Address for correspondence:*** sols3@yandex.ru. S. V. Solntseva

side with random alternation of starting points). When the animal reached the platform, it was left there for 30 sec, and then transferred to the home cage for 60 sec. Rats that did not reach the platform were gently guided to it. The time of finding the platform was registered in each trial.

Maze performance was tested in one session with two trials with animal placement to the maze using the same two starting points that were used in training (order of the points was random).

Experimental groups equal in terms of skill formation were formed on the basis of training results to be tested at different time points: group 1 was tested 5 days after training (n=8), group 2 was tested 10 days after training (n=17), group 3 was tested 20 days after training (n=9), and group 4 (control) was tested 24 h after training (n=15). Rats from all groups were housed in home cages under vivarium conditions during the entire period between training and test.

During the test, the mean time of finding the platform was used to assess retention and retrieval of spatial memory. This parameter was used to compare different groups, and significance of differences from the same parameter during training day was assessed.

The results were processed statistically by nonparametric Wilcoxon and Mann–Whitney tests using Statistica software.

RESULTS

Analysis of spatial skill performance on the day of training (pooled for all groups) showed that the distribution of the mean time of finding the platform significantly differs from normal distribution (p<0.01). Two subgroups were distinctively allocated in the sample (Fig. 1). In one subgroup this parameter was close to 60 sec, *i.e.* these rats demonstrated virtually no skill.

In light of this, the animals in each group were divided into good learners and poor learners in relation to the median value (48.5 sec) for further analysis. Subgroups of good learners included animals that successfully found the platform at least two times during training. Poor learner subgroups comprised (85-100%) rats that have not found the platform by themselves or their latency exceeded 40 sec, which attested to accidental finding the platform.

Analysis of maze performance in good learners showed that the time of finding the platform 24 h after training was similar to that on the day of training. Statistically significant reduction in latency was observed during testing on day 5 after training in comparison with both training day and control group (Fig. 2). Testing in 10 and 20 days after training revealed no significant differences in the latency from both the baseline level and control group (Fig. 2).

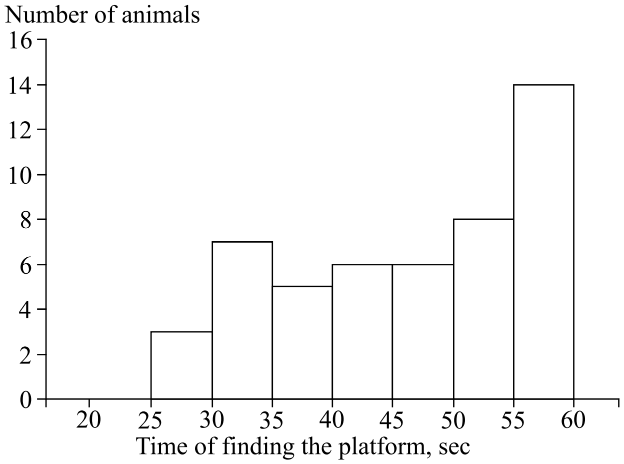

Fig. 1. Distribution of animals by the mean time of finding the platform on the day of training.

Comparison of poor learners from different groups showed revealed significant improvement of test performance on day 20 after training (Fig. 3), but the differences from the values observed on the day of training did not reach the level of statistical significance.

These data suggest that the transformation of long-term spatial memory trace proceeds during relatively protracted period after training (up to 20 days) and that discovered spontaneous memory enhancement after training confirms "prolonged" memory consolidation. Improvement of maze performance in the period from 24 h to 20 days after training was also observed in passive avoidance paradigm [8]. However, it should be noted that these results could reflect prolonged consolidation or changes in memory trace accessibility for retrieval.

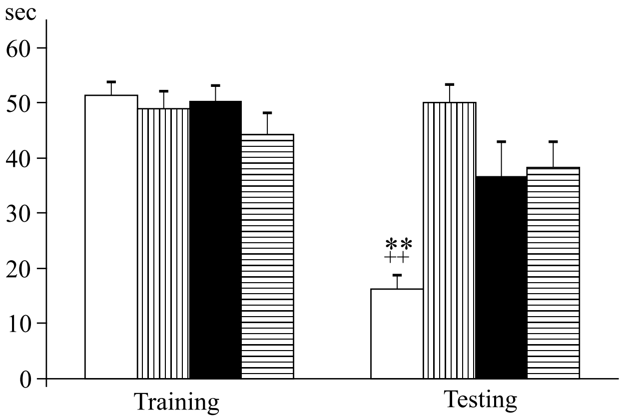

Fig. 2. Dynamics of spatial test performance at different times after single training session in good learners. Light bars: testing 5 days after training (n=4); vertical shading: testing 10 days after training (n=8); dark bars: testing 20 days after training (n=4); horizontal shading: testing 24 h after training (n=7). Here and in Fig. 3: ordinate: mean time of finding the platform for the first two trials. p<0.01 in comparison with: **training, $^{++}$control group (testing 24 h after training).

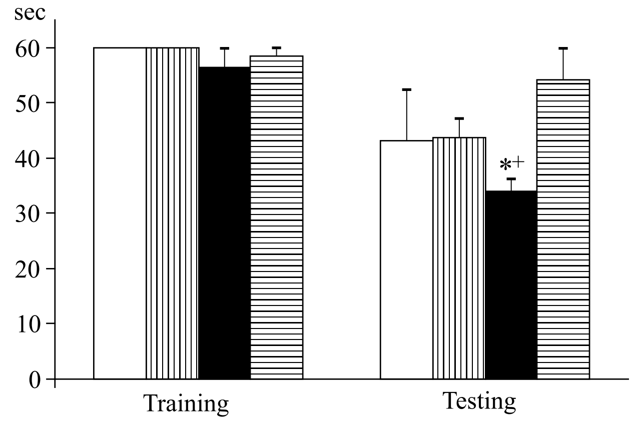

Fig. 3. Dynamics of spatial test performance at different terms after single training session in poor learners. Light bars: testing 5 days after training ($n=4$); vertical shading: testing 10 days after training ($n=9$); dark bars: testing 20 days after training ($n=5$); horizontal shading: testing 24 h after training ($n=8$). $p<0.05$ in comparison with: *training, +control group (testing 24 h after training).

Differences in memory retrieval dynamics between good learners and poor learners are of particular interest. These findings may point at the differences in neurophysiological and neurochemical mechanisms of memory trace formation, consolidation, and storage in animals with different learning capacities. It should be noted that poor learners had almost no reinforcement experience during training (*i.e.* unguided finding of the platform). In this regard, the formation of long-term spatial memory in these animals can be regarded as latent training, *i.e.* training without reinforcement [6,15]. There are data on the possibility of latent spatial training in rats [15], in addition, some investigators suggest that latent training (so-called “cognitive training’) is associated with activation of specific pattern of brain structures, that differs from that in training with classical protocols [6]. Moreover, we found that delayed enhancement (or changed accessibility for representation) of memory trace acquired in single short training session in animals which demonstrated almost no evidences of learning may manifest after a relatively long period after training. This fact is of interest not only in terms of investigation of lingering memory trace transformation path also for psychopathological investigations, since changes in latent training, as reflected by available literature [11], are one of the most typical cognitive impairments in endogenous psychoses.

Generally, the obtained results are indicative of presence of multiple mechanisms of memory trace formation and transformation. Particularly, one may assume that these mechanisms have substantial differences in good learners and poor learners. Literature data also indicates that individual peculiarities in dynamics of memory formation, consolidation as well as in resistance to extinction are associated with selective activation of various neurotransmitter and hormonal systems [10] and coupled neurogenesis/apoptosis processes in adult brain [13]. Investigation of individual peculiarities in dynamics of memory trace transformation at delayed time periods after training is one of timely issues in investigation of cognitive mechanisms.

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