
Step-down passive avoidance in the rat ontogeny

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Abstract. Ontogeny of step-down passive avoidance (PA) was studied in 174 Wistar rats at the age of 2, 3, 4, 6, 8 and 13 weeks. Latency to the first descent from the safe bench (DL), number of descents (DN), time to criterion meeting (TC) and time during which animals were shocked (TS), were evaluated within learning (L) and two consecutive retention tests (R₁ and R₂); R₁ took place at short to intermediate intervals (5 min - 6 h), R₂ 24 h after learning. None of 2-week pups mastered the task. The most efficient learning was in 6-week pups, and also three indices of R₁ (DN, TC and TS) were best at this age. However, the longest DL (most commonly used memory index in PA) was found in R₁ and R₂ of 3-week pups, due probably to high fear motivation. In 3-month animals DL was zero in R₁. It is emphasized that the development of learning and memory is non-monotonous, which was also seen in our previous studies. There were differences between DL recalled from memory and other three indices (DN, TC and TS) in which further reinforcement within the retention test facilitated the retrieval.

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INTRODUCTION

The ontogenetic development of learning and memory has attracted a great deal of interest of many investigators during the last decades, and was the object of several monographs (e.g. Spear and Campbell 1979, Kail and Spear 1984). Usually, learning and memory are considered as a process ameliorating during the ontogeny up to reaching a definite adult level which, in turn, deteriorates with aging. Obrázová (1972) has concluded, on the basis of the data of her laboratory, that an "exaltation period" in the ontogeny occurs when all functional parameters of the brain, including learning and memory, culminate. We, on the other hand, have shown that learning and memory peaks are unevenly distributed throughout the ontogeny depending on a variety of factors, including the complexity and difficulty of the experimental task, animal species and strain, and the stringency of the chosen criteria (Mysliveček 1976, Mysliveček et al. 1980, Mysliveček and Hassmannová 1987). Differential peaks have been shown for one-way active avoidance with the criterion of 9 correct responses out of 10 trials and with 5 correct consecutive responses (Mysliveček and Hassmannová 1973, Hassmannová et al. 1977, Mysliveček and Hassmannová 1979), rectangular maze escape (Mysliveček 1985), one-way and two-way active avoidance in Long Evans and Wistar rat strains (Mysliveček et al. 1983, Hassmannová and Mysliveček 1984). At the age between 4 and 6 weeks we were able to show, in a one-way active avoidance paradigm, an inversion of a typical Kamin effect (1957) and, moreover, a characteristic "W" shaped curve at very short retrieval intervals up to 1 h (Hassmannová et al. 1977).

Considerable data have been accumulated in the literature concerning ontogenic development of various inhibitory conditioned reactions, mainly in the rat, but also in other animal species (Campbell and Campbell 1962, Riccio et al. 1968, Rohrbaugh and Riccio 1968, Feigley and Spear 1970, Schulenburg et al. 1971, Egger and Livesey 1972, Ernst 1972, Nyakas and Endröczy 1972, Riccio and Marrazo 1972, Spear et al. 1972, Sprott 1972, Essman 1973, Meinecke 1974, Ernst 1975, Davis and Jensen 1976, Ray and Nagy 1978, Collier and Mast 1979, Mysliveček 1979, Blozovski and Cudennec 1980, Mysliveček et al. 1980). A general conclusion has been drawn from these investigations that learning and memory of inhibitory reactions, as passive avoidance (PA) and similar phenomena, are maturing in the ontogeny with a delay if compared with other simple types of conditioning that are based

on central excitatory processes. We have shown that in Wistar rats between 1 and 3 months of age the highest incidence of memory within 24 h after learning in a step-through PA paradigm is found at the age of 40-49 days (Mysliveček 1979, Mysliveček et al. 1980). On the other hand, taking into consideration the developmental specificities and capabilities, we were able to show that an inhibitory PA reaction in newborn rat pups may be established as early as several hours after birth (Mysliveček 1982, Mysliveček and Hassmannová 1983, 1990). Taken together, these data indicate that the possibility to get an inhibitory learning and memory depends very much on the actual conditions of the experiment. There were no step by step investigations of passive-avoidance ontogeny throughout a longer developmental period. Neither was published any description of the step-down passive avoidance (PA-SD). We use a PA-SD paradigm, that makes it possible to evaluate several characteristics of learning and memory.

Here we present a detailed description of the development of PA-SD from 2 weeks up to 3 months of age; an abstract of a preliminary report has been published (Mysliveček and Hassmannová 1986).

METHODS

Animals

A total of 174 Wistar rats in the following age groups were studied (number of animals given in parentheses); 2 weeks (10), 3 weeks (17), 4 weeks (53); 6 weeks (35), 8 weeks (25) and 3 months (30). Experiments started when the animals reached precisely the given age. Unequal numbers of animals in groups are due to special attention paid to the ages of 4 and 6 weeks, in the attempt to find out if phenomena analogous to Kamin effect (1957) and our previous findings take place with PA-SD paradigm. The pups stayed with their mothers up to the age of 30 days, when they were weaned. Males and females were evenly represented in each age group.

Apparatus

The apparatus was a brown plastic box 30 x 30 x 22 cm with an electrified grid of stainless-steel rods 2 mm in diam. and 15 mm apart. The grid was electrified with scrambled electric shocks (0.5 s duration at the frequency of 1 Hz, 1.1-1.9 mA - the strength was stepwise increased with age, which elicited escape and avoided

convulsions). A safe bench of size varying from 2 x 6 cm up to 5 x 12 cm was situated close to the middle of one wall of the apparatus, 2 to 5 cm above the grid. There were four bench sizes, length increasing by 2 cm, width and height by 1 cm, which corresponded to the animals' size increasing with age; they could stay but not move on the bench. A plexiglass ceiling was magnetically fixed to the walls of the box.

Procedure

The animal was positioned on the bench and the experimenter measured the time to the first descent, the number of descents and the duration of each animal's stay on the bench starting from its positioning by the experimenter up to the chosen criterion of 100 s on the safe bench without descent to the electrified grid. Thus, four indices could be evaluated: latency to the first descent (DL), number of descents (DN), time to criterion meeting - i.e. the time of the last ascent on the safe bench (TC), and the time of exposition to shocks (TS), i.e. actually the time to criterion minus total time on the safe bench before criterion meeting.

Memory retrieval was tested and evaluated again with the grid electrified by the same way at intervals of 5, 10, 20, 40 min, 3, 6 and 24 h (first retention), and then, in those tested between 5 min and 6 h, once more 24 h after learning (second retention). Retention indices (RI) were computed for DN, TC and TS in the 1st

retention (to reveal if there were any significant changes of memory retrieval) according to the formula $RI = \frac{L-R}{L}$ where L are values within learning and R are values within retention test. As there were no interval effects in the retention (neither in any age group nor in the whole sample) the data were pooled for further evaluation. By this way we obtained 4 indices each with 1 parameter of learning and 2 parameters of memory for each age group.

Statistics

The data were evaluated by ANOVA within and among age groups. Post hoc comparisons between treatments and between individual age groups were effectuated by *t*-test. Differences among age groups in the number of animals meeting and failing the chosen criterion were computed by means of Chi square test and by Fischer test.

RESULTS

Criterion meeting

Twenty-seven animals did not meet the chosen criterion - not to leave the platform for 100 s. Among these animals there were two different groups: those not coping with the experimental situation, and those finding another kind of avoidance than stipulated: they stepped with their hind legs on one rod only while their forelegs leaned against the wall of the experimental box. No significant difference was recorded between the ratios of animals meeting and failing the criterion among the age groups from 3 weeks to 3 months. The percentage of animals meeting 100 s criterion; and of all rats avoiding shocks is shown in Fig. 1. None of ten 2-week-old pups met the criterion; so further attempts with the training of this age group were stopped. The ratio of meeting and failing the criterion was significantly different in 2-week animals compared with all older rats (Fischer test: $p = 1.566 \times 10^{-9}$).

Learning and memory in age groups

ANOVA (3 x 2 factors, i.e. procedure: learning, 1st and 2nd retention tests, vs. sex) in rats fulfilling the chosen criterion showed highly significant or significant effects of procedure in all age groups and all four indices. On the other hand, gender proved significant in one index of 4 weeks old animals only

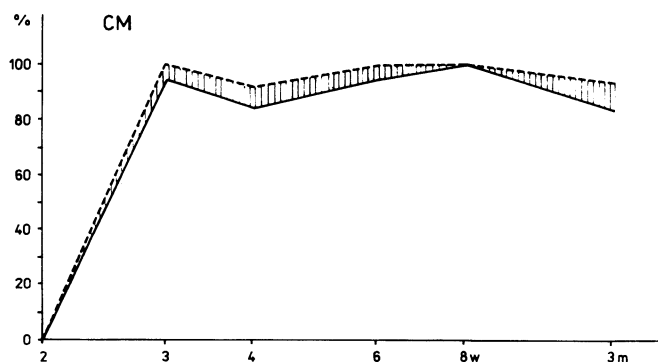


Fig. 1. Percentage of animals (ordinate) meeting the criterion (CM) of 100 s versus age (abscissa) plotted in logarithmic scale (2-8 weeks, 3 months). Full line, animals staying without electric shocks on the safe bench; broken line, all animals without shocks during 100 s; shaded area represents animals standing on one rod of the grid.

(shorter time to criterion within learning and first retention in males) and tended to do so in latency to the first descent of the same age group; number of descents and duration of shocks showed a similar tendency in 3 months old rats. Procedure-gender interaction was significant in time to criterion of 4 weeks old rats, and number of descents in 3 months old rats (Table I). The differences between learning and both retention tests were significant in all four indices studied in every age group, whereas differences between the first and second (24-h) retention were only sporadic (Figs. 2-5): 6 weeks number of descents and time to criterion, 3 months – latency to the first descent.

Developmental changes

Latencies of the first descent, even if generally low, showed a highly significant age factor within learning - $F(4,137) = 11.429, P < 0.001$ (Fig. 2), due mainly to higher latencies in the 4 week group that differed from rats at the age of 3 weeks ($P < 0.01$), 6 weeks ($P < 0.001$), 8 weeks ($P < 0.05$) and 3 months ($P < 0.05$); the difference between 6 and 8 weeks was significant as well

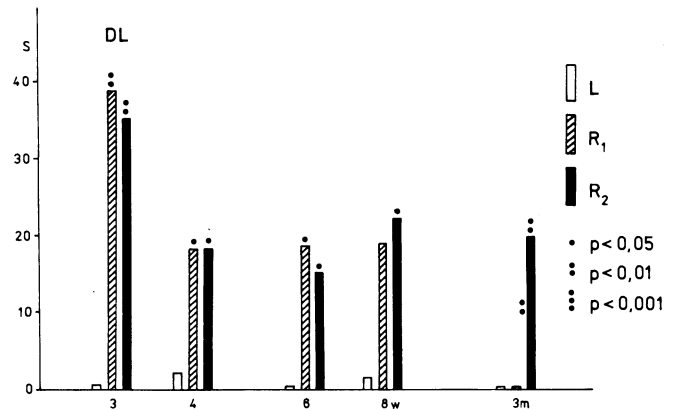


Fig. 2. Average latencies to the first descent (DL) of the safe bench in s (ordinate) within learning (L, white columns), within 1st (R_1 , shaded columns) and 2nd retention test (R_2 , black columns). Significant difference between learning and retention indicated by dots above columns, differences between both retention tests marked by dots between corresponding columns: one dot, $P < 0.05$, two dots, $P < 0.01$, three dots, $P < 0.001$. Age on the abscissa.

($P < 0.05$). The age factor was also significant in the 1st retention test $F(4,137) = 3.179, P < 0.02$. The longest mean latencies of 3-weeks old pups differed from the 4-weeks ones ($P < 0.005$), and 3 months old animals

TABLE I

ANOVA in age groups										
Age	Factor	df	Number of descents-F		Latency of the first descent-F		Time to criterion-F		Duration of shocks-F	
3 weeks	Treatment	2/40	16.956	***	4.856	*	20.408	***	22.827	***
	Sex	1/40	< 1	NS	< 1	NS	2.717	NS	2.324	NS
	T-S interaction	2/40	< 1	NS	< 1	NS	< 1	NS	<< 1	NS
4 weeks	Treatment	2/132	21.367	***	6.098	**	73.279	***	67.414	***
	Sex	1/132	1.354	NS	3.080	°	6.960	**	2.293	NS
	T-S interaction	2/132	< 1	NS	1.541	NS	10.235	**	1.858	NS
6 weeks	Treatment	2/89	13.782	***	3.592	*	16.701	***	21.062	***
	Sex	1/89	<< 1	NS	<< 1	NS	<< 1	NS	<< 1	NS
	T-S interaction	2/89	<< 1	NS	1.270	NS	< 1	NS	<< 1	NS
8 weeks	Treatment	2/65	15.578	***	3.946	*	21.333	***	24.356	***
	Sex	1/65	< 1	NS	< 1	NS	< 1	NS	< 1	NS
	T-S interaction	2/65	1.079	NS	< 1	NS	1.301	NS	1.546	NS
3 months	Treatment	2/65	23.507	***	5.781	**	17.870	***	17.760	***
	Sex	1/65	2.774	°	<< 1	NS	1.644	NS	2.517	°
	T-S interaction	2/65	4.619	*	<< 1	NS	2.391	NS	1.349	NS

Significance: ° $P < 0.10$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, NS, not significant

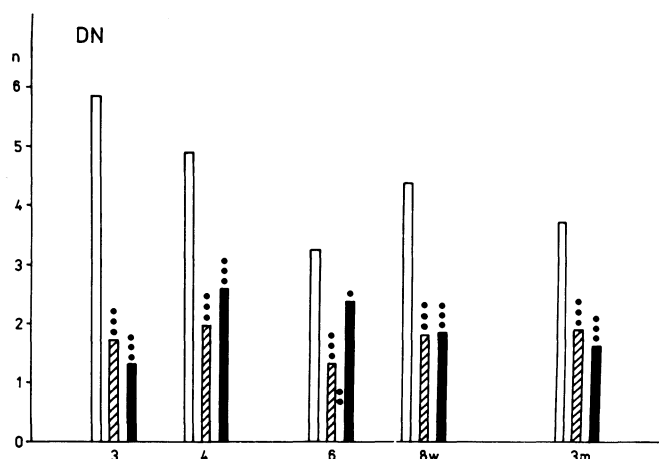


Fig. 3. Average number of descents (DN) of the bench (ordinate). Other explanations as in Fig. 2.

($P < 0.001$) and tended to do so from 6 and 8 weeks old rats. The last group (3 months) differed, moreover, from those of 4 weeks old ($P < 0.05$), 6 weeks old ($P < 0.005$), and tended to differ from 8 weeks old rats. The age factor did not reach significance in the second retention test, but when both retention data were analyzed together, the age factor became highly significant - $F(4,264) = 3.497$, $P < 0.01$; neither sex, nor age-sex interaction proved significant.

Number of descents decreased within learning up to 6 weeks, and then rose again (Fig. 3). The factor of age was significant $F(4,137) = 7.222$, $P < 0.02$, but neither sex, nor sex-age interaction were significant. The 6-weeks group, needing the lowest number of descents to criterion, differed significantly from both younger groups of 3- and 4-weeks old rats ($P < 0.01$). The age factor was significant neither in the first nor in the second retention test.

In time to criterion meeting (Fig. 4) within learning, both main factors were reliable: age - $F(4,137) = 6.526$, $P < 0.001$ and sex - $F(1,137) = 6.389$, $P < 0.05$; males met the criterion earlier in all but the 8-weeks old group. The efficient learning in 6-weeks old rats differed from the age groups of 3-weeks ($P < 0.001$), 4 weeks ($P < 0.001$), 8 weeks ($P < 0.05$) and 3-months old animals ($P < 0.01$); further differences were found between ages: 3 and 8 weeks ($P < 0.05$) 4 and 8 weeks ($P < 0.01$), and a tendency between 4 weeks and 3 months. Also in the first retention test the minimum of time was needed in 6 weeks old animals; the age factor was, however, only marginally significant:

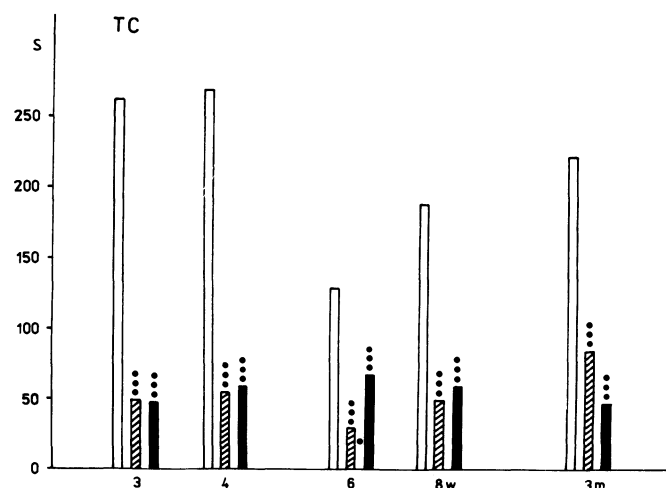


Fig. 4. Average time to criterion meeting (TC), i.e. to the last ascent on the bench before the criterion of 100 s. Other explanations as in Fig. 2.

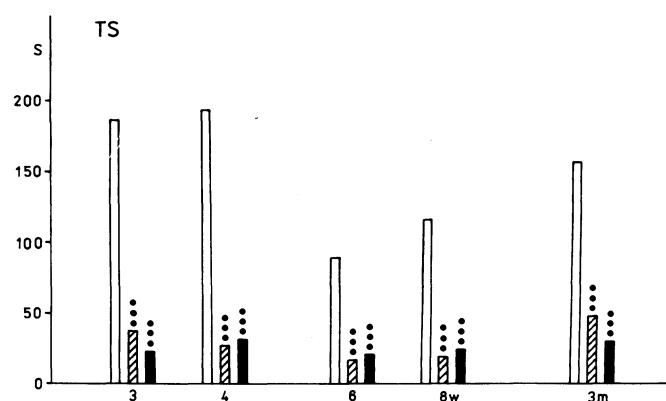


Fig. 5. Average time of shocks (TS) undergone before criterion meeting. Explanations as in Fig. 2.

$F(4,137) = 2.148$, $P < 0.07$. Neither gender main factor nor age-gender interaction were significant. No significant factor was found in the second retention. Duration of shocks (Fig. 5) showed an almost identical picture as did the time to criteria with a reliable age factor in the first retention test. ANOVA yielded the following significant factors within learning: age - $F(4,137) = 5.934$, $P < 0.001$, gender - $F(1,137) = 3.728$, $P < 0.06$; first retention age $F(4,137) = 2.936$, $P < 0.025$; first and second retention combined, age - $F(4,264) = 2.800$, $P < 0.05$.

DISCUSSION

Our present results indicate, similarly as data obtained with other learning - and memory paradigms, that the PA-SD development is not monotonic. Its time course, however, considerably varies. Three of four evaluated indices: number of descents, time to criterion, and duration of shocks showed unambiguously that 6-weeks rats learned PA-SD more efficiently than any other age group. The latent period of the first descent, i.e. the remaining parameter, has no importance for learning evaluation, as it estimates only the first movement after the animal's positioning on the bench. No systematic sex differences were observed; only two parameters (pointing to a common process), i.e. time to criterion and duration of shock reinforcement, were attained better by males than females in all but the 8-weeks group (this might be due to different rates of sexual maturation). Several processes might be hypothetically responsible for the prolonged time to criterion meeting and duration of shocks in 3 months old rats, indicating a slower learning than in two preceding younger age groups, e.g. decreased motivation or worse coping with the experimental situation represented by the relatively small compartment. Larger males coped, however, better with the situation than smaller 3 months old females, and this points, however, against the last-mentioned possibility. The inability of rats aged 2 weeks to master the PA-SD task might be related rather to performance inability than to a general lack of learning or inhibitory mechanisms, as in another paradigm, involving a working memory component, 15-day pups were also unable to master the task (Green and Stanton 1988) whereas a simple PA task was efficiently learned and remembered several hours after birth (Mysliveček 1982, Mysliveček and Hassmannová 1990).

In all but one age (3 months, first retention), the retention data showed reliable memory. The three indices (DV, TC and TS) had an optimum in the first retention test also in the 6-weeks group. Latency to the first descent (usually used as a main indicator of memory in PA paradigms) was an exception, here the longest times were observed in 3 weeks old pups, i.e. the youngest group mastering the task, with minimum differences in the others; the surprising zero latency in the first retention test of 3 months old rats may be hardly explained, but identical findings in 25 animals of both genders, progeny of various litters, cannot be obtained by chance or by an experimental error. Changed reactivity at short and intermediate af-

ter-learning intervals seems to be a tentative explanation. The longest descent latencies in the 3 weeks old animals are probably due, as we suppose, to increased motivation and a fear-provoking effect of shocks at that age.

Our present data show that the age of 6 weeks is an ontogenetic period when the ability of learning and first memory retrieval of PA-SD in our experimental design culminates, and is followed by an impairment at later ages, which is evident in three out of four indices monitored. We do not believe that best parameters of learning and memory (as e.g. in 3 indices of 6 weeks old rats) mean a higher learning and memory capacity at this age per se, but this increased performance is due to a favourable interaction of various factors and internal mechanisms, as e.g. changes of motivation, emotionality or motor reactivity, which is specific for each experimental paradigm and, moreover, for each experimental index. This is evident namely for the remaining index of memory - latency to the first descent from the safe bench with an optimum (longest latency) in the 3-weeks group and zero latency in the first retention test in 3 months old rats.

Memory and its development must be, therefore, viewed also in experimental models as a complex phenomenon whose individual features do not need to coincide absolutely. The latency to the first descent in the PA-SD paradigm indicates evidently a memory recall, whereas in the other three indices a reminder of the original learning characteristics with aversive reinforcement participates as well, and might be thus considered as a recognition indicator. When learning is repeatedly reinforced within the first retention test (which might be thus considered as a reminder procedure), then no significant age factor appears in the second (24-h memory) retention test.

There is a question, if it is possible to correlate our findings on PA-SD development culminating at 6 weeks of postnatal age with the present knowledge of structural, biochemical and functional maturation of the nervous system. It has to be emphasized that PA-SD postnatal ontogeny differs from the development in other kinds of learning and memory (Mysliveček and Hassmannová 1987). This is in good agreement with two principal statements that may be derived from the research work done during the last decades. First, there are several kinds of learning and memory, and even if a general common mechanism may be supposed, each of them is characterized by specific features allowing to consider them as an individual entity (e.g. Warrington 1981, Broadbent

1983, Thompson 1988). Second, there are recent as well as earlier literature data showing that many structural, biochemical and functional parameters of the central nervous system develop differentially, some having a typical ontogenic peak, several of them culminating between 3 and 4 weeks of age, others raising slowly up to adulthood (e.g. Aghajanian and Bloom 1967, Bär 1983, Erdö and Wolff 1989, Rozenberg et al. 1989, Sales et al. 1989, Leroux-Nicollet et al. 1990). The changing role of neural structures during ontogeny is also shown by uneven effects of identical brain lesions at various stage of ontogeny (Kolb and Whishaw 1989). From what has been said it is obvious that manifold time coincidences and correlations between the maturation of various kinds of learning and memory and of other neural characteristics appear, but no causal relationship and direct implication may be firmly established as yet, even if it is very likely to occur.

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