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Two months makes a difference in spatial orientation learning in very old FBNF1 rats☆

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Abstract

Age-related changes in cognitive performance may be more pronounced in the period near or exceeding the median life span. Therefore, we compared the acquisition of a Morris water escape task by two groups of very old Fischer344 × Brown Norway hybrid rats. The mean age difference between the two groups of rats (a 33- to 34-month-old group versus a 35- to 36-month-old group) was about 2 months.

Both groups of rats initially had the same level of performance, but then the younger group learned to escape onto the submerged platform faster, swimming a shorter distance, than the older group. By the fifth acquisition session, the younger rats needed only half the time and swam a shorter distance before they reached the platform than the older rats. These differences in learning were not due to different locomotor abilities as both groups had a similar swimming speed. These results suggest that age-related changes in cognitive performance are indeed more pronounced in the period around the median life span.

We also discussed different set-ups to perform cross-sectional age-comparison studies. If there are not sufficient animals from one batch, it may be worthwhile to combine animals from different batches per age group, provided that breeding, rearing, housing, and testing conditions are highly standardized.

Keywords: Aging; Rat; Cross-sectional design; Morris task

1. Introduction

In order to assess the rate of decline of performance due to aging, longitudinal studies, or cross-sectional studies, preferably with multiple age points, are necessary [1,2]. It has been suggested that age groups that differ by as little as 1 or 2 months should be compared, because aging proceeds at a different rate for different behavioral domains [3–5], and the most profound age-related decline may occur over a relatively narrow age range [6]. In a previous study, we found that 26-month-old FBNF1 rats had a worse performance in the Morris water escape task than 6-month-old conspecifics [7], whereas Hebda-Bauer et al. [8] reported that 23- to 25-month-old FBNF1 hybrids still had a spatial orientation performance similar to that of young conspecifics, although 31-month-old FBNF1 hybrids showed impaired acquisition. Markowska and Savonenko [9] observed a mild decline in spatial discrimination in the Morris task in 18-month-old FBNF1 rats, compared with a group of 9-month-old rats. They observed, however, a further, much stronger decline in 30-month-old FBNF1 rats. These studies show that old hybrids are still able to acquire the Morris water escape task, albeit at slower pace [7–9], and suggest that age-related impairments in acquisition of the Morris water escape task in FBNF1 rats become more pronounced in rats older than 25 months.

To test whether the age-related decline in spatial memory becomes more pronounced in animals older than the median life expectancy, we compared the acquisition of a Morris water escape task by two groups of very old Fischer344 × Brown Norway hybrid (FBNF1) rats. The median life span of FBNF1 hybrids appears to be approximately 31 to 33 months [9–11]. Because it proved difficult to obtain sufficient numbers of animals from the same batch, we combined rats from two different batches per age group. The two age groups were tested at different time points. However, they had been bred, reared, and housed under strictly standardized conditions at the breeder,

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and they were housed and tested under strictly standardized conditions in our laboratory. The age difference between the two age groups was about 2 months: the younger rats were 33 to 34 months old and the older rats were 35 to 36 months old.

2. Material and methods

2.1. Animals

Four batches of aged male F344/NHsd × BN/RijHsd F1 rats (FBNF1/Hsd) – hereafter called FBNF1 – were supplied by Harlan–Sprague Dawley (Indianapolis, Indiana, USA; see Table 1, part A) in two separate shipments. At the breeder's facility, the FBNF1 rats had been maintained in barriers and were provided with standard animal care. The aged rats were fed on 2014S diet and filtered water. They were socially housed, typically 2 or 3 rats per cage. They were maintained on inventory by month of birth.

Each batch originally consisted of 25 animals. After shipment from the USA to Europe, the rats were kept in an air-conditioned (humidity: 60%, temperature: 22C) animal room. They were housed in groups of four in standard Makrolon™ type IV cages with sawdust bedding. If a rat died, the cage was not restocked, and consequently, some cages were occupied by fewer than 4 rats by the end of the study, but all cages were occupied by at least two animals. Lights were on from 6:00 to 18:00.

After 2 or 3 months in our animal room, all animals were transferred to the laboratory where behavioral testing was performed. Here, the rats were allowed to habituate to the new environment for 3 days over the weekend, before training in the Morris water maze started. Of the animals supplied, only those appearing healthy and without cataracts (no obvious abnormalities) were tested in the Morris water escape task (see Table 1, part A).

2.2. Apparatus

The Morris water tank and the escape platform were made of gray Poly-Propylene (PP). The color of the maze and escape platform very closely resembled the gray defined by RAL 7032. The dimensions of the tank were diameter 1700 mm; depth 450 mm; water level 450 mm; diameter of platform 110 mm; height of platform 250 mm. The center of the platform was located half the radius of the maze from the rim of the tank. The video-tracking system EthoVision for Windows (Noldus, Wageningen, The Netherlands; [12]) was used to register the movements of a rat in the water tank.

Table 1

A				B	
Age at test	Number of rats per batch, 1 week before start testing	Number of rats, selected per batch and trained		Number of rats that found the platform	
33-month-old	18	14		11	
34-month-old	18	15	Total of 29 rats	9	Total of 20 rats
35-month-old	19	17		11	
36-month-old	18	15	Total of 32 rats	9	Total of 20 rats

Part A: age of male FBNF1 rats during acquisition on the Morris water escape task, number of animals in the original batch that had survived till 1 week before testing, number of animals selected from the batches for training. Part B: number of animals that were able to locate the submerged platform in the Morris water escape task.

2.3. Procedure

All rats were trained to find a submerged escape platform in the Morris water tank. Training took place for five successive daily sessions. A trial was started by placing a rat into the pool, facing the wall of the tank. Each of four starting positions (north, east, south, and west) was used once in a series of four trials; their order was randomized. The escape platform was always in quadrant west. A trial was terminated as soon as the rat had climbed onto the escape platform or when 90 s had elapsed, whichever event occurred first. A rat was allowed to stay on the platform for 30 s. Then it was taken from the platform and the next trial was started. If a rat did not find the platform within 90 s it was put on the platform by the experimenter and was allowed to stay there for 30 s. After completion of the fourth trial, the rat was gently dried with crêpe paper and returned to its home cage. The animal was kept warm under an infrared bulb (Original Hanau Solilux, 150 W) fixed about 60 cm above the floor of the cage. The body weights of the rats ranged from 430 to 621 g during behavioral testing.

The data of animals that did not find the platform or that found it in less than 80% of the trials during the last two acquisition sessions were removed from the statistical analysis. Note that the proportion of animals excluded due to poor health (difference between number of animals in batch and number of animals trained) or to obvious inability to find the platform (difference between number of animals trained and number of animals that found the platform) was similar in batches and age groups (see Table 1, part B). A common characteristic of all rats that did not find the platform was that they persisted in swimming along the rim of the Morris tank, i.e. they appeared to apply a thigmotaxic strategy and may have been unable to switch to an efficient search strategy [13–15].

The rats received further training after the first five acquisition sessions that are reported in this paper, including a probe trial and training in a repeated acquisition version of the Morris water escape task that assesses short term memory performance [16]. In this phase, the rats received test compounds. Therefore, data on probe trial performance in a drug-naïve state are, unfortunately, not available.

2.4. Statistical analysis

Five different measures were taken to evaluate the performance of the rats during acquisition of the Morris water escape task: escape latency, traveled distance, mean distance to platform, swimming speed, and speed of locomotion.

- Escape latency was the time (s) taken to find and escape onto the submerged platform [17].