

An Evaluation of Spatial Information Processing in Aged Rats

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The spatial learning abilities of young, middle-age, and senescent rats were investigated in two experiments using several versions of the Morris water maze task. In Experiment 1, Long-Evans hooded rats were trained to find a submerged escape platform hidden within the water maze. During this phase of testing, aged rats exhibited acquisition deficits compared with either young or middle-age subjects. With continued training, however, all age groups eventually achieved comparable asymptotic levels of performance. Subsequent testing in Experiment 1 revealed that following original training, aged rats were not impaired in learning a novel escape location or in their ability to locate a visible, cued escape platform. In an attempt to identify the basis of the age-related impairments observed in Experiment 1, naive young and aged rats in Experiment 2 were initially tested for their ability to locate a cued escape platform in the water maze. During this phase of testing, the escape latencies of both young and aged rats rapidly decreased to equivalent asymptotic levels. Subsequent analyses revealed that following cue training, young subjects exhibit a significant spatial bias for the region of the testing apparatus where the platform was positioned during training. In contrast, aged rats showed no spatial bias. Training was continued in Experiment 2 using a novel submerged platform location for each subject. During these place training trials, the escape latencies of senescent rats were longer than those of young subjects. These impairments were also accompanied by a lack of spatial bias among aged rats relative to young control subjects. In combination, the results of these investigations indicate that age-related impairments in water maze performance reflect a specific deficit in the ability of aged rats to utilize spatial information.

In recent years the number of investigations focusing on the identification of age-related changes in learning and memory has risen dramatically. Related to this intensified research effort is an increasing growth in the proportion of aged individuals in the population. Because the incidence of various forms of cognitive deterioration is well documented to increase with increasing age (Botwinick, 1978), an important focus of current research is to delineate age-related changes in learning and memory in laboratory animals. Such investigations may, therefore, highlight specific cognitive processes that are compromised in senescence, as well as provide insight into possible neural sites and mechanisms of senescent memory decline.

In this context, a number of investigations utilizing a wide range of behavioral testing procedures have demonstrated that the performance of aged animals is impaired relative to young subjects (see Kubanis & Zornetzer, 1981, for a recent review). Perhaps the most consistent finding across investigations using rodents is that aged rats are impaired in tasks that young animals solve using spatial information. Specifically, spatial information processing in aged rats has been studied using a number of testing procedures including the Barnes hole-board task (Barnes, 1979; Barnes, Nadel, & Honig, 1980), the 8-arm

radial maze (Barnes et al., 1980; Davis, Idowu, & Gibson, 1983; de Toledo-Morrell, Morrell, & Fleming, 1984; de Toledo-Morrell, Morell, Fleming, & Cohen, 1984; Gallagher, Bostock, & King, 1985; Wallace, Krauter, & Campbell, 1980), the 12-arm radial maze (Ingram, London, & Goodnick, 1981), as well as the Morris water maze (Gage, Dunnett, & Bjorklund, 1984). Despite differences in testing procedures and animal strains across these studies, old animals have exhibited acquisition deficits in each case. These findings therefore suggest that spatial memory testing procedures may be particularly sensitive to changes in learning and memory in aged rats. In attempts to assess age-dependent changes in cognitive function, however, it has proven difficult to dissociate the involvement of learning and memory processes, *per se*, from the contribution of nonspecific factors to learned performance. That is, because aging is accompanied by a broad range of sensory, motoric, and motivational changes in addition to impaired cognitive function, it is important to assess the relative contributions of these various factors to observed behavioral deficits in aged animals. To date, however, relatively few studies have provided such an analysis.

Recently, a behavioral testing procedure has been developed that permits a direct measurement of many nonspecific factors that contribute to learned performance. In this task, known as the Morris water maze, young rats learn the location of a submerged escape platform hidden in a tank of clouded water (Morris, 1981). The nature of the information learned during training can then be assessed by imposing infrequent probe trials in which the escape platform is removed from the maze and the subject is permitted to swim for some fixed period of time. During these "free swim" trials, well-trained rats consistently spend the greatest amount of time swimming

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in the quadrant of the maze that formerly contained the escape platform. In addition, trained rats cross the former location of the platform more often than other areas of equal size located in the centers of the remaining three quadrants of the apparatus (i.e., the platform locations used for other subjects). Because no visual or olfactory cues are available within the maze, it appears that the spatial bias exhibited by animals trained in the Morris water maze is supported by the presence of extramaze cues in the testing environment. This interpretation is also consistent with the demonstration that manipulations which disrupt performance in other spatial tasks (i.e., lesions of the hippocampus or its major connections, O'Keefe & Nadel, 1978) also impair acquisition in the water maze (Morris, Garrud, Rawlins, & O'Keefe, 1982; Morris, Garrud, & Woodhouse, 1980; Schenk & Morris, 1985; Sutherland & Dyck, 1983). In addition, because both quadrant times and annulus crossings are not latency measurements, they provide information concerning spatial learning that is largely unconfounded by the motoric capacity of the subjects tested. This consideration is especially important in research investigating cognitive changes in aging because, as has been noted, age-dependent alterations in many nonspecific factors can contribute to performance differences between young and senescent subjects.

Importantly, a second variety of testing in the Morris task measures sensory, motor, and motivational contributions to learned performance. On these trials, animals are permitted to escape onto a black platform that protrudes slightly above water level. During this cue training procedure, young rats rapidly learn to escape onto the visible platform even when the platform is moved randomly to various locations in the maze (Morris, 1981). In the context of research on aging, cue training in the Morris task permits an analysis of whether aged animals have sufficient sensory and motoric capabilities to swim to a goal object, and whether they are motivated to escape. This information is critical because it directly measures those capacities of animals that are required for normal acquisition in the earlier described place version of the task which, in addition, requires the retention and utilization of spatial information.

In light of the above considerations, we hypothesized that performance in the Morris task might prove sensitive to age-related changes in spatial behavior, and that this testing procedure could yield a more detailed analysis of the variables contributing to observed behavioral deficits in aged subjects than has previously been reported (Gage et al., 1984). The following therefore reports the results of investigations designed to study spatial information processing in young, middle-age, and senescent rats utilizing the Morris water maze.

Experiment 1

Method

Young (6 months, $n = 11$), middle-age (12 months, $n = 11$), and aged (23–28 months, $n = 11$) male Long-Evans hooded rats were obtained from Charles River Laboratories. The ages indicated above denote the age of subjects at the conclusion of behavioral testing. All middle-age and senescent animals were obtained as retired breeders

at 8–9 months of age. Subjects were singly housed in the Department of Psychology vivarium for at least 1 month prior to testing. The animal colony is maintained at an ambient temperature of 24 °C with a 12 hr light/dark cycle (lights on at 0700 hour). Animals were provided with water and standard laboratory rat chow ad lib throughout all experiments.

The testing apparatus used in these experiments was constructed from a large animal watering tank (FCX Corporation, Carrboro, NC), which measured 1.83 m in diameter and 58.4 cm in depth. The interior of the tank was flat white. Prior to testing, the maze was filled to a depth of 35.5 cm with water maintained at 26 °C \pm 1 °C. The two escape platforms used in the task were constructed from 10.2 cm diameter PVC piping covered at one end with wire mesh. One platform was white and measured 34.5 cm in height, and the other was black and measured 36.5 cm in height. Thus, when placed in the filled apparatus, the white platform remained submerged 1 cm below water level, whereas the black platform protruded 1 cm above the surface of the water. Only one platform was placed in the tank during any phase of testing. The white and black platforms, respectively, were used in the place and cue versions of the Morris task described below. Before testing, water in the maze was opacified by the addition of 0.9 kg of dry powdered milk (Land O'Lakes Corp., WI). Following each day of testing, the tank was drained and cleaned.

For all trials, subjects were videotaped through a wide-angle lens attached to a camera mounted directly above the center of the maze. In addition to this equipment, the testing environment contained an abundance of extramaze cues, which included several standard laboratory items (e.g., supply cabinets, sink, shelves, etc.) as well as the experimenter.

Behavioral testing procedures. Prior to behavioral testing, all subjects were handled daily (approximately 2 min/day) for 1 week. On Day 1 of testing, animals were habituated to the apparatus by placing each subject in the maze for 90 s with no escape platform present. Immediately following this habituation trial, subjects were returned to the home cage. Beginning on Day 2, all subjects were tested in the place version of the task for 31 trials, 2 trials per day, 5 days per week. For each animal, the submerged platform was fixed in the center of one quadrant of the maze and remained in that location across these training trials. The platform location among animals in each group, however, was counterbalanced. Subjects were placed in the maze facing away from the center of the apparatus from one of four equally spaced points along the perimeter of the tank. Entry points were randomly varied with the qualification that each animal was placed in the maze at each entry point once across every four trials. During training, escape latencies were measured as the time after being released in the maze until the subject escaped onto the platform. For all trials, after escaping, subjects were allowed to remain on the platform for 60 s. Trial 2 of each day's training began immediately following this 60-s period. A 120-s cutoff was imposed on all trials. If an animal failed to escape during this 2-min period, it was placed on the platform by the experimenter for 60 s. Following the second trial of the day, animals were returned to the home cage.

Subjects were trained as described above for 31 trials. Immediately following Trial 31, the escape platform was removed from the apparatus and the subject was placed in the maze for a 90-s interval. From video tapes filmed during this free swim, it was possible to derive two measures of spatial behavior in the task. One measure, *quadrant time*, is the number of seconds animals spent in each of the four quadrants of the maze. Another measure, *annulus crossings*, refers to the number of times subjects traversed the actual location of the escape platform used during testing compared with the number of crossings made over the three remaining platform locations used for other animals. These measures are important because they directly reflect the degree to which behavior in the task is based on extramaze spatial information.

Training was subsequently continued for Trials 33–40 by returning the submerged platform to its former location for each animal and testing subjects exactly as before for two trials per day. Beginning on Trial 41, animals were tested in a transfer training procedure in which the escape platform was moved to the center of the quadrant opposite to the original training location used during Trials 1–40. Subjects were tested in this manner for 13 trials (two trials/day) following which a second free swim trial (see above description) was interposed on Trial 54.

In the final stage of testing, animals were trained for 7 trials (two trials/day) in a cued version of the Morris task. During these trials (55–61), animals were tested exactly as described above with the exception that a visible black platform (see above description) was placed for each animal in one of the two remaining quadrants not used during earlier phases of testing. The location of the platform across these cued trials remained constant for individual animals.

Two weeks following behavioral testing, subjects were sacrificed by decapitation, and necropsy data were obtained by grossly inspecting the pituitary gland of each subject for evidence of tumors.

Results

Over the course of the first 31 training trials in the place version of the Morris task, the mean escape latencies of all age groups decreased from >90 s to <10 s (see Figure 1). A two-way analysis of variance with repeated measures revealed a significant age effect, $F(2, 20) = 4.70, p < .02$, a significant trials effect, $F(30, 900) = 31.90, p < .001$, as well as a significant Age \times Trials interaction, $F(60, 900) = 1.39, p < .05$. Subsequent separate analyses of the first half (Trials 1–16) and second half of training (Trials 17–31) indicated a significant age effect, $F(2, 30) = 5.81, p < .001$, and trials effect, $F(15, 450) = 28.71, p < .001$, for Trials 1–16 with no

significant interaction. Separate between-groups comparisons revealed that aged subjects were impaired during the first half of training compared with either young, $F(1, 20) = 8.63, p < .01$, or middle-age subjects, $F(1, 20) = 6.62, p < .02$. Inspection of the group data for Trials 1–16 also indicated that aged subjects generally exhibited longer escape latencies on the first trial of each day (i.e., Trials 5, 7, 9, and 13) compared with their performance on the second trial of that day (Trials 6, 8, 10, and 14; see Figure 1). No statistically significant differences were obtained for any variable during the second half of training (Trials 17–31). Finally, between-groups comparisons revealed no significant differences at any point in training between young and middle-age animals.

On Trial 32, all subjects were permitted to swim in the maze for 90 s with the escape platform removed. During this free swim, all groups spent significantly more time in the quadrant of the apparatus that had previously contained the escape platform compared with other quadrants of the maze as revealed by one-way analyses of variance (see Figure 2): young, $F(2, 40) = 56.87, p < .001$; middle-age, $F(2, 40) = 28.61, p < .001$; senescent, $F(2, 40) = 38.83, p < .001$. (Note that in this and all subsequent analyses of quadrant time measures, the numerator degrees of freedom for the F values have been reduced by one to reflect the fact that the total quadrant times necessarily add to 90 s. This adjustment is not necessary for the annulus crossing measure since these crossings are independent of each other.) Despite the slightly stronger spatial bias exhibited by young rats (see Figure 2), subjects of different ages appeared to spend equivalent amounts of time swimming in the training quadrant because no significant age differences were obtained. Parallel results

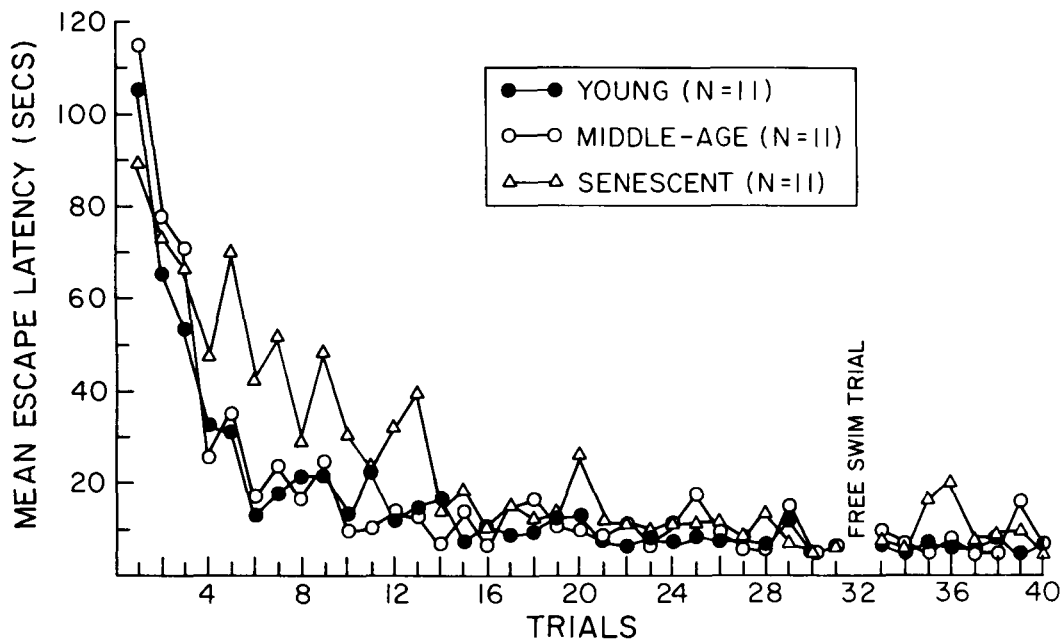


Figure 1 Mean escape latencies across Trials 1–40 for young, middle-age, and senescent rats during place training in Experiment 1. (On Trial 32, the animals were given a 90-s free swim with no escape platform present.)

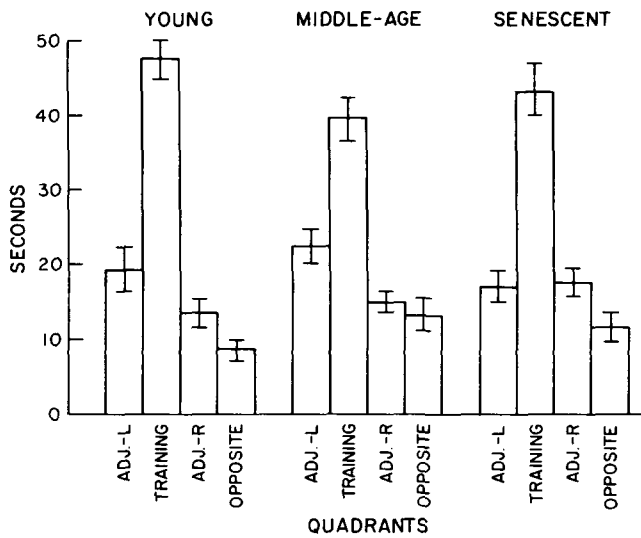


Figure 2 Mean number of seconds (\pm SE) spent by young, middle-age and senescent animals in each quadrant of the water maze during the Trial 32 free swim in Experiment 1 (Quadrants are designated as follows: Training = the quadrant of the maze that contained the submerged escape platform during Trials 1-31, ADJ-L = the quadrant of the maze to the left of the training quadrant, ADJ-R = the quadrant of the maze to the right of the training quadrant, Opposite = the quadrant of the maze directly opposite to the training quadrant)

to the quadrant times were observed in the annulus crossing data derived during this free swim trial (see Figure 3). Specifically, all groups crossed the training location of the escape platform significantly more often than other annuli of equal area in the center of the three remaining quadrants: young, $F(3, 40) = 85.52, p < .001$, middle-age, $F(3, 40) = 43.59, p < .001$, and senescent, $F(3, 40) = 20.94, p < .001$. Subsequent between-groups comparisons failed to reveal a significant age difference in the number of training annulus crossings. Finally, both the quadrant measure and annulus crossings re-

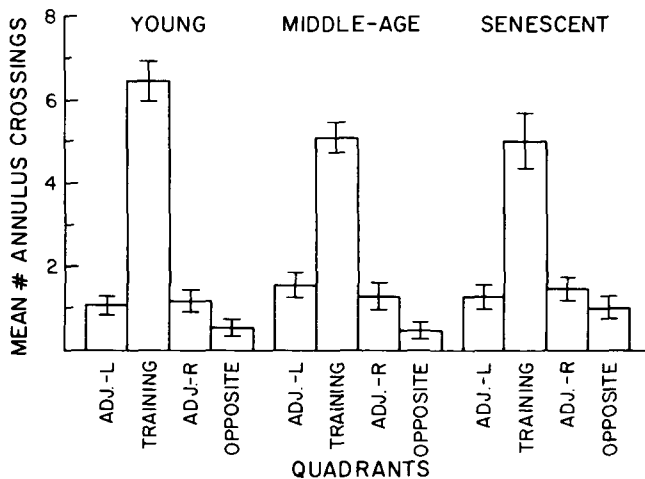


Figure 3 Mean number of annulus crossings \pm SE for young, middle-age, and senescent rats during the Trial 32 free swim in Experiment 1 (Quadrants are designated as in Figure 2)

vealed a similar profile of spatial behavior in all age groups: animals showed the greatest bias for the training quadrant and annulus location, the least preference for the quadrant and annulus opposite to the training location, and an intermediate bias divided among the two quadrants adjacent to the training quadrant.

During Trials 33-40, subjects were tested in the place version of the task with the escape platform located in the same quadrant of the maze as during Trials 1-31 (see Figure 1). Statistical analysis of these data revealed no significant effect of age or trials on performance indicating that the free swim trial did not disrupt escape behavior in any group.

For Trials 41-53 the hidden escape platform was moved to the center of the quadrant opposite to the original training location. During this transfer training procedure, the mean escape latencies of all groups rapidly decreased from >60 s on Trial 41 to comparable asymptotic levels of performance (see Figure 4). Statistical analysis verified the presence of a significant trials effect during transfer training, $F(12, 360) = 31.08, p < .001$. Despite the somewhat longer escape latencies of aged subjects on the second and third trials of transfer training, statistical analysis revealed no significant age effect during this phase of testing. A comparable acquisition of spatial information across age groups was also indicated by the quadrant time and annulus crossing measures derived during the Trial 54 free swim (data not shown). Specifically, all groups showed a significant spatial bias for the quadrant of the maze which had contained the escape platform during Trials 41-53: young, $F(2, 40) = 16.42, p < .001$, middle-age, $F(2, 40) = 9.02, p < .001$; senescent, $F(2, 40) = 20.17, p < .001$. Parallel results were obtained in the annulus crossing measure such that all age groups showed a significant bias for the training location of the platform: young, $F(3, 40) = 21.4, p < .001$, middle-age, $F(3, 40) = 17.10, p < .001$, senescent, $F(3, 40) = 23.68, p < .001$. No statistically significant differences, however, were observed between age groups as assessed by either the quadrant time or annulus crossing measure.

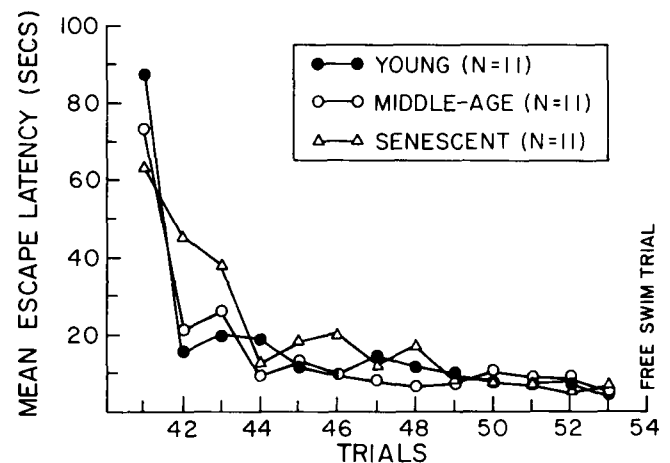


Figure 4 Mean escape latencies for young, middle-age, and senescent subjects during transfer training (Trials 41-53) in Experiment 1 (On Trial 54, the animals were given a 90-s free swim with no escape platform present)

For the final phase of testing in Experiment 1, subjects were tested across Trials 55–61 in a cued version of the Morris task with a visible escape platform fixed in the center of a quadrant of the maze that, for individual animals, was not used during prior training. The mean escape latencies of all groups during these trials decreased to equivalent asymptotic levels of <5 s (see Figure 5). This observation was reflected in statistical analysis that revealed a significant trials effect, $F(6, 174) = 26.71$, $p < .001$. This analysis did not, however, reveal a significant age effect.

Finally, necropsy data obtained 2 weeks following behavioral testing revealed that 2 aged rats had large pituitary tumors which involved the entire gland. During behavioral testing, however, escape latencies, quadrant times, and annulus crossings for these 2 subjects fell well within the range of values exhibited by other senescent rats.

Discussion

The results of the present experiment demonstrate that aged subjects exhibit initial deficits in the acquisition of water maze performance. In addition, the specific pattern of senescent escape performance early in training provides evidence that aged animals are more profoundly impaired on the first trial of each day relative to their performance on the second trial of the same day. This finding suggests that one important determinant of the observed impairment in the Morris task may be due to an age-related deficit in the retention of information important for task performance across days. This interpretation is consistent with other findings, which suggest that one prominent feature of senescent memory decline is an increase in the rate of forgetting of newly acquired information among aged subjects (Zornetzer, Thompson, & Rogers, 1982). The present results further demonstrate that with continued training, senescent rats achieve asymptotic levels of performance equivalent to young and middle-age subjects. This general pattern of results is consistent with a number of previous investigations that have reported significant senescence-related initial deficits in 8-arm radial maze performance

(Barnes et al., 1980; Gallagher et al., 1985). Furthermore, the amelioration of original acquisition deficits with continued training is also a consistent finding across the studies cited. In contrast, other investigations have demonstrated that aged animals exhibit persistent impairments in spatial behavior across a variety of training procedures (Barnes, 1979; Davis et al., 1983; de Toledo-Morrell et al., 1983; de Toledo-Morrell et al., 1984; Gage et al., 1984; Ingram et al., 1981; Wallace et al., 1980). Because all age groups in the present experiment eventually reached equivalent asymptotic levels of performance, however, these results are important in as much as they suggest that aged rats have sufficient motoric capacity to perform well in the task. Based on these findings, then, the hypothesis that deficits early in training in the Morris task result from generalized motor deterioration in aged animals would seem less tenable.

The interpretation that learning in the Morris maze is primarily supported by the presence of spatial information is consistent with the data obtained during the free swim on Trial 32. During this trial, all age groups showed as an equivalent and significant spatial bias for the previous location of the escape platform as well as for that quadrant of the maze that had contained the platform. Since, as these data demonstrate, learning in the water maze is accompanied by a significant acquisition of spatial information, it appears reasonable to suggest that age-related impairments early in training in this task could reflect a specific deficit in the acquisition and/or retention of spatial information. The notion that the senescent deficits observed in the present experiment specifically reflect impaired spatial information processing is also consistent with results obtained during latter phases of training. Specifically, during transfer training trials, all age groups showed similar acquisition of a novel platform location within the original testing environment. The equivalence of learning across age categories in this phase of testing is reflected by the lack of significant differences in escape latency across Trials 41–53, as well as similar annulus crossing and quadrant time measures obtained during the second free swim on Trial 54. In conjunction, these findings provide evidence that given extensive exposure to the testing environment, aged rats acquire sufficient spatial information to support levels of learning in the Morris task comparable to young control subjects.

Although the preceding hypotheses appear tenable on the basis of the findings obtained, the results discussed thus far provide no direct evidence as to the possible contribution of other nonspecific factors to senescent deficits seen early in training in the water maze. The final phase of testing during Experiment 1 therefore used a cued version of the Morris task to assess whether sensory or motivational alterations in aged subjects might contribute to performance deficits among these animals. Data obtained during Trials 55–61 demonstrate that age does not differentially affect performance in swimming to a novel, but visible escape location. Therefore, to the degree that behavior in the cued version of the Morris task is guided by the presence of the visible goal, these data suggest that aged rats have sufficient sensory capacity to locate a visible escape platform and that they are motivated to perform in the task.

Although these findings are consistent with the interpretation that age-related deficits in the Morris task reflect a

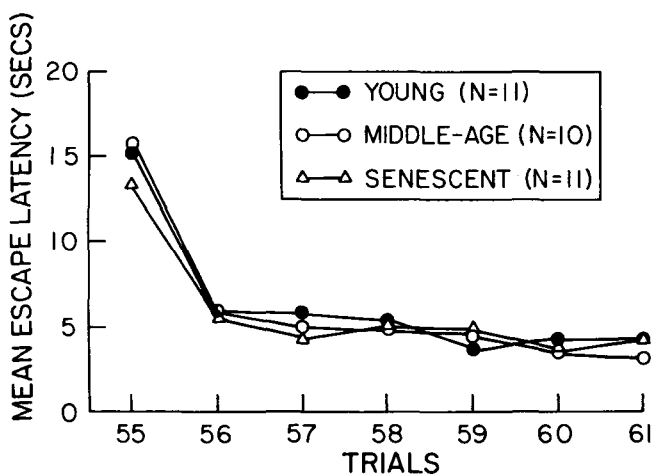


Figure 5. Mean escape latencies for young, middle-age, and senescent rats during cue training (Trials 55–61) in Experiment 1.

senescent decline in the ability to acquire or utilize spatial information, a plausible alternative is that aged subjects are impaired in learning other nonspatial task contingencies. If, for example, aged rats require more trials than young subjects to learn that a means of escape is provided in the maze, acquisition deficits among senescent animals might reflect impaired retention for this information rather than impaired spatial information processing, *per se*. Furthermore, because aged rats are known to exhibit increased neophobia in other behavioral testing procedures (Brennan, Blizard, & Quarterman, 1982, Collier & Sladek, 1984, Goodrick, 1967), it may be that a persistence of neophobic reactions among aged animals during water maze training interferes with the acquisition or retention of information that is critical for normal task performance. Note that neither of these possibilities is well addressed by the inclusion of cue training in Experiment 1 since, by this point in training, senescent subjects had been extensively tested and were found to have acquired sufficient spatial information to support normal performance in the task. Experiment 2, therefore, investigated water maze acquisition in naive young and old rats in the cued version of the task that does not require the utilization of spatial information. Initial cue training should thereby provide evidence as to whether nonspatial task variables contribute importantly to performance differences between young and aged rats. Two weeks following cue training in Experiment 2, young and senescent subjects were tested in the place version of the task exactly as described in Experiment 1. Thus, by providing extensive prior experience in the maze, this design was intended to minimize the neophobic response of aged animals during subsequent place training.

Experiment 2

Method

In Experiment 2, naive groups of young (4 months, $n = 13$) and aged (23–25 months, $n = 11$) male Long-Evans hooded rats (Charles River Laboratories) were initially trained in the cued version of the Morris task as described above. For this experiment, the testing environment and apparatus were the same as in Experiment 1. Subjects were trained over Trials 1–13, 2 trials per day, with the visible black platform always located in the center of one quadrant for each individual animal. The platform location among animals in each group, however, was counterbalanced. As in Experiment 1, a 60-s intertrial interval was imposed, during which the animal remained on the escape platform. A 120-s cutoff was used on all trials. Immediately following the last cue training trial, animals were given a 90-s free swim as described above.

Following training as outlined, animals were not tested in the maze for 2 weeks. Subsequently, all subjects in Experiment 2 were trained in the place version of the Morris task exactly as described in Experiment 1 for 7 trials. During this phase of testing, the submerged platform was fixed for each subject in the center of the quadrant of the maze opposite to the cued platform location used earlier in training. Immediately following Trial 7, subjects were given a 90-s free swim as described above.

Finally, 2 weeks following behavioral testing, all subjects were sacrificed by decapitation, and necropsy data were obtained by inspecting the pituitary gland of each subject for evidence of tumors.

Results

During cue training Trials 1–13, the mean escape latencies of young animals and senescent subjects decreased from

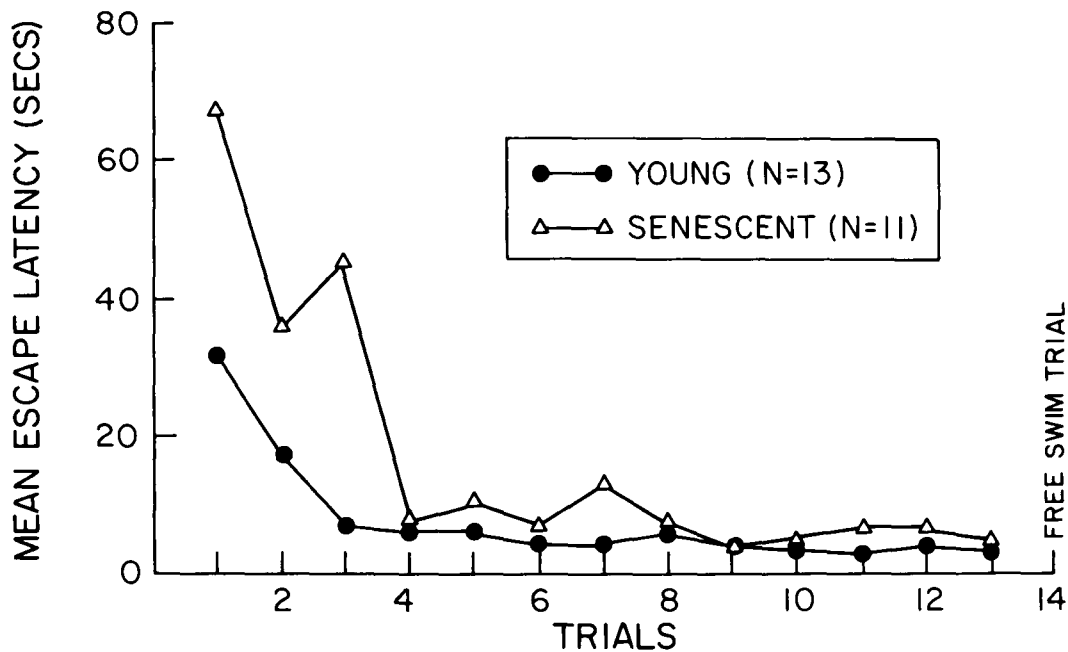


Figure 6 Mean escape latencies across Trials 1–13 for young and senescent rats during cue training in Experiment 2. (On Trial 14, subjects were given a 90-s free swim with no escape platform present.)

greater than 35 s and 65 s, respectively, to below 8 s (see Figure 6) A two-way analysis of variance with repeated measures revealed a significant trials effect, $F(12, 264) = 16.37, p < .001$, a significant age effect, $F(1, 22) = 23.03, p < .001$, as well as a significant Trials \times Age interaction, $F(12, 264) = 3.81, p < .001$ Individual trial comparisons, however, revealed that by the end of cue training, both groups achieved equivalent asymptotic levels of performance Immediately following Trial 13, subjects were given a 90-s free swim Aged subjects showed no spatial bias during this trial as assessed by either the quadrant or annulus crossings measures (see Figures 7 and 8) In contrast, quadrant time measures derived during the Trial 14 free swim showed that young animals spent the greatest amount of time swimming in that quadrant of the maze which had contained the cued escape platform (see Figure 7) Statistical analysis revealed this effect to be significant, $F(2, 48) = 5.08, p < .01$ For young animals, the pattern of time spent in each quadrant was also observed to be similar to results obtained in Experiment 1, with the greatest amount of time spent in the training quadrant, the least amount of time spent swimming in the opposite quadrant, and the remaining time approximately equally distributed among the half of the maze adjacent to the training quadrant Among young subjects, the pattern of annulus crossings also paralleled these quadrant measure results (see Figure 8) There were, however, no statistically significant differences in the number of times young animals crossed the four annuli locations A

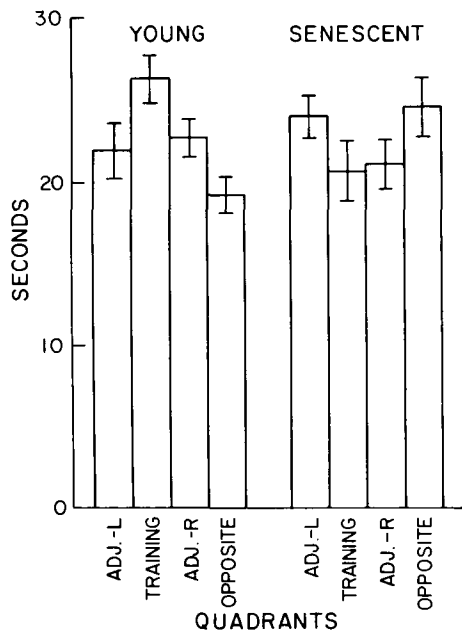


Figure 7 Mean number of seconds \pm SE spent by young and senescent rats in each quadrant of the maze during the Trial 14 free swim in Experiment 2 (Quadrants are designated as follows: Training = the quadrant of the maze that contained the cued escape platform during Trials 1-13. ADJ.-L = the quadrant of the maze to the left of the training quadrant. ADJ.-R = the quadrant of the maze to the right of the training quadrant. Opposite = the quadrant of the maze directly opposite to the training quadrant)

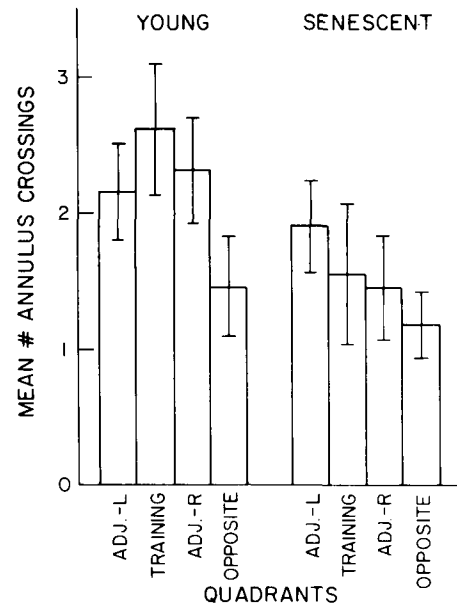


Figure 8 Mean number of annulus crossings \pm SE for young and senescent rats during the Trial 14 free swim in Experiment 2 (Quadrants are designated as in Figure 7)

finer grained analysis of these data was performed by measuring each animal's latency to its first crossing of the training location of the platform These data yielded a median latency of 7.0 s for young animals and a median latency of 40.7 s for senescent subjects. Statistical analysis by a Mann-Whitney *U* test (two-tailed) revealed these results to be significant, $p < .05, U = 32$

Two weeks following the end of cue training, subjects were tested in the place version of the Morris task, with the hidden platform located in the quadrant of the maze opposite to the cued platform location used earlier in testing During Trials 1-7, the mean escape latencies of both groups decreased as revealed in a significant trials effect for these data (see Figure 9), $F(6, 132), p < .001$ A significant age effect was also obtained, $F(1, 22) = 4.23, p < .05$, which reflected the longer escape latencies of aged subjects throughout place training

Immediately following the last training trial, subjects were provided a second free swim Quadrant times measured during this trial revealed that young subjects spent the greatest proportion of time swimming in the quadrant of the maze that had contained the submerged platform (see Figure 10) This effect was statistically significant, $F(2, 48) = 17.65, p < .001$ A similar bias among young rats was also observed for the training location of the platform as assessed in the annulus crossing measure (see Figure 11). Again, this effect was significant, $F(3, 48) = 13.91, p < .001$ In contrast, Trial 8 free-swim data revealed no significant spatial bias among aged rats in either quadrant time or annulus crossings measures

Finally, 2 weeks following the completion of behavioral testing, subjects from Experiment 2 were sacrificed by decapitation. Necropsy data revealed no evidence of pituitary tumors in any subjects used in this investigation

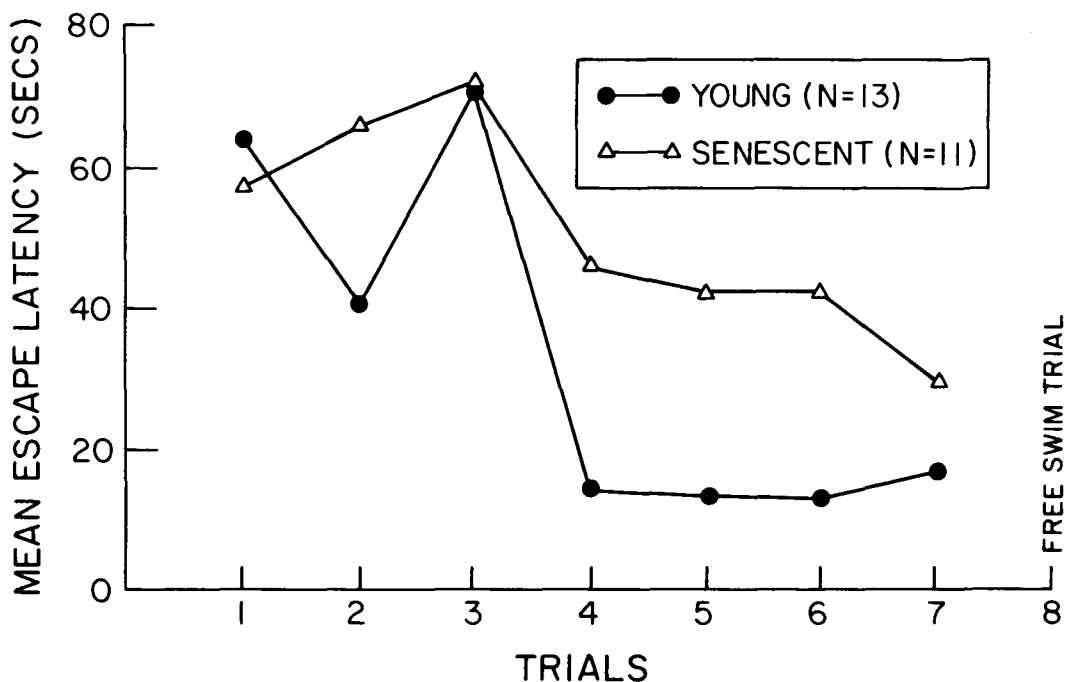


Figure 9 Mean escape latencies across Trials 1-7 for young and senescent rats during place training in Experiment 2 (On Trial 8, the animals were given a 90-s free swim with no escape platform present)

Discussion

The results of Experiment 2 demonstrate that naive aged subjects are impaired during early phases of cue training in the Morris water maze. Importantly, however, the results obtained indicate that age-related deficits in the cued version of the task are primarily confined to the first three trials of training (see Figure 6). Therefore, because the impaired performance of senescent subjects in Experiment 1 became apparent only after the first three trials (see Figure 1), it would appear unlikely that the factors contributing to senescent deficits in cued performance are responsible for the impairments observed during place training. Furthermore, the results of cue training in Experiment 2 indicate that nonspatial learning impairments in senescent subjects do not prevent rapid and substantial acquisition in the task as reflected in the good performance of aged animals after Trial 3. Indeed, the impaired performance of older rats during the first several trials of cue training in the present experiment may, in part, reflect impaired spatial information processing among senescent subjects, since a spatial strategy could be used to solve the cued version of the task used here. Additional data relevant to this proposal are discussed below. In any case, the confluence of these data provide strong support for the proposal that sensory and motor dysfunctions in aged rats are not sufficient to account for the senescent deficits observed during place training. Direct evidence that aged animals do have a specific deficit in processing spatial information is also provided by the results of Experiment 2. Data obtained during the first free swim on Trial 14 clearly demonstrate that during

cue training in the Morris maze, young subjects acquire a significant amount of spatial information, whereas aged rats exhibit no evidence of similar learning. Moreover, this age difference occurs despite senescent subjects having had greater exposure to the testing environment by virtue of their initially longer escape latencies. These results are consistent with other data demonstrating that compared with young subjects, aged animals preferentially use nonspatial strategies to solve tasks when such alternative strategies are available (Barnes et al., 1980).

In the final phase of testing in Experiment 2, aged subjects exhibited impaired escape performance during place training in the Morris task. Because both age groups appeared to benefit substantially and equally from their prior experience in the maze (i.e., compare Trial 1 escape latencies in Figures 1 and 9), it does not appear likely that a persistence of neophobia in senescent subjects contributes importantly to age-related deficits during subsequent place training. Furthermore, age-related acquisition deficits in place training in Experiment 2 are probably not due to behavioral inflexibility among senescent subjects (i.e., a persistence of swimming to the former cued platform location), since the results of transfer training in Experiment 1 demonstrate that aged rats are not impaired in learning a novel spatial location within the original testing environment. Direct evidence that the deficits observed among senescent rats primarily reflect impaired spatial information processing is provided by the free swim data obtained following place training. These results demonstrate that deficits early in place training in the Morris task are accompanied by a profound lack of acquisition of spatial

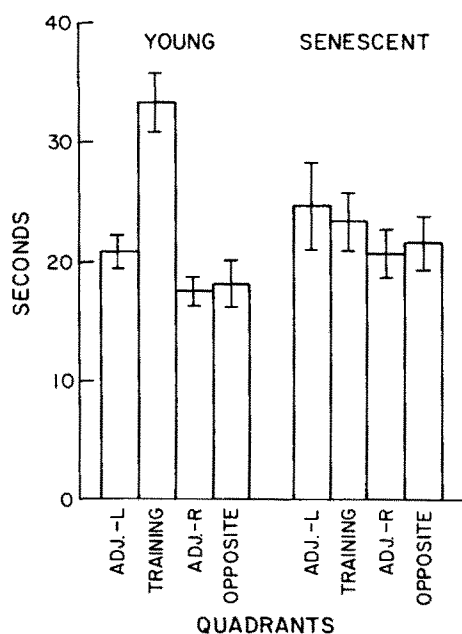


Figure 10 Mean number of seconds \pm SE spent by young and senescent rats in each quadrant of the maze during the Trial 8 free swim in Experiment 2 (Quadrants are designated as follows: Training = the quadrant of the maze that contained the submerged escape platform during Trials 1-7. ADJ-L = the quadrant of the maze to the left of the training quadrant, ADJ-R = the quadrant of the maze to the right of the training quadrant, Opposite = the quadrant of the maze directly opposite to the training quadrant)

information among aged subjects. Indeed, given the results described, it is not unreasonable to suppose that the acquisition of spatial information among young subjects during prior cue training may have served to facilitate later place learning in these subjects.

General Discussion

The experiments described here demonstrate that aged rats exhibit marked impairments during place training in the Morris water maze. These findings are in general agreement with other recently reported data (Gage et al., 1984) and provide substantial additional evidence supporting the interpretation that aged rats have a specific impairment in their ability to process spatial information. In addition, this research suggests that the Morris water maze may be a particularly sensitive procedure with which to test the nature of cognitive dysfunctions in senescence. Given the substantial literature delineating neuroanatomical sites and neurochemical mechanisms involved in mediating spatial learning, the present experiments may also facilitate efforts to identify candidate neural substrates of age-related spatial learning impairments. Current experiments are, therefore, underway in our laboratory to investigate age-related neurochemical dynamics and their relation to deficits in processing spatial information.

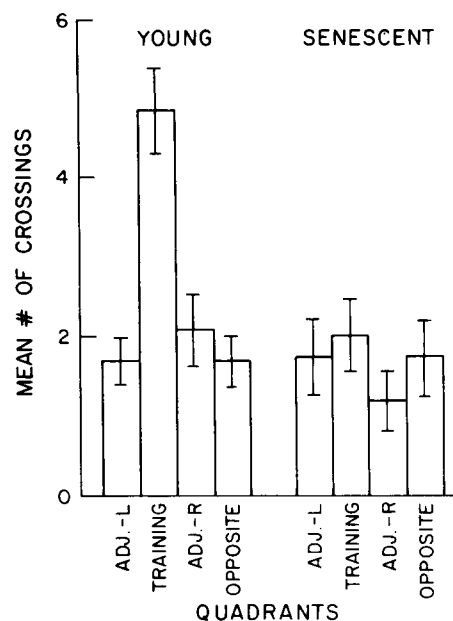


Figure 11 Mean number of annulus crossings \pm SE for young and senescent rats during the Trial 8 free swim in Experiment 2 (Quadrants are designated as in Figure 10)

References

- Barnes, C. A. (1979). Memory deficits associated with senescence: A neurophysiological and behavioral study in the rat. *Journal of Comparative and Physiological Psychology*, 93, 74-104.
- Barnes, C. A., Nadel, L., & Honig, W. K. (1980). Spatial memory deficits in senescent rats. *Canadian Journal of Psychology*, 34, 29-39.
- Botwinick, J. (1978). *Aging and Behavior* (2nd ed.). New York: Springer.
- Brennan, M. J., Blizard, D. A., & Quartermain, D. (1982). Amelioration of age-related deficits in exploring behavior by preexposure to the test environment. *Behavioral and Neural Biology*, 34, 55-62.
- Collier, T. J., & Sladek, J. R. (1984). Increased neophobia: Behavioral identification of a subpopulation of memory-impaired norepinephrine-deficient aged F344 rats. *Society for Neuroscience Abstracts*, 10, 772.
- Davis, H. P., Indow, A., & Gibson, G. E. (1983). Improvement of 8-arm maze performance in aged Fischer 344 rats with 3,4-diaminopyridine. *Experimental Aging Research*, 9, 211-214.
- de Toledo-Morrell, L., Morrell, F., & Fleming, S. (1984). Age-dependent deficits in spatial memory are related to impaired hippocampal kindling. *Behavioral Neuroscience*, 98, 902-907.
- de Toledo-Morrell, L., Morrell, F., Fleming, S., & Cohen, M. M. (1984). Pentoxifylline reverses age-related deficits in spatial memory. *Behavioral and Neural Biology*, 42, 1-8.
- Gage, F. H., Dunnett, S. S., & Bjorklund, A. (1984). Spatial learning and motor deficits in aged rats. *Neurobiology of Aging*, 5, 43-48.
- Gallagher, M., Bostock, E., & King, R. (1985). Effects of opiate antagonists on spatial memory in young and aged rats. *Behavioral and Neural Biology*, 44, 374-385.
- Goodrick, C. L. (1967). Exploration of nondeprived male Sprague-Dawley rats as a function of age. *Psychological Reports*, 20, 159-163.

- Ingram, D K, London, E D, & Goodrick, C L (1981) Age and neurochemical correlates of radial maze performance in rats *Neurobiology of Aging*, 2, 41-47
- Kubanis, P, & Zornetzer, S F (1981) Age-related behavioral and neurological changes: A review with emphasis on memory *Behavioral and Neural Biology*, 31, 115-172
- Morris, R G M (1981) Spatial localization does not require the presence of local cues *Learning and Motivation*, 12, 239-260
- Morris, R G M, Garrud, P, Rawlins, J N P, & O'Keefe, J (1982) Place navigation is impaired in rats with hippocampal lesions *Nature*, 297, 681-683
- Morris, R G M, Garrud, P, & Woodhouse, I Q (1980) Fornix lesions disrupt location learning by the rat *Behavioral Brain Research*, 2, 266
- O'Keefe, J, & Nadel, L (1978) *The hippocampus as a cognitive map* Oxford Clarendon Press
- Schenk, F, & Morris, R G M (1985) Dissociation between components of spatial memory in rats after recovery from the effects of retrohippocampal lesions *Experimental Brain Research*, 58, 11-28
- Sutherland, R J, & Dyck, R H (1983) Hippocampal and neocortical contributions to spatial learning and memory *Society for Neuroscience Abstracts*, 9, 638
- Wallace, J E, Krauter, E E, & Campbell, B A (1980) Animal models of declining memory in the aged: Short-term and spatial memory in aged rats *Journal of Gerontology*, 35, 355-363
- Zornetzer, S F, Thompson, R, & Rogers, J (1982) Rapid forgetting in aged rats *Behavioral and Neural Biology*, 36, 49-60

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Correction to Thomas and Gash (1986)

In the article "Differential Effects of Posterior Septal Lesions on Dispositional and Representational Memory" by Garth J Thomas and Don M Gash (*Behavioral Neuroscience*, 1986, Vol. 100, No 5, pp 712-719), a phrase was erroneously deleted from the text. In the seventh paragraph on p. 713, the second sentence should read as follows: Early in training individual differences were great, but by the end of adaptation training, individual differences were quite small and all rats responded at close to asymptotic speeds.
