Neurobiology of Aging, Vol. 19, No. 6, pp. 589–597, 1998

0197-4580/98 $–see front matter

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PII:S0197-4580(98)00107-9

Environmental Influences on Cognitive Decline in Aged Rats

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Received 20 July 1998; Revised 30 November 1998; Accepted 14 December 1998

WINOCUR, G. *Environmental influences on cognitive decline in aged rats.* NEUROBIOL AGING **19**(6) 589–597, 1998.—Two experiments are reported in which young and old rats, housed in an impoverished (IE), enriched, (EE), or standard (SE), environment, were tested on a series of complex, blind-alley mazes. In Experiment 1, 3-months exposure to IE exacerbated age differences in maze performance, relative to the differences between young and old rats in EE and SE. Old rats in the EE and SE conditions did not differ from each other. In Experiment 2, rats were raised for an additional 3 months in either IE or EE before further maze testing. The main findings were that the maze performance of old rats, transferred from IE to EE, improved significantly, whereas the performance of old rats, transferred from SE or EE to IE, declined. These results indicated that the deleterious effects of an impoverished environment on learning and memory are, at least partly, reversible, and that experience in a stimulating environment can protect old rats from the adverse effects of relocation to a deprived environment. Taken together, the results highlight the impact of environmental influences on cognitive function in old age, and emphasize the need to consider nonbiological factors in understanding the process of cognitive aging. © 1999 Elsevier Science Inc.

Aging Cognitive function Environmental influences

THERE IS growing awareness that cognitive decline in old age is related to a number of factors, in addition to biological processes that cause structural changes in the brain. Older people, of course, are at risk for a variety of physical and mental health problems and it is well known that health status can directly or indirectly impact on neurocognitive function. In the pursuit of other relevant variables, recent research has shown that personal (1,18), psychosocial (3,32), and lifestyle-related (15,24,52) factors can also interact with chronological aging to affect cognitive performance. Attempts to study nonbiological influences on cognitive function in animal models have yielded similar relationships. Several reports have highlighted the potential benefits of early handling (39), dietary restrictions (26), and physical exercise (22).

Over the last 15 years, our research has identified environmental conditions as another significant contributor to cognitive aging in humans (41,57,59,61,62). In a series of experiments, involving a variety of learning and memory tasks (e.g., paired-associate learning; negative transfer; release from proactive interference, and standard neuropsychological tests), normal old people living in their own homes in the community, consistently performed better than carefully matched counterparts living in various institutional settings. These differences could not be attributed to differences in health, education, socioeconomic status, or other potentially confounding factors. Rather, there were strong indications that they were related to environmental influences and older people's adjustment to environmental stressors.

A well-established tradition of animal research points to the importance of environmental influences on brain function (see reviews (45,46)). While much of this work has been conducted on animals in early stages of development, effects of environment on the aging brain also have been examined. The latter research, performed mainly on aged rats, has consistently shown that environmental enrichment induces a variety of brain changes that include increases in dendritic growth (22), cortical thickness (13), levels of nerve growth factor (40), and brain weight (40). Environmental effects on age-related changes in cognitive function have been investigated in a few studies and, in general, the results indicate that old rats, housed in complex, stimulating environments, performed better on tests of learning and memory than rats raised in standard or impoverished conditions (6,11,14,27,51).

In most studies of environmental influences on cognitive aging, animals were reared in special housing throughout most of their life span. The present research extends this work by comparing the effects of limited exposure to an enriched, impoverished, or standard laboratory environment on maze-learning performance. In Experiment 1, groups of young and old rats were transferred from group cages to one of three experimental environments and, after 3 months, administered a series of 12 complex mazes

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designed to assess general learning and memory abilities. The second study employed a cross-over design to assess the permanence of environmentally-induced effects, the ability of old rats to recover from negative effects of an impoverished environment, as well as the extent to which experience in a stimulating environment can protect against subsequent adverse effects of being transferred to an impoverished environment.

METHODS

Subjects

The subjects were male, Long–Evans rats obtained from the Trent University Breeding Center (Peterborough, Ontario, Canada). The same rats were used for Experiments 1 & 2, and only the data for animals that completed both experiments are reported. A total of 52 old rats and 53 young rats were used in this research.

Old rats were between 19 and 20 months of age when they were assigned to their respective environments in Experiment 1. Previously, for most of their adult lives, they were housed in small groups in plastic cages. At different stages of development, all old rats had participated in several experiments, involving operant conditioning or discrimination learning procedures. During these experiments, they were housed in individual wire-mesh cages, located in a room that contained other racks of cages. There were no systematic differences in the experiences of rats that were assigned to the various environmental conditions.

Young rats were 6–7 months old at the beginning of Experiment 1. Their histories were similar to those of the old rats, except that the young rats had participated in only one behavioral study before the present research.

The health status of all rats was regularly assessed by a consulting veterinarian. Over the course of the two experiments, for reasons of death, poor health, or inability to perform the tasks, 12 old rats and 4 young rats were moved from the research, and their data are not included.

Test Apparatus

A Hebb–Williams Closed Field Test was constructed according to specifications described by Rabinovitch and Rosvold (42). It consisted of a square field (76 × 76 cm) with start (28 × 52 cm) and goal (28 × 52 cm) boxes located at diagonally opposite corners. The square field, which was covered by a wire-mesh screen, was divided into 36 clearly marked squares. The squares defined error zones in blind alleys and served as markers for placing the barriers to create 12 maze problems. The configurations of the problems were identical to those described by Rabinovitch and Rosvold (42).

Environments

For Experiment 1, all rats were assigned to one of three environmental conditions in which they were housed for 3 months and, as well, for the duration of testing: enriched (old, $n = 16$; young, $n = 18$); impoverished (old, $n = 17$; young, $n = 18$); standard (old, $n = 19$; young, $n = 17$). Illumination for all environments was provided by central lights that were controlled by a 12-h on/off schedule. To familiarize the rats with their new environments, for 1 week before the transfer, each rat was placed in its assigned environment for approximately 2 h each day.

Enriched Environment (EE). This environment consisted of a wire cage (95 × 95 × 45 cm) that contained various objects (toys, tunnels, etc.) that could be entered, manipulated, or moved. Objects that deteriorated with use were replaced as needed. An activity wheel was attached to one wall. A second level (95 × 30 cm), attached midway up the back and side walls, was connected to the floor by two wire-mesh ramps. Several water bottles and food hoppers were attached to the walls at various locations. A total of four such cages were constructed, each housing 8–10 old or young rats.

Impoverished Environment (IE). This environment was created in a separate, quiet room that contained a single rack of individual wire-mesh cages. The front of the cages was covered by a dark curtain that permitted diffuse light during the light-on periods. The only activity in the room was that of an animal attendant who performed routine maintenance duties every other day and the veterinarian during his periodic visits.

Standard Environment (SE). This environment consisted of individual wire-mesh cages in a rack that was located in one of the colony rooms that also contained other similar racks. Students, research assistants, and lab attendants created regular traffic in this room. In the 3 months before the beginning of maze testing, rats in this environment were routinely handled every 3 or 4 days. SE rats were handled to provide rats in this condition with a level of stimulation that was intended to be intermediate between that received by the IE and EE groups.

Procedure

After rats had lived in their respective environments for 3 months, they were placed on a restricted food schedule to reduce their weight to 80% of normal body weight. Throughout the experiment, individually housed rats were maintained at a constant weight by being fed 15–20 g of standard lab chow each day. Rats housed in group cages were fed on a feeding stand in groups of four or five. During group feeding, the rats remained on a stand for about 1 h until they had all stopped eating. Once maze training began, all feeding took place after each day's session.

Initially, rats were given four adaptation sessions (one per day) in which they were paired and placed in the maze apparatus, which contained only a few randomly located barriers. During these sessions, the rats were allowed 1 h to explore freely and eat wet mash in the goal box.

On the 5th day, preliminary training was introduced in which rats were administered a series of practice problems. Each rat received 10 trials per day in which it was individually placed in the start box and allowed to run to the goal box where it could eat for 10 s. A different practice problem was introduced each day for a total of 6 days. The problems corresponded to those described by Rabinovitch and Rosvold (42). The criterion for advancing to the test problems was running the 10 trials of the last practice problem within a total of 70 s. Most young rats reached this criterion but a few that did not were given up to five additional sessions on mirror images of the practice problems. At this point, two young rats that did not reliably navigate the mazes during practice were eliminated. Approximately half the old rats reached the set training criterion but many old rats ran slower and failed to reach the criterion within six additional sessions. Consistent with previous practice (58), old rats were allowed to enter the test phase if they averaged about 15 s per trial on the last practice problem. At this point, four old rats that failed to meet the more liberal criterion were withdrawn from the experiment.

During testing, which began the day after criterion was reached on the practice problems, rats were administered the 12 mazes of the Rabinovitch and Rosvold series. Each rat received 10 trials on a different maze each day for a total of 12 days. Records were kept of the number of error zones that each rat entered while moving from the start box to the goal box. An error was scored when a rat's two forepaws crossed an error line. Each error-zone entry constituted an error. When a rat reached the goal box, it was allowed to eat from the wet mash for about 10 s before being returned to a

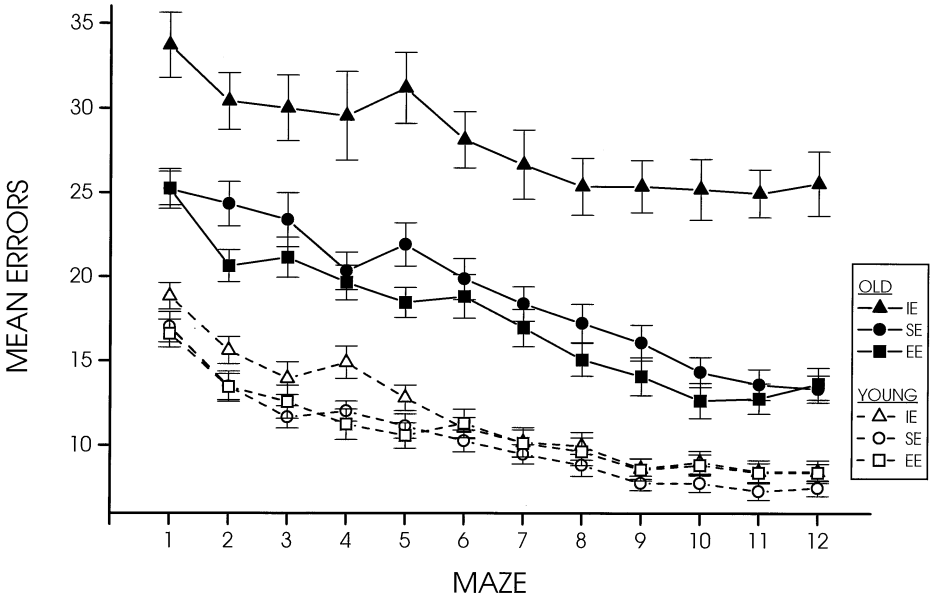

FIG. 1. Mean number of errors made by young and old rats, housed in enriched, impoverished, or standard environments on the 12 mazes of Experiment 1.

holding cage to await the next trial. Rats were run in squads of five to six, so that intertrial intervals generally ranged between 5 and 10 min, depending on the rat's running speed.

RESULTS AND DISCUSSION

The average number of errors made by old and young groups, housed in the different environments, on each of the 12 maze problems, are presented in Fig. 1. It is readily apparent that, in each of the environmental conditions, young rats out-performed old rats. ANOVA revealed significant main effects of age in SE conditions [$F(1, 34) = 74.86$, $p < 0.0001$; EE, $F(1, 34) = 45.59$, $p < 0.0001$; and IE, $F(1, 33) = 36.75$, $p < 0.0001$]. The data also revealed significant main effects of training over the 12 mazes in each environmental condition (all p values $<$ 00001), and significant age $\times$ training interactions in SE [$F(11, 374) = 3.70$, $p < 0.001$; and EE, $F(11, 352) = 3.96 = p < 0.001$]. In IE, the group $\times$ training interaction was not significant ($F < 1$).

The results also show that environmental factors influenced the performance of old rats on the maze problems. Overall error scores, as presented in Fig. 2, confirm the robust age effect over

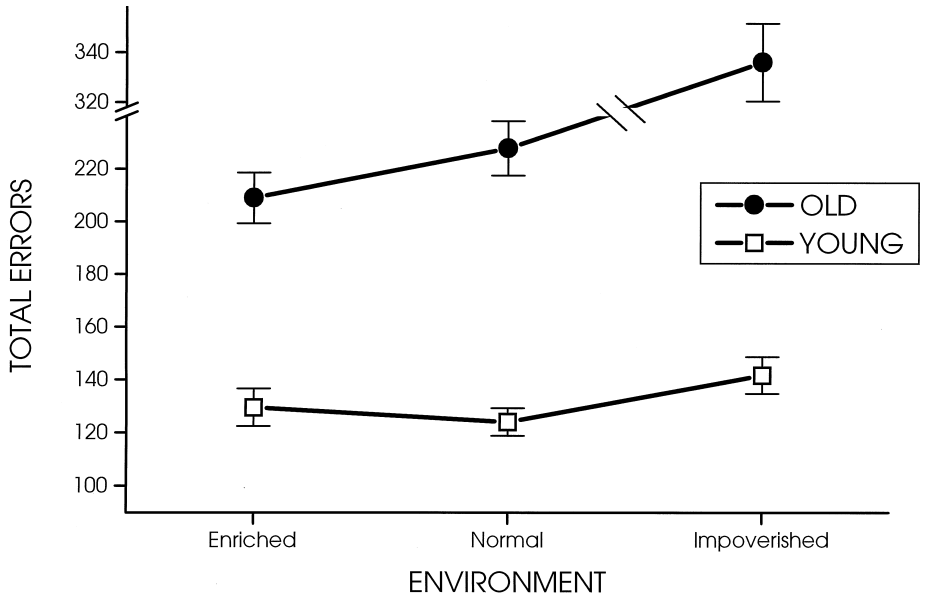

FIG. 2. Mean number of errors made by young and old rats, housed in enriched, impoverished, or standard environments in Experiment 1.

the three environmental conditions [$F(1, 99) = 254.75$, $p < 0.0001$] and, in addition, highlight the significant main effect of environment [$F(2, 99) = 31.56$, $p < 001$]. Of particular interest, the effect of environment was modified by the effect of age [$F(2, 99) = 19.56$, $p < 0.001$], especially in IE, where aged rats were more adversely affected by restriction than young rats. Post hoc comparisons with the Tukey test confirmed that old rats, housed in IE, performed significantly worse than old rats in SE and IE (both p values < 0.001), conditions, whereas the latter groups' performance did not differ from each other (p values > 0.05). Comparisons of young groups' performance across environmental conditions yielded no significant differences (all p values > 0.05).

The differential effects of environment are also reflected in the significant group $\times$ training interactions that were observed in the SE and EE conditions, but not in IE. In SE and EE, the old rats' deficits were greatest in the first six mazes (Fig. 1). Differences between old and young groups in these environments decreased when, with further training, the old rats began to improve at a somewhat faster rate. This pattern probably reflects the old rats' impairment in learning basic maze-learning skills that could be transferred from one maze to another. The steady improvement of young rats from the beginning of testing suggests that these skills were acquired during exposure to the practice problems and had generalized readily to the test problems. The age-related deficit in acquiring nonspecific, maze information was reported by Winocur and Moscovitch (58), and attributed to a failure of frontal-lobe function. The finding, in IE, that the exaggerated impairment of old rats was relatively constant across the 12 problems, indicates that environmental restriction disproportionately affected their ability to learn and remember information that was specific to each maze and exacerbated their difficulties in acquiring a general maze-learning strategy.

Experiment 2

An important finding of Experiment 1 is that old rats, transferred from a standard laboratory environment to an impoverished environment for a relatively brief (3-month) period, were profoundly impaired on maze testing, relative to a similar group that was always housed in the standard environment. By comparison, transfer to a more stimulating, group-cage environment had little effect on old rats' performance. The question arises as to whether the exaggerated maze-learning deficits of the aged, IE rats reflected an accelerated and permanent loss of brain function or an environmentally induced change that may be reversible.

Work with older humans indicates that restricted environments can have adverse effects on cognitive performance but there is evidence that, under certain conditions, their effects are situationally dependent and, to some extent, reversible. In a recently completed longitudinal study, Winocur and Moscovitch (see (12)) found that older people, confined to periods of inactivity in a restricted institutional environment, often performed worse on cognitive tests than comparable individuals who lived in richer environments. When circumstances of the confined individuals changed in favorable ways, their cognitive performance improved significantly. The reverse pattern was also found to be the case when normal older people, for various reasons, found themselves isolated from their broader social environments.

The aim of Experiment 2 was to determine if parallel effects can be demonstrated in an animal model. That is, if the environmentally induced cognitive deficits of IE rats in Experiment 1 reflect a shut-down of brain function rather than permanent physiological changes, it may be possible to restore some function by improving their environments. To address this issue, IE rats were divided into two subgroups: one that remained in the impoverished environment for an additional 3 months, and another that was transferred to the enriched, group-cage environment. They were then tested once again on a series of similar maze-learning problems. If the severe impairment of IE rats was linked directly to a reversible environmental effect, it was expected that rats transferred to EE would display some functional recovery. Similarly, the SE and EE groups of Experiment 1 were divided into subgroups and housed in the impoverished or enriched environment for the same 3-month period. The latter groups enabled comparisons of behavioral effects of relocating between different environments, and provided the opportunity to assess whether exposure to stimulating environments can protect against the deleterious effects of subsequent relocation to a restricted environment.

Methods

Following completion of testing in Experiment 1, all rats were maintained in their pretest environments on an ad lib. food and water schedule. After 1 week, each environmental group was divided approximately in half and assigned to environmental conditions in the following manner. Rats previously housed in IE remained in their isolated cages (IE-IE: old, $n = 8$; young, $n = 9$) were transferred to a group cage (IE-EE: old, $n = 9$; young, $n = 9$). Rats previously housed in EE remained in their group cage (EE-EE: $n = 8$; young, $n = 9$) or were transferred to isolated cages (EE-IE: old, $n = 8$; young, $n = 9$). Rats in the SE condition were transferred to isolated cages (SE-IE: old, $n = 10$; young, $n = 9$) or group cages (SE-EE: old, $n = 9$; young, $n = 8$). The respective environmental conditions were identical to those of Experiment 1.

After 3 months, rats were placed on a restricted-food schedule for 2 weeks. During this time, rats in IE or SE cages were fed approximately 20 g of chow in pellet form while rats in EE were removed from their group cages for 1 h per day and fed the same food in the form of wet mash. EE rats were fed in this way to ensure that all rats in this group were satiated at the end of each feeding session. Maze testing was then initiated. Initially, all rats received 3 days of training in which they were administered 10 trials per day in one of three practice problems selected from the six that were used in the training phase of Experiment 1. By the end of this training period, old and young rats were running well and were ready to advance to the test phase. For testing, mazes 10–12 of the Hebb–Williams series was used. However, for this experiment, the start- and goal-boxes were reversed and the mazes were transformed to mirror images of the original versions. The order of maze presentation was changed in semi-random fashion. In all other respects, testing procedure was identical to Experiment 1. Ten trials were administered daily on each maze with errors recorded in the usual way.

RESULTS AND DISCUSSION

The main findings of Experiment 2 are presented in Fig. 3. The scores represent the average total errors made by the various old and young subgroups in the last three mazes of Experiment 1 and their mirror-image transformations in Experiment 2.

Considering first the groups that, in Experiment 1, were housed in IE, it can be seen (Fig. 3, Panel 1) that old rats transferred from IE to EE dramatically improved their maze performance, relative to the old rats that remained in IE. As expected, the young group in this environmental condition generally performed at a higher level. A comparison of the young IE-IE and IE-EE subgroups' performance reflected little response to the shift in environment. Overall, this outcome contributed to a highly significant group $\times$ test $\times$ environmental-shift interaction [$F(1, 31) = 18.86$, $p < 0.001$].

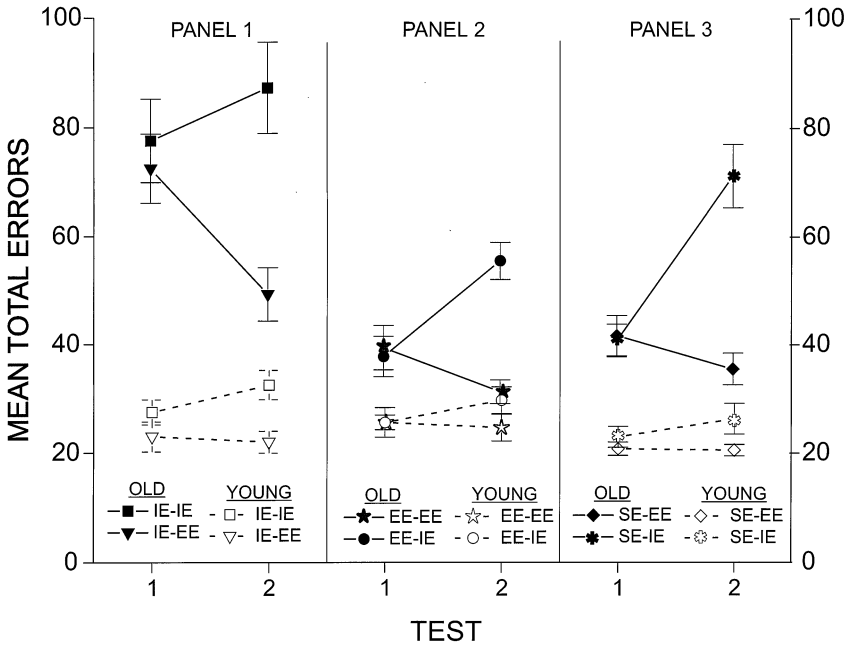

FIG. 3. Mean number of errors made by all subgroups on the last three mazes of Experiment 1 and the three mazes of Experiment 2.

Separate ANOVAs of the old and young groups' scores confirmed that the old rats recovered much more than the young rats following transfer to EE. These analyses revealed a significant test × environmental-shift interaction in the old group [$F(1, 15) = 36.90$, $p < 0.0001$] but not the young group [$F(1, 16) = 3.44$, $p = 0.082$]. Further evidence of this effect is provided by a comparison of each rat's proportional change in performance in the IE-IE and IE-EE conditions. Old rats transferred from IE to EE reduced their error scores on essentially the same mazes by an average of 32%, whereas the young, IE-EE subgroup improved by only 6%. This difference is statistically significant [$t(16) = 3.54$, $p = 0.003$]. By comparison, old and young rats in the IE-IE condition increased their error scores by an average of 14% and 23%, respectively—a difference that was not statistically significant ($t < 1$).

The maze scores of rats that were housed originally in EE are presented in Fig. 3, Panel 2. These data yielded a significant age × test × environmental-shift interaction [$F(1, 30) = 20.35$, $p < 0.0001$] that was due primarily to the substantial drop in performance by the old EE-IE subgroup. Performance changes in the old, EE-EE subgroup and the two young subgroups were negligible. Separate ANOVAs yielded a significant test × environmental-shift interaction for the old [$F(1, 14) = 39.40$, $p < 0.0001$] but not for the young [$F(1, 16) = 1.33$, $p = 0.267$] groups. Comparisons of the proportional changes in performance indicated that the old EE-IE subgroup declined by about 52%, as compared to a decline of 16% in the young EE-IE subgroup [$t(15) = 2.84$, $p = 0.012$]. In the EE-EE condition, the old and young rats improved by about 16% and 10%, respectively [$t(15) = 1.67$, $p = 0.116$].

The pattern observed in the scores of old and young rats that were housed in SE in Experiment 1 (Fig. 3, panel 3) was essentially the same as that of the EE groups, described in the preceding paragraph. A significant age × test × environmental-shift interaction [$F(1, 32) = 39.43$, $p < 0.0001$] was due mainly to a disproportionate decline in performance by the old SE-IE subgroup. Separate analyses yielded a significant test × environmental-shift interaction in the old [$F(1, 17) = 74.30$, $p < 0.00001$] but not in the young [$F(1, 15) = 1.52$, $p = 0.236$]. Comparisons of proportional change indicated that the old SE-IE subgroup declined, on average, by about 74%, and the young SE-IE subgroup by 16% [$t(17) = 5.43$, $p < 0.0001$]. In the SE-EE condition, the old rats improved by about 12%, and the young rats declined by less than 1%, a difference that was not statistically significant [$t(15) = 1.31$, $p = 0.209$].

Despite the considerable recovery by the old, IE-EE rats in Experiment 2 (32% improvement over Experiment 1 vs. 16% and 13% for the old EE-EE and old SE-EE subgroups, respectively), their performance on the mazes of Experiment 2 did not quite reach that of the other subgroups housed in EE. A comparison of the three subgroups' error scores in Experiment 2 indicated a significant main effect [$F(2, 23) = 6.77$, $p = 0.005$] that was attributable to differences between the old IE-EE subgroup and each of the other two EE subgroups (both p values < 0.03). However, it is noteworthy that the old IE-EE subgroup's performance in Experiment 2 did improve to the level of the SE group's performance on the last three mazes of Experiment 1 [$t(26) = 1.72$, $p = 0.098$] but not quite to that of the EE group [$t(23) = 2.09$, $p = 0.048$]. These results indicate that 3 months of enrichment was sufficient to reverse a substantial amount of the negative effects experienced by old rats after 3 months of isolation.

Along the same lines, it can be seen in Fig. 3 that, despite the decline in performance observed in the old, EE-IE rats, they performed better in Experiment 2 than rats in the IE-IE condition. A comparison of error scores of old rats housed in IE in Experiment 2, yielded a significant main effect [$F(2, 23) = 6.15$, $p = 0.007$] that was due to a significant difference between the old EE-IE and old IE-IE subgroups [$t(14) = 3.53$, $p = 0.003$]. The scores of the old SE-IE subgroup fell between those of the other two old subgroups that were transferred to IE, and did not differ statistically from either of them. Related to this was the finding that the old EE-IE subgroup performed

better in Experiment 2 than the IE group on the last three mazes of Experiment 1 [$t(23) = 2.61$, $p = 0.016$]. Taken together, these results indicate that, despite the lack of difference between the old EE and old SE groups in Experiment 1, and between the old EE-EE and SE-EE subgroups in Experiment 2, environmental enrichment provided protective benefits that were over and above those of the standard lab environment.

GENERAL DISCUSSION

The results of the present study confirmed that normal, old rats are severely impaired, relative to young adult rats, in performing complex maze problems [(11,20,25); see (4) for review] and, in addition, provide clear evidence that environmental factors contribute significantly to cognitive aging. In Experiment 1, apart from robust age differences in maze performance, a principal finding was that old rats, housed in an impoverished environment for 3 months, were especially impaired, when compared with old rats that were housed in standard or enriched conditions. The EE group consistently made fewer errors than the SE group but, statistically, the differences were not reliable. Experiment 2 revealed that switching environments had significant effects on maze performance of old rats. When old rats were transferred from the impoverished environment to the enriched environment (IE-EE) for an additional 3 months, their performance improved dramatically, reaching the level of old rats that had always lived in the standard lab environment. Old rats, transferred from SE or EE to IE, were adversely affected by the shift but, following transfer, both groups performed at a higher level than old rats, housed in IE for 6 consecutive months. In contrast, the maze performance of the young rats was virtually unaffected by housing conditions or environmental shift.

The susceptibility of aged rats to the negative effects of isolation was reported previously by Cummins et al. (11), who also found that old rats, housed in a restricted environment, performed worse on a test of complex maze learning than old rats living in a more stimulating environment. The present study extends these results in several ways. In the Cummins et al. study, rats were housed in their experimental environments from the time of weaning until 17 months, when they were tested. By comparison, in Experiment 1, rats were transferred to IE or EE when they were 19–20 months old and were housed in these environments for only 3 months before maze testing. Thus, the present results show that even short periods of restriction can affect cognitive function in aged animals, a finding that is in line with evidence that exposure to impoverished or enriched environments for as little as 30 days can produce significant brain changes in young or middle-aged animals (43,49). Moreover, by including a group of old rats in a standard lab environment, the present design enabled comparisons between the effects of extreme environments and conditions that are typical of most investigations of cognitive aging in rats. Finally, the inclusion of young, adult groups in each experimental environment allowed direct examination of the effects of aging as well as the combined effects of age and environment on cognitive performance.

The exaggerated deficits of the aged, IE group in Experiment 1 may be due in part to environmentally-induced changes in brain structure and function. Although most research in this area has focused on the effects of increased stimulation in relatively young animals, there is little doubt that environmental enrichment produces similar changes across the life span (22,30,46). There is a need for greater specificity in describing relationships between such changes and behavior, particularly in brain regions known to mediate learning and memory. However, available evidence suggests that enhanced cognitive performance associated with environmental stimulation can be linked directly to morphological changes involving, e.g., increases in synaptic connections and dendritic growth (29) as well as increased metabolic activity (19). To the extent that synaptogenesis and other physiological changes are supported by external stimulation, it follows that reduced stimulation associated with environmental isolation could contribute to a failure of neural mechanisms that translates into impaired neurocognitive function.

From a neuropsychological perspective, several lines of evidence suggest that the hippocampus and prefrontal cortex may be implicated in the effects observed in the present study. It is well established that these structures are involved in performing complex mazes, although it is likely that they contribute in different ways (58). The hippocampus and prefrontal cortex are extremely susceptible to the aging process (2,8,53), and there is evidence, that aged animals (4,9,16,54,55) and humans (10,17,34,60) have particular difficulty on tasks that require the integrity of these brain regions. As well, reports suggest that the functional and structural organization of the hippocampus and frontal lobes are modulated by environmental influences [(31,40,44), but see also (29)].

The pattern of deficit observed in rats housed in IE offers further evidence that hippocampal and prefrontal function were affected by environmental influences. Successful performance on a series of complex mazes requires that animals adopt a general maze-running strategy that can be appropriately and efficiently transferred to the various problems. In addition, they must draw on specific learning and memory processes to find and navigate the correct route in each maze. Using selective lesion techniques, Winocur and Moscovitch (58) were able to identify strategy formation with prefrontal function and the more specific abilities with hippocampal function. In Experiment 1, the old IE group displayed exaggerated deficits on measures that reflected both of these functions. In addition to performing poorly on each of the 12 mazes, over the testing period, these rats, unlike other groups, failed to show a progressive decline in the number of errors per maze. It would be simplistic to suggest that only the hippocampus and prefrontal cortex respond to the combined influences of aging and environment but, clearly, these brain regions qualify as important candidates.

Apart from environmental influences on cognitive function, it is important to consider the impact of environment on other psychological processes that affect maze performance in more indirect ways. In Experiment 1, rats housed in IE were slower than other groups to reach the training criterion and, generally, they were slower to complete test trials (although slower running times were confounded by increased numbers of errors). These observations raise the possibility that attentional, motivational, and stress-related factors contributed to environmentally induced deficits. Other investigators have raised this issue (7,25,50) and, in particular, there is growing evidence of an important link between environmental stress and cognitive function in old age (36,47). Several studies have shown that handling and other forms of external stimulation protect old animals from potential stressors and, at the same time, preserve learning and memory function by reducing glucocorticoid toxicity in hippocampal cells (37,38,40) The present study was not designed to assess such variables but informal observations revealed behavioral signs of high stress levels in old rats. In Experiment 1, old, IE rats were more fearful in the mazes, as evidenced by fecal droppings and long periods of immobility, particularly in the early stages of training. To some extent, this subsided with experience but the old IE rats were generally more distractible, irritable, and less active throughout testing and it is likely that these characteristics interfered with overall performance. Clearly, examination of the effects of environmental restriction on independent measures of performance-

related factors and their relationship to cognitive function in old age is in order.

Evidence that environmental stimulation can influence brain mechanisms in old age speaks to the high degree of plasticity that is built into neural systems. The results of Experiment 2 provide dramatic expressions of this plasticity in behavioral terms. For example, old rats transferred from IE in Experiment 1 to EE in Experiment 2 displayed considerable recovery of function in the maze task and achieved a level of performance that compared favorably with old rats that had been housed in more stimulating environments. It is unlikely that this improvement was simply the result of continued training since other old rats that received the same amount of training, and especially those that continued to be housed in IE, did not show the same improvement. At the same time, previous experience in a stimulating environment helped to protect old rats from the adverse effects of transfer to IE. This effect was most apparent in the old EE-IE subgroup in Experiment 2. Although these rats declined somewhat from their performance in Experiment 1, they made substantially fewer errors than the old IE group in Experiment 1 and the IE-IE subgroup in Experiment 2. The relatively good performance of the EE-IE and SE-IE subgroups in Experiment 2 may be due in part to their superior maze learning in Experiment 1. However, this factor cannot account entirely for their reduced impairment in Experiment 2. The significant difference in performance between the EE-IE and IE-IE subgroups is strong evidence that environmental enrichment served to protect the brain from the disruptive effects of subsequent transfer to a less stimulating environment.

In the present study, the effects of housing old rats in an enriched environment, that was designed to provide increased stimulation, were relatively modest when their performance was compared with that of old rats in a standard lab environment. In Experiment 1, the old EE group generally made fewer errors than the old SE group on the various mazes although, statistically, the differences were not reliable. As can be seen in Fig. 3, by the end of testing on the 12 mazes, SE and EE rats were performing at the same level. As noted above, the exception to this pattern, was that three months of housing in EE protected old rats from the deleterious effects of relocating to IE better than the same period in SE. The similarity in effects of SE and EE should not be interpreted as a lack of stimulation in EE. Rather, it was probably the case that SE was stimulating enough to produce brain and behavior changes that were similar to those associated with complex environments. Ongoing activity in the SE provided considerable stimulation but the critical factor may have been the regular handling that these rats received. Indeed, research indicates that handling and other forms of tactile stimulation is highly conducive to producing neural growth and accompanying benefits to cognitive function (35,39).

Whereas the effects of environment and environmental shift were quite clear in the old rats, young rats appear to have been less affected by environmental influences. By the end of maze testing in Experiment 1, young rats in all environments were performing well so that there may have been little room for improvement. This point is particularly relevant to the IE-EE and SE-EE conditions of Experiment 2, where it is of interest to know if young and old rats responded equally when transferred to more complex environments. While it is conceivable that young rats were performing at near-optimal capacity, there is evidence that they were genuinely unaffected by the environmental conditions. In Experiment 1, there were no differences between young groups in the three environments across the full range of maze testing. As well, in Experiment 2, transfer from SE or EE to IE had negligible effects on performance. Given that the young rats were unaffected by the severely restricted conditions of the impoverished environment, it is improbable that they were sensitive to the more subtle differences between SE and EE. The latter point is reinforced by the finding, in Experiments 1 and 2, that the effects of SE and EE on the maze performance of old rats were very similar.

The finding that environmental conditions did not substantially affect the young rats is somewhat surprising, given evidence that young rats, raised in different environments often perform differently on tests of learning and memory [(6,21,31), but see also (23)]. These discrepancies are important and are probably linked to a variety of procedural differences that include the animals' prior experience, the nature of the environments, and the tests employed. In the present study, e.g., young rats had participated previously in a behavioral study and that experience may have helped compensate for the negative effects of the restricted environment. A careful examination of historical and other factors that interact with environmental influences to affect cognitive function in young adult animals would appear to be a fruitful subject for further research.

Finally, there are parallels between the present results and evidence that environmental factors influence cognitive function in older humans. The poor maze-learning performance of old rats in the impoverished environment may be compared with reports that old people, living in institutions or other restricted environments, perform worse on cognitive tests than counterparts living in more stimulating environments (12,32,56). The finding that some of this impairment is reversible is also consistent with reports that the level of cognitive function in older humans varies with environmentally related factors. For example, studies have shown that restructuring the environments of older people in favorable ways (1,12,32,33,59), can result in improved cognitive performance. The findings, in the present study, that environmental enrichment did not provide benefits over and above those of the standard environment, in a sense, is also consistent with the human literature. There is no evidence that exposing active, well-adjusted, older humans to more complex environments is necessarily beneficial in terms of cognitive or psychological function. Indeed, it may be, as Schaie (48) suggests, that older people derive the greatest benefits from continuing to live in familiar, stimulating environments where they can participate in known and successful activities, and where there is opportunity for development and growth. Clearly, there is much to be learned about the complexities of age/environment interactions. With growing awareness of the benefits of stimulation and the hazards of stimulus-deprivation, it may be possible to incorporate environmental factors into programs aimed at enhancing cognitive function in older adults, as well as other populations that experience degrees of brain dysfunction.

ACKNOWLEDGMENTS

This research was supported by a grant from the Natural Sciences and Engineering Research Council of Canada. The author gratefully acknowledges the technical assistance provided by Chris Conley, John Zomer, Gordon Figuerro, and Heidi Roesler. Thanks also to Morris Moscovitch and Brian Levine for their constructive contributions to the paper.

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