Neurobiology of Aging, Vol. 6, pp. 17–24, 1985. © Ankho International Inc. Printed in the U.S.A. 0197-4580/85 $3.00 + .00

Effect of Exercise on Longevity, Body Weight, Locomotor Performance, and Passive-Avoidance Memory of C57BL/6J Mice

T. SAMORAJSKI,[1] COURTNEY DELANEY AND LISA DURHAM

Neurobiology Section, Texas Research Institute of Mental Sciences, Houston, TX 77030

J. M. ORDY AND J. A. JOHNSON

Department of Pharmacology, Penwalt, Pharmaceutical Division, 755 Jefferson Rd., Rochester, NY 14623

W. P. DUNLAP

Tulane University, New Orleans, LA 70118

Received 7 March 1984

SAMORAJSKI, T., C. DELANEY, L. DURHAM, J. M. ORDY, J. A. JOHNSON AND W. P. DUNLAP. *Effect of exercise on longevity, body weight, locomotor performance, and passive avoidance memory of C57BL/6J mice.* NEUROBIOL AGING 6(1) 17–24, 1985.—Studies of human and animal subjects have suggested that exercise may retard aging, help prevent age-related diseases, and prolong life span. Earlier studies focused on the effects of exercise on the heart, skeletal muscles, lungs, metabolism, and longevity. Researchers recently have begun to direct their attention to possible benefits of exercise on the brain. The goals of this study were to examine the effects of voluntary wheel-running exercise on life span, body weight, food and water intake, locomotor performance, and one-trial passive-avoidance memory of mature (10–14 month), middle-aged (20–24 month), and old (28–30 month) C57BL/6J male mice. No significant differences in life span, expressed in months, were found between control and exercised mice when exercise was carried out during maturity, senescence, intermittently across both periods, or continuously throughout maturity and senescence. Exercised adult mice maintained body weight compared to adult controls, an effect not apparent in old mice. Locomotor performance was reduced in old mice, and exercise increased performance much more in adult than in old mice. In the passive avoidance test of recent memory, exercise significantly increased latency, that is, it improved retention, in adult, middle-aged, and old mice. The effect was greatest in middle-aged, next in old, and lowest in adult mice. The findings indicate that exercise may be an important modulator of the rate of aging.

Aging Locomotor activity Passive avoidance Memory Exercise

IT is generally accepted that maximum life span among species is set by genetic codes whereas average life span and rate of aging within a species are determined by genetic and environmental interactions [16]. Correlations among body weight, metabolic rate, caloric intake, physical activity, and life span have indicated that the rate of aging, as well as the onset of age-related diseases, may be amenable to intervention by nutrition and exercise [19]. Although controlled human studies are few, evidence is accumulating that regular, long-term exercise may retard the normal aging process and help prevent age-related diseases in human beings [15]. In one study it was reported that cross-country skiers survived an average of 4.3 years longer than age-matched controls from the general population [14]. However, since the skiers had lower blood pressure and lower body weight, and smoked less than the controls, it is not clear whether the longer life span was due to lower blood pressure, fewer heart attacks and strokes, or other unidentified factors.

Since the effects of exercise on human aging are generally confounded by factors of nutrition, socioeconomic status, alcohol, smoking, life style, and many other variables, several investigators have begun to use animal models to focus more directly on the effects of exercise on body weight, metabolic rate, and life span. A recent investigation exam-

[1]Requests for reprints should be addressed to T. Samorajski, Ph.D., Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Texas Medical Center, Houston, TX 77030.

ined the effects of voluntary wheel exercise on life span, body weight, growth rate and duration, and metabolic rate in male and female Wistar rats. Rats allowed wheel exercise from weaning to maturity had slower growth rates and longer growth durations, lower body weights, higher metabolic rates, and longer life spans [9]. In another multivariate correlation study with Wistar rats, gender, exercise, and growth rate accounted for 50% of the variance in life span [13]. These findings suggest that exercise may retard aging in rats, and perhaps in humans, by maintaining a higher ratio of muscle to body fat and thus preventing the decrease in metabolic rate associated with aging. The animals' exercise took place during growth, however, so that differences in life spans among groups may also be associated with decreased growth rate and longer growth duration, as defined by body weight increments. The findings suggest that lifelong exercise may increase life span in a manner similar to early food restriction.

In addition to assessing the effects of exercise on body weight, metabolism, and life span in most human and animal studies, the effects of exercise on neuromuscular performance, cardiovascular efficiency, blood cholesterol, high-density lipoproteins, and heart disease have been examined [15]. More recently, investigators have begun to explore the effects of exercise on the human brain in terms of cerebral blood flow and metabolism [17], regional variations in cerebral blood flow in the dog [11], rat brain norepinephrine and serotonin levels [3], and the release of acetylcholine from the rat hippocampus during sensory stimulation and treadmill running [6].

Although human sensory, cognitive, and motor functions have been shown to decline with age, at least in studies with cross-sectional designs, researchers have reported significant improvements in cognitive functions [8] and in psychomotor speed in middle-aged and even old individuals after exercise [22]. In recent reports, loss of short term or recent memory has been cited as an inevitable manifestation of normal aging and the dementing illness of late life, Alzheimer's disease [2]. In an earlier study with young human subjects, short-term memory was reported to have improved significantly after the subjects exercised on a bicycle ergometer [4]. In a more recent study, it was reported that aerobic exercise improved cognitive functions in healthy elderly subjects [7].

Although the effects of exercise on short-term memory have not been examined in animal studies, significant correlations have been reported between passive-avoidance learning and life span in C57BL/6J mice [12]. In another study, the impairment of one-trial passive-avoidance retention, or memory with age, was established as one of the more dramatic manifestations of aging in C57BL/6J mice [5].

Few investigators have examined limits, or a diminution of beneficial effects, if exercise is begun and continued during maturity and senescence. The goals of this study were to examine the effects of voluntary wheel-running on life span, body weight, and food and water intake, locomotor performance, and one-trial passive-avoidance learning and memory of mature (10–14 month), middle-aged (20–24 month), and old (28–30 month) C57BL/6J male mice. Specific aims were to (1) determine whether or not voluntary wheel exercise had differential effects on life span if it is carried out either during maturity, senescence, intermittently across maturity and senescence, or continuously throughout maturity and senescence; (2) examine the effects of exercise on body weight, food and water intake, as well as on locomotor performance

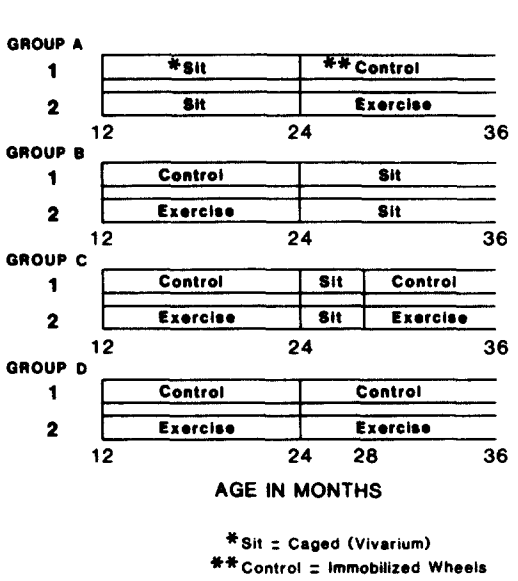

FIG. 1. Schematic representation of the experimental design.

of mature and senescent mice; and (3) evaluate the effects of exercise on one-trial passive-avoidance learning and memory among mature, middle-aged, and old mice.

METHOD

Subjects

Male C57BL/6J mice (Jackson Laboratories, Bar Harbor, ME) were obtained at nine months of age and housed six per cage with free access to a standard diet of Lablox and water before and during the experimental phase. All animals were maintained in the same room at 20–22°C and with light from 6 a.m. to 6 p.m. Animals selected for the three experiments ranged from 12 to 30 months of age, and different animals were used for each experiment.

Procedures and Apparatus

Experiment 1 (exercise and longevity). Twelve-month-old mice were divided by weight into four groups, each consisting of 12 to 18 experimental (exercise) and 12 to 18 control (nonexercise) mice. For exercise, each mouse was placed in an activity wheel and allowed to run spontaneously for two hours, five days a week. The number of revolutions was recorded by an electronic counting device. Control mice were handled similarly, except that the activity wheels were immobile. The four groups were exercised (or placed in immobile wheels) according to the following schedule: *Group A* began locomotor activity at 24 months of age and continued until death. *Group B* exercised from 12 to 24 months of age and was sedentary (in animal colony) therafter. *Group C* exercised from 12 to 24 months of age, was sedentary (in animal colony) from 24 to 28 months of age, and resumed exercising at 28 months and continued until death. *Group D* exercised from 12 months of age until death. The experimental design is shown in Fig. 1. Mice were weighed and inspected weekly for abnormalities.

Experiment 2 (age, exercise, food and water consump-

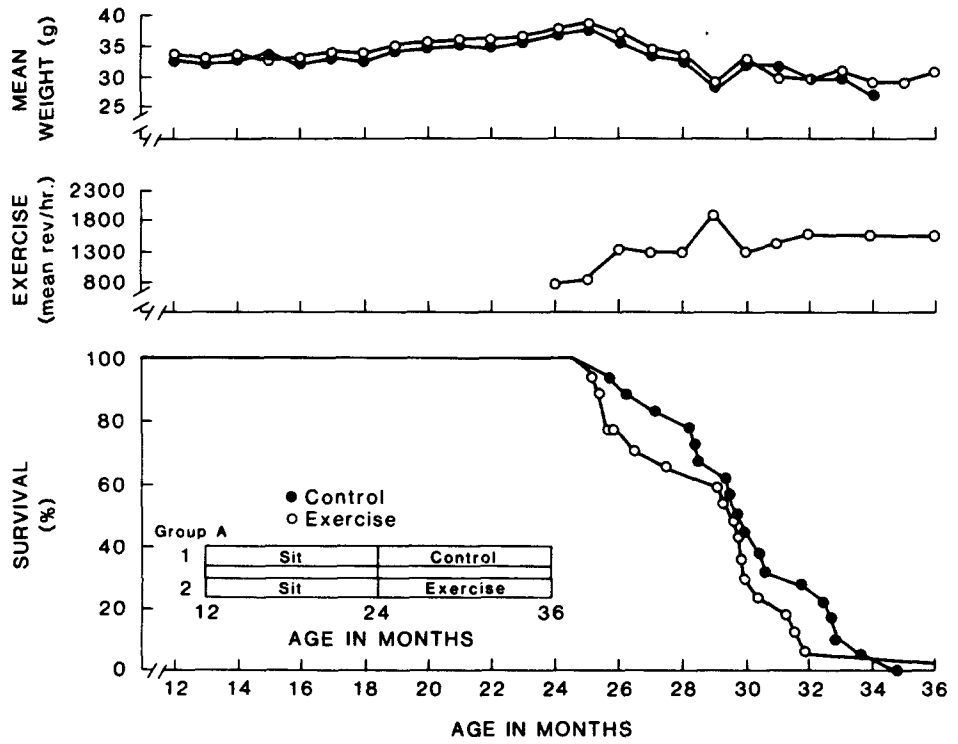

FIG. 2. Exercise (from 24 months of age until death) and changes in mean weight, locomotor activity, and survival of Group A mice (12–18 mice per subgroup).

tion). Two groups of 12 mice each were used. At the beginning of the experiment, one group was 13 months old, the other 26 months old. The experiment was divided into periods of pre-exercise (two weeks), exercise (three weeks), and post-exercise (two weeks). Body weight, food and water consumption were recorded during the three periods. In addition, activity scores of exercising mice were recorded during the exercise period.

Experiment 3 (age, exercise, and one-trial passive-avoidance behavior). Three groups of 24 mice each were used, one between 10 and 14 months of age, the second 20 to 24 months, and the third 28 to 30 months old. Each age group was subdivided into a control and exercise group. For exercise, each mouse was allowed to run spontaneously for two hours, five days a week, for four weeks, with the number of revolutions recorded. Control mice were handled similarly, except that the activity wheels were immobilized. At the end of the experimental period, all mice were tested in a two-compartment step-through passive-avoidance apparatus [5]. The test consisted of a training trial with each mouse placed individually in the apparatus' lighted front chamber. After 60 seconds, a raised door allowed the mouse to explore freely and to enter the second, darker chamber. Then the door was lowered quickly, preventing the mouse from escaping to the lighted side. A 0.3 mA shock was applied to the grid floor for 3 seconds with a shocker-scrambler. Testing was done by placing the mouse into the front chamber in the same manner as during the training trial and the animal's latency in entering the darker chamber was measured. Tests were conducted 24 hours after the shock. The passive-avoidance procedure is intended to measure an animal's ability to remember to avoid a noxious stimulus (after one exposure) by inhibiting a response that has a high probability of occurring [5].

RESULTS

Exercise Effects on Life Span (Study 1)

The aims of the first study were to establish whether voluntary wheel-running exercise during senescence (Group A), maturity (Group B), intermittently across both (Group C), and uninterrupted exercise throughout maturity and senescence (Group D) produce differential effects on life span. Nonexercised control groups were compared to experimental groups exercised under the above four conditions using a 2×4 analysis of variance (ANOVA). No significant differences in life span, expressed in months, were found between control and exercised mice in groups A, B, C, and D (p's>0.05, for main effects and interactions). The effects of exercise and age on body weight and life span are illustrated for group A in Fig. 2, group B, in Fig. 3, group C in Fig. 4, and group D in Fig. 5.

Significant correlations have been reported for exercise, body weight, and life span if body measurements were made during growth or late senescence in mice. In this study, however, correlations were essentially zero and were not statistically significant between body weight (measured at 24 months of age) and life span for the pooled controls (r=.039) and exercised mice in groups A (r=−.122), B (r=.100), C (r=.289), and D (r=.244).

Effects of Exercise on Body Weight, Food and Water Intake, and Locomotor Performance (Study 2)

A second study was undertaken with 13- and 26-month-old mice to assess the effects of age and exercise on body weight, food and water intake, and locomotor performance. Body weights were monitored for 2 weeks pre-exercise, 3

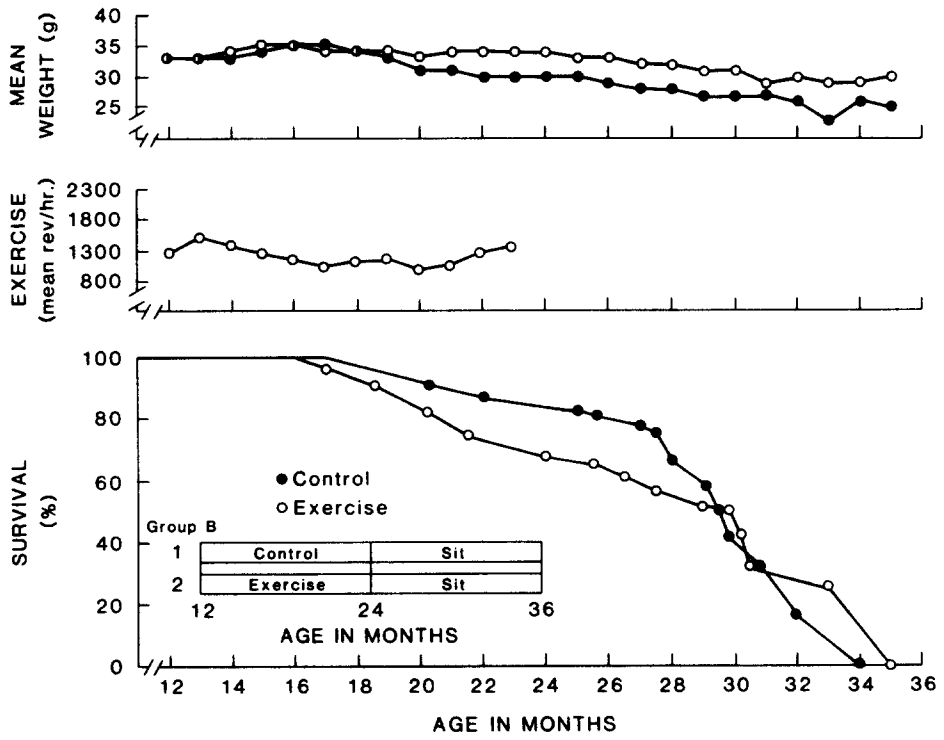

FIG. 3. Exercise (from 12 to 24 months of age) and changes in mean weight, locomotor activity, and survival of Group B mice (12–18 mice per subgroup).

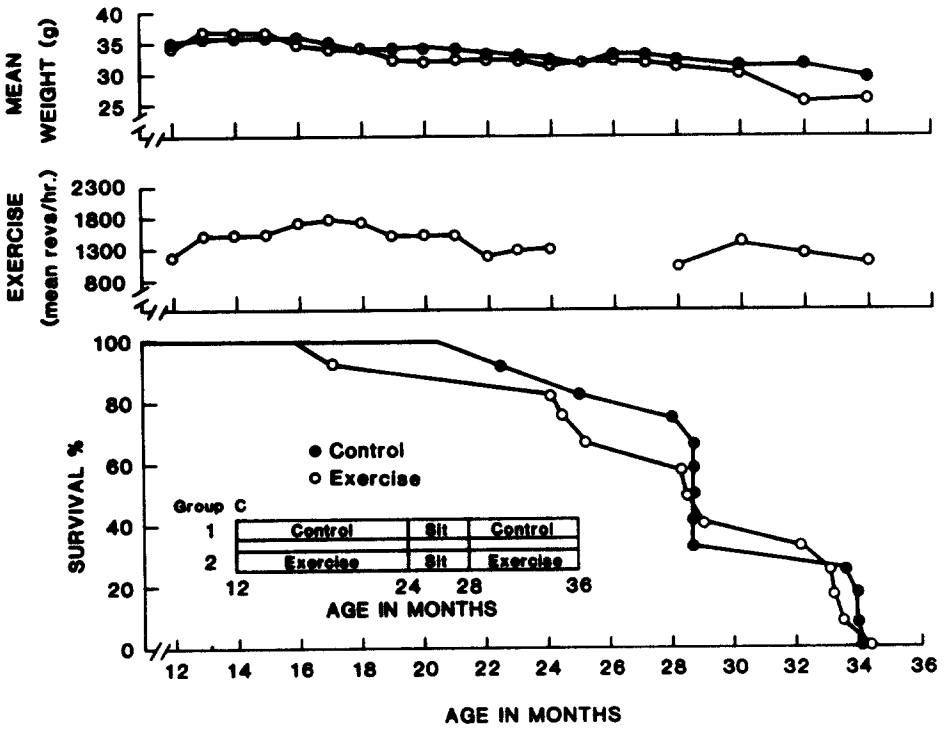

FIG. 4. Exercise (from 12 to 24 months of age, vivarium for 4 months, and again exercised from 28 months of age until death) and changes in mean weight, locomotor activity, and survival of Group C mice (18 mice per subgroup).

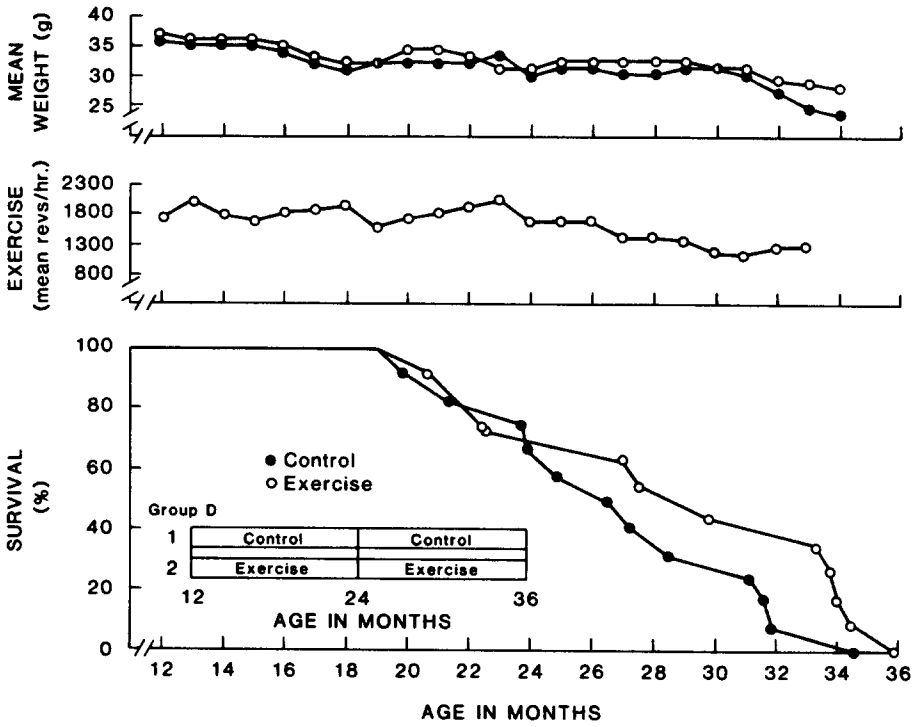

FIG. 5. Exercise (from 12 months of age until death) and changes in mean weight, locomotor activity, and survival of Group D mice (18 mice per subgroup).

TABLE 1

THE EFFECT OF WHEEL EXERCISE AND AGE ON BODY WEIGHT, FOOD AND WATER CONSUMPTION (MEAN ± S.E.)

Age (months)	Pre-exercise (2 weeks)	During Exercise (3 weeks)	Post-exercise (2 weeks)
	Body Weight (g)		
13 months			
Control	32.98 ± 0.56	31.95 ± 0.42	31.04 ± 0.32
Exercise	32.36 ± 0.05	32.01 ± 0.19	31.56 ± 0.22
26 months			
Control	31.86 ± 0.32	31.40 ± 0.24	30.84 ± 0.50
Exercise	31.95 ± 0.71	30.82 ± 0.09	30.09 ± 0.02
	Food (g/Ss/day)		
13 months			
Control	3.30 ± 0.09	2.96 ± 0.12	2.77 ± 0.09
Exercise	2.93 ± 0.13	2.93 ± 0.26	2.89 ± 0.21
26 months			
Control	2.95 ± 0.14	2.93 ± 0.06	2.71 ± 0.12
Exercise	2.94 ± 0.14	2.99 ± 0.25	2.71 ± 0.11
	Water (ml/Ss/day)		
13 months			
Control	4.15 ± 0.26	3.95 ± 0.24	3.89 ± 0.31
Exercise	3.71 ± 0.24	4.09 ± 0.39	4.17 ± 0.12
26 months			
Control	3.59 ± 0.30	4.01 ± 0.35	4.10 ± 0.39
Exercise	3.89 ± 0.29	3.92 ± 0.24	3.84 ± 0.17

weeks during exercise, and 2 weeks post-exercise. Control and exercised groups were compared in a repeated-measures ANOVA in which exercise and age were between-subject variables, and weeks of observation was the repeated-measures variable. Although the effects of age, exercise, and treatment time were not significant, the three-way interaction of exercise × age × weeks was significant, $F(6,120)=3.07$, $p=0.0079$. When 13-month weights were analyzed separately, exercise interacted significantly with weeks of observation, $F(6,60)=4.47$, $p=0.0008$, indicating that exercised mice maintained body weight across the seven weeks whereas the controls lost weight during this period. Similar analyses of the effects of age and exercise on body weights of old mice (26 month) showed no significant effects.

Food and water consumption was monitored during 4 periods before exercise, 5 periods during exercise, and 3 periods after exercise. The monitoring was done biweekly. Since the animals were housed in groups, individual data were pooled for average consumption per group. The three-way ANOVA, age × exercise × weeks, revealed no significant main or interactive effects for either food or water consumption (Table 1). The effects of age and exercise on locomotor performance in activity wheels were also examined with activity recorded in revolutions per hour. The control mice of each group had no previous experience running in the activity wheels. The exercised mice of each age group had 4 weeks of prior wheel-running experience, so that the data represented their fifth week of locomotor activity. A two-way age × exercise ANOVA indicated a significant effect of exercise, $F(1,32)=5.75$, $p=0.0225$, as well as a significant effect of age on locomotor performance, $F(1,32)=5.04$, $p=0.0318$ (Fig. 6).

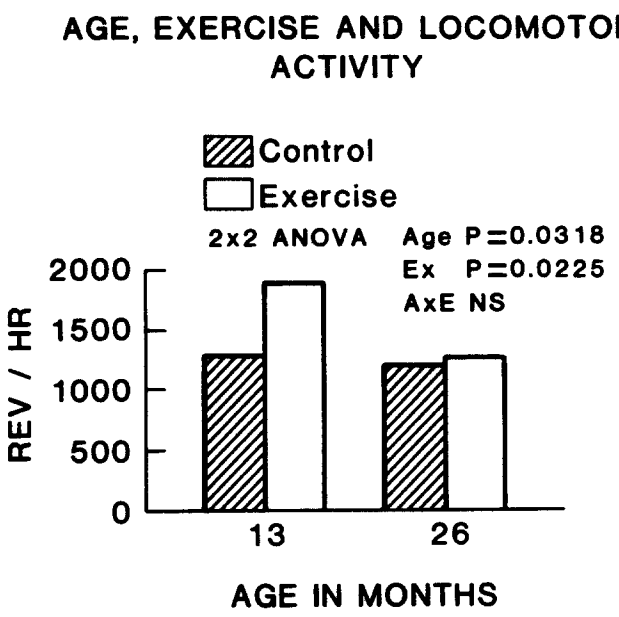

FIG. 6. Locomotor activity in revolutions per hour in control and exercised mice at 13 and 26 months of age.

Age and Exercise Effects on Passive-Avoidance Learning and Memory (Study 3)

During the training phase mice were individually placed in the illuminated part of the chamber, and their latency in entering the dark chamber was recorded in seconds. After 3 seconds in the dark chamber, all mice received a 3-second shock. Then all mice were removed and tested 24 hours later for passive-avoidance retention. Latency in re-entering the dark chamber, in seconds, served as a measure of retention. An activity group × age (12 month, 22 month, or 29 month) ANOVA was performed on the training trial data and no pretest age differences in speed to enter the dark compartment were found to be significant (Fig. 7). A similar analysis was performed for the memory trial data in which a significant main effect was found for exercise, $F(1,56)=6.72$, $p=0.0121$, and an interaction of exercise × age, $F(2,56)=4.29$, $p=0.0185$. The effect of exercise on memory was greatest for mice in the middle-aged 22-month group, $F(1,56)=16.37$, $p=0.0002$. The positive effects of exercise were also apparent in the 29-month-old group, whereas they were least evident in the mature 12-month-old group.

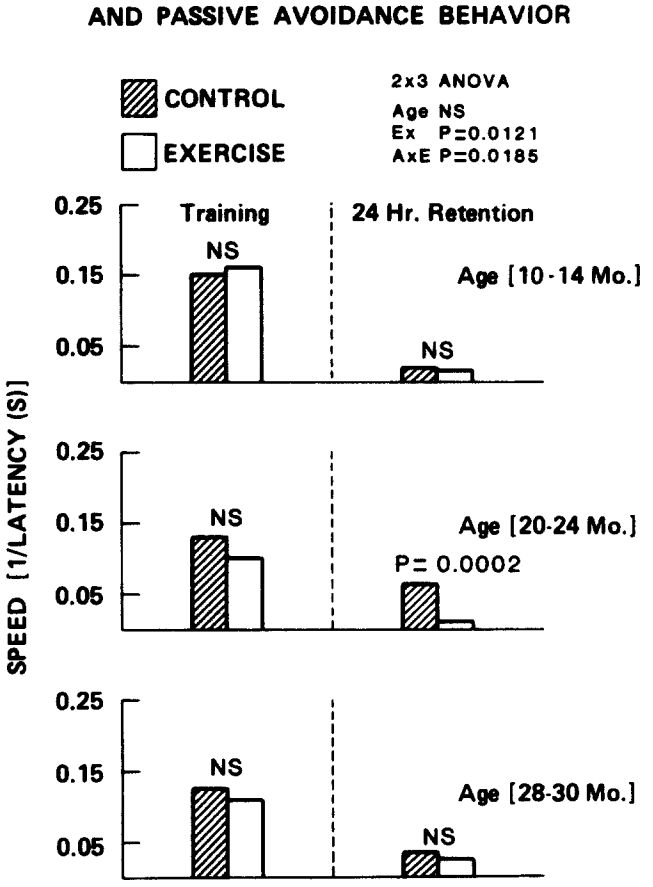

FIG. 7. Latency in seconds as a function of age and exercise when the subject had been previously shocked. Retention period was 24 hours, post-foot shock. N=12.

DISCUSSION

In a previously cited laboratory study with rats [10], the mean life span of male rats that were allowed voluntary wheel-running exercise from 1.5 months of age to the end point of death was 4 months 19.3% longer than that of male controls, and that of exercised female rats was 3 months or 11.5% longer than that of female controls. These increases were significant statistically as large numbers of rats were used in that study. In the present study, voluntary wheel exercise was initiated only during maturity, senescence, intermittently across both periods, or continuously across both periods. When carried out during these periods of the life span, exercise did not increase life span significantly. The differences in findings between the present study and the previous study [10] may be attributed to the earlier onset of exercise in the latter or to species differences. It is interesting that the strongest trend for an exercise effect in the present study was in the group that received the most and continuous exercise, Group D.

In addition to significant correlations among rate, growth duration, exercise, and life span in rats, significant correlations have been reported also among exercise, body weight, metabolic rate, and life span for these animals [10]. In contrast to these findings, measures of body weight during development did not correlate with exercise and life span [13], and in a study of the effects of dietary protein on body weight and life span of C57BL/6J mice, body weight did not correlate with life span [9]. Although there was no significant correlation between body weight and life span for control or exercised mice in our Study 1, we found in Study 2 that the younger, 13-month-old exercised mice maintained their body weight for seven weeks, whereas the controls lost weight. The 26-month-old mice showed no significant effect of exercise on body weight. Since metabolic rate has been shown to decrease with age in nonexercised rats [10], it seems likely that age differences in body weight response to exercise in our study were associated with age and exercise-induced differences in metabolic rate. When mice allowed exercise for the first time were compared to mice previously exercised for 3 weeks, the former group ran fewer revolutions per hour; this was particularly true for mice tested at 13 months of age. Although

this difference might be interpreted as differential capacity of desire for locomotor performance due to exercise, it might also be an effect of learning to run in the wheel or interference by neophobia (dread or fear of new things) to the wheel-running situation. Our study showed that exercise and age had significant effects on locomotor performance as well. It appears that exercise increased locomotor performance considerably more in the 13-month-old compared to the 26-month-old mice, however, the age × exercise interaction was not significant statistically.

The mice were housed in groups during the seven weeks of this study, and no significant effects of exercise were observed on food and water consumption. Questions of relationships among exercise, body weight, and life span remain to be resolved by future studies in which body weight is measured at frequent intervals across the life span, with attention to the presence of tumors and other diseases during senescence [13].

In contrast to the extensive literature on the effects of environmental stimulation, enrichment, and physical exercise on the brain in terms of its plasticity during development, research on environmental modifiability of the brain during maturity and aging is quite fragmentary [18]. Earlier studies focused on the effects of exercise on psychomotor speed from maturity to senescence [22]. Recent studies have focused more on loss of short-term or recent memory during aging in man [2] and in rodents, particularly the C57BL/6J mouse [5]. In one earlier study, it was reported that short-term memory improved significantly even in healthy young adult humans after they exercised on a bicycle ergometer [4]. The beneficial effects of exercise on short-term memory in this study were attributed to increased attention and/or level of arousal. In a more recent study, the beneficial effects of aerobic exercise on digit span memory and other measures of cognitive function were attributed to effects on central neural memory mechanisms rather than improvements in sensory acuity or affective states [7]. In two previously cited studies on the effects of age on recent memory in the C57BL/6J mouse, it was reported that one trial passive-avoidance memory declined with age [5], and that superior performance on passive-avoidance learning correlated significantly with longer life span [12]. In the present study, the beneficial effects of exercise on passive-avoidance memory were highly significant across the three age groups of male mice. The interaction effect of exercise and age was also highly significant, and a post-hoc comparison indicated that the greatest effects were in the middle-aged group (20–22 months), followed by the old group (28–30 months), with the least effects on retention in the adult group (10–14 months). These results are consitent with reported findings of greatest benefits on sensory, cognitive, and motor skills due to exercise occurring in middle-aged human subjects, compared to old and young adults [22].

Research on the interactive effects of age and exercise on passive-avoidance memory in terms of neural mechanisms, cholinergic circuits of the cortex, hippocampus, basal forebrain, and the amygdala have received considerable attention in the anatomical localization of recent memory function [23]. Treadmill exercise has been shown to increase blood flow in sensory and motor regions of the cerebral cortex in dogs [11]. Treadmill exercise has also been reported to increase norepinephrine levels and decrease serotonin levels in the cerebral cortex of rats [3]. Similar treadmill exercise has been shown to increase acetylcholine release in the septo-hippocampal pathway in the rat [6]. In addition to the direct effects of exercise on cerebral blood flow and neurotransmitters in neural memory circuits, other studies have shown that exercise-trained rats had increased plasma corticosterone concentrations and that this response decreased with age in rats [21]. Since the hippocampus is known to have corticosterone receptors, the beneficial effects of exercise on passive-avoidance memory of mice observed in this study may be attributed to direct stimulation of the cholinergic septo-hippocampal pathway, as well as indirect exercise effects on autonomic system arousal through the activation of the hypothalamic-pituitary-adrenal axis.

So far, despite increasing individual and social interest, relatively little is known concerning the interactive effects of exercise and aging in man. Earlier studies focused on the effects of exercise on the heart, skeletal muscles, lungs, metabolism, and longevity. Recent studies have begun to focus on the possible benefits to the brain. In terms of possible prolongation of life span, only caloric restrictions during growth, reduced body temperature and metabolism, and the use of some anti-toxidants, have proved to be effective in prolongation of average, and possibly maximum, life span of animals [20]. The findings of the present study, as well as the accumulating evidence cited from other studies with human and animal models, indicate that exercise may be a significant modulator of longevity. Clinically, exercise may become an important adjunct or even necessity in the judicious use of many drug therapies in the elderly, since exercise may reduce not only dosage requirements but adverse side effects of many drugs [1].

REFERENCES

1. Aloia, J. Estrogen and exercise in prevention and treatment of osteoporosis. *Gerontology* **37**: 81–85, 1982.
2. Bartus, R. T., R. L. Dean, B. Beer and A. S. Lippa. The cholinergic hypothesis of geriatric memory dysfunction. *Science* **217**: 408–417, 1982.
3. Brown, B. S., T. Payne, C. Kin, G. Moore, P. Kregs and W. Martin. Chronic response of rat brain norepinephrine and serotonin levels to endurance training. *J Appl Physiol* **46**: 19–23, 1979.
4. Davey, C. P. Physical exertion and mental performance. *Ergonomics* **16**: 595–599, 1973.
5. Dean, R., J. Scozzafava, J. Goas, B. Regan, B. Beer and R. Bartus. Age-related differences in behavior across the life span of the C57BL/6J mouse. *Exp Aging Res* **7**: 427–451, 1981.
6. Dudar, J., I. Q. Whishaw and J. Szerb. Release of acetylcholine from the hippocampus of freely moving rats during sensory stimulation and running. *Neuropharmacology* **18**: 673–678, 1979.
7. Dustman, R. E., R. O. Ruhling, E. M. Russell, D. E. Shearer, H. W. Bonekat, J. W. Shigeoka, J. S. Wood and D. C. Bradford. Aerobic exercise training and improved neuropsychological function of older individuals. *Neurobiol Aging* **5**: 35–42, 1984.
8. Elsayed, M., A. Ismail and T. Young. Intellectual differences of adult men related to age and physical fitness before and after an exercise program. *J Gerontol* **35**: 383–387, 1980.
9. Goodrick, C. Body weight increment and length of life: the effect of genetic constitution and dietary protein. *J Gerontol* **33**: 184–190, 1978.

10. Goodrick, C. L. Effects of long term voluntary wheel exercise on male and female Wistar rats. *Gerontology* **26:** 22–33, 1980.
11. Gross, P. M., M. L. Marcus and D. D. Heistad. Regional distribution of cerebral blood flow during exercise in dogs. *J Appl Physiol* **48:** 213–217, 1980.
12. Ingram, D., J. Archer and D. Harrison. Physiological and behavioral correlates of life span in aged C57BL/6J mice. *Exp Gerontol* **17:** 295–303, 1982.
13. Ingram, D. K., M. Reynolds and C. Goodrick. Relationship of sex, exercise, and growth rate to life span in the Wistar rat: a multivariate correlational approach. *Gerontology* **28:** 23–31, 1982.
14. Karvonen, M. J., H. Klemola and J. Virkajarvi *et al.* Longevity of endurance skiers. *Med Sci Sports Exerc* **6:** 49–51, 1974.
15. Kent, S. Exercise and aging. *Geriatrics* **37:** 132–135, 1982.
16. Kohn, R. *Principles of Mammalian Aging*, 2nd Edition. Englewood Cliffs, NJ: Prentice-Hall, Inc., 1978.
17. Metter, E., W. Reige, D. Kuhl and M. Phelps. Cerebral metabolic relationships for selected brain regions in healthy adults. *J Cerebral Blood Flow Metab* **4:** 1–7, 1984.
18. Ordy, J. M. Neurochemical aspects of aging in humans. In: *Handbook of Biological Psychiatry, Part IV, Brain Mechanisms and Abnormal Behavior-Chemistry*, edited by H. M. Van Praag, M. H. Lader, O. J. Rafaelsen and E. J. Schar. New York, NY: Marcel Dekker, Inc., 1981, pp. 355–416.
19. Ordy, J. M. Nutrition as a modulator of rate of aging, disease and longevity. In: *Nutrition in Gerontology*, vol 26, edited by J. Ordy, D. Harman and R. Alflin-Slater. New York, NY: Raven Press, 1984, pp. 1–18.
20. Sacher, G. A. Life table modification and life prolongation. In: *Handbook of the Biology of Aging*, edited by C. Finch and L. Hayflick. New York: Van Nostrand Reinhold, 1977.
21. Severson, J., R. Fell, J. Vander Tuig and D. Griffith. Adrenocortical function in aging exercise-trained rats. *J Appl Physiol* **43:** 839–843, 1977.
22. Spirduso, W. Physical fitness, aging, and psychomotor speed: a review. *J Gerontol* **35:** 850–865, 1980.
23. Thomas, G. Memory: Time-building in organisms. In: *Neuropsychology of Memory*, edited by L. Aquire and N. Butters. New York, NY: Guilford Press, 1984.