Exercise for the aged brain

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진 영 수

- **“It is exercise alone that supports the spirits, and keeps the mind in vigor”** : Marcus Tullis Cicero –65 BC

- Exercise invigorates, enlivens all the faculties of body and of mind

Benefits of Exercise

- Muscular-skeletal
- Cardio-pulmonary
- Endocrino-metabolic
- Psycho-Neuro-Immunology
- <u>**Brain**</u>

Regular physical exercise

- Health promotion .
- **Enhances cognitive function** in older adults decreased risk for decline in cognitive function (odds ratio [OR], 0.58), Alzheimer disease (OR, 0.50), and any dementia (OR, 0.63)

- **An effective strategy to delay onset of dementia**. improved cerebral blood flow and oxygen delivery and inducing fibroblast growth factor in the hippocampus reduced loss of hippocampal brain tissue in the aging brain is related to level of physical fitness

Walking was associated with a reduced risk for dementia and Alzheimer disease in a cohort of Japanese-American men

Diverse physical activities was associated with a reduced risk for dementia in the Cardiovascular Health Study .

Brain Study & Physical Activity

- EPIDEMIOLOGICAL STUDIES OF EXERCISE AND PHYSICAL ACTIVITY EFFECTS
- HUMAN CLINICAL TRIALS: COGNITION AND BRAIN
- EXERCISE EFFECTS ON THE BRAIN: MOLECULAR AND CELLULAR BIOLOGY

EPIDEMIOLOGICAL STUDIES OF EXERCISE AND PHYSICAL ACTIVITY

- Larson et al. (2006):1,740 men and women over the age of 65 yr without cognitive impairment were asked to report the number of times per week (i.e., walking, hiking, bicycling, aerobics or calisthenics, swimming, water aerobics, or weight training) for at least 15 min per time over the past year.
- Podewils et al. (2005) studied the relationship between physical activity and dementia in 3,375 men and women over the course of 5.4 yr. Physical activity in these individuals over the age of 65 yr was assessed via the Minnesota Leisure Time Questionnaire in which participants are asked about the frequency and duration of 15 types of physical activities over the past 2 wk.
- Yaffe et al. (2001) found an inverse relationship between the number of blocks walked per week and energy expended and cognitive decline as assessed by performance on a general test of cognitive function, the Mini Mental State Examination, indicating that cognitive performance
- Weuve et al(2004). This study involved 5,925 women over 65 yr of age over the course of a 6- to 8-yr period.
- Barnes et al. (2003) A prospective study of physical activity by included both self-report and objective (i.e., peak oxygen consumption) measures of cardiorespiratory fitness in a 6-yr study of 349 individuals over the age of 55 yr.

Ann Intern Med. 2006;144:73-81.
Eric B. Larson, MD, MPH; Li Wang, MS; James D. Bov
Linda Teri, PhD; Paul Crane, MD, MPH; and Walter Ku

Exercise Is Associated with Reduced Risk for Incident Dementia among Persons 65 Years of Age and Older

Figure 1. **Kaplan–Meier survival estimates for the probabilities of being dementia-free.**

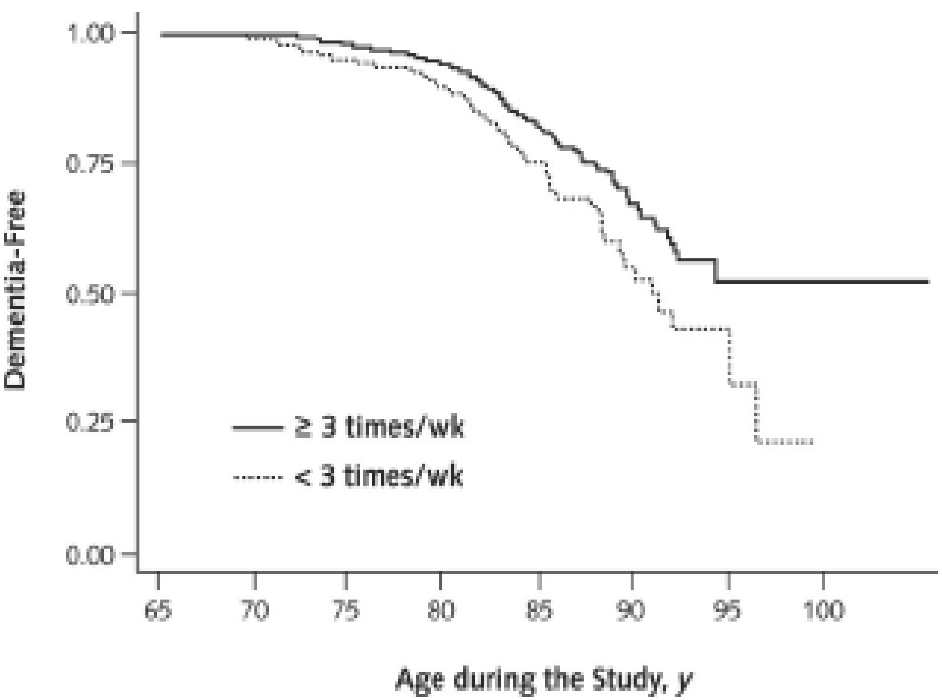
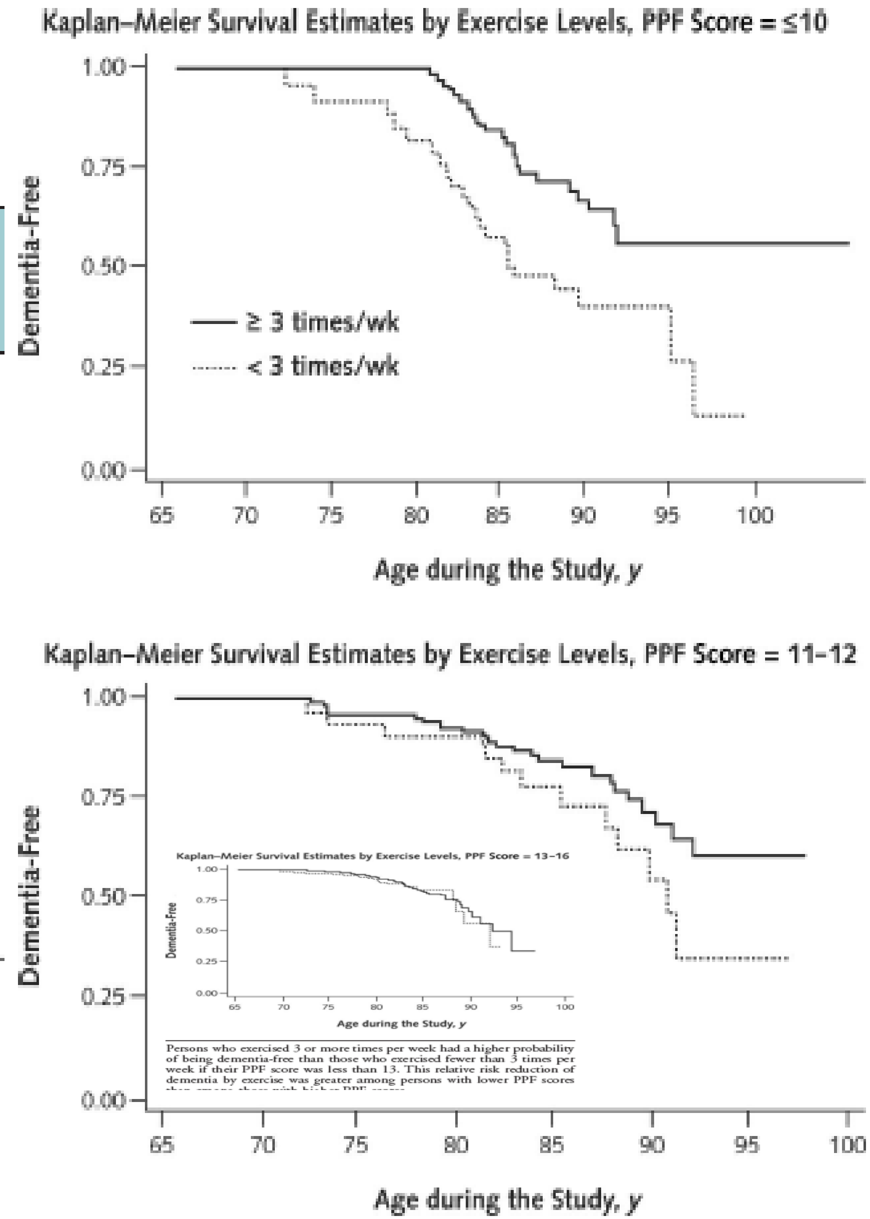


Figure 2. **Kaplan–Meier survival estimates by exercise and performance-based physical function (*PPF*) levels.**



American Journal of Epidemiology Vol. 161, No. 7 2005
Laura Jean Podewils1, Eliseo Guallar1,2, Lewis H. Kuller3, Linda P. Fried4, Oscar L.

Physical Activity, APOE Genotype, and Dementia Risk: Findings from the Cardiovascular Health Cognition Study

TABLE 5. Hazard ratios of incident dementia by activity index (no. of activities during the previous 2 weeks), Cardiovascular Health Cognition Study, United States, 1992–2000*

	0–1 activity	2 activities	3 activities	≥4 activities	*p*-trend
All-cause dementia					
No. of incident cases	130	152	113	84	
Incidence rate (per 1,000 PY†)	39.5	29.8	23.7	16.5	
Crude HR† (95% CI†)	1.0 (referent)	0.76 (0.60, 0.96)	0.60 (0.47, 0.78)	0.42 (0.32, 0.55)	<0.001
Age-adjusted HR (95% CI)	1.0 (referent)	0.88 (0.69, 1.11)	0.76 (0.59, 0.97)	0.55 (0.42, 0.73)	<0.001
Multivariate‡ HR (95% CI)	1.0 (referent)	0.90 (0.69, 1.18)	0.90 (0.66, 1.22)	0.58 (0.41, 0.83)	0.004
Alzheimer's disease					
No. of incident cases	69	72	61	43	
Incidence rate (per 1,000 PY)	21.0	14.1	12.8	8.4	
Crude HR (95% CI)	1.0 (referent)	0.68 (0.48, 0.94)	0.61 (0.43, 0.86)	0.40 (0.27, 0.58)	<0.001
Age-adjusted HR (95% CI)	1.0 (referent)	0.78 (0.56, 1.09)	0.76 (0.54, 1.08)	0.52 (0.36, 0.77)	0.001
Multivariate‡ HR (95% CI)	1.0 (referent)	0.73 (0.49, 1.08)	0.85 (0.57, 1.29)	0.55 (0.34, 0.88)	0.03
Vascular dementia					
No. of incident cases	55	71	50	37	
Incidence rate (per 1,000 PY)	16.7	13.9	10.5	7.3	
Crude HR (95% CI)	1.0 (referent)	0.85 (0.60, 1.20)	0.64 (0.43, 0.94)	0.44 (0.29, 0.67)	<0.001
Age-adjusted HR (95% CI)	1.0 (referent)	0.98 (0.69, 1.39)	0.81 (0.55, 1.19)	0.59 (0.39, 0.90)	0.01
Multivariate‡ HR (95% CI)	1.0 (referent)	1.09 (0.74, 1.60)	1.01 (0.64, 1.58)	0.65 (0.39, 1.08)	0.08

* No. of participants in crude and age-adjusted models = 3,373; n = 3,041 for fully adjusted models.
† PY, person-years; HR, hazard ratio; CI, confidence interval.

A Prospective Study of Physical Activity and Cognitive Decline in Elderly Women

Yaffe K, Barnes D *Arch Intern Med.* 2001;161:1703–1708.

Table 2. Frequency of Cognitive Decline According to Physical Activity Quartile in 5925 Older Women*

Physical Activity Quartile	No. of Subjects	Cognitive Decline, %	OR (95% CI) Unadjusted	Age and Education Adjusted	Multivariate Adjusted†
Blocks Walked per Week					
Lowest	1450	24.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Second	1438	21.6	0.87 (0.73-1.04)	0.87 (0.73-1.04)	0.87 (0.72-1.05)
Third	1581	17.6	0.68 (0.57-0.81)	0.70 (0.59-0.84)	0.63 (0.52-0.77)
Highest	1456	16.6	0.63 (0.53-0.76)	0.70 (0.58-0.84)	0.66 (0.54-0.82)
Total Kilocalories (Energy) Expended per Week‡					
Lowest	1470	24.1	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Second	1491	20.5	0.81 (0.69-0.96)	0.91 (0.76-1.08)	0.90 (0.74-1.09)
Third	1480	18.0	0.69 (0.58-0.83)	0.79 (0.66-0.95)	0.78 (0.64-0.96)
Highest	1480	17.0	0.65 (0.54-0.78)	0.77 (0.64-0.92)	0.74 (0.60-0.90)

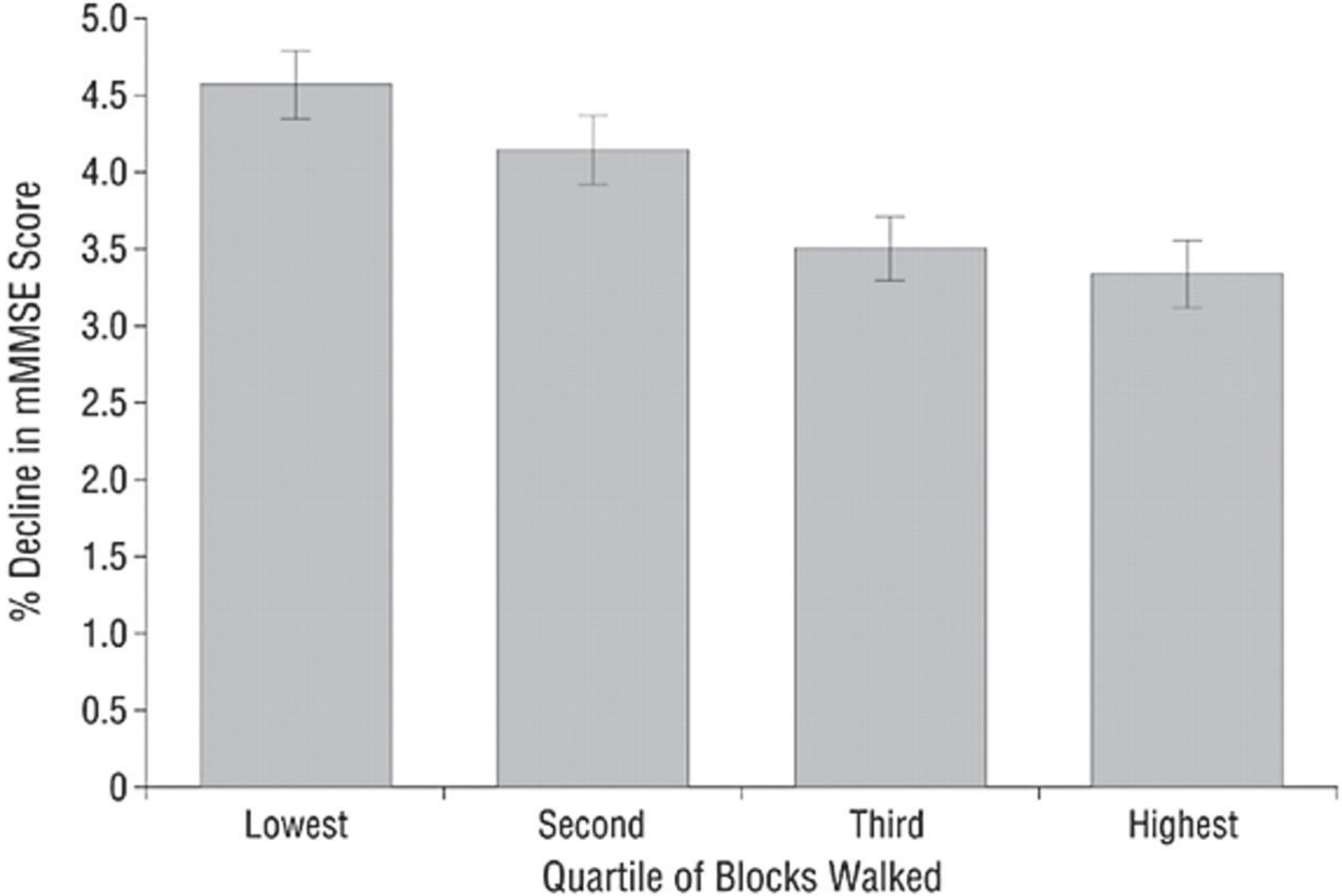
**A complete description of the quartiles is given in the "Results" section of the text. OR indicates odds ratio; CI, confidence interval.*

†Adjusted for baseline age, educational level, health status, functional limitation, depression score, stroke, diabetes, hypertension, myocardial infarction, smoking, and estrogen use.

‡n = 5921 because 4 women did not provide information on total kilocalories expended per week.

Arch Intern Med. 2001;161:1703–1708.

A Prospective Study of Physical Activity and Cognitive Decline in Elderly Women Yaffe K, Barnes D



JAMA. 2004;292:1454-1461

Jennifer Weuve, ScD Jae Hee Kang, ScD JoAnn E. Manson, MD Monique M. B. Breteler, MD

Physical Activity, Including Walking, and Cognitive Function in Older Women

Table 2. Mean Differences in Baseline Cognitive Function Scores by Quintile of Physical Activity*

Test	Quintile of Physical Activity: 1 (Lowest)	2	3	4	5 (Highest)	P Value for Trend
TICS (n = 18 766)						
Adjusted mean difference (95% CI)	Reference	0.20 (0.07 to 0.32)	0.27 (0.15 to 0.40)	0.28 (0.15 to 0.40)	0.28 (0.21 to 0.47)	<.001
Category fluency (n = 18 047)						
Adjusted mean difference (95% CI)	Reference	0.59 (0.38 to 0.81)	0.74 (0.52 to 0.95)	0.76 (0.54 to 0.98)	0.95 (0.73 to 1.17)	<.001
Working memory and attention (n = 16 382)						
Adjusted mean difference (95% CI)	Reference	0.15 (0.03 to 0.27)	0.16 (0.04 to 0.28)	0.27 (0.15 to 0.39)	0.34 (0.22 to 0.46)	<.001
Verbal memory score (n = 16 370)†						
Adjusted mean difference (95% CI)	Reference	0.04 (0.01 to 0.07)	0.03 (0 to 0.07)	0.07 (0.04 to 0.10)	0.08 (0.05 to 0.12)	<.001
Global score (n = 16 353)†						
Adjusted mean difference (95% CI)	Reference	0.06 (0.03 to 0.09)	0.06 (0.03 to 0.09)	0.09 (0.06 to 0.12)	0.10 (0.07 to 0.13)	<.001

Abbreviations: CI, confidence interval; TICS, Telephone Interview for Cognitive Status.

*Mean differences are adjusted for age, education, husband's education, alcohol use, smoking status, aspirin use, ibuprofen use, vitamin E use, balance problems, health limitations in the ability to walk a block, osteoarthritis, emphysema or chronic bronchitis, fatigue, poor mental health (see Table 1), antidepressant use, and moderate to severe bodily pain.

†Verbal memory score averages performance in immediate and delayed 10-word recalls and immediate and delayed East Boston Memory Tests. Global score averages performance on all cognitive tests. Composite scores were computed only for women who completed all component tests.

- 신체활동과 인지기능 및 치매, 연관성?
- 무산소 운동과 유산소성 운동 사이에 대한 연구가 미흡, 운동시간,강도 빈도에 평가가 부족-운동의 방법론 연구 필요
- 참가자의 subclinical signs of dementia 에 대한 평가?
- 체력에 대한 유전자요소(apoe), neurotransmitter system functions and those with neurotrophic effects.

Human Clinical trials

- **Colcombe S and Kramer AF.** Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci* 14: 125–130, 2003
- **Heyn P, Abreu BC, and Ottenbacher KJ.** The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Arch Phys Med Rehabil* 85: 1694–1704, 2004
- **Raz N, Lindenberger U, Rodrigue KM, Kenedy KM, Head D, Williamson A, Dahle C, Gerstorf D, and Acker JD.** Regional brain changes in health aging adults: general trends, individual differences and modifiers. *Cereb Cortex* 15: 1676–1689, 2005
- **Colcombe SJ, Kramer AF, Erickson KI, Scalf P, McAuley E, Cohen NJ, Webb A, Jerome GJ, Marquez DX, and Elavsky S.** Cardiovascular fitness, cortical plasticity, and aging. *Proc Natl Acad Sci USA* 101: 3316–3321, 2004
- **Erickson KI, Colcombe SJ, Elavsky S, McAuley E, Korol DL, Scalf PE, and Kramer AF.** Interactive effects of fitness and hormone replacement treatment on brain health in postmenopausal women. *Neurobiol Aging*: January 4, 2006

Cardiovascular fitness, cortical plasticity, and aging
Stanley J. Colcombe*†, Arthur F. Kramer*†‡§, Kirk I. Erickson*†§, Paige Scalf*†§, Edward McAuley¶, Neal J. Cohen*†§,
Andrew Webb*, Gerry J. Jerome¶, David X. Marquez¶, and Steriani Elavsky

These data suggest that increased cardiovascular fitness can affect improvements in the plasticity of the aging human brain, and may serve to reduce both biological and cognitive senescence

Cognitive Status, Muscle Strength, and Subsequent Disability in Older Mexican Americans

J Am Geriatr Soc 53:1462–1468, 2005.

Mukaila A. Raji, MD,w Yong-Fang Kuo, PhD,w Soham Al Snih, MD,wz Kyriakos S. Markides, PhD,wz M. Kristen Peek, PhD,wz and Kenneth J. Ottenbacher, PhD

Table 3. General Estimation Equations Models Examining the Potential Mediating Effect of Handgrip Strength on 7-Year Incidence of ADL Disability in Older Subjects Initially Not Disabled in Activities of Daily Living with Low Cognition (Mini-Mental State Examination (MMSE) <21) Versus High Cognition (MMSE ≥21)

	Model 1	Model 2	Model 3	Model 4
Explanatory Variable	Odds Ratio (95% Confidence Interval)			
Age	1.07 (1.05–1.09)	1.04 (1.02–1.06)	1.04 (1.02–1.06)	1.05 (1.03–1.08)
Female vs male	1.47 (1.13–1.92)	0.53 (0.38–0.72)	0.53 (0.38–0.72)	0.60 (0.43–0.83)
Low cognition (MMSE <21*)	2.01 (1.60–2.52)	1.66 (1.31–2.10)	1.66 (1.31–2.10)	1.62 (1.26–2.10)
Time	1.31 (1.25–1.38)	1.28 (1.21–1.35)	1.35 (1.15–1.59)	1.39 (1.17–1.65)
Handgrip strength		0.89 (0.87–0.91)	0.91 (0.87–0.95)	0.92 (0.88–0.96)
Handgrip strength × time			1.00 (0.99–1.00)	1.00 (0.99–1.00)

OP with poor cognition had steeper decline in handgrip muscle strength over 7 years than those with good cognition, independent of other demographic and health factors.

Predictors of Combined Cognitive and Physical decline

Hal H. Atkinson, MD, Matteo Cesari, MD, PhD, Stephen B. Kritchevsky, PhD, Brenda W. J. H. Penninx, PhD,§ Linda P. Fried, MD, MPH,w Jack M. Guralnik, MD, PhD,z and Jeff D. Williamson, MD, MHS

Table 2. Logistic Regression Models Assessing the Association Between Baseline Characteristics and Cognitive Decline Only, Physical Decline Only, or Combined Decline

Characteristic	Physical Decline (n = 112)	Cognitive Decline (n = 68)	Combined Decline (n = 60)
	Odds Ratio (95% Confidence Interval)		
Age	1.10 (1.05–1.16)	1.09 (1.03–1.16)	1.07 (1.00–1.15)
White	0.40 (0.19–0.86)	1.00 (0.37–2.71)	0.55 (0.19–1.56)
Smoking			
Never	1	1	1
Former	1.97 (1.02–3.80)	1.03 (0.43–2.46)	1.38 (0.48–4.00)
Current	2.16 (0.76–6.13)	1.19 (0.31–4.54)	5.66 (1.49–21.54)
Education ($\leq 8^{th}$ grade)	0.55 (0.27–1.15)	1.38 (0.60–3.19)	0.97 (0.36–2.57)
Number of diseases	1.17 (0.97–1.41)	0.94 (0.72–1.23)	0.75 (0.53–1.05)
Pulmonary disease	0.95 (0.49–1.83)	0.49 (0.17–1.33)	1.96 (0.69–5.56)
Hemoglobin, g/dL	0.97 (0.77–1.23)	0.86 (0.60–1.21)	0.68 (0.47–0.98)
Baseline walking speed (per SD increase[†])	0.70 (0.48–1.00)	0.99 (0.64–1.54)	0.46 (0.22–0.97)
Baseline Mini-Mental State Examination score	1.02 (0.85–1.23)	0.56 (0.44–0.70)	0.70 (0.54–0.92)
Baseline instrumental activities of daily living	2.04 (1.46–2.86)	1.40 (0.86–2.29)	2.58 (1.58–4.20)
Baseline activities of daily living	0.86 (0.65–1.12)	0.79 (0.55–1.12)	0.80 (0.53–1.20)

Note: Reference group: No physical or cognitive decline (n = 318). Analysis was performed using separate logistic regression models adjusted for age, race, smoking, education, number of diseases, pulmonary disease, hemoglobin, baseline walking speed, baseline Mini-Mental State Examination score, baseline instrumental activities of daily living, and baseline activities of daily living.

Improvement of Cognitive Function by Mental and/or Individualized Aerobic Training in Healthy Elderly Subjects

C. Fabre[1], K. Chamari[2], P. Mucci[3], J. Massé-Biron[2], C. Préfaut[2]

Abstract

Thirty-two healthy elderly subjects (60 - 76 years) were assigned to one of four groups: aerobic training, mental training, combined aerobic and mental training and a control group.. After the training period, the results showed a significant improvement in $\dot{V}O_2max$ ($F = 4.45$, $DF = 1$, $p < 0.05$) of 12 % and 11 % in aerobic training and combined aerobic and mental training groups, respectively. Logical memory ($F = 4.31$, $DF = 1$, $p < 0.05$), as well as paired associates learning scores ($F = 5.47$, $DF = 1$, $p < 0.05$) and memory quotient ($F = 6.52$, $DF = 1$, $p < 0.01$) were significantly improved in the three trained groups. The mean difference in memory quotient between pre and post training was significantly higher in the combined aerobic and mental training group compared to aerobic training or mental training groups ($F = 11.60$, $DF = 3$, $p < 0.001$). We conclude that the specific aerobic training and mental training used in this study could induce the same degree of improvement in cognitive function and that combined training seemed to lead to greater effects than either technique alone.

Erickson KI, Colcombe SJ, Elavsky S, McAuley E, Korol DL, Scalf PE, and Kramer AF.

Interactive effects of fitness and hormone replacement treatment on brain health in postmenopausal women.

Neurobiol Aging: January 4, 2006

First, all women, regardless of HRT status, showed cognitive and brain volume benefits of being more physically fit.
Second, short-term HRT use (within 10 yr) was beneficial on brain volume and executive control, whereas long-term HRT use (longer than 16 yr) negatively affected both cognition and brain volume.

The effects of exercise training on elderly persons with cognitive impairment and dementia: A meta-analysis1

A total of 2020 subjects participated

Significant summary effect sizes (ES) were found for strength (ES=.75; 95% confidence interval [CI], .58–.92), physical fitness (ES=.69; 95% CI, .58–.80), functional performance (ES=.59; 95% CI, .43–.76), cognitive performance (ES=.57; 95% CI, 0.43–1.17), and behavior (ES=.54; 95% CI, .36–.72). The overall mean ES between exercise and nonexercise groups for all outcomes was .62 (95% CI, .55–.70).

Conclusions

Exercise training increases fitness, physical function, cognitive function, and positive behavior in people with dementia and related cognitive impairments.

- 체력훈련과 인지기능의 향상, 효율적 뇌기능, 뇌용적의 보전과는 인과관계가 있을 것이다
- *체력훈련의 프로토콜의 세분화가 필요*
- *인지기능의 평가나 뇌기능 및 구조의 측정 도구에*

Exercise & Brain &Cellular Biology Animal trials

voluntary-wheel running protocols to examine

1) whether aerobic exercise improves behavioral performance on learning and memory paradigms in young and old animals;
2) whether neural activity and long-term potentiation (LTP), a cellular model of memory, are enhanced with exercise;
3) whether molecular factors associated with brain plasticity are upregulated during exercise in young and old animals
4) whether exercise promotes the growth of new neurons and vasculature in aged animals.

- **Fordyce DE and Wehner JM.** Physical activity enhances spatial learning performance with an associated alteration in hippocampal protein kinase C activity in C57BL/6 and DBA/2 mice. *Brain Res* 619: 111–119, 1993
- **Garza AA, Ha TG, Garcia C, Chen MJ, and Russo-Neustadt AA.** Exercise, antidepressant treatment, and BDNF mRNA expression in the aging brain. *Pharmacol Biochem Behav* 77: 209–220, 2004
- **Gomez-Pinilla F, So V, and Kesslak JP.** Spatial learning and physical activity contribute to the induction of fibroblast growth factor: neural substrates for increased cognition associated with exercise. *Neuroscience* 85: 53–61, 1998
- **Kim YP, Kim H, Shin MS, Chang HK, Jang MH, Shin MC, Lee SJ, Lee HH, Yoon JH, Jeong IG, and Kim CJ.** Age-dependence of the effect of treadmill exercise on cell proliferation in the dentate gyrus of rats. *Neurosci Lett* 355: 152–154, 2004
- **Rhodes JS, van Praag H, Jeffrey S, Giard I, Mitchell GS, Garland T, and Gage FH.** Exercise increases hippocampal neurogenesis to high levels but does not improve spatial learning in mice bred for increased voluntary wheel running. *Behav Neurosci* 117: 1006–1016, 2003
- **Van Praag H, Shubert T, Zhao C, and Gage FH.** Exercise enhances learning and hippocampal neurogenesis in aged mice. *J Neurosci* 25: 8680–8685, 2005
- **Farmer J, Zhao X, van Praag H, Wodtke K, Gage FH, and Christie BR.** Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult-male Sprague-Dawley rats in vivo. *Neuroscience* 124: 71–79, 2004

Age-dependence of the effect of treadmill exercise on cell proliferation in the dentate gyrus of rats

Young-Pyo Kima,b, Hong Kima, Mal-Soon Shina, Hyun-Kyung Changa, Mi-Hyeon Janga, Min-hul Shina, Sam-Jun Leea, Hee-Hyuk Leea,b, Jin-Hwan Yoonb, Ill-Gyu Jeongb, Chang-Ju Kim

Neuroscience Letters 355 (2004) 152–154

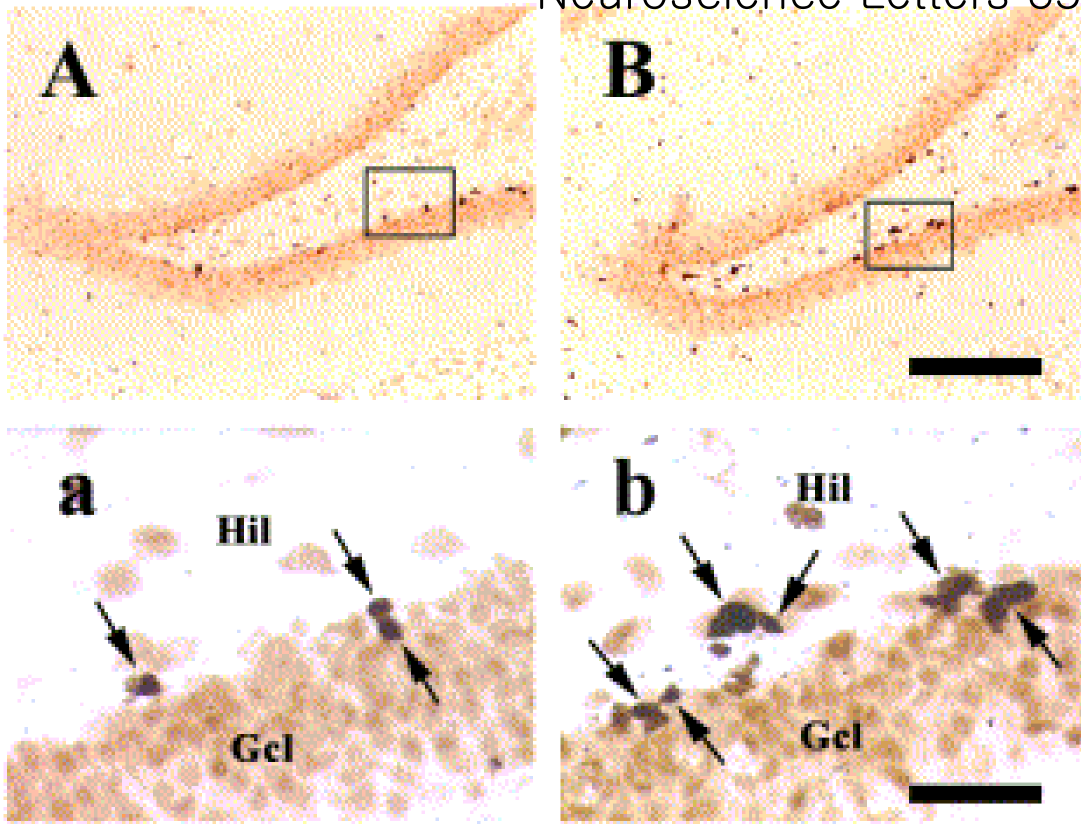


Fig. 1. Photomicrographs of BrdU-positive cells in the dentate gyrus. (A) Eight-week-old control group; (B) 8-week-old exercise group. The scale bar represents 100 μm in (A,B). The scale bar represents 25 μm in (a,b). Arrows indicate the location of BrdU-positive cells in the subgranular layer. Gcl, granule cell layer; Hil, hilus.

Physical activity enhances spatial learning performance with an associated alteration in hippocampal protein kinase C activity in C57BL/6 and DBA/2 mice

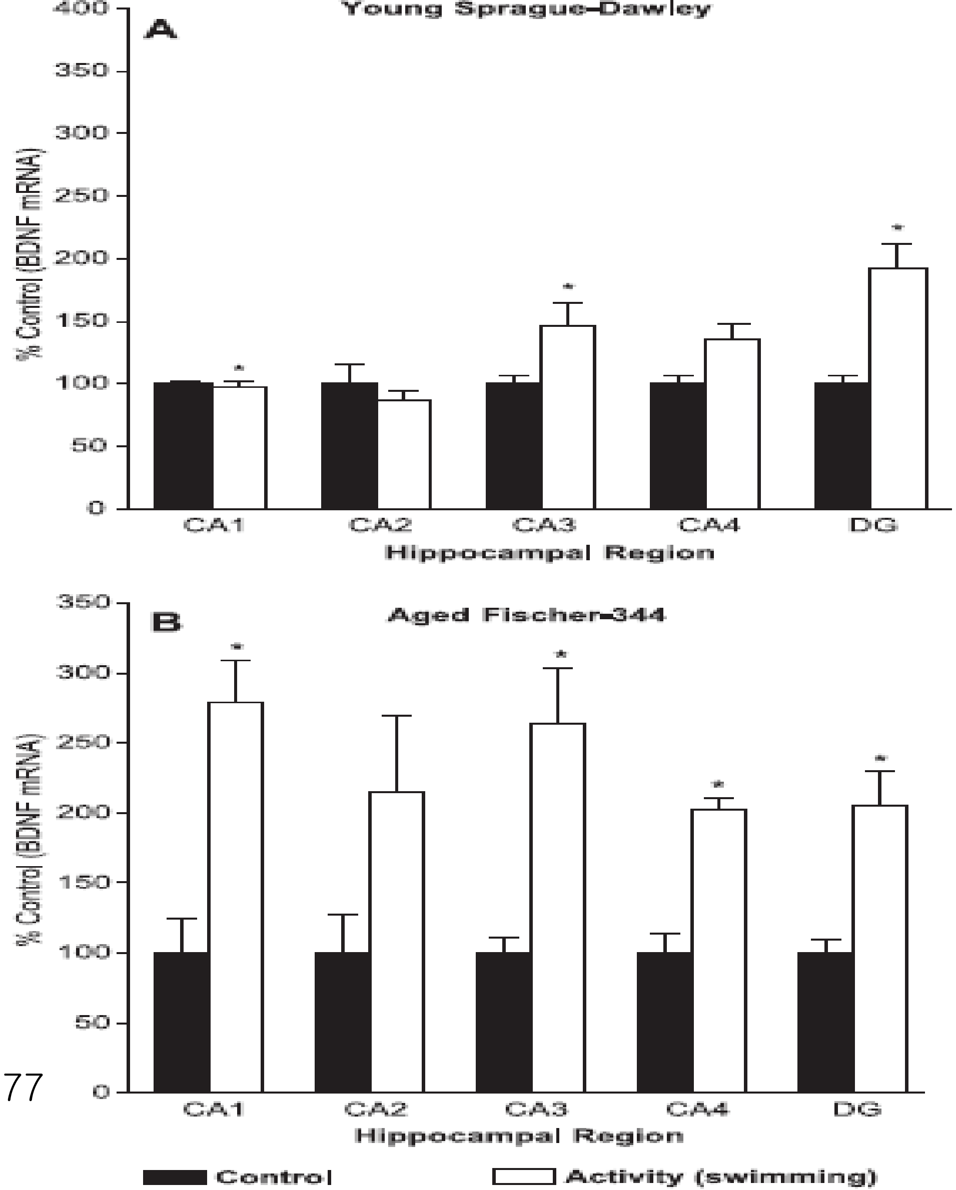
D.E. Fordycea and J.M. Wehner

C57BL/6Ibg (C57) and DBA/2Ibg (DBA) mice. C57 and DBA mice, 3 months of age, were subjected to 8 weeks of a physical activity regime (consisting of moderate-pace treadmill running 5 days/week, 60 min/day, 0% grade, 12 m/min) or remained sedentary in their cages.
the Morris water maze task for 6 days followed by 12 days of testing on the place learning-set task (8 trials/day with each task).
Physical activity produced a 2- to 12-fold enhancement in spatial learning performance on both the Morris ($P < 0.0001$) and place learning-set ($P < 0.02$) probe trials in both C57 and DBA mice.
hippocampal bound PKC activity ($P < 0.05$).
These data provide further support for our previous hy
activity involvement in spatial learning and enhanceme
performance in rodents by physical activity. In additior
indicate that hippocampal PKC activity may be involve
activity-induced enhancement of spatial learning perf

Exercise, antidepressar treatment, and BDNF mRNA expression in the aging brain

Antonio A. Garza, Tony G. Ha, Celithelma Garcia, Michael J. Che and Amelia A. Russo-Neustadt

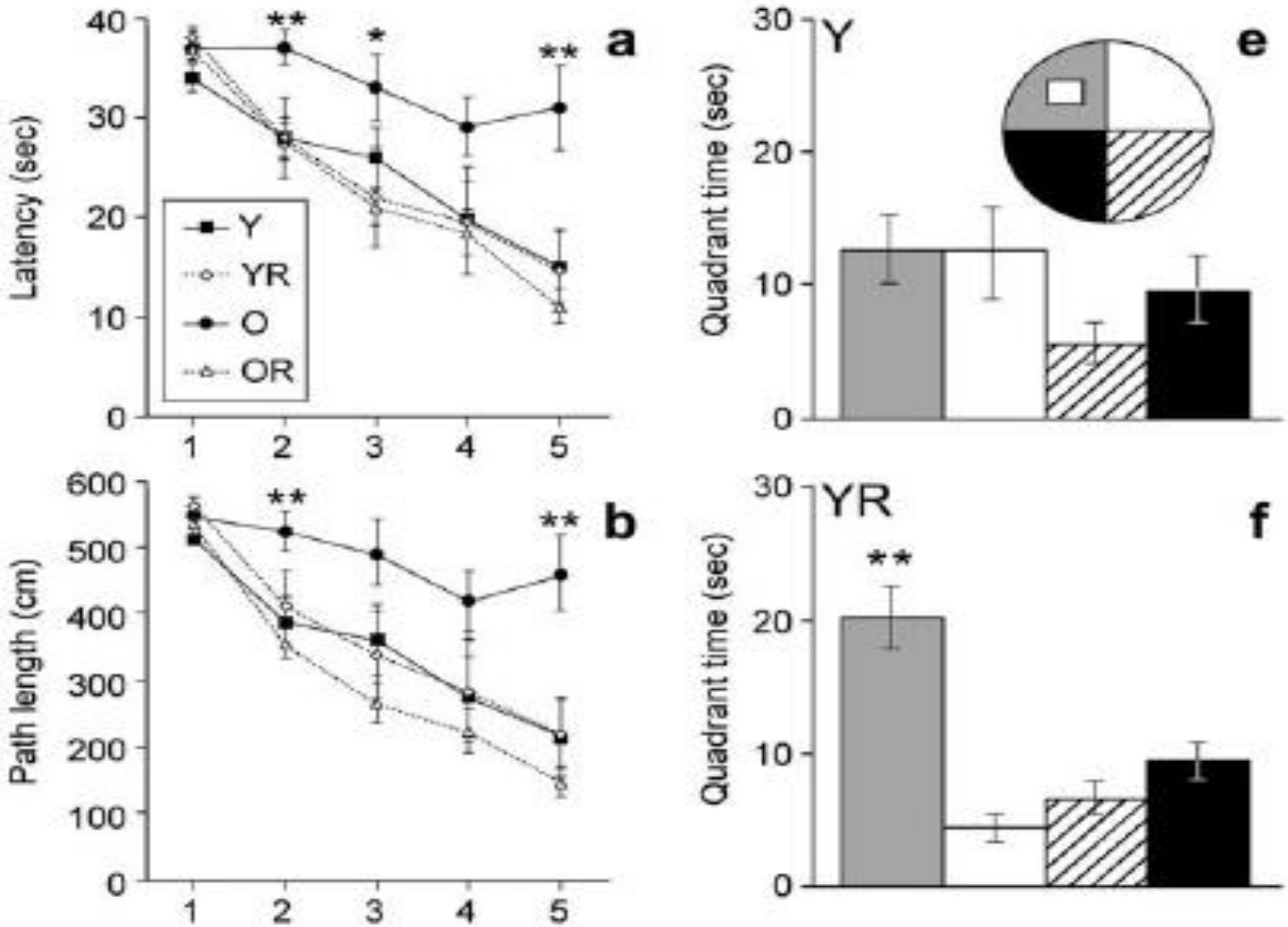
Pharmacology, Biochemistry and Behavior 77 (2004) 209–220



ig. 4. Swimming activity (8 min/day total) for 2 days significantly creased BDNF mRNA levels in the CA3 and DG subregions of the young) rat hippocampus. In older animals (B) swimming activity led to marked creases in BDNF mRNA in all hippocampal subregions compared to edentary controls. Results are displayed as the percentage of control and present the mean ± S.E.M. Asterisks denote statistically significant ifferences from the control group (SS), $P < .05$.

Exercise Enhances Learning and Hippocampal Neurogenesis in Aged Mice

The Journal of Neuroscience, September 21, 2005 • 25(38):8680–8685



The majority of animal studies:

exercise on neuronal systems have focused on **the hippocampus,**

a dramatic alterations in cell number in persons with Alzheimer's disease and has also been associated with some forms of amnesia.

In rodents, the hippocampus has been frequently associated with spatial learning and memory tasks such as the Morris water maze

The hippocampus also has several subfields that play distinct roles in the formation of new memories and may be disproportionately affected with exercise.

Exercise increases cognitive performance in both young and aged animals and increases mRNA and protein levels of BDNF,

IGF-I may be mediating the effects of exercise on BDNF, neurogenesis, and cognitive performance.

Exercise is an effective enhancer of neurocognitive functioning in both young and old animals.

결론
The animal and human studies

- 신체활동과 유산소훈련이 인지기능, 뇌기능, 뇌구조에 나이에 따른 바람직하지 않은 영향을 조정할 수 있을 것이다.
- Aging brain에 운동의 긍정적 영향이 동물이나 질환이 없는 집단에서 있을 것이다.

향후

- 어떤 운동이? 얼마 정도의 신체활동이 인지 기능이 뇌에 영향을 미칠 것인가???
- 훈련이 끝나고 얼마 동안 운동효과가 지속될 것인가. 과거의 운동효과를 회복시키는데 얼마큼의 운동이 필요할 것인가.