

Exercise & the Brain

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Apart from its physical benefits, new findings show that exercise also can boost brain function, tone neural connections, and shape up memory and learning.

One study found that joggers consistently performed better than non-joggers on learning and memory tests that required the use of the prefrontal cortex. This area of the brain is located behind the forehead and is known for its ability to carry out complex functions involving learning and memory.

In the study, Kisou Kubota, MD, and his colleagues at the Nihon Fukushi University in Japan compared seven healthy joggers with seven healthy non-joggers. The joggers ran for 30 minutes, several times a week for 12 weeks. Before and after the training period, the researchers tested prefrontal function with three memory tasks using a computer.

"The tests showed that joggers had a clear improvement in prefrontal function over non-joggers," says Kubota. "These improvements, however, went down when the joggers stopped their training, which suggests that ongoing exercise is required to maintain the benefit."

A key mediator of exercise's effect on learning and memory is brain-derived neurotrophic factor (BDNF), which is a protein known to have a critical role in the repair and maintenance of neural circuits. Fernando Gomez-Pinilla, PhD, and his colleagues at the University of California in Los Angeles, found that voluntary exercise increased levels of BDNF in the hippocampus, a brain area involved with learning and memory.

The researchers found that exercise helped rats overcome poor cognitive function caused by nutritional factors. "A typical diet of most industrialized western societies, high in saturated fat and refined carbohydrates, can contribute to cognitive decline," says Gomez-Pinilla. These new studies suggest that "exercise can be used as a compensatory strategy to ameliorate the effects of an unhealthy diet on both cognition and neural function," he adds.

Researchers at the University of Colorado in Denver, led by David Albeck, PhD, found that even a light exercise routine can create the beneficial BDNF effect in rats. Previous reports showed that rigorous physical exercise, like high-intensity treadmill running, stimulated BDNF expression in the brain. The downside is that sometimes high-intensity workouts can be stressful experiences that increase the release of stress hormones. Stress hormones can suppress BDNF production, thereby canceling the positive effects of the BDNF rise from the exercise.

As a next step, the researchers plan to test whether mild exercise can boost BDNF in aged rats with low BDNF levels. "Aged rats often develop problems with short-term memory processing, similar to symptoms often reported in older people," says Albeck. "Enhancing BDNF expression in the brains of older rats may enhance their memory."

Study is first to confirm link between exercise and changes in brain

Three key areas of the brain adversely affected by aging show the greatest benefit when a person stays physically fit. The proof, scientists say, is visible in the brain scans of 55 volunteers over age 55.

The idea that fitness improves cognition in the aging is not new. Animal studies have found that aerobic exercise boosts cellular and molecular components of the brain, and exercise has improved problem solving and other cognitive abilities in older people. A new study in the February 2003 issue of the *Journal of Gerontology: Medical Sciences*, however, is the first to show - using high-resolution magnetic resonance imaging - anatomical differences in gray and white matter between physically fit and less fit aging humans.

Gray matter consists of thin layers of tissue of cell bodies such as neurons and support cells that are critically involved in learning and memory. White matter is the myelin sheath containing the nerve fibers that transmit signals throughout the brain.

As people age, especially after age 30, these tissues shrink in a pattern closely matched by declines in cognitive performance, Kramer said.

The authors, led by Arthur F. Kramer of the University of Illinois at Urbana-Champaign, said that the findings "provide the first empirical confirmation of the relationship between cardiovascular fitness and neural degeneration as predicted" in various academic studies on aging and cognition in both animal and human populations.

"We found differences in three areas of the brain, the frontal, temporal and parietal cortexes," Kramer said. "There were very distinct differences particularly in two types of tissue, the gray matter and white matter. Nobody has reported this before."

A second Kramer-led study - a meta-analysis of 18 previous studies - published in March 2003 in *Psychological Science*, suggests that older women, especially those on hormone replacement therapy, benefit more cognitively than do men from increased physical activity as they age.

The *Journal of Gerontology* study involved well-educated men and women aged 55-79. Their fitness ranged from sedentary to very fit, competitive-ready athletes. Fitness was measured by results of 1-mile-walking and treadmill stress tests. Three-dimensional scans of the participants' brains were done using MRI equipment at Carle Foundation Hospital in Urbana. Applying voxel-based morphometry, researchers estimated tissue atrophy in a point-by-point fashion in the targeted regions of the brain.

"Interestingly, we found that fitness per se didn't have any influence on brain density," said Kramer, a professor of psychology and member of the Beckman Institute for Advanced Science and Technology at Illinois. "It is fitness as it interacts with age that has the positive effects. Older adults show a real decline in brain density in white and gray areas, but fitness actually slows that decline."

In the study, most other potential negative attributes - smoking, diabetes, drinking,

dieting, etc. - were factored out of the data equation, Kramer said.

"This, to our knowledge, is the first human data providing a potential anatomical account of the cognitive effects that we and others have found over the years," Kramer said. "Our data also suggest that more research is clearly needed to actually do a thorough examination of brain structure and functioning, and the impact of interventions such as fitness and cognitive training."

In 1999, Kramer and colleagues reported in the journal *Nature* that previously sedentary people over age 60 who walked rapidly for 45 minutes three days a week can significantly improve mental processing abilities that decline with age, and particularly tasks that rely heavily on the frontal lobes of the brain.

For their meta-analysis paper, researchers reviewed 18 intervention studies done between 1966 and 2001 and involving hundreds of participants ages 55 and older. Fitness training was found to show "robust but selective benefits for cognition, with the largest fitness-induced benefits occurring for executive-control processes."

Few studies done in the early part of the time included women, but as data were analyzed from later studies, Kramer said, "We found that gender had a large effect; men simply don't benefit as much, so we went back through our own data and asked why."

In previous studies of mice whose ovaries had been removed, they noted a decline in exercise and a drop in production of brain-derived neurotrophin. When mice were put back on estrogen, production of the brain molecule increased and so did exercise activity.

In women, Kramer said, the data showed a similar trend: Women on estrogen replacement therapy benefited more than women not on it.

Other main conclusions from the meta-analysis:

- * Exercise programs involving both aerobic exercise and strength training produced better results on cognitive abilities than either one alone.
- * Older adults benefit more than younger adults do, possibly, Kramer said, because older adults have more to gain as age-related declines become more prevalent.
- * More than 30 minutes of exercise per session produces the greatest benefit, a finding consistent with many existing guidelines for adults.

The studies were funded by the National Institute on Aging (National Institutes of Health) and the New York-based Institute for the Study of Aging.

"These intriguing data suggest there may be one more possible benefit from regular exercise," said Molly V. Wagster, program director for the Neuropsychology of Aging, Neuroscience and Neuropsychology of Aging Program of the NIA, which supported the work. "The study emphasizes the importance of continued research on the potential role that exercise might play in reducing cognitive decline with age."

Illinois contributors to the *Journal of Gerontology* paper were Kramer; postdoctoral researcher Stanley J. Colcombe; doctoral student Kirk I. Erickson; Andrew G. Webb,

professor of electrical and computer engineering; Neal Cohen, professor of psychology; and Edward McAuley, professor of kinesiology. Naftali Raz of Wayne State University in Detroit also was a coauthor. Colcombe and Kramer performed the meta-analysis study. This article was prepared by Obesity, Fitness & Wellness Week editors from staff and other reports.