Exercise increases brain growth factor and receptors, prevents stem cell drop in middle age

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A new study confirms that exercise can reverse the age-related decline in the production of neural stem cells in the hippocampus of the mouse brain, and suggests that this happens because exercise restores a brain chemical which promotes the production and maturation of new stem cells.

Neural stem cells and progenitor cells differentiate into a variety of mature nerve cells which have different functions, a process called neurogenesis. There is evidence that when fewer new stem or progenitor cells are produced in the hippocampus, it can result in impairment of the learning and memory functions. The hippocampus plays an important role in memory and learning.

The study, "Exercise enhances the proliferation of neural stem cells and neurite growth and survival of neuronal progenitor cells in dentate gyrus of middle-aged mice," was carried out by Chih-Wei Wu, Ya-Ting Chang, Lung Yu, Hsiun-ing Chen, Chauying J. Jen, Shih-Ying Wu, Chen-Peng Lo, Yu-Min Kuo, all of the National Cheng Kung University Medical College in Taiwan. The study appears in the November issue of the *Journal of Applied Physiology*, published by The American Physiological Society.

Rise in corticosterone or fall in nerve growth factor?

The researchers built on earlier studies that found that the production of stem cells in the area of the hippocampus known as the dentate gyrus drops off dramatically by the time mice are middle age and that exercise can slow that trend. In the current study, the researchers wanted to track these changes in mice over time, and find out why they happen.

One hypothesis the researchers investigated is that the age-related decline in neurogenesis is tied to a rise in corticosterone in middle age. Elevation of corticosterone has been associated with a drop in the production of new stem cells in the hippocampus.

The second hypothesis is that nerve growth factors -- which encourage new neural cell growth but which decrease with age -- account for the drop in neurogenesis. Specifically, the study looked at whether a decrease in brain-derived neurotrophic growth factor leads to a decline in new neural stem cells.

Variables studied

The researchers trained young (3 months), adult (7 months), early middle-aged (9 months), middle-aged (13 months) and old (24 months) mice to run a treadmill for up to one hour a day.

The study tracked neurogenesis, age, exercise, serum corticosterone levels and brain-derived neurotrophic factor (BDNF) and its receptor TrkB levels in the hippocampus. The researchers focused on middle age as a critical stage for the decline of neurogenesis in the mice.

As expected, the study found that neurogenesis drops off sharply in middle-aged mice. For example, the number of neural progenitor and mitotic (dividing) cells in the hippocampus of middle-aged mice was only 5% of that observed in the young mice.

The researchers also found that exercise significantly slows down the loss of new nerve cells in the middle-aged mice. They found that production of neural stem cells improved by approximately 200% compared to the middle-aged mice that did not exercise. In addition, the survival of new nerve cells increased by 170% and growth by 190% compared to the sedentary middle-aged mice. Exercise also significantly enhanced stem cell production and maturation in the young mice. In fact, exercise produced a stronger effect in younger mice compared to the older mice.

How does this happen?

Based on these results, it appears that nerve growth factor has more to do with these findings than the corticosterone:

-- The middle-aged exercisers had more brain-derived neurotrophic factor and its receptor, TrkB, compared to the middle-aged mice that did not exercise. This suggests that exercise promotes the production of brain-derived neurotrophic factor which, in turn, promotes differentiation and survival of new brain cells in the hippocampus.

-- Exercise did not change the basal level of serum corticosterone in middle-aged mice. This suggests that the reduction of neurogenesis during aging is not due to the drop in corticosterone levels.

Source: American Physiological Society