Does physical activity influence the health of future offspring?

April 11 2018

Credit: CC0 Public Domain

Physical and mental exercise can affect the learning ability of future offspring, at least in mice. This particular form of inheritance is mediated by certain RNA molecules that influence gene activity. These molecules accumulate in both the brain and germ cells following physical and mental activity. Prof. André Fischer and colleagues from the German Center for Neurodegenerative Diseases (DZNE) in Goettingen and Munich and the University Medical Center Goettingen (UMG) report these findings in the journal *Cell Reports*.

For a long time, geneticists believed that acquired skills do not modify the DNA sequence and therefore cannot be passed on to the offspring. However, in recent years, scientists have found some circumstances that refute this principle. A poor diet, for example, increases the risk of disease for unborn offspring. Lifestyle factors such as stress and trauma can also influence the next generation. Scientists call this phenomenon "epigenetic" inheritance, as it is not associated with changes in DNA sequence.

Prof. André Fischer and colleagues investigated the inheritance the ability for learning, another acquired characteristic. It is well known that physical and mental activity improves learning ability and reduces the risk of diseases such as Alzheimer's. In mice, the scientists showed that learning ability was passed onto the next generation by epigenetic inheritance. When Fischer and co-workers exposed mice to a stimulating environment in which they had plenty of exercise, their offspring also benefited. Compared to the mice of a control group, they achieved better results in tests that evaluate learning ability. These rodents were also found to have improved synaptic plasticity in the hippocampus, a region of the brain important for learning. Synaptic plasticity is a measure of how well nerve cells communicate with each other. It thus forms the cellular basis for learning.

Next, the scientists sought to determine which mechanism was responsible. They focused on epigenetic inheritance by fathers and looked for its material basis in sperm. Sperm contains paternal DNA and also RNA molecules. The scientists therefore conducted experiments to find out about the role played by these RNA molecules in the inheritance of learning skills. They extracted RNA from the sperm of mice that were physically and mentally active. These extracts were injected into fertilized egg cells. The resulting offspring were also found to have enhanced synaptic plasticity and learning ability. Physical and mental activity therefore had a positive effect on the cognitive skills of the offspring. This effect was mediated through the RNA in the sperm.

Tracking down the responsible RNA

In further experiments involving injections of RNA extracts, the scientists were able to identify more closely the RNA molecules responsible for epigenetic inheritance: They showed that two so-called microRNA molecules—miRNA212 and miRNA132—could account for at least some of the inherited learning capacity. microRNAs are control molecules that influence gene activity. "For the first time, our work specifically links an epigenetic phenomenon to certain microRNAs," says Fisher, a senior scientist at the DZNE Goettingen and the UMG.

The researchers also found that miRNA212 and miRNA132 accumulated in the brains and sperm of mice after physical and mental activity. It was previously known that these molecules stimulate the formation of synapses in the brain, thus improving learning ability. Through the sperm, they are transmitted to the next generation. "Presumably, they modify brain development in a very subtle manner improving the connection of neurons. This results in a cognitive advantage for the offspring," says Fischer.

It is known that physical activity and cognitive training also improve learning ability in humans. However, it is not so easy to study in humans whether learning ability can be inherited epigenetically. Nevertheless, the results obtained by Fischer and colleagues may point towards answers to this question. The researchers now intend to find out whether miRNA212 and miRNA132 also accumulate in human sperm after phases of physical and mental activity.

More information: Eva Benito et al, RNA-Dependent Intergenerational Inheritance of Enhanced Synaptic Plasticity after Environmental Enrichment, *Cell Reports* (2018). DOI: 10.1016/j.celrep.2018.03.059

Provided by German Center for Neurodegenerative Diseases