EXERCISE

Intergenerational inheritance of exercise benefits

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Although the beneficial effects of exercise for health are well known, few reports have addressed whether these exercise-mediated effects are inheritable. According to a new study in mice, paternal exercise positively influences offspring's brain physiology and cognitive behavior.

In 2018, Benito and colleagues reported that exposure of adult male mice to environmental enrichment (EE) enhances hippocampal synaptic plasticity in the mice themselves and also in the next generation, via changes in the father's sperm RNA composition. The effects of EE on cognition, however, seemed to be limited in the offspring. In the present study, McGreevy and colleagues followed a 'gold standard' approach to evaluate the effects of paternal physical activity on offspring's cognitive behavior and performed three experiments: in experiment A, litters of sedentary fathers were compared with litters born from the same fathers after exercising; in experiment B, litters from sedentary males were compared with litters from different exercised males; in experiment C, in vitro fertilization (IVF) and embryo transfer were used to produce and compare litters from different exercised and sedentary males. Memory and pattern separation performance were assessed in fathers and their litters using the novel object recognition (NOR) test and a pattern separation task. Both the NOR test and the pattern separation task were evaluated by measuring the discrimination index (DI), an indicator of the difference between the exploration time of novel and familiar objects. DI scores revealed that NOR memory and spatial pattern separation were enhanced in exercised fathers compared with sedentary fathers, as well as in their offspring compared with offspring of sedentary fathers (experiment B) or offspring of the same father before exercising (experiment A). Similar behavioral differences were observed in litters generated from IVF and embryo transfer, confirming the germline transmission of exercise benefits.

Immunohistochemistry analysis showed that exercise increased the number of immature neurons in the hippocampus of the father, and that this effect was transmitted to the progeny. Analysis of RNA sequencing data from hippocampal tissues indicated that mitochondrial-related gene sets were enriched in exercised fathers compared with sedentary fathers and in litters from exercised fathers compared with litters of the sedentary ones. Next, the investigators analyzed the activity of citrate synthase, which revealed that this marker of mitochondrial functionality was increased in the hippocampus of the offspring from exercised fathers.

Altogether, these results suggest that paternal exercise enhances offspring's cognition by reprogramming hippocampal mitochondria in the offspring.

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