Study shows that paternal nutrition affects offsprings' mental fitness

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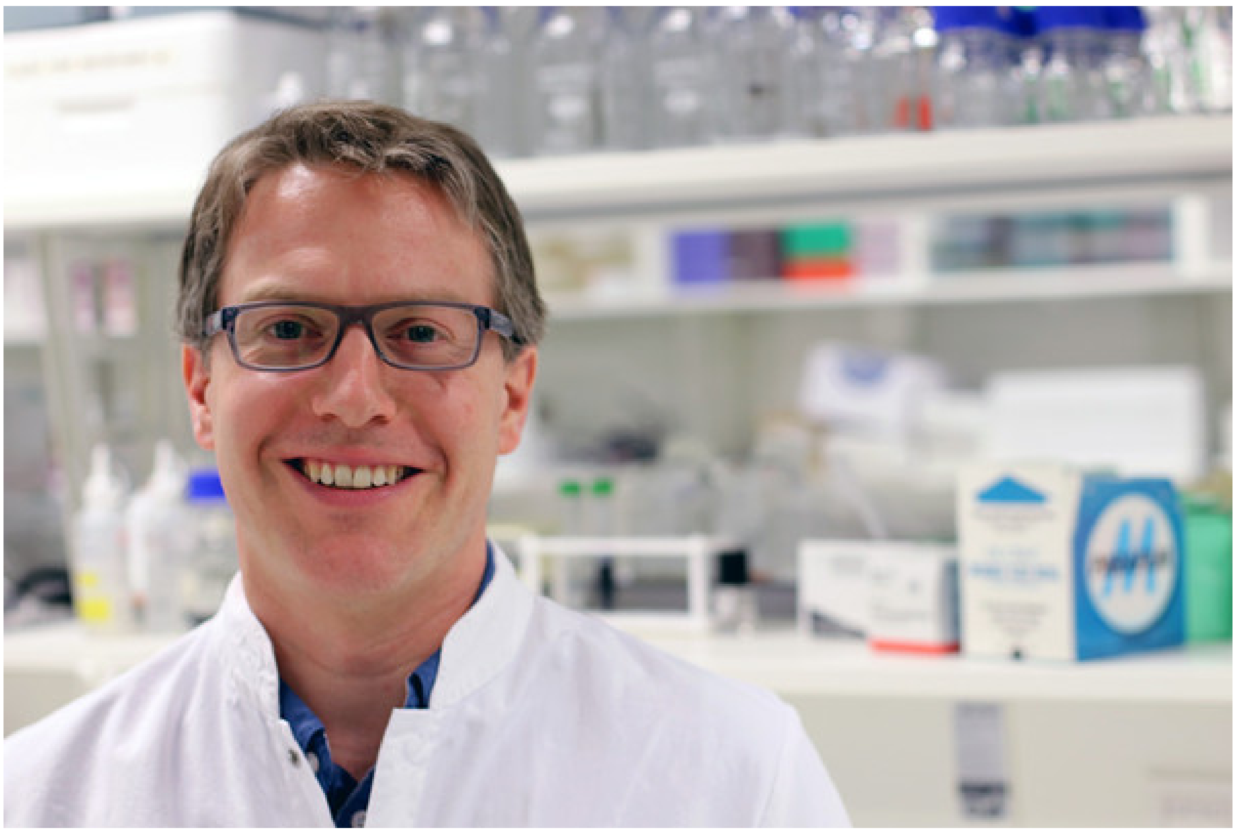

In a laboratory study Dr. Dan Ehninger and colleagues examined whether epigenetic changes are associated with cognitive alterations. Credit: DZNE / Daniel Bayer

The father's lifestyle affects the cognitive skills of his offspring—at least in mice. Scientists at the German Center for Neurodegenerative Diseases (DZNE) have now shown that if male rodents are fed a diet rich in folic acid, methionine and vitamin B12, their progeny do not perform well in memory tests. The diet influences so-called epigenetic patterns in the genome, and this reprogramming is transferred to some degree to the next generation through the sperm. This suggests that the intake of high concentrations of such methyl donors could also have side effects in humans, for example if they consume excessive amounts of energy drinks or folic acid pills. Dan Ehninger and colleagues report on these findings in the journal *Molecular Psychiatry*.

Evidence is accumulating, at least in animal studies, that child development is affected not only by the mother's diet and lifestyle prior to conception, but also by environmental factors the father is exposed to. For example, if male rodents are put on a diet particularly rich in fats, they will pass on a tendency to become diabetic to their offspring. One possible cause for phenomena like this are diet-induced DNA methylation changes, i.e. alterations in tiny chemical tags attached to the DNA that can control the activity of genes. If particularly large quantities of these methyl tags are supplied in the diet, this may hamper the expression of genes affected by increased DNA methylation.

The effects of a methyl donor-rich diet

"For a long time, it was assumed that these paternal epigenetic marks are erased completely after the fusion of sperm and egg cell," explains Dr. Dan Ehninger, who leads a research group at the DZNE's Bonn site. However, we know today that part of the paternal DNA methylation survives this process. In collaboration with colleagues at the Helmholtz Zentrum München and the Federal Institute for Drugs and Medical Devices, Ehninger's team examined whether these epigenetic changes are associated with cognitive alterations in offspring mice. Towards this end, the scientists put male mice on a diet rich in methyl donors and cofactors required for methyl group metabolism: This diet contained high concentrations of methionine, folic acid, vitamin B12, choline, betaine and zinc. A second group of male rodents was given a standard diet. After six weeks, the male mice were mated with female mice and their offspring subjected to careful analyses. The result: the offspring of the male mice fed with methyl donors performed less well in all learning and memory tests. "We were able to show that even a transient change in the paternal diet can cause impaired learning skills in offspring. This affected in particular the ability to properly learn a spatial navigation task," says Ehninger.

Abnormalities were found not only in the animals' behavior, but also in their brains: Nerve connections in the hippocampus—a brain region which is important for memory—reacted quite sluggishly to electrical stimuli, indicating that their adaptiveness—the so-called neuronal plasticity—was impaired in offspring mice. In line with this, a gene called "Kcnmb2" which is involved in neuroplasticity, was downregulated in progeny of the fathers that received the methyl donor-rich diet.

Excessive amounts of food supplements could have side effects

All this are merely results of animal experiments. However, humans can also be exposed to high doses of methyl donors, says Ehninger. This may apply in particular to countries like the USA, where there is a widespread consumption of products fortified with folic acid. "Methyl donor deficiencies are well known to have adverse health consequences that can be prevented with dietary supplements. However, our study suggests that excessive consumption may be associated with adverse effects as well," says the scientist. In the future, he intends to determine whether epigenetic traits can also be passed on by humans to their offspring and which environmental factors may have an influence on this. Does the father's age alter DNA methylation patterns, thus influencing health of the next generation? Ehninger reckons: "To date, such epigenetic mechanisms and their intergenerational influences have certainly received too little attention."

More information: D P Ryan et al, A paternal methyl donor-rich diet altered cognitive and neural functions in offspring mice, *Molecular Psychiatry* (2017). DOI: 10.1038/MP.2017.53

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