Vitamin E-deficient embryos are cognitively impaired even after diet improves

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Credit: Oregon State University

Zebrafish deficient in vitamin E produce offspring beset by behavioral impairment and metabolic problems, new research at Oregon State University shows.

The findings are important because the neurological development of zebrafish is similar to that of humans, and nutrition surveys indicate roughly 95 percent of women in the U.S. have inadequate intakes of this critical micronutrient.

The problem may be exacerbated in women of child-bearing age who avoid high-fat foods and may not have a diet rich in oils, nuts and seeds, which are among the foods with the highest levels of vitamin E, an antioxidant necessary for normal embryonic development in vertebrates.

Corresponding author Maret Traber and collaborators at OSU compared offspring from fish on vitamin E-deficient diets - the E-minus group - with those on vitamin E-adequate diets, the E-plus fish.

The E-minus embryos had more deformities and greater incidence of death as well as an altered DNA methylation status through five days after fertilization; five days is the time it takes for a fertilized egg to become a swimming zebrafish.

For the next seven days, all of the normal-looking fish, irrespective of diet history, were fed a vitamin E-adequate diet.

Both groups grew normally and showed similar DNA methylation, but the E-minus fish failed to learn and were afraid. They also continued to have metabolic defects and indications of mitochondrial damage.

Because insufficient vitamin E reached the E-minus embryos' brains, those brains continued to lack choline and glucose and simply did not develop correctly, said Traber, a professor in the OSU College of Public Health and Human Sciences, and Ava Helen Pauling Professor in the Linus Pauling Institute.

"They managed to get through the critical period to get the brain formed, but they were stupid and didn't learn and didn't respond right," Traber said. "They had so much oxidative damage they essentially had a screwed-up metabolism. These outcomes suggest embryonic vitamin E deficiency in zebrafish causes lasting impairments that aren't resolved via later dietary vitamin E supplementation.

"What that means for people is that many people are walking around with inadequate intakes, and how is their metabolism being affected and especially the brain, which is highly polyunsaturated and has specific mechanisms for retaining vitamin E? It takes awhile to get vitamin E into the brain to protect it, and this has me concerned about teenage girls who eat inadequate diets and get pregnant."

Traber said a lack of vitamin E causes a chain reaction that dramatically changes cell metabolism.

"It's the secondary ripples of having inadequate vitamin E that are really causing the problems, and it takes a fair amount of time to correct all of those

things that go wrong," she said. "It's very frightening is what it really comes down to."

Traber's collaborators included OSU colleagues Melissa McDougall, Jaewoo Choi, Lisa Truong and Robert Tanguay.

Findings were recently published in *Free Radical Biology and Medicine*. The National Institutes of Health and the National Institute of Environmental Health Sciences supported this research.

More information: Melissa McDougall et al, Vitamin E deficiency during embryogenesis in zebrafish causes lasting metabolic and cognitive impairments despite refeeding adequate diets, *Free Radical Biology and Medicine* (2017). DOI: 10.1016/j.freeradbiomed.2017.06.012