Prenatal choline intake increases grey and white matter in piglets

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Austin Mudd and Ryan Dilger from the University of Illinois show that piglets from choline-deficient mothers have smaller brains with less grey and white matter. Credit: Stephanie Henry, University of Illinois

Choline intake during pregnancy can influence infant metabolism and brain development, according to a series of studies from the University of Illinois. Although the role of choline in neurodevelopment has been studied before in rodents, the new research, done with pigs, has more relevance to humans.

"We know the pig is a good model for humans because they have the same nutrient requirements, similar metabolic function, and also have very similar brain development, following the same growth trajectories," explains Austin Mudd, a doctoral student in the Neuroscience Program at U of I. "The pig is bridging the gap between the mechanistic work we see in rodents and that higher-level cognitive function that they're looking at in humans."

Choline, found in liver, eggs, wheat germ, and other foods, is an essential nutrient in human and animal diets. It's required to make cell membranes, neurotransmitters, and myelin, the fatty sheath surrounding nerve cells. But most adults, including pregnant women, don't consume enough.

"In the U.S., 90 percent of us don't meet our choline requirement," Mudd says. "And the most recent data says pregnant women, who should consume 450 milligrams per day, may not even be reaching 300 milligrams."

To understand how choline deficiency affects the developing brain during and after pregnancy, Mudd and his collaborators gave pregnant sows choline-deficient or choline-sufficient diets through the second half of their pregnancies. After weaning, piglets were fed choline-deficient or choline-sufficient milk replacer for 30 days. Then the month-old piglets were scanned by magnetic resonance imaging (MRI).

Mudd analyzed images of the piglet brains in terms of volume and makeup. The first analysis, reported in a 2016 article in *Nutritional Neuroscience*, compared the volumes of 19 brain regions in piglets that had received deficient or sufficient choline prenatally and postnatally. The second analysis, published last week in *Current Developments in Nutrition*, corrected for volume differences to isolate differences in grey and white matter concentration in the piglets' brains.

"In pigs from choline-deficient moms, their brains were about 10 percent smaller overall," Mudd says. And 11 of the 19 regions were significantly smaller in choline-deficient brains.

When Mudd corrected for these volume differences to look specifically at grey and white matter concentration, the story was the same. Piglets whose mothers consumed sufficient choline during pregnancy had higher concentrations of grey and white matter in the brain's cortical regions.

Grey matter is primarily made up of the neurons themselves, while white matter comprises the material that connects neurons and bridges different parts of the brain.

"In our first paper, we saw that the left and right cortex were larger in the choline-sufficient pigs," he says. "After our second analysis, that makes sense. If you have a greater density of grey matter in the cortex, it is likely that brain region will have a greater volume as well."

Decades of research has shown particular nutrients play specific roles in the neurodevelopmental process. The use of MRI technology has allowed researchers to identify the global influence of a specific nutrient on particular aspects of brain development. In an earlier study, the researchers found that another nutrient, iron, influenced aspects of both grey and white matter development.

"Our research shows that choline, like iron, does not appear to be specific to one part of brain development, it's important for all of it," Mudd says.

All of these results were for piglets born to choline-deficient mothers. But, as part of the study, some of the pigs from choline-deficient mothers were given adequate amounts of choline after birth. Was it enough to offset the deficiency during pregnancy?

The short answer is no, at least not for the brain. "Postnatal supplementation cannot correct for prenatal deficiency. It has to occur during development. We can't recover that after the fact," says Ryan Dilger, associate professor in the Department of Animal Sciences, Division of Nutritional Sciences, and Neuroscience Program at U of I.

However, another graduate researcher who collaborated on these papers led an earlier study on the same piglets in 2015. The study, led by Caitlyn Getty, showed lower brain weights in piglets from choline-deficient mothers, but her study focused more on overall health and metabolism of the piglets. From that perspective, it was postnatal choline intake that was most important, particularly for liver and kidney function.

The research, taken together, suggests a cellular-level mechanism to back up a 2013 study that concluded children born to mothers whose choline intake was well below the recommendation have lower academic outcomes by age seven.

"We know that the structural alteration is there, but it may not manifest in ways we can see until later in life. That's why it's important to think about this during gestation because the changes are occurring then," Mudd says.

Dilger adds, "We're not talking about an overt developmental disorder or saying if you don't eat eggs when you're pregnant, you cause a disorder. Instead, these are subtle pieces where we see individual variation and it could be related to your mother's diet during pregnancy."

More information: Austin T Mudd et al, Maternal Dietary Choline Status Influences Brain Grey and White Matter Development in Young Pigs1–3, *Current Developments in Nutrition* (2018). DOI: 10.1093/cdn/nzy015

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