Iron deficiency and cognitive development: New insights from piglets

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University of Illinois researchers have developed a model that uses neonatal piglets for studying infant brain development and its effect on learning and memory. To determine if the model is nutrient-sensitive, they have done some research on the effects of iron-deficient diets.

"Iron deficiency is a major problem worldwide," said Rodney Johnson, professor of animal sciences and director of the Division of Nutritional Sciences. "Infants who experience iron deficiency during the first 6 to 12 months of age can have irreversible developmental delays in cognition."

He said that, even in the United States, iron deficiency is a significant problem. "Babies born to obese mothers are at risk for iron deficiency," said Johnson. "Furthermore, the incidence of child obesity is increasing, and being overweight or obese is a risk factor for iron deficiency. Overweight toddlers are nearly three times more likely to suffer from iron deficiency than are those with a healthy weight."

Johnson and his collaborators took 2-day-old piglets and fed them one of three diets. The diet for the control group contained the recommended levels of iron, the second was mildly deficient, and the third was severely deficient.

The piglet brain grows to approximately half of its maximum volume in the first 4 weeks of life. It continues to grow rapidly for the next 8 weeks, which is very similar to the way that human infant brains grow in the postnatal period.

At 4 weeks, the researcher began testing the piglets in a T-shaped maze. In an acquisition phase, piglets were trained to locate a milk reward in a constant place in space as well as direction, using visual cues from outside the maze. Pigs on the control diet learned the task quite well.

"Piglets provided the diet severely deficient in iron just didn't learn the task," Johnson said. "It's a T-maze so they have a 50 percent chance of getting it right. Even after 6 days of training, they never performed above chance levels. The piglets given the mildly deficient diet showed intermediate performance, but their performance was not significantly different from that of piglets given the control diet."

In the second phase of the test, the reward location was reversed. The piglets were retested to assess reversal learning.

"We changed the rules so the piglets had to change their strategy," Johnson explained. "It's more demanding, cognitively speaking. The piglets fed an adequate diet learned this task very well. However, piglets fed a diet severely deficient in iron continued to perform poorly while those given a mildly deficient diet showed intermediate performance."

Johnson said that one of the strengths of this paper is that it shows that this test is sensitive to a nutrient in a dose-dependent fashion.

The researchers then examined iron levels in different parts of the brain. They found reduced iron levels in the hippocampus, a brain region that is important for spatial learning and memory, of pigs in both experimental groups.

Johnson said that this work highlights a new translational model for studying micronutrient deficiencies. Traditional rodent models are less suited for examining these kinds of questions because they cannot be weaned early and placed on experimental diets. Pigs, however, are a precocial species, which means that their motor and sensory skills are quite well developed at birth. This facilitates early weaning and behavioral testing.

Johnson has recently received a 5-year NIH grant to do further work with this model. "We are investigating the effects of maternal viral infection during pregnancy," he said. "At a critical period during pregnancy, gilts are inoculated with a virus that causes pneumonia. When the piglets are born, we study their brain and cognitive development."

More information: "Early Life Iron Deficiency Impairs Spatial Cognition in Neonatal Piglets" by Jennifer L. Rytych, *Journal of Nutrition*, 2012.

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