Pig brain models provide insights into human cognitive development

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A mutual curiosity about patterns of growth and development in pig brains has brought two University of Illinois research groups together. Animal scientists Rod Johnson and Ryan Dilger have developed a model of the pig brain that they plan to use to answer important questions about human brain development.

"It is important to characterize the normal brain growth trajectory from the neonatal period to sexual maturity," said Johnson.

"Until we know how the brain grows, we don't know what is going to change," added Dilger.

In cooperation with the Beckman Institute, they performed MRI scans on the brains of 16 piglets, starting at the age of 2 weeks, then at 4 weeks, and then at 4-week intervals up to 24 weeks.

"We have world-class people at the Beckman Institute who are pushing and developing the next generation of neuroimaging technology, so we're able to connect with them and take advantage of their expertise," said Johnson.

Matt Conrad, a student in Johnson's lab, used three-dimensional visualization software on over 200 images to manually segment each region on three planes. The software put the information together into a three-dimensional image of the pig brain. This is used to determine the volume of the different structures.

When the piglets were at Beckman for their imaging sessions, Dilger performed other tests, including diffusion tensor imaging (DTI), which shows how neural tracks develop, allowing the exploration of brain complexity and of how neurons form. It was also possible to measure neurochemicals, including creatine and acetylcholine, in the brain, which provides a unique insight into brain metabolism.

The end result of this work is what they call the deformable pig brain atlas.

"We are taking 16 pigs and averaging them, so it's more representative of all pigs," said Dilger. "You can then apply it to any individual pig to see how it's different."

"It's called a deformable brain atlas because the software takes information from an individual and deforms it until it fits the template, and then you know how much it had to be deformed to fit," Johnson explained. "So from that, you can tell whether a brain region is larger or smaller compared to the average."

Johnson and Dilger said that the goal is to develop a tool for pigs that is equivalent to what is available for the mouse brain and make it publicly available. But they don't want to stop with tool development.

"We want to use this to address important questions," Johnson said.

One research direction being pursued in Johnson's lab is to induce viral pneumonia in piglets at the point in the post-natal period when the brain is undergoing massive growth to see how it alters brain growth and development. They are also looking at effects of prenatal infections in the mother to see if that alters the trajectory of normal brain growth in the offspring. The risk for behavioral disorders and reduced stress resilience is increased by pre- and post-natal infection, but the developmental origins are poorly understood.

Dilger's group is interested in the effects of early-life nutrition on the brain. They are looking at the effects of specific fatty acids as primary structural components of the human brain and cerebral cortex, and at choline, a nutrient that is important for DNA production and normal functioning of neurons.

"Choline deficiency has been tied to cognitive deficits in the mouse and human, and we're developing a pig model to study the direct effects choline deficiency has on brain structure and function," Dilger said. "Many women of child-bearing age may not be receiving enough choline in their diets, and recent evidence suggests this may ultimately affect learning and memory ability in their children. Luckily, choline can be found in common foods, especially eggs and meat products, including bacon."

More information: More information about the model is available in "Brain growth of the domestic pig (Sus scrofa) from 2 to 24 weeks of age: a longitudinal MRI study," by M.S Conrad, R.N. Dilger, and R.W. Johnson, which was recently published in *Developmental Neuroscience*. It is available online at www.ncbi.nlm.nih.gov/pubmed/22777003.

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