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Piglet brain atlas new tool in understanding human infant brain development

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A new online tool developed by researchers at the University of Illinois will further aid studies into postnatal brain growth in human infants based on the similarities seen in the development of the piglet brain, said Rod Johnson, a U of I professor of animal sciences.

Through a cooperative effort between researchers in animal sciences, bioengineering, and U of I's Beckman Institute, Johnson and colleagues Ryan Dilger and Brad Sutton have developed a magnetic resonance imaging (MRI) based brain atlas for the four-week old piglet that offers a three-dimensional averaged brain and anatomical regions of interest.

This averaged brain atlas, created from images from multiple piglets, will serve as a template for future studies using advanced MRI techniques that can provide important information on brain macro- and microstructure during this critical period of development. The template, as well as tissue probability maps that were also created, are available online and are freely distributed.

"The piglet brain is similar to the human brain in that it is gyrencephalic and experiences massive growth and development in the late prenatal and early postnatal periods. We are concerned that environmental insults such as infection or poor nutrition during these early periods may alter the trajectory of brain development," Johnson said.

"Pigs provide an excellent translational model for biomedical research. This is a new tool that may be useful to others in the biomedical

community," he added.

While an atlas did already exist for the adult pig, Matthew Conrad, a doctoral student in Johnson's lab said the previous atlas was created from a single adult animal. "The benefit to using an averaged brain is that it will produce a template that is a better representation of the population. The more animals included the better."

The atlas was created by taking MRI images of the brains of 15 four-week-old York breed piglets—nine females and six males. The images were then reconstructed into 3D volumes for each pig. Through a series of deformations and averaging of the data sets, the images were eventually aligned to create the final averaged brain.

Conrad explained that having an averaged brain template available will allow better use of the software needed for more advanced techniques in studying the volume of brain regions.

An example of these techniques includes voxel-based morphometry (VBM), which can be used to detect volume difference in the brain. Additionally, diffusion tensor imaging (DTI), which looks at white-matter track development and connectivity in brain regions, and magnetic resonance spectroscopy (MRS), which looks at white matter and neurochemical changes in the brain, are being conducted.

"The atlas will be used as the population average. When new data sets are brought in, you first line up the new brain images to this template," Conrad said.

In addition to the average brain atlas, Conrad said they also created population averages for white and gray matter as well as cerebrospinal fluid (CSF). "This is another data set that helps predict the tissue classification," he said.

Previous studies using MRI imaging of piglets have looked at the effects of iron deficiency on brain development. "For that we did MRI imaging and manual segmentation, and with manual segmentation you are looking at volume changes within very large areas of the brain, but with VBM we can pinpoint smaller changes within discrete brain areas," Conrad said. "We are now reanalyzing data from those piglets and replicating this study with new protocols, which will allow us to see changes that we didn't see before."

Another study is looking at the effects of postnatal infections, such as pneumonia, on brain development. "These types of infections are common in infants, and again it's a period of time when the brain is undergoing rapid development," Johnson said.

A third study funded by the National Institutes of Health is focused on maternal viral infection during pregnancy. "The goal is to assess how mom's immune response to infection influences brain development and future behavior of her piglets," Johnson explained.

Conrad added that the piglet brain is now being recognized for its potential as a translational animal model for neurodevelopmental studies.

"Much of the research on the effects of pre- and postnatal factors on brain development has been done in rodent models, but the rodent brain develops very differently. Therefore, the piglet can provide a complementary model wherein results better translate to humans," Johnson said.

More information: An in vivo three-dimensional magnetic resonance imaging-based averaged brain collection of the neonatal piglet (Sus scrofa), *PLOS ONE*, DOI: 10.1371/journal.pone.0107650