



CHDD Outlook 2012 Issue #7

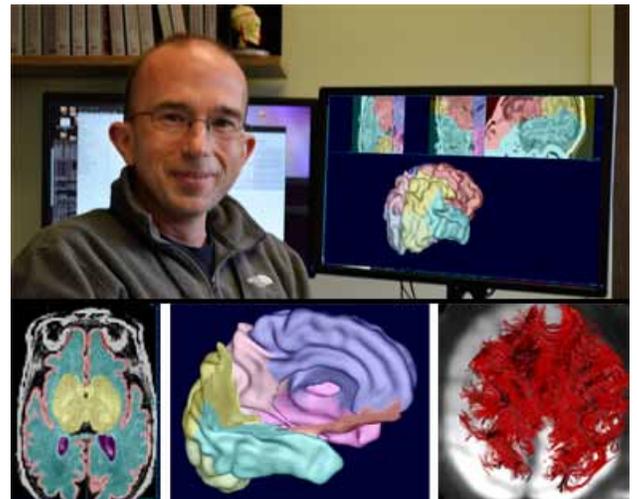
News from the Center on Human Development and Disability at the University of Washington
 Health Sciences Center

CHDD | IDDRC | UCEDD

Picture This: Researchers Try to Build an Atlas of How Human Brain Develops In Utero

by Joel Schwarz

Nearly a century after cosmologists and physicists devised the big bang theory to explain the expansion of the universe, some of their scientific descendants are busy with a more confined but perhaps equally daunting task: trying to create a three-dimensional and four-dimensional map of how the human brain develops before birth. By first understanding and characterizing this period of rapid brain growth, researchers hope to be able to use this knowledge to better detect, understand and perhaps treat developmental and related disabilities at the very earliest stages of growth. This work, driven by the development of improved in utero magnetic resonance imaging (MRI) and new computational techniques to study developing anatomy, is being carried out at the Biomedical Image Computing Group at UW led by Colin Studholme, PhD, a University of Washington professor of pediatrics and bioengineering, and adjunct professor of radiology. He is the principal investigator of an NIH funded project that has for the first time mapped in 4D when and where the furrows, or sulci, in the cerebral cortex are formed in utero in the healthy fetal brain.



Colin Studholme is leading a group that is constructing an atlas of human brain development in utero. The lower images illustrate components of the atlas showing tissue boundaries and connectivity.

Studholme, who is also a Center on Human Development and Disability research affiliate, calls the use of MRI to study the fetal brain “the big bang” of brain mapping, a field that began with the study of the adult brain. “In cosmology being able to measure and model the rapid changes that happened in the big bang is crucial in understanding the large scale structure of the universe we see today. In the same way, studying the earliest stages of brain formation when tissues are expanding rapidly to form the basic organization of the adult brain helps us understand how the brains of children and adults are organized and how this organization may vary and be perturbed by conditions during the early stages of development. Our research seeks to link basic developmental neuroscience at a cellular level with resulting organization of large scale anatomy, to examine how a brain is built from the ground up,” he said. Our task is complicated by the fact that it is much easier to scan the brain of an adult or even a child than it is to get sharp images of the smaller moving fetal brain. There are several reasons for this. “With an adult and some children you can tell them to stay still allowing you to capture a full 3D image in one scan. You can’t do that with a fetus,” Studholme explained. “The structure of the fetal brain is also entirely different from that of an adult or child who have gray matter layers on the outside of the brain and white matter connections on the inside. With a fetus you have many different tissue zones that are changing dynamically during only a few weeks, and those zones may actually require the use of different types of MR imaging to study different gestational ages.

“In our work we are trying to describe the average fetal brain and normal variations around it at any given age of development, to build a true 4D statistical map of growth. Such a map opens up the possibility of learning what might influence the brain during pregnancy. For example, by studying a range of different fetuses we might be able to examine what the effects of maternal diet or maternal stress are on specific brain regions,” he said.

One area that Studholme is particularly interested in is the folding patterns, those distinctive convoluted furrows in the human cerebral cortex. “Folding patterns are like fingerprints and are unique. While there is a genetic component to folding, and identical twins share many common features in their folding patterns, they are not a perfect match,” he said. In a recently published paper, Studholme and colleagues in California and France reported on the early development of this folding in healthy fetuses over the period of 20 to 28 weeks after conception. “Studying brain folding is difficult. Typically, it has been done with post-mortem data or from single slice images captured through the living fetal brain. In our group we use computer vision methods to build true 3D MR images of the healthy fetal brain. The time period we looked at is when the brain starts off basically smooth with only a few folds, where individuals are still very similar. Then, the number of folds quickly increases and the brain shape becomes more individualized approaching that of the child or adult. This is a time when a great number of new cells are being created in the brain, and these migrate outward to regions where the outer layers of the brain are expanding in area more rapidly. These folds importantly correspond to much of the underlying functional organization of the cortex in the adult brain,” said Studholme.

In some countries MRI is used for clinical imaging of fetuses where there are known problems, using sedation to reduce motion. This approach however cannot be used to study healthy fetuses in order to provide a normative reference for evaluating developmental abnormalities. In Studholme’s work, his group has focused on techniques that can be used without sedation that allow images to be corrected for fetal movements after they have been acquired. By combining faster slice based imaging techniques with advances in computational techniques, Studholme can capture many snapshots of parts of the moving fetal brain within the maternal anatomy and put these pieces back together after the scan has finished, separating maternal anatomy from that of the moving fetal brain.

This research has also provided the earliest look at asymmetry in the brain, and shows when it emerges and how it changes over time. These asymmetries may be related to future functional specialization in different brain regions, he believes. “For example, language areas correspond to regions of known asymmetry so understanding why and when they form early is important. Their correct and timely development in utero may be fundamental in determining language abilities later in life.” Another avenue explored in Studholme’s work looks at the ventricles deep inside the brain (structures that contain cerebrospinal fluid) to see if they have become enlarged. This causes a condition called ventriculomegaly that is the most commonly diagnosed fetal brain abnormality in utero. In mild cases, there is a strong chance of a normal outcome, but depending on the severity of the enlargement, it has been related to learning disabilities in later life. Studholme and his colleagues are searching for a better biomarker for these cases of ventriculomegaly that radiologists can use to diagnose the condition in utero.

An important second application of this work is using these new in utero derived brain maps to better understand and detect injuries in the brains of very premature babies of similar age. Working with collaborators in Vancouver, British Columbia, Studholme is examining white matter brain injuries and blood clots in premature babies to discover when and where those types of injuries may be critical to brain function. “The focus of this work is on whether we can develop biomarkers that will tell us how drugs that may be used in treating premature babies can prevent longer term brain injury,” he said. This work involves 175 premature babies and Studholme said follow-up testing and MRI scans will be vital so that a growth atlas of the brain that relates early brain injury to later developmental problems can be built for this population.

CHDD is an interdisciplinary center dedicated to the prevention and amelioration of developmental disabilities through research, training, clinical service, and community outreach. CHDD includes the University Center of Excellence in Developmental Disabilities and the Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center.

CHDD Outlook

Center on Human Development and Disability, University of Washington, Box 357920, Seattle, Washington 98195-7920

© 2012 Center on Human Development and Disability, University of Washington