The human brain undergoes a remarkable transition *in utero*, but until recently scientists have had few tools to study how this process unfolds.

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Pioneering study images activity in fetal brains

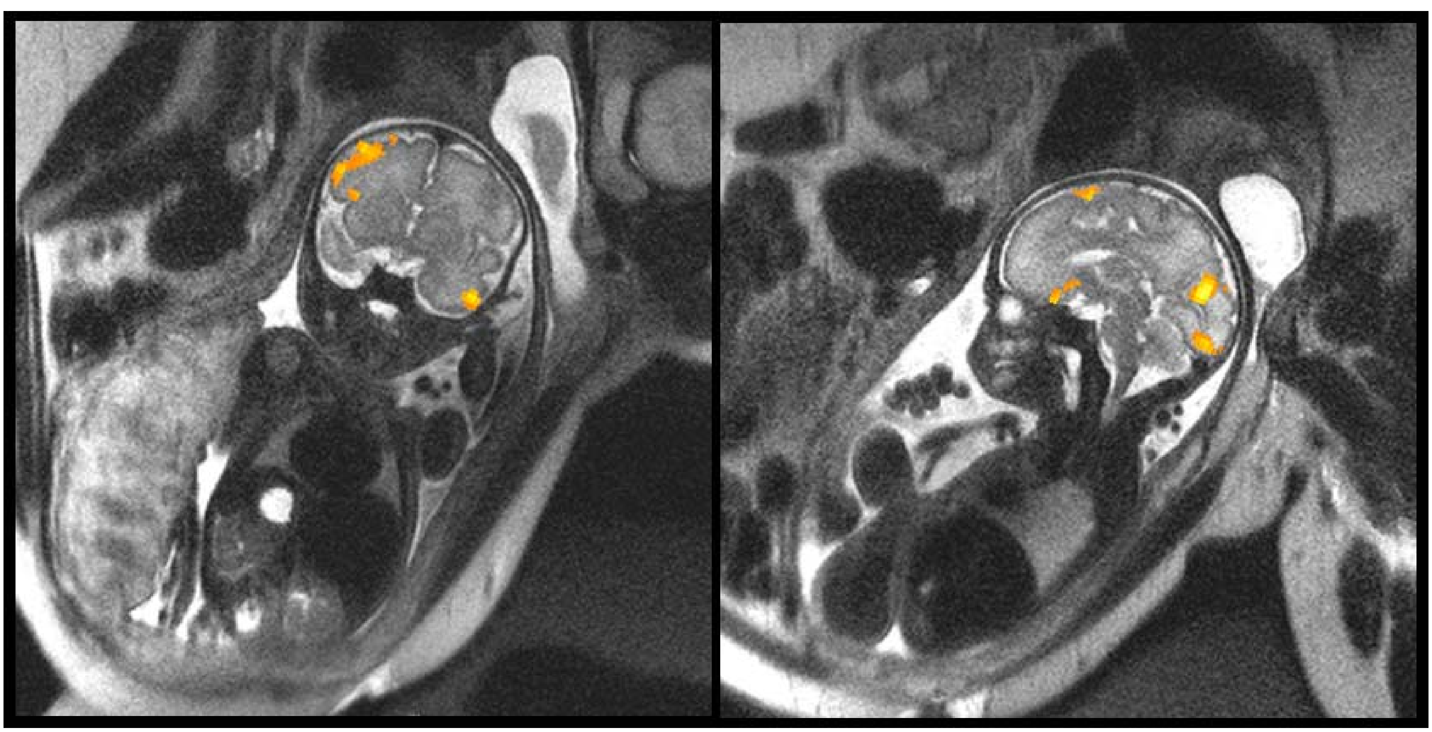
By Greg Miller | Jan. 9, 2017 , 5:00 AM

Babies born prematurely are prone to problems later in life—they're more likely to develop autism or attention deficit hyperactivity disorder, and more likely to struggle in school. A new study that's among the first to investigate brain activity in human fetuses suggests that the underlying neurological issues may begin in the womb. The findings provide the first direct evidence of altered brain function in fetuses that go on to be born prematurely, and they might ultimately point to ways to remediate or even prevent such early injuries.

In the new study, published 9 January in *Scientific Reports*, developmental neuroscientist Moriah Thomason of Wayne State University School of Medicine in Detroit, Michigan, and colleagues report a difference in how certain brain regions communicate with each other in fetuses that were later born prematurely compared with fetuses that were carried to term. Although the findings are preliminary because the study was small, Thomason and other researchers say the work illustrates the potential (and the challenges) of the emerging field of fetal neuroimaging. “Harnessing the power of these advanced tools is offering us for the very first time the opportunity to explore the onset of neurologic insults that are happening in utero,” says Catherine Limperopoulos, a pediatric neuroscientist at Children’s National Medical Center in Washington, D.C.

Thomason and colleagues **used functional magnetic resonance imaging (fMRI) to investigate brain activity in 32 fetuses**. The pregnant mothers were participants in a larger, long-term study of brain development led by Thomason. “The majority have just normal pregnancies, but they’re drawn from a low-resource population that’s at greater risk of early delivery and developmental problems,” she says. In the end, 14 of the fetuses were born prematurely.

The team’s approach relied on methods developed in the past decade or so to study “functional connectivity” in the adult human brain—essentially using fMRI to determine which brain regions have synchronized activity when the subject is not engaged in any particular task. Synchronized activity between brain regions, the thinking goes, shows that those regions are well connected and sharing information.



Colored regions in these MRI images of a human fetus (shown from two perspectives) indicate brain regions where connectivity grows stronger between the 20th and 40th weeks of gestation.

Data courtesy of Moriah E. Thomason, Wayne State University School of Medicine

One feature stood out in the brains of the fetuses that were ultimately born prematurely: A small patch on the left side of the brain, in an area that develops into a language processing center, had weaker connectivity with other brain regions than it did in fetuses carried to full term. “That they can detect this difference in connectivity so early is something interesting,” says Hao Huang, who studies neonatal brain development at the University of Pennsylvania. “Usually with earlier detection you have better chances for intervention.” Language problems are common in children born prematurely, and Thomason plans to track these children as they develop.

Previous studies by Huang and others have reported altered connectivity in the brains of premature infants, but only after birth, leaving open the possibility that stress, oxygen deprivation, or other injury during delivery is to blame. But Thomason and her colleagues not only found that the impairment starts earlier; they also found a hint of a cause. The mothers who delivered prematurely had more inflammation in their placental tissue, which leads Thomason to suspect that maternal infection or inflammation might play a role.

This type of study would have been impossible only a short time ago. One of the biggest problems in fetal neuroimaging is that a fetus is a moving target, bobbing around inside the amniotic sac. “A fetus has so many degrees of freedom,” says Veronika Schöpf, a mathematician at the University of Graz in Austria who is developing computational tools for fetal neuroimaging. That’s a problem because an MRI scan is like a stack of pancakes—thin slices piled neatly on top of one another. Any movement throws the slices out of register. But Schöpf says better algorithms are helping scientists stitch together slices thrown off by the subject’s movement. At the same time, MRI machines have gotten faster, making it possible to collect more slices in a shorter time. That’s a big deal, Thomason says, because it means getting more data during periods when a fetus is staying still.

The fetal brain is a moving target in another sense, too. Its anatomy is in constant flux as it matures, which means researchers need templates and atlases for different developmental time points to be able to make comparisons across subjects. Several research groups around the world are currently developing these resources.

The ability to image the fetal brain at work opens up questions in basic science, too, Huang says. In the course of a pregnancy, the human brain transforms from a simple fluid-filled tube into a complex organ ready to perceive and interact with the outside world. How this process unfolds is largely a mystery, and Huang is eager to probe such questions as how and when the networks found in the mature brain develop and become active for the first time. At last, he says, “The techniques are catching up” to the questions.

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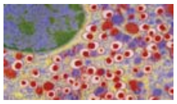

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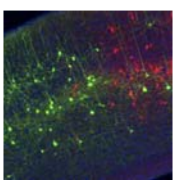

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