Prenatal stress changes brain connectivity in-utero
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Boston - The time babies spend in the womb is far from idle. The brain is changing more rapidly during this time than at any other time in development. It is an active time for the fetus to grow and explore, and of course connect to its mother. And new evidence from in-utero fetal brain scans shows, for the first time, that this connection directly affects brain development: A mother's stress during pregnancy changes neural connectivity in the brain of her unborn child.

"It has long been thought that the stress of a mother during her pregnancy may imprint on the brain of her developing child," says Moriah Thomason of Wayne State University who is presenting this new work at the 25th meeting for the Cognitive Neuroscience Society in Boston today. "Despite the clear importance of this time frame, we presently possess very little understanding of how functional macroscale neural networks build during this precious time in human life, or the relevance of this to future human health and development."

This prenatal work is part of a growing body of research to better understand how the human brain develops across its lifespan, from fetus to old age. "We are interested in how a human brain constructs over time to become the adult brain," says Nim Tottenham of Columbia University, whose work focuses on identifying sensitive periods of brain development from childhood into adolescence. She is chairing a session on new findings in brain development at the CNS meeting: "The talks aim to bridge across the very long brain development that gives rise to mature functioning."

**Seeing the changing fetal brain**

Research in newborns and older children to understand prenatal influences has been confounded by the postnatal environment, Thomason explains. But recent advancements in fetal imaging allowed her and her team to gain insight into a critical time period in brain development never previously accessible.

Using fetal resting-state fMRI, they examined functional connectivity in 47 human fetuses scanned between the 30th and 37th week of gestation. The researchers recruited the participating mothers from a low-resource and high-stress urban setting, with many reporting high-levels of depression, anxiety, worry, and stress.

They found that mothers reporting high stress had fetuses with a reduced efficiency in how their neural functional systems are organized. It is the first time, imaging has shown a direct influence of maternal stress on fetal brain development, independent of influences of the postnatal environment.

"The major thrill is that we have demonstrated what has long been theorized, but not yet observed in a human, which is that the stress of a mother during her pregnancy is reflected in connectional properties of her child's developing brain," Thomason says. The data suggest that the brain does not develop in a sequence from simplest systems (e.g., vision, motor) to more complex high-order systems, but perhaps instead first develops the areas that will be most critical in bridging across systems.

The researchers found that the cerebellum played a central role in the observed effects, suggesting it may be especially vulnerable to the effects of prenatal or early life stress. The cerebellum has the highest density of glucocorticoid receptors, which are involved in stress responses, than any other place in the brain. Thomason and her team plan to further investigate this as a possible mechanism for the stress responses they observed.

Although conducting in-utero brain scans are challenging - first and foremost because of the always wriggling babies - working with expectant mothers is quite rewarding, Thomason says. "A lot
of our moms are interested in being part of this research, not because of concerns they have in their pregnancy," she says, "but because they appreciate the heightened vulnerability of budding human life, and this is an opportunity to help other women that may not have the same fortune in their circumstances."

Making connections into adulthood

Cognitive neuroscientists are especially interested in understanding sensitive periods of time when the environment has the largest influence on future brain functions. To identify such times, Tottenham of Columbia University has honed in on connections between the prefrontal cortex (PFC) and the amygdala.

"A majority of developmental change during childhood and adolescence are the changes in connections," she explains. "We have largely focused on the connections between the amygdala and prefrontal cortex because of the very large changes we have observed there across childhood and adolescence and their central role in emotional behaviors."

Studying awake children as young as 4-years old, Tottenham and colleagues identified developmental periods when the nature of the communication between the amygdala and the PFC operates differently than in an adult. The connections develop very slowly over childhood, with a dramatic shift toward the end of childhood when the transition to adolescence brings about more adult-like characteristics. Looking at coincidental environmental events in childhood, the researchers also found data to suggest that amygdala-medial PFC connections are highly impressionable to external forces.

"The human brain is designed to learn from the environment. This is thanks to the long period of infancy, childhood, and adolescence that humans enjoy," Tottenham says. "What has amazed me most about the developing brain is that it is not simply an immature version of the adult brain but instead is designed to collaborate with the expected caregiving ecology."

Indeed, says Thomason: "We must consider the developing brain in context, thinking about the role of the environment in shaping the brain. It is a topic that inspires us to promote healthy brain growth, to ask what it is that we do for children in the lifestyles, opportunities, and learning conditions we create for them."

More information: Thomason and Tottenham will be presenting in the symposium "Developmental Cognitive Neuroscience: Brain Construction from the Fetus through Old Age at the CNS annual meeting in Boston. More than 1,500 scientists are attending the meeting from March 24-27, 2018. http://www.cogneurosociety.org … symposium_sessions#7

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