New study links placental oxygen levels to fetal brain development

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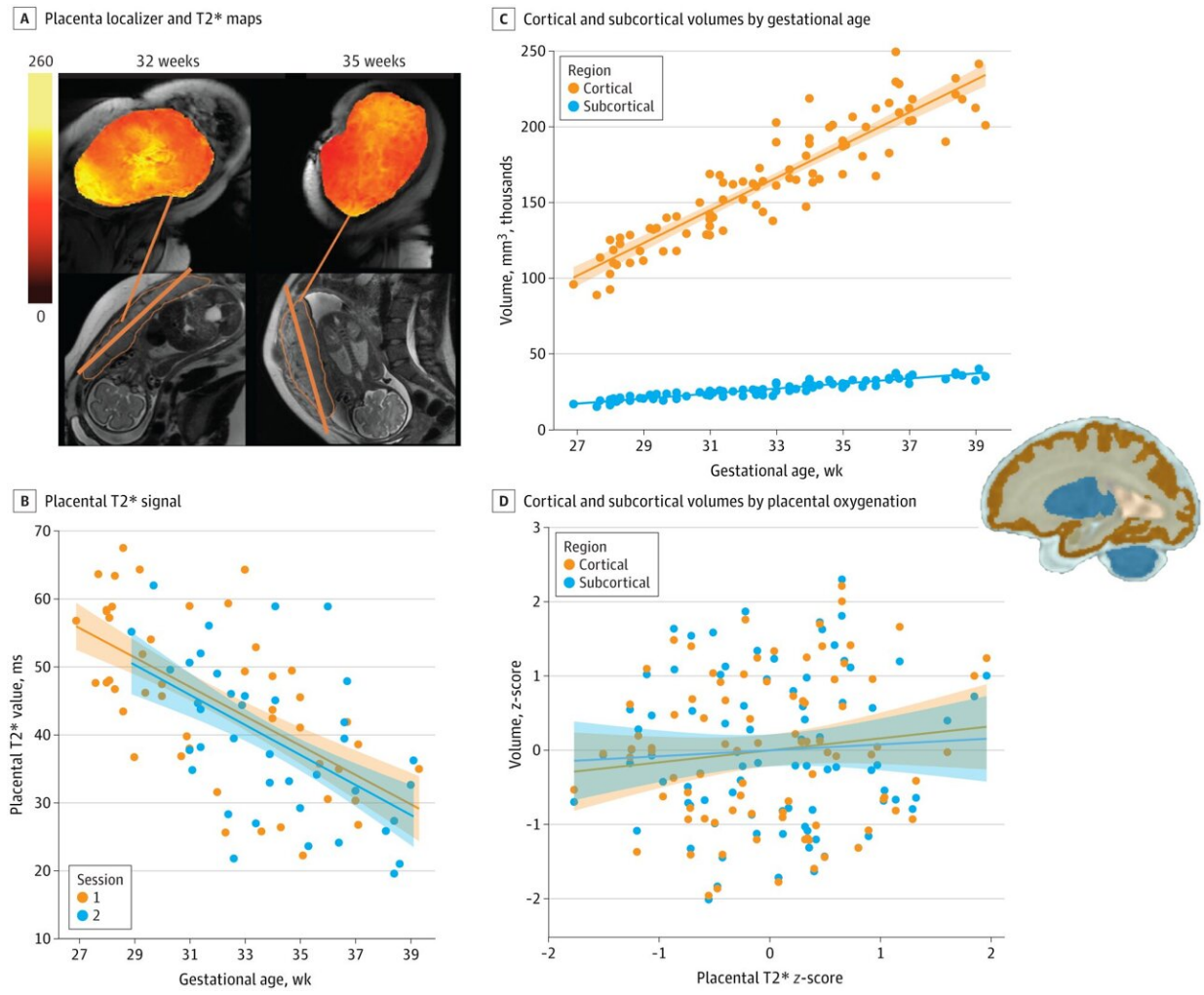

Placental T2* Values and Cortical and Subcortical Volumes A, Placenta localizer and T2* maps in a representative participant at 32 (time point 1, a) and 35 weeks (time point 2, b) of gestation. B, Placental T2* signal (time point 1 [n = 49]; time point 2 [n = 38]) in relation to gestational age in weeks at time point 1 (orange)

and 2 (blue). C. Cortical and subcortical volumes in relation to gestational age in weeks. D. Cortical and subcortical volumes by placental oxygenation (T2*). Both volumes and T2* values have been z-scored. Shaded regions indicate 95% CIs and are based on the mean. Credit: *JAMA Network Open* (2024). doi:10.1001/jamanetworkopen.2024.0456

A new study shows oxygenation levels in the placenta, formed during the last three months of fetal development, are an important predictor of cortical growth (development of the outermost layer of the brain or cerebral cortex) and is likely a predictor of childhood cognition and behavior.

"Many factors can disrupt healthy brain development in utero, and this study demonstrates the placenta is a crucial mediator between maternal health and fetal brain health," said Emma Duerden, Canada Research Chair in Neuroscience & Learning Disorders at Western University, Lawson Health Research Institute scientist and senior author of the study.

The connection between placental health and childhood cognition was demonstrated in previous research using ultrasound, but for this study, Duerden, research scientist Emily Nichols and an interdisciplinary team of Western and Lawson researchers used magnetic resonance imaging (MRI), a far superior and more holistic imaging technique. This novel approach to imaging placental growth allows researchers to study neurodevelopmental disorders very early on in life, which could lead to the development of therapies and treatments.

"While ultrasound provides some measure of placental function, it is imprecise and prone to error, so MRI is just a bit more specific and precise," said Nichols, lead author of the study. "You wouldn't use MRI

necessarily to diagnose placental growth restriction, you would use ultrasound, but MRI gives us a much better way to understand the mechanisms of the placenta and how placental function is affecting the fetal brain."

The study, published in *JAMA Network Open*, was led by Duerden and Nichols and co-authored by researchers from the Faculty of Education, Schulich School of Medicine & Dentistry, Western Engineering and Lawson Health Research Institute.

The placenta, an organ that develops in the uterus during pregnancy, is the main conduit for oxygenation and nutrients to a fetus and a vital endocrine organ during pregnancy.

"Anything a fetus needs to grow and thrive is mostly delivered through the placenta, so if there is anything wrong with the placenta, the fetus might not be receiving the nutrients or the levels of oxygenation it needs to thrive," said Nichols.

Poor nutrition, smoking, cocaine use, chronic hypertension, anemia, and diabetes may result in fetal growth restriction and may cause problems in the development of the placenta. Fetal growth restriction is relatively common and happens in about six percent of all pregnancies and globally impacts 30 million pregnancies each year.

"There can be many issues related to the healthy development of the placenta," said Duerden. "If it does not develop properly, the fetal brain may not get enough oxygen and nutrients, which may affect childhood cognition and behavior."

Impact, affect, and change

The study revealed that a healthy placenta in the third trimester

particularly impacts the cortex and the prefrontal cortex, regions of the child's brain that are important for learning and memory.

"An unhealthy placenta can place babies at risk for later life learning difficulties, or even something more serious, like a neurodevelopmental disorder," said Duerden. "This research can open a lot of doors as we still don't really understand everything there is to know about the placenta. We are just scratching the surface."

The study is also an important first step in biomarking the impact of oxygenation levels in the placenta and considering changes for expectant mothers to deal with less-than-ideal placental conditions.

While oxygenation in the placenta in the third trimester predicts fetal cortical growth (development of the outermost layer of the brain—the cerebral cortex), results of the study indicate it may not affect subcortical maturation or the deep gray and white matter structures of the brain.

Subcortical structures in the brain, responsible for children's temperament or motor functions, such as the amygdala and basal ganglia, may be more vulnerable to factors affecting the placenta in the second trimester.

"We now have a better understanding of how the placenta affects the cortex. With this basic knowledge, we now have an idea of how these two things are related and we can identify or benchmark healthy levels that lead to brain cortical growth," said Nichols. "The subcortical regions of the brain appear to be unaffected by placental growth, at least in the healthy samples from our study."

Duerden, Nichols, and the team scanned pregnant women twice (during their third trimester) for the study at Western's Translational Imaging

Research Facility.

"This is one of the few datasets in the world where there are two scans collected in utero during the third trimester. There are not many groups in the world doing fetal MRI, so it is a super-rich data set that allows us to look at growth over time," said Duerden. "Western is probably one of the few places where we can do the research because we have the expertise and the facilities to do it."

More information: Emily S. Nichols et al, T2* Mapping of Placental Oxygenation to Estimate Fetal Cortical and Subcortical Maturation, *JAMA Network Open* (2024). DOI: 10.1001/jamanetworkopen.2024.0456 jamanetwork.com/journals/jaman… /fullarticle/2815476

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