

Placental function linked to brain injuries associated with autism

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Anna Penn, M.D., Ph.D., a neonatologist in the divisions of Neonatology and Fetal Medicine, and a developmental neuroscientist at Children's National
Credit: Children's National

Allopregnanolone (ALLO), a hormone made by the placenta late in

pregnancy, is such a potent neurosteroid that disrupting its steady supply to the developing fetus can leave it vulnerable to brain injuries associated with autism spectrum disorder (ASD), according to Children's research presented during the Pediatric Academic Societies 2019 Annual Meeting.

In order to more effectively treat vulnerable babies, the Children's research team first had to tease out what goes wrong in the careful choreography that is pregnancy. According to the Centers for Disease Control and Prevention, about 1 in 10 babies is born preterm, before 37 weeks of gestation. Premature birth is a major risk factor for ASD.

The placenta is an essential and understudied organ that is shared by the developing fetus and the pregnant mother, delivering oxygen, glucose and nutrients and ferrying out waste products. The placenta also delivers ALLO, a progesterone derivative, needed to ready the developing [fetal brain](#) for life outside the womb.

ALLO ramps up late in gestation. When babies are born prematurely, their supply of ALLO stops abruptly. That occurs at the same time the cerebellum—a brain region essential for motor coordination, posture, balance and [social cognition](#)- typically undergoes a dramatic growth spurt.

"Our experimental model demonstrates that losing placental ALLO alters cerebellar development, including white matter development," says Anna Penn, M.D., Ph.D., a neonatologist in the divisions of Neonatology and Fetal Medicine, and a developmental neuroscientist at Children's National. "Cerebellar white matter development occurs primarily after babies are born, so connecting a change in placental function during pregnancy with lingering impacts on later brain development is a particularly striking result."

The research team created a novel [experimental model](#) in which the gene encoding the enzyme responsible for producing ALLO is deleted in the placenta. They compared these preclinical models with a [control group](#) and performed whole brain imaging and RNAseq gene expression analyses for both groups.

"We saw long-term cerebellar white matter alterations in male experimental models, and behavioral testing revealed social impairments and increased repetitive behaviors, two hallmark features of ASD," says Claire-Marie Vacher, Ph.D., lead study author. "These male-specific outcomes parallel the increased risk of brain injury and ASD we see in human babies born prematurely."

ALLO binds to specific GABA receptors, which control most inhibitory signaling in the nervous system.

"Our findings provide a new way to frame poor placental function: Subtle but significant changes in utero may set in motion neurodevelopmental disorders that children experience later in life," adds Dr. Penn, the study's senior author. "Future directions for our research could include identifying new targets in the placenta or [brain](#) that could be amenable to hormone supplementation, opening the potential for earlier treatment for high-risk fetuses."

More information: Pediatric Academic Societies 2019 Annual Meeting presentation: "Placental allopregnanolone loss alters postnatal cerebellar development and function."

Provided by Children's National Medical Center

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