

How immune response in pregnancy may lead to brain dysfunction in offspring

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A pregnant woman's immune response to viral infections may induce subtle neurological changes in the unborn child that can lead to an increased risk for neurodevelopmental disorders including schizophrenia and autism. Research published in the online journal *mBio* provides new insights into how this may happen and suggests potential strategies for reducing this risk.

"Infection during pregnancy is associated with increased risk of damage to the developing nervous system. Given that many agents have been implicated, we decided to focus on mechanisms by which the maternal <u>immune response</u>, rather than direct infection of the fetus, might contribute to behavioral disturbances in the offspring of mothers who suffer infection during pregnancy," says W. Ian Lipkin of Columbia University, senior author on the study.

To better understand how the immune response causes these neurological changes, the researchers exposed pregnant mice to a synthetic molecular mimic of a replicating virus. Offspring of the exposed mice had impaired locomotor activity compared to controls. Further testing determined that the exposure inhibited embryonic neuronal stem <u>cell replication</u>, affecting brain development.

They also looked at the potential role of an immune protein known as Toll-like receptor 3 (TLR3) which is commonly activated in <u>viral</u> <u>infections</u>. Using TLR3-deficient mice they determined that the effects of exposure were dependent on TLR3. They also investigated whether



the drug carprofen, a non-steroidal anti-inflammatory drug, would have any effect. Pretreatment with the drug abrogated the effects of exposure.

"Our findings provide insights into mechanisms by which maternal infection may induce subtle changes in brain and behavior and suggest strategies for reducing the risk of neuropsychiatric diseases following exposures to infectious agents and other triggers of innate immunity during gestation," says Lipkin.

More information: mbio.asm.org/

Provided by American Society for Microbiology

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