NEWS

Serotonin may mediate effects of infection in the womb

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Infection during pregnancy blunts development of the fetal brain by boosting levels of the chemical messenger serotonin, a new study suggests[1].

A wealth of data tie infection in a pregnant woman to a slightly **increased risk of autism** in her child. Prenatal exposure to inflammation is known to **disrupt brain development** and **produce autism-like behaviors** in mice.

But how inflammation in the womb leads to these effects is unclear, says lead researcher **Alexandre Bonnin**, assistant professor of cell and neurobiology at the University of Southern California in Los Angeles. His study shows that inflammation in the womb not only boosts serotonin production in the placenta but halts the growth of fetal neurons that produce the chemical messenger.

The findings, published 1 June in the *Journal of Neuroscience,* hint at a role for serotonin in the observed autism risk.

“[Serotonin] is a potentially very important mediator of the effects of maternal immune activation on the developing brain,” says **Sarah Canetta**, assistant professor of clinical neurobiology at Columbia University, who was not involved in the work.

Serotonin swell:

Bonnin and his colleagues injected pregnant mice with a substance that mimics a mild flu infection. The timing of the injection corresponds to the end of the first trimester of a human pregnancy, when neuron production peaks and the placenta is fully developed.

After 24 hours, the placentas of the mice have higher levels of tryptophan, a precursor to serotonin, than do those of pregnant mice injected with saline. And at 48 hours, an enzyme that converts tryptophan to serotonin is more active in the placentas of the mock-infected mice than in those of the controls.

By 48 hours, the fetuses exposed to inflammation in the womb also have higher concentrations of serotonin and fewer neurons that produce the **neurotransmitter** in their forebrains than controls do. Giving the pregnant mice a drug that blocks serotonin production prevents these effects on the fetal brain.

The findings suggest that inflammation in the mother causes the placenta to produce excess serotonin and deliver it to the fetal brain. Serotonin neurons stop growing to compensate, Bonnin says.

“If you have too little or too much serotonin, in both cases, there are pretty bad consequences,” he says.

These findings jibe with results suggesting that taking antidepressants called **selective serotonin reuptake inhibitors during pregnancy** may increase autism risk in the child, Canetta says. “It’s always intriguing when you see different risk factors that are coming from different pathophysiological places converge at similar common endpoints.”

Scratching the surface:

Other studies have suggested that infection has a direct effect on the fetal brain through the inflammatory molecule IL-6. Researchers have found **IL-6 to be elevated in the brains** of the pups of pregnant rats with activated immune systems, leading to social deficits.

The new study revealed elevated IL-6 in the blood of pregnant mice that received the mock infection, but not in their placentas or the pups’ brains — a finding consistent with an indirect link through serotonin.

Bonnin plans to test some of the pups exposed to inflammation for behaviors that mirror those seen in autism and schizophrenia, which is also **tied to maternal infection**. He is also investigating whether infectious diseases seen outside the lab, **including the Zika virus**, trigger a similar serotonin surge.

“This is scratching the surface of all that you could explore once you really start to think that you have a handle on a potential mechanism,” Canetta says.

REFERENCES:

1. Goeden N. *et al. J. Neurosci.* **36**, 6041-6049 (2016) **PubMed**