Examining how hormonal birth control may affect the adolescent brain

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Reproductive health experts consider hormonal contraceptives good choices for adolescents because they're safe and highly effective at

preventing pregnancy, but one aspect of their effect on the teenage body remains a mystery—whether and how they modify the developing brain.

New research in young rats links the synthetic hormones found in birth control pills, patches and injections with disordered signal transmission between cells in the prefrontal cortex, an area of the brain that continues to develop throughout adolescence. Compared to control rats, the animals receiving hormonal contraceptives also produced higher levels of the stress hormone corticosterone, which is similar to cortisol in humans.

The Ohio State University scientists launched this line of study in the prefrontal cortex, a region where mood is regulated, because some previous research has associated early adolescent use of hormonal contraceptives with risk for depression in adulthood. But what's most important, the researchers said, is learning how birth control affects the developing brain so individuals can weigh the risks and benefits of their reproductive health choices.

"Birth control has had a major positive impact for women's health and autonomy—so it's not that we're suggesting adolescents should not take hormonal contraceptives," said senior study author Benedetta Leuner, associate professor of psychology at Ohio State.

"What we need is to be informed about what synthetic hormones are doing in the brain so we can make informed decisions—and if there are any risks, then that's something that needs to be monitored. Then if you decide to use hormonal birth control, you would pay more attention to warning signs if you knew of any possible mood-related side effects."

The research poster was presented at Neuroscience 2022, the annual meeting of the Society for Neuroscience.

An estimated 2 in 5 teenage girls in the United States have sexual intercourse between age 15 and 19, and the vast majority use a contraceptive—condoms in particular. Of those using birth control, almost 5% use hormonal contraceptives, also known as long-acting reversible contraceptives. These products are also prescribed to treat acne and heavy periods.

Despite their popularity, "there isn't a lot known about how hormonal birth control influences the teen brain and behavior," said co-author Kathryn Lenz, associate professor of psychology at Ohio State. "Adolescence is a crucially under-investigated period of dramatic brain change and dramatic hormonal change that we really haven't understood."

The researchers gave a combination of synthetic estrogen and progesterone typically found in hormonal contraceptives to female rats for three weeks beginning about a month after they were born, an age equivalent to early adolescence in humans. Researchers confirmed the drugs disrupted the animals' reproductive cycling—these birth control products work by stopping ovaries from producing hormones at levels necessary to generate eggs and making the uterine lining inhospitable for an egg to implant.

Blood samples showed the treated rats were producing more corticosterone than untreated animals, a sign that they were stressed. And after being subjected to and recovering from an experimental stressor, the treated rats' corticosterone level remained high. Their adrenal glands were also larger, suggesting their stress hormone production was consistently higher than that of control animals.

An analysis of gene activation markers in the animals' prefrontal cortex showed a decrease in excitatory synapses in that region of treated rats' brains compared to controls, but no change to inhibitory synapses—a

phenomenon that could set up an imbalance of normal signaling patterns and result in altered behavior. The loss of only excitatory synapses in the prefrontal cortex has been linked to exposure to chronic stress and depression in previous research.

"What this means for the function of particular circuits, we don't know yet. But this gives us a clue of where to look next in terms of what the functional outcomes might be," Lenz said.

The researchers are moving forward with additional studies targeting hormonal contraceptive effects on the brain between puberty and late adolescence—a tricky time to study the developing brain because it is undergoing constant change, Leuner said. The reasons behind the drugs' effects are an open question, as well.

"These are synthetic hormones, so are they affecting the brain because of their synthetic properties, or are they affecting the brain because they're blocking the naturally produced hormones?" she asked. "It's a difficult question to answer, but an important one."

More information: Conference: www.sfn.org/meetings/neuroscience-2022

Conference abstract: www.abstractsonline.com/pp8/#! … 9/presentation/70469

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