

Synthetic estrogen associated with increased anxiety-like behaviors in a rat model

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The type of estrogen in hormonal birth control may influence anxiety-like behaviors, according to data presented by Abigail Hegwood, M.S., from the Prakapenka Lab at [ENDO 2024](#), the Endocrine Society's annual meeting in Boston, Mass.

"It is plausible that estrogen type is a key player in mood or cognitive related side effects of hormone-based contraceptive use," said Alesia Prakapenka, Ph.D., an assistant professor in the Biomedical Sciences program at Northwestern University in Downers Grove, Ill.

According to the CDC, 12.6% of women in the United States between the ages of 15 and 49 reported using [oral contraceptives](#) from 2015 to 2017. Prakapenka and colleagues acknowledged that behavioral side effects are one of the reasons why many women stop taking combination birth control.

The researchers sought to understand whether or not identifying an estrogen type matters when it comes to evaluating behaviors like anxiety and cognition.

In this rat model study, the researchers randomly assigned 36 young adult female rats (aged 3 to 4 months old) to synthetic ethinyl estradiol plus dienogest, natural estradiol valerate plus dienogest, or vehicle control treatment.

After four weeks, the rats were evaluated on a delayed spontaneous alternation task to examine spatial memory and elevated plus maze to analyze anxiety-like [behavior](#).

Then, Prakapenka explained, serum was extracted and examined for estradiol, progesterone, androstenedione, and [testosterone levels](#) using

liquid chromatography-mass spectrometry and corticosterone levels using radioimmunoassay.

"We found that [female rats](#) treated with the [synthetic estrogen](#) exhibited elevated anxiety-like behaviors compared to females that received a vehicle control or the natural estrogen," Prakapenka said, adding that spatial memory was similar across the three treatment groups.

Of note, navigation on the spatial memory task differed. The synthetic estrogen increased habitual turn strategy use compared to the control and natural estrogen—a finding that is associated with anxiety-like behaviors.

"Altogether, our findings support the notion that estrogen type matters for behavioral outcomes associated with contraceptive use, identifying estrogen type as a potential clinical tool for management of behavioral side effects in females," Hegwood said.

Provided by The Endocrine Society

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