Medical Xpress

Researchers uncover biological trigger of early puberty

May 20 2024, by Alena Kuzub

Heather Brenhouse, associate professor of psychology, says disrupting the caretaker relationship can really traumatize a child or a developing rodent. Credit: Ruby Wallau/Northeastern University

New research conducted by the Brenhouse Lab reveals how early life adversity triggers early puberty and late-life anxiety, paving the way for

potential interventions.

The onset of puberty has been creeping downward for decades.

In the United States, the average age of girls reaching puberty ranges from 8.8 to 10.3 years old. The early start of puberty, which is associated with many health risks, can be triggered by chronic stress in children.

New research by Northeastern scientists published in *Hormones and Behavior*, has identified for the first time that early life stress affects the part of the brain—specifically, a protein in the membrane of a cell—responsible for preventing premature inception of puberty.

The brain receptor can suppress the release of hormones, or put the "brakes" on early puberty. The receptor malfunctions under chronic stress, unleashing a cascade of messaging that leads to early initiation of puberty, according to Northeastern researchers.

Children with early puberty are at risk of developing cancers of the reproductive tract, metabolic syndromes such as diabetes, cardiovascular disease, emotional and social problems later in adulthood, according to studies.

Researchers hope the findings will lead to medical interventions in the future.

"Early puberty is very important because it seems to be associated with later life psychopathologies like anxiety-related disorders," says Heather Brenhouse, professor of psychology at Northeastern University. "Physiological medical conditions also seem to be potentially linked to early puberty."

The biological mechanism of how early childhood stress leads to early

puberty, Brenhouse says, had remained largely unknown.

The new research conducted by the Brenhouse Lab at Northeastern identified a receptor—a part of a brain cell that receives messages from another cell—in the hypothalamus, a region in the brain that controls many body functions via hormones.

The scientists knew from previous studies, Brenhouse says, that premature pubertal development in girls is associated with early life adversity and that early puberty predicts anxiety later in adolescence and adulthood.

They set out to confirm these findings and identify a biological trigger of early puberty in the brain.

Lauren Granata, a Northeastern graduate with a doctoral degree in psychology, co-authored the study and conducted the investigation in animal models. The idea of a stress triggering puberty, she says, seemed counterintuitive to her at first.

"It's pretty well understood nowadays that stress is dampening reproduction," Granata says. "I thought there was a lot of opportunity to find out something new."

First, the scientists confirmed the hypothesis that early childhood adversity indeed triggered early puberty in rats. Working with the animal model, Granata says, allowed them to isolate one specific factor—a disrupted relationship with the mother—aside from other factors such as nutrition, for example.

Of course, Granata says, what's happening in humans does not correlate one-to-one with the animal model, but it is good evidence that dysfunction of maternal care early in life may be one factor that's

regulating early puberty.

"The way you can really traumatize a child or a developing rodent is by manipulating and disrupting the caretaker relationship," Brenhouse says.

Other childhood adverse experiences in humans, she says, could be neglect, resource scarcity and maltreatment.

To find a biomarker, a biological molecule in the brain whose state indicates early or normal puberty, Granata looked at the hypothalamus as it is widely known that it controls whether somebody is going to undergo puberty, among other important functions.

"There are cells that are basically activated, and they release certain proteins and peptides [hormones] that initiate puberty," Brenhouse says.

Granata found, she says, that those brain cells actually start expressing and releasing these proteins earlier in female rats that have been exposed to maternal separation. She has identified a specific receptor—CRH-R1—in the hypothalamus that suppresses preliminary puberty and gets affected by chronic stress stimulation.

"You can think of this as there's always a battle between a go signal and a stop signal [in the brain]," Granata says.

Stress hormones usually act as "brakes" on puberty, she says, because they cause the receptor CRH-R1 to suppress the release of hormones essential for puberty. So they hypothesized that it is not one stressful event but chronic stress that wears down puberty brakes, or reduces responsiveness of the receptor to stress hormones.

That unleashes a cascade of signaling in the brain and in the body.

"Now all of the go signals just have free reign to just say go ahead. It's time for puberty," Granata says.

The hypothalamus releases specific hormones that tell the system to release the brakes and produce estrogen and testosterone that are involved in the growth and maintenance of reproductive tissues.

The scientists did not observe accelerated puberty in male rats also exposed to maternal separation.

To study the relationship between adversity and childhood trauma and anxiety in adolescents and adults, the scientists used acoustic startle—startle noise bursts interrupting white noise background—on female rats after puberty. The experiment showed significant negative correlation between the age of puberty and the magnitude of response to the acoustic startle, which is associated with disorders.

A rat that had earlier puberty, Granata says, experienced higher levels of anxiety in adolescence.

She hopes these findings could be used to potentially create interventions and treatments for girls who are at a higher risk of anxiety and depression in adolescence and adulthood because of early puberty.

More information: Lauren Granata et al, Early life adversity accelerates hypothalamic drive of pubertal timing in female rats with associated enhanced acoustic startle, *Hormones and Behavior* (2024). DOI: 10.1016/j.yhbeh.2024.105478

Provided by Northeastern University