Study suggests that estrogen may drive nicotine addiction in women

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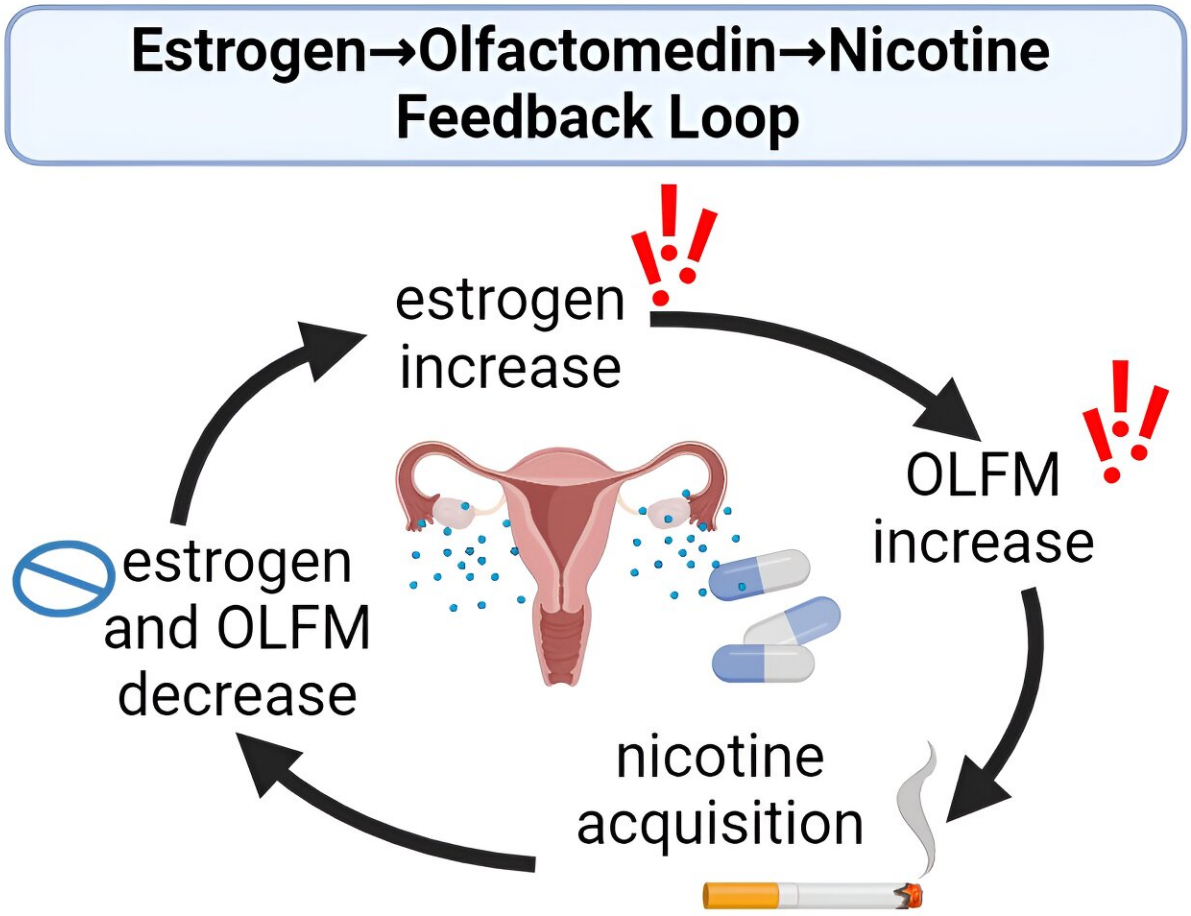


Researchers discovered that estrogen induces the expression of olfactomedins (OLFM), proteins that are suppressed by nicotine in key areas of the brain involved in reward and addiction. The research could lead to new targeted therapies that help women control nicotine consumption. Credit: Sally Pauss, University of Kentucky College of Medicine; created with BioRender.com

A newly discovered feedback loop involving estrogen may explain why women might become dependent on nicotine more quickly and with less nicotine exposure than men. The research could lead to new treatments for women who are having trouble quitting nicotine-containing products such as cigarettes.

Sally Pauss is a doctoral student at the University of Kentucky College of Medicine in Lexington. She led the project.

"Studies show that women have a higher propensity to develop addiction to nicotine than men and are less successful at quitting," said Pauss, who is working under the supervision of Terry D. Hinds Jr., an associate professor. "Our work aims to understand what makes women more susceptible to nicotine use disorder to reduce the gender disparity in treating nicotine addiction."

The researchers found that the sex hormone estrogen induces the expression of olfactomedins, proteins that are suppressed by nicotine in key areas of the brain involved in reward and addiction. The findings suggest that estrogen–nicotine–olfactomedin interactions could be targeted with therapies to help control nicotine consumption.

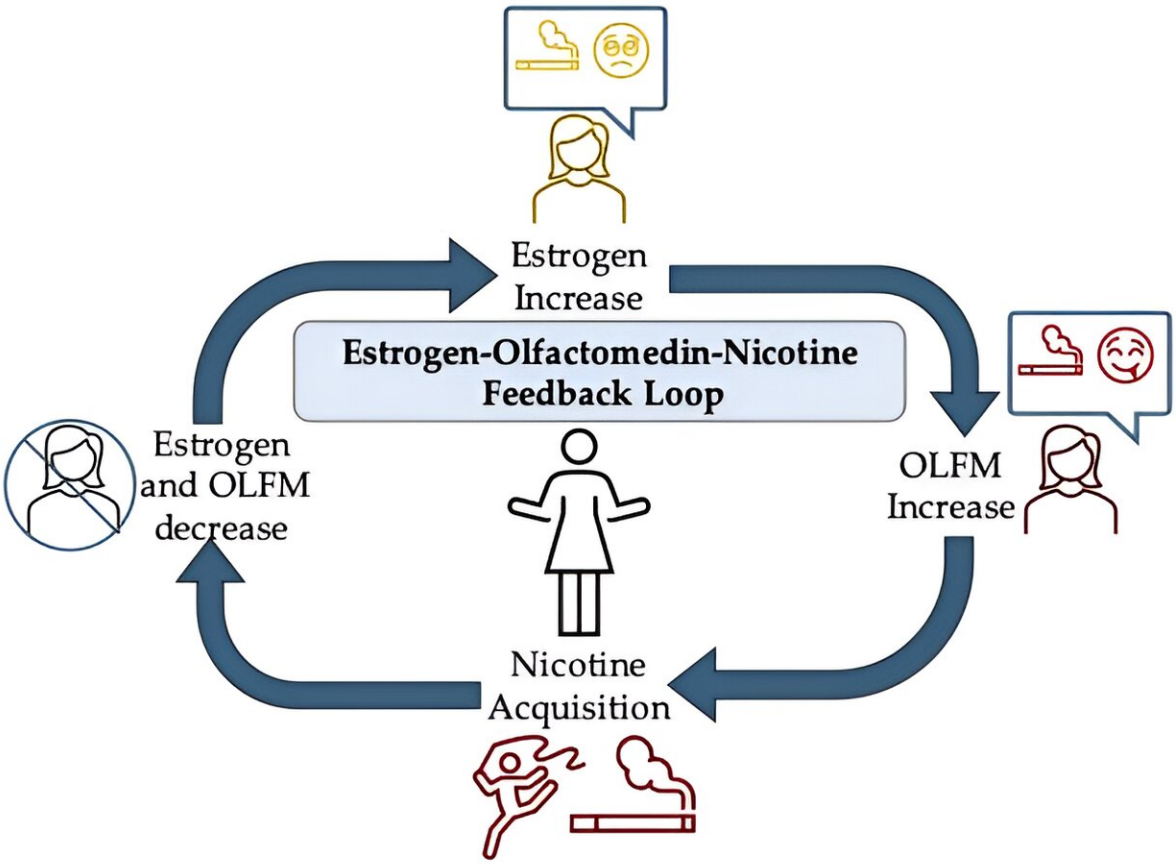
Pauss will present the research at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, which will be held March 23–26 in San Antonio.

"Our research has the potential to better the lives and health of women struggling with substance use," she said. "If we can confirm that estrogen drives nicotine seeking and consumption through olfactomedins, we can design drugs that might block that effect by targeting the altered pathways. These drugs would hopefully make it easier for women to quit

nicotine."

For the new study, the researchers used large sequencing datasets of estrogen-induced genes to identify genes that are expressed in the brain and exhibit a hormone function. They found just one class of genes that met these criteria: those coding for olfactomedins.

They then performed a series of studies with human uterine cells and rats to better understand the interactions between olfactomedins, estrogen and nicotine. The results suggested that estrogen activation of olfactomedins—which is suppressed when nicotine is present—might serve as a feedback loop for driving nicotine addiction processes by activating areas of the brain's reward circuitry such as the nucleus accumbens.



Researchers discovered that estrogen induces the expression of olfactomedins (OLFM), proteins that are suppressed by nicotine in key areas of the brain involved in reward and addiction. The research could lead to new targeted therapies that help women control nicotine consumption. Credit: Sally Pauss, University of Kentucky College of Medicine

The researchers are now working to replicate their findings and definitively determine the role of estrogen. This knowledge could be useful for those taking estrogen in the form of oral contraceptives or hormone replacement therapy, which might increase the risk of developing a nicotine use disorder.

The investigators also want to determine the exact olfactomedin-regulated signaling pathways that drive nicotine consumption and plan to conduct behavioral animal studies to find out how manipulation of the feedback loop affects nicotine consumption.

Provided by American Society for Biochemistry and Molecular Biology

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