

Mouse study links changes in microbiome to prenatal opioid exposure

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Prenatal exposure to opioids had been linked to a range of adverse outcomes in infants, including poor fetal growth, low birthweight, possible congenital defects and a higher risk of admission to neonatal intensive care. Less information is known, however, on how developmental opioid exposure shapes an infant's microbiome and how that influence, in turn, may trigger neurological or behavioral effects

later in life.

For a study on mice published this week in *mSystems*, researchers from the University of Missouri, Columbia, identified significant changes to the infant gut microbiome associated with maternal exposure to [oxycodone](#), a commonly used and abused [opioid](#). Those bacterial changes are associated with alterations in [metabolic pathways](#), a connection that suggests maternal opioid use influence the metabolism of infants.

"Physicians prescribe oxycodone, but they don't have all the data for the implications on the fetus and long-term health," said microbiologist Cheryl Rosenfeld, Ph.D., who co-led the study with bioinformatics scientist Trupti Joshi, Ph.D. "What happens in utero can lead to [long-term health](#) consequences."

Rosenfeld and Joshi hypothesized that developmental exposure to oxycodone would induce gut dysbiosis—a disruption to the natural balance of bacteria in the gut—and that those bacterial changes could be connected to other alterations previously reported in adult offspring. To find out, the researchers administered oxycodone to [female mice](#) in the experimental group starting two weeks before breeding and continuing until the birth of offspring. The amount of oxycodone, 5 mg per kilogram of body weight, was calculated to mimic levels recorded in humans with [opioid use disorder](#).

The researchers collected [fecal matter](#) from the mouse offspring at 120 days of age and isolated bacterial DNA from the samples. They used 16s rRNA sequencing to identify the [bacterial populations](#) in each sample and bioinformatics tools to find sex-linked differences in bacterial abundances, as well as differences between the experimental and control groups. Using these tools in succession, said Joshi, allowed the researchers to map connections among biological systems.

"Bioinformatics really allows you to get in deeper, build more insights and connect the data to the biology," she said.

Notably, males and females did not respond the same when their mothers had been exposed to oxycodone. Males exposed to oxycodone showed higher abundances of Coriobacteriaceae, Roseburia spp., Sutterella spp., and Clostridia than those not exposed to the drug. Females showed higher abundance of Butyricimonas spp., Bacteroidetes, Anaeroplasma spp., TM7, Enterococcus spp., and Clostridia. For both sexes, the identified bacterial changes were associated with changes in metabolite pathways, which ultimately influence an individual's metabolism.

Rosenfeld cautioned that the new study identifies important connections between opioid exposure and microbiome changes, but it doesn't demonstrate causation or elucidate the underlying mechanisms. In future studies, she and Joshi plan to continue using an informatics approach to better understand the microbiome's role in connecting drug exposure to long-term effects. She also said she'd like to see studies investigating whether this connection in mice holds in humans—and what it means for the health of infants prenatally exposed to the drugs.

"We can't just be thinking of neonates," she said. "We need long-term studies on these children."

More information: Zhen Lyu et al, Long-Term Effects of Developmental Exposure to Oxycodone on Gut Microbiota and Relationship to Adult Behaviors and Metabolism, *mSystems* (2022). [DOI: 10.1128/mSystems.00336-22](https://doi.org/10.1128/mSystems.00336-22)

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