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Why some children are harmed by mother's alcohol, but others aren't

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Exposure to alcohol in the womb doesn't affect all fetuses equally. Why does one woman who drinks alcohol during pregnancy give birth to a child with physical, behavioral or learning problems -- known as fetal alcohol spectrum disorder -- while another woman who also drinks has a child without these problems?

One answer is a gene variation passed on by the mother to her son, according to new Northwestern Medicine research. This gene variation contributes to a fetus' vulnerability to even moderate alcohol exposure by upsetting the balance of thyroid hormones in the brain.

The Northwestern Medicine study with rats is the first to identify a direct genetic mechanism of behavioral deficits caused by fetal alcohol exposure. The study is published today in the FASEB Journal.

"The findings open up the possibility of using dietary supplements that have the potential to reverse or fix the dosage of the thyroid hormones in the brain to correct the problems caused by the alcohol exposure," said Eva E. Redei, senior author of the study and the David Lawrence Stein Professor of Psychiatry at Northwestern University Feinberg School of Medicine.

"In the not-too-distant future we could identify a woman's vulnerability to alcohol if she is pregnant and target this enzyme imbalance with drugs, a supplement or another method that will increase the production of this enzyme in the hippocampus, which is where it's needed," Redei

said.

Efforts to educate pregnant women about the risks of alcohol have not changed the percentage of children born with fetal alcohol spectrum disorder, Redei noted.

The gene involved, Dio3, makes the enzyme that controls how much active thyroid hormone is in the brain. A delicate balance of the thyroid hormone is critically important in the development of the fetal brain and in the maintenance of adult brain function. Too much of it is as bad as too little.

When males inherit this variation of the Dio3 gene from their mother, they don't make enough of this enzyme in their hippocampus to prevent an excess of thyroid hormones. The resulting overdose of the hormones makes the hippocampus vulnerable to damage by even a moderate amount of alcohol. The rat mothers in the study drank the human equivalent of two to three glasses of wine a day. Their male offspring showed deficits in social behavior and memory similar to humans whose mothers drank alcohol.

The alcohol causes the problem by almost completely silencing the father's copy of the Dio3 gene in animals whose mother has the gene variation. As a result, the offspring don't make enough of this enzyme, disrupting the delicate balance of the thyroid hormone levels. This is an example of an interaction between genetic variation in the DNA sequence, and epigenetics, which is when the environment, such as alcohol in utero, modifies the DNA.

"The identification of this novel mechanism will stimulate more research on other genes that also influence alcohol-related disorders, especially in females," said Laura Sittig, the lead author of the study and a graduate student in Redei's lab.

In the study, the rats' social behavior was measured by putting a pup into a cage with an adult. Normal adult behavior is to lick and smell the pup. The adults exposed to alcohol in utero, however, interacted with the pup half as much as normal. They also forgot where to navigate in a maze that evaluated spatial memory.

"These results show they had social and memory deficits," Redei said. "This indicates the damage to the hippocampus from the alcohol exposure."

Provided by Northwestern University