

NEWS

Smoking during pregnancy may up autism risk in grandchildren

BY SARAH DEWEERDT

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A woman who smokes while pregnant may increase autism risk in her daughter's children, according to a new study¹. What's more, maternal granddaughters have an elevated incidence of some autism traits.

The new work does not prove that cigarette smoking during pregnancy increases autism risk in grandchildren. It is possible that shared genetic factors boost both a woman's propensity to smoke and a granddaughter's vulnerability to autism. The researchers also cannot rule out the possibility that smoking affects daughters, who then pass autism traits on to their children.

Rather the findings, published 27 April in *Scientific Reports*, merely hint at an environmental risk factor for autism that operates across generations.

"We would call this a hypothesis-generating study," says **Marcus Pembrey**, visiting professor of pediatric genetics at the University of Bristol in England, who co-led the analysis.

It's rare for studies to assess how a woman's environment affects her grandchildren's development.

"This is one of the first studies that I know of that has been able to do a three-generation study" of environmental risk factors in autism, says **Amy Kalkbrenner**, assistant professor of environmental health sciences at the University of Wisconsin-Milwaukee, who was not involved in the work.

The findings are surprising, because there is little support for a link between cigarette smoking and autism risk.

"The literature on maternal smoking and autism largely shows that there isn't an association," says **Heather Volk**, assistant professor of mental health at Johns Hopkins University in Baltimore, who was not involved in the new work. A study published earlier this year contradicts the idea that maternal smoking contributes to bipolar disorder or schizophrenia².

Time machine:

The researchers analyzed data from the **Avon Longitudinal Study of Parents and Children**, a long-term study of 14,500 children born in southwestern England in 1991 and 1992. Before the children were born, researchers asked the parents about their own and their parents' smoking histories.

"Short of jumping into a time machine and observing the grandmothers smoking in pregnancy, this really is the best way to assess their exposure," says **Brian Lee**, associate professor of epidemiology and biostatistics at Drexel University in Philadelphia. Lee was not involved in the work, but is collaborating with the researchers on a different analysis of Avon data.

As the children grew up, the researchers periodically evaluated them at a local clinic. They also mailed the mothers a series of questionnaires about their children's behavior when the children were about 3, 6, 7 and 9 years old.

Children whose maternal grandmothers smoked during pregnancy are more likely to have certain autism traits than those whose grandmothers did not smoke. The effect is stronger in girls than in boys, and most pronounced in girls whose mothers did not smoke while pregnant.

Mixed mechanisms:

The researchers identified 212 children from the Avon group who have autism, using medical and school records, along with information from mothers. Information about at least one grandparent is available for 174 of these individuals.

They found that children whose maternal grandmothers smoked during pregnancy are more likely to have autism than those whose grandmothers did not smoke. The study included too few children with autism to reveal any sex differences.

The researchers did not find any link between autism and smoking in paternal grandmothers. This raises the possibility that the link involves **mitochondria**, energy-producing structures inside cells that are inherited from the mother. Mounting evidence **implicates mitochondria** in autism.

Alternatively, **epigenetic** changes — modifications to DNA that affect gene expression — could account for the link. Maternal smoking during pregnancy is thought to affect the epigenetic regulation of several candidate genes for autism risk, including **DLGAP2**, **NRP2** and **CNTNAP2**.

So far, most research on epigenetics and autism has focused on fathers. The new study suggests scientists should pay more attention to mothers and grandmothers. Pembrey and his colleagues are examining epigenetic markers in DNA samples from the children and their mothers.

REFERENCES:

1. Golding J. *et al.* *Sci. Rep.* **7**, 46179 (2017) [PubMed](#)
2. Quinn P.D. *et al.* *JAMA Psychiatry* Epub ahead of print (2017) [PubMed](#)