

Maternal stress hormones and maternal smoking increase daughter's risk of nicotine dependence

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Tobacco smoking by pregnant women has long been viewed as a public health risk because of smoking's adverse effects on the development of a that began in 1959 and enrolled over 50,000 fetus.

Smoking during pregnancy is linked to numerous negative outcomes, including low birth weight, sudden infant death syndrome, and increased risk for attention deficit disorder, conduct disorder, and nicotine use in offspring. Despite this extensive literature, it is estimated that 13%-30% of women in the United States continue to smoke while pregnant.

Now, a new 40-year longitudinal study, published in Biological Psychiatry, provides strong evidence that prenatal exposure to maternal stress hormones predicts nicotine dependence later in life - but only for daughters. It also confirms previous research that babies born to moms who smoked when pregnant have an increased risk of nicotine addiction in adulthood.

"While maternal smoking during pregnancy has been shown to be an independent risk factor for nicotine dependence, we didn't really know which pathways or mechanisms were responsible. Most prior research involving biological mechanisms had been conducted in animals not humans," said Dr. Laura Stroud, first author on this study and a researcher with the Centers for Behavioral and Preventive Medicine at The Miriam Hospital in Providence, RI.

"Our study suggests that maternal smoking and high stress hormones represent a 'double-hit' in terms of increasing an offspring's risk for nicotine addiction as an adult. Because mothers who smoke are often more stressed and living in adverse conditions- these findings represent a major public health concern."

To conduct the study, Stroud and her colleagues used data from a large, national, long-term project pregnant women. The offspring of those women were ultimately followed by researchers for 40 vears.

For this particular project, 1,086 mothers participated, where their hormone levels (cortisol and testosterone) were measured during pregnancy and their smoking status was recorded. Their children, 649 of whom were daughters and 437 of whom were sons, were interviewed as adults and their smoking status was also recorded.

The findings revealed that in female but not male offspring, elevated prenatal cortisol exposure and exposure to maternal smoking during pregnancy were associated with increased rates of nicotine dependence as adults. No links were found between elevated prenatal testosterone exposure and adult nicotine dependence. There were also no findings among male offspring.

"Our findings highlight the particular vulnerability of daughters to long-term adverse outcomes following maternal stress and smoking during pregnancy. We don't yet know why this is, but possible mechanisms include sex differences in stress hormone regulation in the placenta and adaptation to prenatal environmental exposures," added Stroud. "Also, cortisol and nicotine may affect developing male and female brains differently. Furthermore, if daughters of smoking mothers are more likely to grow up nicotine dependent, the result is dangerous cycle of intergenerational transmission of nicotine addiction."

"These new data may help us to focus our attention on individuals at greatest risk for later smoking," said Dr. John Krystal, Editor of Biological



Psychiatry. "It is interesting that female, but not male, offspring seemed to be at greatest risk. Sex differences in the vulnerability to smoking are important and merit further study."

More information: The article is "Prenatal Glucocorticoids and Maternal Smoking During Pregnancy Independently Program Adult Nicotine Dependence in Daughters: A 40-Year Prospective Study" by Laura R. Stroud, George D. Papandonatos, Edmond Shenassa, Daniel Rodriguez, Raymond Niaura, Kaja Z. LeWinn, Lewis P. Lipsitt, and Stephen L. Buka (DOI: 10.1016/j.biopsych.2013.07.024). The article appears in *Biological Psychiatry*, Volume 75, Issue 1 (January 1, 2014)

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