

Cocaine exposure during pregnancy leads to impulsivity in male, not female, monkeys

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Adult male monkeys exposed to cocaine while in the womb have poor impulse control and may be more vulnerable to drug abuse than female monkeys, even a decade or more after the exposure, according to a new study by researchers at Wake Forest University School of Medicine. The findings could lead to a better understanding of human drug abuse.

The study was presented yesterday at the annual Society for Neuroscience meeting in Chicago.

"This is the first time that so many different measures of impulsivity, which is considered a risk factor for drug abuse, have been looked at in the same group of animals," said Lindsey Hamilton, lead investigator and a graduate student working in the laboratory of Michael Nader, Ph.D., a professor of physiology and pharmacology. "We're looking for ways to predict which individuals are going to take drugs during their lives. It was very surprising to see that, even more than a decade after the prenatal cocaine exposure, the monkeys ended up being more impulsive and possibly more susceptible to drug use. It was particularly interesting, however, that this effect was only seen in the males. Something is either protecting the females from the effects of the cocaine exposure in the womb or making the males more susceptible to the lasting effects."

For the study, researchers compared adult monkeys - both male and female - prenatally exposed to cocaine more than 15 years ago, to monkeys who were raised under similar conditions, but not exposed to cocaine during gestation. To determine if the animals differed in impulse

control, they performed four tests. For one of the tests, the researchers gave the animals the choice between pushing a lever that delivered a single banana pellet reward immediately or a lever that delivered several banana pellets, but required the animals to wait up to five minutes before the reward was delivered.

"That's where we saw very large differences between the groups," Hamilton said. "The males who were exposed to cocaine in-utero had no patience or impulse control whatsoever."

Those monkeys were less willing to wait for a larger food reward and preferred the immediately available, though much smaller, reward, indicating they were more impulsive than the adult male monkeys who had never been exposed to cocaine. There was, however, no difference in the preference of female monkeys prenatally exposed to cocaine and those never exposed to the drug.

After all of the impulsivity tests were administered, the researchers ranked each monkey from least to most impulsive and compared their average impulsivity score across the four tests. They found that the male, but not female, monkeys prenatally exposed to cocaine were more impulsive overall compared to control monkeys who weren't exposed.

"A lot of the differences we saw were subtle," Hamilton said. "We've done several different kinds of impulsivity tests and, on their own, each task resulted in only slight differences. But together, they paint a really clear picture of the effects of this early cocaine exposure. The more challenging the test, the more obvious the difference between the groups was.

"The fact that we are seeing differences at all is particularly striking because this is 15 years after the monkeys were exposed in the womb to cocaine," she added. "Fifteen years is the equivalent of middle age for

monkeys. The fact that fairly large differences are still turning up is fascinating."

Hamilton described the findings further, explaining that dopamine is a chemical in the brain that has been associated with drug abuse. When dopamine is released, it is broken down into homovanillic acid (HVA), which can be readily measured from a sample of cerebrospinal fluid (CSF). The researchers found that the less HVA present in a monkey's CSF, the less impulse control that monkey demonstrated. This finding is the first time a relationship between this dopamine metabolite and impulsivity has been documented, and indicates that there is a biological correlation associated with the alterations in impulse control observed in the monkeys exposed to cocaine in the womb.

Since decreased impulse control is a defining characteristic of cocaine addicts, Hamilton and her colleagues are currently working on an ongoing study to assess whether the monkeys that were prenatally exposed to cocaine will be more likely to self-administer drugs in adulthood.

So far, Hamilton said, it appears that the male monkeys exposed to cocaine in utero are more likely to self-administer the drug, even in low doses, than controls. Again, the difference is not being observed in the female [monkeys](#).

"Our studies indicate that males may be more vulnerable to the long-lasting behavioral and neurobiological consequences of cocaine exposure during gestation than females, suggesting male children who were exposed to cocaine during their mothers' pregnancies may be predisposed to abuse drugs in adulthood," Hamilton said.

It has been estimated that there are about 7.5 million children in the United States that were exposed to cocaine during gestation and between

30,000 and 160,000 infants born each year who have been prenatally exposed to cocaine, according to the National Pregnancy and Health Survey, the Department of Health and Human Services and previous research. The effects of cocaine use during pregnancy on children's development are not well established.

"Whether or not these children who were exposed to cocaine in the [womb](#) may be more vulnerable to drug use is a timely question," Hamilton said, "both because these children are now young adults, a time when a lot of drug experimentation occurs, and because cocaine abuse among young women of childbearing age is a growing problem in this country."

It is challenging to study children exposed to cocaine in utero because there are many other factors that could affect their behavior, such as less-than-optimal prenatal care, inadequate nutrition, and exposure to multiple types and doses of drugs during their mothers' pregnancies, Hamilton explained. By using a monkey model, researchers are able to control these variables and determine the long-term effects of prenatal cocaine exposure.

"We know that drug abusers are more impulsive than non drug users," Hamilton said. "But what is not as clear is whether people become drug abusers because they are impulsive or if people become impulsive because they're drug abusers. It's a bit of the chicken or the egg puzzle. We'll probably find that it's a little bit of both. The more we learn about the causes of [drug abuse](#), the more likely that, one day, we'll be able to prevent it."

Source: Wake Forest University Baptist Medical Center ([news](#) : [web](#))

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