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Three studies in rodents suggest prenatal exposure to the drug may pose risks for infants

By Dana G. Smith on November 7, 2018

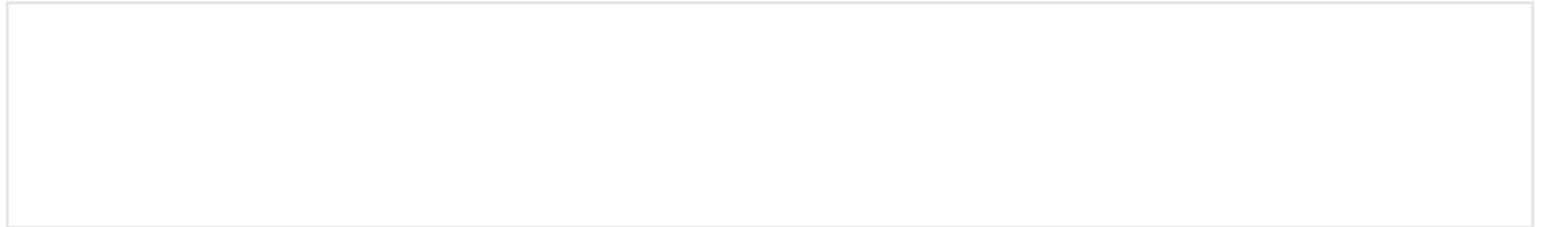


Credit: Getty Images

Marijuana has been legalized in some capacity in 31 U.S. states, in large part due to a softening stance around the potential harms of the drug and recognition of its medical benefits. As a result, cannabis has become the most commonly used illicit drug during pregnancy.

One recent study revealed that in 2016 7 percent of pregnant women in California used marijuana, with rates as high as 22 percent among teenage mothers. In Colorado 69 percent of dispensaries recommended the drug to pregnant women to help with morning sickness.

Whereas marijuana is not a major health risk for most adults, prenatal drug exposure can be harmful to unborn babies. Previous research has shown infants exposed to cannabis in the womb are 50 percent more likely to have a lower birth weight. Now three new studies presented in November at the Society for Neuroscience annual meeting in San Diego suggest prenatal cannabis exposure—at least in rodents—could have serious consequences for fetal brain development. “There’s become this relaxation—in part because [marijuana] is becoming legal in many states around the country—that it’s fine,” says Yasmin Hurd, who is director of the Addiction Institute at the Icahn School of Medicine at Mount Sinai and was not involved in the new research. But, she adds, just because a drug is not very dangerous to adults does not mean it is harmless to the developing brain.



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In one study researchers at Washington State University in Pullman showed rat pups born to mothers exposed to high amounts of cannabis vapor during pregnancy had trouble with cognitive flexibility. Twice a day the scientists filled the pregnant rats’ containers with marijuana vapor from an e-cigarette, elevating levels of the psychoactive chemical THC (tetrahydrocannabinol) in the rats’ blood to roughly the human equivalent of smoking a joint. After the pups grew up the researchers trained them on a task that measured their ability to think flexibly and learn new rules. The young rats first learned to follow a light cue to push one of two levers in order to receive a sugary treat. The next day, pushing only the left lever would deliver the reward, regardless of which side the light had been on.

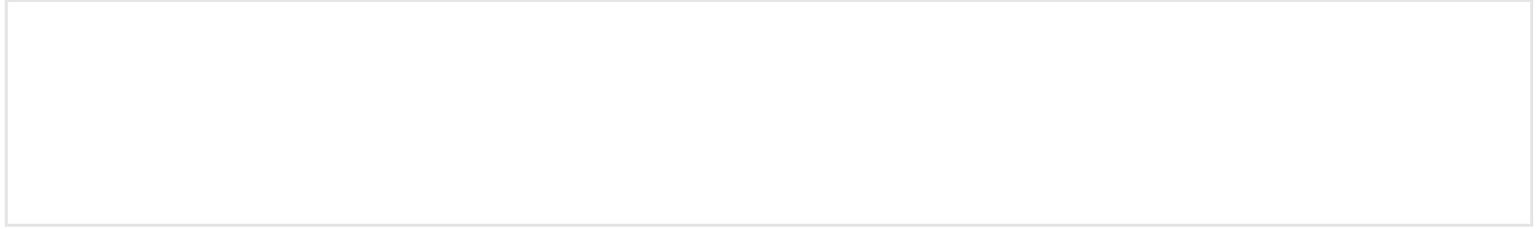
The rats exposed to cannabis in utero learned the first rule (following the light cue) without a problem, but they took significantly longer to learn the new rule (pushing the left lever) than did rats

not exposed to the drug. The cannabis-exposed rats also made many more mistakes on the second day. They would respond correctly for a couple rounds, making it seem like they knew the new rule, but then they would press the wrong lever again. “It was like something wasn’t really clicking with them,” says Ryan McLaughlin, an assistant professor of integrative physiology and neuroscience at Washington State and lead author of the study, which has not yet been published. He says they never got that “‘Aha!’ moment, where it’s like, ‘Oh, this is what I’m supposed to do.’”

In a similar study, scientists at Auburn University in Alabama found rats born to mothers that had been injected with a low, continuous dose of synthetic cannabis during pregnancy were significantly impaired on several different memory tasks involving mazes. “The rats that were exposed to cannabinoids [chemicals like those found in marijuana] prenatally were performing less efficiently than the control rats” that were not exposed, says Priyanka Pinky, a graduate student at Auburn who conducted the research. “There was a gap in the acquisition of the memory and the consolidation of the memory.”

The young rats whose mothers were dosed with the drug also had abnormalities in the hippocampus, the brain’s primary memory center. Specifically, they had difficulty creating new connections between neurons—the basis for forming new memories. The researchers think the differences in the hippocampus stem from changes in levels of glutamate, the brain’s main excitatory neurochemical involved in learning and memory.

In the third study researchers at the University of Maryland School of Medicine and the University of Ferrara in Italy again found impairments in memory and changes in levels of glutamate in the brains of rats exposed to THC in the womb. They also discovered an increase in another molecule in the brain, which they think may be the missing link between prenatal cannabis exposure, glutamate and cognitive impairments: kynurenic acid. This chemical acts like a puppet master in the brain, regulating glutamate and other important neurochemicals; high levels of the molecule result in lower glutamate levels. Kynurenic acid has also previously been implicated in cognitive impairments in both people and animals.



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“We think that prenatal marijuana exposure can induce an increase in kynurenic acid, and this may be responsible for the cognitive impairment observed in the offspring of marijuana users,” says Sarah Beggiato, a postdoctoral researcher at the University of Ferrara in Italy and co-author of the study. “Why is glutamate going down? It’s because kynurenic acid is going up.” The scientists are now researching drugs that block the acid’s synthesis, which may help defend against the problems associated with prenatal cannabis exposure.

The findings, which are in rodents, may not necessarily translate to humans. Mount Sinai’s Hurd, who has been researching the effects of marijuana on the developing brain in both humans and animals for 15 years, says the new studies do not reveal anything “shockingly new.” But they show “that there are indeed multiple systems being affected,” she says, “and given that more pregnant women today are starting to smoke marijuana, it’s really important for us to get that word out.”

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Dana Smith is a freelance science writer specializing in brains and bodies. She has written for *Scientific American*, the *Atlantic*, the *Guardian*, NPR, *Discover*, and *Fast Company*, among other outlets. In a previous life, she earned a Ph.D. in experimental psychology from the University of Cambridge.

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