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NIDA
NATIONAL INSTITUTE
ON DRUG ABUSE

NewsScan

NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

RESEARCH NEWS

Studies Show Effects of Cocaine Use During Pregnancy on Infants' Brains

Babies born to mothers who abuse cocaine during pregnancy often are delivered prematurely, have low birth weights, smaller head circumferences, and tend to be shorter. However, the full consequences of prenatal cocaine exposure on children are still unclear and are difficult to study.

In a series of recently published studies, a team of NIDA-supported researchers at the University of Maryland, Baltimore, led by Dr. Michael S. Lidow, examined the effects of prenatal cocaine exposure in rhesus monkeys. The researchers found that such exposure interferes with the production of nerve cells and leads to a significant increase in cell death in the developing cerebral cortex. They also found that, as a result of these actions of cocaine, the number and density of nerve cells (neurons) in the cerebral cortex of monkeys born from cocaine-exposed mothers is reduced, their positioning is abnormal, and the cortex lacks its usual layered structure.

"The results of these studies provide important information on the effects of prenatal cocaine exposure on the developing brain," says NIDA Director Dr. Alan I. Leshner. "Particularly noteworthy is the finding that a mother's use of cocaine during pregnancy can lead to long-lasting abnormalities in her infant's cerebral cortex, the part of the brain that is largely responsible for our higher brain functions, including visual perception, social behavior, and learning, memory and attention."

More detailed information about these studies follows.

Rhesus Monkeys as a Model for Cocaine Abuse in Pregnant Humans

To determine the dosage and route of cocaine administration for studies in pregnant monkeys that would be relevant to humans, Dr. Lidow and his colleagues looked at the absorption and elimination of cocaine administered by mouth (orally) and intravenously in pregnant monkeys and in their fetuses. Based on their results, they decided to use oral administration of cocaine, which closely resembles the snorting of cocaine in humans, at a dose of 20 milligrams per kilogram body weight per day, which produces maternal blood concentrations of cocaine in the range of those seen in people who are heavy users of cocaine.

- WHAT IT MEANS: Studying the effects of fetal exposure to cocaine in humans is difficult. This study provides evidence that rhesus monkeys given 20 milligrams of cocaine per kilogram body weight daily by mouth can serve as a model for studying the effects of cocaine abuse by pregnant women.

The study appears in the May 2001 issue of the *Journal of Pharmacology and Experimental Therapeutics*. An abstract of the article is available online at jpet.aspetjournals.org.

Prenatal Cocaine Exposure Interferes With New Cell Formation and Increases the Incidence of Cell Death in the Developing Cerebral Cortex

The University of Maryland researchers looked first at the ability of prenatal cocaine exposure to interfere with the generation of neurons destined for the cerebral cortex in the developing fetal brain. They injected pregnant rhesus monkeys either 1.5 hours or 10 hours after cocaine administration with a radioactive compound that marks dividing cells. Cocaine levels in the fetal circulation peak at 1.5 hours after oral administration and are undetectable 10 hours after the drug is given.

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The researchers found that when cocaine levels are highest, formation of new neurons in the developing cortex is cut roughly in half. However, when fetal cocaine levels are undetectable, new neuron formation is nearly doubled. These fluctuations in cell division suggest that the initial suppression of new nerve cell formation caused by a single dose of cocaine is followed by a significant compensatory burst of cell division when the drug level drops. Therefore, the net amount of new neuron formation may not change. Nevertheless, Dr. Lidow says, the abnormal fluctuations in the production of cortical neurons caused by cocaine may ultimately affect these cells" survival.

The researchers also used chemical markers of cell death to determine whether cocaine exposure of fetuses increases neuronal death in the developing cerebral cortex. They treated pregnant animals with cocaine for 10 days at the beginning of the second trimester and then looked at the number of dying cells in the fetal brain. They found that the number of such cells in the developing cortex nearly triples in cocaine-exposed fetuses, suggesting that cocaine kills fetal cortical neurons.

- WHAT IT MEANS: Cocaine-induced increases in cell death in the fetal cerebral cortex are likely to play a role in the reduced number and density of cortical neurons in monkeys that were prenatally exposed to the drug. Prenatal cocaine exposure also interferes with new cell generation in the developing cortex, but how or whether this contributes to the decreased density and number of cortical neurons is still unclear.

These studies appear, respectively, in the June 2001 issue of Cerebral Cortex, and the December 1999 issue of *Neuropathology and Applied Neurobiology*.

Chronic Prenatal Cocaine Exposure Leads to Long-term Changes in the Primate Brain

To determine how the actions of cocaine on neurons affect the cerebral cortex, the researchers examined this brain region in adult monkeys born from cocaine-treated mothers. They gave pregnant rhesus monkeys cocaine during the second trimester of pregnancy and allowed the monkeys to deliver at the normal time (day 165 of pregnancy). When the offspring reached 3 years of age, the researchers examined the anatomy of the cerebral cortex.

They found that the cortex in the offspring lacked its normal multilayered, highly organized, structure. The cortex also contained nearly 50 percent fewer neuronal cells than the cortex of non-drug-treated monkeys. The researchers also found a significant increase in the number of cells below the cortex in the white matter of the brain, which normally contains few neurons. However, even counting these neurons, which did not assume their normal position in the cortex, the total number of neurons was lower than in normal animals.

Finally, the researchers determined the time during pregnancy when cocaine can produce all these abnormalities in the developing cerebral cortex. In this study, they examined the cerebral cortex in monkeys exposed to cocaine during the first, second, or third trimester of pregnancy. They found that the cortex was affected only in monkeys exposed to cocaine during the second trimester. However, Dr. Lidow emphasizes, "while the abnormalities we detected seem to be caused by cocaine exposure in the second trimester, this does not mean that cocaine use in other trimesters is safe," because cocaine use at other times could and probably does have other effects.

- WHAT IT MEANS: Prenatal cocaine exposure in rhesus monkeys during the second trimester of pregnancy affects the organization of the cerebral cortex and the number and positioning of nerve cells in this brain region. The abnormalities in cortical structure and neuronal positioning persist in 3-year-old monkeys, indicating that these effects are long-lasting and may be permanent.

The study on long-term effects of cocaine appears in the July 2001 issue of the *Journal of Comparative Neurology*. The article on the timing of cocaine administration appears in the May 2001 issue of *Developmental Brain Research.*

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NEW PUBLICATIONS

New Brochure Helps Spanish-Speaking Families Discuss Drug Abuse and Related Health Risks

A new NIDA publication developed in Spanish provides a science-based discussion tool for Hispanic/Latino families. *Juventud Latina - Hable con Sus Hijos Sobre las Drogas y Sus Peligros (Latino Youth - Speak to Your Children About Drugs and Their Dangers)* includes the latest information on the health effects of inhalants, marijuana, cocaine, methamphetamine, and heroin. The publication also informs parents about the signs of drug use in their children as well as information about drug abuse prevention and treatment strategies.

The brochure was produced with the active involvement and input from Hispanic/Latino parents, young people, and community health professionals.

The release of the brochure was accompanied by radio public service announcements in Spanish. The PSAs encourage listeners to learn about the health effects of drug abuse and to talk to their children about them.

Free copies of the brochure are available from the National Clearinghouse for Alcohol and Drug Information (NCADI). Call 1-800-729-6686 and request publication number PHD854S. The brochure can also be downloaded from NIDA's Web site at www.drugabuse.gov.

UPCOMING EVENTS

- September 24-26, 2001: *Bridging Science and Culture to Improve Drug Abuse Research in Minority Communities*, Wyndham Franklin Plaza Hotel, Philadelphia, PA.

  Watch upcoming issues of *NewsScan* for more information on this event, or call NIDA at 301-443-6245.

For more information about any item in this *NewsScan:*

- Reporters, call Michelle Muth, NIDA Press Office, at 301-443-6245
- Congressional staffers, call Keith Van Wagner, NIDA Office of Science Policy and Communications, at 301-443-6071.

The National Institute on Drug Abuse is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports more than 85 percent of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics can be ordered free of charge in English and Spanish by calling NIDA Infofax at 1-888-NIH-NIDA (644-6432) or 1-888-TTY-NIDA (889-6432) for the deaf. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at http://www.drugabuse.gov.