Study reveals possible genetic risk for fetal alcohol disorders

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New research in primates suggests that infants and children who carry a certain gene variant may be more vulnerable to the ill effects of fetal alcohol exposure.

Reported online today (Sept. 21) in *Biological Psychiatry*, the findings represent the first evidence of a genetic risk for fetal alcohol spectrum disorder — a condition that is characterized by profound mental retardation in its most severe form, but which is also associated with deficits in learning, attention, memory and impulse control.

By identifying a genetic marker that might signal susceptibility to these more subtle fetal alcohol-induced problems, the research fills a pressing need, says Mary Schneider, the University of Wisconsin-Madison professor of kinesiology and psychology who led the study.

"The big concern used to be the link between fetal alcohol exposure and mental retardation, but today there is increased concern over behavioral problems in these children," says Schneider. "If this genetic marker could provide a way of recognizing the most vulnerable fetal alcohol-exposed children early in life, perhaps we could help them to live more successful and satisfying lives."

The study's results may also help to explain why some children of mothers who drink during pregnancy suffer birth defects, while others seem to escape unharmed.

"Children who are exposed to alcohol because their mothers drank during pregnancy have varying degrees of problems, and the same is true for monkeys who are exposed to moderate levels of alcohol in utero," says Schneider. "So we know there are other factors involved."

With colleagues at UW-Madison, the University of Toronto and the National Institutes of Health, Schneider investigated two forms of a gene called the serotonin transporter gene promoter, which helps regulate the brain chemical serotonin. Past studies of both people and primates suggest that carriers of a short form of this gene are at increased risk for depression, but only if they also experience adverse life events.

To test whether the gene's short form might also raise the risk of fetal alcohol-induced problems, Schneider's team analyzed data from an ongoing, long-term study into the impacts of moderate fetal alcohol exposure on behavior and brain function in rhesus monkeys. Although fetal alcohol syndrome was first recognized in children of alcoholic mothers, attention has shifted in recent years to moderate drinking because of its potential to affect many more children, says Schneider.

"We know that 60 percent of women of child-bearing age consume alcohol and more than 50 percent of pregnancies are unplanned," she says. "So it doesn't take much to figure out that prenatal exposure to alcohol — at least in the weeks before pregnancy is detected — is substantial."

In line with this, the mother monkeys in the study's experimental group consumed the equivalent of just two alcoholic beverages five times a week during breeding and pregnancy. After the infants were born, the scientists recorded their irritability during a standard battery of developmental tests, measured their reactivity to stress when separated from their mothers at six months for weaning, and determined whether they carried the short or long form of the serotonin transporter gene

promoter.

What the researchers found is that fetal alcohol-exposed infants who carried a copy of the short form were more irritable and reactive to stress than either control group infants who weren't exposed to alcohol or those who were exposed but had two copies of the gene's long form. Overall, says Schneider, the results indicate a "substantial interaction" between fetal alcohol exposure and genotype.

She and her colleagues are now conducting additional studies to see if these findings fit a larger pattern of fetal alcohol-induced problems as the monkeys grow up. At the same time, extreme irritability and stress responsiveness in infants can themselves lead to problems, she says.

"If a baby is very irritable and stress reactive, one of the things this can interfere with is the caregiver-infant interaction," she says. "In real life, negative events tend to cluster. So if there's alcohol in the environment, there may also be stress. And then if you have an irritable baby, this all could have cascading effects on the child's psychological development."

Recognizing that complex behaviors are seldom, if ever, governed by a single gene, Schneider and her colleagues are also investigating other gene alleles for their potential to interact with fetal-alcohol exposure and put children at risk.

"Genetics by themselves rarely tell us much, because life experiences may trigger the actual effects of our genetic vulnerabilities," says Schneider. "So the more knowledge we have about the ways that genes interact with environmental factors, the more we can envision interventions early in life to help a vulnerable child."

Source: UW-Madison