NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD
SCIENCE BRIEFS

NEUROSCIENCE

Fetal Alcohol Exposure Reduces Adult Brain Plasticity

A review of a recent study focusing on the long-lasting effects of alcohol consumption by pregnant mothers.

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Why was the study done? Drugs, alcohol, and chemicals are known to interfere with typical neurodevelopmental processes in fetuses. There are a large number of animal and human studies that illustrate that fetal exposure damages brain architecture and chemistry, with long-lasting effects on cognition and mental and physical health. However, we know that some brain systems remain open to functional changes, a form of brain plasticity that can be elicited through behavioral interventions or even drug therapy. The phenomenon of adult plasticity takes different forms, from more effective communication at synapses to the enhanced production and survival of new neurons in certain brain areas, including the hippocampus. It is as if the brain architecture reserves the option to remodel itself in adulthood, through a biological process known as "adult neurogenesis." Therapies such as enriched environments or anti-depressant drugs are believed to work in part by increasing the production of a certain type of neuron in the adult hippocampus in depressed animals and humans. The hippocampus, involved in memory, learning, and emotional regulation, is one of the few brain structures that normally continue to produce new neurons in adult life. Given the functional importance of producing new neurons, scientists wanted to determine whether moderate fetal alcohol exposure impairs not only ongoing developmental processes, but also the later ability of the mature brain to remodel itself by producing new hippocampal neurons, part of the brain's response to interventions and therapies that are designed to improve behavioral functions. The scientists were able to use a well-defined animal model to test the impact of moderate fetal alcohol exposure on adult brain plasticity.

What did the study find? The study discovered a novel, detrimental, and long-lasting impact of even moderate prenatal exposure to alcohol in a mouse model. Fetal alcohol is a well-known neurotoxin that directly alters the development of brain architecture. Here, the authors show that prenatal exposure can also permanently disturb a form of adult brain plasticity—adult neurogenesis—in the hippocampus. While the study found that there was no difference in the number of new hippocampal neurons produced, the number of neurons that survived for an extended period of time after they were newly produced was far fewer in animals exposed to fetal al-

SCIENCE BRIEFS summarize the findings and implications of a recent study in basic science or clinical resesarch. Studies are selected for review based on their scientific merit and contributions to understanding early development. No single study is definitive, of course. Understanding of early development is based on many studies that, taken together, permit broad conclusions and human applications. Generalizing to human children the results of studies with animals, for example, must be done cautiously and confirmed by research with children and their families. The National Scientific Council rests its work on a rigorous discussion of the validity of many studies like these conducted over many years and using different methodologies and samples.

cohol than in the control animals exposed to an enriched environment. Thus, the fetal alcohol exposure had a negative impact on the survival of neurons produced through adult neurogenesis. These observations suggest that the impact of fetal alcohol exposure extends well into adulthood, where early exposure may result in an impaired ability to respond to behavioral or drug treatments. In effect, early exposure impairs the brain's later ability to remodel itself, closing off functions that provide the healthy brain architecture with suitable adult refinements and repairs.

How was the study conducted? Female mice were exposed to diminishing concentrations of alcohol or a stable amount of saccharin in their drinking water during pregnancy. Previous animal studies have defined this model as exposing fetuses to clinically moderate levels of maternal blood alcohol. The offspring were raised by their mother until weaning at 23 days after birth. The pups then were placed in either a standard or enriched cage, the latter containing toys and multiple climbing objects. It is well know that this type of enriched environment will stimulate adult neurogenesis in the hippocampus when compared to a standard cage environment. At 3 months of age, when mice are considered to be post-pubertal young adults, each animal was injected daily for two weeks with a chemical that labels newly produced neurons in the hippocampus, a measure of adult neurogenesis. Immediately following or one month after the last injection, the hippocampus was collected and the number of labeled neurons was determined using sophisticated counting methods. The number of neurons was compared across four experimental groups: saccharin and standard environment, alcohol and standard environment, saccharin and enriched environment, and alcohol and enriched environment.

What do the findings mean? The authors note that their study defines a new and persistent defect in adult animals exposed to moderate levels of fetal alcohol. Well after exposure, there is normal production but impaired survival of newly generated adult neurons in the hippocampus in response to enriching environments. This finding shows that, beyond disrupted function of the brain due to prenatal alcohol exposure, adult brain plasticity, in the form of the survival of new adult neurons, is also vulnerable to early toxic stressors. The study has implications for intervention strategies. For example, we know that brain circuitry that is not functioning properly may be amenable to improvement through behavioral or drug therapies. However, the circuits need to be receptive to such therapies in order for the interventions to be effective. In the case of trying to improve behaviors that involve the hippocampus, this would involve adult neuron production and survival. This study suggests that fetal alcohol can impair the ability of mature circuits to change, and may therefore cause long-term damage that is more irreparable than was previously believed. It is

important to note that the authors did not examine whether fetal alcohol impairs the ability of new neurons to survive in response to anti-depressant drugs, or whether other forms of adult brain plasticity are influenced by moderate fetal alcohol exposure. New studies are underway to further examine these findings using other measures of brain plasticity.

Title and Authors: Choi, I.Y., Allan, A.M., Cunningham, L.A. (2005) Moderate fetal alcohol exposure impairs the neurogenic response to an enriched environment in adult mice. Alcoholism: Clinical and Experimental Research 29:2053-2062