Study shows lithium chloride blunts brain damage linked to fetal alcohol syndrom

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A single dose of lithium chloride, a drug used to treat bipolar disease and aggression, blocks the sleep disturbances, memory loss, and learning problems tied to fetal alcohol syndrome, new experiments in mice show.

Published in the journal *Neuroscience* online Nov. 26, and led by researchers at NYU School of Medicine, the new study found that giving the drug to newborn mice 15 minutes after "binge" alcohol consumption eliminated the hyperactivity and sleep deficits seen when rodents exposed to alcohol became adults. Moreover, the researchers report, lithium chloride-treated mice were much less likely to show the 25 percent drop in memory and cognitive test scores seen in untreated mice given the same amount of alcohol.

"Our study showed that lithium chloride prevented many of the damaging neurological effects of alcohol abuse on the still-developing brain, especially the impact on the parts of the brain controlling sleep," says co-senior study investigator Donald Wilson, PhD.

Mice given alcohol just after birth are a good model for measuring the impact on human fetal development because the brains of mice pups achieve developmental milestones after birth that are comparable to those in other mammals, including humans.

Wilson, a professor at NYU Langone Health, cautions that it is too early to propose lithium chloride as a treatment or preventive therapy for fetal alcohol syndrome. The drug is "likely far too risky for pregnant

mothers," with known organ toxicities, he says. Further experiments would have to proceed under strict medical supervision to ensure the safety of mothers and children.

A more likely future therapy, says co-senior study investigator Mariko Saito, PhD, would be one that takes advantage of chemistry related to the action of lithium chloride, but with fewer side effects. "Lithium chloride is known to block many pathways that lead to brain cell death, while promoting others that lead to survival, like brain-derived neurotrophic factor, or BDNF," says Saito, a research assistant professor at NYU Langone. Further experiments are needed, she says, to determine if chemicals that stimulate BDNF production also blunt the effects of alcohol abuse in newborn mammals.

Of equal importance, the study brings scientists closer to determining if fixing sleep issues tied to fetal alcohol syndrome alone is key to countering the other developmental effects tied to alcohol abuse, says co-lead study investigator Monica Lewin, MS, a doctoral student at NYU Langone.

Among the study's key findings was that mice given lithium chloride after alcohol consumption and mice that never consumed alcohol had the same duration of undisrupted sleep of about 10 hours per day, while untreated mice given alcohol woke up as many as 50 times per hour. Sleep disturbances in animals and humans have long been linked to cognitive and emotional damage.

Recent work by the same group of researchers showed that such disruptions in sleep were also a hallmark of fetal alcohol syndrome, both in animal models and in people. Mice that slept better and longer, whether suffering from alcohol abuse or not, had better brain function than those that slept more poorly. The brain damage associated with fetal alcohol syndrome is believed to afflict one in 33 newborns in the United

States and occurs when the developing fetus' mother drinks large amounts of alcohol.

Wilson says the team next plans to investigate if lithium chloride can blunt other forms of neurological damage, such as that resulting from trauma and stroke, both of which can kill large groups of brain cells.

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