A family history of alcoholism may add to damaging effects of prenatal alcohol exposure

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Prenatal exposure to alcohol (PAE) can lead to serious deficiencies associated with fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD), such as impairments in general intelligence, adaptive function, verbal learning and memory, attention, executive function, and visual-spatial functioning. The role of family history of alcoholism (FHP) in the neurocognitive effects of PAE has not yet been studied. This study used neuroimaging to examine spatial working memory (SWM) in children with histories of heavy PAE and children with confirmed FHP but not PAE, finding that FHP may in fact have an impact on neural functioning of children with PAE.

Results will be published in the January 2013 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Children with histories of heavy PAE exhibit a broad range of neurocognitive deficits, including deficits in spatial working memory (SWM), which was the focus of this paper," explained Sarah N. Mattson, a professor of psychology at San Diego State University and corresponding author for the study. "Previous studies demonstrated that children with PAE may exhibit difficulties learning spatial locations and later recognizing if an object is in a previously learned location. This type of deficit could impact a variety of real-life behaviors and abilities like route finding, and remembering where personal items are located.

This will be especially true when working memory is taxed, that is, when they have to hold one idea or object in memory while trying to do or remember something else."

Mattson explained that the main goal of this study was to tease apart what neurocognitive effects were due to PAE and what effects were due to having an FHP. "In order to address this question it was imperative to investigate a cognitive function that has been examined in both groups, children with PAE and children with an FHP," she said. "One such function is SWM. This is the first study to address the role of FHP in reported neurocognitive effects of PAE and to suggest there are multiple processes leading to differences in brain function in children with prenatal exposure."

"It is extremely important to examine the influence of FHP on the neurobehavioral effects of PAE," said Piyadasa W. Kodituwakku (Kodi), associate professor of pediatrics and neurosciences at the University of New Mexico School of Medicine. "Atypical brain development in children with FASD results from the interactive effects of PAE, genetic/epigenetic factors, and the quality of postnatal environment," he explained. "Investigators have hitherto been reluctant to include an FHP group in their research designs because of the difficulty of ruling out PAE in children from alcoholic families. Given that family members, particularly spouses, often drink together, one can always suspect that the child may have been exposed to some alcohol during pregnancy."

Mattson and her colleagues selected 53 right-handed children, aged 12 to 18 years, from two ongoing neuroimaging studies, one examining the teratogenic effects of alcohol, and one examining family history of alcohol use disorders (AUDs). The children were divided into three groups: 18 youth (14 males, 4 females) with histories of heavy PAE (ALC), 18 youth (12 males, 6 females) without PAE but with an AUD

family history (FHP), and 17 youth (8 males, 9 females) with no PAE or AUD family history (CON). All participants underwent structural and functional imaging while engaging in a task designed to assess memory for spatial locations relative to a vigilance condition that assessed attention.

"This comparison of brain functioning during SWM, in children with PAE relative to children with an FHP and no exposure, suggests that some but not all aspects or regions of neural functioning within the alcohol-exposed population may in fact be associated with factors other than prenatal exposure, like an FHP," said Mattson. "Other aspects or regions were more specific to the effects of prenatal alcohol exposure and did not occur in the group of subjects without prenatal exposure."

Differences between the ALC group and the FHP and CON groups suggest that the left middle and superior frontal regions may be specifically affected among alcohol-exposed children. Conversely, differences among the ALC and FHP groups versus the CON group in the lentiform nucleus and insular region indicate these areas may be associated with FHP rather than PAE.

"The finding of increased BOLD response in the middle and superior frontal gyri in alcohol-exposed children during working memory task performance is interesting," said Kodituwakku. "Until this finding is replicated, it is hard to say what it signifies. The main contribution that this paper makes to the field of prenatal alcohol research is making an attempt to estimate the effects of FHP on neurocognitive functioning in children with FASD. However, this is a complex methodological issue because the effects of PAE, family history of alcoholism, and postnatal experiences are interactive, not just additive."

"The main idea is that there may be more than one brain functioning mechanism leading to SWM impairment in children prenatally exposed

to alcohol," said Mattson. "Within the context of research on PAE, this paper suggests that differences in brain function in children with heavy PAE may stem from multiple developmental mechanisms, including the insult from PAE and functional differences based on family history. As the alcohol field moves towards intervention, these results suggest multiple approaches may be necessary to address difficulties in SWM or other neurocognitive impairments."

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