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# Youths with a family history of substance use disorders have less efficient forebrain

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Researchers and clinicians know that youths with a family history of alcohol and other drug use disorders (FH+) have a greater risk of developing substance-use disorders (SUDs) than their peers with no such family histories. This increased risk may be related to impaired maturation of forebrain circuitry. A new study examines forebrain activity in youths with a family history of SUDs, finding they had greater activity in several forebrain regions during a specially designed task than their peers with no such family histories, indicating their forebrain regions function less efficiently.

Results will be published in the December 2014 online-only issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"The forebrain is important for several major cognitive processes, including decision-making and impulse control, and activity in several forebrain regions increases when people perform tasks that involve those processes," explained Ashley Acheson, an assistant professor at The University of Texas Health Science Center at San Antonio as well as corresponding author for the study. "Not surprisingly, dysfunctions in the forebrain are involved in many psychiatric disorders, including alcohol and other drug use disorders. FH+ youths and young adults often have impairments in cognitive processes controlled by the forebrain such as decision-making and impulse control, and we think those cognitive impairments may contribute to their increased risk for developing alcohol and other drug problems."

"The term forebrain encompasses large areas of the cerebral cortex that collectively do three things," added William R. Lovallo, professor of psychiatry and behavioral sciences at the University of Oklahoma Health Sciences Center. "The forebrain classifies and identifies events in the environment. It develops a response strategy to the classification step. Finally, it starts the motor process of actually making the motor response."

"We looked at brain activity when kids did a computer task requiring them to quickly respond to some cues but not to others," said Acheson. "Previous studies have focused on how FH+ kids' brain activity looked during the parts of the task when they weren't supposed to respond to cues to see how inhibition circuitry was affected. We looked at brain activity in all parts of the task compared to the rest to see if there were more general differences in brain functioning."

"This study used a task that is especially sensitive to a person's ability to inhibit a response when that response is the one most likely to occur," explained Lovallo. "In the Go/NoGo paradigm, persons have a tendency to respond with a button press when a signal appears on their screen and stopping that requires significant cognitive processing. So, we usually think of the Go/NoGo tasks as being sensitive to impulsive tendencies. Persons who are impulsive are likely to perform worse than less impulsive persons. This is of interest in alcoholism research because of data and theories that view impulsive and less-inhibited persons as being at higher risk of misusing alcohol and recreational drugs."

Acheson and his colleagues tested 72 FH+ (37 females, 35 males) and 32 FH- (18 males, 14 females) youths performing a Go/NoGo task. Go/NoGo tasks activate forebrain circuitry that regulates selective attention and inhibitory control by requiring subjects to selectively respond only to appropriate stimuli (Go cues) and withhold responding to inappropriate stimuli (NoGo cues). The researchers also examined

activations in blocks with only Go trials, blocks with 50-percent Go and 50-percent NoGo trials, and a contrast of those two blocks.

"FH+ kids had more activity than FH- kids in several forebrain regions during all parts of the task, not just when they were supposed to inhibit responding," said Acheson. "Forebrain regions that had increased activity included the medial superior frontal gyrus, which is important for planning movements, and the striatum, which is important for reward and motivation. We think this increased activity is at least partially due to some forebrain regions working less efficiently in FH+ kids. Interestingly, people who had more parents and grandparents with alcohol and other drug use disorders had the greatest activity in these regions."

"In other words, the results were stronger in persons that had a greater number of alcoholic relatives," said Lovallo. "This tends to point to a genuine inheritance of a risk factor and not at some incidental characteristic of these youths. However, this study found differences in the family history of alcoholism subjects on both the Go and the NoGo parts of the task. So the results tell us that there is a generalized information-processing deficit here that may not be specific to impulsivity."

"I think the results show FH+ kids have some forebrain regions that function less efficiently," observed Acheson. "We think this because we and others have found FH+ kids and young adults have poorer development of myelin or the insulation that allows neurons to send fast electrical impulses. Other researchers have found poorer myelination is linked with increased activations, and they think this means neurons are functioning less efficiently."

Lovallo agreed. "The greater cognitive resources expended by the FH+ group might be related to other findings showing that persons with a

family history of alcoholism have poorer functioning white-matter pathways in the brain," he said. "These pathways are the long ones that connect up distant brain regions. It is like trying to talk on a long-distance phone call with static on the line. You need to work harder at your conversation. The present results are consistent with such an explanation. And again, the finding that this is worse in persons with more alcoholic relatives is critical."

"I think our findings help shed light on brain mechanisms that may be important for risk for alcohol and other drug use disorders," said Acheson. "We are following these kids as part of a longitudinal study and will be able to see how the brain differences we are seeing in FH+ kids relate to developing alcohol and drug problems. We hope that better understanding underlying mechanisms that make people vulnerable to addictions will lead to more effective treatment and prevention strategies. I tend to think of alcohol and other drug use disorders as a kitchen sink overflowing with the consequences of chronic heavy use being the water soaking the floor. I think we need to know what makes people misuse alcohol and drugs in the first place in order to treat addictions, like how you need to stop the sink from overflowing before you start mopping up the water on the floor. If we could prevent the sink from overflowing we wouldn't have a mess on the floor to clean up."

"The real-world, take-away message here is that risk for alcoholism in persons with a family history might be a rather generalized effect of less efficient brain function leading to poor behavior regulation," said Lovallo. "In this scenario, persons might be more susceptible to the attractions of alcohol and drugs and less able to control these tendencies once these behaviors begin."

"That said, we need to remember that having a family history of alcohol or other drug use disorders doesn't automatically mean someone will have problems themselves," said Acheson. "Likewise, many teenagers

with no alcohol or drug problems in the family still go on to develop drug problems. What parents can do to help their children avoid serious substance use problems includes knowing who their children's friends are, decreasing unsupervised time, promoting organized activities and generally keeping kids busy, and communicating with their children about potential negative consequences of alcohol and drug use."

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