Brain chemistry ties anxiety and alcoholism

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Doctors may one day be able to control alcohol addiction by manipulating the molecular events in the brain that underlie anxiety associated with alcohol withdrawal, researchers at the University of Illinois at Chicago College of Medicine and the Jesse Brown VA Medical Center report in the March 5 issue of the Journal of Neuroscience.

"The association of anxiety with increased alcohol use is a key factor in the initiation and maintenance of alcohol addition," says Dr. Subhash Pandey, UIC professor of psychiatry and director of neuroscience alcoholism research, the lead author of the study.

Previous research has shown that people with inherently high levels of anxiety are at an increased risk of becoming alcoholics. In addition, withdrawal of alcohol in chronic users is often accompanied by extreme anxiety.

"Alcoholics may feel a need to continue to drink alcohol in an attempt to self-medicate to reduce their anxiety and other unpleasant withdrawal symptoms," said Pandey.

Pandey and his colleagues have discovered the molecular basis for the link between anxiety and alcohol addiction, which may help in identifying new therapeutic strategies for the treatment of alcohol addiction.

The researchers found that a protein within neurons in the amygdala --

the area of the brain associated with emotion and anxiety -- controls the development of alcohol withdrawal symptoms and drinking behaviors in laboratory animals by changing the shape of the neurons. This change in shape affects the communication between neurons, leading to changes in behavior.

Neurons communicate by sending signals through branches called dendritic spines. The researchers found that short-term alcohol exposure increased the number of dendritic spines in certain regions of the amygdala, producing anti-anxiety effects. Alcohol-dependent animals eventually developed a tolerance to the anxiety-lowering effects of alcohol.

The researchers traced the anti-anxiety effect to the production of a particular protein, Arc, in response to a nerve growth factor called BDNF that is stimulated by alcohol exposure. BDNF is vital in the functioning and maintenance of neurons.

When alcohol was withheld from animals that had been chronically exposed, they developed high anxiety. Levels of BDNF and Arc -- and the number of dendritic spines -- were decreased in the amygdala. But the researchers were able to eliminate the anxiety in the alcohol-dependent animals by restoring BDNF and Arc to normal levels.

Pandey suggested that an initial easing of anxiety may encourage people to begin to use alcohol, while for chronic users, a lack of alcohol provokes high anxiety, creating a need to continue drinking to feel normal.

The researchers blocked Arc production in normal rats by injecting a complementary sequence to Arc gene DNA into the central amygdala. They found that when levels of Arc in the central amygdala were lowered, the spines decreased and anxiety and alcohol consumption

increased. When levels of Arc were returned to normal three days post-injection, anxiety and alcohol consumption also returned to normal. In a previous study, researchers found that lowering BDNF in amygdala promoted anxiety and alcohol drinking.

"This is the first direct evidence of the molecular processes occurring in the neurons that is responsible for the co-morbidity of anxiety and alcoholism, which we believe plays a major role in the addictive nature of alcohol," said Pandey.

"This offers the possibility of new therapeutic target -- BDNF-Arc signaling and associated dendritic spines in the amygdala -- or new drug development."

"These observations by Dr. Pandey's research group provide an insight into the link between alcohol and anxiety and could be used to identify new targets for developing medications that alleviate withdrawal-induced anxiety and potentially modify a motivation for drinking," said Antonio Noronha, director of neuroscience and behavior research at the National Institute on Alcohol Abuse and Alcoholism.

Source: University of Illinois at Chicago