Excessive drinking and relapse rapidly cut in new approach

9 June 2008

Boosting the level of a specific brain protein quickly cut excessive drinking of alcohol in a new animal study, and also prevented relapse -- the common tendency found in sober alcoholics to easily return to heavy drinking after just one glass.

In addition, the treatment did not block other "pleasure-seeking behaviors" -- in this case, craving sweets. Interference with these normal behaviors has been a problem with drugs developed for alcoholism treatment. Nor did the brain chemical boost appear to carry any side effects, the study researchers report.

The findings are being published June 9 in *The Proceedings of the National Academy of Sciences.*

The research by scientists at theUCSF-affiliatedErnest Gallo Clinic and Research Center builds on their earlier work. In 2005, they reported the first hints that increased levels of this brain protein, known as GDNF, cut down alcohol consumption. The new study established how quickly the effect kicks in, and shows for the first time that the chemical blocks relapse and does not interfere with normal cravings. The research also pinpointed the brain site where GDNF acts to control drinking.

"Alcoholism is a devastating and costly psychiatric disease with enormous socioeconomic impact," said Dorit Ron, PhD, senior author on the paper and principal investigator at the Gallo Center. "There is a tremendous need for therapies to treat alcohol abuse."

"Unfortunately, only three drugs are currently approved to treat excessive drinking, and all have serious limitations. Our findings open the door to a promising new strategy to combat alcohol abuse, addiction and especially relapse." Ron is also associate professor of neurology at UCSF.

GDNF, or glial cell-derived neurotrophic factor, is already a focus of strong interest for treating Parkinson's disease. A new orally-delivered, experimentaldrug has been shown to raise brain GDNF levels in rats, suggesting its promise against Parkinson's. Research by Ron and her colleagues suggests such a drug might also treat alcoholism.

The Gallo Center scientists set out to test the actions of GDNF in a brain site known as the Ventral Tegmental Area, or VTA, a region of the brain thought to be strongly involved in drug-seeking behavior. The first part of the study was designed to model both human social and excessive drinking. Researchers first trained rats to seek alcohol for two months. GDNF was then injected into the VTA brain region, and their motivation to drink in both models dropped significantly within as little as 10 minutes. The effect lasted at least three hours, the scientists reported.

In a second part of the study, rats had access to sugar water, and the scientists showed that after GDNF treatment, the animals still sought sugar -- convincing evidence that increased GDNF did not decrease other, related pleasure-seeking behaviors.

In a third research arm designed to model the risk of relapse behavior, the rats were trained to press a lever to get alcohol. Once they became highly motivated to seek alcohol, it was taken away. At first, they still pressed the lever to get their drink, but eventually they gave up – like people after rehab, Ron says. When alcohol was reintroduced, they relapsed, pressing for the same amount as before. But when they were treated with GDNF, they quickly lost their taste for alcohol.

The scientists are now studying whether any FDA-approved drugs might stimulate GDNF activity in the brain. If an already-prescribed drug has this capacity, it could become a valued addition to the woefully small arsenal of treatments for alcoholism, Ron says.

Source: University of California - San Francisco