New study reveals brain cell mechanism of alcohol dependence

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A study released today reveals a cellular mechanism involved in alcohol dependence. The study, in the May 28 issue of *The Journal of Neuroscience*, shows that gabapentin, a drug used to treat chronic pain and epilepsy, reduces alcohol intake in alcohol-dependent rats by normalizing chemical communication between neurons, which is altered by chronic alcohol abuse.

The central amygdala, a part of the brain involved in emotions such as stress and fear, is important in regulating alcohol consumption. Most central amygdala neurons communicate via a chemical signal known as GABA, which is an inhibitory neurotransmitter. Alcohol dependence has been associated with the strengthening of inhibitory synapses in this brain region.

Gabapentin (known commercially as Neurontin) is structurally similar to GABA and increases GABA neurotransmission. In alcoholics, gabapentin has been shown to effectively treat alcohol withdrawal and reduce alcohol consumption and cravings following detoxification. However, how gabapentin acts in the brain to combat alcohol dependence has been unclear.

The study's authors, led by Marisa Roberto, PhD, at the The Scripps Research Institute, made rats dependent on alcohol by chronically exposing them to ethanol in an aerosol or in their food. They then tested how much alcohol the rats voluntarily drank and examined neural signaling in the central amygdala.

The study authors found that gabapentin reduced alcohol intake in rats chronically exposed to alcohol, but not in rats that were chronically unexposed. Gabapentin reduced alcohol intake in alcohol-dependent rats whether it was given systemically or infused directly into the central amygdala, supporting the importance of the central amygdala in alcohol dependence.

“What I find to be important about this paper is that gabapentin’s effect on alcohol consumption is only seen in alcohol-dependent rats,” said Julie Blendy, PhD, at the University of Pennsylvania, an expert unaffiliated with the study. “For me, this speaks volumes to the addiction field, in that therapeutic targets for addiction—which have been few and far between—may be missed when examined in animal studies that use only minor exposures of alcohol,” said Blendy.

Gabapentin corrected the cellular effects of chronic alcohol exposure. Both gabapentin and alcohol increase GABA neurotransmission in the central amygdala of non-alcohol-dependent rats, but in alcohol-dependent rats, gabapentin reduced it, suggesting that altered GABA neurotransmission is key to alcohol dependence.

In the study, gabapentin and chronic alcohol exposure both affected GABA B (GABAB) receptors. The authors believe that alcohol abuse alters the function of these receptors, and gabapentin may be able to counteract alcohol dependence by regulating their function.

“This study provides important mechanistic insights,” said Robert Messing, MD, at the Ernest Gallo Clinic and Research Center at the University of California at San Francisco, an expert also uninvolved with the study. “Because gabapentin is well tolerated, this paper provides a strong rationale for large clinical trials testing whether gabapentin is an effective treatment for alcoholism in both detoxified and actively drinking alcoholics,” Messing said.

Source: Society for Neuroscience