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FEATURED ARTICLES

Kicking the habit

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A new treatment that blocks a neurotransmitter receptor involved in anxiety may benefit people with alcoholism.

After a stressful day, many people reach for a drink. Similarly, chronic stress increases alcohol consumption in rats. In people with alcohol dependence, or alcoholism, stress is a strong trigger for relapse, and prolonged alcohol use increases sensitivity to stress. Now George *et al*. report that blocking a neurotransmitter receptor active in stress reduces alcohol intake in mice and alcohol cravings in people in a recent article in *Science*.

Although best known for involvement in pain, substance P and its receptor neurokinin 1 receptor (NK1R) localize to brain regions involved in fear and anxiety. Psychological stressors induce substance P release, and NK1R antagonists reduce social anxiety. Animal studies suggest that NK1R is also involved in drug reward. Because of its role in stress and drug reward, the authors wondered whether NK1R mediates stress-associated aspects of alcohol abuse.

NK1R deficiency reduced the motivation to drink. Given a choice between water and alcohol, NK1R knockout mice drank less alcohol than wild-type mice. Relative to people who drink occasionally, people with alcoholism tend to be more sensitive to alcohol. After treatment with a sedating dose of alcohol, NK1R knockout mice were slower to wake than wild-type mice, suggesting that NK1R deficiency makes mice more sensitive to alcohol.

Current treatments for alcoholism include the deterrent disulfiram, which induces headaches and vomiting when combined with alcohol, and naltrexone, which is not effective for everyone. Does an NK1R antagonist reduce alcohol craving in people? The authors treated people with alcoholism who had completed withdrawal and had high scores in tests of anxiety with an NK1R antagonist that is currently in Phase II clinical trials. Relative to placebo, the NK1R antagonist decreased self-reported alcohol cravings. Clinicians blind to treatment group rated disease severity as lower in people treated with the NK1R antagonist relative to placebo.

The NK1R antagonist decreased stress-induced cravings in people with alcoholism. Researchers asked people to make a spontaneous speech and do math problems in front of an audience. Then, they showed them alcohol-related cues. Relative to people treated with placebo, people treated with the NK1R antagonist reported fewer stress- and alcohol-induced cravings and had a smaller stress response. The NK1R antagonist also decreased brain activity in the insula, a region associated with drug craving.

These data suggest that blocking NK1R may benefit people who abuse alcohol or other drugs. However, this small clinical trial only examined people with alcoholism and anxiety, so it will be important to address whether this treatment will be effective for people with different temperaments.

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1. George, D. T. *et al.* Neurokinin 1 receptor antagonism as a possible therapy for alcoholism. *Science* **319**, 1536–1539 (2008). | Article | PubMed | ChemPort |