# How alcohol consumption contributes to chronic pain

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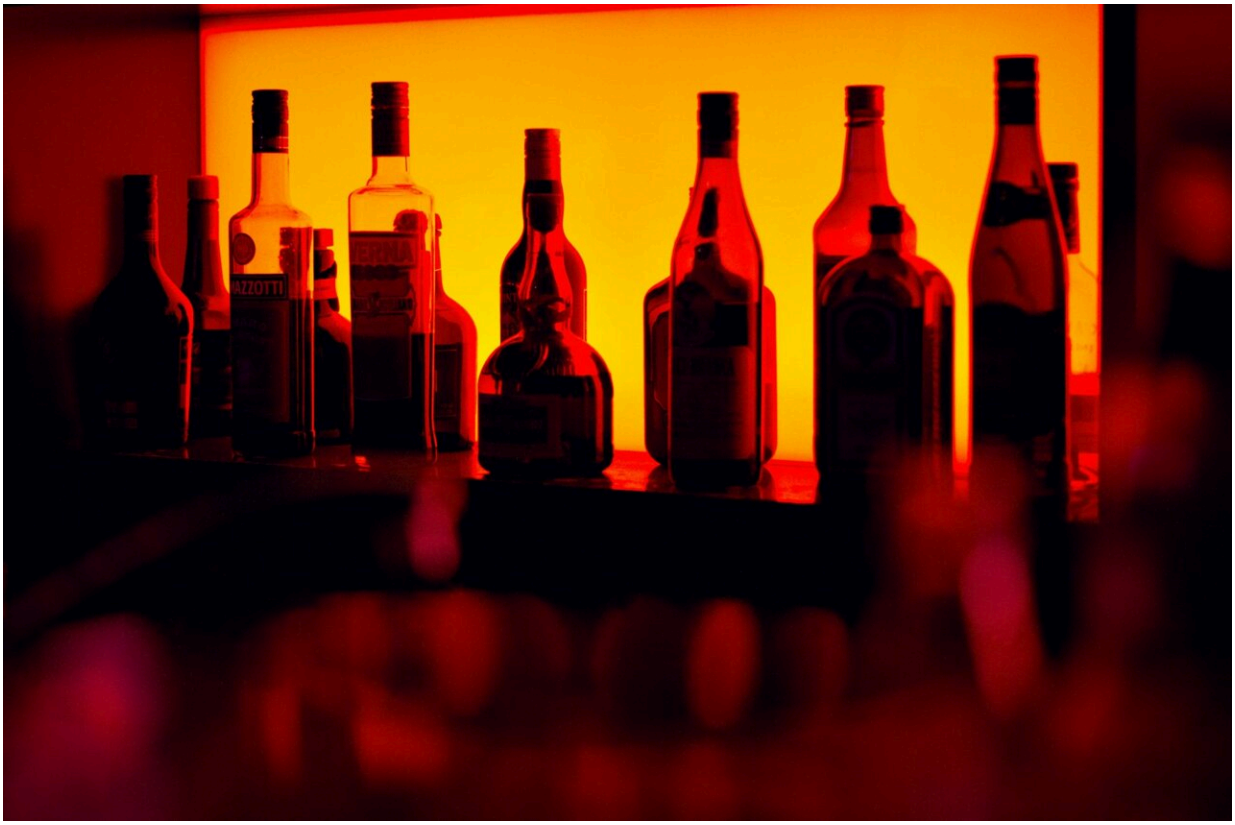

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Chronic alcohol consumption may make people more sensitive to pain through two different molecular mechanisms—one driven by alcohol intake and one by alcohol withdrawal. That is one new conclusion by

scientists at Scripps Research on the complex links between alcohol and pain.

The research, published in the *British Journal of Pharmacology* on April 12, 2023, also suggests potential new drug targets for treating alcohol-associated chronic pain and hypersensitivity.

"There is an urgent need to better understand the two-way street between chronic pain and alcohol dependence," says senior author Marisa Roberto, Ph.D., the Schimmel Family Chair of Molecular Medicine, and a professor of neuroscience at Scripps Research. "Pain is both a widespread symptom in patients suffering from alcohol dependence, as well as a reason why people are driven to drink again."

Alcohol use disorder (AUD), which encompasses the conditions commonly called alcohol abuse, alcohol dependence and alcohol addiction, affects 29.5 million people in the U.S. according to the 2021 National Survey on Drug Use and Health. Over time, AUD can trigger the development of numerous chronic diseases, including heart disease, stroke, liver disease and some cancers.

Among the many impacts of long-term alcohol consumption is pain: more than half of people with AUD experience persistent pain of some type. This includes alcoholic neuropathy, which is nerve damage that causes chronic pain and other symptoms. Studies have also found that AUD is associated with changes in how the brain processes pain signals, as well as changes to how immune system activation occurs. In turn, this pain can lead to increased alcohol consumption. Moreover, during withdrawal, people with AUD can experience allodynia, in which a harmless stimulus is perceived as painful.

Roberto and her colleagues were interested in learning the underlying causes of these different types of alcohol-related pain. In the new study,

they compared three groups of adult mice: animals that were dependent on alcohol (excessive drinkers), animals that had limited access to alcohol and were not considered dependent (moderate drinkers), and those that had never been given alcohol.

In dependent mice, allodynia developed during alcohol withdrawal, and subsequent alcohol access significantly decreased pain sensitivity. Separately, about half of the mice that were not dependent on alcohol also showed signs of increased pain sensitivity during alcohol withdrawal but, unlike the dependent mice, this neuropathy was not reversed by re-exposure to alcohol.

When Roberto's group then measured levels of inflammatory proteins in the animals, they discovered that while inflammation pathways were elevated in both dependent and non-dependent animals, specific molecules were only increased in dependent mice. This indicates that different molecular mechanisms may drive the two types of pain. It also suggests which inflammatory proteins may be useful as drug targets to combat alcohol-related pain.

"These two types of pain vary greatly, which is why it is important to be able to distinguish between them and develop different ways to treat each type," says first author Vittoria Borgonetti, Ph.D., a postdoctoral associate at Scripps Research.

Roberto's group is continuing studies on how these molecules might be used to diagnose or treat alcohol-related chronic pain conditions.

"Our goal is to unveil new potential molecular targets that can be used to distinguish these types of pain and potentially be used in the future for the development of therapies," says co-senior author Nicoletta Galeotti, Ph.D., associate professor of preclinical pharmacology at the University of Florence.

**More information:** Vittoria Borgonetti et al, Chronic alcohol induced mechanical allodynia by promoting neuroinflammation: a mouse model of alcohol-evoked neuropathic pain., *British Journal of Pharmacology* (2023). DOI: 10.1111/bph.16091