

Chronic alcohol use reshapes the brain's immune landscape, driving anxiety and addiction

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Deep within the brain, a small almond-shaped region called the amygdala plays a vital role in how we exhibit emotion, behavior and

motivation. Understandably, it's also strongly implicated in alcohol abuse, making it a long-running focus of Marisa Roberto, Ph.D., professor in Scripps Research's Department of Molecular Medicine.

Now, for the first time, Roberto and her team have identified important changes to anti-inflammatory mechanisms and cellular activity in the amygdala that drive [alcohol addiction](#). By countering this process in mice, they were able to stop [excessive alcohol consumption](#)—revealing a potential treatment path for [alcohol](#) use disorder. The study is published in *Progress in Neurobiology*.

"We found that chronic alcohol exposure compromises brain immune cells, which are important for maintaining healthy neurons," says Reesha Patel, Ph.D., a postdoctoral fellow in Roberto's lab and first author of the study. "The resulting damage fuels anxiety and alcohol drinking that may lead to alcohol use disorder."

Roberto's study looked specifically at an immune protein called Interleukin 10, or IL-10, which is prevalent in the brain. IL-10 is known to have potent anti-inflammatory properties, which ensures that the immune system doesn't respond too powerfully to disease threats. In the brain, IL-10 helps to limit inflammation from injury or disease, such as stroke or Alzheimer's. But it also appears to influence key behaviors associated with chronic alcohol use.

In mice with chronic alcohol use, IL-10 was significantly reduced in the amygdala and didn't signal properly to neurons, contributing to increased alcohol intake. By boosting IL-10 signaling in the brain, however, the scientists could reverse the aberrant effects. Notably, they observed a stark reduction in anxiety-like behaviors and motivation to drink alcohol.

"We've shown that inflammatory immune responses in the brain are very much at play in the development and maintenance of [alcohol use](#)

[disorder](#)," Roberto says. "But perhaps more importantly, we provided a new framework for therapeutic intervention, pointing to anti-inflammatory mechanisms."

Alcohol use disorder is widespread, affecting some 15 million people in the United States, and few effective treatments exist. By examining how brain cells change with prolonged exposure to alcohol, Roberto's lab has uncovered many possible new therapeutic approaches for those with alcohol addiction.

In the latest study, Roberto's lab collaborated with Silke Paust, Ph.D., associate professor in the Department of Immunology and Microbiology. Paust and her team determined the precise immune cells throughout the whole brain that are affected by chronic alcohol use. The findings revealed a large shift in the brain immune landscape, with increased levels of [immune cells](#) known as microglia and T-regulatory cells, which produce IL-10.

Despite a higher number of IL-10-producing cells in the whole brain of mice with prolonged alcohol use, the amygdala told a different story. In that region, levels of IL-10 were lower and their signaling function was compromised—suggesting that the [immune system](#) in the amygdala responds uniquely to chronic alcohol use.

This study complements recent findings by the Roberto lab demonstrating a casual role for microglia in the development of alcohol dependence.

Future studies will build on these findings to identify exactly how and when IL-10 signals to neurons in the amygdala and other addition-related [brain](#) circuits to alter behavior.

More information: Reesha R. Patel et al, IL-10 normalizes aberrant

amygdala GABA transmission and reverses anxiety-like behavior and dependence-induced escalation of alcohol intake, *Progress in Neurobiology* (2020). [DOI: 10.1016/j.pneurobio.2020.101952](https://doi.org/10.1016/j.pneurobio.2020.101952)

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