

# Treatment keeps alcoholic monkeys from drinking as much

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A hormone produced by the liver called fibroblast growth factor 21 (FGF21) suppresses alcohol consumption in primates, finds a study published February 1 in the journal *Cell Metabolism*. Vervet monkeys

with a strong preference for ethanol that were given an FGF21 analogue consumed 50% less alcohol. The study also studied the brain circuits involved in mice and found that the protein, known to also reduce sugar intake, acts on different circuits to reduce alcohol and sugar consumption.

"When considering how and why these modality specific mechanisms evolved, it is interesting to note that mammals were primarily exposed to alcohol from fermenting fruits, which possess high levels of simple sugars," says senior study author Matthew Potthoff of the University of Iowa Carver College of Medicine. "Despite this, [neural circuits](#) regulating FGF21-mediated suppression of sugar and alcohol intake apparently developed independently and not in response to a shared selective pressure."

Excessive alcohol consumption is a major health and social issue in our society. Given that [excessive alcohol consumption](#) negatively impacts health and survival, it is not surprising that numerous physiological systems have evolved to sense and regulate it in mammals.

Unfortunately, efforts to therapeutically target pathways that regulate alcohol consumption have been limited in their ability to effectively treat alcohol use disorder.

Recently, [genome-wide association studies](#) have shown that FGF21 genetic variants are linked to increased alcohol consumption in humans. In rodents, pharmacologic administration of this protein, which is produced in the liver, reduces alcohol consumption through actions in the brain. But until now, the neural circuits through which FGF21 inhibits alcohol consumption were unknown, as were its effects on alcohol consumption in higher organisms.

In the new study, Potthoff and co-first author Kyle Flippo of the University of Iowa and international collaborators, including co-first

authors Drs. Matthew Gillum and Samuel Trammell of the University of Copenhagen, showed that administration of an FGF21 analogue reduces alcohol intake by 50% in vervet monkeys with a strong innate preference for ethanol. FGF21 and the FGF21 analogue decrease [alcohol intake](#) even when administered after prolonged ethanol exposure in mice and primates.

FGF21 alters neural transmission in the nucleus accumbens, a brain region that plays a complex role in reward and addiction, and suppresses alcohol consumption through a sub-population of neurons in the basolateral amygdala. Specifically, FGF21 signaling in neurons that project from the basolateral amygdala to the [nucleus accumbens](#) suppresses alcohol consumption by changing the activity of a specific subpopulation of these neurons. Previous studies have shown that this pathway is involved in reward-seeking behavior. According to the authors, more research is needed to investigate the specific effects of FGF21 on the activity of these neurons during [alcohol consumption](#) in animal models.

"Our results provide a mechanism for a liver-to-brain endocrine feedback loop that presumably functions to protect the liver from damage," Flippo says. "The central molecular and cellular effects of FGF21 represent an opportunity for future research, and the present data indicates that FGF21 analogues may provide a potential treatment option against alcohol-use disorder and related diagnosis."

**More information:** Matthew J. Potthoff, FGF21 suppresses alcohol consumption through an amygdalo-striatal circuit, *Cell Metabolism* (2022). [DOI: 10.1016/j.cmet.2021.12.024](https://doi.org/10.1016/j.cmet.2021.12.024). [www.cell.com/cell-metabolism/f ... 1550-4131\(21\)00690-2](https://www.cell.com/cell-metabolism/f...1550-4131(21)00690-2)

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