Neurons in the dorsomedial striatum play a critical role in excessive alcohol consumption

Exciting D1 medium spiny neurons and Inhibiting D2 medium spiny neurons leads to excessive alcohol consumption in mice.

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Approximately 14.4 million people ages 18 and older were diagnosed with Alcohol Use Disorder (AUD) in 2018. Of these people, only 7.9% received treatment. The striatum is a brain area that has been implicated in drug and alcohol addiction. The dorsomedial striatum (DSM) controls goal-directed behaviors. Neurons are the basic working unit of the brain. Specifically, the DSM contains specialized neurons called medium spiny neurons. MSN are medium-sized units that contain many little spines. These neurons express either dopamine D1 receptors, which are excitatory, or dopamine D2 receptors, which are inhibitory. There have been gaps in how these D1 and D2 expressing neurons are involved in alcohol addiction. The goal of this paper was to look at the role of D1 and D2 MSNs in alcohol consumption to identify a target for the development of a new therapeutic approach to alcoholism.

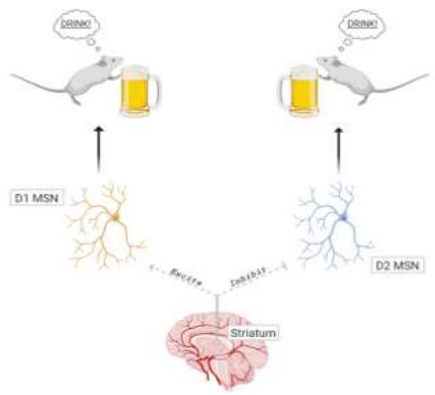

Figure 1. Excitation of D1 MSN and inhibition of D1 MSN promotes alcohol consumption.

A paper published in the Biological Psychiatry (2017) by Yifeng Cheng and colleagues investigates the role of MSN expressing different dopamine receptors, D1 and D2, on alcohol consumption in mice. They used twelve-week old male mice that were housed individually under 12-hour light and dark cycles. The mice were given intermittent accesses to two bottle choices: one containing 20% alcohol (ethanol) and another containing water. The bottles were alternated every session to control for side preference among the mice. This was done for 8 weeks. 24 hours after the last alcohol consumption, the mice were sacrificed, and their brains were sectioned sagittally or coronally.

The first part of their analysis included observing N-methyl-D-aspartate receptor (NMDAR) transmission since these receptors are the main target for alcohol. What they found is that NMDAR transmission was dramatically increased in D1 MSN where mice exposed to alcohol. However, D2 MSN did not have such a drastic increase. Instead, they found that these D2

MSNs increase the effect of GABAergic transmissions. GABA is a type of chemical signal in the brain that inhibits or blocks signals. So, what this means is that these D2 MSNs are sending inhibitory signals. The second finding was that D2 receptors can inhibit these GABAergic signals from D2 MSN through the use of GSK3β (an enzyme) activity. This means that D2 receptors and GSK3β play a significant role in alcohol consumption.

The main finding was that exciting D1 MSN in the dorsomedial striatum increased alcohol consumption in mice, as well as inhibiting D2 MSN. These findings revealed that D2 and D1 expressing MSN play a critical role in alcohol abuse. They also provided a mechanism for alcohol consumption in the dorsomedial striatum. Excessive alcohol consumption results in excitatory strengthening of D1 MSN and inhibitory strengthening of D2 MSN. Therefore, increasing and decreasing the strength of their correlating pathways. This information gives insight into a new target site for future treatment approaches.

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