

Window to brain's reward system could lead to better treatments for alcoholism

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Credit: Imperial College London

Scanning the brains of alcoholics taking medication to beat their addiction has revealed new insights into how the treatments work.

In a small trial, carried out at Imperial College London, researchers have provided a unique view into the brains of active alcoholics taking a newly licensed treatment, showing that the medication blunts the brain's reward pathway.

The team believes the findings could help to improve existing drug treatments for alcoholism by targeting them to those who are most likely to benefit, and even lead to the development of more effective treatments.

Led by Professor Anne Lingford-Hughes, a consultant psychiatrist and addiction expert in Imperial's Department of Medicine, the group set out to explore the effects of nalmefene – a compound which modulates opioid receptors in the brain – in alcoholics.

Nalmefene has been successfully shown to treat

alcoholism and also pathological gambling. It appears to work by effectively dulling the desire for alcohol, or the need for a 'win', but exactly how it affected the brain was unclear.

Now, findings from the Imperial team's latest study suggest that the drug blunts the response in key areas of the brain involved in habit formation. The researchers believe nalmefene effectively reduces the anticipation of alcohol by interfering with the brain's dopamine-based reward systems.

"The findings indicate that the mechanism proposed to explain how the drug works is correct," said Professor Lingford-Hughes. "Certainly this fits with my clinical experience, where people describe how being on these opiate blocking drugs means that they may start drinking, but then they just don't want any more – they don't crave it, they don't desire it, it doesn't taste nice or give them a good feeling."

Blunting the reward system

In the latest study, published in the journal *Biological Psychiatry*, the team recruited 22 alcoholics who were not currently seeking treatment to see the effect of nalmefene. The volunteers were asked to perform tasks in an MRI scanner and were administered the single dose of the drug, equivalent to what they would receive in the real world setting (18 mg).

As part of a classic reward anticipation set up, participants were shown a screen with symbols flashing up, some of which meant they would win a small cash reward.

Throughout the task, snapshots of their brain activity were taken using the fMRI, highlighting when they were anticipating the reward.

However, unlike other studies, the volunteers were under the influence of alcohol, receiving an

intravenous infusion to bring their blood-alcohol levels up to the English [drink drive limit](#) (80 mg per 100 mL of blood).

Scans revealed that when patients took nalmefene with alcohol, activity in two areas of the brain, the dorsal and ventral striatum, decreased.

Neuroscientists believe that these regions are key in habit-formation, with activity shifting from the ventral to the dorsal region as the habit develops. But in the heavy drinking volunteers, the feedback system was dampened down by nalmefene, which was linked with reduced anticipation of a reward.

Professor Lingford-Hughes explained: "We are trying to understand the underlying brain mechanisms in addiction and one of the ways of doing this is that if you know a [treatment](#) can help people, you can look at what it is doing to brain processes and see what it is modulating."

The team believes that not only could the work lead to better targeting of existing drugs, it could also help to develop new drug treatments for alcoholism. They stress that one of the limitations of the study is the lack of a control scan, where the volunteers would have been imaged without the influence of alcohol.

However, previous studies testing similar drugs in patients who were not under the influence of alcohol showed a lack of modulation of brain pathways, hinting that the treatments are most effective in the presence of alcohol - something consistent with clinical findings.

"What our findings show is that if patients have been pre-treated with this [drug](#), we blunt the response to that monetary reward, so they seem to be getting less [brain](#) activation to the rewarding stimulus," added Professor Lingford-Hughes.

"We can infer from that that it may be helpful in blunting the drive that makes them want more of the same thing – such as [alcohol](#) – and is consistent with the hypothesis on how the drugs work, by activating the [reward](#) system less."

More information: Darren R. Quelch et al.

Nalmefene Reduces Reward Anticipation in Alcohol Dependence: An Experimental Functional Magnetic Resonance Imaging Study, *Biological Psychiatry* (2017). [DOI: 10.1016/j.biopsych.2016.12.029](#)

Provided by Imperial College London

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