

One step closer to a new drug for alcohol dependence

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Researchers at Karolinska Institutet and the Sahlgrenska Academy in Sweden might be one step closer to finding an effective drug for alcohol dependence. In two separate studies, they show that the dopamine stabilizer OSU6162 can reduce the craving for alcohol in alcohol dependent people and normalises the level of dopamine in the brain reward system of rats that have consumed alcohol over a long period of time. However, thorough clinical studies are needed to determine if the OSU6162 also can help alcohol dependent people drink less alcohol.

"The results of our studies are promising, but there is still a long way to go before we have a marketable drug," says Pia Steensland, PhD, Associate Professor at the Department of Clinical Neuroscience of Karolinska Institutet, and co-author of both studies. "The socioeconomic costs of alcohol are huge, not to mention the human suffering. It is inspiring to continue working."

Roughly a million Swedes over 15 years of age drink so much alcohol that they risk damaging their health, and it is estimated that some 300,000 of these people are dependent. Despite the pressing need, there are only a few approved drugs for the treatment of alcohol dependence, but their effects vary from person to person and the prescriptions rates are low. Consequently the hunt for new, more efficacious drugs for alcohol dependence continues.

The studies of OSU6162 are based on the knowledge of how the [brain reward](#) system stimulates us to act in the interests of our own survival. Since [dopamine](#) creates a feeling of wellbeing, such as when we exercise or eat good food, the memory associates the two so that we will repeat the behaviour. Alcohol makes the brain reward system release more dopamine than normal, creating a pleasant euphoric sensation. However, the more alcohol drunk, the more the reward system is desensitised and the less

dopamine is released. With time, greater volumes of alcohol are needed to cause intoxication and eventually to attain a state of physical and emotional normality - addiction has set in.

In the clinical study, which is published in the [scientific journal](#) *European Neuropsychopharmacology*, the scientists examined for the first time if OSU6162 can reduce the craving for alcohol in people with [alcohol dependence](#). Half the participants were treated with OSU6162 and half with placebo for a fortnight, after which both groups were exposed to different situations that could be assumed to elicit a craving for alcohol. The results show that the experimental group experienced less of a craving for alcohol after drinking one glass of an alcoholic beverage.

"At the same time, the OSU6162 group reported not enjoying the first sip of alcohol as much as the placebo group," says Dr Steensland. "One interesting secondary finding was that those with the poorest impulse control, that is those thought to be most at risk of relapse after a period of abstinence, were those who responded best to the OSU6162 treatment."

A study of rats published at the same time in the scientific journal *Addiction Biology* adds to the understanding of how OSU6162 works, as it shows that rats that voluntarily consumed alcohol for almost a year had lower levels of dopamine in their brain reward system than rats that had never drunk alcohol. However, when the "alcohol rats" were treated with OSU6162 it was found that the substance counteracted the low concentrations of dopamine in the brain reward system.

"We therefore think that OSU6162 can reduce the [alcohol](#) craving in dependent people by returning the downregulated levels of dopamine in their brain [reward system](#) to normal," says Dr Steensland.

More information: 'The Effects of the Monoamine

Stabilizer (-)-OSU6162 on Craving in Alcohol Dependent Individuals: A Human Laboratory Study', Lotfi Khemiri, Pia Steensland, Joar Guterstam, Olof Beck, Arvid Carlsson, Johan Franck, Nitya Jayaram-Lindström, *European Neuropsychopharmacology*, online 6 October 2015, doi:org/10.1016/j.euroneuro.2015.09.018.

'The Monoamine Stabilizer (-)-OSU6162 Counteracts Down-Regulated Dopamine Output in the Nucleus Accumbens of Long-Term Drinking Wistar Rats', Kristin Feltmann, Ida Fredriksson, Malin Wirf, Björn Schilström, Pia Steensland, *Addiction Biology*, online 14 October 2015, DOI: [10.1111/adb.12304](https://doi.org/10.1111/adb.12304).

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