

# RESEARCH HIGHLIGHTS

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## ADDICTION

### Herbal remedy

Ibogaine, which is derived from an African shrub, has long been thought to help alcoholics and drug addicts to kick the habit, but its side effects, such as hallucinations, have kept it off pharmacy shelves. Now, a new study has identified a molecular pathway that is responsible for ibogaine's anti-addiction effects, which might open the door for the development of other drugs to reverse addiction without undesirable side effects.

Reporting in the *Journal of Neuroscience*, He and colleagues found that systemic administration of ibogaine decreased alcohol consumption in rats that had been trained to drink alcohol voluntarily. The treatment was also effective in a relapse model, in which rats were re-exposed to alcohol after a period of abstinence. As the ventral tegmental area (VTA) is one of the main brain regions in the 'reward' circuitry that is altered in alcohol addicts, the authors injected ibogaine into this part of the rat brain and found that this also kept alcohol consumption at bay.

But how does ibogaine interfere with the rewarding effects of alcohol? Previous research has shown that chronic cocaine or morphine administration results in decreased activity of the glial cell line-derived neurotrophic factor (GDNF) pathway in rats, and that injection of GDNF into the VTA can block the behavioural effects of these drugs. In this study, systemic ibogaine administration increased the expression of GDNF mRNA in the midbrain dopaminer-

gic region that includes the VTA.

As dopamine is the key neurotransmitter that is consistently associated with reward, the authors used a dopaminergic neuroblastoma cell line to study the downstream signalling events that are activated by ibogaine. Ibogaine induces an increase in GDNF mRNA expression, which leads to increased secretion of GDNF and activation of downstream signalling molecules such as mitogen-activated protein kinases. Importantly, injection of GDNF into the VTA also reduces alcohol intake in rats, and anti-GDNF neutralizing antibodies markedly attenuate the effect of ibogaine on alcohol consumption.

This study shows a direct link between GDNF and ibogaine's desirable effect on alcohol addiction. Therefore, the development of agents that activate the GDNF pathway might be useful for treating drug and alcohol abuse.

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#### References and links

**ORIGINAL RESEARCH PAPER** He, D. Y. *et al.* Glial cell line-derived neurotrophic factor mediates the desirable actions of the anti-addiction drug ibogaine against alcohol consumption. *J. Neurosci.* **25**, 619–628 (2005)

**FURTHER READING** Airaksinen, M. S. & Saarna, M. The GDNF family: signalling, biological functions and therapeutic value. *Nature Rev. Neurosci.* **4**, 383–394 (2003)

#### WEB SITE

Ron's laboratory: <http://www.egcrc.org/pis/ron-c.htm>

