

Discovery offers new hope for drug addiction treatments

Victoria Hollick | 0401 711 361, 02 9351 2579, victoria.hollick@sydney.edu.au

Users of heroin and other addictive opioids may be spared from distressing withdrawal symptoms in the future thanks to a research breakthrough by University of Sydney scientists.

In an article just published in [Nature Neuroscience](#) the researchers describe for the first time a protein in nerve cells that drives the withdrawal response - a complex and intensely unpleasant syndrome that includes chills, sweating, cramps, elevated heart rate and blood pressure and increased sensitivity to pain.

"We have identified a protein in nerve cells that is driving the withdrawal response," said [Professor MacDonald Christie](#), the paper's senior author and professor of pharmacology at the University of Sydney and researcher at the [Brain and Mind Research Institute](#) (BMRI).

"When we either remove that protein from the brain or block it with experimental medications, then we can block withdrawal response and the aberrant activity of the nerves responsible for the painful withdrawal."

The protein identified by the researchers is called GABA transporter 1 (GAT-1). The researchers have found it causes a problem due to its excessive electrical activity in the brain during withdrawal from opioids.

"The electrical activity of the protein becomes excessive in the withdrawal phase. This stimulates the nerves to behave aberrantly and causes withdrawal symptoms," said the article's lead author [Dr Elena Bagley](#), a senior lecturer in pharmacology and researcher at the BMRI.

"This increased nerve excitability triggers the cascade of event that drives the opioid withdrawal syndrome. These highly excited nerve cells release more GABA, the neurotransmitter associated with the protein GABA transporter, and this GABA release decreases the chemical messages sent to other brain regions. The downstream dampening of signals to key brain regions such as the hypothalamus produces many of the withdrawal symptoms."



Lead author of the study Dr Elena Bagley.

The researchers made the finding in a study using mice and rat models, but they are confident the discovery will lead to the development of new medications that can be used for humans. The finding also explains for the first time why certain medications currently used to treat withdrawal symptoms work.

Professor Christie commented:

"Now that we now know why compounds that block the GAT-1 protein work, we hope to be able to design medications that better target the activity that causes the withdrawal symptoms without targeting the other functions of the protein."

The discovery also has the potential to lead to the development of medications for use when withdrawing from other addictive substances such as cocaine and nicotine.

The paper, 'Drug-induced GABA transporter currents enhance GABA release to induce opioid withdrawal behaviours', is published in the latest edition of *Nature Neuroscience*.

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