

GWAS identifies genetic alteration associated with opioid dependence

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A genome-wide association study has identified a new genetic alteration in European-Americans with opioid dependence. The study, published in *Biological Psychiatry*, included over 3,000 opioid-exposed people. The new findings provide insight into the biological origins of opioid dependence, which has become an epidemic of historical proportions in the US, driven by dangerous use of prescription painkillers and heroin.

"It's widely recognized that we need a better understanding of the biological influences on [opioid](#) use—it is possible that biological understanding can lead to treatments," said senior author Joel Gelernter, M.D., of Yale University.

In the midst of this opioid crisis, the study provides a timely identification of new genetic risk factors, said John Krystal, M.D., Editor of *Biological Psychiatry*. Genes responsible for opioid dependence have been difficult to identify, as the disorder stems from a complex combination of genetic alterations and environmental influences, such as drug availability.

To tease out some of the genetic contribution to opioid dependence, first author Zhongshan Cheng, Ph.D., and colleagues performed a scan of the entire genome to search for new genetic factors. Of the 3,058 opioid-exposed European-American patients included in the study, 1,290 met the criteria for a diagnosis of opioid dependence. Rather than analyzing patients based on the presence or absence of a diagnosis, the analysis took into account opioid dependence severity, based on the number of

criteria each person met for a clinical diagnosis.

The analysis identified an alteration, or variant, near the gene *RGMA* associated with opioid dependence. "If you have a certain *RGMA* variant, you're more likely to have opioid dependence symptoms than if you have the alternative form," said Dr. Gelernter. *RGMA* also associated with several [genes](#) critical for normal brain function that have been linked to other mental disorders, including schizophrenia, Alzheimer's disease, and autism.

To get an idea of how the gene might be involved in opioid dependence, Dr. Gelernter and colleagues examined the effect of morphine on protein levels of *Rgma* in mice. *Rgma* increased with chronic morphine treatment. Previous studies have also found that *Rgma* regulates cell death and nerve growth in the brain, giving researchers a clue as to how the gene might alter the brain's response to opioids.

"We believe this is a good new lead and hope it encourages novel pharmacological approaches to treating [opioid dependence](#)," said Dr. Gelernter.

More information: Zhongshan Cheng et al, Genome-wide Association Study Identifies a Regulatory Variant of *RGMA* Associated With Opioid Dependence in European Americans, *Biological Psychiatry* (2018). [DOI: 10.1016/j.biopsych.2017.12.016](#)

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