



Media contact
Rhiannon Bugno
+1 214 648 0880
Biol.Psych@UTSouthwestern.edu

GWAS identifies genetic alteration associated with opioid dependence

A genome-wide association study in Biological Psychiatry investigates the biological origins of opioid dependence in European-Americans

Philadelphia, February 22, 2018 – A genome-wide association <u>study</u> has identified a new genetic alteration in European-Americans with opioid dependence. The study, published in <u>Biological Psychiatry</u>, 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.

Notes for editors

The article is "Genome-wide association study identifies a regulatory variant of RGMA associated with opioid dependence in European Americans," by Zhongshan Cheng, Hang Zhou, Richard Sherva, Lindsay Farrer, Henry R. Kranzler, and Joel Gelernter (https://doi.org/10.1016/j.biopsych.2017.12.016). It appears in *Biological Psychiatry*, published by Elsevier.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at <u>Biol.Psych@UTSouthwestern.edu</u> or +1 214 648 0880. Journalists wishing to interview the authors may contact Joel Gelernter at <u>joel.gelernter@yale.edu</u>.

The authors' affiliations and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, M.D., is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available here.

About Biological Psychiatry

<u>Biological Psychiatry</u> is the official journal of the <u>Society of Biological Psychiatry</u>, whose purpose is to promote excellence in scientific research and education in fields that investigate the nature, causes, mechanisms and treatments of disorders of thought, emotion, or behavior. In accord with this mission, this peer-reviewed, rapid-publication, international journal publishes both basic and clinical contributions from all disciplines and research areas relevant to the pathophysiology and treatment of major psychiatric disorders.

The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

Biological Psychiatry is one of the most selective and highly cited journals in the field of psychiatric neuroscience. It is ranked 6th out of 142 Psychiatry titles and 10th out of 258 Neurosciences titles in the Journal Citations Reports® published by Thomson Reuters. The 2016 Impact Factor score for *Biological Psychiatry* is 11.412.

About Elsevier

Elsevier is a global information analytics business that helps institutions and professionals progress science, advance healthcare and improve performance for the benefit of humanity. Elsevier provides digital solutions and tools in the areas of strategic research management, R&D performance, clinical decision support, and professional education; including ScienceDirect, Scival, ClinicalKey and Sherpath. Elsevier publishes over 2,500 digitized journals, including The Lancet and Cell, more than 35,000 e-book titles and many iconic reference works, including Gray's Anatomy. Elsevier is part of RELX RELX Group, a global provider of information and analytics for professionals and business customers across industries. www.elsevier.com

Media contact

Rhiannon Bugno, Editorial Office Biological Psychiatry

+1 214 648 0880

Biol.Psych@UTSouthwestern.edu