

## Genetic analysis of risk for painkiller dependence points to nervous system

By Bill Hathaway

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An analysis of the genomes of 12,000 of addicts and non-addicts revealed some unexpected risk factors for dependence on opiates, a class of drug that includes both heroin and commonly-used painkillers, a new study in the journal Biological Psychiatry shows.



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Most previous investigations of genetic risk have focused on brain receptors that respond directly to opioids such as Vicadin and Oxycodone. However, the new research found that the most significant genetic variations associated with opioid dependency occurred in areas of the genome that encode proteins governing potassium and calcium signaling in the nervous system.

"Potassium and calcium signaling were brought to the fore as the most important systems in terms of contribution to genetic risk in our sample," said Joel Gelernter, Foundations Fund Professor of Psychiatry and lead author of the study. "Findings like these will help provide insight into new therapeutic and prevention strategies."

The most significant associations were found in African American subjects, something Gelernter suspects is attributable both to chance and racial differences in genetic risk factors.

Genomewide association studies previously have been used previously to identify variants linked to nicotine and cocaine dependence. The new study was first to employ this type of analysis to opioid dependence - despite estimates that on average 60 percent of the addiction risk for this trait in an individual is inherited. Gelernter stressed that eventually the number of genetic variants involved in addiction may number in the thousands as more studies are conducted. His lab has begun to sequence genes of opioid dependent subjects.

"We hope that study will provide us with more insight into specific risk variants for this trait," he said.

Hongyu Zhao of Yale is a co-author of the study.

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Source: Yale University

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