Researchers identify gene possibly linked with methamphetamine addiction

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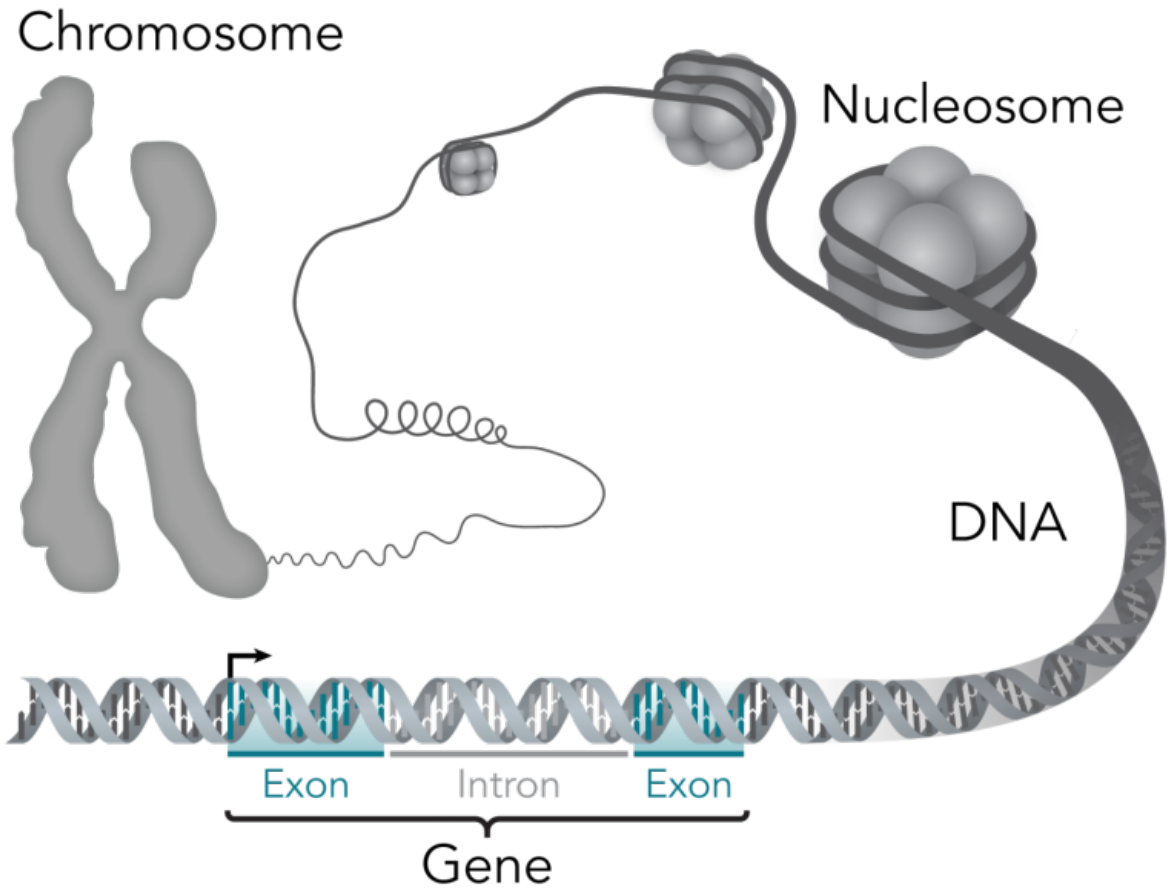

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas

A new study sheds light on the significance of a potential genetic risk factor for drug addiction and possibly other neuropsychiatric disorders. Both genetic and environmental factors are known to influence susceptibility to substance use disorders. However, the genetic basis of these disorders is largely unknown.

Researchers at Boston University School of Medicine (BUSM) have for the first time identified a gene that is casually associated with the behavioral stimulant response to the drug methamphetamine. The gene, known as heterogeneous nuclear ribonucleoprotein H1 (Hnrnph1) has never been previously implicated in the behavioral effects of psychostimulants such as amphetamines or cocaine.

These findings could have implications for understanding the genetic basis of methamphetamine addiction in humans and the development of novel therapeutics forprevention and treatment of substance abuse and possibly other psychiatric disorders. The study appears in the journal *PLOS Genetics*.

Using an experimental model, researchers were able to identify a region of a chromosome that was causally associated with differences in sensitivity to the stimulant properties of methamphetamine. Utilizing genetic approaches such as "fine mapping" and "genome editing," the researchers narrowed the region of the chromosome and targeted each gene to responsible for affecting the behavioral response to the drug.

According to the researchers, Hnrnph1 codes for an RNA binding protein that regulates the processing of hundreds of other genes in the brain. A top priority now is to identify the direct genetic targets of

Hnrnph1 within the reward circuitry.

"A better understanding of the brain region and cell type-specific binding targets of Hnrnph1 will tell us more about the function of this gene and possibly identify new therapeutic strategies for minimizing risk and treating psychostimulant addiction - a disorder for which there is currently no FDA-approved drug," explained corresponding author Camron Bryant, PhD, assistant professor of Pharmacology and Experimental Therapeutics & Psychiatry at BUSM.

The researchers believe this discovery may be potentially relevant to other neuropsychiatric disorders involving dopaminergic dysfunction (ADHD, schizophrenia and bipolar disorder) and have implications for neurodegenerative disorders that affect dopamine circuits, including Parkinson's and Huntington's disease.

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