Study identifies genetic variant that can lead to severe impulsivity

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A multinational research team led by scientists at the National Institutes of Health has found that a genetic variant of a brain receptor molecule may contribute to violently impulsive behavior when people who carry it are under the influence of alcohol. A report of the findings, which include human genetic analyses and gene knockout studies in animals, appears in the Dec. 23 issue of *Nature*.

"Impulsivity, or action without foresight, is a factor in many pathological behaviors including suicide, aggression, and addiction," explains senior author David Goldman, M.D., chief of the Laboratory of Neurogenetics at the NIH's National Institute on Alcohol Abuse and Alcoholism (NIAAA). "But it is also a trait that can be of value if a quick decision must be made or in situations where risk-taking is favored."

In collaboration with researchers in Finland and France, Dr. Goldman and colleagues studied a sample of violent criminal offenders in Finland. The hallmark of the violent crimes committed by individuals in the study sample was that they were spontaneous and purposeless.

"We conducted this study in Finland because of its unique population history and medical genetics," says Dr. Goldman. "Modern Finns are descended from a relatively small number of original settlers, which has reduced the genetic complexity of diseases in that country. Studying the genetics of violent criminal offenders within Finland increased our chances of finding genes that influence impulsive behavior."

The researchers sequenced DNA of the impulsive subjects and compared those sequences with DNA from an equal number of non-impulsive Finnish control subjects. They found that a single DNA change that blocks a gene known as HTR2B was predictive of highly impulsive behavior. HTR2B encodes one type of serotonin receptor in the brain. Serotonin is a neurotransmitter known to influence many behaviors, including impulsivity.

"Interestingly, we found that the genetic variant alone was insufficient to cause people to act in such ways," notes Dr. Goldman. "Carriers of the HTR2B variant who had committed impulsive crimes were male, and all had become violent only while drunk from alcohol, which itself leads to behavioral disinhibition."

"Discovery of a genetic variant which predicts impulsive behavior under certain conditions in one human population may have much wider implications," says NIAAA Acting Director Kenneth R. Warren, Ph.D. "The interaction with alcohol intoxication is interesting, as is the apparent involvement of a neurotransmitter pathway that has been regarded as important in addictions and other behavior."

The researchers then conducted studies in mice and found that when the equivalent HTR2B gene is knocked out or turned off, mice also become more impulsive. Studies of any alcohol interaction in the knockout mice are ongoing.

Taken together, the findings could lead to a better understanding of some aspects of impulsivity and ultimately may lead to strategies for diagnosing and treating some clinically important manifestations of impulsive behavior. The researchers caution, however, that impulsivity is a complex trait with multiple genetic and environmental causes.

"Although relatively common in Finland, the genetic variant we

identified in this study is unlikely to explain a large fraction of the overall variance in impulsive behaviors, as there are likely to be many pathways to impulsivity in its various manifestations," says Dr. Goldman.

Provided by National Institutes of Health

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