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Faulty signaling in brain increases craving for sugar and drugs

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When glutamate and dopamine do not collaborate as they should in the brain's signal system, the kick that alcohol, sugar, or other drugs induce increases. This is shown in a new Swedish-Canadian study on mice being published today in the prestigious *Journal of Neuroscience*. It provides a key piece of the puzzle about the mechanisms behind both substance abuse and obesity.

"Our data indicate that the brain becomes hypersensitive to rewards when this co-signaling of glutamate and dopamine does not function. Lower doses than normal are enough to increase the propensity to ingest the substance, and this is true of both sugar and cocaine," says Asa Mackenzie, associate professor of neuroscience at Uppsala University and the researcher who led the study.

Addiction disorders are a major social problem, and we lack sufficient knowledge of how they arise and how various substances impact the brain. The brain's reward system gives us feelings of pleasure and happiness, for example when we have eaten or drunk something good, had sex, or worked out. This pleasure arises when certain signal substances, primarily dopamine, are released in the brain. But this reward system can be "kidnapped" by other rewarding substances, such as alcohol and abuser drugs like cocaine. They provide feelings of reward initially, but they are so strong that nerve cells in the system are rewired, and addiction occurs. More natural substance, such as food rich in sugar, can also produce addiction-like conditions.

The Uppsala researchers and their colleagues have recently shown that dopamine cells in the reward system can send signals in cooperation with glutamate, so called co-signaling. Its physiological role was not previously known, however. For instance, how important is it for the inclination to ingest reward substances?

In studies of mice that lack the ability to send the above signals because their glutamate transporter, so-called VGLUT, has been inactivated, the scientists studied how prone the mice were to ingest sugar and cocaine. The results showed that they both ingested more and responded to lower dosages than control mice.

Since there is a strong correlation between memory and consumption substances, and ultimately also for the risk of addiction, the researchers also looked into this. They are able to present the interesting finding from the study that mice that lack the ability to co-signal developed dramatically improved memory of environments that could be associated with the ingestion of drugs. They also found changes in genetic expressions in the reward system that indicate that the brain has become hypersensitive and that dopamine levels have dropped.

"This is extremely interesting, but more research is needed in order to understand how this can be used in drug development, for instance," says Asa Mackenzie.

These scientists have now gone on to study these mechanisms in connection with abuse in humans and are looking for direct connections between low VGLUT levels and addiction.

Provided by Uppsala University