Researchers find cocaine disinhibits natural inhibitor allowing continued release of dopamine

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(Medical Xpress)—A team of researchers working at the University of Geneva and Geneva University Hospital have found during experiments with test mice, that injections of cocaine can cause naturally occurring inhibiting neurons in the brain to stop preventing the release of dopamine. In their paper published in the journal *Science*, the team describes their experiments and how their results suggest a new type of treatment for cocaine addicts might be on the horizon.

Most research conducted to learn more about how cocaine works on the brain has been primarily focused on how the drug stimulates the brain. In this new study, the research team took a new approach—they looked at how cocaine can disinhibit activity in the brain, leading they say, to changes in personality that can lead to an addictive personality.

To find out more about why cocaine addicts appear to experience a change in personality, the researchers injected test mice with different amounts of cocaine then used brain scanners to try to see what was happening to them. They looked specifically at two areas of the brain: the nucleus accumbens and ventral tegmental area—both are impacted by cocaine—the former is believed to be active in pleasure, reinforcement and reward, while the latter is generally associated with cognition and motivation. Careful study of how the two areas work when exposed to cocaine revealed that the drug caused a neural channel of sorts to be created between the nucleus accumbens and GABA neurons

in the ventral tegmental area. The creation of this channel resulted in dopamine being released on a nearly constant basis, which, the researchers suggest, accounts for the addictive behavior exhibited by addicts. In essence, they claim, cocaine disinhibts a natural dopamine inhibitor, releasing the brakes, so to speak, causing changes in personality.

The research team has previously been involved in using optogenetics—a fiber-optic based approach to stimulating nerve cells in the brain—they suggest using it might prove beneficial in treating cocaine addicts. They note that since such therapy has already been approved by the FDA in the US for Parkinson's patients, it might not be long before it can be tried in people addicted to cocaine to see if it can close the channel that was created resulting in reduction of addictive tendencies.

More information: Cocaine Disinhibits Dopamine Neurons by Potentiation of GABA Transmission in the Ventral Tegmental Area, *Science* 27 September 2013: Vol. 341 no. 6153 pp. 1521-1525 DOI: 10.1126/science.1237059

ABSTRACT
Drug-evoked synaptic plasticity in the mesolimbic system reshapes circuit function and drives drug-adaptive behavior. Much research has focused on excitatory transmission in the ventral tegmental area (VTA) and the nucleus accumbens (NAc). How drug-evoked synaptic plasticity of inhibitory transmission affects circuit adaptations remains unknown. We found that medium spiny neurons expressing dopamine (DA) receptor type 1 (D1R-MSNs) of the NAc project to the VTA, strongly preferring the GABA neurons of the VTA. Repeated in vivo exposure to cocaine evoked synaptic potentiation at this synapse, occluding homosynaptic inhibitory long-term potentiation. The activity of the VTA GABA neurons was thus reduced and DA neurons were disinhibited. Cocaine-evoked potentiation of GABA release from D1R-MSNs

affected drug-adaptive behavior, which identifies these neurons as a promising target for novel addiction treatments.