

Research team uses optogenetics to reverse effects of cocaine

December 8 2011, by Bob Yirka

(Medical Xpress) -- A team of Swiss researchers, led by Christian Lüscher of the University of Geneva, has found the first casual link between cocaine use and physical brain changes and in so doing, as they describe in their paper published in *Nature*, have also come up with a means to reverse it.

It has been known for a while that when cocaine is introduced into the [brain](#), the firing potential of [neurons](#) of the nucleus accumbens (a part of the brain responsible for reward and pleasure) is increased. It has been suspected that this is what leads to the jittery behavior seen in addicts, though until now has never been fully proven.

To both prove and counter this particular impact cocaine has on the brain, Lüscher and his team turned to optogenetics, a process whereby certain kinds of algae that have light-sensitive ion channels are used to cause some action in a cell in response to light. In this case, it was used to reduce the firing potential of certain neurons brought about by the introduction of cocaine.

In their experiment, the team expressed such channels in cortical neurons that communicate with neurons in the accumbens in [mice](#) that had been given several rounds of cocaine to cause the change in brain activity. They then fired laser pulses at them to cause a virtual storm of chatter between the two cell types resulting in overkill, which caused them to reduce their firing on their own, effectively nullifying the initial impact caused by the cocaine.

By applying the procedure to several mice, and finding virtually the same results each time, i.e. that brain chatter lessened, as did the jittery behavior associated with cocaine use, the team has proven there is a link between the two.

And while it might seem the team has found a technique for helping addicts get off [cocaine](#), it's not as simple as that. This is because the technique only appears to work on the brains of mice that are newly addicted, whose brains haven't been changed in other less understood ways after extended drug use. Thus a true therapy is, as the team notes, still in the distant future.

The next step for the team is to see if they can find other brain changes due to drug use in mice to see if their process can undo those as well.

More information: Reversal of cocaine-evoked synaptic potentiation resets drug-induced adaptive behaviour, *Nature* (2011)

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Abstract

Drug-evoked synaptic plasticity is observed at many synapses and may underlie behavioural adaptations in addiction. Mechanistic investigations start with the identification of the molecular drug targets. Cocaine, for example, exerts its reinforcing and early neuroadaptive effects by inhibiting the dopamine transporter, thus causing a strong increase in mesolimbic dopamine. Among the many signalling pathways subsequently engaged, phosphorylation of the extracellular signal-regulated kinase (ERK) in the nucleus accumbens is of particular interest because it has been implicated in NMDA-receptor and type 1 dopamine (D1)-receptor-dependent synaptic potentiation as well as in several behavioural adaptations. A causal link between drug-evoked plasticity at identified synapses and behavioural adaptations, however, is missing, and the benefits of restoring baseline transmission have yet to be

demonstrated. Here we find that cocaine potentiates excitatory transmission in D1-receptor-expressing medium-sized spiny neurons (D1R-MSNs) in mice via ERK signalling with a time course that parallels locomotor sensitization. Depotentiation of cortical nucleus accumbens inputs by optogenetic stimulation in vivo efficiently restored normal transmission and abolished cocaine-induced locomotor sensitization. These findings establish synaptic potentiation selectively in D1R-MSNs as a mechanism underlying a core component of addiction, probably by creating an imbalance between distinct populations of MSNs in the nucleus accumbens. Our data also provide proof of principle that reversal of cocaine-evoked synaptic plasticity can treat behavioural alterations caused by addictive drugs and may inspire novel therapeutic approaches involving deep brain stimulation or transcranial magnetic stimulation.

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