

Enzymatic pathway common to drugs of abuse could lead to new treatment options

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The extracellular-signal regulated kinase (ERK) pathway plays a role in multiple drug addictions and appears to modulate neuronal plasticity through epigenetic mechanisms, say French scientists.

The discovery could pave the way for new therapeutic options for treating [drug](#) addictions, the researchers claim.

"The molecular adaptations induced by ERK include epigenetic regulation that causes a stable response that modifies the structure of DNA, hence accounting for long-term neuronal plasticity," says Dr Jocelyne Caboche, from the Pierre-and-Marie-Curie University, Paris, France.

Dr Caboche and her colleague Dr Peter Vanhoutte have been researching the neuronal adaptations that occur in the brain in response to chronic drug use, and that are responsible for addiction. Using mice models and cell cultures, Drs. Caboche and Vanhoutte examined enzymatic pathways that were activated in specific brain areas after exposure to addictive drugs – the so-called reward circuitry.

They found that ERK appears to be a common enzymatic pathway to drugs of abuse, with genetic and epigenetic regulations playing a key role in long-lasting behavioral adaptations.

"We found that injecting cocaine into mice induces the nuclear accumulation of the active form of ERK (di-phospho ERK1/2) in the

striatum," says Dr Caboche, explaining their research.

"We extended this observation to most drugs of abuse, including amphetamine, nicotine, morphine and delta-9 tetrahydrocannabinol. ERK activation is functionally important since its pharmacological blockade prevents gene expression and long-term behavioral effects of the drugs," adds Dr Caboche.

Drs Caboche and Vanhoutte further characterised the mechanism of ERK activation, and showed that it required concomitant stimulation of both D1 and NMDA receptors. The researchers have also confirmed that ERK activation is necessary for long-term synaptic plasticity induced by electrical stimulation in slices or by cocaine injection in vivo.

"Our work thus described, shows that addiction can be considered as a pathological memory, that can be a priori reversed using new therapeutic approaches", says Dr Caboche.

She proposes that their strategy for targeting the ERK pathway may be a suitable target for therapeutics to treat addiction and other neuronal plasticity-related disorders.

Provided by European College of Neuropsychopharmacology

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