

ADDRESS Colloquia

Centre for Addiction Research und Science (AddResS)

Venue: Medical University Vienna

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Wednesday 15.01.2020 12:00 s.t. Host: Harald H. Sitte

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“From drug-evoked synaptic plasticity to addiction ”

Addictive drugs evoked-dopamine surge results in neural adaptations especially in the Nucleus accumbens (NAc).

Cocaine-evoked synaptic plasticity at excitatory synapses to medium-sized spiny neurons of the NAc has been linked to locomotor sensitization, cue-associated seeking and relapse.

These molecular and behavioural alterations were found in every animal exposed to addictive drugs.

However, it is established that only a fraction of drug consumers will reach more severe criteria of addiction. Drug consumption despite harmful consequences is

considered as a compulsive behaviour in addicts and represents a latest stage of addiction.

Compulsivity to obtain drug self-administration can be observed in rodents using an operant task during which a punishment has to be endured to obtain an infusion.

In a mouse model of addiction, perseverance is observed in a fraction of mice in which the transmission of Orbitofrontal Cortex (OFC) to Dorsal striatum (DS) synapses is strengthened.

Importantly, we established bidirectional modulation of synaptic plasticity that was able to invert behaviour in both persevering and renouncing mice. Together these demonstrate that synaptic potentiation of OFC-DSt transmission drives expression of compulsive reinforcement, a defining symptom of addiction.

In addition, a majority of compulsive mice continues VTA (Ventral Tegmental Area) DA (dopamine) neurons self-stimulation despite the opportunity to obtain an alternative natural reward.

During this choice task, a reduced DA signal evoked by reward predictive cues in the Nucleus Accumbens was detected in compulsive animals. DA was measured with a biosensor, called D-light.

This DA sensor is a genetically modified DA D1 receptor that emits fluorescence while binding DA. The biased reward signal due to the pharmacological property of addictive drugs represents a leading theory of addiction.

Here data suggest that an alteration of the prediction signal may also contribute to both the transition and the maintenance of compulsive drug use.