

# **Acute and chronic effects by stimulants on behavior and striatal neurotransmission in the rat**

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## **Abstract**

Nicotine and amphetamines are the most widely abused stimulants. The main aim of the studies in this thesis was to investigate how these two drugs of abuse affect distinct regions of the rat brain involved in development of habitual and compulsive behavior, namely subregions of striatum in the rat. To this end, using a battery of tests including behavior, brain slice electrophysiology, and molecular biology, we have evaluated acute effects by nicotine and amphetamine, as well as progressive changes induced by their chronic use and discontinuation. We show that nicotine acutely depresses synaptic activity in dorsal striatum, an effect that involves multiple receptors. In chronic experiments, we show that a brief exposure to nicotine (15 days) or amphetamine (five days) induces persistent behavioral changes, which sustain over long periods of withdrawal. In addition, we demonstrate that following the drug exposure period, dorsal striatal subregions are engaged in a temporal manner, such that effects in lateral portions only appear after protracted withdrawal, where they sustain for a long time. We also demonstrate that drug-induced effects on behavior and synaptic activity are enhanced in younger animals. In summary, we show acute and long-lasting effects by stimulants on behavior and neurotransmission in striatal subregions, where they also reveal spatiotemporal and age-dependent components.

**Keywords:** withdrawal, nicotine, amphetamine, striatum, GABA, glutamate, dopamine, sensitization, locomotor activity

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- I. **Lotfi A\***, Licheri V\*, Patton MH, Lagström O, Mathur B, Ericson M, Söderpalm B, Adermark L. *Long-lasting inhibition of striatal excitability following nicotine exposure ex vivo*  
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- II. Adermark L, Morud J, **Lotfi A**, Jonsson S, Söderpalm B, Ericson M. *Age-contingent influence over accumbal neurotransmission and the locomotor stimulatory response to acute and repeated administration of nicotine in Wistar rats*  
Neuropharmacology. 2015, 97:104-12
- III. Adermark L, Morud J, **Lotfi A**, Danielsson K, Ulenius L, Söderpalm B, Ericson M. *Temporal rewiring of striatal circuits initiated by nicotine*  
Neuropsychopharmacology. 2016, 41:3051-3059
- IV. **Lotfi A**, Licheri V, Lagström O, Söderpalm B, Ericson M, Adermark L. *Temporal and spatial suppression of striatal excitability elicited by amphetamine in Wistar rats*  
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