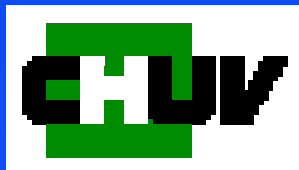


Cocaine-induced molecular and cellular adaptations in brain reward systems: role of the C/EBP transcription factors.

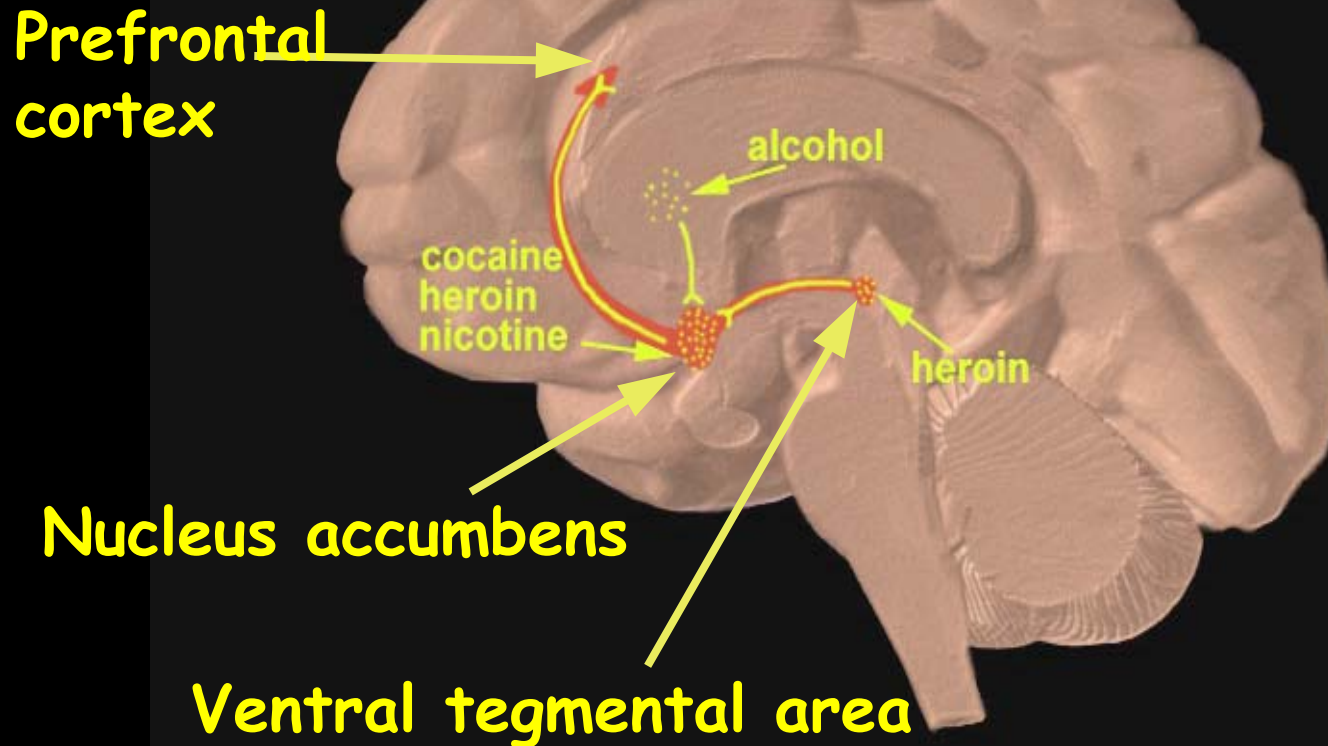
J-R. Cardinaux, K.A. Kovács, M. Steinmann,

P.J. Magistretti, O. Halfon.

Service Universitaire de Psychiatrie de l'Enfant et de l'Adolescent (SUPEA), Centre de Neurosciences Psychiatriques, Lausanne.

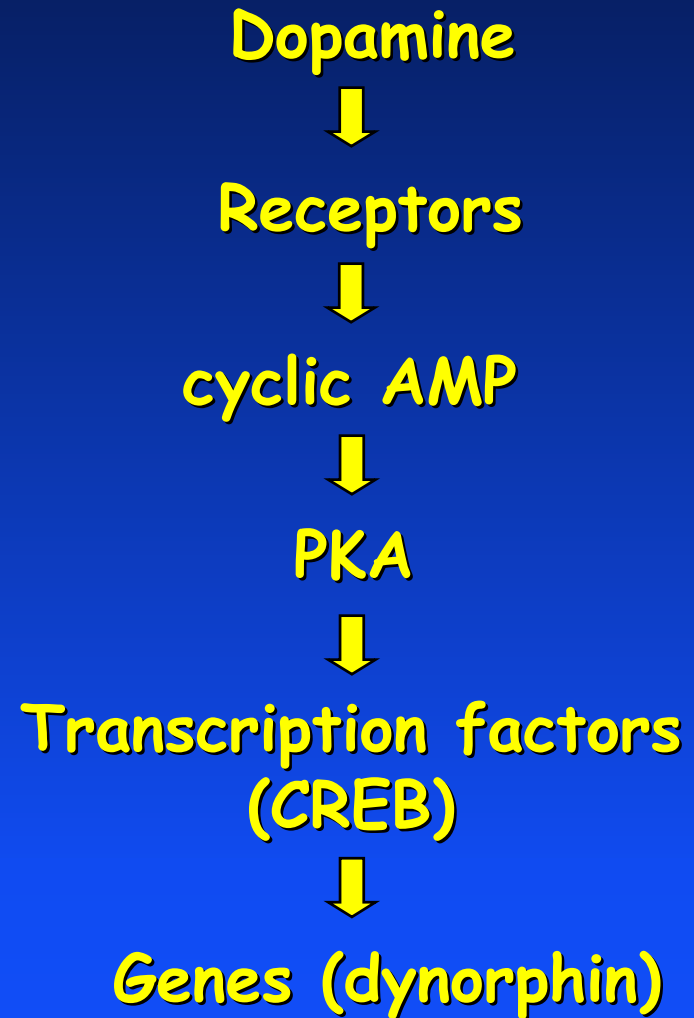
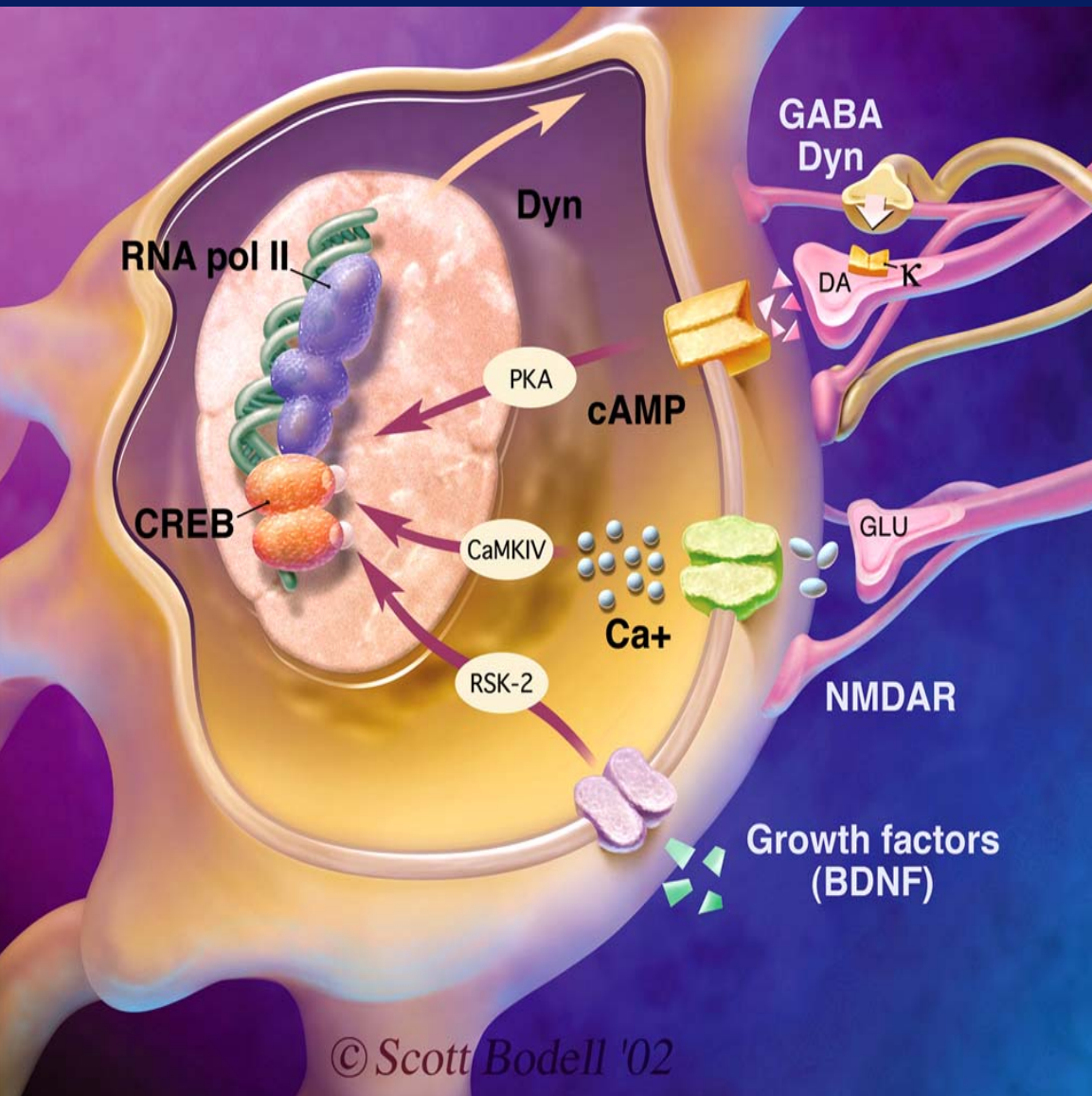


Activation of the reward pathway by addictive drugs

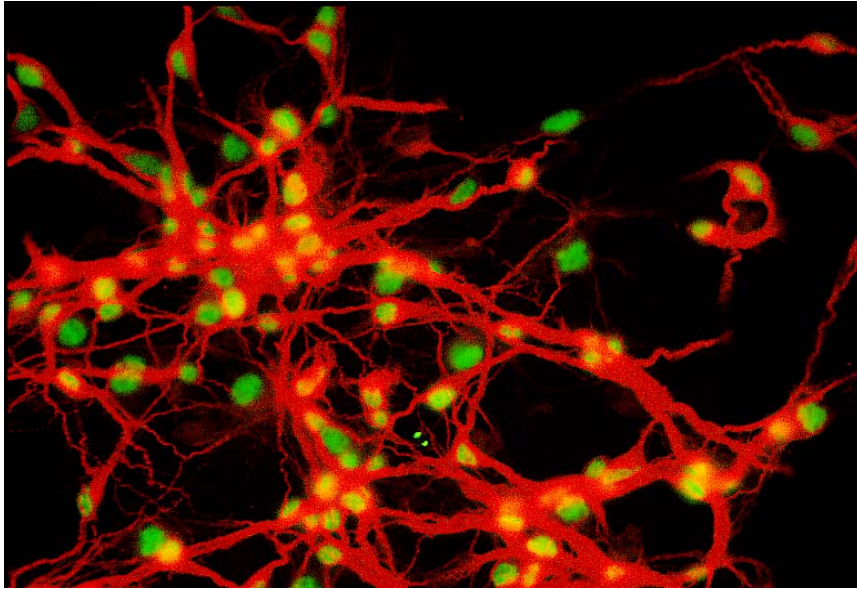


The mesolimbic dopamine system is activated by virtually all drugs of abuse. Compulsive use that characterizes substance dependence produces neuroadaptive changes in this system, resulting in a compromised reward system.

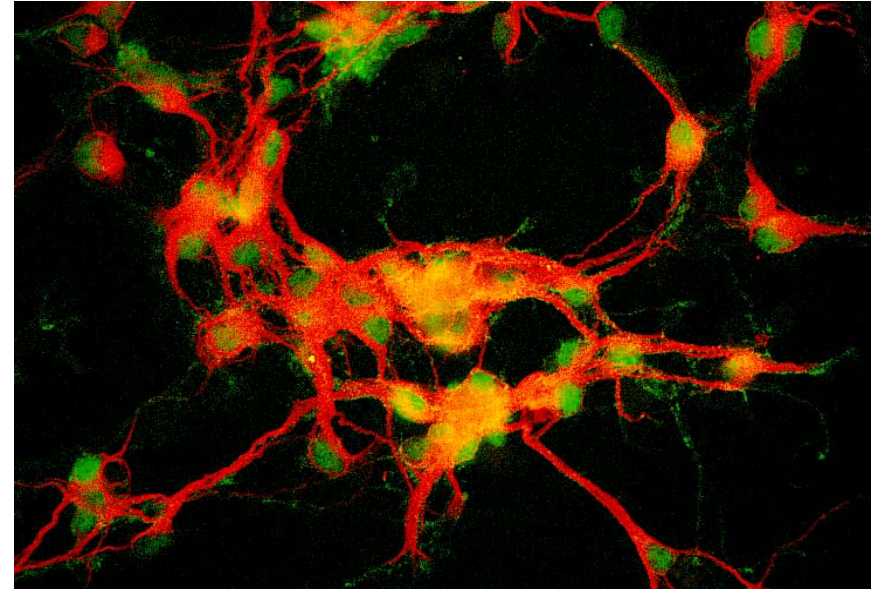
Dopamine-mediated changes in gene expression. Role of the transcription factor CREB



Mouse striatal neurons express C/EBP β and C/EBP δ



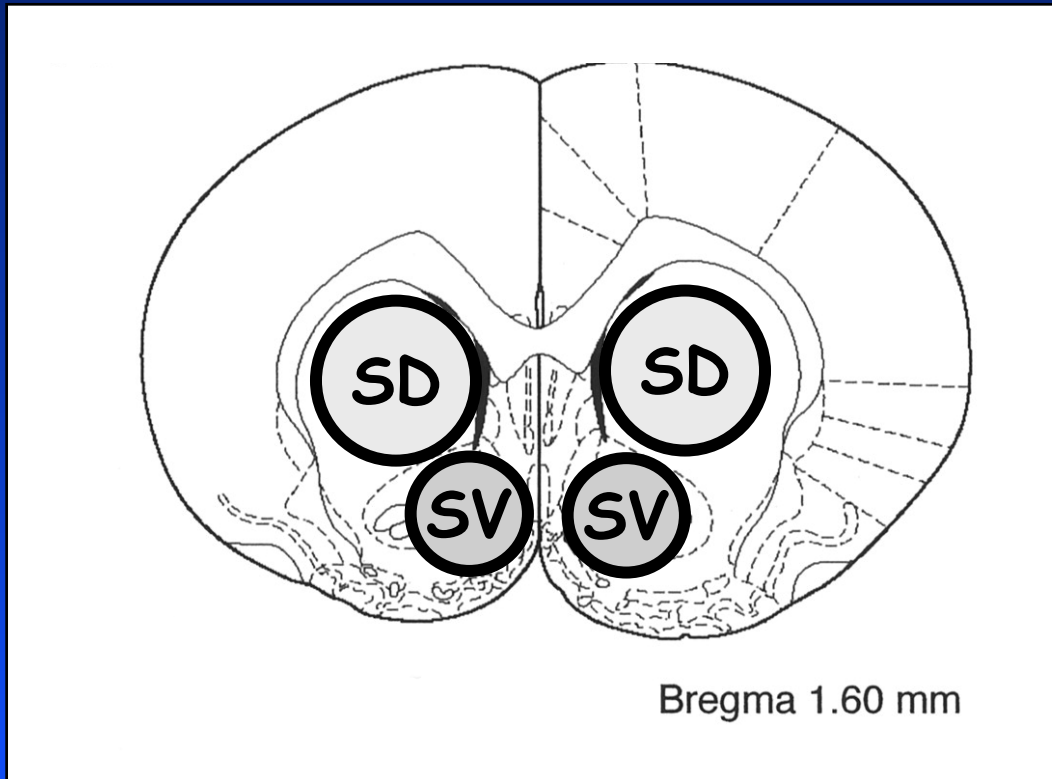
C/EBP β and MAP-2



C/EBP δ and MAP-2

Quantitative RT-PCR analysis of mouse chronically exposed to cocaine

C57/BL6J males daily injected with 20 mg/kg cocaine or vehicle (controls) for 7 days.

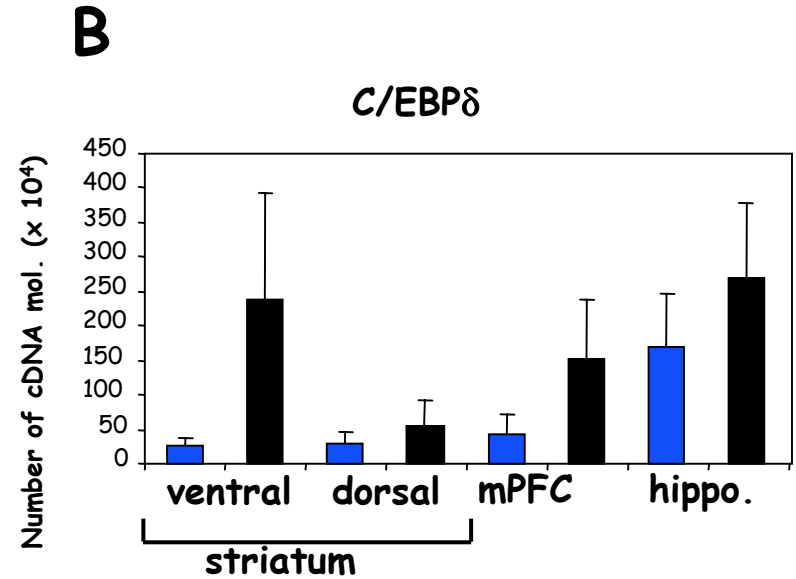
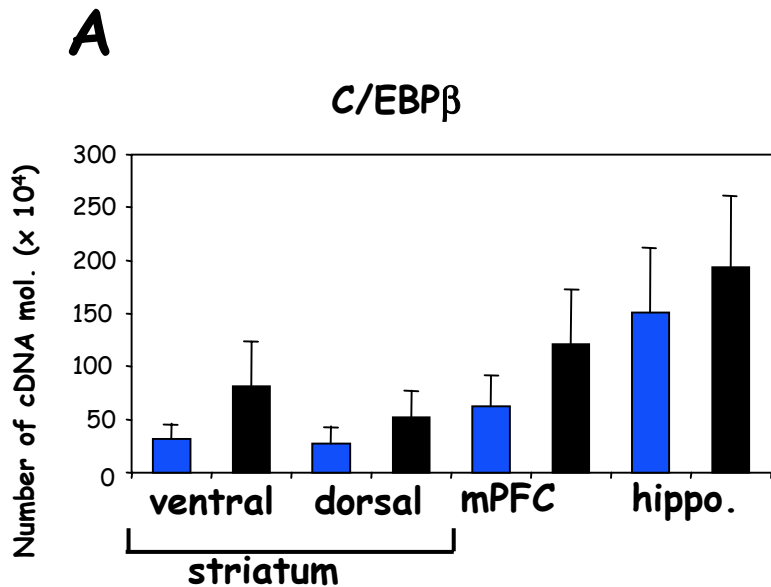


After sacrifice, 4 brain regions were dissected:

- Dorsal and ventral striatum (micropunches)
- Medial prefrontal cortex
- Hippocampus

Total RNA of these regions was extracted and analyzed by quantitative RT-PCR (TaqMan, ABI).

C/EBP β and - δ mRNA levels in brain of mice exposed to cocaine for 14 days



■ = saline 1 inj./day for 14 days

■ = cocaine 20 mg/kg 1 inj./day for 14 days

Conclusions and future perspectives :

C/EBP mRNA levels are increased in the striatum of mice exposed to cocaine for 14 days.

This has to be confirmed with more animals and on the protein level (immunohistochemistry, Western blot).

The specific aims of our future studies are to :

- 1/ Study the regulation of *c/ebp β* and *c/ebp δ* gene expression in adult mouse striatum after self-administration of cocaine.
- 2/ Investigate whether C/EBP β or C/EBP δ -deficient mice have an altered behaviour in cocaine self-administration experiments.
- 3/ Determine the target genes of the C/EBP isoforms that could play a role in drug addiction.