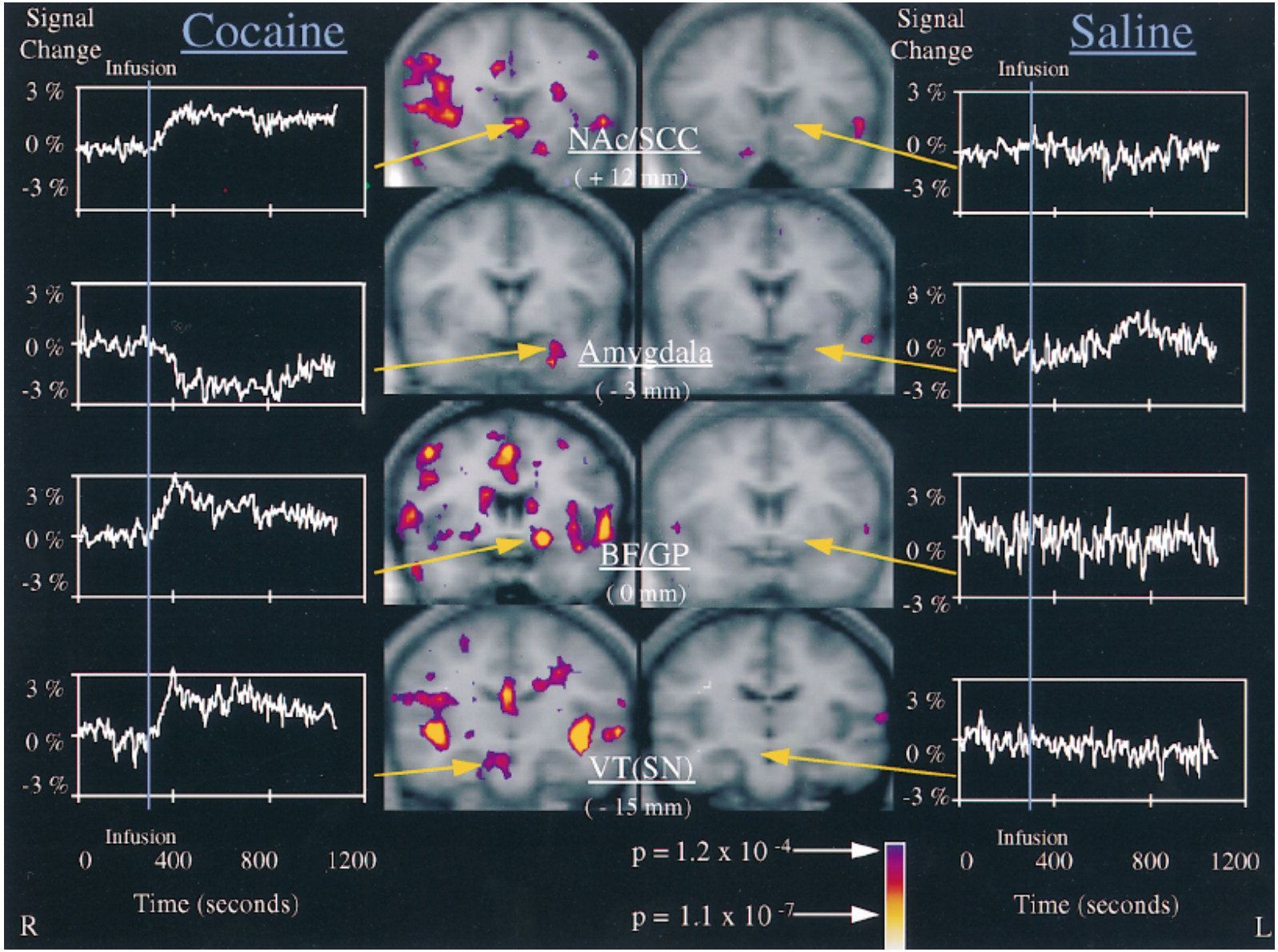
N2100 – Human Neuroanatomy

Dopamine, Reward and Addiction

Mark J. Thomas, PhD
Department of Neuroscience

How do drugs affect the brain?



Breiter et al., Neuron, 1997

What use is a reward system?

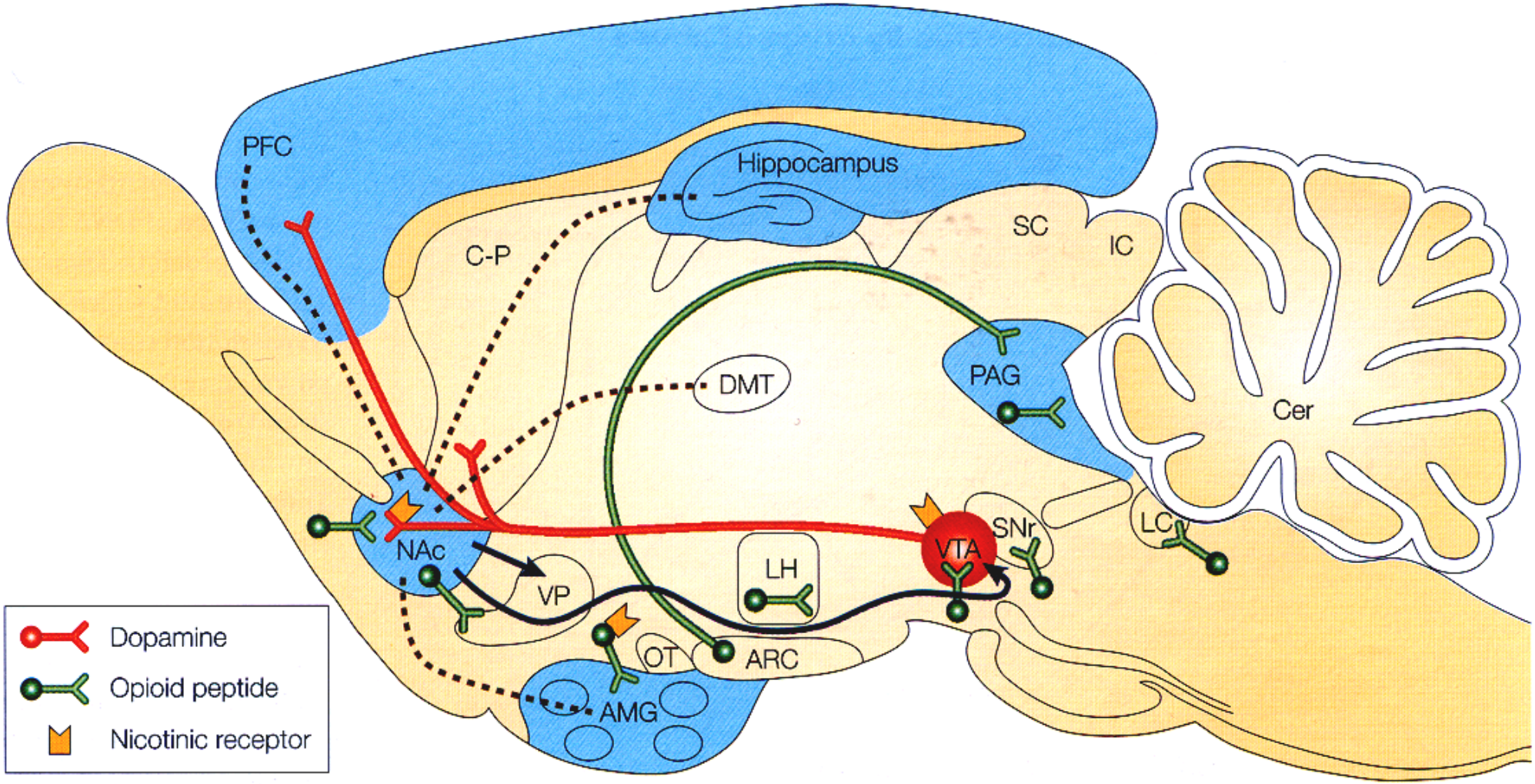
Direct behavior towards
"advantageous" stimuli

Food

Sex

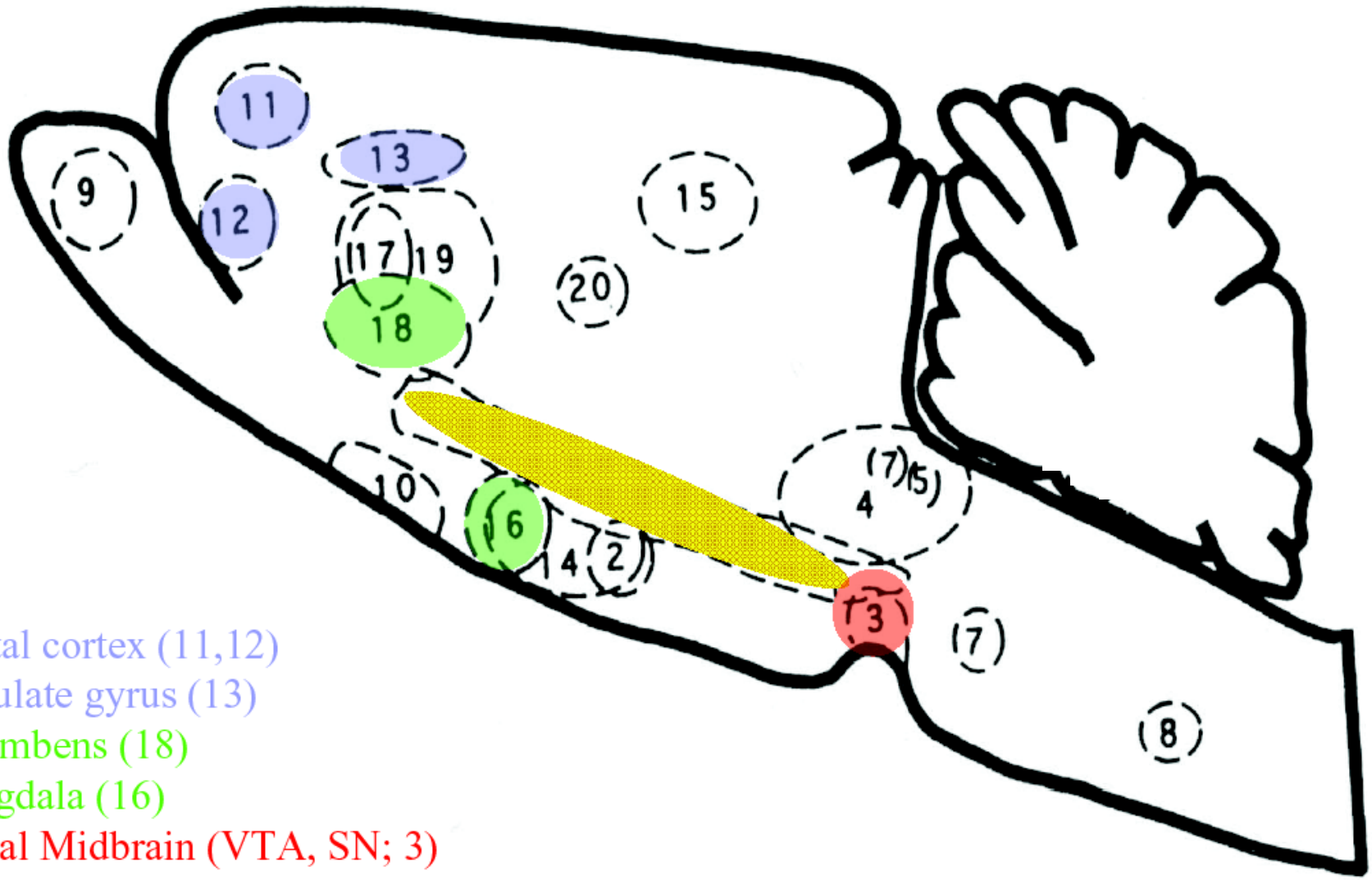
Social network

Reward Circuitry



(from EJ Nestler, Nature Reviews Neuroscience, 2001)

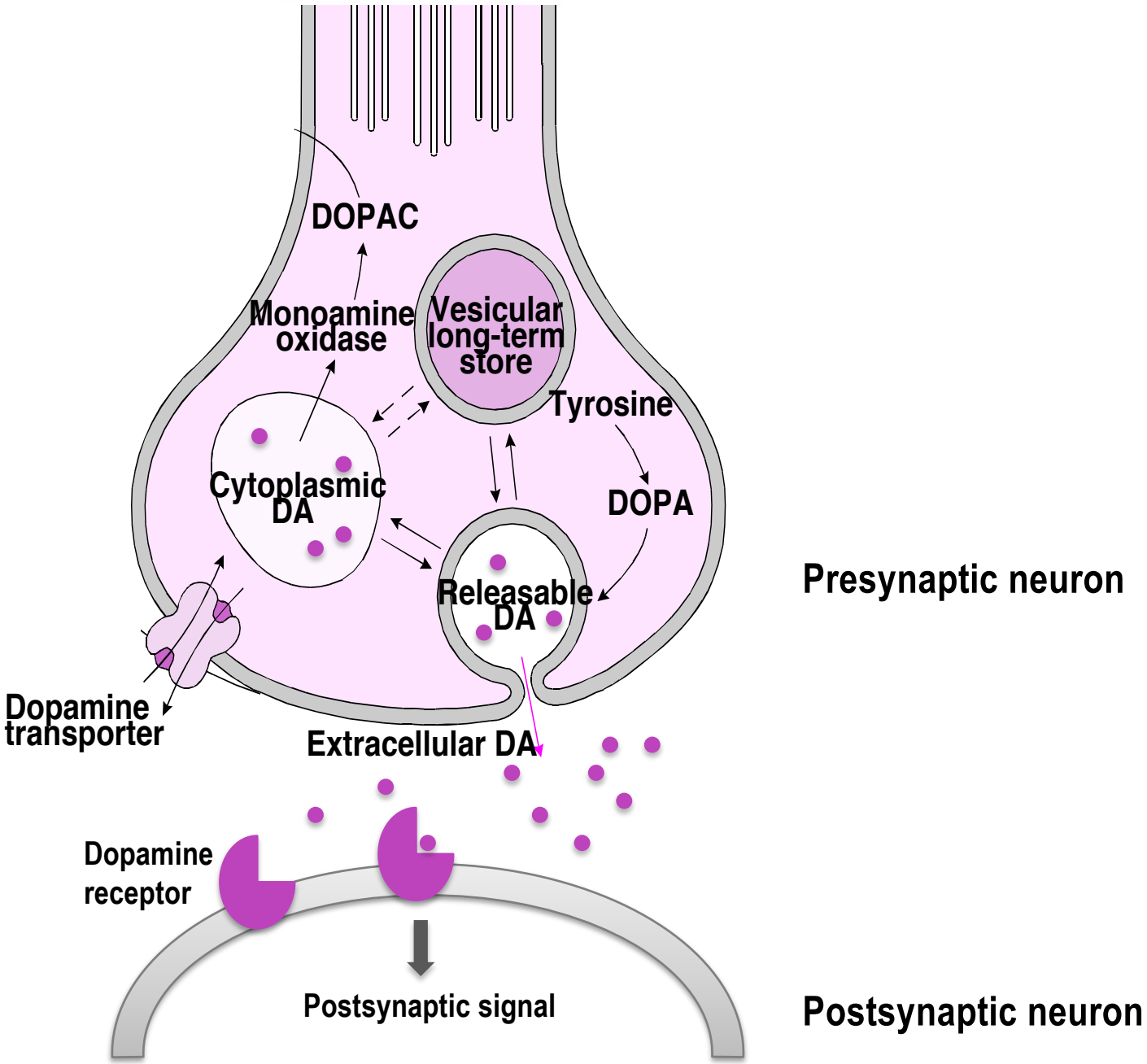
Brain Stimulation Reward (BSR) regions



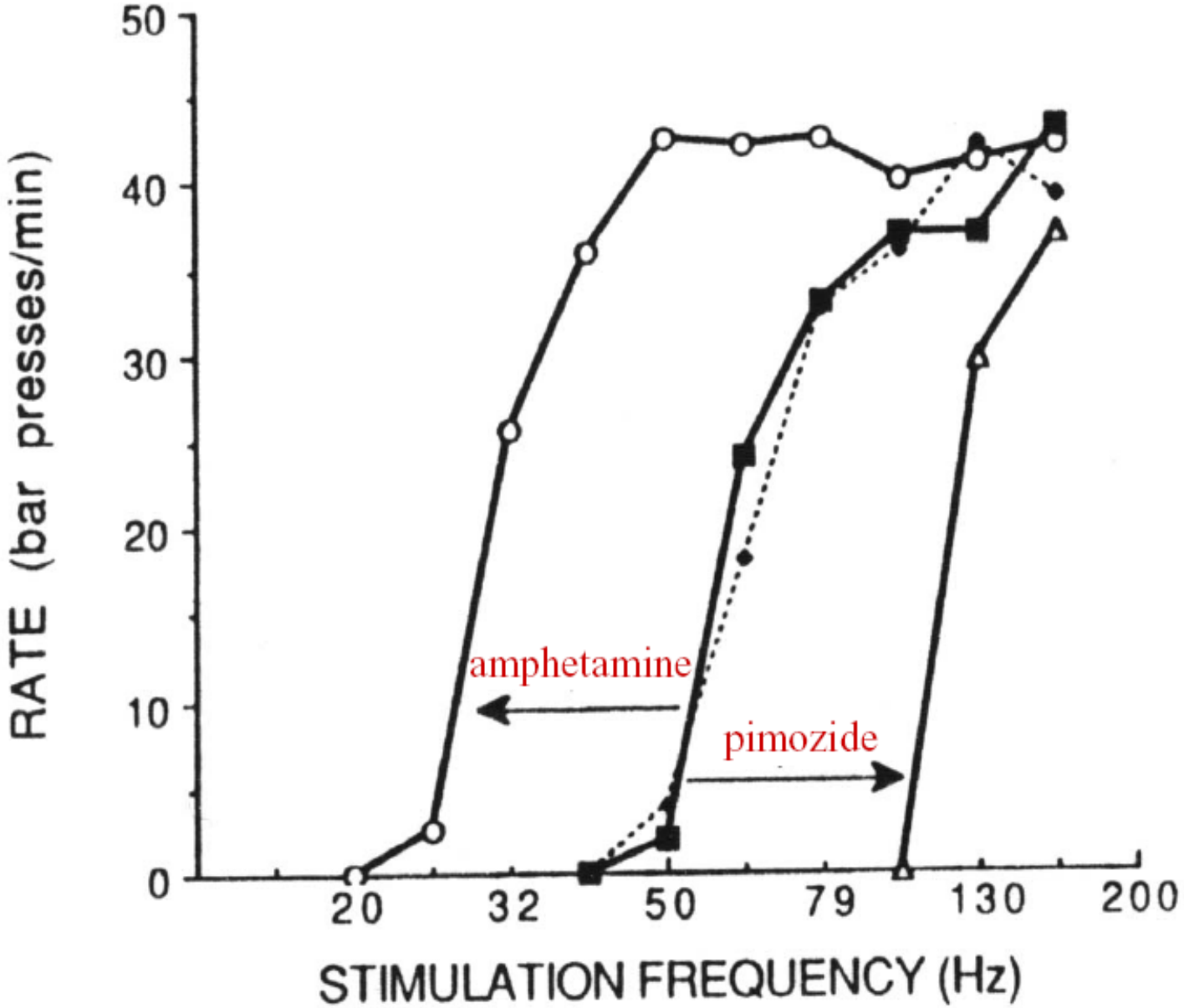
Frontal cortex (11,12)
Cingulate gyrus (13)
Accumbens (18)
Amygdala (16)
Medial Midbrain (VTA, SN; 3)
Medial Forebrain Bundle (1)

(Wise, 1996)

Dopamine synapse – form and function



Dopamine signaling enhances BSR

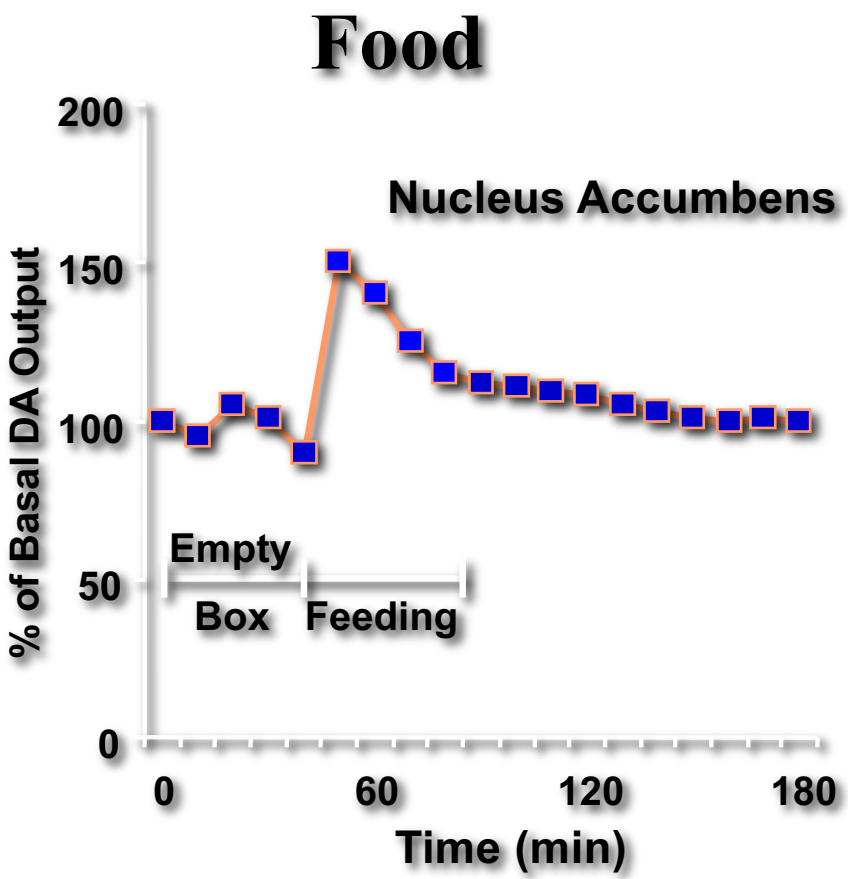


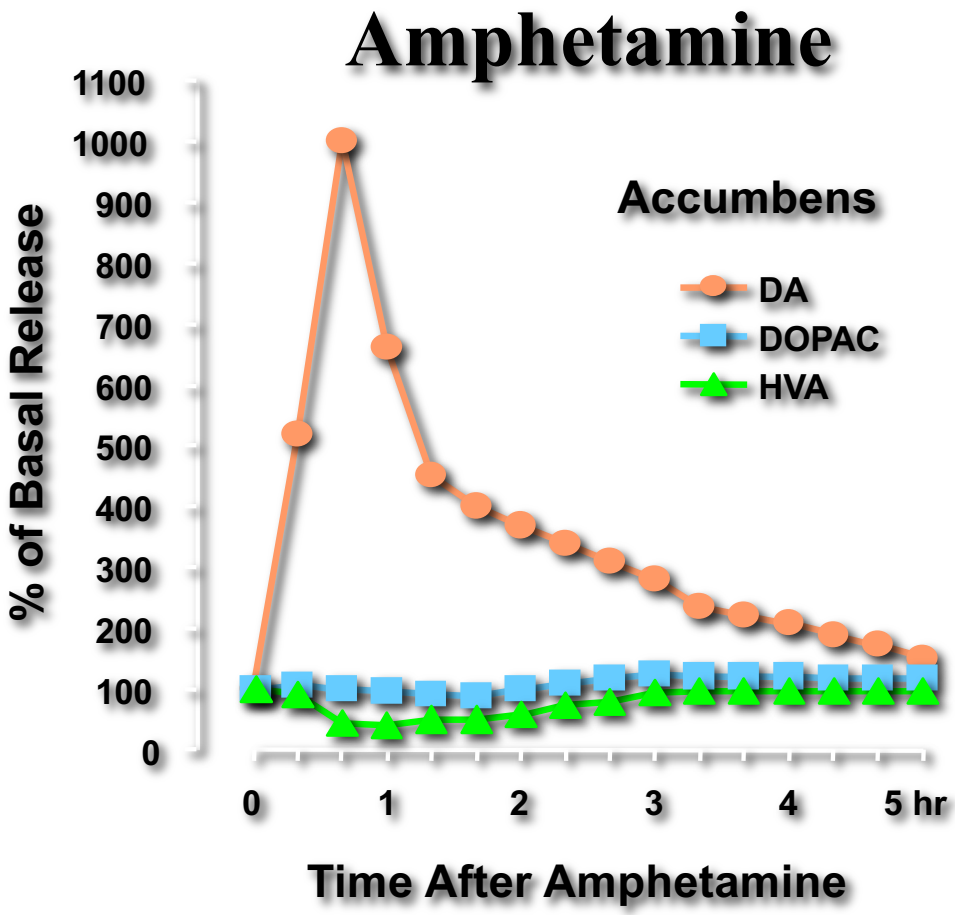
Gallistel and Karras (1984)

Is dopamine necessary for "liking" responses?

Berridge and Robinson, Trends in Neurosci, 2003

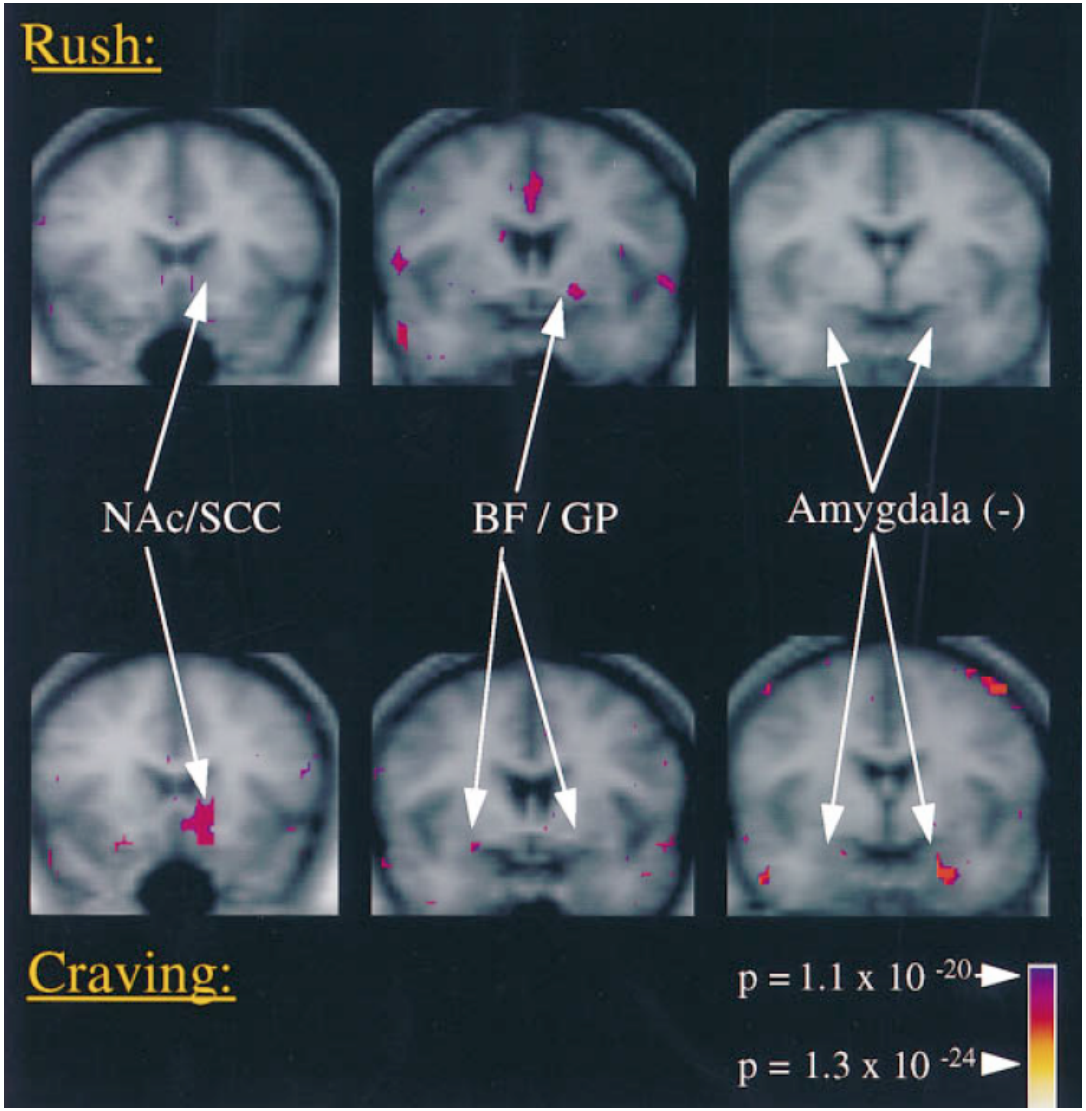
Dopamine release: "natural" vs. drug reward





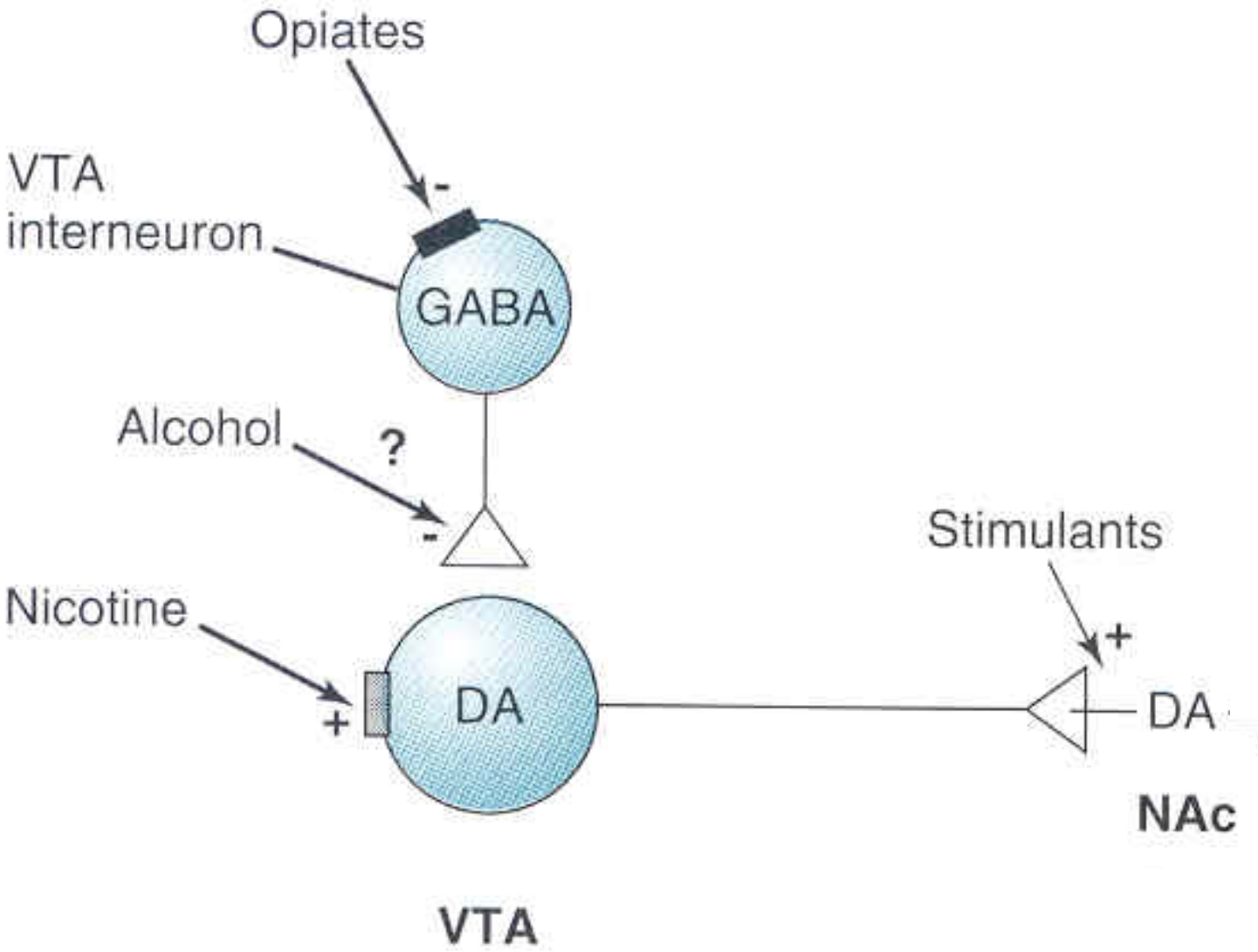
Source: Di Chiara et al.

NAc activity: correlated with euphoria (rush) or craving?

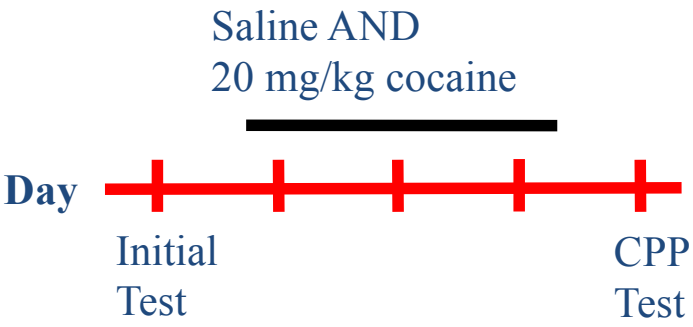


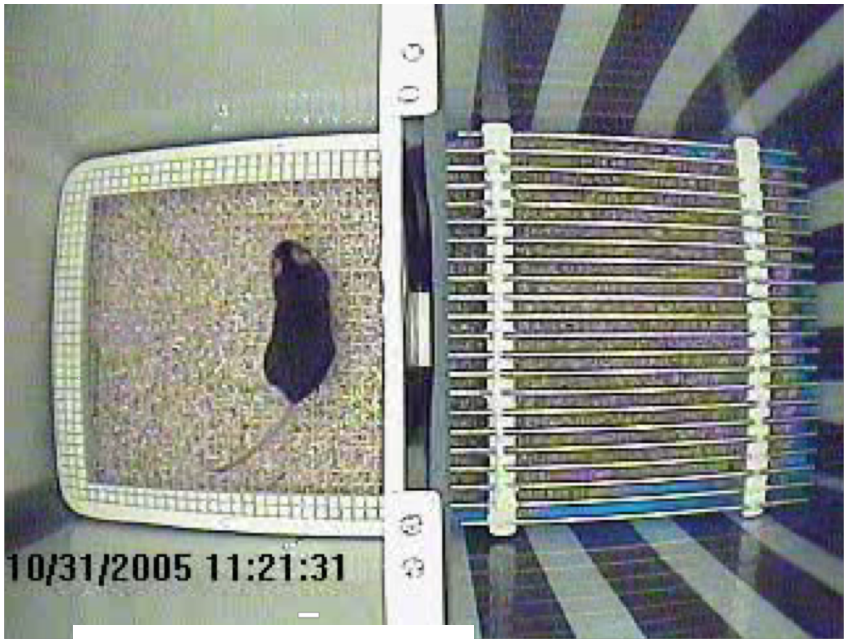
Breiter et al., Neuron, 1997

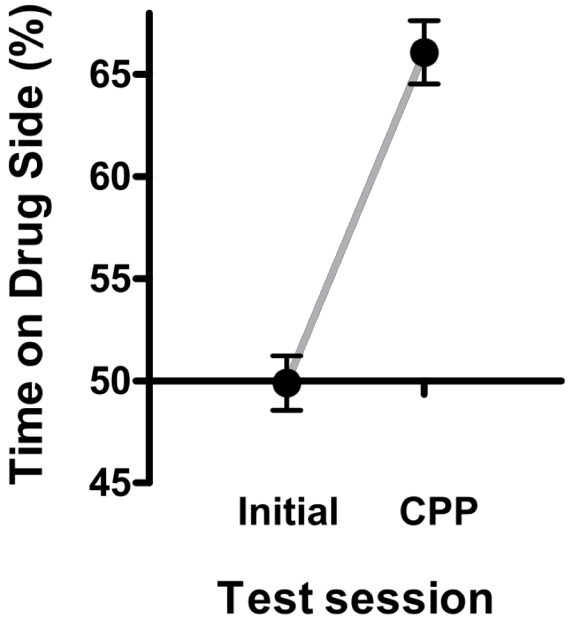
Different drugs, different mechanisms → same result



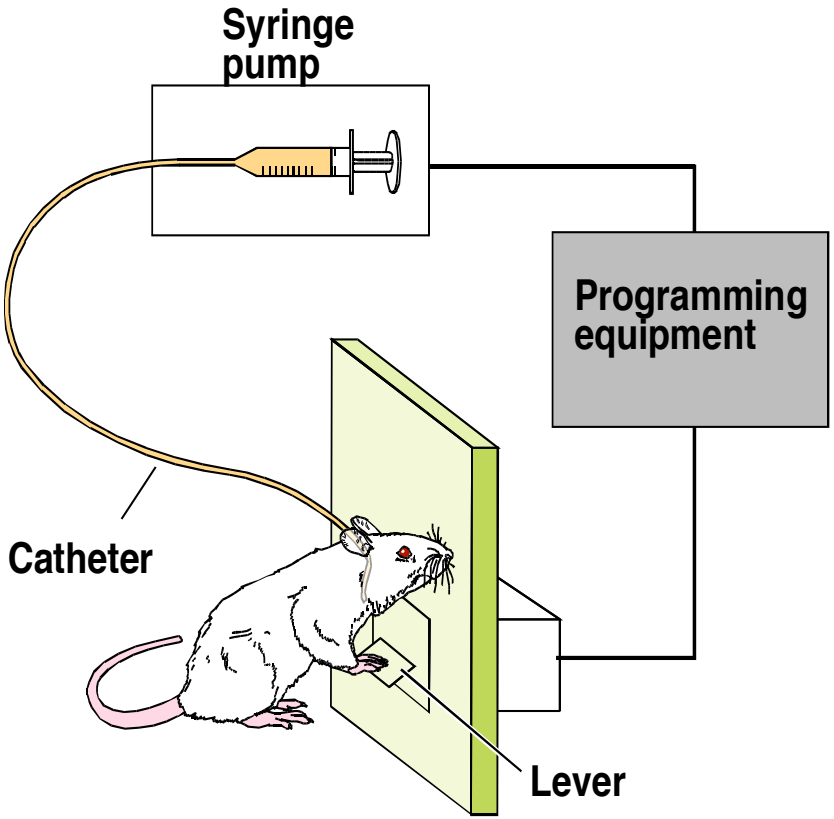
Conditioned place preference (CPP)







Drug self administration



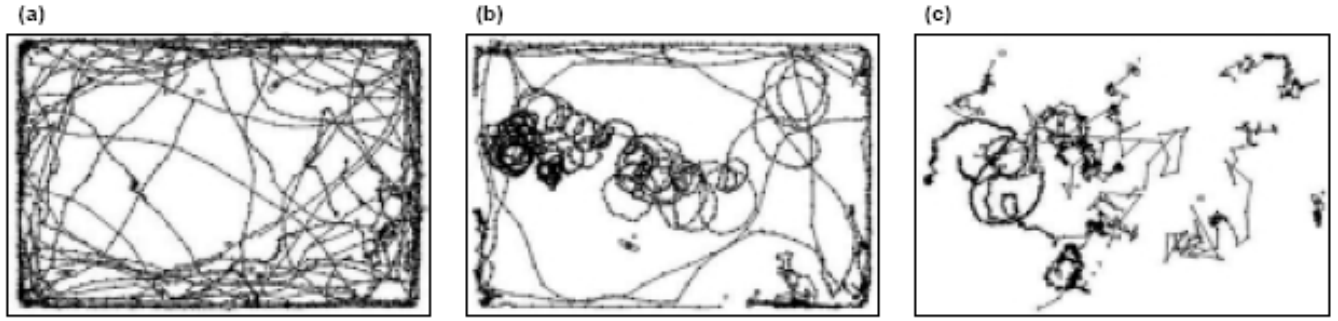
Rosenzweig/Leiman (Sinauer)

Modeling addiction in "simple systems"

Time flies like an arrow.
Fruit flies like crack?

J Hirsh

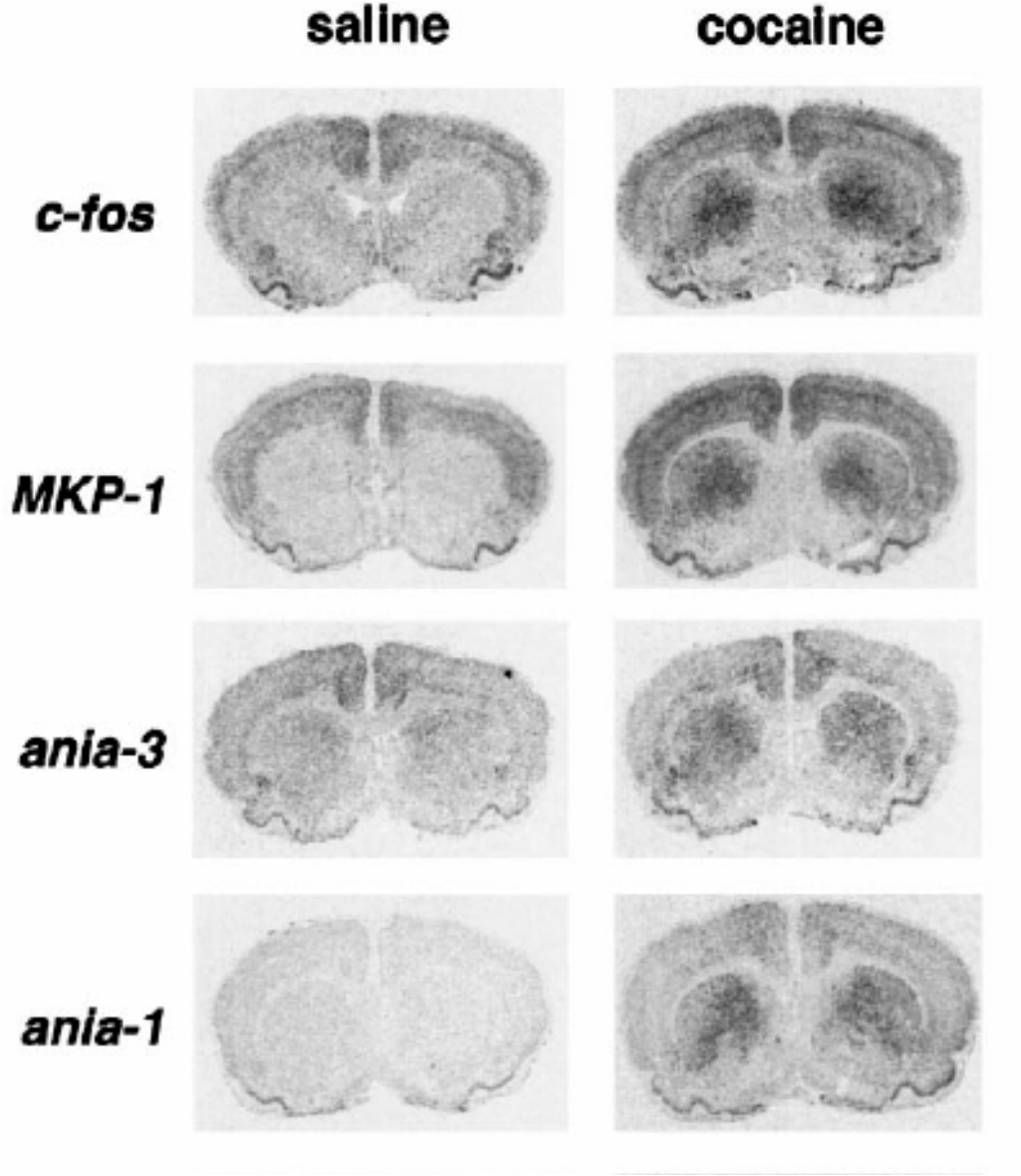
Department of Biology, University of Virginia, Charlottesville, VA, USA



normal low cocaine high cocaine

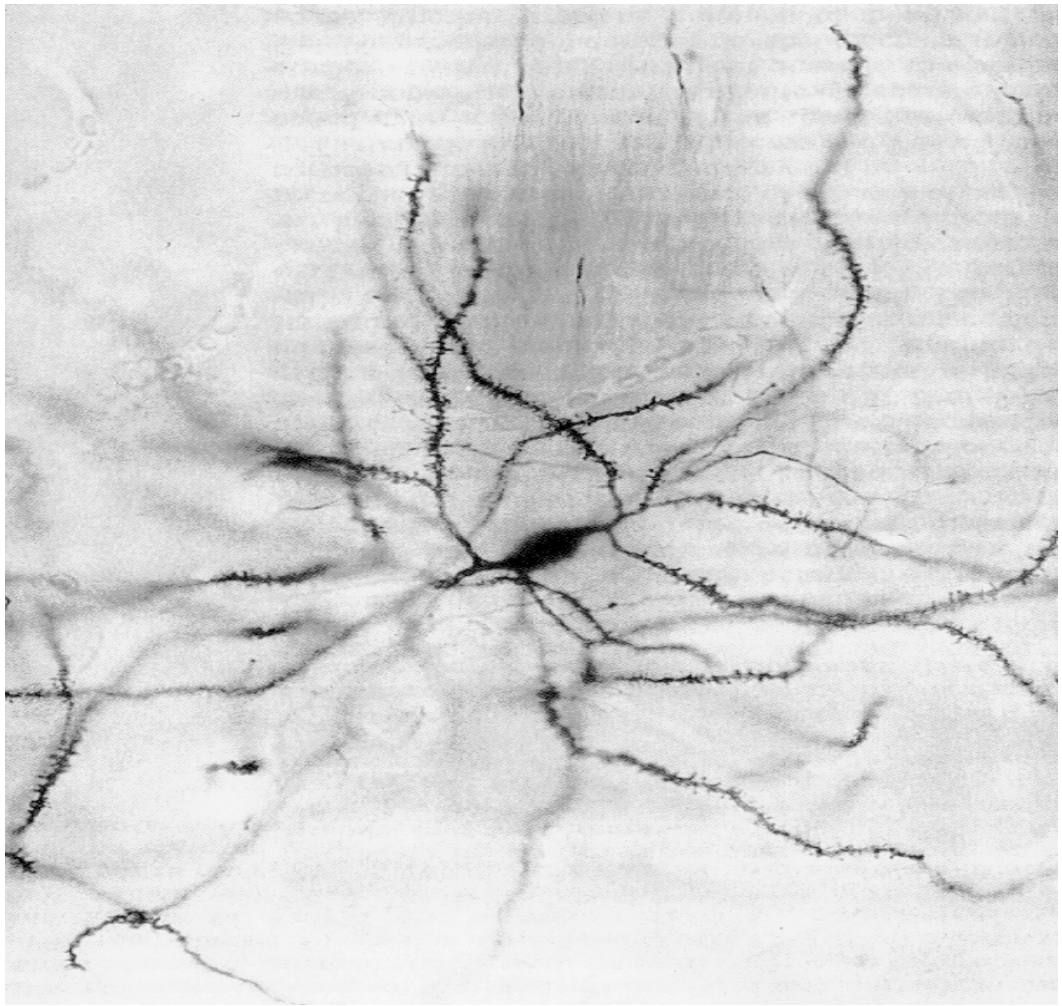
Hirsh, Pharmacogenomics, 2001

Changes in gene expression occur with a single exposure to cocaine



Berke et al., J Neurosci, 1998

Normal structure of nucleus accumbens "medium spiny" neurons

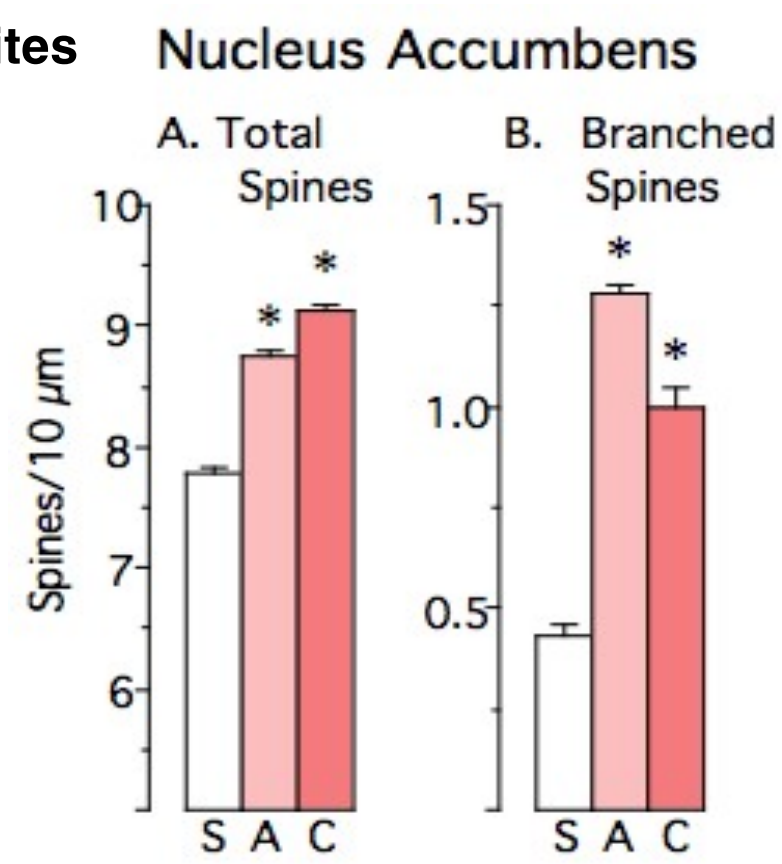


(from Smith & Bolam, *Trends Neurosci.*, 1990)

Addictive drugs alter structure of neuronal dendrites

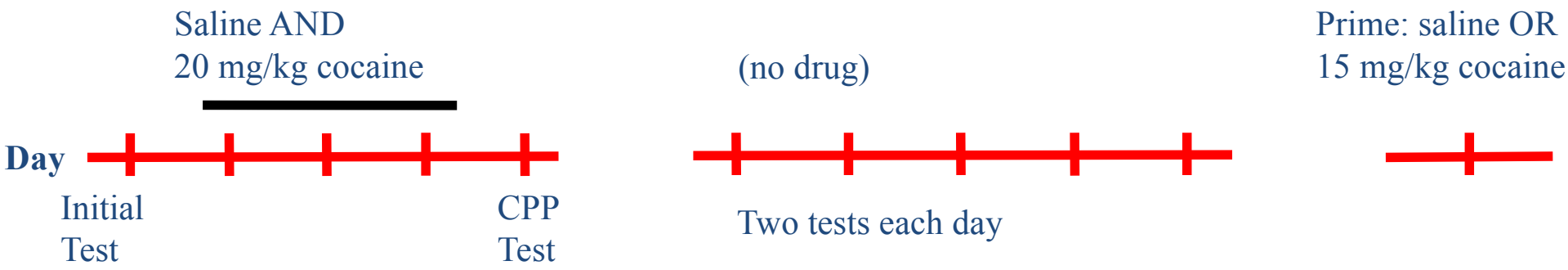
Terminal tips of medium spiny dendrites

saline amph

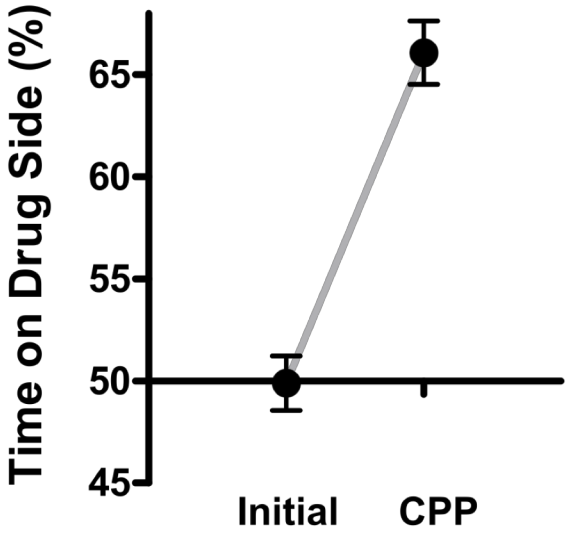


T.E. Robinson & B. Kolb, J. Neurosci., 1997

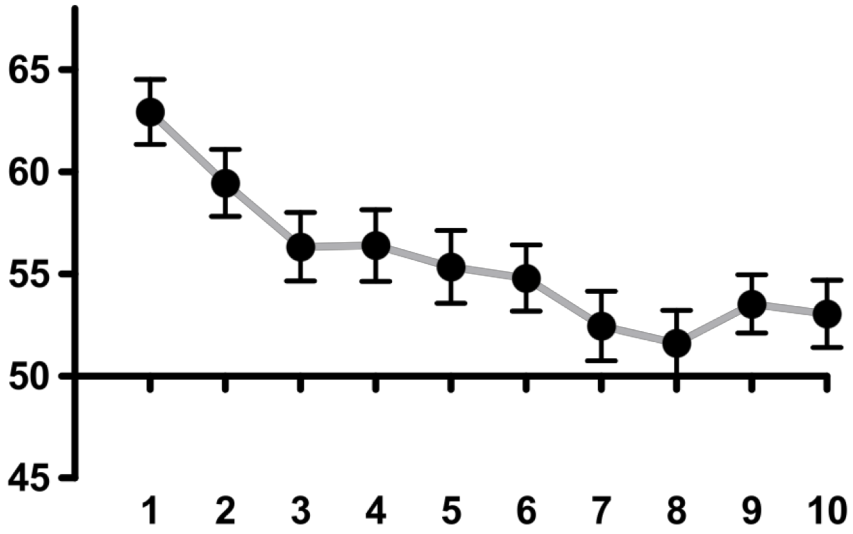
CPP reinstatement – modeling relapse?



Conditioning



Extinction



Reinstatement