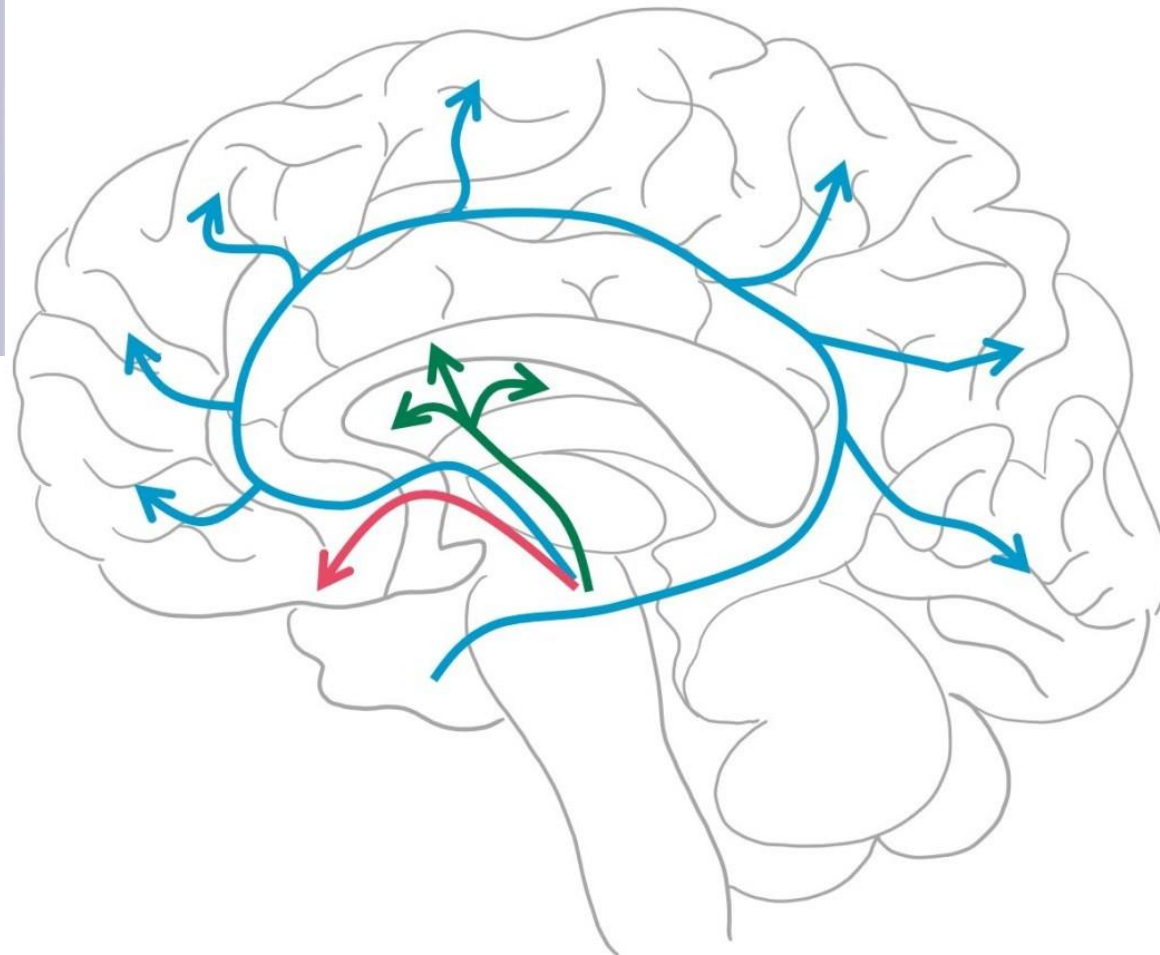
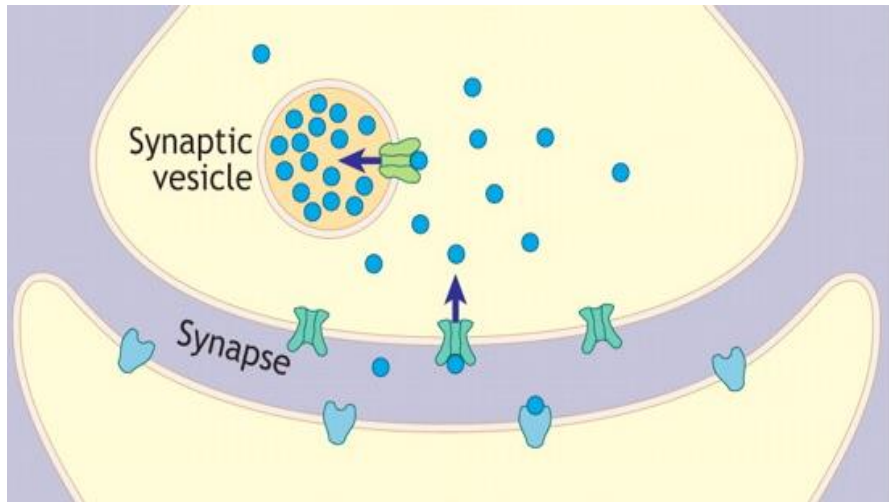


The Pharmacology of Methamphetamine Addiction

Susan Ferguson, PhD
University of Washington
Seattle Children's Research Institute

June 28, 2019

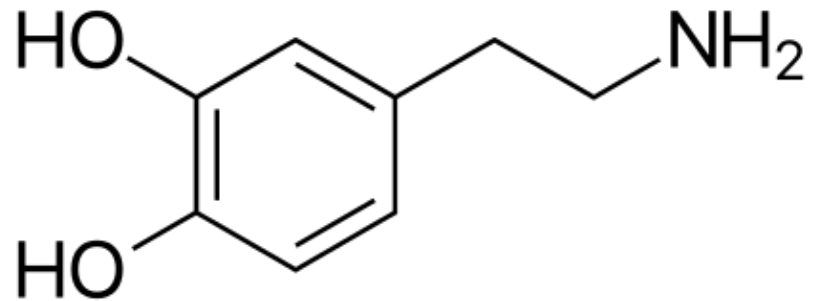
Dopamine pharmacology



MESOCORTICAL
Cognition, Memory,
Attention, Emotional
Behavior, & Learning

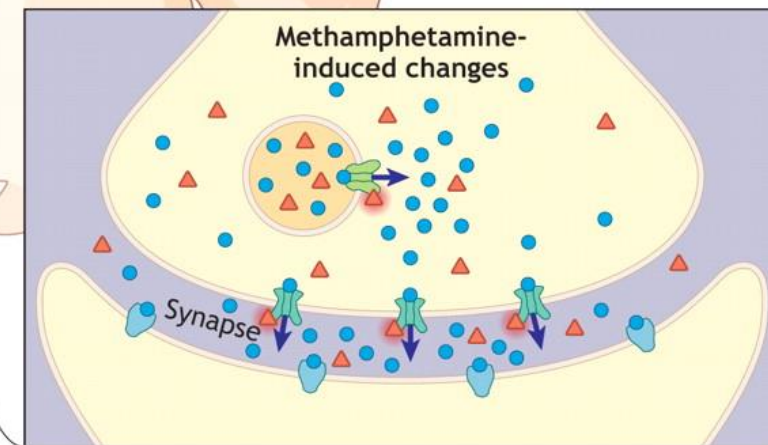
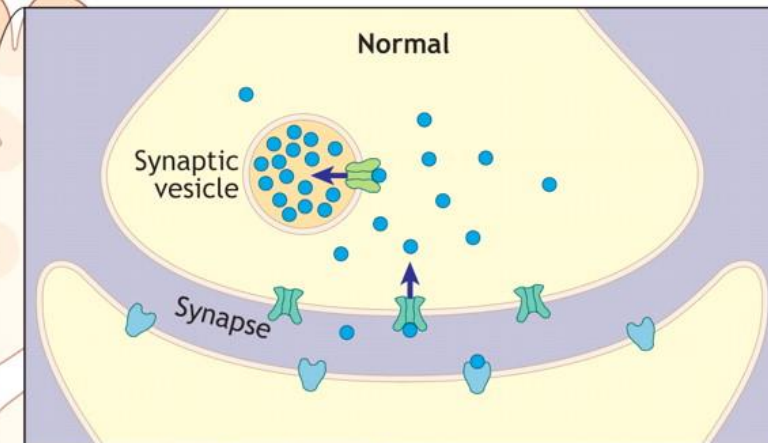
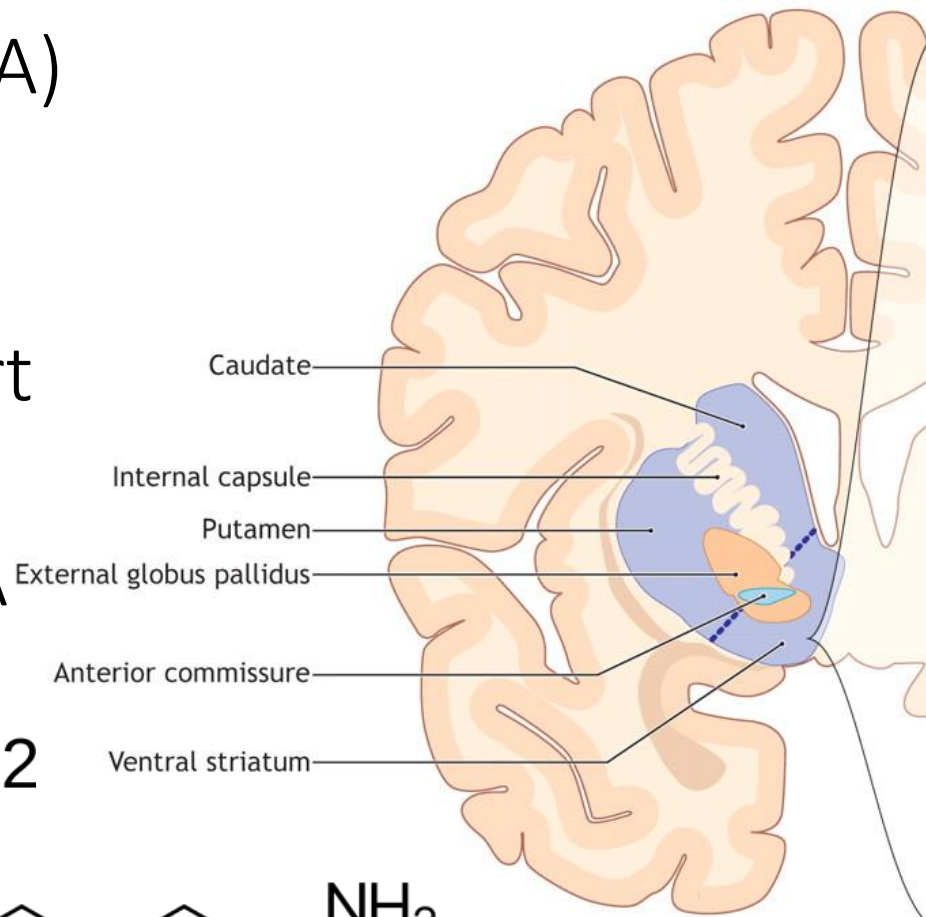
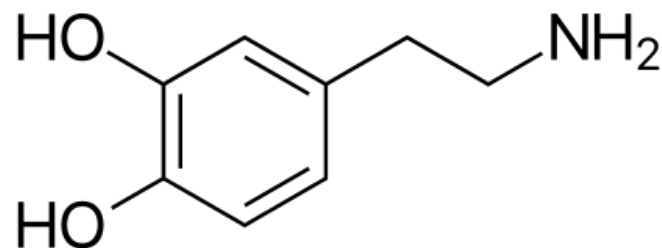
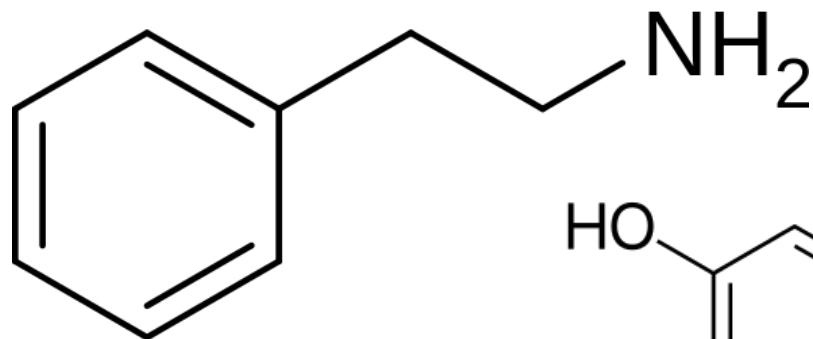
NIGROSTRIATAL
Movement & Sensory
Stimuli

MESOLIMBIC
Pleasure & Reward
Seeking Behaviors;
Addiction, Emotion,
Perception



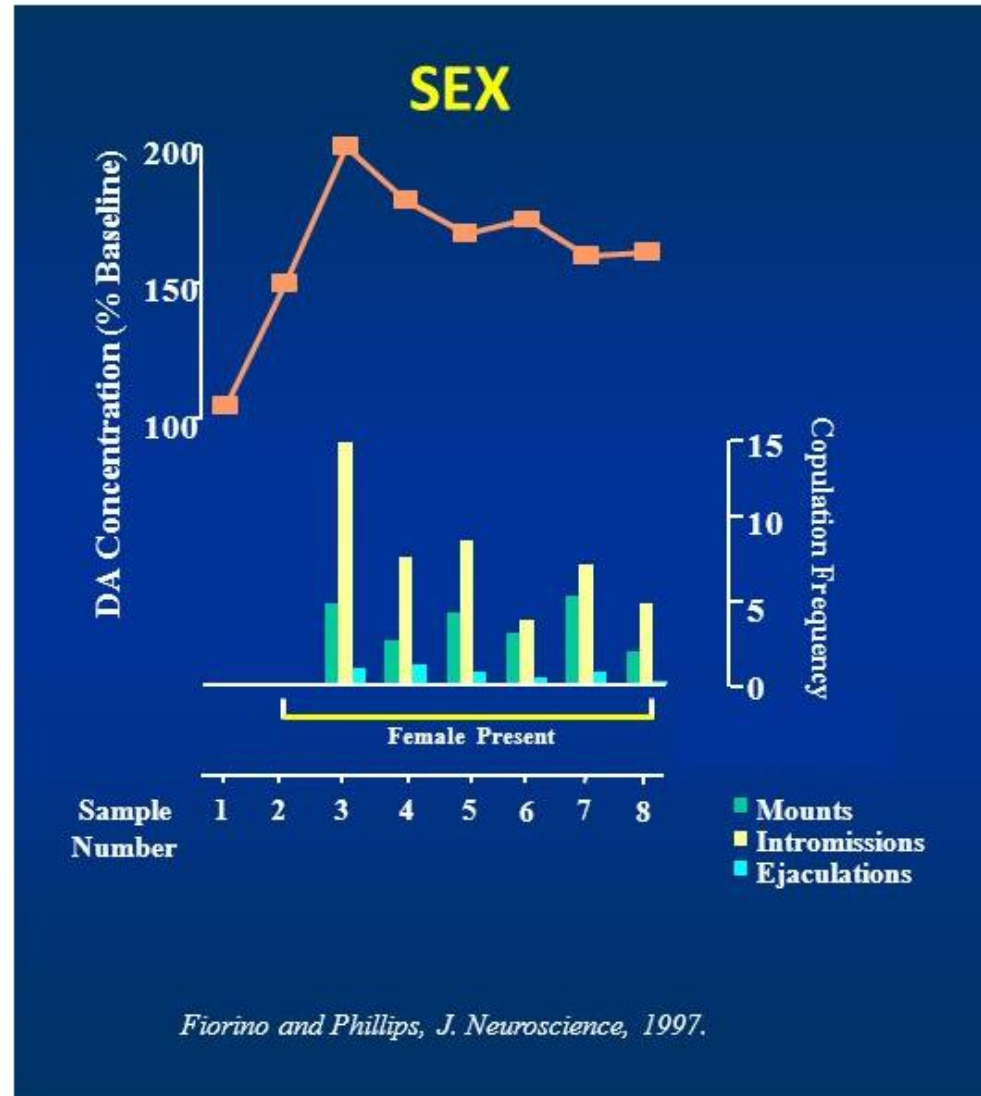
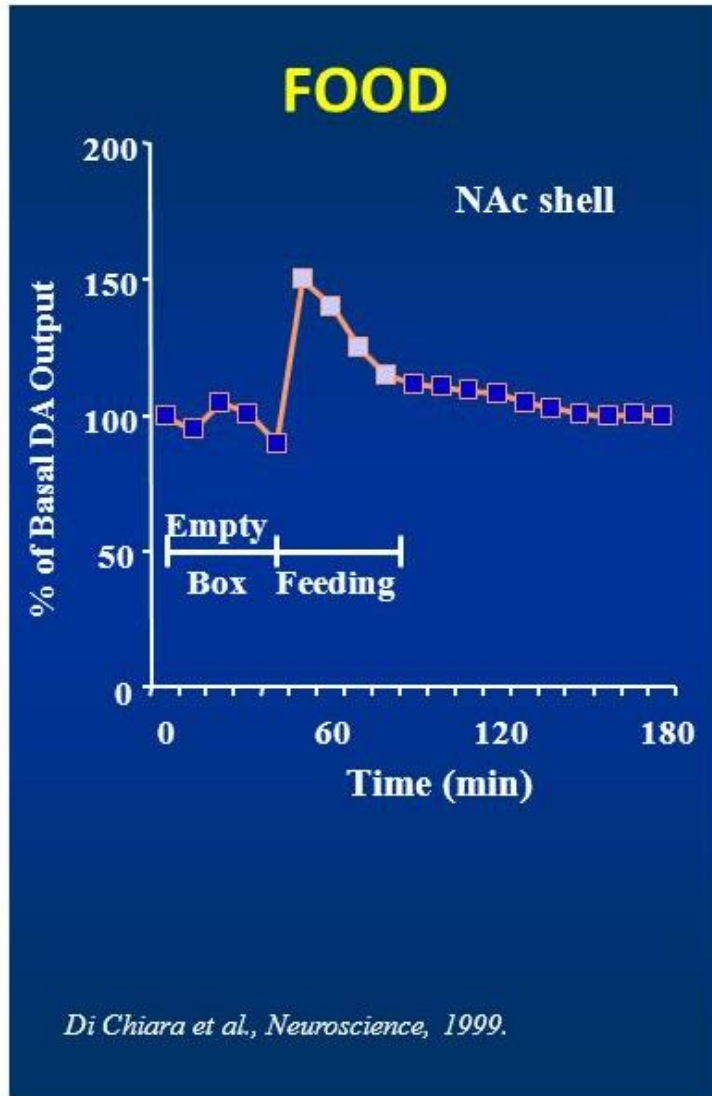
Meth: Mechanism of action

- Inhibits dopamine (DA) reuptake by DAT and VMAT
- Reverses DA transport
Internalizes DAT
- Impairs storage of DA

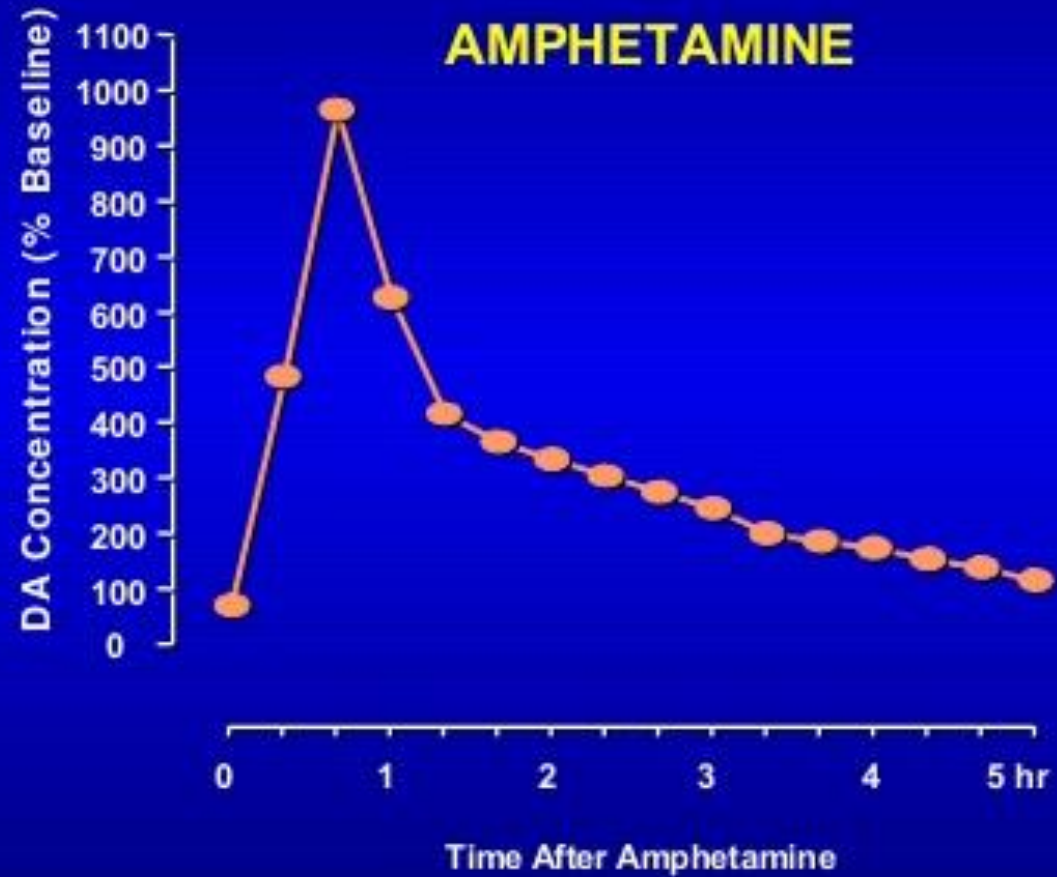
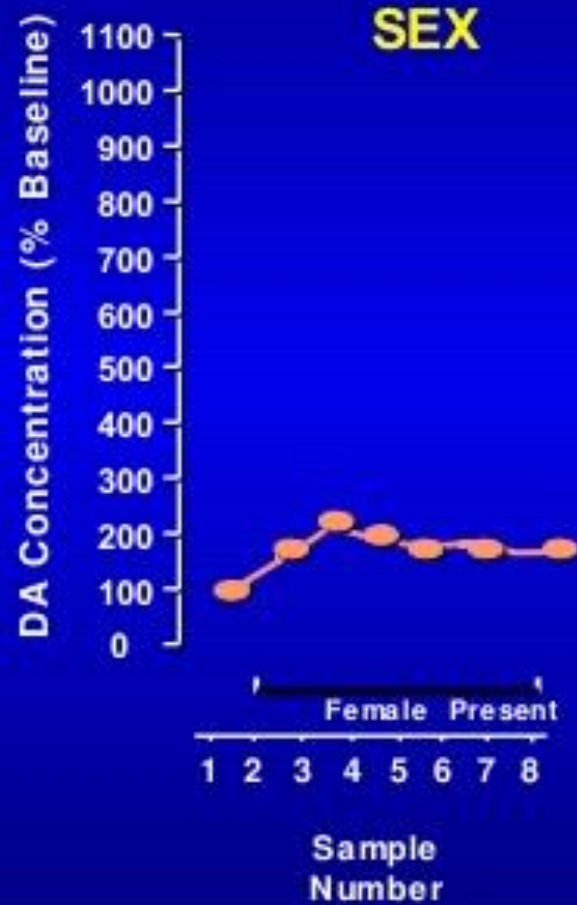


- ▲ Methamphetamine
- Dopamine
- ◀ Dopamine transporter
- ◀ Vesicular monoamine transporter 2
- ◀ Dopamine receptor

Natural rewards increase dopamine



But, amphetamines do it better!!!



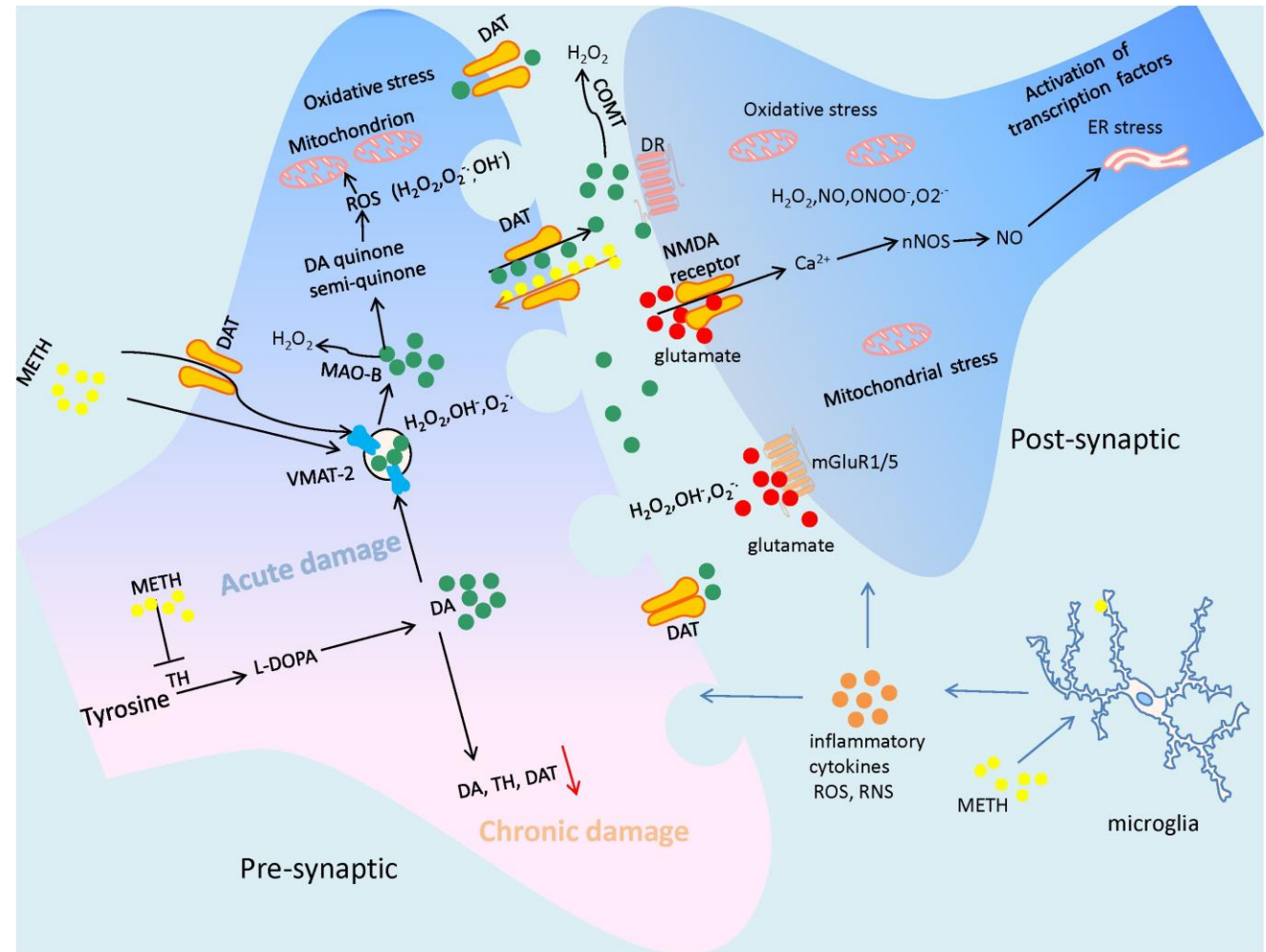
*Fiorino and Phillips,
J. Neuroscience, 1997.*

Short-term effects

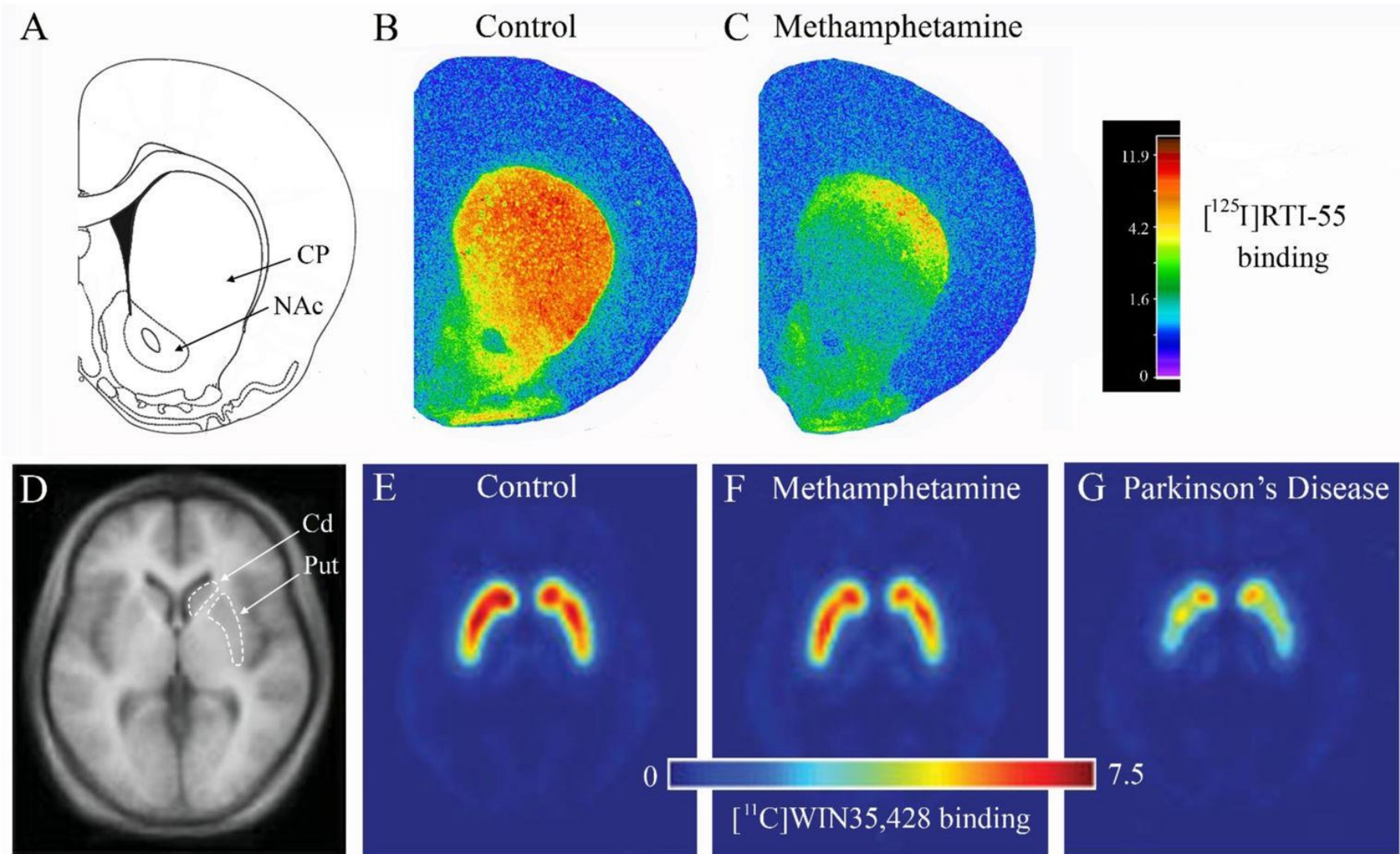
- Euphoria/“Rush”
- Increased wakefulness/physical activity
- Increased attention
- Decreased appetite
- Faster breathing
- Increased heart rate and blood pressure
- Increased body temperature

Meth neurotoxicity

- Damage to dopamine and serotonin neurons
- Neuronal apoptosis
- Neuroinflammatory response from activated astroglia and microglia



Chronic meth use decreases DAT



Chronic meth use: Addiction

- Decreased frontal cortex activation/gray matter/DA D2 receptors
 - Impaired decision-making, impulsivity
 - Attention deficits
- Structural/metabolic changes in striatum
 - Reinforcement, motivation, craving, compulsive behavior
- Decreased hippocampal volume
 - Impaired cognition and memory

Medical risks of chronic meth use

- Increased infection risk (HIV, hepatitis)
- Periodontal disease
- High body temperature
- Pulmonary hypertension
- Cerebrovascular events, stroke, kidney failure
- Develop psychiatric diseases
 - Parkinson's, depression, psychosis

Meth Abstinance: Reversal of DAT effects

