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

\[
\text{HO} - \text{C}_6\text{H}_4 - \text{CH} - \text{NH}_2
\]

\[
\text{HO} - \text{C}_6\text{H}_4
\]
Meth: Mechanism of action

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

**FOOD**

- NAc shell

**SEX**

- DA Concentration (% Baseline)

*Di Chiara et al., Neuroscience, 1999*

But, amphetamines do it better!!!
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 Abstinence: Reversal of DAT effects