Health and Safety Consequences of Psychostimulant Use

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Objectives

- Discuss the root causes and neurobiology of substance use
- Understand the pharmacology and effects of stimulants and hallucinogens
- Describe the presentation and treatment of stimulant and hallucinogen toxicity
- Review trends in the use, misuse, and overdose on stimulants, hallucinogens, and synthetics analogues
Neurobiology of Addiction

• Genetic
  – Increased risk in first degree relatives of individuals with any substance use disorder

• Psychosocial
  – Increased environmental availability and decreased perceived threat
  – Physical and/or psychological trauma
  – Impaired coping mechanisms

• Pharmacologic
  – Dopamine-mediated reward
  – Tolerance
  – Long term changes in stress response pathways
Nature vs. Nurture?

YES!

- 23-54% due to genetics in multiple studies\textsuperscript{1,2}
- 25% attributable to family environmental factors
- 44% attributable to non-family environmental factors

Environmental Risk Factors for Addiction Development

- Adolescent exposure to drugs or heavy drinking
- Low socioeconomic status
- Lack of social support systems
- Parental drug or alcohol use
- Parental depression
- Peer/sibling influences
- Drug availability
- School and neighborhood characteristics
- Trauma (ACES)

ACES can have lasting effects on:

- Health (obesity, diabetes, depression, suicide attempts, STDs, heart disease, cancer, stroke, COPD, broken bones)
- Behaviors (smoking, alcoholism, drug use)
- Life Potential (graduation rates, academic achievement, lost time from work)

Risk for Negative Health and Well-being Outcomes

ACES have been found to have a graded dose-response relationship with 40+ outcomes to date.

2. Sloboda Z, Glantz MD, Tarter RE. Revisiting the concepts of risk and protective factors for understanding the etiology and development of substance use and substance use disorders: implications for prevention. Substance Use Disord 2012; 47: 944–62
• ~8 million children live with an adult who has a substance use disorder

• Parents with SUD are 3x more likely to physically or sexually abuse their children

• From 1999-2014, incidence of parental substance use as a reason for child removal doubled (15.8→31.8%)²

• From 2004-2013, incidence of neonatal abstinence syndrome more than tripled (7 cases/1,000 admissions → 27 cases/1,000 admissions)³
Neuropharmacology of Drug Addiction

- Neurotransmitters Involved
  - Dopamine
  - Opioid
  - GABA
  - Glutamate
  - Serotonin
  - Acetylcholine
  - Endocannabinoids
  - Enkephalins
  - Norepinephrine
  - Corticotropin-releasing factor
  - Dynorphin
  - Neuropeptide Y
Stimulant Purity and Availability

- Cocaine and methamphetamine purity and availability have increased
- Price per gram has also decreased

![Price and Purity of Domestic Meth](source: DEA)

Figure 70. Methamphetamine Purity and Potency.

Source: DEA Methamphetamine Profiling Program

Substances Associated with Overdose Deaths

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018
Stimulant Misuse

- New stimulant misuse surpasses new opioid misuse
  - 2,079,000 vs. 2,017,000
Methamphetamine Exposures Reported to Poison Centers-PA and U.S.
Hospital Costs Associated with Stimulants

- Amphetamine-related hospital costs increased almost 400% from 2003 to 2015\(^1\)
  - 2003: ~$436 million
  - 2015: ~$2.17 billion

- Pennsylvania\(^2\):
  - Cocaine related hospitalizations +27% from 2016 to 2019
  - Amphetamine related hospitalizations +66% from 2016 to 2019

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Stimulants and Hallucinogens-Examples

- Cocaine
- Amphetamines, Rx and illicit
- Methamphetamine
- Cathinones (“bath salts”)
- Synthetic hallucinogenic stimulants
  - 25i-NBOMe (“N-bombs”, “acid”)
  - 2C, 2C-I
- Dissociative Agents
  - Phencyclidine, methoxetamine
- Serotonergic hallucinogens
  - Dimethyltryptamine (DMT)
  - MDMA (“Molly”)
• Synthetic Stimulants and Hallucinogens seized by DEA in 2018
  – 2C-B
  – 25i-NBOMe
  – 25B-NBOMe
  – 25C-NBOMe
  – 2C-H
  – 2C-I
  – 3-MeO-PCP
  – 2F-Deschloroketamine
  – 2-Oxo-PCE
  – MMMP
  – 4-Fluoroamphetamine
  – 5-MeO-DALT
  – 5-MeO-DiPT
Stimulant Pathophysiology

- Cocaine, amphetamine-based stimulants, and cathinones
- Direct receptor activation
- Inhibition of reuptake of biogenic amines
  - Serotonin
  - Norepinephrine
  - Dopamine
- Toxicity is related to relative effects on each transmitter/receptor system

![Chemical structures of stimulants](image)
Variety of serotonin receptor subtypes

Activation results in euphoria

Hallucinogenic effects
  - Primarily visual and tactile; synesthesias

Serotonin syndrome

SIADH with low sodium (particularly with MDMA)
Stimulant Pathophysiology-Norepinephrine and Dopamine

• Norepinephrine
  – Tachydyssrhythmias
  – Agitation
  – Delirium
  – Hypertension
  – Seizures
  – Mydriasis

• Dopamine
  – Tachydyssrhythmias
  – Hallucinations (visual and tactile)
  – Choreathetosis

http://archivetemp.iqscloud.net/NIDA_Notes/NNVol13N2/Brain.html
Dissociative Agents

- Ketamine, phencyclidine, dextromethorphan, methoxyphencyclidine, methoxetamine

- NMDA receptor antagonists
  - Dissociated high; out of body
  - Stupor or agitation
  - Analgesic properties
  - Horizontal and vertical nystagmus
  - Tachycardia and mild hypertension
  - Mydriasis
Acute Stimulant Toxicity

- Vital signs:
  - Hypertension and tachycardia
  - HYPERTHERMIA
- Agitation, delirium
- Seizures
- Intracranial hemorrhage, myocardial infarction and dysrhythmia
- Rhabdomyolysis
- Metabolic and/or respiratory acidosis
- Mydriasis
- Diaphoresis
Treatment of Hallucinogenic-Stimulant Toxicity

- Control agitation and/or seizures
  - Benzodiazepines
  - Antipsychotics
  - Ketamine
  - Propofol
  - NO NALOXONE-LIKE ANTIDOTE

- Airway management as needed

- Once adequately sedated, additional cardiovascular management

- Cooling and hydration
Chronic Stimulant Health Effects

- Pulmonary hypertension
  - 10x increased risk in patients with stimulant use

- Vasculitis
  - Drug-induced
  - Levamisole adulteration

- Increased platelet aggregation

- Atherosclerotic artery disease

- Psychosis

References:
Synthetic Cannabinoids

- Alkylindoles and cyclohexylphenols
- JWH, HU, and CP series Compounds
  - Sold as incense or potpourri in the U.S. since ~2010
  - Originally popularized in the U.K. and Europe in the mid-2000s
  - “Spice” and “K2” are common slang
- Full cannabinoid agonists leading to potent clinical effects
“-INACA” Compounds

- Indazole carboxamides
- Marked increase in use reported in early 2015
- True prevalence difficult to assess given limited testing capabilities
- Chemicals sprayed onto dried vegetative material, e.g. tobacco or marijuana
- ADB-CHMINACA identified in PA overdose patients
  - Allentown area in 4/15/15 with 8 associated deaths
  - ~100 to UPMC Hamot in 10/15-12/15 with ~15% requiring intubation
SYNTHETIC CANNABINOIDs

There were 984 synthetic cannabinoid identifications in 2016. FUB-AMB and SF-UR-144 were the most commonly reported synthetic cannabinoids, accounting for approximately 34% of the synthetic cannabinoid identifications during the reporting period. Of the 37 different synthetic cannabinoids identified, three (~8%) of these substances, PK-2, MMDM-CHMICA, and A8-CHMICA, were seized and reported for the first time in 2016.

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MAB-CHMINACA = A8-CHMINACA
Synthetic Cannabinoid Clinical Effects

- Severe agitation/psychosis
- Delirium
- Sinus tachycardia and hypertension
- Rhabdomyolysis
- Respiratory failure
- Initial agitation often followed by deep sedation
Chronic Cannabinoid Health Effects

• Largely unknown for newer synthetic cannabinoids

• Chronic adverse health effects associated with cannabinoid use
  – Addiction (9% of users; 17% in adolescents)
    – Lower IQ and increased dropout rates in adolescents
    – Diminished life satisfaction and achievement
  – Chronic bronchitis
  – Increased risk of psychosis

Just a Click Away…

all different amounts ranging from 5g to 1kg retail and also large amounts at wholesale prices, orders will be sent next day delivery.
Shipping from multiple warehouses: China, EU, USA, Russia
AB-CHMINACA

$20.00 Per Gram

**Formal Name:** N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide

**CAS Number:** 1185987-21-1

**Molecular Formula:** C20H28N4O2

**Formula Weight:** 356.5

**Formulation:** A crystalline solid

**Purity:** ≥98%

**λ<sub>max</sub>:** 210, 303 nm

**Stability:** 2 years

Category: CANNABINOIDS Tags: AB-CHMINACA
Canadian Connection
Thank you!