Methamphetamine use disorder (+ HIV): Trials, Trends and Tribulations

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WHAT-IF? Learning Collaborative
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Outline

• Background
• Physiology and health effects
• Epidemiology
• Treatment
Why the fuss?

- Higher rates of meth use in populations at risk for HIV
  - Up to 20% of MSM may report meth use within past 6mo \(^1\)
- Meth use is associated with an increased risk of contracting HIV
  - Higher rates of risky behaviours (high risk injection and/or sexual practices) \(^2\)
  - Impaired/altered immunity? \(^3\)
- Meth use is associated with worse HIV outcomes
  - Decreased ART adherence, slower rates of RNA suppression, decreased CD4 counts, poor overall health outcomes \(^3,4\)

HIV prevalence among MSM who primarily injected meth was almost 50% higher than among MSM who primarily injected other drugs, and this association was mediated by sexual risk.
Background
Ephedra sinica
Methamphetamine

- Methamphetamine powder
  - PO or insufflated

- Methamphetamine base
  - PO or injected

- Crystal methamphetamine
  - Smoked, insufflated or injected

Half-life for all 3 close to \(~10\) hours!

\(\text{Ice, crystal, glass, speed, meth, jib, side, gak, chalk, crank, tina, go, geek, tweak, amp, P2P, zip, shards, goofball}^*\)
Narcolepsy, exhaustion, weight loss, schizophrenia, asthma, morphine addiction, barbiturate intoxication, alcoholism, excessive anaesthesia administration, migraine, heart block, myasthenia gravis, myotonia, enuresis, dysmenorrhea, Meniere’s disease, colic, head injuries, infantile cerebral palsy, codeine addiction, tobacco smoking, pediatric behaviour issues, Parkinson’s disease, epilepsy…
Physiology and effects
# Pharmacology

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
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</thead>
<tbody>
<tr>
<td>Methamphetamine</td>
<td><img src="structure1.png" alt="Methamphetamine" /></td>
</tr>
<tr>
<td>Ephedrine</td>
<td><img src="structure2.png" alt="Ephedrine" /></td>
</tr>
<tr>
<td>MDMA</td>
<td><img src="structure3.png" alt="MDMA" /></td>
</tr>
<tr>
<td>MDPV</td>
<td><img src="structure4.png" alt="MDPV" /></td>
</tr>
<tr>
<td>Amphetamine</td>
<td><img src="structure5.png" alt="Amphetamine" /></td>
</tr>
<tr>
<td>Pseudoephedrine</td>
<td><img src="structure6.png" alt="Pseudoephedrine" /></td>
</tr>
<tr>
<td>Mephedrone</td>
<td><img src="structure7.png" alt="Mephedrone" /></td>
</tr>
<tr>
<td>Cocaine</td>
<td><img src="structure8.png" alt="Cocaine" /></td>
</tr>
</tbody>
</table>

All of the above compounds belong to the phenethylamine class of psychostimulants except cocaine; MDMA = methylenedioxyamphetamine; MDPV = methylenedioxyprovalerone

![Diagram of neurotransmission](diagram.png)
Acute intoxication

- Mania/paranoia/psychosis
- Hypertension, agitation, sweating
- Skin-picking/formication (delusions of insects under the skin)
- Abnormal movement (choreoathetosis, ataxia)
- Miosis
**Meth-associated health complications**

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Infectious</th>
<th>Hematologic</th>
<th>Gastrointestinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>HIV</td>
<td>Necrotizing angiitis</td>
<td>Acute liver injury</td>
</tr>
<tr>
<td>CAD</td>
<td>Viral hepatitis</td>
<td></td>
<td>Mesenteric infarction</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>MSK</td>
<td>Ischemic colitis</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Neurologic</td>
<td>“Meth mouth”</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Hypertension</td>
<td>ICH</td>
<td>Rhabdomyolysis</td>
<td></td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td>Ischemic stroke</td>
<td>Traumas</td>
<td>Pulmonary</td>
</tr>
<tr>
<td>Dilated CMO</td>
<td>Seizure</td>
<td>Osteomyelitis</td>
<td>Pulmonary edema</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Cognitive impairment</td>
<td></td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatologic</td>
<td>Fetal growth restriction</td>
<td></td>
<td>Renal</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Picking/excoriations</td>
<td>Premature delivery</td>
<td>Myoglobinuria</td>
</tr>
<tr>
<td>STIs</td>
<td>Cellulitis</td>
<td>Abruption</td>
<td>Necrotizing angiitis</td>
</tr>
<tr>
<td></td>
<td>Abscesses</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Societal harms: environmental hazards/pollution, crime, violence.*

Adapted from Vearrier et al. Dis Mon, 2012.
Neurotoxicity (dopamine neurons)

Comparison Subject  Methamphetamine Abuser

\(^a\) PET scan was performed 80 days after detoxification.

Epidemiology
FIG. 27 Global quantity of amphetamine-type stimulants seized, 1998–2017
## US National Survey on Drug use and Health: Prevalence of Illicit Drug Use

### Table 1.6B  Types of Illicit Drug Use in Lifetime, Past Year, and Past Month among Persons Aged 18 or Older: Percentages, 2015 and 2016

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>ILIlicit Drugs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana</td>
<td>46.9</td>
<td>47.0</td>
<td>12.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.1</td>
<td>8.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.1</td>
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<tr>
<td>Cocaine</td>
<td>15.9</td>
<td>15.8</td>
<td>1.9</td>
<td>2.0</td>
<td>0.8</td>
<td>0.8</td>
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<tr>
<td>Crack</td>
<td>3.7</td>
<td>3.6</td>
<td>0.3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.2</td>
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<tr>
<td>Heroin</td>
<td>2.1</td>
<td>2.0</td>
<td>0.3</td>
<td>0.4</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>16.5</td>
<td>16.7</td>
<td>1.7</td>
<td>1.8</td>
<td>0.5</td>
<td>0.5</td>
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<tr>
<td>LSD</td>
<td>10.3</td>
<td>10.5</td>
<td>0.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.7</td>
<td>0.1</td>
<td>0.1</td>
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<tr>
<td>PCP</td>
<td>2.6</td>
<td>2.6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>Ecstasy</td>
<td>7.4</td>
<td>7.4</td>
<td>1.0</td>
<td>0.9</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Inhalants</td>
<td>9.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.1</td>
<td>0.4</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>5.9</td>
<td>5.9</td>
<td>0.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.6</td>
<td>0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.3</td>
</tr>
<tr>
<td>Misuse of Psychotherapeutics&lt;sup&gt;++&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Relievers&lt;sup&gt;4&lt;/sup&gt;</td>
<td>nr</td>
<td>nr</td>
<td>7.2</td>
<td>7.1</td>
<td>2.4</td>
<td>2.4</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>nr</td>
<td>nr</td>
<td>4.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.3</td>
<td>1.4</td>
<td>1.3</td>
</tr>
<tr>
<td>Stimulants</td>
<td>nr</td>
<td>nr</td>
<td>2.3</td>
<td>2.3</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Sedatives</td>
<td>nr</td>
<td>nr</td>
<td>2.0</td>
<td>2.1</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>OPIOIDS (HEROIN USE OR PAIN RELIEVER MISUSE)</strong>&lt;sup&gt;4&lt;/sup&gt;</td>
<td>nr</td>
<td>nr</td>
<td>4.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.5</td>
<td>1.5</td>
<td>1.4</td>
</tr>
</tbody>
</table>
Methamphetamine Lab Distribution in the US

DEA National Clandestine Laboratory Registry, 2004-2012.
Figure 1. Amphetamine-Related Hospitalizations in the United States, 2003 to 2015

Regression models were used to examine in-hospital mortality and length of stay. Analysis of these data was conducted from November 2017 to August 2018.

**EXPOSURE**  Amphetamine dependence or abuse or amphetamine poisoning.

**MAIN OUTCOMES AND MEASURES**  Annual hospitalizations, in-hospital mortality, length of stay.
Psychostimulant-related overdose deaths in US, 1999-2017

- Total psychostimulants (including methamphetamine)
- Psychostimulants and any opioid
- Psychostimulants without any opioid
- Psychostimulants and other synthetic opioids
Treatment
Approach to treatment for stimulant use disorder

Stimulant use disorder

Mild
Drug counseling

Sustained remission
Continued use or relapse

Moderate to severe

Intensive outpatient therapy

Sustained remission
Continued use or relapse

Augment with contingency management or CBT or motivational interviewing

Sustained remission
Continued use or relapse

Refer to UpToDate topic on the implementation of continuing care of addiction
Referral to addiction specialist for adjunctive medication

CBT: cognitive-behavioral therapy.
Stimulant Use Disorder
Treatment

Pharmacologic

- SSRIs
  - Mirtazapine
- Anti-Psychotics
  - Aripiprazole
  - Risperidone
- Anti-Depressants
  - Modafinil
  - Methylphenidate
  - Bupropion
- Agonist Therapies
  - Dextroamphetamine

Non-pharmacologic

- CBT (+/- MI)
- Contingency Management
  - Others: gabapentin, baclofen, vigabatrin, topiramate, ondansetron, naltrexone, ibudilast...
# Trial medications

<table>
<thead>
<tr>
<th>Study Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychostimulants (dexamphetamine, methylphenidate)</td>
<td>9 RCTs: may decrease use, craving, and/or severity of addiction?</td>
</tr>
<tr>
<td>Topiramate</td>
<td>2 RCTs: may decrease use, and/or severity?</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>1 RCT: may decrease use?</td>
</tr>
<tr>
<td>Bupropion</td>
<td>5 RCTs: may decrease use?</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>2 RCTs: may decrease use and/or craving?</td>
</tr>
<tr>
<td>Modafinil</td>
<td>3 RCTs: may decrease use?</td>
</tr>
</tbody>
</table>

*Studies limited by retention, adherence, primary outcomes.*

Adapted from Lee et al., Drug Alc Dep. 2018.
Treatment of Stimulant Use Disorder: Psychosocial Treatments

1. Contingency management
2. Cognitive behavioural therapy
3. Motivational interviewing
4. Relapse prevention
5. Psychodynamic therapy
6. Combinations programs

- Overall small to moderate effects (dropout rates are typically >40%)
- Immediate effects noted, long-term benefits for meth use disorder not clear
Treatment of Stimulant Use Disorder: Psychosocial Treatments

Contingency Management

- Goal is to reduce reinforcement provided by drug use while simultaneously increasing reinforcement for healthier activities
- Applies contingencies in the form of reinforcement and consequences in order to reduce substance use
- Often uses a voucher-based system to give possible rewards for staying in treatment or remaining drug-free
- A 2016 systematic review found that contingency management helped to decrease use in a diverse group of substance use disorders, with a treatment effect that weakened but did not disappear following treatment termination

Clinical responses to CM in PROP were similar to CM delivered in drug treatment programs. [...] Further expansion of programs like PROP could address the increasing needs for acceptable, feasible, and cost-effective methamphetamine treatment in this group with exceptionally high rates of HIV-infection.
Conclusions

• The prevalence of methamphetamine use continues to rise and it is associated with numerous physical, psychiatric, and social harms

• Methamphetamine use is associated with an increased risk of contracting HIV and worse HIV treatment outcomes

• Evidence-based treatments are available for stimulant use disorder, psychosocial approaches (esp. CM) remain the gold standard and can be implemented in settings with high rates of HIV
Questions?

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