Welcome!

Mute
Minimize Interruptions
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Chat
Go Ahead, Speak Up!
Use the Zoom chat to ask questions and participate in activities.

Naming
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Represent your team and add your organization’s name to your name.

Tech Issues
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While we wait, please rename yourself.
Addiction Treatment Starts Here
Prescriber Forum Session #3

“Didactic Teaching on Stimulant Use Disorders Prescribing”

November 19, 2021 | 12 – 1pm (PT)
Today’s Presenter

Joe Sepulveda, MD, FAPA, FASAM
Chief of Psychiatry
Medical Director, Substance Use Disorder Services

Family Health Centers of San Diego
Stimulant Use Disorder & Evidence-based Treatment 101

Joe Sepulveda, M.D., FAPA, FASAM
Chief of Psychiatry, Family Health Centers of San Diego (FHCSD)
Medical Director, Substance Use Disorder Services
Medication-Assisted Treatment (MAT) Program
Psychiatric Nurse Practitioner Program
Voluntary Assistant Clinical Professor, UCSD Health Sciences—Dept. of Psychiatry
Diplomate of the American Board of Psychiatry and Neurology
Diplomate of the American Board of Preventive Medicine—Addiction Medicine
Fellow of the American Psychiatric Association
Fellow of the American Society of Addiction Medicine
• Overview of Amphetamines
• Methamphetamines vs. Cocaine
• Physical and Psychological effects of Amphetamines
• Toxicology testing for stimulants
• Evidence-based psychosocial interventions
• Medications for Stimulant use (none are FDA approved)
• Key Principles for treating Stimulant Use Disorder – “Take Home Message”
• Stimulants and Fentanyl
• Comprehensive care
Disclosures

Joe Sepulveda, M.D., FAPA, FASAM

No financial conflicts of interest

None of the medications discussed in this presentation are FDA approved for any Stimulant Use Disorder
Amphetamine-Type Stimulants & Cocaine

Examples of Stimulants

- Cocaine
- Methamphetamine
- Amphetamine-type stimulants (e.g. MDMA/Ecstasy)
- Prescription stimulants (e.g. mixed amphetamine salts, dextroamphetamine, methylphenidate)
- Other Amphetamine-type stimulants (e.g. bath salts)
Methamphetamine Use Disorder in the U.S.
Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years

Han, B., et al., JAMA 2021
Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years

Adjusted past-year prevalence of methamphetamine use disorder (no injection) by sex and sexual orientation

Han, B., et al., JAMA 2021
Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years

Adjusted past-year prevalence of methamphetamine use disorder (no injection) by race/ethnicity

Han, B., et al., JAMA 2021
# Cocaine vs. Methamphetamine

<table>
<thead>
<tr>
<th>Cocaine</th>
<th>Methamphetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Plant-derived</td>
<td>• Synthetic</td>
</tr>
<tr>
<td>• Effects last 1-2 hours</td>
<td>• Effects last 10-20 hours</td>
</tr>
<tr>
<td>• T½: 1 hour</td>
<td>• T½: 12 hours</td>
</tr>
<tr>
<td>• Mechanism: mainly DA/NE</td>
<td>• Mechanism: mainly DA/NE release</td>
</tr>
<tr>
<td>reuptake</td>
<td>• Neurotoxicity</td>
</tr>
<tr>
<td>• <em>NOT</em> directly neurotoxic</td>
<td>• Withdrawal ➡ 1-2 days</td>
</tr>
<tr>
<td>• Withdrawal ➡ 1-2 days</td>
<td>• Withdrawal ➡ <em>SEVERAL</em> days</td>
</tr>
</tbody>
</table>
Pharmacology of Cocaine
Methamphetamine
Pharmacology of Methamphetamine

- Blocks Reuptake
- Facilitates release of newly formed catecholamine
- Blocks break down of catecholamine in the neuron
Destruction and Recovery of Dopamine Transporter in Meth Users

Nora D. Volkow et al., J. Neurosci. 2001
Meth is toxic to the brain triggering glial activation and neuroinflammation

Neuroinflammation persists despite years of abstinence and may trigger relapse

### Acute Physical & Psychological Effect of Stimulants

<table>
<thead>
<tr>
<th>Physical</th>
<th>Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Increase</strong></td>
<td><strong>Increase</strong></td>
</tr>
<tr>
<td>- Energy/productivity</td>
<td>- Energy</td>
</tr>
<tr>
<td>- Heart Rate</td>
<td>- Confidence</td>
</tr>
<tr>
<td>- Blood pressure</td>
<td>- Alertness</td>
</tr>
<tr>
<td>- Respiration</td>
<td>- Mood/Euphoria</td>
</tr>
<tr>
<td>- Pupil size</td>
<td>- Sex Drive</td>
</tr>
<tr>
<td><strong>Decrease</strong></td>
<td><strong>Decrease</strong></td>
</tr>
<tr>
<td>- Appetite (weight loss)</td>
<td>- Boredom</td>
</tr>
<tr>
<td>- Sleep</td>
<td>- Loneliness</td>
</tr>
<tr>
<td>- Reaction Time</td>
<td>- Timidness</td>
</tr>
</tbody>
</table>

NIDA, 2019
Chronic Psychological Effects of Stimulants

- Hallucinations
- Paranoia
- Psychosis
- Depression
- Concentration
- Memory loss

- Irritability
- Anger
- Panic reactions
- Fatigue
- Insomnia
- Confusion

NIDA, 2019
Organ system damage

Cardiac
- Heart Failure
- Cardiomyopathy
- Myocarditis
- Myocardial infarction
- Arrhythmia → Sudden Death
- Tachycardia
- Reduced heart rate variability
- Microvascular Dz
- Accelerated CAD → Catacholamine excess

Respiratory
- Pulmonary HTN
- Pleuritic chest pain
- Edema
- Decrease capacity

Neurological
- Movement disorders
  - Parkinson’s
  - Tremor
- Neurocognitive Impairment
- Seizures
- Hemorrhage
- Cerebral vasculitis

Dental
- Cavities
- Tooth Erosion
- Periodontal Dz

Hepatic Failure
- Rhabdomyolysis

Renal failure
- Rhabdomyolysis → Renal tubular obstruction

NIDA, 2019; Lappin et al, 2018; Curtin et al, 2015; Callaghan et al, 2011; Turnipsee et al, 2003; Karch, 2002; Rhee et al., 1998; Wallace et al, 1999
Drug Testing: Stimulants

Oral fluid testing
• Shorter detection windows than urine

Serum Testing
• For acute intoxication

Hair testing
• Longer period of detection (e.g. up to 90 days)
• Better for detection of heavy, frequent use
Urine Drug Testing: Stimulants

Amphetamine, Methamphetamine
- Detection window approximately 2-3 days
- False positives: pseudoephedrine, bupropion, labetolol, ranitidine, trazodone, TCA’s
- Low sensitivity for detection of MDMA
- 2 methamphetamine isomers: D (CNS) and L (Peripheral)

Cocaine
- Detection window 2-4 days
- Primary metabolite: Benzoyleconnine
- False positives RARE
EVIDENCE-BASED RESOURCE GUIDE SERIES

Treatment of Stimulant Use Disorders

https://store.samhsa.gov/product/Treatment-of-Stimulant-Use-Disorder/PEP20-06-01-001
Four psychosocial treatments

<table>
<thead>
<tr>
<th>Summary of Evidence Review</th>
</tr>
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<tbody>
<tr>
<td>Practice</td>
</tr>
<tr>
<td>Review rating</td>
</tr>
<tr>
<td>Focus of the practice</td>
</tr>
<tr>
<td>Can be used in outpatient healthcare settings</td>
</tr>
<tr>
<td>Can be used in inpatient healthcare setting</td>
</tr>
<tr>
<td>Specific training available</td>
</tr>
<tr>
<td>Web-based version available</td>
</tr>
<tr>
<td>Can be practiced by peers</td>
</tr>
<tr>
<td>Has been used successfully with males and females</td>
</tr>
<tr>
<td>Special populations with whom the practice has been successfully implemented</td>
</tr>
<tr>
<td>Intensity and Duration of Treatment</td>
</tr>
</tbody>
</table>

https://store.samhsa.gov/product/Treatment-of-Stimulant-Use-Disorder/PEP20-06-01-001
Motivational Interviewing (MI)

- Evoke change talk from individuals overcome ambivalent feelings and insecurities
- In the process, individuals become more likely to make the changes that they verbalize.
- MI does not have a prescribed time period
Motivational Interviewing (MI)

- Five principles
  - Empathy through reflective listening
  - Identify discrepancies between patient's goals/values and current behaviors
  - Avoid arguments and direct confrontations
  - Adjust to a patient's resistance rather than opposing it directly
  - Support self-efficacy and optimism
Motivational Interviewing: Resources

Available at: http://pcssnow.org/event/motivational-interviewing-brushing-up-on-the-basics and http://motivationalinterviewing.org
Contingency Management (CM)

• Basic Assumptions of CM
  
  • Substance use can be reduced using operant conditioning
  
  • Useful in promoting treatment retention and adherence
  
  • Incentives for negative urine tests useful in decreasing drug use
Applications of Contingency Management

• Behavioral targets:
  • Counseling attendance
  • Drug use

• Reinforcing consequences:
  • Money (or vouchers)
  • Privileges (e.g. take-home doses)

Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, ctndisseminationlibrary.org/PPT/485Stitzer.ppt
Contingency Management (CM)

• Key Concepts

  • Behavior to be modified (e.g. stimulant use) must be objectively measured

  • Behavior to be modified (e.g. urine toxicology tests) must be monitored frequently

  • Reinforcement must be immediate

  • Penalties for unsuccessful behavior (e.g. +UDS) include withholding the reinforcer
Fishbowl Method

Incentive = draws from a bowl

- Draws earned for each negative urine
- Number of draws can escalate
- Bonus draws can be given for consecutive weeks of abstinence

Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, cndisseminationlibrary.org/PPT/485Stitzer.ppt
Half the fishbowl slips are winners
Win frequency inversely related to cost

➢ largest chance of winning a small $1 prize
➢ moderate chance of winning a large $20 prize
➢ small chance of winning a jumbo $100 prize
Voucher Incentives in Treatment


Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, cndisseminationlibrary.org/PPT/485Stitzer.ppt
Community Reinforcement Approach (CRA)

Elements of Community Reinforcement Approach

- Functional Analysis of Substance Use
- Relationship Counseling
- Vocational Guidance and Job Skills Training
- Therapy Focused on Building Social and Drug Refusal Skills
- New Recreational Activities and Social Networks
Cognitive Behavioral Therapy (CBT)

• Patients trained to evaluate faulty patterns of thinking, actions, and negative feelings associated with their drug use

• Tailored to the needs of the individual and their unique experiences with their stimulant use

• Standard therapeutic session last ~50 minutes

• Counseling period last ~5-10 months
Medications for Stimulant Use Disorder (MAT for StUD)
Medications for Methamphetamine Use Disorder (none are FDA approved)

• Naltrexone LAI and high dose bupropion (small effect)
• Mirtazapine (two small studies)
• Bupropion (low-level users who will adhere)
• Topiramate (low-level users)
• Naltrexone (for those who had already stopped using methamphetamine for 2+ weeks)

• Dextroamphetamine (one small study)
• Methylphenidate (moderate to high dose in frequent users/those with ADHD)

http://custom.cvent.com/10D3BAE39269457884C1D96DE1DF8D8D/files/f9dd789e619c417e8d753a1c767a28b8.pdf

http://vimeo.com/390978438/7e844d0b02
Mirtazapine 30mg QD vs. placebo in meth dependent MSM (N=60)

Colfax, GN, et al., Arch Gen Psychiatry. 2011 Nov.; 68(11): 1168-1175
Mirtazapine

- Start mirtazapine at 15 mg qHS and increase to 30mg qHS after 7 days
- Treats Depression, Anxiety and helps with Insomnia
- Common side effects:
  - Weight gain
  - Sedation
Bupropion: dopamine-norepinephrine re-uptake inhibitor for meth?

Randomized trial of bupropion SR 150 mg bid vs placebo for 12 weeks in methamphetamine users with *less than daily meth use*

<table>
<thead>
<tr>
<th>Total sample</th>
<th>Bupropion (N=41)</th>
<th>Placebo (N=43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of treatment abstinence</td>
<td>29% (12)</td>
<td>14% (6)</td>
<td>0.087</td>
</tr>
</tbody>
</table>

Only 32% (13/41) of bupropion participants were deemed medication adherent via week 6 plasma bupropion level. Adherence was strongly associated with end of treatment meth abstinence.

<table>
<thead>
<tr>
<th>Bupropion only</th>
<th>Adherent (N=13)</th>
<th>Non-adherent (N=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of treatment abstinence</td>
<td>54% (7)</td>
<td>18% (5)</td>
<td>0.018</td>
</tr>
</tbody>
</table>
Bupropion

- Start Bupropion XL 150 mg daily for 7 days, then 300 mg daily thereafter

- **Avoid** in those who:
  - Abuse ETOH/Sedatives or undergoing abrupt ETOH/Sedative discontinuation
  - Bulimia/Anorexia Nervosa
  - Patients with increase risk of Seizures

- Common side effects: Dry mouth, anxiety, insomnia
Topiramate

Topiramate

- Start 25mg qHS and titrate up in 25 to 50mg increments as tolerated over a month until the patient is taking either 100mg BID or 200mg qHS, or until the patient’s maximum tolerated dose is reached.

- Do NOT neglect to provide contraceptive treatments to appropriate patients of childbearing age who are prescribed topiramate.

- Kidney Stones: Use with other carbonic anhydrase inhibitors, other drugs causing metabolic acidosis, or in patients on a ketogenic diet should be avoided.
Naltrexone LAI + Bupropion XL

A. Response

- Percentage of Participants with a Response
- Stage 1: 16.3%
- Stage 2: 11.4%
- Weighted average: 12.6%
- Naltrexone-Bupropion Group
- Placebo Group
- Difference, 11.3 percentage points

B. Methamphetamine-Negative Urine Samples

- Percentage of Negative Urine Samples
- Naltrexone-Bupropion
- Placebo
- Placebo/Naltrexone-Bupropion
- Placebo/placebo
- Stage 1 evaluation period
- Stage 2 evaluation period

Trivedi, M.H., NEJM, 2021
Naltrexone PO and Naltrexone LAI + Bupropion XL

- Patients must be opioid-free for a minimum of 7-10 days before starting Naltrexone treatment

- Administer Naltrexone extended-release injectable suspension 380mg via intramuscular injection monthly or oral naltrexone 50mg daily

- Naltrexone extended-release injectable suspension in combination with bupropion XL (In the study previously shown):
  - Administer Naltrexone extended-release injectable suspension 380mg via intramuscular injection every three weeks in combination with Buproprion XL
  - Titrated Buproprion XL 150mg on day 1, 300mg on day 2, and 450mg daily beginning day 3.
  - Doses can be reduced to alleviate adverse effects although in the trial the prescribing clinicians were encouraged to attempt to raise the dose back up to the 450mg daily dose.
Medications for Cocaine Use Disorder (none are FDA approved)

- Sertraline (abstinent from cocaine and experiencing depression)
- Topiramate (low-level users)
- Modafinil (if the client does not have alcohol use disorder)
- Methamphetamine Sustained Release
- Combination of Mixed Amphetamine Salts-Extended Release and Topiramate
- Mixed Amphetamine Salts-Extended Release (high dose if +ADHD)
- Dextroamphetamine Sustained Release

http://custom.cvent.com/10D3BAE39269457884C1D96DE1DF8D8D/files/f9dd789e619c417e8d753a1c767a28b8.pdf

http://vimeo.com/390978438/7e844d0b02
Stimulant Use Disorder Treatment Key Principles

- Avoid Confrontation
- Therapeutic Alliance
- Meeting the patient where they are at
- Motivational Interviewing
- CM ± CRA
- CBT
- Counseling plus meds
- Frequent Follow-up Visits
- Exercise
Stimulant Use Disorder Treatment Key Principles

Follow-Up

- Monitor whether patient is achieving their goals
  - If patient not responding to treatment → reassess and adapt or change treatment(s)
  - Develop tracking protocols (e.g., EHR registry) for ensuring population-based follow-up
Methamphetamines and Fentanyl

LaRue et al, 2019
“Goofball” = Risky Use leading to Deadly results
Don’t forget to provide comprehensive care

• StUD patients require comprehensive care!
  • Physical health issues
  • Co-morbid substance use
  • Mental Health
  • Psychosocial issues
• Patient education
  • Narcan!!!

• Laboratory workup recommended
  • CBC
  • CMP
  • Hepatitis A, B & C
  • Pregnancy test
  • STD/HIV screen
  • Urine toxicology, comprehensive
References


References


The California Substance Use Line: A resource for health care providers

Free, confidential, on-demand, 24/7 teleconsultation on substance use evaluation & management for any health care provider in California

<table>
<thead>
<tr>
<th>Evidence-based, person-centered guidance on topics such as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Assessment &amp; treatment of opioid, stimulant, and other use disorders</td>
</tr>
<tr>
<td>• Medications for substance use disorder treatment (e.g., buprenorphine)</td>
</tr>
<tr>
<td>• Withdrawal management</td>
</tr>
<tr>
<td>• Opioid safety and harm reduction</td>
</tr>
<tr>
<td>• Special circumstances (e.g., co-occurring pain, polysubstance use, pregnancy)</td>
</tr>
</tbody>
</table>

• Staffed by experienced physicians and pharmacists from the California Poison Control System & National Clinician Consultation Center

• For more information, please call or visit our website | Please send program-related inquiries to David Monticalvo, Project Manager (David.Monticalvo@ucsf.edu)
### Poll

1. **On a scale of 1-5, please select the number that best represents your experience with today’s session.**
   - 5 - Excellent
   - 4 - Very Good
   - 3 - Good
   - 2 - Fair
   - 1 - Poor

2. **Please select the number that best represents your response to the statement: Today’s session was a valuable use of my time.**
   - 5 - Strongly Agree
   - 4 - Agree
   - 3 - Neutral
   - 2 - Disagree
   - 1 - Strongly Disagree

3. **I can apply learnings from today’s webinar to my MAT work.**
   - 5 - Strongly Agree
   - 4 - Agree
   - 3 - Neutral
   - 2 - Disagree
   - 1 - Strongly Disagree
Coming Up – Session #4 (final session)

Friday, December 3, 12-1pm PT

**Topic:** Office Hours – Prescribing Medications for OUD and StUD

Come with questions, challenges, and case examples you’d like to discuss on the call with Dr. Sepulveda and other attendees.

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For registration information, go here: https://www.careinnovations.org/events/atsh-peer-forums-registration/#prescriber

Any questions? Email meaghan@careinnovations.org