SUDs Masquerading as Other Psychiatric Illnesses

Better Understanding Diagnoses & Treatment Considerations

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A Primary Care Approach to Treating Substance Use Disorders
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Objectives

1. Understand how substance use disorders (SUDs) can mimic other psychiatric diagnoses.
2. Learn how substances impact mood, anxiety, psychosis, cognition, and behavior
3. Explore in detail substance-induced psychosis vs primary psychosis and implicated substances of abuse, highlighting:
    - Methamphetamine
    - Cannabis
4. Assess diagnostic differentiation strategies.
5. Explore treatment strategies in primary care settings.
6. Review Takeaways

Overlap Between SUDs and Other Psychiatric Disorders

- **High Comorbidity:** Over 50% of individuals with a SUD have a co-occurring mental health disorder.
- **Diagnostic Pitfalls:** Symptoms of intoxication, withdrawal, and impaired function 2/2 substance use can be mistaken for primary psychiatric conditions.
- **Examples of Potential Misdiagnosis:**
  - A patient with stimulant-induced manic symptoms diagnosed as bipolar disorder.
  - A patient with alcohol use disorder with 2ndary mood symptoms mistakenly diagnosed with depression.

Neurobiological Basis of Substance-Induced Symptoms

Neurotransmitter Effects:

- **Dopamine:** Psychosis, impulsivity (Stimulants: e.g. Methamphetamine)
- **Serotonin:** Mood instability, hallucinations (MDMA, LSD)
- **GABA:** Sedation, disinhibition and impaired cognition, (Alcohol, Benzos)
- **Glutamate:** Excitotoxicity, agitation (Ketamine), anxiety, seizures (withdrawal from Alcohol/Benzos)

Structural & Functional Brain Changes:

- Prefrontal cortex impairment → Poor impulse control, emotional dysregulation.
- Limbic system hyperactivity → Heightened anxiety and mood swings.

Mood Symptoms & Substance Use

Substance	Mania-like Symptoms	Depression-like Symptoms
Stimulants (Meth, Cocaine)	Grandiosity, insomnia, agitation	Crash phase: fatigue, appeared depressed (suicidal ideation)
Cannabis	Mood swings, irritability	Long-term Amotivation, depression
Alcohol	Disinhibition, emotional lability	Long-term: Depressive symptoms
Opioids	Initial euphoria, dysphoria on withdrawal	Long-term: Anhedonia, apathy

DDx and Treatment Considerations

- Many mood symptoms associated with substance use are **acute** and **resolve with abstinence**.
- Chronic SUD can present with persistent mood symptoms that often benefit from treatment (in addition to abstinence).

Anxiety Symptoms Associated with Substance Use

Substances Use Patterns that Induce Anxiety:

- Use of Stimulants (e.g. meth and cocaine): Panic attacks, generalized anxiety.
- Use of Cannabis: anxiety and panic symptoms.
- Alcohol/Benzodiazepine Withdrawal: Severe anxiety, tremors, autonomic instability.
- Opioid Withdrawal: Restlessness, dysphoria, somatic anxiety.

DDx and Treatment Considerations

- Alcohol-induced anxiety disorders typically resolve within 3-4 weeks of abstinence.
- Primary anxiety disorders persist regardless of substance use.

Psychosis: associated with some SUDs

Psychosis = gross impairment of reality testing

Core symptoms

- Hallucinations
- Delusions
- Disorganized thinking and speech
- Disorganized behavior
- Negative symptoms
- Cognitive deficits

•Functional impairments

- Relationships, work, education, activities of daily living

Substance-Induced Psychosis per DSM5

“Substance/medication-induced psychotic disorder” has:

- The presence of **delusions** and/or **hallucinations** during or soon after **intoxication/exposure** or **withdrawal**
- Disturbance **not better explained** by another type of **psychotic disorder**
- The disturbance cannot **“occur exclusively during the course of a delirium”**
- Must cause **significant distress** or impairment in function

Substance-Induced Psychosis

- Withdrawal from substances
  - Alcohol, benzodiazepines
- Intoxication
  - Amphetamines, cocaine, hallucinogens, PCP, inhalants, cannabis, bath salts
- Prescribed medications
  - Steroids, dopamine agonists, stimulants
- Implicated pathophysiology is similar to that of primary psychosis: → **overactivation of dopamine pathways**

Substance or medication	Examples
Alcohol and sedatives/hypnotics	Alcohol (intoxication or withdrawal), barbiturates and benzodiazepines (particularly withdrawal)
Anabolic steroids	Testosterone, methyltestosterone
Analgesics	Meperidine, pentazocine, indomethacin
Anticholinergics	Atropine, scopolamine
Antidepressants	Bupropion, others if triggering a manic switch
Antiepileptics	Zonisamide, other anticonvulsants at high doses
Antimalarial	Mefloquine, chloroquine
Anti-parkinsonian	Levodopa, selegiline, amantadine, pramipexole, bromocriptine
Antivirals	Abacavir, efavirenz, nevirapine, acyclovir
Cannabinoids	Marijuana, synthetic cannabinoids (i.e., "spice"), dronabinol
Cardiovascular	Digoxin, disopyramide, propafenone, quinidine
Corticosteroids	Prednisone, dexamethasone, etc.
Hallucinogens	LSD, PCP (phencyclidine), ketamine, psilocybin-containing mushrooms, mescaline, synthetic "designer drugs" (eg, 2-CB, "N-Bomb" [25I-NBOMe]) , salvia divinorum
Inhalants	Toluene, butane, gasoline
Interferons	Interferon alfa-2a/2b
Over-the-counter (OTC)	Dextromethorphan (DXM), diphenhydramine, some decongestants
Stimulants	Cocaine, amphetamine/methamphetamine, methylphenidate, certain diet pills, "bath salts" (MDPV, mephedrone), MDMA/ecstasy
Toxins	Carbon monoxide, organophosphates, heavy metals (eg, arsenic, manganese, mercury, thallium)

Source: Fiorentini A, Volonteri LS, Dragogna F, et al. Substance-induced psychoses: a critical review of the literature. Curr Drug Abuse Rev 2011; 4:228.

Differentiating between primary vs. substance-induced psychosis

Often there is a distinct presentation

- Withdrawal
  - Alcohol, benzodiazepines
- Visual hallucinations (e.g., Meth intoxication)
- Tactile hallucinations (e.g., alcohol/benzo withdrawal)
- Positive symptoms often predominate
  - Often there is lack of negative symptoms.
  - Chronic use though may shift presentation: → Psychosis in chronic meth abuse appears similar to schizophrenia (though normally there is a lack of negative symptoms)

Differentiating between primary vs. substance-induced psychosis

Course of illness matters!

- Cannot diagnose primary psychosis unless symptoms persist after at least one month of abstinence
  - Exception: chronic meth abuse can result in long-term psychotic sx.*
- Higher suspicion for substance-induced vs. primary psychosis if onset of symptoms coincide with substance use, intoxication or withdrawal

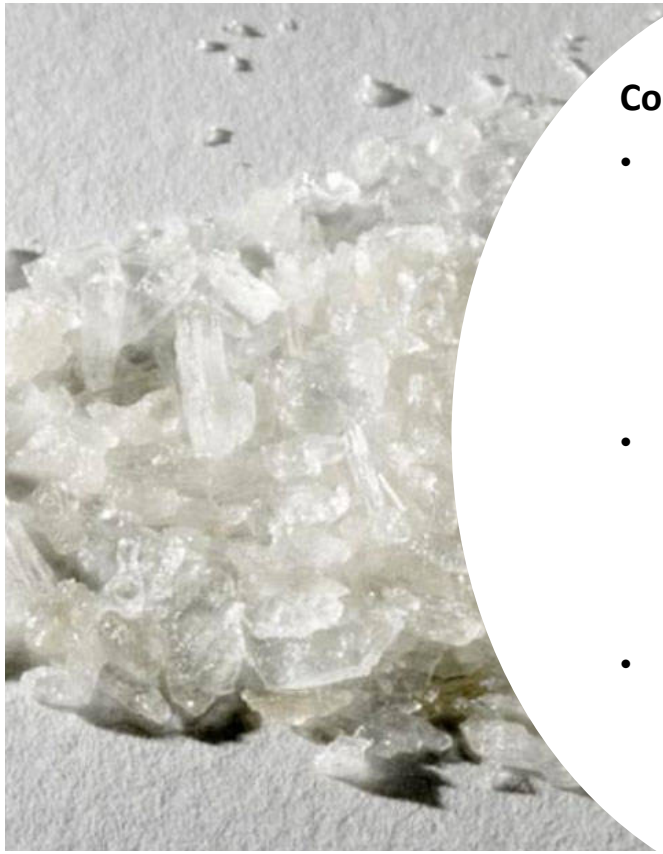
Note: substance-induced psychosis may be transition to primary psychosis

- 25% of substance-induced psychosis may progress to have diagnosis of Schizophrenia**

*Wearne, Travis A., and Jennifer L. Cornish. "A comparison of methamphetamine-induced psychosis and schizophrenia: a review of positive, negative, and cognitive symptomatology." *Frontiers in psychiatry* 9 (2018): 491.

**Fusar-Poli, Paolo, et al. "Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk." *European Psychiatry* 40 (2017): 65-75.

Methamphetamine



Common Stimulant of Abuse: 1.6M users last (NSDUH)

- Explosive psychostimulant with dual mechanism of action
  - Indirect neurotransmitter: displaces epinephrine, norepinephrine and dopamine from inside neurons into synapses
  - Blocks reuptake of these neurotransmitters from the synaptic cleft
  - Increases dopamine production
- Highly Dopaminergic:
  - Increased activation of dopamine pathway: more marked with higher frequency of use/doses
  - Pathophysiology of methamphetamine-induced psychosis
- Approximately 1/3 of recreation users experience psychosis
  - Chronic users have >50% likelihood of psychotic sx

Cannabis

•Wide variety of cannabis-based products offering various concentrations of cannabinoids

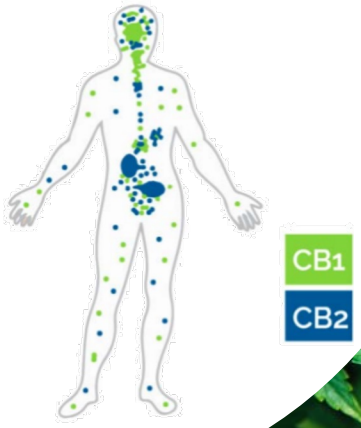
- 85 different cannabinoids have been isolated from the plant (El-Alfy et al 2018)
- The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC)
- Various different strains of cannabis exist, offering relatively different concentrations of CBD and THC

•THC: CB1 agonist

- Psychoactive: altered mood, cognition

•CBD: Indirect CB1 and CB2 antagonist

- Immunologic and anti-inflammatory effects
- Antipsychotic?



Cannabis Use and Schizophrenia

Strong Association

•Cross-sectional study indicates regular cannabis use associated with two to three times higher lifetime prevalence of schizophrenia compared with non-users. (Gage, et al, 2016)

- Strongly associated with:
  - earlier age of onset of use
  - higher frequency of use/amount used
  - Use of products with high THC/CBD ratios

•In a systematic review including 53 studies of patients with schizophrenia-spectrum disorders (Green, et al, 2005)

- 23.1% prevalence of cannabis use over the past six months
- 42.2% prevalence of lifetime cannabis use

Cannabis-Induced Psychosis

Associated with Higher THC Concentrations

Case studies demonstrate general association between use of high dose THC products (e.g., wax) and cannabis-induced psychosis. (Volkow, et al, 2016; and Di Forti, et al, 2015)

- Acute THC administration causes increased dopamine release
  - Increased activation of dopamine pathway. More marked with higher frequency of use/THC doses

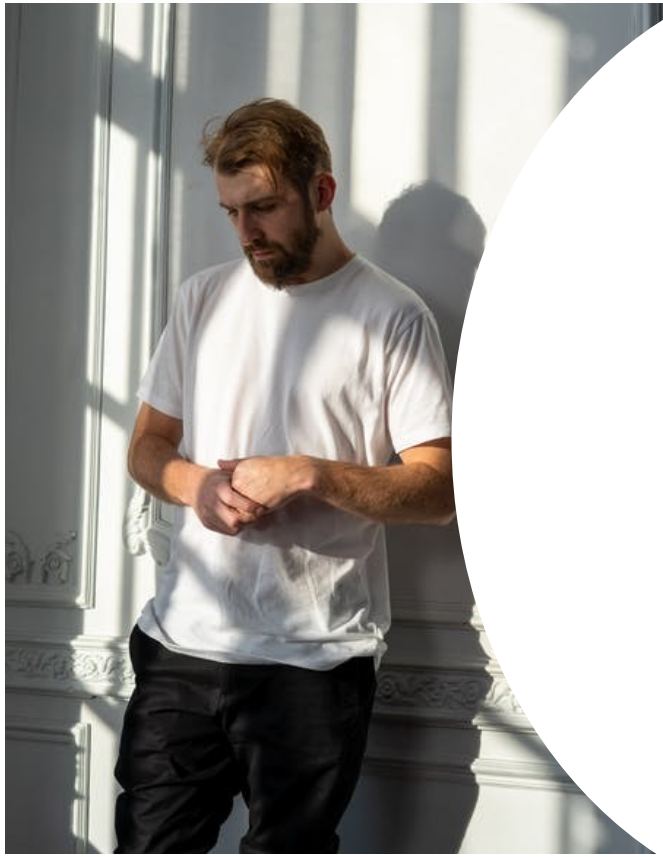
Unclear whether this acute effect is related to the development of schizophrenia associated with chronic cannabis use.

- Danish study using national registry (~1500 patients who received a diagnosis of cannabis-induced psychosis from 1994 and 2014, and followed them through August 2014) found: 41.2% conversion rate to schizophrenia (Starzer 2018)

Cannabis Use and Psychosis

- Systematic review of 35 longitudinal studies (Moore, et al, 2007) found:
  - Increased risk of psychosis associated with any lifetime use of cannabis (OR 1.41, 95% CI 1.20-1.65)
  - Dose-response relationship: two times increase in risk among highest frequency users (OR 2.09, 95% CI 1.54-2.84).
- Finnish Prospective Longitudinal study (Mustonen, 2018): Significantly increased risk of psychosis among subjects who used cannabis more than or equal to five times by age 16-years-old versus those who never used:
  - ~6500 individuals born in northern Finland in 1986
  - Evaluated at age 15 to 16 years
  - Evaluated again at age 30 years
  - Adjusted HR ratio 3.02, 95% CI 1.14-7.98

Cannabis Use Among Psychotic Patients



Worsens positive symptoms

- In their 2016 systematic review/meta-analysis of 24 longitudinal studies (> 16.5k participants), Schoeler T, Monk and coauthors found the following:
  - Cannabis use was associated with increased relapse, rehospitalization and positive symptoms (but not negative symptoms)
  - Cannabis use was associated with poorer overall level of functioning
- Two-year-long prospective longitudinal study of 220 adults with first-episode psychosis found the following:
  - Increased risk of relapse with hospitalization during periods of cannabis use (OR 1.13) (Schoeler T, Petros N et al 2016)

Treatment of Substance-Induced Psychosis

Driven by severity of symptoms, underlying cause.

- Always treat medically if related to withdrawal
- Ensure appropriate level of care setting depending on level of severity
- For severe positive symptoms/agitation: First (e.g., Haldol) vs. second generation antipsychotics (e.g., Olanzapine)
- Beware of hemodynamic instability in meth-induced psychosis

General considerations for SUDs & psychosis:

Time Course and presence of negative symptoms help differentiate between primary vs. substance-induced psychosis

Methamphetamine: Remarkably high likelihood of inducing psychosis

- Chronic use may result in lasting psychotic symptoms

Cannabis: High THC consumption associated with both acute psychosis and increased life-time risk of psychotic disorder

- Associated with worse positive sx
- Evidence suggestive of casual link, change in dopamine pathways

Differentiating Primary vs. Substance-Induced Psychiatric Symptoms

Feature	Primary Non-SUD Psychiatric Disorder	Substance-Induced Disorder
Symptom Onset	Gradual, chronic course	Abrupt onset with use
Duration	Persistent despite sobriety	Resolves with abstinence
Family History	Often present	May be absent
Course with Treatment	Responds to psychiatric treatment	Improves with detox and abstinence

Time Course of Symptoms & Substance Use in Psychiatric Diagnosis

- **No strict 1-month rule,** but 4 weeks of abstinence is often a best practice.
- If symptoms resolve within withdrawal period → **Likely substance-induced.**
- If symptoms persist beyond withdrawal (especially after 4 weeks**) → Primary psychiatric disorder more likely.**
- **For thought disorders** (e.g., schizophrenia), symptoms must persist **at least 1 month post-substance effects.**
- Clinical judgment is key—**consider half-life of substance & individual patient history.**

Best Practices for Management in Primary Care

1. **SBIRT**
2. **Ensure Detox & Abstinence Before Diagnosing Non-SUD Psychiatric Concern**
3. **Use Motivational Interviewing** to Discuss Substance Use Reduction/Cessation
4. **Referral to Co-Occurring Disorder Treatment Programs**
5. **Consider Medication-Assisted Treatment (MAT)**
6. **Monitor for Prolonged Symptoms Beyond Detox**

Key Takeaways

1. SUDs can closely **mimic** psychiatric disorders, leading to misdiagnosis.

2. A structured diagnostic approach using **timeline, collateral history, toxicology, and abstinence trials** helps differentiate conditions.

3. **Integrated, co-occurring treatment** is critical for patients with co-occurring disorders.

Questions?

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