Psychosis and Substance Misuse

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Disclosure

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Concurrent Disorders

- Lifetime prevalence of substance use disorders are significantly higher among individuals with psychiatric disorders

- Lifetime prevalence of psychiatric disorders are significantly higher among individuals with substance use disorders

ECA Data: Risk of Dual Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>any alcohol disorder</th>
<th>any drug disorder</th>
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<tbody>
<tr>
<td>ASPD</td>
<td>74% 21.0</td>
<td>42% 13.4</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>34% 3.3</td>
<td>28% 6.2</td>
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<tr>
<td>Bipolar Disorder</td>
<td>43% 5.1</td>
<td>34% 8.3</td>
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<tr>
<td>Major Depression</td>
<td>17% 1.3</td>
<td>18% 3.8</td>
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<tr>
<td>Dysthymia</td>
<td>21% 1.7</td>
<td>19% 3.9</td>
</tr>
<tr>
<td>Phobias</td>
<td>17% 1.6</td>
<td>11% 2.2</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>29% 2.6</td>
<td>17% 3.2</td>
</tr>
<tr>
<td>OCD</td>
<td>24% 2.1</td>
<td>18% 3.7</td>
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(Regier et al, 1990)
Concurrent Disorders: Origins?

Both disorders may be caused by a common risk factor
- biological risk factors, such as 5HT, DA, GABA polymorphisms
- environmental risk factors, such as childhood trauma

Genetic linkage of risk factors
- i.e. genes that influence psychiatric disorders may be located near genes that influence alcohol risk

Assortative mating

Psychiatric disorder may cause alcohol use disorder
- i.e. “self medication” hypothesis

Alcohol use disorder may cause psychiatric disorder
- i.e. traditional AA philosophy

Self Medication Hypothesis:

Substance abuse relieves psychological suffering.

Painful affects and subjective states of distress are important determinants in using, becoming dependent upon, and relapsing on substances.

Criticisms:
- many individuals suffer but do not use alcohol or drugs
- substance abuse causes more distress than it relieves

Empathically appreciating and tuning in to the subjective states of distress that substance abusers self-medicate can improve engagement and treatment adherence.

(Khantzian, 1985 & 1997)
Example of a Concurrent Disordered Client Presenting at Mental Health Services

Clinical Vignette

Kenny, age 17, adopted at age 2 months of age, lives with parents in rural NS, works in landscaping/tree planting/picking berries, dropped out in Grade 10, illiterate

Hearing problems as infant, speech delayed and impaired

Diagnosed at age 6 with ADHD, later with LD
Clinical Vignette

Brought to ER by parents for severe and persistent personality/behavioral changes

Two week history of increasing self-isolation, disruptive and disrespectful

Began making peculiar gestures, grabbing at unseen objects in the air, talking to someone who wasn’t there, increasingly restless, removed mirrors, walked about naked, openly masturbating, drank from dog’s dish

Clinical Vignette

Began walking down middle of highway, screaming obscenities, became incontinent, lay down on highway spinning around and pretending to fly

Ran into barn, got rope and made a noose
Family tried to intervene, he fled into the forest
During drive to ER, Kenny grabbed the steering wheel and attempted to strangle father

Appeared to be disorientated and confused
Clinical Vignette

Brought to ER by police - at ER, he tried to go AWOL

Extremely disrupted and aggressive in ER, shouting, cursing, spitting, kicking

Family felt this might be drug related

Clinical Vignette

Initially, Kenny admitted to using LSD, hash oil and 2 lines of cocaine

Later denied heavy drug use

Urine tox screen negative for cocaine, PCP, amphetamines but positive for cannabis

Actually level of drug use never determined, but suspected daily cannabis use
Clinical Vignette

Diagnosis:

– Axis I - Bipolar Affective Disorder, Type I, Manic Episode with Psychotic Features
  Cannabis Dependence
  Learning Disability
  Past diagnosis of ADHD
  R/O Polysubstance Abuse/Dependence

– Axis II - Borderline Intelligence
  R/O Cluster A traits

DSM-IV Guidelines for Dual Diagnosis: Primary vs. Substance-Induced Disorder

Psychiatric sx developed prior to substance use

Psychiatric sx persist despite a significant period of abstinence

Psychiatric sx have occurred during periods of remission of substance use disorder

Psychiatric sx are in excess of what would be expected given type or amount of substance patient uses

FH of primary psychiatric disorder(s)
Models of Treatment for Concurrent Disorders

Sequential Treatment:
- most common approach; sequence depends on relative severity of dual disorders
- risk of delaying necessary interventions

Parallel Treatment:
- usually conducted at 2 different treatment facilities
- risk of conflicting interventions and advice

Integrated Treatment:
- particularly suited for treatment of concurrent disorders
- possibility of better outcomes

Schizophrenia & Substance Use Disorders: Prevalence

the most common concurrent disorder among individuals with schizophrenia is a substance use disorder

inpatients range from 48 - 72% (lifetime)
- Cantwell et al, 1999 (inpatients, first episode)
  • 37% lifetime diagnosis of a SUD

outpatients range from 32 - 60% (lifetime)
- Fowler et al, 1998 (outpatients)
  • 59.8% lifetime diagnosis of SUD

highest rates found in services attending to less stable, more severe cases:
- community link / emergency / walk-in clinics
Schizophrenia & Substance Use Disorders: Prevalence

- None: 52%
- Polyabuse: 6%
- Stimulants: 7%
- Cannabis: 16%
- Alcohol: 19%

Schizophrenia & Substance Use Disorders: Prevalence

- Binge rather than regular use
  - i.e. polymorphous, chaotic, opportunistic use
- Use is highly sensitive to environmental prompting
- Dependence more likely with the more accessible drugs (nicotine, alcohol, cannabis, Rx drugs)
- Specific vulnerability for DA-agonist substances (nicotine, cocaine)
  - augment positive symptoms
  - reduce negative symptoms
  - counteract DA-blockade of antipsychotics
Schizophrenia & Substance Use Disorders: Diagnostic Issues

primary vs. substance-induced psychotic disorder

– unclear connection between the emergence of psychotic symptoms and states of substance intoxication or withdrawal
– sluggish onset of illness and early evidence of “core disturbances”
  • i.e. negative, deficit and thought disorganization symptoms
– persistence of symptoms beyond 4 wks of abstinence
– a positive family history for SZ-spectrum disorders

Schizophrenia & Substance Use Disorders

Does substance use cause schizophrenia?

Does substance use influence the clinical expression of schizophrenia?

Does substance use affect the symptoms of schizophrenia?

Does substance use interfere with the treatment of schizophrenia?
Schizophrenia & Substance Use Disorders

Substance use causes schizophrenia?

NOT REALLY…

– despite the sharp increase in substance abuse over the last 40 years, there has been no commensurate rise in the rate of schizophrenia

– the “psychotic” symptoms directly caused by intoxication or withdrawal (i.e. “substance induced psychosis”), are temporary (do not meet 6-month duration criterion)

Schizophrenia & Substance Use Disorders

substance use influences the clinical expression of schizophrenia?

PROBABLY…

– excess addiction / schizophrenia comorbidity could be due to drugs causing the clinical expression of SZ which otherwise would not have developed
Is Cannabis Use a Contributory Cause of Psychosis?

A 15-year prospective study of cannabis use and schizophrenia

- 50,465 18-year-old Swedish conscripts in 1971-72
- cannabis use prior to age 18 (nil, 1-50x, >50x)
- schizophrenia diagnoses, as documented in the Swedish psychiatric case register, during the subsequent 15 years (up to age 33)

- the risk of schizophrenia was related in a dose-response way to cannabis use prior to age 18
  - any use 3x risk
  - >50x use 6x risk

- cannabis use precipitates the clinical expression of schizophrenia in vulnerable individuals

(Andreasson et al., 1987)

Is Cannabis Use a Contributory Cause of Psychosis?

Alternatively, the schizophrenia prodrome could render an individual prone to substance abuse (self-medication)

If affected men were experiencing prodromal symptoms at age 18, they may have been self-medicating with cannabis

Studies have shown that most patients with schizophrenia believe drugs medicate their “depression” and lack of energy (i.e. the negative symptoms of the illness itself, and the affective components of EPS)

(Dixon et al, 1990)
Is Cannabis Use a Contributory Cause of Psychosis?

27-year follow-up of the Swedish cohort
   – i.e. covering most of the risk period for the onset of psychotic disorders (up to age 45)

The study distinguished between cases that occurred in the first 5 years of the study period and those that occurred more than 5 years afterwards

The relation between cannabis use and schizophrenia was the same for the individuals diagnosed during the first 5 years after assessment, and those diagnosed during the subsequent 22 years

(Zammit & Lewis, 2004)

Is Cannabis Use a Contributory Cause of Psychosis?

Findings were replicated by a 3-year follow-up study of 4848 individuals in the Netherlands

Among individuals who had no psychosis at baseline, there was an increased risk of psychotic symptoms if they used cannabis
   – cannabis was responsible for 13% of the risk of new psychotic sx

Among those reporting some psychotic symptoms at baseline, there was an increased risk of developing schizophrenia if they used cannabis
   – cannabis was responsible for 50% of the risk of developing a full blown psychotic disorder among vulnerable individuals

(Van Os et al., 2002)
Biological Plausibility of Cannabis as a Contributory Cause of Psychosis

THC is the principal psychoactive ingredient of cannabis, and acts on a specific cannabinoid receptor (CB1) in the brain. CB1 receptor knockout mice show behaviors consistent with some schizophrenia symptoms, such as reduced goal-directed activity and memory for temporal representations (Fritzsche, 2001). Elevated levels of anandamide, an endogenous cannabinoid agonist, have also been found in the cerebrospinal fluid of individuals with schizophrenia (Leweke et al., 1999). Individuals with schizophrenia had a greater density of CB1 receptors in the prefrontal cortex compared with control subjects (Dean et al., 2001).

Schizophrenia & Substance Use Disorders

substance use affects the symptoms of SZ?

YES…

- an earlier onset of illness
- a more sudden and dramatic onset of illness
- a more significant conduct disorder / antisocial behavior history
- increases the severity of positive and other symptoms
- increases agitation, impulsiveness and violent behavior
Schizophrenia & Substance Use Disorders: Symptomatology

substance use affects the symptoms of SZ? YES…

Increases the severity of positive and other symptoms

- cannabis -- increased delusional and hallucinatory symptoms
  (Negrete et al., 1986)
- alcohol -- more likely to report hallucinations and depressive episodes
  (Pulver et al., 1989)
- cocaine -- more depressed, less socialized, more impaired on memory tasks
  (Sevy et al., 1990)

Schizophrenia & Substance Use Disorders: Symptomatology

substance use affects the symptoms of SZ? YES…

Increases agitation, impulsiveness and violent behavior

- ECA study: violence reported in 30.3% of DD vs 8.3% of SZ
  (Swanson et al., 1990)
- Finnish birth cohort of 11,017; 36.4% of DD males committed violent crimes compared to 7.5% SZ
  (Rasanen et al., 1998)
- inpatient sample of 331; relationship between DD and violence mediated by medication non-compliance
  (Swartz et al., 1998)
Schizophrenia & Substance Use Disorders

substance use interferes with the treatment of schizophrenia?

YES...

– miss more appointments, more likely to move from service to service, forming no lasting alliances
– require more services, more inpatient and outpatient contacts (Woog, 1990; Maynard and Cox, 1998)
– higher institutional (hospital, jail), emergency and legal costs (Bartels et al, 1993)
– shorter inpatient stays, but higher readmission rates (30 vs 17%) (Leon et al, 1998)

– lesser therapeutic response, higher rate of relapse
– inpatients with SZ and cocaine abuse require larger doses of antipsychotics during the acute treatment (Seibyl et al, 1993)
– at equivalent IM doses, patients with SZ and EtOH have lower antipsychotic blood levels, lower prolactin levels, less EPS (Soni & Brownlee, 1991)
– correlation between drug use and poor response to antipsychotics extends beyond compliance (Bowers et al, 1990)
Schizophrenia & Substance Use Disorders: Treatment Issues

Cannot assume that substance use is an epiphenomenon which will resolve with remission of the psychosis

SZ patients are usually ineligible for treatment at traditional addiction programs

Conversely, if actively using, SZ patients are not offered follow-up at many mental health services

Current guidelines recommend “integrated” treatment, where both psychosis and addiction are treated concurrently in a single program, by a team of clinicians adequately trained in both fields

Schizophrenia & Substance Use Disorders: Integrated Treatment

Basic components of an integrated treatment program for dual diagnosis patients include:

– systematic base-line and on-going assessment of substance use problems, including regular urine toxicology screening

– assertive case management

– adapted psychiatric treatment

– adapted addiction treatment

– controlled low-risk housing
**Schizophrenia & Substance Use Disorders: Adapted Psychiatric Treatment**

Adjust expectations regarding compliance with prescribed pharmacotherapy

Use higher doses of antipsychotics
   – expect accelerated metabolic breakdown of antipsychotics associated with nicotine / cannabis use

Be prepared to make more frequent medication changes, due to poor response

Avoid long-term prescription of benzodiazepines, particularly if there is evidence of alcohol abuse

**Schizophrenia & Substance Use Disorders: Adapted Psychiatric Treatment**

Meds with stronger binding affinity for D2 receptors carry the potential to increase substance abuse
   – more severe EPS (self-medication)
   – more significant receptor up-regulation
      • which enhances the dopamine-mediated effects of drugs, and makes them more reinforcing

Decreased substance use among dual-diagnosis patients on atypical vs. conventional antipsychotics
   • uncontrolled trials with clozapine, olanzapine and risperidone
**Schizophrenia & Substance Use Disorders: Atypical Antipsychotics**

362 adults with SZ
- followed for 3 years in a naturalistic study
- with structured interviews at 6-month intervals

Three medication classes
- atypical antipsychotic, typical antipsychotic and no medication

Participants who were compliant with atypical antipsychotics for 90 days were significantly less likely to use substances during the next 6-month period than patients who were compliant with typical antipsychotics, or than those who were not prescribed medication.

Atypical antipsychotics may offer an advantage in reducing substance use among schizophrenia patients

*(Swanson et al, 2007)*

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**Schizophrenia & Substance Use Disorders: Atypical Antipsychotics**

249 US veterans with SZ and comorbid SUD
- assessed with the Addiction Severity Index
- compared outcomes among those switched or maintained on an atypical antipsychotic to those treated with typicals

Multivariate analysis showed no greater improvement in alcohol, drug, or psychological scores in individuals who were switched to \((n = 33)\) or maintained on \((n = 161)\) an atypical antipsychotic as compared to those who were treated with conventional at the final assessment \((n = 55)\)

Patients treated with atypical antipsychotics achieved no greater improvement in substance-related outcomes

*(Petrakis et al, 2007)*
Schizophrenia & Substance Use Disorders: Adapted Addiction Treatment

Longer phase of engagement and motivation enhancement prior to beginning detoxification

Active addiction treatment

Include component of relapse prevention

Longer, more flexible maintenance interventions

Regular urine toxicology screening

• “Drug and alcohol use among patients with schizophrenia and related psychoses: levels and consequences”

• Margolese et al, 2004
  – 207 CCC outpatients
  – 114 single disorder, 93 dual disordered (lifetime or current)
  – 49% current or lifetime DD
  – Nicotine, alcohol and cannabis most commonly abused
Margolese et al., 2004

\[ p < 0.05 \]

Margolese et al., 2004

\[ p < 0.05 \]
Margolese et al., 2004

\[ p < 0.05 \]

Margolese et al., 2006

Medication Non-Compliance
PANSS positive scores

Margolese et al., 2006