Substance use and psychosis: more common than you think?

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Talk Outline

• How much first episode psychosis is related to substance use?
• Does substance-related psychosis progress to schizophrenia?
• Why is comorbid psychosis and substance use so common?
• What are outcomes like for individuals with substance-related psychosis?
• Assessing comorbid substance use in psychosis
• Managing comorbid substance use and psychosis
How much first episode psychosis is related to substance use?
Hospital admissions for First Episode Psychosis

All first psychosis in NSW
Hospital admissions
July 2005-July 2015
Aged 16-64
Total: n=41794
17460 (41.8%) females
24334 (58.2%) males
First psychosis

Any substance diagnosis
- Alcohol: 14%
- Sedative: 1%

Any illicit drug
- Cannabis: 30%
- Stimulant: 16%
- Polydrug: 11%
- Opiate: 4%
- Hallucinogen: 1%

Substance diagnoses at first admission with psychosis.

9,919 NSW residents aged 15-29. Min 5 year clearance period

Cannabis
- 2107 (21%)

Cannabis + Stimulant
- 857 (9%)

Stimulant
- 685 (7%)

First Episode Psychosis across the age span

Total FEP: n=41794
Amphetamine-related: n=4645

Psychosis peaks from late adolescence

Amphetamine-related psychosis peaks from late adolescence to early 30’s

Psychosis onset can occur at any age and *may* be related to drug use
The role of cannabis

Cannabis use is common in individuals presenting with first psychosis

Cannabis-related psychosis peaks earlier

Cannabis plus amphetamine peaks earlier

Amphetamine alone peaks later but risk persists
Does substance-related psychosis progress to schizophrenia?
Substance/drug induced psychosis

Brief psychotic syndromes triggered by substance use

Persisting for days or weeks after intoxication has resolved

Estimated incidence 1.5-6.5 per 100,000 person years

Up to 25% of first hospital admissions may include this diagnosis

Often excluded from studies of early psychosis
Substance/drug induced psychosis

A significant proportion of people later transition to a diagnosis of schizophrenia

Estimates vary widely:
- as high as 66% (Addington et al 2006)
- as low as 17% (Starzer et al 2017)

Examined this question in recent meta-analysis to synthesize the results of longitudinal observational studies of transition from substance-induced psychosis to schizophrenia
Transition of Substance-Induced, Brief, and Atypical Psychoses to Schizophrenia: A Systematic Review and Meta-analysis

Benjamin Murrie¹, Julia Lappin²,³, Matthew Large², and Grant Sara*⁴,⁵
Transition Rate to Schizophrenia by initial type of Psychosis(%)
Transition Rate to Schizophrenia (% by Substance Type)

- Alcohol: 9%
- Sedatives: 10%
- Opioids: 12%
- Amphetamines: 22%
- Mixed or not specified: 22%
- Hallucinogens: 26%
- Cannabis: 34%
Progression to schizophrenia

Niemi-Pynttari et al. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. J Clinical Psychiatry 2013
• Transition rates vary by substance
• **More than one third** with cannabis-induced psychosis develop schizophrenia
• Consistent with literature that cannabis use doubles the risk of developing schizophrenia in vulnerable people
• Rates of transition are higher among younger people
• **Familial risk and genetic predisposition** play a key role in the development of cannabis-induced psychosis and later transition to schizophrenia
• No association between transition rate and
  • Sex
  • Duration of follow-up
  • Proportion followed up or
  • Year of publication
Why is comorbid psychosis and substance use so common?
Reasons for high rates of comorbidity

Possible explanations include:

• shared genetic or environmental factors (such as childhood trauma or neglect, social deprivation) that increase risk for both mental illness and substance use

• a possible causal link between substance use and the development of new onset psychotic disorders

• self-medication with substances to lessen symptoms of severe mental illness

• a further important consideration in the maintenance of these persistently high-rates is that people with severe mental illness are known to have
  • Inadequate access to cessation services (incl. smoking cessation)
  • Poor social supports
  • Impaired cognition
  • Poor coping strategies
Childhood trauma and mental illness

Childhood abuse is a well-established risk factor for a range of psychiatric disorders and other health problems

Childhood adversity may be experienced as

- Physical abuse
- Sexual abuse
- Emotional abuse
- Neglect
- Family member experiencing domestic violence, mental illness or substance abuse, or imprisonment
Adverse Childhood Experience (ACE) Study

Survey of all adults receiving any form of US healthcare over 10-year period

- 11% had experienced emotional abuse
- 30% physical abuse
- 20% sexual abuse

About half have experienced 1 or more ACE

16% have experienced 4+ ACEs

(Felitti et al., *American Journal of Preventive Medicine* 1998)
How many of us grew up with ACEs?

ACE studies: 50% of the population has an ACE of 1 or more; 16% have an ACE of 4 or more

Felitti, 1998
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</table>
Childhood trauma and risk for psychosis

- Social experience across the life course interacts with genes, and impacts on biological development, to shape adult outcomes
- Biological models of adverse social experiences such as childhood trauma, and adult psychosis
- Dopamine continues to be implicated in the aetiology of psychosis
- Formation of persecutory delusions: due to perceived role of dopamine in the interpretation of threat-related stimuli
- Extended exposure to trauma may increase risk for psychosis through direct effects on dopamine function

(Morgan & Fisher, 2007)
Possible explanations include:

- shared genetic or environmental factors (such as childhood trauma or neglect, social deprivation) that increase risk for both mental illness and substance use
- a **possible causal link between substance use and the development of new onset psychotic disorders**
- self-medication with substances to lessen symptoms of severe mental illness
- a further important consideration in the maintenance of these persistently high-rates is that people with severe mental illness are known to have
  - Inadequate access to cessation services (incl. smoking cessation)
  - Poor social supports
  - Impaired cognition
  - Poor coping strategies
Substances consistently identified in studies of comorbid substance use and psychosis:

- Alcohol
- Cannabis
- Psychostimulants (methamphetamine/amphetamine)

Biological models suggest that the effects of these substances on a variety of brain neurotransmitters may both precipitate and maintain psychotic symptoms with adverse impact on outcomes.
Cannabis-associated psychosis

• Heavy use of cannabis increases the risk of later psychosis
• Administration of THC to volunteers induces transient psychosis and increases release of dopamine in striatum
• There are plausible biological explanations for the psychotogenic effects of cannabis
• The proportion of THC in “street” cannabis is rising
• Early use of high-potency cannabis increases risk for psychosis particularly in those with other risk factors (family history; genetic risk; childhood adversity; migration; minority status)

(Murray et al, 2017)
Methamphetamine-related Psychosis

- high prevalence of psychosis in methamphetamine users *(Farrell, 2002)*

- dose-related psychotic symptoms in chronic users *(McKetin, 2013)*

- significantly increased risk of schizophrenia development in methamphetamine users *(Callaghan, 2012)*
Psychosis with Methylphenidate or Amphetamine in Patients with ADHD


ABSTRACT

BACKGROUND
The prescription use of the stimulants methylphenidate and amphetamine for the treatment of attention deficit–hyperactivity disorder (ADHD) has been increasing.
RESULTS
We assessed 337,919 adolescents and young adults who received a prescription for a stimulant for ADHD. The study population consisted of 221,846 patients with 143,286 person-years of follow up; 110,923 patients taking methylphenidate were matched with 110,923 patients taking amphetamines. There were 343 episodes of psychosis (with an episode defined as a new diagnosis code for psychosis and a prescription for an antipsychotic medication) in the matched populations (2.4 per 1000 person-years): 106 episodes (0.10%) in the methylphenidate group and 237 episodes (0.21%) in the amphetamine group (hazard ratio with amphetamine use, 1.65; 95% confidence interval, 1.31 to 2.09).

CONCLUSIONS
Among adolescents and young adults with ADHD who were receiving prescription stimulants, new-onset psychosis occurred in approximately 1 in 660 patients. Amphetamine use was associated with a greater risk of psychosis than methylphenidate. (Funded by the National Institute of Mental Health and others.)
Possible explanations include:

• shared genetic or environmental factors (such as childhood trauma or neglect, social deprivation) that increase risk for both mental illness and substance use

• a possible causal link between substance use and the development of new onset psychotic disorders

• self-medication with substances to lessen symptoms of severe mental illness

• maintenance of persistently high-rates in people with SMI contributed to by
  • Inadequate access to cessation services (incl. smoking cessation)
  • Poor social supports
  • Impaired cognition
  • Poor coping strategies
Schizophrenia is associated with increased risk of subsequent substance abuse diagnosis: A nation-wide population-based register study

Stine Mai Petersen¹², Nanna Gilliam Toftdahl¹², Merete Nordentoft¹² & Carsten Hjorthøj¹²³
Aims We aimed to investigate whether or not a diagnosis of schizophrenia increases the risk of a substance abuse diagnosis. Design Prospective cohort study using a longitudinal study design. Setting and participants Individuals born in Denmark from 1955 to 1999 and registered in the Danish registers between 1 January 1968 and 1 July 2013. Measurements We investigated the associations between schizophrenia and ICD diagnoses of substance abuse, both established through various Danish registers. The Cox regression model was used and adjusted for calendar year, gender, urbanicity, co-abuse, other psychiatric diagnoses, parents' substance abuse and psychiatric history, parents' immigration and parents' socio-economic position. Individuals diagnosed with substance abuse less than a year after diagnosis of schizophrenia were classified as not diagnosed with schizophrenia. Findings The cohort consisted of 3,133,968 individuals. During follow-up (103,212,328 person-years at risk), a total of 14,007 individuals developed schizophrenia, with 28,855 subsequently diagnosed with substance abuse. A diagnosis of schizophrenia was positively associated with the risk of developing substance abuse [hazard ratio (HR) = 3.69, 95% confidence interval (CI) = 3.56–3.83]. Additionally, adjusting for a co-abuse markedly affected the associations, making schizophrenia primarily associated with an increased risk of abuse of cannabis, alcohol, stimulants and other substances (adjusted HR = 2.48, 95% CI = 2.34–2.64 for cannabis; HR = 1.94, 95% CI = 1.87–2.02 for alcohol; HR = 1.77, 95% CI = 1.61–1.95 for stimulants; HR = 1.36, 95% CI = 1.20–1.54 for other substances). The association was still significant 10–15 years subsequent a diagnosis of schizophrenia (HR = 2.50, 95% CI = 2.26–2.76). Conclusions In Denmark a diagnosis of schizophrenia is significantly associated with increased risk of subsequent diagnosis of substance abuse.
Commentary on Petersen et al. (2019): Development of problematic substance use in the years that follow diagnosis of schizophrenia

The development of problematic substance use is common in the years that follow a diagnosis of schizophrenia. While the risk for substance use in precipitating psychosis has received much attention, there is a clear need for clinicians to screen and offer intervention for emerging substance use in all individuals with psychosis, even many years following onset. Increased rates of not only relapse and re-hospitalization, but also violence, suicide and all-cause mortality [6–9]. Barriers to effective treatment include that those with comorbid substance use are less adherent to treatment, engage poorly in care and often present when in crisis [3,10,11]. Nonetheless, for those who do engage, evidence-based approaches exist, including group counsel-
What are outcomes like for individuals with substance-related psychosis?
Second admission

Readmission within 2 years

- 37% at 2 years
- 28% at 1 year
- 10% at 28 days

$N = 6841$

Factors:
- Male
- Younger
- Drug-induced psychosis
- Prior admissions
- Prior stimulant Dx

- Baseline cannabis Dx
- Baseline stimulant Dx
- Prior cannabis Dx
- Disadvantage
- Rurality

- Affective psychosis
- Brief/NOS psychosis
Outcomes better for those who cease drug use after FEP

Sara G et al. Cannabis and stimulant disorders and readmissions 2 years after first episode psychosis. B J Psychiatry 2014
Greater harms associated with comorbidity

- Higher rates of relapse and rehospitalisation
- Higher rates violence
- Higher rates suicide
- Higher rates all-cause mortality
- Additional mental health and physical health issues
Are there missed opportunities for early intervention in substance-related FEP?
Methamphetamine-related psychosis: an opportunity for assertive intervention and prevention

Methamphetamine-related psychosis is a growing public health concern. All individuals with transient amphetamine-related psychotic symptoms should be considered to be at risk for future development of an enduring psychotic illness, and prioritized for early intervention of integrated care across substance use and mental health services.

Contemporary views of psychosis challenge the simple categorical distinction between brief drug-induced psychoses and more enduring disorders such as schizophrenia. Psychoses are seen increasingly as heterogeneous disorders with a spectrum of illness profiles and course trajectories [11]. Substantial evidence exists that diagnoses of drug-induced psychosis have poor predictive validity. A high

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Service use differences

- Less likely to seek help
- Less adherent to treatment
- Engage poorly in care
- Often present in crisis
- Commonly receive treatment for psychosis but not for drug use
Substance-related psychoses are not all equivalent

Care should be assertive early intervention, as for other brief psychotic disorders

Need for monitoring and ongoing support

Decisions regarding care should consider
- the different risks associated with each substance
- *for example* considering a heightened risk for transition from cannabis-induced psychosis versus alcohol-induced psychosis
- comorbid use of other substances
- individual risk factors for psychosis (family history, early life trauma)
Assessing comorbid substance use in psychosis
Assessing use of common substances

- Alcohol
- Tobacco
- Cannabis
- Methamphetamine/psychostimulants
- Hallucinogens/NPS
- Opioids
- Painkillers
Drug use characteristics

- Drug of use
- Pattern of use (alone/occasional/daily)
- Escalating use
- Effect on relationships/function
- Polysubstance use
- Mental health symptoms – do they make link with pattern of use?
Assessing Use and Misuse

- Escalating use
- Use preferred over previously enjoyed activities
- Effect on relationships
- Effect on occupational/scholastic function
- Related social harms (criminal offences, debt)
Harms associated with use

- Suicide
- Driving
- Overdose
- Injecting
- Sexual disinhibition or sex work
- Drug-dealing
- Criminal charges
- Physical health harms: multiple and beyond scope of today!
Common issues to look out for

• High rates of other mental health issues:
  • Depression
  • Anxiety (including PTSD)
  • Suicidal behaviours
• Polysubstance use (Comorbid alcohol or substance use)
• Increasing use of prescribed meds, eg analgesics, benzos
• Smoking
Managing comorbid substance use and psychosis
Approach to management

- Individual-centred
- Holistic
- Willingness to engage in ongoing mental health care
- Family/carer involvement
- Local options for integrated/co-ordinated care with D&A services
- Local NGOs for support (housing/employment)
Immediate

- Non-judgemental
- Assess risks to self (self-harm; vulnerability; STDs)
- Assess risks to others (driving; machinery operation; minors in home)
- Check supports (family/partner)
- Assess readiness for change
- Make substance use monitoring part of the care plan
Short term

- Treatment of conditions concurrently is gold standard

- Discuss options for outside help
  - Refer D&A or liaise
  - Refer psychologist (if motivated!)
  - NGOs
  - Family support
Long term

- Expect relapse
- Contain anxiety
- Be available through successes and failures
- Deal with physical and mental health harms opportunistically
- CBT
- Residential rehabilitation
Treatment options

Evidence-based approaches for substance use:

- group counselling
- contingency management
- residential treatment
Co-ordinated approach to care

Compared to parallel or sequential care:

- Fewer ED presentations
- Faster recovery times
- Shorter and fewer hospitalisations
- Reduced relapse into substance abuse
- Less deterioration in mental illness symptoms
Integrated care for both issues concurrently

- Reduced drop-outs from care
- Improved outcomes in
  - substance use
  - psychiatric symptoms
  - quality of life
Conclusions

Substance-induced psychosis is a common reason for seeking mental health care

> 1 in 5 first hospital admissions for psychosis in young Australians

Often excluded from early psychosis services due to perception that self-resolve

Not a benign or self-limiting condition: transition rate to schizophrenia approx. 30%

Treat psychosis and substance use concurrently

Outcomes better if abstain but abstinence does NOT ensure no further psychosis
The Clinician’s Guide to Illicit Drugs and Health by NDARC’s Professor Shane Darke, Dr Julia Lappin and Professor Michael Farrell has been officially launched by Silverback Publishing.