Introduction

People who use alcohol and other psychoactive drugs, especially heavy users, are prone to develop psychotic episodes that are not always recognized as being due to acute intoxication or withdrawal. Some medication use can cause the same syndrome. Since the current first episode psychosis programming supported by the Mental Health Block Grant set-aside is based upon a Coordinated Specialty Care model that was tested on individuals with first-episode non-affective psychosis (Heinssen, Goldstein & Azrin, 2013), appropriate recognition of substance-induced and affective psychosis is important. Differing treatment approaches may be used depending upon the underlying causes of the psychotic disorder. Tailoring approaches requires adequate diagnosis, which can be challenging in first psychotic episodes.

The Diagnostic and Statistical Manual, 5th edition (DSM-V), defines substance/medication-induced psychotic disorder (SIPD) as delusions and/or hallucinations related to the physiological effects of a substance or medication, based on evidence from the history, physical examination, or laboratory findings (American Psychiatric Association, 2013). SIPD can produce the full range of psychotic symptoms: hallucinations, delusions, psychomotor changes, impaired cognition, disorganized speech, mania, and so on.

While diagnosis is critical in the early treatment of psychotic symptoms, information on the diagnosis, treatment, and outcomes for SIPD remains inadequate (Mathias, Lubman & Hides 2008). As we describe below, this area needs systematic research, because an initial episode of SIPD increases the risk for conversion to a long-lasting psychotic illness that is not directly related to substance use.

Epidemiology

According to the DSM-V, between 7% and 25% of people presenting with an initial episode of psychosis have SIPD due to substance or medication use (American Psychiatric Association, 2013). People with heavy substance use, especially marijuana, amphetamine, psychedelics, or cocaine are at highest risk (Aldandashi, 2009). Nevertheless, a wide range of substances and other conditions can produce psychosis (Caton, 2005; Sacks, 2012). Prescribed medications that cause psychosis include steroids and non-steroidal anti-inflammatory drugs, antiviral agents and antibiotics, anticholinergics, antihistamines, antiparkinsonian agents, muscle relaxants, opioids, and some psychotropic medications (e.g., antidepressants, anticonvulsants, and stimulants). Recent trends, including legalization of cannabis, the availability of more potent forms of cannabis, the opioid epidemic, and increased use of multiple medications, may be affecting the prevalence of SIPD, but few data are available.
Presentation

People with SIPD often present in emergency rooms because families, friends, or the affected individuals may feel a need for urgent intervention and often call the police, an ambulance, or other emergency personnel to help. The individual’s substance use, often heavy and long-term, suddenly transforms his/her perceptions or cognitions into frightening experiences that are not recognized as due to acute intoxication and require an emergent response. Some people may have been experiencing substance-induced psychotic symptoms for months before the symptoms become dysphoric and motivate seeking help.

An initial episode of psychosis may put the individual experiencing the symptoms in danger, both personal risk and occasionally risk to others. It warrants careful evaluation and treatment, and often results in hospitalization. Thus, people with a presumed SIPD should be watched closely in the emergency room and hospitalized if they do not clear rapidly.

Diagnosis

Diagnosis should be based on history, physical and mental exam, and laboratory tests as indicated for drugs and medications use. Understanding the history of substance and medication use and recent changes in the pattern of use is important. Significant others may help to provide this history and provide information regarding whether or not the patient has experienced a month or more of abstinence and his or her condition during that time. This information will help to identify substance use as a primary cause of the psychosis.

Nevertheless, psychosis in the presence of heavy alcohol, other drug, or medication use involves a diagnostic dilemma because a variety of substances and medications can produce all types of psychotic experiences. People often arrive at emergency clinical settings with early psychosis (symptoms for less than six months) following heavy substance use, but the use may have been occurring for years before psychosis appears (Caton, 2005).
According to the DSM-V (American Psychiatric Association, 2013), the diagnostic criteria include:

A. Presence of one or both of the following symptoms:
   
   1. Delusions
   2. Hallucinations

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):
   
   1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a medication
   2. The involved substance/medication is capable of producing the symptoms in Criterion A

C. The disturbance is not better explained by a psychotic disorder that is not substance or medication-induced. Such evidence of an independent psychotic disorder could include the following:
   The symptoms preceded the onset of substance/medication use; the symptoms persist for a substantial period of time (e.g., about 1 month) after the cessation of acute withdrawal or severe intoxication; or there is other evidence of an independent non-substance/medication –induced psychotic disorder (e.g., a history of recurrent non-substance/medication-related episodes)

D. The disturbance does not occur exclusively during the course of delirium

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other areas of functioning.

(DSM-5, American Psychiatric Association 2013, page 110)

The common diagnostic dilemma regarding SIPD is that many people who present with an episode of early psychosis have been using psychoactive drugs or medications continuously for months or years, precluding the opportunity for anyone to observe them in a substance-free state. In the absence of any recent drug-free observation, the diagnosis of SIPD is often made, but the patient may appear much different when drug-free. To complicate matters further, these patients are often started on antipsychotic medications to more rapidly reduce or eliminate their symptoms. If they become non-psychotic while on medications, does the transition reflect drug-abstinence or antipsychotic treatment? How long should the antipsychotic medication be continued? These questions complicate diagnosis and care (Dawson, et al 2008).
In a study of 386 patients presenting to emergency rooms in Northern Manhattan with early psychosis and regular use of alcohol or other drugs, 169 (44%) were diagnosed with SIPD based on research diagnostic interviews, interviews with significant others, laboratory tests, and observation for several days or weeks (Caton, 2005). Among those with SIPD, 40% had been using two or more substances, most commonly alcohol and cocaine or alcohol and cannabis. Key differentiating factors were: the SIPD group was more likely to have parental substance abuse, a diagnosis of dependence on any drug (rather than abuse or regular use only), and visual hallucinations. Those with primary psychosis had higher positive and negative symptoms than persons with SIPD. By one-year follow-up, 25% of those initially diagnosed with SIPD were re-diagnosed as having a primary psychosis (Caton, et al 2007). Predictors of change in diagnosis to primary psychosis included poor premorbid functioning, lack of insight, and family history of mental illness. Similarly, in a cohort of 3,500 people admitted to hospitals in Scotland with SIPD, 17% were later diagnosed with schizophrenia, most (80%) in the first five years after the admission (Alderson, 2017). In a Finnish cohort of 18,000, the rate of conversion to schizophrenia varied by substance used, between 5% with alcohol-induced psychosis to 46% in cannabis-induced psychosis (Niemi-Pynttäri, et al 2013).

Treatment

**Early treatment.** Patients in the emergency setting should be safely detoxified and carefully monitored by medical personnel. In theory, these patients should be observed without antipsychotic medications for 30 days to aid in diagnosis. In practice, however, clinicians often start antipsychotic medications rapidly to hasten the decrease or elimination of symptoms. Most are also transferred to inpatient settings for further observation (Caton, 2005).

**Intermediate treatment.** Optimal outpatient treatment for patients with SIPD should include co-located mental health and addiction interventions, often termed integrated dual diagnosis treatment. Because these patients may have alcohol or other substance use disorder or a history of dysfunctional use, helping them to become abstinent and to maintain abstinence is paramount. Family and group interventions, along with supported employment/education and safe housing, are critical. If psychotic symptoms are in remission, a slow taper over several months of antipsychotic medication makes clinical sense. In real-world situations, however, about half of early psychosis patients who experience SIPD become abstinent from abused substances with mental health treatment only (Wisdom, Manuel & Drake, 2011), and most patients take themselves off antipsychotic medications within weeks of recovery (Drake, et al 2011). Nevertheless, mental health and addiction providers should try to follow them closely because addiction relapse is common and change from SIPD to primary psychosis is also common; both changes should trigger rapid treatment.
**Long-term treatment.** People with SIPD are a high-risk group, even if they do well over the first year after an initial psychotic episode. Several factors enhance relapse prevention and long-term recovery: safe housing, peer support for abstinence, employment, and careful follow-ups. As with other long-term illnesses, social determinants probably outweigh medical treatments in importance, and the provision of vocational, educational, housing, and peer supports may help to alleviate some of the risk associated with these social factors. Involvement in peer-support groups may also be beneficial. Treatment providers should do their best to maintain contacts with these patients and attend to their overall needs. When the diagnosis changes to non-affective psychosis, referral to early psychosis treatment programs may be optimal.

**Conclusions**

SIPD is a common but poorly understood and unreliably diagnosed condition. Patients have often been using several substances and medications for long periods of time, without opportunity to observe their condition free of the substances/medications. SIPD is considered a psychiatric emergency, and these patients are usually hospitalized for safe detoxification and observation. When psychotic symptoms do not remit quickly, patients typically receive antipsychotic medications. The diagnostic picture often remains uncertain because observation off substances and antipsychotic medications proves challenging. Because these patients often have a severe drug and alcohol use disorder, and are clearly vulnerable to psychosis, long-term abstinence is the primary goal. Discontinuation of antipsychotics should be considered and done slowly with careful observation. The diagnosis often changes to a primary psychosis over time.
References


