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Clinical characteristics of primary psychotic disorders with concurrent substance abuse and substance-induced psychotic disorders: A systematic review

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ABSTRACT

Background: Distinguishing between a primary psychotic disorder with concurrent substance abuse (PPD + SA) and a substance-induced psychotic disorder (SIPD) can be diagnostically challenging. We aimed to determine if these two diagnoses are clinically distinct, particularly in relation to psychopathology. In addition, we aimed to examine the specific clinical features of cannabis-induced psychotic disorder (CIPD) as compared to primary psychotic disorder with concurrent cannabis abuse (PPD + CA) and also to SIPD associated with any substance.
Methods: A systematic review of SIPD literature using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
Results: Using strict inclusion criteria, a total of six studies examining SIPD were included in the review (two of which only considered psychosis induced by cannabis alone). The findings did not reveal many consistent differences in psychopathology. However, we did find that that compared to PPD + SA, individuals with SIPD have a weaker family history of psychotic disorder; a greater degree of insight; fewer positive symptoms and fewer negative symptoms; more depression (only in CIPD) and more anxiety.
Conclusion: There remains a striking paucity of information on the psychopathology, clinical characteristics and outcome of SIPD. Our review highlights the need for further research in this area.

1. Introduction

Substance abuse is common among individuals with primary psychotic disorders. Nearly half of those with a history of schizophrenia report a lifetime coexisting substance use disorder (Kavanagh et al., 2004; Regier et al., 1990). Alcohol and cannabis are the predominant substances abused by patients with psychotic disorders (Barnett et al., 2007; Kavanagh et al., 2004; Weaver et al., 2003). More recently, the use of novel psychoactive substances (NPS) has become more widespread due to their availability on the internet and in so called "head shops". Their use appears to be significantly more common in people with psychiatric illnesses compared to healthy people (Martinotti et al., 2014). A recent systematic review on the effects of NPS on individuals with severe mental illness suggested that NPS can have a relatively severe effect on people with psychotic disorders, resulting in an exacerbation in symptoms with increased agitation, aggression and violence (Gray et al., 2016).

Multiple agents have been implicated in the development of substance-induced psychotic disorder (SIPD) including alcohol, cocaine, amphetamines and hallucinogens (Engelhard et al., 2015; Harris and Batki, 2000; Murray et al., 2013; Vardy and Kay, 1983). Much of the research however has focused on cannabis-induced psychotic disorder (CIPD). The intimate relationship between cannabis use and psychosis is well recognized (Andreasson et al., 1987; Arseneault et al., 2002; Fergusson et al., 2005; Fergusson et al., 2003; Henquet et al., 2005a; Henquet et al., 2005b; Imade and Ebie, 1991; Kristensen and Cadenhead, 2007; Kuepper et al., 2011; Semple et al., 2005; Solomons et al., 1990; van Os et al., 2002). Overall, cannabis use appears to confer a twofold risk of later schizophrenia or schizophreniform disorder (Arseneault et al., 2004).

There is still debate as to whether SIPD is a separate entity from schizophrenia and whether the diagnosis is stable over time. Some authors argue that there are no consistent differences in the symptomatology of SIPDs and primary psychotic disorders (PPDs) and that there is little evidence to support the validity of "cannabis psychosis" as a diagnostic entity (Boydell et al., 2007; Imade and Ebie, 1991; McGuire et al., 1994; Thornicroft, 1992). Others maintain that in spite of certain

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similarities the possibility of a nosologically distinct diagnosis remains (Basu et al., 1999).

In relation to the effect of comorbid drug use on specific symptomatology in those with psychotic disorders, varying outcomes have been reported. The most consistent finding has been that drug abusing patients with an underlying psychotic illness tend to experience fewer negative symptoms than non-drug abusing patients (Baeza et al., 2009; Baldacchino et al., 2009; Bersani et al., 2002; Buckley et al., 1994; Compton et al., 2004; Dixon et al., 1991; Dubertret et al., 2006; Swartz et al., 2006). However, several studies have noted no difference in negative symptomatology (Addington and Addington, 2007; Barrowclough et al., 2015; Grech et al., 2005; Kamali et al., 2009; Katz et al., 2010). More positive symptoms of schizophrenia are generally observed in patients with drug abuse (Addington and Addington, 2007; Allebeck et al., 1993; Baeza et al., 2009; Baldacchino et al., 2009; Bersani et al., 2002; Buhler et al., 2002; Dubertret et al., 2006; Grech et al., 2005; Kamali et al., 2009; Katz et al., 2010; Swartz et al., 2006). But once again discrepancies exist, with some studies reporting fewer or no difference in incidence of positive symptoms (Barrowclough et al., 2015; Buckley et al., 1994; Compton et al., 2004; Dixon et al., 1991).

Aggarwal et al. (2012) determined that the incidence of patients presenting with SIPD to an Indian Drug De-addiction and Treatment Centre over a 13-year period was 1.4%. Over an average follow up of 6 months, 20.3% of patients had a change in diagnosis to either schizophrenia or affective psychosis. Arendt et al. (2005) found that of 535 individuals who were initially treated for CIPD and followed up for at least three years, 238 (44.5%) later developed a schizophrenia-spectrum disorder. According to Chen et al. (2015) who observed 284 Taiwanese patients with SIPD over a 15 year period, the progression time from transient to permanent psychotic disorder was 2.2 years with the majority of transformations occurring in the first year after diagnosis. Patients who receive an initial diagnosis of PPD in the context of substance abuse have more diagnostic stability and are more likely than SIPD patients to retain their diagnosis over time (Singal et al., 2015).

Given that the diagnosis has significant implications for future management, it is important to correctly identify SIPD. If psychotic symptoms can be attributed to drug use rather than to a PPD then antipsychotic treatment can be seen as a short term option with the main emphasis being placed on substance abuse treatment.

The fourth edition of the Diagnostic and Statistical manual of Mental Disorders (DSM-IV) introduced the term SIPD in 1994 (American Psychiatric Association. and American Psychiatric Association. Task Force on DSM-IV., 1994). It was intended to distinguish substance-induced psychotic states from primary psychotic disorders. In the DSM-5, the diagnostic criteria for SIPD essentially remain unchanged (American Psychiatric Association. and American Psychiatric Association. DSM-5 Task Force., 2013). They require the presence of hallucinations and /or delusions that arise during or soon after substance intoxication or withdrawal, that are judged to be due to the physiological effects of the substance, and are not better accounted for by a primary psychotic disorder. The symptoms cannot occur exclusively during the course of a delirium and must cause significant distress or impairment.

In clinical practice, distinguishing between SIPDs and PPDs with concurrent substance use remains a diagnostic difficulty (Schanzer et al., 2006). There has been criticism of the DSM diagnostic criteria (Mathias et al., 2008; Rounsaville, 2007). A diagnosis of SIPD is based on the assumption that most of the symptoms are transient and disappear after sustained abstinence. In practice, individuals who have an established pattern of abusing substances may not report any sustained drug-free periods. Therefore, psychotic symptoms which appear during periods of heavy drug use may indeed be substance-induced, but they may also be manifestations of an underlying PPD.

Regardless of the pathophysiology, patients with psychotic illness who abuse substances are a complex group of individuals with multiple different needs. Severe mental illness and co-morbid substance misuse is associated with a range of negative outcomes including non-adherence, increased relapse and more frequent hospitalisations (Caspari, 1999; Caton et al., 2000; Zammit et al., 2008).

To our knowledge no previous systematic reviews have examined the specific psychopathology of individuals presenting with a DSM diagnosis of SIPD. There is a remarkable paucity of research in this area. We identified only one major systematic review examining the specific psychopathology of "cannabis psychosis" compared to other psychotic disorders (Baldacchino et al., 2012). However, this study used a very broad definition of "cannabis psychosis" and only included studies conducted in an inpatient setting.

2. Aims and objectives

2.1. Aim

The aim of this review was to determine if SIPD is distinct from primary psychotic disorder with concurrent substance abuse (PPD + SA), in relation to psychopathology. Furthermore we aimed to examine the specific clinical features of CIPD as compared to primary psychotic disorder with concurrent cannabis abuse (PPD + CA) and also to SIPD associated with any substance.

2.2. Objectives

The objectives of this paper were to review the demographics, general psychopathology, positive and negative symptoms, insight and premorbid adjustment of individuals with SIPD and CIPD.

3. Methods

We identified studies examining SIPD associated either with any substance use or with cannabis alone. The former included studies that did not differentiate between illicit drugs, instead examining more than one type of substance within the same study. Studies investigating SIPD associated with a single substance of abuse other than cannabis were not included in the review due to the methodological difficulties in meaningfully comparing outcomes between these trials. Therefore two types of studies were considered of interest:

1. Those examining the psychopathology of SIPD (associated with any substance) compared to PPD + SA.
2. Those examining the psychopathology of CIPD compared to PPD + CA.

3.1. Search strategy

The PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines (Moher et al., 2009) were used as a framework for our review and reporting procedures. The search criteria were collaboratively established with assistance from a research librarian. We searched the following databases in February 2016: Pubmed, Psychology and Behavioral Sciences, PsycINFO, Medline and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). The search strategy used both free-text words and Medical Subject Headings (MeSH) terms. We conducted eight separate searches using a combination of the key words "substance-induced psychosis", "cannabis", "THC", "psychopathology", "diagnosis", "clinical features", "schizophrenia",

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