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Pre-illness cannabis use and the early course of nonaffective psychotic disorders: Associations with premorbid functioning, the prodrome, and mode of onset of psychosis

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ABSTRACT

Introduction: Limited research indicates that pre-illness cannabis use may result in an earlier age at onset of psychosis, though little is known about the influence of prior cannabis use on the premorbid and prodromal phases. This study examined the effects of prior or concurrent cannabis (as well as nicotine and alcohol) use on: (1) early adolescent (12–15 years) premorbid functioning, (2) late adolescent (16–18 years) premorbid functioning, (3) two features of the prodrome, and (4) mode of onset of psychosis.
Methods: Participants included 109 well-characterized first-episode patients hospitalized in public-sector settings. Assessments included ages at initiation of first, weekly, and daily use of substances, the *Premorbid Adjustment Scale*, the *Symptom Onset in Schizophrenia* inventory, and a consensus-based best estimate of mode of onset.
Results: Participants having used cannabis at ≤15 years had better early adolescence social functioning than those who had not used cannabis ($p = 0.02$). Conversely, those who had used cannabis at ≤18 years had poorer late adolescence academic functioning ($p < 0.001$). Participants having used cannabis before onset of psychotic symptoms did not differ from those who had not in terms of having had an identifiable prodrome or the number of prodromal symptoms experienced. Whereas 42% of those having used cannabis daily had an acute mode of onset of psychosis, only 20% of those without prior daily cannabis use had an acute onset ($p = 0.04$).
Conclusions: Findings suggest that cannabis use is associated with premorbid social and academic functioning and mode of onset. Further research is warranted to elucidate the complex associations between cannabis use and diverse early-course features.

1. Introduction

Among individuals with schizophrenia, the most commonly abused substances are nicotine, alcohol, cannabis, and cocaine (Mueser and McGurk, 2004). Cannabis misuse is of particular interest for several reasons. First, cannabis appears to be the most commonly abused substance in samples of patients with schizophrenia (DeQuardo et al., 1994; Sevy et al., 2001), including first-episode patients (Barnett et al., 2007; Van Mastrigt et al., 2004). Second, pre-illness cannabis use may be an independent risk factor for psychosis (Semple et al., 2005) and appears to be associated with an earlier onset of psychotic symptoms (Barnes et al., 2006; Compton and Ramsay, 2009). Third, even among first-episode patients, heavy substance use, including cannabis use, is associated with increased risk of inpatient admission, poorer symptomatic and functional outcomes, and shorter time to relapse (Wade et al., 2006, 2007). Further research is needed to examine how cannabis use influences early-course features, given that premorbid

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functioning, prodromal features, age at onset, and mode of onset of psychosis each has prognostic implications for the longer-term course of nonaffective psychotic disorders.

A previous report from the present first-episode sample documented associations between pre-illness cannabis, alcohol, and tobacco use and the age at onset of prodrome and age at onset of psychosis; specifically, analysis of change in frequency of use prior to onset indicated that progression to daily cannabis and tobacco use was associated with an increased risk of onset of psychotic symptoms, and similar or even stronger effects were observed when onset of illness or prodromal symptoms was the outcome (Compton et al., 2009b). (However, it should be noted that it has been suggested that the association between age at onset and cannabis use is a spurious one because those using cannabis are more likely to be young; Wade, 2005). Yet, aside from associations with age at onset, very little is known about the influence of cannabis use on these other aforementioned early-course features. Given the sequential onset of nonaffective psychotic disorders and the need to further characterize early-course epochs including the premorbid and prodromal phases, this study examined the effects of prior or concurrent cannabis (as well as nicotine and alcohol) use on: (1) premorbid functioning in early adolescence (12–15 years), (2) premorbid functioning in late adolescence (16–18 years), (3) two features of the prodrome (presence of a retrospectively identifiable prodrome and the number of prodromal features experienced), and (4) mode of onset of psychosis.

2. Methods

2.1. Setting and sample

This analysis was conducted using data from a well-characterized sample of first-episode patients enrolled in a study on the determinants of treatment delay, or the duration of untreated psychosis (Compton et al., 2008, 2009a,c, in press). The sample included individuals, aged 18–40 years, who were hospitalized for recent-onset or previously untreated nonaffective psychosis at a large, urban, university-affiliated, public-sector hospital ($n=99$) or a suburban county psychiatric crisis center ($n=10$). Exclusion criteria included: known or suspected mental retardation, a Mini-Mental State Examination (Cockrell and Folstein, 1988; Folstein et al., 2001) score of <23, a significant medical condition compromising ability to participate, prior antipsychotic treatment of >3 months duration, previous hospitalization for psychosis >3 months prior to the index hospitalization, or inability to provide written informed consent.

Demographic and clinical characteristics of the present sample have been described in detail elsewhere (Compton et al., in press, 2010). Briefly, participants' mean age at recruitment was 23.1 ± 4.7 years. The majority of the sample was male (76.1%) and African American (89.9%). Coming from a socioeconomically disadvantaged milieu, many participants had not completed high school (44.0%, Goulding et al., 2010), reported a prior history of incarceration (57.8%, Ramsay et al., in press), and were unemployed (61.5%) at the time of first treatment contact. All participants met *Structured Clinical Interview for DSM-IV Axis I Disorders* (SCID; First et al., 1998) criteria for schizophreniform disorder, schizophrenia, schizoaffective disorder, brief psychotic disorder, delusional disorder, or psychotic disorder not otherwise specified, as described in greater detail elsewhere (Compton et al., in press, 2010).

2.2. Procedures and materials

Participants were first approached several days after their admission to the inpatient units, allowing for adequate stabilization of symptoms and initiation of treatment planning. The research assessment typically lasted 3–4 h and occurred on hospital day 9.1 ± 6.7. Data on substance use were collected by inquiring about the age at initiation of any use, weekly use, and daily use of cannabis, alcohol, and tobacco (Compton et al., 2009b; Stewart et al., 2010). As noted previously (Stewart et al., 2010), the majority of participants (87, 79.8%) had previously used cannabis; furthermore, 66 (60.6%) had used it weekly and 49 (45.0%) had previously used it daily.

The *Premorbid Adjustment Scale* (PAS; Cannon-Spoor et al., 1982), a reliable and valid instrument widely used in schizophrenia research, was used to assess the degree of attainment of specific developmental goals preceding initial onset of psychosis (Alvarez et al., 1987; Cannon-Spoor et al., 1982). Premorbid functioning was rated (0–6 for normal to severe impairment) during two age periods: early adolescence (12–15 years) and late adolescence (16–18 years), in two domains typically considered as subscales of the PAS. That is, in both early adolescence and late adolescence, *academic functioning* is comprised of scholastic performance and adaptation to school, and *social functioning* includes sociability and withdrawal, peer relationships, and social–sexual functioning. As described in a previous report (Monte et al., 2008), premorbid functioning was not assessed in the early or late adolescence age periods if these periods included the year before the onset of prodromal symptoms, as a conservative measure to safeguard against inadvertently assessing prodromal impairments during the rating of premorbid functioning.

As described previously (Compton et al., 2010), a consensus-based determination of the presence of a prodrome relied on both patient and informant/family member data derived from the *Symptom Onset in Schizophrenia* (SOS) inventory (Perkins et al., 2000) and select items from the semi-structured *Course of Onset and Relapse Schedule/Topography of Psychotic Episode* (CORS/TOPE) interview (Norman and Malla, 2002). Regarding the latter, participants were asked questions such as: "When were you last your usual self?", "When did you first notice a change?", "What was the first change that you noticed?", "What do you believe is the cause of these problems that you are currently having?", and "When did you think that it was important to seek help for yourself?" The SOS elicits information about 14 well-defined symptoms that are commonly observed during the prodromal phase of psychotic disorders. Each item is rated on a 4-point scale based on the frequency and duration of the disturbance, which determines whether it was clinically relevant as a harbinger of the subsequent psychotic episode. Of note, non-specific features such as dysphoric mood must be relatively more severe, while attenuated or brief psychotic experiences may be considered a marker of the subsequent disorder after occurring only a few times. To qualify as