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Evaluating the relationship between cannabis use and IQ in youth and young adults at clinical high risk of psychosis

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ABSTRACT

Among people with psychosis, those with a history of cannabis use show better cognitive performance than those who are cannabis naïve. It is unknown whether this pattern is present in youth at clinical high risk (CHR) of psychosis. We evaluated relationships between IQ and cannabis use while controlling for use of other substances known to impact cognition in 678 CHR and 263 healthy control (HC) participants. IQ was estimated using the Vocabulary and Block Design subtests of the Wechsler Abbreviated Scale of Intelligence. Drug and alcohol use severity and frequency were assessed with the Alcohol and Drug Use Scale, and we inquired participants' age at first use. CHR were further separated into early and late age at onset of cannabis use sub-groups, and low-, moderate- and high-frequency sub-groups. No significant differences in IQ emerged between CHR or HC cannabis users vs. non-users, or between use frequency groups. CHR late-onset users showed significantly higher IQ than CHR early-onset users. Age at onset of cannabis use was significantly and positively correlated with IQ in CHR only. Results suggest that age at onset of cannabis may be a more important factor for IQ than use current use or use frequency in CHR.

1. Introduction

Cannabis is the most widely used illicit substance in both schizophrenia and in those at clinical high risk (CHR) of developing psychosis (Addington et al., 2014). Furthermore, cannabis use severity is associated with greater positive symptoms in CHR (Caspi et al., 2005; Moore et al., 2007; Kuepper et al., 2011; Fusar-Poli et al., 2012) and epidemiological data suggest a role for cannabis in the onset of psychosis (Arseneault et al., 2002). Recent prospective data in CHR individuals have indicated that among lifetime cannabis users, higher baseline use severity (Buchy et al., 2015a), frequency (Valmaggia et al., 2014) and first use before the age of 15 (Arseneault et al., 2002; Valmaggia et al., 2014) are associated with an increased rate of conversion to psychosis.

It is well documented that among people diagnosed with a psychotic disorder, those with a history of cannabis use show better cognitive performance than those who are cannabis naïve (Potvin et al., 2008; Rabin et al., 2011; Yucel et al., 2012). A recent meta-analysis (Rabin et al., 2011) excluded studies with people with a current comorbid diagnosis of drug abuse and reported a medium effect size (Cohen's $d=0.48$) for higher IQ in cannabis-using individuals with schizophrenia compared to non-users. Stratifying patients according to cannabis use frequency has suggested higher IQ in low- vs. high-frequency users (Leeson et al., 2012), although another study failed to observe this relationship

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(Tosato et al., 2013). Yucel et al. (2012) did not observe differences in IQ in psychosis patients with a lifetime exposure to cannabis compared to never-users, or in users with an early vs. late age at onset of cannabis use. Thus there is some evidence that patients with psychosis with a positive lifetime exposure to cannabis and/or who are current users show higher IQ than abstinent patients, and that use frequency may associate with IQ. The relationship between IQ and age at onset of cannabis use in people with psychoses is less clear. No published studies have characterized IQ in youth at CHR of psychosis who use cannabis compared to those who do not.

Several explanations have been proposed to explain the higher cognitive abilities in cannabis-using vs. abstinent patients with schizophrenia. One suggestion is that among people who develop a psychosis, those who have used cannabis have better cognitive functioning because they have fewer neurodevelopmental risk factors compared to those who did not use cannabis (Loberg and Hugdahl, 2009; Schnell et al., 2009; Leeson et al., 2012). Another explanation is that early cannabis use may induce psychosis onset in less cognitively vulnerable individuals, i.e., those with better cognitive capacities, thereby facilitating the onset of psychosis that may otherwise not have occurred (Yucel et al., 2012). A related suggestion is that the better cognition in patients who use cannabis may have facilitated their recreational drug use like in typical adolescents (Ferraro et al., 2013), or that superior social skills enable cannabis-using patients to acquire and sustain a drug habit, which is reflected in their cognition (Solowij and Michie, 2007; Potvin et al., 2008).

When assessing the relationship between cannabis and IQ, it is important to control for the effects of the consumption of other substances. Tobacco and alcohol are the most frequently used substances among people with schizophrenia and in CHR than in the general population (de Leon and Diaz, 2005; Addington et al., 2014; Buchy et al., 2015a) and have been associated with neurocognitive function in schizophrenia (Fowler et al., 1998; Allen et al., 1999; Cantor-Graae et al., 2001; Manning et al., 2009; Yip et al., 2009; Wing et al., 2011; Morisano et al., 2013). Stimulant use also has a deleterious effect on cognitive functions in people diagnosed with a psychotic disorder (Serper et al., 2000a, 2000b; Smelson et al., 2003; Bahorik et al., 2014; van der Meer et al., 2014), and other studies have reported elevated neurocognition in people with schizophrenia currently using cocaine (Bahorik et al., 2014; Benaiges et al., 2013). Therefore, these variables must be taken into account when interpreting results of the relationship between cannabis use and IQ across the schizophrenia spectrum.

The goal of the present study was to assess the relationship between cannabis use patterns and IQ in CHR youth, while controlling for any use of other substances known to impact cognition such as tobacco, alcohol and stimulants, as well as antipsychotic medications. This cohort offers a unique opportunity to examine these associations prior to the onset of psychosis, in people with a greater probability of developing a psychotic disorder relative to the general population, but who do not have potential confounds seen in patient studies such as lengthy antipsychotic treatment. Based on the literature in schizophrenia, we hypothesized that: 1) CHR youth using cannabis will have a higher IQ compared to those who do not; 2) CHR youth with a lifetime exposure to cannabis will have a higher IQ compared to never-users; and 3) CHR low-frequency cannabis users will have a higher IQ than CHR high-frequency users. Additionally, we conducted exploratory analyses of IQ in relation to age at onset of cannabis use in CHR youth, and in CHR separated dichotomously by early vs. late age at onset of cannabis. We also conducted an exploratory analysis of IQ in CHR converters vs. non-converters separated by baseline cannabis use (Y/N).

2. Methods

2.1. Participants

Participants were recruited for the second phase of the multi-site North American Prodrome Longitudinal Study (NAPLS-2) (Addington et al., 2012). The final NAPLS-2 sample consists of 764 CHR participants and 280 healthy controls (HC). The present paper reports on the 678 CHR and 263 HC participants in NAPLS 2 who provided baseline IQ data and completed an assessment on cannabis use. All CHR participants were required to meet the Criteria of Prodromal Syndromes (COPS) using the Structured Interview for Prodromal-Risk Syndromes (SIPS) (McGlashan et al., 2010). The age range for NAPLS-2 was 12–35.

Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ < 70, past or current history of a central nervous system disorder or DSM-IV criteria for a current substance dependence disorder. HC participants were also excluded if they had a first-degree relative with a current or past psychotic disorder. HC and CHR participants were not matched for IQ; however, we made every attempt to match groups on age, sex and parental socioeconomic status. A more detailed description of ascertainment, inclusion and exclusion criteria, and participant details is provided elsewhere (Addington et al., 2012).

2.2. Measures

The SIPS and the Scale of Prodromal Symptoms (SOPS) (McGlashan et al., 2010) were used to assess criteria for a prodromal syndrome and severity of attenuated positive symptoms.

Diagnosis of conversion to psychosis was made with the SCID (First et al., 1998). Conversion criteria is that at least one of the five SOPS positive symptoms reached a psychotic level of intensity (rated 6) for a frequency of ≥ 1 h per day for 4 days per week during the past month or that symptoms seriously impacted functioning (e.g., severely disorganized or dangerous to self or others).

Alcohol and drug use for cannabis, cocaine and amphetamine severity over the last month was rated using the Alcohol and Drug Use Scale (AUS/DUS) (Drake et al., 1996) as 1=abstinent, 2=use without impairment, 3=abuse, 4=dependence. Frequency of use was rated as 0=no use, 1=once or twice per month, 2=3–4 times per month, 3=1–2 times per week, 4=3–4 times per week, or 5=almost daily. Frequency of tobacco use was rated differently as 0=no use, 1=occasionally, 2=less than 10 per day, 3=11–25 per day, 4=more than 25 per day. Based on commonly used measures and interview questions in the literature (Arseneault et al., 2002; Caspi et al., 2005; Henquet et al., 2005), we also enquired whether they had ever used cannabis during their lifetime (i.e. “Have you ever smoked/used cannabis?”) and the age at first use.

IQ was estimated with the Vocabulary and Block Design subtests of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).

2.3. Cannabis groups

First, we separated CHR participants into three groups of users: early-onset (< age 15), late-onset (≥ age 15), and cannabis naïve.

Next, CHR individuals were grouped according to baseline cannabis use frequency and compared on IQ: Abstinent, low-frequency (< 5 times per month), moderate-frequency (< 5 times per week), and high-frequency users (Daily).

Lastly, we separated CHR youth into four sub-groups according to baseline cannabis use and subsequent conversion vs. non-conversion to psychosis: CHR who converted and were using cannabis (Converter+Cannabis), CHR who converted and were abstinent (Converter−Cannabis), CHR who did not convert and were using cannabis (NonConverter+Cannabis), and CHR non-converters abstinent from cannabis (NonConverter−Cannabis).

2.4. Procedures

All eight NAPLS sites (Emory University, Harvard University/Beth Israel Deaconess Medical Center, University of Calgary, University of California at Los Angeles, University of California at San Diego, University of North Carolina at Chapel Hill, Yale University, and Zucker Hillside Hospital) recruited CHR and HC participants. Raters were experienced research clinicians who demonstrated adequate reliability at routine reliability checks. Post-training agreement on the critical threshold for determining initial eligibility, subsequent conversion status and prodromal diagnoses based on the SIPS was excellent (kappa=.90). All testers across sites received training on IQ measures at the beginning of the study under the supervision of LJS and WS and ongoing within site and across site supervision was carried out at least a few times every month (Meyer et al., 2014). The Principal Investigator or clinical psychiatrist or psychologist at each site conducted a comprehensive clinical assessment to determine if entry criteria were met (Addington et al., 2012). Clinical assessments that included the AUS/DUS were conducted at baseline. The study protocols and informed consents were reviewed and approved