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Are Cannabis Use Disorders Associated with an Earlier Age at Onset of Psychosis? A Study in First Episode Schizophrenia

Serge Sevy, MD,

The Zucker Hillside Hospital of the North Shore Long Island Jewish Health System, Psychiatry Research; Albert Einstein College of Medicine, psychiatry

Delbert G Robinson, MD,

Feinstein Institute for Medical Research, Center for Translational Psychiatry; The Zucker Hillside Hospital of the North Shore Long Island Jewish Health System, Psychiatry Research; Albert Einstein College of Medicine, psychiatry

Barbara Napolitano, MA,

Feinstein Institute for Medical Research, Biostatistics Unit; The Zucker Hillside Hospital of the North Shore Long Island Jewish Health System, Psychiatry Research

Raman C Patel, MD,

Bronx Lebanon Hospital, Psychiatry

Handan Gunduz-Bruce, MD,

Yale University School of Medicine, Psychiatry

Rachel Miller, LCSW,

National Institute of Mental Health

Joanne McCormack, LCSW,

The Zucker Hillside Hospital of the North Shore Long Island Jewish Health System, Psychiatry Research

Beth S Lorell, LCSW, and

Bronx Lebanon Medical Center, Psychiatry

John Kane, MD

Dr. Serge Sevy, MD, Psychiatry Research, The Zucker Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004, Phone: (718) 470-8175, Fax: (718) 343-1659, Sevy@lij.edu.

Contributors

Dr. Sevy assessed and treated subjects, participated in the statistical analysis, and wrote the first draft of the manuscript. Dr. Robinson wrote the protocol, recruited and assessed subjects, and participated in the statistical analysis. Ms. Napolitano undertook the statistical analysis and wrote part of the Results section. Dr. Patel, Dr. Gunduz-Bruce, Ms. Miller, Ms. McCormack, and Ms. Lorell recruited, assessed, and treated subjects. Dr. Kane participated in the writing of the protocol. All authors contributed to and have approved the final manuscript.

Conflict of Interest

Dr. Robinson has received grant support from Bristol-Meyers Squibb, Eli Lilly, and Janssen Pharmaceutica. He has served as a speaker for Astra Zeneca and Janssen Pharmaceutica. Dr. Kane has served as a consultant or speaker for Astra-Zeneca, Bristol-Myers Squibb, Cephalon, Eli Lilly, GSK, Janssen Pharmaceutica, Johnson and Johnson, Lundbeck, Organon, Otsuka, Pfizer Inc, PgXHealth, Proteus, Vanda, and Wyeth. He is a shareholder of MedAvante. Dr. Sevy, Ms. Napolitano, Dr. Gunduz-Bruce, Dr. Patel, Ms. Miller, Ms. McCormack, and Ms. Lorell report no competing interests.

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Feinstein Institute for Medical Research, Center for Translational Psychiatry; The Zucker Hillside Hospital of the North Shore Long Island Jewish Health System, Psychiatry Research; Albert Einstein College of Medicine, psychiatry

Delbert G Robinson: robinson@lij.edu; Barbara Napolitano: bnapolit@nshs.edu; Raman C Patel: rpatel@bronxleb.org; Handan Gunduz-Bruce: handan.gunduz-bruce@yale.edu; Rachel Miller: mrachel@mail.nih.gov; Joanne McCormack: jmccorma@lij.edu; Beth S Lorell: bethlorell@gmail.com; John Kane: psychiatry@lij.edu

Abstract

Introduction—The purpose of this study is to determine if an earlier age at onset of positive symptoms in schizophrenia is associated with cannabis use disorders (CUD).

Methods—49 first-episode schizophrenia subjects with CUD were compared to 51 first-episode schizophrenia subjects with no substance use disorders for demographic and clinical variables. A multivariate logistic regression was performed to determine the joint relationship between variables significantly associated with CUD on univariate testing and ascertain if these variables independently predict CUD. Significance level was set at $p < 0.05$.

Results—74% of CUD subjects had the onset of CUD before the onset of positive symptoms. Compared to non-substance abusing subjects, CUD subjects were predominantly male, younger at study entry, had an earlier age at onset of positive symptoms, less educational attainment, a lower own socioeconomic status, better premorbid childhood social adjustment, a trend for poorer premorbid childhood academic adjustment, less motor abnormalities but more severe hallucinations and delusions. In the multivariate analysis, only male gender, worse socioeconomic status, better premorbid childhood social adjustment, and more severe positive symptoms at study entry were associated with a lifetime history of CUD.

Discussion—although cannabis use precedes the onset of illness in most patients, there was no significant association between onset of illness and CUD that was not accounted by demographic and clinical variables. Previous studies implicating CUD in the onset of schizophrenia may need to more comprehensively assess the relationship between CUD and schizophrenia, and take into account additional variables that we found associated with CUD.

Keywords

schizophrenia; first-episode; onset; cannabis; abuse; dependence

1. Introduction

Lifetime prevalence of cannabis use disorders (CUD) in schizophrenia ranges from 13% to 64% (Barnes, et al., 2006, Barnett, et al., 2007, Buhler, et al., 2002, Cantwell, et al., 1999, Cantwell, et al., 2004, Hambrecht and Hafner, 1996, Kovasznay, et al., 1997, Linszen, et al., 1994, Sevy, et al., 2001, Van Mastrigt, et al., 2004, Wade, et al., 2006). Several epidemiological studies in Sweden (Allebeck, et al., 1993, Andreasson, et al., 1987, Andreasson, et al., 1989, Zammit, et al., 2002), New Zealand (Arseneault, et al., 2002), The Netherlands (van Os, et al., 2002), and Israel (Weiser, et al., 2002) report an increased likelihood of developing schizophrenia in individuals who abuse cannabis. Several studies also suggest that the onset of cannabis use precedes the onset of positive symptoms in most schizophrenia subjects with cannabis use disorders (Allebeck, et al., 1993, Buhler, et al., 2002, Linszen, et al., 1994, Mauri, et al., 2006, Rabinowitz, et al., 1998), and the age at onset of psychosis is earlier in cannabis-abusing than non-substance abusing first-episode (Buhler, et al., 2002, Green, et al., 2004, Van Mastrigt, et al., 2004) and multi-episode (Andreasson, et al., 1989, Green, et al., 2004, Hambrecht and Hafner, 1996, Veen, et al., 2004) schizophrenia patients.

Several hypotheses have been put forward to explain an earlier age at onset of schizophrenia in patients abusing cannabis. A first hypothesis suggests that cannabis abuse precipitates the onset of schizophrenia in patients at risk for the illness. The neurobiological mechanisms underlying this increased vulnerability to psychosis may be related to increased cannabinoid receptors in the dorsolateral prefrontal cortex (Dean, et al., 2001), and increased release of dopamine in the mesolimbic pathway by Δ^9 -tetrahydrocannabinol (Tanda, et al., 1997). Dopamine activation in the striatum involves direct interactions between the dopamine D2 receptors and CB1 receptors. Functional interactions between the endogenous cannabinoid anandamide and dopamine suggest a possible participation of the endogenous cannabinoid system in disorders that involve dysregulated dopamine neurotransmission (Giuffrida, et al., 1999). A second hypothesis postulates that cannabis abuse and schizophrenia share common etiologic factors such as genetic vulnerability (Caspi, et al., 2005) or developmental neuropathology (Chambers, et al., 2001). A third hypothesis proposes that the earlier age at onset of psychosis in CUD subjects compared to non-substance users is the result of factors unrelated to schizophrenia such as age, gender, pre-morbid adjustment, and cognition. Cannabis is the most widely used illicit drug among adolescents and young adults (SAMHSA, 2006). It is used more by males than females and almost one half of the cannabis users start using it before age 18 (Gfroerer, et al., 2002). Several (Green, et al., 2004, Linszen, et al., 1994, Rabinowitz, et al., 1998, Veen, et al., 2004) but not all (Barnett, et al., 2007) first-episode studies have also reported a higher proportion of males in CUD subjects compared to non-substance abusing subjects. Patients with schizophrenia and substance abuse have better premorbid social adjustments (Arndt, et al., 1992, Breakey, et al., 1974, Ritzler, et al., 1977, Tsuang, et al., 1982). Higher functioning patients may be more social and more exposed to opportunities for substance abuse (Arndt, et al., 1992) or more active in trying to cope with some of their symptoms by using substances (Ritzler, et al., 1977). Regarding cognition, earlier age at onset of psychosis has been associated with worse IQ (Woodberry, et al., 2008), attention (Frangou, et al., 2008, Oie and Hugdahl, 2008, Thaden, et al., 2006), executive function (Gunduz-Bruce, et al., 2007, Jeste, et al., 1998, Tuulio-Henriksson, et al., 2004), psychomotor speed of processing (Hoff, et al., 1996, Tuulio-Henriksson, et al., 2004, White, et al., 2006) and verbal learning and memory (Basso, et al., 1997, Tuulio-Henriksson, et al., 2004). Finally, motor abnormalities have been reported in drug-free first-episode schizophrenia (Honer, et al., 2005, Pappa and Dazzan, 2009, Peralta, et al.). As spontaneous motor abnormalities increase with age (Fenton, 2000), a younger age at the onset of psychosis and at study entry may be associated with less spontaneous motor abnormalities in the CUD group compared to the non-substance abuse group.

Thus, the purpose of this study is to determine how specific is the association between age at onset of psychosis and cannabis use disorders in patients admitted for a first-episode of schizophrenia, schizophreniform or schizoaffective disorder. Previously, we reported on the correlates of substance use disorders in subjects with first-episode schizophrenia and schizoaffective disorder and found higher parental class, better premorbid cognitive functioning, higher IQ, better language skills, but no difference in age at onset of illness in 27 dual-diagnosis patients compared to 91 patients with no substance use disorders (Sevy, et al., 2001). Based on our previous findings and the above hypotheses, the present study focuses on cannabis use disorders and compare first episode schizophrenia subjects who have a lifetime history of cannabis use disorders (CUD) with non-substance abuser first-episode schizophrenia subjects for demographics, pre-morbid childhood adjustment, symptoms, cognition, and abnormal motor movements. By studying first-episode patients, we rule out the use of cannabis for self-medication related to side effects of antipsychotic medication, limit the exposure to prescribed medications that may influence study variables, and reduce problems of diagnosis, poor memory and inconsistent reporting for the onset of cannabis use and psychotic illness.

2. Methods

The present study was part of a prospective, randomized study comparing risperidone and olanzapine for the treatment of first episode patients with a diagnosis of schizophrenia, schizophreniform disorder, or schizoaffective disorder. Further details regarding this study were previously described (Robinson, et al., 2006). The study was conducted under the guidelines of the Institutional Review Board (IRB) of the North Shore - Long Island Jewish Health System (New York) and the Bronx-Lebanon Hospital (Bronx, NY). It was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Informed consent of the participants was obtained after the nature of the procedures had been fully explained.

2.1 Participants

Subjects were recruited from the Zucker Hillside Hospital (Queens, NY) and the Bronx-Lebanon Hospital (Bronx, NY). All new patients referred to psychiatric acute care in both institutions were screened for this study. All adult subjects provided written informed consent. For subjects less than 18 years old, written parental consent and written subject assent were also obtained. Eligible subjects were between the age of 16 and 40, had a current diagnosis of DSM-IV schizophrenia, schizophreniform disorder, or schizoaffective disorder with less than 12 weeks of lifetime antipsychotic medication treatment, and demonstrated either current positive or negative symptoms (as evidenced by a rating of 4 or more on the Schedule for Affective Disorders and Schizophrenia Change Version with psychosis and disorganization items (SADS-C+PD) *or* on the affective flattening, alogia, avolition, or anhedonia global items of the Hillside Clinical Trials version (Robinson, et al., 2000) of the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1989)). Women were included if they had a negative pregnancy test and agreed to use a medically accepted method of birth control. Subjects were excluded from this study if they met DSM-IV criteria for a current substance-induced psychotic disorder, psychotic disorder due to a general medical condition, mental retardation, suffered from any medical condition affecting the brain or requiring treatment with psychotropic medications, medical contraindications to treatment with olanzapine or risperidone, or significant risk of suicidal or homicidal behavior. Because this study intended to detect differences between severe cannabis users and non-substance users in a relatively small sample, we excluded subjects who used cannabis but did not have CUD, and subjects who had a substance use disorder but no CUD.

2.2. Assessments

Subject diagnoses were evaluated using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P). Psychopathology was assessed with SADS-C+PD and the Hillside Clinical Trials version of the SANS. Motor side effects were assessed with the Simpson-Angus Rating Scale (Simpson and Angus, 1970) and Barnes Akathisia Scale (Barnes, 1989). Parental and subject socio-economic status was assessed with the Index of Social Position (Hollingshead and Redlich, 1958). The index is composed of two factors (occupation and income) and includes 5 social classes (the lower the class, the higher the socio-economic status). Premorbid adjustment was assessed with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor, et al., 1982). We only used the childhood (up through age 11) PAS scores for the analyses to capture premorbid functioning before the onset of substance use disorders and psychosis. One subject with substance use disorders before age 12 was excluded from the premorbid adjustment analysis. The childhood PAS includes 2 items for social adjustment and 2 items for academic adjustment. Each item is scored from 0 (good adjustment) to 6 (poor adjustment). Ratings for 'Socialability and Withdrawal' and 'Peer Relationships' were averaged to obtain a composite measure of social adjustment, and 'Scholastic performance' and 'Adaptation to School' were

averaged to obtain a measure of academic adjustment. Raters for all the assessments were blinded to medication treatment to minimize external influence.

Substance use was assessed using the alcohol and substance abuse sections of the SCID interview. Sources of information for these assessments included patient self report and collateral information from health care providers, case managers, family members, friends, and housemates when available. Subjects were longitudinally treated and assessed for up to 3 years. For some subjects, the extent of substance use only became known after study entry. Thus, substance use classifications for the present study are the best assessments of substance use using all data sources at baseline and follow-up.

2.3. Outcome Definitions

The variables to be examined included demographics, symptoms, motor movements, and cognition. Neurocognitive tests included Continuous Performance Test, Identical Pairs version (CPT-IP), Trail Making Test, Wisconsin Card Sorting Test (WCST), WAIS-R digit span and digit symbol, Delayed Match to Sample Task, and the Set Shifting Task, California Verbal Learning Test (CVLT), Judgment of Line Orientation (JLO), WAIS-R, Block Design Subtest, and the Wide Range Achievement Test – Third Edition, Reading (WRAT-3).

2.4 Analyses

Univariate analyses for comparisons between the two groups on baseline characteristics included the two-sample t test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Mean and standard deviations are reported for continuous variables. To determine which variables were independently associated with a lifetime history of cannabis use disorders, we entered in a multivariate logistic regression model the variables that were significantly different between groups in the univariate analyses.

3. Results

3.1. Subject sample

Data for this report were collected from November 1998 to July 2004. Subject flow is described elsewhere (Robinson et al. 2006). 112 subjects participated in the prospective randomized study comparing risperidone and olanzapine. Forty-nine subjects (44% of the total sample) met DSM-IV criteria for cannabis use disorders (cannabis abuse or dependence) (CUD) either prior to or at the time of study entry. Among the 49 CUD subjects, 36 subjects (74%) began using cannabis more than one year prior to the onset of positive symptoms. Six subjects (12%) started cannabis use the same year as the onset of positive symptoms and 4 subjects (8%) started to use cannabis after the onset of positive symptoms. The timing of cannabis use and psychosis was unclear for 3 subjects (6%). Thus, 74% of subjects had the onset of CUD before the onset of positive symptoms. Nineteen CUD subjects (39%) had alcohol use disorders (abuse or dependence) and seven of these 19 CUD subjects (14%) had other substance use disorders (cocaine, n=5; hallucinogens, n=2; opiates, n=1; inhalants, n=1). As mentioned in the Methods section, we excluded from the analyses six subjects who were using cannabis at least once a week but were not diagnosed with CUD, and six subjects who had a diagnosis of alcohol use disorder and no diagnosis of CUD. Thus, 49 CUD subjects were compared with 51 non-substance abuser subjects.

3.2. Univariate analyses

3.2.1. Demographic and clinical characteristics—Compared to the non-substance abuser group, there were more males in the CUD group (82% vs. 57%; $p<0.05$). CUD subjects were significantly younger at study entry (22 ± 4 years vs. 25 ± 6 years; $p<0.001$), and had an

earlier age at onset of psychosis (20 ± 4 years vs. 22 ± 7 years; $p < 0.01$). In the CUD group, male subjects ($n=40$) had an earlier age at onset of psychosis (19 ± 4 vs. 23 ± 5) and earlier age at study entry (21 ± 3 vs. 24 ± 4) than female subjects ($n=9$). The CUD group had less educational attainment (Fisher's Exact Test, $p < 0.05$), lower subject socioeconomic status (Fisher's Exact Test, $p < 0.001$), better premorbid childhood social adjustment ($p < 0.05$) and a trend for poorer premorbid childhood academic adjustment ($p = 0.051$) than the non-substance abuser group. The CUD group also had less motor abnormalities ($p < 0.01$) but more severe hallucinations and delusions at study entry ($p < 0.05$) than the non-substance abuser group. No statistically significant differences were found between CUD subjects and non-substance abuser subjects for types of diagnosis, socio-demographics, parental socio-economic status, duration of untreated psychosis before study entry, impaired understanding, thought disorder, negative symptoms, or depressive symptoms. In the CUD group, subjects who were abusing cannabis and alcohol ($n=19$) were more depressed than subjects who were abusing cannabis only ($n=30$) (depressive score 19 ± 7 vs. 15 ± 6 respectively) but these two CUD subgroups did not differ for any other variables. Demographic and clinical characteristics are summarized in Table 1.

3.2.2. Neuropsychological Test Performance—There were no statistically significant differences between the CUD and non-substance abuser groups for episodic memory, attention and working memory, executive functioning, motor and cognitive speed, and current and premorbid intellectual functioning.

3.3. Multivariate analyses

To determine which variables were independently associated with a lifetime history of cannabis use disorders, we entered in a logistic regression the variables that were significantly different between groups in the univariate analysis: sex, educational attainment, childhood social and academic PAS scores, subject socio-economic status, age at onset of positive symptoms, hallucinations and delusions at study entry, and Simpson Angus Scale score (age at study entry was associated with groups, however, was also strongly correlated with age at onset of positive symptoms, and subsequently deleted). Using a backward elimination procedure (greater than 0.05 significance level for removal), the independent variables associated with a lifetime history of cannabis use disorders were male gender, subject socio-economic status, better premorbid childhood social PAS score, and worse positive symptoms at study entry ($R^2 = 0.32$). Regression coefficients, Chi-square values, and odds ratio estimates for the significant variables are summarized in Table 2.

We found similar results by only including subjects who had the onset of CUD before the onset of psychosis ($n=36$).

4. Discussion

In our sample of 112 first-episode subjects who participated in a randomized study comparing the efficacy and safety of two antipsychotics, lifetime prevalence rates of abuse or dependence were the highest for cannabis (44%), followed by alcohol (22%), and cocaine (4%). The lifetime prevalence rate of cannabis use disorders found in our sample of first-episode subjects is within lifetime prevalence rates (13% to 64%) previously reported in subjects with recent-onset schizophrenia. Our rates of alcohol use disorders are also within the reported rates of alcohol use in first-episode patients, which vary between 10 and 43% (Addington and Addington, 2001, Barnes, et al., 2006, Barnett, et al., 2007, Buhler, et al., 2002, Cantwell, et al., 1999, Green, et al., 2004, Hambrecht and Hafner, 1996, Mauri, et al., 2006, Sevy, et al., 2001, Strakowski, et al., 1993, Van Mastrigt, et al., 2004, Wade, et al., 2006). In contrast, our rates of psychostimulant use disorders were lower than those previously reported in first-episode patients, which vary between 5 and 40% (Barnes, et al., 2006, Barnett, et al., 2007,

Buhler, et al., 2002, Hambrecht and Hafner, 1996, Sevy, et al., 2001, Wade, et al., 2006). Similar to previous studies, more than 50% of CUD subjects were polysubstance abusers (Barnett, et al., 2007, Sevy, et al., 2001, Wade, et al., 2006).

Most (74%) of the first-episode CUD subjects had the onset of cannabis use disorders before the onset of positive symptoms. Previous first-episode studies reported that the onset of cannabis use disorders precedes the onset of positive symptoms in most CUD subjects (Allebeck, et al., 1993, Buhler, et al., 2002, Linszen, et al., 1994, Mauri, et al., 2006, Rabinowitz, et al., 1998). CUD subjects had an earlier age at onset of positive symptoms than non-substance abuser subjects. Other first-episode studies also reported an earlier age at onset of psychosis in CUD subjects compared to non-substance abuser subjects (Buhler, et al., 2002, Green, et al., 2004). As reported in other first-episode studies (Linszen, et al., 1994, Mauri, et al., 2006), CUD subjects were admitted for a first episode of psychosis at an earlier age than non-substance abuser subjects. Interestingly, earlier age at onset of positive symptoms and study entry in the CUD group compared to the non-substance group resulted in similar duration of untreated psychosis in both groups. Green et al (2004) reported a longer duration of untreated psychosis in first episode CUD subjects but a study in chronic patients did not find differences in duration of untreated psychosis between groups (Drake, et al., 2000).

In the multivariate analysis, only male gender, worse subject socio-economic status, better premorbid childhood social adjustment, and more severe positive symptoms at study entry were associated with a lifetime history of cannabis use disorder in first-episode patients. Being male increases the likelihood of having a lifetime diagnosis of cannabis use disorder by more than four times. As mentioned previously, several first-episode studies suggest a higher proportion of males in substance abusers compared to non-substance abusers. However, the predominance of males in the CUD group is not specific to schizophrenia. In a recent survey, it was estimated that rates of cannabis use during the past month were around 10% for males compared to 6% for females (SAMHSA 2007). Age at onset of positive symptoms was not in the final model and the high proportion of males in the CUD group may explain the earlier age at onset of psychosis observed in this group. Men have an earlier age at onset of schizophrenia than women (Szymanski, et al., 1995) and younger males are at higher risk of substance use disorders in the community (Blanchard, et al., 2000). This hypothesis is corroborated by our findings of an earlier age at onset of psychosis and study entry in men compare to women in the CUD group.

Compared to non-substance abuser subjects, CUD subjects did not differ for parental socio-economic status, but had a worse socio-economic status associated with their lifetime history of cannabis use disorders. Although the worsening of subject socio-economic status may explain the increased likelihood of CUD, the lack of difference between groups for parental socio-economic status suggest instead that CUD worsen subject socio-economic status.

CUD subjects had better premorbid childhood social adjustment than non-substance abuser subjects. Previous studies reported similar (Dixon, et al., 1991, Kovasznay, et al., 1997, Sevy, et al., 1990) or better (Arndt, et al., 1992, Breakey, et al., 1974, Ritzler, et al., 1977, Tsuang, et al., 1982) premorbid social functioning in subjects with schizophrenia and substance abuse. We also found that severity of positive symptoms at study entry was independently associated with a lifetime history of cannabis use disorders. Our findings are in agreement with previous first-episode studies reporting more severe positive symptoms in CUD subjects compared to non-substance abuser subjects (Buhler, et al., 2002, Green, et al., 2004). Unfortunately, this difference in positive symptoms between groups does not reveal the nature of the association between CUD and positive symptoms: cannabis may be used to self medicate positive symptoms, may worsen positive symptoms, or may be used because of delusional and/or auditory contents. Although a lifetime history of co-occurring alcohol use disorders in CUD

subjects is not associated with psychosis, it is associated with depressive symptoms and CUD subjects with a lifetime history of alcohol use disorders were more depressed at study entry than CUD subjects without a lifetime history of alcohol use disorders. We could not determine the causal relationship between alcohol use and depression from our data.

CUD patients did not differ from non-substance users for cognition. In a previous study, we found better auditory attention and working memory in schizophrenia patients with cannabis use disorders compared to non-substance abuser patients, but no differences between groups for processing speed, executive function, verbal fluency, verbal learning and memory (Sevy, et al., 2007). Loberg and Ugdhal (2009) reviewed 23 studies assessing cognition in schizophrenia patients using cannabis and only one of these studies reported worse cognition in cannabis users compared to non-cannabis users. Thus, our results and those of other studies suggest that cannabis use do not worsen cognition in schizophrenia.

The CUD group had less spontaneous motor abnormalities than the non-substance abuser group, which may be related to the younger age at onset of psychosis and at study entry of the CUD group. However, we cannot rule out a possible therapeutic effect of cannabinoids on spontaneous motor abnormalities. Cannabinoids have been found to improve spasticity in multiple sclerosis (for a review, see Lakhani and Rowland, 2009) and tics in Tourette's syndrome (Muller-Vahl, et al., 2002, Muller-Vahl, et al.), and may improve motor disorders by modulating basal ganglia activity (for a review, see Fernandez-Ruiz, 2009). The use of cannabinoids for treating movement disorders in schizophrenia is intriguing and will need to be further explored.

Finally, it is noteworthy that the correlates of CUD in our first-episode subjects are the same variables that predicted a continuous course of illness at five-year follow-up in first-episode subjects participating in the OPUS trial in Denmark (Bertelsen, et al., 2009). While correlations between these factors and other variables in multivariate models cannot be ruled out, these results suggest that there are common risk factors for cannabis use disorders and poor prognosis.

In summary, we found that a lifetime history of cannabis use disorders in first-episode subjects was associated with male gender, lower subject socio-economics status, better premorbid childhood social adjustment, and more severe positive symptoms at study entry. Although the onset of cannabis use disorder preceded the onset of illness in most patients, our findings suggest that age at onset of psychosis was not associated with cannabis use disorders. Previous studies implicating cannabis use disorders in schizophrenia may need to more comprehensively assess the relationship between cannabis use disorders and schizophrenia, and take into account the additional variables that we found associated with cannabis use disorders. Our study has some limitations including retrospective assessments of the onset of symptoms and substance use, a relatively small sample, and a possible contribution of alcohol and other substance use disorders to our findings. We did not correct for the large number of univariate comparisons, which might possibly increase the risk of type I errors. However, this study was exploratory and intended to screen for possible predictors of cannabis use disorders. Finally, our multivariate logistic regression model only explains 32% of the variation associated with cannabis use disorders. Future studies will have to address these limitations and other factors that may be associated with cannabis use disorders in first-episode subjects such as neurodevelopmental abnormalities and psychiatric symptoms in childhood.

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Table 1

Demographics and Clinical Characteristics of first-episode subjects with and without a history of cannabis use disorders (CUD) (mean $\pm$ standard deviation)

Total sample (n = 100)	No history of cannabis use disorders (n = 51)	History of cannabis use disorders (n = 49)	P-value
Males/females	29/22	40/9	<0.01
Age at study entry	25 $\pm$ 6	22 $\pm$ 4	<0.01
Age at onset of CUD		17 $\pm$ 3	
Age at onset of psychosis	23 $\pm$ 5	20 $\pm$ 4	<0.01
Duration of untreated	117 $\pm$ 175	94 $\pm$ 109	ns
Psychosis in weeks			
Severity of hallucinations and Delusions	4.7 $\pm$ 1.1	5.1 $\pm$ 0.8	<0.05
Simpson-Angus Dyskinesia	0.3 $\pm$ 0.6	0.0 $\pm$ 0.2	<0.01
Premorbid Adjustment Scale (PAS):			
Childhood			
Social adjustment [†]	2.1 $\pm$ 1.5	1.5 $\pm$ 1.3	<0.05
Academic adjustment [‡]	1.9 $\pm$ 1.2	2.4 $\pm$ 1.2	0.051

[†] Average of items 'Socialability and Withdrawal' and 'Peer Relationships'

[‡] Average of items 'Scholastic performance' and 'Adaptation to School'

Table 2

Regression coefficients and Chi-square values for variables independently associated with a lifetime history of cannabis use disorders

Explanatory variables	Coefficient	Wald χ^2	p	Odds ratio	95% CI
Intercept	-6.77	7.49	<0.01		
Female gender	-1.48	5.48	<0.02	0.23	0.07 – 0.79
Own socio-economic Status *	1.13	5.48	<0.001	3.09	1.59 – 6.01
Childhood PAS social score *	-0.65	10.75	<0.002	0.52	0.35 – 0.77
Severity of hallucinations and delusions at study entry	1.02	9.31	<0.01	2.77	1.44 – 5.33

* Socio-economic status and Childhood PAS social scores are scale variables used as continuous variables.