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A comparative study of socio-demographic and substance use correlates in early onset psychosis

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Abstract

Background—Comorbid substance use particularly cannabis among adolescents with mental illness is a major public health concern in developing countries with limited mental health resources. Better understanding of the association between cannabis use and other poly-substance use and early mental illness will provide for more targeted early interventions.

Aim—To examine the socio-demographic profile and cannabis use characteristics among adolescents with first episode early onset psychosis (EOP) and compare to age and gender matched adolescents with first episode non-psychotic mental illness (controls).

Method—Forty-five adolescents with first episode EOP and 45 controls were assessed using a clinical interview, PANSS and WHO ASSIST for substance related problems.

Results—There were significant socio-demographic differences among the adolescents with EOP (73% Black, 64% from low family income, 44% from rural areas) compared to controls (24% Black, 53% from low family income, 2% from rural areas). Whilst there was no difference in lifetime cannabis use, EOP adolescents differed in motivation for cannabis use, had increased current cannabis use (38%, $p=0.01$) and more frequent use (52%, $p=0.04$) compared to controls (16% current and 18% frequent use). EOP adolescents reported more hazardous use with higher ASSIST mean cannabis specific involvement scores (EOP 10.2; controls 2.3; $p=0.004$).

Conclusion—The differences in socio-demographic variables may reflect the marked disparity in access to mental health care for rural Black youth. Psychotic youth may be more vulnerable to comorbid cannabis related problems than other mentally ill adolescents. The study highlights the need for early introduction of substance use interventions among adolescents with mental illness.

Keywords

adolescent; cannabis; early onset; mental health; psychosis

Introduction

The relationship between mental illness and substance use is complex and often reciprocal, requiring an integrated response.¹ Patients who present with comorbid substance use are at increased risk for poor clinical and socio-economic outcomes^{2,3} and present significant challenges in terms of management, especially within resource limited settings. In South Africa, as in many other developing countries, child and adolescent mental health services are scarce, and there are no integrated substance use and psychiatric treatment centers in many areas including in KwaZulu-Natal for mentally ill adolescents with co-morbid substance related disorders.

The prevalence of comorbid substance use disorders in adolescents with mental illness ranges from 20 to 33%, with predominance in males and older adolescents.⁴ Substance use is associated with a variety of adolescent psychopathology particularly the externalizing disorders with varying rates and patterns of substance use.⁵ The prevalence of substance use disorders is especially high among patients with early onset psychosis (EOP) (psychosis onset by age 18) and is often under-detected and untreated.⁶ An American study of 75 youth with EOP reported that 45% of the participants had a history of substance abuse or dependence with alcohol and cannabis being the most commonly abused substances.⁶ Cannabis, alcohol and nicotine are the most commonly used substances globally and there is often polysubstance use in patients with mental illness and particularly psychosis.⁷

Cannabis use is also associated with various other non-psychotic mental illnesses in adolescents including conduct disorders, attention deficit hyperactivity disorder (ADHD), depression and suicidal behavior.⁸ For example, in a review of 236 adolescent psychiatric patients in Israel, the most common diagnoses among cannabis users were ADHD and disruptive behavior disorder.⁸

Studies of cannabis use in adolescents with mental disorders within low- and middle-income countries (LMICs) however, are lacking; although recent prevalence studies from South Africa indicate that rates of use in adolescents with FEP are as high in these contexts as in high-income countries.^{9,10} In the Western Cape, Lachman and colleagues found that 44% of males and 10% females reported cannabis use⁹, while in KwaZulu-Natal, a rate of 68% was reported in FEP adolescents.¹⁰ Notably, there are no prevalence studies for substance use in non-psychotic mentally ill adolescents in the South African context.

Studies have investigated the differential susceptibility to cannabis among adults with psychosis compared to the general population and to other mental illness. A study of cannabis use among 80 youth with schizophrenia spectrum disorder reported no significant difference in prevalence of cannabis use or other substance use among psychotic and non-psychotic youth, however there was an association with earlier age of cannabis initiation and earlier age of onset of psychotic and non- psychotic disorders.¹¹ Studies have also reported that adult patients with psychosis have a different pattern of substance use with earlier tolerance, loss of control and onset of dependence.⁷ This has not been investigated in exclusive adolescent samples.

Understanding the reasons for substance use in adolescents with mental illness is a priority for developing appropriate preventive and treatment interventions. A review in adults with psychosis identified the main reasons for substance use as: the intoxicating effects of drugs; social reasons; and relief from dysphoria, psychotic symptoms and/or medication side effects.² These authors found considerable variability in reported reasons for use and, among other factors, attributed this variability to heterogeneous study methodologies. Nevertheless, they noted that the most frequently cited reason for use was alleviation of dysphoric symptoms, and they argue that this supports the self-medication hypothesis.² In a more recent review of the self-report literature, it was suggested that psychotic patients use cannabis for its intoxicant effect – as do the general population – and to reduce negative symptoms such as dysphoria.¹² Importantly however, studies on self-reported reasons for cannabis use in EOP and other mental illness in youth are lacking.

Thus we need to clarify whether substance use varies in its patterns of use and impact in adolescents with psychotic and non-psychotic mental disorders. This has implications for policies and planning of appropriate early interventions in this vulnerable population. The findings of this study are important as if we address early cannabis use and the associated risk factors in early intervention programs we may potentially be able to delay disease onset or outcome.

Aim

With these issues in mind, we set out to compare the specificity of socio-demographic and cannabis use presentations between adolescents with first-episode early onset psychosis (EOP) and a control group of adolescents with a first episode of non-psychotic mental illness. The rationale for comparing psychotic youth to non-psychotic youth was to establish the specificity of the pattern and influence of these factors on EOP presentation compared to other mental illness.

Method

Study site and population

We conducted a cross-sectional study in a clinical population of adolescents aged 10-18 years with EOP at four public hospital psychiatric units (including the only two adolescent in-patient units) in KwaZulu-Natal, South Africa. A control group matched for age and gender with first episode non-psychotic mental illness were recruited from the same services. This method has been used in previous studies to assess specificity of findings in psychosis compared to non-psychotic illness.¹¹ Consecutive patients meeting inclusion criteria and consented were recruited to the study between March 2013 and May 2015 and all participants and their caregivers provided written informed assent and consent respectively. The study received ethical approval from the biomedical research ethics committee of the University of KwaZulu-Natal.

Patients with autistic spectrum disorders, intellectual disability, concurrent substance use other than cannabis in the month prior to admission, or significant medical conditions that may have contributed to the mental illness (such as epilepsy or HIV) were excluded in both

EOP and control groups. Adolescents with a primary diagnosis of substance induced- mood or psychotic disorder were excluded.

Assessment instruments

All assessments and ratings were conducted by three clinically experienced psychiatrists (SP, SK and KJ) trained in administration of the instruments. Inter-rater reliability was satisfactory (Cronbach alpha values: $r = 0.88$; $r = 0.91$ and $r = 0.86$). A full clinical assessment comprising a participant and caregiver interview was carried out to allocate a DSM-IV TR clinical diagnosis and obtain socio-demographic information.¹³ The World Health Organization (WHO) Alcohol, Smoking and Substance Involvement Screening test (ASSIST v 3.0) was administered to evaluate substance use.

Definitions

Early onset psychosis (EOP) was defined as onset of psychosis before or at age 18 years.

Substance use was recorded as *lifetime history of specific substance use* if subject ever used substance.

Cannabis use (CU) was recorded as *lifetime history of cannabis use (LCU)* if subject ever used cannabis.

Current cannabis use (CCU) was recorded as use in the 3 months prior to first presentation for treatment.

WHO ASSIST Specific Substance Involvement Score is a measure of use and problems in the past 3 months prior to presentation for that specific substance as per the ASSIST tool. A score of 0-3 (0-10 for alcohol) for a substance indicates low risk, 4-26 (11-26 for alcohol) indicates moderate risk of harmful or hazardous use of a substance, and scores greater than 27 indicate a high risk of substance dependence.

WHO ASSIST Total Substance Involvement Score is the total score for all substances.

Statistical analysis

The data was analysed using the Stata 13.0 (Statacorp. 2013 Stata Statistical Software: Release 13. College Station, TX: Statacorp LP) Lins concordance coefficient and 95% Bland and Altman's limits-of-agreement were used for inter-rater agreement. Means (standard deviations), median (Inter Quintile Range (IQR)), and range were calculated. The student's t-test was used to compare mean age by gender. Associations between categorical variables were tested using Pearson Chi-squared (χ^2) tests. If an expected cell count was fewer than 5 observations, then the Fishers exact test was used instead. A p-value of <0.05 was deemed statistically significant.

Results

Socio-demographic and diagnostic characteristics of the sample

Forty-five adolescents with first-episode early onset psychosis (EOP) and 45 controls matched for age and gender with first-episode mental illness other than psychosis were recruited consecutively in this study. Five EOP patients meeting criteria did not consent and nine non-psychotic youth refused to consent. There were no differences between groups in terms of gender, age and educational attainment. However, EOP adolescents were predominantly of Black ethnicity ($p < 0.001$). Adolescents with non-psychotic mental disorders were more likely to live in urban areas ($p < 0.001$). The socio-demographic characteristics for the adolescents with EOP and the adolescents with other mental illness are presented in Table 1.

Thirty-eight (84%) adolescents with EOP were diagnosed with schizophrenia spectrum psychotic disorder and 7 (16%) with an affective psychotic disorder.

Diagnoses in the adolescents with non-psychotic disorders were: major depressive disorder ($n=25$, 55%); ADHD ($n=8$, 17%); disruptive behavioural disorders (conduct disorder and oppositional defiant disorder) ($n=6$, 13%); conversion disorder ($n=2$, 4%); bipolar mood disorder ($n=1$, 2%); trichotillomania ($n=1$, 2%); adjustment disorder ($n=1$, 2%); and post-traumatic stress disorder ($n=1$, 2%).

Cannabis and other substance-use patterns

Adolescents with EOP were significantly more likely to have current cannabis use (37.8% versus 15.6%, $p = 0.017$) and, while not significant, they were more likely to have a history of lifetime cannabis use (55.56% versus 35.56%). EOP adolescents were also significantly more likely to have a strong urge or desire to use cannabis, to have tried to cut down on cannabis use and failed, to have a higher ASSIST Specific Substance Involvement Score for cannabis, and to be at high risk of cannabis dependence (15.6% versus 0%). In terms of alcohol use, EOP adolescents were more likely to have related health, social, legal or financial problems, and were less likely to have low risk use as defined by the ASSIST. Adolescents with EOP also had higher ASSIST Specific Substance Involvement Scores for cocaine, amphetamines, inhalants, sedatives, hallucinogens, opioids and other drugs. The substance use patterns among adolescents with EOP and those with other mental illness are described for each substance in Table 2.

Socio-demographics of lifetime cannabis users (LCU)

Cannabis was the most commonly used illicit substance by psychotic and non-psychotic mentally ill adolescents (LCU prevalence 55.6% and 35.6% respectively). The impact of cannabis use on clinical characteristics of EOP is described in a separate publication.¹⁴ The socio-demographic variables for the adolescents with LCU with and without psychosis are presented in Table 3. In comparison with controls, EOP adolescents with LCU were more likely to be male and were less likely to live in an urban area. They were less likely to have a first-degree relative with a non-psychotic mental illness though not statistically significant.

Patterns of cannabis use

The patterns of cannabis use in the mentally ill adolescents with and without psychosis are compared in Table 4. EOP adolescents with LCU were more likely to report their main reason for using cannabis as being for its intoxicant effect, while non-psychotic adolescents were more likely to give depression as the main reason for their cannabis use.

Discussion

In this study we compared socio-demographic and substance use patterns, as well as patterns of cannabis use, in psychotic and non-psychotic mentally ill adolescents at disease onset. A number of our findings have particular public health relevance to the prevention and management of comorbid substance use in adolescents with mental disorders in our context. Firstly, the differences between the EOP and control groups is significant in that these differences likely relate to disparities in access to mental health care for certain youth (see discussion below). Secondly, although LCU prevalence did not differ significantly between groups, use in adolescents with EOP was more frequent, more likely to be of high risk, use preceded onset of symptoms and was for different reasons compared with use in non-psychotic adolescents. This possibly suggests differential susceptibility to the effects of cannabis in psychotic youth compared to other mentally ill adolescents.

Disparities in mental health care access

This study reported some important differences in the socio-demographic profile of EOP and other mentally ill adolescents, which we believe reflect disparities in access to mental health services for the latter group of adolescents. While the profile of EOP adolescents closely mirrors the general population demographics and is consistent with the literature,^{9,15} youth of Black ethnicity, rural residence, and low socioeconomic status were under-represented in the control group of non-psychotic adolescents.

Whilst risk factors related to socioeconomic status and ethnicities are associated with the development of psychosis,¹⁶ and may in part account for some demographic characteristics of the EOP group, one has to consider alternative explanations.

Other explanations include potential socio-cultural influences on accessing mental health care such as parental educational differences, lack of awareness of mental health or facilities, stigma and use of alternative health services such as traditional healers.¹⁷

In addition, the demographic profile of the non-psychotic sample may to reflect persistent inequalities in access to mental health care services for adolescents with common and other non-psychotic mental disorders. Specifically, we contend that within our poorly resourced context, Black youth, youth from rural areas, and those from low socio-economic backgrounds have difficulty accessing mental health care unless they are severely ill with psychosis. This is supported by literature reporting the inequalities in mental health care in developing countries with only 15-30% of children and adolescents who require treatment receiving care.^{17, 18} This is also consistent with our clinical experience within these services.

Cannabis and other substance use

Alcohol and nicotine were the most commonly used substances by all mentally ill adolescents, while cannabis was the most commonly used illicit substance. Lifetime prevalence rates of alcohol, nicotine and cannabis use in this study were high compared to an adolescent in-patient study in Israel,¹ but comparable with previous adult^{19,20} and local adolescent studies.⁹ Different definitions of substance use are likely to account for significant variability in substance use prevalence rates in the literature.² The prevalence of current cannabis use was higher in adolescents with EOP and more common in males as has been reported previously.²¹ Lifetime prevalence rates of other illicit substances were low and did not differ between groups. This may be due to socio-cultural and geographical differences in patterns of use. It may also be due to exclusion of current use in past month of substances other than cannabis as the study aimed to assess cannabis impact on presentation. Psychotic youth were however more likely to have problematic use of other substance related problems and this is consistent with adult literature.^{2, 22}

There were significant differences in current use and patterns of cannabis use between adolescents with and without psychosis. Adolescents with EOP had more intense and regular cannabis use (Table 4), a stronger urge to use cannabis and had greater problematic use (Table 2) compared to other mentally ill adolescents. This is consistent with the literature that individuals with psychosis appear to be more vulnerable to the effects of cannabis.²³ Possible reasons for this include genetic susceptibility to cannabis use among individuals with a psychosis vulnerability; increased neurobiological vulnerability to effects of cannabis in adolescent onset psychosis and gender dependent differences in cannabis vulnerability in adolescents.²⁴⁻²⁶ This is particularly concerning as intensive current cannabis use is significantly associated with a greater negative effect on mental health than past use. In addition, the impact of cannabis on mental health increases with increasing intensity of use.²⁷ Early and regular cannabis use is also associated with negative effects on psychopathology and psychosocial functioning.⁸ Thus the more frequent and hazardous use of cannabis by adolescents with EOP suggests a poorer outcome for not only the psychotic disorder,²⁸ but for mental health generally.

The main reasons reported for cannabis use in the current study was markedly different among psychotic and non-psychotic adolescents. The main reason for cannabis use by non-psychotic adolescents was depression and cannabis use was initiated after symptom onset. This reinforces the need for earlier screening and intervention for adolescent mental health problems to prevent progression to substance use. The reason for cannabis use may have been confounded by the selection of a heterogeneous group of psychiatric disorders as controls. In contrast, the finding that EOP adolescents mainly used cannabis for its intoxicant effect and the majority of EOP adolescents initiated cannabis before the onset of positive psychotic symptoms is not in keeping with the self-medication hypothesis. The findings of this study support the suggestion that there are multiple risk factors for substance use in adolescents with EOP including socio-demographic factors such as gender, living environment, socio-economic status and family history.^{2,12, 29} This multifactorial causation hypothesis of substance use in psychosis is supported in this study as EOP adolescents with LCU were predominantly male, from urban areas and had marginally higher family income

than other mentally ill adolescents with LCU. Understanding when, why and who is at risk of cannabis use among mentally ill adolescents is critical to planning appropriate intervention programs.

In this study there were no significant associations between cannabis use and family history of mental illness or a family history of psychosis in first degree relatives; however EOP adolescents with LCU were less likely to have a first degree relative with a non-psychotic mental illness. This is not in keeping with the literature that proposes that individuals with a genetic vulnerability to psychosis are more susceptible to cannabis use,^{11,30} but the finding is supported by the Edinburgh High Risk study that also reported no association between family history of mental illness and cannabis use.³¹ However this requires further study due to the small sample size.

Finally it is also important to note that only one-third (36.5 %) of the adolescents with LCU reported receiving information on substance prevention from their clinic (table 4). The primary health care clinic serves as the first point of health care contact. The study findings suggest that busy and under-resourced clinics may not be detecting and managing substance use in adolescents. The lack of substance use counseling at clinics in this study reinforces the need for an integrated youth friendly service offering comprehensive mental health and substance use treatment at primary health care level to address the inequalities in mental health care. Whilst this may be challenging it could be addressed by training community lay counselors and primary health care nurses and reviewing our resource allocations to primary health care facilities.

Limitations of study

There were several limitations in this study. Whilst incident EOP is relatively rare, our sample size of 45 adolescents is small and limited the power of the analyses to detect potential associations between variables. In addition, this study relied on self-reporting of substance use and family history of mental illness by the caregiver and patient, which may not always be accurate.

This study is based on a clinical hospital based sample and this could present an issue of selection bias. However we recruited from four different mental health care units serving a large part of the province, and in addition, two adolescent in-patient psychiatric units in KwaZulu-Natal that receive all the admissions were included in the study, thus the sample may be considered a fair representation of the clinical population attending state sector mental health services. Importantly, socio-demographic profile and substance use patterns may vary in the private health sector. The clinical sample also limits generalisability and large epidemiological studies are still needed.

The exclusion of substance induced psychotic disorder, neurodevelopmental disorders and significant medical illness may be considered a strength of this study as this strategy ensured a homogenous sample of 'functional' EOP. The exclusion of individuals with substance induced-psychosis and substance use other than cannabis in the month prior to presentation may also have under-reported the prevalence of substance use in mentally ill adolescents.

Conclusion

The disparity in access to mental health care for Black youth from rural and low socio-economic backgrounds is a major public health concern. Strategies to improve access to care via the integrated primary health care system, education system and traditional healers in the communities need to be urgently addressed. The significantly increased frequency, different motivation for use and more problematic use of cannabis by adolescents with EOP suggest that adolescents with psychosis are more vulnerable to cannabis related problems than adolescents with other mental illness. Thus adolescents with EOP and cannabis use are more likely to require management of both the psychosis and substance use and hence a need for integrated mental health care and substance use treatment centers to address the current deficits in care.

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References

1. Lev-Ran S, Aviram A, Braw Y, Nitzan U, Ratzoni G, Fening S. Clinical correlates of cannabis use among adolescent psychiatric inpatients. *European Psychiatry*. 2012; 27:470–475. [PubMed: 22512931]
2. Gregg L, Barrowclough C, Haddock G. Reasons for increased substance use in psychosis. *Clinical Psychology Review*. 2007; 27:494–510. [PubMed: 17240501]
3. Scourfield J, Stevens DE, Merikangas KR. Substance abuse, comorbidity, and sensation seeking; gender differences. *Comprehensive Psychiatry*. 1996; 37(6):384–392. [PubMed: 8932962]
4. Hollen V, Ortiz G. Mental Health and substance use comorbidity among adolescents in psychiatric in-patient hospitals: prevalence and covariates. *Journal of Child and Adolescent Substance Abuse*. 2015; 24:102–112.
5. Storr CL, Pacek LR, Martins SS. Substance use disorders and Adolescent Psychopathology. *Public Health Reviews*. 2012; 34
6. Hsiao R, McClellan J. Substance abuse in early onset psychotic disorders. *Journal of Dual Diagnosis*. 2008; 4(1):87–99.
7. Sadiachha S, Sur S, Sinha BNP, Khess CRJ. How is substance use linked to psychosis? A study of the course and patterns of substance dependence in psychosis. *Substance Abuse*. 2010; 31:58–67. [PubMed: 20391271]
8. Rey JM, Martin A, Krabman P. Is the Party over? Cannabis and juvenile psychiatric disorder: the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2004; 43(10): 1194–1205. [PubMed: 15381886]
9. Lachman A, Nassen R, Hawkrigde S, Emsley RA. A retrospective chart review of the clinical and psychosocial profile of psychotic adolescents with co-morbid substance use disorders presenting to acute adolescent psychiatric services at Tygerburg hospital. *South African Journal of Psychiatry*. 2012; 18(2):53–60.
10. Paruk S, Burns JK, Caplan R. Cannabis use and family history of mental illness in adolescent first episode psychosis in Durban, South Africa. *Journal of Child and Adolescent Mental Health*. 2013; 25(1):61–68. [PubMed: 25860308]
11. Estrada G, Fatjo-Vilas M, Munoz MJ, et al. Cannabis use and age at onset of psychosis: further evidence of interaction with COMT Val158Met polymorphism. *Acta Psychiatrica Scandinavica*. 2011; 123(6):485–492. [PubMed: 21231925]

12. Kolliakou A, Joseph C, Ismail K, Atakan Z, Murray RM. Why do patients with psychosis use cannabis and are they ready to change their use? *International Journal of Developmental Neuroscience*. 2011; 29:335–346. [PubMed: 21172414]
13. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4. Washington DC: American Psychiatric Association Press; 1994.
14. Paruk S, Jhazbhay K, Singh K, Sartorius B, Burns JK. Dynamics of cannabis use and its impact on early onset first episode psychosis. in press.
15. Castro Fornieles J, Parellada M, Gonzalez-Pinto A, et al. CAFEPS group. The child and adolescent first episode psychosis study (CAFEPS): design and baseline results. *Schizophrenia Research*. 2007; 91:226–237. [PubMed: 17267179]
16. Brown AS. The environment and susceptibility to schizophrenia. *Progress in Neurobiology*. 2011; 93:23–58. [PubMed: 20955757]
17. Ngui EM, KhasaKhala L, Ndeti D, Roberts LW. Mental disorders, health inequalities and ethics: A global perspective. *Int Rev Psychiatry*. 2010; 22(3):235–244. [PubMed: 20528652]
18. World Health Organisation/WONCA. Integrating mental health into primary care: a global perspective. Geneva: World Health Organisation and World Organisation of Family Doctors (WONCA); 2008. Available from apps.who.int/iris/bitstream/10665/43935/1/9789241563680_eng.pdf
19. Sevy S, Robinson DG, Solloway S, et al. Correlates of substance misuse in patients with first episode schizophrenia and schizoaffective disorder. *Acta Psychiatrica Scandinavica*. 2001; 104:367–374. [PubMed: 11722318]
20. Lambert M, Conus P, Lubman DJ, et al. The impact of substance use disorders on clinical outcome in 643 patients with first episode psychosis. *Acta Psychiatrica Scandinavica*. 2005; 112(2):141–148. [PubMed: 15992396]
21. Barnett JH, Werners U, Secher SM, et al. Substance use in a population-based clinic sample of people with first episode psychosis. *British Journal of Psychiatry*. 2007; 190:515. [PubMed: 17541112]
22. Reigier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and drug abuse. Results from the Epidemiologic Catchment Area (ECA) study *JAMA*. 1990; 64(19):2511–2518.
23. Parukh P, Basu D. Cannabis and psychosis: have we found the missing links? *Asian Journal of Psychiatry*. 2013; 6:281–287. [PubMed: 23810133]
24. Agrawal A, Lynskey MT. Candidate genes for cannabis use disorders: findings, challenges and directions. *Addiction*. 2009; 104:518–532. [PubMed: 19335651]
25. James, A., James, C., Thomas, T. The brain effects of cannabis in healthy adolescents and in adolescents with schizophrenia: a systematic review. *Psychiatry Research: Neuroimaging*. 2013. <http://dx.doi.org/10.1016/j.psychres.2013.07.012>
26. McQueeney T, Padula CB, Price J, et al. Gender effects on amygdala morphometry in adolescent marijuana users. *Behav. Brain Res*. 2011; 224(1):128–134.
27. Van Ours JC, Williams J. Cannabis use and mental health problems. *Journal of Applied Econometrics*. 2011; 26:1137–1156.
28. Drake RE, Wallach MA. Substance use among the chronic mentally ill. *Hospital and Community Psychiatry*. 1989; 40:1041–1046. [PubMed: 2807205]
29. Atakan Z. Cannabis use by people with severe mental illness- is it important? *Advances in Psychiatric Treatment*. 2008; 14:423–431. DOI: 10.1192/apt.bp.105.002006
30. McGuire PK, Jones P, Harvey I, William SM, McGuffin P, Murray RM. Morbid risk of schizophrenia for relatives of patients with cannabis associated psychosis. *Schizophrenia Research*. 1995; 15(3):277–281. [PubMed: 7632625]
31. Miller P, Lawrie SM, Hodges A, Clafferty R, Cosway R, Johnstone EC. Genetic liability, illicit drug use, life stress and psychotic symptoms: preliminary findings from the Edinburgh study of people at high risk for schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*. 2001; 36:338–342. [PubMed: 11606002]

Table 1
Patients and controls by socio-demographic characteristics

Socio- demographic variables	EOP n=45 n (%)	Non psychotic controls n=45 N (%)	p- value
Age (years, SD)			
Mean	15.9 (1.8)	15.3 (1.9)	0.126
Median (IQR)	16 (15-17)	15 (14-17)	0.216
Male Gender	31 (69%)	29 (64%)	0.655
Ethnicity			
Black	33 (73.33)	11 (24.44)	<0.001
Other	12 (36.66%)	34 (75.66)	
Family Income (ZAR per month)			
< R1500	13 (28.89)	8 (17.78)	0.417
R1500- R4000	16 (35.56)	15 (33.33)	
> R4000	16 (35.56)	21 (46.67)	
Education			
Mean grade achieved (SD)	9 (2.2)	9 (2.2)	0.876
From urban area	25 (55.56)	44 (97.78)	<0.001
From rural area	20 (44.44)	1 (2.22)	
Consulted a traditional healer	22 (48.89)	16 (35.56)	0.420
Referral source			
Self	2 (4.44)	1 (2.22)	0.009
Family	24 (57.78)	20 (44.44)	
Clinic/hospital service	10 (22.22)	8 (17.78)	
School	3 (6.67)	11 (24.44)	
Other	6 (13.33)	5 (11.11)	
Primary caregiver:			
Parents	19 (42.22)	16 (35.56)	0.003
single parent	13 (28.89)	12 (26.67)	
Other	13 (28.89)	17 (37.78)	
History of child abuse	7 (15.56)	11 (25)	0.302
Substance use			
nicotine	22 (50.00)	29 (64.44)	0.202
alcohol	29 (64.44)	29 (64.44)	1.000
cannabis	25 (55.56)	16 (35.56)	0.090

Table 2
Substance use patterns in adolescents with EOP and other mental illness

	EOP n=45	Other mentally ill adolescents n=45	p- value
	n (%)	n (%)	
Lifetime use			
Nicotine	22 (48.9%)	29 (64.4%)	0.202
Alcohol	29 (64.4%)	29 (64.4%)	1.000
Cannabis	25 (55.6%)	16 (35.6%)	0.090
Cocaine	4 (8.9%)	4 (8.9%)	1.000
Amphetamines	6 (13.3%)	3 (6.7%)	0.315
Inhalants	5 (11.1%)	2 (4.4%)	0.434
Sedatives	5 (11.1%)	8 (17.8%)	0.550
Hallucinogens	2 (4.4%)	2 (4.4%)	1.000
Opioids	5 (11.1%)	3 (6.7%)	0.714
Current use			
Nicotine	18 (40%)	17 (37.8%)	0.829
Alcohol	15 (33.3%)	12 (26.7%)	0.490
Cannabis	17 (37.8%)	7 (15.6%)	0.017
Cocaine	2 (4.4%)	0 (0)	0.494
Amphetamines	2 (4.4%)	1 (2.2%)	1.000
Inhalants	1 (2.2%)	0 (0)	1.000
Sedatives	3 (6.7%)	3 (6.7%)	1.000
Hallucinogens	0 (0)	1 (2.2%)	1.000
Opioids	1 (2.2%)	1 (2.2%)	1.000
*Strong urge or desire to use substance			
Nicotine	16 (35.6%)	8 (17.8%)	0.094
Alcohol	5 (11.1%)	1 (2.2%)	0.203
Cannabis	12 (26.7%)	2 (4.4%)	0.004
*Frequency of health, social, legal or financial problems			
Nicotine	6 (13.3%)	3 (6.7%)	0.485
Alcohol	12 (26.7%)	1 (2.2%)	0.001
Cannabis	0 (0)	0 (0)	
*Tried to cut down and failed			
Nicotine	5 (11.1%)	5 (11.1%)	1.000
Alcohol	3 (6.7%)	0 (0)	0.242
Cannabis	11 (24.4%)	1 (2.2%)	0.004
*ASSIST specific substance involvement Score (mean, SD)			
Nicotine	8.24 (10.35)	6.16 (8.08)	0.719

	EOP n=45	Other mentally ill adolescents n=45	p- value
	n (%)	n (%)	
Alcohol	5.18 (6.07)	2.89 (3.08)	0.072
Cannabis	10.2 (13.56)	2.27 (4.84)	0.004
Cocaine	2.02 (0.26)	0.13 (0.63)	<0.001
Amphetamines	2.07 (0.5)	0.53 (3.58)	<0.001
Inhalants	1.93 (0.45)	0 (0)	<0.001
Sedatives	2.44 (2.35)	0.98 (3.41)	<0.001
Hallucinogens	2.0 (0.0)	0.09 (0.6)	<0.001
Opioids	1.98 (0.26)	0.84 (5.66)	<0.001
Other	1.89 (0.44)	0 (0)	<0.001
ASSIST Alcohol involvement score			
0-11	32 (71.1%)	40 (88.9%)	0.035
12-26	12 (26.7%)	5 (11.1%)	0.059
>than 26	1 (2.2)	0 (0%)	1.000
ASIST Nicotine involvement score			
0-3	32 (71.1%)	37 (82.2%)	0.213
4-26	11 (24.4%)	6 (13.3%)	0.178
>26	2 (4.4%)	2 (4.4%)	1.000
ASSIST Cannabis involvement score			
0-3	28 (62.2%)	41 (91.1%)	0.001
4-26	10 (22.2%)	4 (8.9%)	0.081
>26	7 (15.6%)	0 (0%)	0.012

Table 3
Socio-demographic characteristics of lifetime cannabis users

	EOP with cannabis use n=25 Mean (%)	Non psychotic controls with cannabis use n= 16 Mean (%)	p-value
Mean age at presentation (years, SD)	16.28 (1.86)	15.69 (1.62)	0.848
Gender			
Male	24 (96%)	8 (50%)	0.001
Female	1 (4%)	8 (50%)	
Ethnicity			
Black	2 (8%)	4 (25%)	0.008
Other	23 (92%)	12 (75%)	
Mean Educational level (SD)	9.29 (2.27)	9.63 (1.63)	0.308
Family income (ZAR/month)			
< R1500	4 (16%)	2 (12.5%)	0.764
R1500- R4000	8 (32%)	5 (31.3%)	
> R4000	13 (52%)	8 (50%)	
Family history of any mental illness	4 (16.0%)	6 (37.5%)	0.316
Family history of psychosis	7 (24%)	3 (18.8%)	0.712
Family history of non- psychotic illness	2 (8%)	8 (50%)	0.007
Child abuse	4 (16.0%)	6 (37.5%)	0.150
Urban residence	18 (72.0%)	16 (100%)	0.031

Table 4
Cannabis use patterns in FEP and other mentally ill adolescents

	FEP with lifetime cannabis use n=25 n (%)	Other mental illness with lifetime cannabis use n=16 n (%)	Significance
Current cannabis use	17 (68%)	7 (43.8%)	0.124
Frequency of use			
Daily	12	2	0.047
Weekly	3	0	
once a month	1	2	
once in past 3 months	1	3	
Mean Age of first cannabis use (years, SD)	13.96 (2.01)	14.2 (1.42)	0.733
Number of joints used/week			
1-3	4	5	0.043
4-6	3	0	
>6	10	2	
First use of cannabis:			
before symptom onset	22 (88%)	4 (25%)	<0.001
after symptom onset	1(4%)	8 (50%)	
Other substance use			
Nicotine	18 (72%)	10 (62.5%)	0.524
Alcohol	15 (60%)	9 (56.3%)	0.812
Main Reason for use			
Intoxicant effect	10 (40%)	1 (6.3%)	0.017
Depression	3 (12%)	7 (43.8%)	0.030
Psychosis	2 (8%)	0 (0)	0.512
Peer pressure	9 (36%)	6 (37.5%)	0.923
Other	1 (4%)	1 (6.3%)	1.000
Substance prevention			
Parents	19 (17%)	12 (75%)	1.000
School	24 (96%)	16 (100%)	1.000
Television	16 (96%)	12 (75%)	0.513
Religious	10 (40%)	11 (68.8%)	0.111
Hospital	21 (84%)	11 (68.8%)	0.276
Clinics	9 (36%)	6 (37.5%)	1.000