Cannabis and Psychosis

Madhavan Seshadri, Mark Agius, Anton Grech, Stanley Zammit

Madhavan Seshadri*
ST4 registrar in Psychiatry, SEPT: South Essex Partnership University NHS Foundation Trust.
Mark Agius, SEPT: South Essex Partnership University NHS Foundation Trust and
Academic Department of Psychiatry, University of Cambridge.
Anton Grech, Victoria Hospital, Gozo.
Stanley Zammit, Department of Psychological Medicine, School of Medicine,
Cardiff University.

Keywords: cannabis, psychosis, psychotic illness, schizophrenia

* Corresponding author

Abstract

Several studies have established a link between cannabis and psychosis. However the causal role of cannabis in schizophrenia is still not clear. The aim of this paper is to summarise the literature pertaining to whether cannabis causes psychosis, whether the continued use of cannabis by patients with schizophrenia affects the course of the disease and its treatment, and whether it is possible to reduce cannabis use in patients who have a psychotic disorder.

Introduction

Cannabis is the most commonly used illicit drug in the world, the main age group misusing cannabis being 15-34 years of age. 75.5 million Europeans use cannabis at least once in their lifetime, and an estimated 23 million Europeans have used cannabis last year. Population survey data suggest that, on average, 31.6 % of young European adults (15–34 years) have ever used cannabis in their lifetime, while 12.6 % have used the drug in the last year. The data from the 2007 European School Survey project on alcohol and other drugs (ESPAD) and 2008 national school surveys reveal that the lifetime prevalence of cannabis use among 15 to 16-year-old school students in the United Kingdom ranged from 26 % to 32 % (1).

Although there are more than 400 constituents in cannabis, Δ9THC is the main psychoactive cannabinoid. The home office cannabis potency study in 2008 showed that over the past decade the concentration of Δ9THC in cannabis has increased, particularly with increasing use of intensively-grown cannabis (Skunk) (2).

Association between cannabis misuse and psychosis

Various studies have shown that psychotic disorders are more common in patients who are dependent on cannabis or misuse cannabis significantly, compared to the general population. In a case-control study in the Netherlands, patients with first episode schizophrenia (59%) were found to misuse cannabis significantly more often compared to their siblings (21%) and general hospital controls (21%)(3). A number of epidemiological studies including the US National Epidemiological Catchment Area (ECA) study, the Australian National Survey of Mental Health and Well-Being (NSMHWB), and the Netherlands Mental Health Survey and Incidence Study (NEMESIS) all reported that psychotic disorders, including schizophrenia, were more common in individuals who used cannabis or were dependent on this drug, compared to non-users (4).

A causal relationship between cannabis use and psychosis could be manifest in the form of any of the following clinical presentations:

a) Intoxication with cannabis (with or without presence of confusion) leading to psychotic symptoms that remit once exogenous cannabinoids are eliminated from the body.

b) Acute and transient psychotic disorder following cannabis use, where symptoms persist beyond a period reasonably attributable to the effects of exogenous cannabinoids.

c) Chronic psychosis, which persists after abstinence from cannabis.

Persistent cannabis misuse may be a risk-factor for serious mental illness such as schizophrenia or other chronic psychoses (5). The relationship between cannabis and persisting psychosis (b and c above) has been the focus of much study in recent years. Cannabis use has been consistently associated with increased incidence of psychosis, but it is very difficult to be certain that cannabis is a causative factor for schizophrenia. The association between cannabis and psychosis could also be due to bias, confounding, or reverse causality.

In this paper the authors addressed three questions.

1) Does cannabis cause schizophrenia or other psychoses?

2) Does the continued use of cannabis by patients with schizophrenia affect the course of the disease and its treatment?

3) What interventions can reduce cannabis use in patients who have a psychotic disorder?

Does cannabis cause schizophrenia or other psychoses?

There has been much debate as to whether cannabis use increases the risk of developing chronic psychotic disorders such as schizophrenia. Andreasson & Allebeck (6) carried out a 15-year follow-up of 50087 Swedish conscripts who had self-reported on their cannabis use at age 18. They found that those who tried cannabis by age 18 years were 2.4 times more likely to develop schizophrenia than those who had not. The risk of developing schizophrenia was related in a dose–response way to the number of times cannabis had been used. Although they concluded that these findings supported a causal relationship between cannabis and schizophrenia, attention was drawn to a number of limitations in this study, relating to the possible effects of confounding by other drug misuse or personality traits of the individuals who used cannabis. To address these limitations, a follow-up study of the same cohort was conducted with an extended 27-year follow-up period that covered most of the risk period for the onset of psychotic disorders. The authors still concluded that cannabis use at baseline predicted an increased risk of schizophrenia during the follow-up period in a dose–response manner. This relationship persisted after controlling for the effects of other drug use and other potential confounding factors, and remained after excluding cases occurring within 5-years of conscription, indicating that the association was very unlikely to have been due to 'self-medication', i.e. use of cannabis after onset of schizophrenia (7,8).

The Dunedin birth cohort study (9) followed-up a general-population birth cohort of 1037 individuals born in Dunedin, New Zealand, in 1972-1973. Self-reports of cannabis use were obtained at ages 15 and 18, and information was also obtained on self-reported psychotic symptoms at age 11, before the onset of cannabis use. At age 26 the cohort members were reassessed. Cannabis use by age 15 was associated with an increased likelihood of meeting diagnostic criteria for schizophreniform disorder at age 26, with 10.3% meeting criteria compared to 3% for non-users. After controlling for age-11 psychotic symptoms, the risk for adult schizophreniform disorder remained elevated, although it was attenuated.

In the NEMESIS study (10), 4,045 subjects without any symptoms of psychosis at baseline were followed up at 1 year and 3 years. There was a dose response relationship between cannabis use at baseline and development of a psychotic disorder at follow-up, both before (OR for trend across 4 categories of cannabis use = 4.0, 95% CI 2.2, 7.1) and after (adjusted OR = 3.5, 95% CI 1.6, 7.4)

adjustment for other drug use, ethnic group, marital status, educational level, urban living, and discrimination.

In the Early Developmental Stages of Psychopathology (EDSP) study (11), a prospective cohort study conducted in Germany, Keupper et al followed up 1923 individuals aged 14-24 at baseline, from the general population, for a period of 10 years. This was to determine whether use of cannabis in adolescence increases the risk for psychotic outcomes by affecting the incidence and persistence of psychotic symptoms in the general population. In individuals who had no reported lifetime psychotic symptoms and no reported lifetime cannabis use at baseline, cannabis use over the period from baseline to 3.5 years increased the risk of later incident psychotic symptoms over the period from 3.5 – 8.4 years (adjusted odds ratio 1.9, 95% confidence interval 1.1 to 3.1; p=0.021). The incidence of psychotic symptoms over the period from baseline to 3.5 years was 31% in exposed individuals compared with 20% in non-exposed individuals; over the period from 3.5 – 8.4 years, these rates were 14% and 8%, respectively.

Moore et al. (12) carried out a systematic review of cannabis use and risk of psychotic or affective mental health outcomes and attempted to clarify whether cannabis can cause psychotic symptoms that persist beyond transient intoxication. Studies were included if they were longitudinal and population based, and only 7 studies were found that met these criteria. There was an increased risk of any psychotic outcome in individuals who had ever used cannabis (pooled adjusted odds ratio=1·41, 95% CI 1·20–1·65). Findings were consistent with a dose-response effect, with greater risk in people who used cannabis most frequently (2·09, 1·54–2·84). Results of analyses restricted to studies of more clinically relevant psychotic disorders were similar. The authors examined to what extent results from each study could have been due to alternative (non-causal) explanations. A substantial confounding effect was present for both psychotic outcomes, but the authors nevertheless concluded that the evidence that cannabis use increased the risk of psychotic illnesses such as schizophrenia was strong enough that individuals using cannabis should be advised about this risk.

Association between continued use of cannabis by patients with schizophrenia and the course of the disease and its treatment.

The EDSP study (11) also examined the persistence of psychotic symptoms in individuals who used cannabis. Continued use of cannabis increased the risk of persistent psychotic symptoms over the period from 3.5 – 8.4 years (OR 2.2, CI 1.2 to 4.2; p=0.016). The authors concluded that cannabis use is a risk factor for the development of incident psychotic symptoms and continued cannabis use might increase the risk for psychotic disorder by impacting on the persistence of symptoms.

In a study that spanned two different cultural settings, South London and Malta (13), psychotic patients abused substances much more than controls in both centres, although use of cannabis and other substances was much more widespread in the former. An extension of this study within the London sample tested the hypothesis that recent-onset psychotic patients who use cannabis would have psychotic symptoms that were more severe and more persistent than those who did not use cannabis. They carried out a 4-year follow-up study of a cohort of 119 patients with recent onset psychosis. Patients who continued to misuse cannabis had more positive symptoms and suffered from a more continuous illness at follow-up. They concluded that it is possible that psychotic patients who use cannabis are at a greater risk of a more continuous illness with more positive symptoms than those who do not.

Zammit et al. (14) carried out a systematic review of the effects of cannabis use on outcomes of psychotic disorders to examine whether research findings support clinical opinion that cannabis use leads to worse outcomes in people with psychosis, or whether this impression is confounded by other factors. They reviewed 13 studies and examined rehospitalisation, readmission, measures of psychopathological symptoms, measures of treatment response and adherence to treatment as outcomes. Cannabis was consistently associated with increased relapse and rehospitalisation and with decreased treatment adherence in the studies that examined these outcomes, whereas associations with psychotic symptoms and other psychopathology scores were much more inconsistent.

However, it was noted that few studies adjusted for baseline illness severity and most made no adjustment for alcohol or other potentially important confounders. It was therefore difficult to be confident that most of the associations reported were specifically due to cannabis. The authors concluded by suggesting that further research was needed to establish whether cannabis is harmful, what outcomes are particularly affected by cannabis use and how these effects occur. Furthermore, unlike determining whether or not cannabis use increases risk of rare disorders such as schizophrenia, studies that examine questions about the effects of cannabis on the outcome of people with psychosis are very feasible.

In a study that addressed a number of the limitations highlighted in the systematic review above, Foti et al. (15) assessed 229 patients with a schizophrenia spectrum disorder over 10 years of follow-up after first psychiatric hospitalization. These patients were assessed five times: during the first admission and 6 months, 2 years, 4 years, and 10 years later. The aim was to examine the relationship between cannabis use and the course of the illness in schizophrenia. The authors rated cannabis use and psychiatric symptoms (psychotic, negative, disorganized, and depressive) at each assessment. Results showed the lifetime frequency of cannabis use was 66.2%, and survival analysis revealed that lifetime use was associated with an earlier onset of psychosis. Cannabis status was moderately stable, with tetrachoric correlation coefficients between waves ranging from 0.48 to 0.78. Mixed-effects logistic regression revealed that changes in cannabis use were associated with changes in psychotic symptoms over time even after gender, age, socioeconomic status, other drug use, antipsychotic medication use, and other symptoms were controlled for. The association between cannabis use and psychotic symptoms was bidirectional. The authors concluded that cannabis use is associated with an adverse course of psychotic symptoms in schizophrenia, and vice versa, even after taking into account other clinical, substance use, and demographic variables.

Can cannabis use be reduced by psychoeducation in psychotic patients?

Most of the psychosocial interventions for cannabis misuse are based on motivational interviewing, cognitive behavioural therapy and relapse prevention. Maddock and Babbs (16) reviewed these studies and concluded that in adult patients, brief interventions were useful in helping to reduce or stop using cannabis. Agius and colleagues (17, 18) reported on the outcomes of early intervention service working for three years with patients who had suffered a first episode of psychosis. A group of patients in the early intervention (EI) service were compared with a group of patients who were treated by the community mental health teams. Patients in the early intervention group received more structured psycho-education about cannabis use and education in identifying the early warning signs. Patients in the CMHT group received routine care which involved outpatient reviews, treatment with antipsychotic medication and involvement of a care co-ordinator (only if necessary). Many patients in the CMHT group might not have received a systematic psycho-education regarding cannabis misuse. More patients in the EI group than in the CMHT group admitted to using illicit drugs at the beginning of the intervention. Less patients in the EI group than in the CMHT group were using illicit drugs especially cannabis at the end of three years, indicating that significantly more patients stopped using illicit drugs in the EI group than in the CMHT group (P=0.003). This might be because of more effective psychoeducation in the EI group. Given that cannabis use appears to increase relapse, delays the recovery and reduces the effectiveness of treatment for psychosis, interventions that can effectively reduce cannabis use in this group could be very important. Recent NICE guidance on the management of psychosis with coexisting substance misuse emphasizes the importance of psychoeducation and psychosocial interventions in this patient group (19).The psychoeducation provided within the EI group described above is a relatively simple and cheap intervention but it could make a substantial difference to morbidity at a population level if further studies support this as an effective approach to reducing cannabis use in individuals with psychotic disorders.

Conclusion

There is little dispute that cannabis intoxication can cause short-lived psychotic experiences (hallucinations, delusions and periods of thought disorder). Although uncertainty regarding causation is inevitable in the absence of RCTs, epidemiological studies support the belief that cannabis use leads to an increased risk of more severe and prolonged psychotic states. Further work in this area, including neuroimaging and animal model studies, as well as epidemiological studies focusing on the effects of more potent forms of cannabis, are on-going, and although beyond the scope of this review, also support a causal role of cannabis on psychotic outcomes. Current psychosocial interventions for reducing cannabis use should be based on the new NICE guidance relating to the management of psychosis with co-existing substance misuse. Research to enable us to understand the reasons why patients at risk of psychosis use cannabis and why those who have already had an episode of cannabis-associated psychosis continue to use it, could be of particular value. The outcomes of such research might enable the psychosocial management of this complex group of patients to be more focussed and more effective.

GP comment

What have I learned from this paper?

1. Despite the limitations in the research, there seems to be strong evidence that cannabis can increase the risk of developing schizophrenia.

2. The more the cannabis use, the higher the risk of developing schizophrenia seems to be.

3. Continued cannabis risk is associated with an increased risk of relapse and re-hospitalisation.

4. Knowing this information, I would very strongly recommend abstinence to anyone who has had a psychotic episode with cannabis and people at high risk of psychosis e.g. 1st degree relatives of someone with schizophrenia.

Sarah Morris,
GP Flitwick, Bedfordshire.

References

1. Annual report. European monitoring centre for drugs and drug addiction.2010; 44-46.

2. Hardwick S, King L. Home Office Cannabis Potency Study. Home Office. 2008; (http://drugs.homeoffice.gov.uk/publication-search/cannabis/potency).

3. Veling W., Mackenbach J. P., van Os J. & Hoek H. W. Cannabis use and genetic predisposition for schizophrenia: a case-control study. Psychol Med:2008; 38, 1251-6.

4. Hall W. & Degenhardt L. (2000). Cannabis use and psychosis: a review of clinical and epidemiological evidence. Aust N Z J Psychiatry 34, 26-34.

5. Johns A. Psychiatric effects of cannabis. British Journal Psychiatry 2001; 178; 116-122.

6. Andreasson S, Allebeck P, Rydberg U. Cannabis and schizophrenia: a longitudinal study of Swedish conscripts. Lancet.1987; 2:1483–6.

7. Zammit S, Allebeck P, Andreasson S,Lewis G . Self reported cannabis use as a risk factor for schizophrenia in Swedish Conscripts of 1969: historical cohort study. BMJ. 2002;325:1199 -201.

8. Zammit S, Lewis G. Exploring the relationship between cannabis use and psychosis. Addiction. 2004; 99:1353–5.

9. Arseneault L, Cannon M, Poulton R, Murray R, Caspi A. & Moffitt T E. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. BMJ 325,2002; 1212-3

10. Van Os J, Bak M, Bijl R V, et al (2002) Cannabis use and psychosis: a longitudinal population-based study. American Journal of Epidemiology, 156, 319 -327.

11. Kuepper R, Van Os J, Lieb R, Wittchen H-U, Hofler M, Henquet C. Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study; BMJ 2011;342:d738

12. Moore T, Zammit S, Lingford-Hughes A et al;Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review.Lancet. 2007;370: 319 – 328.

13. Grech A, Takei N, Murray RM. Comparison of cannabis use in psychotic patients and controls in London and Malta. Schizophrenia Research.1998; 29: 22.

14. Zammit S, Moore T, Lingford-Hughes A et al. Effects of cannabis use on outcomes of psychotic disorders: A systematic review: The British Journal of Psychiatry. 2008; 193: 357-363

15. Foti DJ, Kotov R, Guey LT, Bromet EJ. Cannabis use and the course of schizophrenia: 10-year follow-up after first hospitalization. Am J Psychiatry. 2010 ;167:987-93.

16. Maddock C and Babbs M. Interventions for cannabis misuse Adv. Psychiatr. Treat. 2006 12: 432-439

17. Agius M, Shah S, Ramkisson R, Murphy S, Zaman R. Three year outcomes of an early intervention for psychosis as compared to treatment as usual for first psychotic episodes in a standard community mental health team. Final results. Psychiatria Danubina. 2007, 19:130-8.

18. Agius M, Shah S, Ramkisson R, Murphy S, Zaman R. Further development of early intervention in psychosis. Early Intervention in Psychiatry. 2008;2:116-7.

19: NICE Guidance: Psychosis with coexisting substance misuse. Assessment and management in adults and young people;March 2011