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Cannabis use and non-clinical dimensions of psychosis in university students presenting to primary care

Skinner R, Conlon L, Gibbons D, McDonald C. Cannabis use and non-clinical dimensions of psychosis in university students presenting to primary care.

Objective: To explore the relationship between cannabis use and self-reported dimensions of psychosis in a population of university students presenting for any reason to primary care.
Method: One thousand and forty-nine students attending the Student Health Unit, National University of Ireland, Galway, completed self-report questionnaires on alcohol and substance misuse, non-clinical dimensions of psychosis [Community Assessment of Psychic Experiences (CAPE)], anxiety and depression [Hospital Anxiety and Depression Scale (HADS)]. Association of cannabis use with psychiatric symptoms was explored whilst controlling for confounds.
Results: More frequent cannabis use was independently associated with greater intensity of positive, negative and depressive psychotic symptoms. The earlier the age of onset of cannabis use, the more positive psychotic symptoms were reported.
Conclusion: These findings support the hypotheses that cannabis use increases the risk of developing psychotic symptoms and that this risk is further increased in those individuals who use cannabis more heavily and commence it at a younger age.

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Key words: cannabis; psychotic symptoms; Community Assessment of Psychic Experiences; age of onset

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Significant outcomes

- Frequent cannabis use is independently associated with higher ratings on non-clinical dimensions of psychosis.
- The earlier the age of first exposure to cannabis the greater the risk of developing positive psychotic symptoms.

Limitations

- Representativeness of sample unknown.
- Psychotic symptoms were self-reported.

Introduction

Cannabis is the most commonly used illicit drug amongst Irish university students, with 45% of men and 32% of women reporting use of this drug in the previous 12 months (1). Widespread cannabis use amongst university populations has also been reported in other European countries and in the United States (2, 3). In recent years, a substantial body of evidence has accumulated to support the hypothesis that cannabis use is a risk factor for the development of positive and negative psychotic symptoms (4, 5). Furthermore, exposure to large amounts of cannabis and exposure early in adolescence is associated with even greater risk for developing psychotic experiences in a dose–response type pattern, providing suggestive evidence of a causal relationship (6–10).

Several community studies have indicated that psychotic symptoms are relatively common

in non-clinical populations, supporting the concept of a continuum of psychosis, from clinical psychotic disorders through to normality (11, 12). Three previous studies have reported a relationship between cannabis use and dimensions of psychosis in non-clinical populations (2, 7, 8). One of these studies examined female undergraduate university students in France and reported that the frequency of cannabis use was independently associated with the intensity of positive and negative psychotic symptoms (2). This study did not assess age of onset of cannabis use and how this related to symptom development.

Aims of the study

The aim of this study was to investigate the relationship between cannabis use (frequency of use and age of first use) and self-report psychotic, anxious and depressive symptoms in a sample of Irish university students. We hypothesised that: i) students who used cannabis more frequently and ii) who started using cannabis at a younger age would be more likely to report higher scores on dimensions of psychosis and affective symptoms.

Material and methods

Subjects

University students presenting for any reason to the Student Health Unit, National University of Ireland Galway, between April and October 2008 were invited to participate in the study by filling anonymous questionnaires whilst awaiting their appointment. The Student Health Unit provides on-campus primary health care for the 15 000 students enrolled in undergraduate and postgraduate courses at the university.

Instruments

Demographic data (gender, age, marital status, ethnicity, year of entry to University, course of study), past history of mental health problems, family history of psychiatric illness and detailed information on use of alcohol (on average how many units of alcohol per week do you drink, on average how many units of alcohol at one sitting do you drink) cannabis and other drugs [age at first use, frequency of use (never, 1–30 times/light use, 30 times or more/heavy use)] were assessed using a self-report questionnaire.

Psychotic experiences were assessed using the Community Assessment of Psychic Experiences (CAPE), a 42-item self-report instrument measuring lifetime psychotic experiences (13). It has a three-factor structure of positive, negative and depressive dimensions. Frequency of lifetime symptoms is measured on a four-point scale, from 'never' to 'nearly always'. Weighted scores were calculated for the positive, negative and depressive dimensions of the CAPE and scores were treated as continuous variables in all analyses.

Participants also completed the Hospital Anxiety and Depression scale (HADS), a 14-item self-report questionnaire measuring symptoms of depression and anxiety which has been used extensively in primary care and non-clinical populations (14).

Analysis

Initially a univariate analysis was performed to identify those explanatory variables that were significantly related to the response variables of interest (CAPE, HADS scores). Explanatory variables were then included in all subsequent ANCOVA models to compare mean response variables to key explanatory variables of interest (freq. of lifetime cannabis use, age of onset of cannabis use), whilst adjusting for those explanatory variables identified as significant. Bonferroni *post hoc* analysis was utilised for further subset comparisons. SPSS version 15 was used for all analyses and the level of statistical significance was set at $P < 0.05$.

Results

One thousand and forty-nine students completed the questionnaires. The mean age of the sample was 21.2 years (range 17–54), and 863 (82%) were female. Participants represented all levels of study, with 168 (16%) in first year, 283 (27%) in second, 292 (27.8%) in third and 297 (28.3%) in fourth year or beyond. Most participants were Irish Caucasian 985 (93.9%) and the majority 1009 (96.2%) were single. One hundred and sixty-nine (16%) participants reported having at one time sought professional help for emotional or psychiatric problems. Two hundred and forty-two (23%) participants reported a family history of mental illness and 49 (4.7%) reported a family history of psychotic disorder (schizophrenia, bipolar disorder, schizoaffective disorder). Participants drank an average of 9.38 units of alcohol per week (range 0–120) and an average of 5.86 units in one sitting (range 0–35).

The rate of lifetime cannabis use (smoked cannabis at least once) was 40% ($n = 423$) with 327 participants reporting light use and 86 report-

ing heavy use of the drug. The mean age of commencing cannabis use was 16.96 years (range 10–40, SD = 2.4). Lifetime use of other drugs was reported as follows; 6.9% ecstasy, 5.8% cocaine, 2.1% lysergic acid diethylamide, 5.1% magic mushrooms and 0.1% heroin.

Of the subjects who had never tried cannabis, a minority only (0.79%) had used the other drugs, either alone or in combination. The mean weighted CAPE frequency scores were 1.29 (range 1–3, SD = 0.24) for positive symptoms, 1.57 (range 1–4, SD = 0.40) for negative symptoms and 1.66 (range 1–3.6, SD = 0.41) for depressive symptoms.

Of those who reported experiencing these symptoms at least 'sometimes', the average distress ratings were1.42 (range 1 = 4, SD = 0.47) for positive symptoms, 1.62 (range 1–3.8, SD = 0.53) for negative symptoms and 1.80 (range 1–4, SD = 0.63) for depressive symptoms.

Mean score for the anxiety subscale of HADS was 6.76 (range 0–19, SD = 3.6). Twenty-one per cent of participants scored between 8 and 10 (borderline abnormal) and 15% scored 11 or above, which is considered an abnormal level of anxiety. The mean score for the depressive subscale of HADS was 2.33 (range 0–18, SD = 2.4), with 2.8% reporting borderline abnormal levels and 1% reporting abnormal levels of depression.

The CAPE positive psychotic symptom scores were significantly related to personal history of mental health problem $F(1,987) = 18.59$, $P < 0.001$, family history of psychiatric disorder $F(1,987) = 4.59$, $P < 0.05$, age $F(1,987) = 5.86$, $P < 0.05$ (younger subjects reporting on average higher levels of symptoms) and gender $F(1,987) = 4.32$, $P < 0.05$ (males having higher scores). CAPE negative psychotic symptom scores were significantly related to personal history of mental health problem $F(1,985) = 30.6$, $P < 0.001$ and family history of psychiatric disorder $F(1,985) = 4.59$, $P < 0.05$ whilst CAPE depressive symptoms were significantly related to personal history of mental health problem $F(1,987) = 69.93$, $P < 0.001$, family history of psychiatric disorder $F(1,987) = 6.72$, $P < 0.05$ and gender $F(1,987) = 16.72$, $P < 0.001$ (females having higher scores than males).

Hospital Anxiety and Depression Scale anxiety scores were significantly related to personal history of mental health problem $F(1,959) = 65.94$, $P < 0.001$, family history of psychiatric disorder $F(1,959) = 9.21$, $P < 0.01$ and gender $F(1,959) = 5.99$, $P < 0.05$ (females having higher scores than males). HADS depressive scores were significantly related to personal history of mental health problem $F(1,958) = 49.33$, $P < 0.001$. After controlling for the effects of personal history of mental health problem, family history of psychiatric disorder, age and gender, the following results were obtained.

There was a significant effect of frequency of cannabis use on positive psychotic symptoms, $F(2,987) = 6.35$, $P < 0.01$, whereby those in the heavy-use group had on average more symptoms than those in the light-use group $P < 0.01$ or those in the never-use group $P < 0.01$, and there was no significant difference between those in the light-use and never-use groups (Fig. 1).

There was a significant effect of frequency of cannabis use on negative psychotic symptoms $F(2,985) = 8.19$, $P < 0.001$, whereby those in the heavy-use group had on average more symptoms than those in the never-use group $P < 0.01$, those in the light-use group had more symptoms than those in the never-use group $P < 0.05$ and there was no significant difference between the heavy-use group and the light-use groups (Fig. 2).

There was a significant effect of frequency of cannabis use on CAPE depressive symptoms $F(2,987) = 3.82$, $P < 0.05$, whereby those in the light-use group had more symptoms than those in the never-use group $P < 0.05$ (Fig. 3). There was no significant effect of frequency of cannabis use on HADS scores.

After controlling for the effects of age, gender, personal history of mental health problems, family history of psychiatric disorder and frequency of cannabis use, there was a significant effect of age at

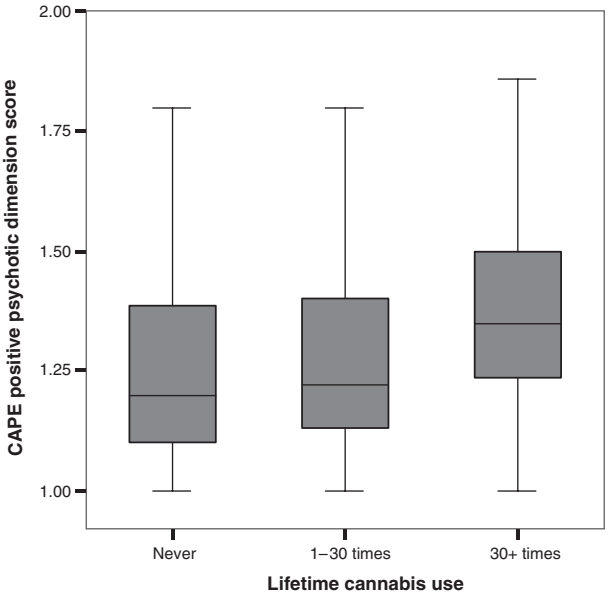

Fig. 1. Frequency of cannabis use and positive psychotic symptoms.

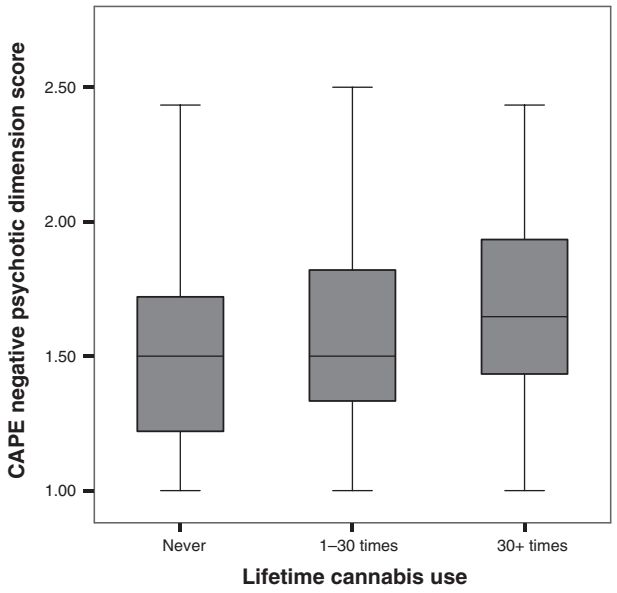

Fig. 2. Frequency of cannabis use and negative psychotic symptoms.

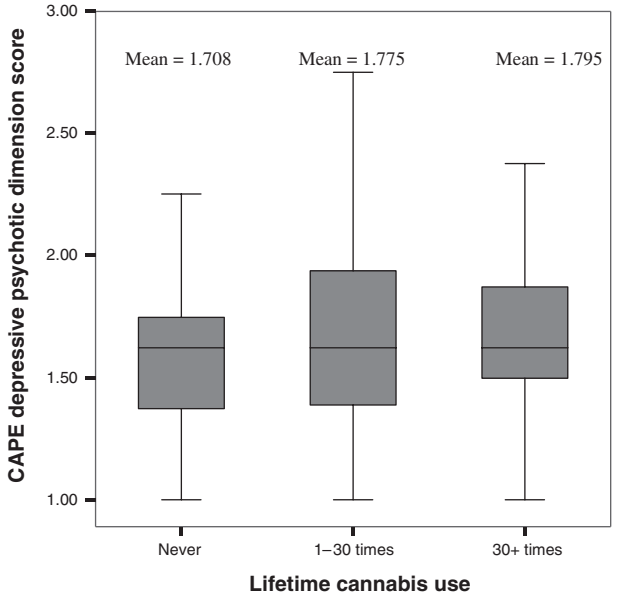

Fig. 3. Frequency of cannabis use and depressive psychotic symptoms.

first cannabis use on positive psychotic symptoms $F(20,327) = 2.24$, $P < 0.01$. Further analysis revealed a significant negative correlation between the two variables, $r = -0.16$, $P < 0.01$, indicating that the younger a person started using cannabis, the more positive psychotic symptoms they reported (Fig. 4). There was no significant effect of age at first cannabis use on other CAPE scores or on HADS scores.

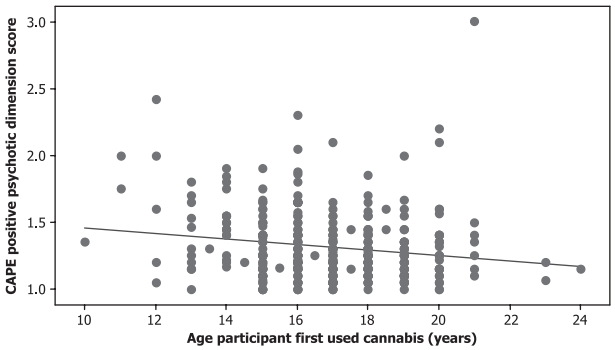

Fig. 4. Age at first cannabis use and positive psychotic symptoms.

Discussion

This study examined illicit drug use and self-reported dimensions of psychosis in a non-clinical population of over 1000 students who presented, for any reason, to a primary healthcare unit of a university and confirmed both our hypotheses. After controlling for confounders, heavy cannabis users reported significantly more experiences than those who had never used cannabis. For positive psychotic symptoms, heavy users reported on average more symptoms than the light users and for negative psychotic symptoms, light users reported on average more symptoms than those who had never used cannabis. These findings are consistent with previous studies of non-clinical populations. Verdoux et al. reported that female university students who had not used cannabis had lower scores on positive and negative dimensions of the CAPE than those in heavy use (more than once a week) and light use (once a month to once a week) groups (2). An Australian study by Hides et al. found that the frequency of cannabis use in the past year was associated with the CAPE's positive symptom scale total score in a community sample of 880 adolescents in Melbourne (15). Stefanis et al. examined a cohort of 3500 representative 19 year olds in Greece, and found that those who had never used cannabis had lower levels of psychotic experiences than those who had used cannabis between two and four times, more than four times or systematically. In addition, use of cannabis was positively associated with both positive and negative psychotic symptoms thereby adding strength to the theory that cannabis contributes to the population level expression of psychosis (7).

Our study found a significant relationship between cannabis use and CAPE depressive symptoms, although not depressive symptoms as measured by HADS, whereby light users reported

more depressive symptoms than those who had never used cannabis. This was not found in previous studies (2, 7, 16). In summary, for all three dimensions of the CAPE (positive, negative and depressive) the overall trend in our findings was for a dose–response effect with heavy users reporting more symptoms than light users, who in turn reported more symptoms than those who had never used cannabis. This apparent dose–response relationship mirrors the relationship between cannabis use and psychotic disorders in clinical populations (6, 9, 17) lending further support to the hypothesis that cannabis may be a causal risk factor for the development of psychosis.

After controlling for frequency of cannabis use, we found a negative correlation between the age cannabis was first used and positive psychotic symptoms. This is consistent with previous work which found that the association between cannabis use and positive CAPE scores was stronger for those who had used cannabis before the age of 16 years than for those 16 years or over (7). It is also consistent with the effect of cannabis use on clinical psychotic disorder outcomes at age 26 years, where these disorders were commonly found in those who had used cannabis before age 16 years compared with those who started using the drug after the age of 16 (an effect which remained significant after adjusting for psychosis liability at 11 years) (6). A recent study of adolescents in Trinidad (8) found that cannabis use increased the risk of experiencing psychotic symptoms and that this effect was conditional on early exposure before the age of 14 years.

At present, the role of both cannabis and the endogenous cannabinoid system (18) in the pathogenesis of schizophrenia and schizophrenic-like psychotic experiences is not fully understood, but research in this area continues to advance. The psychotropic effects of cannabis are thought to be mainly because of the effects of delta-9-tetrahydrocannabinol on specific cannabinoid receptors in the brain and these regulate the release of a number of key neurotransmitters including GABA, glutamate, dopamine, noradrenaline, serotonin and acetylcholine (19, 20).

Evidence from human and animal studies suggest that delta-9-tetrahydrocannabinol has transient effects on behaviour and cognitive functioning (21, 22) and it is thought that in susceptible people, repeated exposure to delta-9-tetrahydrocannabinol may lead to permanent changes in neurotransmitter functioning and so may contribute to psychotic illness. The neurobiological pathways linking cannabis use and increased psychotic symptoms most likely involve the effects of delta-9-tetrahydrocannabinol on the regulation of dopamine and serotonin and studies have shown that depending on their site in the brain, stimulation of cannabinoid receptors by delta-9-tetrahydrocannabinol may either inhibit or increase the release of dopamine (23, 24). Further support for the view that dopamine effects may indeed be one of the key mechanisms linking cannabis use with the development of psychotic symptoms and psychosis comes from behavioural genetic research. It has been found that people with the Val/Val variant of the COMT gene (which regulates dopamine metabolism in the prefrontal regions) have a greater susceptibility to cannabis-induced psychosis (25). Such lines of evidence support a model whereby early cannabis exposure may cause later psychosis by enhancing pre-existing dysregulation of the prefrontal cortex and mesolimbic dopamine system (26). This model is also supported by animal studies demonstrating that cannabinoid exposure during puberty, but not in adult rats, induced behavioural and cognitive changes (27). There is also a considerable body of evidence emerging from neuroimaging studies which focus on the possible role that age of onset of first use of cannabis may play on brain morphology, in particular on white matter structure, and function (28, 29). In one study of fifty-seven subjects using magnetic resonance imaging and positron emission topography scanning techniques, subjects who started using cannabis before age 17, compared with those who started later, had smaller whole brain and per cent cortical grey matter and larger per cent white matter volumes (30).

Our study is limited by the fact that the representativeness of the sample of primary healthcare attendees is unknown. However, it does contain an even distribution of students at different levels of study and our findings of 40% rate of lifetime cannabis use amongst students sampled is similar to prevalence rates in other studies of Irish student populations. The College Lifestyle and Attitudinal National survey (1) reported cannabis use in the previous 12 months of 37% in Irish college students. In addition, the prevalence of self-report psychotic symptoms in our sample is in keeping with previous research in general populations (17). A further methodological limitation is the cross-sectional design, and the fact that the CAPE does not measure the age of onset of psychotic experiences. It may be argued that development of psychotic symptoms could have preceded cannabis exposure and that drug use occurred subsequently, in an attempt to alleviate

symptoms through self-medication. Therefore, the possibility of reverse causality cannot be outruled. However, the specificity of the findings in relation to cannabis, from studies also examining alcohol and other illicit drug use, does not support the self-medication hypothesis (2, 7), nor do findings that associations between cannabis and psychosis are not influenced by levels of distress associated with the experiences (7). Further work in this area should therefore include longitudinal studies of general population cohorts that incorporate repeated measures of subclinical psychopathology, use of cannabis, alcohol and other drugs, as well as measures of function and illness severity.

In conclusion, our findings contribute to the existing body of work linking cannabis use to the expression of psychosis and add strength to the suggestion that younger cannabis users are at greatest risk.

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Declaration of interest

None.

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