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What every adolescent needs to know: Cannabis can cause psychosis

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Abstract

Objective: Cannabis is a widely used substance that may be becoming more socially accepted, legally tolerated, and utilized by younger individuals. This review explores the relationship between cannabis and the onset of psychosis as well as the policy ramifications of current research. **Method:** This article synthesizes published work that was considered by the author to be relevant to the discussion of cannabis and the onset of psychosis. **Results:** The evidence suggests that, along with other harms, cannabis is a significant risk factor in the etiology of psychosis. Adolescents are more vulnerable to using cannabis, and because of their stage of mental development, the cognitive effects are more pronounced. The mechanism for this change is thought to be neuro-chemical with a stronger effect in those with a diathesis for psychosis. **Conclusion:** The risk that cannabis poses to adolescent health should not be neglected. Policy measures should use a multifaceted and strategic perspective in order to prevent adolescents from using this drug.

Keywords: Cannabis; Psychosis; Adolescents; Public Health; Policy

Introduction

Cannabis use and acceptance have increased among adolescents worldwide [1]. Currently, cannabis is the most widely used illicit drug in most English-speaking countries such as Canada, New Zealand, Australia, and the United States [2]. Despite being an illicit drug in Canada, one in seven adults and one in four students reportedly use cannabis [3]. There are reports of an even higher prevalence of cannabis use in students (one in three) [4]. A recent survey of middle and high school students in Nova Scotia found cannabis to be more widely utilized than cigarettes, and while 16.2% of adolescents used cigarettes, 32.4% used cannabis in 2007 [5]. Furthermore, in a study carried out in New Zealand it was shown that almost 70% of a 21-year-old cohort population used cannabis [6]. Cannabis use is even more striking in certain demographic groups. For example, in one survey 92% of street youth report using cannabis 'in the past year' and 16% report 'daily use' [7]. Adolescents appear to be at a double disadvantage as they are more vulnerable to using cannabis [8] and the effects of cannabis on cognitive measures are more pronounced in adolescence [9,10].

In 1991, Boyle and Offord [11] wrote, "Despite the many studies that have reported associations between maladjustment and substance use in adolescence, we know little about the relationship between adolescents substance abuse and specific types of psychiatric disorders." Other articles have made light of cannabis use, one calling it "safer than aspirin" [12]. However, with such a high prevalence of adolescents using cannabis it is imperative to firmly conclude whether the result of this action causes psychosis. At this point in time there are strikingly contradictory views regarding the possible neurobiological role of cannabis in triggering long-term psychosis, with some viewing the likelihood of long-term brain effects as unlikely [13] and others arguing that a lasting effect is likely [14]. This article will review the relationship of cannabis and psychosis as well as discuss the policy implications of these findings.

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Background

Cannabis refers to marijuana and other preparations made from the hemp plant *Cannabis sativa*. The active ingredient in Cannabis is primarily Δ-9-tetrahydrocannabinol (THC), although there are over 60 other related compounds. All these forms act as agonists at the CB1 receptor [15]. If THC is taken orally, it will take 1–3 h for the drug to have an effect; however, if inhaled, it reaches the brain tissue within minutes. Users typically feel lightheaded, calm, drowsy, a subjectively sharpened sense of humor, and an increased appetite [15].

There has been significant public and political interest recently concerning the decriminalization (a reduction from criminalization to a fine penalty) and legalization (a regulated system of supply and distribution) of cannabis as well as regarding the prescribed use of cannabis [16,17]. For example, before 2001, cannabis was only legally accessible in Canada via medical regulation to aide with medical treatment. In February 2004, Bill C-17 was reintroduced into parliament in Canada to advocate a reduction in the penalties for possessing small amounts of cannabis [18]. The bill focused on decriminalization, whereby possession of 15 g or less would be faced with a fine without further criminal charges. With the federal government changes in 2006 this bill died. Currently, the possession of marijuana in any quantity is a criminal offense in Canada [18]. Current governmental initiatives (i.e., Bill C-15) seek to place an even greater emphasis on law enforcement. Though the minority Conservative government is opposed to decriminalizing cannabis (and therefore stifled Bill C-17), this is in contrast with the position of other Canadian political parties. The lack of political agreement on this issue is not specific to Canada, but similar rapid changes in cannabis policy have recently been observed in Britain, New Zealand, and Australia. In reality, cannabis use is broadly tolerated in Canada and enforcement is inconsistently applied [18]. Hall and Pacula [19] report that in Canada, similar to Australia and New Zealand, fewer than 2% of cannabis users are arrested and the arrests disproportionately affect those who are socially disadvantaged.

Because of the rapid growth in the number of users (especially) among adolescents, it becomes important to understand the impact of cannabis and to fully evaluate the premise that cannabis use may be increasing the risk of developing schizophrenia or other long-term psychotic disorders. The odds ratio of developing psychosis in a series of longitudinal studies comparing young cannabis users to nonusers ranges from 2.0 to 24.2, clustering around 5 [20–25]. A key issue is that, in assessing risk, many adolescents might view a consequence with a low percent risk as fairly negligible. However, this approximately fivefold increase might be viewed by a health professional as clinically and fiscally significant [26]. This article reviews the literature and attempts to establish whether cannabis use in adolescence increases the risk of psychosis in later life. Only work that has been published or translated into English was analyzed.

Cannabis use and schizophrenic symptoms

There is controversy in the literature over whether cannabis causes psychosis. In Kendell's 2003 article [27] entitled "Cannabis Condemned: The Proscription of Indian Hemp," he describes how cannabis historically gained a reputation as a drug of addiction based on politics, not on medical evidence. Although Kendell [27] acknowledges that cannabis can lead to acute psychotic episodes, his review did not find sufficient evidence to infer a causal relationship with chronic psychosis. Kendell [27] therefore concludes that cannabis is less of a health risk than alcohol or tobacco, and he points to three reviews (an American, Australian, and British), which similarly conclude that cannabis is of a relatively low risk [28–30]. Although Kendell [27] acknowledges that "…cannabis certainly produces short-lasting psychotic states," he argues that there is insufficient evidence to support the notion that cannabis use leads to long-term psychotic conditions. However, recent epidemiological studies with large samples contradict Kendell's [27] conclusions.

For over a decade, there has been considerable evidence that among schizophrenic patients cannabis abuse can act as a stressor leading to a relapse, particularly if the use is heavy [31]. Cannabis use among people diagnosed with schizophrenia has been shown to be associated with more intense delusions and hallucinatory experiences compared to patients not using cannabis [32]. Tien and Anthony [33] have shown that, after controlling for use of cocaine and alcohol, there was a twofold increased risk of the onset of psychosis in cannabis users. Fifteen percent of cannabis users indicate that they have experienced psychotic symptoms [34], and evidence of a cross-sectional study supports the emergence of psychotic symptoms in those who did not have previous psychosis [35]. More recently, Zammit et al. [23] showed in a survey of approximately 50,000 Swedish conscripts that the use of cannabis was linked to the development of schizophrenia with increasing use being associated with higher risks. This echoes an earlier article [22] on the same cohort. They noted that with more than 50 episodes of use the risk increases close to sevenfold. This dramatic observation does not clarify the issue of whether there was some preexisting problem that led to the cannabis use rather than cannabis being the causative factor in triggering and perpetuating psychosis. This point is addressed by the incisive analysis by Arseneault et al. [36] who showed (drawing upon a longitudinal study in New Zealand) that cannabis users before age 15 were four times more likely to have developed schizophrenia by the age of 26. Furthermore, information from the sample at age 11 allowed the authors to control for any psychotic symptoms at that time. It is notable that in this study a 10th of cannabis users at age 15 developed "schizophreniform disorder" by

age 26 [36]. These recent studies definitively negate the prior ambiguities of the etiological role of cannabis in schizophrenia (see Refs. [37–39]). However, an earlier report from the New Zealand study demonstrated that a mental disorder at the age of 15 led to an increase use of cannabis at the age of 18 [40]. Cannabis is also the most commonly used illicit drug in those with schizophrenia [17]. This emphasizes the complexity of the interaction, which can be clarified by the use of longitudinal studies.

Longitudinal studies in five countries, Greece [24], Israel [20], the Netherlands [21], New Zealand [25,36], and Sweden [23], have provided strong evidence indicating a causal link between cannabis use and schizophrenia. For example, the study by Weiser et al. [20] encompassed 270,000 male adolescents, of whom 50,413 were specifically questioned after the initial screening concerning their drug use. The researchers, using a population-based psychiatric hospitalization registry, established that drug abuse in adolescence led to more than double the rate of hospitalizations for schizophrenia. Furthermore, the study from Greece emphasizes that exposure early in adolescence "may increase the risk for subclinical positive and negative dimensions of psychosis" [24].

A review by a Dutch group concluded that of five hypotheses concerning the link between cannabis use and psychosis, "self-medication" or "the effect of other drugs" can be summarily dismissed [41]. They state that there has been converging evidence to support the notion of cannabis having a stronger effect in "predisposed people" and that it is an "etiological cause of psychosis." Similarly, another review concluded that "all these studies support the concept of temporal priority by showing that cannabis use most probably preceded schizophrenia" [36]. A study published this year uses a sibling-pair analysis to minimize the possibility of confounding variables in their analysis of cannabis use in 228 sibling pairs [42]. Using a range of indices of psychosis, they found that the duration since first cannabis use was related to psychotic phenomena. The conclusion by McGrath et al. [42] that "early cannabis use is associated with psychosis-related outcomes in young adults" complements and concurs with the larger epidemiological studies that are cited above.

A further support for a causal relationship is provided by the observation of a dose–response relationship in the exposure to cannabis and likelihood of psychosis [21]. The finding that there is not a close temporal relationship between the consumption of cannabis and the acute occurrence of the psychotic experience suggests a patho-plastic role for cannabis in the development of psychosis. The observation that there is a close proximity in the brain between cannabinoid and dopaminergic systems may suggest a possible mechanism by which cannabis contributes to the development of psychosis [43].

Very recently, Di Forti et al. [44] have shown that the potency of cannabis used and the duration of use are both key factors in triggering a first episode of psychosis. This adds to the work by Murray et al. [45], who showed that both transitory psychotic features and the triggering of schizophrenia are dependent on dose-related cannabis use. It is noteworthy that cannabidiol may have protective qualities in relation to psychosis triggers [44,46]. This work needs to be considered in the context of the potency of the causative agent that leads to psychosis and the vulnerability of the individual in becoming psychotic [47]. A study recently published in *Psychological Medicine* extends this observation by suggesting a multiplicative effect of cannabis use and brain trauma leading to psychosis in adolescents [48]. This is in contrast to the effect of cannabis and panic in adolescents, which are both suggested to be independent triggers of psychosis [49].

Those who contest a causative relationship of cannabis on psychosis argue that there has not been an increase in the prevalence of schizophrenia as cannabis has become more commonly used in Western nations over the recent decades [50]. This logic is spurious as cannabis is clearly not the only factor that causes psychosis and the impact of cannabis will be muted if the potency of some of the other factors has declined. Others who are skeptical about the evidence that cannabis is a cause of schizophrenia argue that the relationship is modest in size and can be explained by confounding variables and noncausal mechanisms [51,52].

Bradford Hill's criteria of causation (1965) have been summarized (Streiner et al. [53]) as including (1) the demonstration of a strong association between the causative agent and the outcome; (2) consistency of the finding across research sites and methodologies; (3) the demonstration of specificity of the causative agent in terms of the outcomes it produces; (4) the demonstration of the appropriate temporal sequence, so that the causative agent occurs prior to the outcome; (5) the demonstration of a biological gradient, in which more of the causative agent leads to a poorer outcome; (6) the demonstration of a biologic rationale, such that it makes sense that the causative agent leads to a poorer outcome; (7) coherence of the findings, such that the causation argument is in agreement with what we already know; (8) experimental evidence; and (9) evidence from analogous conditions. All of these bar "(3)" and "(8)" have been fulfilled, substantiating the argument that cannabis causes psychosis. Realistically, animal studies would be needed to fulfill "(8)" and these are impractical (because of lack of subjective report), and "(3)" seems inappropriate as one agent may impact on several brain functions. In a systematic review, Moore et al. [26] conclude that "there is now enough evidence to inform people that using cannabis could increase their risk of developing a psychotic illness later in life" and that this warrants public education campaigns to alert people of the associated risks of cannabis use.

Other notable effects of cannabis

Cannabis use is related to emotional distress, depression, and lack of a sense of purpose [54]. In addition, cannabis can

interfere with learning and personal development in teenagers. Short-term memory is impaired by the use of cannabis [55] and in particular the impact on cognitive function is more severe in younger users [9,10]. This result is contradicted by Müller-Vahl et al. [56] who investigated the cognitive effects of THC over a 6-week period and did not observe any differences on acute or long-term cognitive tasks between Tourette's syndrome patients who consumed THC and a control group. However, this result could be due to the less potent doses given by doctors to their patients with Tourette's syndrome (up to 10 mg in this study), compared to what is typically found in unregulated, "street" cannabis. The impact of cannabis upon cognitive function should be clarified by larger and longer-duration controlled studies.

Regarding driving and cannabis use, one survey reported that 82% of drug users indicated that they had driven immediately after consuming illicit drugs (primarily heroin and cannabis), 41.4% of whom had an accident following drug consumption [57]. Tellingly, these individuals reportedly believed that unlike alcohol these drugs would not cause impairment [57].

Cannabis is also recognized as a gateway drug to more serious drugs [58]. However, going against this theory is the observation that the actual proportion of cannabis users who graduate to harder drug use is less than 1% [59]. This has led some to suggest that the association between cannabis and harder drugs is not necessarily causal but rather due to an underlying factor such as "drug-use propensity" [59].

Cannabis has a number of other detrimental effects including the development of cannabis dependence, cardiovascular disease, chronic bronchitis, and impaired respiratory function [60]. Furthermore, many adolescents do not appreciate that cannabis is 50–70% more carcinogenic compared to tobacco [61]. It is also notable that THC may be effective in treating tics and behavioral problems in individuals with Tourette's syndrome [56].

Policy implications

It is becoming increasingly accepted that cannabis use is harmful to adolescents especially with early, frequent, and chronic use [62]. The recent plethora of evidence suggesting that cannabis is a causative agent in the development of schizophrenia/chronic psychosis adds to a multiplicity of other documented adverse health consequences. The logical conclusion is that it would be sensible to pursue policies that will reduce the use of cannabis amongst adolescents.

The negative health repercussions of using cannabis, and the resulting cost for nationalized health care, have supported the argument advocating the criminalization of cannabis users [60]. However, the constantly high rates of cannabis users, despite the criminalization of cannabis, suggest that the current deterrence-based policies have not had the intended effect of reducing use [3]. This may in large part be due to the difficulty and high cost in policing the possession of cannabis. While some would argue that the costly increase in police enforcement is the solution to reducing adolescent use, others have contended that the harms of cannabis do not necessitate criminalization but instead would be better assuaged by the decriminalization or legalization of cannabis in conjunction with other prevention programs [62].

Promoters of cannabis legalization explain that the harms of cannabis are not manifestly more serious than those of alcohol and tobacco. They therefore conclude that, like alcohol and tobacco, cannabis should be regulated, monitored, and taxed, which would create safer and more responsible use rather than pressuring users into an illicit drug market. Moreover, experiences of decriminalization (e.g., in the Netherlands or American states that decriminalized cannabis in the 1970s) indicate that cannabis use incidence is not dependent on the degree of law enforcement [17]. Furthermore, more enforcement of the law would only swamp the system with minor cannabis offenders and is arguably not a cost-effective policy [62]. This position is not marginal. The Angus Reid Strategy 2009 survey reported that 50% of Canadians support the legalization of cannabis [63]. Even if legalized, the law would certainly maintain restrictions on cannabis especially with regard to driving under the influence and adolescent use. As driving under the influence of cannabis causes potential harm to oneself and others, a zero-tolerance policy should be enforced while driving [3]. The policy direction for adolescent use is more ambiguous. Because criminal enforcement of cannabis may put adolescents on a road to deviancy, decriminalization (whereby fines rather than criminal charges are enforced) may be a better solution than criminalization [18].

A significant problem with legalizing cannabis is the concern over the resulting increased access that may increase use [64]. However, if selling to minors becomes a criminal offense that is strongly enforced (similar to cigarettes), then we might expect to observe a reduced access among adolescents, despite greater general access. The experience of tobacco regulation can inform the likelihood of this result. Despite a dramatic and sustained increase in merchants' compliance in refusing to sell cigarettes to young people, the tobacco regulation policies have had limited success with preventing tobacco access in youth. Rigotti et al. [65] report a discrepancy between compliance checks that measure access and self-reported access by youths. They conclude that the law underestimates young people's ability to access tobacco and therefore the ability of these laws to reduce adolescents' smoking behavior. Before legalizing cannabis, the government would have to consider an improved system to better monitor cannabis access.

The law certainly has a role in preventing cannabis use, but instead of focusing on controlling access, a more effective way to decrease adolescent use of cannabis is through teaching youth the dangers of cannabis and encouraging them to make informed decisions that minimize their risk [18]. Tellingly, in a large sample (N=82,106), the

most common reason why youth report abstaining or quitting cannabis use is their concern of psychological and physical damage [66]. This is substantiated by the Substance Abuse and Mental Health Services Administration's (2007) findings that adolescents who perceived the risks of smoking cannabis to be high were less likely to have used marijuana in the past month than those who perceived moderate to no risk (1.4% vs. 9.5%) [67]. It is therefore arguable that the best way to prevent cannabis use is to provide education regarding cannabis safety.

The most common problem with education programs is their one-dimensional perspective, the unrealistic and judgmental message of these programs, and their inability to be sustained in the long-term. Education campaigns need to be multidimensional: occurring in school, in homes, as well as utilizing media outlets. It has been recommended by Fischer et al. [3] that secondary schools would be a good setting for preventive public health intervention and systematic monitoring; however, it is perhaps wise to begin education earlier as the onset of cannabis use can occur before high school. In this regard, it is important to investigate whether early education would have the undesired effect of encouraging experimentation with cannabis [59].

Education programs would also benefit from the dissemination of knowledge through use of multiple agents including peers, who have a very potent influence, and "neutral" agents (e.g., public health staff) so screening and interventions can be direct, swift, and confidential [3]. Education programs should also be layered. The initial aim of programs should be to inform youth that the most reliable way to avoid the harms of cannabis is by practicing abstinence. However, abstinence should not be the only message of education programs. In this regard, it is important to consider that liberal countries have low rates of cannabis use (the Netherlands), whereas countries that emphasize prohibition and abstention have high rates of cannabis use (e.g., Unites States) [17]. For the significant adolescent population who are engaged in cannabis use, education campaigns must hone in on a message regarding "safe use," i.e., not driving intoxicated. In this regard, there are probably many lessons to be learnt from "safe sex" and "anti-smoking" programs. For example, Jha et al. [68] report the reduction of smoking in high-income countries to be due to tobacco tax increases, dissemination of information about the health risks of smoking, restrictions on smoking in public places, bans on advertising and promotion, and increased access to treatment.

As many adolescents become dependent on cannabis [69] and more users are seeking specialists' help for their problem [17], it would also be useful to incorporate modes of treatment into educational programs. It is also extremely important that interventions not be a one-off workshop, but that the program occurs on multiple occasions to reinforce the initial effort and increase efficacy [70].

A commentary by Anthonisen and Murray [71] on the issue of cigarette smoking notes that "substantial efforts are underway to identify genetic characteristics that render people susceptible to the malignant effects of tobacco smoke." The same is necessary for cannabis, but the process is probably less advanced [72]. Anthonisen and Murray [71] recognize the need to consider whether educational efforts should be focused on the genetically vulnerable or on the whole population, and this may be as or more true in the case of cannabis users. The issue of "a public education campaign" is strongly promoted by Hall and Degenhardt [73]. According to Hall and Room [62], educating adolescents about the risk of cannabis is a "moral imperative." Evaluating and implementing evidence-based cannabis education programs should therefore be an urgent priority.

Conclusion

Although there has been a long history of suggestion that cannabis consumption may be a causative agent in the development of schizophrenia, the influential review by Kendell [27] in 2003 seemed to negate this notion or at the very least indicate that there was insufficient evidence to come to this conclusion. It is therefore remarkable that in the last few years there have been a plethora of studies all pointing to an increased risk of schizophrenia/chronic psychosis when adolescents use cannabis on a frequent basis. This may be further compounded by the greater potency of the cannabis that is currently available. The adverse health ramifications are becoming clearer, but the policy direction remains more questionable.

The ambiguous enforcement of the law regarding cannabis use has likely led to a blasé attitude towards cannabis and a postponement in developing a successful cannabis health policy action plan. Governments and public health agencies can no longer defer their responsibility regarding the protection of their population [3]. It is the right of young individuals to know the effects of cannabis so that they are able to make an educated decision regarding cannabis consumption.

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