The Mental Health Risks of Adolescent Cannabis Use

Wayne Hall

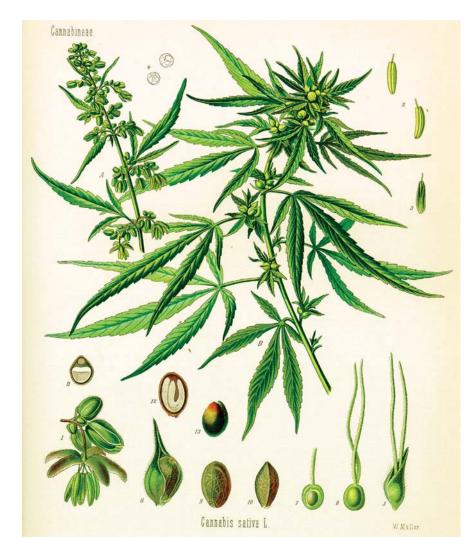
Since the early 1970s, when cannabis first began to be widely used [1], the proportion of young people who have used cannabis has steeply increased and the age of first use has declined [2,3]. Most cannabis users now start in the mid-to-late teens [1], an important period of psychosocial transition when misadventures can have large adverse effects on a young person's life chances.

Dependence is an underappreciated risk of cannabis use [1]. There has been an increase in the numbers of adults requesting help to stop using cannabis in many developed countries, including Australia [4] and the Netherlands [1,5]. Regular cannabis users develop tolerance to many of the effects of delta-9-tetrahydrocannabinol [6–8], and those seeking help to stop often report withdrawal symptoms [9-11]. Withdrawal symptoms have been reported by 80% of male and 60% of female adolescents seeking treatment for cannabis dependence [12,13].

In epidemiological studies in the early 1980s [14] and 1990s [15], it was found that 4% of the United States population had met diagnostic criteria for cannabis abuse or dependence at some time in their lives. Surveys in Australia, Canada, and New Zealand have produced similar estimates [16-19]. About one in ten of those who use cannabis meet criteria for dependence [15], but this risk is much higher for daily users and persons who start using at an early age [20,21]. Only a minority of cannabis-dependent people in surveys report seeking treatment (Chapter 7 of [1]), but among those who do, fewer than half succeed in remaining abstinent for as long as a year [9,10,22].

Those who use cannabis more often than weekly in adolescence are more likely to develop dependence, use other illicit drugs, and develop

The Essay section contains opinion pieces on topics of broad interest to a general medical audience.



DOI: 10.1371/journal.pmed.0030039.g001

Scientific drawing of Cannabis sativa, circa 1900

psychotic symptoms and psychosis [1]. Establishing whether cannabis use is a contributory cause of these outcomes [1] requires two things: (1) longitudinal research on the effects that cannabis use in adolescence has on psychosocial outcomes in young adulthood [23], and (2) statistical methods to control for the fact that young people who regularly use cannabis differ from their peers who do not in ways that increase regular cannabis users' risk of these adverse psychosocial outcomes [1,23]. **Citation:** Hall W (2006) The mental health risks of adolescent cannabis use. PLoS Med 3(2): e39.

Copyright: © 2006 Wayne Hall. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Wayne Hall is Professor of Public Health Policy at the School of Population Health, University of Queensland, Herston, Australia. E-mail: w.hall@sph. uq.edu.au

Competing Interests: The author declares that he has no competing interests.

DOI: 10.1371/journal.pmed.0030039

Is Cannabis a Gateway Drug?

Surveys of adolescents in the United States over the past 30 years have consistently shown [24] that: (1) almost all adolescents who had tried cocaine and heroin had first used alcohol, tobacco, and cannabis, in that order [25,26], (2) regular cannabis users are the most likely to use heroin and cocaine [27], and (3) the earlier the age of first cannabis use, the more likely a young person is to use other illicit drugs [26].

Three explanations have been offered for these patterns: that those who use cannabis at an early age are more likely for other reasons to use other illicit drugs; that cannabis users obtain the drug from the same black market as other illicit drugs (providing more opportunities to use these drugs); and that the effects of cannabis on the brain increase an adolescent's propensity to use other illicit drugs [28].

Animal studies of the neurobiology of drug effects provide some biological plausibility for a causal relationship in showing that cannabis and other illicit drugs act on the same brain reward centres [29–31]. Nevertheless, the role that cannabis plays remains controversial because it is difficult to exclude the hypothesis that these patterns of use are substantially explained by the personal characteristics of cannabis users and the shared environments that make those who use cannabis more likely to use other drugs [24,32].

Several studies have recently suggested that the pattern cannot be wholly explained in this way. A wellcontrolled longitudinal study of a birth cohort found that the pattern did not disappear after statistical adjustment for plausible common factors [33]. Two studies of twins who were discordant for cannabis use have found that the relationship between cannabis use and the use of other illicit drugs persisted after controlling for the effects of shared genes and environment [34,35].

Cannabis Use and Psychosis

Cannabis use and psychotic symptoms and disorders are associated in the population [37–38] and in persons with schizophrenia [39–41]. The major explanations of this association have been that: (1) cannabis use precipitates schizophrenia in persons who are vulnerable to the disorder [1], (2) cannabis is used to self-medicate symptoms of schizophrenia, or (3) the association arises from uncontrolled confounding by variables that predict an increased risk of both cannabis use and schizophrenia [23,42].

The first explanation was supported by a 15-year prospective study of 50,465 Swedish conscripts [43] that found a dose–response relationship between the risk of developing schizophrenia and the number of times cannabis had been used by age 18. These risks remained significant after statistical adjustment for confounding variables. A later 27year follow-up of this cohort [44] also found a dose–response relationship between the frequency of cannabis use and the risk of schizophrenia, which persisted after statistically controlling for confounding factors.

It is worth trying to change adolescent views about the health risks of cannabis.

These findings have been recently replicated in: a three-year study of 4,848 young people in the Netherlands [45]; a 4-year follow up of a cohort of 2,437 young Germans [46]; and two New Zealand birth cohorts (n = 759[47]; n = 900 [48]). All of these studies found a relationship between regular cannabis use and psychosis (with a RR of 2–3) that persisted after controlling for confounding variables [49].

In the Dutch, German and New Zealand cohorts, young people who reported psychotic symptoms at baseline were much more likely to report psychotic symptoms at followup if they used cannabis than were cannabis-using peers who did not report these symptoms at baseline. In one of the New Zealand studies, young people with a variant allele of the COMT gene who used cannabis had a risk of reporting psychotic symptoms that was ten times higher than young people who did not have the allele who used cannabis [50].

The self-medication hypothesis was not supported in the van Os or Henquet studies [45,46], both of which found that early psychotic symptoms did not predict an increased use of cannabis. These results have been supported by Verdoux et al. [51], who found that cannabis users were more likely to report unusual perceptions after using cannabis than to report using cannabis in response to experiencing unusual perceptions, and that this relationship was stronger in individuals with a history of psychotic experiences.

Communicating the Risks

In most developed countries, the debate about cannabis policy is often simplified to a choice between two options: (1) to legalize cannabis because its use is harmless, or (2) to continue to prohibit its use because it is harmful [1]. As a consequence, evidence that cannabis use causes harm to adolescents is embraced by supporters of cannabis prohibition and is dismissed as "flawed" by proponents of cannabis liberalization (e.g., [52]).

A major challenge in providing credible health education to young people about the risks of cannabis use is in presenting the information in a persuasive way that accurately reflects the remaining uncertainties about these risks. The question of how best to provide this information to young people requires research on their views about these issues and the type of information they find most persuasive. It is clear from US experience that it is worth trying to change adolescent views about the health risks of cannabis; a sustained decline in cannabis use during the 1980s was preceded by increases in the perceived risks of cannabis use among young people [53].

The following are brief summaries of the evidence intended for health professionals.

Cannabis dependence. Cannabis users can become dependent on cannabis. The risk (around 10%) is lower than that for alcohol, nicotine, and opiates, but the earlier the age a young person begins to use cannabis, the higher the risk.

Cannabis and other illicit drug use. Regular users of cannabis are more likely to use heroin, cocaine, or other drugs, but the reasons for this remain unclear. Some of the relationship is attributable to the fact that young people who become regular cannabis users are more likely to use other illicit drugs for other reasons, and that they are in social environments that provide more opportunities to use these drugs. It is also possible that regular cannabis use produces changes in brain function that make the use of other drugs more attractive. The most likely explanation of the association between cannabis and the use of other illicit drugs probably involves a combination of these factors.

Cannabis and psychosis. As a rule of thumb, adolescents who use cannabis more than weekly probably increase their risk of experiencing psychotic symptoms and developing psychosis if they are vulnerable—if they have a family member with a psychosis or other mental disorder, or have already had unusual psychological experiences after using cannabis. This vulnerability may prove to be genetically mediated.

Acknowledgments

An earlier version of this paper was presented at the Annual Congress of the Royal Australian and New Zealand College of Psychiatrists in Sydney, Australia, in May 2005 and also at the Centre for Public Health and History, London School of Hygiene and Tropical Medicine (London, United Kingdom) in July 2005. The article overlaps to a small extent with a much longer and more detailed review of the topic, entitled "Cannabis Use and the Mental Health of Young People," that will be published by the Australian and New Zealand Journal of Psychiatry. I would like to thank Sarah Yeates for her invaluable assistance in locating the literature and preparing this paper for publication.

References

- Hall WD, Pacula RL (2003) Cannabis use and dependence: Public health and public policy. Cambridge: Cambridge University Press. 298 p.
- Degenhardt L, Lynskey M, Hall WD (2000) Cohort trends in the age of initiation of drug use in Australia. Aust N Z J Public Health 24: 421–426.
- Monshouwer K, Smit F, de Graaf R, van Os J, Vollebergh W (2005) First cannabis use: Does onset shift to younger ages? Findings from 1988 to 2003 from the Dutch National School Survey on Substance Use. Addiction 100: 963–970.
- Australian Institute of Health and Welfare [AIHW] (2003) Alcohol and other drug treatment services in Australia 2001–02: Report on the National Minimum Data Set. Canberra (Australia): AIHW. 98 p.
- Dutch National Alcohol and Drug Information System (2004) Treatment demand of cannabis clients in outpatient addiction care in the Netherlands (1994–2001). LADIS Bulletin. Available: http://www.ivv.nl/content/_files/ LADIS_Bulletin_Cannabis_april_2004_eng.pdf. Accessed 19 December 2005.
- Adams IB, Martin BR (1996) Cannabis: Pharmacology and toxicology in animals and humans. Addiction 91: 1585–1614.
- Maldonado R (2002) Study of cannabinoid dependence in animals. Pharmacol Ther 95: 153–164.
- 8. Cook SA, Lowe JA, Martin BR (1998) CB1 receptor antagonist precipitates withdrawal in

mice exposed to delta9-tetrahydrocannabinol. J Pharmacol Exp Ther 285: 1150–1156.

- Copeland J, Swift W, Rees V (2001) Clinical profile of participants in a brief intervention program for cannabis use disorder. J Subst Abuse Treat 20: 45–52.
- Stephens RS, Roffman RA, Simpson EE (1994) Treating adult marijuana dependence—A test of the relapse prevention model. J Consult Clin Psychol 62: 92–99.
- Swift W, Hall WD, Copeland J (1998) Characteristics of long-term cannabis users in Sydney, Australia. Eur Addict Res 4: 190–197.
- Crowley TJ, Macdonald MJ, Whitmore EA, Mikulich SK (1998) Cannabis dependence, withdrawal, and reinforcing effects among adolescents with conduct symptoms and substance use disorders. Drug Alcohol Depend 50: 27–37.
- Tims FM, Dennis ML, Hamilton N, Buchan BJ, Diamond G, et al. (2002) Characteristics and problems of 600 adolescent cannabis abusers in outpatient treatment. Addiction 97: 46–57.
- 14. Robins LN, Reiger DA, editors (1991) Psychiatric disorders in America: The Epidemiological Catchment Area Study. New York: The Free Press. 449 p.
- 15. Anthony JC, Warner L, Kessler R (1994) Comparative epidemiology of dependence on tobacco, alcohol, controlled substances and inhalants: Basic findings from the National Comorbidity Survey. Exp Clin Psychopharmacol 2: 244–268.
- Hwu HG, Compton WM (1994) Comparison of major epidemiological surveys using the Diagnostic Interview Schedule. Int Rev Psychiatry 6: 309–327.
- Russell JM, Newman SC, Bland RC (1994) Drug abuse and dependence. Acta Psychiatr Scand 89: 54–62.
- Wells J, Bushnell J, Joyce PR, Oakley-Browne M, Hornblow A (1992) Problems with alcohol, drugs and gambling in Christchurch, New Zealand. In: Abbot M, Evans K, editors. Alcohol and drug dependence and disorders of impulse control. Auckland (New Zealand): Alcohol Liquor Advisory Council. pp. 3–13.
- Hall WD, Teesson M, Lynskey M, Degenhardt L (1999) The 12-month prevalence of substance use and ICD-10 substance use disorders in Australian adults: Findings from the National Survey of Mental Health and Well-Being. Addiction 94: 1541–1550.
- 20. Chen CY, O'Brien MS, Anthony JC (2005) Who becomes cannabis dependent soon after onset of use? Epidemiological evidence from the United States: 2000–2001. Drug Alcohol Depend 79: 11–22.
- Coffey C, Carlin JB, Lynskey M, Li N, Patton GC (2003) Adolescent precursors of cannabis dependence: Findings from the Victorian Adolescent Health Cohort Study. Br J Psychiatry 182: 330–336.
- Budney AJ, Moore BA (2002) Development and consequences of cannabis dependence. J Clin Pharmacol 42: S28–S33.
- MacLeod J, Oakes R, Copello A, Crome I, Egger M, et al. (2004) The psychosocial consequences of use of cannabis and other illicit drugs: Systematic review of longitudinal, general population studies. Lancet 363: 1579– 1588.
- Morral AR, McCaffrey DF, Paddock SM (2002) Reassessing the marijuana gateway effect. Addiction 97: 1493–1504.
- 25. Kandel DB (1975) Stages in adolescent involvement in drug use. Science 190: 912–914.
- 26. Kandel DB, Yamaguchi K (2002) Stages of drug involvement in the U.S. population. In: Kandel DB, editor. Stages and pathways of drug involvement: Examining the gateway hypothesis. New York: Cambridge University Press. pp. 65–89.
- 27. Kandel DB (1984) Marijuana users in young adulthood. Arch Gen Psychiatry 41: 200–209.

- Hall WD, Lynskey M (2005) Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. Drug Alcohol Rev 24: 39–48.
- Gardner EL (1999) Cannabinoid interaction with brain reward systems. In: Nahas G, Sutin KM, Harvey D, Agurell S, editors. Marihuana and medicine. Towa (New Jersey): Humana Press. pp. 187–205.
- 30. Manzanares J, Corchero J, Romero J, Fernandez-Ruiz JJ, Ramos JA, et al. (1999) Pharmacological and biochemical interactions between opioids and cannabinoids. Trends Pharmacol Sci 20: 287–294.
- 31. Tanda G, Pontieri FE, Di Chiara G (1997) Cannabinoid and heroin activation of mesolimbic dopamine transmission by a common mu1 opioid receptor mechanism. Science 276: 2048–2050.
- 32. Agrawal A, Neale MC, Prescott CA, Kendler KS (2004) Cannabis and other illicit drugs: Comorbid use and abuse/dependence in males and females. Behav Genet 34: 217–228.
- Fergusson DM, Horwood LJ (2000) Does cannabis use encourage other forms of illicit drug use? Addiction 95: 505–520.
- Lynskey MT, Heath AC, Bucholz KK, Slutske WS (2003) Escalation of drug use in early-onset cannabis users vs co-twin controls. JAMA 289: 427–433.
- 35. Agrawal A, Neale MC, Prescott CA, Kendler KS (2004) A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. Psychol Med 34: 1227–1237.
- Tien AY, Anthony JC (1990) Epidemiological analysis of alcohol and drug use as risk factors for psychotic experiences. J Nerv Ment Dis 178: 473–480.
- Thomas H (1996) A community survey of adverse effects of cannabis use. Drug Alcohol Depend 42: 201–207.
- Degenhardt L, Hall WD (2001) The association between psychosis and problematical drug use among Australian adults: Findings from the National Survey of Mental Health and Well-Being, Psychol Med 31: 659–668.
- 39. Warner Ř, Taylor D, Wright J, Sloat A, Springett G, et al. (1994) Substance use among the mentally ill: Prevalence, reasons for use, and effects on illness. Am J Orthopsychiatry 64: 30–39.
- Hambrecht M, Hafner H (1996) Substance abuse and the onset of schizophrenia. Biol Psychiatry 40: 1155–1163.
- Mueser KT, Bellack AS, Blanchard JJ (1992) Comorbidity of schizophrenia and substance abuse: Implications for treatment. J Consult Clin Psychol 60: 845–856.
- Thornicroft G (1990) Cannabis and psychosis: Is there epidemiological evidence for association? Br J Psychiatry 157: 25–33.
- 43. Andreasson S, Engstrom Á, Allebeck P, Rydberg U (1987) Cannabis and schizophrenia: A longitudinal study of Swedish conscripts. Lancet 2: 1483–1486.
- 44. Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G (2002) Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. BMJ 325: 1199–1201.
- 45. van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, et al. (2002) Cannabis use and psychosis: A longitudinal population-based study. Am J Epidemiol 156: 319–327.
- 46. Henquet C, Krabbendam L, Spauwen J, Kaplan C, Lieb R, et al. (2005) Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. BMJ 330: 11.
- 47. Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, et al. (2002) Cannabis use in adolescence and risk for adult psychosis: Longitudinal prospective study. BMJ 325: 1212–1213.

- Fergusson DM, Horwood JL, Swain-Campbell NR (2003) Cannabis dependence and psychotic symptoms in young people. Psychol Med 33: 15–21.
- Semple DM, McIntosh A, Lawrie SM (2005) Cannabis as a risk factor for psychosis: A systematic review. J Psychopharmacol 19: 187–194.
- 50. Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, et al. (2005) Moderation of the

effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene x environment interaction. Biol Psychiatry 57: 1117–1127.

- 51. Verdoux H, Ginde C, Sorbora, F, Tournier, M. Swendsen J (2003) Effects of cannabis and psychosis vulnerability in daily life: An experience sampling study. Psychol Med 33: 3–6.
- 52. Zimmer L, Morgan JP (1997) Marijuana myths, marijuana facts: A review of the scientific evidence. New York: The Lindesmith Center. 241 p.
- 53. Johnston LD, O'Malley PM, Bachman JG (1991) Drug use among American high school seniors, college students and young adults, 1975–1990, Volume 1. Rockville (Maryland): National Institute on Drug Abuse. 199 p.

What if I can't afford What if I can't afford Can't afford

We realize that not everyone who does medical research can afford to pay publication charges through their grants. PLoS waives those fees, no questions asked, for anyone who can't pay. Our editors and peer reviewers have no knowledge of who can pay, so papers are accepted only on their merit.