

EDITORIALS



High potency cannabis

A risk factor for dependence, poor psychosocial outcomes, and psychosis

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A recent study by Di Forti and colleagues suggests that daily use of “skunk”—cannabis with high levels of $\Delta 9$ -tetrahydrocannabinol ($\Delta 9$ -THC) and low levels of cannabidiol—is a contributory cause of schizophrenia.¹ The study compared patterns of cannabis use in first episode cases of psychosis and matched controls recruited from areas in south London. It found equally high rates of cannabis use in cases and controls, but cases were three to five times more likely to report daily use of skunk than controls, and this association persisted after statistical adjustment for confounders. The researchers estimated that one in four new cases of schizophrenia in this area of London were attributable to skunk, if the association is causal.

Their finding fits with prospective studies of the association between cannabis and schizophrenia. For example, a 27 year follow-up of 50 000 Swedish conscripts found a dose response relation between the number of times cannabis had been used by age 18 and the risk of receiving a diagnosis of schizophrenia.² This relation persisted after adjustment for potential confounders. Prospective studies in Australia,³ Germany,⁴ the Netherlands,⁵ and New Zealand^{6 7} have found that regular cannabis users are twice as likely to report psychotic symptoms as peers who do not use cannabis.⁸

Other explanations

Whether the association is causal has been debated.^{1 9 10} Sceptics offer two other explanations. One is that young people who are developing a psychotic illness use cannabis as a form of self medication. The other—residual confounding—is that there are some unmeasured factors that explain both why some young people become regular cannabis users and why they develop schizophrenia.^{10 11}

Self medication does not rule out a causal effect of skunk on psychotic symptoms. Cannabis may improve mood in the short term but at the cost of increasing psychotic symptoms, as young people with schizophrenia seem to recognise.^{12 13} A time sampling study suggests that psychotic symptoms more often follow cannabis use than the reverse.¹⁴

It is harder to rule out residual confounding. The association could be explained by other types of drug use (such as

stimulants) that are more common among heavy cannabis users, or due to pre-existing differences in social and genetic risks of developing psychoses between cannabis users and their non-using peers. Some longitudinal studies have controlled for the effects of these other types of drug use,⁸ although critics suggest that they may not have adequately controlled for tobacco smoking.¹⁰

Studies of cannabis use in genetically characterised populations have assessed the degree to which shared genetic risk factors may explain the association. These have included studies of sibling pairs,³ an analysis of the strength of the relation between cannabis and psychosis in people with differing genetic relationships,¹⁵ and correlations between polygenic risks scores for schizophrenia and cannabis use in large twin samples.¹⁶ They suggest that shared genetic factors are unlikely to explain all the association between cannabis and psychosis.

Plausible links

Those who favour a causal explanation place weight on its biological plausibility.¹ They point to double blind studies in which $\Delta 9$ -THC has produced dose related increases in positive and negative symptoms of psychosis in people who do not have psychoses.¹⁷ There are also reports of psychotic syndromes in people with multiple sclerosis who have been treated with the cannabinoid extract, Sativex,¹⁸ which has $\Delta 9$ -THC and cannabidiol as the major constituents.

The existing evidence does not prove a causal relation beyond reasonable doubt. Nonetheless, the remarkable consistency of multiple types of individually fallible evidence makes it much more likely than not that regular cannabis use is a contributory cause of psychosis.^{6 8 19 20} We should accordingly advise young people about the risks of daily cannabis use, given the devastating effects that a psychotic illness can have on a young person's life.²¹ This is especially pertinent advice for young people with affected first degree relatives, whose risk of developing psychosis is 10 times that of their peers.

The debate about whether cannabis contributes to psychosis has overshadowed a much more common and underappreciated risk of daily cannabis use—namely, dependence. In the early 1990s,

this risk was estimated to be one in 10 for all users, one in six among those who started in their mid-teens, and perhaps one in three to one in two among those who used daily.²² These risks may also be higher for daily users of skunk.

Cannabis dependence can be a problem in itself, as shown by an increase in people seeking treatment for problem cannabis use in many developed countries over the past few decades, including the Netherlands, where cannabis use was decriminalised in 1976.²³ Young people who become cannabis dependent are also at higher risk of leaving school early, educational underachievement, using other illicit drugs, and suffering cognitive impairment.²³ There are also debates about whether these associations are causal, but these uncertainties should not prevent us advising cannabis users that using skunk, especially daily, probably increases their risks of dependence and other adverse psychological outcomes as well as psychosis.

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