PERSPECTIVE

Be clear about the real risks

The assertion that cannabis use can cause schizophrenia is not borne out by the evidence, says **Matthew Hill**.

The 1936 film *Reefer Madness* depicted cannabis as a drug that provoked uncontrollable insanity, leading to manslaughter, suicide and attempted rape. This was a ridiculous characterization of the effects of cannabis, but there is a long history of associating the drug with psychotic disorders. In research terms, the first evidence came from a 1987 study, which found that Swedish conscripts had an increased risk of developing schizophrenia if they had consumed cannabis more than 50 times in their life[1]. This finding has been replicated, implying, at the very least, an intricate relationship between cannabis use and schizophrenia[2]. The nature of this relationship is still a matter of debate and is not as clear as some researchers or policymakers would suggest.

One interpretation is that cannabis is an instigating factor in the development of schizophrenia. Some researchers have argued that removing cannabis, particularly high potency strains, from society would reduce the prevalence of the disease[3]. Although this may seem alluring from a drug regulatory standpoint, from a scientific one we need look at the evidence. The history of cannabis use in the Western world stands as an enlightening social experiment. Before the 1960s, cannabis use in Europe and North America was relatively uncommon; today, use varies between countries, but in certain regions upwards of 20% of the adolescent population use the drug. If cannabis is causally related to the development of schizophrenia, then it would be expected that the incidence of the disease would have increased significantly with increased use of the drug. Yet schizophrenia rates since the 1960s have remained stable worldwide, and in fact even declined slightly in the West between the mid-1960s and the mid-1990s[4]. Although changes in diagnostic practices and disease classification may have contributed to this drop, if cannabis does induce schizophrenia, then we would expect to have seen a jump in the number of cases. There also seems to be no difference in schizophrenia rates between countries where cannabis use is prevalent and those where its use is rare. Again, if the drug were an instigating factor alone, we would expect to see differences in the population data.

Other evidence purporting to support the causal hypothesis is also inconclusive. Clinical studies have shown that pure tetrahydrocannabinol (the psychoactive constituent of cannabis) can produce an acute psychotic state. But these states are transient and do not lead to mental illness. It is also known that people with schizophrenia consume cannabis more than the general population[2]. Although cannabis may worsen schizophrenic symptoms such as delusions and hallucinations, it might also mitigate negative symptoms, such as anxiety and social withdrawal — explaining why people with schizophrenia would want to use it[5]. As with any correlation, there is the possibility that a third variable mediates the relationship. The finding[6] that genetic variance could predispose a person to schizophrenia and also increase risk of cannabis use could explain the co-occurrence of these variables on a biological basis.

What does seem to be clear is that heavier than average cannabis use, particularly in early adolescence, can accelerate the onset of schizophrenia[7]. Although this seems damning at first glance, it is less so when examined more closely. A reasonable interpretation is that individuals with schizophrenia, in their attempt to self-medicate, tend to use the drug more frequently than the general population. A vicious circle could develop whereby an adolescent in the early phases of psychosis begins to use cannabis to mitigate some aspects of their developing symptoms, but in fact speeds up disease onset. In this sense, cannabis would be one influence in an already developing illness as opposed to a stimulus that induces the development of the disease itself.

In support of the hypothesis that cannabis only triggers the onset of schizophrenia, gene variants have been identified[8] that predict the development of schizophrenia in response to cannabis use. This suggests that cannabis promotes the development of schizophrenia only in people with a specific biological predisposition. Imagine that the disease is like a campfire: adding fuel to a pile of sticks has little effect, but throwing fuel on a weakly burning fire will increase its strength. Regardless of whether fuel is added, the embers will continue to burn. This hypothesis would also explain the epidemiological data: that higher rates of cannabis use are associated with schizophrenia, but cannabis use does not affect disease rate at a population level. Importantly, this would mean that cannabis does not induce schizophrenia in non-vulnerable individuals. The distinction between the causal and the trigger hypothesis is significant in the message that is conveyed to the public. The former suggests that cannabis use alone can cause the disease, whereas the latter indicates that cannabis is merely a risk factor for someone who would probably develop schizophrenia anyway.

IF CANNABIS IS RELATED TO THE **DEVELOPMENT** OF SCHIZOPHRENIA THEN INCIDENCE OF **THE DISEASE** WOULD HAVE INCREASED.

Clearly, understanding the nature of the risk of schizophrenia is important when developing social policies surrounding cannabis. Education about the drug's effects on mental health should highlight the association of cannabis use with schizophrenia. But scientists should be careful with the language that they use, particularly when presenting this relationship to the public. It is important to ensure we do not confuse correlation with causation and incite another *Reefer Madness*-style panic. By offering careful, evidence-based interpretations of the data, scientists can effectively contribute to policy decisions related to cannabis use and mental health. ■

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