

Invited Commentary

Long-term Marijuana Use and Cognitive Impairment in Middle Age

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During the last 20 years, there have been substantial changes in the legal status and public perception of marijuana in the United States. Decriminalization, medical dispensaries with marijuana for those with a physician's note, and legalization of marijuana in several states have resulted in increased availability and more relaxed views toward marijuana use. However, to our knowledge, relatively little research has been done on the risks of long-term marijuana use.

In this issue of *JAMA Internal Medicine*, Auer and colleagues¹ report an association between cumulative lifetime marijuana exposure and cognitive performance in a prospective study of 3385 middle-aged adults who were followed up for 25 years. Their findings suggest that those who used marijuana on a long-term daily basis have poorer verbal memory in middle age than do their peers who have not smoked marijuana habitually.

The study has several strengths. It followed up two-thirds of a large, representative cohort of adults who were aged 18 to 30 years at baseline for 25 years and assessed 96.7% using validated neuropsychological tests of cognitive functioning.

Detailed information regularly collected on marijuana use (which was comparable with that in US national surveys) showed that 11.6% of the participants used marijuana regularly for a substantial part of the follow-up period. The cohort members were also assessed on other factors that may have affected cognitive performance (eg, use of alcohol, tobacco, and illicit drugs; educational level; depression; and cardiovascular risk factors). The authors statistically controlled for the effects of these variables and excluded participants currently using marijuana to ensure that poorer cognitive performance in those with heavier use of marijuana was not attributable to intoxication.

Participants with the greatest cumulative exposure to marijuana had the poorest verbal memory, processing speed, and executive functioning. The difference in verbal memory persisted after adjusting for confounders, but the other 2 differences did not persist. The absence of baseline data on cognitive performance makes it more difficult to exclude the possibility that participants with lower cognitive abilities were more likely to become long-term users of marijuana.

These findings fit well with other evidence on the effects of long-term marijuana use on cognitive performance. Case-control studies have generally found poorer verbal learning, memory, and attention in those who regularly use marijuana than in controls.² The size of these differences usually has been related to the duration and frequency of marijuana use and, hence, to the cumulative dose of tetrahydrocannabinol received.²

A New Zealand birth cohort study also found that those with heavy marijuana use over several decades had poorer cog-

nitive performance than did those without such use.³ This study assessed IQ at age 13 years (before marijuana was used) and again at age 38 years. It found that the early initiators and persistent users showed the largest decline in IQ scores (8 points vs peers who had not used marijuana or those who had used marijuana but then discontinued use).

Detailed analyses of the New Zealand study point to persistent use of marijuana as the most plausible explanation for the decline in IQ.⁴ First, the decline was largest in those who began using marijuana in adolescence and who continued to use marijuana daily throughout adulthood. Second, the decline persisted after statistical adjustment for recent marijuana use; use of alcohol, tobacco, and other drugs; educational level; and symptoms of schizophrenia. The difference also persisted after controlling for social class. Among those with heavy, sustained marijuana use, IQ scores were a mean of one-half standard deviation lower than those of their peers and close friends; family reported that individuals with heavy marijuana use had more problems with memory and attention in everyday life than did their peers.

Functional neuroimaging studies provide supportive evidence that those with heavy marijuana use have impaired cognitive functioning.⁵ These studies have generally shown reduced activity in those with long-term marijuana use in brain regions involved in memory and attention, as well as structural changes in the hippocampus, prefrontal cortex, and cerebellum.

The available evidence does not establish beyond a reasonable doubt that heavy use of marijuana impairs verbal memory and lowers IQ. Individual studies can always be criticized, but we think considerable weight should be given to the confluence of findings from case-control, neuroimaging, and now 2 long-term, prospective, epidemiologic studies. These cognitive effects are of particular concern because young people with low cognitive abilities seem most likely to start using marijuana at an early age and to continue using the drug regularly throughout young adulthood.⁶

There are also other good reasons why we should discourage early and regular marijuana use by adolescents and young adults. This pattern of marijuana use increases the risks of developing dependence,⁶ which is associated with an increased risk of other adverse psychosocial outcomes in adolescence and young adulthood. These outcomes include leaving school early, experiencing psychotic symptoms, receiving a diagnosis of schizophrenia and bipolar disorder, using other illicit drugs, and developing depression and anxiety disorders.⁶

It is unclear whether heavy use of marijuana is a cause of all of the disorders with which it is correlated. There are nonetheless good reasons to believe that regular use of marijuana is a contributory cause of psychosis in vulnerable individuals.⁶



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Such use probably also worsens the health and psychosocial outcomes in young people who are struggling with their schooling and are at a higher risk of developing anxiety and depressive disorders and psychoses.⁶

The liberalization of medical marijuana laws in the United States since 1996 has made it easier for young adults in some states to engage in sustained daily use of marijuana, particularly in the states that have effectively legalized marijuana use by allowing anyone with a physician's letter to purchase marijuana from a dispensary.⁷ This change has made marijuana more readily available, at a lower price, and with higher tetrahydrocannabinol content than may have been the case for the participants in the study by Auer et al.¹ Regular use of marijuana and symptoms of dependence appear to have increased among young adults who use marijuana in states that have legalized marijuana for medical use.⁸ So far, medical marijuana laws do not appear to have increased adolescent marijuana use.⁹

The public health challenge is to find effective ways to inform young people who use, or are considering using, marijuana about the cognitive and other risks of long-term daily use. Young adults may be skeptical about advice on the putative adverse health effects of marijuana, which they may see

as being overstated to justify the prohibition on its use. More research on how young people interpret evidence of harm from marijuana and other drugs would be useful in designing more effective health advice.

It will be even more challenging to provide effective health advice to adolescents and young adults in states that have legalized retail sales of marijuana to adults.⁹ It is too early to assess the long-term effects on marijuana use of allowing legal sales of marijuana to adults, but it would be remarkable if marijuana use did not increase among adults when retailers are allowed to promote and advertise their products. In a fully legal marijuana market, retailers will do what for-profit industries do, namely, increasing their profits by expanding their markets, reducing prices to increase use among existing users, and attempting to recruit new users to replace those who stop.¹⁰ In these states, health educational messages about the adverse effects of regular use of marijuana will have to compete with the promotional activities of an industry that will highlight the benefits of using its products and discount any evidence that users may be harmed. Federal and state regulators should consider requiring explicit warnings of the adverse effects of marijuana on the package, as we do with prescription and over-the-counter medications and with cigarettes.

ARTICLE INFORMATION

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