

Study Demonstrates That Marijuana Smokers Experience Significant Withdrawal

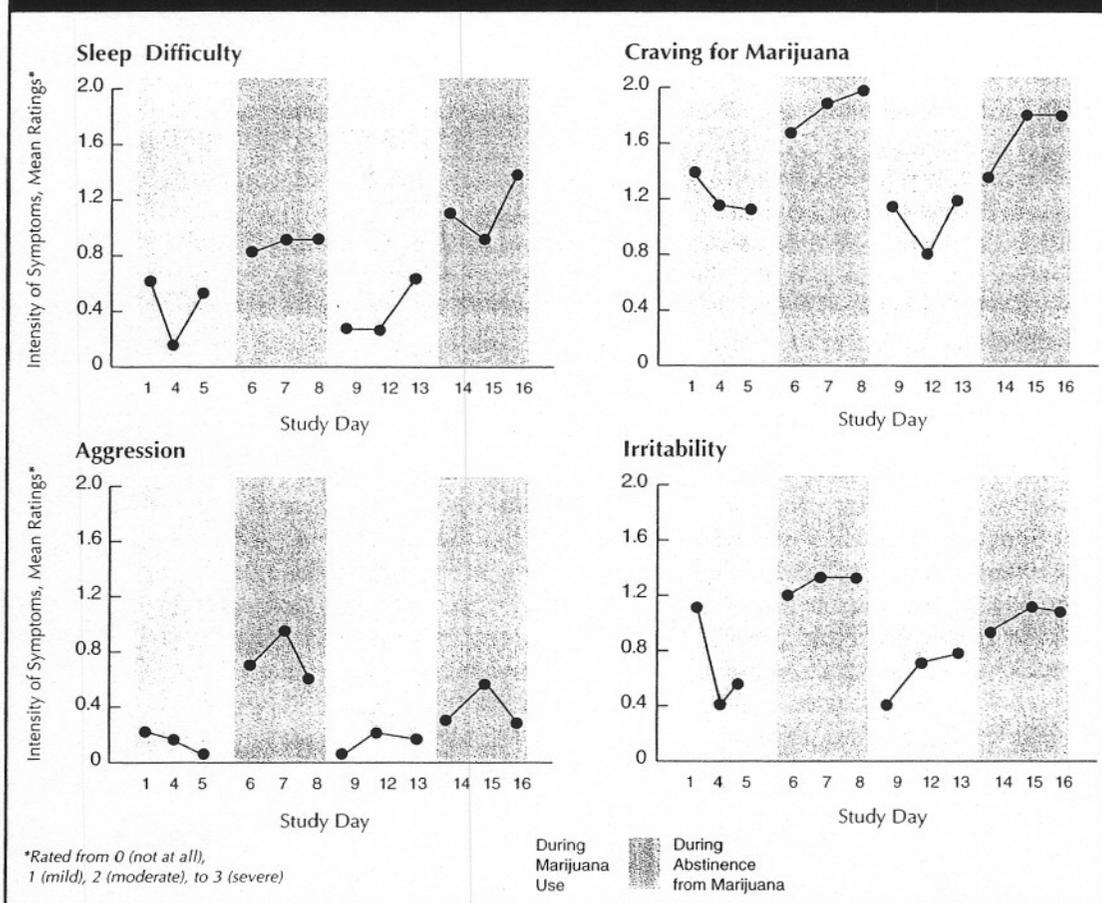
By Patrick Zickler
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Animal research and controlled studies of marijuana smokers during inpatient treatment suggest that marijuana dependence, like dependence on other addictive drugs, is associated with withdrawal symptoms—such as irritability, anger, depressed mood, headaches, restlessness, lack of appetite, and craving—that can make it difficult to stop using the drug (see “Evidence Accumulates That Long-Term Marijuana Users Experience Withdrawal,” *NIDA NOTES* Vol. 15, No. 1).

Now, NIDA-supported research conducted by Dr. Alan Budney and colleagues at the University of Vermont in Burlington has found that marijuana smokers who stop using the drug while in their home environment suffer withdrawal symptoms that appear as severe as those associated with tobacco-smoking.

“These findings represent a significant step toward general acceptance of withdrawal as a key aspect of chronic marijuana use,” says Dr. Jag Khalsa of NIDA’s Center on AIDS and Other Medical Consequences of Drug Abuse. Treatment providers may not

Severity of Symptoms During Marijuana Use Versus Abstinence



Marijuana smokers living at home reported “clinically significant” withdrawal symptoms—such as sleep difficulty, marijuana craving, aggression, and irritability—during periods of abstinence from the drug. The participants’ self-reports were confirmed, in part, by observers who reported increased restlessness and irritability among the marijuana users when they were not smoking.

address the problem of marijuana withdrawal because the condition is not currently included in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*, the standard reference published by the American Psychiatric Association.

Dr. Budney and his colleagues evaluated withdrawal symptoms in 12

adult marijuana smokers (7 male, 5 female, average age 30 years) over 3-day abstinence periods that followed 5-day periods when participants could smoke marijuana at will. “We found consistent emotional and behavioral symptoms that increased during abstinence and dramatically decreased when marijuana smoking resumed,

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Cannabinoid Antagonist Reduces Marijuana's Effects in Humans

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THC or a marijuana cigarette without THC. Immediately after smoking and up to 65 minutes later, participants rated the strength of marijuana's effects on a scale ranging from 0 (no effect at all) to 100 (extremely strong effect).

"Participants who received the 90-mg dose of SR141716 reported 40 to 75 percent less drug effect than those who didn't receive the compound. Those who received lower doses of the compound also reported less drug effect," Dr. Huestis says. "This demonstrates, first, that CB-1 receptors play a major role in THC's effects in humans and, second, that SR141716 can be used to at least partially block the drug's effects."

In addition to its psychological effects on humans, marijuana increases the heart rate. Heart rates of

men who smoked marijuana with THC but received no SR141716 increased by roughly 30 percent above baseline within 10 minutes of smoking marijuana and were 15 percent higher at 1 hour after smoking. Increases in heart rate after marijuana with THC was smoked were diminished in a dose-related manner by SR141716.

Blood tests showed that men who smoked marijuana with THC and who received 90 mg SR141716 had blood concentrations of THC similar to those of participants who did not receive SR141716. This demonstrates that reduction of marijuana's effects is attributable not to any effect of SR141716 on THC concentration, but to blockade of CB-1 receptors, Dr. Huestis says.

Because SR141716 partially blocks THC's intoxicating effects, the compound may prove valuable in treating marijuana addiction, the researchers say. If marijuana does not provide its usual high, patients in treatment would be less tempted to

The participants made daily laboratory visits during which their abstinence was confirmed by urine tests.

During the abstinence periods, participants reported increases in the severity of craving and sleep difficulty, decreased appetite, and increased aggression, anger, and irritability. In addition, participants reported an increase in "strange dreams" during the second abstinence period. Observers reported increased irritability and restlessness among the participants during abstinence.

"Marijuana withdrawal doesn't include dramatic physical symptoms such as the pain, nausea, heavy sweating, and cramps associated with opiate withdrawal. Nevertheless, the symptoms of marijuana withdrawal appear clinically significant. It seems clear now that withdrawal from mari-

juana produces identifiable behavioral and emotional distress that may be as important as, if not more important than, physical symptoms in the development of dependence and undermining attempts to quit using the drug," Dr. Budney says.

"Confirming withdrawal as part of marijuana dependence will increase the likelihood that treatment providers will alert patients to its symptoms and will help them cope with it through behavioral or pharmacological treatments," says Dr. Khalsa.

Source

• Huestis, M.A., et al. Blockade of effects of smoked marijuana by the CB1-selective cannabinoid receptor antagonist SR141716. *Archives of General Psychiatry* 58(4):322-328, 2001. **NN**

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suggesting that these types of symptoms are the hallmark of acute marijuana withdrawal," Dr. Budney says. "The symptoms most closely resembled many of those observed during nicotine withdrawal."

During the study, participants lived at home and made daily records rating the intensity of withdrawal symptoms (on a scale from 0, "not at all," to 3, "severe") over the preceding 24 hours. In addition, each participant designated an observer—a friend or family member who spent at least 2 hours each day with the participant—to provide an independent rating of the participant's withdrawal symptoms.

Source

• Budney, A.J.; Hughes, J.R.; Moore, B.A.; Novy, P.L. Marijuana abstinence effects in marijuana smokers maintained in their home environment. *Archives of General Psychiatry* 58(10):917-924, 2001. **NN**