Your brain on marijuana: two views

Neuroscience writer Laura Sanders had little idea what she was walking into when she wrote a short news story about marijuana earlier this year. The finding was interesting if not Earth-shattering: A hormone blocks some of the intoxicating effects of marijuana in rats and mice (*SN: 2/8/14, p. 12*). The work, she wrote, "may lead to drugs that help people curb cannabis dependence."

The scolding began as soon as the story went up on the *Science News* website. Marijuana, many online commenters said, is simply not addictive. One wrote: "Cannabis was proven to be nonaddictive quite a long time ago.... I am sad to see a respected publication like *Science News*, which I read and appreciate, spreading this misinformation."

Yet, in her reporting, Sanders had heard something quite different. Most scientists believe that marijuana can be classified as addictive (though less so than tobacco and alcohol), with about 10 percent of users becoming hooked. With recent moves toward legalization and decriminalization of marijuana, it seemed well worth a deeper look at what the evidence actually shows, or doesn't show, about marijuana's dangers and how it affects the brain.

As revealed on Page 16 of this issue, many of the "facts" that people believe to be true about marijuana are not supported by science. And while the pro-pot lobby cherry-picks data to support its arguments (denying marijuana's addictiveness, for example), so too do anti-marijuana groups, which play up pot's dangers. Studies do show that marijuana may harm the developing brains of adolescents, but there's little science to support the idea that occasional use by an adult causes lasting damage.

What strikes Sanders is that the fierce debate over whether to legalize marijuana is largely fought by people with personalized "facts." The disagreement seems rooted in conflicting world views. "Science can help clarify some of these issues," she says, "but for research to have an effect on policy, people must first shed their biases and actually examine the evidence. And that seems a tall order." But, for those of us interested in truth, it's also an especially worthy one.

—Eva Emerson, Editor in Chief

CHIEF EXECUTIVE OFFICER, INTERIM Rick Bates
EDITOR IN CHIEF Eva Emerson

EDITORIAL
EDITOR, SCIENCE NEWS FOR STUDENTS Janet Raloff
DEPUTY MANAGING EDITOR, NEWS Lila Guterman
DEPUTY MANAGING EDITOR, DEPARTMENTS Erika Engelhaupt
DEPUTY MANAGING EDITOR, DIGITAL Kate Travis
PRODUCTION EDITOR Erin Wayman
WEB PRODUCER Ashley Yeager
ASSISTANT EDITOR Allison Bohac
ASTRONOMY Christopher Crockett
BEHAVIORAL SCIENCES Bruce Bower
BIOMEDICINE Nathan Seppa
CHEMISTRY AND ENVIRONMENT Beth Mole
LIFE SCIENCES Susan Milius
MOLECULAR BIOLOGY Tina Hesman Saey
NEUROSCIENCE Laura Sanders
PHYSICS Andrew Grant
STAFF WRITER Meghan Rosen
SCIENCE EDUCATION WRITER Bethany Brookshire
EDITORIAL ASSISTANT Bryan Bello
CONTRIBUTING EDITOR Cori Vanchieri
CONTRIBUTING CORRESPONDENTS
Laura Beil, Susan Gaidos, Alexandra Witze

DESIGN
DESIGN DIRECTOR Beth Rakouskas
ASSISTANT ART DIRECTORS Marcy Atarod, Stephen Egts, Erin Otwell
FRONT-END DEVELOPER Brett Goldhammer

BUSINESS SERVICES
SPONSORSHIP AND ADVERTISING Melissa Pewett
SUBSCRIBER AND MEMBER SERVICES Kerwin Wilson
PERMISSIONS Evora Swoopes

BOARD OF TRUSTEES
CHAIRMAN H. Robert Horvitz
VICE CHAIR Jennifer Yruegas **SECRETARY** Alan Leshner
TREASURER Robert W. Shaw, Jr. **AT LARGE** Michela English
MEMBERS Craig R. Barrett, Mary Sue Coleman, Tom Leighton, Paul J. Maddon, Stephanie Pace Marshall, Joe Palca, Vivian Schiller, Frank Wilczek, George Yancopoulos

EXECUTIVE OFFICE
CHIEF EXECUTIVE OFFICER, INTERIM Rick Bates
CHIEF CONTENT OFFICER Mike Mills
EXECUTIVE ASSISTANT Amy Méndez

FINANCE **CHIEF FINANCIAL OFFICER** Greg Mitchell
ACCOUNTING MANAGER Lisa M. Proctor
SENIOR ACCOUNTANT Sivakami Kumaran

EXTERNAL AFFAIRS
CHIEF ADVANCEMENT OFFICER Rick Bates
SENIOR COMMUNICATIONS MANAGER Sarah Wood
SOCIAL MEDIA Patrick Thornton
EXTERNAL AFFAIRS Nancy Moulding
DEVELOPMENT ASSISTANT Carolyn Carson

EVENTS MANAGEMENT **DIRECTOR** Cait Goldberg
ASSOCIATE Marisa Gaggi

SCIENCE EDUCATION PROGRAMS
DIRECTOR Michele Glidden
INTEL SCIENCE TALENT SEARCH MANAGER Caitlin Sullivan
BROADCOM MASTERS MANAGER Allison Hewlett
INTERNATIONAL FAIRS MANAGER Sharon Snyder
DOMESTIC FAIRS Laurie Demsey
VOLUNTEERS AND SPECIAL AWARDS Diane Rashid
AWARDS AND EDUCATION PROGRAMS June Kee
INTERNATIONAL FAIRS SPECIALIST Jinny Farrell
STUDENT SCIENCE SPECIALIST Laura Buitrago
OUTREACH Victor Hall **ASSOCIATE** Sarah Conner

INTERNAL OPERATIONS
DIRECTOR Harry Rothmann
NETWORK MANAGER James C. Moore
OPERATIONS MANAGER Anthony Payne
FACILITIES Paul Roger
IT PROJECT MANAGER Angela Kim
DRUPAL DEVELOPMENT Craig Bozman
WEB AND DATABASE DEVELOPER Ilya Mekeda
DATA OPERATIONS MANAGER Alan Gordon
INFORMATION TECHNOLOGY Gregory A. Sprouse
MAILROOM Randy Williams

EDITORIAL, ADVERTISING AND BUSINESS OFFICES
Audit Bureau of Circulations
1719 N Street NW, Washington, DC 20036
Phone: (202) 785-2255
Customer service: member@societyforscience.org
Editorial/letters: editors@sciencenews.org
Sponsor content: snsales@sciencenews.org

Science News (ISSN 0036-8423) is published biweekly by Society for Science & the Public, 1719 N Street, NW, Washington, DC 20036.

Online and iPad access: Activate your subscribing member account, including digital access and the ability to opt out of print, at sciencenews.org/activate

Subscribe:
Web Visit sciencenews.org/join to become a subscribing member or renew at sciencenews.org/renew
Phone Call (800) 552-4412 in the U.S. or (570) 567-1191 outside of the U.S.
E-mail member@societyforscience.org
Mail *Science News*, PO Box 1205, Williamsport, PA 17703-1205

Subscribing memberships include 26 issues of *Science News* and are available for $50 for one year (international rate of $68 includes extra shipping charge). Single copies are $3.99 (plus $1.01 shipping and handling). Preferred periodicals postage paid at Washington, D.C., and an additional mailing office.

Postmaster: Send address changes to *Science News*, PO Box 1205, Williamsport, PA 17703-1205. Two to four weeks' notice is required. Old and new addresses, including zip codes, must be provided.

Society for Science & the Public is a 501(c)(3) nonprofit membership organization founded in 1921. The Society seeks to promote the understanding and appreciation of science and the vital role it plays in human advancement: to inform, educate, inspire. Learn more at societyforscience.org. Copyright © 2014 by Society for Science & the Public. Title registered as trademark U.S. and Canadian Patent Offices. Republication of any portion of Science News without written permission of the publisher is prohibited. For permission to photocopy articles, contact eswoopes@societyforscience.org. Sponsor content and advertising appearing in this publication do not constitute endorsement of its content by *Science News* or the Society.

SANDY SCHAFFER

High TIMES

Legalization trend forces consideration of pot's dangers

By Laura Sanders

Some people think marijuana is nature's gift to humankind: a nonaddictive drug, safe at any dose, that opens the mind, lifts the spirit and transports the user to a more profound reality.

"The illegality of cannabis is outrageous, an impediment to full utilization of a drug which helps produce the serenity and insight, sensitivity and fellowship so desperately needed in this increasingly mad and dangerous world," a user named Mr. X wrote in the 1971 book *Marihuana Reconsidered*.

Close to 30 years later, Mr. X was revealed to be the legendary science communicator and astronomer Carl Sagan. His message still reverberates with many Americans, whose support for legalizing marijuana has tripled since 1989 — from 16 percent to 54 percent today. In Colorado and Washington state, voters legalized recreational marijuana use in November 2012. That formal embrace of marijuana may signal a growing shift in acceptance. Today, 21 states and the District of Columbia sanction medical use (up from 16 in 2010) and 17 have curbed punishments for possession of small amounts of recreational cannabis.

Marijuana as medicine is gaining support in studies, both to tamp down nausea and pain and to directly counter insidious diseases such as epilepsy, cancer and multiple sclerosis (*SN: 6/19/10, p. 16*). But what about for healthy people? Is marijuana really a safe way to rise above the tumult and distress of daily life?

Michele Leonhart, the head of the U.S. Drug Enforcement Administration, says no. In congressional testimony in 2012, she portrayed marijuana as a dangerous addictive drug on par with methamphetamines or heroin. Like other drugs cordoned off by her agency to a list called Schedule I, she said, marijuana has no medical use and a high potential for abuse.

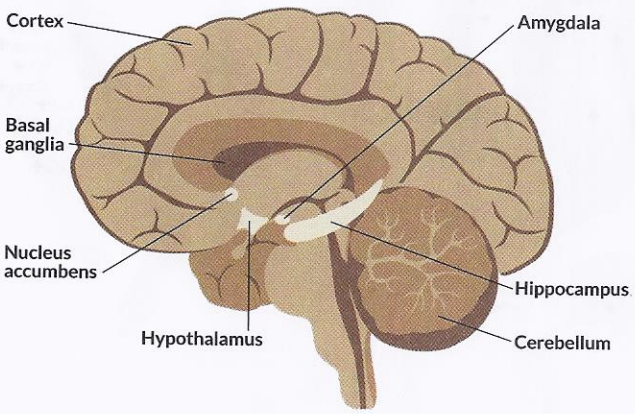
Convinced of marijuana's dangers, the DEA and vocal groups of police officers, educators and public health officials remain steadfastly opposed to the growing legalization movement. Legalization poses significant health and safety risks to Americans, they argue. This addictive drug wipes out memories, steals IQ points and triggers psychosis, leaving behind a zombie nation of slackers vegetating in their parents' basements, opponents say. The consequences may be especially damaging for teens.

Who is right? The people who contend that marijuana is a misunderstood salve for the soul or those who claim it's a dangerous narcotic that turns people into dimwitted potheads?

Turns out it's neither. Though the research is far from definitive, the scientific evidence that does exist suggests that marijuana is far less dangerous than highly addictive drugs like heroin, methamphetamines and alcohol. But it is not harmless. Pot can probably cause permanent changes in the developing brains of adolescents. And though marijuana is not highly addictive, about 10 percent of users become dependent.

It's unlikely that existing research will be able to provide a clear-cut answer about whether legalization is a good idea. But in a way, that debate is already over. As popular sentiment shifts and laws become more lenient, marijuana becomes a bigger piece of the social fabric.

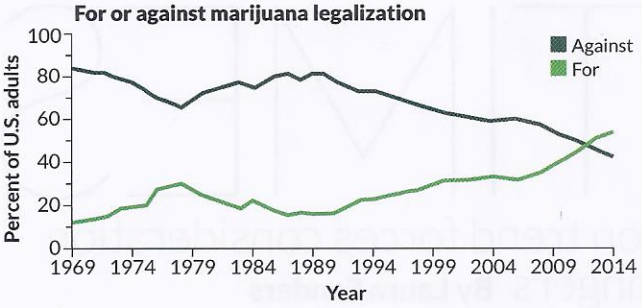
Altered states Marijuana can speed up the heart, expand blood vessels in the eye and make the mouth feel cottony. It also has several targets in the brain.



Brain structure	Effect of marijuana on brain region
Amygdala	Can alter emotional states
Basal ganglia	Reduces motor activity; users may move less
Cerebellum	Can impair coordination
Cortex	May alter complex thinking, making it hard to pay attention or switch quickly between two tasks
Hippocampus	Memory center becomes less efficient, making it harder to learn and remember new information
Hypothalamus	Stimulates appetite, giving marijuana users the well-known "munchies" effect
Nucleus accumbens	Can make users want to use again by targeting this area, which is part of the brain's reward system

SOURCE: K. FRANSON

OPPOSITE PAGE: TANG YAU HOONG; THIS PAGE: ALILA MEDICAL MEDIA/SHUTTERSTOCK



Leaning green From the 1960s until about four years ago, the majority of Americans thought pot should be illegal. Today, views have shifted, with 54 percent supporting the legalization of marijuana.
SOURCE: PEW RESEARCH CENTER 2014

"We're at this point, whether we like it or not, where things are changing, and they're changing fast," says Susan Weiss, associate director for scientific affairs at the National Institute on Drug Abuse (NIDA) at the National Institutes of Health. Her agency is funding studies to better understand the effects of marijuana, she says, so that the science can better inform public policy.

Your brain on pot

When a person tokes, eats or vapes cannabis, a wave of THC, or tetrahydrocannabinol, washes into the brain. Thought to be the major psychoactive ingredient in marijuana, THC latches on to a protein in the brain called cannabinoid receptor type 1, or CB1. These receptors are sprinkled liberally throughout the brain, especially in the cortex, where thinking takes place; the basal ganglia, which helps control movement; the appetite-regulating hypothalamus; and the hippocampus, a structure involved in forming memories.

CB1 receptors are an important part of how the brain works, says neuroscientist Valerie Curran of University College London. "They're not put there by God so we can all enjoy cannabis," she says. "They're put there because we have our own cannabis in our brains."

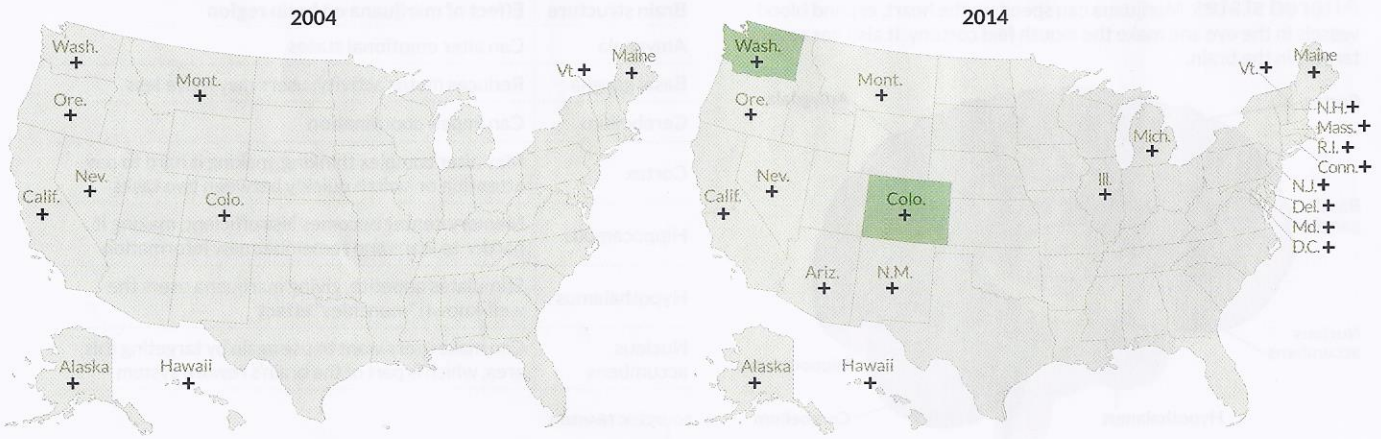
The brain's self-made cannabis consists of molecules called endocannabinoids, which hit the targets that cannabis hijacks. One of the primary endocannabinoids is named anandamide, after the Sanskrit word for bliss. The brain's endocannabinoid system influences pain, memory, mood and appetite, and plays a role in helping the brain grow.

So when foreign THC taps into this system, the effects can feel profound, says psychologist Mitch Earleywine of the University at Albany in New York. "It's got a novelty," he says. "It's got its own receptor system and its own set of effects. The fact is that not a lot of other substances hit that CB1 receptor." That's how cannabis elicits its particular brand of euphoria and cognitive flexibility, says Earleywine, who also serves on the board of NORML, the National Organization for the Reform of Marijuana Laws, which pushes to legalize the drug.

Unlike some other reality-altering drugs, cannabis doesn't seem to be lethal, even in high doses. "Can you die from alcohol just by drinking yourself to death? Yes, you can," says pharmacologist Kari Franson of the University of Colorado Denver. "Can you die from marijuana just from ingesting too much or smoking too much? Well, not really. You pretty much have to fall down and hit your head to die from it." (A paper published in the April *Forensic Science International* does describe the deaths of two presumably healthy young men from heart trouble under the acute effects of cannabis. But overall, deaths seem to be rare.)

Marijuana may not be deadly, but there are some clear downsides. A mental juggling act called working memory, the ability to hold pieces of information in mind, is diminished in someone who's high, 40 years' worth of studies show. Marijuana use has been linked to cardiovascular problems, most recently in a paper in the April *Journal of the American Heart Association* that describes heart problems in young cannabis users. Cannabis intoxication may double a driver's risk of a car crash, scientists reported in 2012 in *BMJ*. And heavy smokers

Coast-to-coast In the last decade, a growing number of states have passed laws legalizing marijuana, both for medical and recreational use. The numbers are expected to rise. In April, Maryland became the 18th state to ease punishment for marijuana possession and the 21st to allow medical marijuana. SOURCE: NATIONAL CONFERENCE OF STATE LEGISLATURES, NORML



VECTORAPZ™, ADAPTED BY E. OTWELL

can show more signs of lung damage compared with nonsmokers, though whether that actually leads to more disease is unclear, according to a 2013 review published in the *Annals of the American Thoracic Society*.

"We're worried about having another drug that's highly prevalent and very accepted by society," says Weiss of NIDA. The burden of problems will only get worse, she says, including altered brain development, poorer school and work performance and higher numbers of people who are addicted. Between 2009 and 2011, as use rates went up, the rate of emergency room visits for cannabis intoxication rose by 19 percent, according to the Drug Abuse Warning Network.

Addiction

The concept of addiction plays front and center in the debate. Marijuana proponents are fond of pointing out that the drug is less addicting than tobacco and alcohol, substances that are legal for adults. And that is correct. On a relative scale, marijuana just isn't as addictive as other substances, says Franson.

"Think about those poor little rats pushing levers to get cocaine. They forgo eating, forgo sex, forgo everything because they just want to hit that lever," she says. Marijuana's addictive allure doesn't compete with opiates, or even alcohol or tobacco. But that doesn't let marijuana off the hook, she says. "It's not the worst offender, but it still does have some of those addictive components," Franson says.

It's not clear what goes on in the brain to cause pot addiction, or why so many people escape it. Marijuana somehow reduces the number of CB1 receptors in the brains of people who smoke regularly, an effect that might contribute to addiction, scientists reported in *Molecular Psychiatry* in 2012. But after a month of abstinence, the receptors bounced back to normal levels everywhere except the memory-forming hippocampus. Regular marijuana use might also influence an addiction-linked pathway that involves the neurochemical dopamine, though the details of that interaction aren't clear. Studies, mainly on animals, suggest that over time, cannabis might change the feel-good parts of the brain, including the neurons that produce dopamine, in ways that prompt people to keep using it.

Those changes might explain why some people struggle to stop using marijuana. About one user in 10 becomes dependent, defined by criteria described in the *Diagnostic and Statistical Manual of Mental Disorders*. Those criteria include two key features: tolerance and withdrawal. Experienced marijuana users need to up their dose as they become tolerant. "You need more of the drug to have the same effect," says Franson. Animal studies bear that out: Mice exposed habitually to THC need more and more of the drug to show the same motor deficits.

Marijuana withdrawal is even more contentious than tolerance. After stopping heavy marijuana use, some people — but not everyone — experience irritability, anxiety and loss of appetite. Still, those symptoms are mild compared with an opiate or alcohol withdrawal, Earleywine says. "If you tell an opiate addict you're 'addicted' to marijuana, you're probably going to get kicked in the crotch," he says.

But if cannabis isn't lethal and doesn't cause debilitating withdrawal, then is habitual use really such a bad thing? The answer, it turns out, probably depends on the age of the smoker.

Trouble for teens

Scientists can't say with confidence what marijuana does to the body and brain long-term, for several reasons. It would be unethical to randomly assign study participants to use an illicit drug for months, so the best scientists can do is look for associations — particular traits, abilities or limitations that appear more frequently in people who use cannabis. This approach leaves open all sorts of variables: People are from different backgrounds and smoke marijuana from different sources, for starters. The most these studies can offer is possible links.

Average number of daily U.S. emergency room visits for drug use in teens ages 12–17

197
Alcohol, alone or with other drugs

165
Marijuana

74
Pain relievers

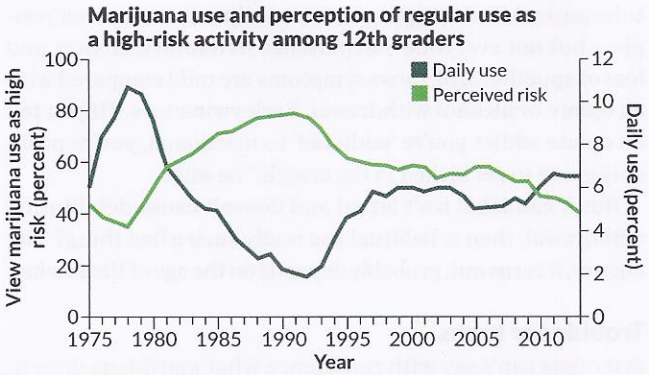
SOURCE: 2011 SAMHSA DRUG ABUSE WARNING NETWORK

One of the strongest links found so far comes from studies of young people. The teenage brain is still growing and refining its neural connections — a process that's regulated in part by the brain's natural endocannabinoid system. Marijuana use when the brain is vulnerable may interfere with its normal development. "The developing brain is at risk," Franson says.

Young adults, ages 18-25, who used marijuana at least once a week were more likely than nonsmokers to have structural differences in two brain areas thought to be involved in addiction, the nucleus accumbens and the amygdala. The differences were more pronounced with increased use, researchers reported April 16 in the *Journal of Neuroscience*. Scientists don't know whether these brain differences track with any behavioral deficits.

Adolescents who heavily use marijuana are more likely to perform poorly in school and drop out, though the effects of cannabis can't be easily separated from other social factors. New Zealanders in one study who used marijuana heavily during their teens showed an IQ drop of about eight points by the time they'd reached age 38. Because the study began before the participants started using marijuana and ran for decades, the results offer some of the strongest evidence yet that marijuana contributes to an IQ decline. But even these results come with caveats and methodological limitations.

Marijuana's long-term effects on people who start using the drug as adults are even less understood, but the hints provided from some studies suggest that it's not as harmful as adolescent use. That same IQ study, for instance, found no decline in people who began using cannabis as adults.



No worries As high school seniors think pot is less of a problem, mirroring adult attitudes, their use of the drug is going up. Marijuana use might be particularly risky for young brains, studies suggest.
SOURCE: MONITORING THE FUTURE STUDY, 2013, UNIV. OF MICHIGAN

A different study, published in the May *Addictive Behaviors*, looked at whether the cognitive effects of marijuana in adults go away when people stop using. "It's generally known that the acute effects are there," says study author April Thames of UCLA. "The question is, do these reverse over time?"

Most of the negative effects of marijuana — poorer attention, working memory and mental nimbleness — were absent in adults who had not used the drug for a month, Thames and her colleagues found. However, a person's ability to plan and make complicated decisions was still impaired a month out.

The results offer just a "snapshot at the time we did the testing," Thames says. They describe an association, not causation. "The question down the road is, what kind of implications does that have for everyday functioning?"

Scientists have largely failed to turn up compelling evidence that adult pot smokers risk permanent brain problems, Earleywine says. "Being stoned all the time is a strange way to live your life," he says, but data just aren't there to argue that a cannabis-fueled lifestyle is permanently harmful to the adult body and brain.

The new reality

As researchers try to make sense of study results, the nascent marijuana industry is charging ahead in a Wild West capitalistic society. That's worrisome, many scientists say. Policies should regulate the quality and strength of marijuana, and keep it away from children, Franson says.

In Colorado, where drug laws have been loosened, first for medical marijuana and then for recreational use, a growing number of children under 12 have been admitted to emergency rooms for acute marijuana intoxication, according to a study in the July 2013 *JAMA Pediatrics*. There ought to be tighter controls over shops, particularly those that sell marijuana-infused products like chocolates and cookies that entice children. Many marijuana retailers "look like sweets shops," Curran says.

NIDA is keeping tabs on ER visits as well as the increasing levels of THC in cannabis seized by law enforcement agencies, and how marijuana legalization has affected the health of people in Colorado and Washington State.

Some researchers see the growing availability of marijuana as inevitable and are advocating ways to keep the drug out of the hands of young people.

"Kids are growing up on a much more toxic form of marijuana than they would have done years ago," Curran says. Today's plants are very high in THC and low in a compound thought to counter its effects called cannabidiol, or CBD. THC levels in marijuana have increased from 3.4 percent in 1993 to 8.8 percent in 2008, according to a marijuana potency-monitoring project at the University of Mississippi. A more regulated market might keep the most potent marijuana out of the hands of young people, Curran says.

More accurate testing and labeling of marijuana products would help, many researchers believe. THC concentrations can vary from seller to seller and even batch to batch. "People need to know what they're getting," Franson says. "It's just named these weird names." Purple Urkel, Girl Scout Cookies and Super Silver Sour Diesel Haze are some of the options available in stores. Colorado is trying to improve labeling to describe important differences, which is particularly urgent for people who rely on certain doses of THC or CBD to treat medical conditions.

When marijuana is eaten, THC takes longer to reach the bloodstream, and its absorption rates can vary greatly. This imprecise delivery system can cause people to take much more than they intended. Proper labeling might help people better titrate their dose, Franson says.

Even Earleywine, who supports legalization, says he's concerned about commercialization of marijuana. "America is so free market and wild that it's going to take some reining in to make sure that no one is penalized for it and medical users have access, but it's not sponsoring every sport event or on TV every five seconds," he says. Current restrictions on cigarettes might be a good model for the burgeoning marijuana industry, he says.

Imperfect science leaves people on both sides of the marijuana debate wanting more. But in a way, the good-or-bad, yes-or-no argument is over: Marijuana is creeping across the country. That's probably not catastrophic for adults, but for young people, the implications are more worrisome. Just how worrisome is something scientists are still figuring out. That knowledge may help ease the transition to an ever-greener world. ■

Explore more

- Drugs Facts: Marijuana. National Institute on Drug Abuse. http://bit.ly/SNpotNIDA
- National Organization for the Reform of Marijuana Laws. www.NORML.org
- DrugScience: Independent Scientific Committee on Drugs. www.drugscience.org.uk