Pot and the Teen Brain

A more relaxed attitude toward legal marijuana may mean more use among teens. The long-term effects may not be good.

By Timothy Gower

The young man was a good scholar and a gifted athlete. But his grades plummeted when he was a junior at Westford Academy, a public high school about 35 miles northwest of Boston. When a drug test ordered by his worried parents confirmed that the student had been using marijuana, the news came as no surprise to James Antonelli, the school’s principal. And although Antonelli met with the family many times, the young man eventually flunked out.

Antonelli has seen at least two dozen students go down the same path. And so he was receptive when researchers from Massachusetts General Hospital’s Center for Addiction Medicine (CAM) approached him about recruiting Westford Academy students to participate in a study of teen marijuana use. The research will examine whether smoking the drug affects teens’ ability to think, learn and remember information—a hypothesis with a growing body of support—and whether users of cannabis products who quit may be able to sharpen their cognitive skills, a question that has not been well studied.

The MGH study will add to research probing the impact of marijuana on the developing teen brain. Past work has indicated that adult pot smokers have somewhat poorer cognitive skills (such as memory and attention span) and worse academic achievement levels. Some (though not all) studies have even found that marijuana devotees have lower IQs than their non-using peers. New research is offering clues about what might cause such problems, suggesting that exposure to cannabis at critical stages of development—perhaps most acutely in those who start smoking pot before age 16—may alter the brain’s structure and lead to changes in how it functions.

Many kids, of course, do use marijuana, and their numbers could be poised to grow. In 2014, 44% of 12th graders said they had used the drug at least once, according to the University of Michigan’s Monitoring the Future survey; the same was true of a third of tenth graders and 16% of eighth graders. And while those figures have remained fairly steady over the past few years, the Michigan survey shows a recent steep decline in the perceived risk of smoking pot among teens. Historically, such changes in how people think about a drug often precede an uptick in use. And indeed, a majority of Americans now favor legalizing marijuana, which is now widely considered to be safer than alcohol, according to a 2014 survey by the Pew Research Center.

“With changes in societal norms, there’s going to be increased use,” says A. Eden Evins, director of the MGH CAM, who is overseeing the Westford Academy study. Like many of her colleagues who study young marijuana users, Evins worries that the growing number of states that are easing prohibitions against pot for medical and so-called recreational purposes will have a “halo effect” on the drug’s reputation. “People think, you wouldn’t legalize something that’s dangerous, right?” says Evins.
Such talk riles proponents of legalization—including organizations such as the Drug Policy Alliance (DPA) and even some physicians who believe pot has medicinal benefits. They insist that Evins and others are raising undue alarm, arguing that recent imaging studies don’t prove that brain changes were caused by marijuana use. Isn’t it just as likely that alterations in brain function and structure came first? “If you’re going to take the leap to causality, I’m concerned that we’re getting too wowed” by the imaging studies, says Sunil Kumar Aggarwal, a palliative care physician in Seattle who studies cannabis’s health benefits, including pain relief.

The brain has never given up its secrets readily, and researchers who have taken a keen interest in marijuana’s impact on the adolescent brain acknowledge that they can’t yet say whether the structural and functional alterations they’re discovering are a cause of pot smoking or a result of it, and whether the changes do affect cognition. A longitudinal study getting under way this year will eventually help answer that question. But in the meantime, converging evidence suggests that getting high may pose a unique threat to young people.

While scientists once believed that the brain is fully formed after puberty, it’s now clear that the organ remains under construction well into the third decade of life. Staci Gruber, an associate professor of psychiatry at Harvard Medical School and director of the Marijuana Investigations for Neuroscientific Discovery (MIND) program at McLean Hospital, in Belmont, Mass., explains that the brain develops from the back forward, and from the bottom to the top, with the frontal cortex the last region to become complete. Among other roles, the frontal cortex governs so-called executive functions, such as the ability to plan, pay attention, follow instructions and juggle multiple tasks. It also helps control impulses—so that someone who feels the urge to do something may choose not to do it.

The brain’s overall structure and functioning become more integrated during adolescence and young adulthood. “We know that white matter connections between certain brain areas become stronger” during those years, says Susan Weiss, director of the division of Extramural Research at the National Institute on Drug Abuse (NIDA). White matter is made up of myelinated nerve fibers, or axons, which are projections from neurons that carry signals—they’re the brain’s transmission lines. Myelin is a white, fatty substance that insulates axons, like plastic coating on electrical wires. As a young person’s brain develops, more axons become myelinated, increasing the speed by which nerves can pass along electrical signals by up to one hundredfold.

Meanwhile, gray matter—the brain’s other chief component, mostly made up of nerve cell bodies, unmyelinated axons and other supporting cells—actually diminishes slightly during healthy development. In a process called synaptic pruning, weak or unnecessary nerve connections are eliminated, and the frontal cortex thins. Pruning increases the efficiency of signal transmission, says Weiss.

The psychoactive compound in marijuana, tetrahydrocannabinol (THC), works by locking into cannabinoid receptors on neurons across much of the brain (as well as in nerves throughout the body and in heart cells, blood vessels and glands). It does this by mimicking compounds that naturally occur in the human body. These endocannabinoids and their receptors play a critical role in protecting neurons and regulating their activity, as well as in shaping brain development and aiding the formation of nerve connections, and they’re needed to form myelin, says Sion Kim Harris, co-director at the Center for Adolescent Substance Abuse Research at Boston Children’s Hospital.

There are several theories about how THC might interfere with normal brain development. By blocking endocannabinoids from locking into their intended receptors, THC may prevent the production of myelin, whose absence could slow the transmission of nerve signals governing thought and behavior. What’s more, while endocannabinoids and THC both can dial down the activity of neurons, the effect of THC is far stronger and longer,
perhaps making it harder for parts of the brain to link up and communicate. “Brain wiring is shaped by neuron activation,” says Harris. “It’s use it or lose it. The more neurons fire, the stronger the connections are [between brain regions]. The less they fire, the less strong they are.”

Recent research suggests that the brains of young marijuana users may truly be different from those of their peers. In a 2015 study published in Developmental Cognitive Neuroscience, psychologist Joanna Jacobus of the Veterans Affairs San Diego Healthcare System in La Jolla, Calif., and her colleagues used magnetic resonance imaging (MRI) to measure cortical thickness in heavy cannabis users who were age 16 to 19 when the study began. (A “heavy” user was defined as someone who had smoked or otherwise consumed cannabis, such as by eating THC-laced cookies, at least 100 times.) Taking several measurements over a three-year period, they consistently found that the frontal cortices of users were thicker than the cortices of nonusers. (Some studies have failed to detect these anomalies.) Jacobus noted that the unusual cortical thickness they measured may have occurred because marijuana was interfering with the normal pruning of synaptic connections that would thin the cortex.

Researchers at MGH also have identified structural differences in the brains even of young people who use the drug only occasionally. Neuroscientist Jodi Gilman of the MGH Center for Addiction Medicine led a 2014 study published in the Journal of Neuroscience that used MRI scans to map the brains of 20 college-age men and women who used marijuana at least once a week. By comparing scans of nonusers and pot users, Gilman and her colleagues (including researchers from Northwestern University) found that only the cannabis users had what she calls “indentations” in two parts of the brain: the nucleus accumbens, an important part of the brain’s “reward” system that contains the cannabinoid receptors stimulated by marijuana and other recreational drugs, which then produce pleasurable sensations; and the right amygdala, a brain region that helps process emotions.

Gilman and her colleagues at MGH are now administering cognitive tests (such as memorizing lists of words) to college-age marijuana users to gauge the possible impact of the structural abnormalities the researchers have detected. She recalls one study participant, a college senior who planned to attend medical school. “His memory seemed to be compromised,” Gilman says. “He performed below average on the cognitive testing. I found myself thinking, ‘This guy’s going to med school?’”

Gruber and her colleagues at McLean Hospital have recently linked structural and functional brain differences in people who began using pot at a young age with impulsive behavior. In a 2014 study, they used diffusion tensor imaging (DTI), which reveals fine details in the brain by tracking the movement of water molecules, to show that the myelinated nerve fibers that make up white matter form disorganized patterns in pot smokers who started at a young age. These same subjects took the Barratt Impulsiveness Scale, in which they rate how often they act in certain ways, such as “I do things without thinking” and “I make up my mind quickly.” A clear trend emerged among young users who started before age 16. “The less organized the white matter, the higher the impulsivity,” says Gruber—though she admits that the study can’t prove that the drug use caused the worrisome behavioral tendencies.

For a 2015 study published in Developmental Cognitive Neuroscience, Gruber performed functional MRI scans on the brains of heavy marijuana users and control subjects as they performed the Stroop Test, which seeks to measure subjects’ ability to inhibit inappropriate responses. Compared with nonusers, early pot smokers had “significantly different patterns of brain activation,” Gruber says. While performing the test, nonusers and those who had started using later showed the most activity in the forward part of the cingulate cortex, part of the brain’s limbic system. In early users, though, fMRI showed the heaviest activity in the rear part of the cingulate cortex, suggesting that their brains had been altered and used different regions to complete the test. Moreover, early users performed poorly on the test, suggesting a
reduced ability to inhibit inappropriate impulses.

Impulse control and making good decisions can be tough for all adolescents, whose brains aren’t yet fully wired, says Gruber. Adding recreational drugs or alcohol to the mix only heightens that challenge, she notes, and marijuana is the most popular illegal substance among adolescents.

Many researchers worry that the ranks of young cannabis users will swell as more states legalize marijuana, and the American Academy of Pediatrics opposes relaxing prohibitions on selling the drug. But proponents of legalization say some doctors and scientists overstate the case against marijuana. “As marijuana laws become less punitive, we see more of this Reefer Madness-style messaging,” says Jerry Otero, youth policy manager for the Drug Policy Alliance, an organization working to reform U.S. drug laws. The 1936 anti-marijuana film he references showed clean-cut young people who lose their minds and even their lives after being introduced to pot.

Searching for brain abnormalities in cannabis users “is kind of like phrenology,” says neurologist Joseph McSherry, of the University of Vermont College of Medicine, comparing the imaging studies of marijuana users with the discredited theory that personality traits could be discerned by feeling bumps on the skull. McSherry, who has written and testified in favor of medical cannabis, notes that several recent studies have failed to detect evidence that using cannabis causes odd activity or defects in the brain. For example, a 2015 MRI study in the Journal of Neuroscience comparing the brains of 50 adolescents who used the drug every day with those of nonusers found no significant differences. And last August, a study in JAMA Psychiatry compared the brains of pairs of siblings, roughly half of whom had used cannabis, and determined that any structural differences were explained by genetics, not exposure to the drug.

Gilman, the MGH neuroscientist who found indentations in the brains of young pot users, points out that the Journal of Neuroscience study lacked a healthy control group—all of the kids, including the nonusers, were referred from the juvenile justice system and many were heavy drinkers—and alcohol is known to be highly toxic to brain cells. The JAMA Psychiatry study, meanwhile, lumped frequent marijuana users with people who might have toked on a joint once at a party and never smoked again, which makes it difficult to gauge pot’s potential effect on their brains. “All studies have limitations, including ours,” says Gilman.

But most are in agreement that the biggest shortcoming of the existing research is that it can’t answer this question: If there are malformations or abnormal activity in the brains of young marijuana users, isn’t it possible that those problems preceded—and perhaps even triggered—the desire to get high?

Researchers around the United States will begin collecting data to help address that issue this year with the launch of the Adolescent Brain Cognitive Development (ABCD) Study, sponsored by NIDA, the National Institute on Alcohol Abuse and Alcoholism, and several other arms of the National Institutes of Health. ABCD investigators will recruit 10,000 nine- and 10-year-olds who haven’t yet used marijuana, alcohol, tobacco or other drugs, and follow them for a decade. The study will track cognitive skills and mental health and the factors that affect them, including substance use, school grades, peer behavior, sleep and other factors. Participants will undergo brain scans every other year.

ABCD will cost about $30 million a year, money well spent to learn more about the adolescent brain, insists NIDA’s Susan Weiss—especially if it provides answers about whether some young people are risking long-term harm for the sake of getting high. “This is a public health emergency,” says Weiss. “This is what keeps us up at night.”