

# The Teen Brain on Marijuana

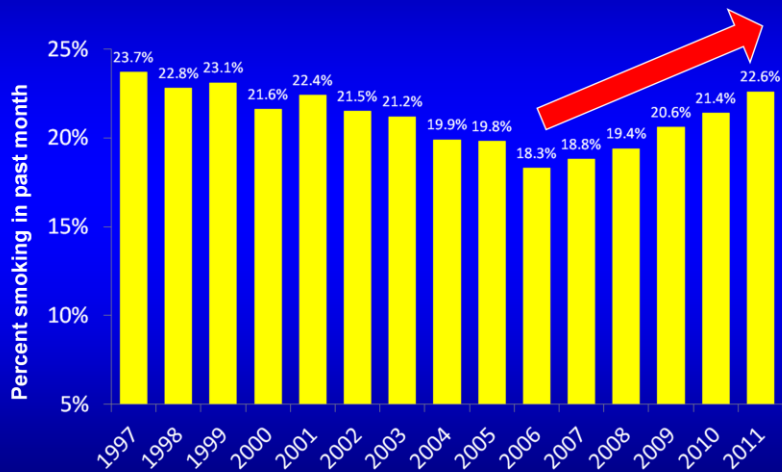


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This presentation was prepared by Sion Kim Harris, PhD, a research scientist with the Center for Adolescent Substance Abuse Research at Boston Children's Hospital, a teaching hospital of Harvard Medical School.

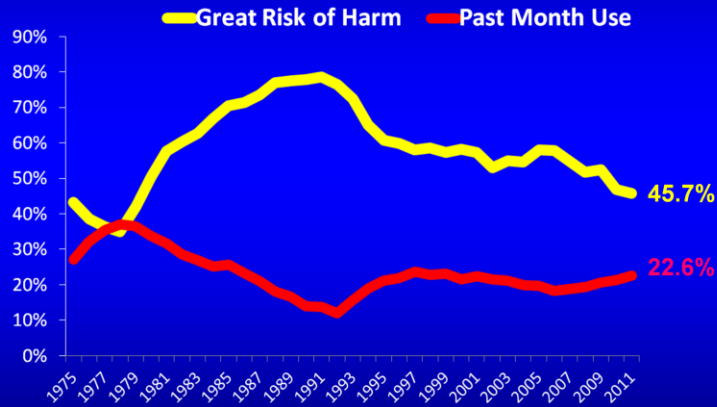
## Trend in Past-Month Marijuana Use among 12<sup>th</sup> graders in the US: 1997-2011



National Monitoring the Future Study, 1997-2011

After a decade of declines, marijuana use has started to go up among U.S. teens and is now more prevalent than tobacco use. Therefore, it is critical to understand the possible short- and long-term effects that marijuana smoking during the teen years could have.

## Perceived Risk of Harm and Marijuana Use, U.S. 12<sup>th</sup> graders: 1975-2011



National Monitoring the Future Study, 2011

This chart shows how marijuana use tends to rise and fall in an opposite, mirror-like fashion relative to how much teens perceive a risk of harm from using marijuana. Not surprisingly, the recent increases in marijuana use have been accompanied by a steady decline in the percent of teens who perceive a great risk of harm from regular marijuana use.

However, there is growing scientific evidence, particularly about how marijuana affects the teen brain, that indicates that marijuana use during the adolescent years may not be as benign as perceived by teens.

# How does marijuana work?

Let's start with the basics about how marijuana works in the brain.

## What is in Marijuana?

- Contains many chemicals called **cannabinoids** such as...
  - delta-9-tetrahydrocannabinol (THC)
  - delta-8-tetrahydrocannabinol
  - cannabidiol
  - cannabinol
  - cannabichromene
  - cannabigerol
  - Etc.

Source: Mechoulam R, Hanus L, The cannabinoid system from the point of view of a chemist. In *Marijuana and Madness*, ed. Castle, Murray, Cambridge University Press, 2004

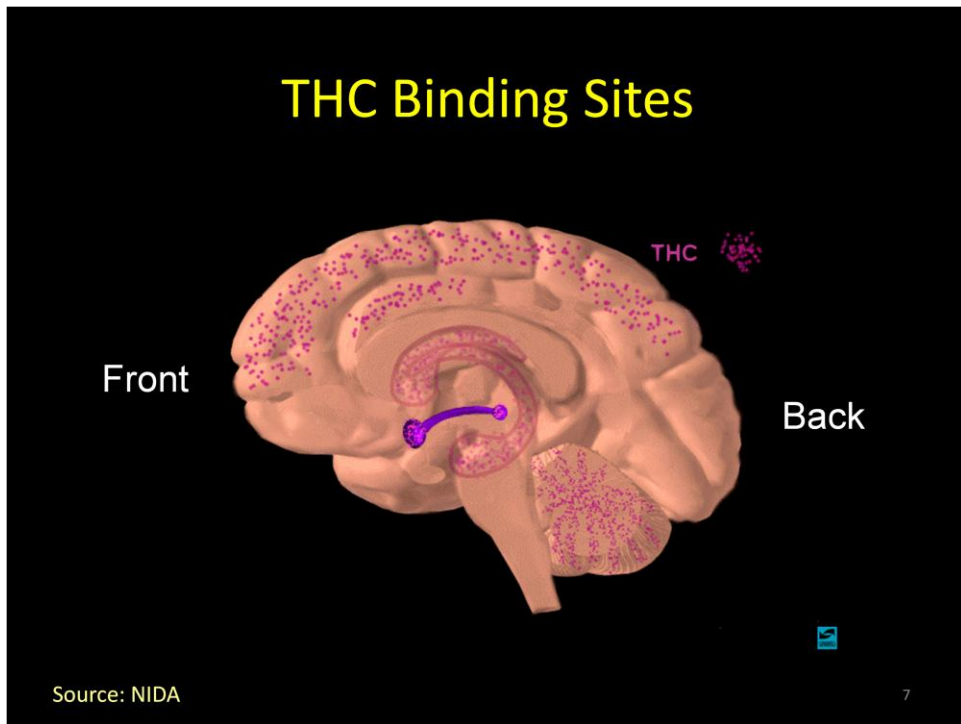
Scientists over the years have discovered that the marijuana plant contains hundreds of different chemicals which have been labeled “cannabinoids.” We don’t know what they all do yet because the focus of research to date has been on the chemical that was found to be the main cause of the psychoactive effects of marijuana.

## What is in Marijuana?

- The main psychoactive chemical is **delta-9-tetrahydrocannabinol** or “**THC**”
- Marijuana’s potency and effects depend on how much **THC** it contains

Source: Mechoulam R, Hanus L, The cannabinoid system from the point of view of a chemist. In *Marijuana and Madness*, ed. Castle, Murray, Cambridge University Press, 2004

The main psychoactive chemical in marijuana is called THC, and marijuana’s potency and effects depend on how much THC it contains.



The human brain is sensitive to marijuana because we are all born with “cannabinoid” receptors on our brain cells to which THC binds. These receptors were discovered when scientists were studying how marijuana worked in the brain. Other psychoactive drugs also bind to receptors in our brain, such as heroin (opioid receptors) and nicotine (nicotinoid receptors).

It turns out that cannabinoid receptors are one of the most common types of receptors in the brain. So far, we know there are two main types of cannabinoid receptors: CB1 receptors are located primarily in the brain, but they also are found in blood vessels and heart cells; CB2 receptors are primarily located outside of the brain, in the peripheral nervous system and glands. Since these receptors are so widespread throughout the brain and body, marijuana can have a widespread effect on the brain, heart, cardiovascular system, nervous system, reproductive system, and immune system.

This slide shows where cannabinoid receptor sites (shown as pink dots) have been found in the brain. They are plentiful in areas from the prefrontal cortex in the front of the brain, to the cerebellum (coordination) and visual center in the back of the brain, to the reward system, hippocampus (memory), hypothalamus (appetite, body temperature, emotions, digestion, etc.), and thalamus (receives and relays sensory information such as pain) in the middle of the brain.

# Cannabinoid receptors in our brains?

Why?

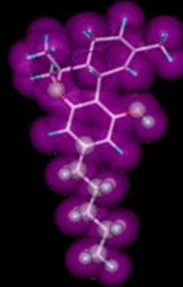
Why do we have cannabinoid receptors in our brain?



## Fooling the brain...

**Brain's Chemical**

**Drug**



**Anandamide**

**THC**

Source: NIDA

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First discovered in 1992, it turns out that our own brain produces some chemicals (called endocannabinoids) that bind to the cannabinoid receptors. One of these chemicals is called anandamide.

Essentially, THC and anandamide have some similarities in chemical structure which is why THC can “fool” the brain by binding to the same receptors that anandamide does. What does anandamide do?

# The Brain's “Endocannabinoid” System

“Endo” = prefix meaning “within” or “inside”

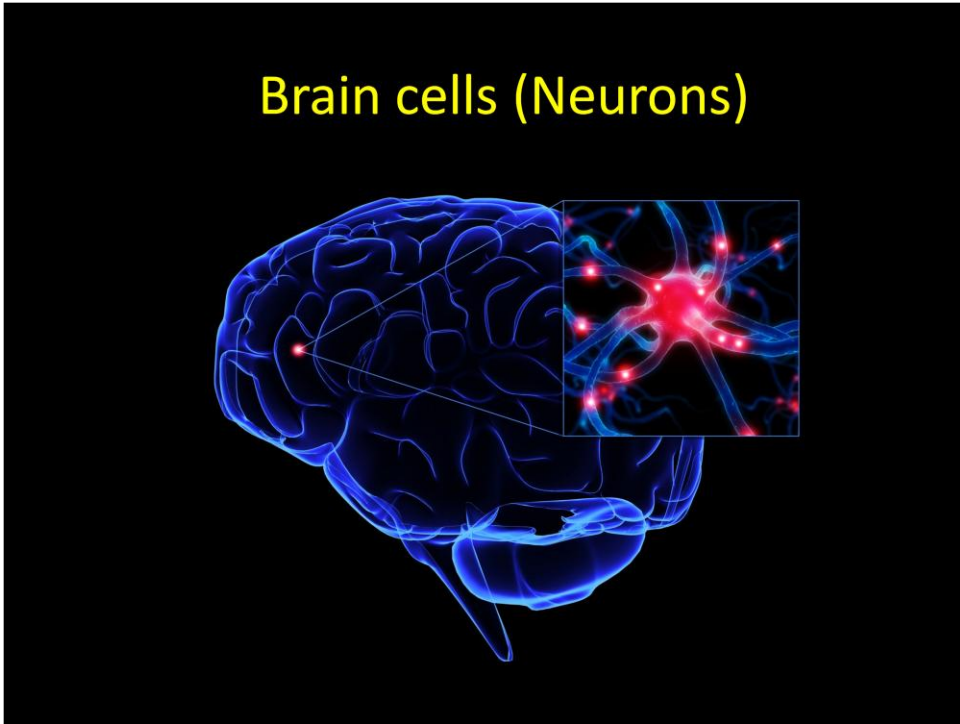
Anandamide, along with the cannabinoid receptors, is part of what is now called the brain's “endocannabinoid system”. “Endo” refers to something from within our own brain, like “endorphins.”

In recent years, there has been a tremendous amount of research to understand what the endocannabinoid system does in our brain.

## A ridiculously brief guide to how the brain works...

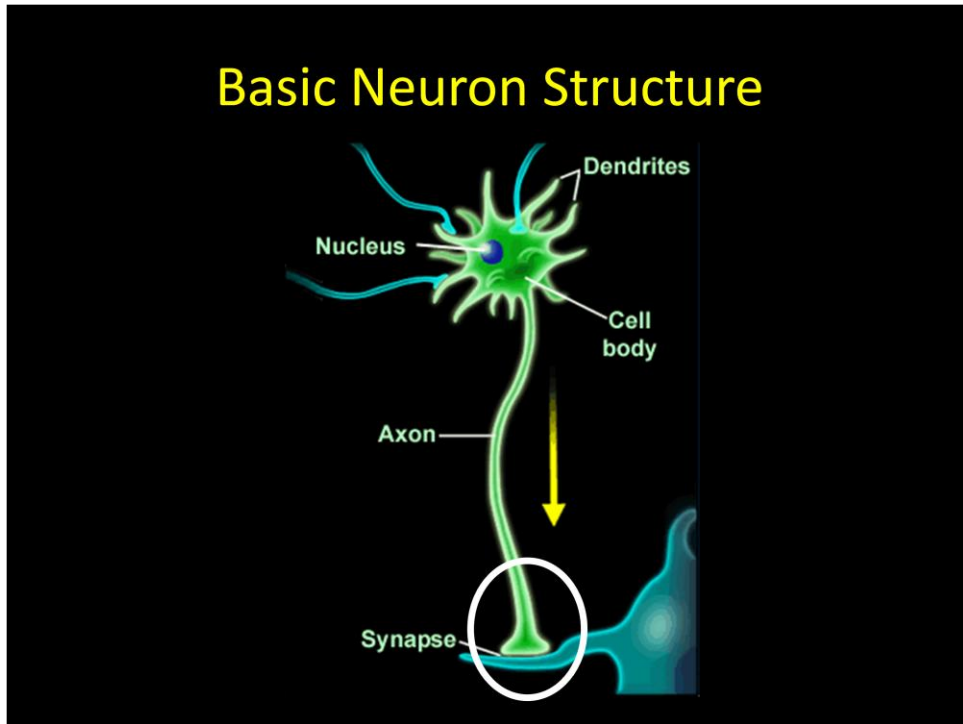
To understand what the brain's endocannabinoid system does, we have to first explain a bit about how the brain works.

## Brain cells (Neurons)



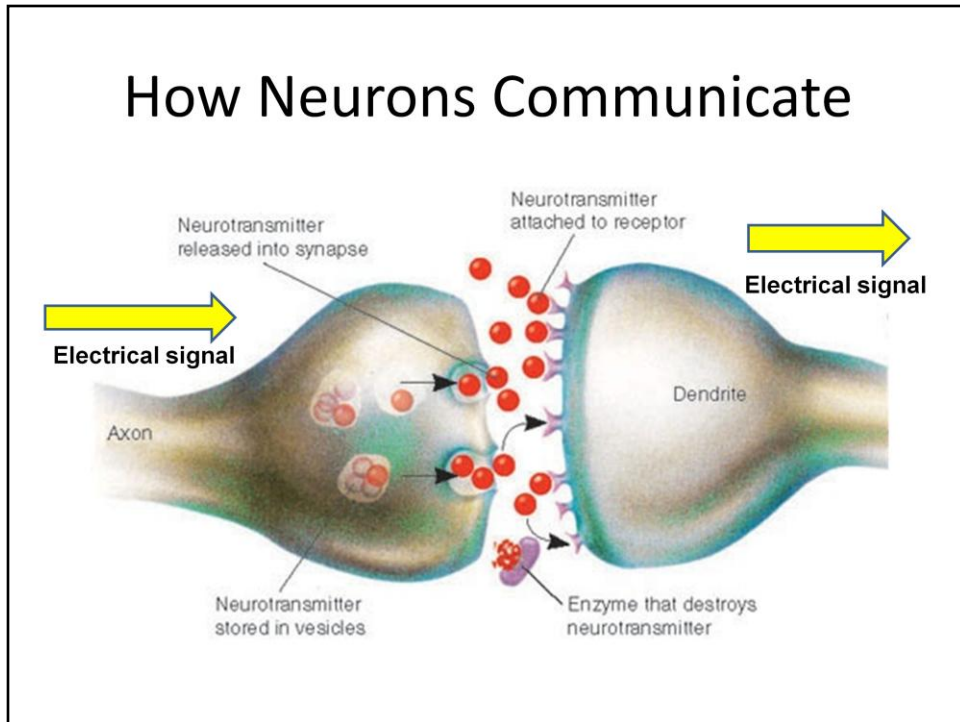
We are able to think, move, sense, feel etc. because of the activity and interaction of neurons in our brains. A typical adult brain has over 100 billion neurons.

## Basic Neuron Structure



Each neuron has a cell body (nucleus) with spiky projections (dendrites) and a long stem (axon) which extends out to connect to other neurons so information can pass from one neuron to the next. One neuron joins to another and communicates with it through synapses. See next slide for a magnified image of the synapse and how it works.

# How Neurons Communicate



If you magnify a single synapse, you'll see that neurons don't actually touch each other. There is a fluid-filled space through which cells send chemical signals, called neurotransmitters, which help one cell (the "sending" neuron) tell the next cell ("receiving" neuron) what to do. These neurotransmitters are stored in pouches on the sending cell. When an electrical signal comes down the axon of the sending cell, that signal makes the cell dump a certain amount of a neurotransmitter into the synaptic space. The neurotransmitter molecules then flow across to become "docked" on receptor sites on the next neuron, like a key fitting into a lock, which causes the receiving neuron to then send an electrical signal to the next neuron, and so on. Some neurotransmitters *excite* the receiving neuron to send electrical signals more often, and some *inhibit* the receiving neuron so that it sends signals more slowly or not at all.

When the electrical signal ends, the neurotransmitter is quickly cleared out of the synaptic space so that the receiving neuron doesn't keep being stimulated.

It turns out that one of the major functions of the brain's own endocannabinoid system is to regulate how active neurons are and how much neurotransmitter they release.

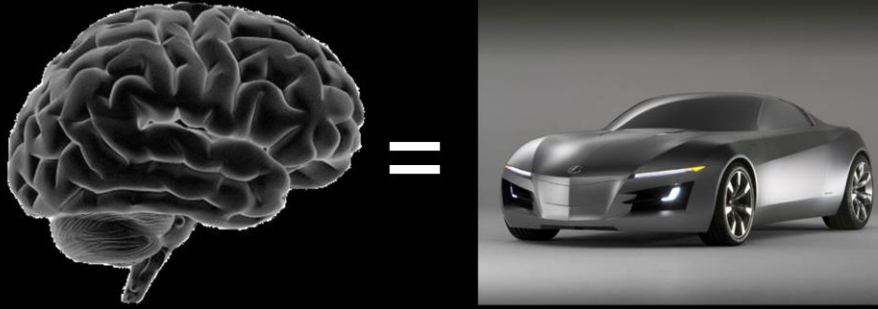
## Endocannabinoid System Functions

- The neuron's "volume control": dampens down neuron activity when too strong
- Regulates levels of important neurotransmitters affecting pleasure, mood, pain, appetite, motivation, memory, etc. (dopamine, serotonin, endorphins)
- Helps keep neuron activity in balance, not underactive or overactive

The endocannabinoid system acts like the brain cell's volume control dial. If the volume or signal coming from one neuron gets too loud, the receiving neuron says "whoa there!" and sends anandamide backwards through the synapse to turn the volume down on that sending neuron.

So, the brain's endocannabinoid system helps to regulate (monitor and control) how active neurons are, and how much neurotransmitter gets released, including neurotransmitters that affect pleasure, mood, pain, appetite, motivation, memory, muscle activity, etc. (e.g., dopamine, serotonin, endorphins). Therefore, the endocannabinoid system helps to keep brain cell activity in BALANCE, not underactive (like in depression or ADHD) or overactive (like in epilepsy or post-traumatic stress disorder).

A healthy brain is a finely-tuned instrument...



To use an analogy that a teen might appreciate, a healthy brain is like a high performance race car. It's a finely-tuned, sensitive instrument which you don't want overheating or getting slow from too much gunk in the engine.



## Endocannabinoid System Part 2

- Shapes brain development by...
  - guiding neurons to grow to the right places in the brain for correct function
  - controlling neuron activity, thereby affecting brain wiring (“neurons that fire together, wire together”)
  - supporting myelin growth on neurons

Source: Galve-Roperh I, Palazuelos J, Aguado T, Guzman M. Eur Arch Psychiatry Clin Neurosci. 2009;259:371-382.

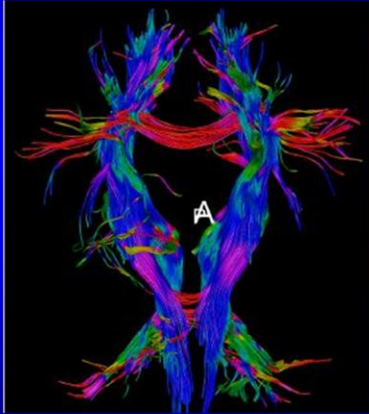
We are also learning more and more about how important the endocannabinoid system is in BRAIN DEVELOPMENT.

The endocannabinoid system is already present in the fetal brain and has been found to help guide neuron growth so that they get to the right places in the brain for correct function.

Also, because it helps to control neuron activity, it plays a major role in brain wiring – that is, how brain cells “learn” whether to grow new synapses and connections to other neurons. The more active neurons are, the stronger their connections get (neurons that fire together, wire together). The less active neurons are, the weaker their connections get, or the more they lose connections altogether.

Finally, the endocannabinoid system appears to play a role in the MYELINATION of brain cells. After neurons grow to a certain point, myelin, a fatty white substance, starts to wrap the long axons of neurons. This myelin sheathing on neurons acts like insulation on an electrical wire, helping the electrical signal pass down the axon more quickly and efficiently, therefore making communication across the brain more efficient.

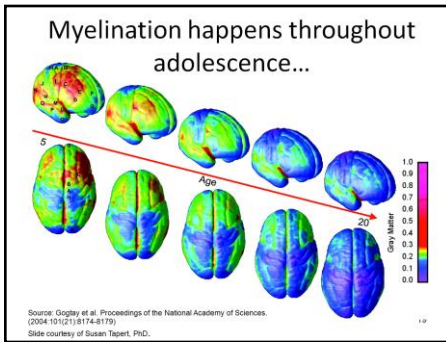
## The Brain's Information Superhighway: Myelin = White Matter Tracts



Source: Gordon J. Harris, PhD.

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The picture on the left shows an actual human brain scan from researchers at Mass General Hospital showing just the myelinated neuron fibers connecting the front and back of the brain and the two hemispheres. These are called “white matter tracts” because of the myelin sheathing. These long “white matter tracts” could be thought of as the brain’s “Information Superhighway” which carries information across different parts of the brain (like an interstate highway system) so that we can carry out complex functions which involve multiple brain areas.



We now know that myelination, and therefore brain maturation, is not complete until the mid-20's. This chart shows 3-D reconstructed MRI images of the human brain across different ages (age 5 on the far left to age 20 on the far right). The more BLUE or PURPLE the brain is, the more the "gray matter" in the brain (unmyelinated neurons) has been taken over by "white matter" (myelinated neurons). As you can see, myelination occurs throughout adolescence, particularly in the front and side of the brain.

So, proper endocannabinoid system function is important for neuron growth, activity, and connectivity, and therefore, for developing a brain that is efficient, balanced, and integrated.

## THC vs. Anandamide

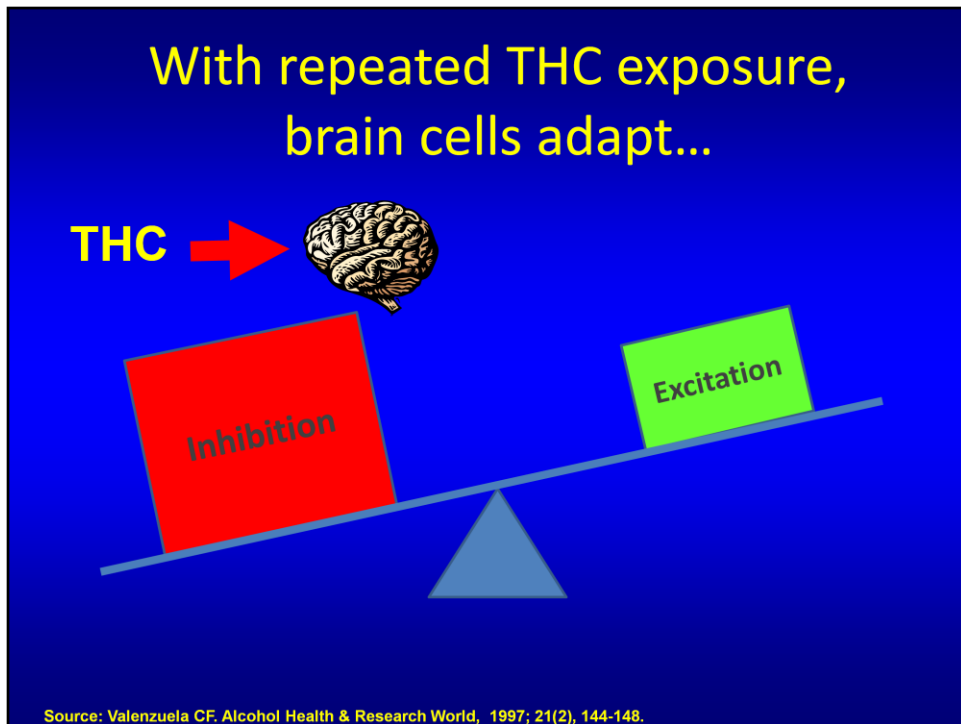
- Both dial down neuron activity to change neurotransmitter release
- THC has a **MUCH STRONGER, LONGER** effect than anandamide on brain cells
- THC interferes with anandamide function, **so it can't do its job to protect and balance cell activity**

So, how does THC compare to anandamide, the chemical which our own brain makes?

Well, both THC and anandamide dial down neuron activity, thereby changing the amount of neurotransmitters released.

However, when THC binds to our cannabinoid receptors, it has a MUCH STRONGER, LONGER effect on brain cell activity than anandamide. THC's effect is like a sledgehammer compared to the precision scalpel of anandamide.

By occupying those cannabinoid receptors, THC interferes with anandamide's ability to naturally protect and balance cell activity.

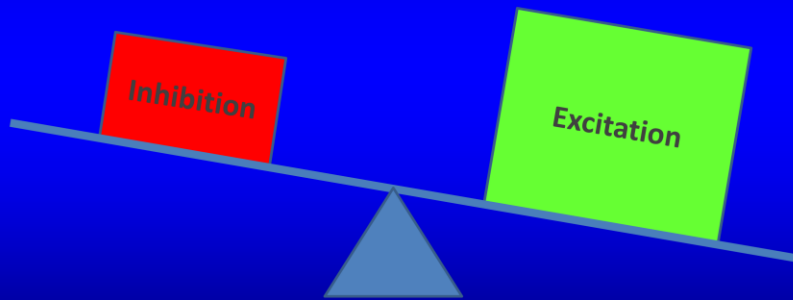


With repeated THC exposure, brain cells start to adapt.

As mentioned before, a balance between inhibition and excitation of neuron activity is important for proper brain functioning. Because THC changes the levels of neurotransmitters in the brain, brain cells that get overstimulated by the effects of THC start to compensate by scaling back the number of receptors (this is why you get “tolerance” after repeated use of a substance, and this happens with all types of substance use).

On the other hand, repeated THC exposure continually dampens down the activity of many brain cells, causing there to be too much INHIBITION.

Chronic inhibition causes brain to increase excitation to compensate...



Source: Valenzuela CF, Alcohol and neurotransmitter actions. Alcohol Health & Research World, 1997; 21(2), 144-148.

In response to this imbalance, the brain tries to compensate by making some cells MORE excitable. When a regular marijuana smoker does not smoke, the inhibitory effect of THC is not there, leaving some parts of the brain with too much excitation. This is why we see marijuana withdrawal symptoms like... (next slide)

## Marijuana Withdrawal Symptoms

- Restlessness, anxiety
- Increased irritability, anger, aggression
- Difficulty falling and staying asleep, nightmares/strange dreams
- Decreased appetite
- Weight loss

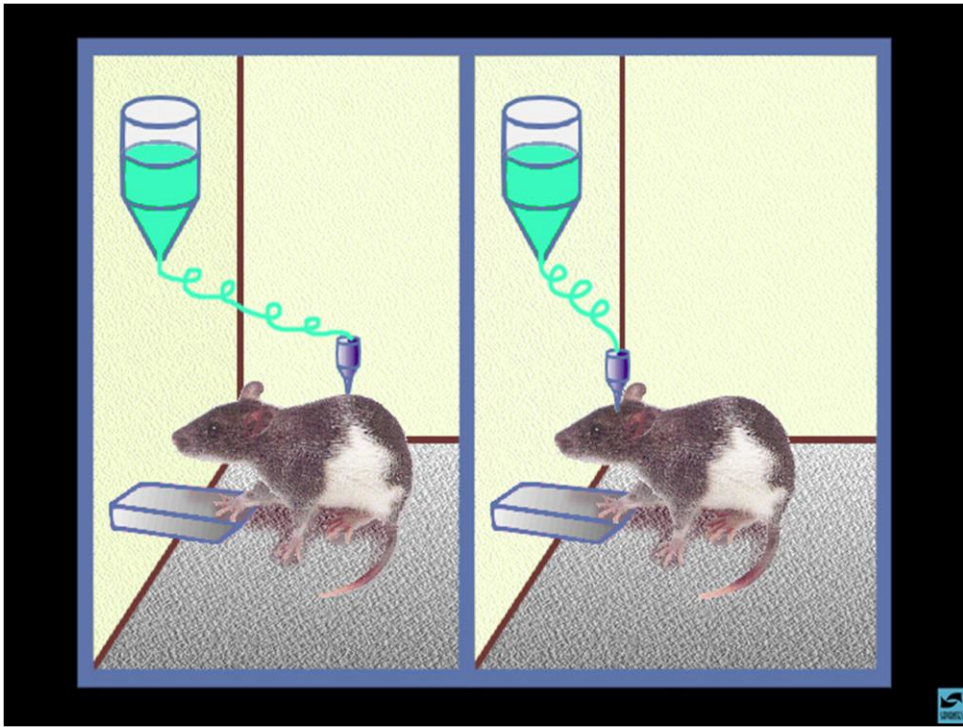
Source: Budney et al. Arch Gen Psych 58(10):917-924, 2001.

...restlessness, anxiety, increased sensitivity or reactivity, difficulty falling and staying asleep, etc. These withdrawal symptoms may not be as dramatic as what is seen for opiate or alcohol withdrawal where people have physical pain, nausea, sweating, cramps, etc. However, people in marijuana withdrawal do report substantial distress over symptoms, particularly with difficulty sleeping, making it hard to quit.

# Is marijuana addictive?

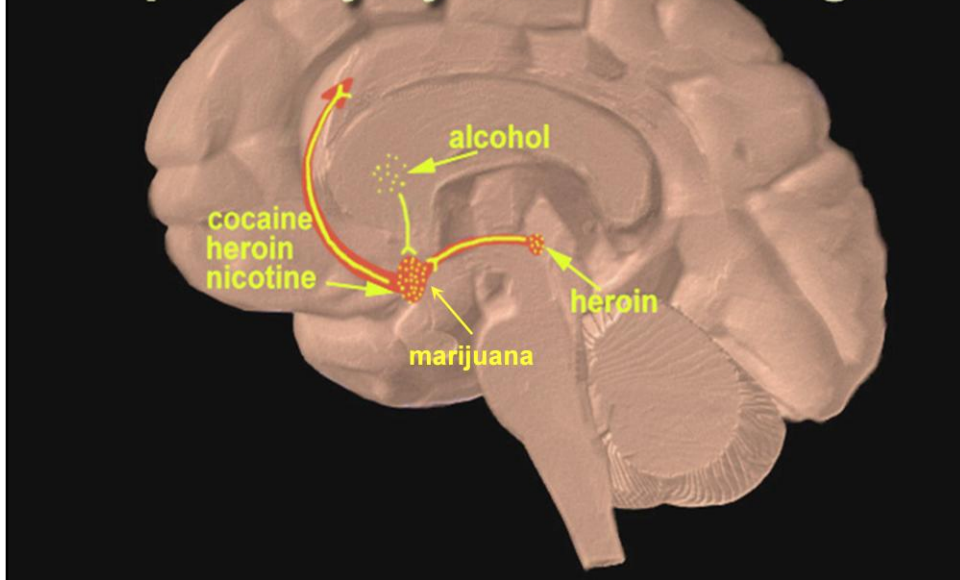
Many people today believe that marijuana is not addictive. Let's look at the science...





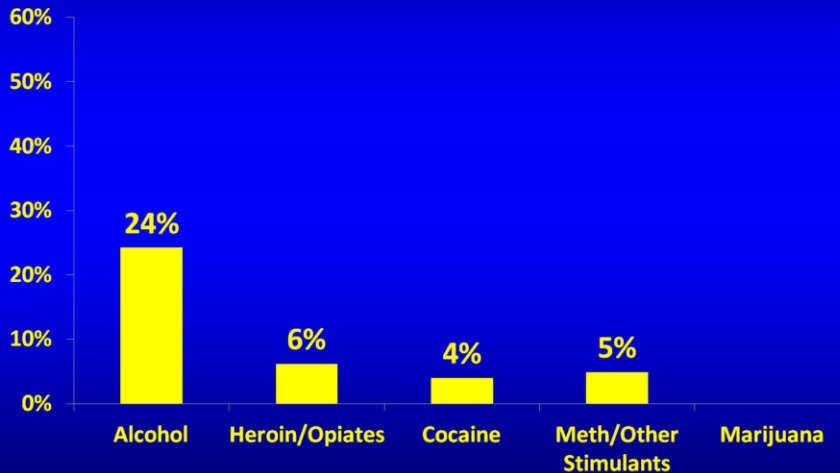
One way that scientists examine whether a substance is potentially addictive is to see if research animals given free access to it will continually self-administer it. In rat experiments, rats were found to self-administer THC doses repeatedly, just as they do other addictive substances like cocaine, heroin, and nicotine.

## Activation of the reward pathway by addictive drugs



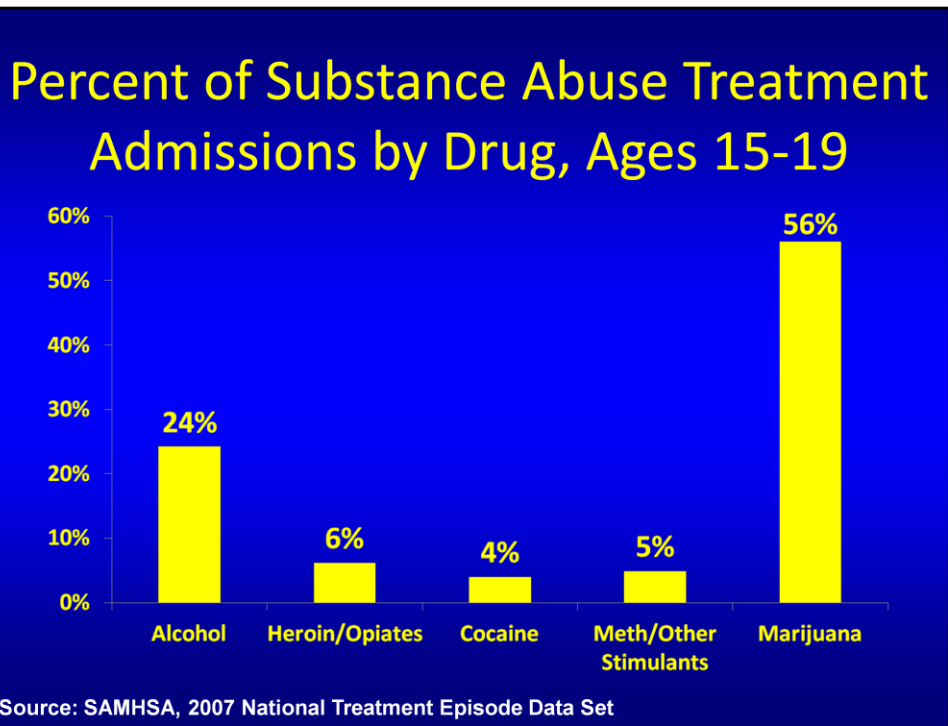
Also, THC has been found to increase dopamine release in the “reward” or pleasure circuit of the brain, just like every other addictive drug. The brain’s reward circuit evolved to motivate us to engage in behaviors that helped our species survive, such as eating, sex, and social connection. Addictive drugs strongly stimulate this reward circuit, giving a “counterfeit” pleasure.

## Percent of Substance Abuse Treatment Admissions by Drug, Ages 15-19



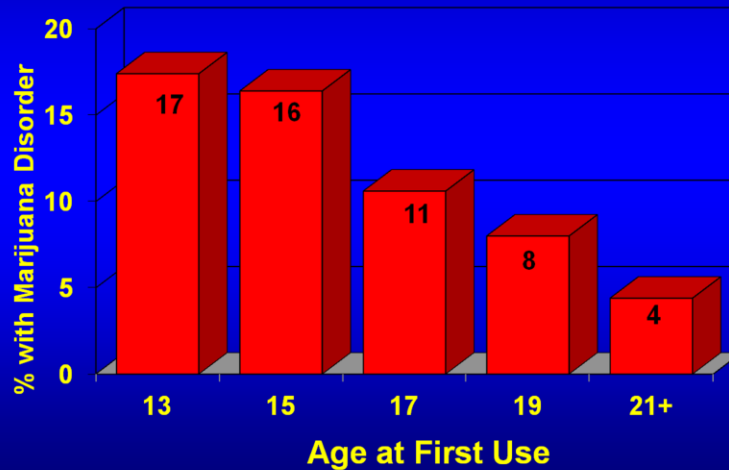
Source: SAMHSA, 2007 National Treatment Episode Data Set

When looking nationally at statistics on why adolescents go into treatment for substance abuse problems, compared to alcohol, heroin, cocaine, etc., substances that everyone agrees are addictive, ....



... marijuana accounts for more teens in substance abuse treatment than any of the other substances combined.

## Younger Age at First Use Has Higher Risk of Marijuana Dependence

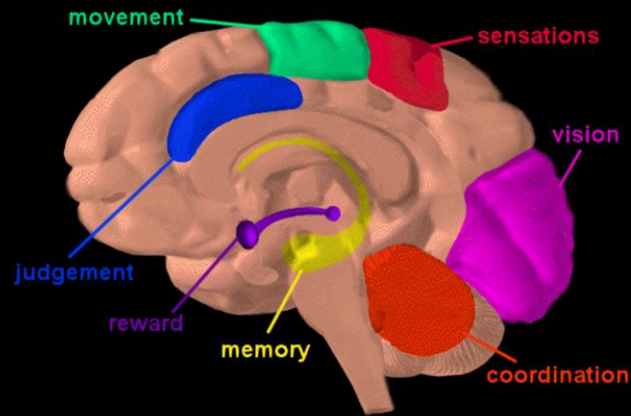


Source: Substance Abuse and Mental Health Services Administration. (2010). *Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings* (Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4586Findings). Rockville, MD.

We now know that adolescent brains are different from adult brains. That is, their brains are still developing, and are more “plastic” and adapt and learn faster than adults. Does this make teens more vulnerable to developing an addiction than adults?

On this bar chart, the percentage of people developing marijuana dependence is shown by their age of first use. As you can see, the risk of marijuana dependence among those who started use before age 16 was over four times the risk (17% vs. 4%) as those starting after 21 (after the brain has mostly matured). That’s 1 in 6 teens who ever smoke marijuana develop addiction 3 out of 4 people in treatment for marijuana dependence (adult or teen) started using marijuana before age 17.

## What else is affected by THC?

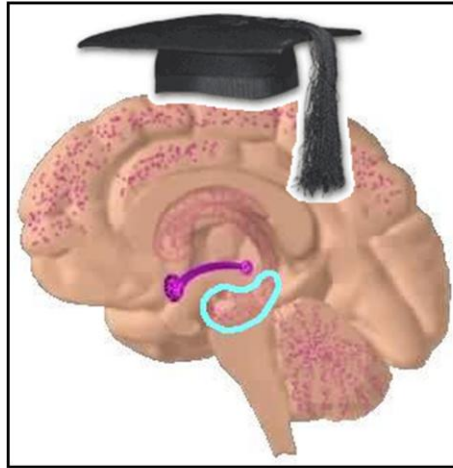


Source: NIDA

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So, what else is affected by marijuana? This slide shows the various areas of the brain that have a lot of cannabinoid receptors and what those brain areas help us to do.

# Hippocampus



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One area of the brain that is particularly sensitive to THC is the hippocampus which is highlighted with a light blue outline on this slide.

The hippocampus is critical for memory formation and retrieval. It is also important for sleep regulation, and for calming down our stress response. The hippocampus develops throughout adolescence, and is one of the few areas in the brain where new brain cells are generated throughout our lives.

## THC and Memory

- THC reduces hippocampal neuron activation, below the level needed to trigger memory formation
- With chronic THC exposure, neuron connections involved in memory **are gradually lost** due to continual suppression
- Brain imaging studies show regular THC users have a smaller hippocampus, and have poorer memory

Source: Iversen L. How cannabis works in the brain. In *Marijuana and Madness*. Ed. Castle & Murray, 2004. Oxford University Press.

One well known effect of marijuana use is memory impairment. Scientists have found that THC dampens down the activity of hippocampal neurons, below the level needed to trigger the formation of a memory.

With chronic THC exposure, and therefore, continual suppression of hippocampal neuron activity, the neurons start to lose connections to other neurons, making it harder to form and retrieve memories.

Brain imaging studies have found that regular marijuana users actually have, on average, smaller hippocampuses than non-users, and poorer memory performance. While we all tend to lose neurons in the hippocampus as we age (which explains why we have a harder time remembering and learning things as we get older), chronic THC exposure will speed up this process. Scientists found that young rats exposed daily to THC for 8 months showed the same level of hippocampal cell loss as unexposed rats twice their age (Source: Marijuana Abuse, NIDA Research Report Series, 2010).



**PNAS**

## Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier<sup>a,b,1</sup>, Avshalom Caspi<sup>a,b,c,d,e</sup>, Antony Ambler<sup>e,f</sup>, HonaLee Harrington<sup>b,c,d</sup>, Renate Houts<sup>b,c,d</sup>, Richard S. E. Keefe<sup>d</sup>, Kay McDonald<sup>d</sup>, Aimee Ward<sup>d</sup>, Richie Poulton<sup>f</sup>, and Terrie E. Moffitt<sup>a,b,c,d,e</sup>

<sup>a</sup>Duke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, <sup>b</sup>Department of Psychology and Neuroscience, and <sup>1</sup>Institute for Genome Sciences and Policy, Duke University, Durham, NC 27708; <sup>c</sup>Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; <sup>e</sup>Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and <sup>f</sup>Dunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand

**Source: Meier et al. Proceedings of the National Academy of Sciences. 2012 Oct 2;109(40):E2657-64**

A limitation of many of the human brain imaging studies is that, because they compared marijuana users and non-users at one point in time, we can't tell whether the differences found were caused by the marijuana use, or were already present before people started to use marijuana.

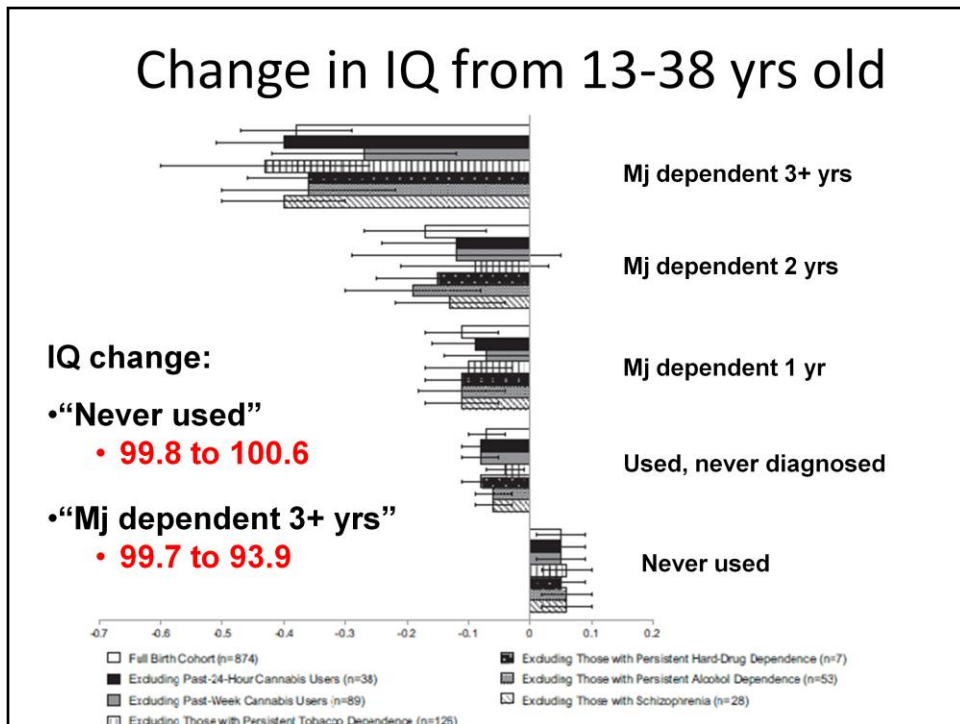
This paper was just published in the Proceedings of the National Academy of Sciences describing the results of a remarkable prospective study examining the effects of marijuana use on cognitive performance over many years.

# The Dunedin Study (New Zealand) (N=1,037)



Source: Meier et al. PNAS, 2012

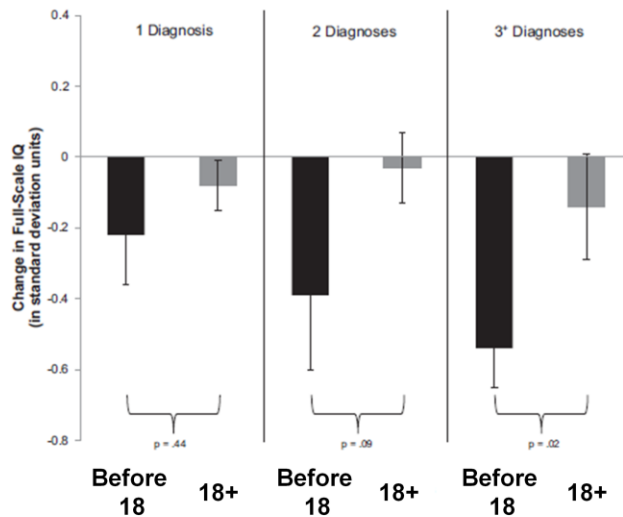
This study conducted in New Zealand followed almost 1000 participants from age 3 to 38. At age 13, before the vast majority had started marijuana use (only 7 had ever tried it by age 13), all participants completed a comprehensive neuropsychological assessment battery which included an IQ test, tests of executive functioning, memory, processing speed, and others. Participants completed this same battery when they were 38 years old. Marijuana use information was collected at all of the assessment timepoints. The authors were then able to determine how marijuana use affected neuropsych performance by comparing the change in individuals' scores between ages 13 and 38 across different levels of marijuana use.



Here is what they found. This chart shows the change in IQ scores as represented by the change in standard deviation units as a function of years of heavy marijuana use. Positive numbers represent an increase in IQ scores, while negative numbers indicate a decrease. The authors report finding a significant relationship between years of marijuana dependence and change in IQ scores between ages 13 and 38, from almost no change for participants who had never used marijuana, (from average IQ score 99.8 at 13 to 100.6 at 38), to a drop of nearly 6 points (99.7 to 93.9) among those who were marijuana dependent at 3 or more of the 5 assessment timepoints.

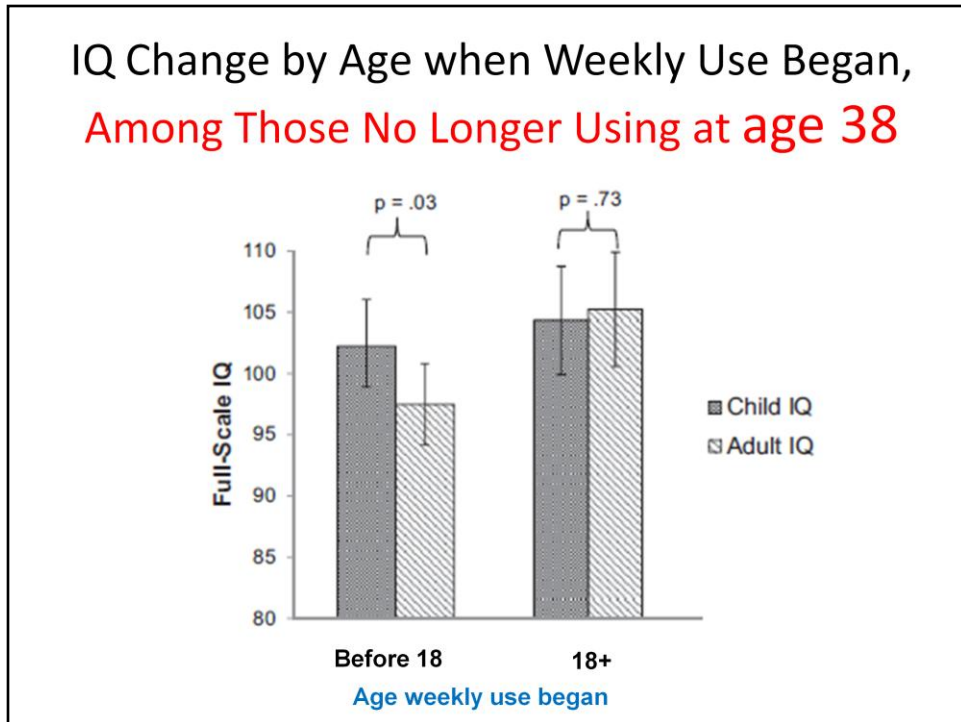
They found this same pattern even after they controlled for potential confounding factors such as alcohol, tobacco, and other drug use, as well as mental illness, and years of education.

## IQ Change by Age when Marijuana Dependence Started



They then looked at how IQ changed depending on the age at which marijuana dependence started. They found that among those with 2 or more years of dependence, those who started before age 18 tended to have bigger drops in IQ than those who had started being dependent AFTER age 18.

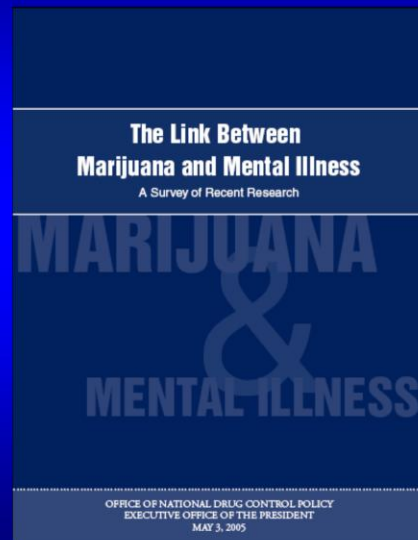
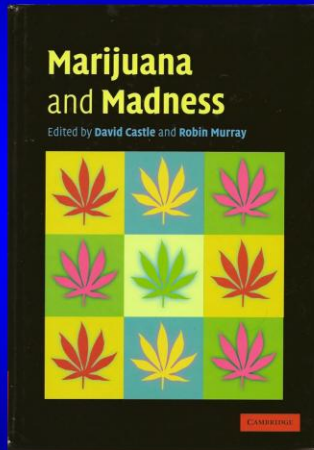
## IQ Change by Age when Weekly Use Began, Among Those No Longer Using at age 38



Another important finding is that among those who had quit using marijuana by age 38, those who had started using weekly *before* age 18 still showed a significant drop in their IQ scores, while those who had started *after* age 18 showed no difference.

This study shows that regular marijuana use among adolescents under age 18, when the brain is undergoing critical development, can have lifelong effects, even when marijuana use is stopped in adulthood.

# Marijuana and Mental Illness



Besides the evidence showing that marijuana affects memory and cognitive performance, there is a growing body of evidence suggesting that marijuana may increase risk for mental illness. The two reports shown on this slide summarize the results of over three decades of research studies showing this link between marijuana and later mental illness.

Regular marijuana use during adolescence found to increase risk 2 to 5 times of developing **psychosis, schizophrenia, anxiety, and depression** in adulthood.



Source: Malone DT et al. Adolescent cannabis use and psychosis: epidemiology and neurodevelopmental models. *Brit J Pharmacol.* 2010;160:511-522 39

Several of these studies followed individuals from childhood (ages 6 or younger), before marijuana use began, all the way into their late 20's. So, they were able to determine whether symptoms of mental illness were present BEFORE marijuana use initiation, and perhaps contributed to individuals becoming marijuana users.

Even after controlling for the confounding effect of mental illness symptoms preceding marijuana use, these studies showed an increased risk of developing schizophrenia or mood disorders (depression, anxiety) in adulthood if individuals regularly smoked marijuana during adolescence. The risk was particularly heightened if there was any family history of mental illness (i.e., "genetics provided the loaded gun and marijuana pulled the trigger"). Also, mental illness, among those at risk, tended to show up earlier with marijuana use.

Why would marijuana use increase the risk for mental disorders?

# White Matter Tracts: The Brain's Information Superhighway



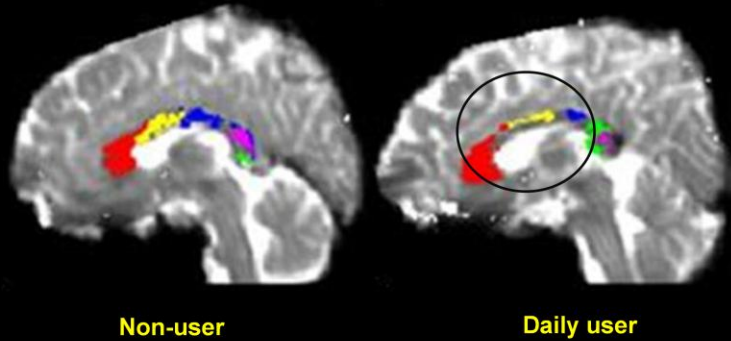
Source: Gordon J. Harris, PhD.

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Remember those white matter tracts and how myelination happens throughout adolescence? There are clues emerging from recent brain imaging studies that suggest that alterations in white matter development among regular marijuana users may be one contributing factor to the increased risk for mental illness.



## White matter structure differences between marijuana users and non-users

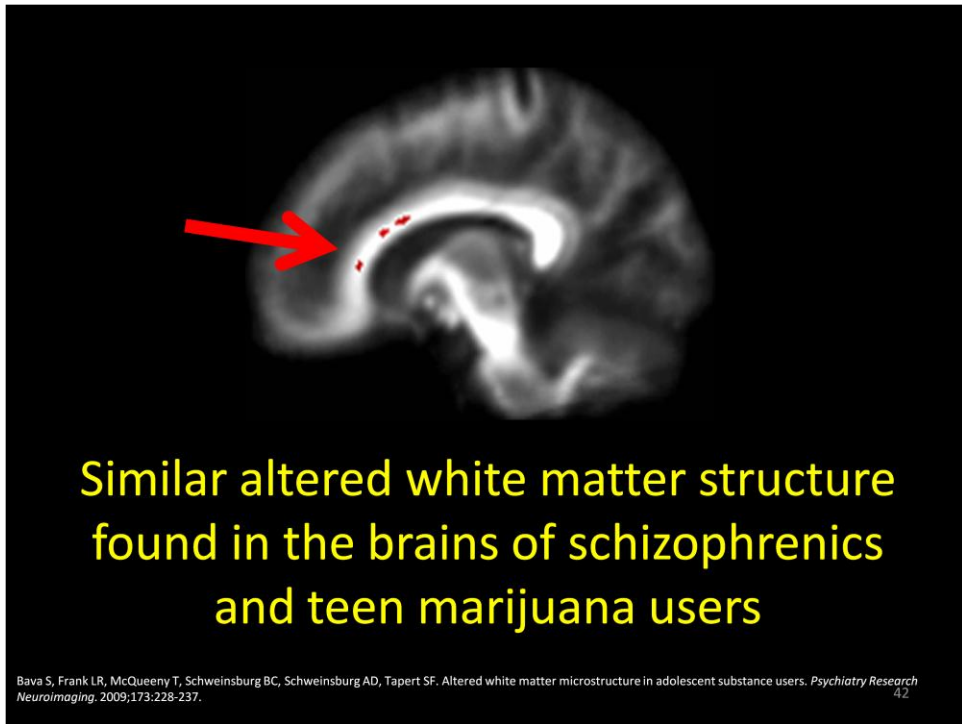


Source: Arnone D, Barrick TR, Chengappa S et al. Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. *NeuroImage*, 2008; 41:1067-1074

This slide shows the results of one such study. These are MRI scans of the corpus callosum, the bundle of fibers connecting the two brain hemispheres, allowing the two hemispheres to communicate and work in a coordinated way. Young adult males who smoked marijuana daily (and started at an average age of 15 yrs) were scanned along with age-matched non-users. All had low levels of alcohol use.

The different regions of the corpus callosum fibers are shown in bright colors on these two scans. The circled area on the scan of the daily user (right) shows thinner corpus callosum fibers than the scan of the non-user (left), indicating that there are white matter integrity issues for the daily user.

Poorer communication across different parts of the brain that need to work together for proper cognitive function may be one cause of cognitive disorders such as schizophrenia.

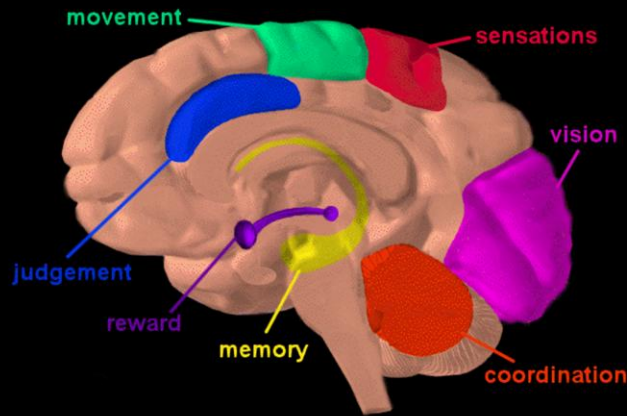


And indeed, imaging studies are finding that there are similar white matter problems in the brains of people with schizophrenia and of regular marijuana users who started using in adolescence. For example, this image is from another study which found white matter alterations in the fibers linking the prefrontal regions of the two hemispheres.

# Marijuana and Driving

A common belief about marijuana is that it does not impair driving. Again, let's look at the science...

## What else is affected by THC?



Source: NIDA

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Referring back to the slide that shows where cannabinoid receptors are in the brain, you can see that vision, coordination, judgement, movement, memory are all affected by THC. These are all, of course, important for driving.

## Marijuana and Driving

Studies of performance show that THC impairs attention, working memory, coordination, reaction time, and visual perception



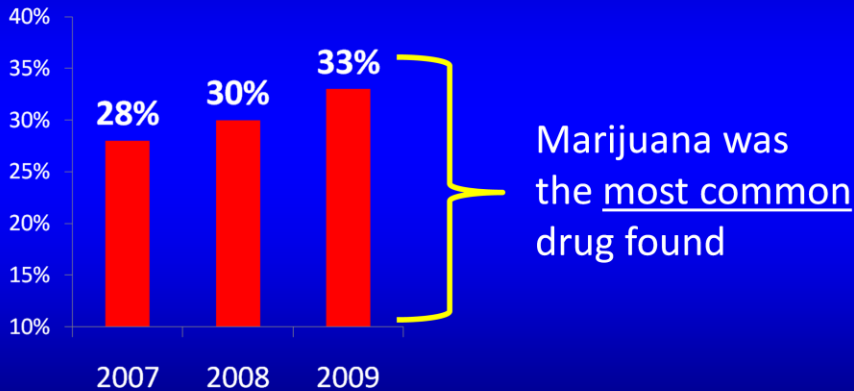
Source: Castle D, Solowij N. Acute and subacute psychomimetic effects of cannabis in humans. In: Castle D, Murray R, eds. *Marijuana and Madness*. Cambridge, UK: Cambridge University Press; 2004:41-53.

45

When researchers tested people's performance during acute THC intoxication, they tended to find that THC did impair attention, working memory, coordination, reaction time, and visual perception.

# Marijuana and Traffic Fatalities

## Percent of Fatally-Injured Drivers Tested who were Drug-Positive



Adapted by CESAR from National Highway Traffic Safety Administration (NHTSA), "Drug Involvement of Fatally Injured Drivers," *Traffic Safety Facts*, November 2010. Available online at <http://www-nrd.nhtsa.dot.gov/Pubs/811415.pdf>.

Recent national statistics show that, among fatally-injured drivers who were randomly selected for drug-testing (excluding tobacco, alcohol, and medications administered after the crash), more and more are testing positive. In 2009, the rate of positive tests had increased to 1 in 3.

Among positive tests, [CLICK] marijuana was the most common drug found.

One caveat about marijuana is that the driver may not have been acutely intoxicated at the time of the crash because marijuana takes longer to excrete from the body than other drugs. Also, the driver may also have been using alcohol or other drugs in addition to marijuana. However, a recent review<sup>1</sup> of the studies to date on the relationship between marijuana use and motor vehicle crashes found a generally consistent increased risk (more than double) of crash involvement for marijuana users, even after controlling for alcohol and other drug use. Also, this risk went up in a dose-dependent way with the amount and frequency of marijuana use.

<sup>1</sup> Li M-C, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. Marijuana use and motor vehicle crashes. *Epidemiologic Reviews*. 2012. 34:65-72.

## Growth and Fertility

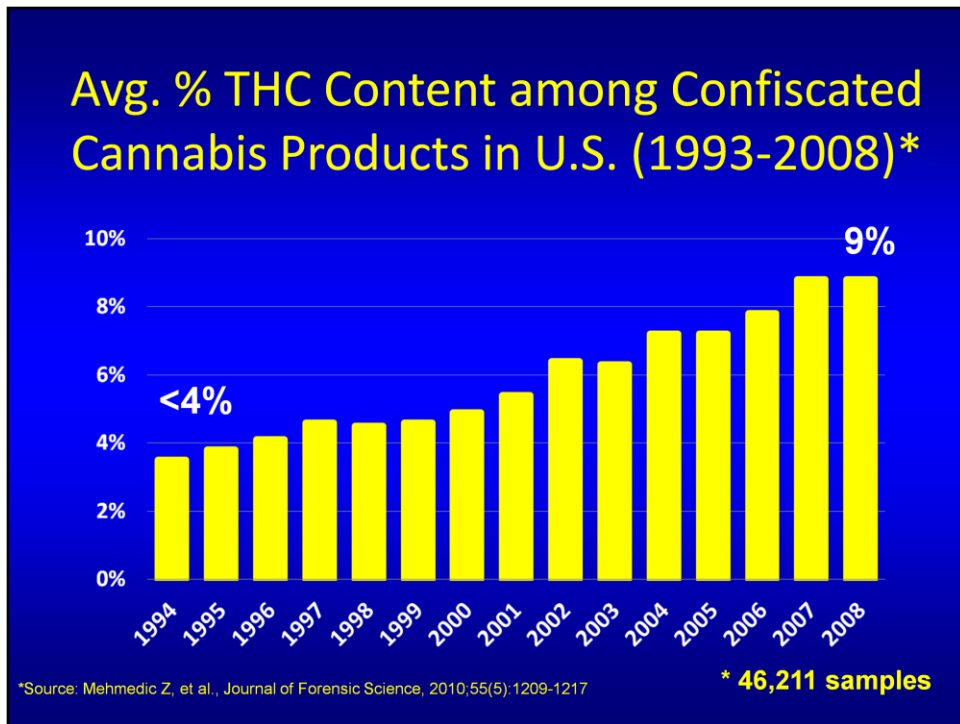
- Marijuana affects glands, organs and hormones involved in overall growth, pubertal development, and energy levels
- People who used regularly before 16 had shorter height
- Possible increased risk for testicular cancer



Source: Wenger T, Croix D, Tramu G. The effect of chronic prepubertal administration of marijuana (delta-9-tetrahydrocannabinol) on the onset of puberty and the post-pubertal reproductive functions in female rats. *Biology of Reproduction*. 1988;39:540-545.; Trabert B, Sigurdson AJ, Sweeney AM et al. Marijuana use and testicular germ cell tumors. *Cancer*. 2011 Feb 15;117(4):848-53.

Finally, because there are cannabinoid receptors in brain areas and glands and organs (testes, uterus) throughout the body involved in growth, pubertal development, fertility, and reproductive hormones, marijuana use can affect all of these things.

Recent studies have found that regular marijuana before the age of 16 is associated with shorter height, and daily use may elevate risk for testicular cancer for males.



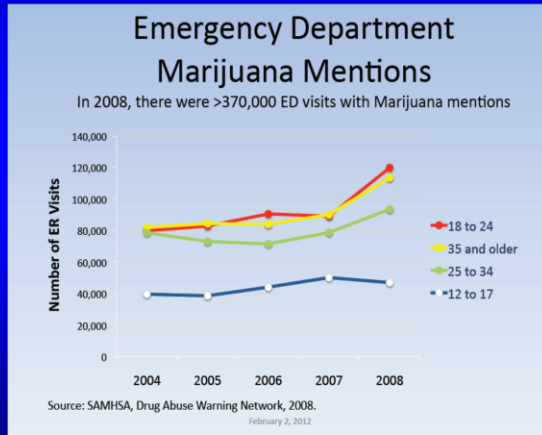
It is important to know that the marijuana of today is, on average, a lot more potent than it was 20 years ago.

This chart shows the average THC content of thousands of samples of marijuana products confiscated each year in the US. From 1993 to 2008, the average THC potency of marijuana available in the USA more than doubled from less than 4% to about 9%. Some samples tested in 2007 were found to have as much as 37% THC!



## As THC content increases, we see more adverse effects:

- Paranoia
- Anxiety and panic
- Hallucinations
- Erratic mood swings
- Aggressive behavior



As THC content of marijuana increases, so does its potential to cause adverse effects such as paranoia, anxiety and panic attacks, hallucinations, erratic mood swings and aggressive behavior.

As you can see in the graph to the right, the number of young people showing up in the emergency department for marijuana-related reasons has risen sharply in recent years. In 2009, over 376,000 emergency room visits nationwide were caused by marijuana use (The DAWN Report, Substance Abuse and Mental Health Services Administration, 12/2010).

Also telling is the huge increase in calls to Poison Control Centers across the country (from 13 calls in 2009 to 9,159 in 2011) by people having such adverse reactions after using “synthetic pot” – plant material sprayed with chemicals developed in labs to study the effects of THC. These chemicals mimic THC by binding to cannabinoid receptors. However, these synthetic chemicals are typically 10 times more potent than THC, which is why they cause more, and more severe, adverse reactions, including heart attacks and seizures.

## “Medical” Marijuana



Source:  
Newsweek, 2010

This slide shows a picture of marijuana samples being sold at a “medical marijuana” dispensary in California. As you can see by the little white cards showing the percent THC of each sample, “medical” marijuana is often even higher in THC content (12% or higher) than the average “street” marijuana.

## Legalized “Medical Marijuana”: the Colorado Experience

- *Nov. 2000*: Passes medical marijuana law
- *July 2010*: The Colorado Medical Marijuana Code allowing commercial scheme for dispensaries goes into effect

Slide courtesy of Dr. Sharon Levy



Currently, 16 states, plus the District of Columbia, have legalized “medical” marijuana. There are as yet few research studies examining the effects of this policy on adolescents. However, it is instructive to look at the experience of one state, Colorado, which now has one of the most liberal marijuana policies in the nation.

Colorado voters approved the legalization of the use of marijuana for “debilitating conditions” in Nov. 2000. These conditions included cancer, glaucoma, HIV/AIDS, or “a chronic or debilitating disease or medical condition that produces cachexia (severe loss of weight), persistent muscle spasms, seizures, or severe nausea or pain which, in the physician’s professional opinion, may be alleviated by the medical use of marijuana.”

However, it was not until July 2010 that the Colorado Medical Marijuana Code allowing for the commercialization of medical marijuana dispensaries went into effect. Since then, medical marijuana dispensaries have proliferated rapidly, and aggressively market themselves. There is even a free iPhone app that makes it easy to locate the nearest dispensary.

**SUMMIT WELLNESS**  
HIGHEST GRADE MEDICINE IN COLORADO INCLUDING  
35+ STRAINS, BEST EDIBLES IN TOWN,  
MULTIPLE FLAVORS OF TINCTURES, HASH,  
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**FREE RAFFLE**  
ENTRY TO WIN 1 OF 3 PRIZES  
BY PURCHASING 10 LBS. WORTH OF MEDICINE,  
OR BUYING 5000 SPANDEX  
AND DRAWING WILL RECEIVE A \$200.00 CASH PRIZE  
AND DRAWING WILL RECEIVE A \$200.00 CASH PRIZE  
AND DRAWING WILL RECEIVE A \$200.00 CASH PRIZE  
NAME: \_\_\_\_\_  
PHONE: \_\_\_\_\_

**FREE MEDICINE FOR ANYONE WHO  
MAKES US THEIR CAREGIVER**  
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**3.5 grams of BLUEBERRY**  
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**3.5 grams of NORTHERN LIGHTS**  
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Medical Marijuana Evaluations  
\$35 \$45  
For Renewals From Any Doctor  
Cultivation Licenses Available  
For New Patient Evaluations  
Walk-ins Welcome  
Tel: 303.944.0437

Slide courtesy of Dr. Sharon Levy

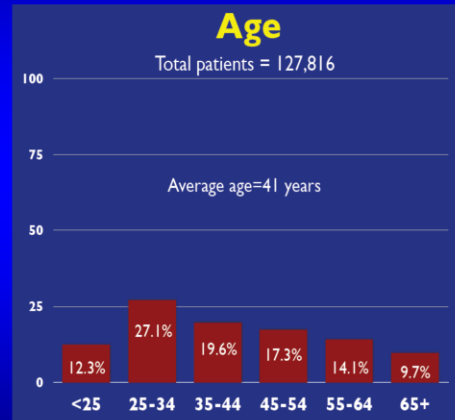
These are pictures of advertisements for some dispensaries, now widely seen throughout Colorado.

With their pictures of busty and scantily-dressed women, these advertisements are likely targeting a particular segment of the Colorado population, one in which rates of cancer, HIV/AIDS, glaucoma, or wasting disease are usually low.

# Who uses medical marijuana in Colorado?

Majority of current medical marijuana card holders are...

- Male (68%)
- Under 45 years olds (59%)
- Using for “severe pain” (94%)



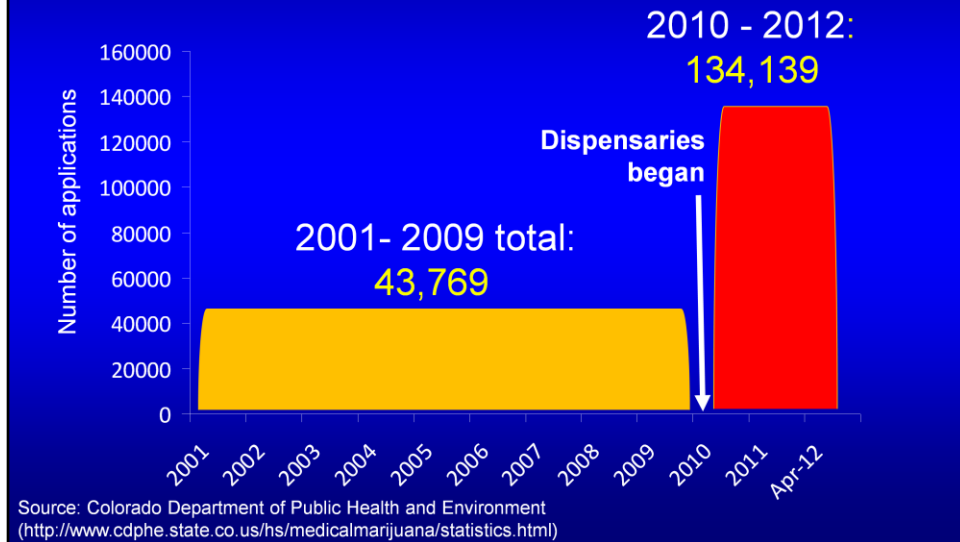
Slide and graph courtesy of Sharon Levy MD MPH, and Christian Thurstone MD.

Source: Colorado Department of Public Health and Environment  
(<http://www.cdphe.state.co.us/hs/medicalmarijuana/statistics.html>)

And sure enough, according to statistics from the Colorado Medical Marijuana Registry, the majority of medical marijuana card holders are male, under 45 years old, and without a history of chronic illness.

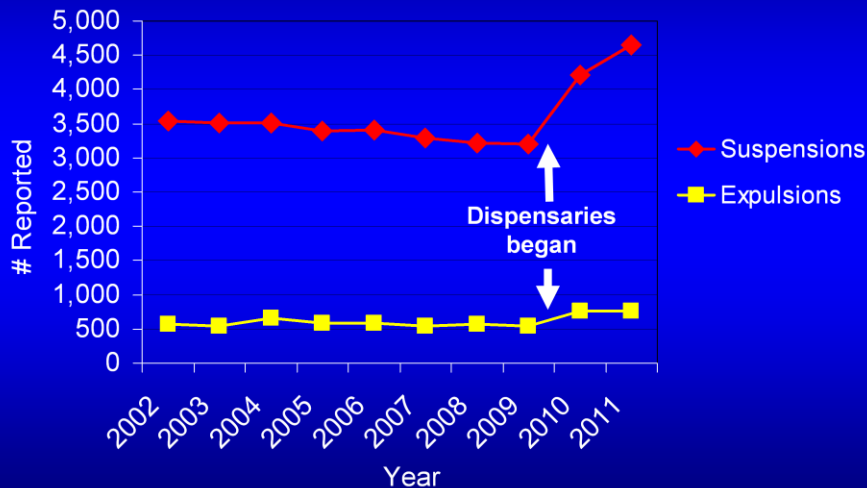
Also, the overwhelming majority (94%) of card holders cite “severe pain” as the reason for use, compared to only 3% for cancer or 17% for muscle spasms.

## Number of Applications for Marijuana Card in CO, by Year



The establishment of the commercial dispensary system in CO resulted in a huge increase in the number of applications for a medical marijuana card. As shown on this graph, there were triple the number of applications for a medical marijuana card in the two years since dispensaries started (over 130,000), compared to the total number over the entire prior 10 years (about 43,000).

## Drug-Related School Suspensions/ Expulsions in Colorado



Slide courtesy of Sharon Levy, MD MPH

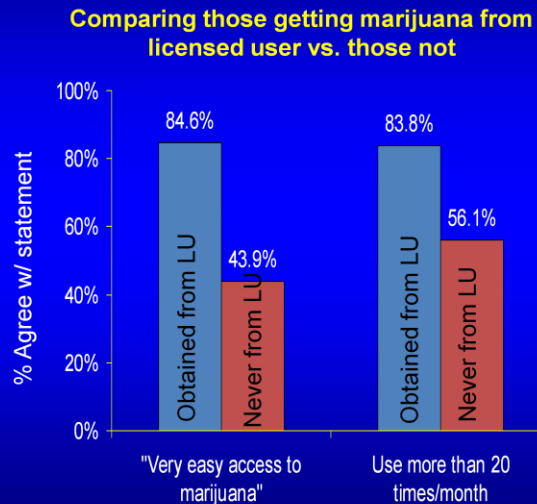
Source: <http://www.cde.state.co.us/cdereval/rv2011sdiincidents.htm>

Curiously, the Colorado Department of Education also saw a steep increase in the number of drug-related school suspensions and expulsions starting between 2009 and 2010, right when the dispensary system started.

While it is difficult to determine cause and effect since the increase may be influenced by other factors, such as other drug use trends or stricter enforcement, there are other indications that greater availability of marijuana through the dispensary system is impacting teen behavior and attitudes.

# Medical Marijuana Diversion to Teens

In sample of 80 adolescents in outpatient substance abuse treatment in Denver, half reported obtaining marijuana from licensed users



Thurstone, C., Lieberman, S.A., Schmiege, S.J. Medical marijuana diversion and associated problems in adolescent substance treatment. *Drug and Alcohol Dependence*; (2011) 118:489– 492

Dr. Christian Thurstone, a pediatrician in Denver CO, and his colleagues recently published a study reporting that, in a sample of 80 adolescents receiving substance abuse treatment, of whom 91% were in treatment specifically for marijuana, half reported having gotten marijuana from someone with a medical marijuana license. Those obtaining marijuana from licensed users and those not were nearly identical in terms of demographics. None of them had their own medical marijuana license.

The bar graph on the right compares the perceptions and behavior of teens in this study in the two groups ("Obtained from licensed users (LU)" vs. "Never from LU") As you can see, teens that obtained marijuana from licensed users were twice as likely to say that marijuana was very easy to access, and 50% more likely to be near-daily users (more than 20 times a month), compared to teens who had never gotten marijuana from a licensed user. They also had more overall problems arising from their substance use.

This November, Massachusetts voters will likely be faced with the question of whether to allow the establishment of 35 "medical" marijuana dispensaries in this state. This ballot initiative would allow licensed individuals ages 25 and older to obtain up to an undefined 60-day supply. Massachusetts already has one of the highest rates of marijuana use among teens in the country (43% ever, 28% in past month [Source: CDC Youth Risk Behavior Survey, 2011]). Based on the experience of Colorado, dispensaries would likely make marijuana even more accessible to Massachusetts teens, and result in more substance abuse and mental/physical health problems among our youth, as well as greater costs for Massachusetts as a whole.



# Tobacco vs. Marijuana Smoke

*Chem. Res. Toxicol.* 2008, 21, 494-502

## A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions

David Moir,<sup>\*,†</sup> William S. Rickert,<sup>‡</sup> Genevieve Levasseur,<sup>§</sup> Yolande Larose,<sup>^</sup>  
Rebecca Maertens,<sup>†</sup> Paul White,<sup>†</sup> and Suzanne Desjardins<sup>^</sup>

*Safe Environments Programme, Tobacco Control Programme, and Drug Strategy and Controlled Substances Programme, Health Canada, Ottawa, ON, Canada K1A 0K9, and Labstat International Inc., Kitchener, ON, Canada N2C 1L3*

Finally, I'd like to address the issue of marijuana and respiratory health. Many people perceive marijuana smoking to be less harmful than tobacco smoking. In fact, "medicalizing" marijuana has led people to view smoking marijuana as an appropriate "medical" therapy for a variety of health problems.

This slide shows a published journal article reporting on the results of a scientifically rigorous comparison of the contents of marijuana and tobacco smoke. While this study did not test how the two different types of smoke, when inhaled, actually affected human lung tissue, it did analyze the contents of each type of smoke.

## Tobacco vs. Marijuana Smoke

- Marijuana smoke contained most of the same cancer-causing chemicals, and as much tar, as tobacco smoke
- Marijuana smoke is usually unfiltered, and held in the lungs longer

What the researchers found was that marijuana smoke contained most of the same cancer-causing chemicals, and as much tar, as tobacco smoke.

Marijuana smokers are actually exposed to more of these chemicals per puff than tobacco smokers because tobacco cigarettes typically have filters through which smokers inhale, whereas marijuana joints do not. Also, marijuana smokers tend to inhale and hold the smoke in their lungs longer than cigarette smokers.

There have been few studies to date of the relationship between marijuana smoking and lung cancer. Isolating the effect of marijuana smoking from tobacco smoking is difficult since many people engage in both. However, a number of studies have looked at the rates of respiratory problems among marijuana smokers, after controlling for tobacco use.

## Marijuana and Respiratory Health

Regular marijuana smokers report more cough, bronchitis, wheezing, shortness of breath, and more days sick than non-smokers (regardless of tobacco use)



These studies have generally found that regular marijuana smokers report more of a range of common respiratory health issues, and more days sick than non-users, regardless of whether they smoked cigarettes.



## Take-Home Points for Parents and Teens



1. The endocannabinoid system is important for maintaining brain health and proper development, and THC interferes with its proper functioning!
2. Repeated exposure to marijuana during adolescence, a time of critical brain development, may have lasting effects on cognitive function, e.g., memory and IQ

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To summarize, here are 5 critical take-home points for parents and teens about marijuana use during adolescence.



## Take-Home Points for Parents and Teens cont'd.

3. Today's marijuana is a lot more potent than 20 years ago
4. Marijuana use increases risk for car crashes, stunted growth, testicular cancer, and respiratory problems
5. The risk of serious mental illness is 2-5 times greater for those starting marijuana use before age 16!!

## Parents Guide



Available for free download at  
[www.maclearinghouse.com](http://www.maclearinghouse.com)

Here is an excellent guide for parents in how to help protect teens from alcohol and other drugs. It was developed by the Massachusetts Department of Public Health in collaboration with Dr. John R Knight, a pediatrician, and director and founder of the Boston Children’s Hospital Center for Adolescent Substance Abuse Research (CeASAR). It is available for free download at the address given above.

Also, please go to our website [www.ceasar-boston.org](http://www.ceasar-boston.org) for more information about CeASAR and our research.

To learn more about the effort to stop the establishment of “medical” marijuana dispensaries in Massachusetts, and to find ways to help, please go to the website of the Massachusetts Prevention Alliance ([www.mapa.org](http://www.mapa.org)).

Thank you.