Effects of Marijuana On Brain, Body & Behavior

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National Institute on Drug Abuse
Marijuana is the Most Commonly Used Illicit Drug In the U.S.

- Over 111 million Americans have tried it at least once
- An estimated 2.4 million Americans used it for the first time in 2012
- What about the rates among adolescents?


Tetrahydrocannabinol (THC) Active Ingredient in Marijuana
## Prevalence of Past Year Drug Use Among 12th graders

<table>
<thead>
<tr>
<th>Drug</th>
<th>%</th>
<th>Drug</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>62.0</td>
<td>Sedatives*</td>
<td>4.8</td>
</tr>
<tr>
<td>Marijuana/Hashish</td>
<td>36.4</td>
<td>Tranquilizers*</td>
<td>4.6</td>
</tr>
<tr>
<td>Hookah</td>
<td>21.4</td>
<td>Hallucinogens</td>
<td>4.5</td>
</tr>
<tr>
<td>Small cigars</td>
<td>20.4</td>
<td>MDMA (Ecstasy)</td>
<td>4.0</td>
</tr>
<tr>
<td>Amphetamines*</td>
<td>8.7</td>
<td>Hall other than LSD</td>
<td>3.7</td>
</tr>
<tr>
<td>Synthetic Marijuana</td>
<td>7.9</td>
<td>OxyContin*</td>
<td>3.6</td>
</tr>
<tr>
<td>Snus</td>
<td>7.7</td>
<td>Salvia</td>
<td>3.4</td>
</tr>
<tr>
<td>Adderall*</td>
<td>7.4</td>
<td>Cocaine (any form)</td>
<td>2.6</td>
</tr>
<tr>
<td>Narcotics o/t Heroin*</td>
<td>7.1</td>
<td>Inhalants</td>
<td>2.5</td>
</tr>
<tr>
<td>Vicodin*</td>
<td>5.3</td>
<td>Ritalin*</td>
<td>2.3</td>
</tr>
<tr>
<td>Cough Medicine*</td>
<td>5.0</td>
<td>LSD</td>
<td></td>
</tr>
</tbody>
</table>

* Nonmedical use

Categories not mutually exclusive

Source: University of Michigan, 2014
Percent of Students Reporting Daily Use of Marijuana, by Grade and Potency (% THC-D9)

SOURCE: University of Michigan, 2013 Monitoring the Future Study, and University of Mississippi Marijuana Project (potency data)
Percent of Students Reporting Use of Synthetic Marijuana in Past Year, by Grade

Denotes significant difference between 2012 and 2013

SOURCE: University of Michigan, 2013 Monitoring the Future Study
Percent Reporting Using Synthetic Marijuana in Past Year, By Past-Year Use of Marijuana

SOURCE: University of Michigan, 2013 Monitoring the Future Study
Percent Perceiving Great Risk of Smoking Marijuana Regularly

SOURCE: University of Michigan, 2013 Monitoring the Future Study
12th Graders’ Past Year Marijuana Use vs. Perceived Risk of Occasional Marijuana Use

SOURCE: University of Michigan, 2013 Monitoring the Future Study
Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol

Is marijuana addictive?
Marijuana is Addictive:

About 9% of users may become dependent, 1 in 6 who start use in adolescence, 25-50% of daily users

Estimated Prevalence of Dependence Among Users

Sources: Anthony JC et al., 1994 and Lopez-Quintero M et al., 2011
ADDICTION IS A DISEASE OF THE BRAIN as other diseases it affects the tissue function.

**Decreased Brain Metabolism in Drug Abuse**

- Control
- Cocaine Abuser

**Decreased Heart Metabolism in Heart Disease**

- Healthy Heart
- Diseased Heart

Sources: From the laboratories of Drs. N. Volkow and H. Schelbert
Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptions that result in addiction.
The fine balance in connections that normally exists between brain areas active in **reward, motivation, learning and memory**, and **inhibitory control** becomes severely disrupted in **addiction**.

**Executive Function**

**Inhibitory Control**

**Motivation/Drive**

**Reward**

**Memory/Learning**
Addictions are common, developmental brain diseases expressed as compulsive behavior through continued use of a drug despite negative consequences: Onset depends on many intrinsic and extrinsic factors.
Addiction Is Developmental: It Starts in Adolescence and Childhood

Age of Onset of Drug Abuse and Dependence

In Adults, Emotional Self Regulation Normally Implemented By A Neural Circuit Comprising Various Subcortical Limbic Structures… & Prefrontal Regions

Adverse Childhood Experiences (ACE) and Illicit Drug Use (n = 8603)

**Ever Addicted**

<table>
<thead>
<tr>
<th>ACE Score</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Does marijuana use negatively affect the brain?
Constituents of MJ and the Cannabinoid System

- Delta-9-tetrahydrocannabinol (Δ⁹-THC)
- Delta-9-tetrahydrocannabinvarin (Δ⁹-THCV)
- Delta-8-tetrahydrocannabinol (Δ⁸-THC)
- Cannabigerol (CBG)
- Cannabichromene (CBC)
- Cannabinol (CBD)
- Cannabidiol (CBD)
Drugs Can be Chemical Imposters
Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

• Brain Development
• Memory and Cognition
• Motivational Systems & Reward
• Appetite
• Immunological Function
• Reproduction
• Movement Coordination
• Pain Regulation & Analgesia
Cannabinoid CB1 Receptors in Human Brain are Downregulated in Marijuana Abusers

Van Loere et al., 2007. Hirvonen et al., Mol Psychiatry 2013
Brain Glucose Metabolism in Controls and Marijuana Abusers

Cerebellar metabolism is decreased in Marijuana Abusers

Correlations between Urine Concentration of THC and D2R availability \( (RAC \ BP_{ND}) \) in Marijuana Users \( (n = 10) \)

Marijuana abusers with heavier consumption had lower striatal D2R

Albrecht DS et al., Drug and Alc Depend 2013;128:52-57.
Brain abnormalities associated with long-term heavy marijuana use

L (yellow) and R (blue) amygdala
L(red) and R(green) hippocampus

morphology and function of hippocampus has been linked to reduced memory performance in heavy cannabis users

Hippocampal and amygdalar volumes were smaller in cannabis users than in controls.

Yucel et al., Arch Gen Psychiatry. 2008 Jun;65(6):694-701.
Marijuana Use may be Associated with Brain Abnormalities in Young Adult Recreational Users.

Gray Matter Density: Marijuana > Control Participants

Associations Drug Use Behavior & Gray Matter Density in Left Nucleus Accumbens

Volume & Associations with Drug Use in Left Nucleus Accumbens

Early (<18y) Long-Term Marijuana Use Decreases Axonal Fiber Connectivity

Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33). Zalesky et al Brain 2012.
High Rates of Comorbid Mood & Anxiety Disorders Among Respondents with Marijuana Dependence (NESARC)

Persistent Marijuana Users Show A Significant IQ Drop between Childhood and Midlife

Followed 1,037 individuals from birth to age 38. Tested marijuana use at 18, 21, 26, 32 and 38. Tested for IQ at ages 13 and 38

Source: Meier MH et al., PNAS Early Edition 2012
Adolescent Marijuana Use Increases the Risk for Adult Psychosis in Genetically Vulnerable Individuals

What harms does marijuana cause?
• Social problems: *School dropout*
• Accidents: *Double risk of motor vehicle accidents*
• Brain: *Impairs motivation and mood; causes addiction and paranoia; may cause schizophrenia and cognitive decline*
• Lung: *Cough and bronchitis*

*Especially with Heavy/Chronic Use*
Early Marijuana (and other drug) Use Linked to Dropping Out of School

Proportion of sample dropping out between ages 16 and 18

- Marijuana: 0.18
- Cigarette: 0.12
- Alcohol: 0.10
- Other drug: 0.12

Initiated prior to age of dropout

Did not initiate prior to age of dropout

Marijuana Use and Later Life Outcomes Are Dose Dependent

% welfare dependent (ages 21-25)

% Unemployed (ages 21-25)

Mean personal income in thousands of NZ $ at age 25

% gained university degree by age 25

Increasing Concentrations of THC In Whole Blood Samples From Drivers Apprehended By The Police Suspected Of Driving Under the Influence in Norway

Emergency Department Visits Involving Selected Drugs: 2008

Source: SAMHSA, 2008 DAWN.
Increased Marijuana Treatment Admissions 1993 and 2007

Source: SAMHSA, TEDS 1993 & 2007
Marijuana Users More Likely to Have Other Drug Disorders: Drug Use Outcomes in Twin Pairs (n = 234) Discordant for Cannabis Use Before Age 17

**Use**

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedatives</td>
<td>3</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>4.5</td>
</tr>
<tr>
<td>Cocaine/Stimulants</td>
<td>3.2</td>
</tr>
<tr>
<td>Opioids</td>
<td>2</td>
</tr>
</tbody>
</table>

**Illicit Drug Abuse/Dependence**

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedatives</td>
<td>5.5</td>
</tr>
<tr>
<td>Cannabis</td>
<td>7</td>
</tr>
<tr>
<td>Cocaine/Stimulants</td>
<td>4.5</td>
</tr>
<tr>
<td>Opioids</td>
<td>6</td>
</tr>
</tbody>
</table>

Changes in Marijuana Policy in the USA

1970

- decriminalized
- medical marijuana
- fully legal
- in legislature
Source of Marijuana* among 12th Graders in 2012 and 2013, by State Policy

*Categories not mutually exclusive
**Statistically significant difference

SOURCE: University of Michigan, 2013 Monitoring the Future Study
Map Of States That Legalized Marijuana By 2004

NESARC: National Epidemiologic Survey on Alcohol and Related Conditions

Marijuana as Medicine?

• Promise lies in purified ingredients or synthetic compounds with more selectivity, less adverse effects

• Applications: pain, nausea, wasting, obesity, muscle spasticity, addiction, inflammatory conditions, HIV

NIDA research focuses on THC, CBD, and compounds that alter the function of the endocannabinoid system
What can be done?
Universal Prevention: Reduced Onset of Marijuana Use in PROSPER over 6.5 Years

Frequency of marijuana use through 6.5 years past baseline. Frequency of marijuana use was scored on a 7-point scale, ranging from 0 (never) to 7 (more than weekly).

A Double-Blind RCT of N-Acetylcysteine in Marijuana-Dependent Adolescents

Proportion of Negative Urine Cannabinoid Tests Over Time Among Cannabis-Dependent Adolescents

• **RFA-DA-11-008 Medical Marijuana Policy Research: Exploring Trends And Impacts (R01)**
  – Awarded 3 grants to inform social, behavioral, and public health impacts of medical marijuana use and policies; 6 grants awarded outside RFA on this topic

• **PA-13-138 Research on Marijuana Legalization in the US (Admin Supp)**

• **PAS-14-020 Public Health Impact of the Changing Policy/Legal Environment for Marijuana (R01)**
Summary

• Marijuana is the most commonly used illicit drug in the U.S.
• Marijuana use generally begins in adolescence
• Use of marijuana can have a wide range of effects on an individual’s brain, body and behavior including short and long term effects on such functions as:
  - Brain development
  - Memory and cognition
  - Motivational systems and reward
  - Addiction
  - Lung health
• In recent years there has been an increase in both treatment admissions for marijuana abuse and in Emergency Department visits involving marijuana
New Online Resources
For teens and those that care about them

**Treatment Publication**
**Principles of Adolescent Substance Use Disorder Treatment: A Research Based Guide**
Outlines thirteen principles and evidence-based approaches for treating adolescent substance use disorders (SUD).

**Medical School Curriculum**
**The Substance Use Disorder in Adolescents: Screening and Engagement in Primary Care Settings**
Provides a series of videos demonstrating effective screening techniques.

**Web interactive Drugs + Your Body: It Isn’t Pretty**
Includes graphics, videos, quizzes and much more on harmful effects of drugs on the brain and body.