The State of the Science: Teen Brain Development and the Impact of Marijuana Use

October 4, 2018
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Today’s Presenter

Dr. Sion Kim Harris
The State of the Science: Teen Brain Development and the Impact of Marijuana Use

Sion Kim Harris, PhD
Associate Professor of Pediatrics
Harvard Medical School
State Marijuana Laws, 2018

- **46** states legalized in some form
- **31** legalized medical marijuana or recreational
- **15** low THC/high CBD only
- **Still Schedule 1 drug at federal level**

Marketing Marijuana

"Let's Be Blunt, It's Good."

"Barack Obama
President of the United States of America"

"When I was a kid, I inhaled frequently. That was the point."

"14 Olympic Gold Medals
37 World Records.
2 Awesome Lungs."

"Marijuana: Inspiring successful Americans since 1776."

"Don't let the government fool you"

"Unlike heavy tobacco smokers, heavy marijuana smokers exhibit no obstruction of the lung's small airway. That indicates that people will not develop emphysema from smoking marijuana."

"Don't let the government fool you"
Images about marijuana that young people see today...
Perceived Risk of Harm and Marijuana Use
U.S. 12th graders: 1975-2017

Perceived risk is at historic low!

Source: National Monitoring the Future Survey, 2017
Percent of U.S. 12th Graders Using Substance in Past Month, 2000-2017

- **Alcohol**: 50% in 2000, decreasing to 33% in 2018
- **Tobacco**: 31% in 2000, decreasing to 11% in 2018
- **Illicit drugs other than marijuana**: 10% in 2000, decreasing to 7% in 2018

Source: National Monitoring the Future Survey, 2017
Percent of U.S. 12th Graders Using Substance in Past Month, 2000-2017

- Alcohol: 50% in 2000, 33% in 2017
- Tobacco: 31% in 2000, 17% in 2017
- Marijuana: 21% in 2000, 11% in 2017
- Vaping: 10% in 2000, 7% in 2017

Source: National Monitoring the Future Survey, 2017
Percent of U.S. 12th Graders Reporting Behavior in Past Month, 2000-2017


Source: National Monitoring the Future Survey, 2017

Top 3 states:
- CO 11.1%*
- VT 10.9%
- RI 10.2%

States with Legalized Marijuana in 2014-2015 (Medical or Recreational)

*Note: CO was ranked #14 in 2005-2006, #4 in 2011-2012, and became #1 starting in 2013-2014

So what?
Common Marijuana Myths

- It’s not addictive
- It’s harmless and natural
Let’s look at the science...
Is marijuana addictive?
Studying the Addictiveness of Drugs
The Reward Pathway

Ventral Tegmental Area

Prefrontal cortex

Nucleus accumbens

VTA

Striatum

Ventral-Tegmental Area

Source: NIDA
Activation of the reward pathway by addictive drugs

- Alcohol
- Cocaine
- Heroin
- Nicotine
- Marijuana
- Heroin
Marijuana (THC) is no exception…

Δ9-Tetrahydrocannabinol Induces Dopamine Release in the Human Striatum

Matthijs G Bossong¹, Bart NM van Berckel²,³, Ronald Boellaard³, Lineke Zuurman⁴, Robert C Schuit³, Albert D Windhorst³, Joop M A van Gerven⁴, Nick F Ramsey¹, Adriaan A Lammertsma³ and René S Kahn²
Marijuana is especially addictive for teens ...
Percent of Substance Abuse Treatment Admissions by Drug, Ages 12-19, 2014

Source: SAMHSA National Treatment Episode Data Set, 2014
Among adolescents, marijuana accounts for more treatment admissions than all other substances combined.

Source: SAMHSA National Treatment Episode Data Set, 2014
Is marijuana harmless?

Not for the teen brain!
What we now know...

- Adolescence is a sensitive period in brain development.
- The brain is still developing until about mid-20’s!!
Critical Period

Definition:
“Window” in brain development when a part of the brain ...

• develops rapidly

• is highly sensitive to being shaped by environmental exposures and experiences
Key Brain Development Processes until Mid-20s

“Pruning”

“Myelination”

Neurons
Basic Neuron Structure

- Axon
- Cell body
- Electrical signal
- Dendrites
- Synapse
- Nucleus
Around age 12, brain cell connections start to undergo **pruning** based on “**use it or lose it**” (connections that are not used are pruned away)

Construction Ahead

- At the same time, myelin starts to cover axons and thicken
- Helps neuron signals travel 100 times faster

Slide courtesy of Ken Winters, PhD.
The Brain’s Information Superhighway:
Myelinated axons = White Matter Tracts

Source: Dr. Gordon J. Harris, MGH, 2008.
Result when pruning and myelination are complete: faster, but fewer, connections in the brain

The Brain’s Connectome


Image source: Dr. Van J. Wedeen, MGH, 2011
Pruning and myelination happen into the mid-20s…

Source: Neuropsychopharmacology Reviews advance online publication 22 October 2014. doi:10.1038/npp.2014.236
It’s speeding up the commute...
To go from this...
To being able to do this...
The teen brain is highly “neuroplastic”

It’s a double-edged sword...

Opportunity

Vulnerability

Adolescence is a great time for getting good at something!
The teen brain is more vulnerable to being harmed by alcohol and drugs than the adult brain.
The Teen Brain on Marijuana
What is in Marijuana?

- Contains many cannabinoid chemicals ...
  - delta-9-tetrahydrocannabinol (THC)
  - cannabidiol (CBD)
  - cannabinol
  - cannabichromene
  - cannabigerol
  - Etc.

THC Properties

• Crosses the blood-brain barrier and the placenta

• Highly absorbed in fat tissue, resulting in long elimination time (several days to 1 week)

• Acts on the body’s cannabinoid receptors, present in the central (CB1 receptors) and peripheral nervous system (CB2 receptors)

Cannabinoid receptors in our brains? Why?
Fooling the brain...

Brain's Chemical

Anandamide

Drug

THC

Source: NIDA
The Brain’s “Endocannabinoid” System

“Endo” = “within” or “inside”
Basic Neuron Structure

- Axon
- Synapse
- Dendrites
- Cell body
- Electrical signal
- Nucleus
Endocannabinoid System Functions

• The neuron’s “volume control” system

• dials down neuron activity and neurotransmitter release when too strong

• regulates levels of many brain chemicals (affects pleasure, mood, pain, appetite, motivation, memory, growth and reproductive hormones)
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 our own brain’s system for protecting neurons and keeping brain activity in balance
Anandamide

THC
Repeated THC exposure causes brain to scale back CB receptors, causing “cannabinoid deficiency”
Marijuana Withdrawal Symptoms
(symptoms of an “out-of-whack” brain)

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

Endocannabinoid System cont’d

• Shapes **brain development** by...
  – guiding neurons to grow to the right places in the brain for correct function
  – controlling neuron activity, thereby affecting **pruning** and brain wiring
  – supporting **myelin** growth on neurons

Pruning and myelination happen throughout adolescence…
If the adolescent brain is regularly exposed to THC, it could alter development of the connectome.
White matter differences in brains of those starting regular use in adolescence vs. not

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
Recent longitudinal brain imaging studies provide confirmation:

**Original Article**

**Adverse Effects of Cannabis on Adolescent Brain Development: A Longitudinal Study**

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What else is affected by THC?

Source: NIDA
The Hippocampus (the key to learning)
Marijuana and Memory

- THC suppresses activity of hippocampal cells below the level needed to trigger memory formation.
- With chronic THC exposure during adolescence, neuron connections involved in memory are gradually lost due to continual suppression.

Marijuana and Hippocampal Size

The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research

A Report of

The National Academies of Sciences • Engineering • Medicine

Available at: https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state
Comprehensive Review of Scientific Research

- 16-member Expert Panel from all areas of medicine, public health, social sciences
- Reviewed >10,700 scientific papers published between 1999-2016
- Generated nearly 100 conclusions about cannabis/cannabinoids’ effects and risks
- Rated strength of scientific evidence for each as substantial, moderate, limited, none
National Academy of Sciences report conclusion:

Moderate evidence for harmful effects of frequent marijuana use on memory and IQ

Marijuana Use and IQ
The Dunedin Study (New Zealand) (N=1,037)

![Image of assessment ages: 13 yrs (Pre-initiation), 18 yrs, 21 yrs, 32 yrs, 38 yrs]

Source: Meier et al. PNAS, 2012
IQ at Age 13 by Mj Use during Follow-up

- 13 yrs old

Never used marijuana: 99.8

Regular use for 3+ yrs: 99.7
Change in IQ from 13 to 38 yrs old

Never used marijuana

- 13 yrs old: 99.8
- 38 yrs old: 100.6

Regular use for 3+ yrs

- 13 yrs old: 99.7
- 38 yrs old: 93.6

Dose-related IQ change

- Regular mj use - 3+ yrs
- Regular mj use - 2 yrs
- Regular mj use - 1 yr
- Used infrequently
- Never used
Adult Social Outcomes

Longitudinal New Zealand study of 1003 youth from birth to age 25

Marijuana-related amotivational syndrome is real...

Marijuana and Psychosis
Strong evidence for link between marijuana and psychotic disorders

Leading Psychosis Expert To His Students: To Avoid Risk, Hold Off On Pot Til 30
Marijuana is very different today from what it was 20 years ago, bringing greater risks...
Avg. % THC Content among Confiscated Cannabis Products in U.S. (1995-2014)

*Source: ElSohly et al., Biological Psychiatry, 2016.

*38,681 samples
Avg. % THC Content among Confiscated Cannabis Products in U.S. (1995-2014)

% Cannabidiol (CBD) (antipsychotic) ~12%

~4%

*Source: ElSohly et al., Biological Psychiatry, 2016.

*38,681 samples
Forms of Butane Hash Oil – contain up to 90% THC!

“Shatter”

“Dabs”

“Budder”

“Earwax”

“Vaping”
As THC increases, we see more negative effects:

- Paranoia
- Anxiety and panic
- Hallucinations
- Erratic mood swings
- Aggressive behavior
Time Course of Marijuana Effects by Ingestion Method

Source: Grotenherman, F. Clin Pharmacokinet 2003; 42 (4): 327-360
Emergency Department Visits Caused by Marijuana Use (Rate per 100,000 people)

2004-2011 Change in Rate of ED Visits Caused by Marijuana Only (no other substance involved), by Age Group

Emergency Department Visits Caused by Marijuana Only (Rate per 100,000 people)

First death in Colorado after legalized recreational marijuana

Levy Thamba-Pongi, 19-year-old college student on Spring Break

Jumped out of 4th floor window after eating whole pot cookie
A Lethal Combination
DENVER -- The family of a Tulsa man who shot himself Saturday night in Keystone, Colorado is blaming his suicide on his ingestion of edible marijuana candies, CBS Denver reports.
Marijuana and Psychosis
Genetic Risk: AKT1 Gene

If people have the AKT1 C/C variant, daily use increases their odds of developing psychosis 7 times higher compared to no use.
Other things teens say:

“My parents smoked pot when they were growing up, so why shouldn’t I?”
Useful Responses

• Because today’s pot is much more potent and dangerous

• We know SO much more today about the harms for teens (other examples: harms of tobacco, trans fats, concussions, etc.)
1. Adolescence/emerging adulthood is a time of **critical brain development**

2. Repeated exposure to marijuana has been shown to have **lasting effects** on cognitive function (e.g., memory and IQ), brain structure and function
3. Today’s marijuana is a **lot more potent**, so it’s more addictive and carries more risks to physical and mental health.

4. Marijuana increases the risk for **car crashes**.

5. Risk of **psychotic disorders** greater for those starting use in adolescence, especially for those with family risk.
Advise DELAYING use until 21+

Dare to delay? The impacts of adolescent alcohol and marijuana use onset on cognition, brain structure, and function

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Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, WI, USA
Marijuana and the Teen Brain: Recent Research Reviews

- Lubman DI et al., Cannabis and adolescent brain development. Pharmacology & Therapeutics. 2015;148:1-16
Questions:
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Questions?

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Additional Questions? Contact Dr. Harris at Sion.harris@childrens.harvard.edu or SBHA at info@sbh4all.org