Marijuana
The Science: What We Know About its Effects on Health

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~70 cannabinoids

THC
Δ9-tetra-hydrocannabinol

CBD
cannabidiol
Marijuana Makes Most People Feel Good

THC

Pleasure
Euphoria
Relaxation
Analgesia*

Hunger

*analgesia is produced at intoxicating doses
Marijuana Makes Some People Feel Bad

THC

- Anxious
- Altered sensory perception
- Time distortion
- Disorientation
How Does Marijuana Work?
Normal Communication Between Neurons

Graham Johnson, 2004
THC Binds to a Target: Cannabinoid Receptors

CB₁ Receptor

THC
Proteins are Made under Instructions From Specific Genes

CB₁ receptor gene

CB₁ receptor protein
Most CB₁ Receptors are on Neuron Terminals

Graham Johnson, 2004
THC Inhibits Release of Neurotransmitters

Graham Johnson, 2004
Cannabinoid Receptors Come in 2 “Flavors”

**CB₁ Receptor**

 Mostly on neurons

**CB₂ Receptor**

 Mostly on immune cells
Cannabinoid Receptors Come in 2 “Flavors”

**CB₁ Receptor**
- Mood
- Cognition
- Appetite
- Nausea

**CB₂ Receptor**
- Immune cell migration
- Inflammation
- Fertility
- Mood?
Why are the CB Receptors Even There?

"Endocannabinoids"
Marijuana’s Effects in the Brain Depend on CB1 Receptor Location
PET Scans Show Location of CB₁ Receptors

K Van Laer et al., 2009
High-Novelty Seekers have Low CB₁ Receptors

K Van Laer et al., 2009
Smoking Marijuana Lowers CB₁ Receptors

Yellow = recovery of CB receptors

J Hirvonen et al., 2012
What About Cannabidiol?
THC & CBD Often Work in Opposition

**THC**
- Euphoria
- Anxiety
- Psychosis
- Cognitive impairment
- Hunger

**CBD**
- No euphoria
- Anti-anxiety
- Anti-psychotic
- No cognitive impairment

Recreational users

Drug companies
CBD
A Drug Developer’s Dream

- Anti-anxiety
- Reduce atherosclerosis
- Anti-psychoic
- Anti-depressant
- Analgesic
- Anti-tumor
- Neuroprotective
- Anti-inflammatory
- Anti-metastasis
- Anti-obesity
- Gum protective

Duke University Medical Center
THC-to-CBD Ratio is Rising

THC concentration is rising and CBD concentration is dropping

JR Burgdorf et al. 2011
Growing “Maximum Yield” Medical Marijuana

Maximum yield marijuana formula for more THC and weight

Sativex™: Oral Spray-THC:CBD = 1
Marijuana is Associated with Several Health Problems
Caveats of Human Studies & Marijuana

- It is difficult to prove causation in humans (animal models are very useful)
- Association or correlation is not causation
- Failure to see an effect doesn’t prove it’s not there
- Many marijuana users also use alcohol or tobacco (this can be controlled in analyses)
- The best studies include longitudinal time-points, varied doses and frequencies, & controls
Marijuana & the Cardiovascular System

- Increases heart rate
- Increases blood pressure (supine)
- Increases $O_2$ demand
Risk of Stroke is High in Young Adults using Marijuana & Tobacco

48 Stroke patients (<45 years old)

11 had Multifocal Intracranial Stenosis (MIS)

10 used cannabis & tobacco (mos.-yrs.)

V Wolff et al. 2011
Occluded Brain Arteries can Recover with Cessation

V Wolff et al. 2011
Marijuana & the Testicles
Marijuana & the Testicles

CB Receptors in testis

X Sun et al. 2009

CB Receptors on sperm

E Agirregiotia et al. 2010
Marijuana Significantly Increases Risk of Testicular Cancer (non-seminous)

Lacson, 2012
1986-1991
Ages 18-35
33% current users
2.5 x as likely if ever used
3 x as likely if a former user
3 x as likely if < 1/week
3 x as likely if < 10 years
6.5 x as likely if > 10 years

Trebert, 2011
1990-1996
Ages 18-50
< 10% current users
2 x as likely overall
3 x as likely if used daily
75% had 1st use < age 18

Dahling, 2009
1999-2006
Ages 18-44
100% current users
2 x as likely overall
3 x as likely if 1st use < age 18
3 x as likely if used weekly
Marijuana & the Lungs

Higher risk of bronchitis
Higher risk of respiratory infections
Increased risk lung cancer in heavy smokers
Marijuana & the Brain
Marijuana Use is Associated with Brain Disorders

- Cannabis Use Disorder
- Anxiety/Mood Disorders
- Cognitive dysfunction
- Psychosis/Schizophrenia
Marijuana & Brain Disorders

• Cannabis Use Disorder

• Anxiety/Mood Disorders

12-18 yr old users are 3-7 x as likely to have CUD than 22-26 yr old users

CUD is 2 x as likely in states with medical marijuana (2.6%)

Patients with mental illness are 3 x as likely to have CUD
Marijuana & Brain Disorders

- Cannabis Use Disorder
  
  14 yr olds using occasionally, weekly, or daily over 15 yrs are 2.5 x as likely to have anxiety disorder at age 29

- Anxiety/Mood Disorders
  
  If non-using at age 29, they are still 2 x as likely to have anxiety disorder
Marijuana & Adolescents: Impacts on Brain Health
The Adolescent Brain: A Key Time for Maturation

- Decision-making
- Judgment
- Impulsivity
- Memory

N Gogtay et al. 2004
Earlier Use of Marijuana is Associated with Lower mo-Prefrontal Cortex Volume

JC Churchwell et al. 2010
Earlier Use of Marijuana is Associated with Altered White Matter Tracts

A Zalesky et al. 2012
IQ Drop Persists in Adults who use Marijuana Infrequently if they Smoked Weekly Before Age 18

MH Meier et al. 2012
Adults with Persistent Cannabis Dependence Show Mental Function Impairment at Age 38

- Memory
- Executive function*
- Processing speed*
- Perceptual reasoning
- Verbal comprehension

*greatest impairment

MH Meier et al. 2012
Marijuana, Genes, and Disease
Chromosomes: Half from Mom & Dad

from Mom

from Dad
COMT Gene Variations: Risk of Schizophrenia

Chromosome 22
Study of Adolescents: Use of Cannabis and Risk of Schizophreniform Disorder, Based on Genetics

Caspi et al., 2005
Adolescents who Smoke Cannabis have Increased Risk of Schizophreniform Disorder, Depending on the COMT Gene

Caspi et al., 2005
Schizophrenia-related Genes on Chromosome #6
Gene for the CB1 Receptor is on Chromosome #6
CB1 Receptor Gene Can Have Many Variations
Effects of Marijuana on Health are Influenced by Genetics

Onset age of use

THC : CBD

Dose & Frequency

GENETICS

Marijuana Health Effects
Take Home Messages

Marijuana’s effects on the developing brain & other organs impacts future health

Delay the onset of marijuana use as long as possible
Cited Studies

Cannabinoid receptor pharmacology:

THC:CBD ratios:

MJ effects on IQ and cognition:

MJ effects on cardiovascular function:

MJ and anxiety disorders:

MJ effects on testicles and cancer:
Cited Studies

**MJ effects on testicles and cancer:**

**MJ and lung cancer:**

**MJ, genes, & schizophrenia:**

**MJ & brain structure changes:**