Marijuana and Teens: Brain Under Construction

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rosecrance
life's waiting

Objectives

- Learn how marijuana interacts with the brain to produce its effects
- Understand the unique aspects of adolescent brain development that make it more susceptible to the impact of marijuana
- Focus on the impact that marijuana has on adolescent brain development and mental health
- Understand the connection between adolescent marijuana use and increased risk for psychotic disorders

Adolescent Brain Development

- Rapid brain development continues from embryonic stage through mid-20s
  - Synaptogenesis
  - Myelination
  - Apoptosis (pruning)

Deborah Rice, Stan Barone. Critical Periods of Vulnerability for the Human Nervous System. Environmental Health Perspectives. 2000.

Synaptic Pruning

- Brain eliminates little-used neurons during adolescence
- Wraps myelin sheath around used neurons to improve efficiency
- Pruning cuts interference between remaining neurons

Marijuana and Gray Matter

- Decreases gray matter in orbifrontal cortex (OFC)
- OFC contributes to impulse control, decision making, and learning
- Less gray matter indicates lower neuron density or volume
- Correlated with higher scores on Marijuana Problem Survey (psychological, social, occupational, legal problems)

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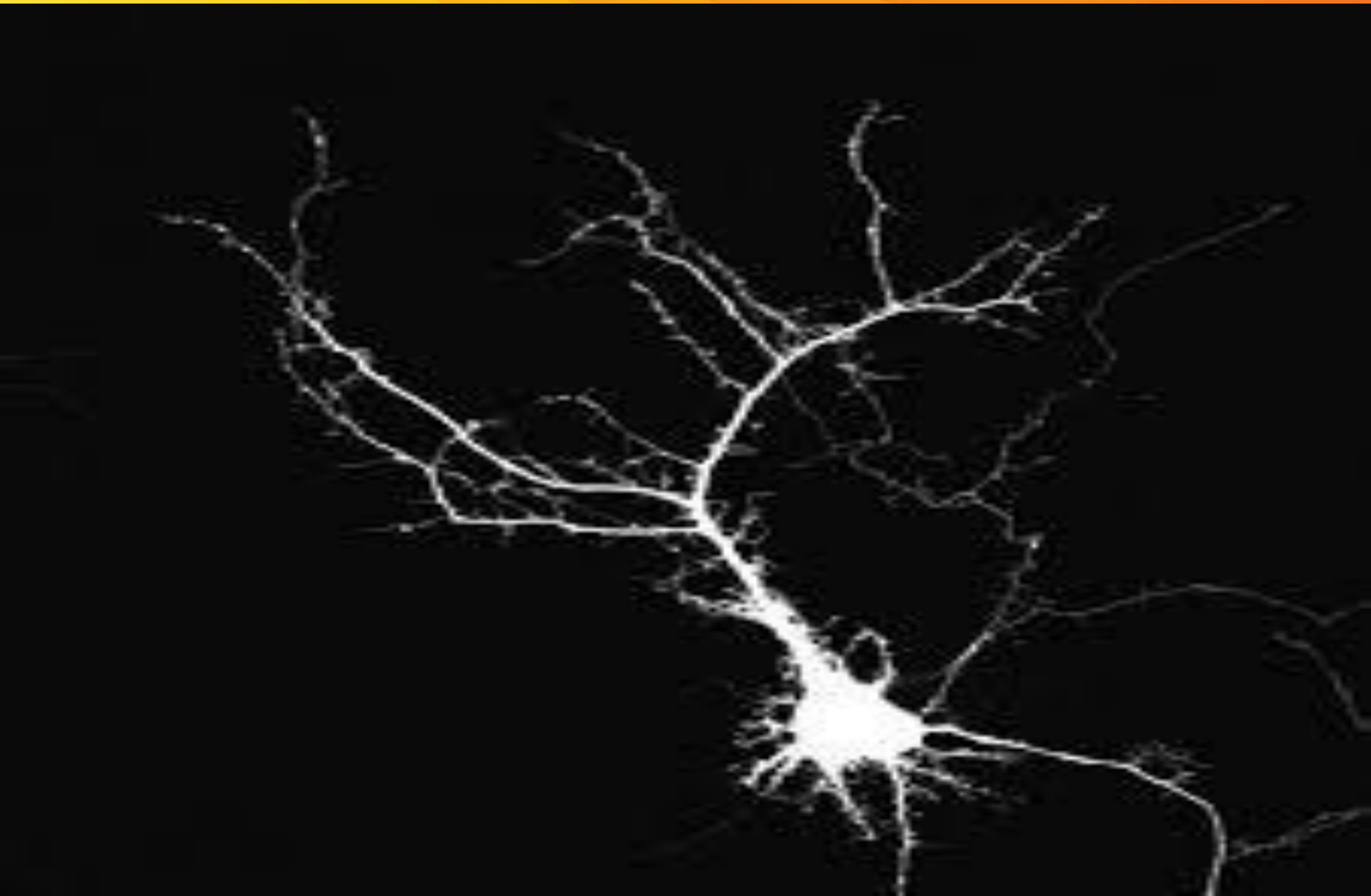


Marijuana and the Brain

- So much attention is being paid to legalization and not enough to impact on teen brain development.
- Hippocampus (memory), amygdala (emotion and anxiety), nucleus accumbens (motivation), hypothalamus (appetite, stress), cerebellum (muscle coordination)

Source: http://www.jneurosci.org/content/34/16/5529.full

Adolescent Behaviors and Marijuana Use

- Increased internal 'reward' for substance use (including marijuana)
- Increased motivation to use these drugs
- Less sensitivity to aversive or negative consequences of these drugs

Marijuana Effects On Brain Function

- Changes in mood – despair and anhedonia
- Changes in cognition (thinking)
  - Memory
  - Attention
- Increased emergence of psychosis
- Increased vulnerability for more harmful use

Risk for Progression of Use

- Over 90% of adults with a severe substance use disorder began use under age 18.
- Children who begin using at or before age 13 have a 47% risk of developing a severe substance use disorder during their lifetime, age 17 run about 25%, age 21 run 10%

Source: http://www.casacolumbia.org/addiction-research/reports/adolescent-substance-use

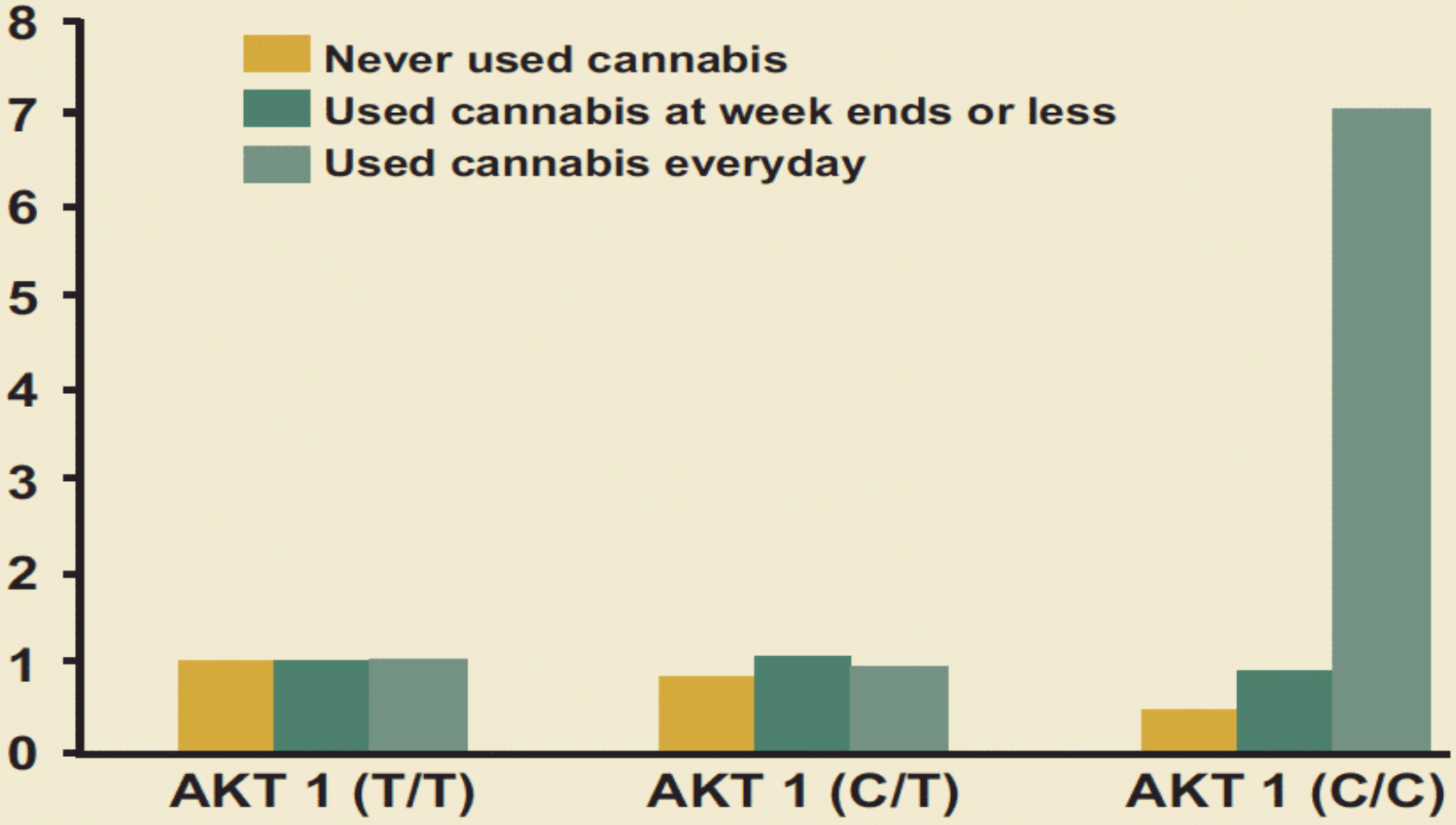
Higher Dose Effects of THC

- Difficulty thinking/making decisions/solving problems
- Distorted perceptions
- Impaired balance and coordination
- Paranoia
- Problems with Learning/Memory
- Acute Psychosis (Delusions, Panic)

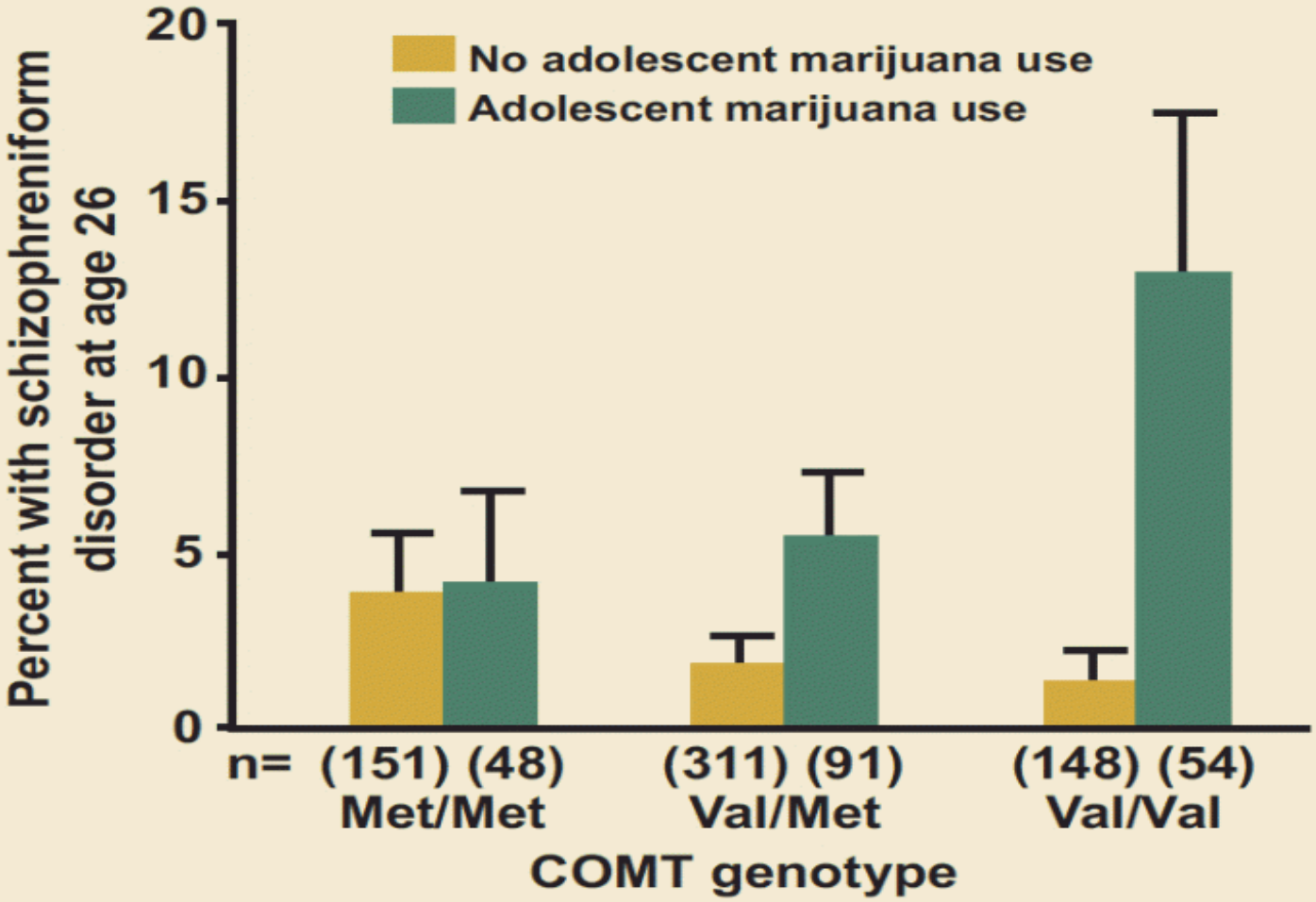
Cannabis and Psychosis

- Smoking high-potency cannabis every day 5x risk for developing psychotic disorder (Lancet)
- C/C variant of AKT1 gene (codes for dopamine signaling) 7x higher risk of psychosis
- Increased schizophrenia risk in adulthood for specific variant of COMT enzyme (degrades dopamine and norepinephrine).

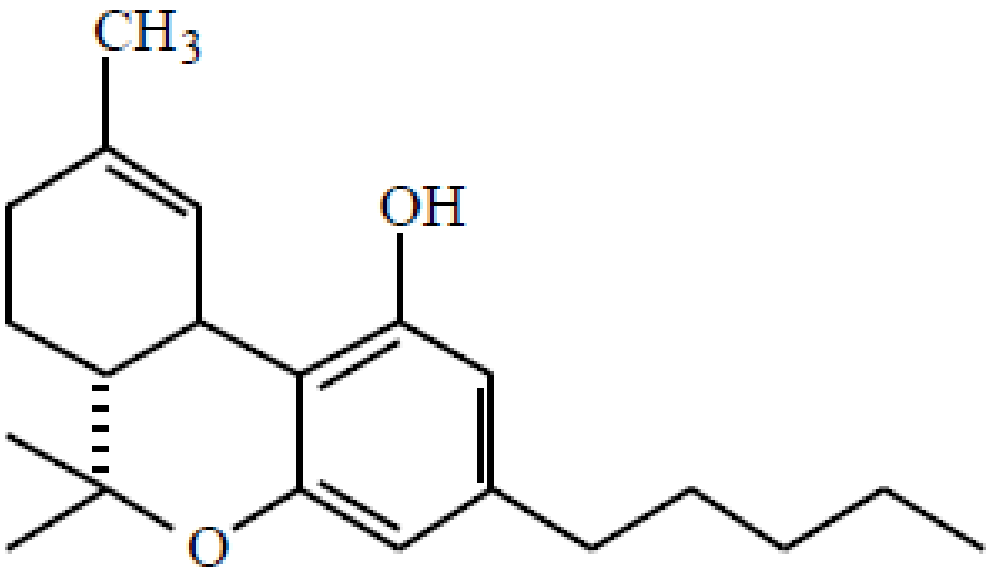
AKT1 Gene Variations and Psychosis



Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs



This is what we are talking about



Δ^9-THC

Important Dates

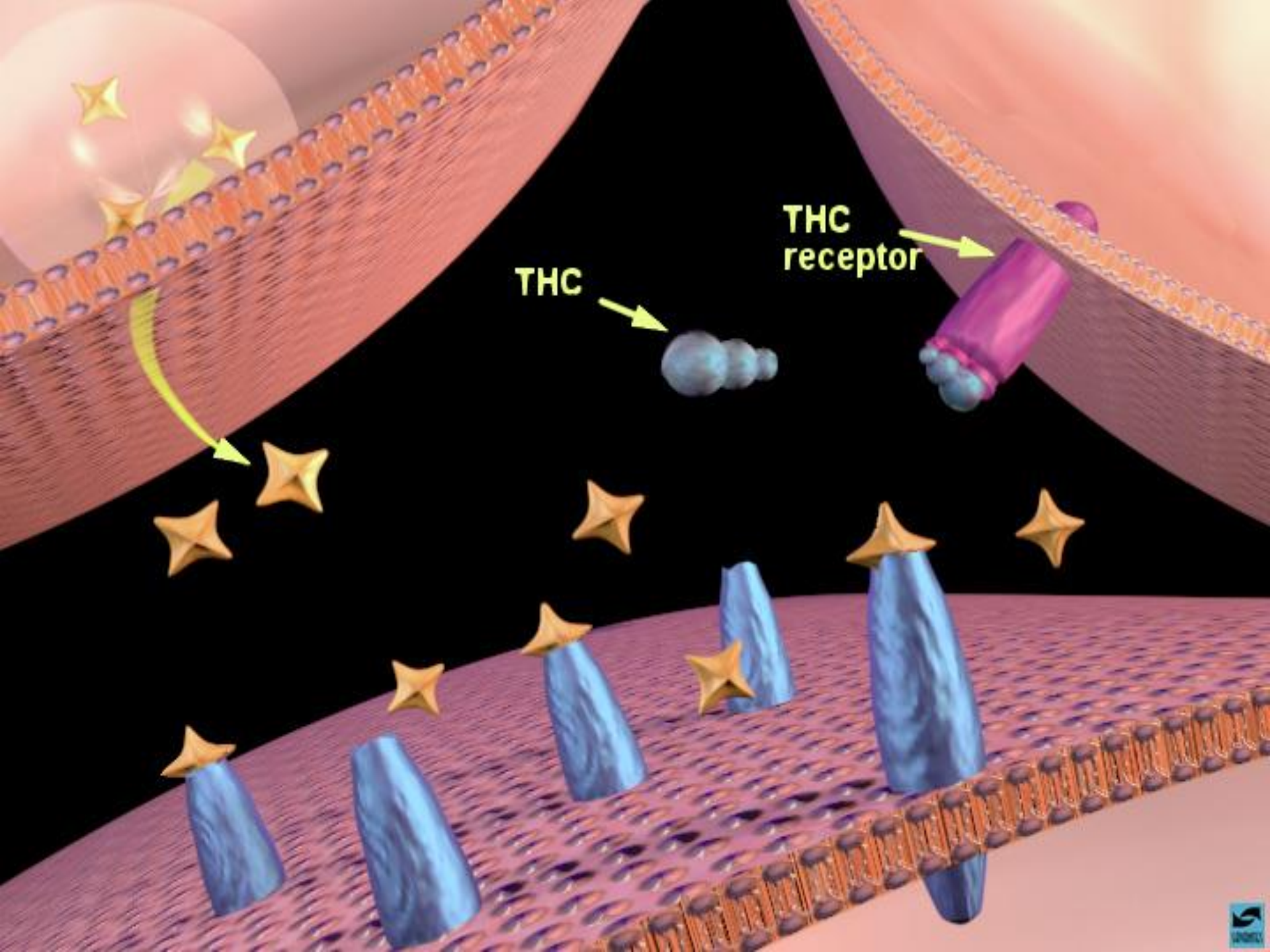
- 1964 THC identified as marijuana's primary active ingredient
- 1988 scientists identified sites in brain and body where it acts (cannabinoid receptors)
- 1992 first known endocannabinoid (anandamide…'dimmer switch')

Endocannabinoid System

- Cell receptor network that regulates a variety of bodily functions
- Regulate functions ranging from appetite, sleep, mood regulation, neuro-protection, and immune function.
- Helps maintain homeostasis (optimal balance and harmony)
- Anadamide plays a critical role in this homeostasis

THC vs. Anandamide

- THC produces the 'high'
- Anandamide breaks down in minutes after binding to receptor
- THC can binds for several days
- THC produces more exaggerated effect
- Anadamide associated with 'runner's high'


THC
receptor
THC

Cannabinoid Receptors

Two types of receptor site have been identified

CB1 receptors – located in CNS (primarily brain)

- Maintenance of homeostasis in health and disease
- Suppression of excessive neuron activity (some reduction in pain and inflammation)
- Inhibits excessive arousal
- Stimulates appetite in GI tract
- The "high"
- Reinstates drug seeking behavior with addiction

Cannabinoid Receptors

Two types of receptor site have been identified

CB2 receptors

- Outside the brain on specific components of the immune system
- Peripheral tissues of spleen, tonsils, and thymus gland
- Localized on immune cells (monocytes, b-cells, t-cells)
- Modulate GI inflammatory response (IBS possibilities?)

Physiological Response

When marijuana is smoked,vaporized,eaten

- THC quickly passes from the lungs into the bloodstream, which carries it to organs throughout the body, including the brain.
- Its effects begin almost immediately and can last from 1 to 3 hours.
- Decision making, concentration, and memory can be affected for days after use, especially in regular users.
- If marijuana is consumed in foods or beverages, the effects of THC appear later—usually in 30 minutes to 1 hour—and may last for many hours.

Neurological Response

- Most of the cannabinoid receptors are found in parts of the brain that influence pleasure, memory, thinking, concentration, sensory and time perception, and coordinated movement.
- Marijuana activates the endocannabinoid system, which causes the pleasurable feelings or "high" and stimulates the release of dopamine in the brain's reward centers, reinforcing the behavior.

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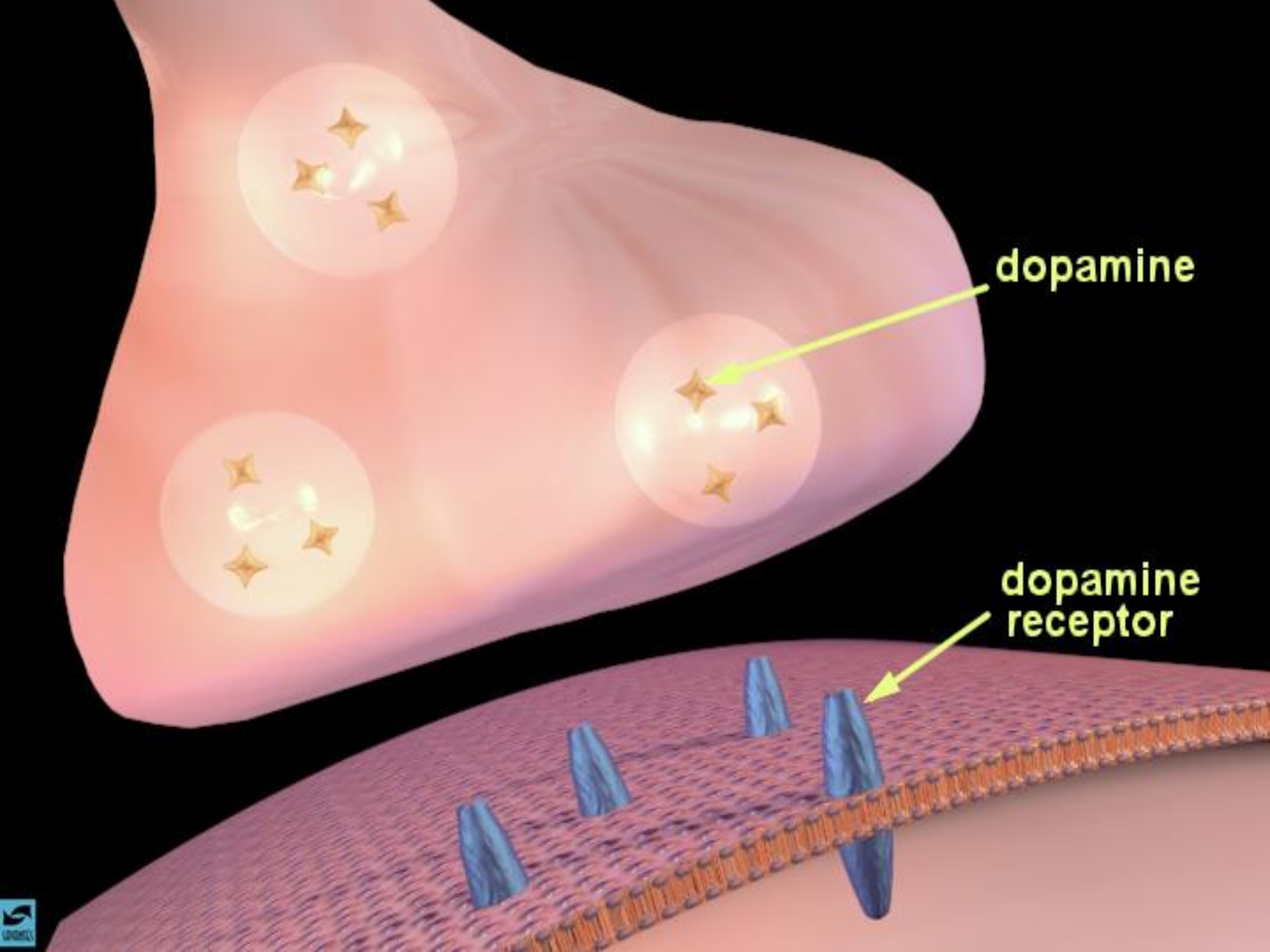
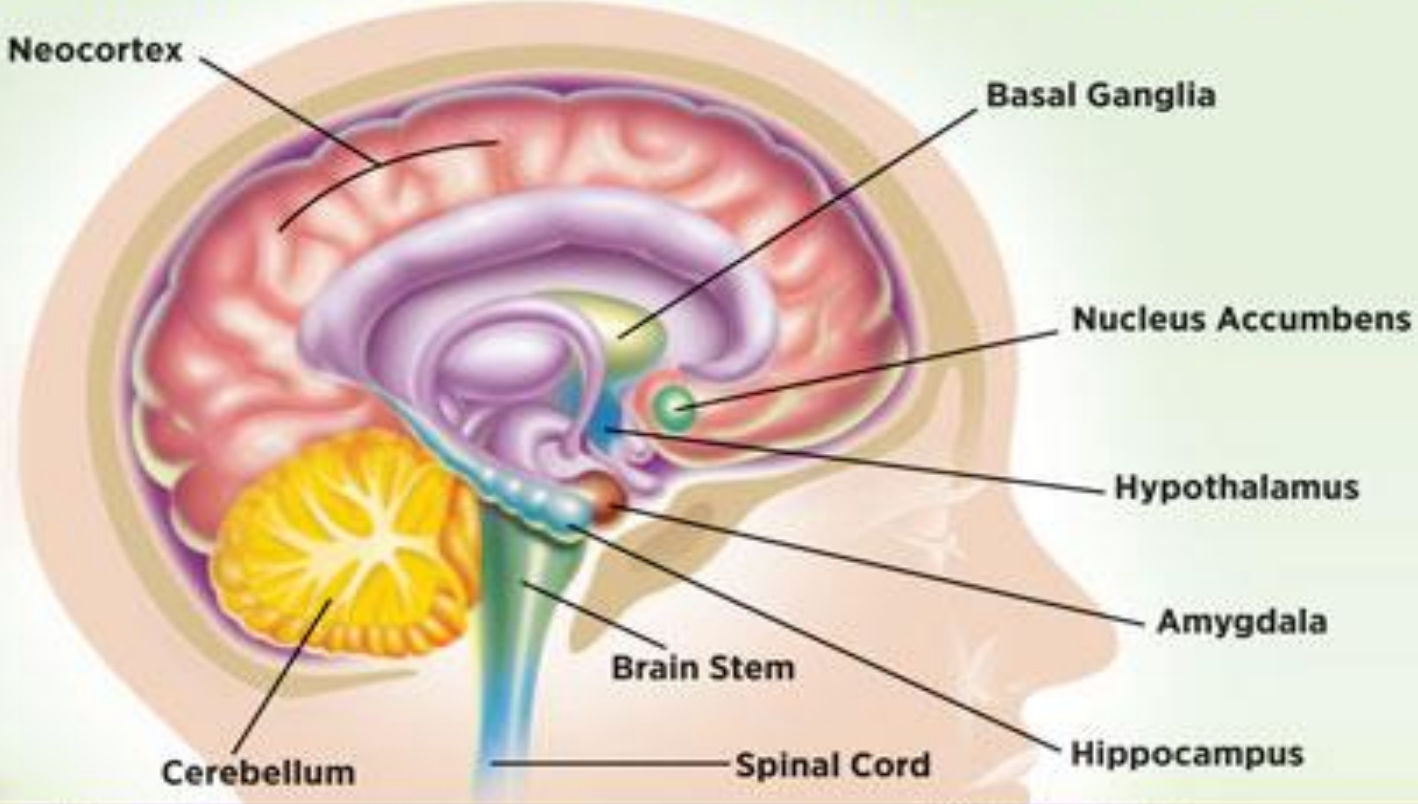

dopamine
dopamine receptor

How does THC affect behavior? *It depends on where the CB receptors are in the brain.*



Brain Structure	Regulates	THC Effect on User
Amygdala	emotions, fear, anxiety	panic/paranoia
Basal Ganglia	planning/starting a movement	slowed reaction time
Brain Stem	information between brain and spinal column	antinausea effects
Cerebellum	motor coordination, balance	impaired coordination
Hippocampus	learning new information	impaired memory
Hypothalamus	eating, sexual behavior	increased appetite
Neocortex	complex thinking, feeling, and movement	altered thinking, judgment, and sensation
Nucleus Accumbens	motivation and reward	euphoria (feeling good)
Spinal Cord	transmission of information between body and brain	altered pain sensitivity

The brain structures illustrated above all contain high numbers of CB receptors

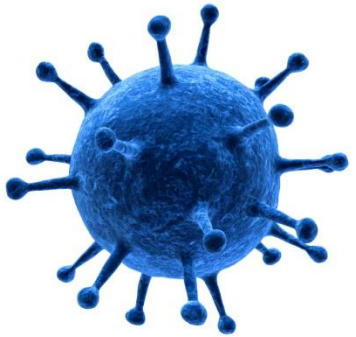
CBD

Abbreviation for Cannabidiol (one of the ingredients in the cannabis plant).

- CBD is not psychoactive (mind-altering) in its pure form
- Doesn’t bind with cannabinoid receptors but increases anandamide levels
- CBD inhibits enzyme that breaks down anadamide
- FDA approved medication for seizures in children with epilepsy

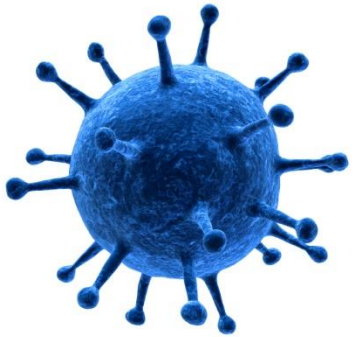
Marijuana and Immune Function

- THC immunological defects in mice and rats
- Defects included decreased antibody responses and reduced lymphocyte proliferation
- THC doses which produced very little behavior effects



Marijuana and Immune Function

- THC significantly inhibits humoral (related to the production of antibodies) and cell-mediated (dependent on the presence of activated T-lymphocytes) immunity
- Immune response of rats is dose-related



Marijuana and Driving

- Moderate doses, cannabis use impairs the functions of:
  - Co-ordination
  - Tracking
  - Perception
  - Vigilance

He proceeded to test drivers on car simulators and confirmed

- Deterioration of the ability to assess time accurately

Marijuana and Driving

- Impairment of short-term memory
- Clear association exists between the dose of cannabis (15-35mg) and reaction times
- Significant deterioration in driving ability, especially keeping the car steady in the middle of a lane and a constant distance from the verge

Sources

- Deborah Rice, Stan Barone. Critical Periods of Vulnerability for the Human Nervous System. Environmental Health Perspectives. 2000.
- https://www.drugabuse.gov/news-events/nida-notes/2016/09/regular-marijuana-use-associated-differences-in-brain-gray-matter-connectivity
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- *https://www.drugabuse.gov/publications/research-reports/marijuana/does-marijuana-use-affect-driving*

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