

<p>NAMI National Alliance on Mental Illness</p>	<p>New Hampshire</p>
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**Cannabis Use and Psychosis:
Science and Practical Considerations**

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1

**Cannabis Use and Psychosis:
The Science**

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2

Cannabis: a brief overview

- Harvested from *Cannabis sativa* since approximately 3,000 BC
 - Naturally, cannabis contains over 100 cannabinoid molecules
 - Two most common are:
 - Delta-9-tetrahydrocannabinol (THC) - euphoria
 - Cannabidiol (CBD) – opposite effects as THC
 - The remaining 100 plus cannabinoids are present in varying concentrations in each strain of cannabis and are poorly understood.
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- During the 1960's, cannabis contained 2% THC and 2% CBD
 - Over the years breeders have enriched THC up to 30% in cannabis.
 - Simultaneously CBD was “bred down” in the cannabis plants.
 - Ratios of THC to CBD in illegally sold cannabis in the US increased from 14:1 THC:CBD in 1995 to 80:1 in 2014.
 - Most potent form is “wax”, which is 50% THC.

3

Legal status of cannabis in the United States

Federally, cannabis is a Schedule 1 drug per the DEA.

Technically, that means it is illegal with no clinical benefits.

This status has greatly impaired research on cannabis/THC/CBD.

June 2018 FDA approved CBD (brand name Epidiolex) for the treatment of 2 seizure disorders: Dravet Syndrome and Lennox-Gastaut Syndrome.

Subsequently, the DEA reclassified CBD as a Schedule (Sch.) 5 drug.

This is the lowest schedule rating (LSD, heroin, bath salts = Sch. 1; stimulants = Sch. 2; most opioids = Sch. 3; benzodiazepines = Sch. 4).

Legal status varies widely from state to state, and this status is in constant flux:

- illegal for any use
- legal medically and illegal recreationally
- legal medically and legal recreationally

4

THC and CBD are 2 VERY DIFFERENT drugs

<u>THC</u>	<u>CBD</u>
Euphoria	Demonstrates effects OPPOSITE to THC
Enhanced sensations	Antipsychotic
Hypoactivity	Anti-inflammatory
Anxiety	Antioxidant
Memory impairment	Treats some seizure disorders
Perceptual distortions	Anti-anxiety
Paranoia	May improve cognition in schizophrenia

Analysing hair samples in daily cannabis users found:
 Higher THC levels increased depression, anxiety, and memory impairment.
 Higher CBD levels lower psychosis-like symptoms and improved memory.

5

Cannabinoid receptors in the human brain

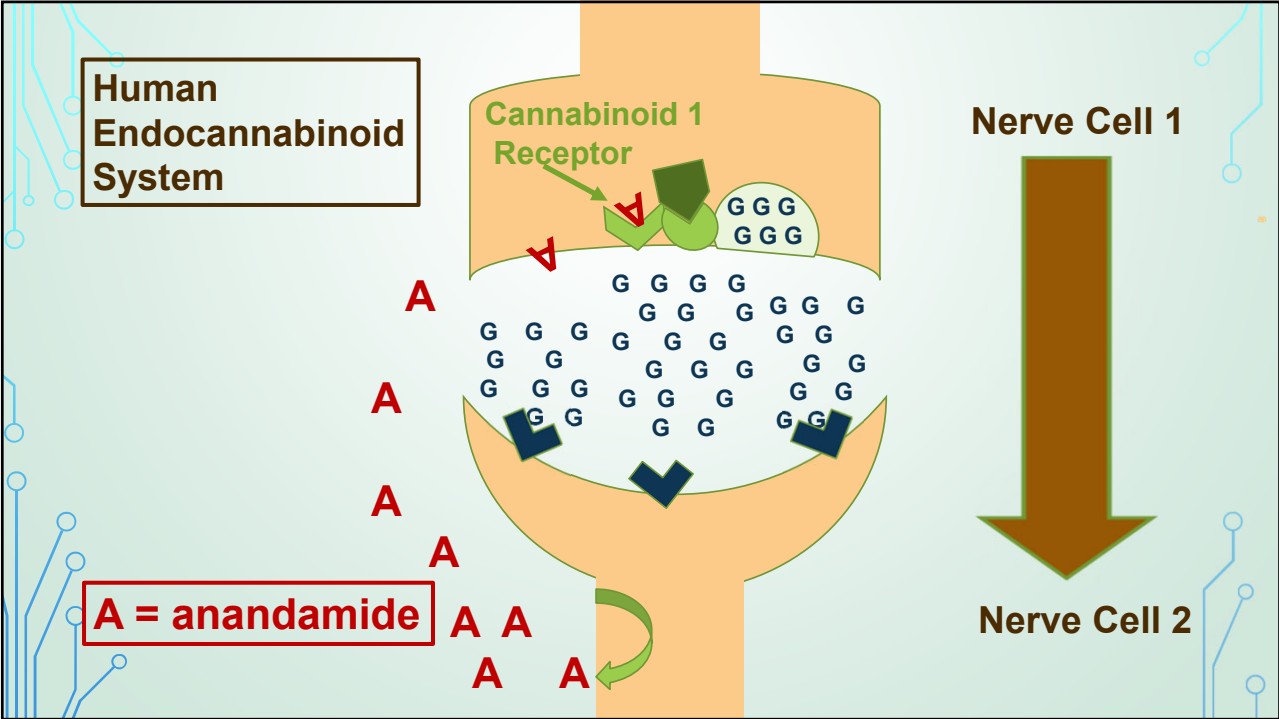
Cannabinoid 1 Receptor (discovered 1990)
 Primary cannabinoid receptor in the human brain.
 THC binds and displaces the naturally occurring cannabinoid.*
CBD DOES NOT bind.

Cannabinoid 2 Receptor
 Some in brain, but primarily in immune cells, GI tract, and spleen.
 THC binds and displaces the naturally occurring cannabinoid.*
CBD DOES NOT bind.

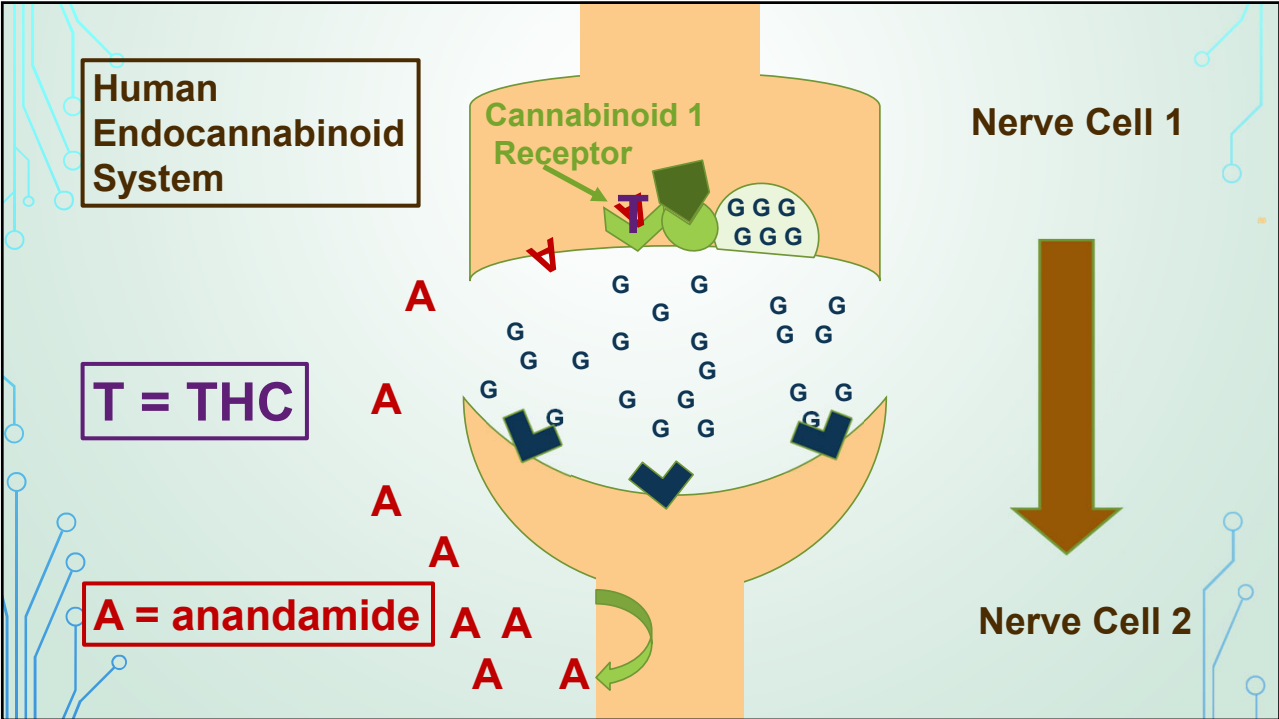
CBD's mechanism is not well established, but it seems to increase brain levels of the natural endogenous cannabinoid anandamide.*

*Endogenous cannabinoids = anandamide and 2-arachidonoyl-glycerol (2-AG)
 Created "on demand" post synaptically. Diffuse up to CB1R and inhibit release of
 Glutamate, GABA, dopamine, norepinephrine, serotonin, and acetylcholine.

6



7



8

Established effects of heavy cannabis use during brain development

10% of THC users develop Cannabis Use Disorder.

Increased risk of psychosis in individuals with other risk factors.

Earlier onset of psychosis in individuals already at risk.

Early evidence of irreversible cognitive decline.

Heavy use in preadolescence and adolescence are neurotoxic.

As brain neurocircuitry develops during the first 20 years of life, heavy daily cannabis use likely impacts how the brain is wired.

9

Heavy cannabis use: a well established risk factor for psychosis

Onset of psychosis 2.7 years earlier in cannabis users compared to non-users.

Onset of psychosis NOT significantly earlier in alcohol users compared to non-users (earlier by 0.3 years).

One third of patients that develop first episode psychosis are cannabis users.

Andrade C; Cannabis and Neuropsychiatry, 2: The Longitudinal Risk of Psychosis as an Adverse Outcome. J Clin Psychiatry. 77(6):e739-e742. 2016

10

Heavy cannabis use: a well established risk factor for psychosis

Increasing cannabis use increases risk of psychosis:

Ten studies showed a dose-dependent increase in the risk of developing psychosis.

Median level of cannabis use doubled the risk of psychosis (OR = 1.97).

Cannabis users in top 20% of amount used increased risk 3.4 times.

Highest level cannabis users increased risk 3.9 times.

Andrade C; Cannabis and Neuropsychiatry, 2: The Longitudinal Risk of Psychosis as an Adverse Outcome. J Clin Psychiatry. 77(6):e739-e742. 2016

11

Cannabis effect on cognition

Prospective studies suggest heavy cannabis use by adolescents can contribute to irreversible cognitive decline.

Study in New Zealand monitored 1,037 individuals born in 1972 or 1973 by evaluating cannabis use every 2 years from birth to age 38 (95% completed the full study). At ages 8, 11, 13, and 38 IQ testing was also performed.

Findings

Ongoing cannabis use beginning during adolescence resulted in a loss of 8 IQ points.

When cannabis use began in adulthood (brain had fully developed) there was no decline in IQ score.

Meier MH, Caspi A, Ambler A, et al: Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA. 2012;109:E2657-E2664.

12

Conclusion

- The term “cannabis” simply describes the source from a plant of over 100 different cannabinoids, some poorly defined and not understood, that includes the two most common: THC and CBD, which have VERY different properties and are unique molecules with oppositional effects.
- The “endocannabinoid” system in humans is complex with diverse roles, and plays an important role in brain development.
- Chronic heavy use of THC, one unique cannabinoid, during preadolescence and adolescence has a well-established effect on shortening the time to a first psychotic episode in individuals already at risk for psychosis.
- CBD has been shown to improve psychosis and cognition in individuals with schizophrenia.
- We have A LOT to learn. The current Schedule 1 DEA status of cannabis has greatly interfered with our ability to further study and understand it.

13

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14



15