THE IMPACT OF MARIJUANA ON PATIENTS WITH DIABETES

Terrence Shenfield MS, RRT-ACCS, RPFT, NPS, AE-C

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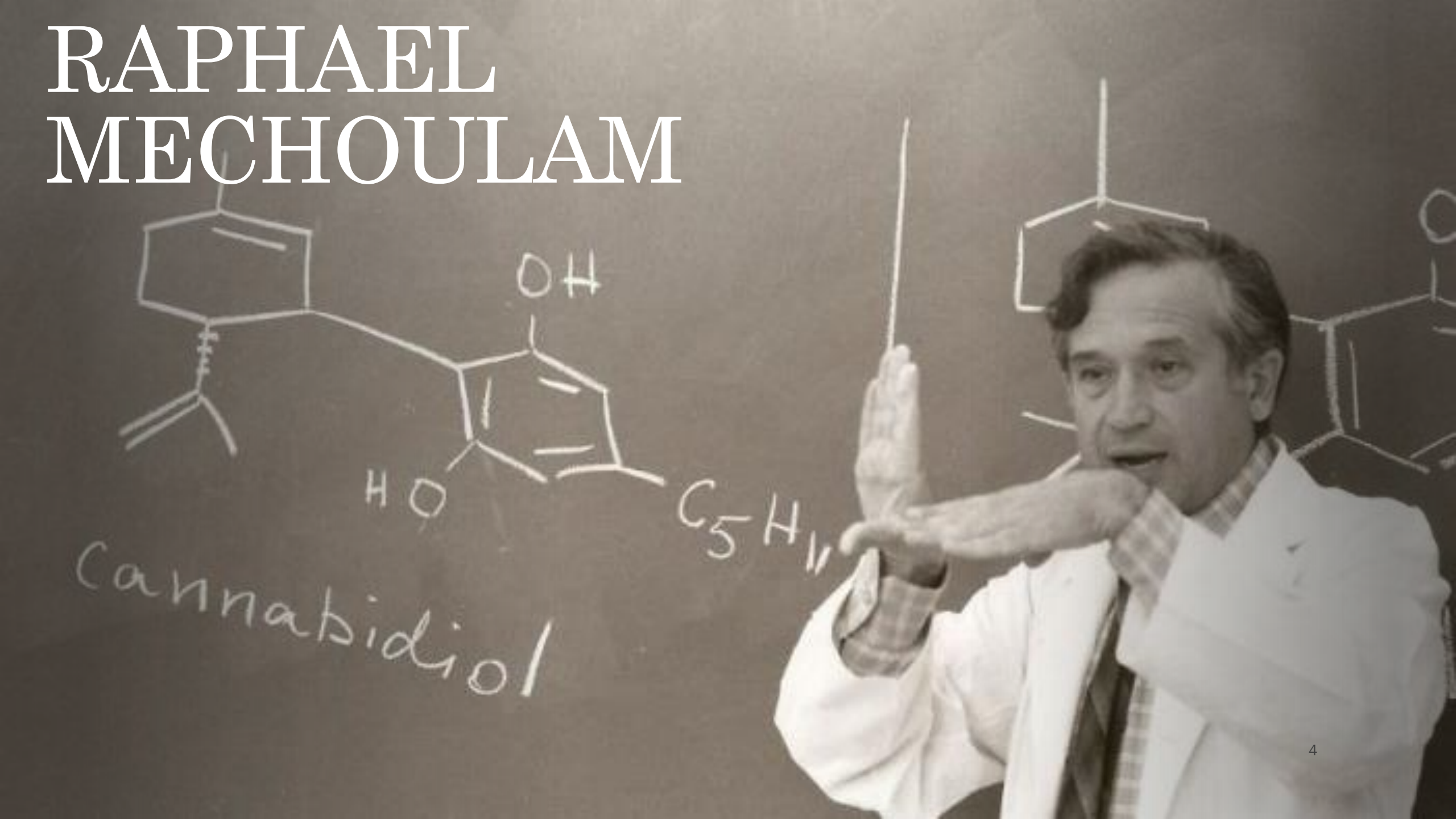
Learning Objectives/ Program Overview

- Describe what is the endocannabinoid system.
- Describe the role of the CB1 and CB2 receptor sites.
- Describe medical conditions that medical marijuana was approved for in the state of New Jersey
- Implications of cannabis on glucose metabolism
- Describe the role of cannabis and weight gain
- Risk/Benefit profile of cannabis

RAPHAEL MECHOULAM



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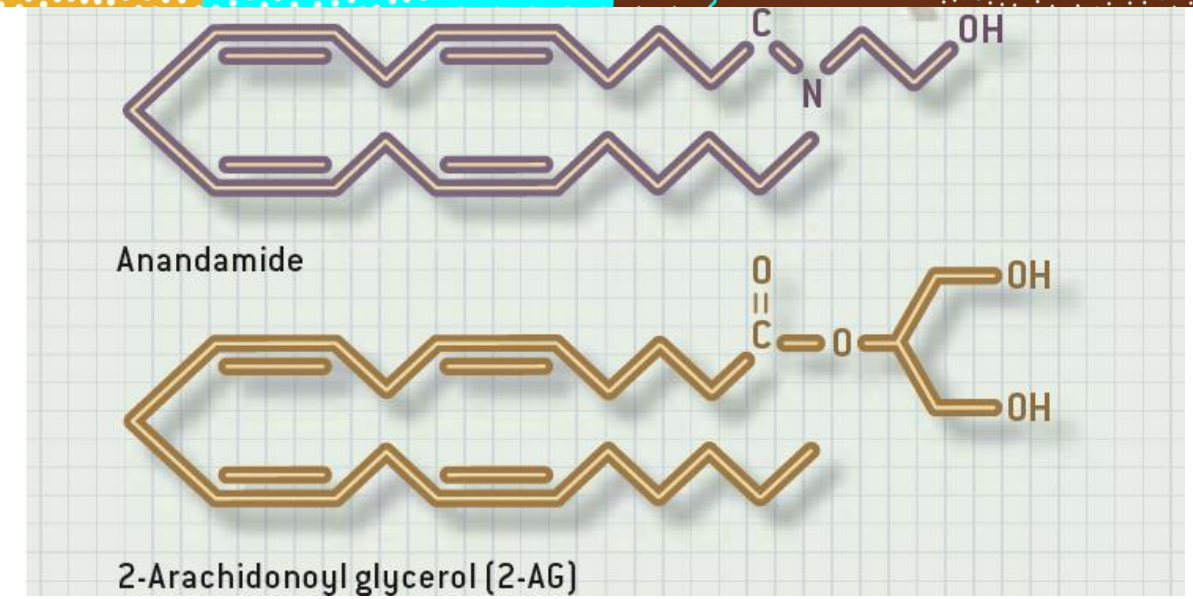


Endocannabinoids: *Bind CB1 > CB 2 structure, related to prostaglandins*

- Annandamide
- (arachidonyl-ethanolamid)

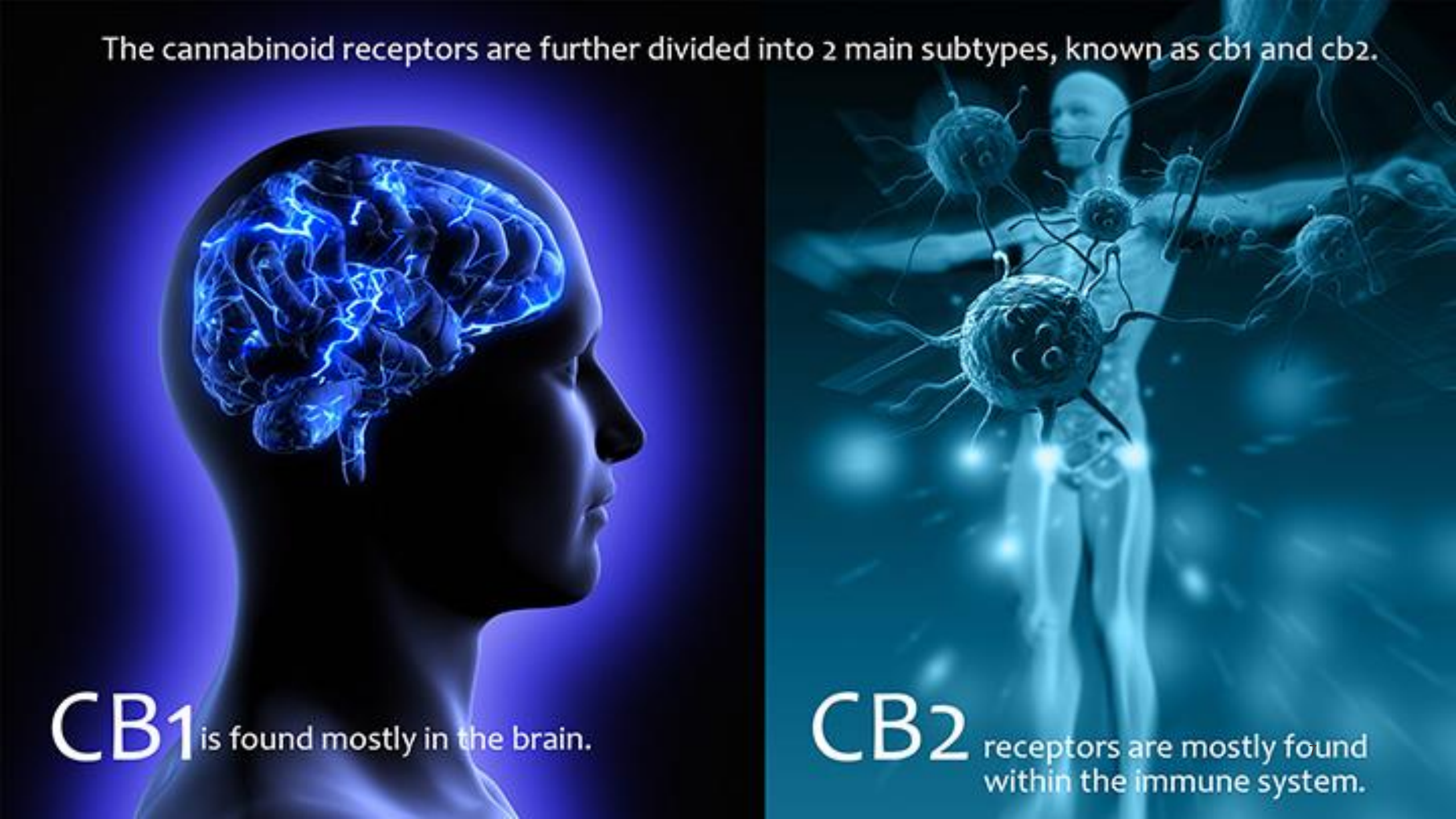
- 2-Arachidonoyl - glycerol (2-AG)
- more abundant, less potent

Nicoll & Alger, 2004

List of known cannabinoids

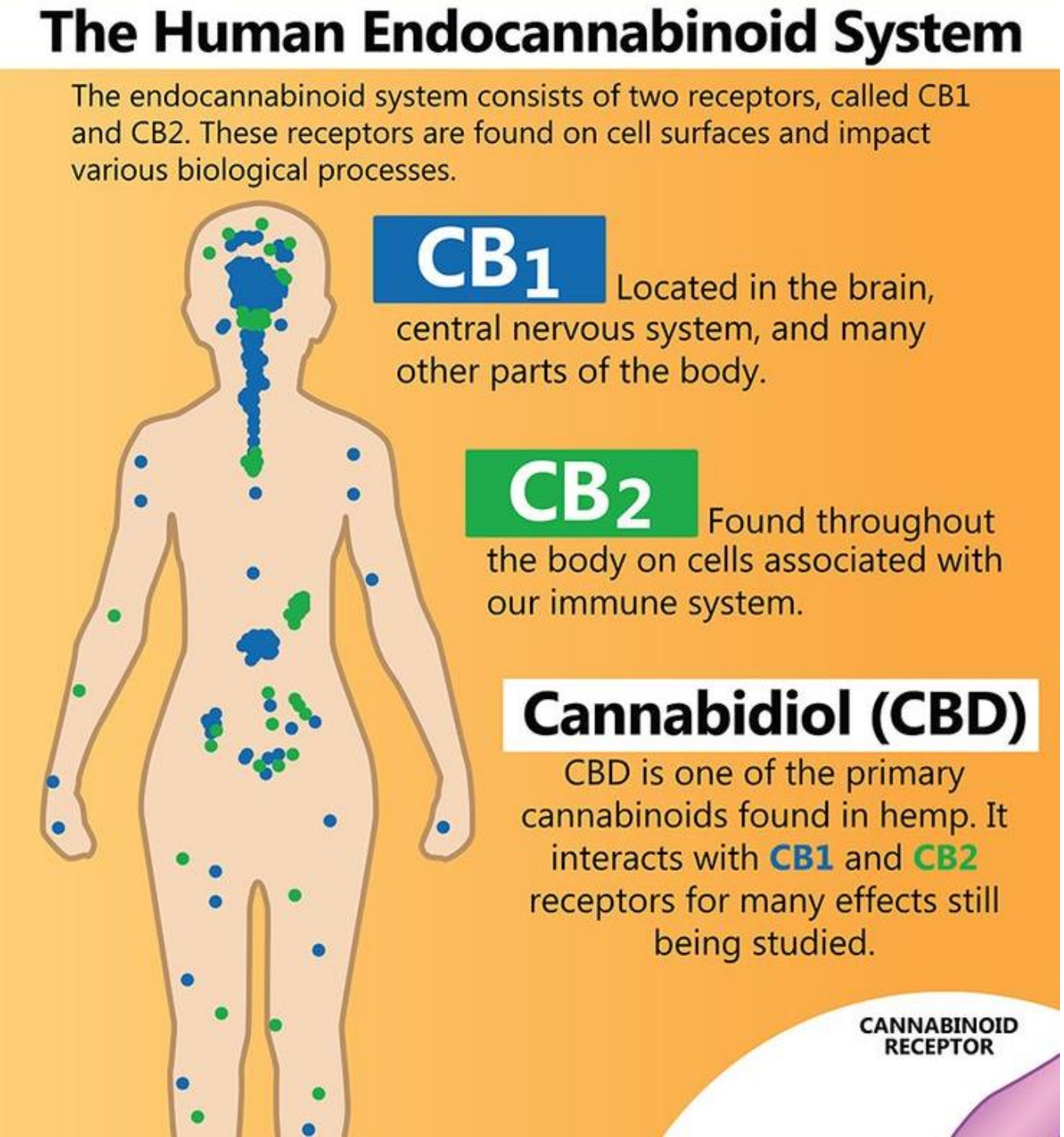
- Cannabidiol (CBD)
- Tetrahydrocannabinol (THC)
- Cannabidiolic Acid (CBDA)
  - Inflammation or infection
- Tetrahydrocannabinolic Acid (THCA)
  - Neuroprotective, cancer research
- Cannabinol (CBN)
  - Insomnia, pain relief, bone cell growth stimulant
- Cannabigerol (CBG)
  - Protect neurons in mice with Huntington's disease (current research)
- Cannabichromene (CBC)
  - Depression and cancer research
- Tetrahydrocannabivarin (THCV)
  - Appetite suppression and diabetes research
- Cannabidivarin (CBDV)
  - Rett syndrome and Autism research

The cannabinoid receptors are further divided into 2 main subtypes, known as cb1 and cb2.



CB1 is found mostly in the brain.

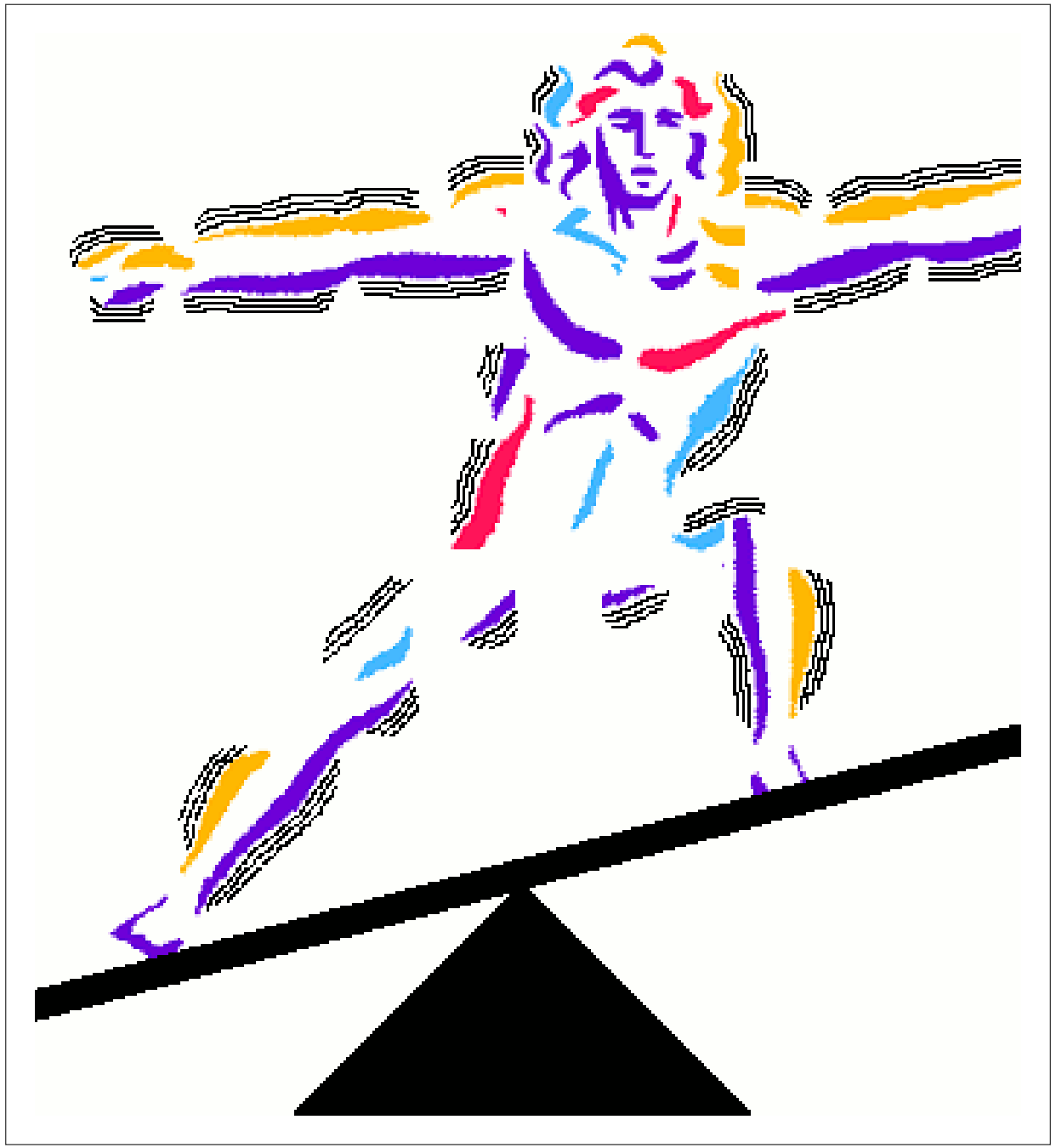
CB2 receptors are mostly found within the immune system.



Endocannabinoid Overview

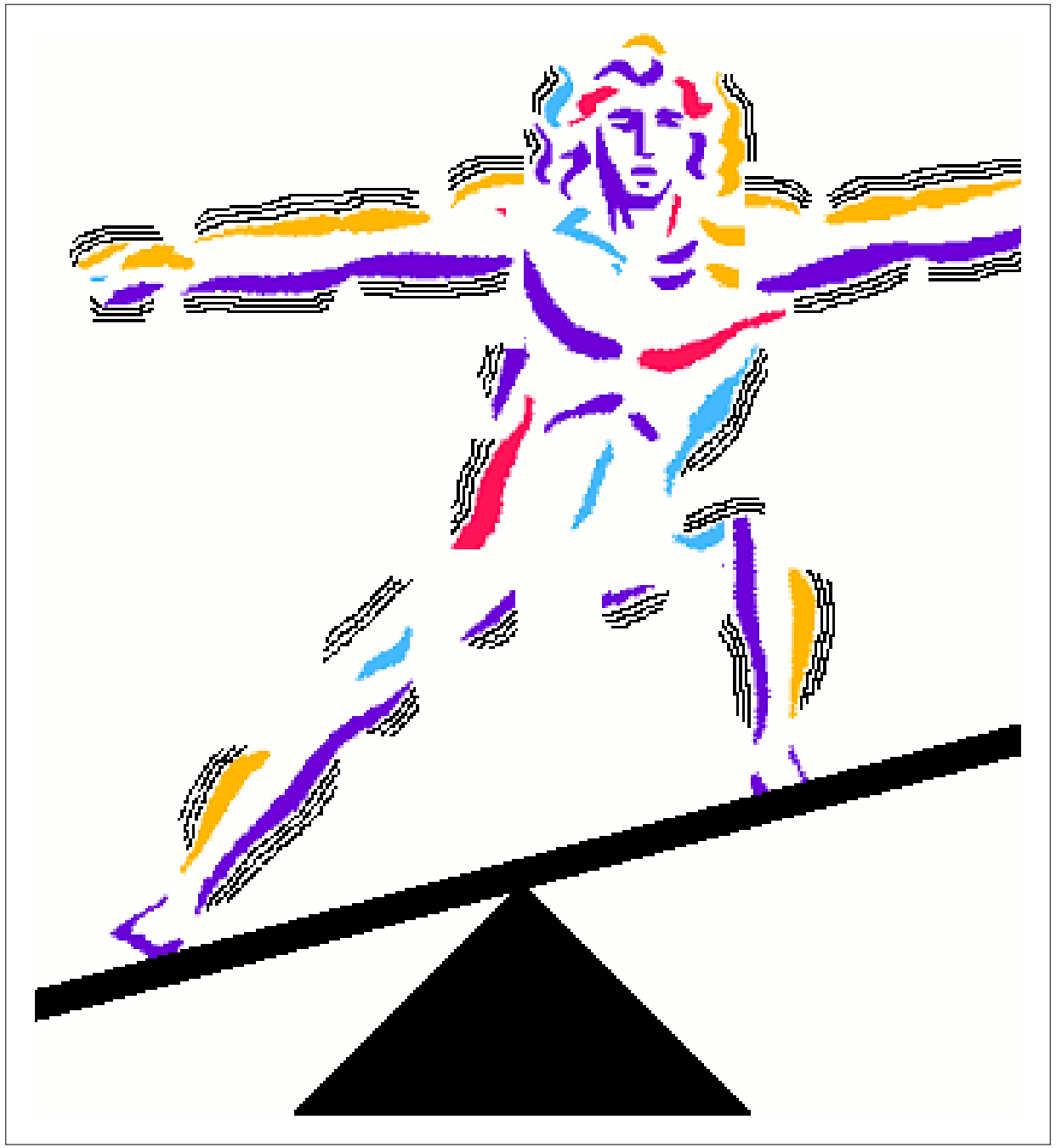
- Endogenous physiologic system
  - Establishes and maintains normal state or homeostasis
  - Key role in food hunger, fat accumulation, glucose and lipid metabolism
- Two well known receptor site
  - CB1 –central and peripheral nervous system
  - CB2 –immune cells
- Endogenous endocannabinoids
  - AEA (Anandamide)
  - 2-AG (2-Arachidonoylglycerol)
- Enzymes degrade AEA and 2-AG

Understanding Endocannabinoid Deficiency



Cannabinoid Receptors:

- CB1
  - THC has high affinity for these receptors
  - Pain , appetite, nausea, and depression
  - Arthritis and Lupus
  - Glucose metabolism
- CB2
  - Receptor's part of immune system
  - Great densities found in GI tract
  - Modulate Crohn’s disease and IBS



CB1 physiologic effects

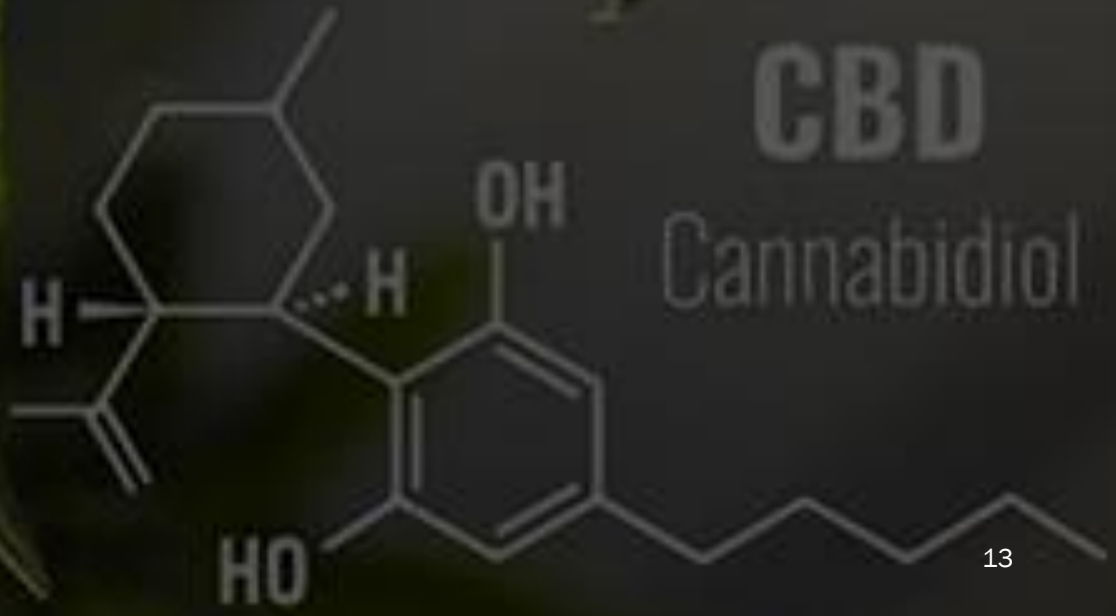
- CB1 blockade helps
  - **Regulate energy intake**
  - **Visceral obesity**
  - **Improves glucose and lipid metabolism**
  - Antinociception
  - Motor control
  - Memory and learning
  - Immunity and inflammatory responses
  - Neuroprotection

Role of CB2 receptors

- Located throughout the immune system and related organs, like the spleen, tonsils, and thymus gland
- Less dense in brain (more CB1)
- Significant role in insulin resistance
  - Considered a promising target for therapeutic development against insulin resistance and obesity-related diabetes
- Modulate inflammatory responses to intestinal diseases such as Crohns and IBS
- Decreases inflammation in Arthritis and Alzheimer's

Role of CBD

- Low affinity for CB1 and CB2 receptors
- Acts as an antagonist on the CB1 and CB2 sites
- Extends duration of Anandamide and 2-AG
- CBD may be helpful in offsetting the damage diabetes can inflict on microvascular system
- Dravet syndrome (Epidiolex)
- Other treatment-resistant epilepsies
- Pain (Nociceptive and Neuropathic)
- Cancer
- Inflammation



New Jersey Approved Medical Conditions For Medical Marijuana

- Amyotrophic lateral sclerosis
- Anxiety
- Cancer
- Chronic Pain
- Dysmenorrhea
- Glaucoma
- Inflammatory bowel disease, including Crohn's disease
- Intractable skeletal spasticity
- Migraine
- Multiple sclerosis
- Muscular dystrophy
- Opioid Use Disorder
- Positive status for Human Immunodeficiency Virus (HIV) and Acquired Deficiency Syndrome (AIDS)
- Post-Traumatic Stress Disorder (PTSD)
- Seizure disorder, including epilepsy
- Terminal illness with prognosis of less than 12 months to live
- Tourette Syndrome

Recreational marijuana is now legal in New Jersey. The New Jersey Cannabis Regulatory, Enforcement Assistance, and Marketplace Modernization Act (known as A21) was signed into law on February 22, 2021.

Some stats

- Risk factors for DM2 are being overweight and obese, physical inactivity, unhealthy food intake, increasing age, smoking, high alcohol intake, genetics, and a family history of diabetes
- Currently about 180 million people use marijuana for nonmedical reasons worldwide
- With decriminalization there is expected increase in marijuana use nationwide
- Compulsive eating disorders had been contributed to marijuana use
- Research on marijuana related diabetes type 2 studies are being conducted
- Studies have shown lower risk of diabetes by lowering fasting insulin levels and insulin resistance
- Cannabis use has been shown to influence glucose metabolism contributing to weight loss

MARIJUANA AND THE MUNCHIES

Is there evidence that smoking cannabis
results in weight gain contributing to type2 diabetes?

Who benefits from the munchies?

HIV + Patients

Chemotherapy Patients

WHAT ABOUT REGULAR CANNABIS USERS?

DOES IT CONTRIBUTE TO OBESITY AND TYPE 2 DIABETES?

Research Article

Cannabis Use as Risk or Protection for Type 2 Diabetes: A Longitudinal Study of 18 000 Swedish Men and Women

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Research question: Whether or not cannabis use may increase or decrease the risk of type 2 diabetes?

- We have all heard that cannabis will increase your appetite (munchies) resulting in weight gain
- Population-based cohort study of 17,967 Swedish men and women (aged 18–84 years)
- **Conclusions. The present study suggests that there is no association between cannabis use and subsequent type 2 diabetes after controlling for age**

Published in final edited form as:

Epidemiology. 2015 July ; 26(4): 597–600. doi:10.1097/EDE.0000000000000314.

Cannabis Smoking and Diabetes Mellitus: Results from Meta-Analysis with Eight Independent Replication Samples

Omayma Alshaarawy[a] and **James C. Anthony**[a,*]

[a]Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI 48823

Research question:
The intersection of cannabis smoking (CS), obesity, and type 2 diabetes mellitus (DM)

- Background—In preclinical animal studies, evidence links cannabis smoking (CS) with hyperphagia, obesity, and insulin resistance.
- In humans, CS shown an inverse relationship to type 2 diabetes mellitus (DM).
- Meta analysis was performed on eight major studies
- (1) National Health and Nutrition Examination Surveys
- (2) National Surveys on Drug Use and Health (2005-12)
- **In conclusion, this epidemiological evidence from eight independent studies**
  - **Lower incidence of obesity**
  - **Less cases of type 2 diabetes**
  - **Decreased insulin resistance**

Caloric intake and diabetes type 2 diabetes

- Activation of CB1 receptors has been shown to promote food craving and hyperphagia
- This led to the development of endocannabinoid receptor antagonists as therapy for obesity and DM2
- Marijuana use is associated with an acute increase in caloric intake, and people who smoke marijuana have higher average caloric intake levels than nonusers
- Despite these associations with increased caloric intake, marijuana use has been associated with
  - Lower body mass index (BMI)
  - Lower prevalence of obesity
  - Less cases of diabetes mellitus
- The mechanisms underlying this paradox have not been determined but research is showing it influencing both lipid and glucose metabolism

Review › Handb Exp Pharmacol. 2011;(203):75-104. doi: 10.1007/978-3-642-17214-4_4.

Cannabinoids and endocannabinoids in metabolic disorders with focus on diabetes

Vincenzo Di Marzo [1], Fabiana Piscitelli, Raphael Mechoulam

Affiliations + expand

PMID: 21484568 DOI: 10.1007/978-3-642-17214-4_4

CB1 receptor role in glucose metabolism

- Anandamide and 2-arachidonoylglycerol are involved in all aspects of the control of energy balance
- Influencing both lipid and glucose metabolism.
- New evidence is showing endocannabinoid regulation of energy balance can become dysregulated and contribute to obesity, dyslipidemia, and type 2 diabetes
- CB(1) antagonists might be used for the treatment of these metabolic disorders.
- Cannabidiol (CBD) can be employed to retard β-cell damage in type 1 diabetes.

› Am J Med. 2013 Jul;126(7):583-9. doi: 10.1016/j.amjmed.2013.03.002. Epub 2013 May 15.

The impact of marijuana use on glucose, insulin, and insulin resistance among US adults

Elizabeth A Penner [1], Hannah Buettner, Murray A Mittleman

Affiliations + expand

PMID: 23684393 DOI: 10.1016/j.amjmed.2013.03.002

The impact of marijuana use on glucose, insulin, and insulin resistance among US adults

- Epidemiologic studies have found lower prevalence rates of obesity and diabetes mellitus in marijuana users compared with people who have never used marijuana.
- Methods: We included 4657 adult men and women from the National Health and Nutrition Examination Survey from 2005 to 2010.
- Marijuana use was assessed by self-report.
- Fasting insulin and glucose were measured via blood samples after a 9-hour fast, and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated to evaluate insulin resistance.
- Results: Current marijuana use was associated
  - 16% lower fasting insulin levels
  - 17% lower HOMA-IR (Homeostatic Model Assessment of Insulin Resistance)
  - Smaller waist circumferences.
- Conclusions: We found that marijuana use was associated with lower levels of fasting insulin and HOMA-IR, and smaller waist circumference.

The role of cannabis and diabetic neuropathy

- Common complication of diabetes and current treatment are relatively refractory to most analgesics
- Cannabis sativa has been used as an analgesic for centuries
- Effective alternative or adjunctive treatment for peripheral neuropathy
- The endocannabinoid system plays a regulatory role in the modulation of pain transmission and in the nociceptive receptive pathways
- Cannabinoids are thought to reduce pain by modifying these events
- CBD oil can achieve significant improvement in pain in patients with peripheral neuropathy

Risk/Benefit of Cannabis Use

Risk

- Anxiety (THC)
- Bronchitis
- Interaction with warfarin (increased INR)
- Additive effect with benzodiazepine‘s
- Acute psychosis or schizophrenia
- Pollen allergies
- Cognitive function
- Dependance
- Cannabinoid Hyperemesis Syndrome

Benefit

- No link with COPD
- No link with Cancer
- CBD decreases anxiety levels

Summary

- Cannabis research is just in the beginning as it's still a scheduled 1 drug here in the United States
- Current cannabis research has led to studies that demonstrate that cannabis does not cause weight gain and may protect humans from getting diabetes
- Cannabis use may lower the risk of diabetes by lowering fasting insulin levels, as well as the risk of insulin resistance
- Cannabidiol (CBD) has been shown to reduce inflammation and protective affect on pancreatic cells
- Neuropathy can be treated with cannabis products
- The risk benefit profile of cannabis is not too extreme considering there are medications which are much more harmful out there

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