

# Introduction to the Endocannabinoid System

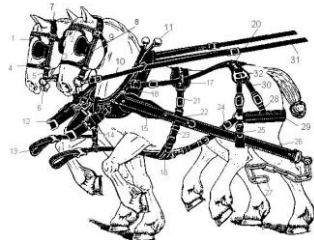
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1

## Defining the cannabinoid system

- Exogenous compounds
  - Phytocannabinoids
    - THC, CBD, combinations
  - Synthetic cannabinoids
    - Nabilone, dronabinol
    - K2, “spice”
- Endogenous cannabinoids
  - Anandamide
  - 2-arachidonyl glycerol
- Receptor targets
  - CB1, CB2



3

## Disclosures

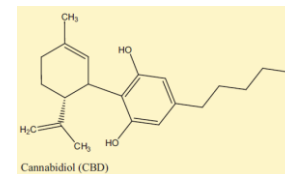
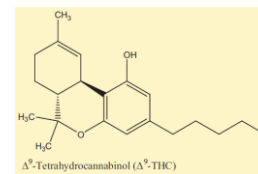
### Scientific Advisory Board

Shoppers Drug Mart

2

## Targets of Phytocannabinoids

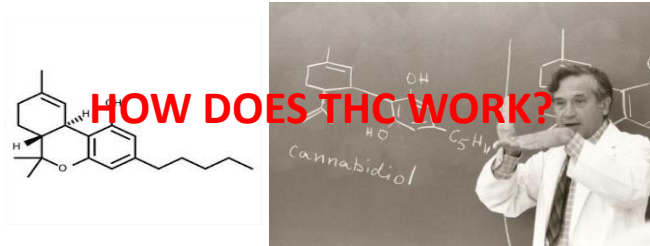
- The two main cannabinoids in cannabis that are studied are:
- THC
- CBD (cannabidiol)



4

## THC

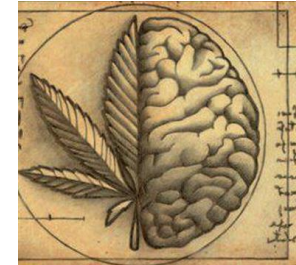
- Discovery of THC as the psychoactive component of cannabis
- Raphael Mechoulam (Hebrew University)
- April 1964 (Happy 55<sup>th</sup> birthday!)



5

## Cannabis and the Endocannabinoid System

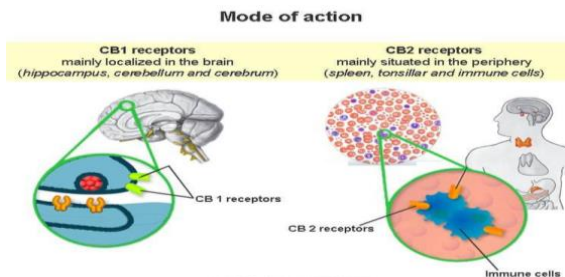
- THC, the psychoactive constituent of cannabis, exerts its effects on the brain and body through activation of the endocannabinoid system



6

## Cannabis and the Endocannabinoid System

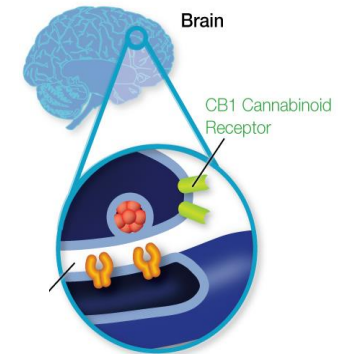
- THC binds to the same receptors that endocannabinoids exert their physiological effects through.
  - CB1 receptors (in the brain)
  - CB2 receptors (in immune cells)



7

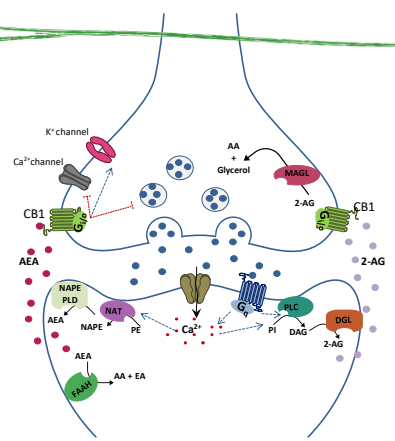
## Cannabinoids 101

- Cannabinoids act at CB<sub>1</sub> receptors to inhibit neurotransmitter release



8

### The Endocannabinoid System



Morena, Patel, Bains and Hill, *Neuropsychopharm* 2016

9

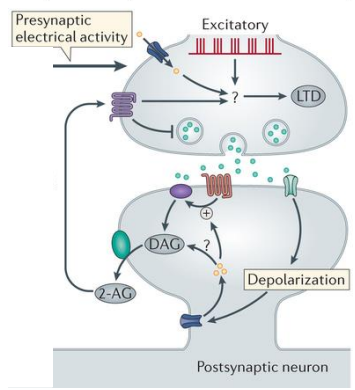
### CB1 Receptors – Its Complicated

- Cannabinoid type 1 receptor (CB<sub>1</sub>)
  - Neuron type matters!!!
  - CB<sub>1</sub> regulates release of both excitatory (glutamate) and inhibitory (GABA) neurotransmitters

10

### CB1 Receptors – Its Complicated

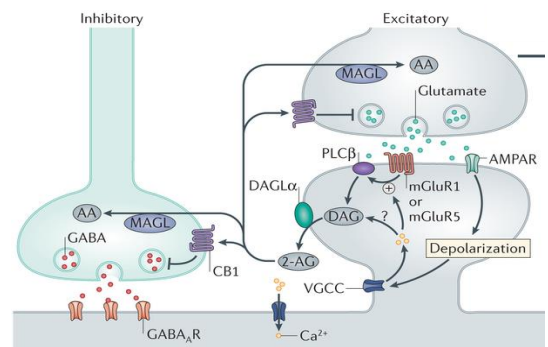
#### CB<sub>1</sub> Receptors as a Circuit Breaker



11

### CB1 Receptors – Its Complicated

#### CB<sub>1</sub> Receptors as Hetero-synaptic Regulators of Plasticity



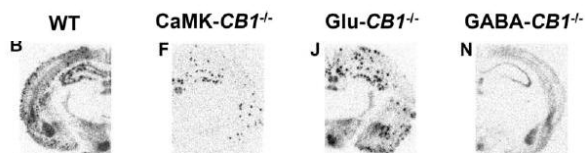
12

## CB1 Receptors – Its Complicated

### Neuronal Subtype Differences

- Most CB<sub>1</sub> expression is on GABA terminals, yet CB<sub>1</sub> on glutamate terminals mediates basically all of the neurobehavioral effects of THC.

Monory et al., 2006

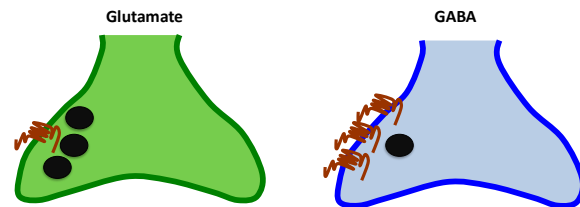


13

## CB1 Receptors – Its Complicated

### Neuronal Subtype Differences

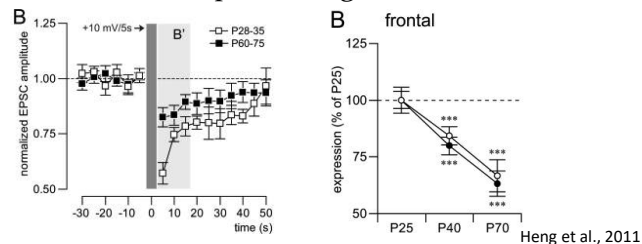
- CB<sub>1</sub> in glutamate neurons is much more efficient at recruiting G proteins than in GABA neurons



14

## CB1 Receptors – Its Complicated

- CB<sub>1</sub> changes over development, prior to puberty CB<sub>1</sub> is very high on glutamate terminals and declines through adolescence, plateauing in adulthood



Heng et al., 2011

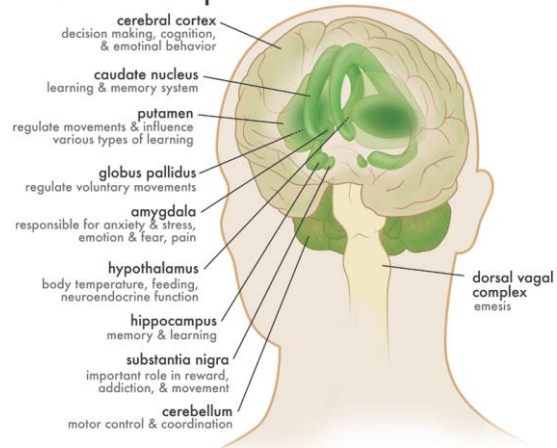
15

## Cannabis and the Endocannabinoid System



16

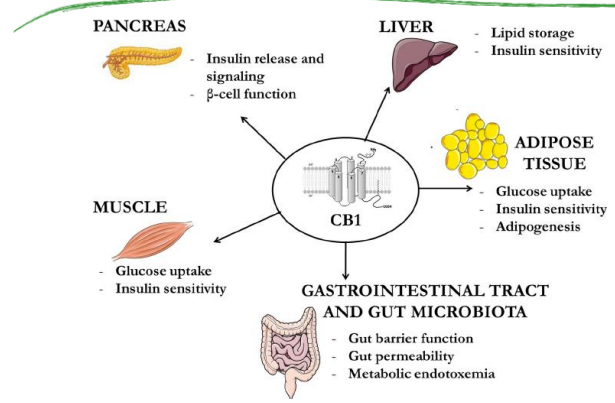
### Distribution of CB1 receptors



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17

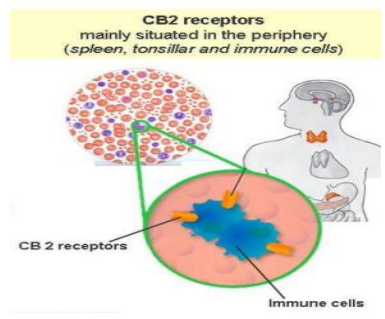
### CB1 Receptors – Its Complicated



18

### Lets Not Forget About CB2!

- Cannabinoid type 2 receptor (CB<sub>2</sub>)
  - Primarily found in immune cells
  - Acts to suppress release of pro-inflammatory molecules
  - Doesn't seem to do much to normal immune system but reduces hyperactivity



19