



UPR *LA UPR*



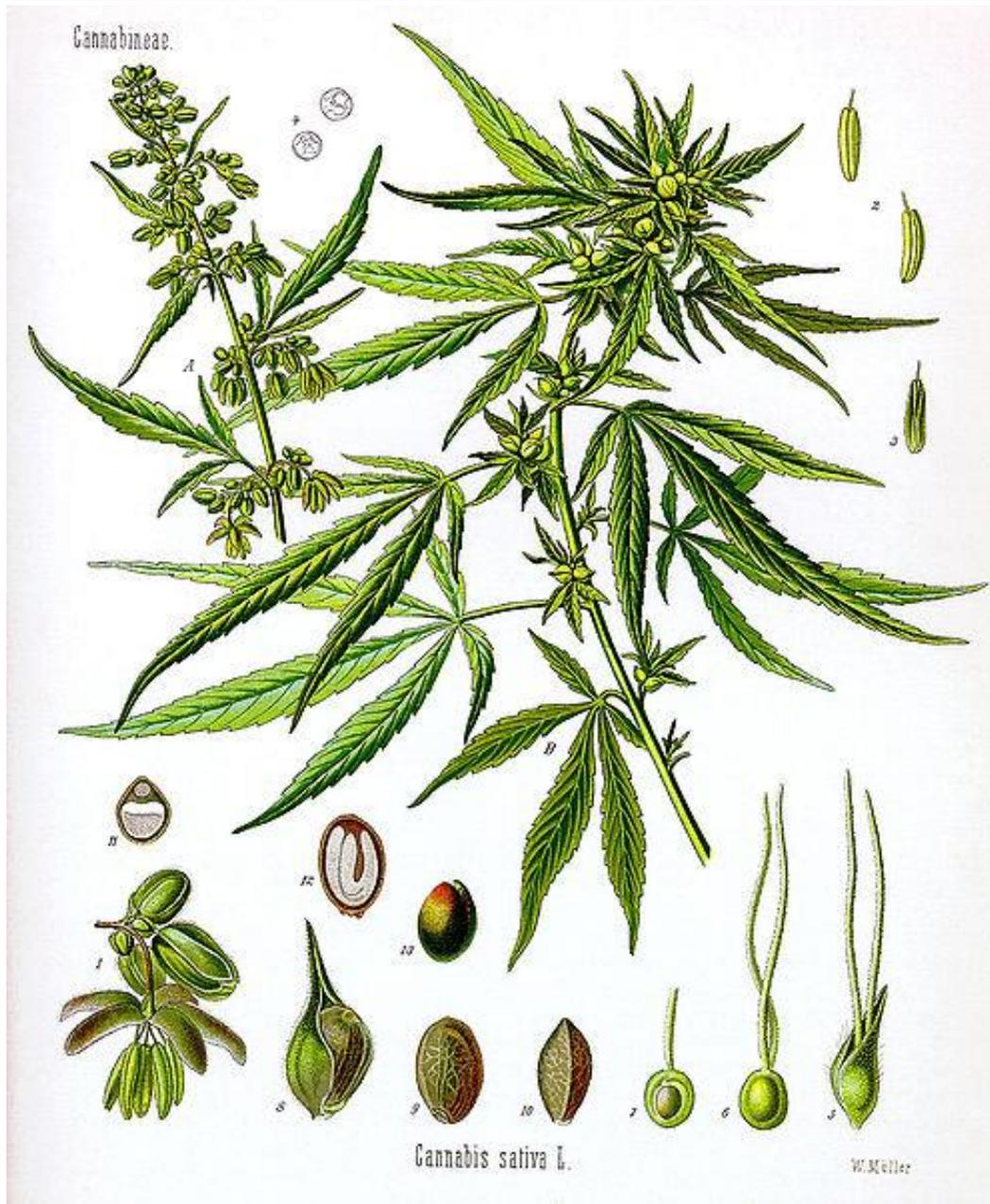
Cannabinoides: Su medicalización desde un enfoque multidisciplinario

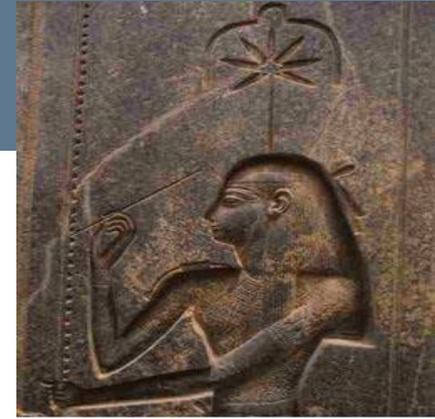
Neurobiología de los cannabinoides



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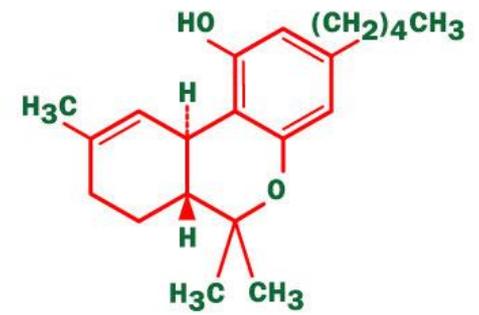
Canabis sativa





Ancient sculpture of the Egyptian god Sheshat with a Hemp plant

- Marijuana es un producto de la planta conocida como *Cannabis sativa*.
- Es la droga ilícita de mas mayor uso en los Estados Unidos.
- La planta de cannabis contiene sobre 500 compuestos de los cuales 100 se les conocen como **canabinoides**
- Los cannabinoides incluyen: Δ^9 -**tetrahydrocannabinol (THC)**, **cannabinol (CBD)** entre otros.

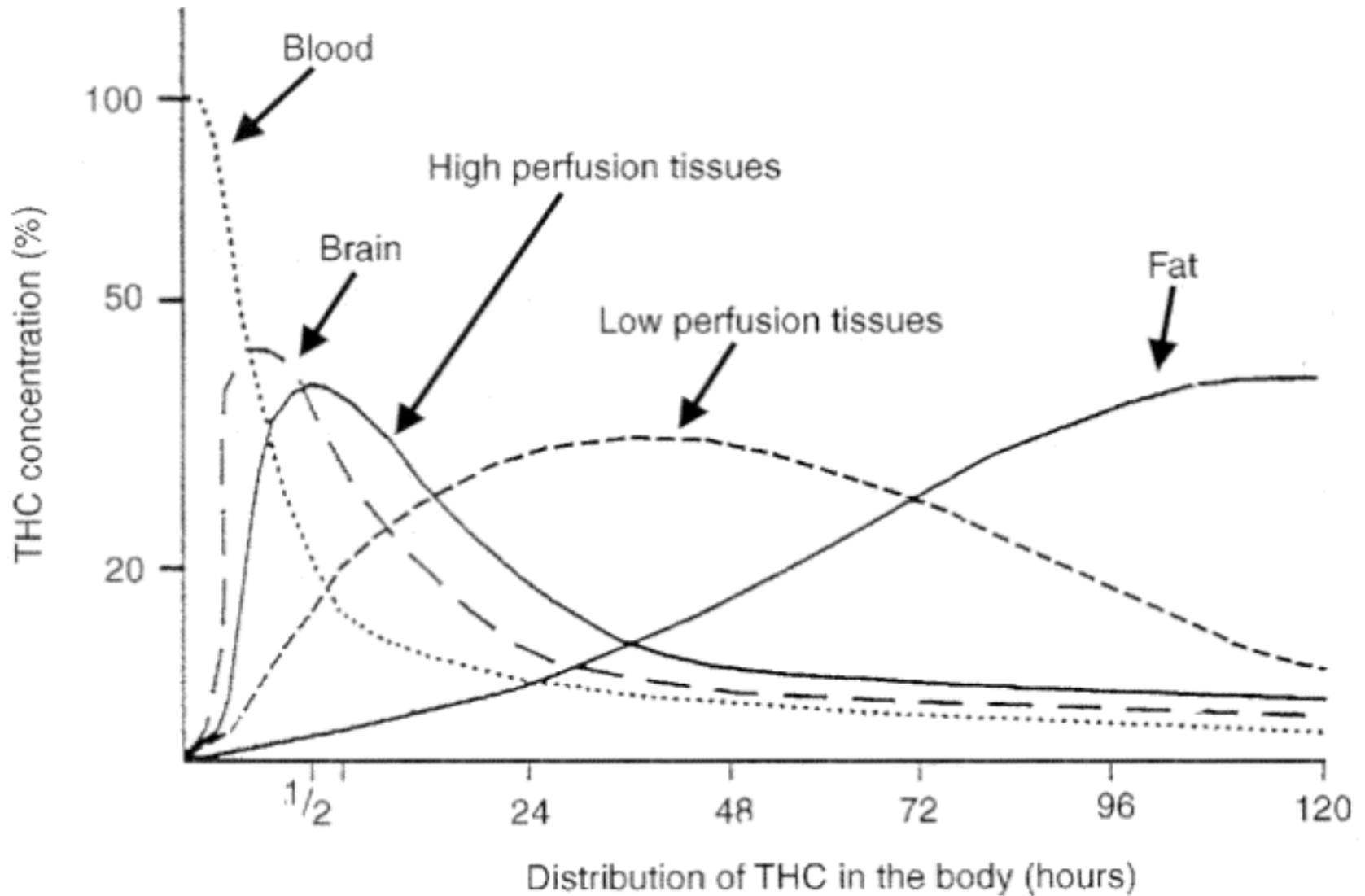


The Molecular Structure of THC
(delta-9-tetrahydrocannabinol)

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- THC es lipofílico
 - se acumula en las grasas
 - cruza la barrera rápidamente pero sus niveles en el corriente sanguíneo son bien bajos
 - Llega al cerebro sin problemas

Distribución de THC por horas



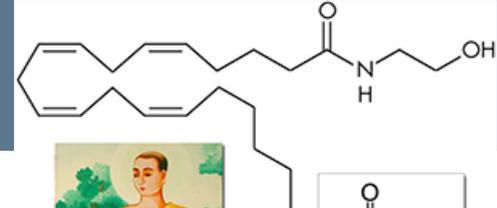
Nuestro cuerpo y cerebro
esta evolutivamente
preparado para recibir y
procesar los canabinoides
gracias a la presencia del
*sistema de
endocanabinoides (SE)*

cannabis *café*
"From our kitchen to yours!"

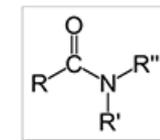


THE BEST FROM ERIC'S KITCHEN

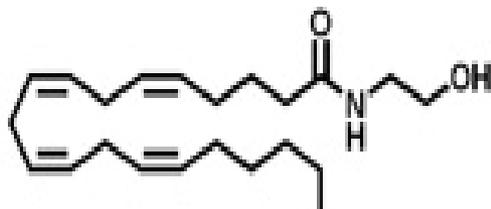
Tipos de endocannabinoides



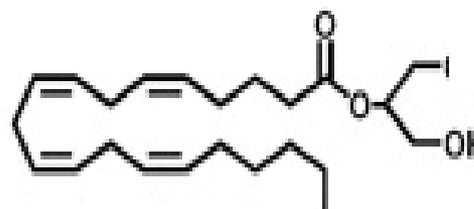
Ananda



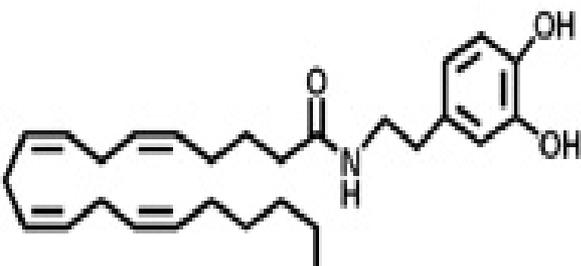
amide



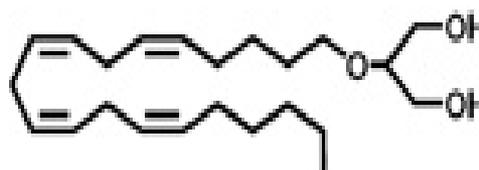
N-Arachidonylethanolamine
(Anandamide, AEA)



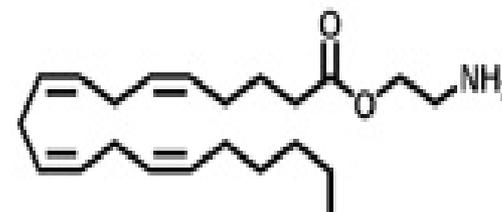
2-Arachidonoylglycerol
(2-AG)



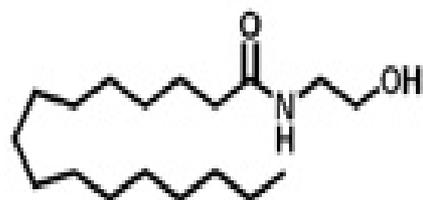
N-Arachidonoyldopamine
(NADA)



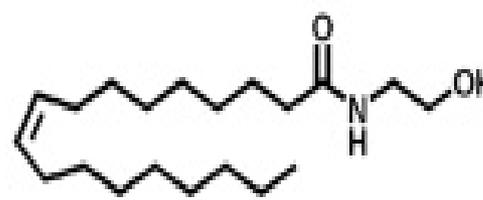
2-Arachidonoylglycerylether
(Noladin ether)



O-Arachidonylethanolamine
(Virodhamine)

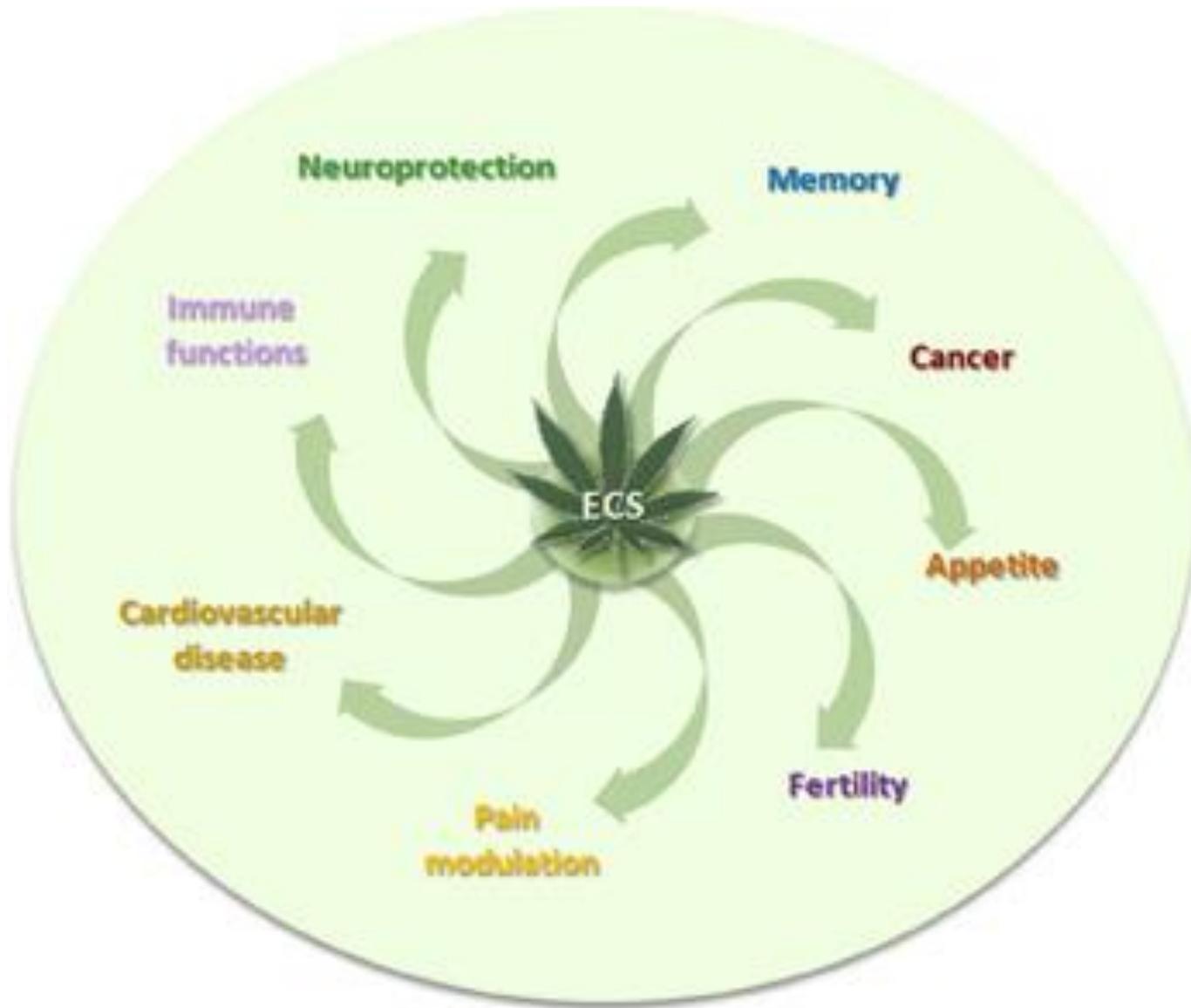


N-Palmitoylethanolamine
(PEA)

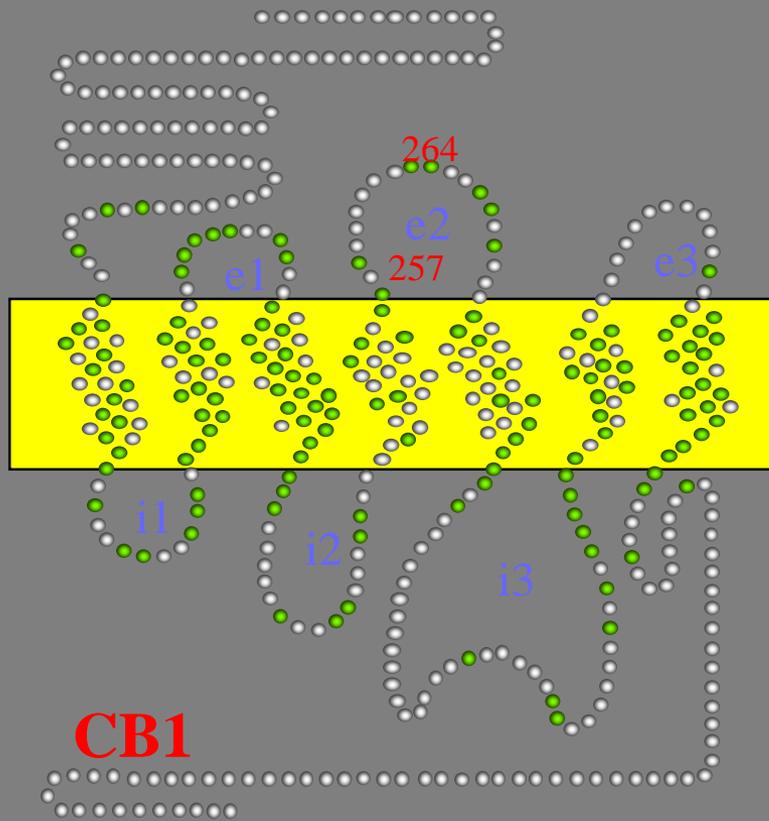


N-Oleoylethanolamine
(OEA)

Efectos fisiologicos de los endocannabinoides

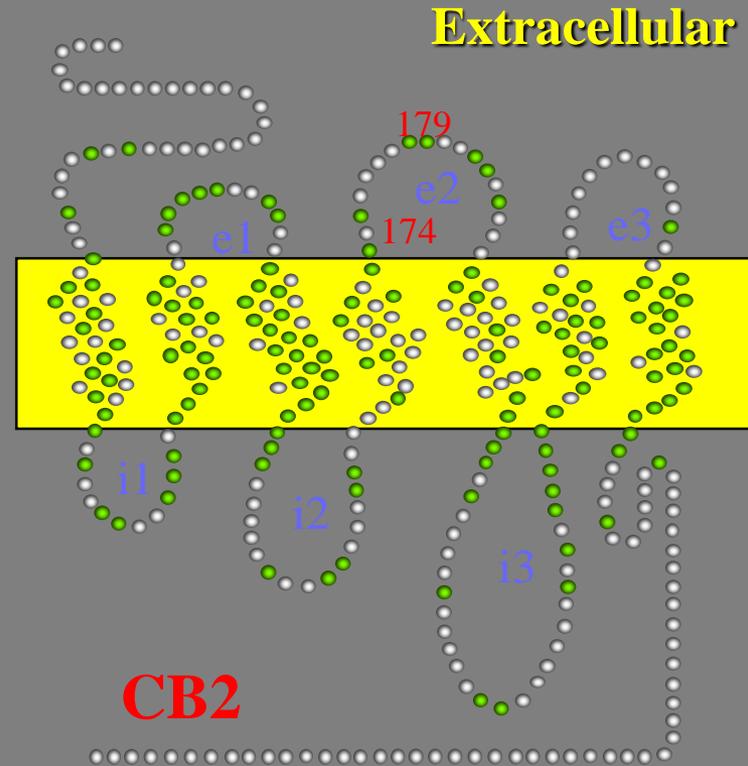


Receptores Cannabinoides : CB1 & CB2



CB1

472 amino acids



CB2

360 amino acids

Diistribucion de receptores CB1 y CB2 en el cuerpo y cerebro

● CB1 present:

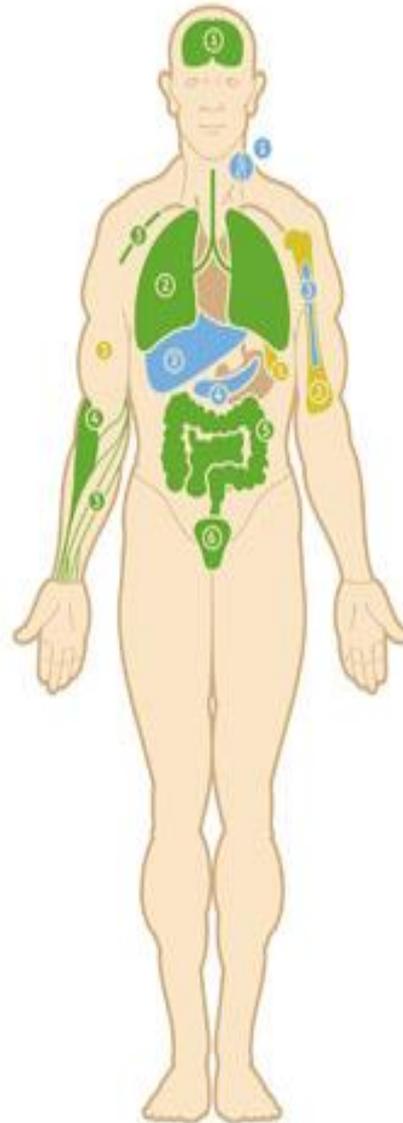
1. brain
2. lungs
3. vascular system
4. muscles
5. gastrointestinal tract
6. reproductive organs

● CB2 present:

1. spleen
2. bones
3. skin

● CB1+CB2 present:

1. immune system
2. liver
3. bone marrow
4. pancreas

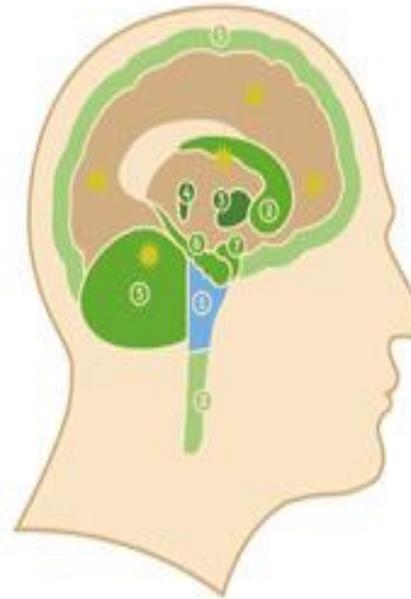


●● CB1 present:

1. cortex
2. caudate nucleus and putamen (nucleus accumbens)
3. basal ganglia
4. hypothalamus
5. cerebellum
6. hippocampus
7. amygdala
8. spinal cord

☀ CB2 present glial cells

● CB1+CB2 present 1. brainstem



CB2: cerebral cortex, hippocampus, striatum, amygdala, thalamic nuclei, periaqueducta grey, cerebellum and several brain stem nuclei

Estructuras del cerebro involucradas

AREAS OF THE BRAIN AFFECTED BY CANNABINOIDS

CEREBRAL CORTEX

PLAYS A ROLE IN MEMORY, THINKING, PERCEPTUAL AWARENESS AND CONSCIOUSNESS

HYPOTHALAMUS

GOVERNS METABOLIC PROCESSES SUCH AS APETITE

AMYGDALA

PLAYS A ROLE IN EMOTIONS

HIPPOCAMPUS

IS KEY TO MEMORY STORAGE AND RECALL

BASAL GANGLIA

GOVERNS MOTOR SKILLS AND LEARNING

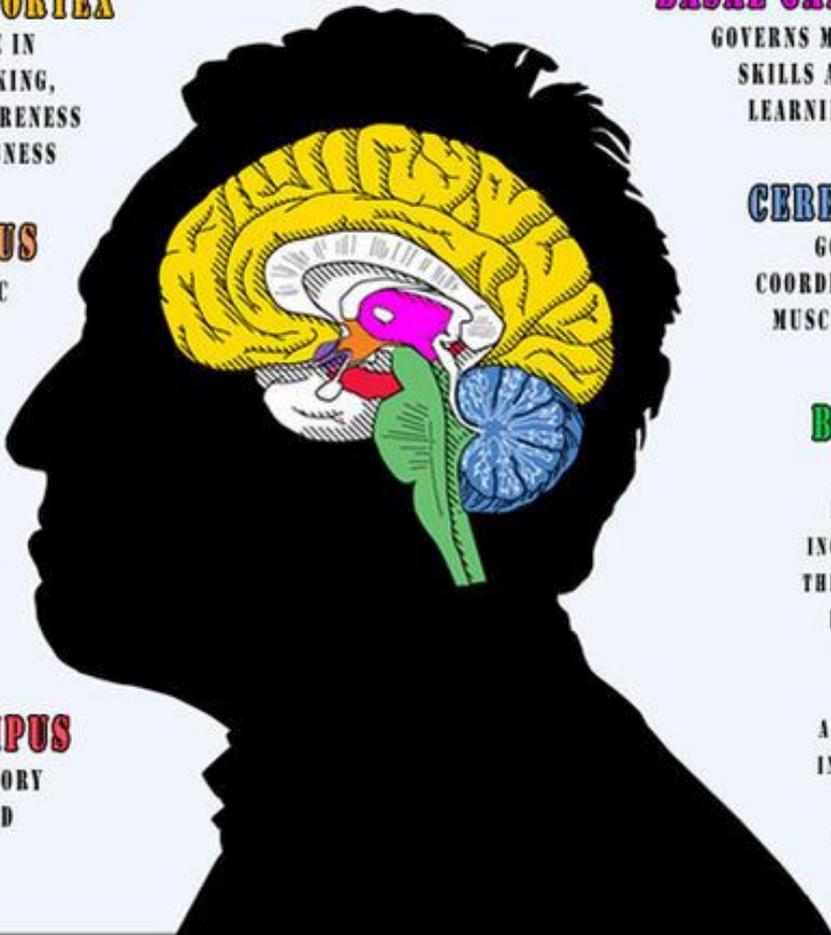
CEREBELLUM

GOVERNS COORDINATION AND MUSCLE CONTROL

BRAIN STEM

CONTROLS MANY BASIC FUNCTIONS INCLUDING AROUSING, THE VOMITING REFLEX, BLOOD PRESSURE AND HEART RATE

ALSO PLAYS A ROLE IN PAIN SENSATION, MUSCLE TONE AND MOVEMENT



Mecanismo celular de acción de señal retrograda

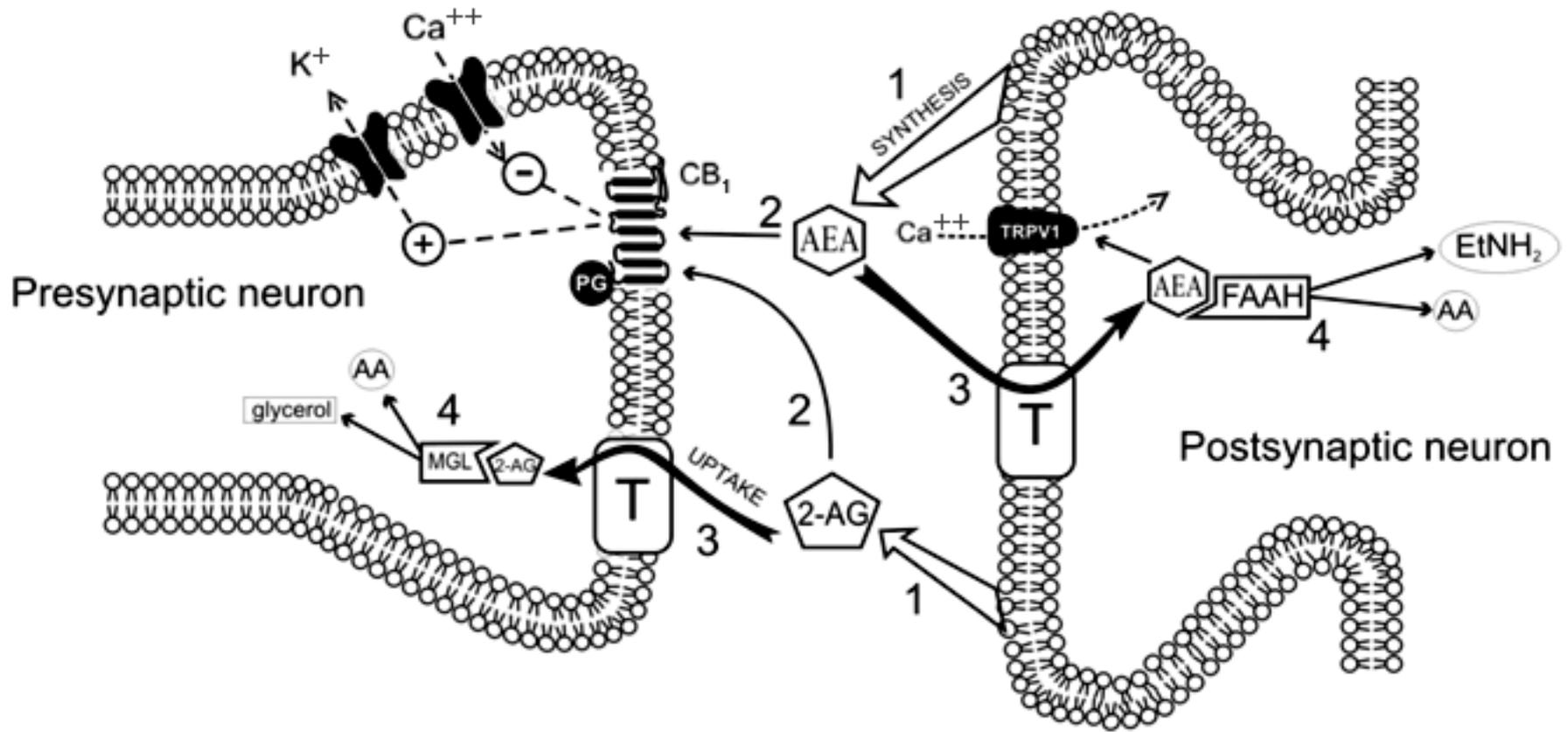
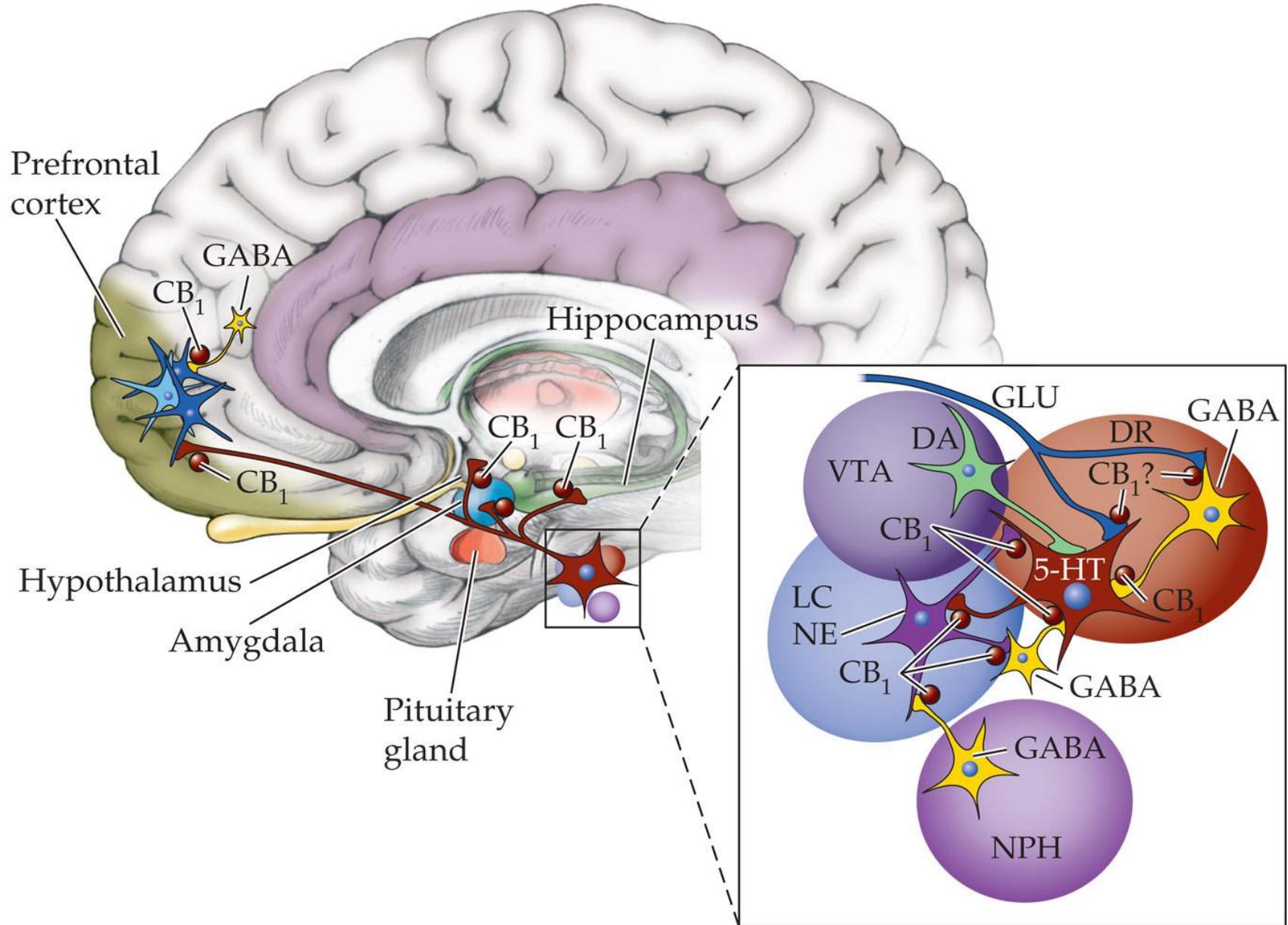


Figure 1 - Schematic representation of endocannabinoid action. Endocannabinoids are synthesised in and released from the membrane of post-synaptic neurons on-demand after calcium influx (1). They activate pre-synaptic CB₁ receptors and restrain neural activity (2). Anandamide and 2-AG are removed from the synaptic cleft by up-take into the post- and pre-synapse, respectively (3). Once inside neurons, anandamide binds TRPV1 (with consequences opposite to those of CB₁ activation) and undergoes hydrolyse by FAAH, whereas 2-AG is hydrolysed by MGL (4).

Box 14.1, Figure A CB₁ receptors are widely expressed in the neural circuitry of the human brain that regulates mood



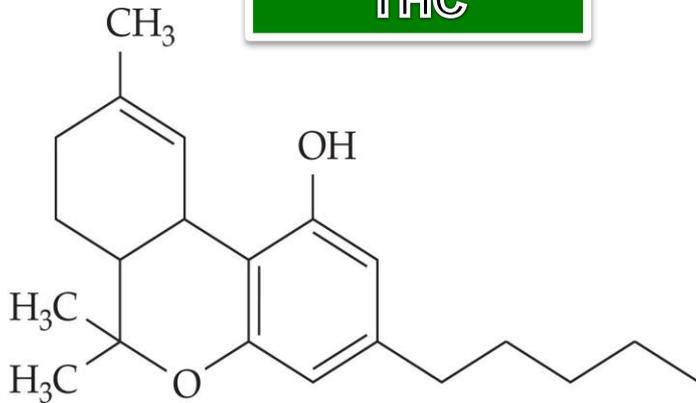
PSYCHOPHARMACOLOGY 2e, Box 14.1, Figure A
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Receptores de cannabis

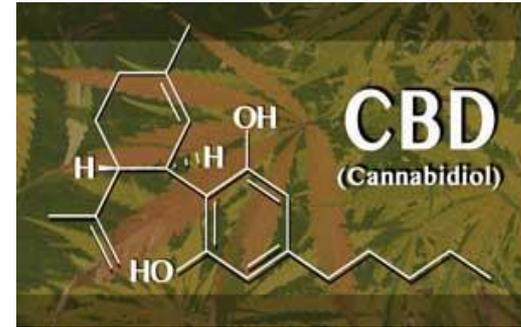
- efectos sedativos: CB1 y receptores de GABA
- efectos activación: CB1 y receptores de dopamina
- Efectos en la memoria: CB1 y receptores de glutamato

THC



PSYCHOPHARMACOLOGY 2e, Figure 14.5
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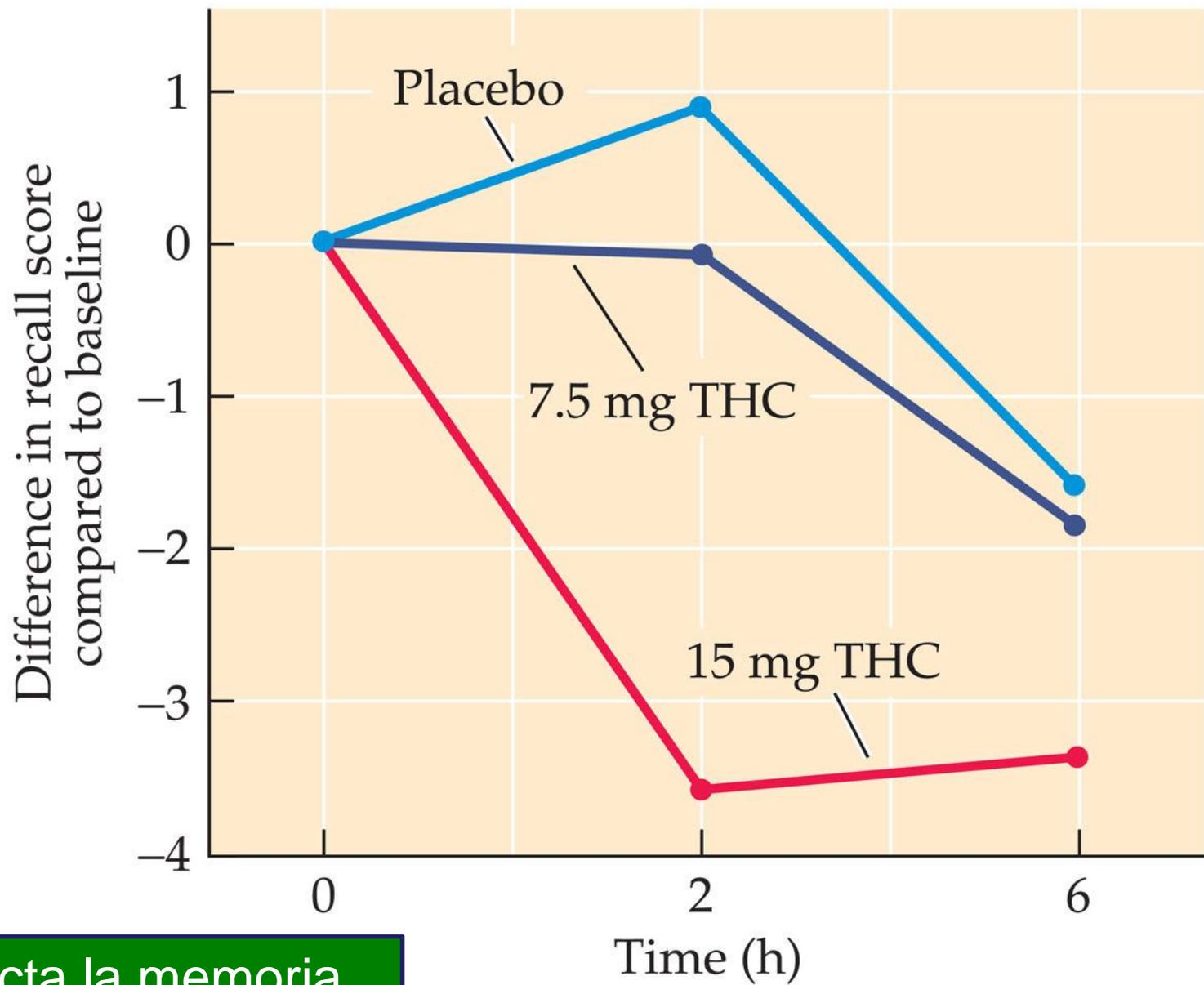
Cannabidiol (CBD)



- ✓ Agonista parcial de receptores CB1 y CB2
- ✓ Tiene efectos psicotrópicos y potencial de abuso

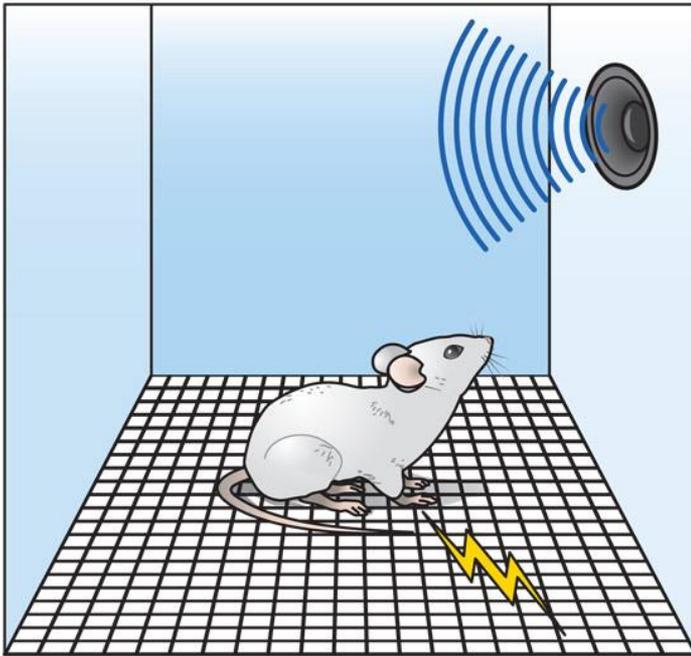
- ✓ Baja afinidad para CB1 y CB2
- ✓ Bloquea la enzima FAAH que degrada los endocannabinoides, por lo tanto mas anandamida se queda disponible para enlazarse con mayor afinidad a los receptores CB1 indirectamente impidiendo que THC se enlace.
- ✓ Si se enlaza a receptores TRPV1 y al receptor de serotonina 1-A
- ✓ No tiene efectos psicotropicos significativos ni potencial de abuso



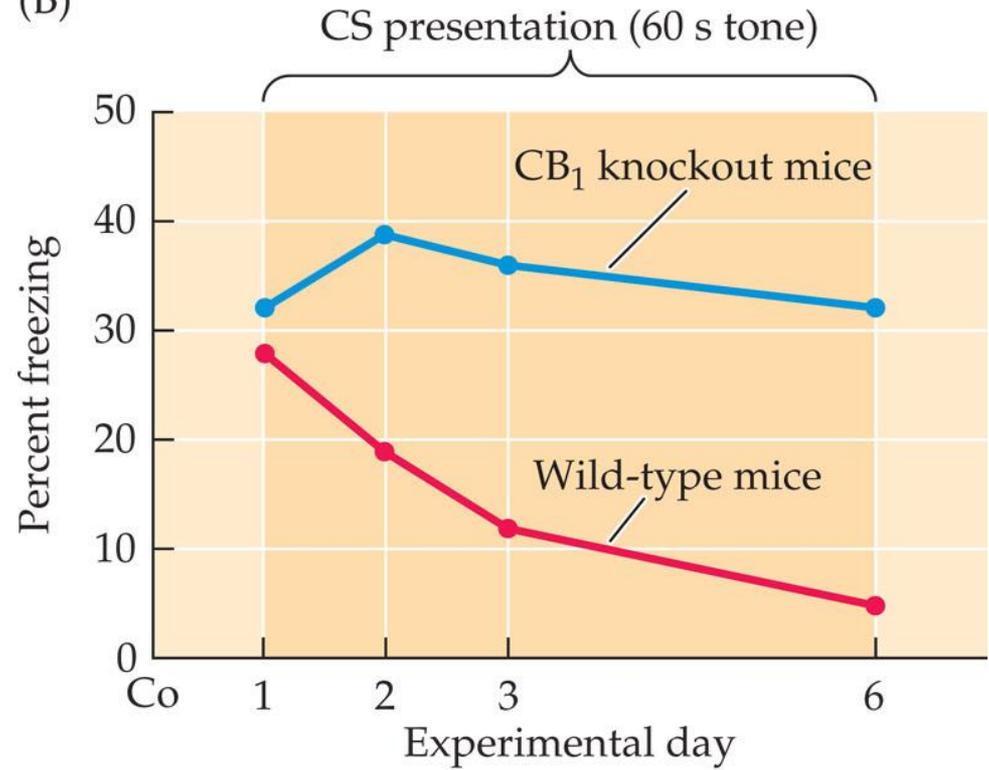


Afecta la memoria

(A)

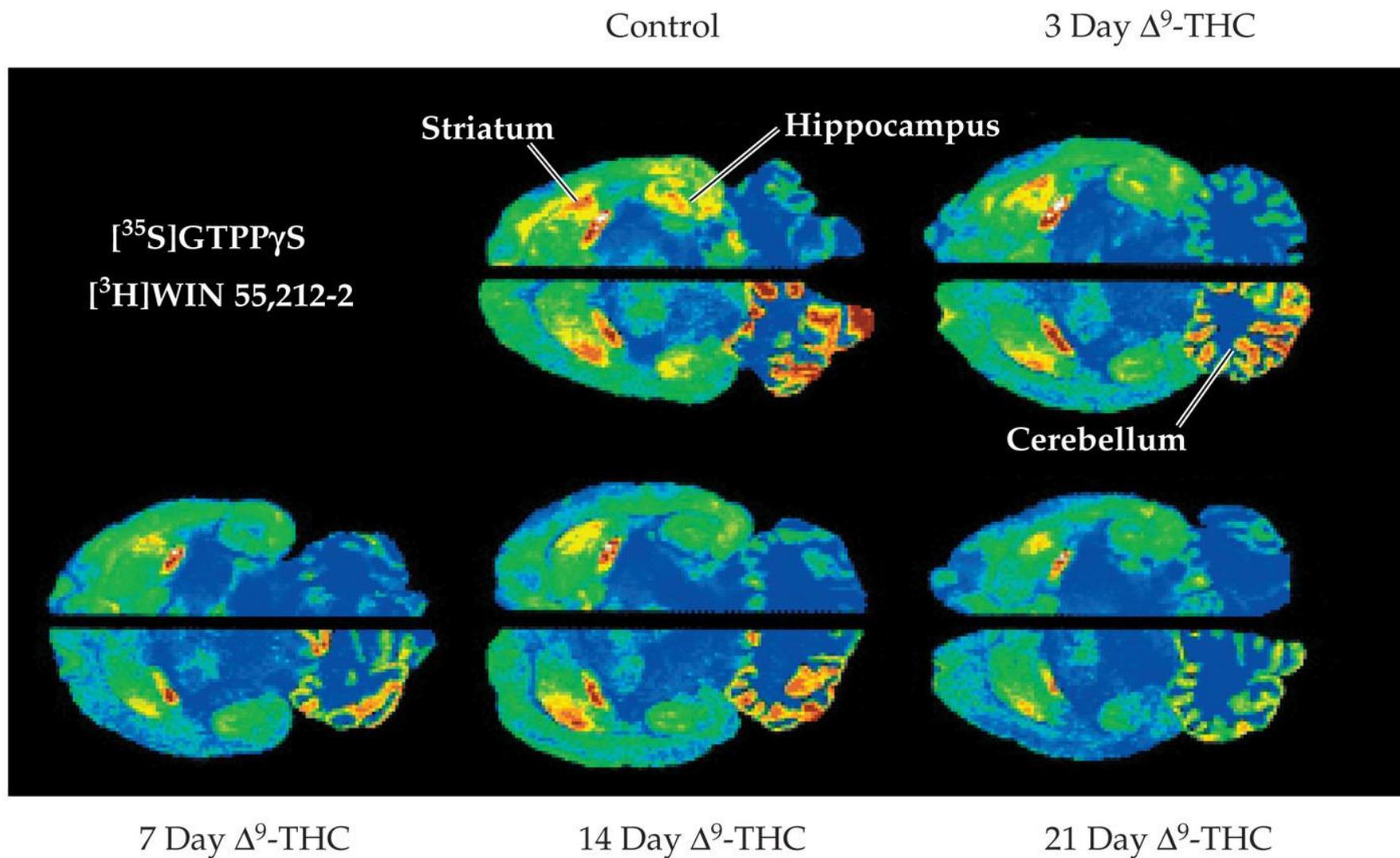


(B)



PSYCHOPHARMACOLOGY 2e, Figure 14.12 (Part 1)
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Afecta las emociones



Afecta el numero de receptores CB1

Let's Have A Talk

**Cannabis Contains Healing
Cannabinoids
Endocannabinoids**

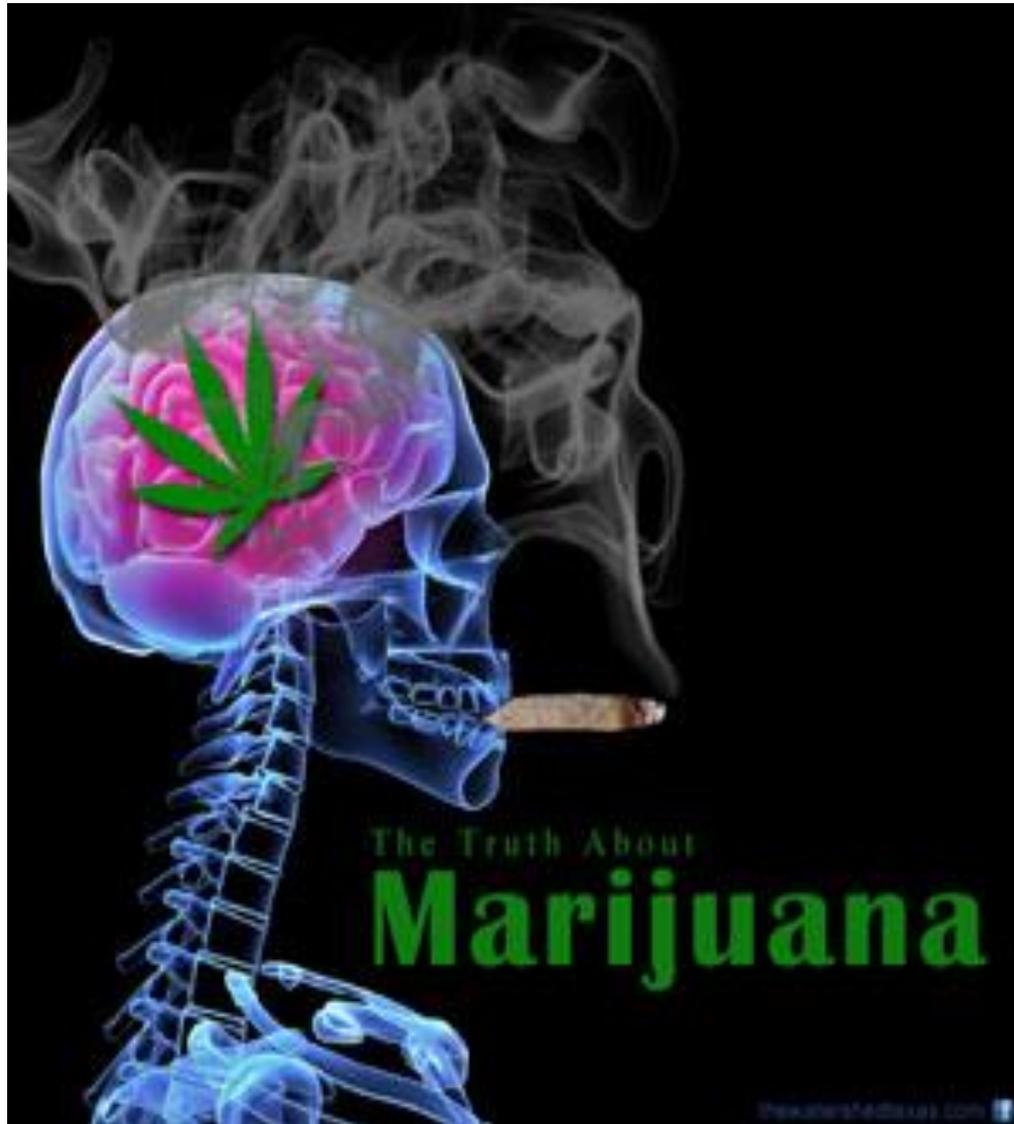


**Also Found In High Concentration In
Breast Milk, Cannabinoids Teach Our
Babies How To Eat, The Munchies.**

- ✓ Investigaciones en animales sugieren que exposicion a pequeñas concentraciones al final del embarazo pueden tener un impacto detrimental al desarrollo del cerebro y la conducta del bebe.
- ✓ En estudios con humanos, niños expuestos pre-natalmente a MJ tienen alta probabilidad de tener problemas de resolver problemas, memoria y de atencion.
- ✓ Mas investigaciones son necesarias para entender mejor los efectos de de la MJ en el proceso de gestacion y la lecha materna.

Efectos en el embarazo

La marihuana ... es adictiva ?



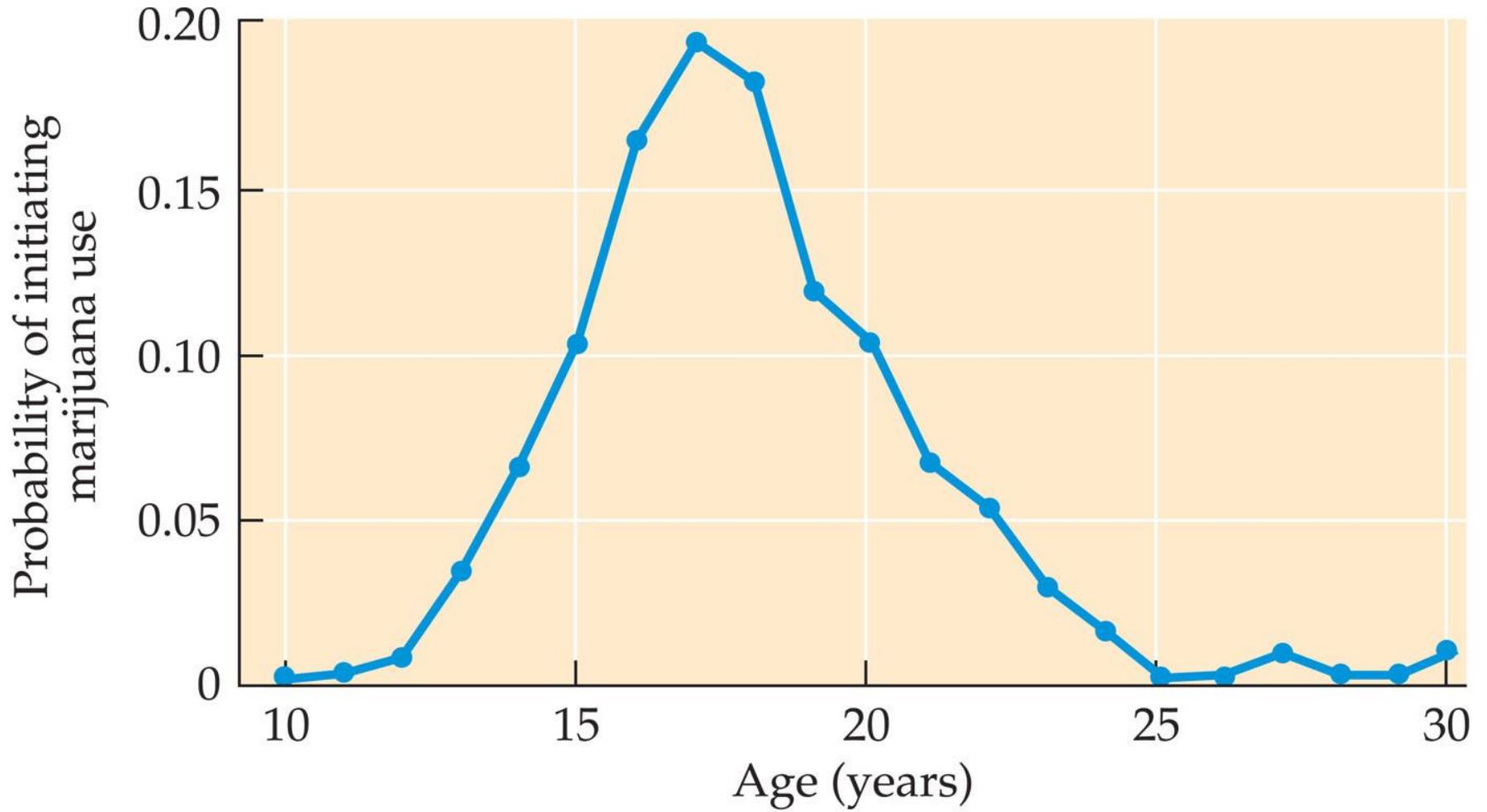
- ✓ Tiene potencial de abuso
- ✓ Presenta síntomas de retirada y farmacodependencia
- ✓ La presencia de comorbidad con otros desordenes psiquaitricos en especial en los adolescentes
- ✓ La retirada se asemeja a la de nicotina
- ✓ Tratamiento para la dependencia a la MJ es diverso pero no hay cura hasta ahora

Marijuana

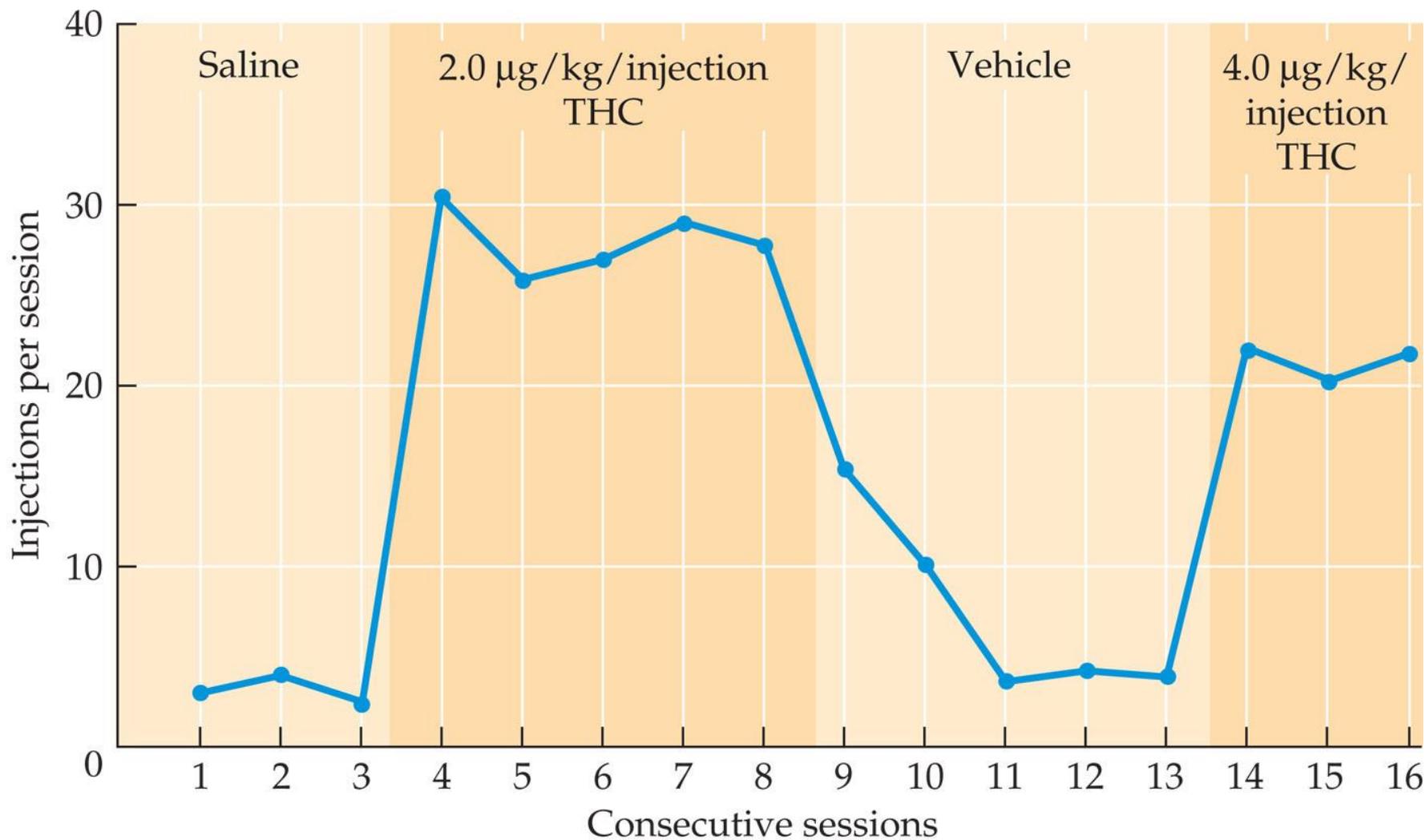
- Mucha de la cannabis sativa que se cosecha actualmente para propósitos de uso recreativo es alta en concentración de THC y baja en CBD.
- En los Estados Unidos, 1 de cada 11 adultos y 1 de cada 6 adolescentes que usan MJ terminan farmacodependientes a la sustancia.



Probability of initiating marijuana use as a function of age

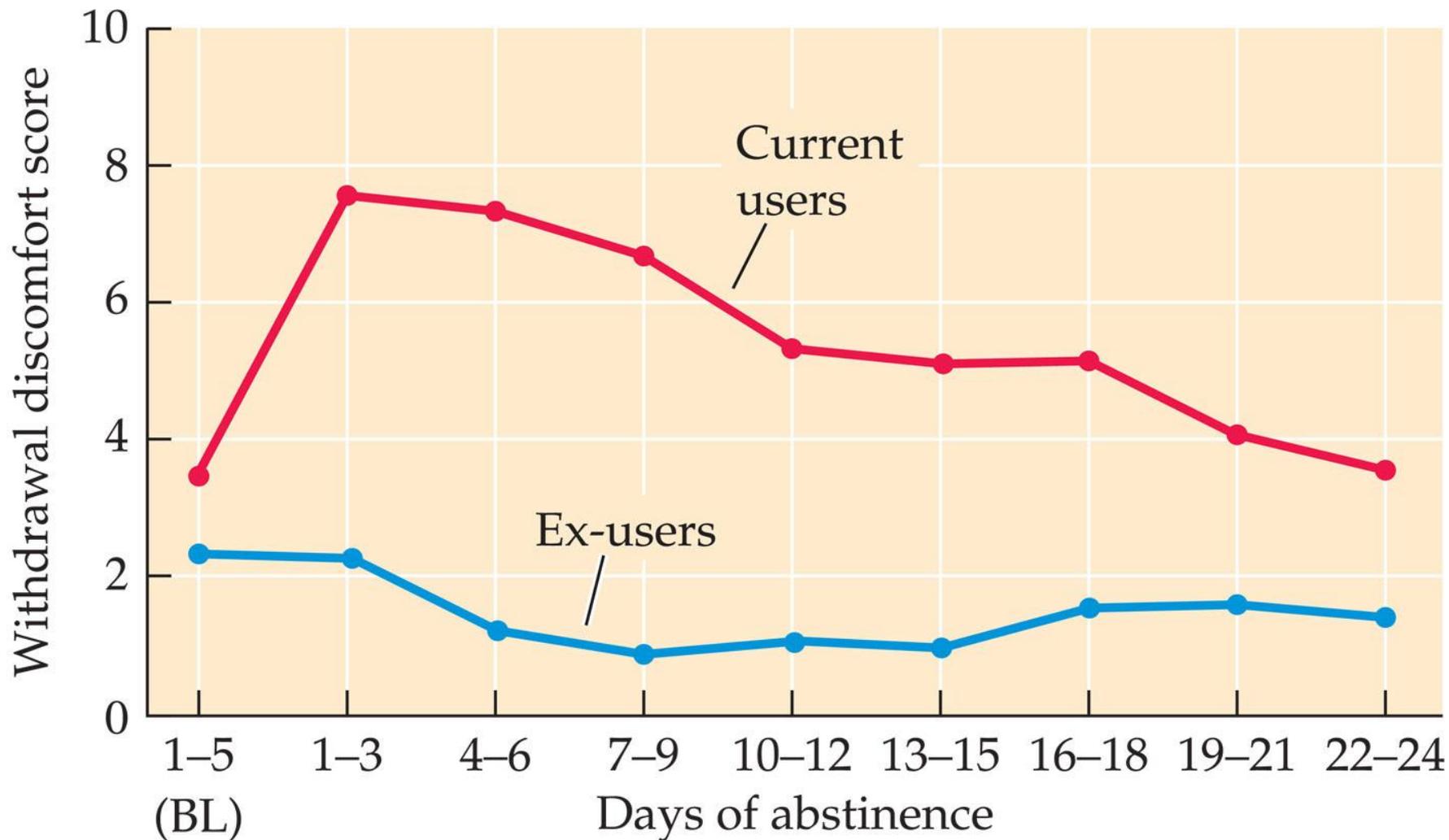


Acquisition of THC self-administration by squirrel monkeys

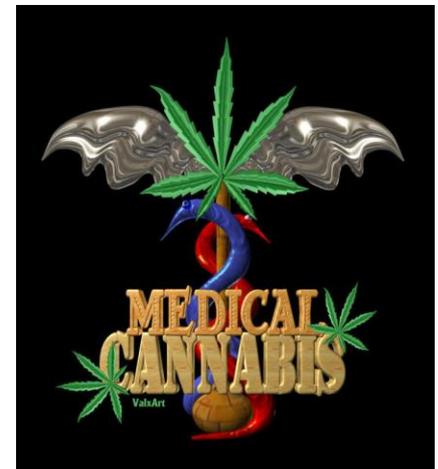


PSYCHOPHARMACOLOGY 2e, Figure 14.16

Time course of overall withdrawal discomfort in heavy marijuana users undergoing abstinence



Usos medicinales para los Cannabinoids



Analgesic

Anticonvulsive

Sedative

Antidepressive

Hypnotic

Antiasthmatic

Immunomodulation

Memory Enhancing

Anesthetic

Birth Control

Appetite Stimulation

Antipyretic

Neuropathic Pain

Antiemetic

Antirheumatic

Antimigraine

Antineuralgic

Reduction of Fatigue

Drogas derivadas de Canabinoides

- **Dronabinol** (Marinol)- THC sintético
- **Nabilone**- analogo de THC (Cesamet) se usa para tratar la nausea y la emesis duranet la quimioterapia.
- **Nabiximols** (Sativex) es un extraxto de cannabis que se usa para tratar dolor y espasticidad en pacientes con esclerosis multiple.
- **CBD**- aceite de canabidiol
- **Epidiolex** – derivado liquido de CBD
- **Rimonabant**- antagonista de receptores CB1



ALCOHOL

- DEPRESSANT
- ADDICTIVE
- HANGOVER
- VOMITING/NAUSEA
- CREATES DRAMA AND
LEADS TO PHYSICAL
VIOLENCE

CANNABIS

- ANTI-DEPRESSANT
- NON-ADDICTIVE
- NO HANGOVER
- TREATS
VOMITING/NAUSEA
- CALMS YOU DOWN/
PREVENTS VIOLENCE

WHY ISN'T CANNABIS LEGAL?