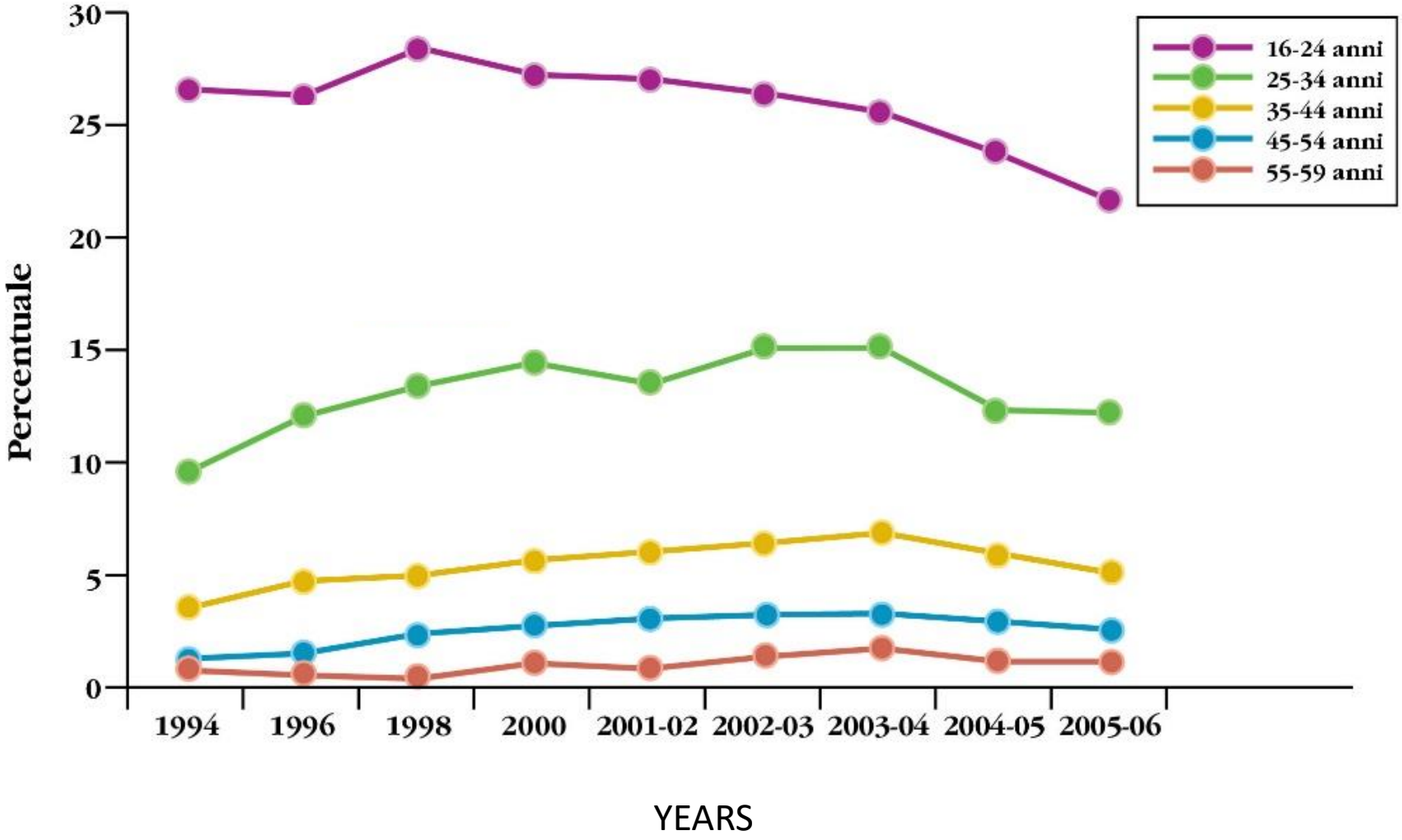
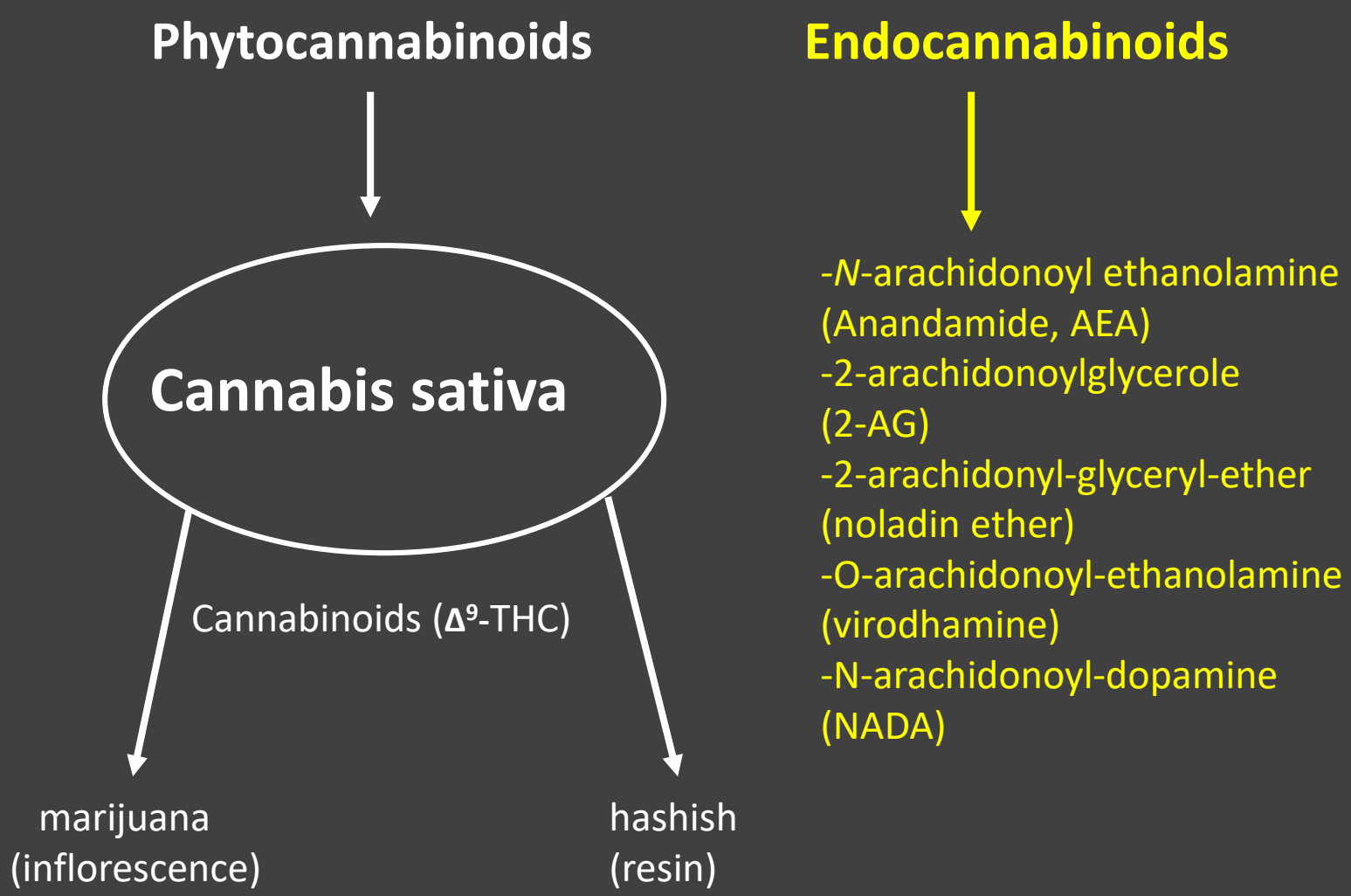
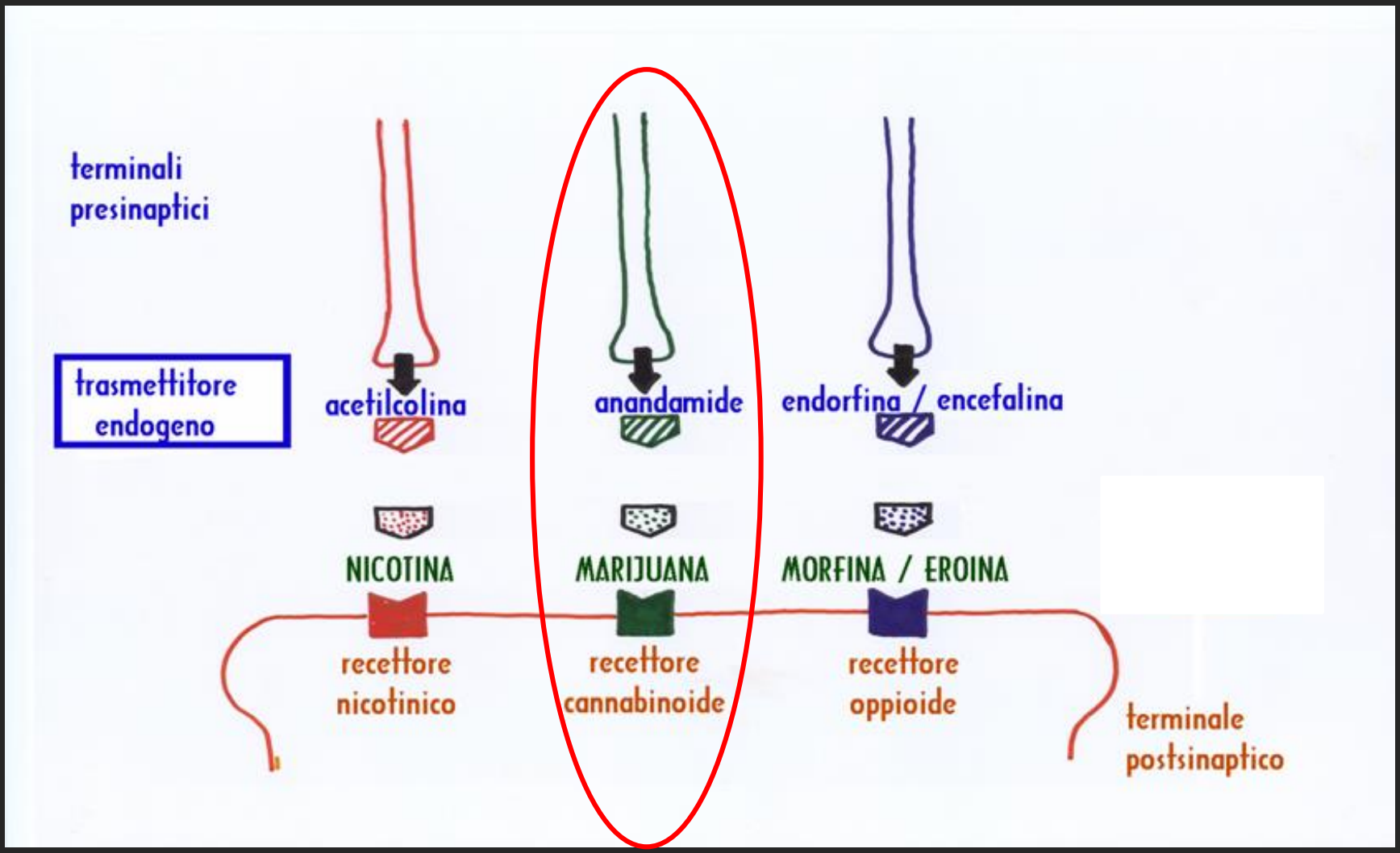
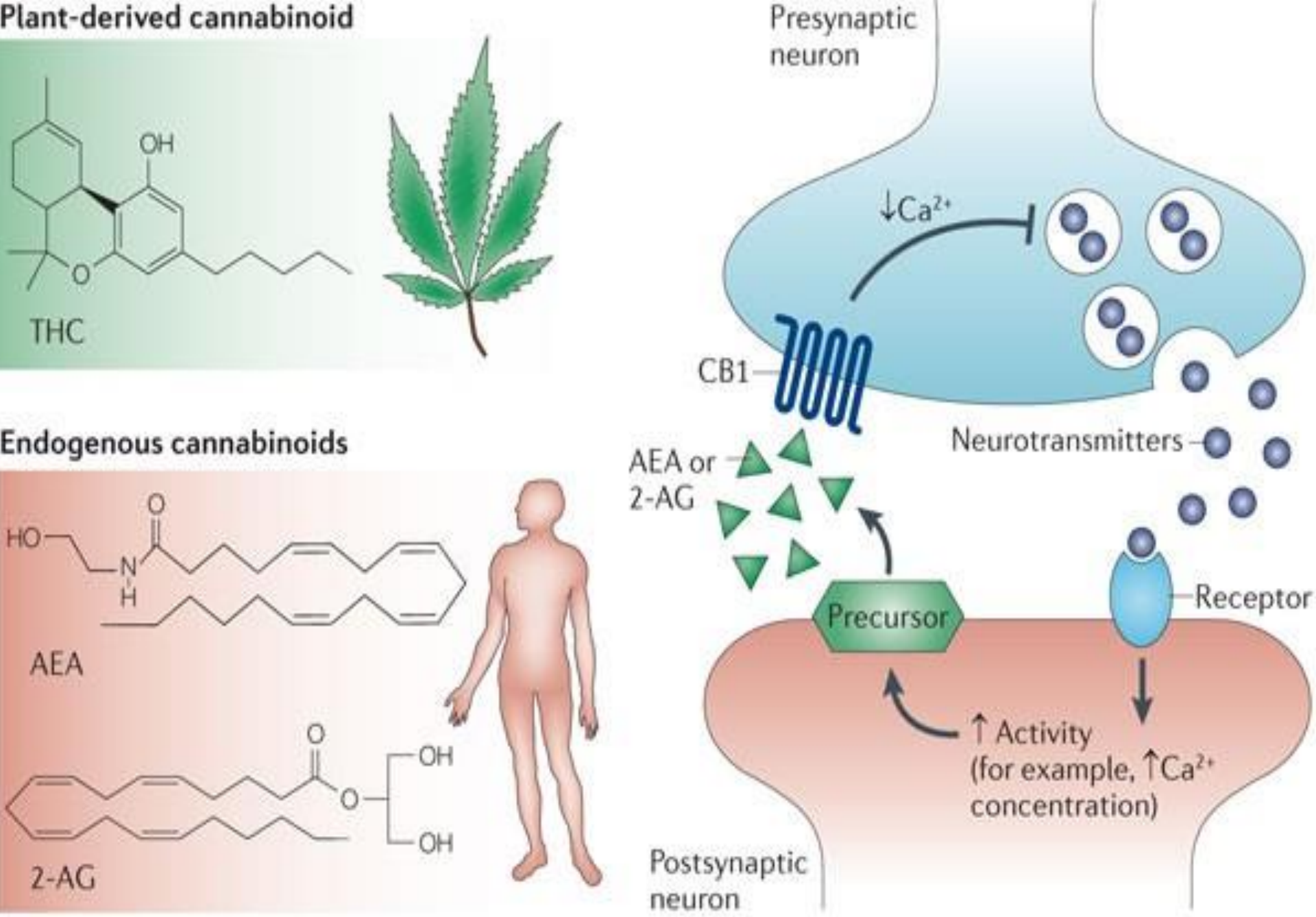
CANNABINOIDS

Prevalence of Cannabis use in UK (1994-2006)

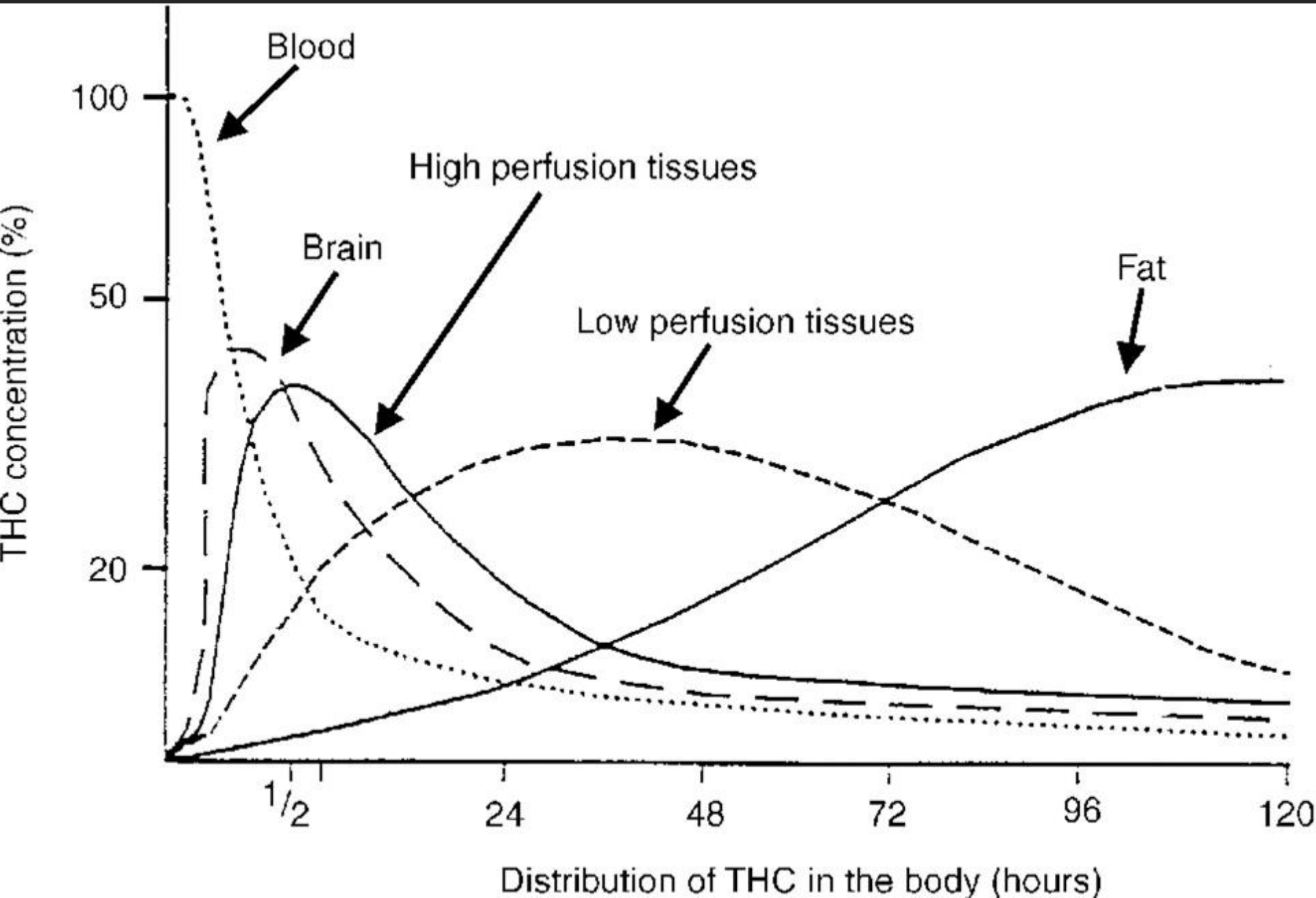



Phytocannabinoids
Endocannabinoids
Cannabis sativa
Cannabinoids (Δ9-THC)
marijuana
(inflorescence)
hashish
(resin)
-N-arachidonoyl ethanolamine
(Anandamide, AEA)
-2-arachidonoylglycerole
(2-AG)
-2-arachidonyl-glyceryl-ether
(noladin ether)
-O-arachidonoyl-ethanolamine
(virodhamine)
-N-arachidonoyl-dopamine
(NADA)


terminali presinaptici
trasmettitore endogeno
acetilcolina
anandamide
endorfina / encefalina
NICOTINA
MARIJUANA
MORFINA / EROINA
recettore nicotinico
recettore cannabinoide
recettore oppioide
terminale postsinaptico


Plant-derived cannabinoid
OH
O
THC
Endogenous cannabinoids
HO
O
N
H
AEA
O
OH
O
OH
2-AG
Presynaptic neuron
↓Ca2+
CB1
Neurotransmitters
AEA or 2-AG
Precursor
Receptor
↑ Activity (for example, ↑Ca2+ concentration)
Postsynaptic neuron

Pharmacokinetics of THC in different tissues



Cannabinoid receptors: CB1 and CB2: G_i protein

CB1: CNS (hippocampus, Ctx, PG)
spinal cord, PNS,
endocrine glands, salivary glands, leukocytes, spleen, heart,
reproductive, urinary, gastrointestinal system

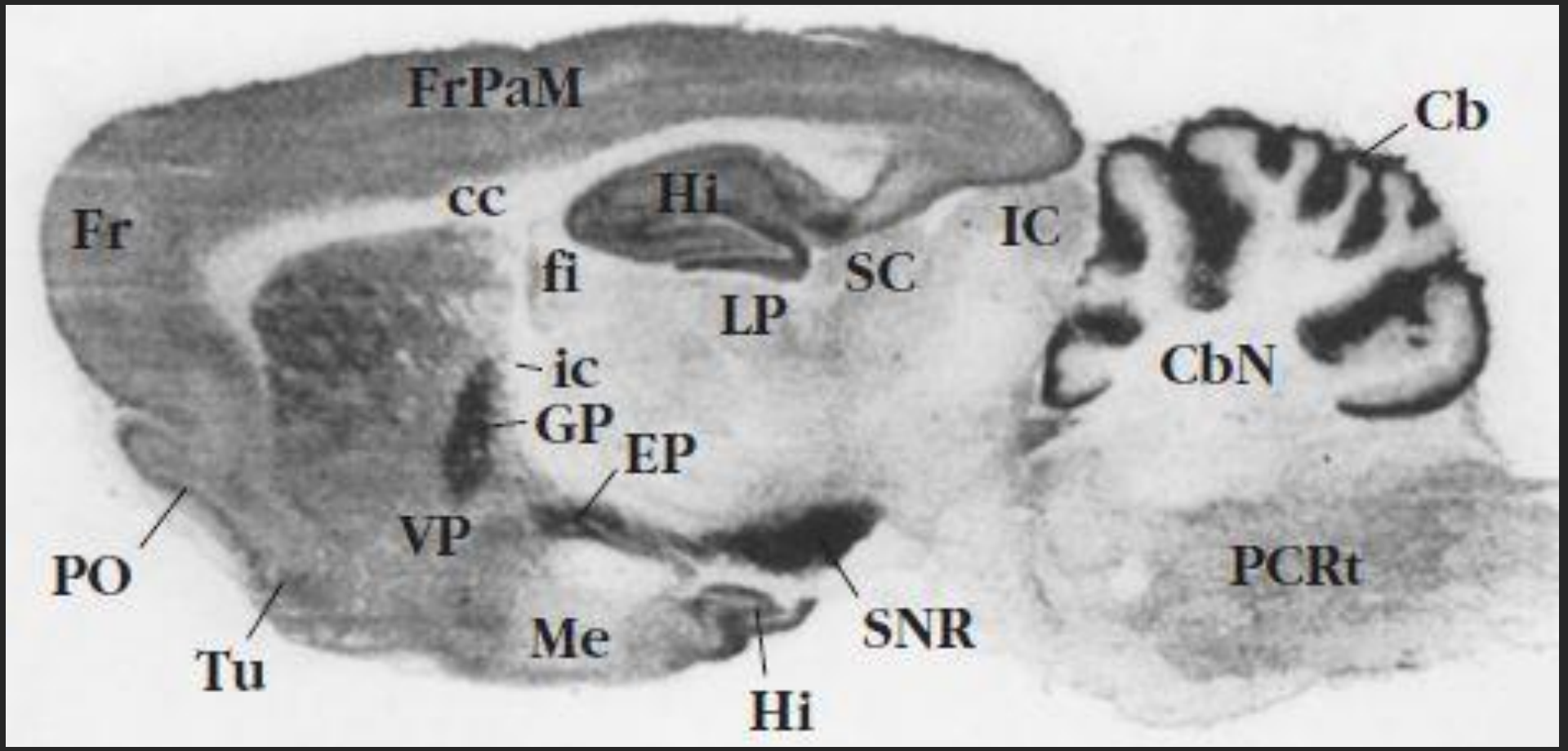
Terminals: inhibition of neurotransmitter release

CB2: leukocytes, spleen, tonsils (immune system)

Pain, spasticity, nausea, appetite

Drugs
Dronabinol, nabilone (agonists)
Rimonabant (antagonist)

Density and autoradiographic distribution of CB1 receptors



Cannabis

- Main active constituent is Δ^9-tetrahydro cannabinol (THC), though pharmacologically active metabolites may be important.
- Actions on CNS include both depressant and psychotomimetic effects.
- Subjectively, subjects experience euphoria and a feeling of relaxation, with sharpened sensory awareness.
- Objective tests show impairment of learning, memory and motor performance.
- THC also shows analgesic and antiemetic activity, as well as causing catalepsy and hypothermia in animal tests.
- Peripheral actions include vasodilatation, reduction of intraocular pressure and bronchodilatation.
- Cannabinoid receptors belong to the G-protein-coupled receptor family, linked to inhibition of adenylate cyclase and effects on calcium and potassium channel function, causing inhibition of synaptic transmission. The brain receptor (CB_1) differs from the peripheral receptor (CB_2), which is expressed mainly in cells of the immune system. Selective agonists and antagonists have been developed.
- Anandamide, an arachidonic acid derivative, is an endogenous ligand for the CNS cannabinoid receptor; its function has not yet been ascertained.
- Cannabinoids are less liable than opiates, nicotine or alcohol to cause dependence but may have long-term psychological effects.
- Nabilone, a THC analogue, has been developed for its antiemetic property.
- trials are in progress for symptomatic treatment of multiple sclerosis and AIDS.

Increased heart rate, decreased blood pressure, conjunctiva redness

Dronabinol (Δ^9-THC). neuropathic pain, anorexia

THC effects

THC: euphoria, relaxation, appetite stimulation, hallucinations, delusional ideas, decreases motor control, sleepiness, memory

- Metabolized by oxidases, eliminated via bile
- Tolerance, weak dependence

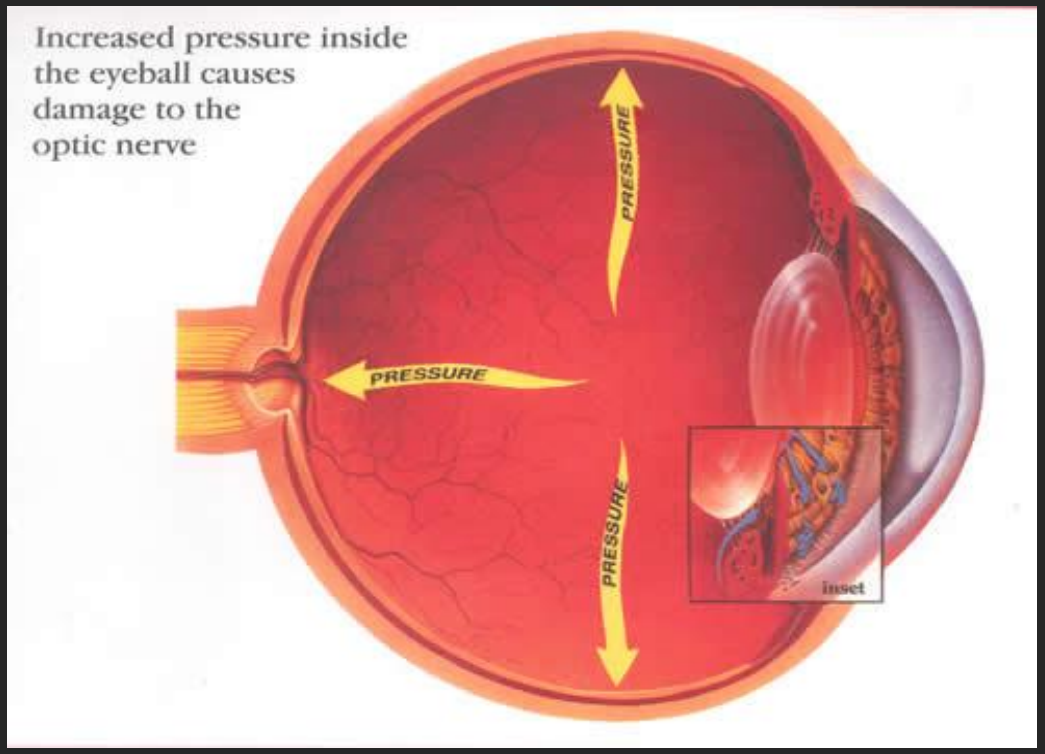
Interactions with THC

Opiates

Ethanol

Glaucoma

affects the optic nerve and leads to a progressive reduction in vision

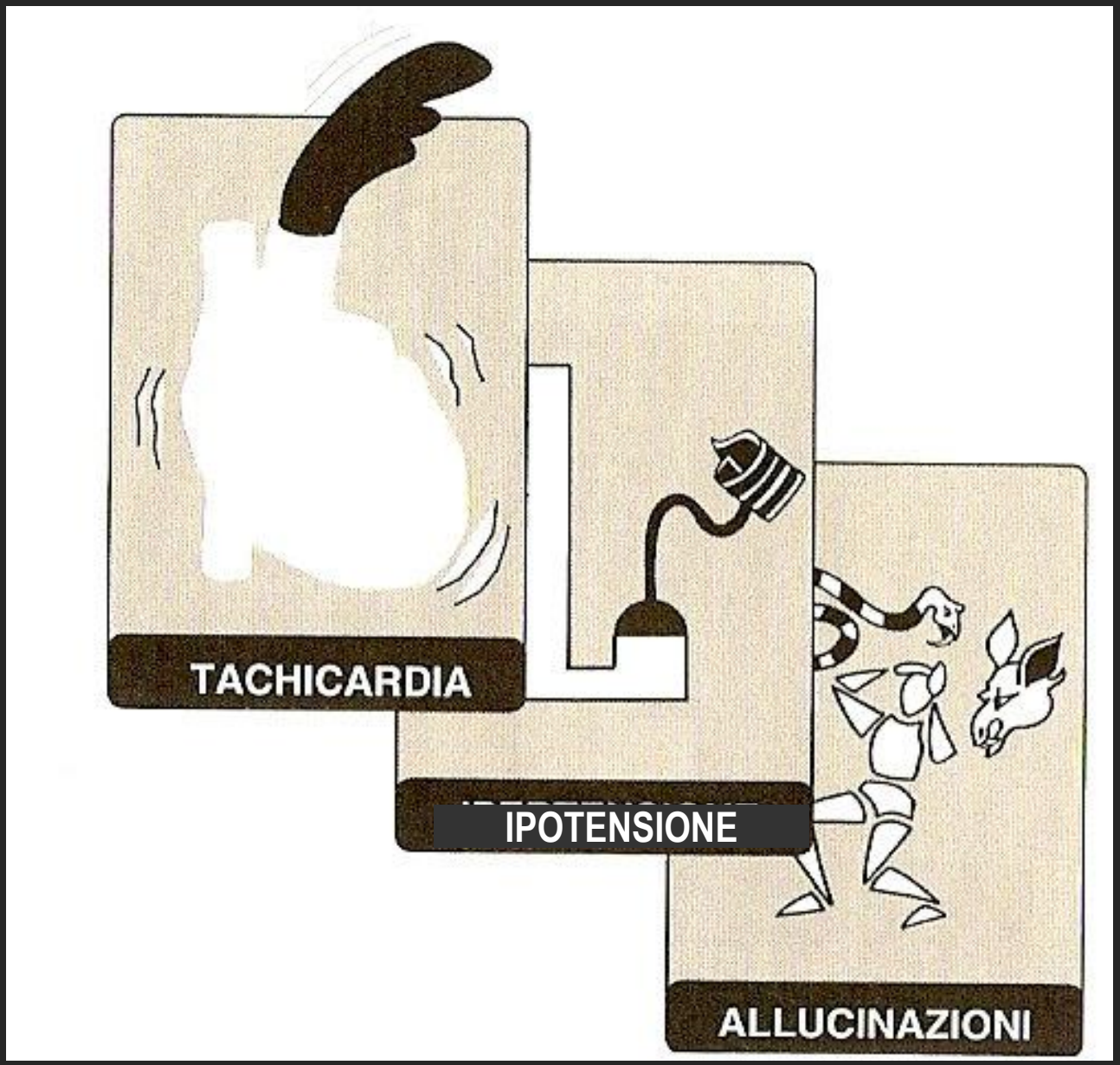


In combination with other drugs.

Stabilizing intraocular pressure THC avoids excessive changes in the internal pressure of the eye, which are very risky

The effect is quite short and cause several side effects

Side effects of tetrahydrocannabinol



Criteri diagnostici per F12.00 Intossicazione da Cannabis [292.89]

A. Uso recente di cannabis.

B. Modificazioni maladattive comportamentali o psicologiche clinicamente significative (per es., compromissione della coordinazione motoria, euforia, ansia, sensazione di rallentamento del tempo, deficit della capacità critica, ritiro sociale) che si sviluppano durante, o poco dopo, assunzione di cannabis.

C. Due (o più) dei seguenti segni, che si sviluppano entro due ore dall'assunzione di cannabis:

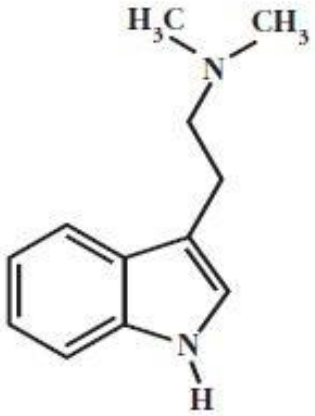
1) iperemia congiuntivale
2) aumento dell'appetito
3) secchezza delle fauci
4) tachicardia.

D. I sintomi non sono dovuti a una condizione medica generale e non risultano meglio spiegati con un altro disturbo mentale.

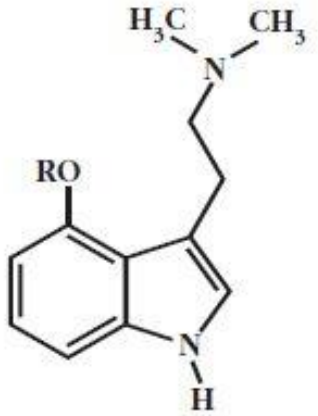
Nota per la codificazione: F12.04 se
Con Alterazioni Percettive

HALLUCINOGENS

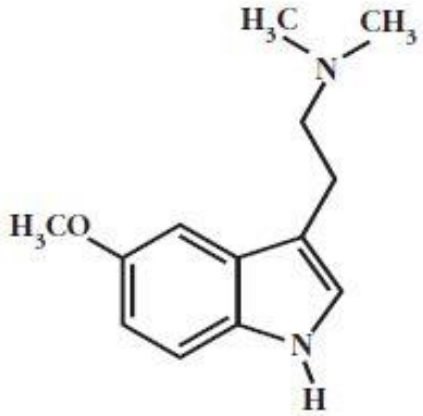
Chemical structure of principal hallucinogens



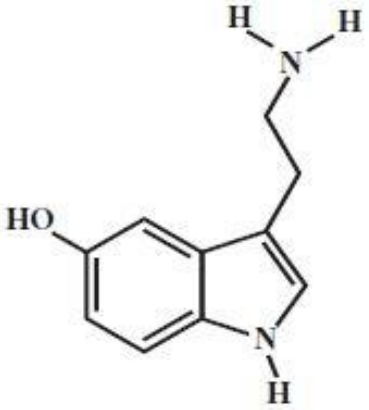
DMT



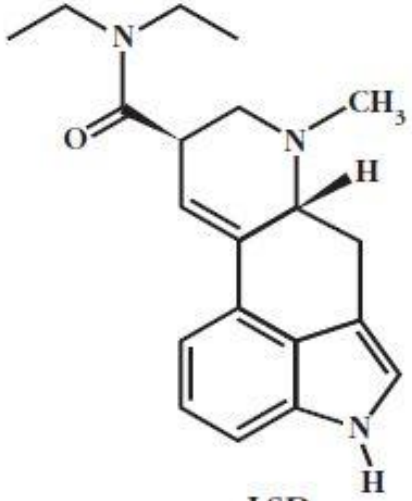
R = H; Psilocina
R = PO_3H; Psilocibina



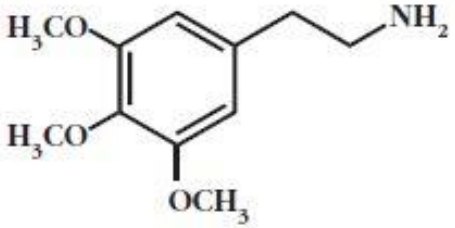
5-Metossi-DMT



Serotonina; 5-HT



LSD



Mescalina

Hallucinogens

- The main types are:
  - —LSD, psilocybin and mescaline (actions related to 5-HT and catecholamines)
  - —phencyclidine.
- Their main effect is to cause sensory distortion of a fantastic and halluciantory nature.
- LSD is exceptionally potent, producing a long-lasting sense of dissociation and disordered thought, sometimes with frightening hallucinations and delusions, which can lead to violence. Hallucinatory episodes can recur after a long interval.
- LSD and phencyclidine precipitate schizophrenic attacks in susceptible patients, and LSD may cause long-lasting psychopathological changes.
- LSD appears to act as an agonist at 5-HT_2-receptors, and suppresses electrical activity in 5-HT raphe neurons, an action that appears to correlate with psychotomimetic activity.
- They do not cause physical dependence and tend to be aversive, rather than reinforcing, in animal models.
- The mechanism of action of phencyclidine is complex; it binds to the σ-receptor and also blocks the glutamate-activated NMDA-receptor channel, as well as interacting with other neurotransmitter systems.

Pupil dilation
piloerection
Increase in body temperature

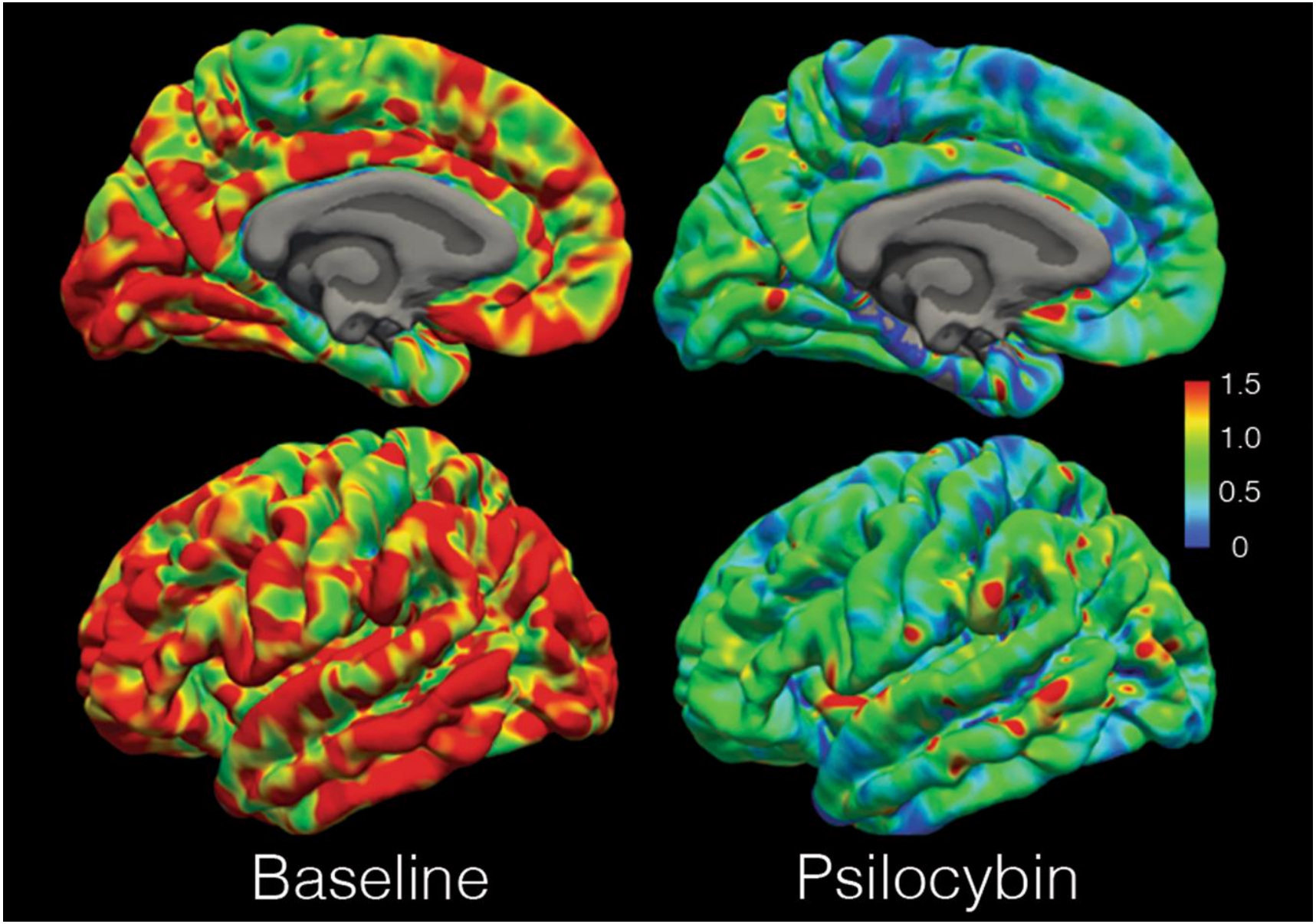
Reuptake DA, 5HT1A, NA

Peyote as a supplement for transcendental practices

Ghost Dance

Peyote (mescaline)

Psilocybe (psilocybin)



PET after psilocybin

Most frequently reported positive effects with recreational use of:		
ecstasy	**amphetamine**	**hallucinogens**
Loquacity	Energy enhancement	Weird thoughts
Open mind	Loquacity	Open mind
Intimacy with others	Alertness	Affability
Happiness	Confidence	Intuition
Fatigability	Affability	Restlessness
Euphoria	Attention towards others	Loquacity
Confidence	Increase in self-estimate	Increase in energy
	Open mind	

Most frequently reported negative effects with recreational use of:		
ecstasy	**amphetamine**	**hallucinogens**
Loss of appetite	Loss of appetite	Visual illusions
Dry mouth	Insonnia	Visual hallucinations
Tachycardia	Tachycardia	Loss of appetite
Tension in the jaw	Tension in the jaw	Insomnia
Insomnia	Teeth grinding	Confusion
Teeth grinding	Dry mouth	Lack of concentration
Hot and cold sensation variation	Palpitations	Auditory hallucinations
Sweating / sweaty hands	Irritability	Anxiety
Lack of concentration	Tremor	Tachycardia

Criteri diagnostici per F16.00 Intossicazione da Allucinogeni [292.89]

A. Uso recente di un allucinogeno.

B. Modificazioni maladattive psicologiche o comportamentali clinicamente significative (per es., rilevante ansia o depressione, idee di riferimento, paura di impazzire, ideazione paranoide, compromissione delle capacità critiche o compromissione del funzionamento sociale o lavorativo) che si sviluppano durante, o poco dopo, l'uso di allucinogeni.

C. Alterazioni percettive ricorrenti in stato di piena consapevolezza e vigilanza (per es., intensificazione soggettiva delle percezioni, depersonalizzazione, derealizzazione, illusioni, allucinazioni, sinestesie) che si sviluppano durante, o poco dopo, l'uso di allucinogeni.

D. Due (o più) dei seguenti segni, che si sviluppano durante, o poco dopo, l'uso di allucinogeni:

1) midriasi
2) tachicardia
3) sudorazione
4) palpitazioni
5) annebbiamenti del visus
6) tremori
7) incoordinazione.

E. I sintomi non sono dovuti a un'altra condizione medica generale e non risultano meglio spiegati con un altro disturbo mentale.