Endocanabinoid system


PSYCHOTROPIC → THC
(Gaoni & Mechoulam, 1964)
hypno/sedative
increasing appetite
antiemetic
bronchodilatatory
neuroprotective
antiinflamatory
snížení nitroočního tlaku
analgesic
imunomodulant
antispastic
EFFECTS
420 cannabinoids
CANNABIS SATIVA
marijuana

Endocannabinoid system (ECS)

- $CB_{1,2}$ receptors (W. Devane et al., 1988)
- endocannabinoids (W. Dewane, L. Hanus , 1992, 1995, 2000)

Piomelli et al., 2000; Wilson R, 2002; Di Marzo V, 2005

Endocannabinoids synthetized on demand from cell membrane

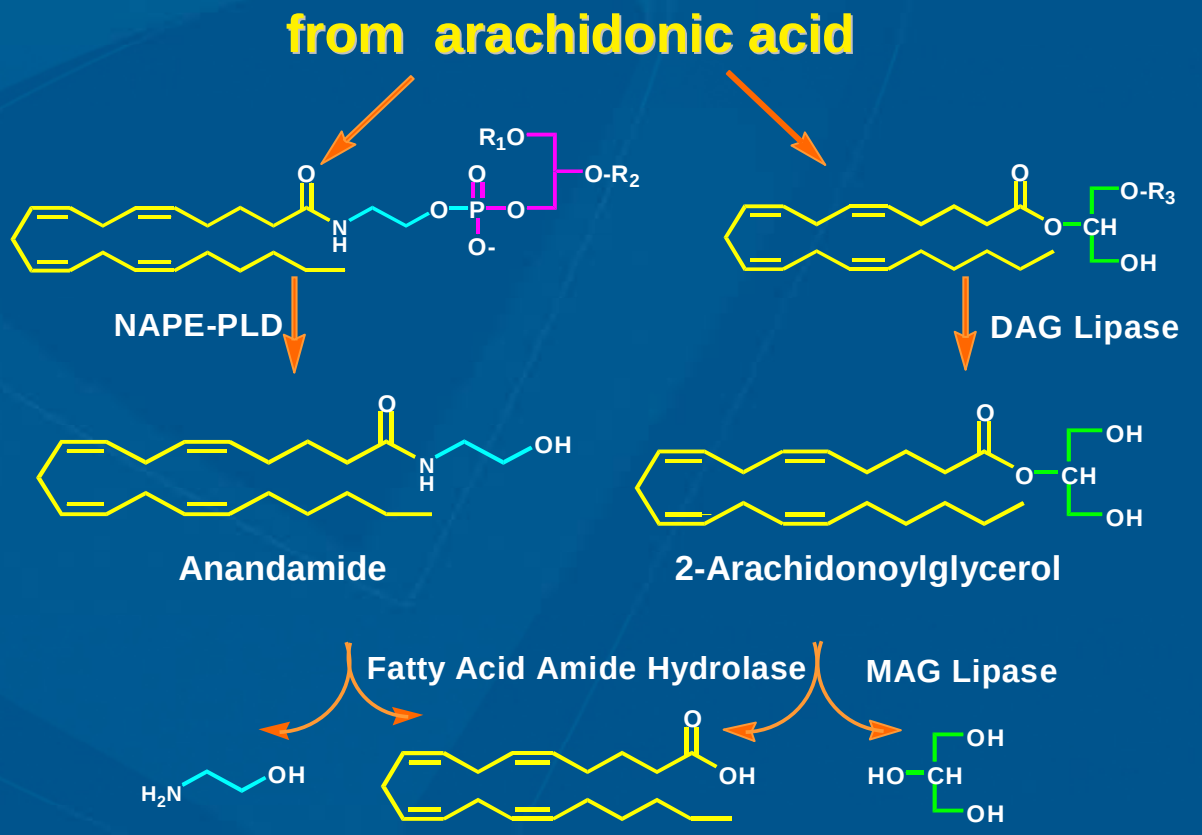
precursors
from phospholipid

⇩

endocanabinoids

⇩

- no storage
- active localy
- fast biodegradation
  (metabolization + uptake)

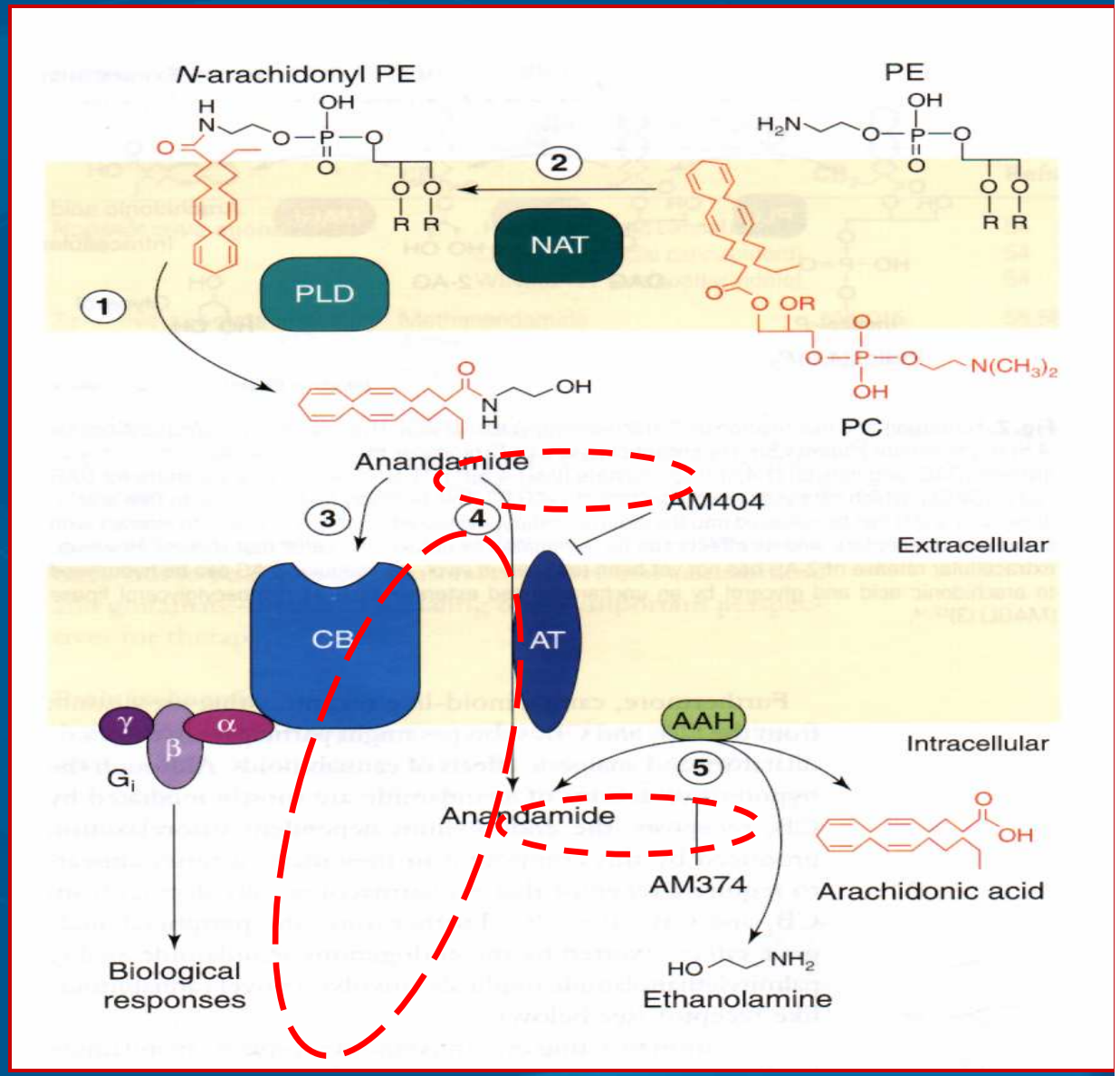


Di Marzo, Nature 2001; Nature reviews 2004

Endocannabinoid system (ECS) = modulatory system of the CNS

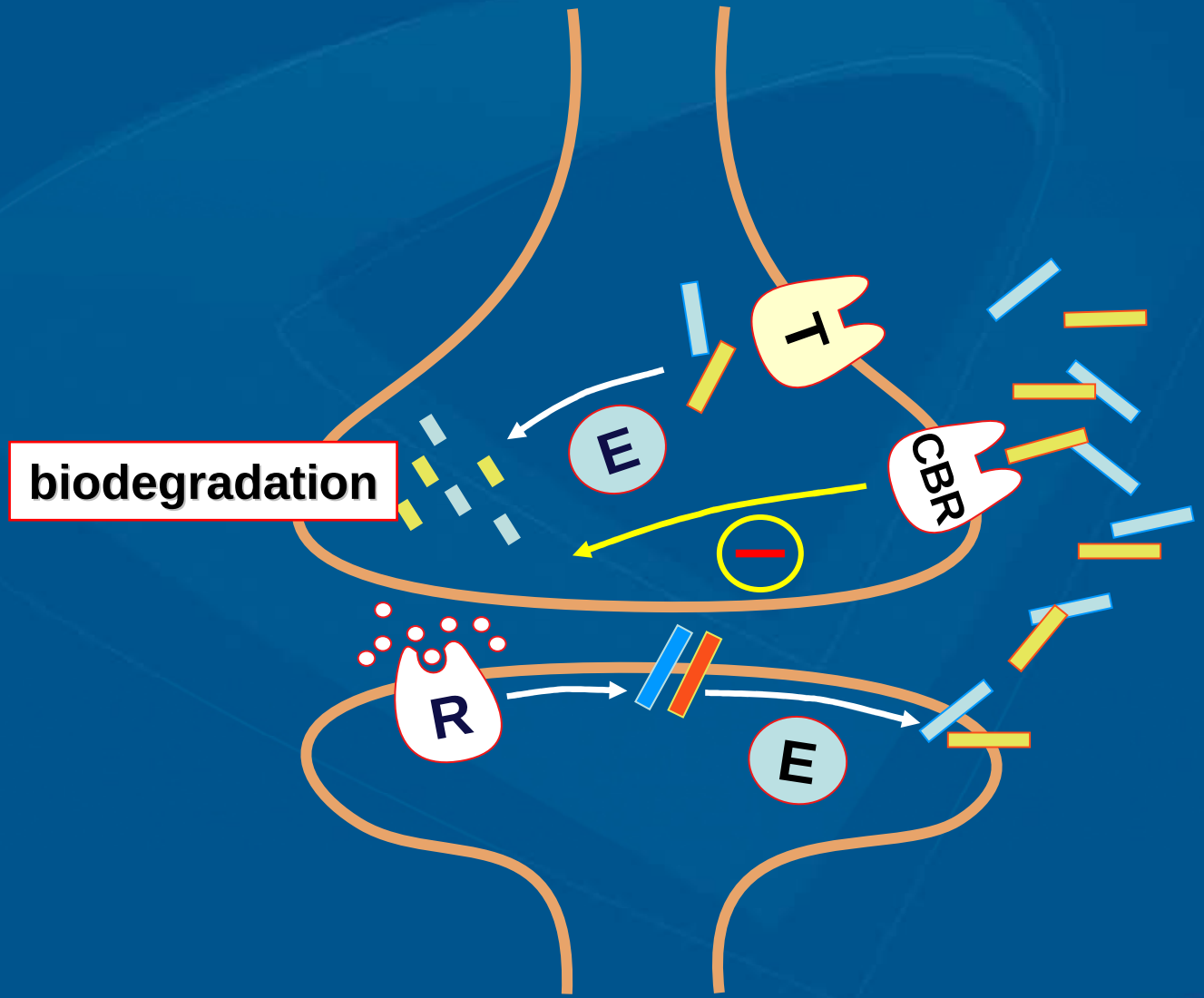
- endocanabinoids

= retrograde synaptic messengers



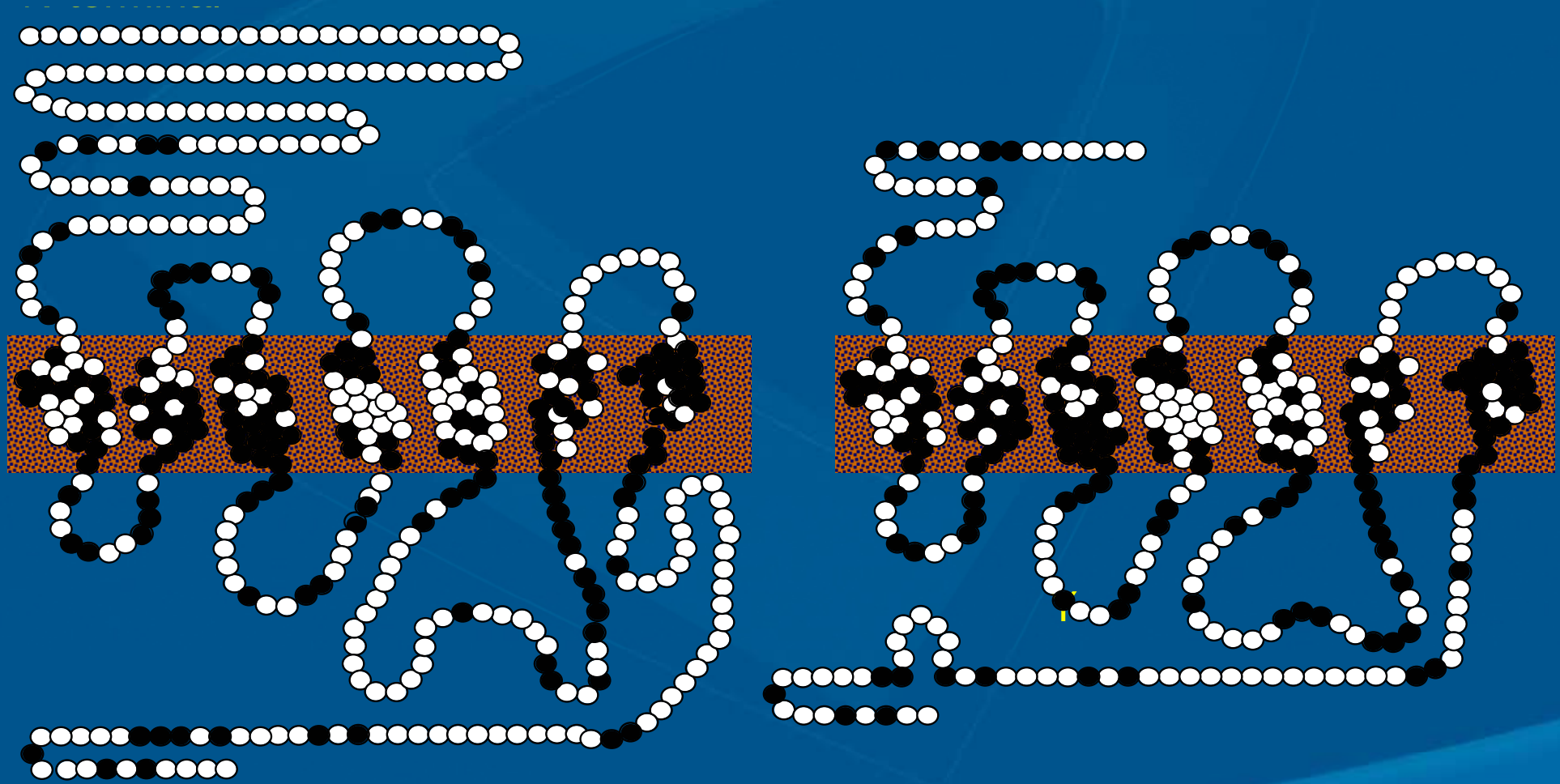
Piomelli et al., 2000; Wilson R, 2002; Di Marzo V, 2005

Function of the endocannabinoid system on synapse



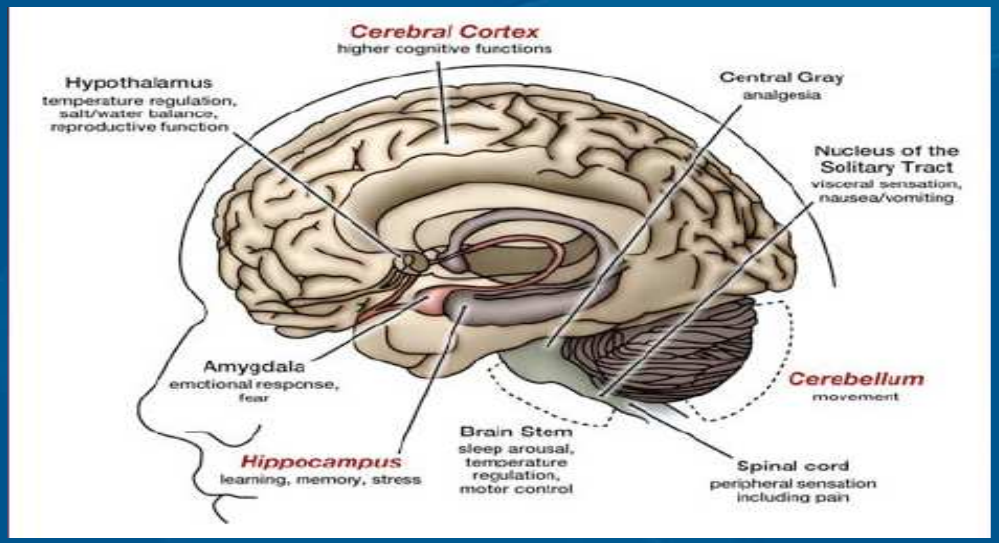
CB_1 Receptor

CB_2 Receptor



Expresion of cannabinoid receptors

CB_1



- cortex, hipocampus
- basal ganglia
- hypothalamus
- cerebellum
- spinal cord
- enteric nervous system

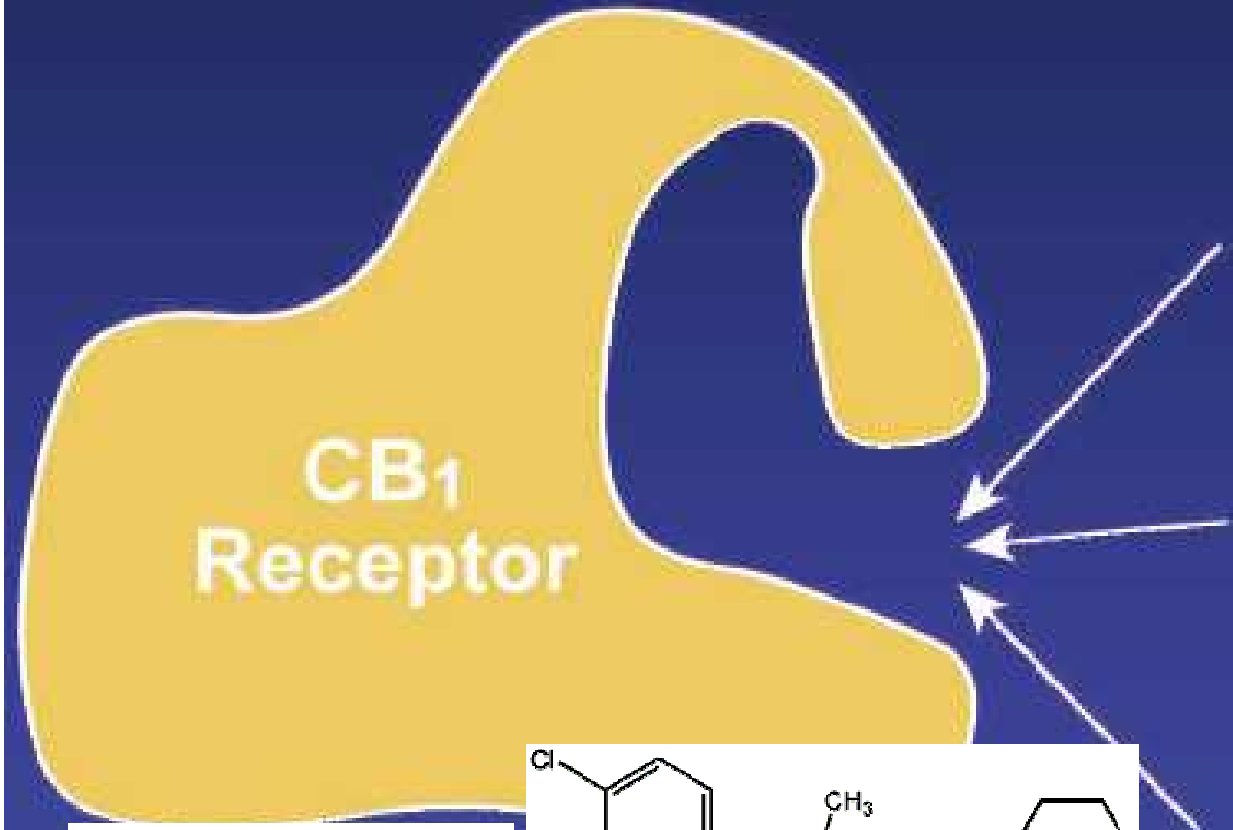
- adipocytes
- endothelial cells
- hepatocytes
- muscles
- GIT

CB_2

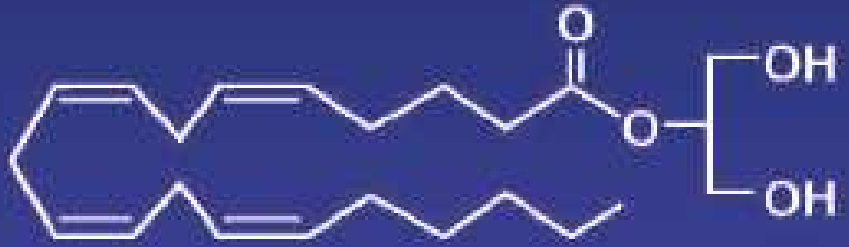
- immun cells:
  T cells, B cells, line, tonsiles
  and
  activovates glial cells, ↑ in neuropathies

Matsuda 1997; Cota et al 2003; Galiègue et al 1995; Pertwee et al 1997; Liu et al 2005; Osei-Hyiaman et al 2005

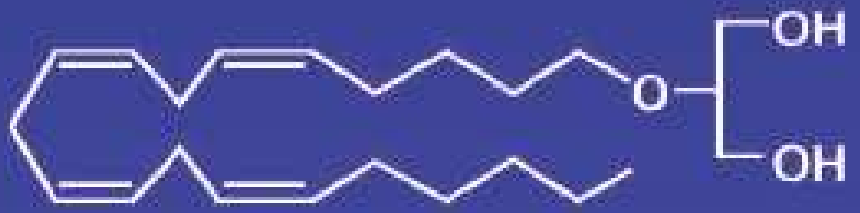
Endocannabinoids



Anandamide

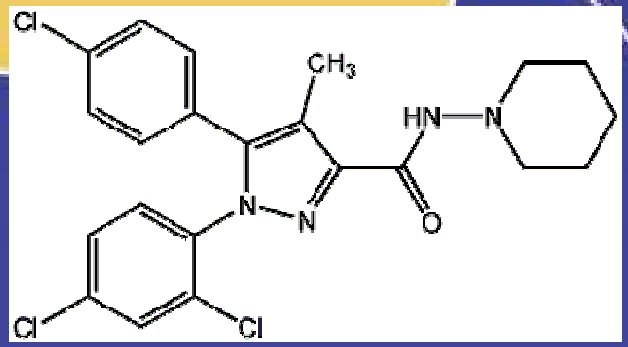


2-Arachidonoyl glycerol



Noladin ether

antagonist
rimonabant



THC

causes dependence

(Costa a kol., 2000; Tanda a kol., 2000; Justinová akol., 2003, 2005)

tolerance and withdrawal syndrom

EFFECTS - psychic + somatic

- euforia, sedation (Howlet, 1995; Ameri, 1999; Chaperon a Thiebot, 1999)
- analgesia (Johnson at al., 1981; Comton et al., 1992)
- antiemetetic (Sallan et al., 1975;, Levitt, 1986; Darmani, 2000)
- anticonvulsive (Consroe et al., 1975; Grinspoon a Bakalar, 1993)
- antispasmoid (" movement disorders") (Clifford, 1983; Meinck., 1993)
- antiasthmatic (Tashkin et al., 1975; Tashkin et al., 1993)
- antiglaucomatic (Adler a Geller, 1986; Porcella et al. 2000)

CB_1 receptors important in :

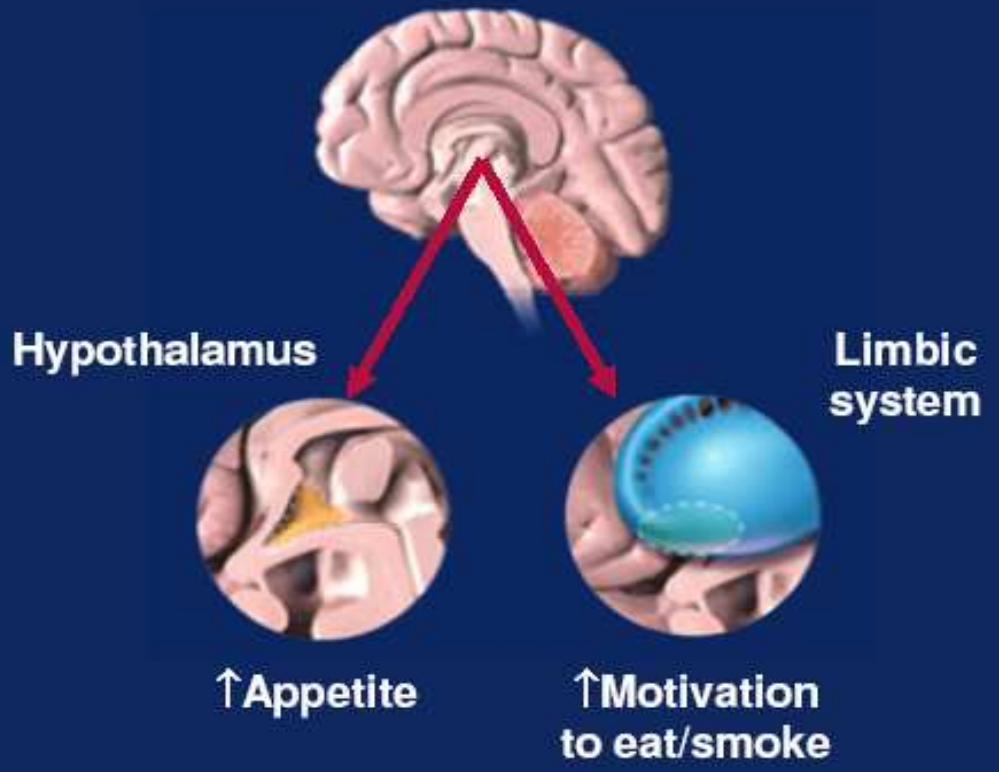
- regultion of food intake
- lipid a glucose metabolism

in development of cardiometabolic risk factors

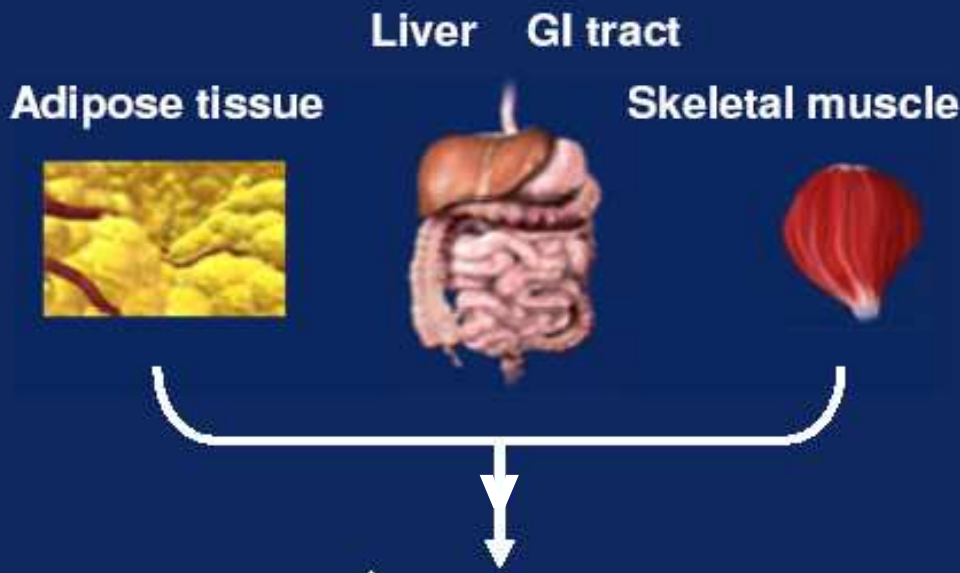
Kirkham et al., 2002; DiMarzo et al., 2001; Jarmshidiet et al., Brit J Pharm., 2001; Ravinet Trillou et al. 2003; Bensaid et al., 2003; Caballero, 2003; Van Gaal et al. 2005; Carr a Brunzell 2004; Pagotto a Pasquali, 2005; Eckel et al., 2005

Implications of CB_1 receptor activation

Central nervous system



Peripheral tissue



Gelfand EV, Cannon CP. *J Am Coll Cardiol*. 2006;47:1919-26.
Pagotto U et al. *Ann Med*. 2005;37:270-5.

PROSPECTIVE USE
of CB_1 cannabinoid receptor blockers

decrease of cardiometabolic risk factors

in smoking secession

? ? treatment of drug addiction? ?