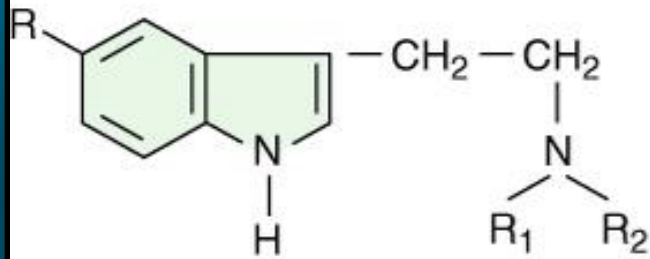


Serotonina

Serotonina



Compound	Position		
	R	R ₁	R ₂
Tryptamine	H	H	H
Serotonin	OH	H	H
Melatonin	OCH ₃	COCH ₃	H
Diethyltryptamine (DET)*	H	CH ₃ CH ₂	CH ₃ CH ₂
Dimethyltryptamine (DMT)*	H	CH ₃	CH ₃
Bufotenine*	OH	CH ₃	CH ₃

*Psychotropic (modifies mental activity)

Histórico-Serotonina (5-HT)

- Final séc. 19: Plaquetas – constrição músculo liso vascular
- 1948: Rapport, Green & Page isolam e identificam a 5-HT
- 1948: Esparmer identifica “enteramina” no trato gastrointestinal
- 1952: enteramina = serotonina
- 1953: Twarog & Page detectam 5-HT no encéfalo
LSD efeitos psicotrópicos e antagonico do efeito constritor da 5-HT
- 1964: Dahlstrom & Fuxe identificam os neurônios serotoninérgicos nos núcleos da rafe

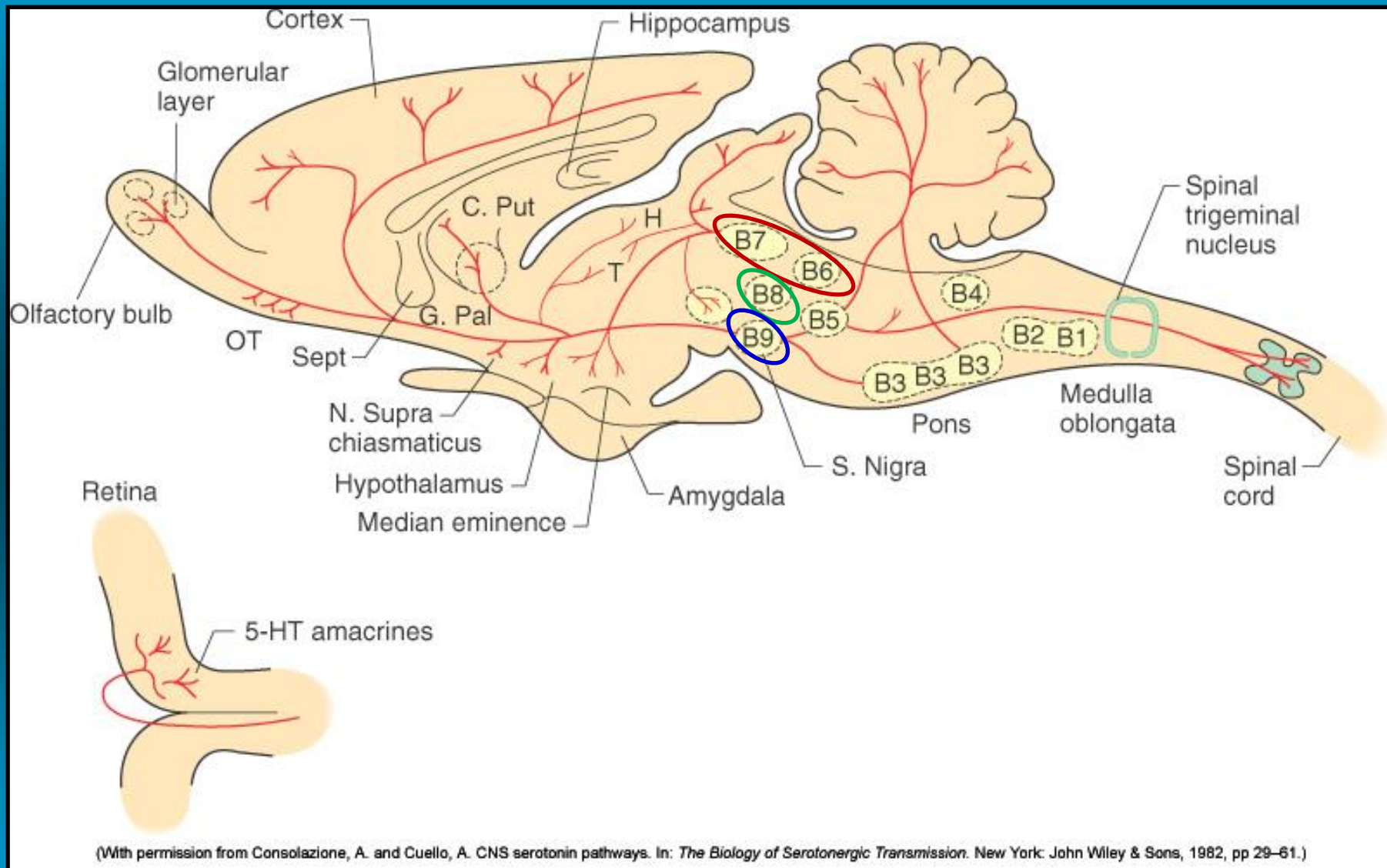
Distribuição de 5-HT no Sistema Nervoso

TABLE 13-1 Classification of serotonergic cell body groups according to Dahlstrom and Fuxe and corresponding anatomical structure

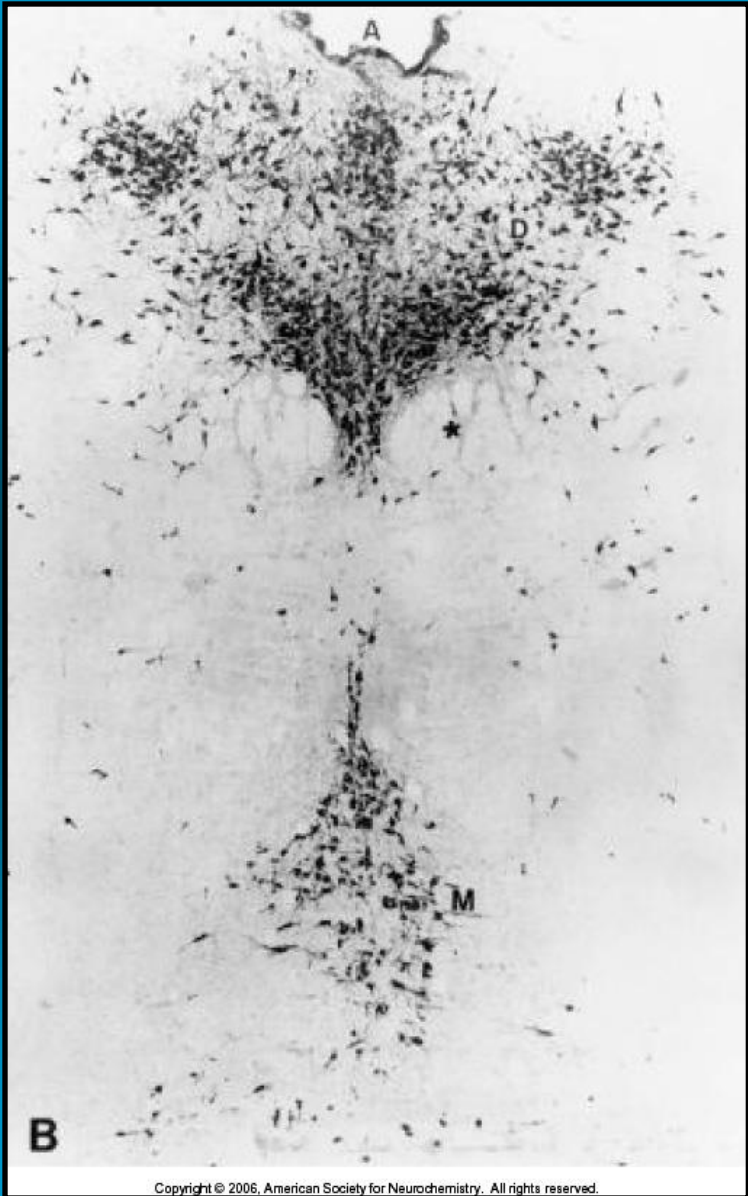
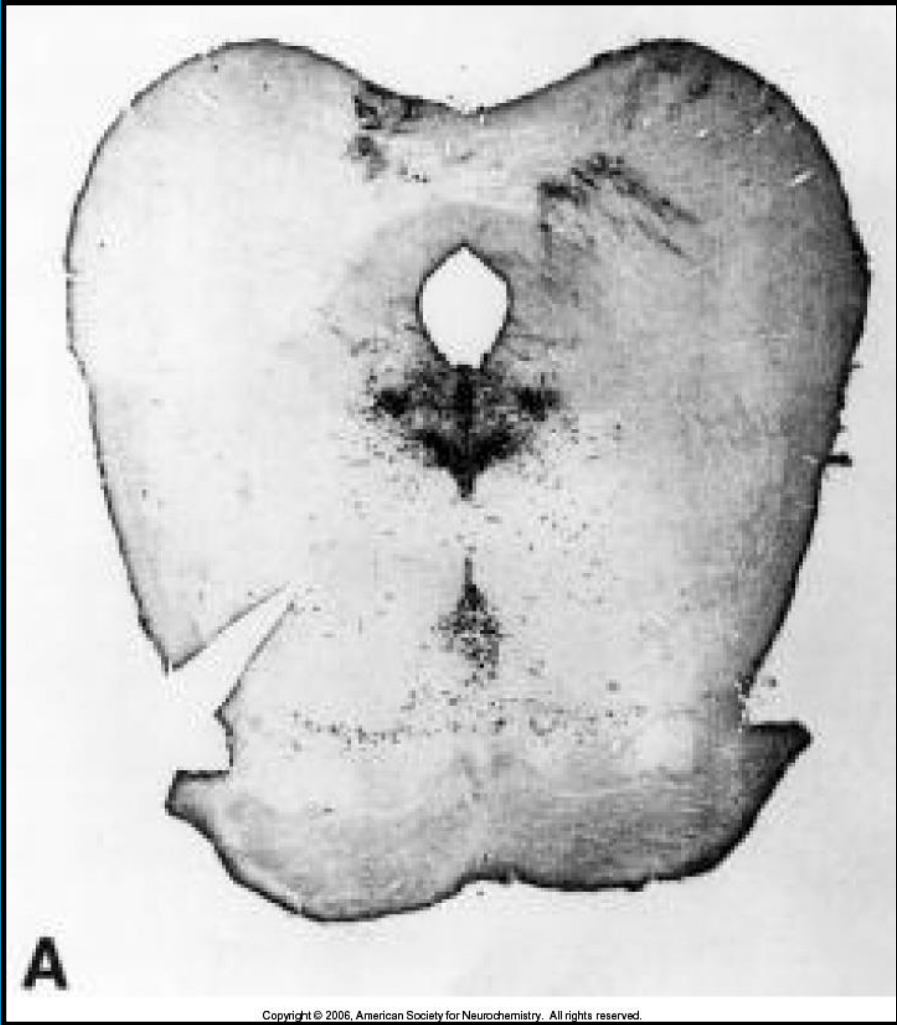
Groups of serotonin-containing cell bodies	Anatomical structure
B ₁	Raphe pallidus nucleus Caudal ventrolateral medulla
B ₂	Raphe obscurus nucleus
B ₃	Raphe magnus nucleus Rostral ventrolateral medulla Lateral paragigantocellular reticular nucleus
B ₄	Raphe obscurus nucleus, dorsolateral part
B ₅	Median raphe nucleus, caudal part
B ₆	Dorsal raphe nucleus, caudal part
B ₇	Dorsal raphe nucleus principal, rostral part
B ₈	Median raphe nucleus, rostral main part Caudal linear nucleus Nucleus pontis oralis
B ₉	Nucleus pontis oralis Supralemniscal region

Source: From Tork [2].

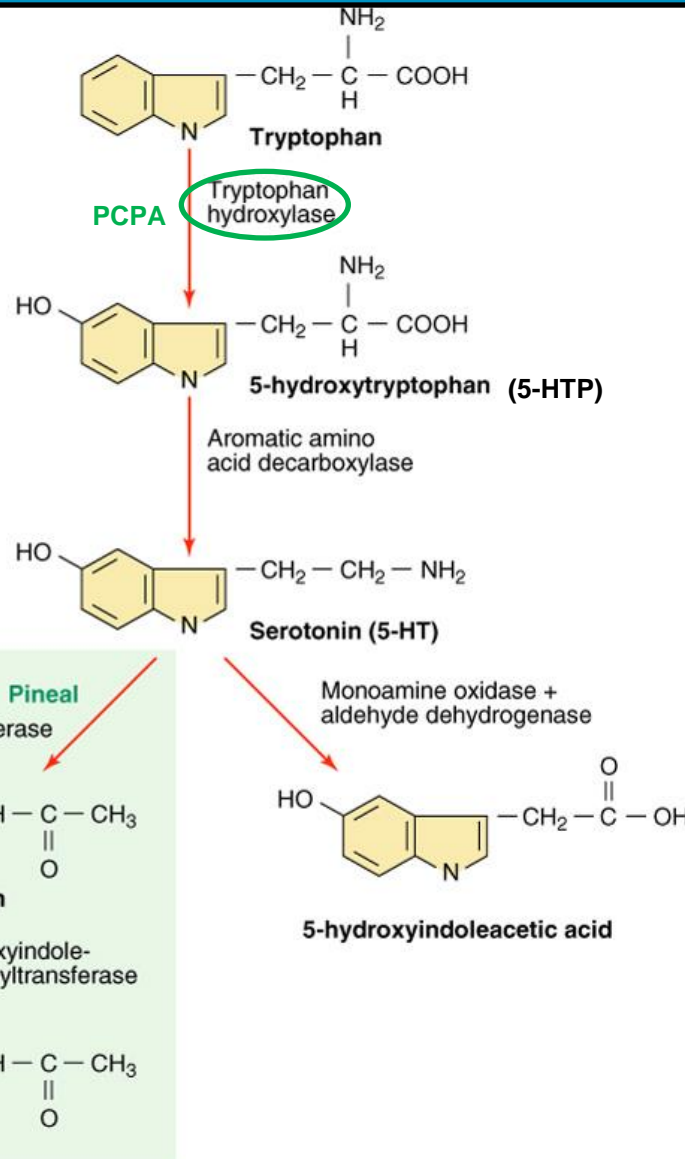
Distribuição de 5-HT no Sistema Nervoso



Distribuição de 5-HT no Sistema Nervoso



Síntese

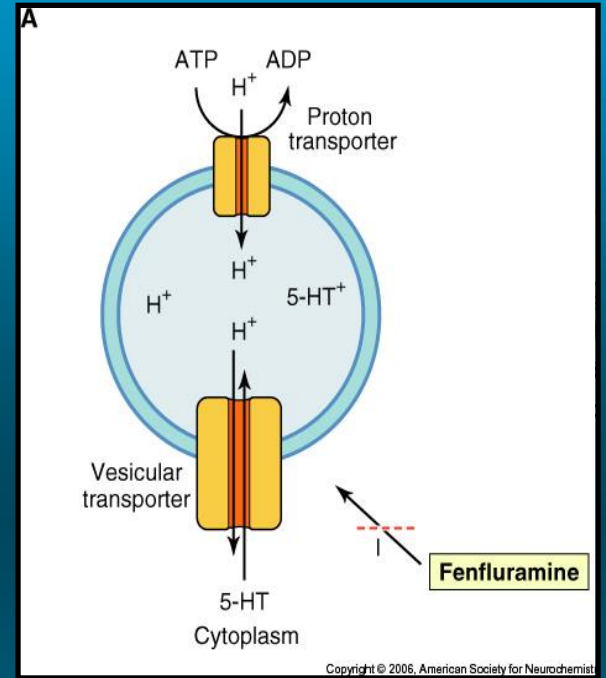
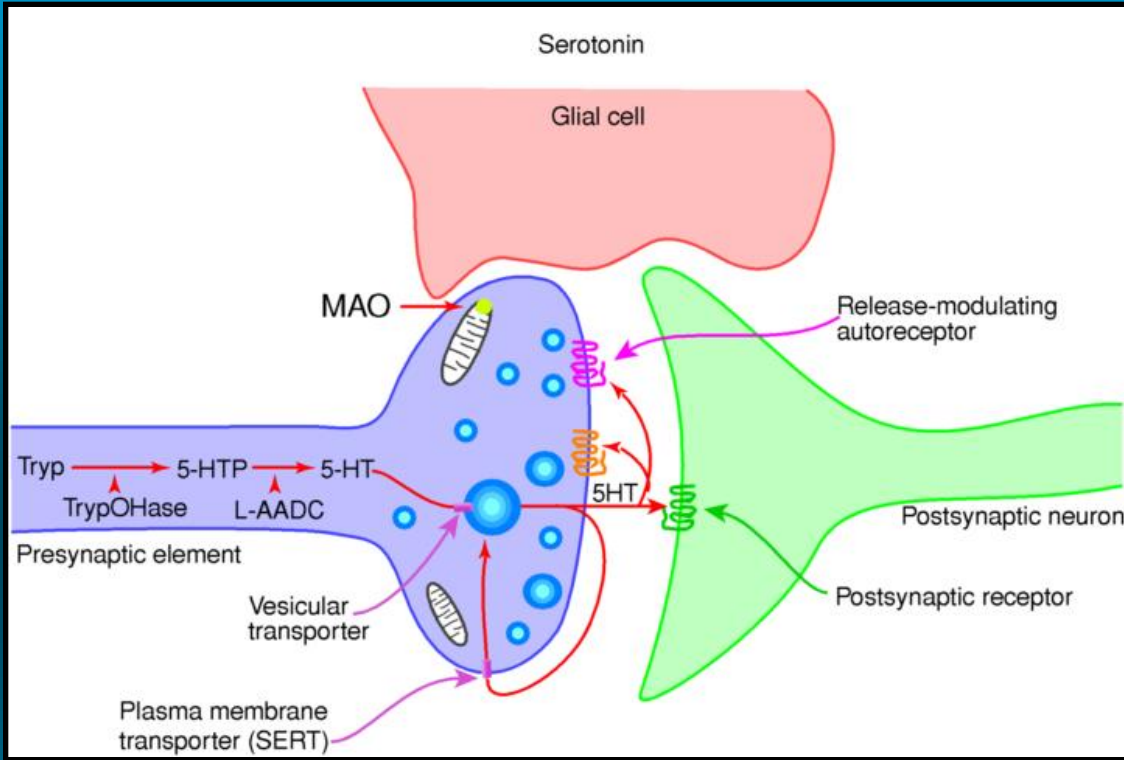


↑ Atividade neuronal

↑ Ca²⁺

↑ Fosforilação pela CaM K II ou PKA

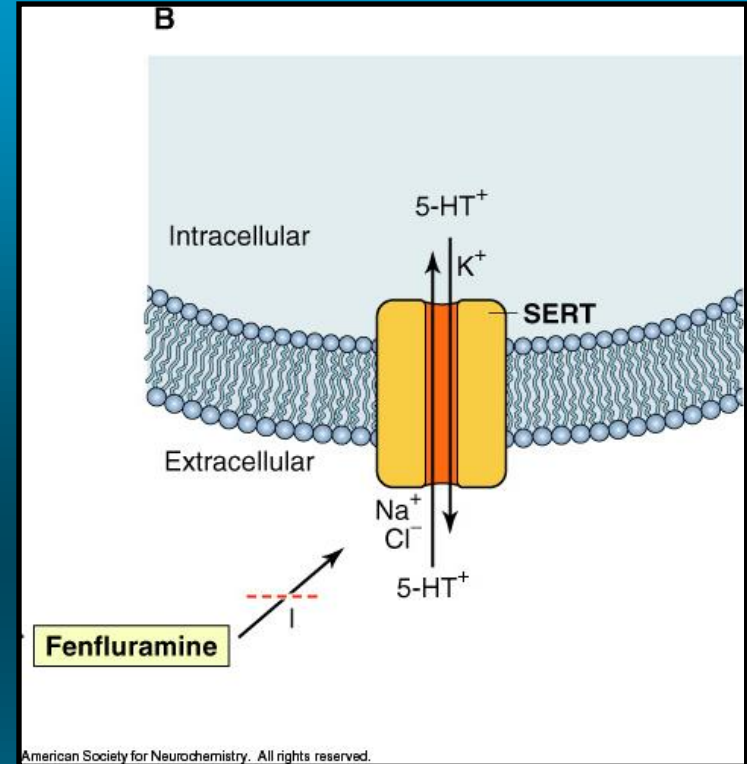
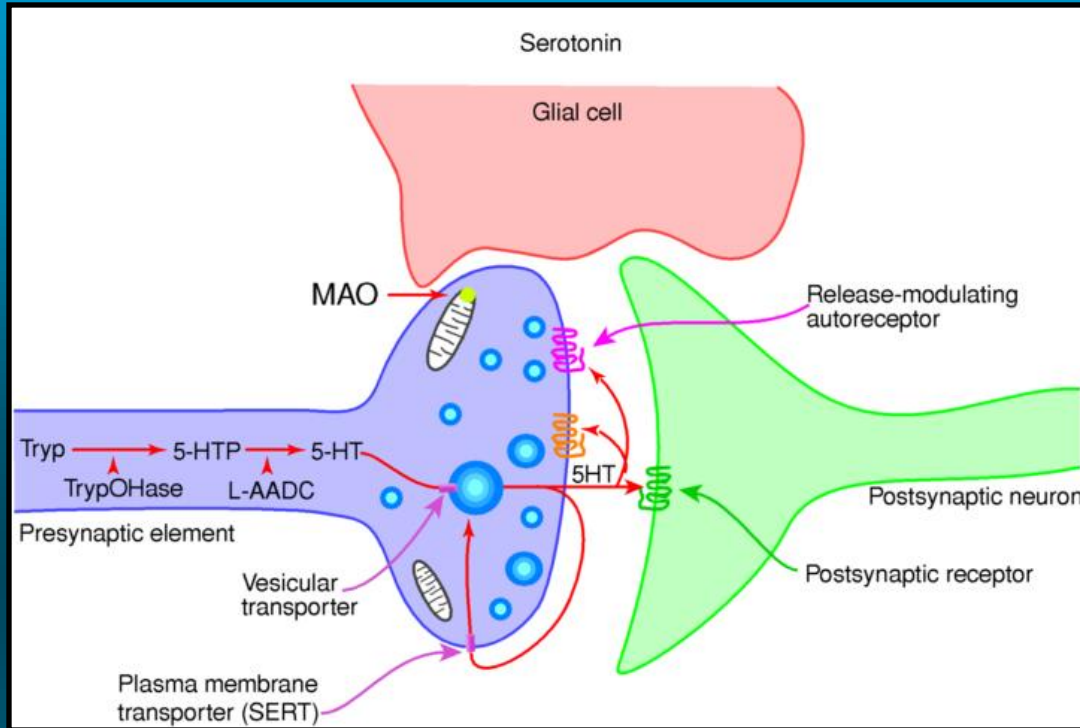
Transportador vesicular de serotonina



MDMA (Ecstasy)

Reserpina

Transportador de serotonina (SERT)



MDMA (Ecstasy)

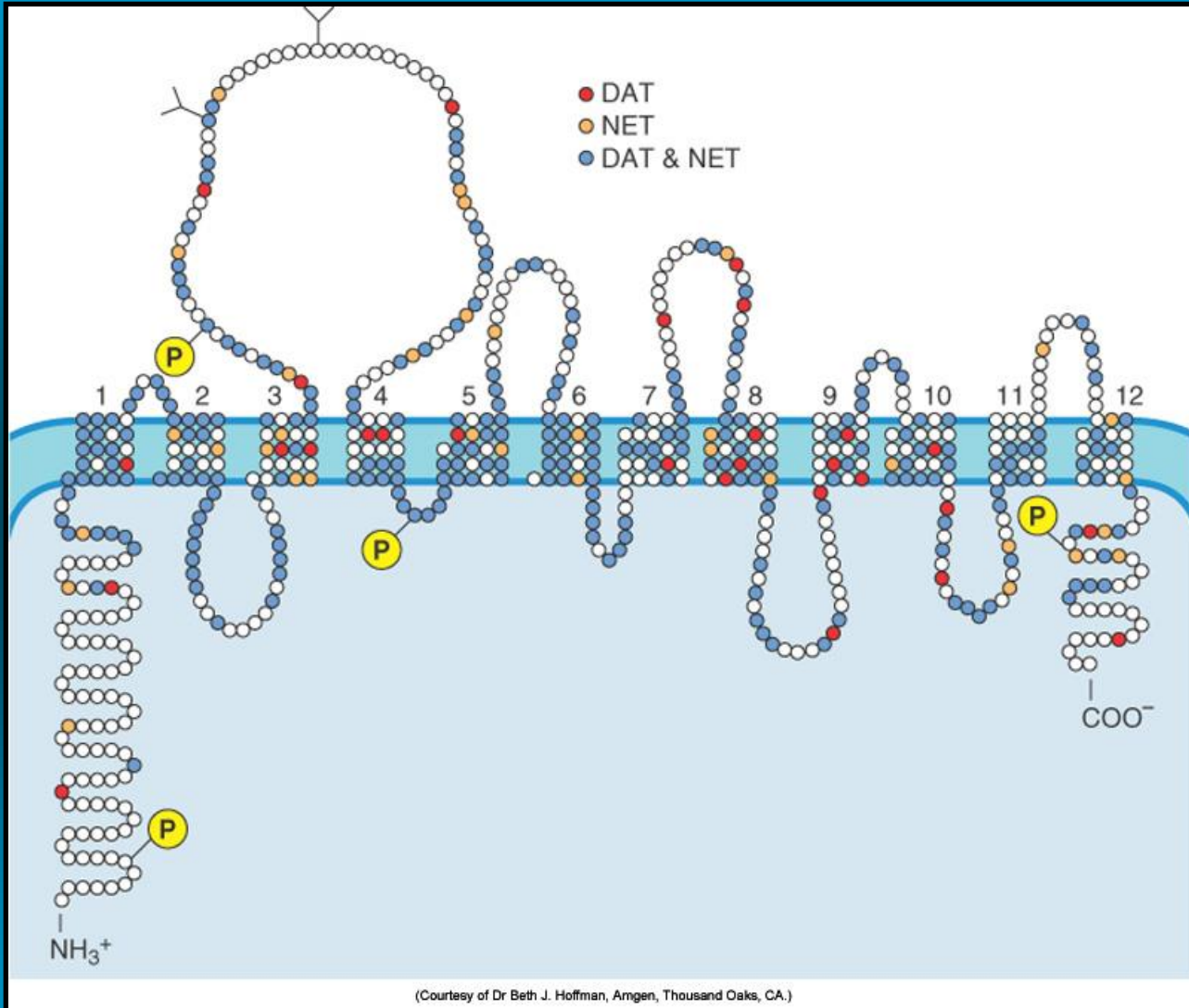
Cocaína

Transportador de serotonina (SERT)

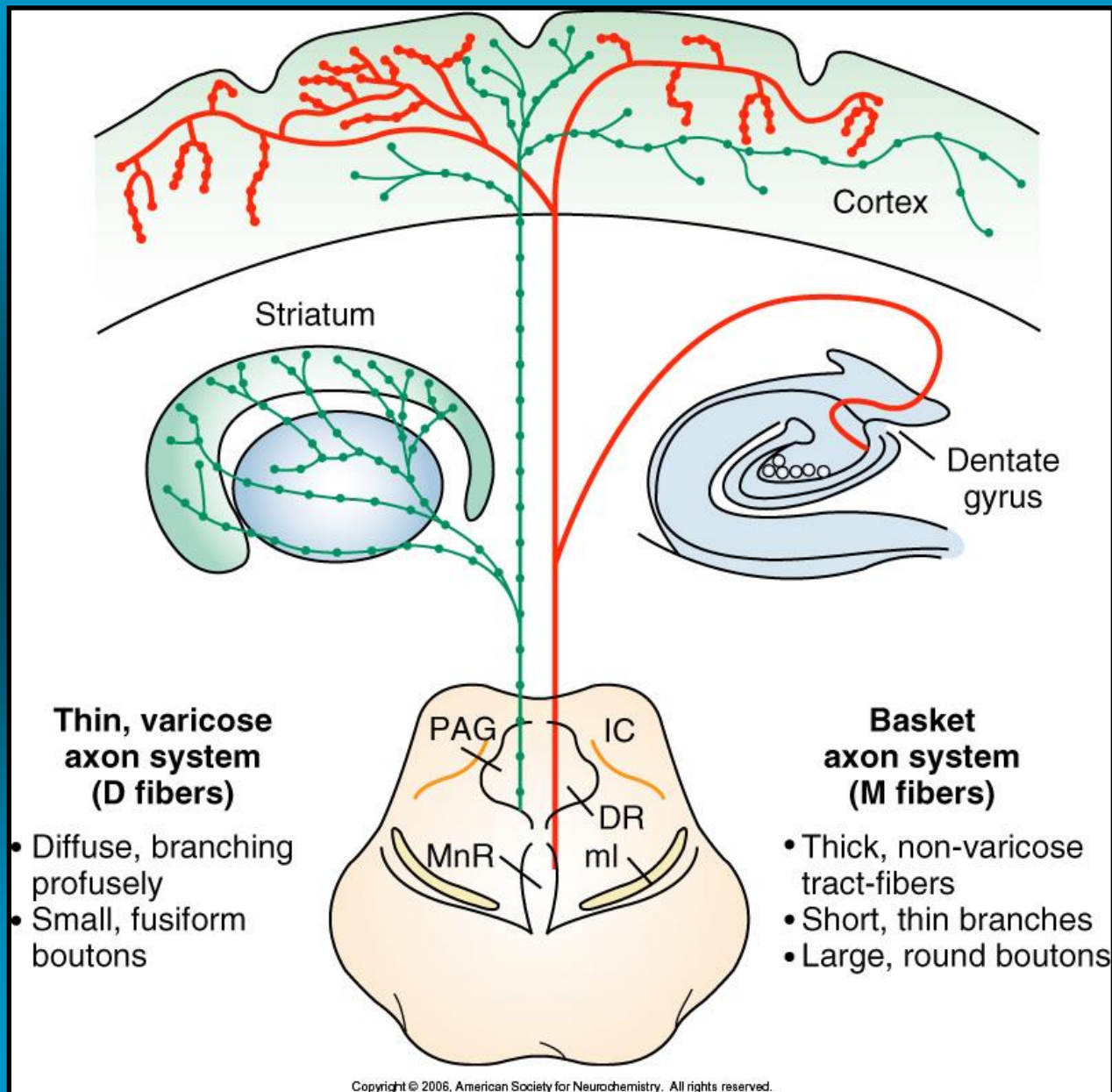
Regulação aguda e crônica da SERT:

- ✓ Uso crônico de drogas que bloqueiam a SERT (ISRSs, cocaína)
- ✓ Exposição ao substrato, mudanças do potencial de membrana, ativação ou inibição de receptores pré-sinápticos, mudanças hormonais, níveis de Ca^{2+}

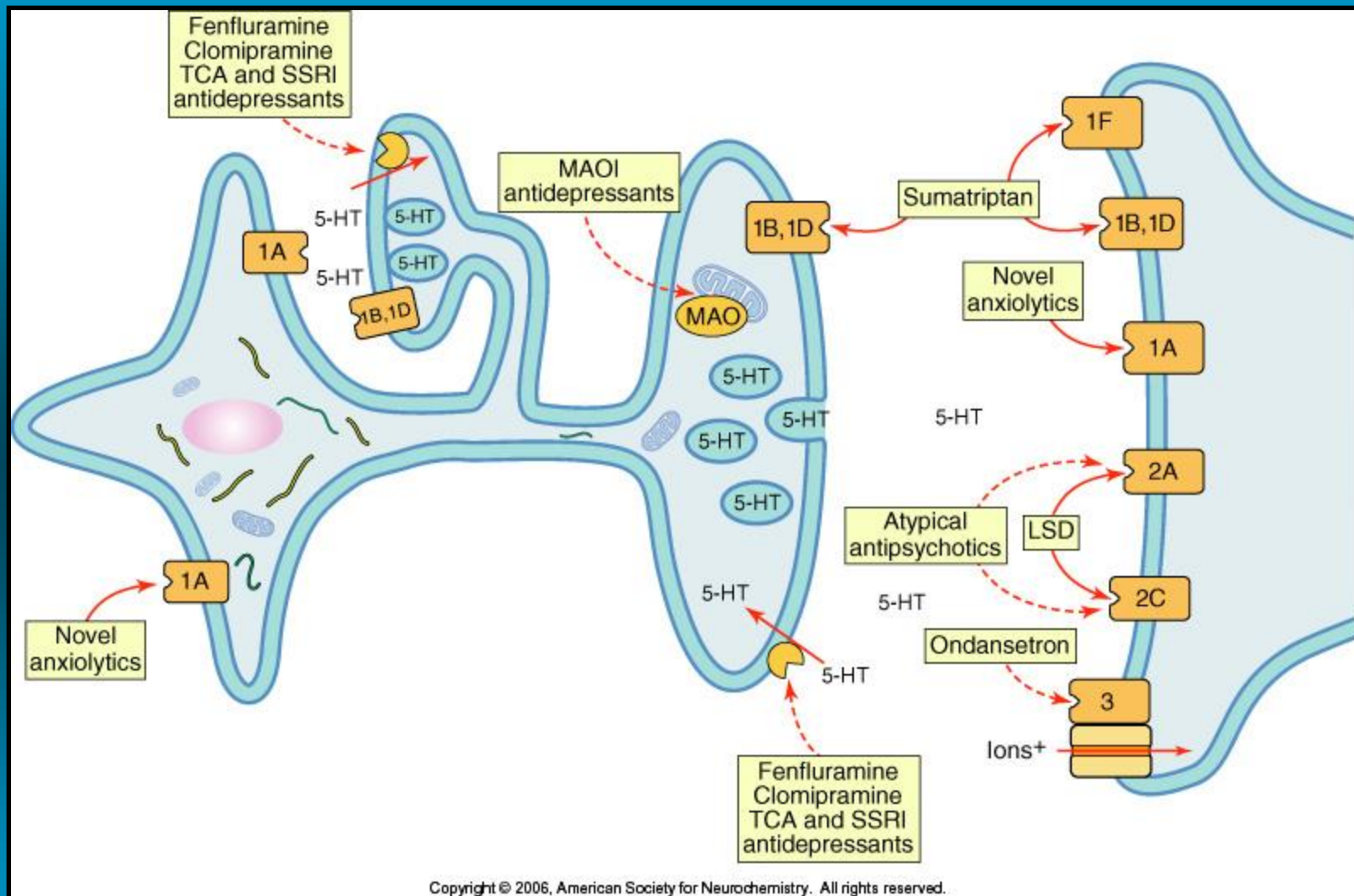
Transportador de serotonina (SERT)



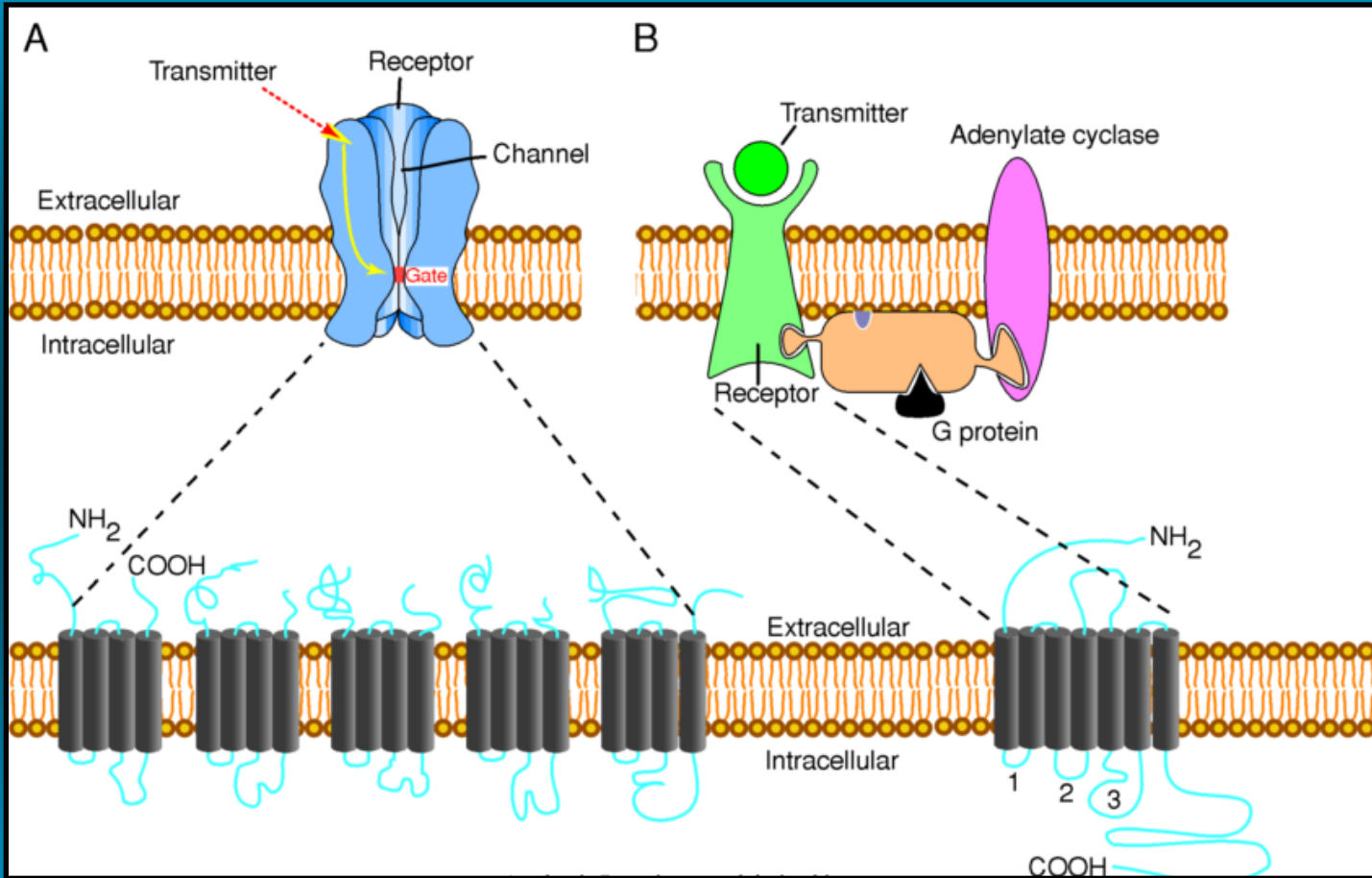
Distribuição no Sistema Nervoso



Sistema serotoninérgico



Receptores



Receptores de Serotonina

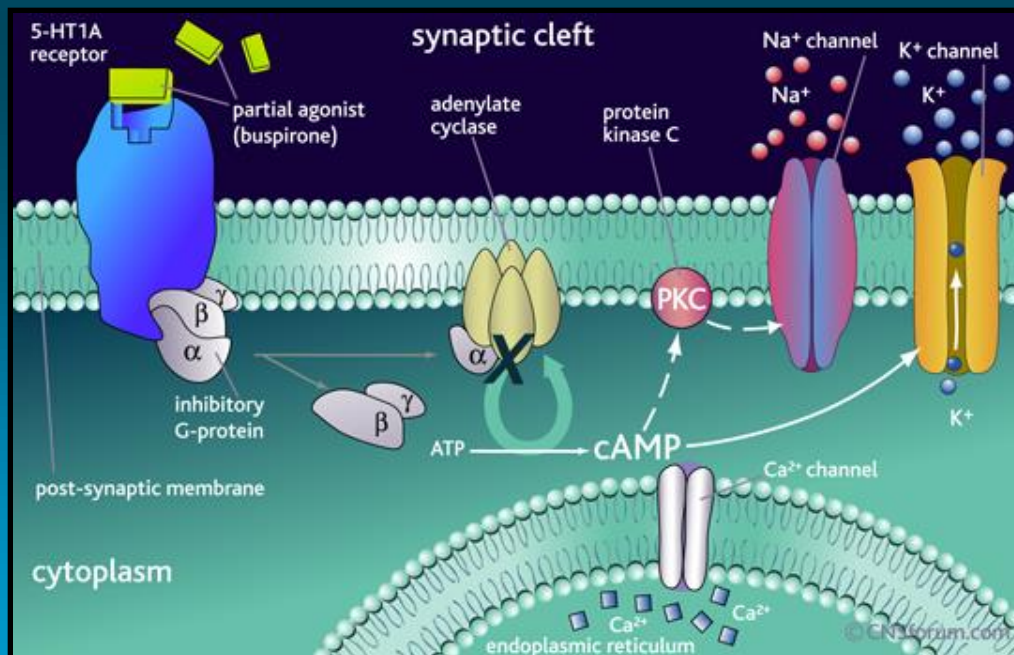
TABLE 13-2 Serotonin receptors present in the central nervous system.

Receptor	Distribution	Effector mechanism
5-HT₁ receptor family		
5-HT _{1A}	Hippocampus, amygdala, septum entorhinal cortex, hypothalamus, raphe nuclei	Inhibition of adenylyl cyclase; opening of K ⁺ channels
5-HT _{1B} (5-HT _{1Dβ})	Substantia nigra, basal ganglia Frontal cortex, superior colliculus, lateral geniculate, deep nuclei of the cerebellum	Inhibition of adenylyl cyclase
5-HT _{1D} (5-HT _{1Dα})	Globus pallidus, substantia nigra, caudate putamen Hippocampus and cortex	Inhibition of adenylyl cyclase
5-ht _{1E}	?	Inhibition of adenylyl cyclase
5-ht _{1F}	Cerebral cortex, striatum, hippocampus,	Inhibition of adenylyl cyclase
5-HT₂ receptor family		
5-HT _{2A} 13q14-21	Clastrum, cerebral cortex, olfactory tubercle, striatum, nucleus accumbens	Stimulation of phospholipase C; closing of K ⁺ channels
5-HT _{2B} 2q36.3-37.1	?	Stimulation of phospholipase C
5-HT _{2C} Xq24	Choroid plexus, globus pallidus, cerebral cortex, hypothalamus septum, substantia nigra, spinal cord	Stimulation of phospholipase C
5-HT₃ receptor family		
5-HT ₃ (5-HT _{3A}) (5-HT _{3B})	Hippocampus, entorhinal cortex, amygdala, nucleus, accumbens, solitary tract nerve, trigeminal nerve, motor nucleus of the dorsal vagal nerve, area postrema, spinal cord	Ligand-gated cation channel
5-HT ₄	Hippocampus, striatum, olfactory tubercle, substantia nigra	Stimulation of adenylyl cyclase
5-ht _{5A}	?	Inhibition of adenylyl cyclase
5-ht _{5B}	?	?
5-ht ₆	?	Stimulation of adenylyl cyclase
5-HT ₇	Cerebral cortex, septum, thalamus hypothalamus, amygdala, hippocampus	Stimulation of adenylyl cyclase

Receptores de Serotonina (5-HT₁)

TABLE 13-2 Serotonin receptors present in the central nervous system.

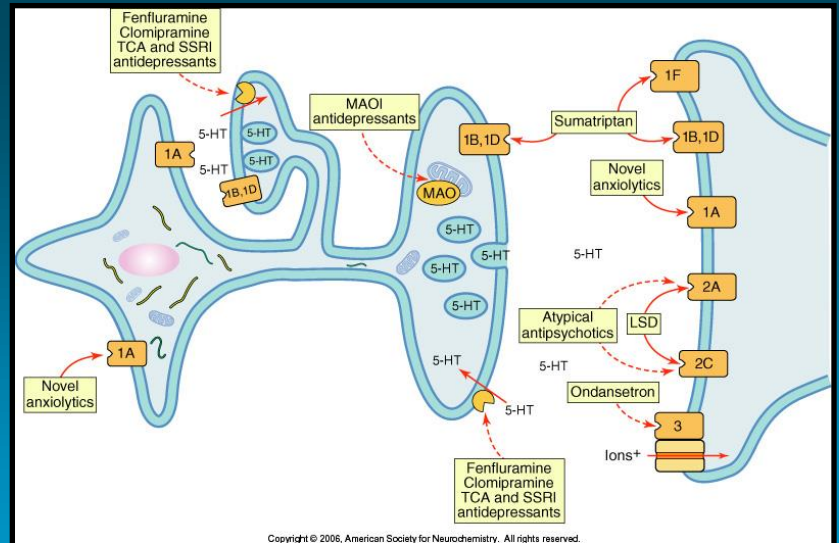
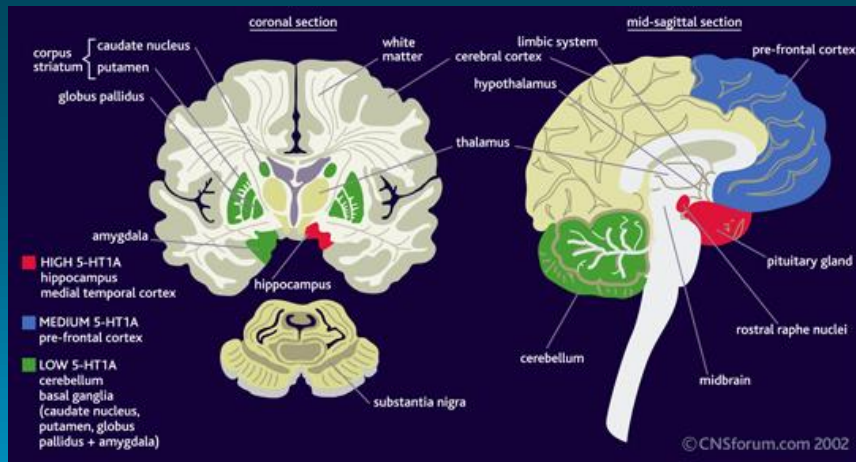
Receptor	Distribution	Effector mechanism
5-HT₁ receptor family		
5-HT _{1A}	Hippocampus, amygdala, septum entorhinal cortex, hypothalamus, raphe nuclei	Inhibition of adenylyl cyclase; opening of K ⁺ channels
5-HT _{1B}	Substantia nigra, basal ganglia	Inhibition of adenylyl cyclase
(5-HT _{1Dβ})	Frontal cortex, superior colliculus, lateral geniculate, deep nuclei of the cerebellum	
5-HT _{1D}	Globus pallidus, substantia nigra, caudate putamen	Inhibition of adenylyl cyclase
(5-HT _{1Dα})	Hippocampus and cortex	
5-ht _{1E}	? I	Inhibition of adenylyl cyclase
5-ht _{1F}	Cerebral cortex, striatum, hippocampus,	Inhibition of adenylyl cyclase



Receptores de Serotonina (5-HT_{1A})

TABLE 13-2 Serotonin receptors present in the central nervous system.

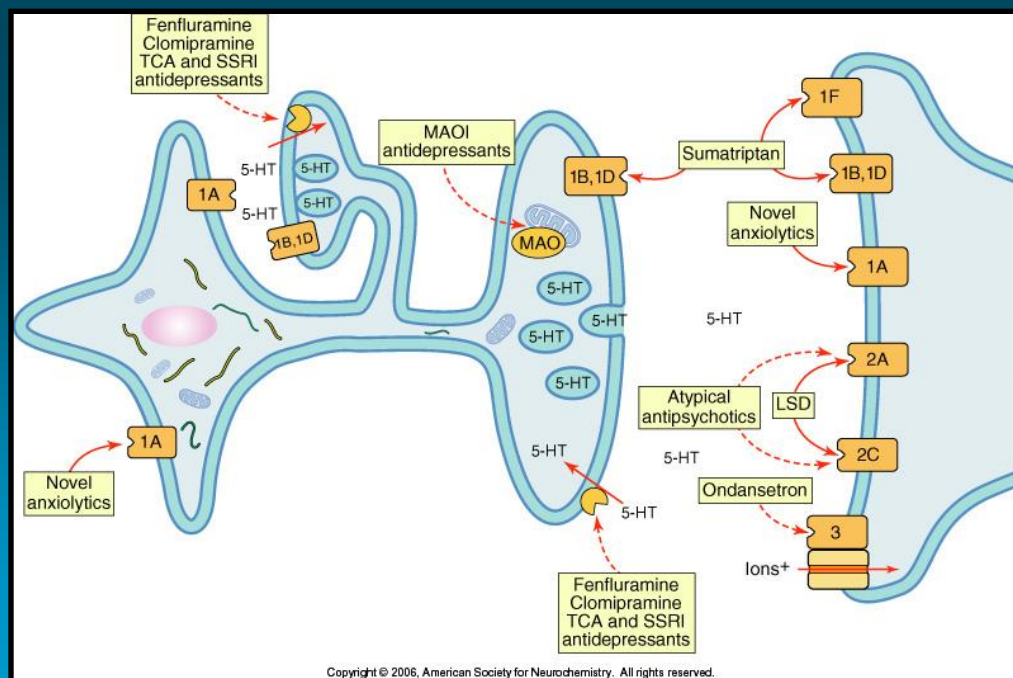
Receptor	Distribution	Effector mechanism
5-HT ₁ receptor family		
5-HT _{1A}	Hippocampus, amygdala, septum entorhinal cortex, hypothalamus, raphe nuclei	Inhibition of adenylyl cyclase; opening of K ⁺ channels
5-HT _{1B} (5-HT _{1Dβ})	Substantia nigra, basal ganglia	Inhibition of adenylyl cyclase
5-HT _{1D} (5-HT _{1Dα})	Frontal cortex, superior colliculus, lateral geniculate, deep nuclei of the cerebellum	Inhibition of adenylyl cyclase
5-HT _{1E}	Globus pallidus, substantia nigra, caudate putamen	Inhibition of adenylyl cyclase
5-HT _{1F}	Hippocampus and cortex	Inhibition of adenylyl cyclase
5-HT _{1E}	? I	Inhibition of adenylyl cyclase
5-HT _{1F}	Cerebral cortex, striatum, hippocampus,	Inhibition of adenylyl cyclase



Receptores de Serotonina (5-HT_{1B} e 5-HT_{1D})

TABLE 13-2 Serotonin receptors present in the central nervous system.

Receptor	Distribution	Effector mechanism
5-HT ₁ receptor family		
5-HT _{1A}	Hippocampus, amygdala, septum entorhinal cortex, hypothalamus, raphe nuclei	Inhibition of adenylyl cyclase; opening of K ⁺ channels
5-HT _{1B} (5-HT _{1Dβ})	Substantia nigra, basal ganglia	Inhibition of adenylyl cyclase
5-HT _{1D} (5-HT _{1Dα})	Frontal cortex, superior colliculus, lateral geniculate, deep nuclei of the cerebellum	Inhibition of adenylyl cyclase
5-HT _{1E}	Globus pallidus, substantia nigra, caudate putamen	Inhibition of adenylyl cyclase
5-HT _{1F}	Hippocampus and cortex	Inhibition of adenylyl cyclase
5-HT ₂ receptor family		
5-HT _{2A}	? I	Inhibition of adenylyl cyclase
5-HT _{2B}	Cerebral cortex, striatum, hippocampus,	Inhibition of adenylyl cyclase



Receptores de Serotonina (5-HT₂)

5-HT₂ receptor family

5-HT_{2A} 13q14-21

Clastrum, cerebral cortex, olfactory tubercle, striatum, nucleus accumbens

Stimulation of phospholipase C; closing of K⁺ channels

5-HT_{2B} 2q36.3-37.1

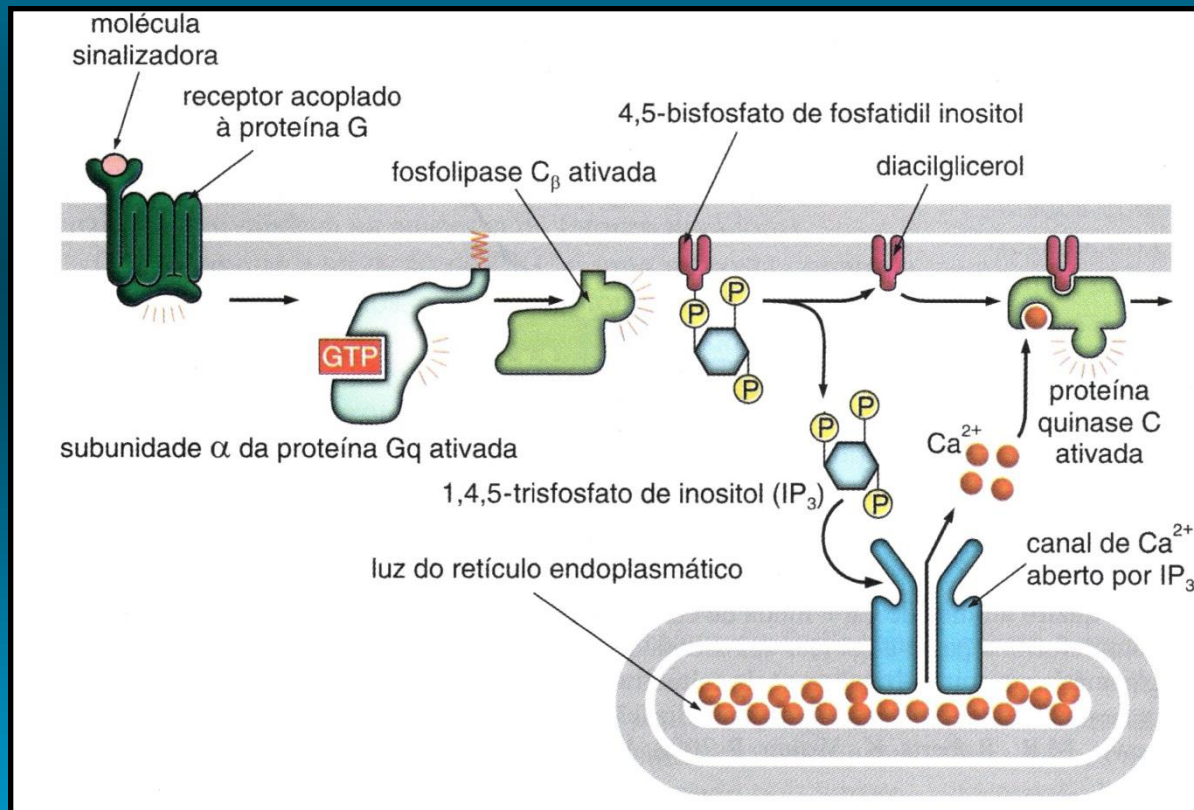
?

Stimulation of phospholipase C

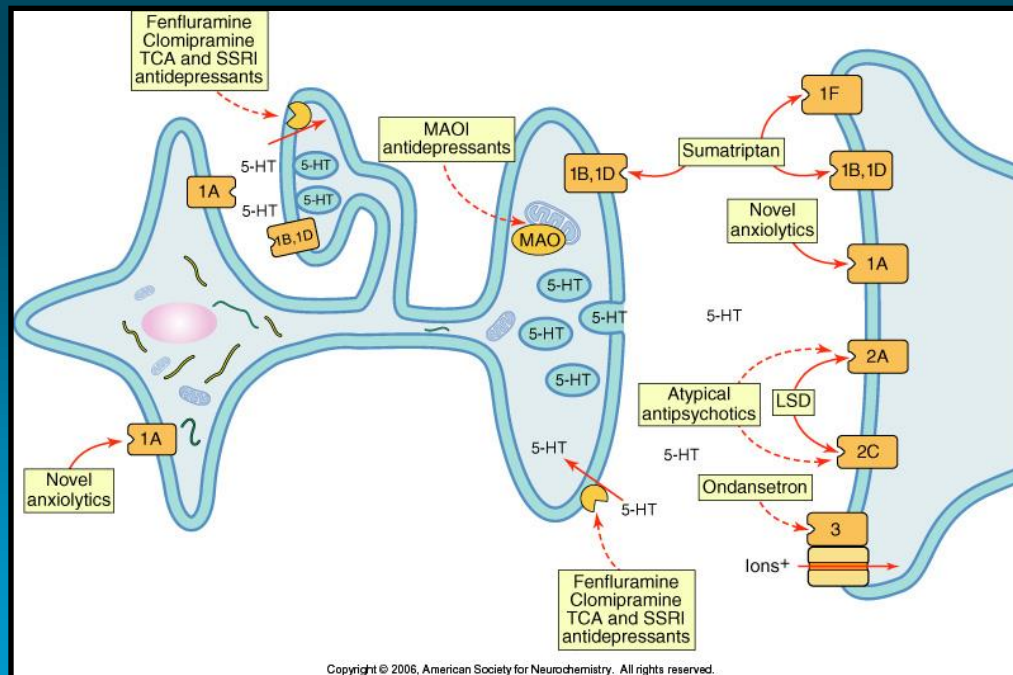
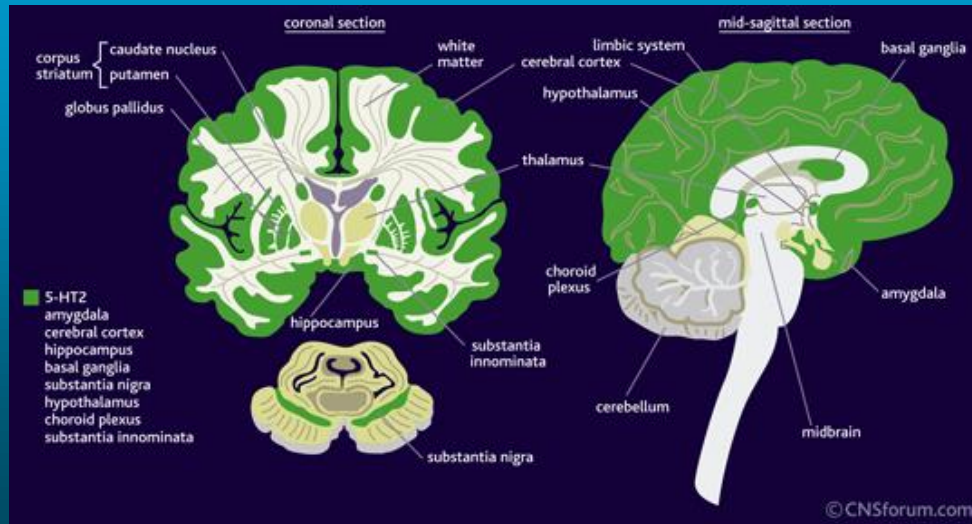
5-HT_{2C} Xq24

Choroid plexus, globus pallidus, cerebral cortex, hypothalamus septum, substantia nigra, spinal cord

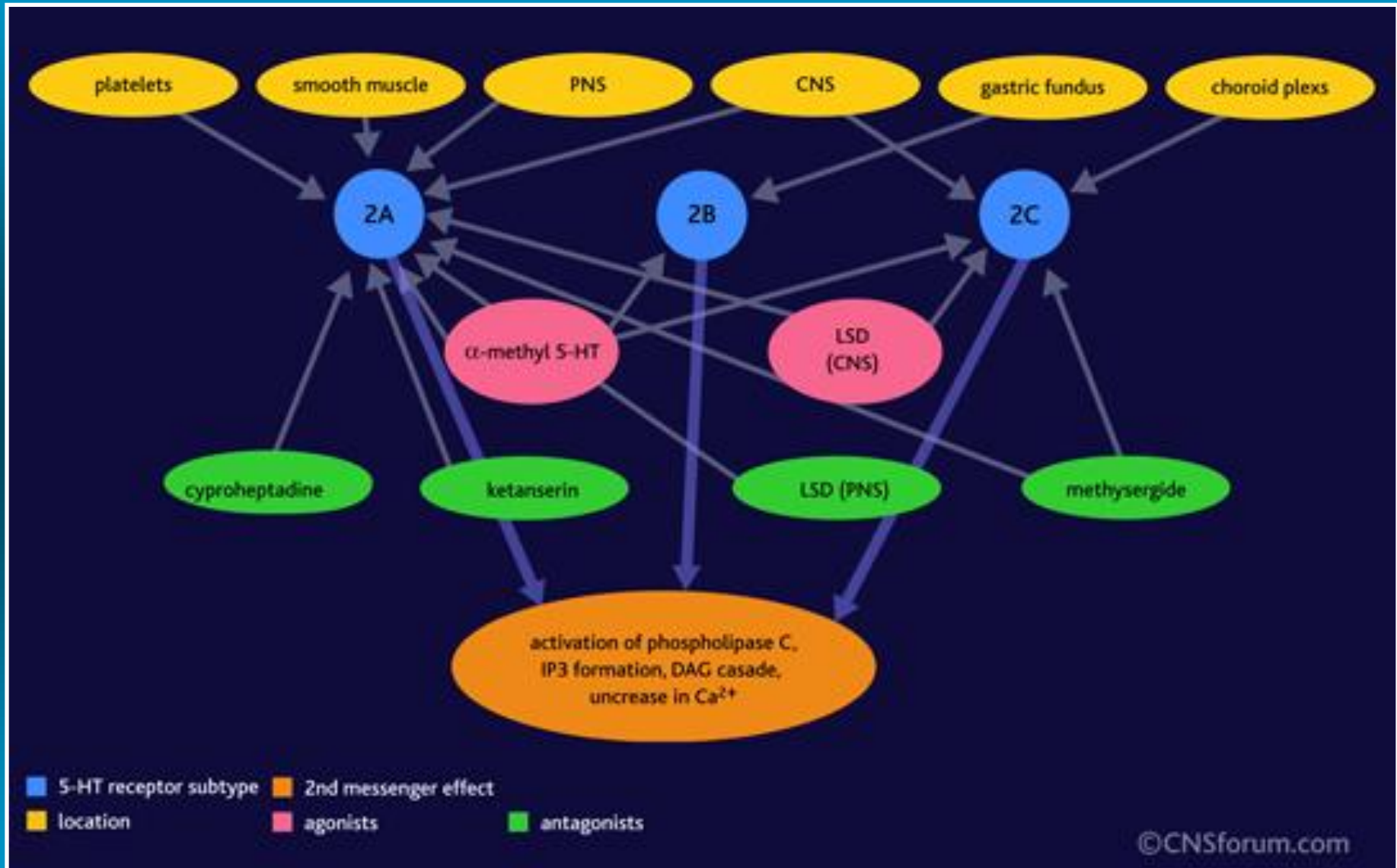
Stimulation of phospholipase C



Receptores de Serotonina (5-HT₂)



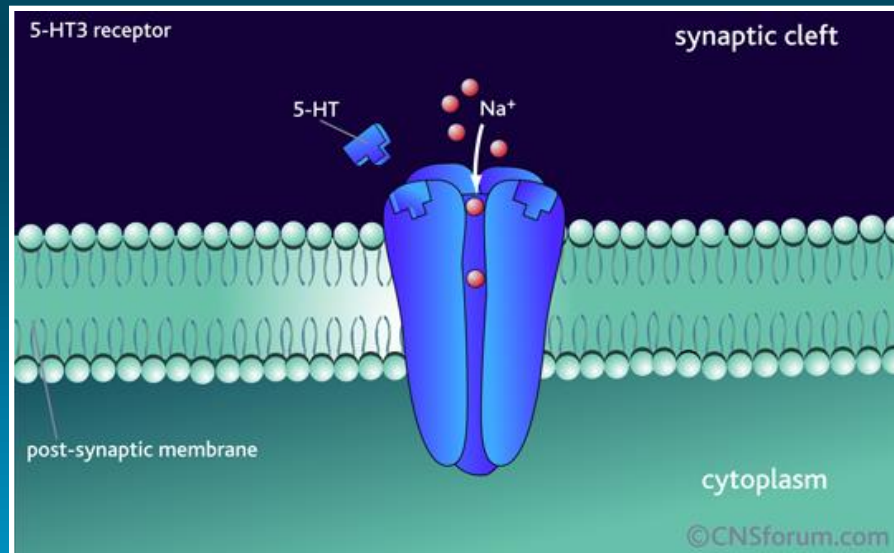
Receptores de Serotonina (5-HT₂)



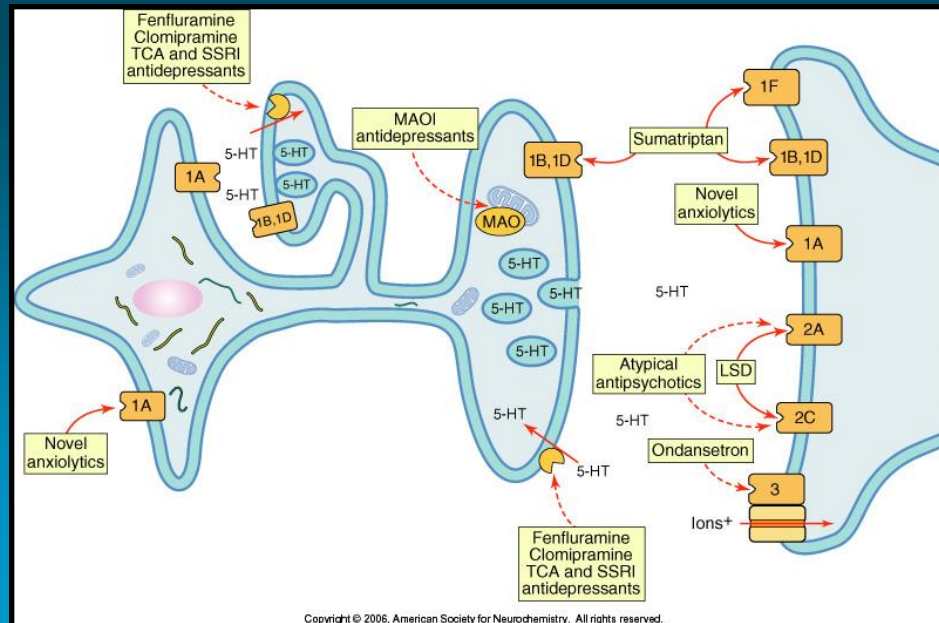
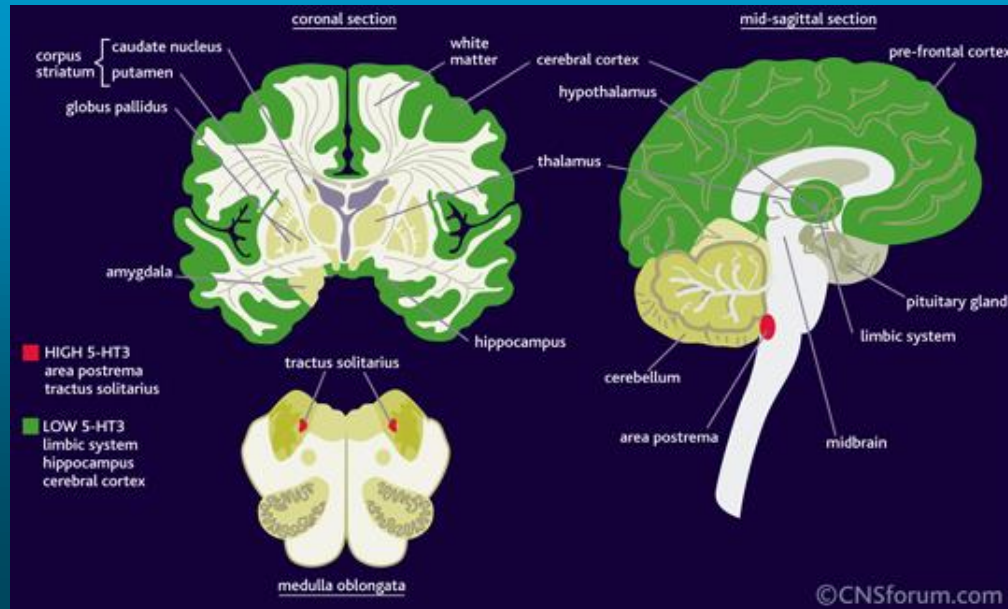
Receptores de Serotonina (5-HT₃)

5-HT₃ receptor family

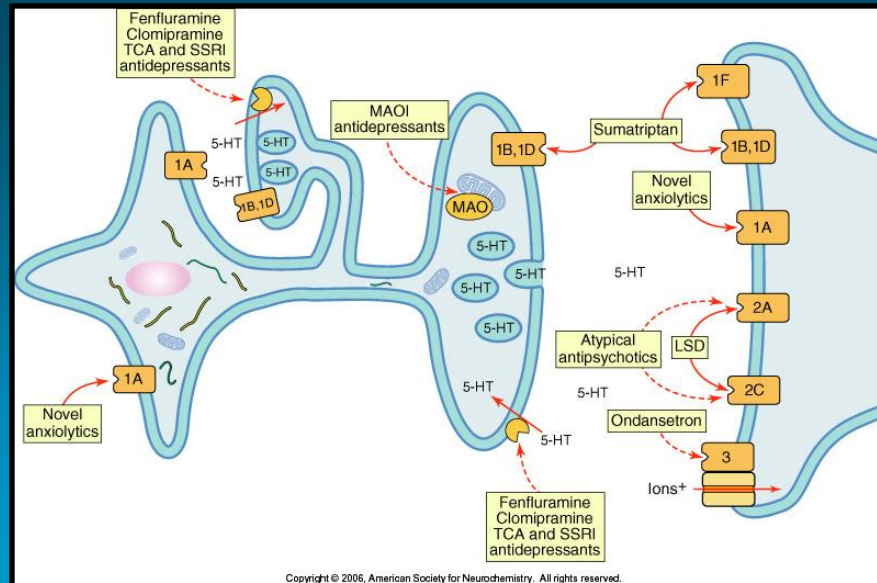
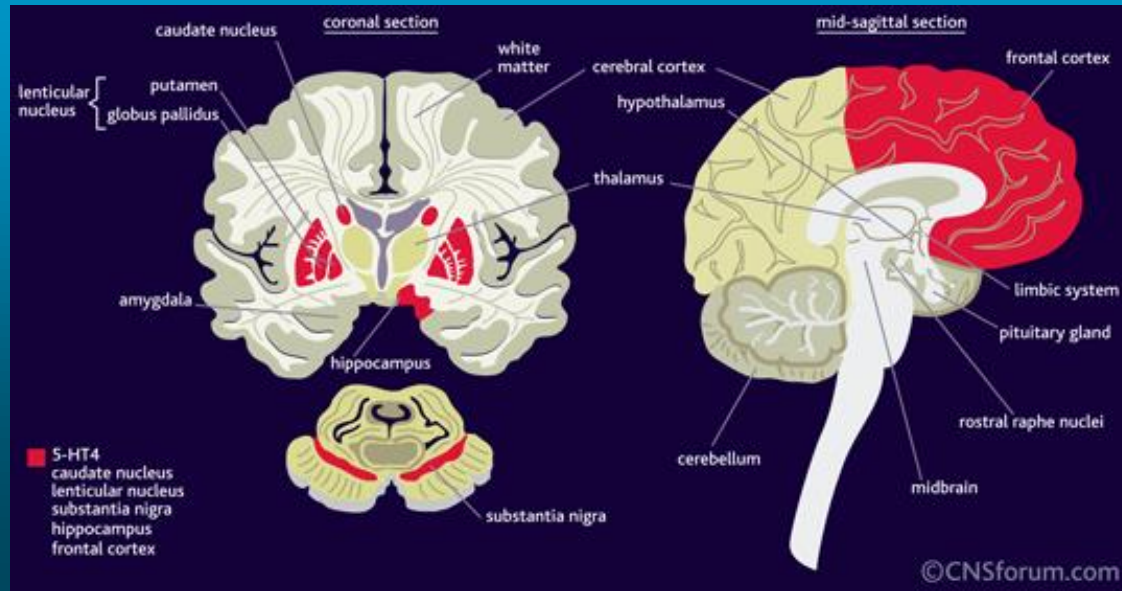
5-HT ₃ (5-HT _{3A}) (5-HT _{3B})	Hippocampus, entorhinal cortex, amygdala, nucleus, accumbens, solitary tract nerve, trigeminal nerve, motor nucleus of the dorsal vagal nerve, area postrema, spinal cord	Ligand-gated cation channel
5-HT ₄	Hippocampus, striatum, olfactory tubercle, substantia nigra	Stimulation of adenylyl cyclase
5-ht _{5A}	?	Inhibition of adenylyl cyclase
5-ht _{5B}	?	?
5-ht ₆	?	Stimulation of adenylyl cyclase
5-HT ₇	Cerebral cortex, septum, thalamus hypothalamus, amygdala, hippocampus	Stimulation of adenylyl cyclase



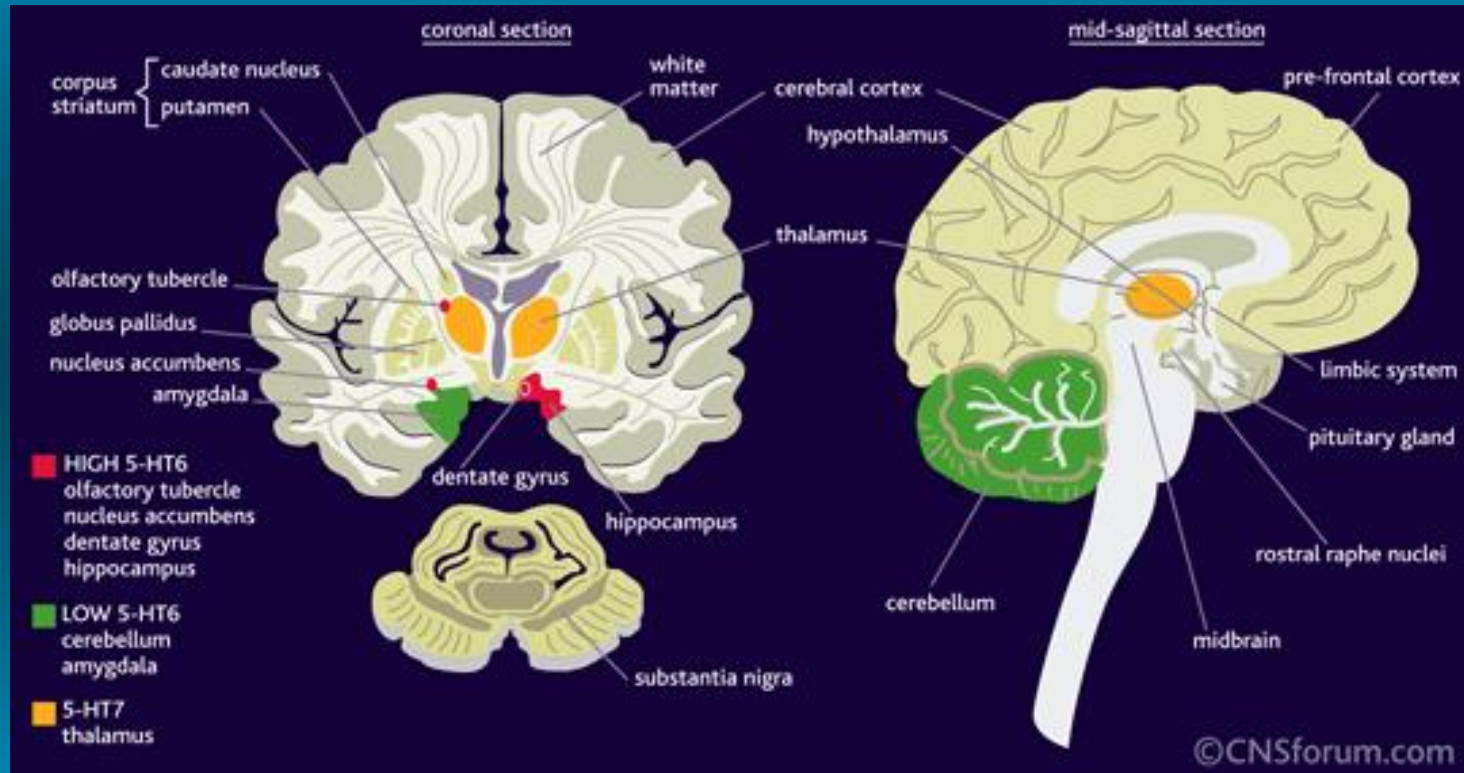
Receptores de Serotonina (5-HT₃)

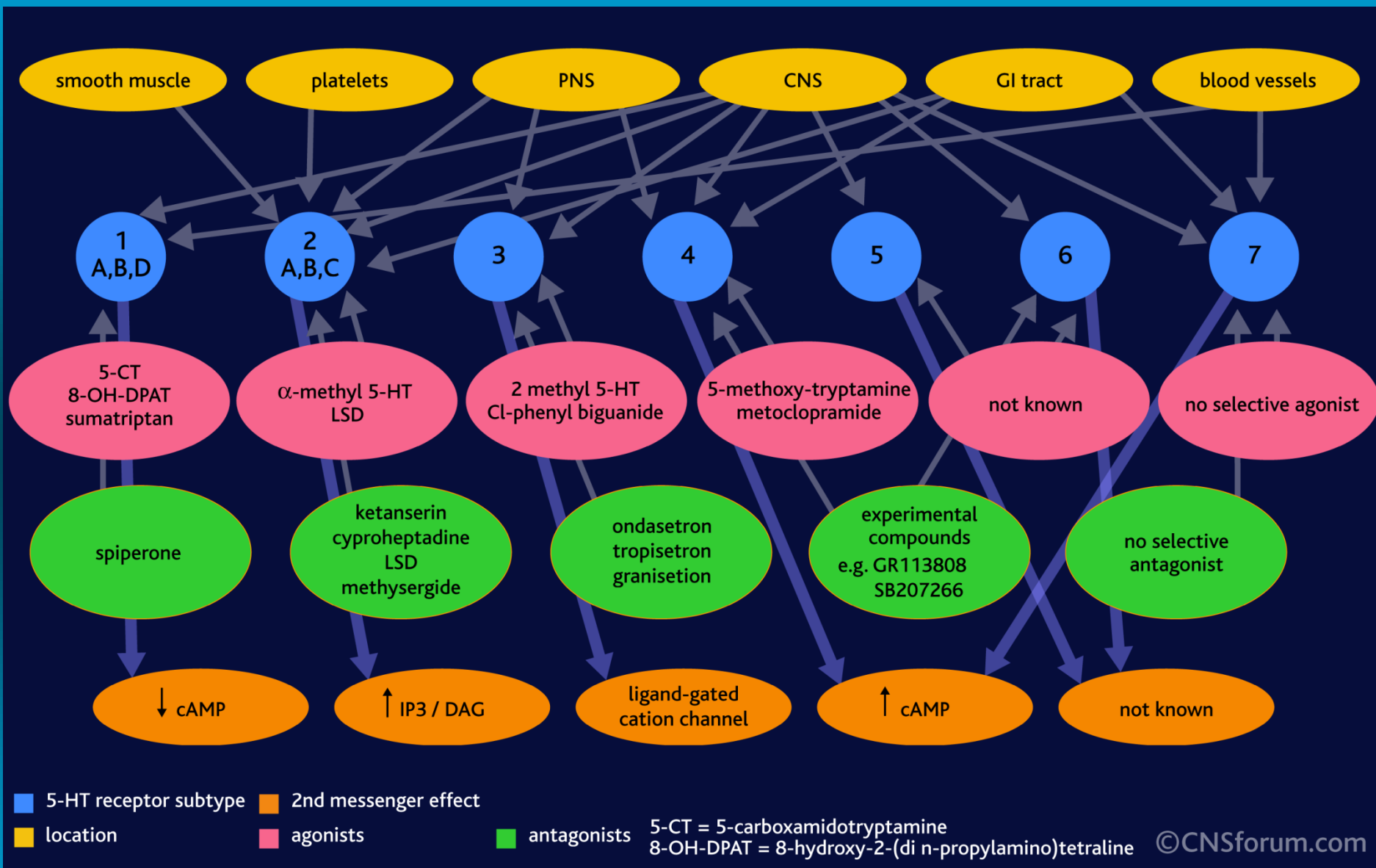


Receptores de Serotonina (5-HT₄)

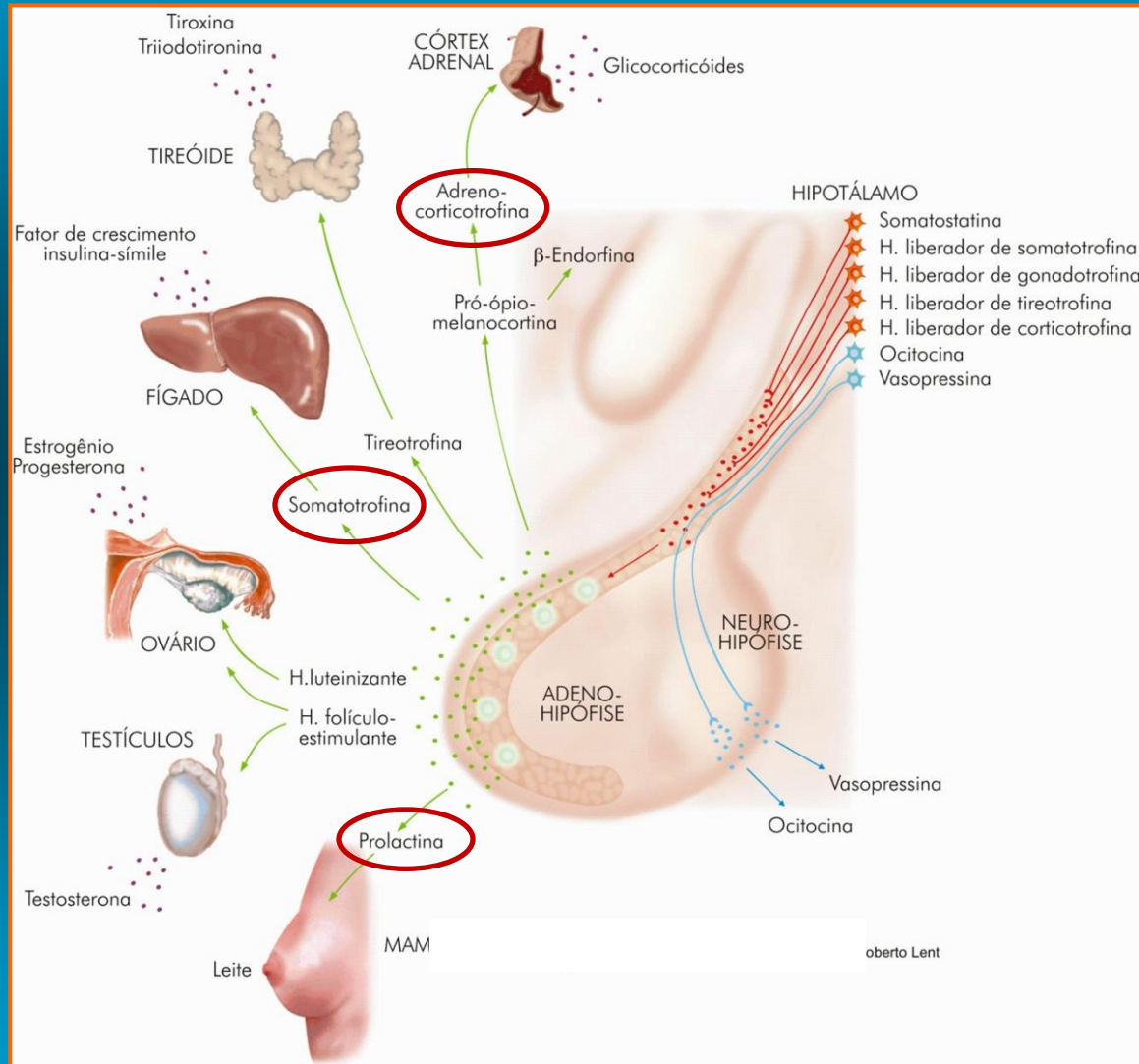


Receptores de Serotonina (5-HT₆ e 5-HT₇)



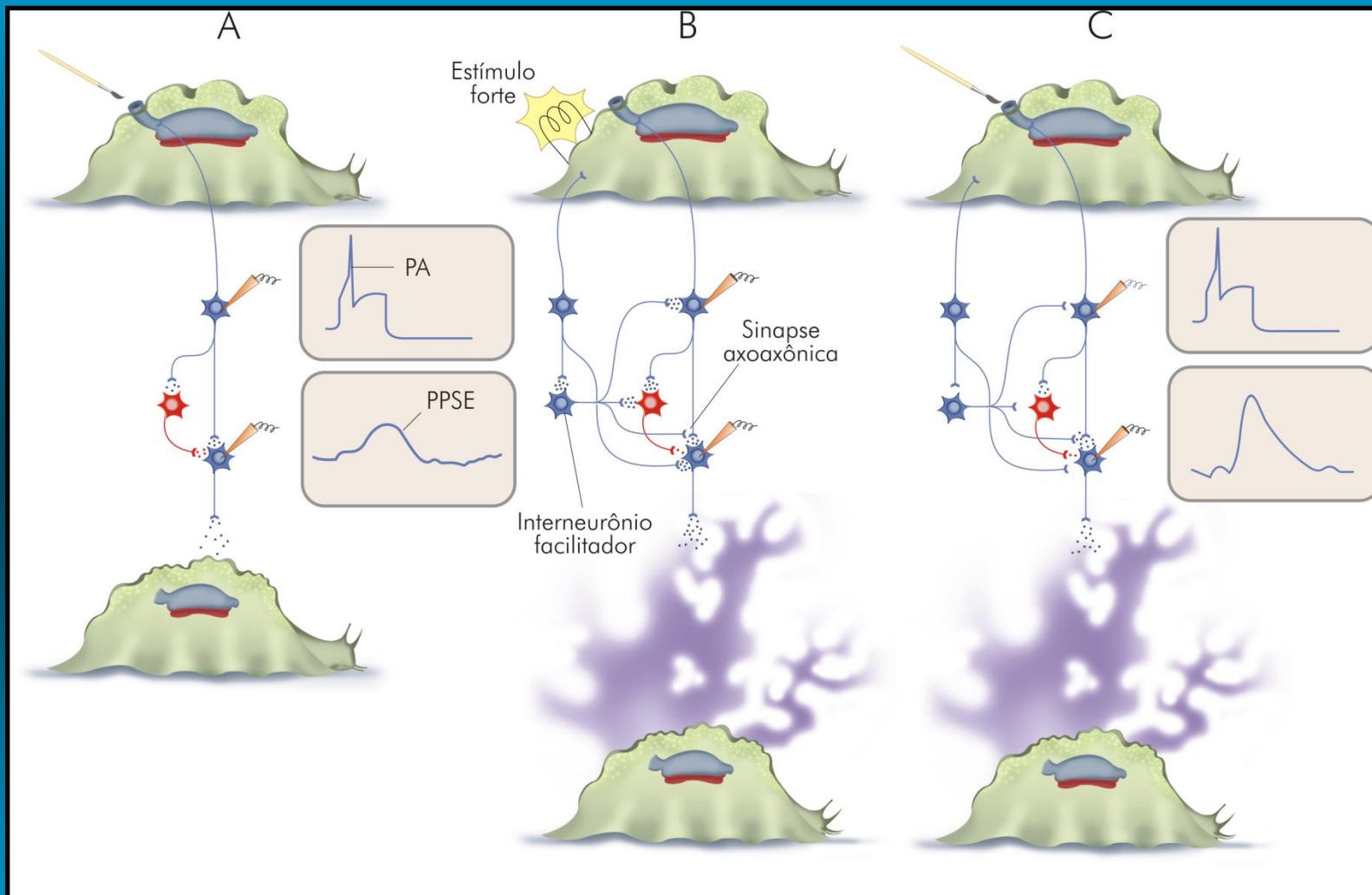


Serotonina e Função Neuroendócrina



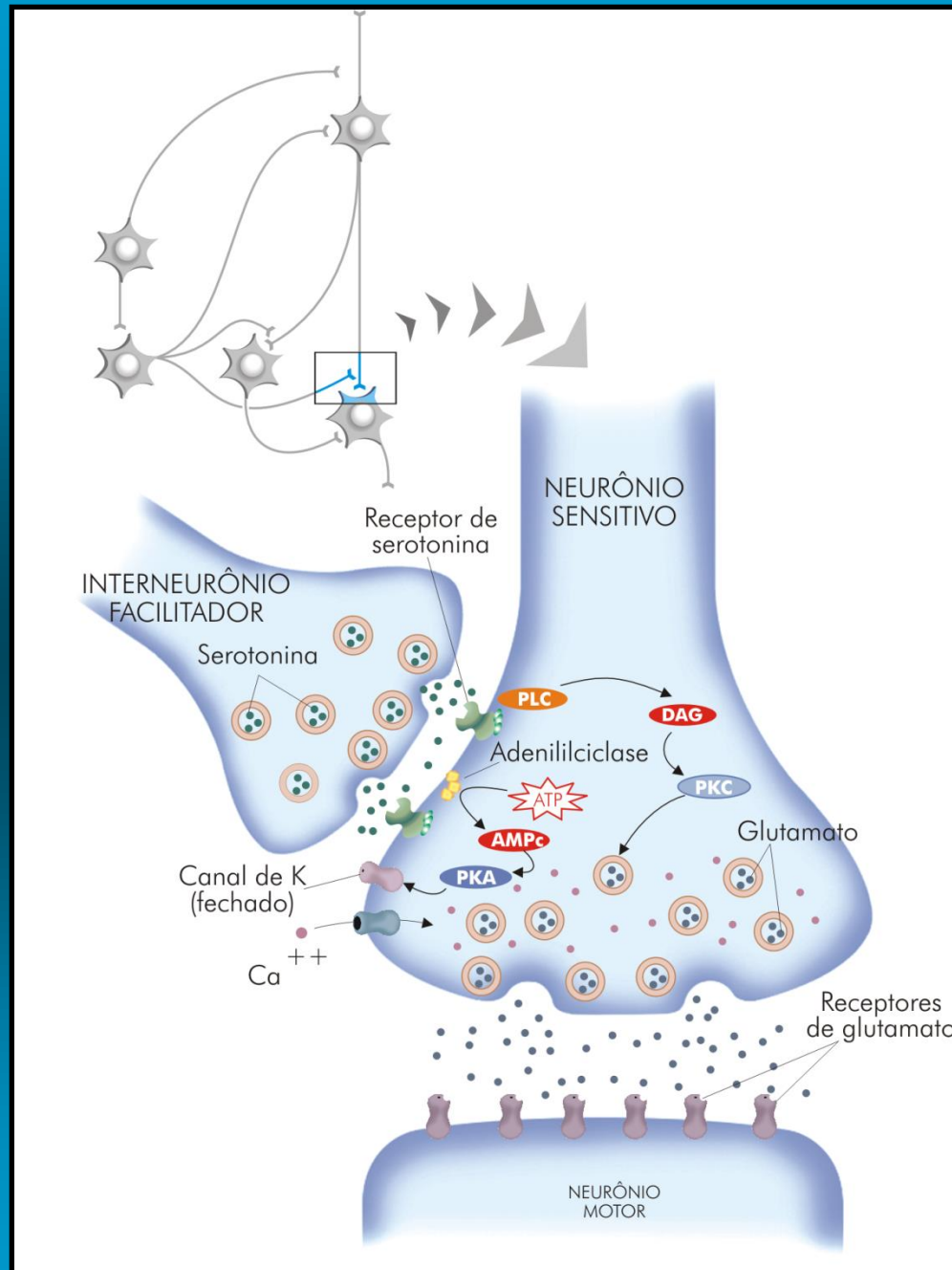
5-HT1A e 5-HT2

Plasticidade sináptica

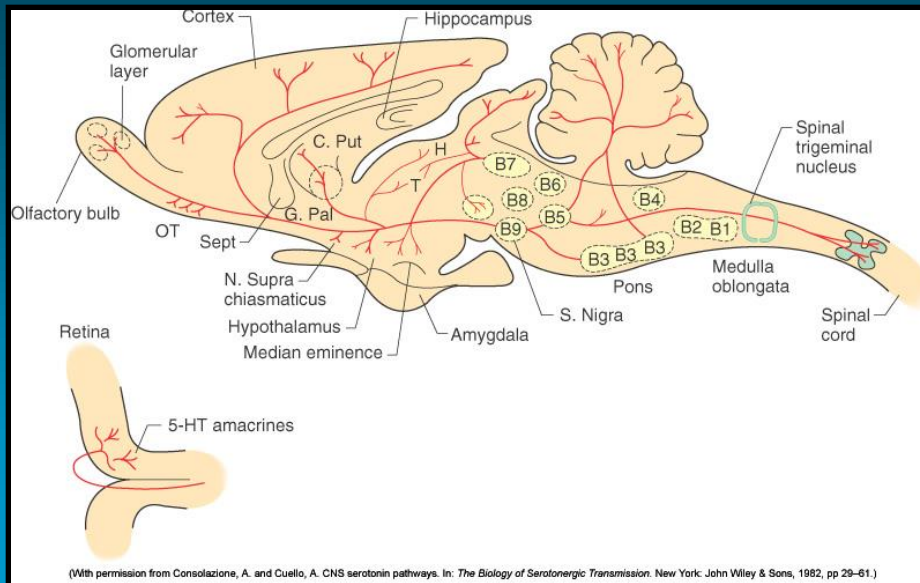
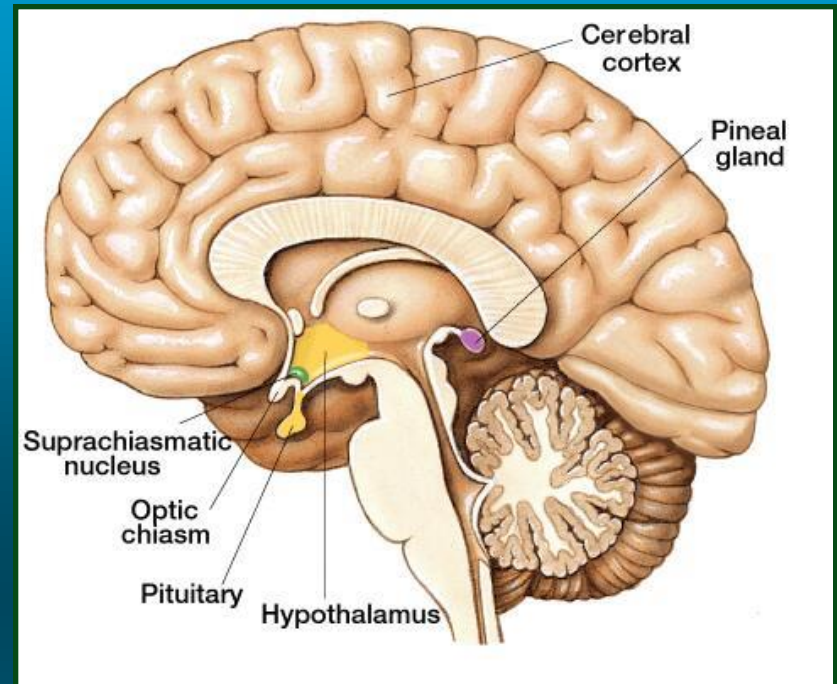
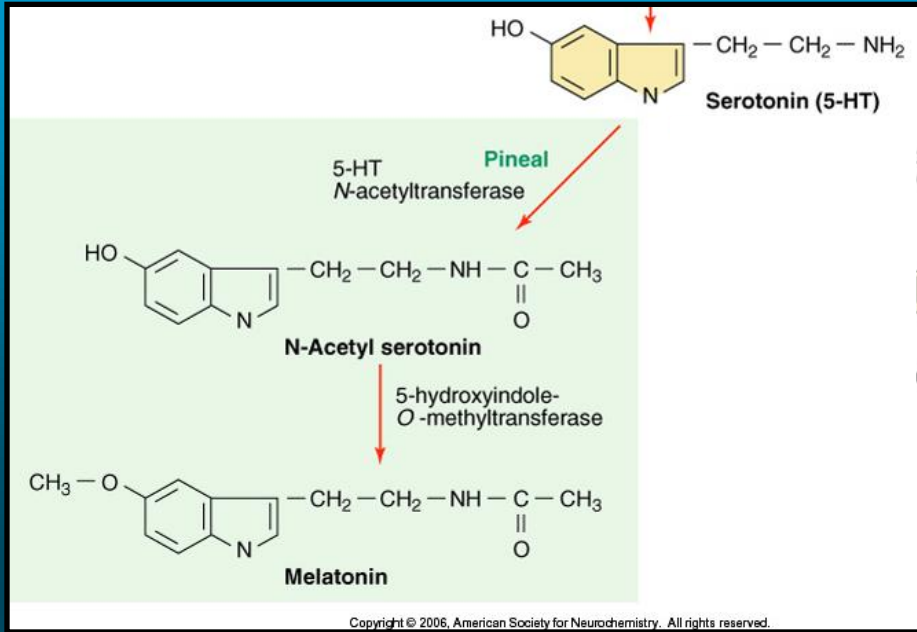


Sensibilização

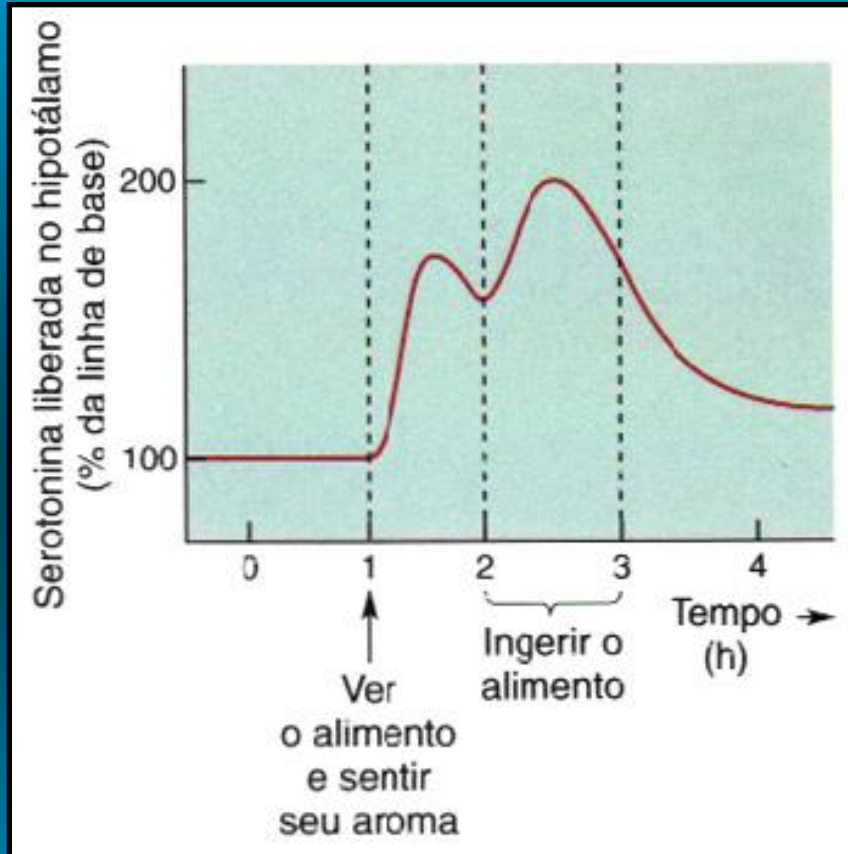
Mecanismos Moleculares da Sensibilização



Serotonina e Ritmicidade Circadiana



Serotonina e Comportamento Alimentar



5-HT1B e 5-HT2C

Serotonina e Transtornos do humor

