Catecolaminas

Aspectos gerais

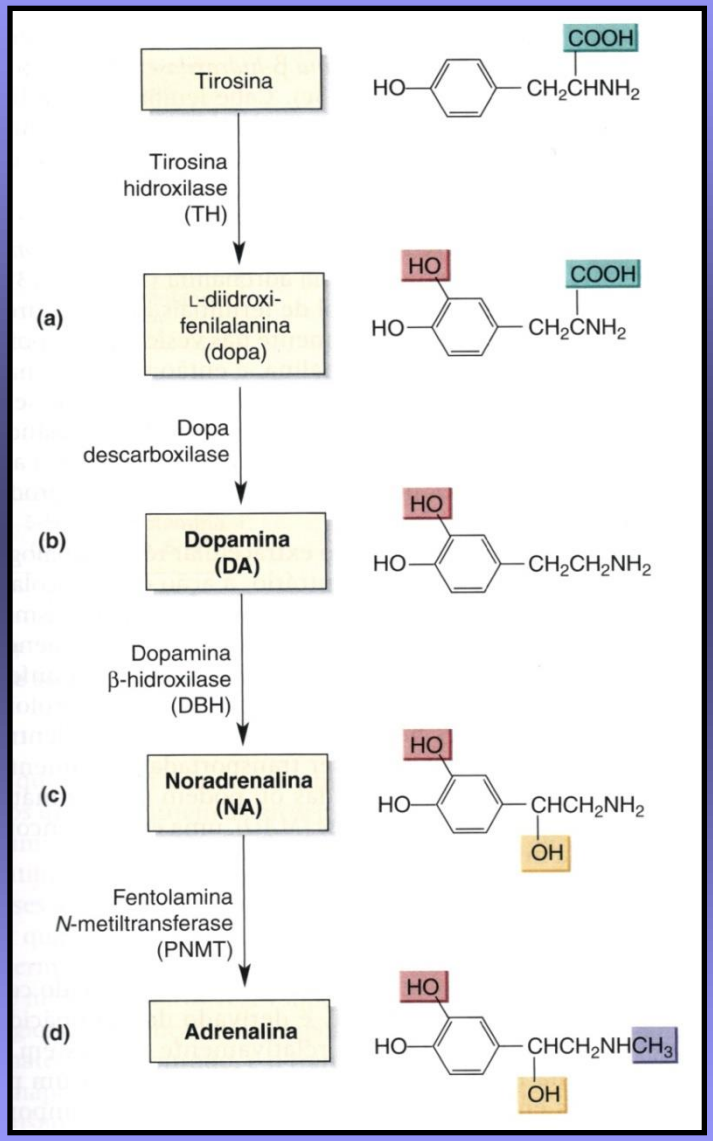
- Rins
- Sistema Nervoso Autônomo
- Sistema Nervoso Central

Catecolaminas

- ✓ Dopamina
- ✓ Noradrenalina
- ✓ Adrenalina

Via de Síntese

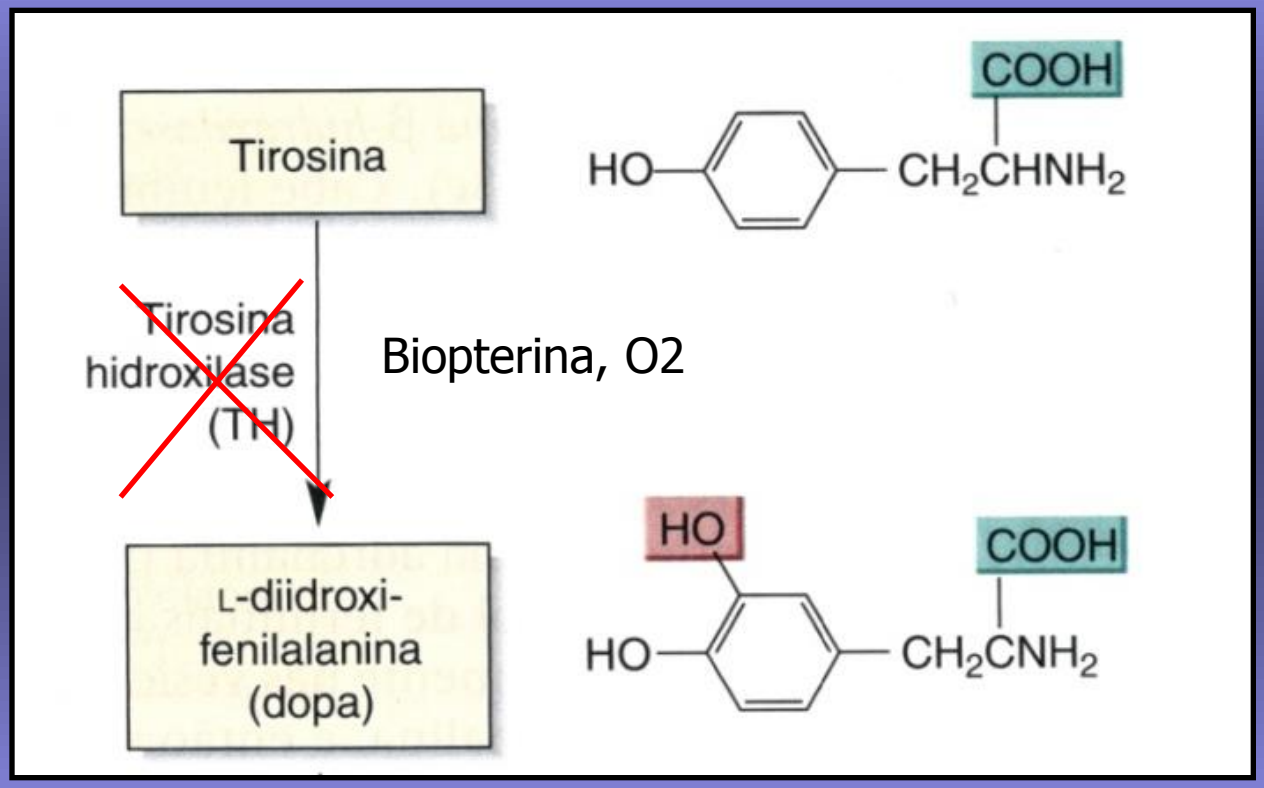
Catecolaminas



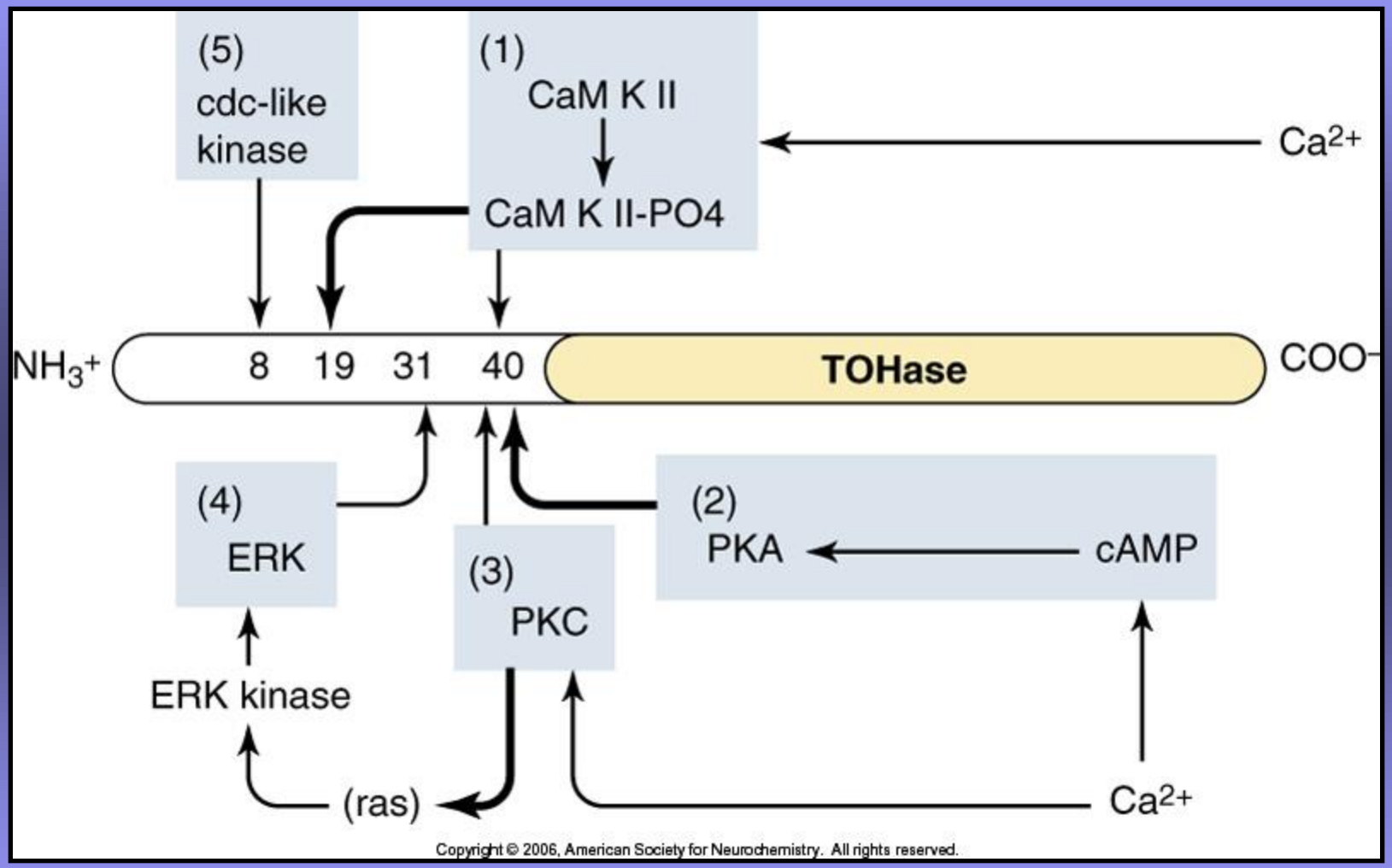
Via de Síntese

Tirosina Hidroxilase

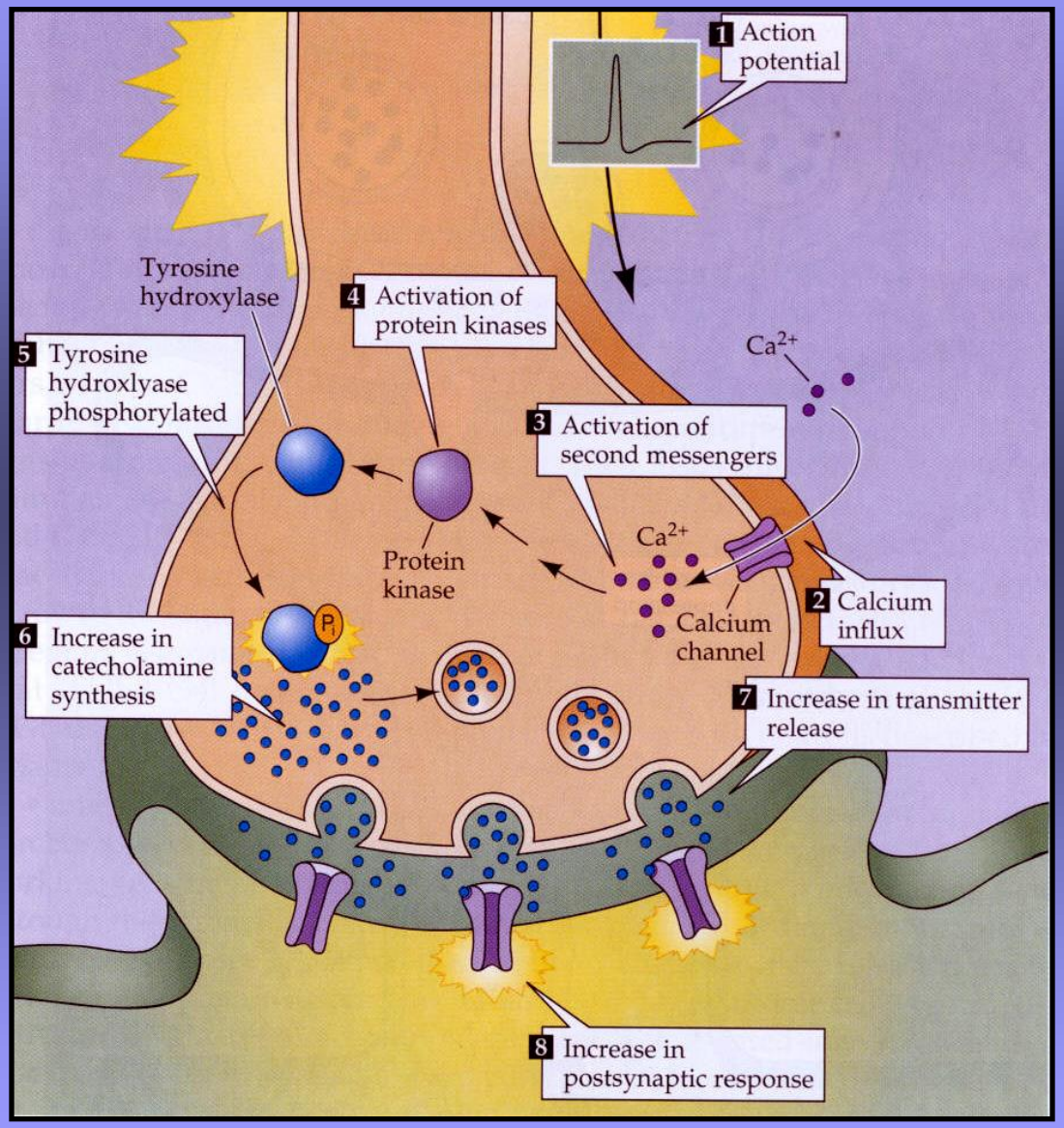
AMPT



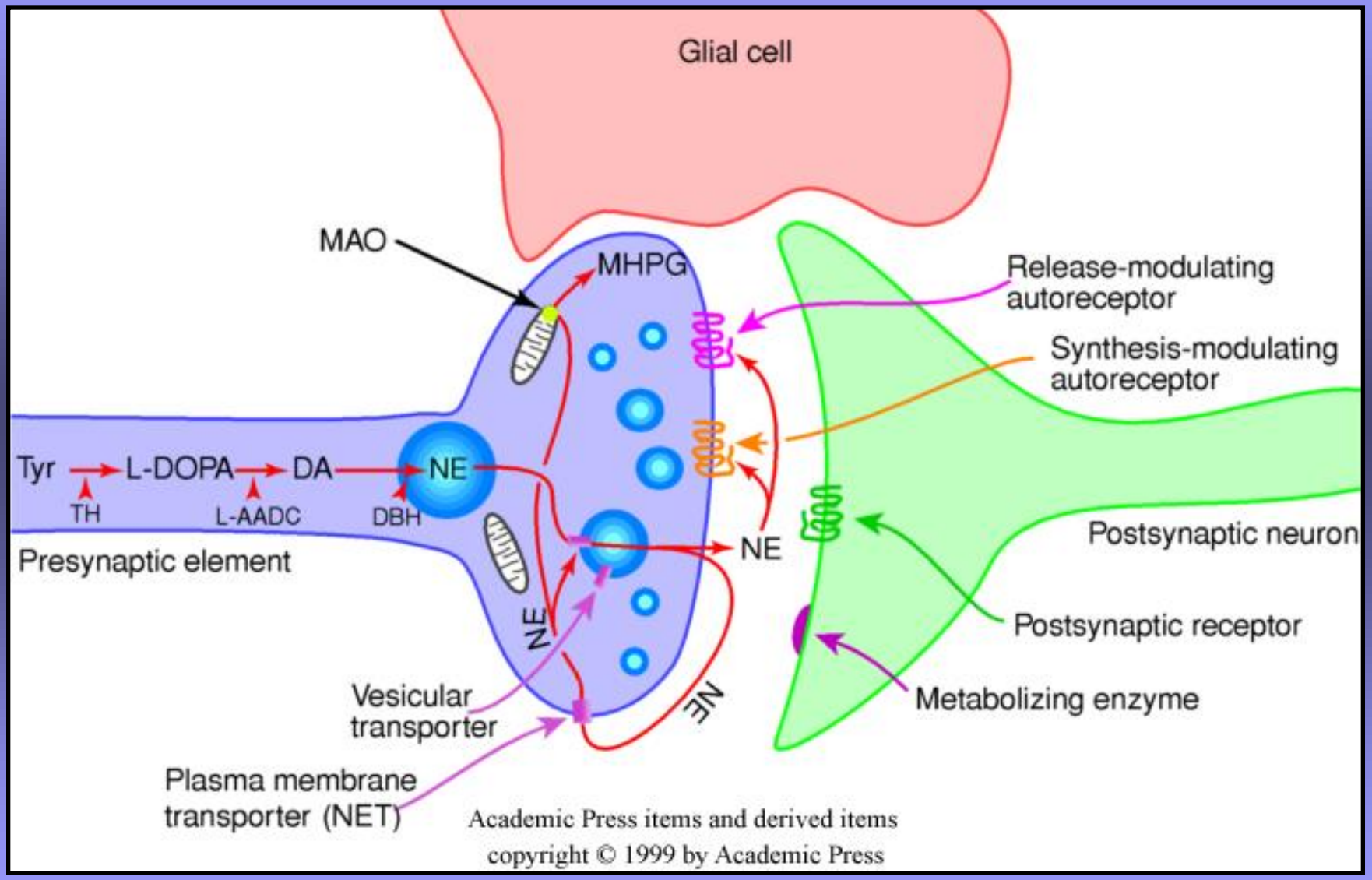
Tirosina Hidroxilase



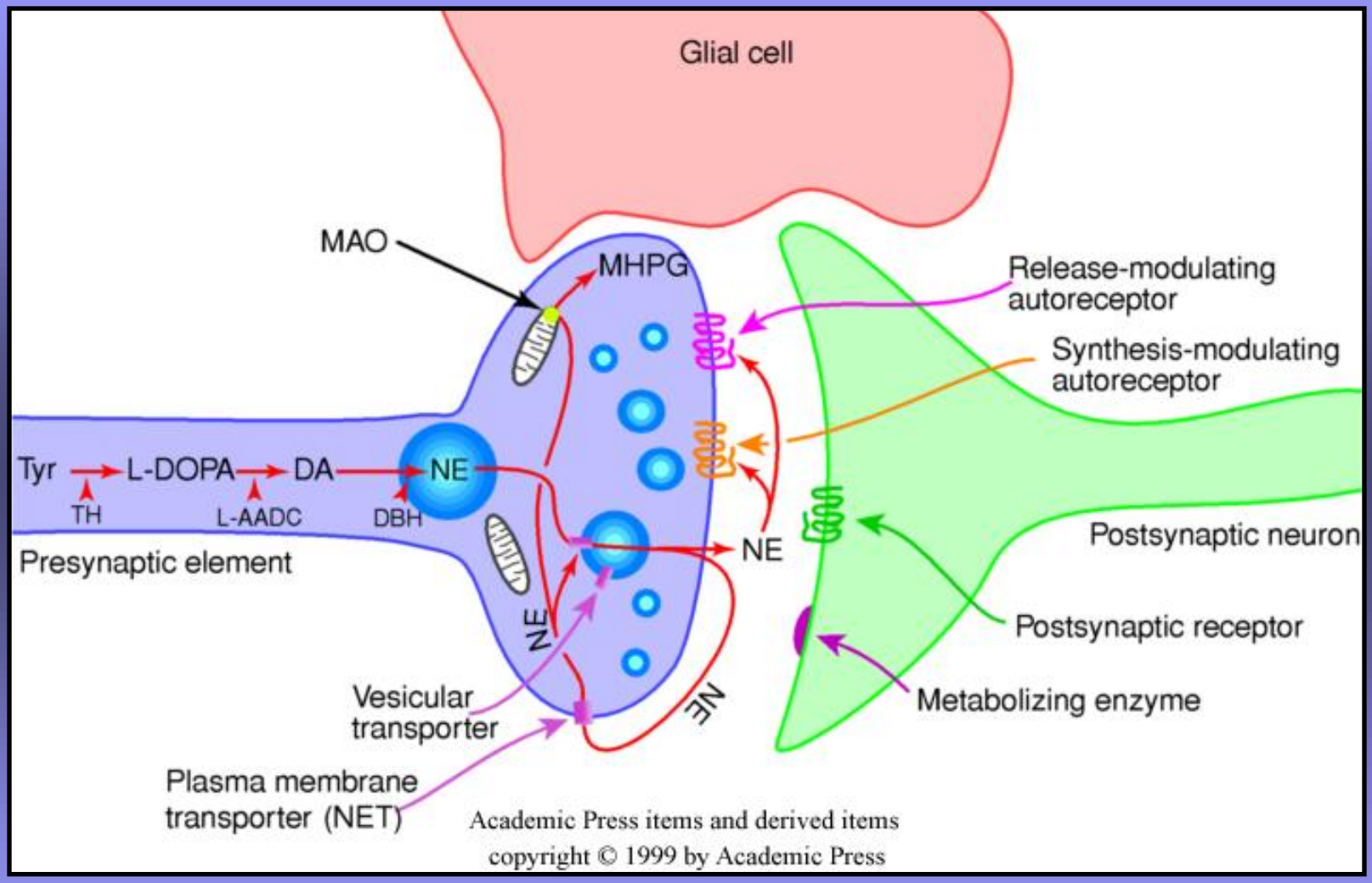
Tirosina Hidroxilase



Via de Síntese

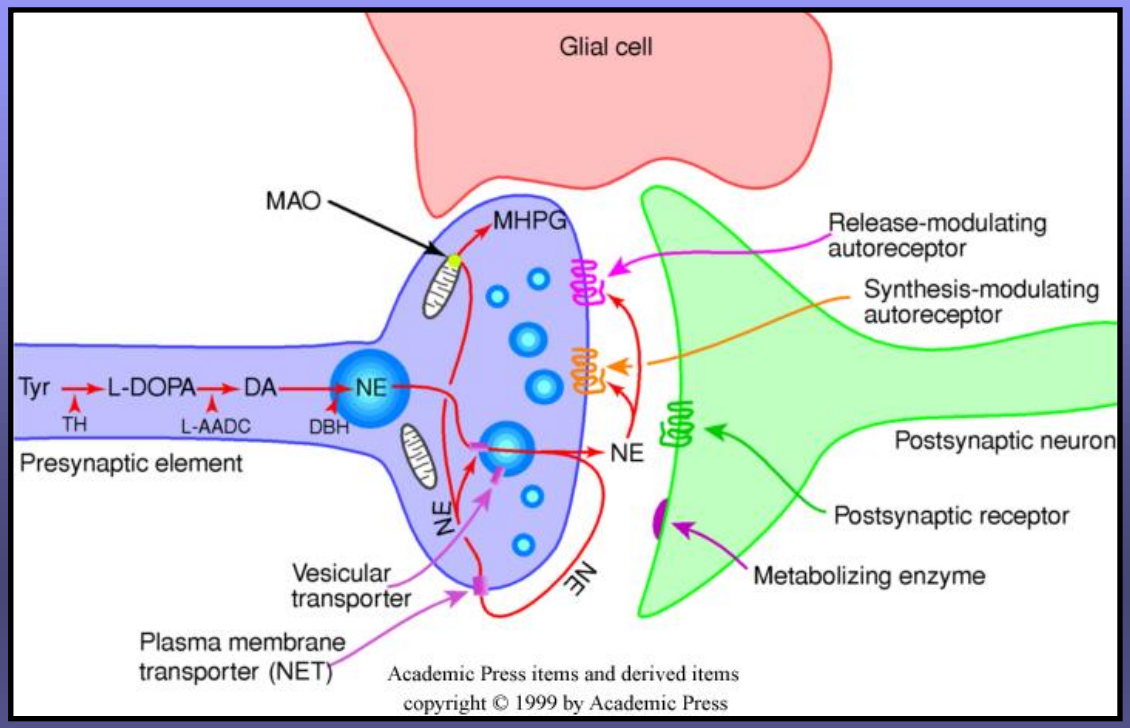


Transportadores vesiculares de aminas (VMAT2)

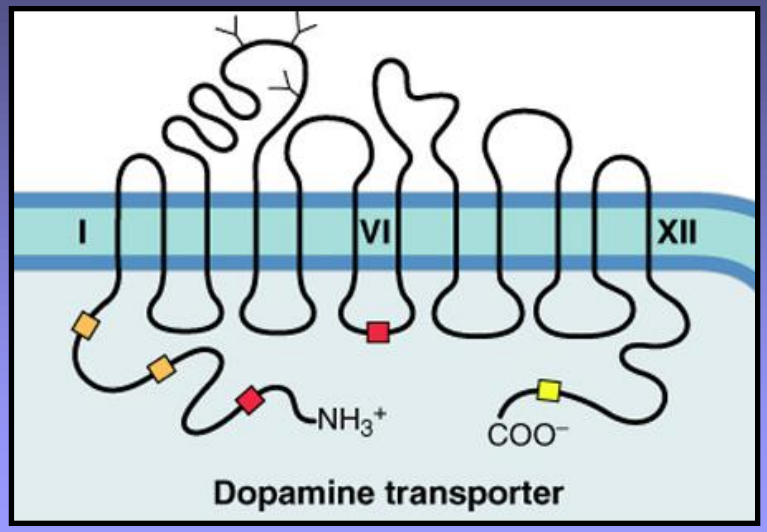


Reserpina

Transportadores de aminas (NET e DAT)



Ouabaína
Veratridina



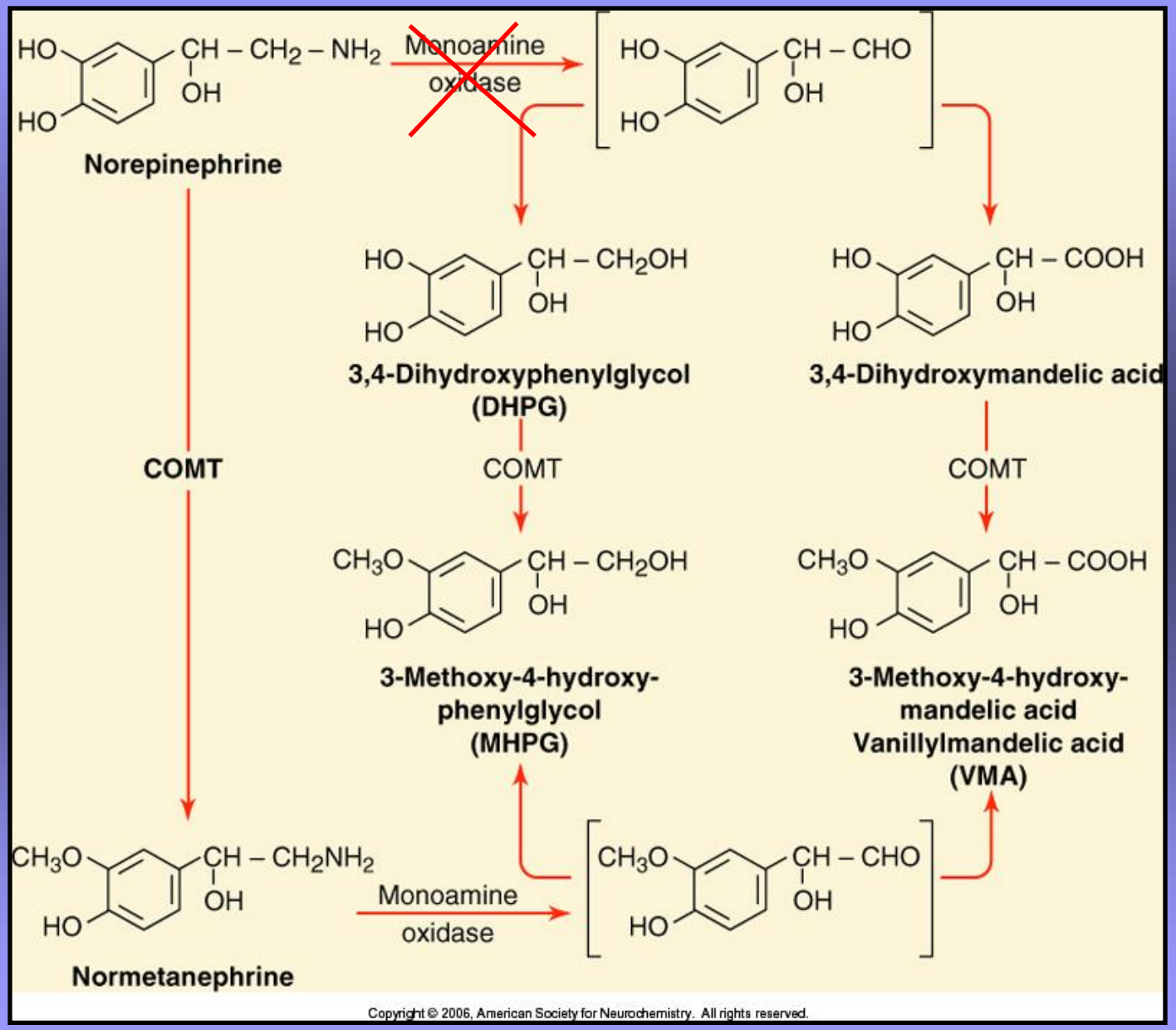
Sistema catecolaminérgico

TABLE 12-2 Properties of amine transporters

	NET	DAT	VMAT-2
Mechanism	NaCl-dependent	NaCl-dependent	H^+-dependent
Transmembrane segments	12	12	12
Amino acids	617	620	742
Chromosome	16	5	10
Blockers	Nisoxetine, desipramine	GBR12909, RTI-121	Reserpine, tetrabenazine

Via de Degradação

Clorgilina
Deprenil



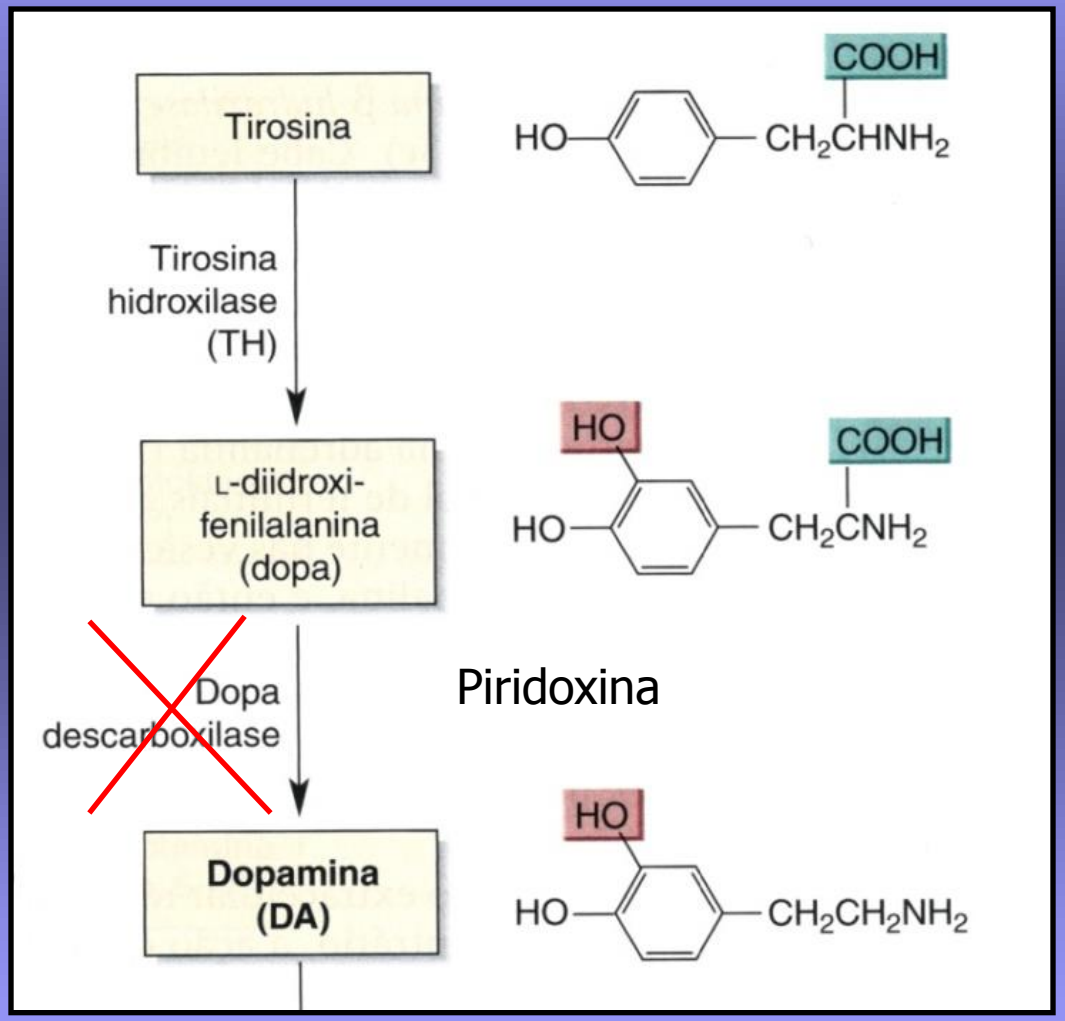
Sistema catecolaminérgico

TABLE 12-1 Studies with knockout mice

Tyrosine hydroxylase	Not viable
Dopamine beta hydroxylase	Hypersensitive to amphetamine
MAO-A	Aggressive behavior
COMT	Complex alterations in anxiety and aggression
VMAT2	Not viable
DAT	Growth retardation and hyperactivity
NET	Enhanced opiate-mediated analgesia and responses to psychostimulants

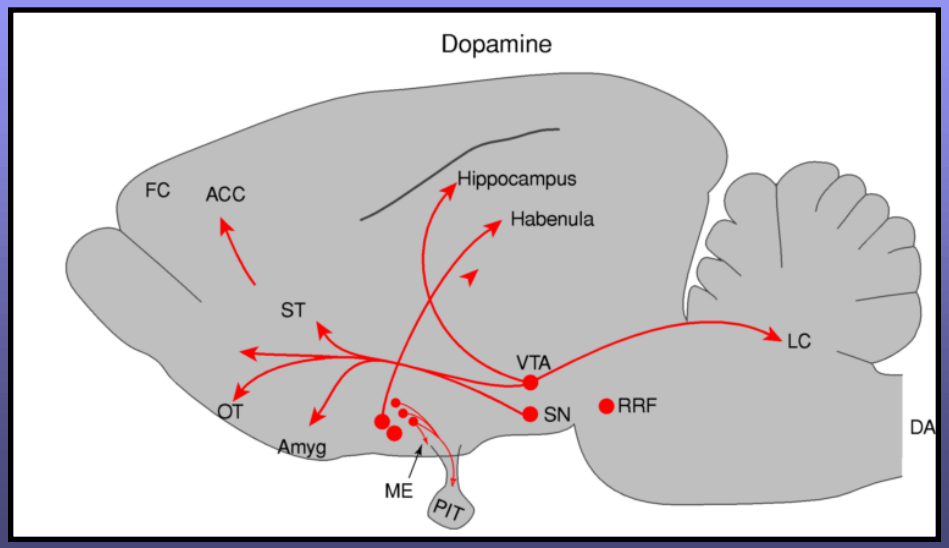
Dopamina

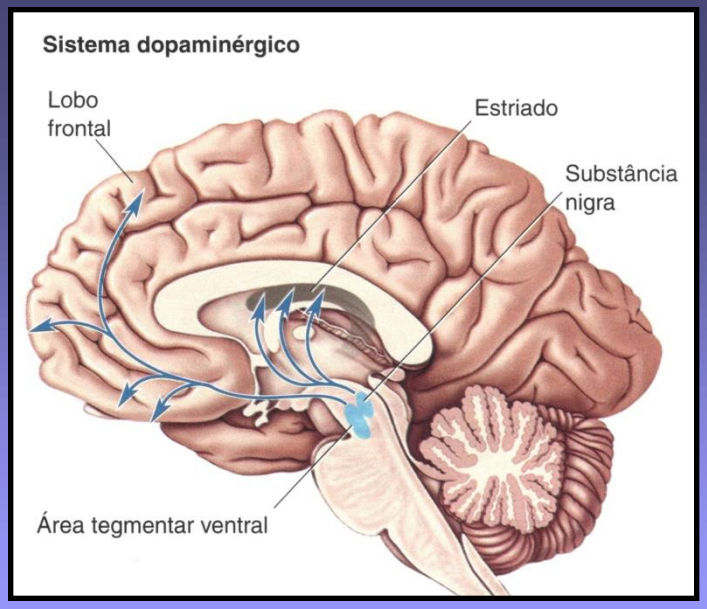
Dopamina descarboxilase



α-metildopa

Distribuição



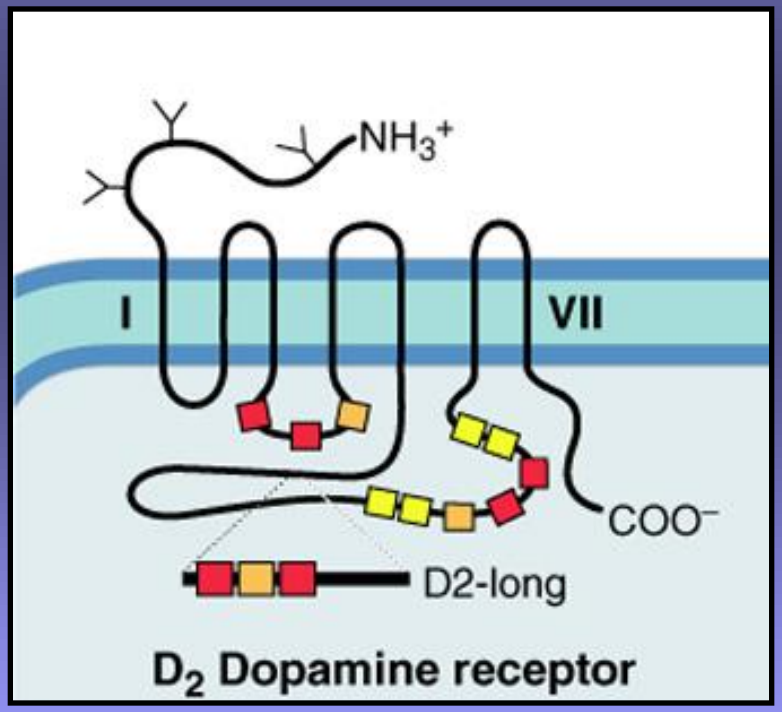


Receptores de dopamina

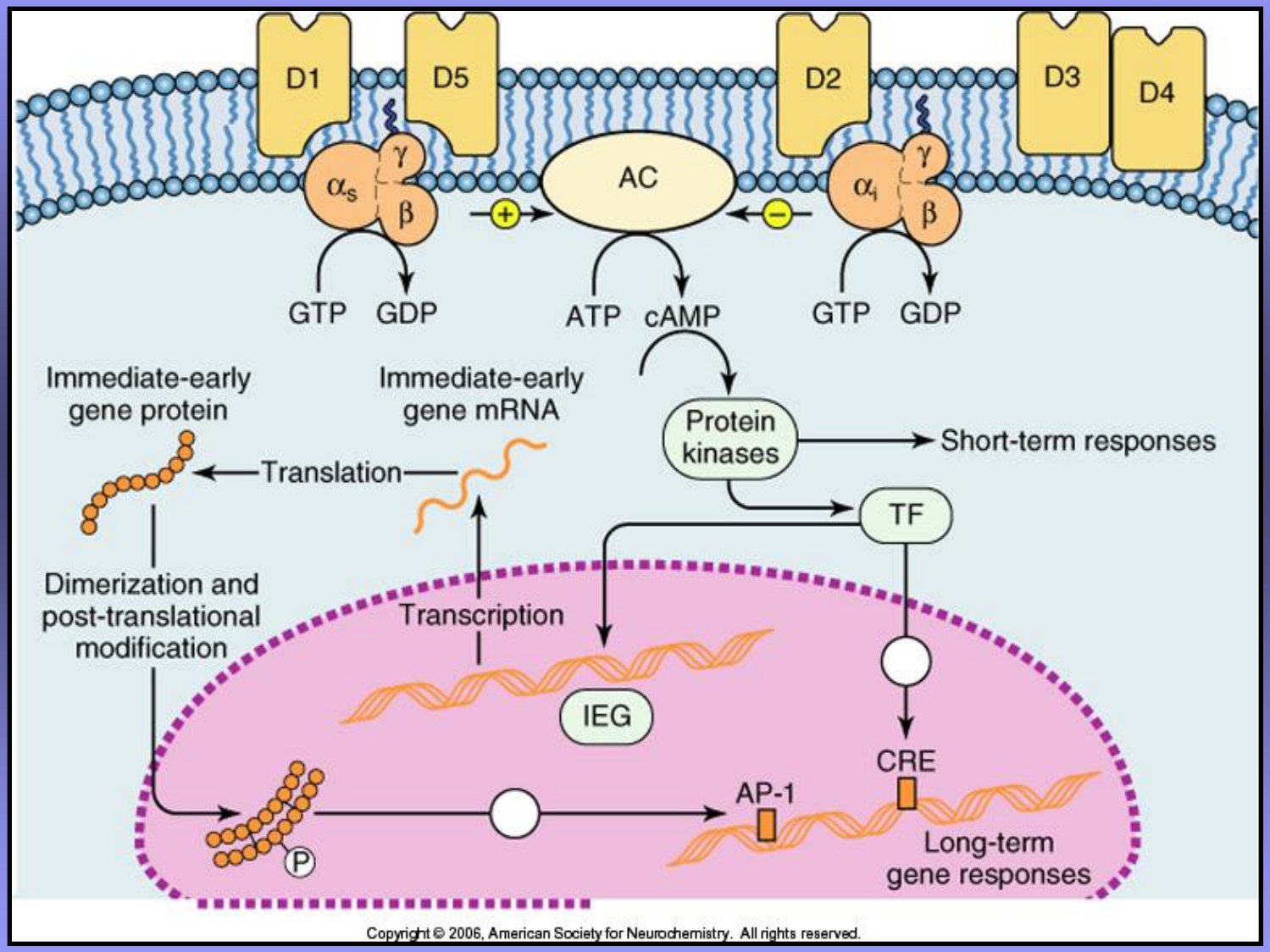
5 subtipos

D_1- like (D_1 e D_5) - G_s

D_2 – like (D_2, D_3 e D_4) - G_i



Receptores de dopamina

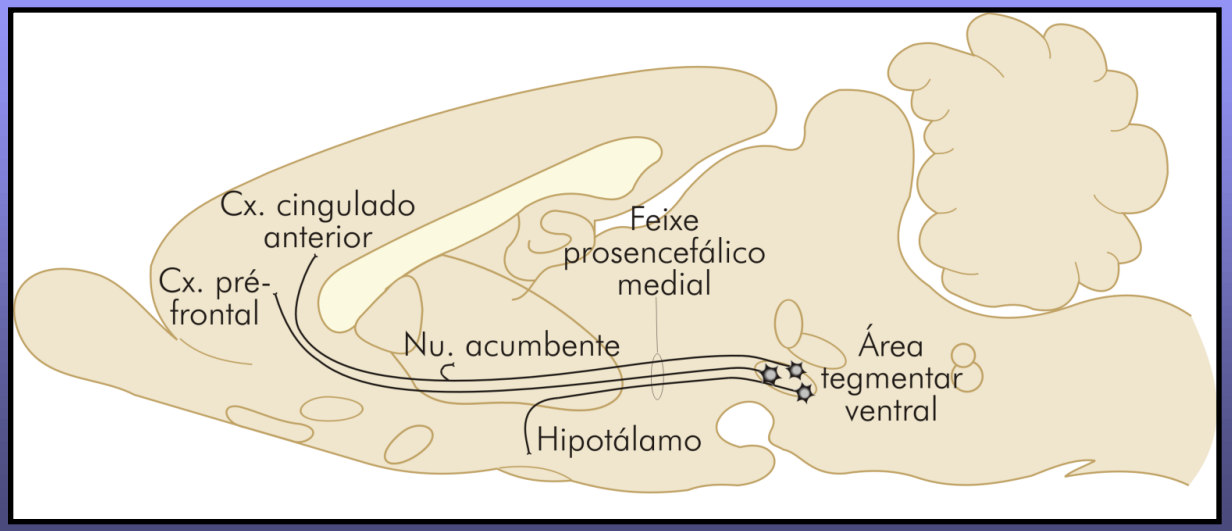


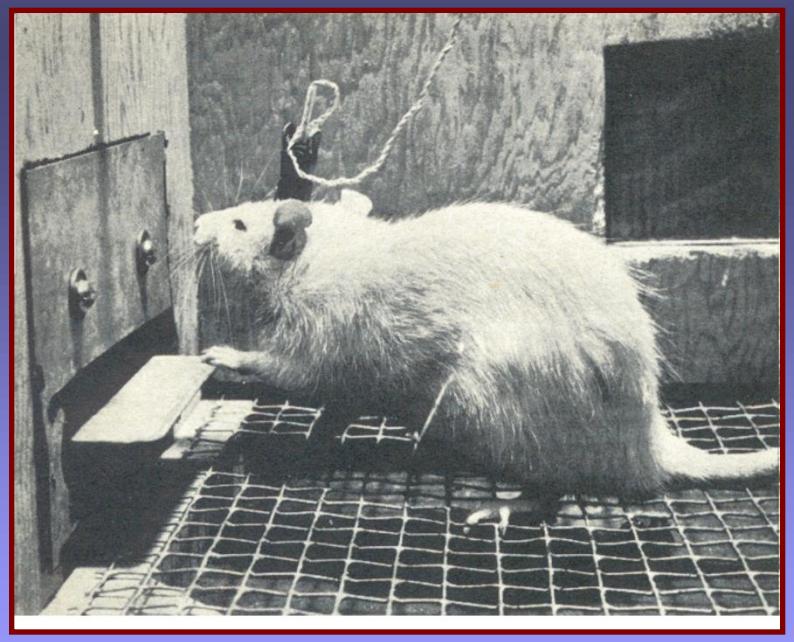
Receptores de dopamina

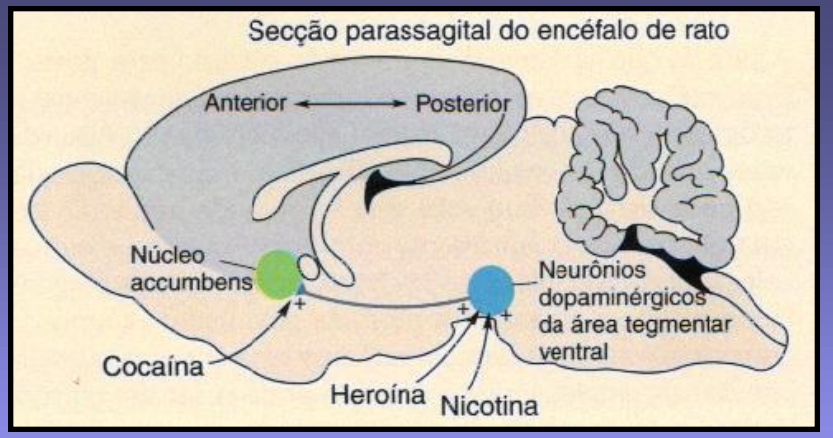
TABLE 12-3 Properties of human dopamine receptor subtypes

	D_1-like		D_2-like		
	D_1	D_5	D_2	D_3	D_4
Amino acids	446	477	415/444	400	387
Chromosome	5	4	11	3	11
Effector pathways	↑cAMP	↑cAMP	↓cAMP ↑K^+ channel ↓ Ca^{2+}channel	↓cAMP ↑K^+ channel ↓Ca^{2+} channel	↓cAMP ↑K^+ channel ↓Ca^{2+} channel
Distribution	Caudate/putamen, nucleus accumbens, olfactory tubercle, cerebral cortex	Hippocampus, hypothalamus, cerebral cortex	Caudate/putamen, nucleus accumbens, midbrain	Olfactory tubercle, hypothalamus,	Frontal cortex, medulla, midbrain, nucleus accumbens

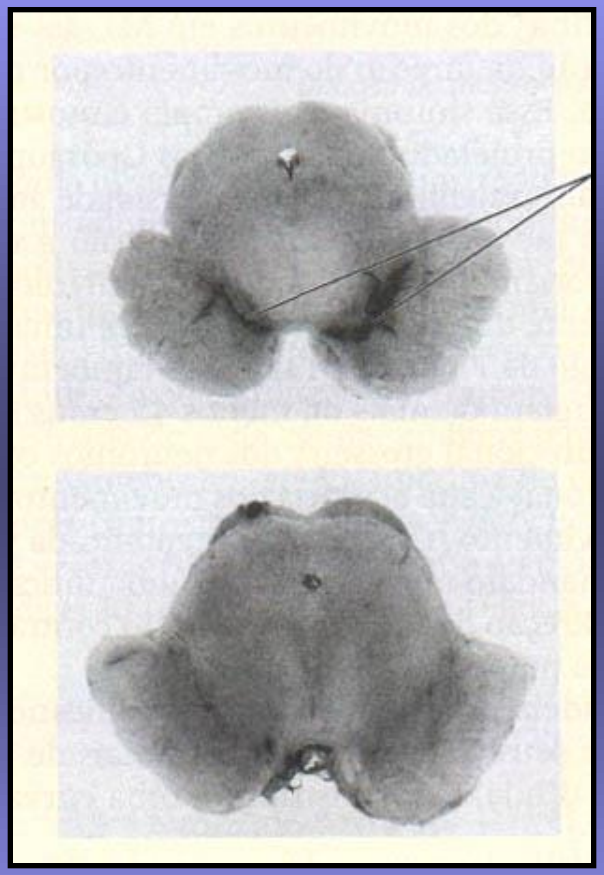
Dopamina e o Sistema córtico-mesolímbico

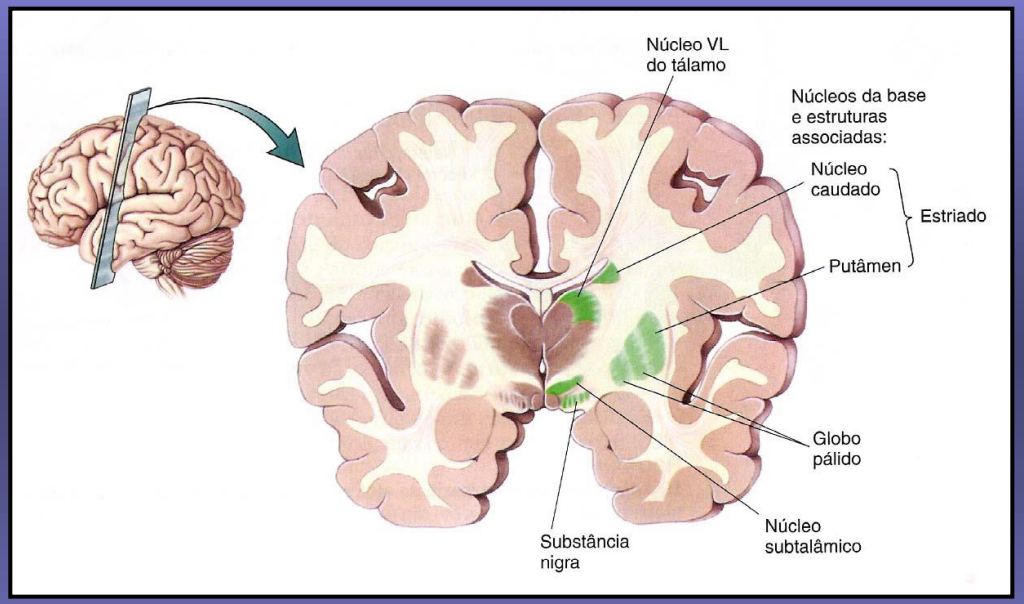




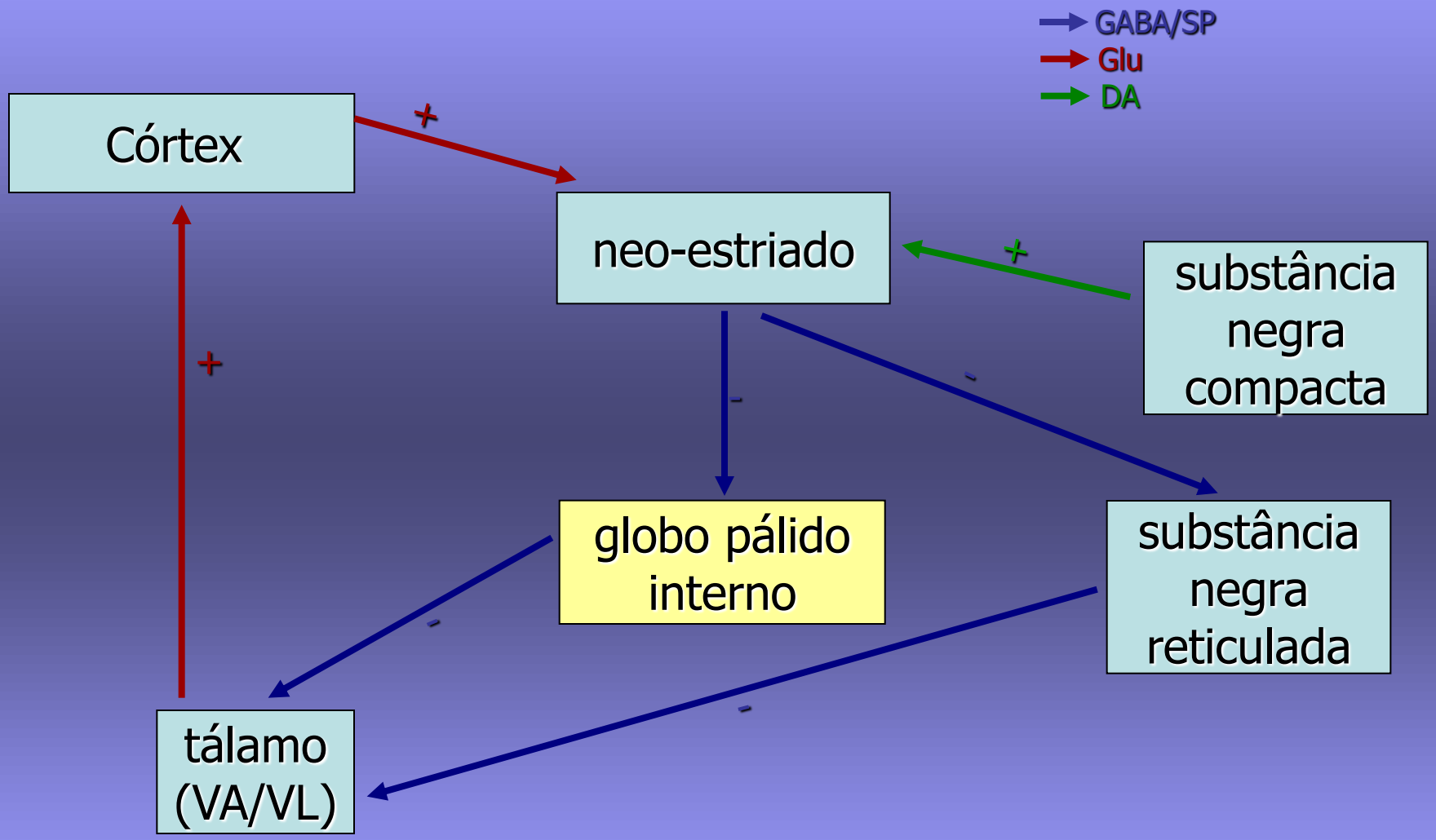


Dopamina e a doença de Parkinson

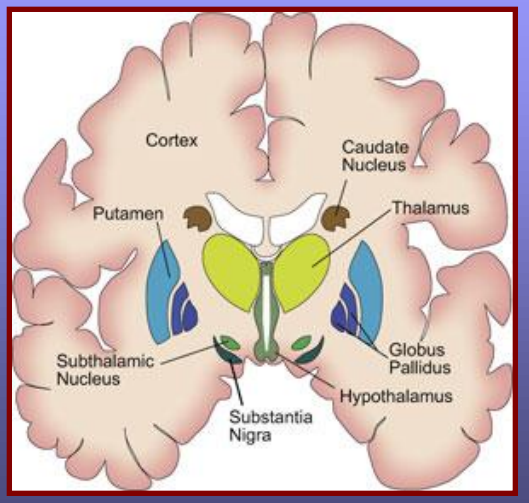


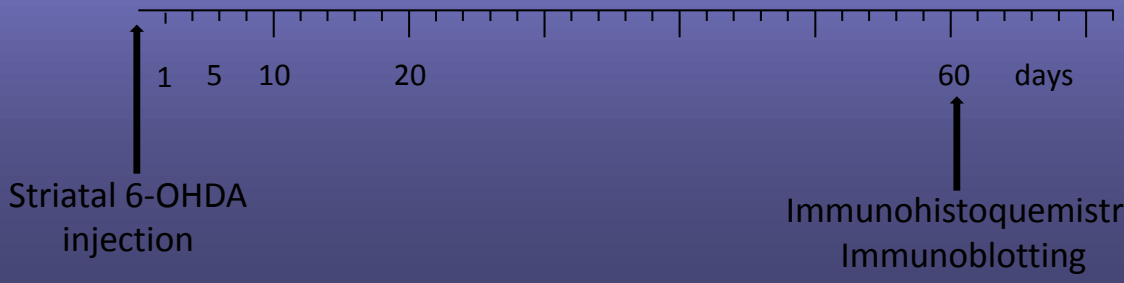


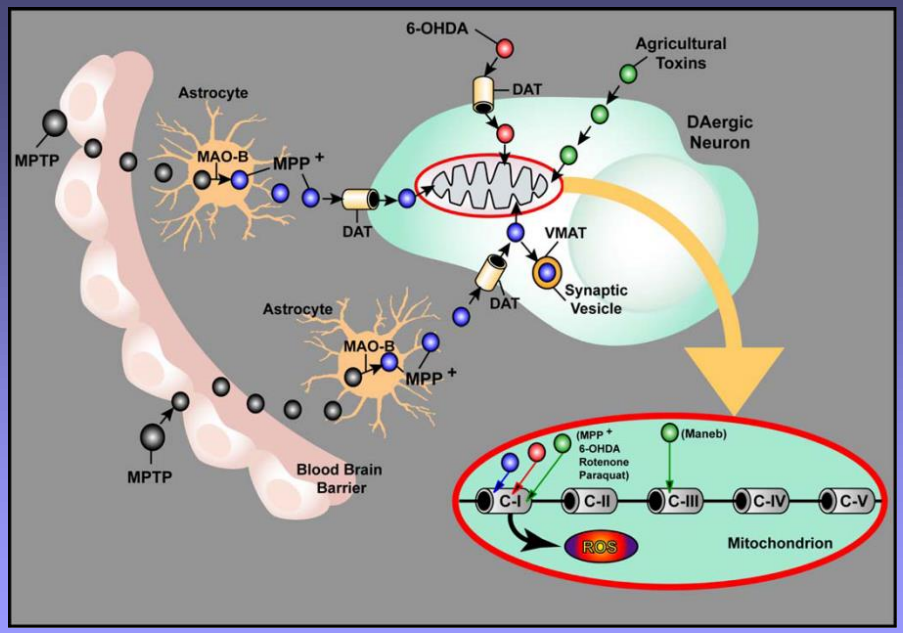
Dopamina e a doença de Parkinson



Dopamina e a doença de Parkinson



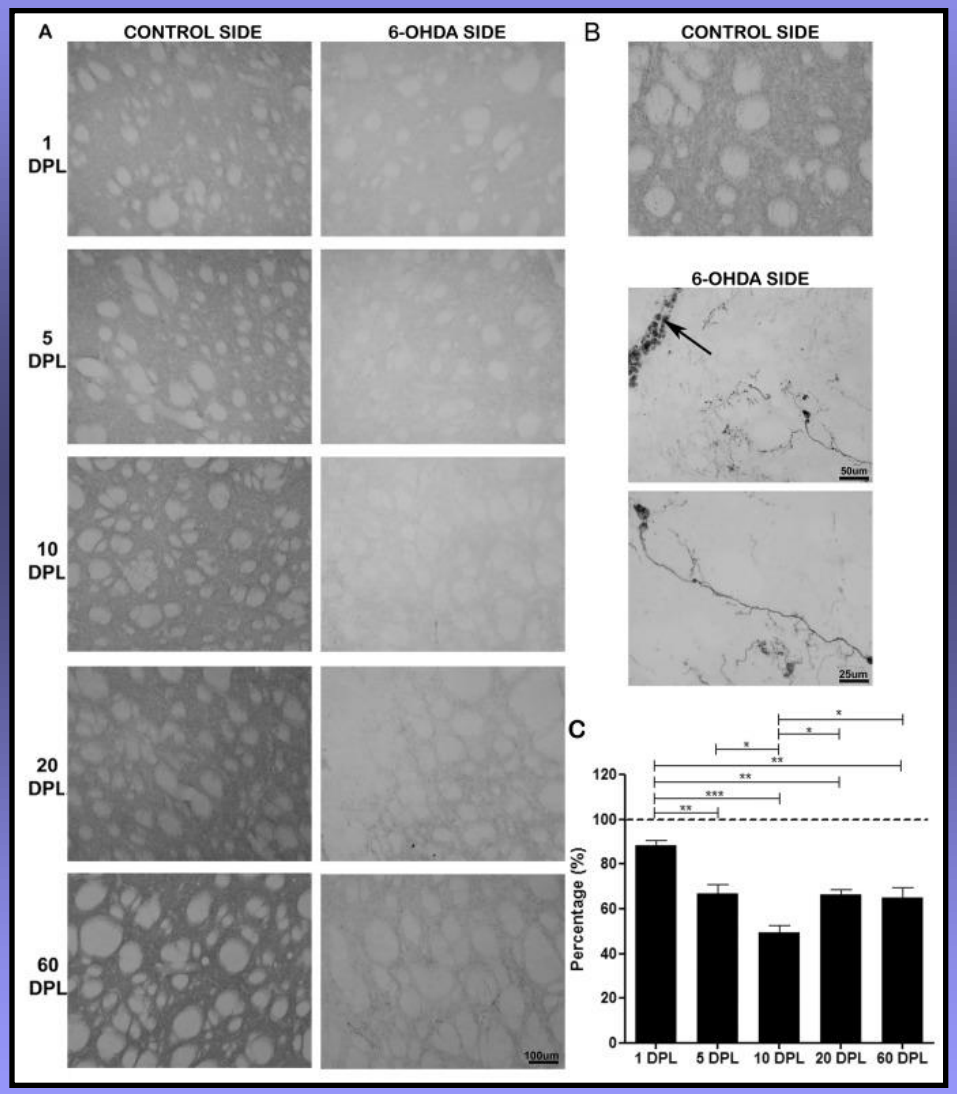


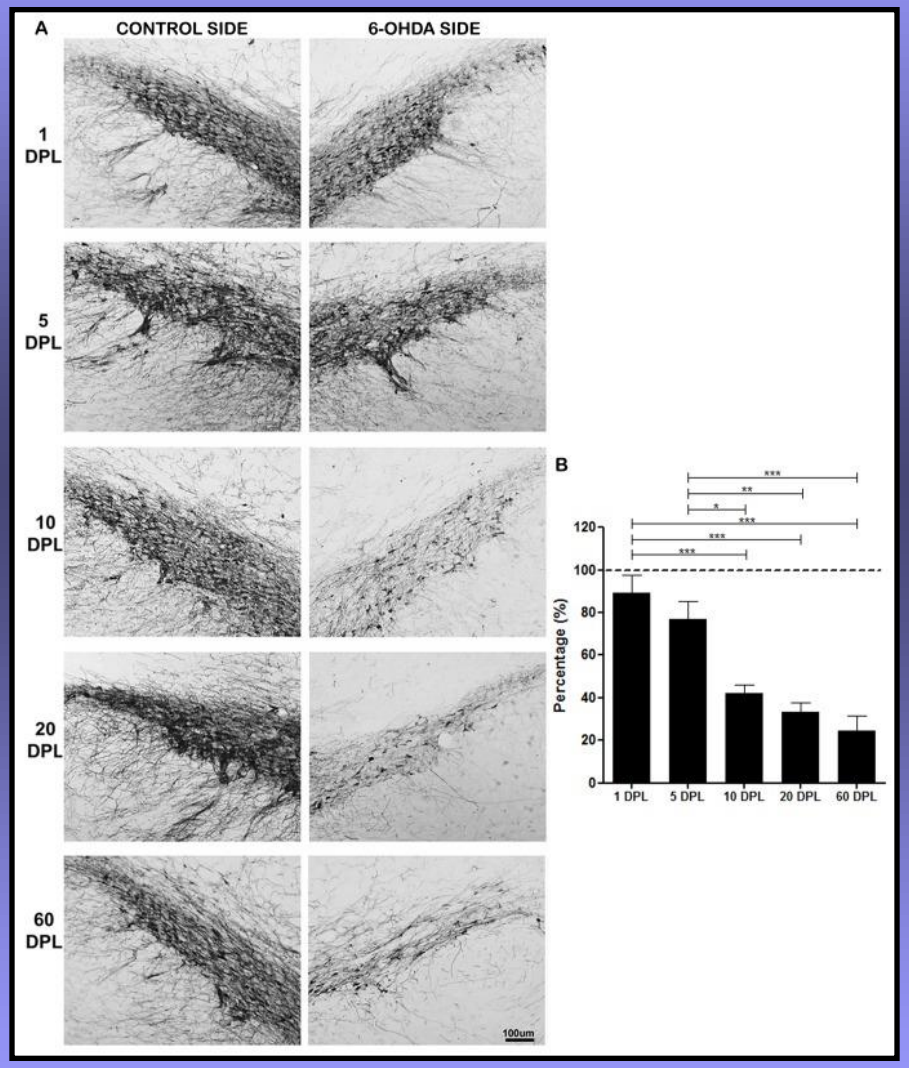


Shober, 2004; Torrão et *al.*, 2012

Dopamina e a doença de Parkinson

6-OHDA PRODUCED A GRADUAL REDUCTION OF TH IN STRIATUM AND SNpc

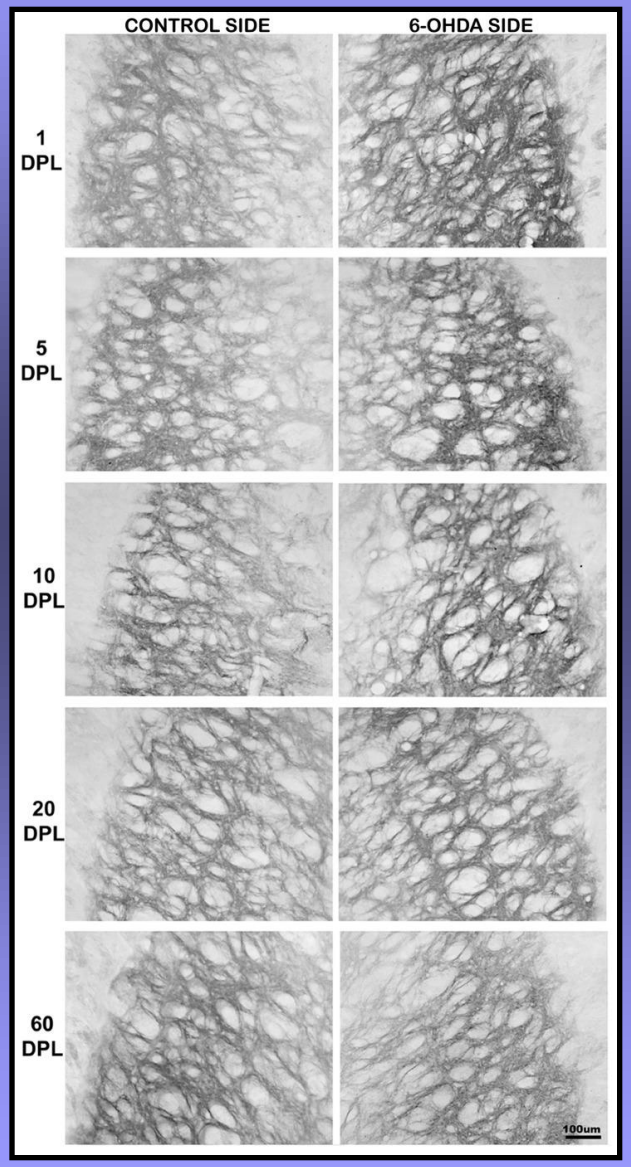


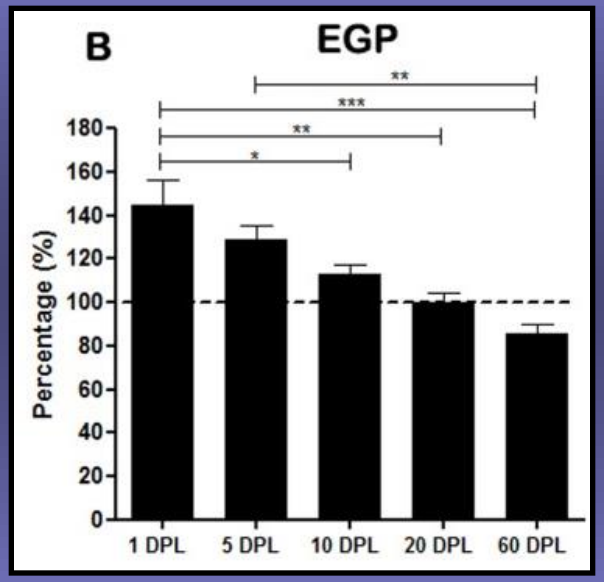


Chaves-Kirsten *et al.*, 2013

Dopamina e a doença de Parkinson

6-OHDA PRODUCED BIPHASIC CHANGES OF CB1 IN GLOBUS PALLIDUS

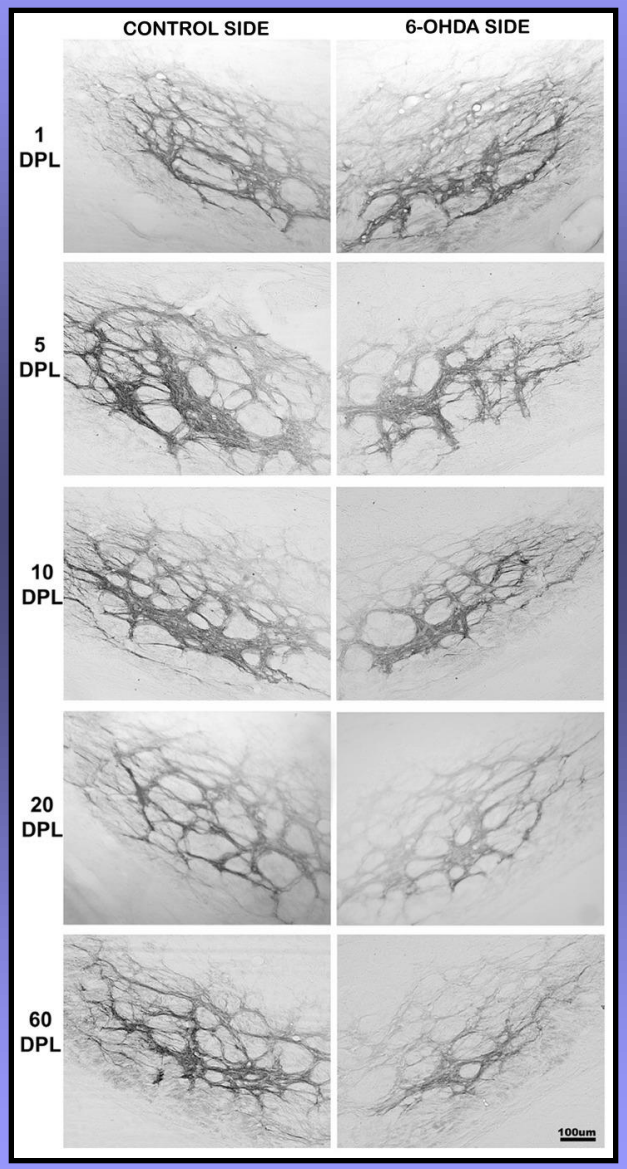


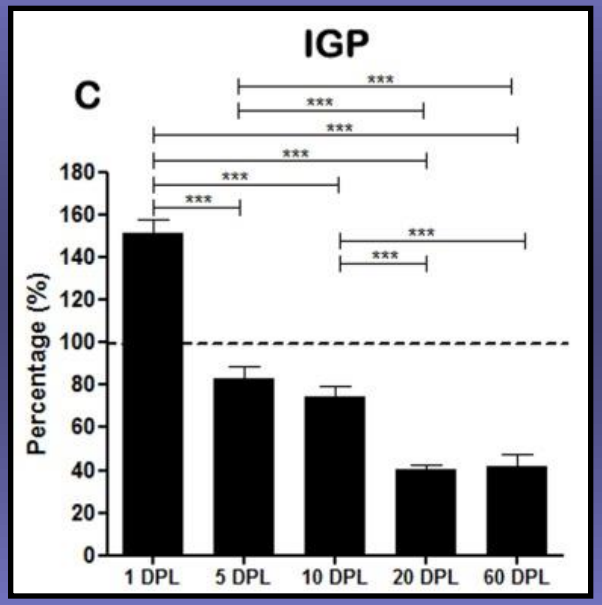


Chaves-Kirsten *et al.*, 2013

Dopamina e a doença de Parkinson

6-OHDA PRODUCED BIPHASIC CHANGES OF CB1 IN GLOBUS PALLIDUS

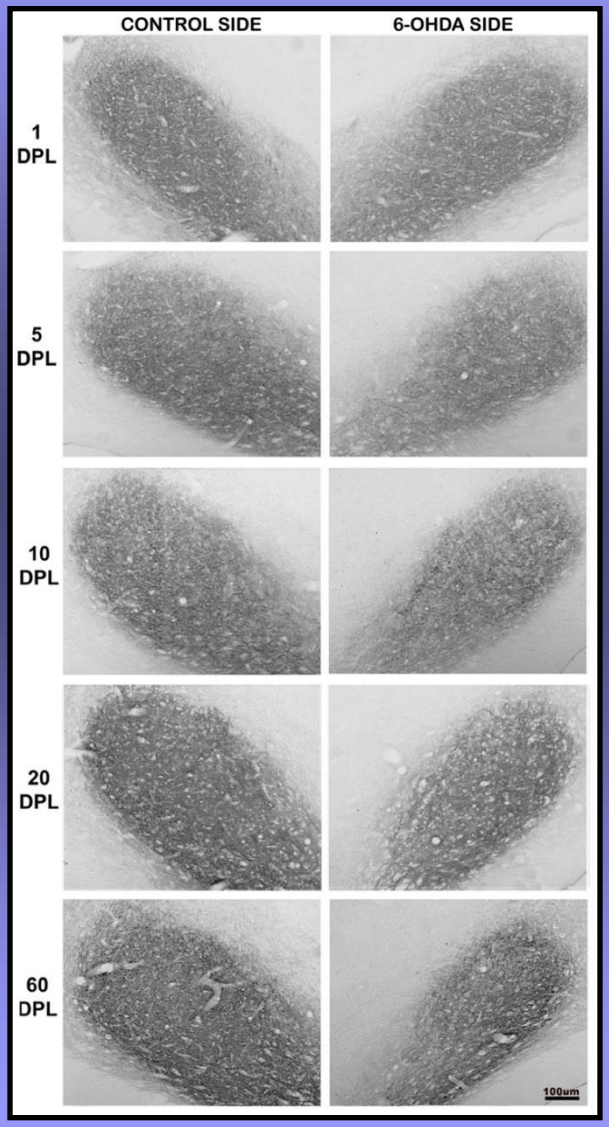


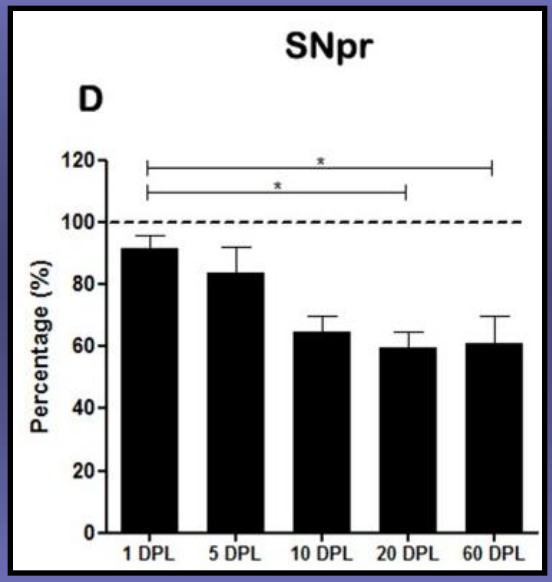


Chaves-Kirsten *et al.*, 2013

Dopamina e a doença de Parkinson

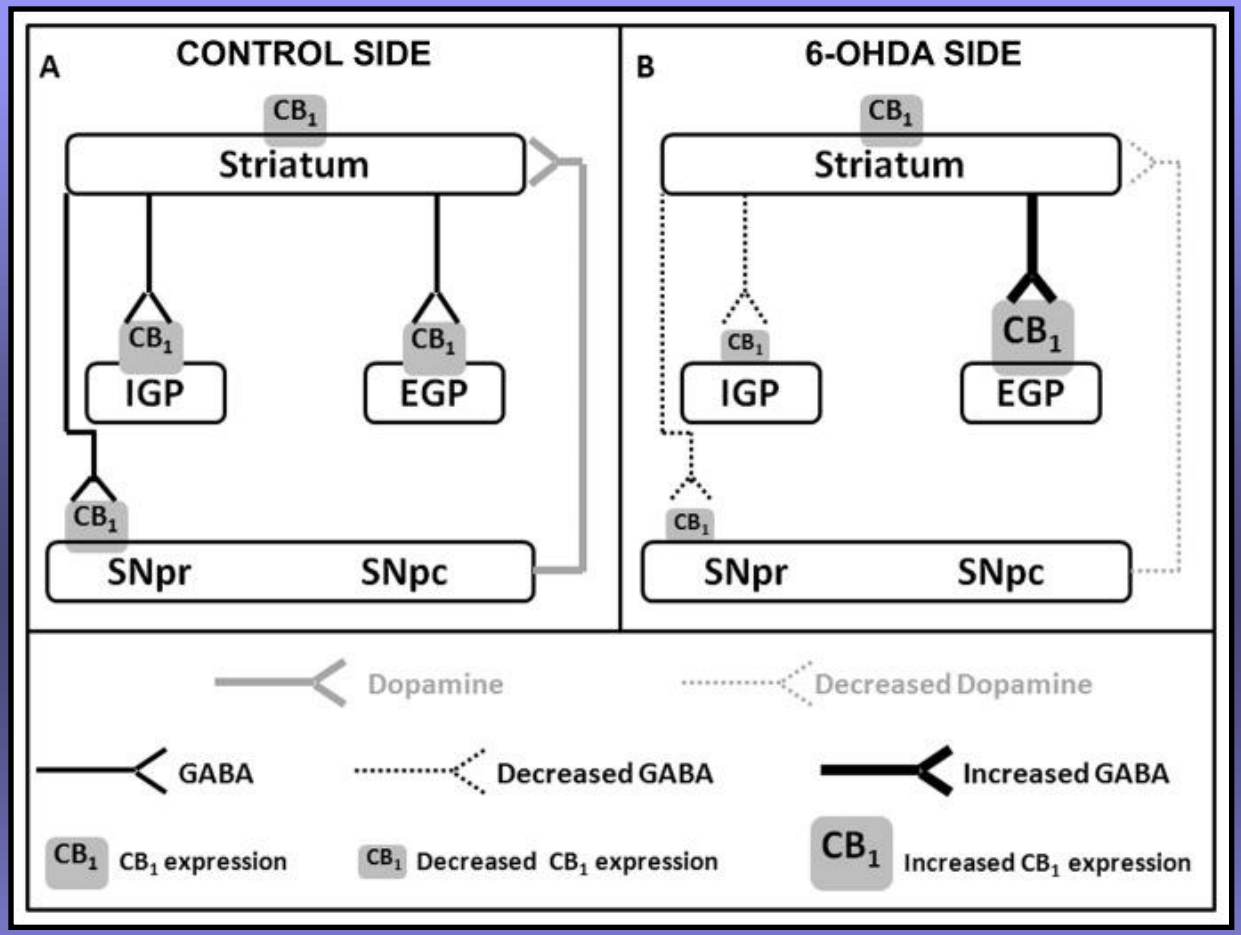
6-OHDA PRODUCED A GRADUAL REDUCTION OF CB1 IN SNpc





Chaves-Kirsten *et al.*, 2013

Dopamina e a doença de Parkinson



OPEN ACCESS Freely available online
PLOS ONE

Temporal Changes of CB1 Cannabinoid Receptor in the Basal Ganglia as a Possible Structure-Specific Plasticity Process in 6-OHDA Lesioned Rats

Gabriela P. Chaves-Kirsten[1*], Caio H. Y. Mazucanti[2], Caroline C. Real[3], Bruna M. Souza[1], Luiz R. G. Britto[3], Andréa S. Torrão[1]

Dopamina e Esquizofrenia

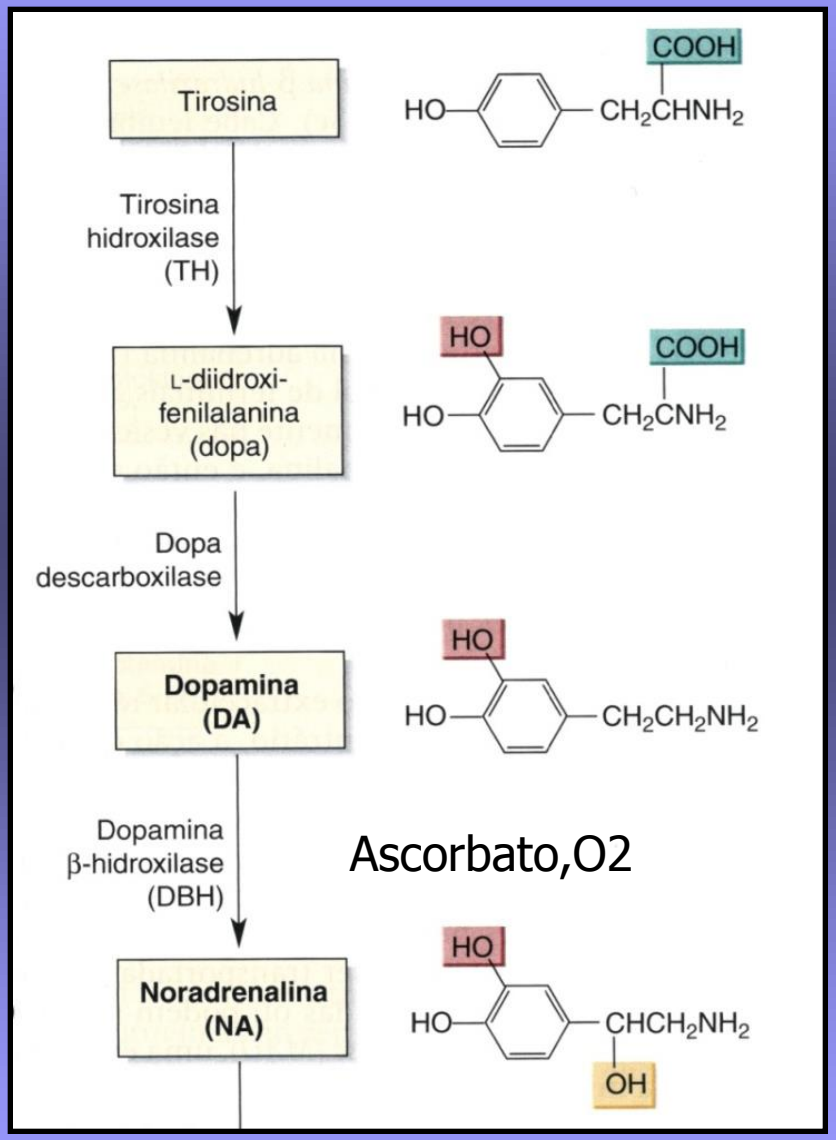
Hipótese dopaminérgica:

anfetamina ⬆DA

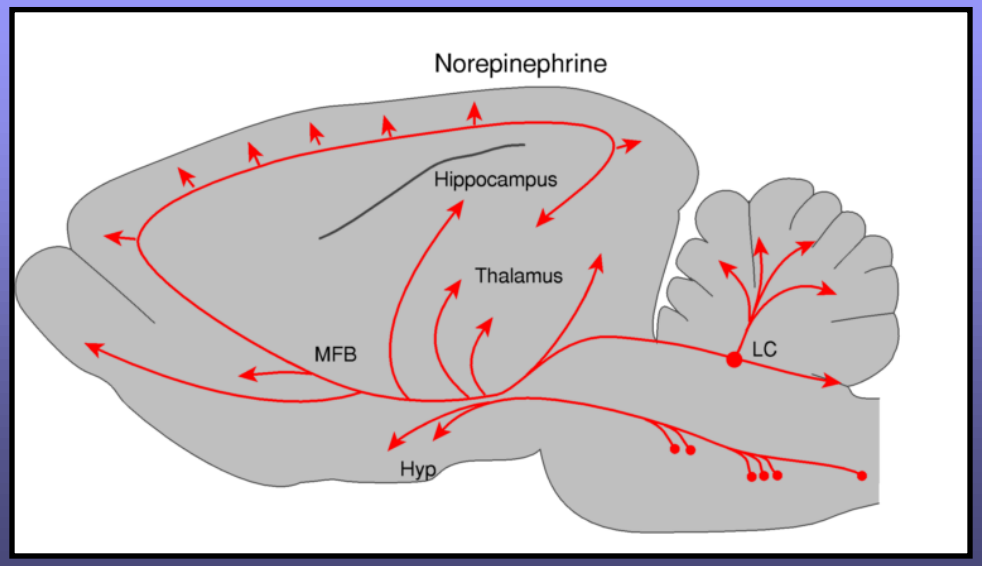
clorpromazina (antipsicótico)

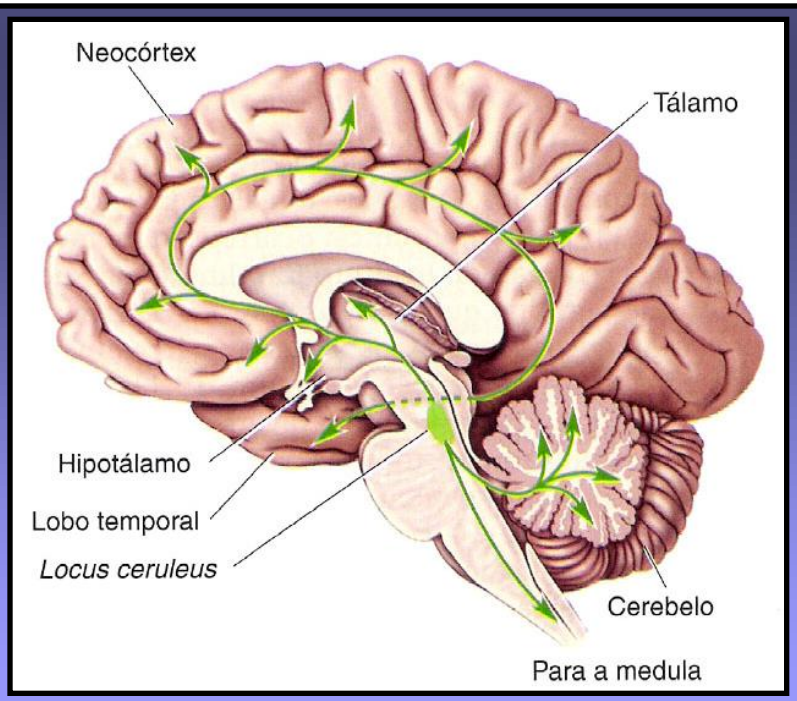
Via de Síntese

Dopamina β-hidroxilase



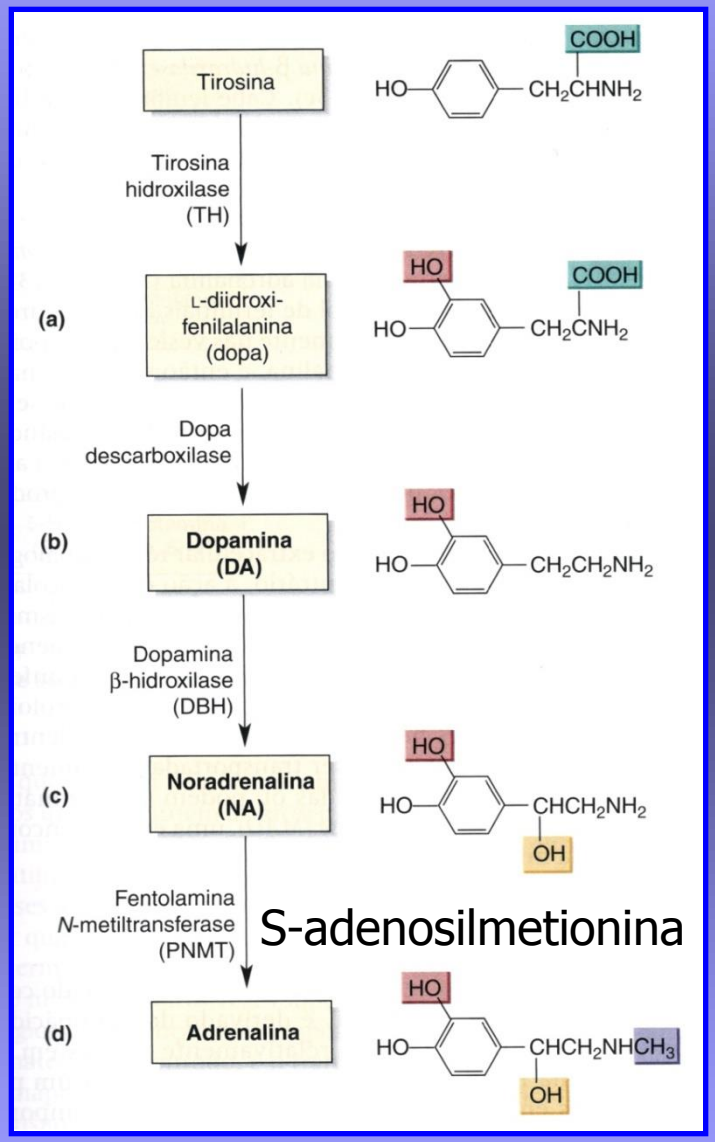
Distribuição





Via de Síntese

Feniletanolamina N-metiltransferase



Receptores de noradrenalina

9 subtipos

α_1- $G_{q/11}$ (músculo liso)

α_2 – G_i (⬇ secreção pancreática)

β – G_s (coração e brônquios)

Receptores de noradrenalina

TABLE 12-4 Properties of human α_1-adrenergic receptor subtypes

	α_{1A}	α_{1B}	α_{1D}
Amino acids	430–476	515	560
Chromosome	8	5	20
Effector pathways	$\uparrow Ca^{2+}$, protein kinase C	$\uparrow Ca^{2+}$, protein kinase C	$\uparrow Ca^{2+}$, protein kinase C
Distribution	Heart, liver, cerebellum, cerebral cortex, blood vessels	Spleen, kidney, fetal brain, blood vessels	Aorta, cerebral cortex

Modified with permission from references [35, 57].

Receptores de noradrenalina

TABLE 12-5 Properties of human α_2-adrenergic receptor subtypes

	α_{2A}	α_{2B}	α_{2C}
Amino acids	450	450	461
Chromosome	10	2	4
Effector pathways	↓cAMP	↓cAMP	↓cAMP
Distribution	Pancreas, small intestine, locus ceruleus, hippocampus	Liver, thalamus	Heart, lung, aorta, hippocampus, olfactory bulb

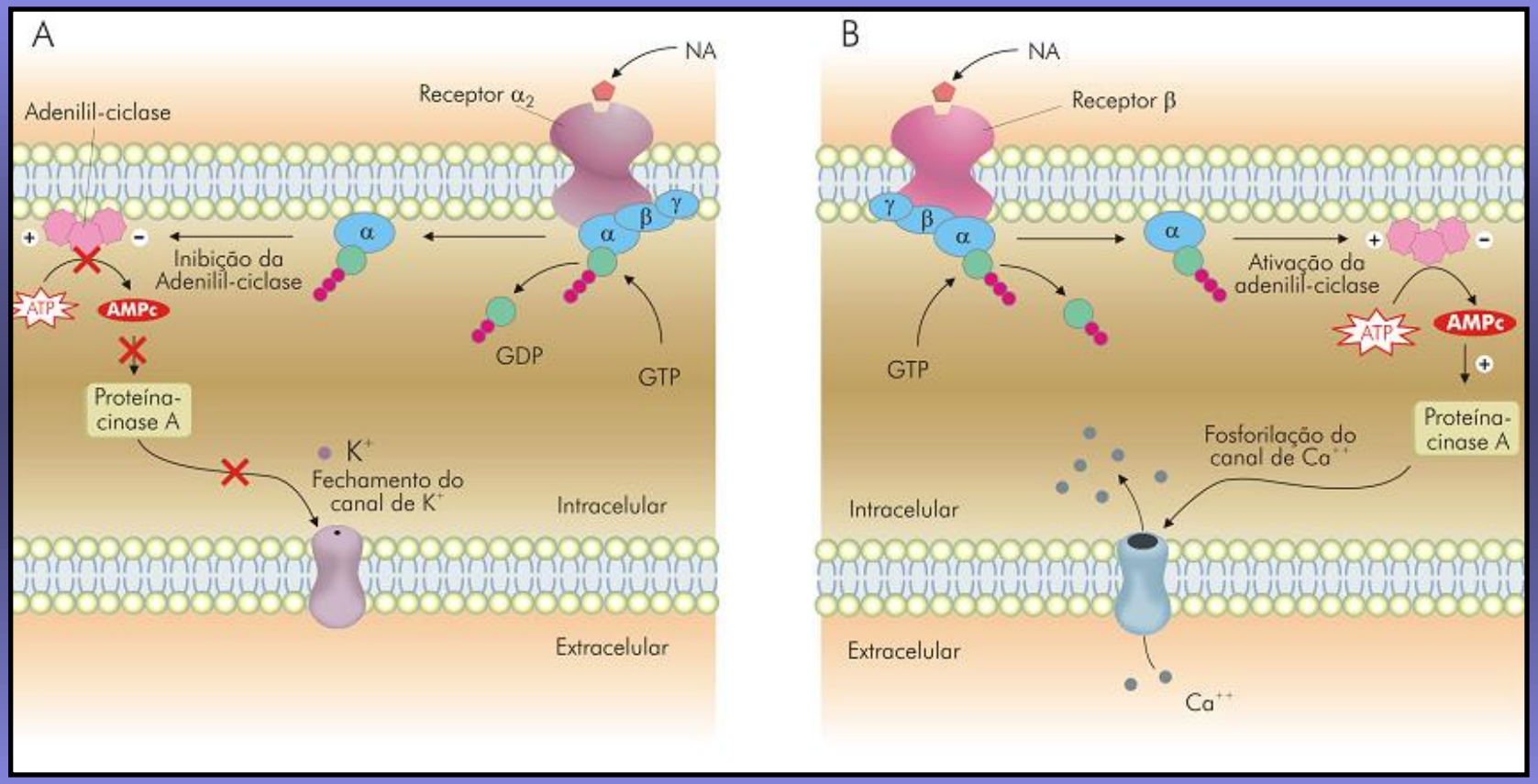
Modified from [57] with permission.

Receptores de noradrenalina

TABLE 12-6 Properties of human β-adrenergic receptor subtypes

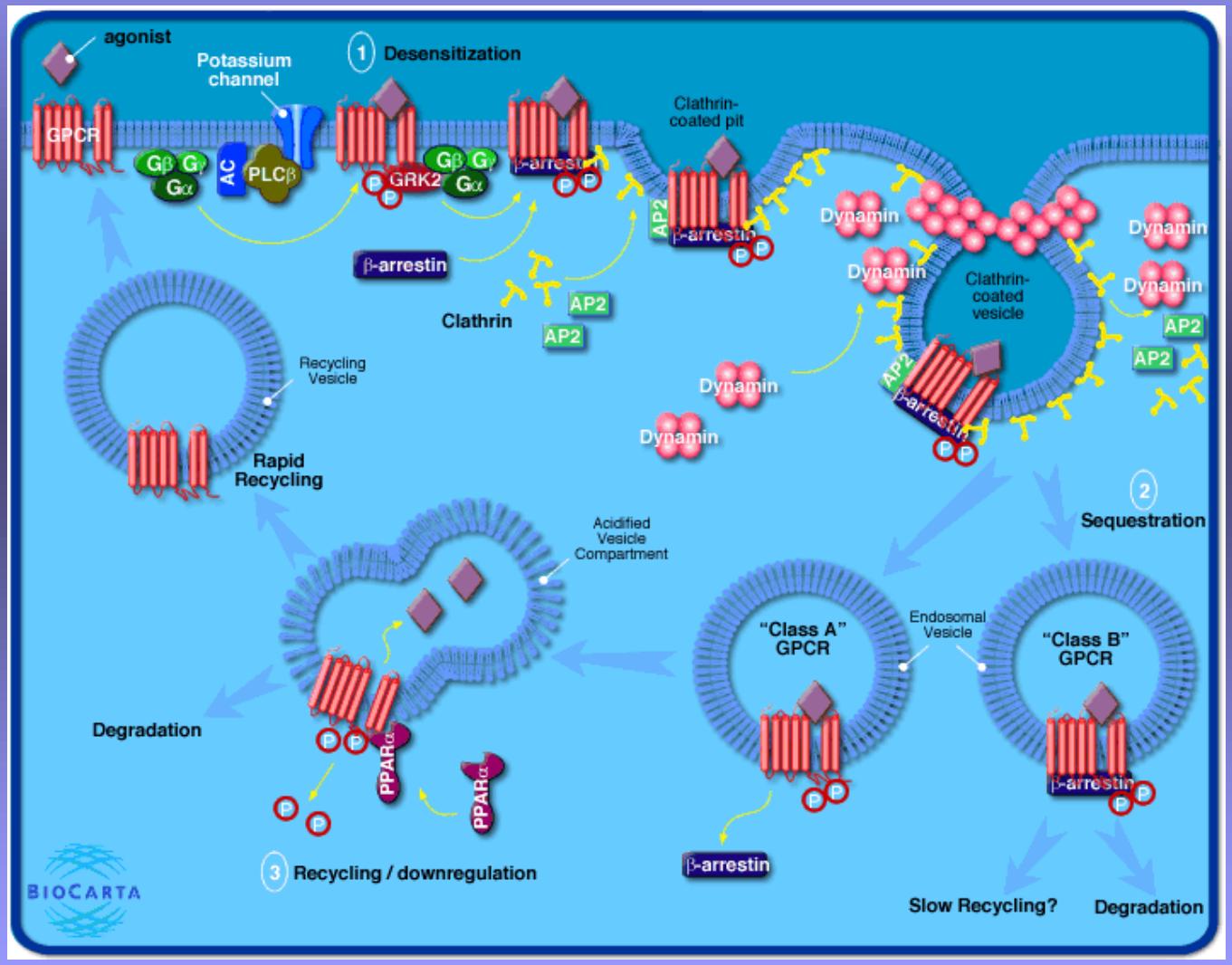
	β_1	β_2	β_3
Amino acids	477	413	402/408
Chromosome	10	5	8
Effector pathways	↑cAMP	↑cAMP	↑cAMP
Distribution	Heart, kidney, cerebral cortex, hypothalamus	Lung, liver, cerebellum, hippocampus, cerebral cortex, smooth muscle, olfactory bulb	Fat, brain (?)

Receptores de noradrenalina



Receptores catecolaminérgicos

Dessensibilização – exposição crônica a agonistas (β2)



Receptores catecolaminérgicos

TABLE 12-7 Characteristics of catecholamine receptor knockout mice

Knockout	Phenotype
α_{1A}-adrenergic receptor	Decreased blood pressure
α_{1B}-adrenergic receptor	Decreased blood pressure, decreased response to CNS stimulants
α_{1D}-adrenergic receptor	Decreased blood pressure
α_{2A}-adrenergic receptor	Increased sympathetic activity, tachycardia, loss of hypotensive response to α_2 agonists
α_{2B}-adrenergic receptor	Decreased vasoconstrictor response to α_2 agonists
α_{2C}-adrenergic receptor	No overt phenotype
β_1-adrenergic receptor	Most die prenatally, survivors have impaired cardiac response
β_2-adrenergic receptor	Changes in vascular tone and energy metabolism during stress
β_3-adrenergic receptor	Altered leptin and insulin concentrations after agonist treatment
D_1-dopamine receptor	Reduced agonist responses, hyperlocomotion
D_2-dopamine receptor	Parkinsonian-like motor impairment
D_3-dopamine receptor	Hyperactivity
D_4-dopamine receptor	Reduced locomotion, hypersensitivity to ethanol and stimulants
D_5-dopamine receptor	Reduced agonist induced locomotion, startle, and prepulse inhibition

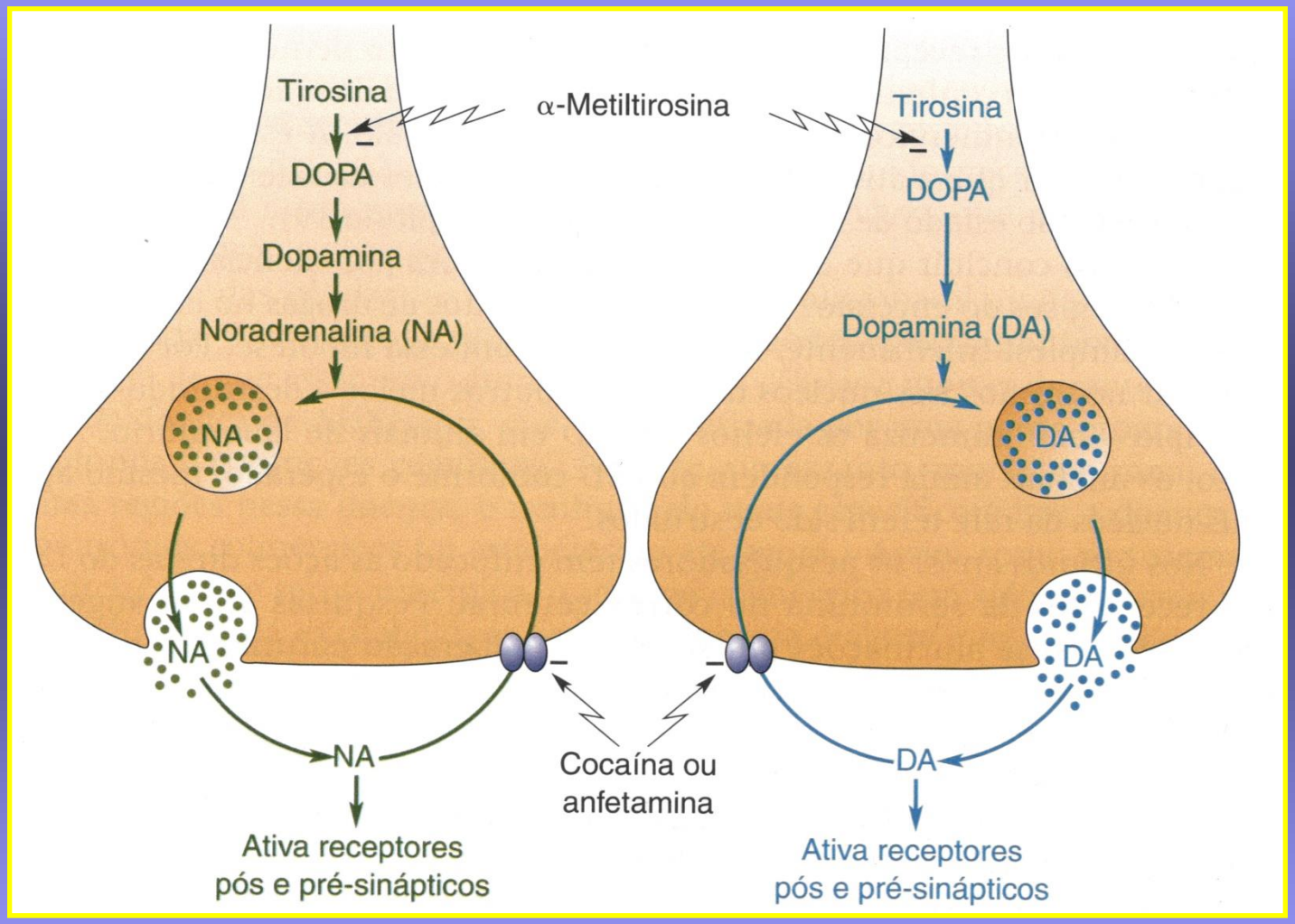
Receptores catecolaminérgicos

Sensibilização – exposição crônica a antagonista (↑ receptores)

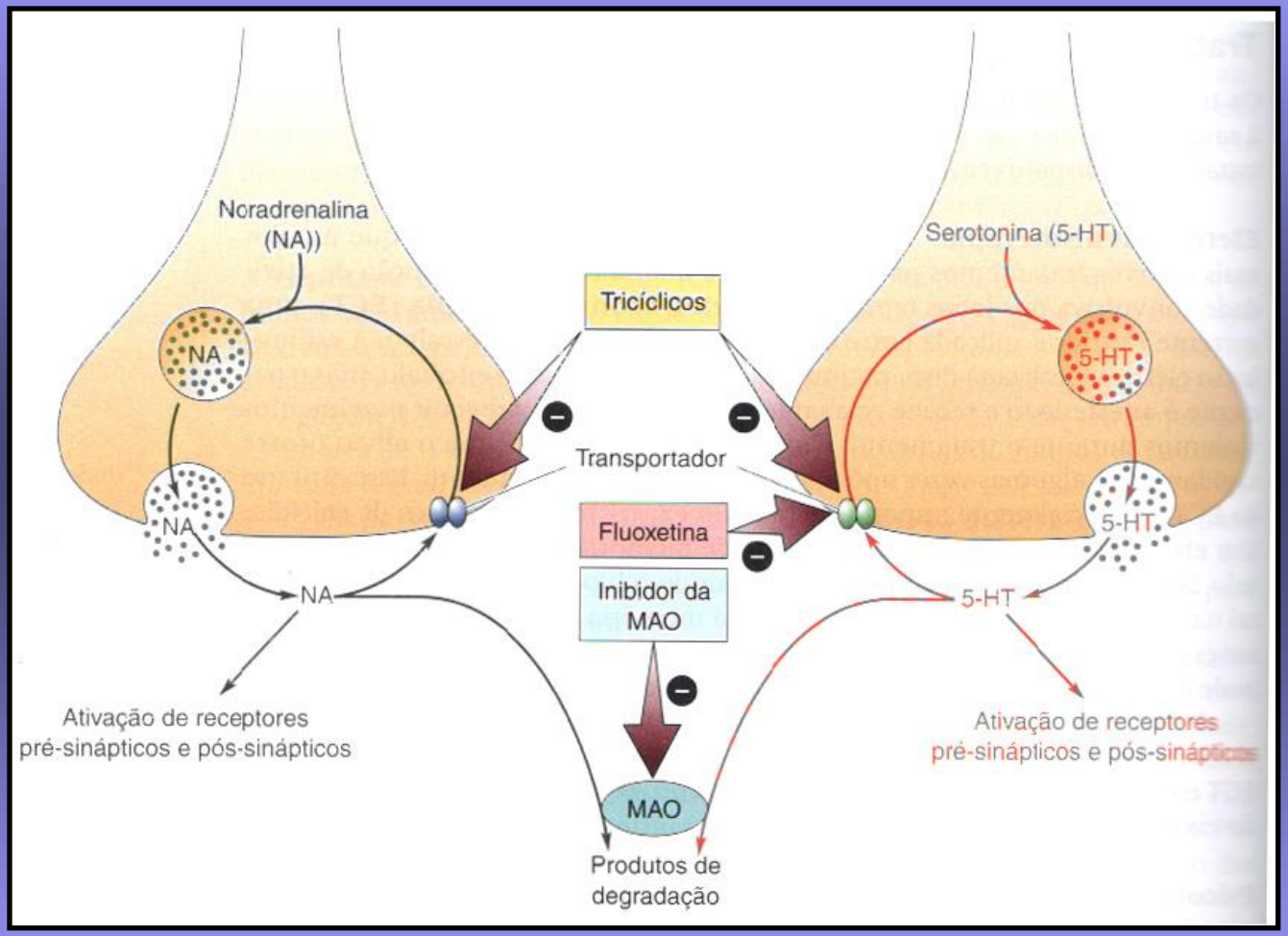
Supersensibilidade efetora – neurotoxinas (6-OHDA)

Subsensibilidade – antidepressivos ou inibidores da MAO

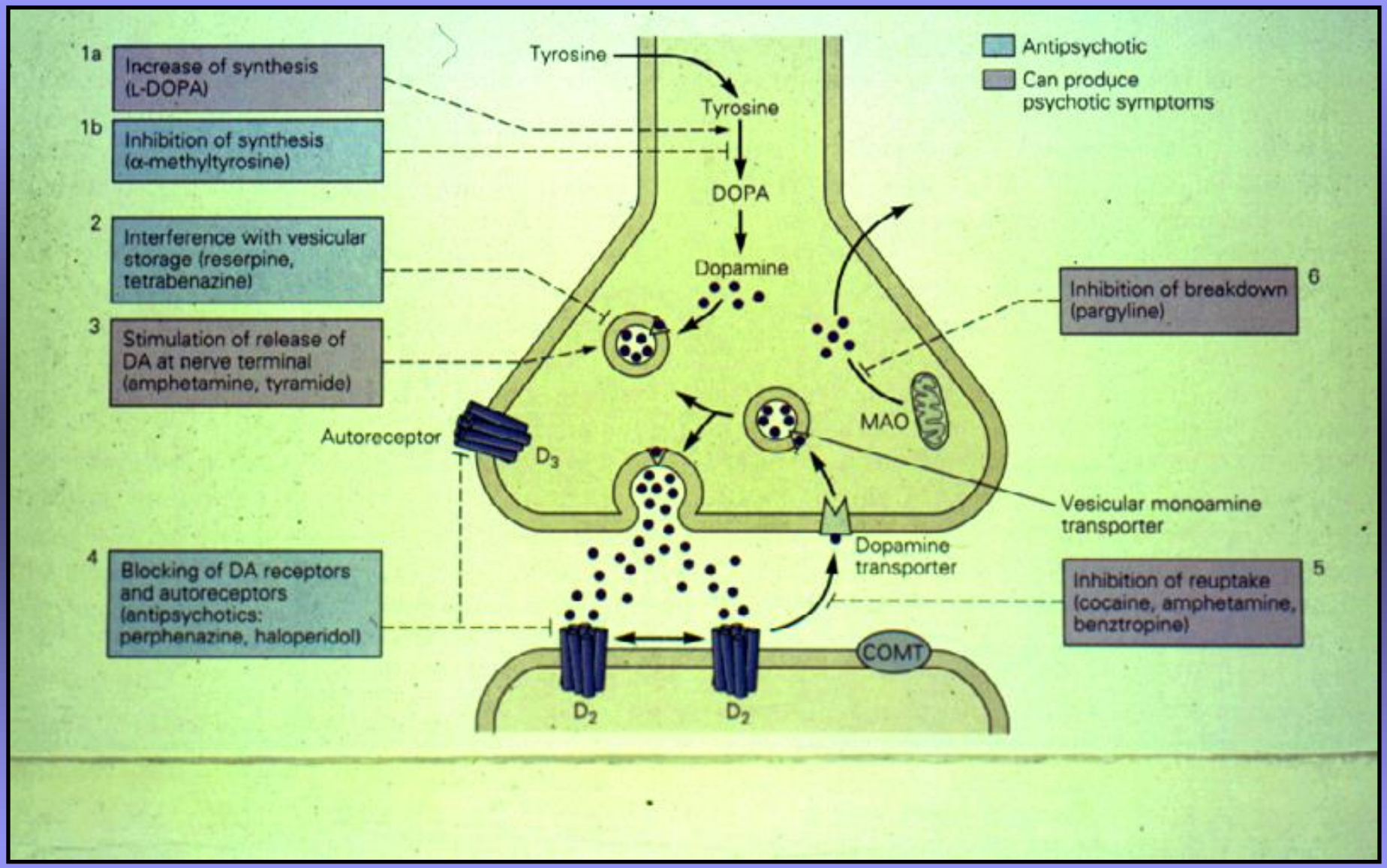
Catecolaminas e ação de drogas



Catecolaminas e transtornos do humor



Catecolaminas e ação de drogas



Adrenergic Transmission