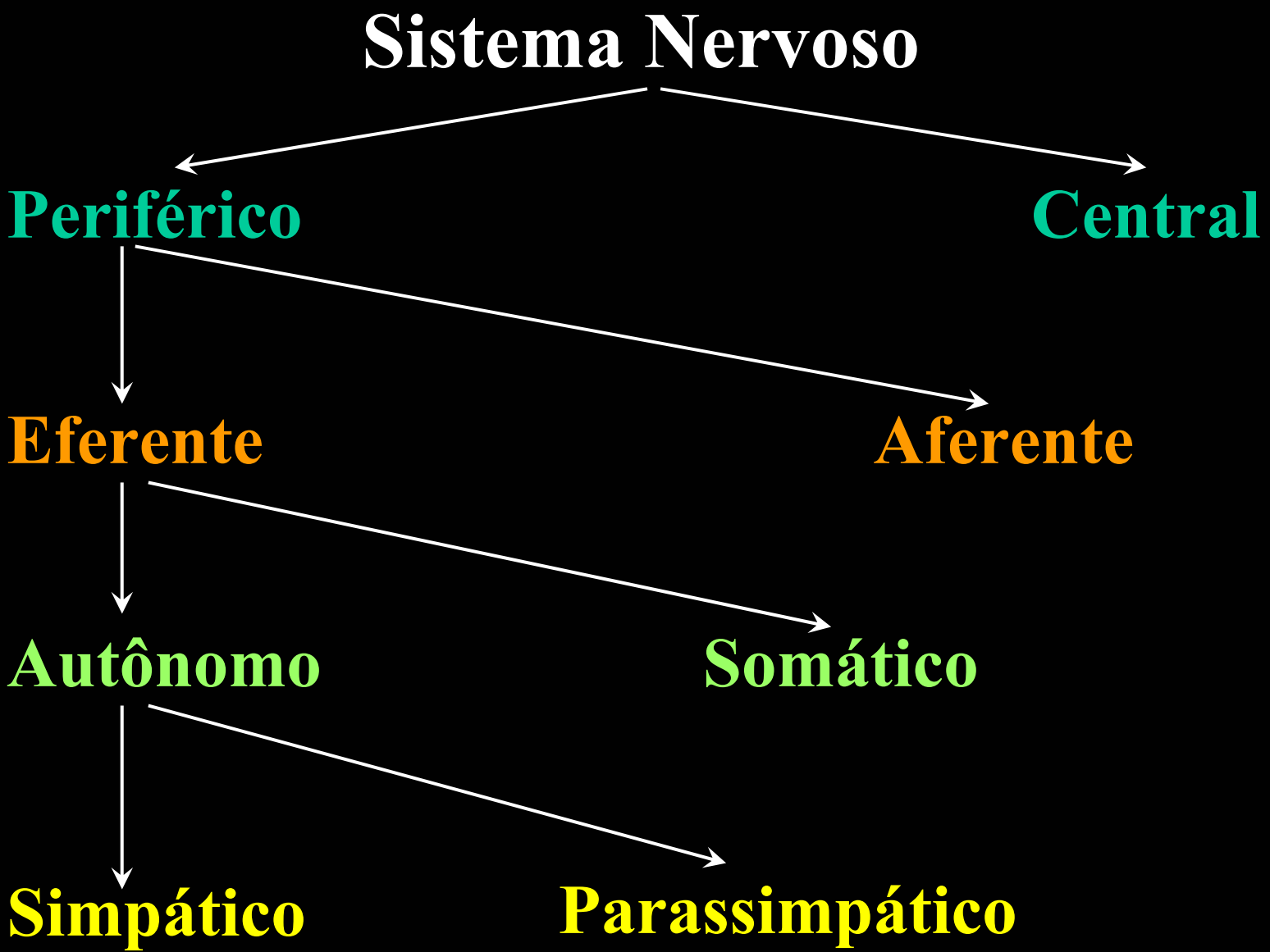
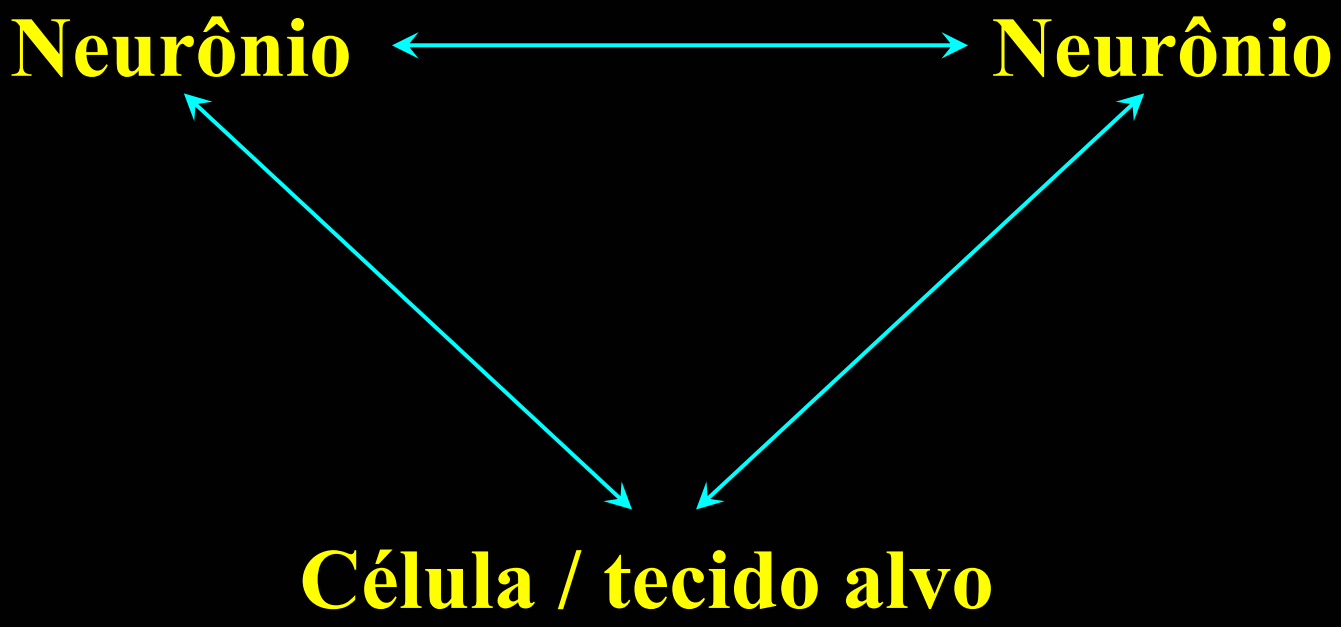
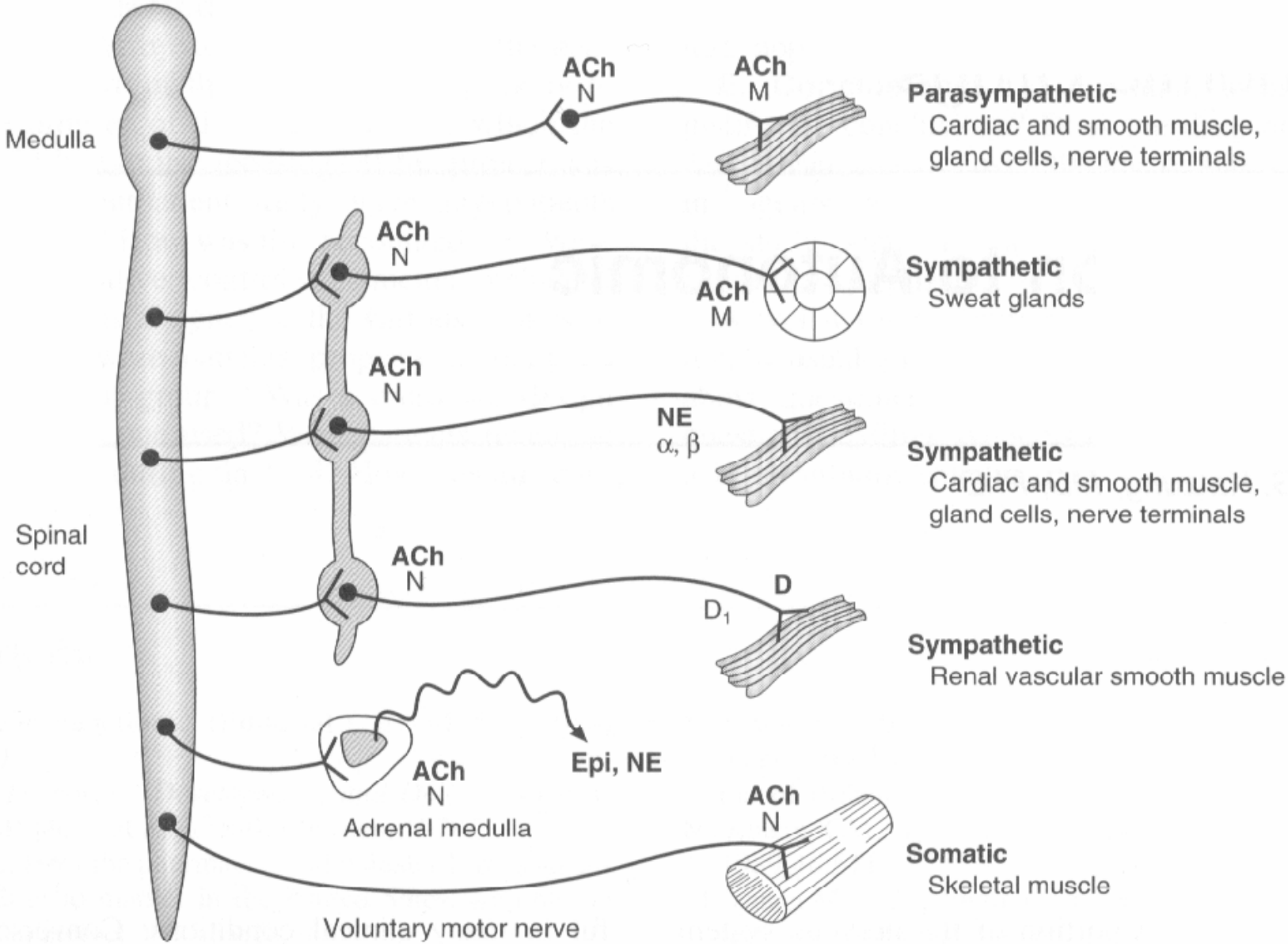
Introdução à Farmacologia do Sistema Nervoso Autônomo (SNA)


Sistema Nervoso
Periférico
Central
Eferente
Aferente
Autônomo
Somático
Simpático
Parassimpático

Sistema Nervoso vs. Sistema Endócrino

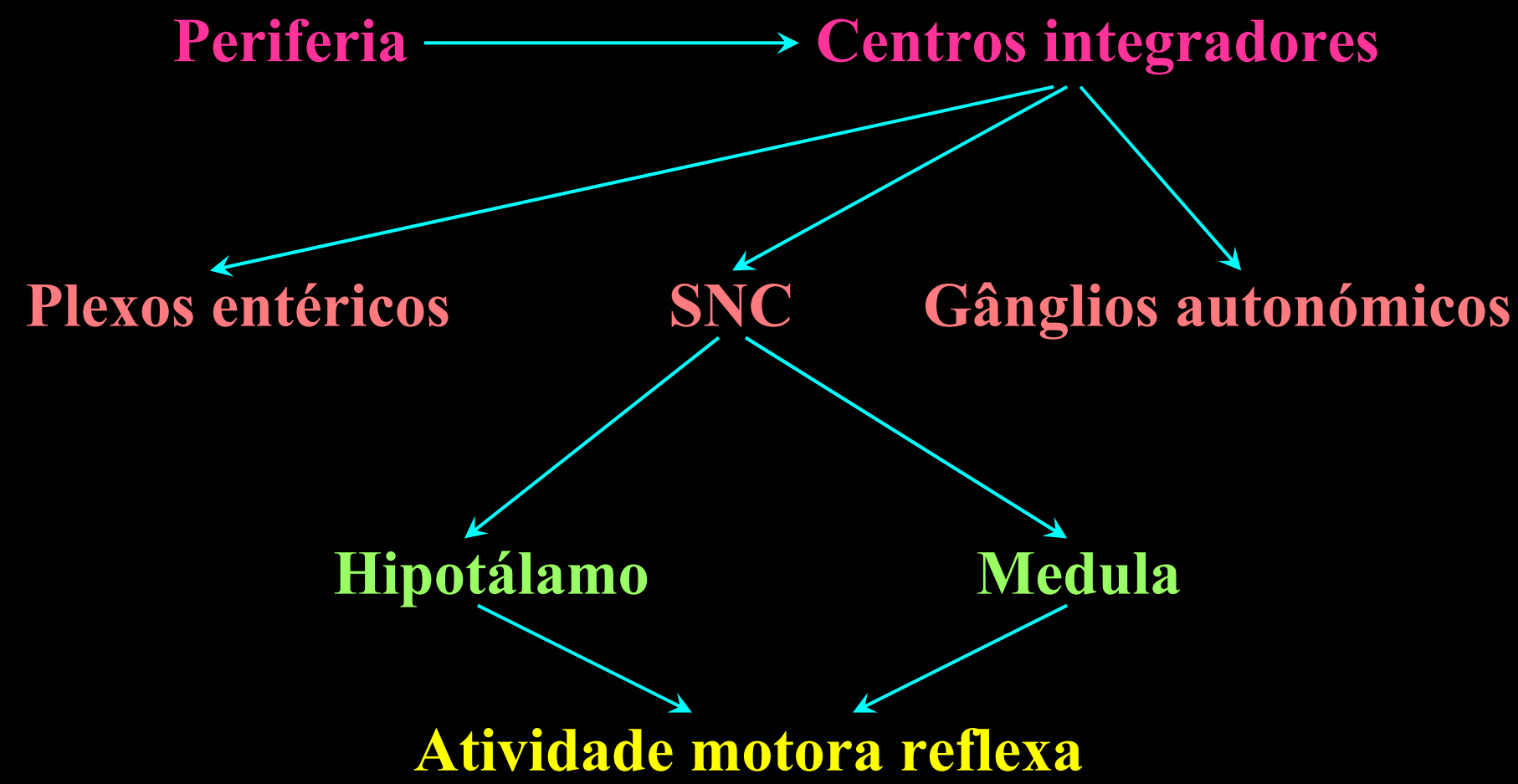
- ✓ Alto nível de integração no cérebro
- ✓ Influência de processos a distância
- ✓ Mecanismos de controle (retro-alimentação)
- ✓ Mediadores químicos

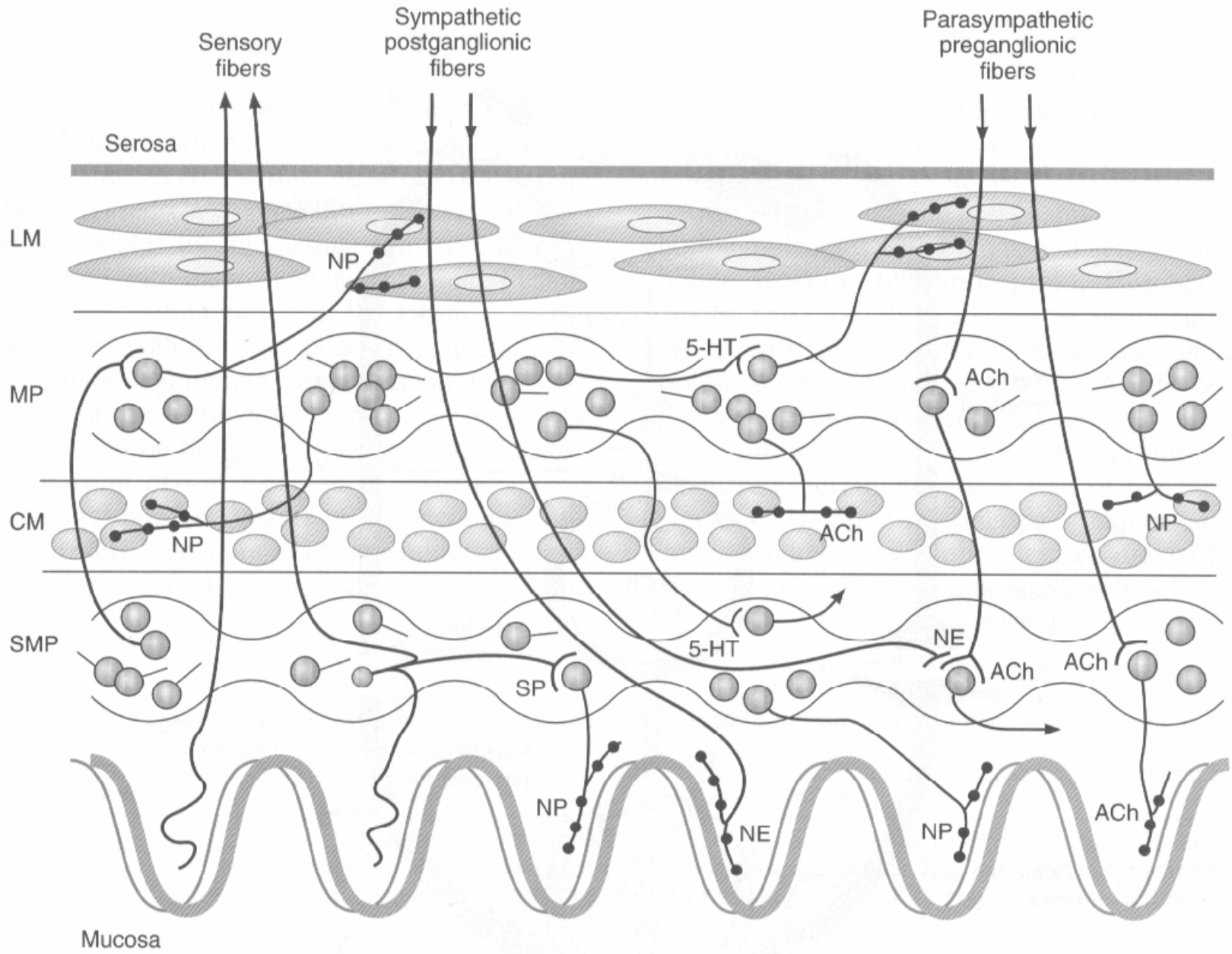

Neurônio
Neurônio
Célula / tecido alvo


Medulla
Spinal cord
ACh N
ACh M
Parasympathetic
Cardiac and smooth muscle, gland cells, nerve terminals
ACh N
ACh M
Sympathetic
Sweat glands
ACh N
NE α, β
Sympathetic
Cardiac and smooth muscle, gland cells, nerve terminals
ACh N
D D1
Sympathetic
Renal vascular smooth muscle
ACh N
Epi, NE
Adrenal medulla
ACh N
Somatic
Skeletal muscle
Voluntary motor nerve

MN

Fibras aferentes:




Sensory fibers
Sympathetic postganglionic fibers
Parasympathetic preganglionic fibers
Serosa
LM
MP
CM
SMP
Mucosa
NP
5-HT
ACh
SP
NE

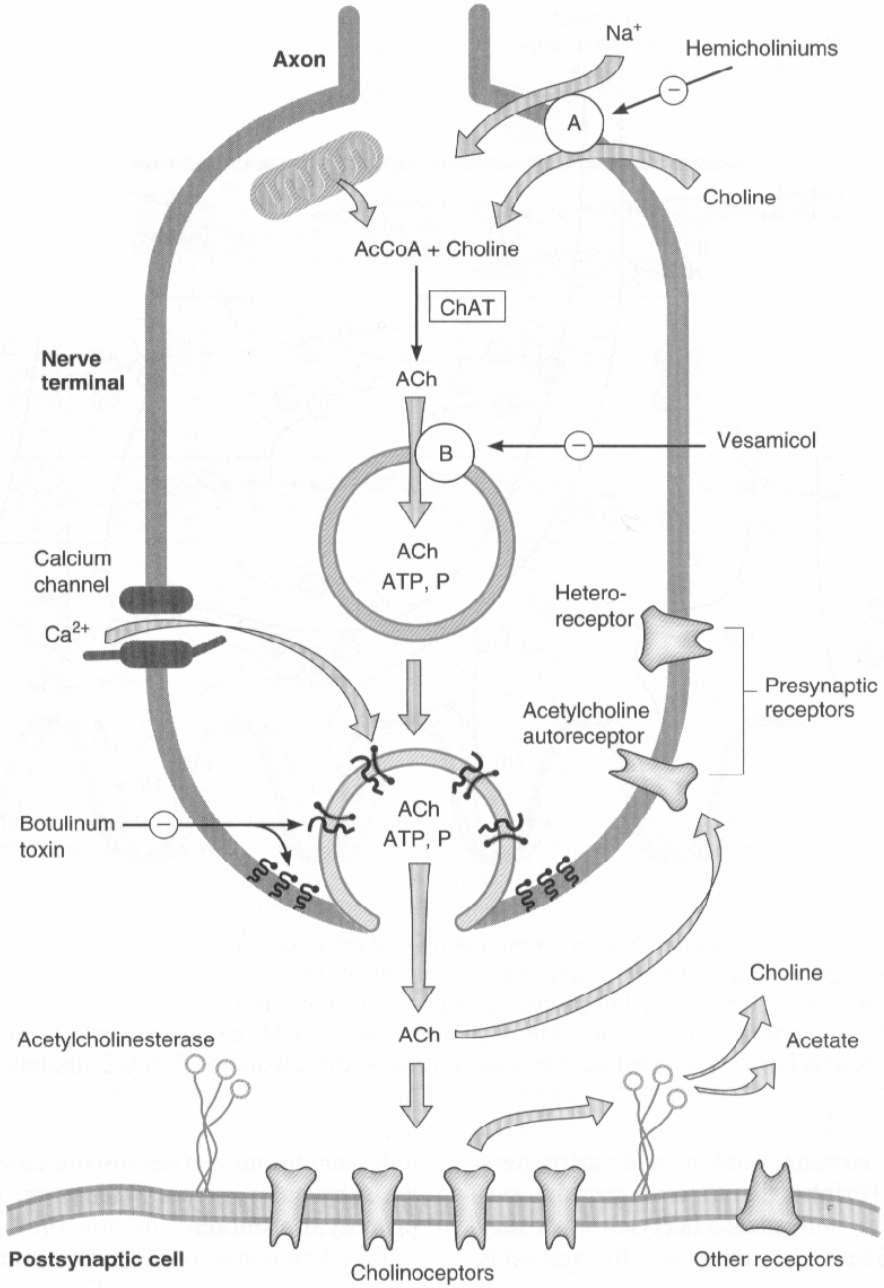
MN

Neurotransmissores do SNA, SNE e NANC

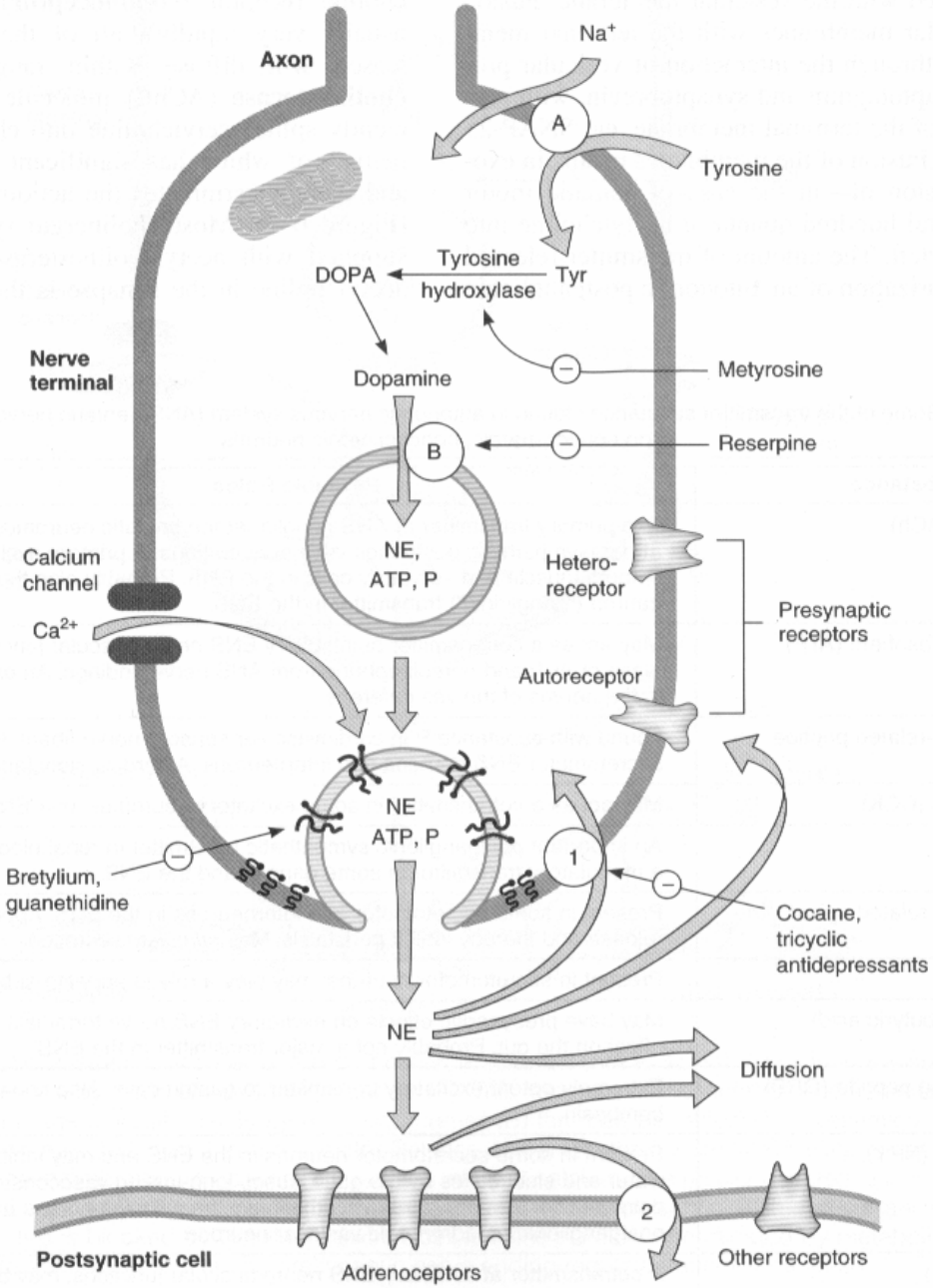
Ach:	• NT primário (gânglios SNA, JNM, parassimpático); • NT primário (céls. ML e secretórias do SNE); • Provável NT principal neurônio-neurônio (SNE).
NE:	• NT principal na maioria das terminações nervosas simpáticas pós-ganglionares.
CGRP:	• Junto com SP em fibras nervosas sensoriais no CV; • Neurônios secreto-motores (SNE).
DA:	• NT simpático pós-ganglionar (vasculatura renal); • Provável NT modulador (gânglios e SNE).
NO:	• Co-NT na JNM inibitória (SNE); • Importante em esfíncteres.
5-HT:	• Co-NT nas junções neurônio-neurônio excitatórias (SNE).

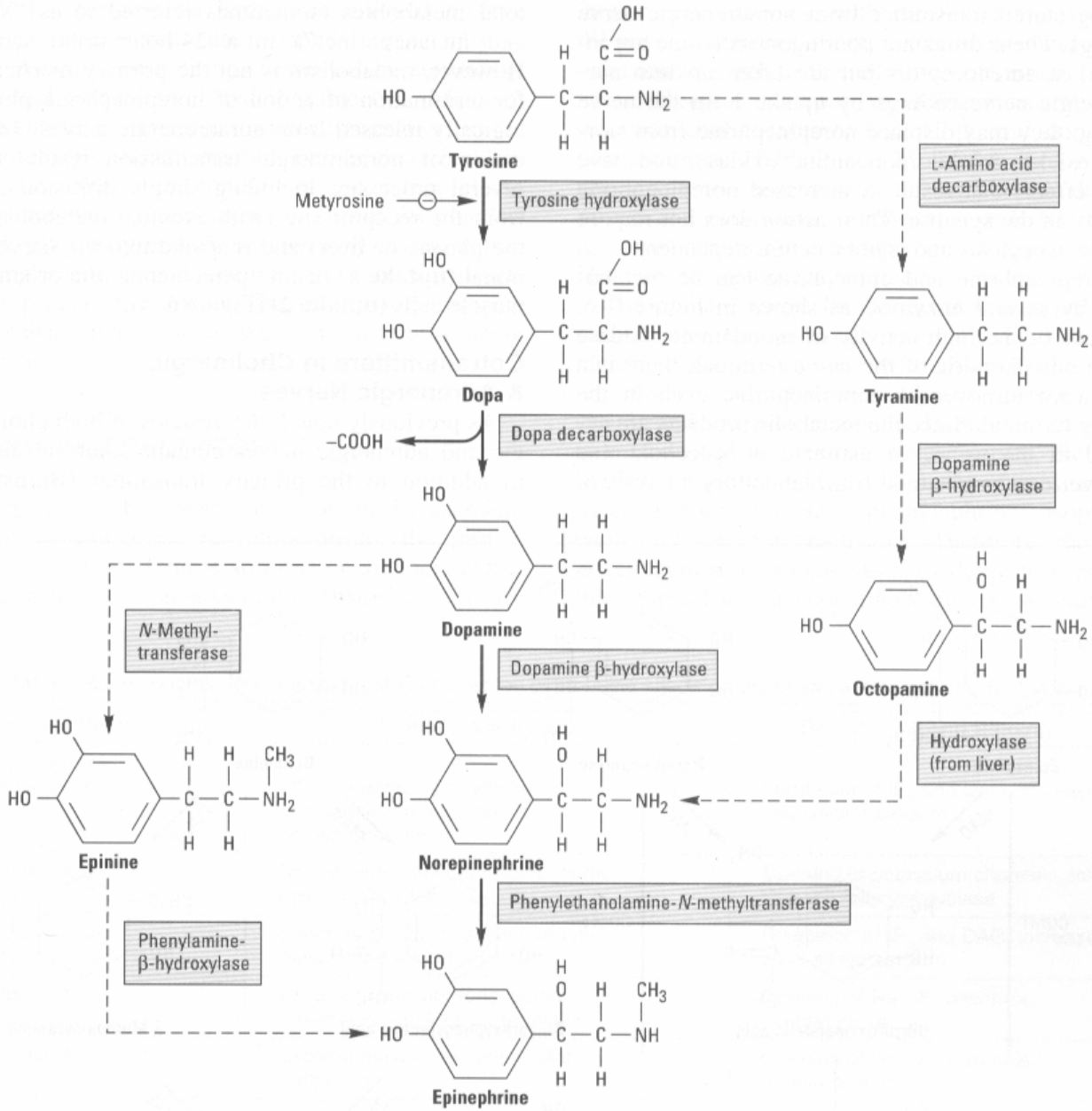
Outros neurotransmissores:

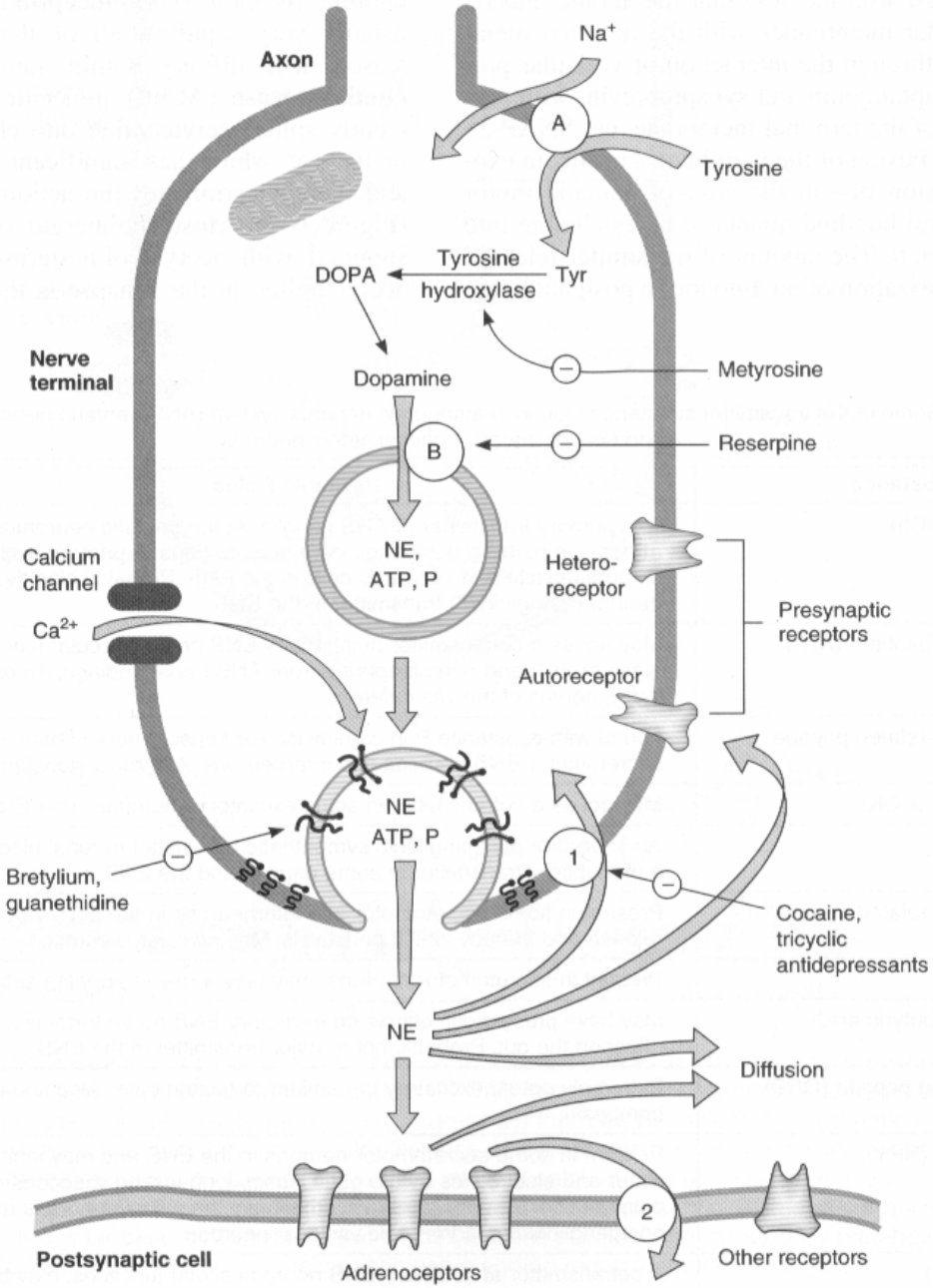
- ATP
- Colecistocinina (CCK)
- Encefalina (opoióides)
- Galanina
- GABA
- Peptídeo liberador de gastrina (GRP)
- NPY
- SP (taquicininas)
- VIP

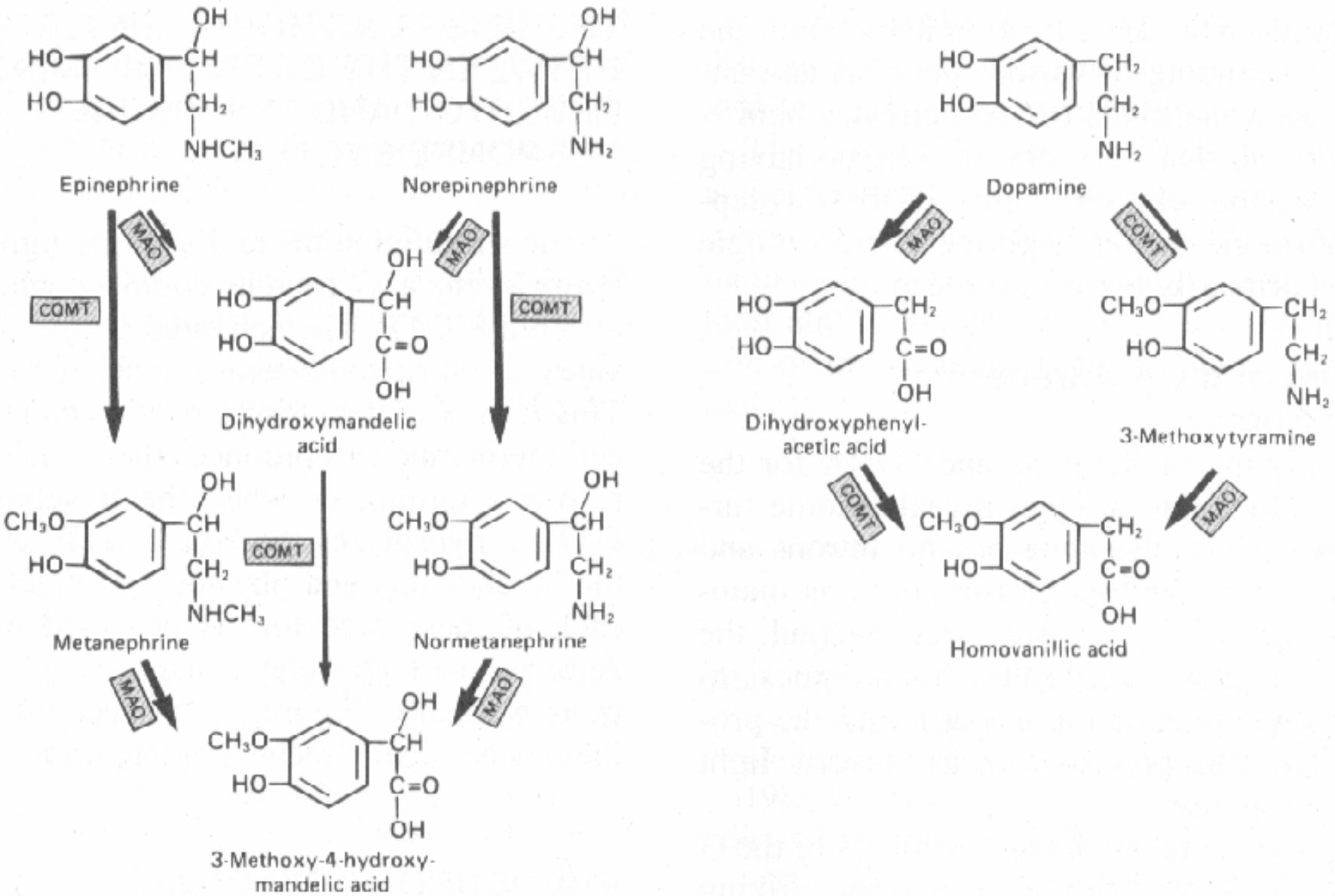

Axon
Na+
Hemicholiniums
A
Choline
AcCoA + Choline
ChAT
Nerve terminal
ACh
B
Vesamicol
ACh
ATP, P
Calcium channel
Ca2+
Hetero-receptor
Presynaptic receptors
Acetylcholine autoreceptor
Botulinum toxin
ACh
ATP, P
Choline
Acetylcholinesterase
ACh
Acetate
Postsynaptic cell
Cholinoceptors
Other receptors

MN


Axon
Na+
A
Tyrosine
Tyrosine hydroxylase
DOPA
Tyr
Nerve terminal
Dopamine
Metyrosine
B
Reserpine
NE, ATP, P
Calcium channel
Ca2+
Hetero-receptor
Presynaptic receptors
Autoreceptor
NE
ATP, P
Bretylium, guanethidine
1
Cocaine, tricyclic antidepressants
NE
Diffusion
2
Postsynaptic cell
Adrenoceptors
Other receptors


Tyrosine
Metyrosine
Tyrosine hydroxylase
L-Amino acid decarboxylase
Dopa
Tyramine
–COOH
Dopa decarboxylase
Dopamine β-hydroxylase
Dopamine
N-Methyl-transferase
Dopamine β-hydroxylase
Octopamine
Hydroxylase (from liver)
Epinine
Norepinephrine
Phenylethanolamine-N-methyltransferase
Phenylamine-β-hydroxylase
Epinephrine


Axon
Na+
A
Tyrosine
Tyrosine hydroxylase
DOPA
Tyr
Nerve terminal
Dopamine
Metyrosine
B
Reserpine
NE, ATP, P
Calcium channel
Ca2+
Hetero-receptor
Presynaptic receptors
Autoreceptor
NE
ATP, P
Bretylium, guanethidine
1
Cocaine, tricyclic antidepressants
NE
Diffusion
2
Postsynaptic cell
Adrenoceptors
Other receptors


Epinephrine
Norepinephrine
Dopamine
MAO
COMT
Dihydroxymandelic acid
Dihydroxyphenyl-acetic acid
3-Methoxytyramine
Metanephrine
Normetanephrine
Homovanillic acid
3-Methoxy-4-hydroxy-mandelic acid

MN

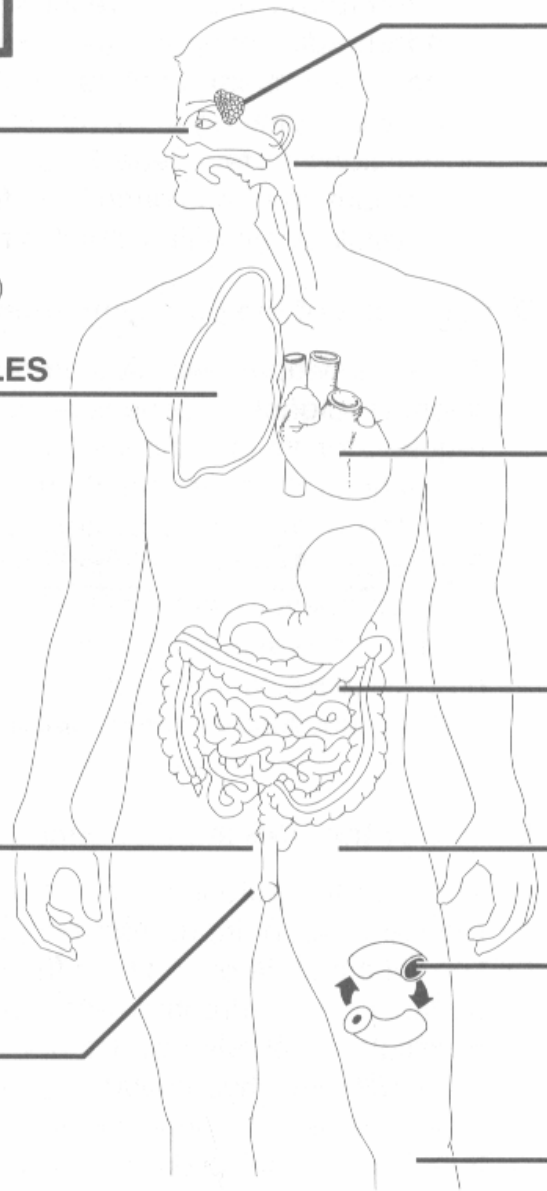
Receptores autonómicos

- Colinérgicos
  - Muscarínicos (M_1, M_2, M_3)
  - Nicotínicos (N_N, N_M)

- Adrenérgicos
  - Alfa (α_1, α_2)
  - Beta (β_1, β_2, β_3)

- Dopaminérgicos
  - D_1, D_2, D_3, D_4, D_5

Bold type = sympathetic actions
Light type = parasympathetic actions



EYE

Contraction of iris radial muscle (pupil dilates)
Contraction of iris sphincter muscle (pupil contracts)
Contraction of ciliary muscle (lens accommodates for near vision)

TRACHEA AND BRONCHIOLES

Dilates
Constricts, increases secretions

URETERS AND BLADDER

Relaxes detrusor; contraction of trigone and sphincter
Contraction of detrusor; relaxation of trigone and sphincter

GENITALIA-MALE

Stimulates ejaculation
Stimulates erection

LACRIMAL GLANDS

Stimulates tears

SALIVARY GLANDS

Thick, viscid secretion
Copious, water secretion

HEART

Increased rate; increased contractility
Decreased rate, and contractility

GASTROINTESTINAL

Decrease in muscle motility and tone; contraction of sphincters
Increased muscle motility and tone

GENITALIA-FEMALE

Relaxation of uterus

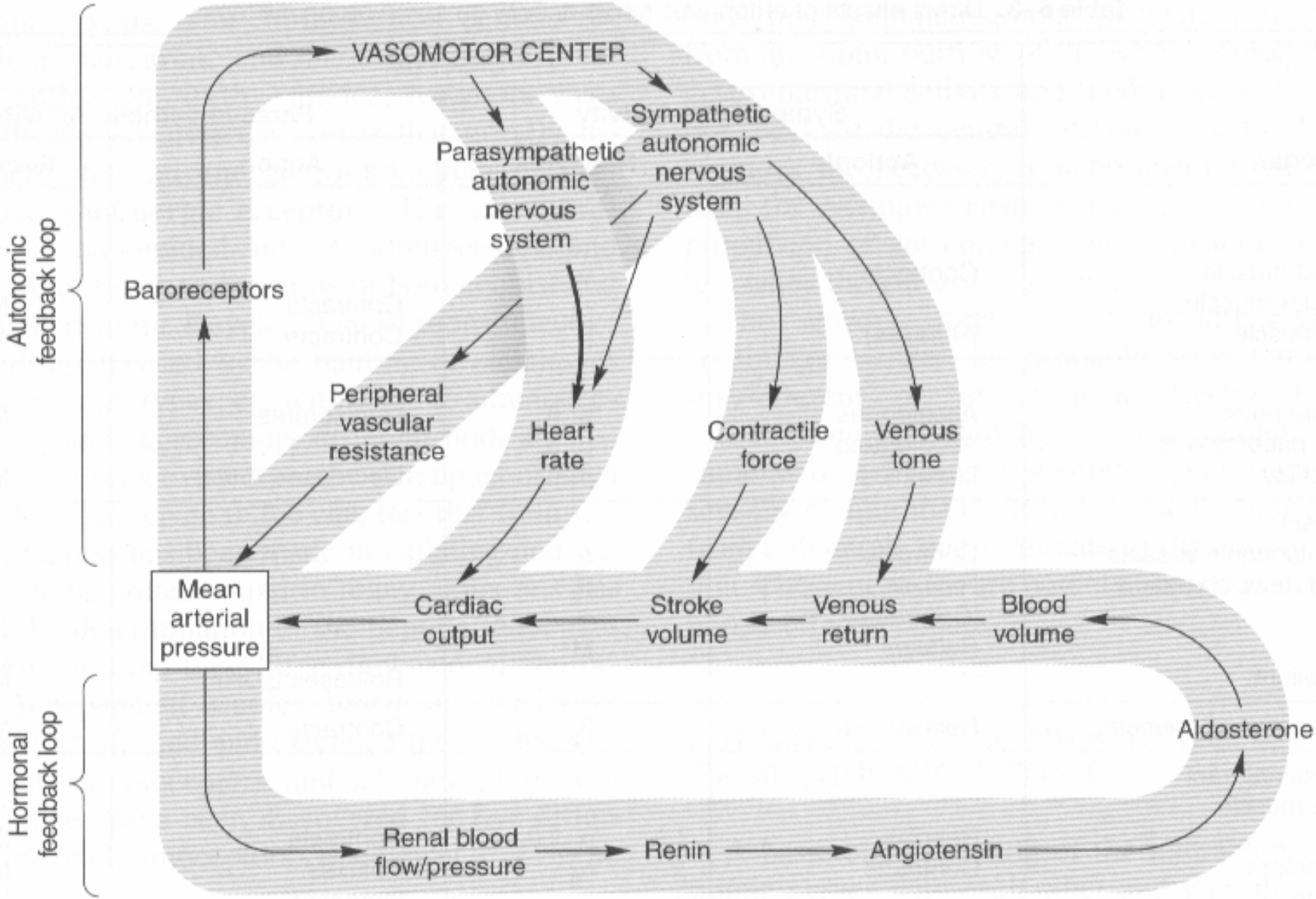
BLOOD VESSELS (skeletal muscle)

Dilatation

BLOOD VESSELS (skin, mucus membranes and splanchnic area)

Constriction

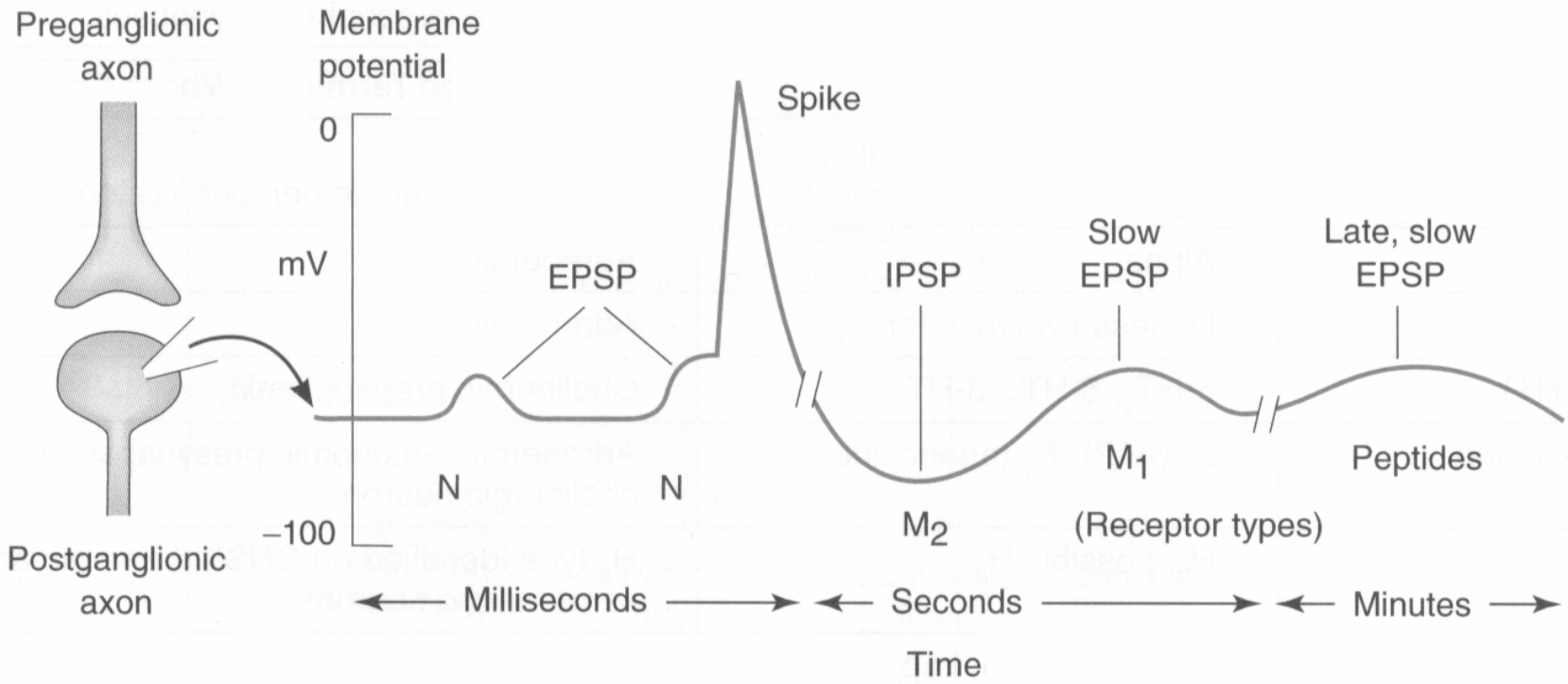
MN


Autonomic feedback loop
VASOMOTOR CENTER
Parasympathetic autonomic nervous system
Sympathetic autonomic nervous system
Baroreceptors
Peripheral vascular resistance
Heart rate
Contractile force
Venous tone
Mean arterial pressure
Cardiac output
Stroke volume
Venous return
Blood volume
Hormonal feedback loop
Aldosterone
Renal blood flow/pressure
Renin
Angiotensin

MN

Modulação de sinapses periféricas (auto / hetero-receptor)

Efeitos inibitórios		
Ach	**M_2**	• Adr; SNE
NE	**α_2**	• Adr
DA	**D_2 (D_1 ?)**	• Adr
5-HT	**5-HT_1, 5-HT_2, 5-HT_3**	• Ch pré-gangl.
PGE_1 / PGE_2	**EP_3**	• Adr
Efeitos excitatórios		
Epi	**β_2**	• Adr; Ch (somático)
ACh	**N_M**	• Ch (somático)
AII	**AT_1**	• Adr


Preganglionic axon
Membrane potential
0
mV
–100
EPSP
Spike
IPSP
Slow EPSP
Late, slow EPSP
N
N
M_2
M_1
(Receptor types)
Peptides
Postganglionic axon
Milliseconds
Seconds
Minutes
Time

MN

Interferência farmacológica na transmissão autônoma

Propagação do potencial de ação	Anestésicos locais / tetrodotoxina, saxitoxina
Estocagem de NT	Vesamicol (Ch), Reserpina (Adr)
Liberação de NT	NE, DA, ACh, AII, PG (moduladores) Toxina botulínica (Ch) Tiramina, anfetamina (Adr)
Captação de NT	Cocaina, antidepressivos tricíclicos, 6-OH DA (Adr)
Ativação / bloqueio de receptor	NE, fentolamina, isoproterenol, propranolol, nicotina, d-tubocurarina, betanecol, atropina.
Inativação enzimática de NT	Neostigmina (Ach-ase), tranilcipromina (MAO)