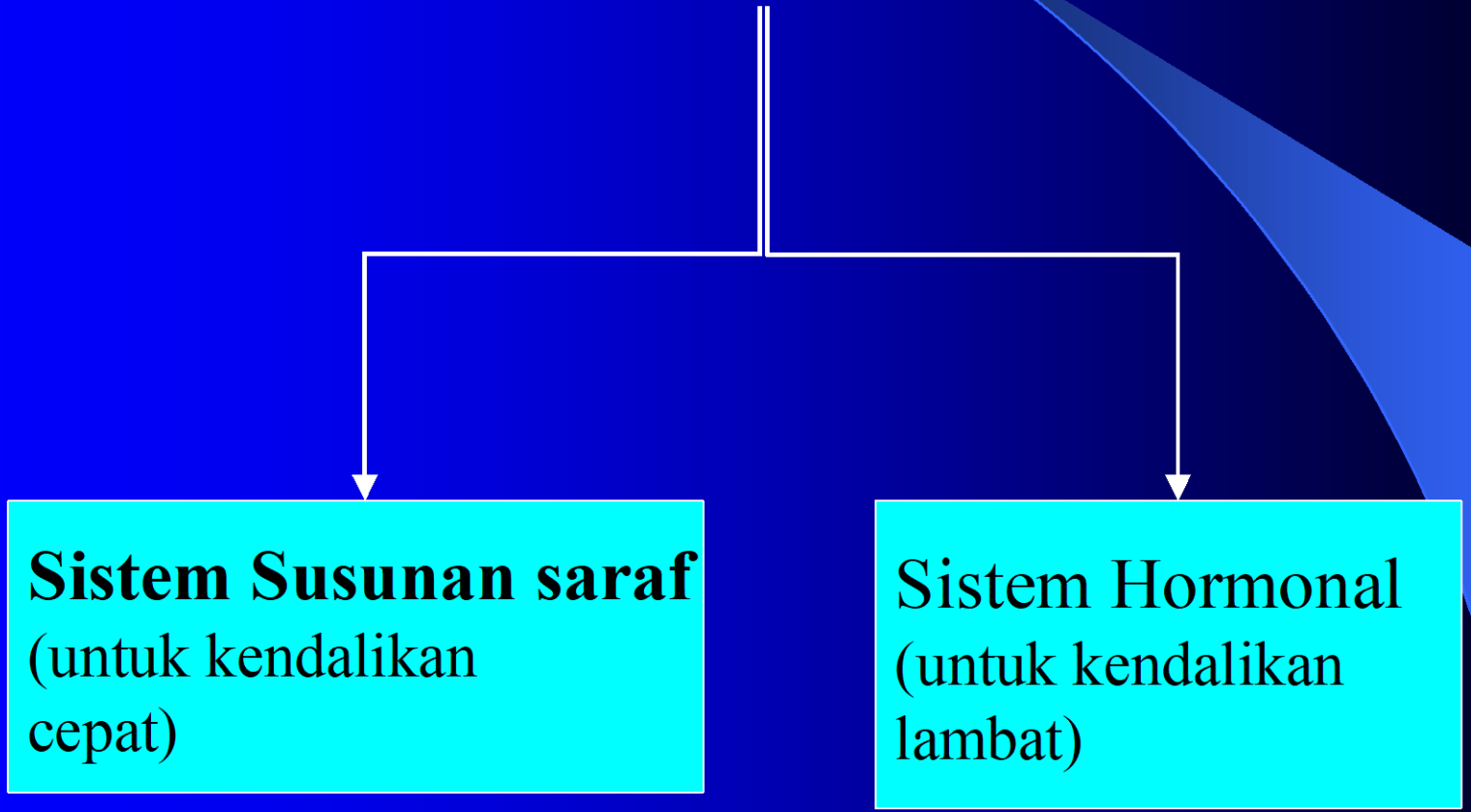
SARAF OTONOM

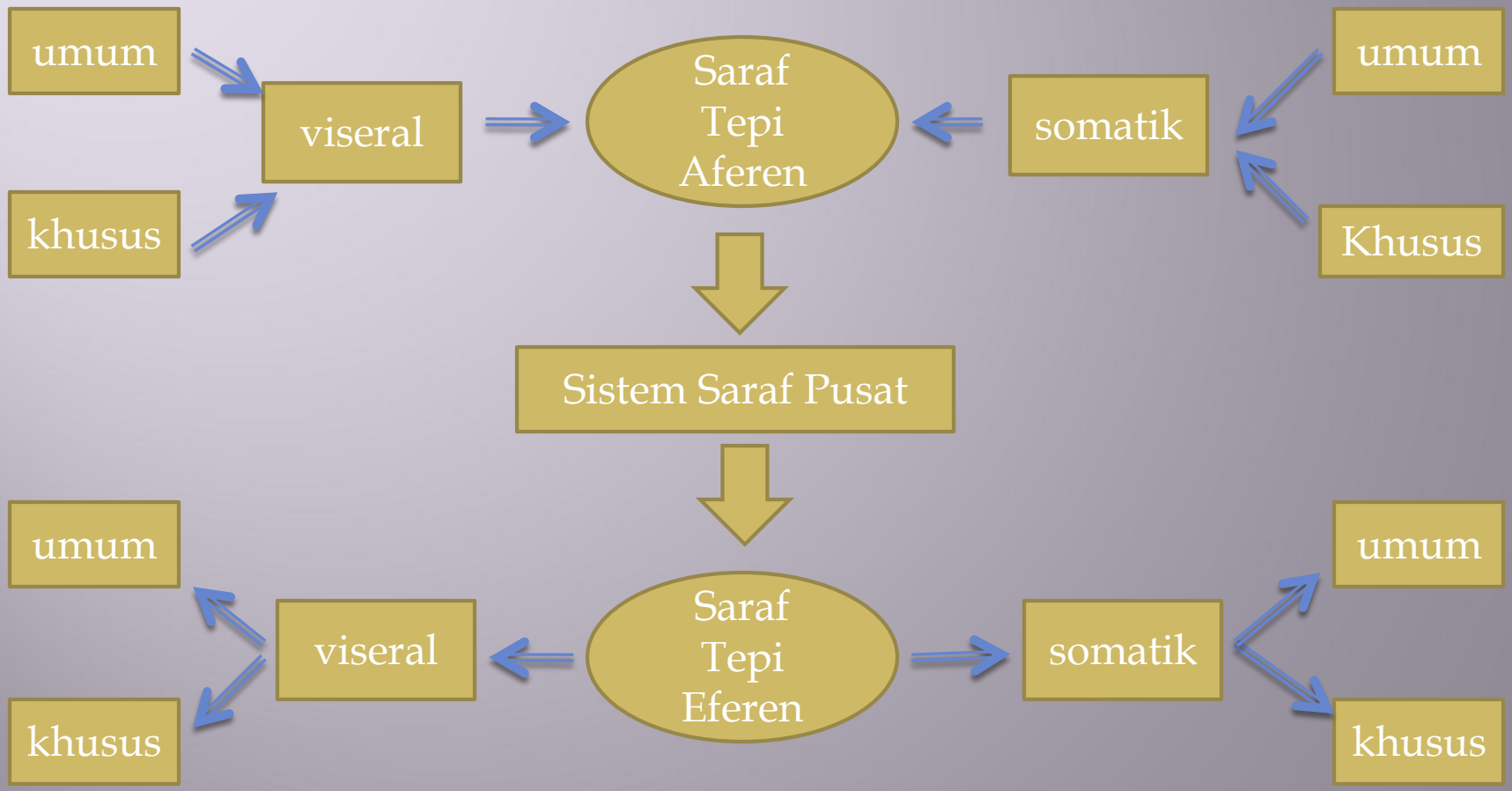
dr. Hadi Sarosa,M.Kes
Physiologist

Dasar pengendalian tubuh manusia (Homeostasis)

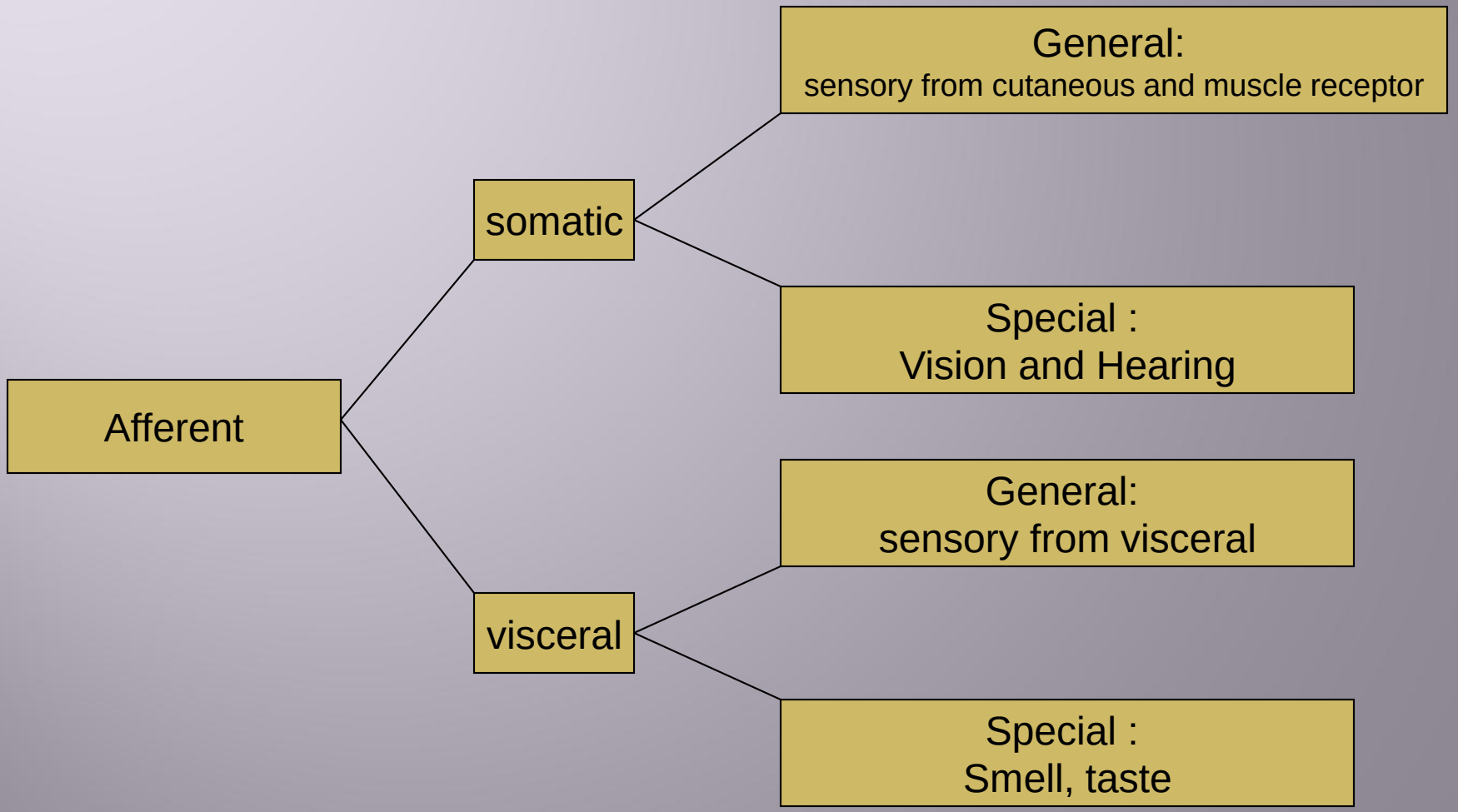
- Dikendalikan oleh 2 sistem utama



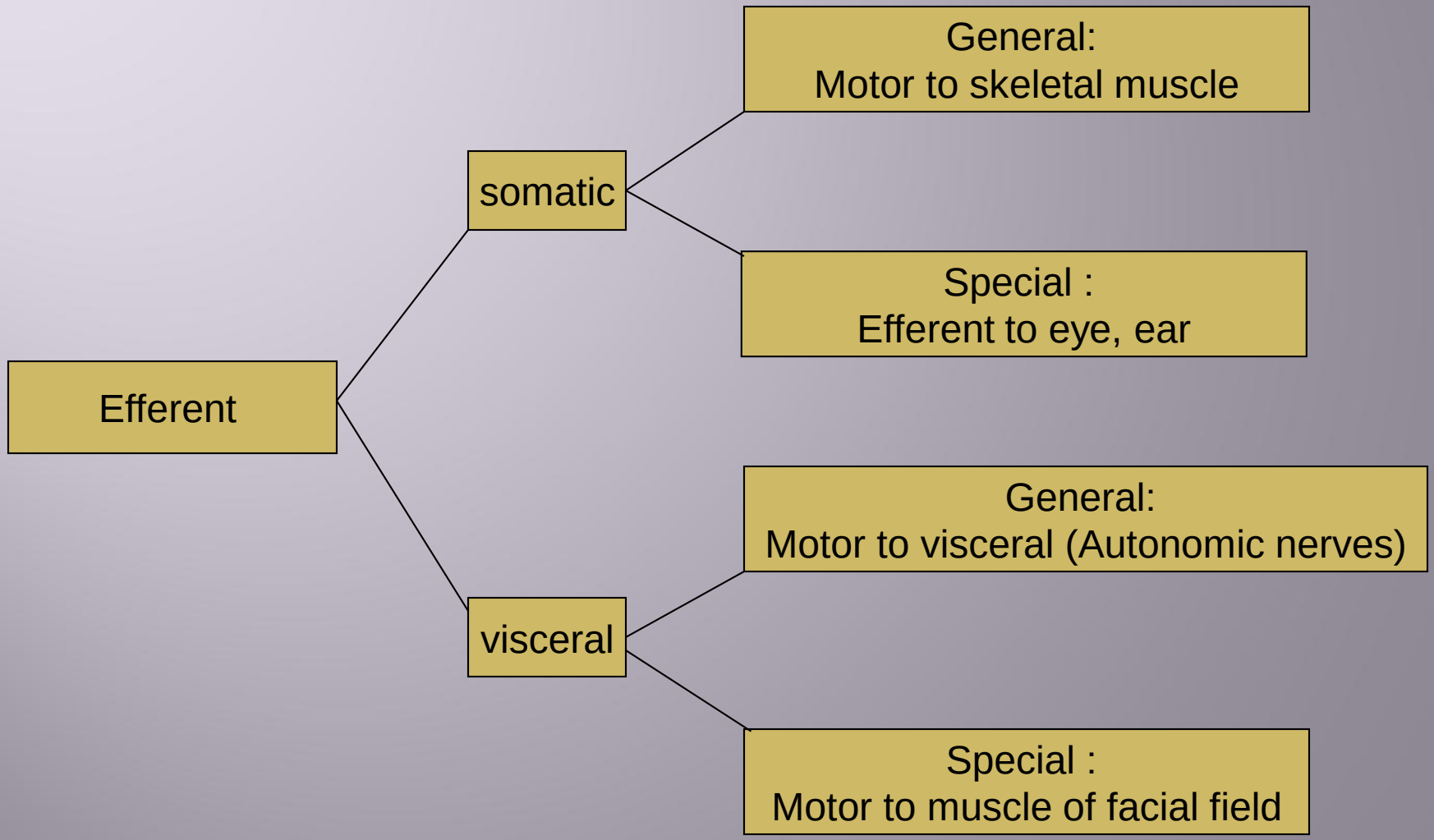
Peripheral and Cranial Nerves



Peripheral and Cranial Nerves



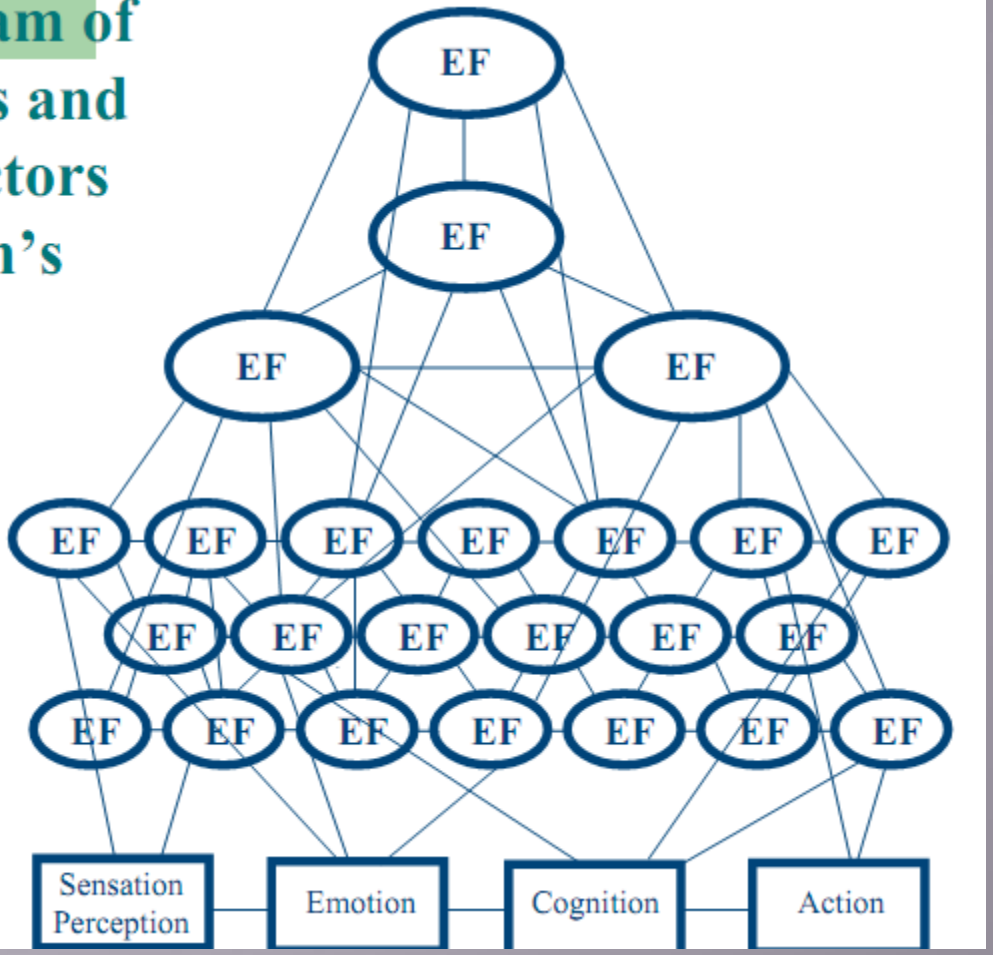
Peripheral and Cranial Nerves

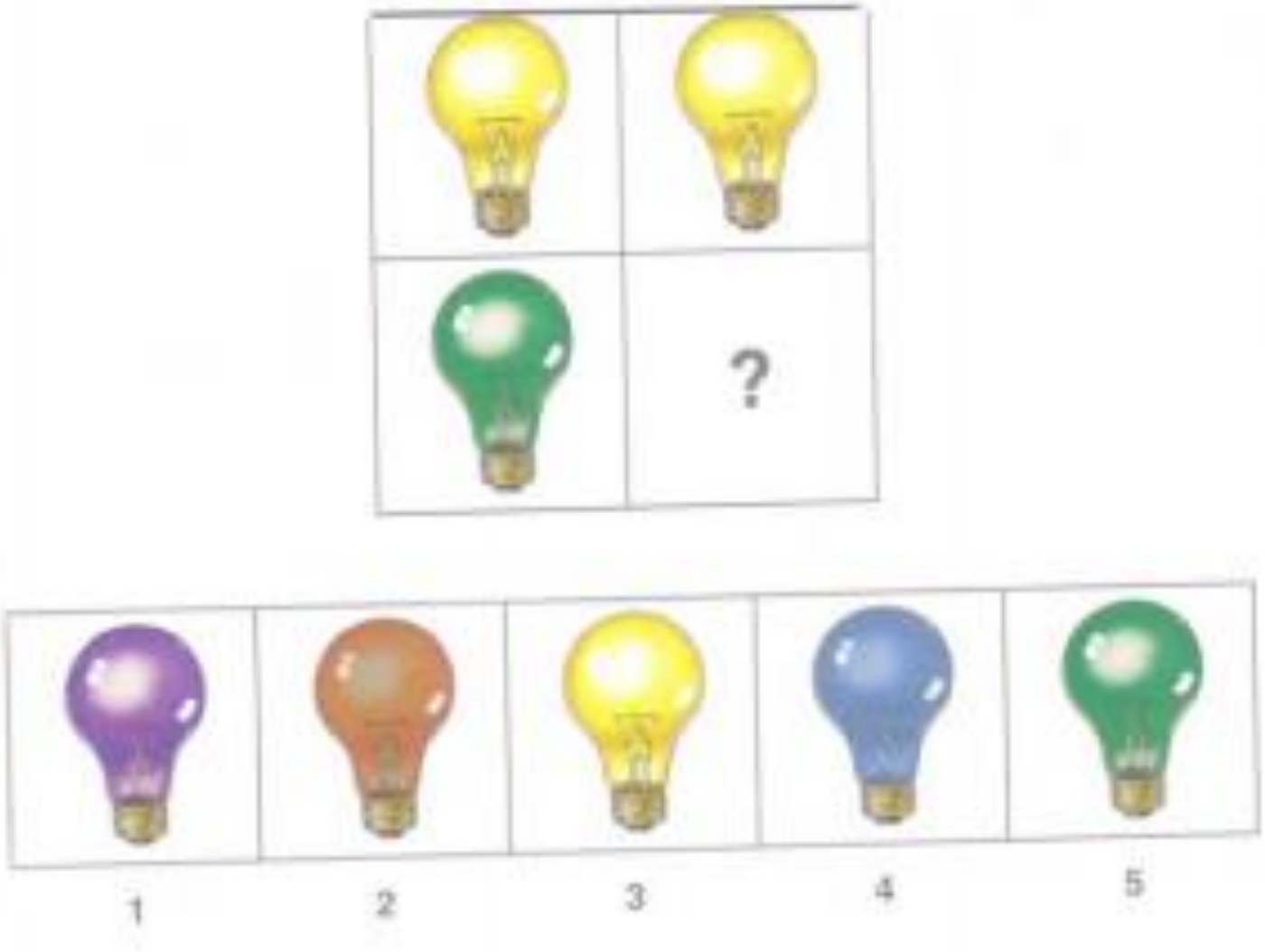


Saraf otonom

- Sistem saraf yang mengatur fungsi visceral tubuh, involunter dan timbul secara reflektoris
- Dipengaruhi oleh emosi
- Mempunyai jaras ascenden dan descenden
- Terintegrasi dengan fungsi luhur, misal fungsi
  - Eksekutif : Planning, Organizing dll
  - Bahasa
  - Memori
  - Emosi
  - spasial
- Terdiri dari bagian pusat dan bagian tepi
  - Bagian pusat
    - Sistem limbik, hipothalamus dan jaras-jaras yang menuju kolomna intermedio lateralis medula spinalis
  - Bagian tepi
    - Ganglion paravertebralis yang berhubungan dengan serabut aferen dan eferen yang berhubungan dengan organ dalam

EF as a Team of Conductors and Co-Conductors of the Brain's Orchestra

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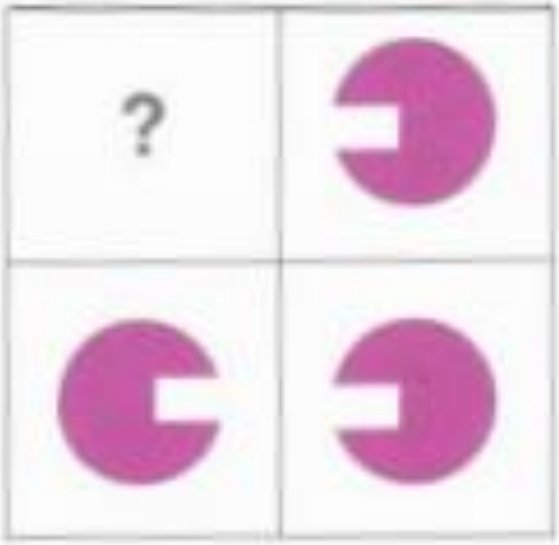
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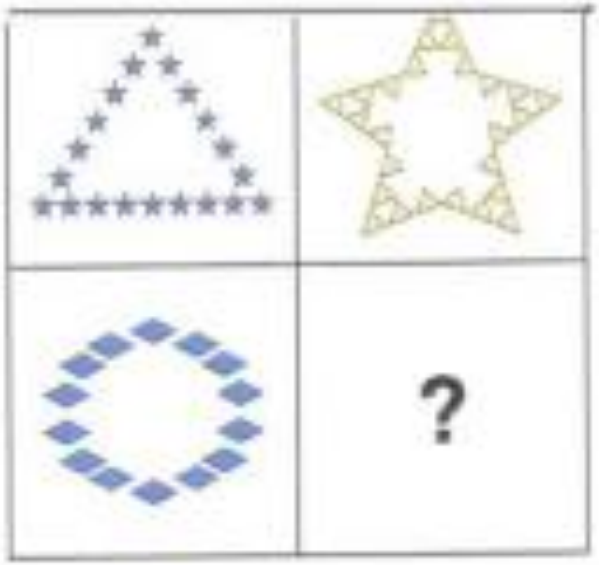
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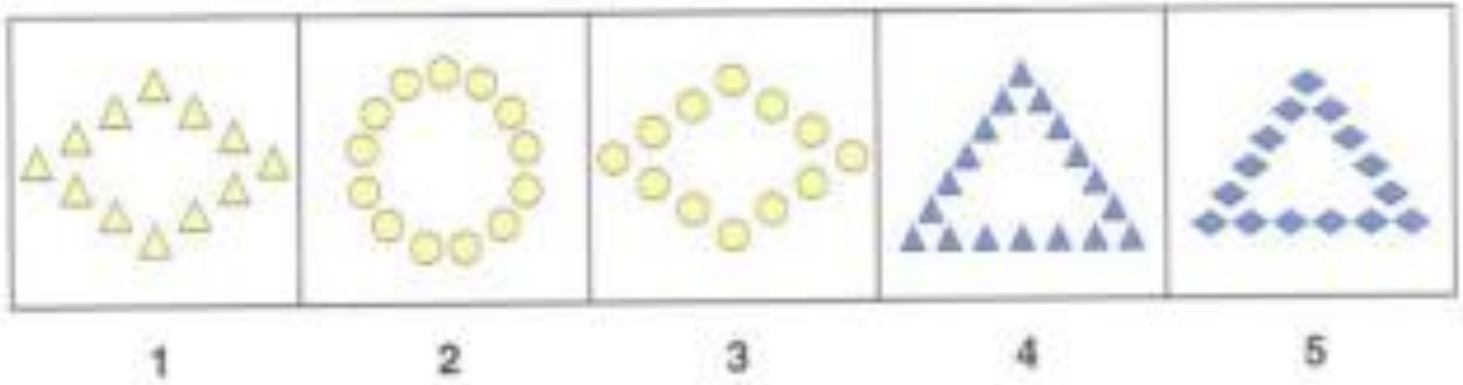
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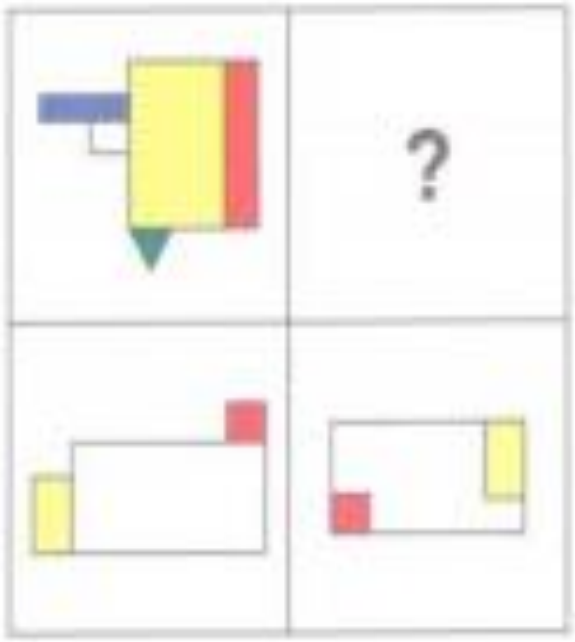
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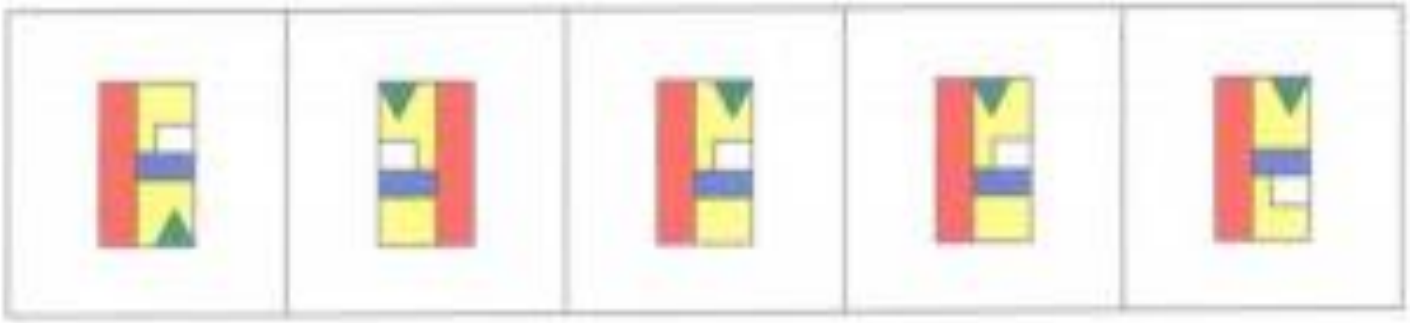
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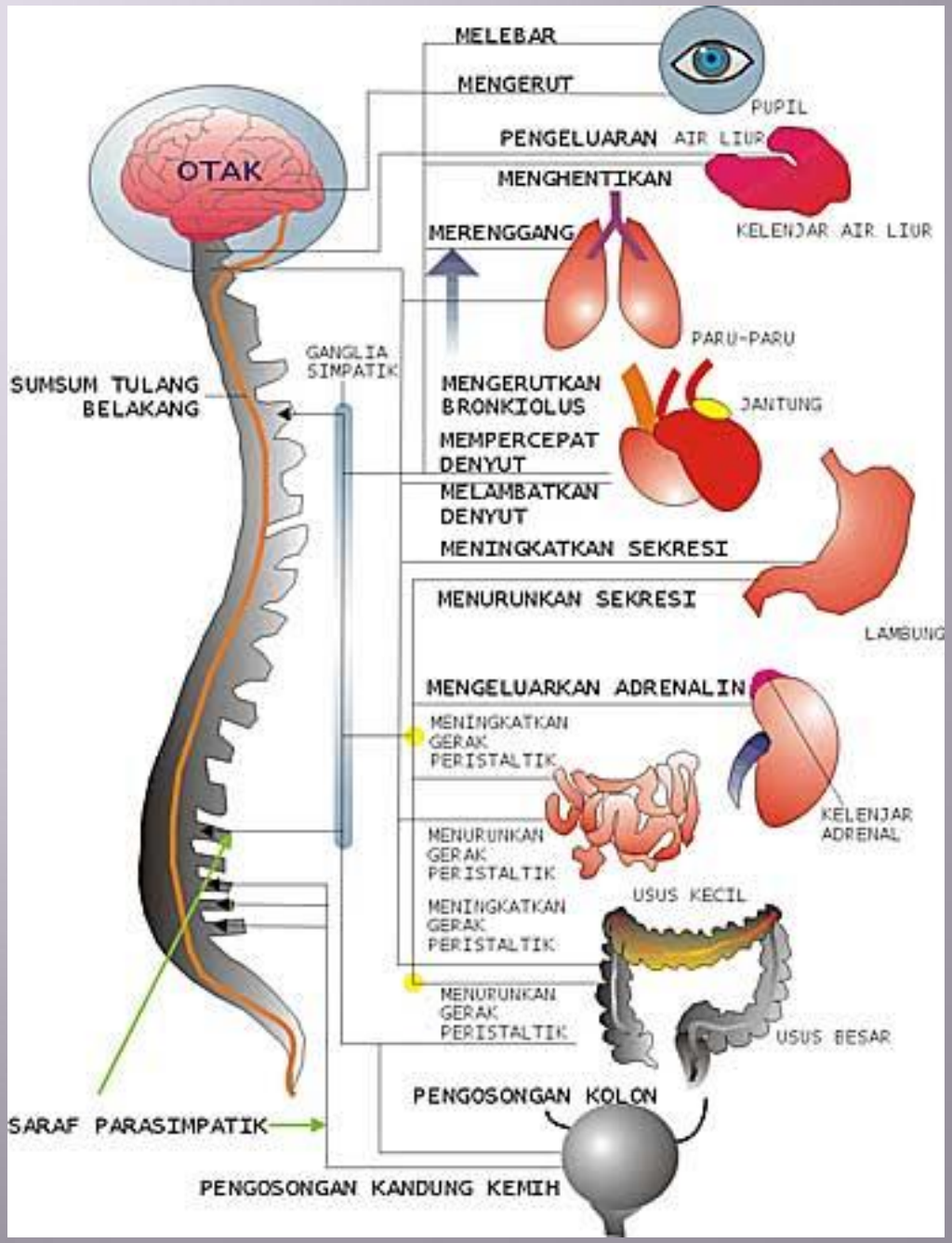
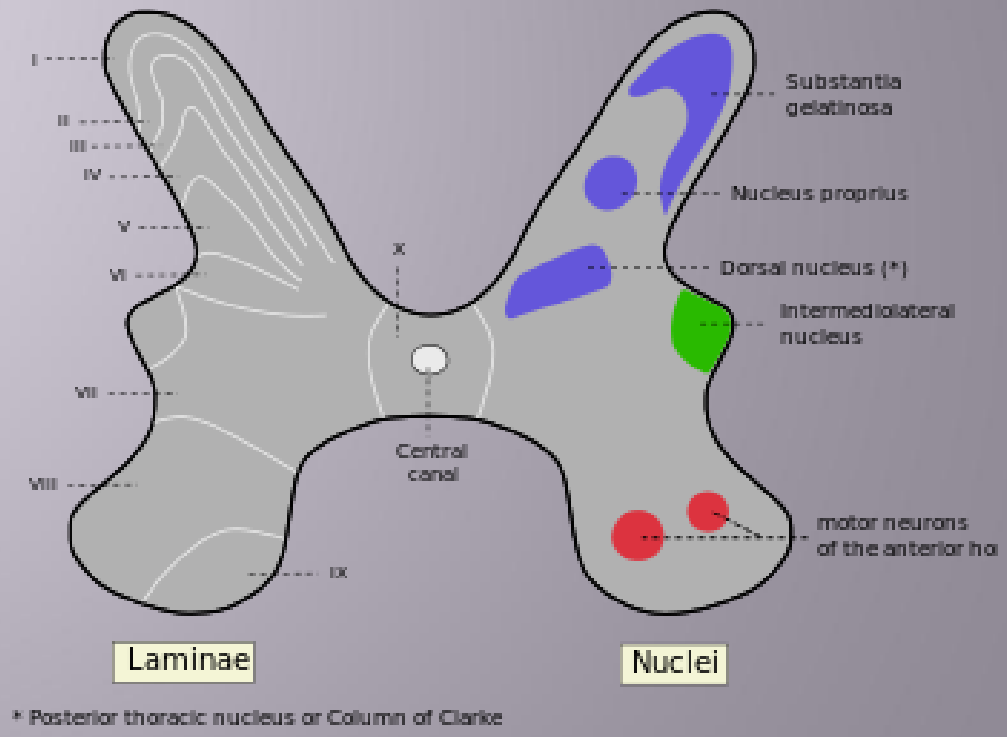
Saraf otonom

- Sistem ini membantu mengatur :
  - Tekanan darah, vasokontriksi-vasodilatasi
  - Motilitas dan sekresi gastrointestinal
  - Output urine
  - Bronkokontrisi - bronkhodilataasi
  - Berkeringat
  - Suhu tubuh
  - Haus, lapar
    dan lain-lain

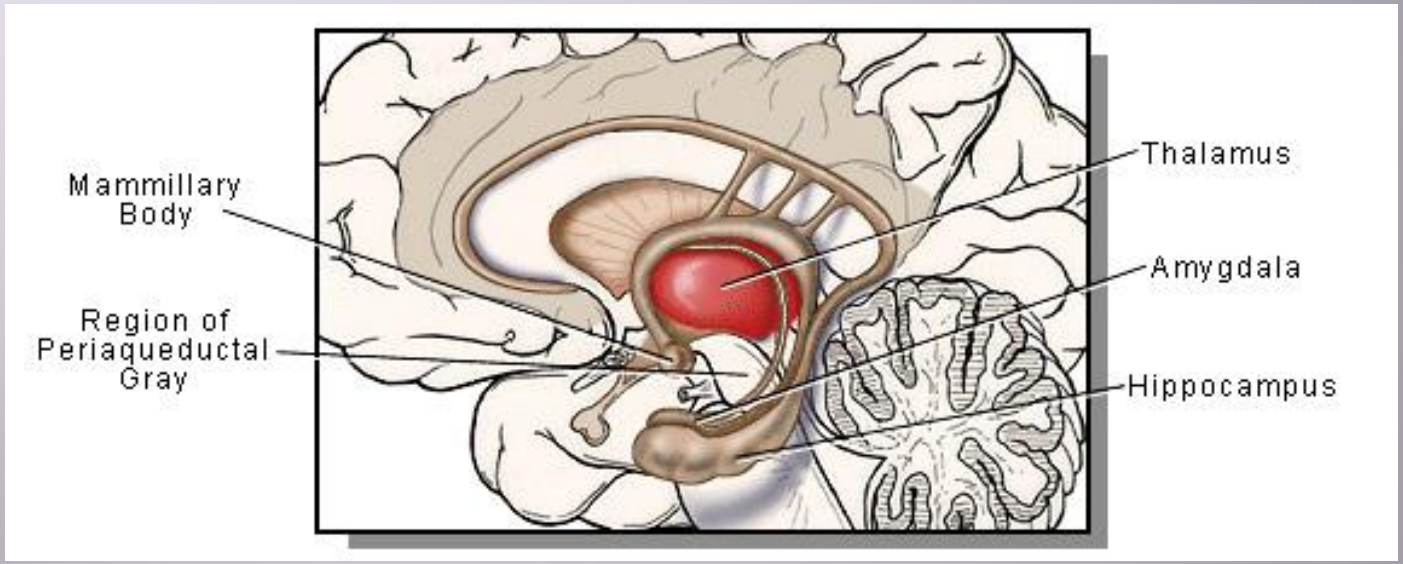

MELEBAR
MENGERUT
PUPIL
PENGELUARAN AIR LIUR
MENGHENTIKAN
KELENJAR AIR LIUR
OTAK
MERENGGANG
PARU-PARU
GANGLIA SIMPATIK
SUMSUM TULANG BELAKANG
MENGERUTKAN BRONKIOLUS
JANTUNG
MEMPERCEPAT DENYUT
MELAMBATKAN DENYUT
MENINGKATKAN SEKRESI
MENURUNKAN SEKRESI
LAMBUNG
MENGELUARKAN ADRENALIN
MENINGKATKAN GERAK PERISTALTIK
KELENJAR ADRENAL
MENURUNKAN GERAK PERISTALTIK
USUS KECIL
MENINGKATKAN GERAK PERISTALTIK
MENURUNKAN GERAK PERISTALTIK
USUS BESAR
PENGOSONGAN KOLON
SARAF PARASIMPATIK
PENGOSONGAN KANDUNG KEMIH

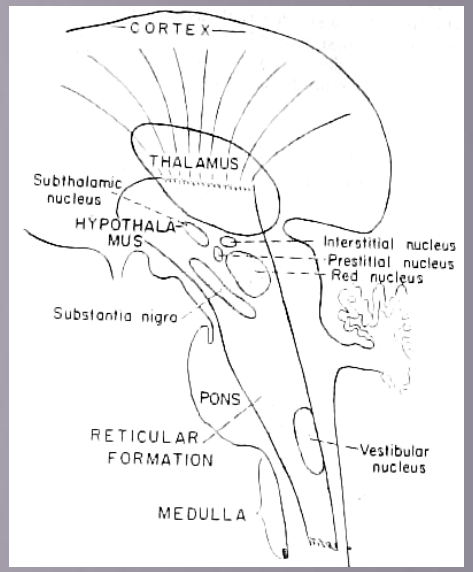
Saraf Otonom bagian Pusat

- Serebrum
- Hipothalamus
- Sistem limbik
- Hipofisis
- Jaras yang menghubungkan intermedio lateralis medula spinalis



Hipothalamus





- Merupakan bagian ujung depan diencephalon yang terletak dibawah sulkus hipothalamic dan di depan nukleus interpudenkular.
- Terdapat hubungan saraf antara hipothalamus
  - Korteks serebri
  - Lobus posterior hipofisa
  - Serta hubungan vaskuler antara hipothalamus dan lobus anterior.

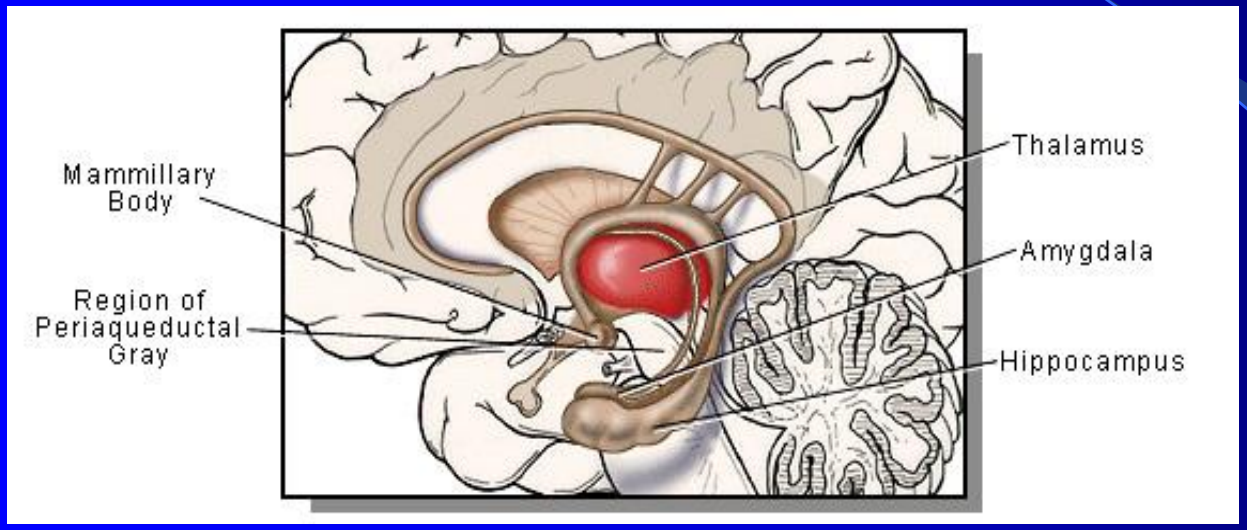
Hipothalamus

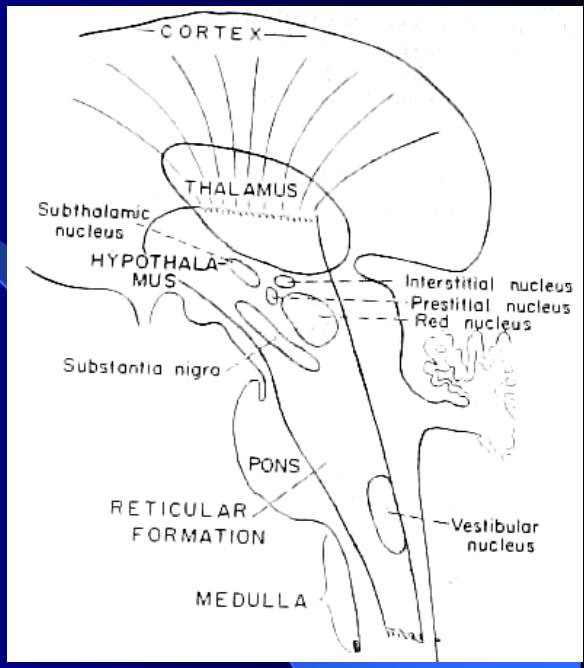
The head ganglion of outonomic nervous system

Fungsi

- Pengaturan endokrin
- Pengaturan nafsu makan
- Pengaturan air tubuh
- Pengaturan suhu
- Pengaturan kardiovaskuler
- Seksual
- Emosi
- Mengatur saraf otonom perifer

Hipothalamus





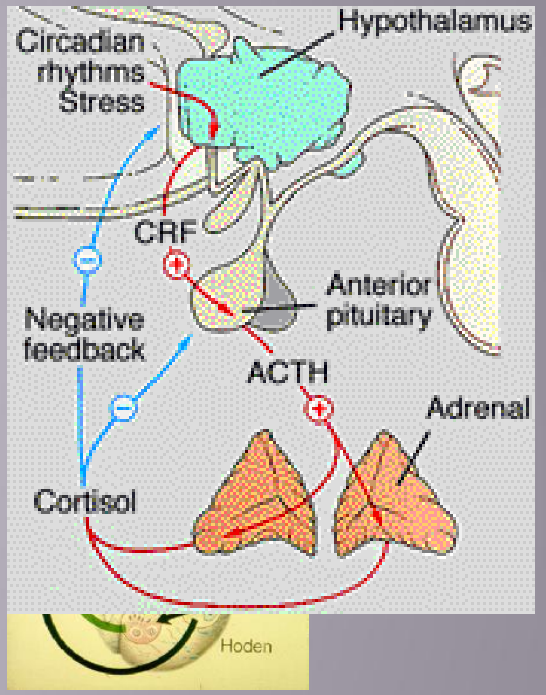
- Merupakan bagian ujung depan diencephalon yang terletak dibawah sulkus hipothalamic dan di depan nukleus interpudenkular. Terdapat hubungan saraf antara hipothalamus dan lobus posterior hipofisa serta hubungan vaskuler antara hipothalamus dan lobus anterior.

Fungsi

- Pengaturan suhu
- Pengaturan kardiovaskuler
- Pengaturan endokrin
- Pengaturan nafsu makan
- Pengaturan air tubuh

Hipothalamus

- Pengaturan endokrin
  - Gland hipofisa anterior
    - Perangsangan timbulkan sekresi :
      - Tirotropin
      - Kortikotropin
      - Pemacu FSH
      - Pemacu LH
  - Gland hipofisa posterior
    - Osmoreseptor mengatur cairan
  - Gland pinealis (h. Melatonin)
  - Gland suprarenalis (h. adrenalin & noradrenalin)
  - Sel Junctaglomerular ginjal (renin)
  - Gland paratiroidea (PTH, CT)
  - Insula langerhans pankreas



Hipothalamus

- Pengaturan nafsu makan
  - Reseptor proses lapar
  - Reseptor kimia darah
  - Hipothalamus
    - Medial —» Pusat kenyang
      - Menentang keinginan makan
      dirangsang –» tak mau makan
      dirusak –» rasa lapar terus
      —» kegemukan
    - Lateral —» Pusat lapar
      dirangsang –» lapar terus
      dirusak –» tidak lapar

- Pengaturan air tubuh
  - Osmoreseptor di hipothalamus lateral
    - Cairan (elektrolit) pekat –» ingin minum.
    - Cairan encer–» hambat sekresi ADH
      —» ingin kencing

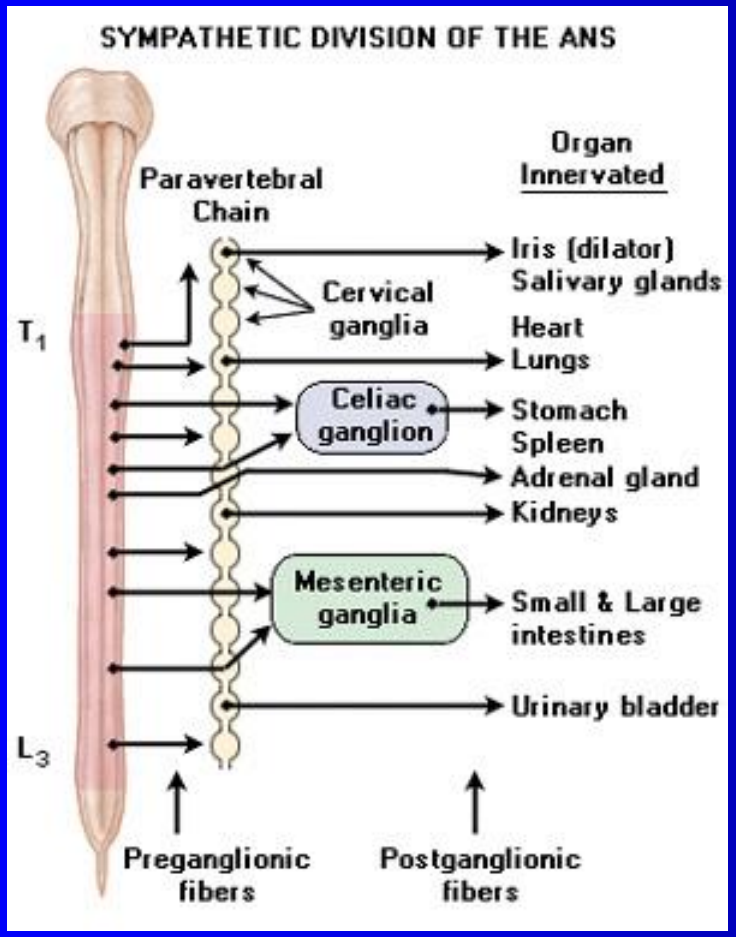
  Aldosteron ↑ merasa haus o.k Na ↑

Hipothalamus

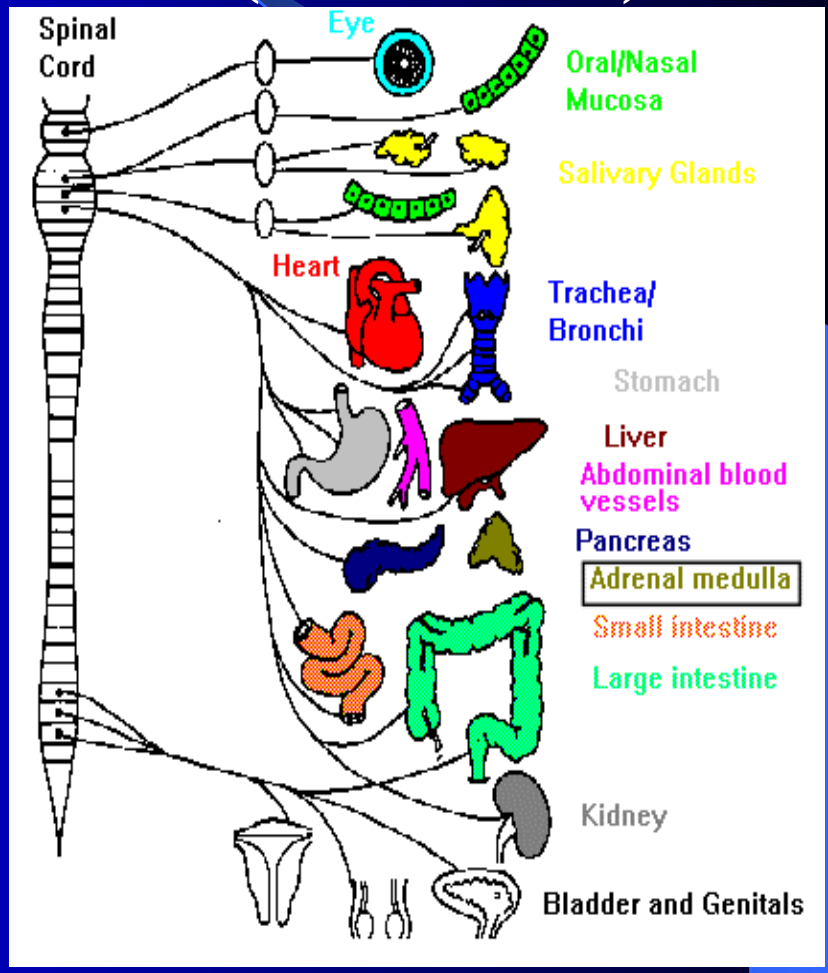
- Pengaturan suhu
  - Hipothalamus anterior
    - Pusat pengaturan panas.
    - Bila dipacu reseptor suhu
      - Vasodilatasi kulit
      - Terengah-engah
      - Menghambat menggigil (dilingkungan dingin)
  - Hipothalamus posterior
    - Pusat konservasi (penahan) dingin
    - Bila digiatkan oleh reseptor suhu:
      - Menggigil
      - Vasokonstriksi
      - Pilo ereksi
- Pengaturan kardiovaskuler
  - Rangsang pada talamus posterior & lateral
    - Tekanan arteri ↑
    - Frekwensi jantung ↑
  - Rangsang pada preoptik
    - Tekanan arteri ↓
    - Frekwensi jantung ↓

Saraf otonom bagian perifer
dibagi 2 :

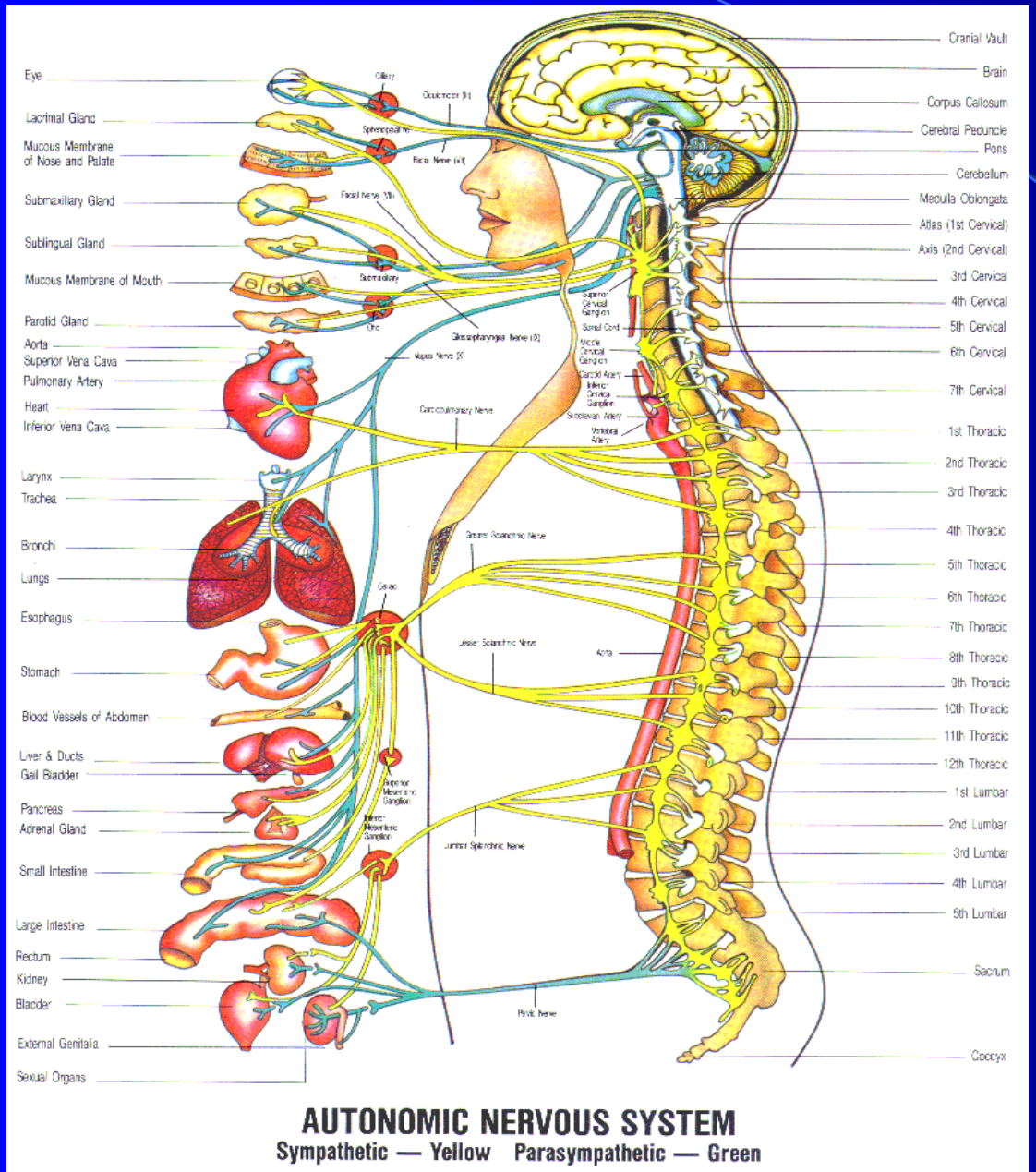
- Saraf simpatis (thoraco lumbal)



- Saraf parasimpatis (craniosacral)



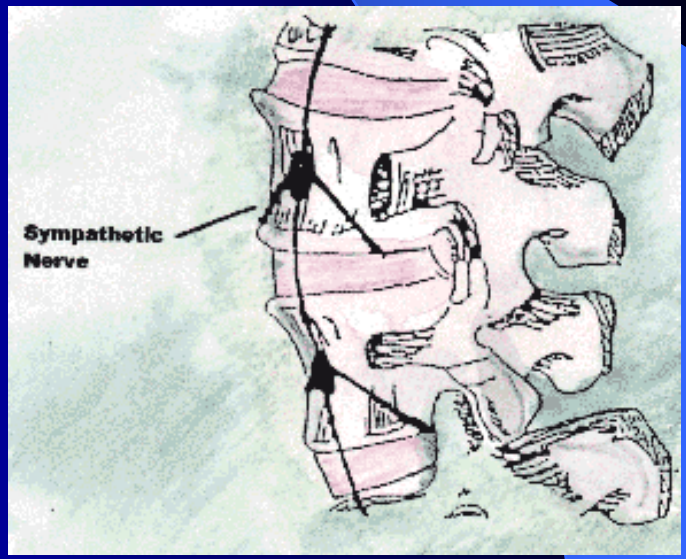
Saraf otonom



AUTONOMIC NERVOUS SYSTEM

Sympathetic — Yellow Parasympathetic — Green

- ***Parasympathetic:***
  - **III** Oculomotor
  - **VII** Facial
  - **IX** Glossopharyngeal
  - **X** Vagus



Serabut saraf simpatis

- Bagian perifer system saraf simpatis
  - Ganglia paravertebralis → 2 rantai
  - 2 ganglia prevertebral
    - Ganglion seliaka
    - Pleksus hipogastrikus
  - Saraf-saraf yang menyebar dari ganglia ke organ interna

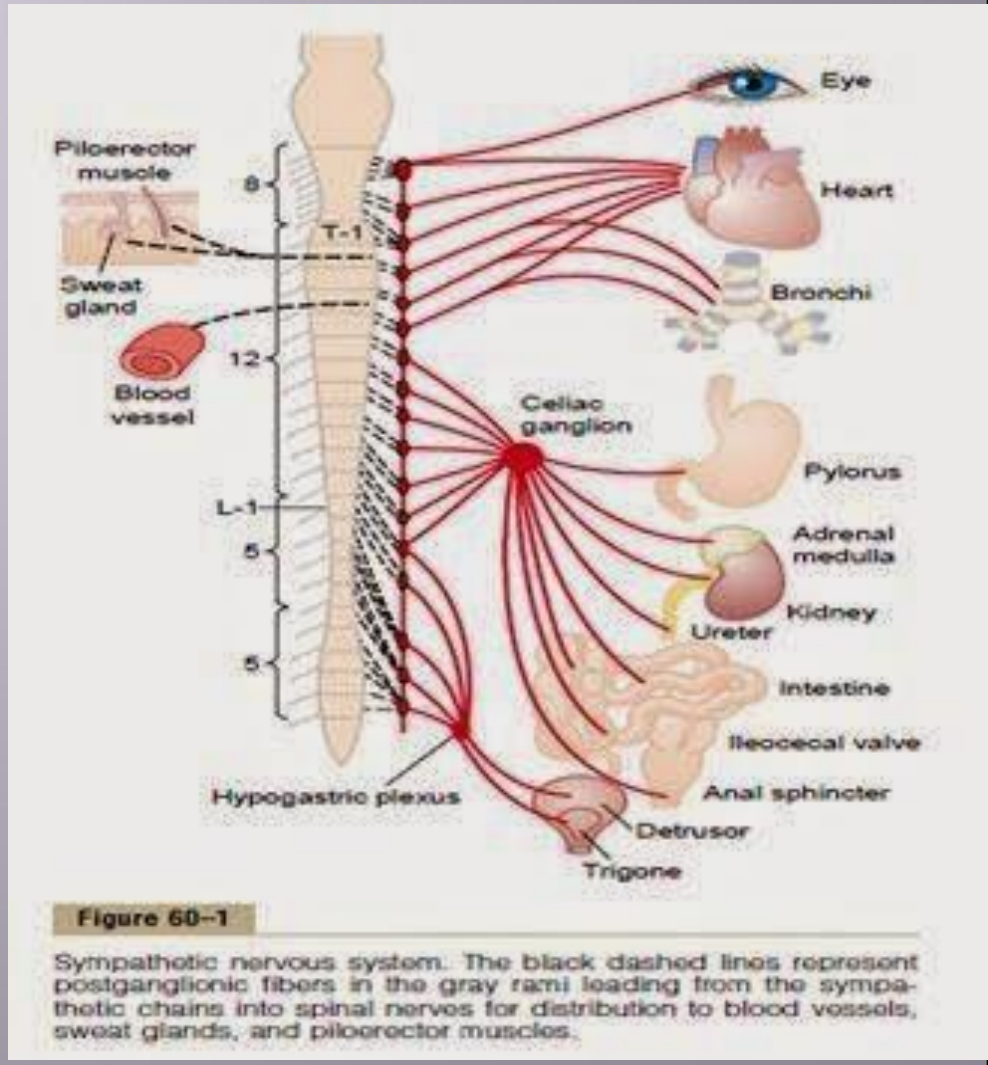


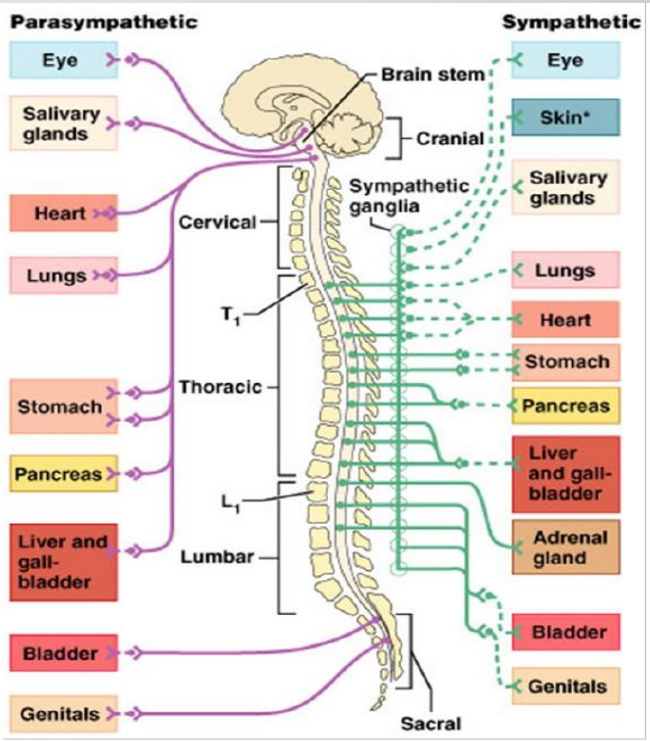
Figure 60–1

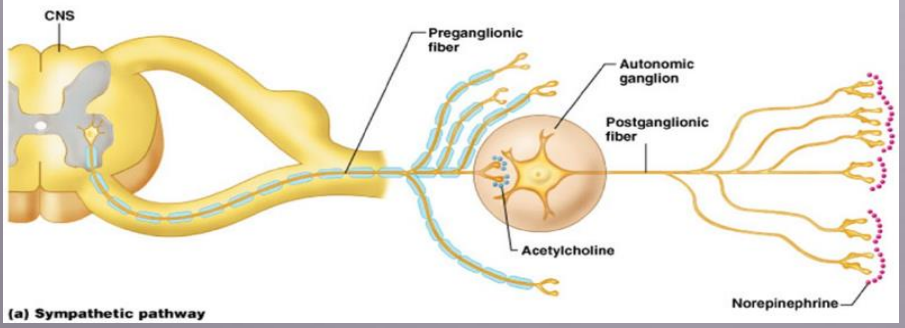
Sympathetic nervous system. The black dashed lines represent postganglionic fibers in the gray rami leading from the sympathetic chains into spinal nerves for distribution to blood vessels, sweat glands, and piloerector muscles.

Serabut saraf simpatis

- Neuron pre dan post ganglion
- Badan sel neuron pregangl terletak di kornu intermediolateral →radiks ant^{or} → saraf spinal→ ramus putih → salah satu ganglia rantai simpatis, selanjutnya
  - Bersinap postganglionik simpatis
  - Berjalan ke atas/bawah dalam rantai → bersinap di salah satu ganglia lain rantai tersebut
  - Berjalan menempuh pada jarak yang berbeda-beda → salah satu saraf simpatis dan bersinap di gangl simpatis perifer

Somatis dan Otonom





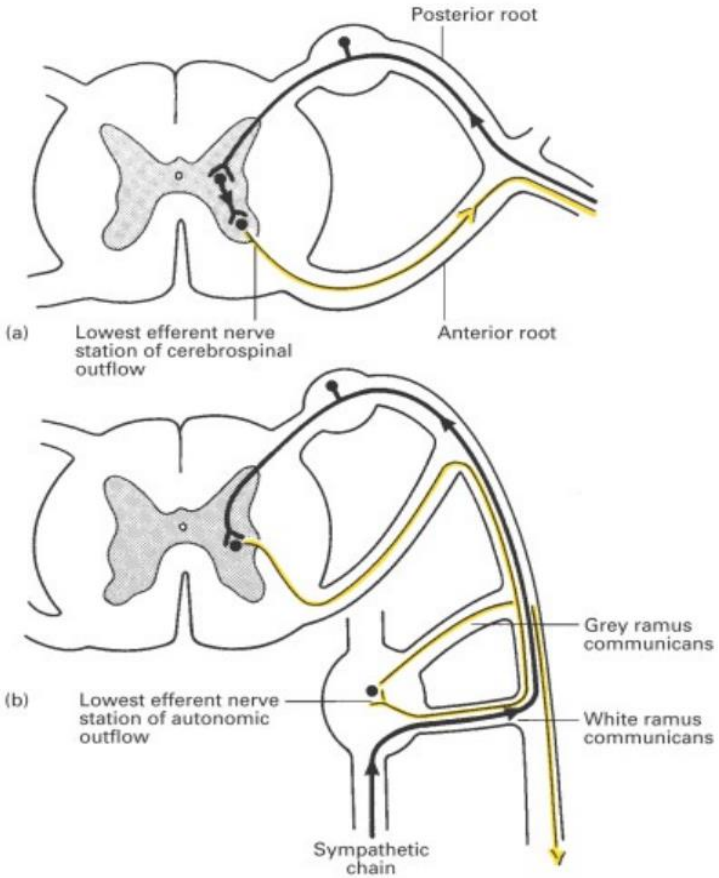


Fig. 149 Diagram to show the essential difference between the cerebrospinal and autonomic outflows: (a) the cerebrospinal system has its lowest efferent nerve cell stations within the central nervous system; (b) the autonomic system has its lowest efferent cell stations in a peripheral ganglion (here illustrated by a typical sympathetic nerve ganglion).

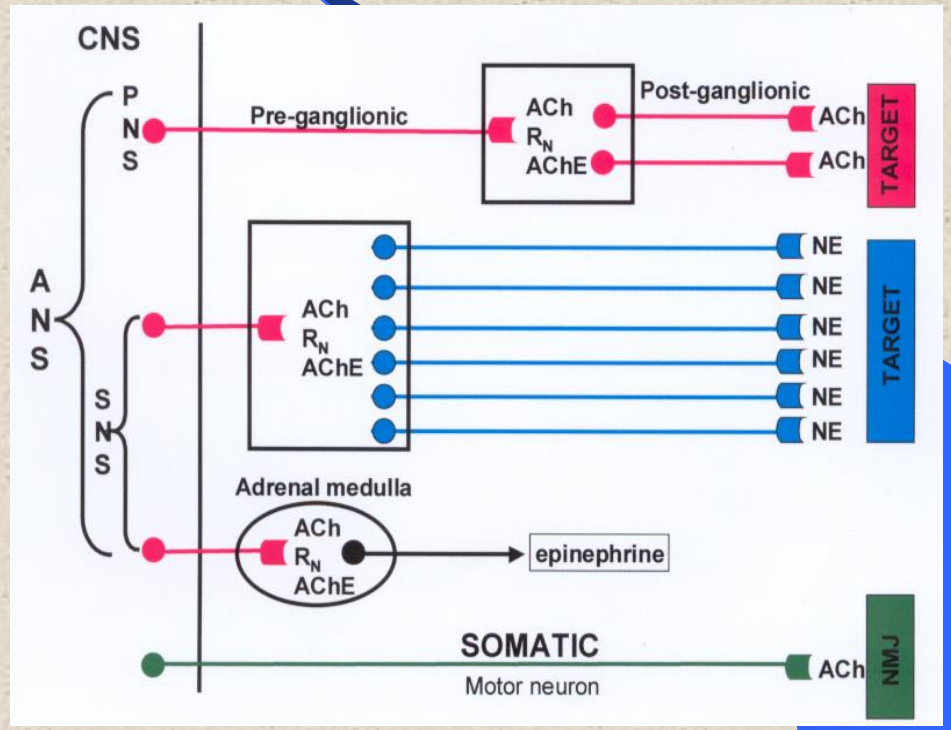
Serabut saraf simpatis

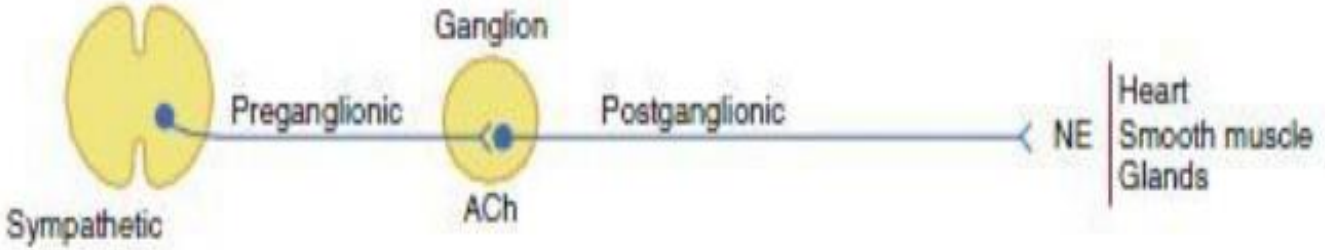
- Saraf skeletal
  - Sebagian serat post ganglionik berjalan kembali dari rantai simpatis ke saraf spinal melalui rami kelabu
  - Serabut tipe C
  - Mengatur pembuluh darah, kelenjar keringat dan otot piloerektor rambut
- Pembagian segmen
  - T1 → rantai simpatis →daerah kepala
  - T2 → leher
  - T3-6 → thoraks
  - T7-11 → Abdomen
  - T12, L1-2 --< tungkai

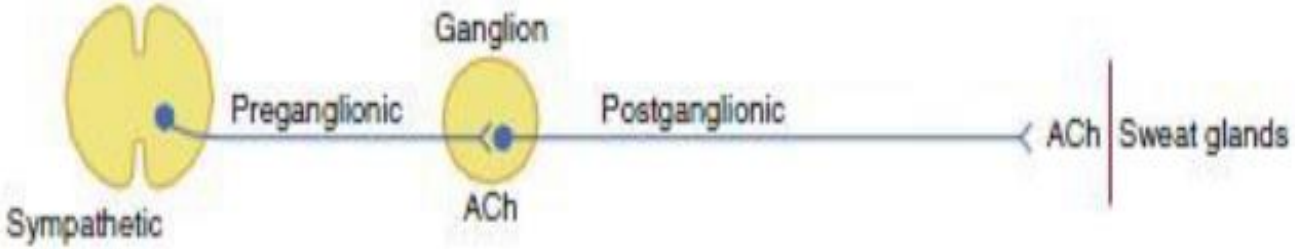
→tumpang tindih

Saraf otonom

- The **AUTONOMIC NERVOUS SYSTEM** consists of the ***Sympathetic*** and the ***Parasympathetic*** Nervous Systems. Both the SNS and the PNS make their first connections outside the CNS in specialized synapses called *ganglia*. Note that the neurotransmitter in PNS *and* SNS ganglia is **ACh** which interacts with **nicotinonic receptors.** Activity in autonomic ganglia is terminated by **acetylcholinesterase (AChE)**-mediated breakdown of ACh. All cholinergic nerves in the Autonomic Nervous System are labeled in red. In the PNS, post-ganglionic nerves release **ACh,** which interacts primarily with **muscarinic receptors** in a variety of target tissues. Here, as in the ganglia, the actions of ACh are terminated by **AChE**.







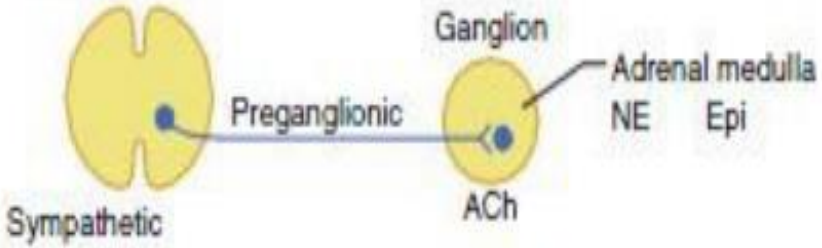
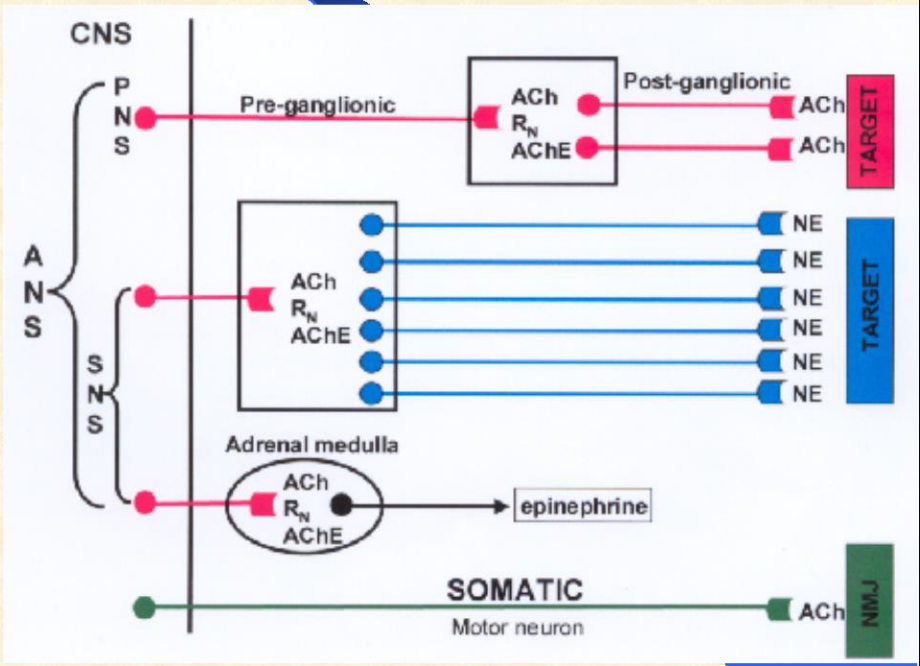


Figure 16-1. Autonomic nervous system neurotransmission. *ACh*, Acetylcholine; *Epi*, epinephrine; *NE*, norepinephrine.

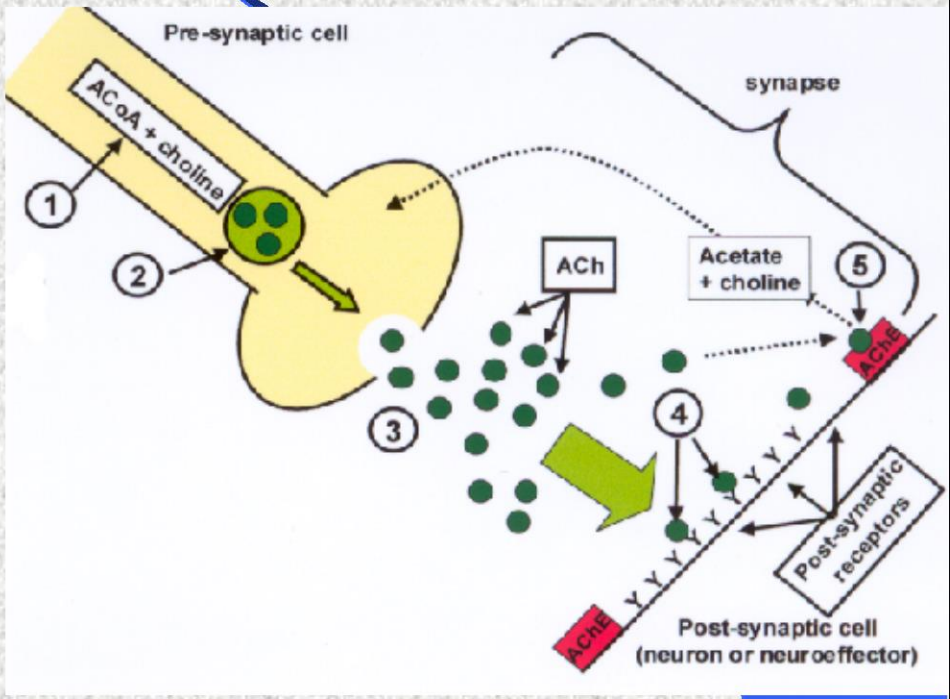
Saraf otonom

- While sympathetic autonomic *ganglia* are **cholinergic synapses**, post-ganglionic sympathetic nerves are *adrenergic* nerves: They release **norepinephrine** which interacts with **α (alpha)** and **β (beta)** receptors All adrenergic nerves in the SNS are labeled in **blue**. The ***Somatic (Voluntary)*** Nervous System is also a cholinergic pathway, but unlike the SNS and PNS, it has no ganglia. Instead, **motor neurons** arising in the spinal cord terminate at a specialized synapse in skeletal muscle called the **neuromuscular junction (NMJ)**. This is still a cholinergic synapse because **ACh** is released by the motor neuron, interacts with **nicotinic receptors** and is broken down by **AChE**



Parasympathetic (Cholinergic) synaps

1. synthesis of acetylcholine (ACh) from acetyl CoA and choline
2. storage of ACh in synaptic vesicles
3. release of ACh (fusion of synaptic vesicle with presysnaptic membrane and release of ACh into the synapse)
4. action of ACh by binding to and activating receptors (nicotinic in autonmic ganglia and NMJ and muscarinic in many sites)
5. inactivation by enzymatic breakdown of ACh by acetylcholinesterase (AChE) located in the synapse



Nor Epinefrin

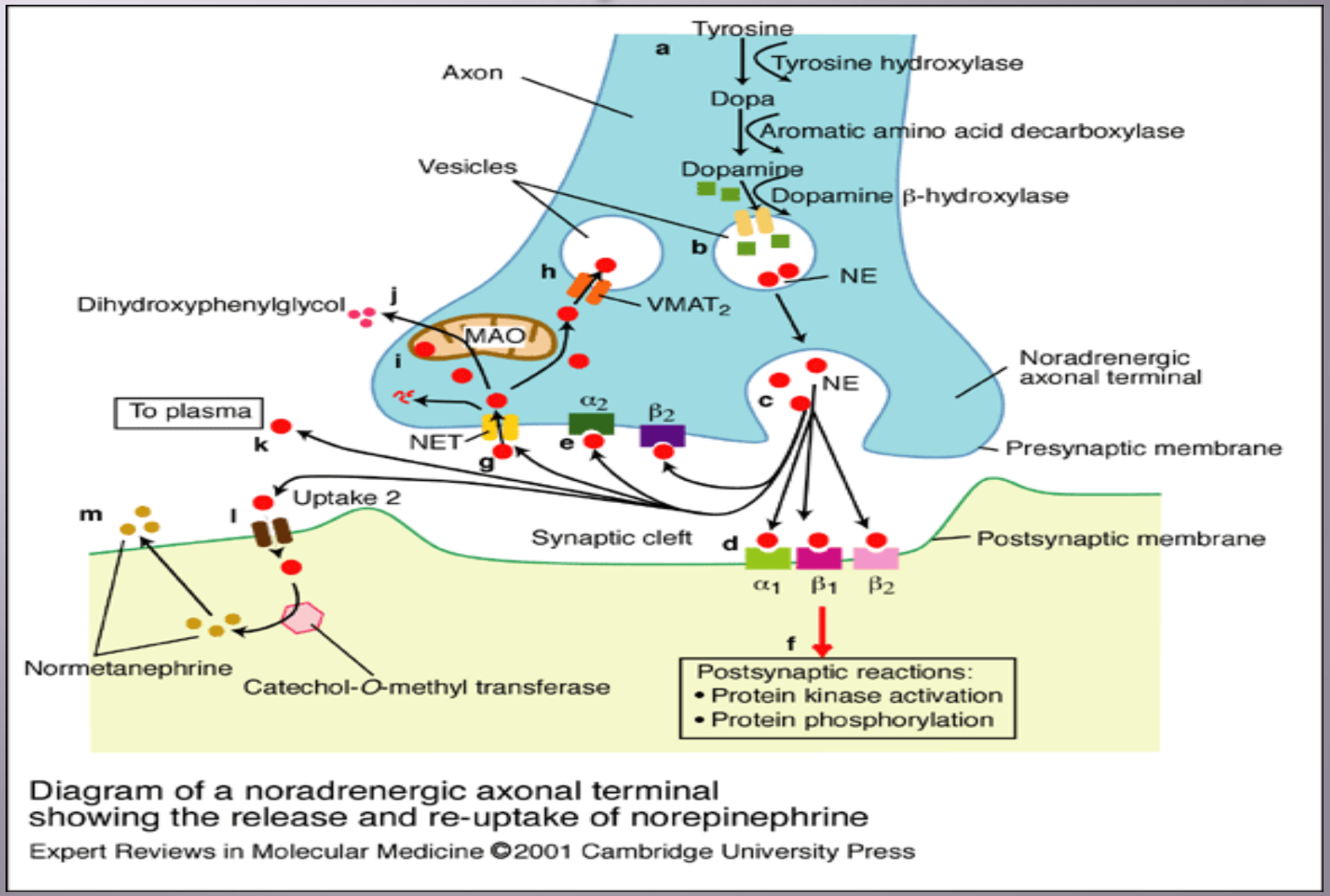
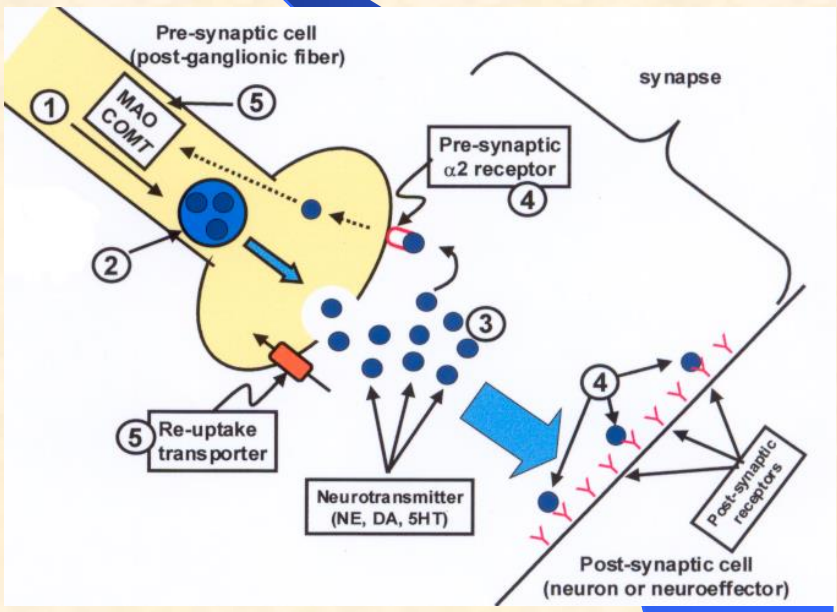


Diagram of a noradrenergic axonal terminal showing the release and re-uptake of norepinephrine

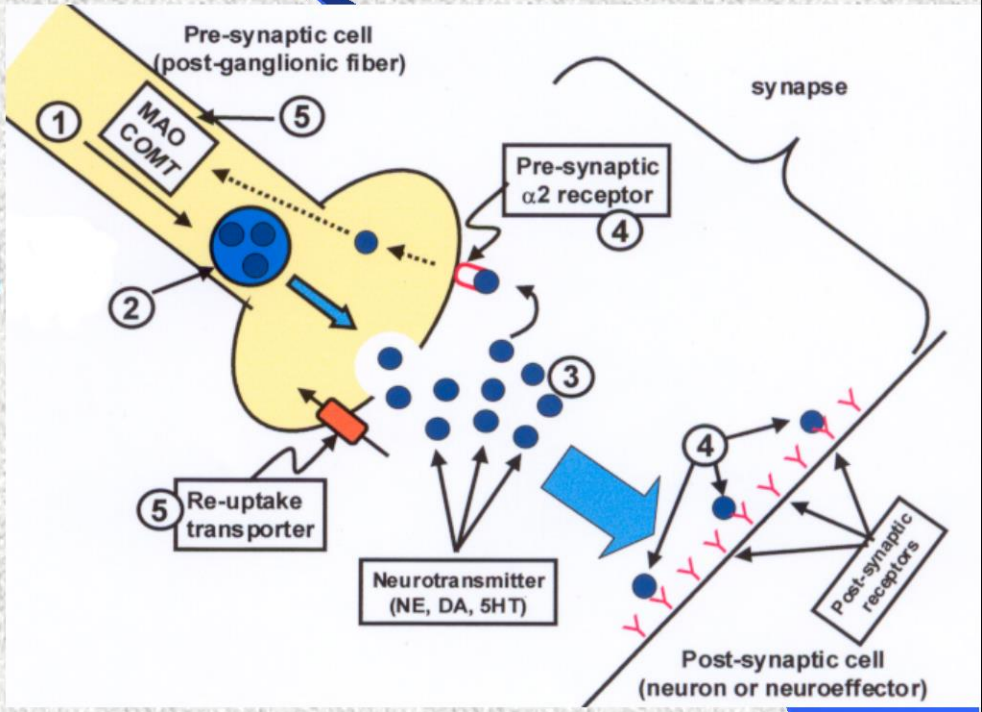
Sympathetic synaps

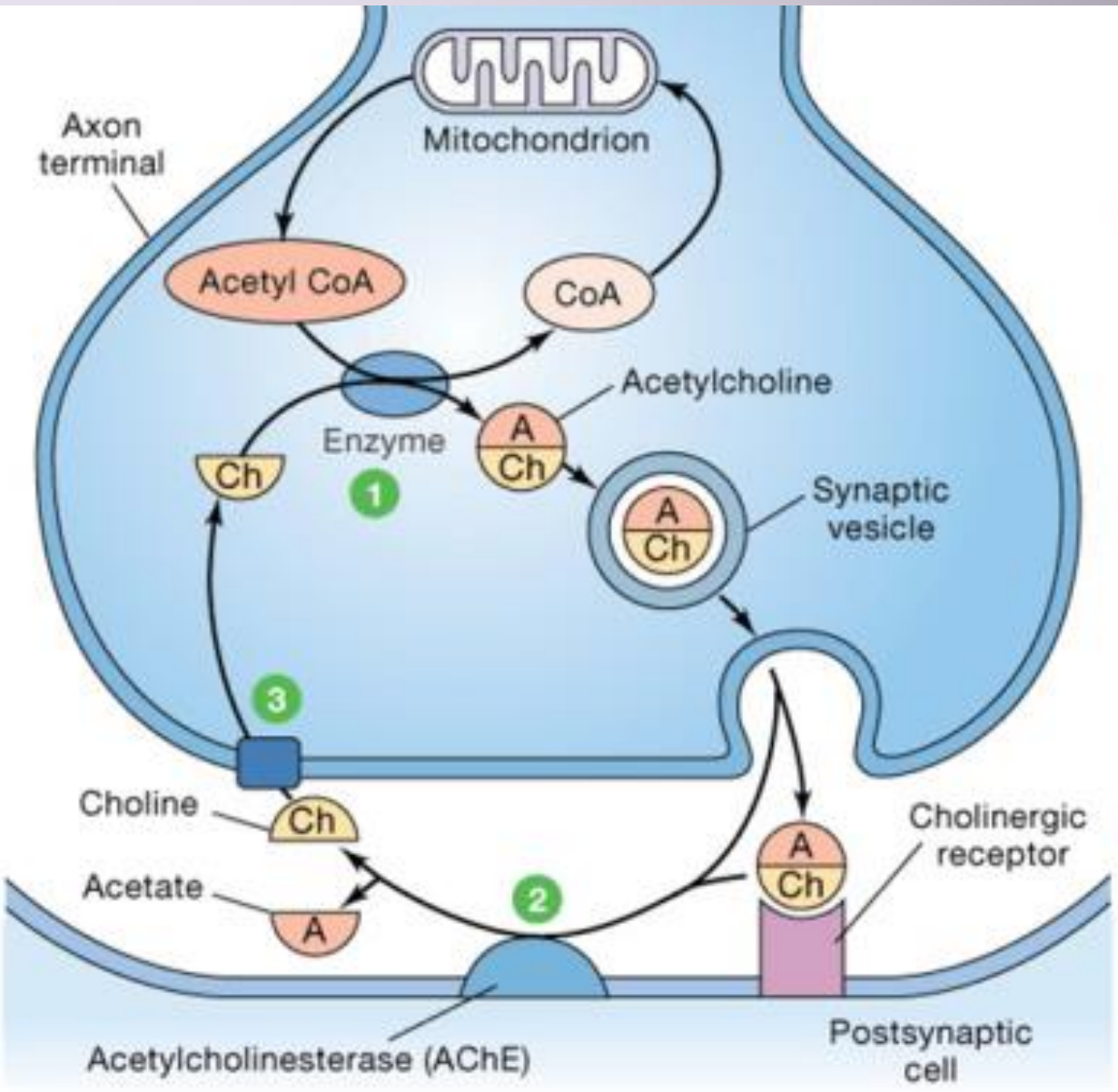
1. synthesis of norepinephrine (NE - not pictured)
2. storage of NE in vesicles
3. release of NE: fusion of synaptic vesicles with presysnaptic membrane and release of NE into the synapse
4. action of NE through binding to and activating receptors (α_2 presynaptic and α and β post synaptic)
5. inactivation by presynaptic re-uptake transporters (also presynaptic receptors shut off further NE release)



Sympathetic (Adrenergic) Drugs

- **Adrenergic agonists** are sub-divided into 3 classes; **direct-acting**, **indirect-acting** and **dual-acting** agonists.
  - Direct-acting agonists bind to and activate a1, a2, b1 and b2 receptors. Fig 3 indicates pre-synaptic a2 receptors and site 4 has a1, a2, b1 and b2 receptors. Naturally -occurring molecules which bind to these receptors include norepinephrine (NE; a neurotransmitter which binds to a1,a2 and b1 receptors), epinephrine (EPI; a hormone produced in and secreted from the adrenal medulla which binds to a1,a2,b1 and b2 receptors -- EPI is a non-selective adrenergic agonist) and dopamine (DA; also a neurotransmitter which binds to DA receptors as well as a1, a2 and b1 receptors). In addition, the synthetic catecholamine isoproterenol binds to b1 and b2 receptors (it is a non-selective b agonist), but has virtually no effect on a receptors.
  - Indirect-acting adrenergic agonists (i.e. amphetamines and cocaine) produce NE-like actions by stimulating NE release (Fig 3 site 3) and preventing its re-uptake (Fig 3 site 5) and thus its inactivation . By preventing NE inactivation, these drugs allow NE to linger in adrenergic synpases. Notice that this is different from the way indirect-acting cholinergic agonists work as they inhibit the activity of AChE, preventing ACh breakdown and allowing it to linger at cholinergic sysnapse.
  - Dual-acting adrenergic agonists (i.e. ephedrine) act as a direct- and an indirect-adrenergic agonists (hence dual-acting) - they bind to adrenergic receptors and stimulate NE release.





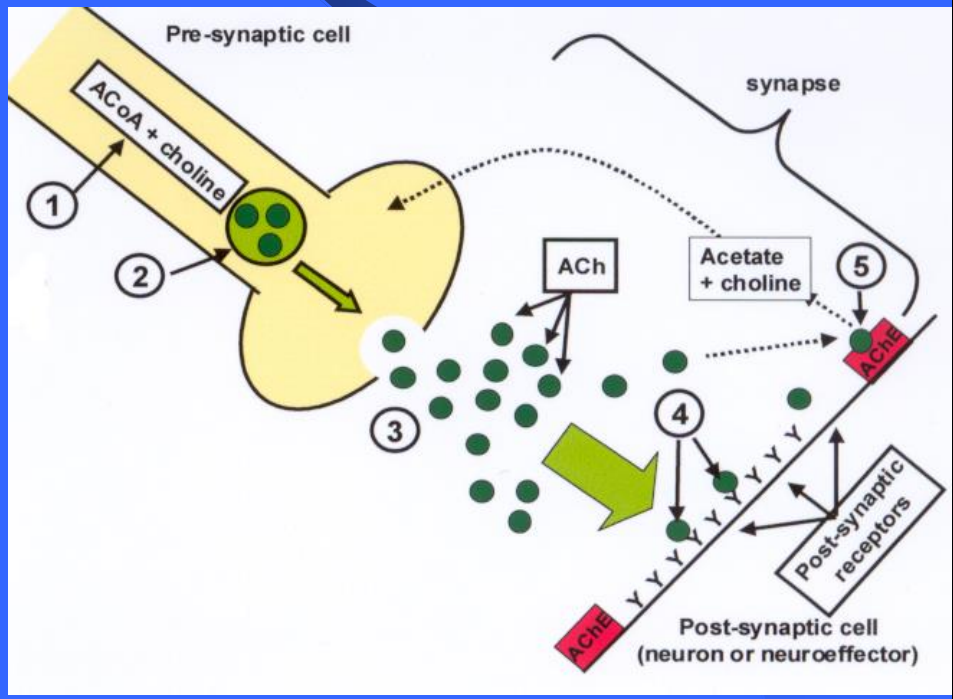
1. **Acetylcholine** (ACh) is made from choline and acetyl CoA.

2. In the synaptic cleft ACh is rapidly broken down by the enzyme **acetylcholinesterase.**

3. Choline is transported back into the axon terminal and is used to make more ACh.

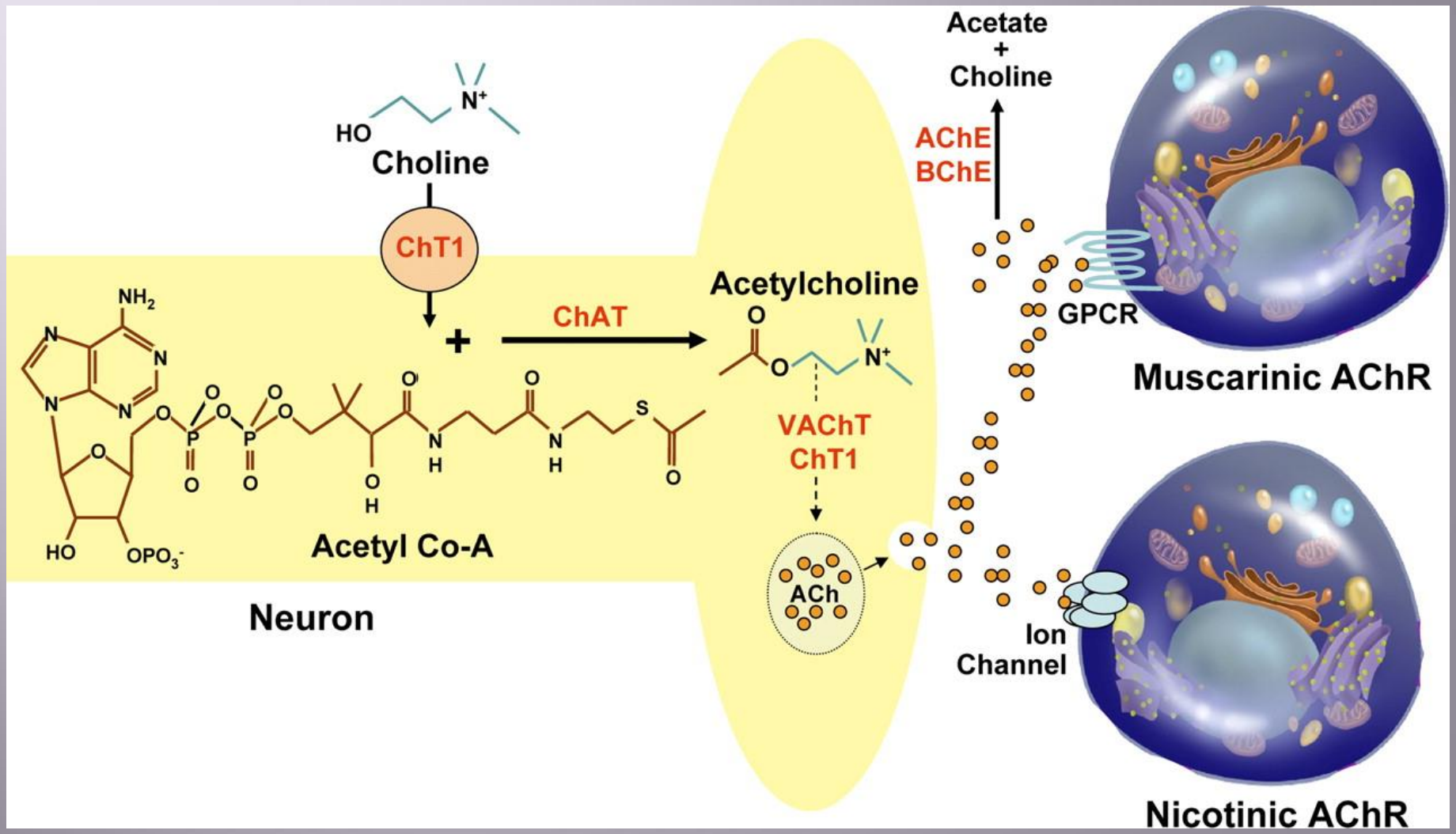
Parasympathetic (Cholinergic) Drugs

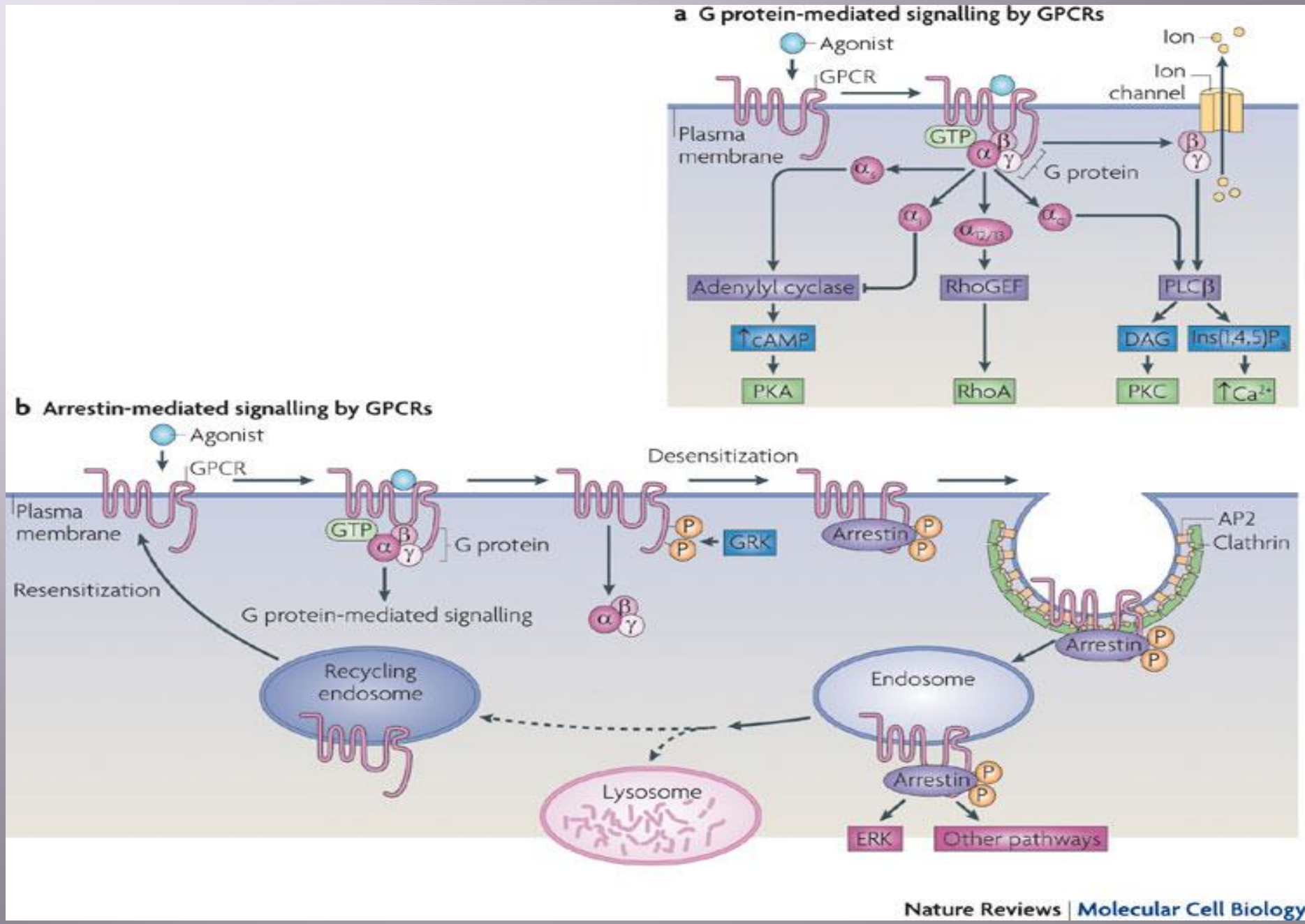
- **Cholinergic agonists** are subdivided into ***direct-acting*** and ***indirect-acting*** agonists. **Direct-acting agonists** bind to and activate receptors (Fig 2, site 4) at autonomic ganglia (nicotinic), the neuromuscular junction (nicotinic), and a variety of tissues such as the GI tract, heart, exocrine glands (muscarinic). Activation of ganglionic nicotinic receptors leads to activation of SNS pathways following by PNS pathways. This is result of the greater number of post-ganglionic fibers in the SNS. Thus ganglionic ***agonists*** activate SNS pathways first and ***antagonists*** block SNS responses first. Activation of nicotinic receptors at the NMJ leads to skeletal muscle contraction. Thus ***agonists*** (***depolarizing neuromuscular blocking agents***) lead to muscle contraction (followed by paralysis) while ***antagonists*** (***non-depolarizing neuromuscular blocking agents***) prevent muscle contraction and produce flaccid paralysis. Activation of muscarinic receptors produce 4 responses we're interested in in this class: increased GI tone and motility, increased urinary bladder tone and motility, increased salivation and sweating and decreased heart rate and blood pressure. Thus muscarinic receptor ***agonists*** produce all these responses and can be used to treat non-obstructive constipation and urine retention. They also cause side effects such as diarrhea, drooling and hyperhidrosis, bradycardia and hypotension. ***Antagonists*** produce the opposite effects and can be used to treat diarrhea, to dry up glandular secretions, and increase heart rate while producing side effects such as constipation, dry mouth and tachycardia. **Indirect-acting agonists** produce ACh-like effects by inhibiting the activity of AChE (Fig 2, site 5). Since AChE is the primary way transmission is terminated at *all* cholinergic synapses . these drugs act at virtually all synapses where ACh is the neurotransmitter (i.e. autonomic ganglia (if they're relatively uncharged), NMJ, and muscarinic receptors



SUMMARY of CHOLINERGIC RECEPTOR ACTION

RECEPTOR	LOCATION	AGONIST	ANTAGONIST
nicotinic	autonomic ganglia neuromuscular junction	activates SNS post-ganglionic fibers then PNS post-ganglionic fibers (uses?) skeletal muscle contraction (used to intensify muscle contractions in myesthenia gravis; as neuromuscular blocking agents)	blocks activation of SNS pos-t ganglionic fibers then PNS fibers (treat hypertension) causes muscle relaxation/paralysis
muscarinic	GI smooth muscle urinary bladder smooth muscle heart blood vessels sweat glands salivary glands	increases GI tone/motility (treat constipation) increases urinary bladder tone and motility (treat urine retention) decreases heart rate decreases blood pressure increases sweating increases salivation	decreases GI tone and motility (treat diarrhea) decrease urinary tone and motility increases heart rate (treat bradycardia) increases blood pressure decreases sweating decreases salivation


Choline
ChT1
Acetyl Co-A
ChAT
Acetylcholine
VAChT
ChT1
ACh
Neuron
Acetate
+
Choline
AChE
BChE
GPCR
Muscarinic AChR
Ion
Channel
Nicotinic AChR


a G protein-mediated signalling by GPCRs
Agonist
GPCR
Plasma membrane
GTP
G protein
Ion
Ion channel
Adenylyl cyclase
RhoGEF
PLCβ
↑cAMP
DAG
Ins(1,4,5)P3
PKA
RhoA
PKC
↑Ca2+
b Arrestin-mediated signalling by GPCRs
Agonist
GPCR
Plasma membrane
GTP
G protein
G protein-mediated signalling
Resensitization
Desensitization
GRK
Arrestin
AP2
Clathrin
Recycling endosome
Endosome
Lysosome
Arrestin
ERK
Other pathways

Lintasan eferen saraf otonom

- Aktivasi simpatis
  - Melebarkan pupil
  - Naikkan frek.jantung
  - Vasokonstriksi vasa kulit dan viscera
  - Vasodilatasi koroner
  - Hambatan pada
    - Peristaltik
    - Otot-otot detrusor
- Aktivasi parasimpatis
  - Kecilkan pupil
  - Turunkan frek.jantung
  - Vasodilatasi vasa kulit dan viscera
  - Konstriksi bronchioli
  - Sekresi air liur&air mata
  - Memberi pacuan pada
    - Peristaltik
    - Otot-otot detrusor

Lintasan eferen saraf otonom

- Untuk memelihara keseimbangan reflek vegetatif (visceral)
  - Misal untuk perasaan :
    - Berdebar
    - Lapar
    - Haus
    - Penuh pada
      - Kandung kencing
      - Rectum
    - Seksual
    - Berkeringat

SUMMARY OF ADRENERGIC RECEPTOR ACTION

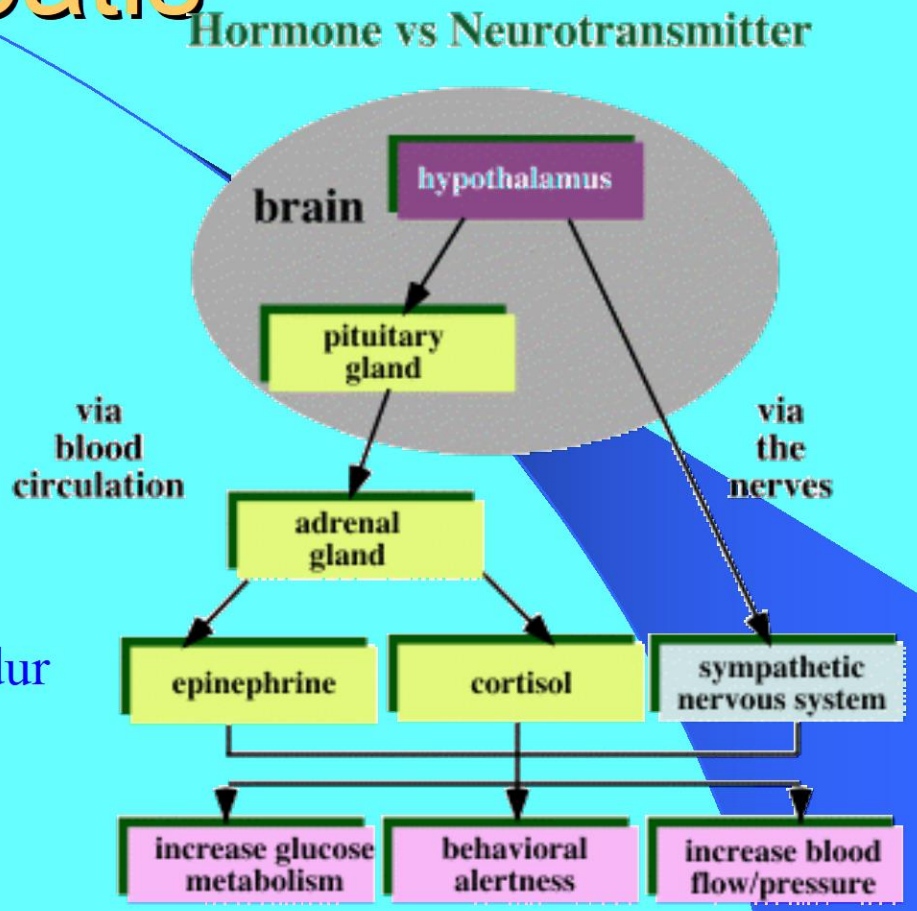
RECEPTOR	LOCATION	AGONIST	ANTAGONIST
$\alpha 1$	blood vessels	vasoconstriction (treat hypotension)	vasodilation (treat hypertension)
$\alpha 2$	blood vessels pre-synaptic membranes in adrenergic nerves	vasoconstriction (treat hypotension) inhibits NE release	vasodilation (treat hypertension) vasodilates and prevent reflex tachycardia (treat hypertension)
$\beta 1$	heart	increases heart rate and force (treat heart failure)	slows heart rate (treat hypertentsion, angina, arrhythmia)
$\beta 2$	bronchiole smooth muscle skeletal muscle arterioles	brochiole dilation (treat asthma etc...) ??	?? ??

Simpatis

Simpatis sebagai fungsi alarm

- Peningkatan kard. vask / tek.arteri
- Peningkatan aliran darah ke otot
- Peningkatan glukosa darah
- Peningkatan glikolisis otot
- Peningkatan kekuatan otot
- Peningkatan kecepatan metabolisme
- Peningkatan kegiatan mental/sukar tidur

- Reaksi tubuh thd stress



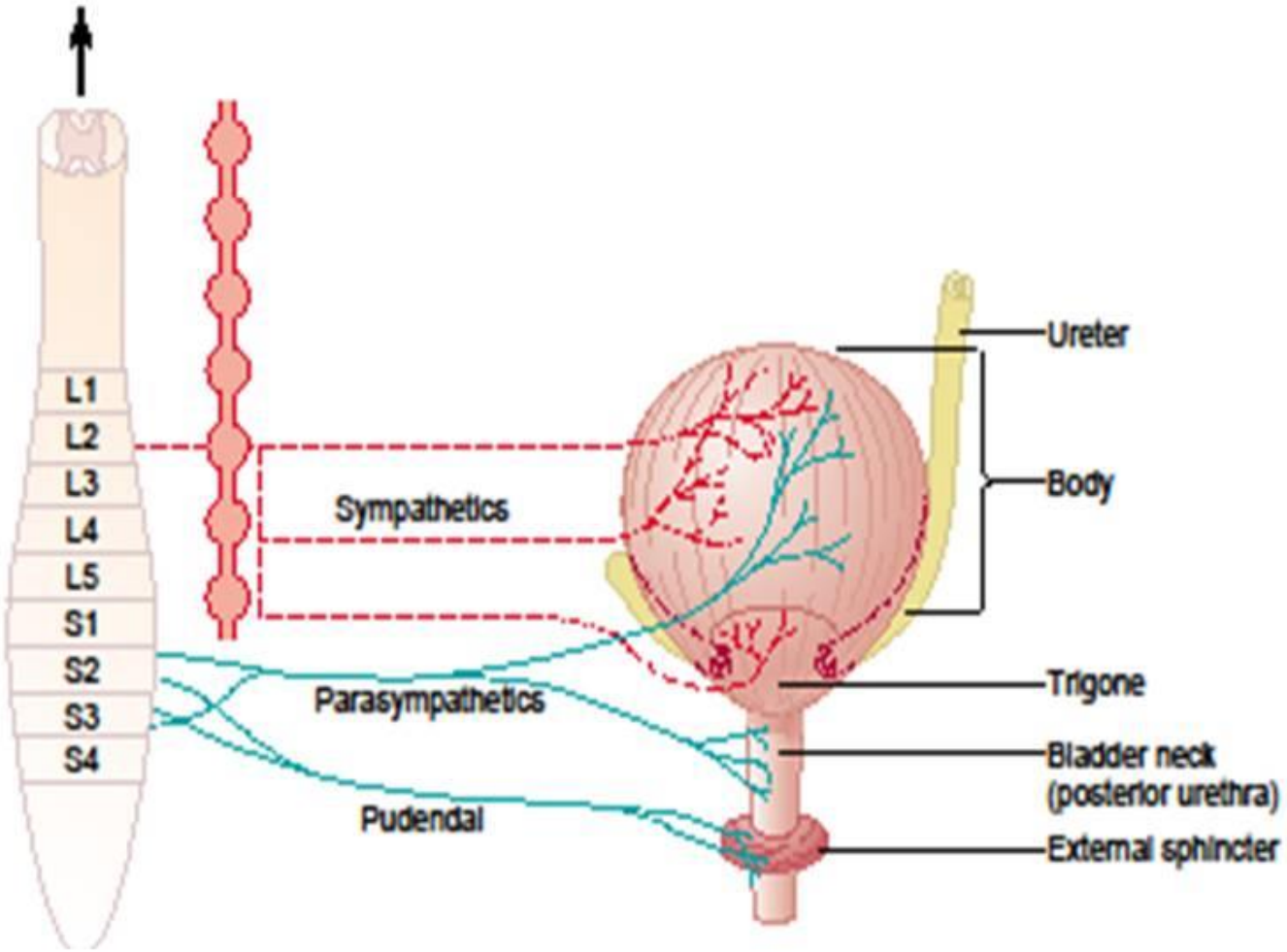
STRESS → Bila berulang & Jangka panjang → Tubuh Adaptasi → Penyakit : Hypertensi/Jantung

Pengaturan Berkemih

- The sacral Micturition Center
  - S2-4 : parasimpatis → kontraksi kandung kemih
  - Aferen : sensasi reganggan kandung kemih
- The pontis micturition center
  - Koordinasi relaksasi sfingter ketika kandung kemih kontraksi
- Corteks cerebri
  - Menginhibisi sacral micturition center

Miksi

- Perpaduan otonom dan somatis
- Kandung kemih dan uretra menerima persarafan simpatik dan parasimpatik
- Simpatik mempunyai sifat inhibisi eksitasi dari komponen parasimpatik
- Pusat parasimpatik di S3 dan S4 untuk merangsang kontraksi otot detrusor
- Otot sfingter eksternus disarafi oleh motorik somatis (nervus pudendus S.1,S.2)

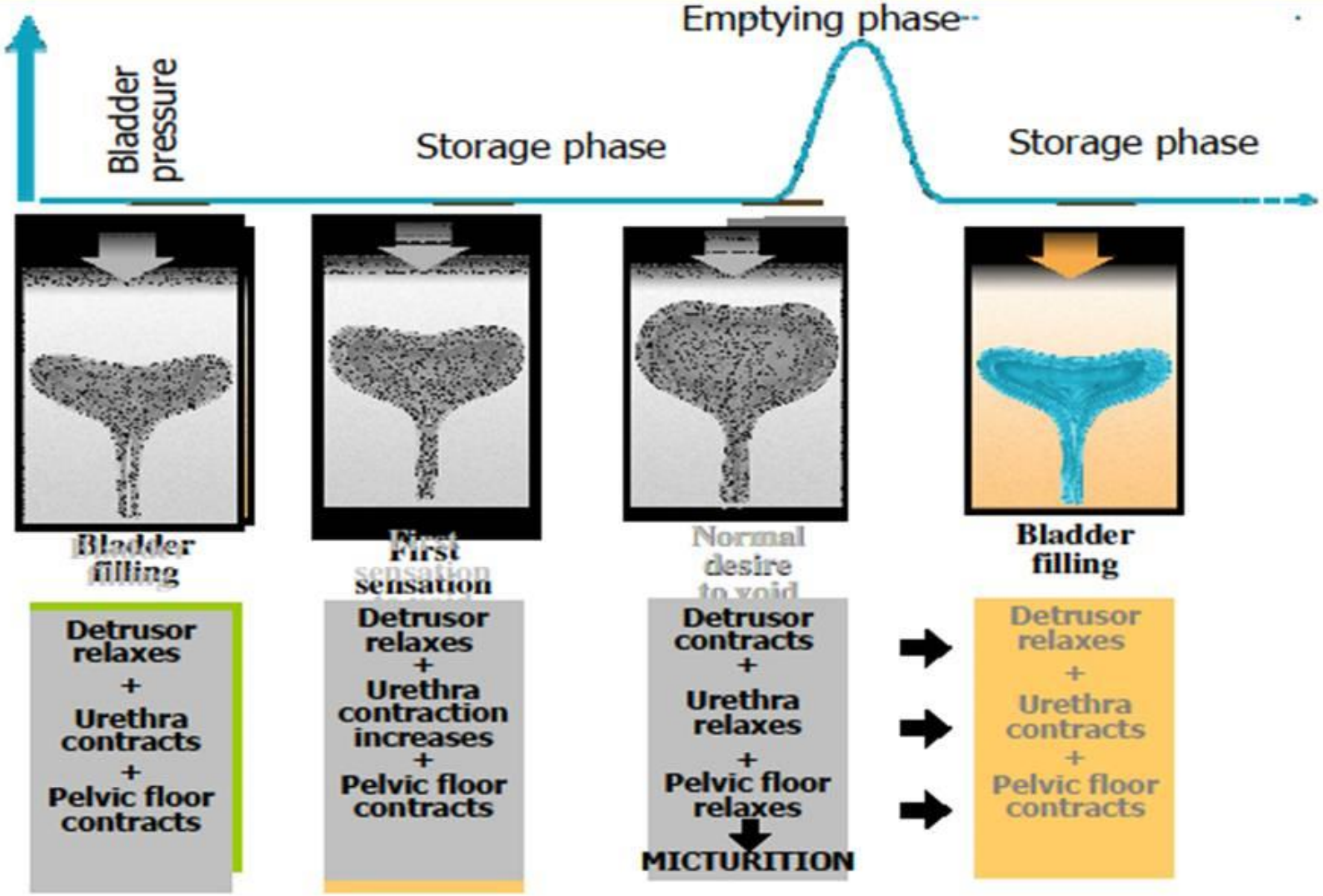


Guyton AC, Hall JE. Textbook of Medical Physiology.11th ed. Philadelphia: Elsevier Inc; 2006.p.311-4

Miksi

- Vesika urinaria penuh → impuls aferen → korteks serebri → keinginan miksi → otot detrusor kontraksi → sfinkter internus melemas (aktifitas parasimpatis) → sfinkter eksternus membuka (n. Pudendus, S2, S3) → miksi

Micturition cycle



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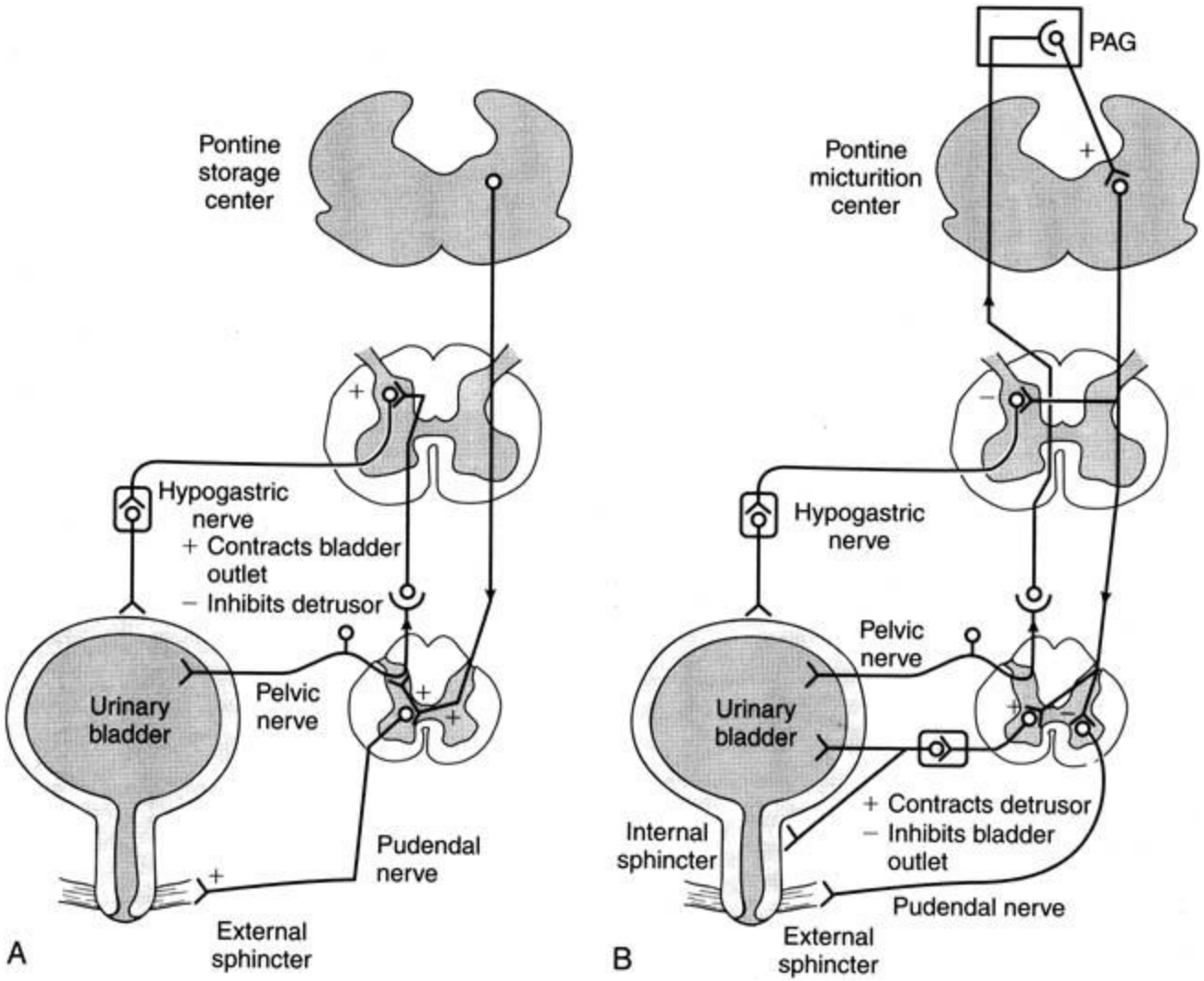
Pontine storage center
Hypogastric nerve
+ Contracts bladder outlet
− Inhibits detrusor
Urinary bladder
Pelvic nerve
Pudendal nerve
External sphincter
A
PAG
Pontine micturition center
Hypogastric nerve
Pelvic nerve
Urinary bladder
+ Contracts detrusor
− Inhibits bladder outlet
Internal sphincter
Pudendal nerve
External sphincter
B

Kelaianan Berkemih

- Jika lesi ascendens → perasaan ingin kencing tidak timbul → kandung kemih penuh → overflow incontinence
- Lesi pada konus medularis atau saraf spinal S3-4 → tonus kandung kemih hilang → kandung kemih atonik → retensio uri
- Automatic bladder :
- neurogenic bladder : spatic atau flaccid

Lesi Spinal

- Inkontinensia, bladder mengosongkan isinya dengan cepat dan sering
- Sphincter uretra eksterna mengalami kontraksi secara paradox
- Dissinergi antara M. Detrusor dan sphincter :
  - Sphincter dan bladder keduanya sama2 spastik pada saat bersamaan
  - Meskipun bladder berusaha mengeluarkan urine, namun sphincter externa kontraksi kuat, mencegah urine jangan keluar.

- Lesi Spinalis sacral – **Otonomic Bladder** – areflek detrusor dengan non-relaksasi uretra; atonic urethra

- Lesi Perifer: **Atoni Bladder** – areflek detrusor dengan gangguan koordinasi sphincter uretra

Defikasi

- Tinja penuh di sigmoid dan rektum → impuls dikirim ke kortek serebri → rasa ingin buang air besar → aktifitas parasimpatis
- Parasimpatetik merangsang kontraksi otot polos sigmoid dan rektum serta relaksasi otot sfingter internus
- Kontraksi otot polos sigmoid dan rektum secara reflekstoris.
- Sfingter eksternus disarafi oleh somatomotorik nervus pudendus (S1, S2 dan S3). Otot sfinkter internus disarafi oleh nervus pelvikus yang bersifat simpatik
- Prosesnya 2 tahap
  - Tinja didorong sampai ke rektum yang berlangsung involunter
  - Volunter dengan melonggarkan sfingkter ani dan dinding perut dikontraksikan untuk meningkatkan tekanan intra abdominal.