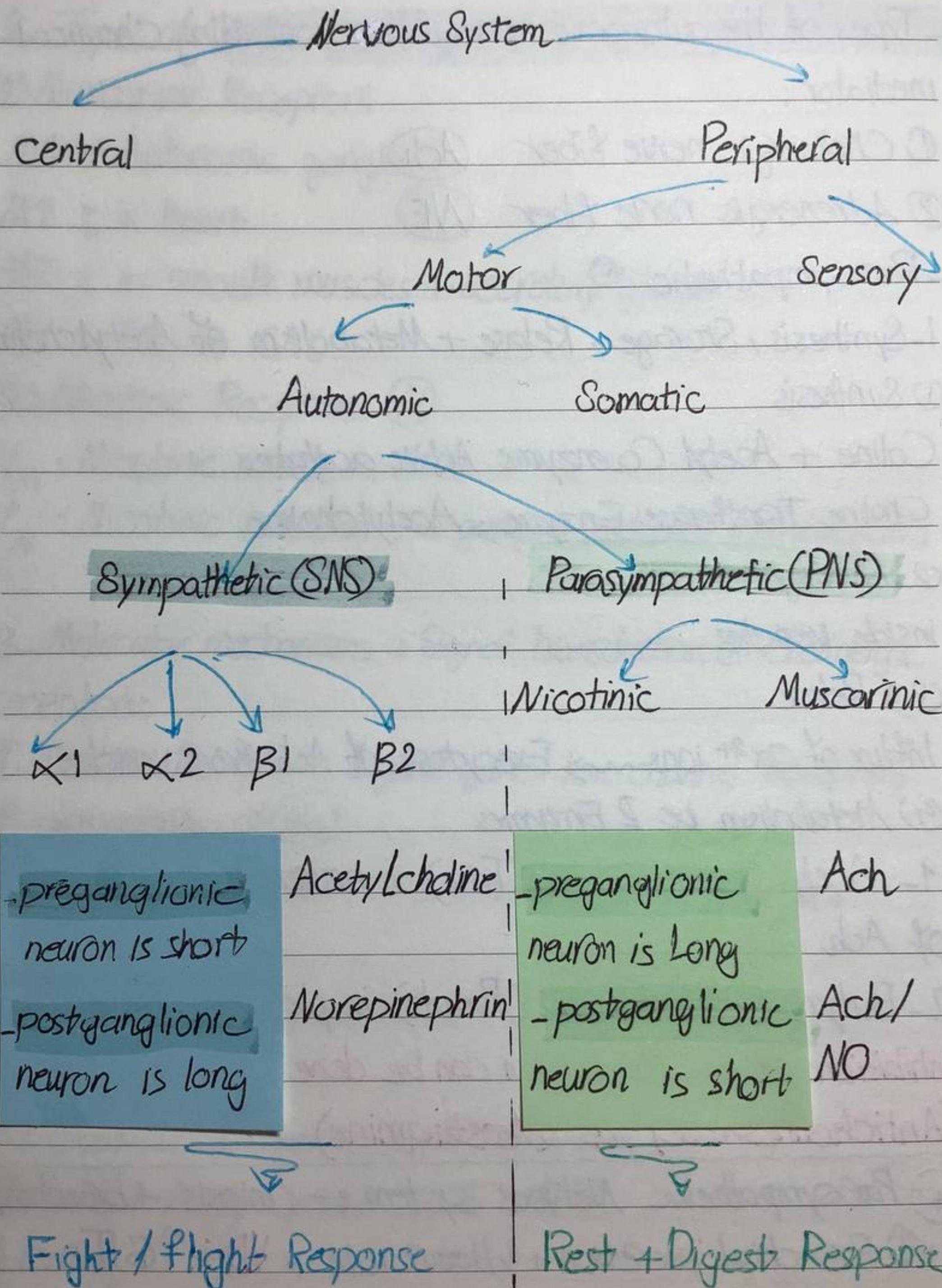


17ec Introduction to Autonomic Drugs

NO Date



- Types of the autonomic nerve fibers according Chemical mediator:

① Cholinergic nerve fiber Ach

② Adrenergic nerve fiber NE

- Parasympathetic ACh

I-Synthesis, Storage, Release + Metabolism of Acetylcholine

(1) Synthesis

Choline + Acetyl Co-enzyme Active acetate

Choline Transferase Enzyme \rightarrow Acetylcholine

(2) Storage

inside vesicles

(3) Release

Influx of Ca^{2+} ions \rightsquigarrow Exocytosis of Ach from vesicles

(4) Metabolism by 2 Enzymes

1- Acetyl Cholinesterase (True) in neurons + NMJ - Hydrolysis of Ach

2- Butyryl Cholinesterase (Pseudo) in plasma + Liver

- Inhibition of this Metabolism can be done by
(Anticholinesterase) as (Neostigmine)

④ Parasympathetic Nervous system :- miosis + bronchospasm
+ ↑ Bronchial secretion + ↓ Heart rate + **VD** + ↑ GIT secretion
+ Salivation + Lacrimal gland + Bladder Contracts + erection

2. Types of Cholinergic Receptors :-

(1) Muscarinic Receptors

M1 : Autonomic ganglia

M2 : in heart

M3 : in smooth muscles + secretory glands

M4 + M5 in CNS

(2) Nicotinic Receptors (N)

N_M : Nicotinic muscle . NMJ

N_N : Nicotinic neuronal . in ganglia , adrenal medulla, CNS

3. Molecular mechanisms + Signal transduction of cholinergic receptors:

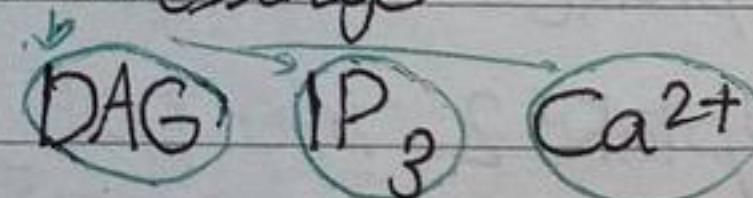
① Nicotinic Receptor: Ligand gated Ion channel Receptors

↑ permeability of Na^+

② Muscarinic Receptor: G protein - coupled receptor

M1 : G_q

stimulate phospholipase C \rightarrow ↑ 2° messenger



M2 : G_i \rightarrow opening of K⁺ channels

G_i inhibit Adeny Cyclase \rightarrow ↓ cAMP

M3: G_q

* Sympathetic:

1 Synthesis, storage, release + Termination of the action of Catecholamine

Tyrosine $\xrightarrow{\text{tyrosine hydroxylase}}$ Dihydroxyphenylalanine DOPA
 $\xrightarrow{\text{DOPA decarboxylase}}$ Dopamine

* α -methadopa $\xrightarrow{\text{DOPA decarboxylase}}$ α -methyl dopamine

* Dopamine is transported into vesicle by carrier inside it will be hydroxylated \rightarrow NE

- in adrenal medulla + Brain: $\text{NE} \xrightarrow{\text{N methyltransferase}}$ EP

- NE is stored in granules at nerve ending

- $\uparrow \text{Ca}^{2+}$ intracellular \rightarrow vesicles exocytosis

expulsion \rightarrow cotransmitter (ATP + polypeptides) + dopamine hydroxylase + $\text{NE} \rightarrow$ Ionic Conductance

- Termination:

① Active Reuptake

\rightarrow Uptake 1 into sympathetic nerve terminal

\rightarrow Uptake 2 into post junctional cell

metabolism by COMT Catechol-O-methyltransferase

② Enzymatic Metabolism: done by MAO + COMT

[] high in liver + kidney

[] little or no in adrenergic neurons

Adrenergic receptors

$\alpha_1 + \alpha_2$

$\beta_1 + 2 + 3$)

Gprotein coupled receptor (D_{1,2,3,4,5})

Dopamine

α_1 similar to M₁

| activate

α_2 similar to M₂

G_s

Adenyl Cyclase
↑ cAMP

α_1 stimulation

V.C + Mydriasis

+ contract of S..

+ HyperKalemia

+ ejaculation

α_2 stimulation

inhibit EP, NE

+ ACh + sympathetic

flow + Insulin release

β_1 stimulation

stimulator

properties of

Heart + Kidney
(renin)

β_2 stimulation

VD + bronchodilat

HypoKalemia

Hyperglycemia

▲ return to

slide num

15 + 30 + 31

of this Lec.

β_3 stimulation Lipolysis