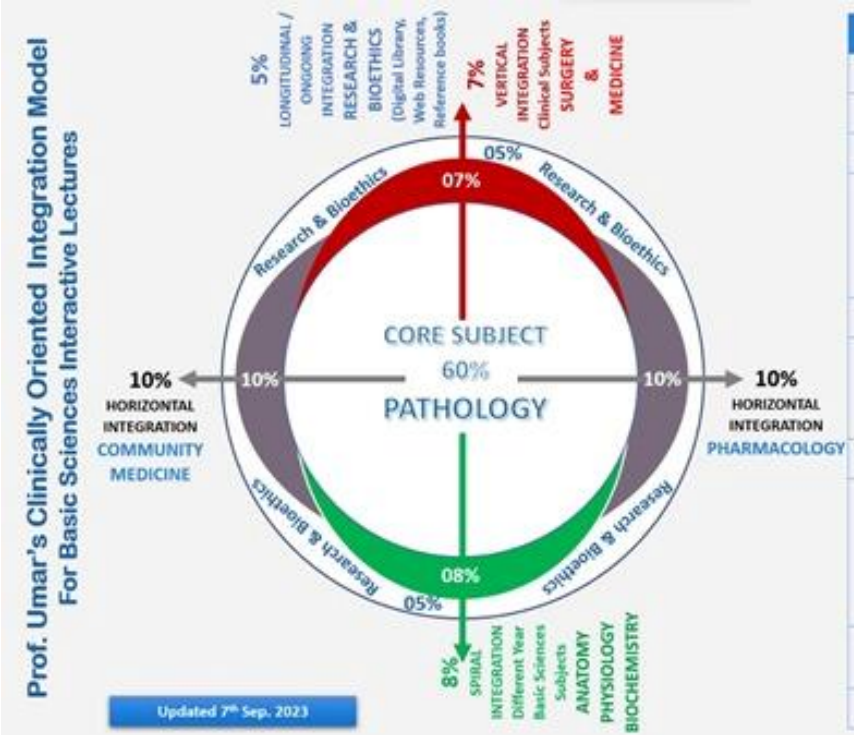
SYMPATHOMIMETICS

- Katzung's Basic & Clinical Pharmacology, 16th Edition
- Goodman and Gilmans The Pharmacological Basis of Therapeutics, 13th Edition

MOTO AND VISION

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

UMAR'S MODEL OF INTEGRATION



Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

PROF. UMAR'S MODEL OF TEACHING STRATEGY

- Self Directed Learning Assessment Program

- Objectives :To cultivate critical thinking, analytical reasoning, and problem-solving competencies.
- To instill a culture of self-directed learning, fostering lifelong learning habits and autonomy.
- How to Assess?
- Ten randomly selected students will be evaluated within the first 10 minutes of the lecture through 10 multiple-choice questions (MCQs) based on the PowerPoint presentation shared on Students Official WhatsApp group, one day before the teaching session.
- The number of MCQs from the components of the lecture will follow the guidelines outlined in the Prof. Umar model of Integrated Lecture.

Component of LGIS	Core Knowledge	Horizontal Integration	Vertical Integration	Spiral Integration
No of MCQs	6-7	1-2	1	1

PRE-LECTURE ASSESSMENT

Which of the following is a characteristic of catecholamines?

A. They are used for local bronchodilation
B. They have a common basic chemical structure
C. They are used for systemic vasodilation
D. They are not destroyed by digestive enzymes
E. They can be given orally

Which of the following structural modifications generally enhance the potency of sympathomimetic drugs?

A) Addition of a bulky group at the para position of the aromatic ring
B) Increasing the length of the side chain between the aromatic ring and the amino group
C) Replacement of the hydroxyl group on the aromatic ring with a methoxy group
D) Introduction of a methyl group on the amine nitrogen
E) Removal of the hydroxyl group on the beta carbon of the side chain

PRE-LECTURE ASSESSMENT

A hypotensive patient in the critical care unit is given an intravenous infusion of an alpha-adrenergic agonist that lacks beta-adrenergic activity. The cardiovascular effects of this drug are:

A. Increased vascular resistance
B. Decrease heart rate
C. Decrease conduction velocity
D. Decrease force of contraction
E. Decrease vascular resistance

A 20-year-old man has been self-treating his nasal congestion with a nonprescription alpha agonist nasal spray for 2 weeks. When he stopped using it he found that he experienced:

A)Increased nasal congestion
B) Decreased nasal discharge
C) Improvement in breathing
D) Reduction in headache
E) Enhanced sense of smell

PRE-LECTURE ASSESSMENT

A 3-year-old child presents to the emergency department with acute asthma. He is given a nebulized bronchodilator that relaxes bronchial smooth muscle through direct action on adrenergic receptors. This drug acts via:

A. Nuclear receptors
B. G protein coupled receptors
C. Voltage gated ion channels
D. Enzyme linked channels
E. Cytoplasmic receptors

The sympathomimetic which may promote diuresis by a direct effect on the kidney is

A. Isoproterenol
B. dobutamine
C. norepinephrine
D. dopamine
E. epinephrine

Which of the following direct-acting drugs is a relatively pure alfa agonist, an effective mydriatic and decongestant and can be used to raise blood pressure?

A. Epinephrine
B. Norepinephrine
C. Phenylephrine
D. Ephedrine
E. Dopamine

A 65-year-old patient is prescribed a drug to treat hypotension. The drug is known to have a rapid onset of action and is metabolized quickly by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT). Which of the following drugs is most likely being prescribed?

A) Epinephrine
B) Phenylephrine
C) Albuterol
D) Isoproterenol
E) Dopamine

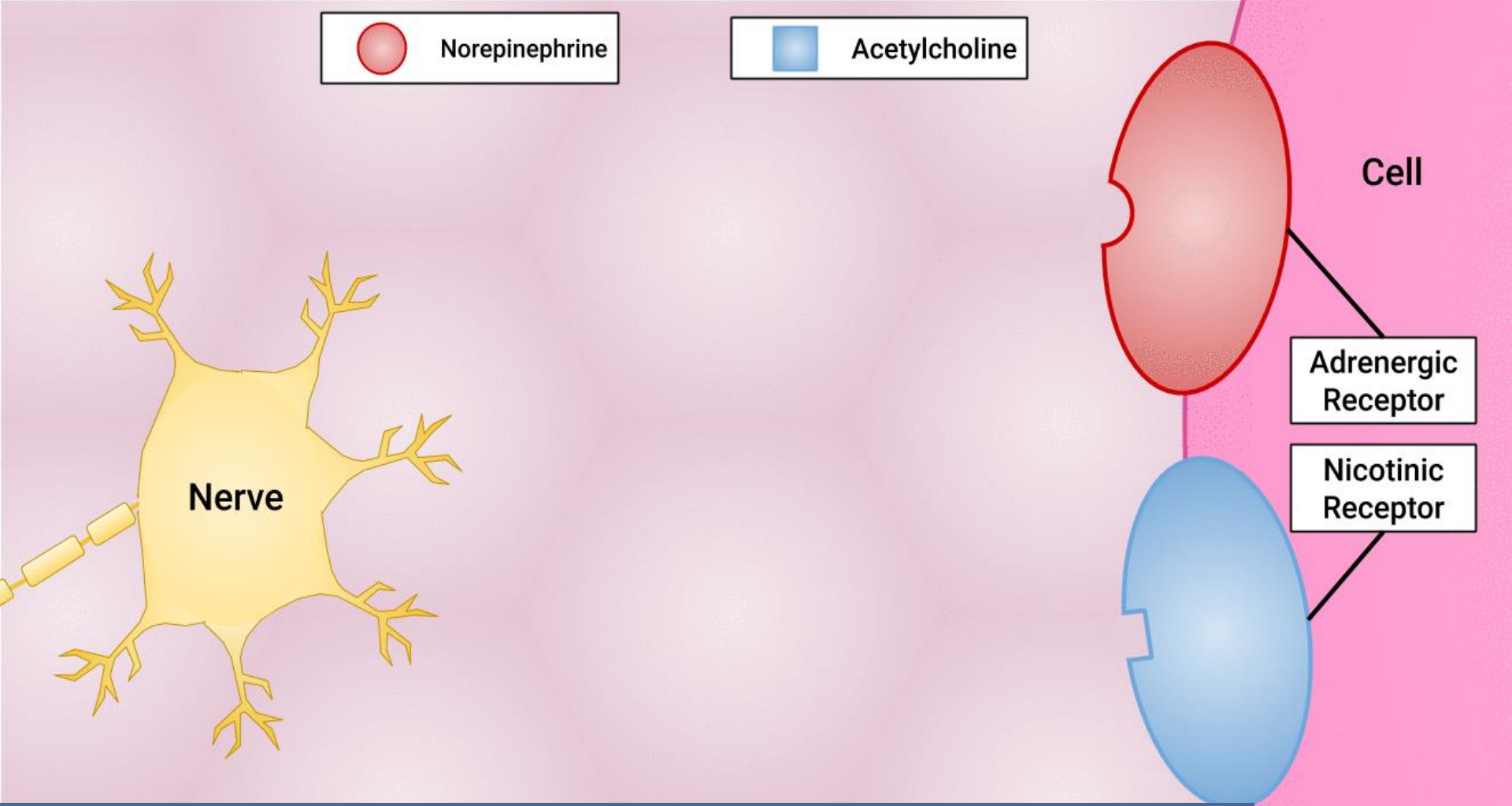
Which of the following mechanisms is commonly associated with sympathomimetics that specifically target beta-adrenergic receptors?
A) Inhibition of cyclic AMP (cAMP) breakdown, leading to increased smooth muscle relaxation
B) Activation of phosphodiesterase to decrease intracellular cAMP levels
C) Direct release of norepinephrine from nerve terminals
D) Inhibition of catecholamine reuptake at presynaptic terminals
E) Activation of alpha-adrenergic receptors to constrict blood vessels

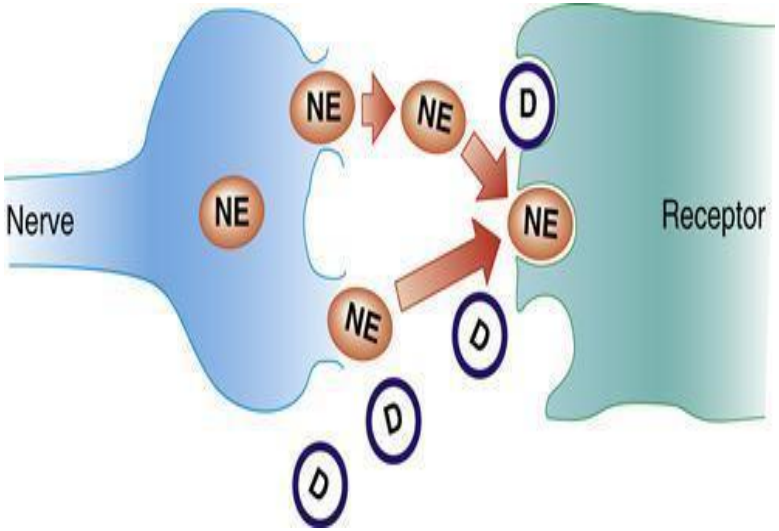
Which of the following mechanisms helps regulate the release of norepinephrine from sympathetic nerve endings?
A) Positive feedback by increasing norepinephrine release with higher blood pressure
B) Negative feedback through alpha-2 receptors that inhibit further norepinephrine release
C) Direct inhibition by acetylcholine at adrenergic nerve endings
D) Activation of dopamine receptors to stimulate norepinephrine release
E) Inhibition of serotonin reuptake to enhance norepinephrine release

Learning Objectives

At the end of the lecture, students of 3rd Year MBBS will be able to ;

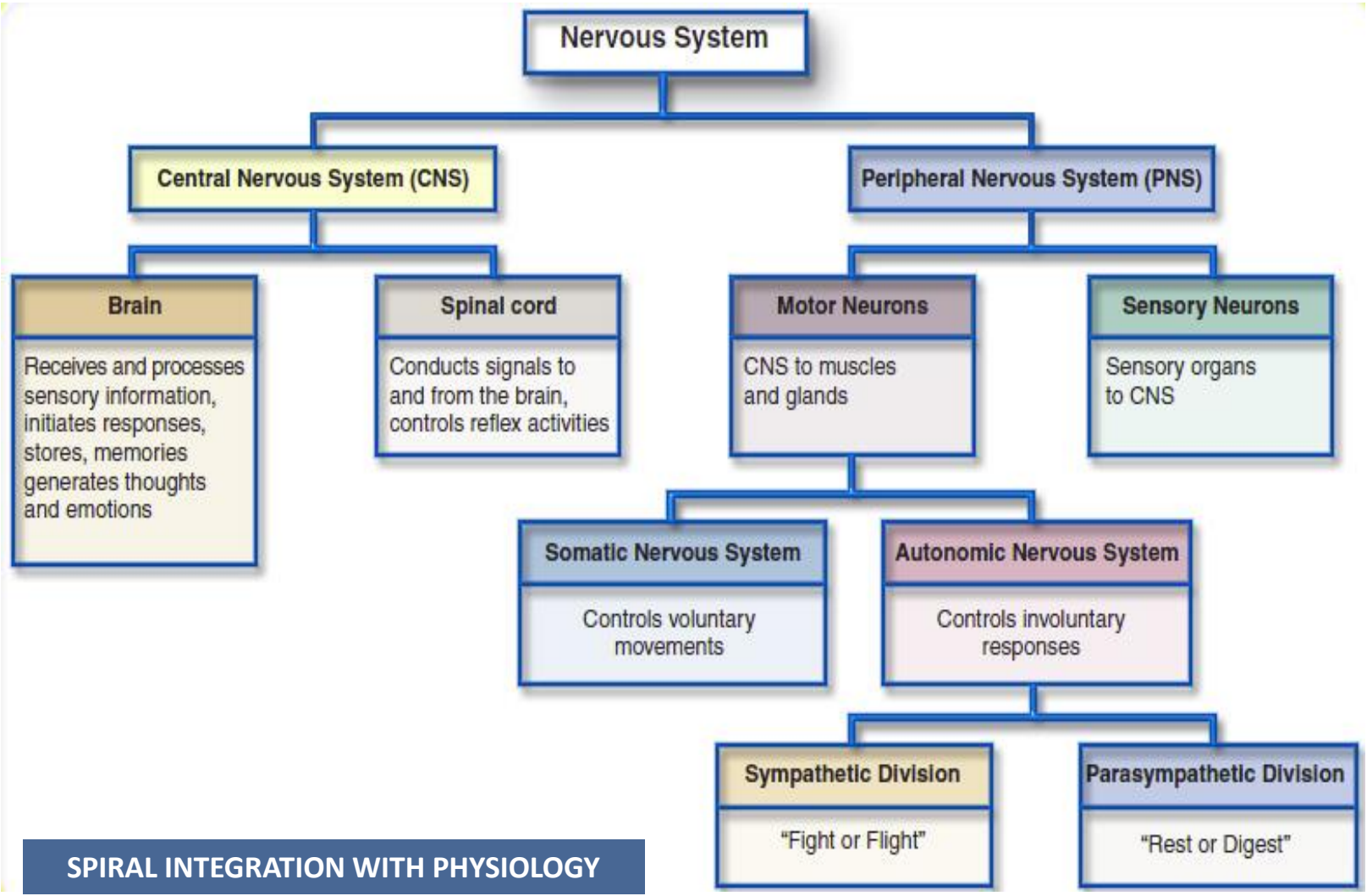
- **Recall components of sympathetic neurotransmission**
- **Identify adrenoceptors and their affiliated signal transduction mechanism**
- **Classify sympathomimetic drugs**
- **Discuss structure activity relationship of symapthomimetics**
- **Differentiate between catecholamines and non catecholamines**


Norepinephrine
Acetylcholine
Cell
Adrenergic Receptor
Nicotinic Receptor
Nerve

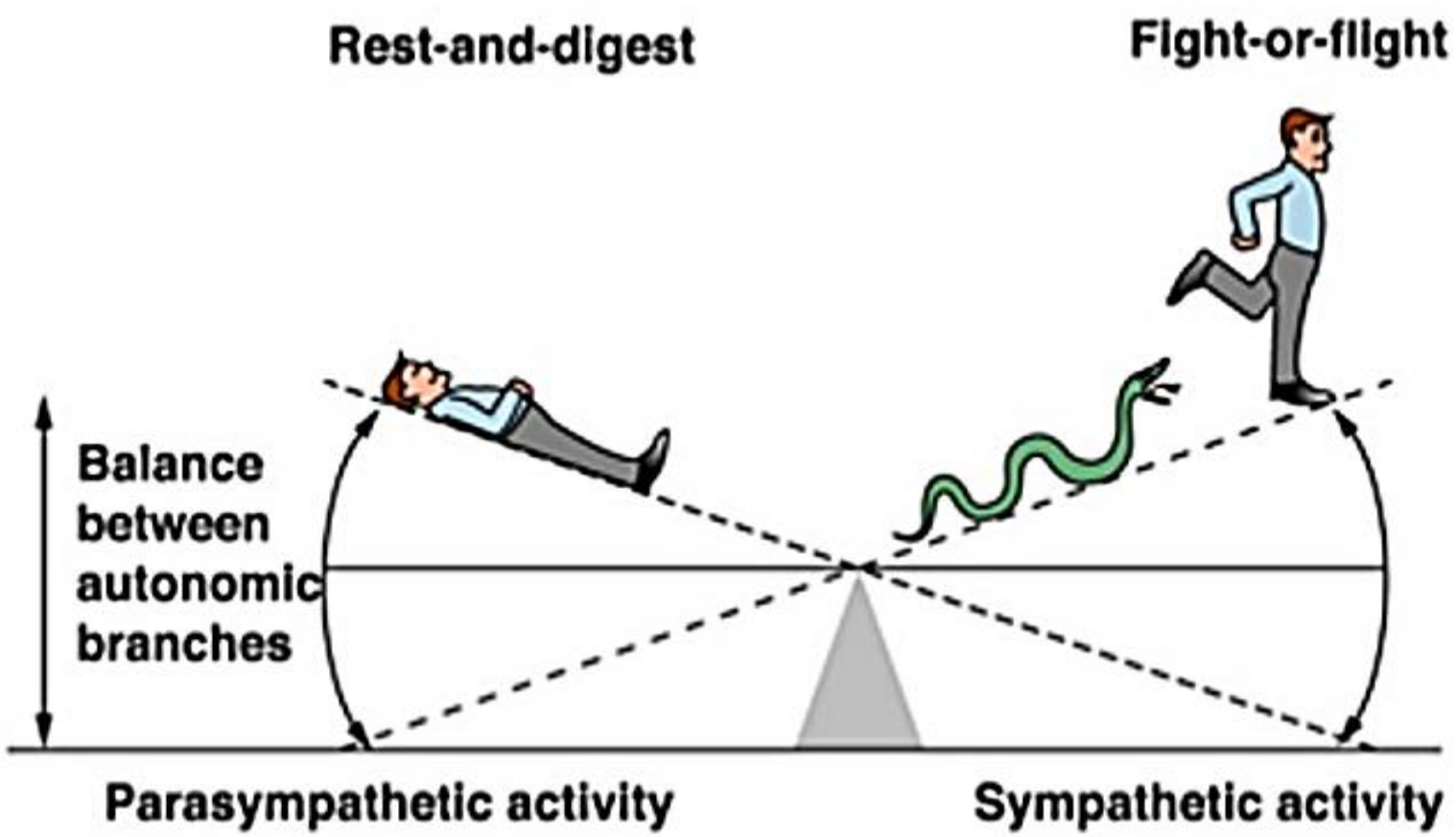


Sympathomimetics

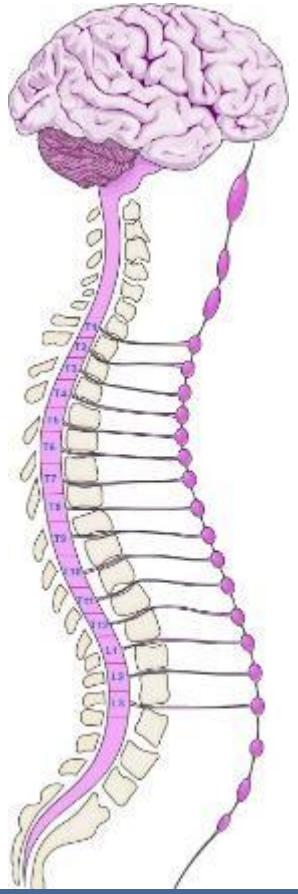
Drugs that facilitate or mimic the actions of the sympathetic nervous system stimulation on sympathetic effectors are called **sympathomimetics, adrenomimetics,** or **adrenergic agonists**.

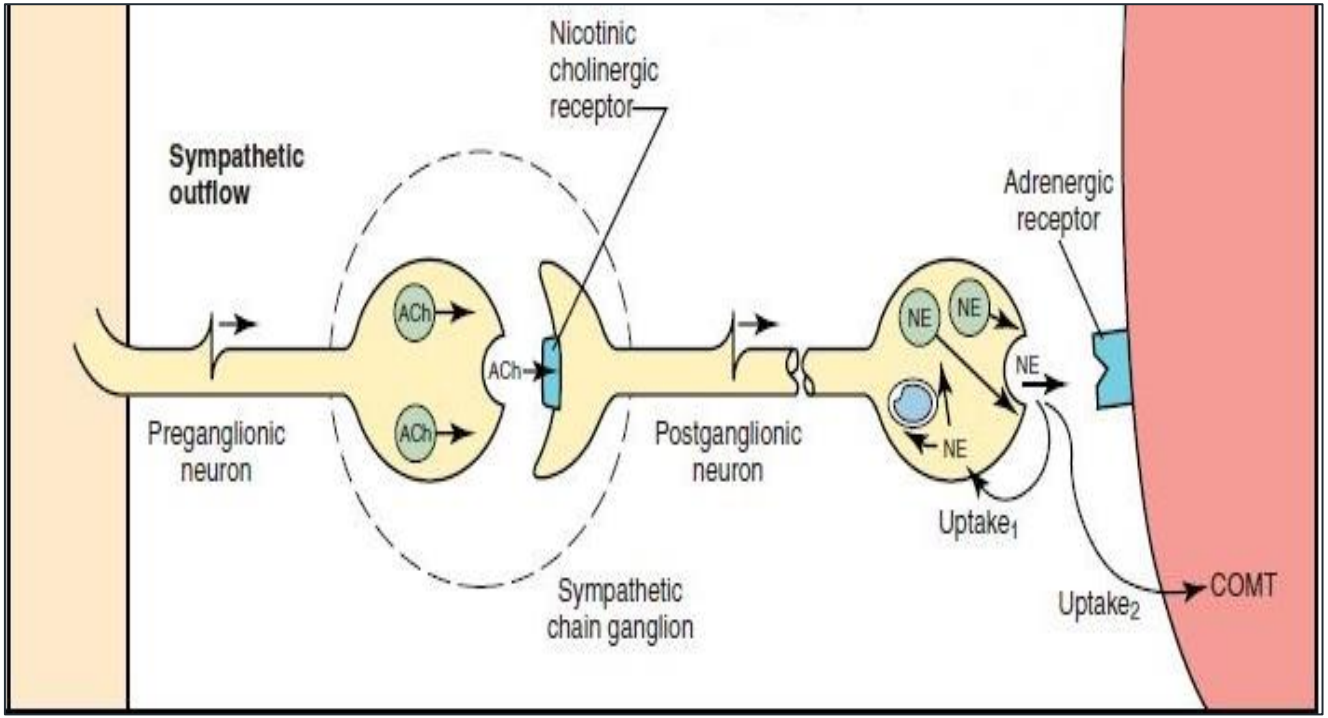


SPIRAL INTEGRATION WITH PHYSIOLOGY

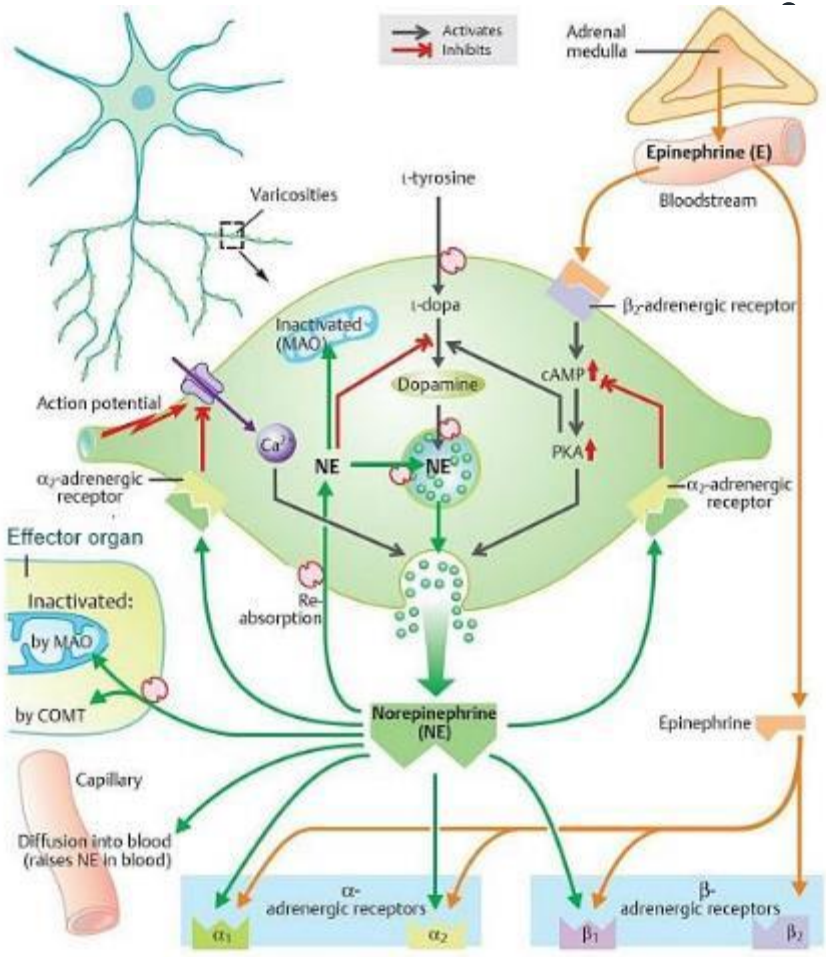

Rest-and-digest
Fight-or-flight
Balance between autonomic branches
Parasympathetic activity
Sympathetic activity

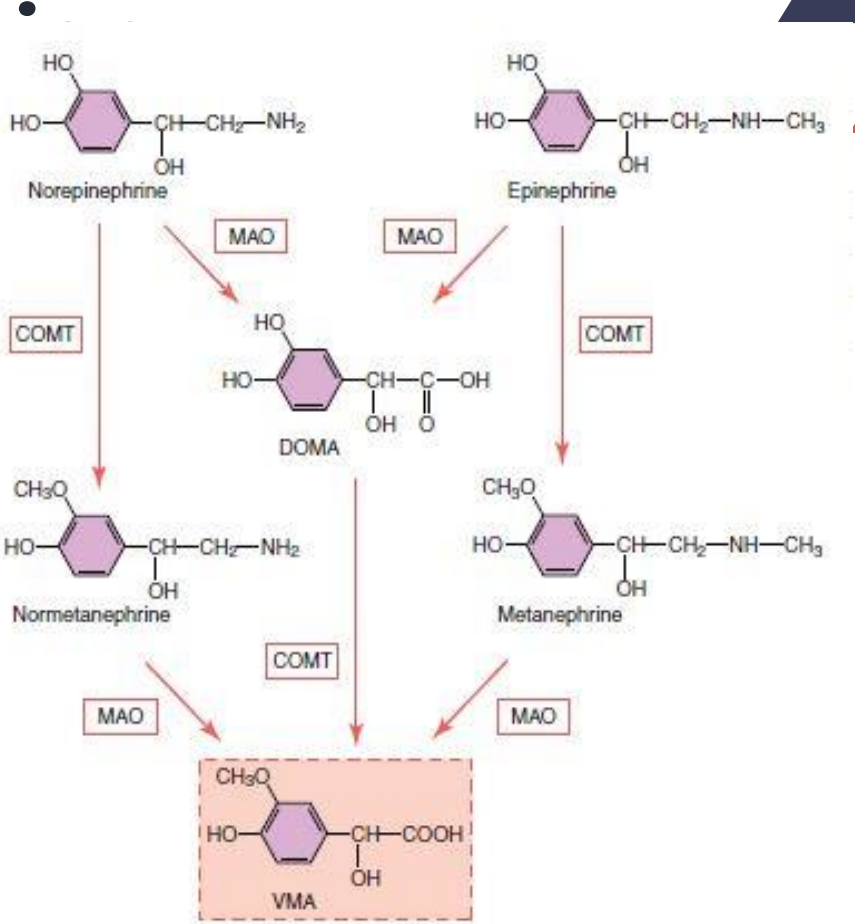
Sympathetic Neurotransmission





Sympathetic





CORE

CORE

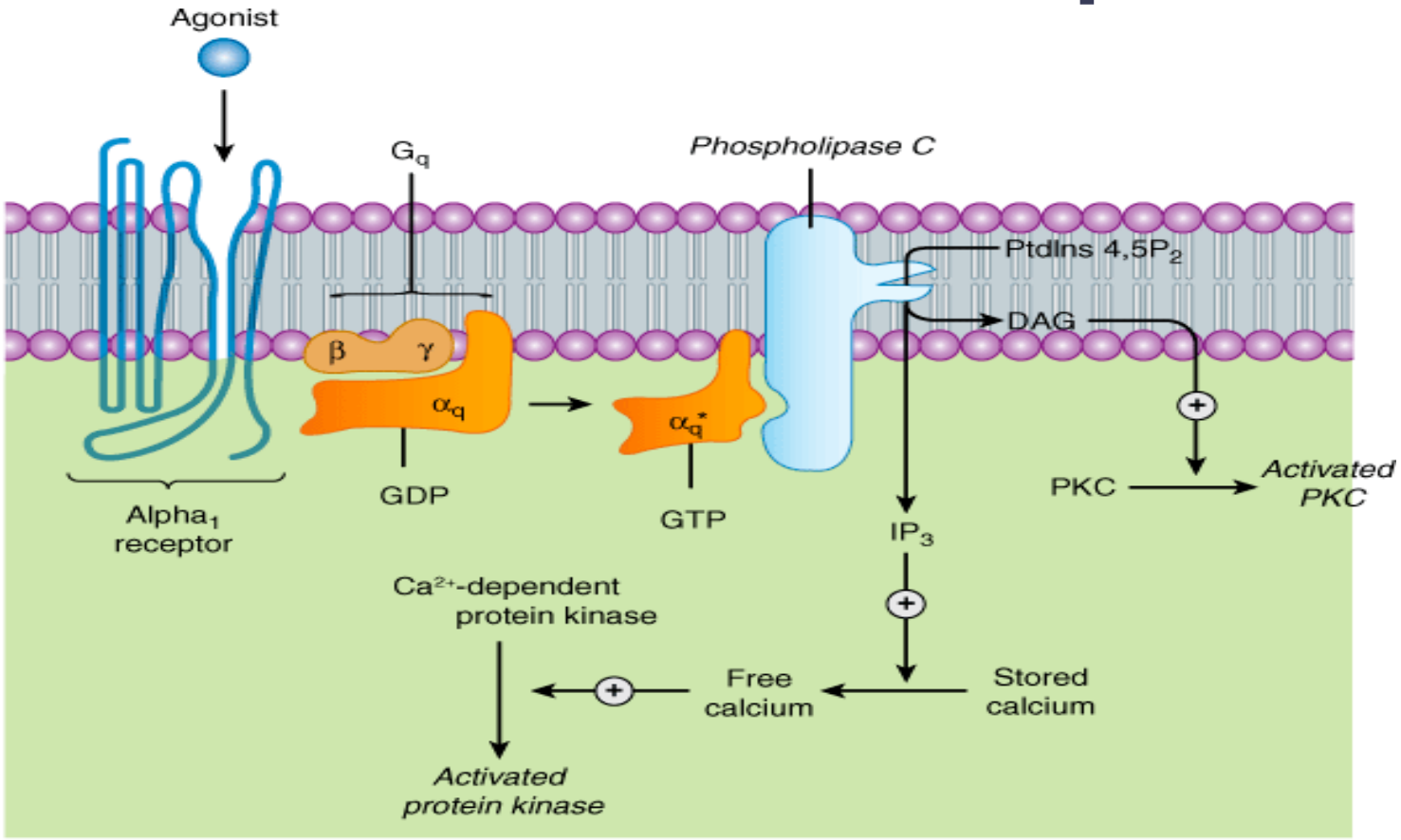
Receptors

1. Adrenergic receptors
   a) Alpha receptors (α)
      i) α1 ($\alpha1_A$ $\alpha1_B$ $\alpha1_D$)
      ii)α2 ($\alpha2_A$ $\alpha2_B$ $\alpha2_C$)
   b) Beta receptors (β)
      i) β 1
      ii) β 2
      iii) β 3
2. Dopamine receptors
3. Imidazole receptors

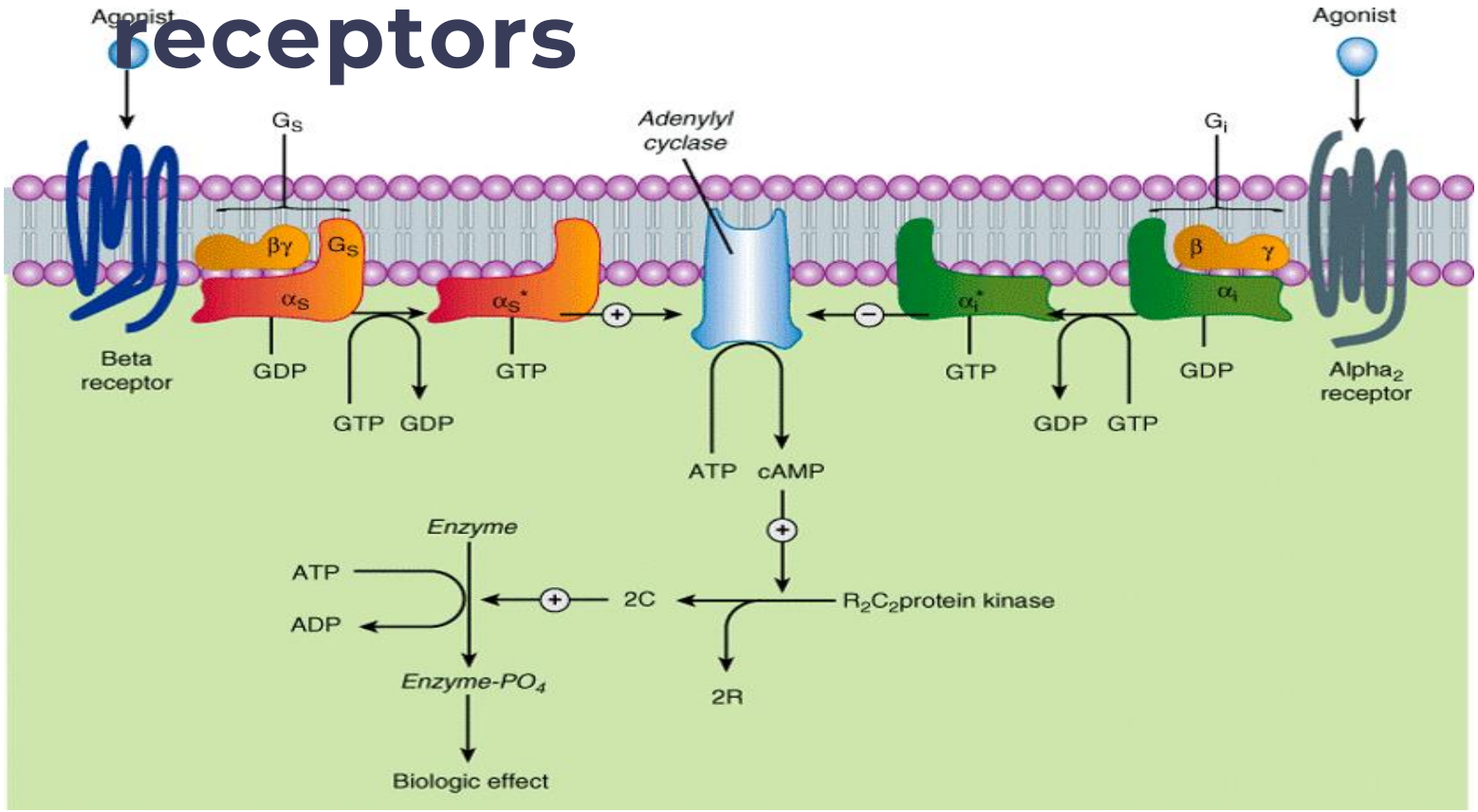
Signal Transduction

Receptor	G-protein	Mechanism
α1	Gq	Phospholipase C activation, increased IP3,DAG and release of calcium
α2	Gi / Go	Inhibition of adenylyl cyclase and decreased cAMP
β1	Gs	Adenylyl cyclase activation, increased cAMP, protein kinase activation
β2	Gs	

Activation of α1 receptors



Activation of β & α2 receptors



Receptor Distribution & Effect

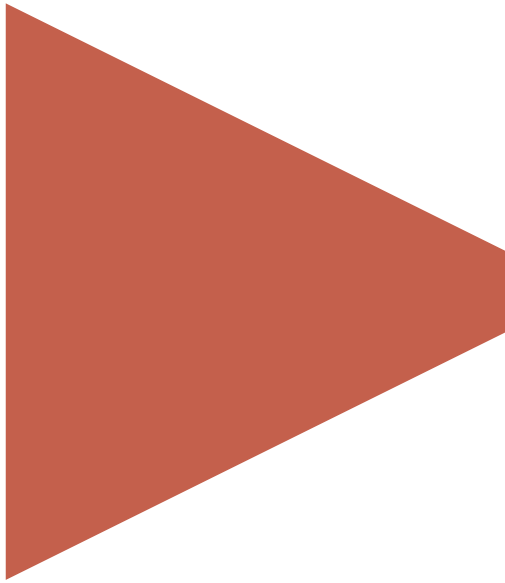
Type	Tissue	Actions
α1	Most vascular smooth muscle	Contraction
	Pupillary dilator muscle	Contraction (dilates pupil)
	Pilomotor smooth muscle	Erects hair
	Urethral sphincter and Prostate	Contraction
	Heart	Increases force of contraction
α2	Synaptic CNS adrenoceptors	Modulate dopamine neurotransmission Decrease sympathetic outflow
	Platelets	Aggregation
	Adrenergic and cholinergic presynaptic nerve terminals	Inhibition of transmitter release
	Some vascular smooth muscle	Contraction
	Fat cells	Inhibition of lipolysis
	Pancrease	Inhibition of insulin secretion

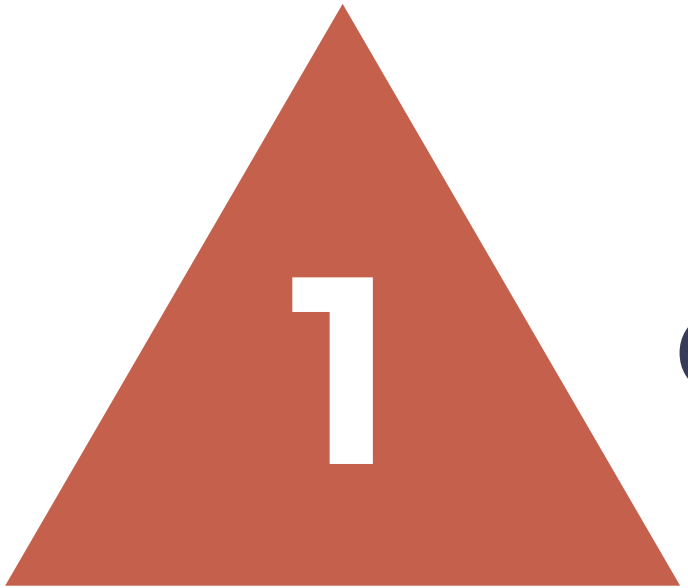
Receptor Distribution & Effect

Type	Tissue	Actions
β1	Heart, juxta-glomerular cells	Increases force and rate of contraction; increases renin release
	Muscle and liver	CHO metabolism
β2	Respiratory, uterine,GIT and vascular smooth muscle	Promotes smooth muscle relaxation
	Skeletal muscle	Promotes potassium uptake Activates glycogenolysis (lactate)
	Liver	Activates glycogenolysis (glucose)
	Pancreas	Secretion of insulin and glucagon
β3	Fat cells	Activates lipolysis
D1	Smooth muscle	Dilates renal blood vessels
D2	Nerve endings	Modulates transmitter release

Classification

1. Chemistry
2. Mode of action
3. Receptor activation
4. Therapeutic uses





Chemical Classification

Chemical Classification

❖ Catecholamines

- **Natural**

  Epinephrine
  Norepinephrine
  Dopamine

- **Synthetic**

  Isoprenaline(Isoproterenol)

  Dobutamine
  Rimiterol
  Isoetharine
  Hexoprenaline

Chemical Classification

Non-catecholamine

Non-selective (α & β)

- Ephedrine,pseudoephedrine, amphetamine,methylphenidate

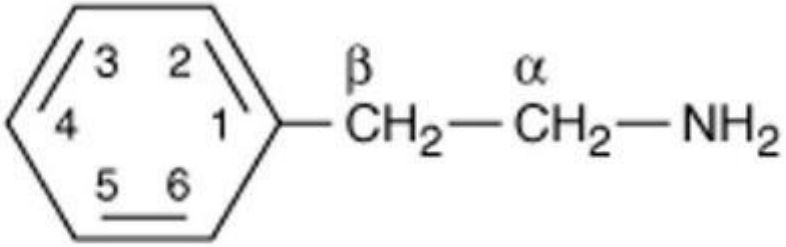
Selective

- α1(phenylephrine,midodrine, xylometazoline)
- α 2 (clonidine, α methyldopa)
- α1 & α2 (Oxymetazoline)

- B1(prenalterol)
- β 2 (salmeterol, terbutaline)
- β1 & β2 (orciprenaline)

CORE

Structure-Activity Relationship



Phenylethylamine

1. Benzene ring
2. α carbon
3. β carbon
4. Amine group

1. Receptor selectivity
2. Lipid solubility (CNS penetration)
3. Metabolism by MAO/COMT

CORE

SUMMARY FOR SAR

1. Direct-acting agonists generally require a hydroxyl group at positions 3 and 4 of the aromatic ring plus a hydroxyl group on the β-carbon atom of the side chain for maximal stimulation of α and β receptors.

2. Indirect-acting agonists have no β-hydroxyl group and either no or one hydroxyl group on the ring. Agents devoid of hydroxyl substitutions can penetrate the blood–brain barrier better and exert prominent CNS effects.

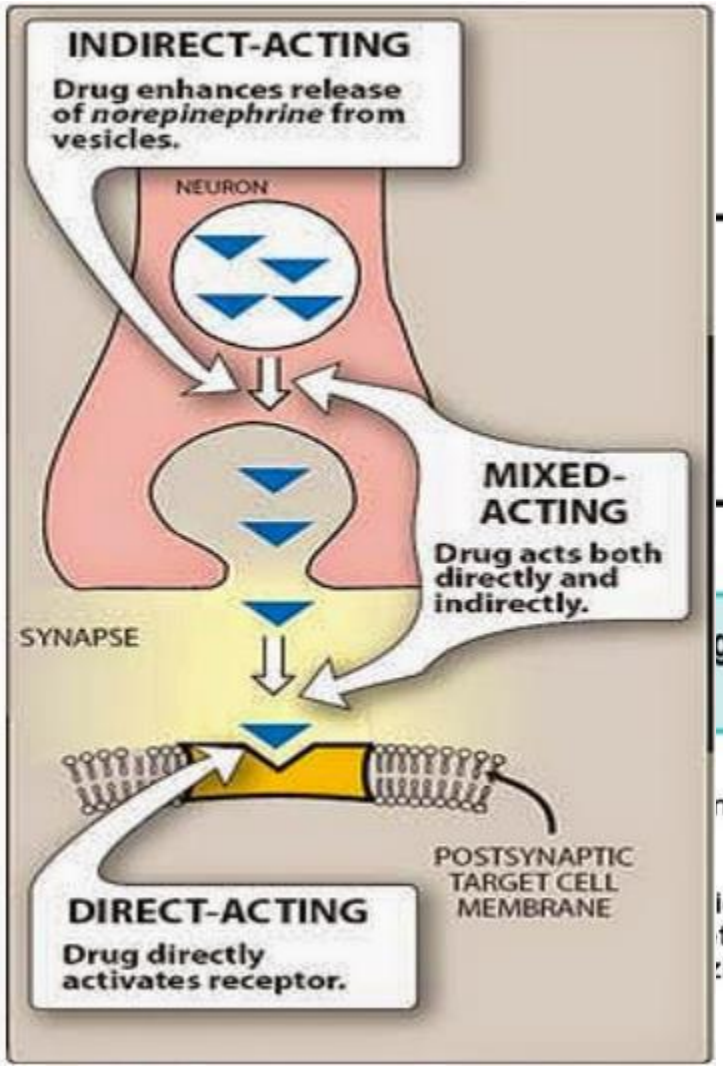
3. Mixed-acting agonists generally have a β-hydroxyl group and a single ring hydroxyl group

4. The alkyl substitution on the nitrogen causes a shift in drug activity toward the β-adrenergic receptor

Catecholamine & Non-catecholamine

CATECHOLAMINE	NON-CATECHOLAMINE
CHEMISTRY: Catechol nucleus	**CHEMISTRY:** Absence of catechol nucleus
ROA: Can not be given orally	**ROA**: can be given orally
DURATION OF ACTION: Shorter as metabolized rapidly by MAO & COMT	**DURATION OF ACTION:** Prolonged as resistant to metabolism to MAO & COMT
CNS EFFECTS: Can not cross BBB so no or minimal CNS effects	**CNS effects**: Can be distributed to CNS produce specific effects there
MOA: Usually direct acting	**MOA:** Act directly, indirectly or by both mechanisms

Mode of Action



Direct-acting

Selective

α_1-phenylephrine
α_2-clonidine
β_1-dobutamine
β_2-terbutaline

Indirect-acting

Uptake Inhibitor*

Cocaine
Atomextine
Sibutramine
Riboxetine
Duloxetine
Milnacipran

MOA Inhibitors*

selegiline

COMT Inhibitors*

entacapone

RESEARCH

Ippolito M, Benovic JL. Biased agonism at β-adrenergic receptors. Cell Signal. 2021 Apr;80:109905. doi: 10.1016/j.cellsig.2020.109905. Epub 2020 Dec 29. PMID: 33385503; PMCID: PMC7878421.

ARTIFICIAL INTELLIGENCE

Shahrokhi Z, Sohrabi MR, Nik SM. The application of artificial intelligence system and regression methods based on the spectrophotometric method for fast simultaneous determination of naphazoline and antazoline in ophthalmic formulation. Optik. 2020 Feb 1;203:164010.

BIOETHICS

Suissa, K., Schneeweiss, S., Kim, D.W. and Patorno, E., 2021. Prescribing trends and clinical characteristics of patients starting antiobesity drugs in the United States. *Diabetes, Obesity and Metabolism*, *23*(7), pp.1542-1551.

FAMILY MEDICINE

Abdullahi S, Cruz EV, Freeman L, Tanlaka E. Anti-obesity Medications Prescribing Measures Utilized by Primary Care Practitioners: Scoping Review.