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EFFECT OF NEUROTRANSMITTER ON ANS

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Abstract : ***The purpose of this manuscript is to discuss about the functions and physiological effects of various excitatory and inhibitory neurotransmitters that effect the parasympathetic and sympathetic nervous systems. The action of this system as its name implies, are in general not under direct voluntary control, these characteristics distinguish the autonomic nervous system from the somatic nervous system. The activity of neurotransmitter action in CNS function, with a clear, comprehensive, and challenging style of writing.***

Index Terms - Autonomic nervous system , Neurotransmitter, Parasympathetic nervous system, Sympathetic nervous system.

INTRODUCTION

Autonomic nervous system is part of nervous system that further has two classification as-

1)Cholinergic or parasympathetic or rest or digest.
2) Adrenergic or sympathetic or flight or fight.

PARASYMPATHETIC NERVOUS SYSTEM –

Parasympathetic nervous system also known as cholinergic system in which functional neurotransmitter is ACETYLCHOLINE. This system is also known as cranio sacral outflow. In this nervous system ganglia is situated near effector organ and away from the spinal chord. Ganglionic chain is not present. Post ganglionic chain is shorter than pre ganglionic chain. It shows effects on physiology of various functions as follows-

Effect on eye-

- **Pupil is constricted or miosis occurs.**
- **There is seen a increase in secretion of lacrimal glands .**
- **IOT or intra ocular tension is increased.**
- **The secretion of overall gland present is increased.**

Effect on heart-

- **Bradycardia or decreased heart rate occurs due to decrease in force of contraction.**
- **Blood pressure is also decreased.**

Effect on blood vessel-

- **All types of blood vessels shows vasodilation.**

Effect on lungs-

- **The parasympathetic system shows constriction in the bronchioles of lungs and decreases the rate of respiration.**

Effect on salivary gland-

- **Increase in the secretion of salivary gland as mostly the secretion is enhanced due to the secretion of cholinergic neurotransmitter.**

Effect on digestive system-

- **In digestive system there is an increase in peristaltic movement or bowel movement .**
- **There is increase in Gastric acid secretion which can further leads to acidity or in rare cases peptic ulcer.**
- **There is also increase in stomach's gland secretion.**

Effect on integumentary system-

- **Cholinergic neurotransmitters decreases or show inhibitory action on sweat glands and sebaceous glands.**
- **Ach also inhibits contraction or relaxation of Arrector pili muscle that joins the base of a hair follicle to dermal tissue.**

Effect on urinary bladder-

- **In this system when the neurotransmitter is released it shows contraction in muscles present in urinary bladder.**
- **Due to which rate of micturition is increased.**

Effect on adrenal gland-

- **It decreases the secretion of adrenaline from adrenaline gland.**

Effect on rest of the physiology-

- **There are many more effect on the body's physiology like in external genitilia in male there is increase in erection and decrease in ejaculation rate.**
- **This system decrease BMR or basal metabolic rate of the metabolism.**
- **It can also sometimes leads to uncontrolled defecation.**

Cholinergic receptors are basically of two types-

A) Muscarinic receptors-

Present on the body parts that are moist in nature like glands of GIT, smooth muscles, heart etc. and are of further subtypes that are as follows-

1) **M1 muscarinic RECEPTORS-**
These receptors are located in the autonomic ganglia , gastric glands, and on CNS. They basically act by Depolarization and increases acid secretion helps in activation of memory and learning centers and shows motor functions. It is a G-protein coupled 7- transmembrane receptor. It acts by the mechanism of IP3-DAG pathway that eventually increases the concentration of Calcium ions in the cytosol.

2) **M2 muscarinic RECEPTORS-**
These receptors are located in the SA node and causes its hyperpolarization which leads to opening of chloride channel leads to decrease in rate pf impulse generation , also AV node (purkinje's fibres) decreases velocity of conduction , also present in atrium and ventricle decreases contractility , in CNS it causes tremors , analgesia and contraction of visceral smooth muscles. It is a G-protein coupled 7-tm receptor. Acts by cAMP pathway of transduction mechanism.

3) **M3 muscarinic RECEPTORS-**
These receptors are located In the visceral smooth muscles, ciliary muscles causing contraction, and Meiosis in Iris and increase release of EDRF in vascular endothelium inducing vasodilation. It is a G- protein coupled 7-tm receptor. It acts by IP3-DAG mechanism increases cytosolic calcium ions.

B) Nicotinic receptors-

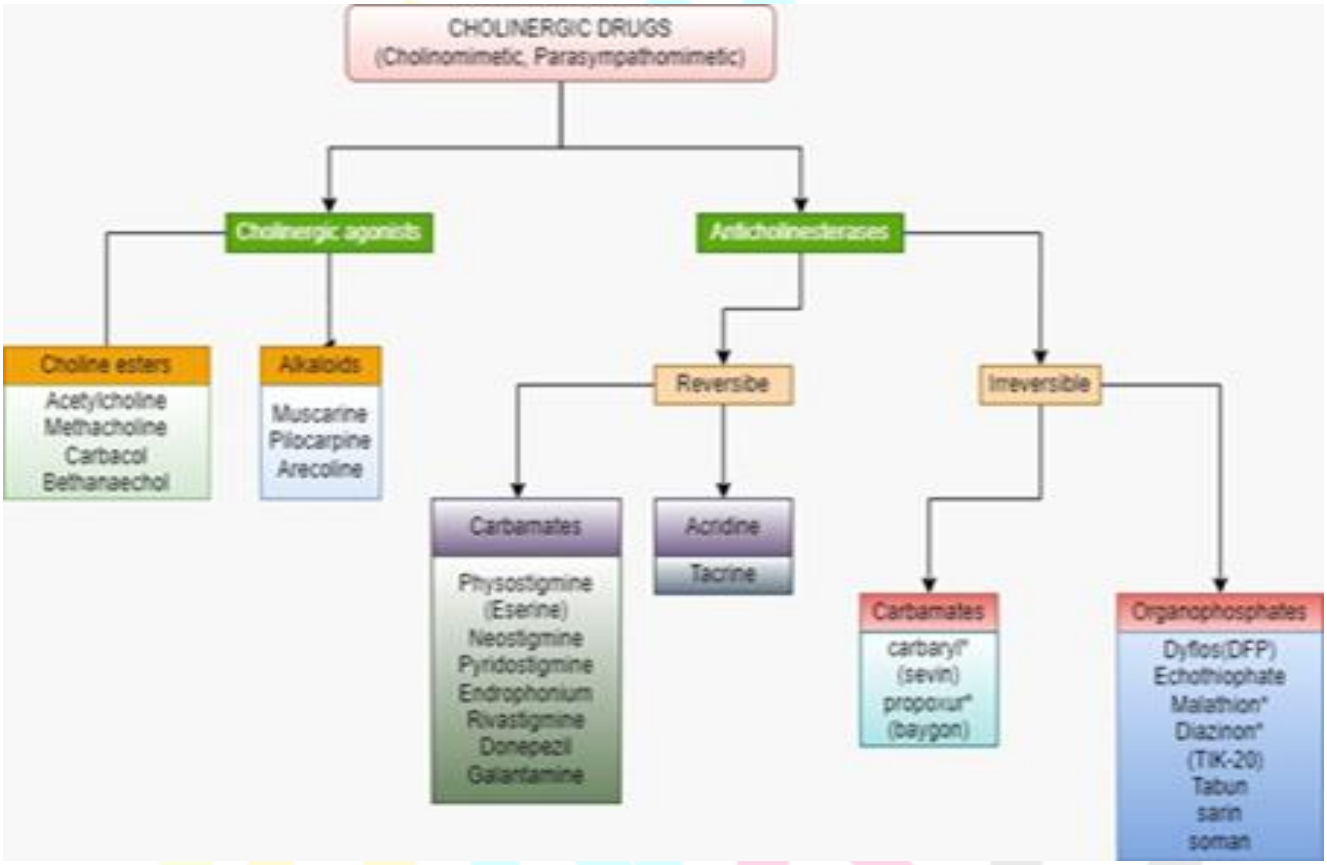
Present on the neuromuscular junctions, autonomic ganglia and are of further subtypes that are as follows-

1) **N m RECEPTORS- it is present on the neuromuscular junctions causing depolarization of muscles and contraction of skeletal muscles. It is a ligand gated intrinsic ion channel pentamer of alpha-2 , beta 0r gamma and delta subunit of 4-TM receptors. It acts by opening of (Na ,k) cation channels which causes muscle contraction.**

2) **N n RECEPTORS- it is present on autonomic ganglia causing depolarization post ganglionic impulse, on adrenal medulla leads to increase in release of catecholamine and causes specific excitation in basal ganglia and inhibition in medulla oblongata. It is same type of receptor as N m receptor and acts by same transduction mechanism.**

There are various drugs that produce actions similar to cholinergic neurotransmitter that are as follows-

A) CHOLINOMIMETIC DRUGS



a) CHOLINE ESTERS-

- **ACETYLCHOLINE**
- **METHACHOLINE**
- **CARBACHOL**
- **BETHANECHOL**

b) ALKALOIDS-

- **MUSCARINE**
- **PILOCARPINE**
- **ARECOLINE**

These choline esters show similar actions as Ach as prototype. Which is mentioned above. These are rarely used and show nonselective action. Alkaloids are the secondary metabolites obtained from plant species in order to show prominent actions to muscarinic receptors and stimulates ganglia.

PILOCARPINE-

it is an alkaloid obtained from the leaf of *Pilocarpus microphyllus* . it causes increase in the glandular secretions . its action is dose dependent in small doses it generally causes fall in BP , and in high doses there is a rise in BP due to ganglionic stimulation.

USES-

There is no oral preparation for this. It comes as an EYE DROPS. (PILOCAR 1% , 2% eye drops, CARPINE 0.5% eye drops)

MUSCARINE-

it occurs in poisonous mushroom *Amanita muscaria* and *inocybe* species and shows muscarinic actions.

ARECOLINE-

it is found in *Areca catechu* . it shows muscarinic as well as nicotinic actions , including those on skeletal muscle endplate. It shows cognitive function but not found useful and has no therapeutic use.

There are various drugs that inhibits the action of cholinergic neurotransmitter that are known are parasympatholytic drugs pr anti-cholinergic drugs or cholinolytic drugs. These drugs acts as a cholinergic blocking agent that are competitive antagonist of Ach. These are reversibly blocks the action of muscuranic agonist. These are classified in above mentioned table(1.1)

A) NATURAL ALKALOIDS-

a) ATROPINE-

It isa tropane alkaloid obtained from flowering tops various plants in the nightshade family like *Atropa belladonna*(deadly nightshade),etc. it shows various anticholinergic actions on various physiology of human body.

Effect on CVS-

- **Decreased cardiovascular response to vagal stimulation resulting in Tachycardia due to antagonist vagal effect.**
- **In CVS it shows some therapeutic effects in symptomatic second degree heart block or in modal bradycardia.**
- **No direct effect on vascular system , except for cutaneous vasodilation.**
- **It blocks hypotensive effect of muscuranic agonists.**

Effect on CNS-

- **At normal doses, it stimulates medullary centers. At higher doses it produces excitement, agitation, hallucination and Coma.**
- **It depresses vestibular excitation and has anti-motion sickness properties.**
- **It suppresses tremor and rigidity of parkinsonism by blocking cholinergic overactivity in basal ganglia.**

Effect on eyes-

- **Mydriasis or dilated pupils also called as blown pupil as it blocks muscuranic interventions.**
- **Cycloplegia or the paralysis of the ciliary muscle of the eye, resulting in a loss of accommodation.**
- **It should not be prescribed while glaucoma.**

Effect on gastrointestinal tract-

- **It relaxes smooth muscles of GI tract.**
- **It decreases intestinal and gastric secretion.**
- **It decreases peristaltic movement and motility.**
- **It also increases contraction of sphincter.**
- **It is used as anti spasmodic agent , in treatment of peptic ulcer and inflammatory bowel syndrome.**

Effect on respiratory system-

- **It decreases bronchial secretion and used as preanesthetic.**
- **It causes bronchodilation.**
- **It can cause ease in the symptoms of asthma , COPD , chronic bronchitis.**

Effect on genitourinary-

- **It decreases detrusor muscles in urinary bladder.**
- **It has a selective inhibitory effect on the bladder.**
- **It may cause urinary retention.**

Effect on glandular secretion-

- **It decreases glandular secretion .**
- **It decreases gastric acid secretion.**
- **It also decreases sweat gland secretion.**

SIDE EFFECTS-

- **It can cause dysrhythmia by increasing heart rate.**
- **It can cause CNS excitation due to which restlessness, irritability, disorientation and hallucination occurs.**
- **It dilates pupils and can cause increase in intra ocular pressure.**
- **It decreases gastric acid secretion as well.**
- **It causes urinary retention.**
- **It inhibits the action of sweat gland and also decreases bronchial.**

Toxic effects-

Sometimes there occurs belladonna poisoning which shows effects like-

- **Delirium**
- **Hypothermia**
- **Dry mouth**
- **Tachycardia**
- **Urinary retention**
- **Seizures**
- **Coma**
- **Respiratory arrest**
- **Sometimes death.**

Treatment of toxicity-

- **Gastric lavage with tannic acid.**
- **Cold sponging.**
- **Subcutaneous administration of physostigmine or intra venous administration of Diazepam to control convulsions.**

Contraindications-

- **In condition of Glaucoma.**
- **Prostatic hypertrophy**
- **Urinary tract obstruction.**
- **Gastro intestinal tract obstruction.**
- **Infectious diarrhea**
- **Reflux oesophagitis**
- **Tachyarrythmias**
- **Angina pectoris**
- **Hyperthyroidism**
- **Pregnancy.**

SYMPATHETIC NERVOUS SYSTEM-

Sympathetic nervous system also known as fight or flight response or adrenergic nervous system in which the functional neurotransmitter is ADRENALINE . this system is also known as thoraco lumbar outflow. In this nervous system ganglia is situated near spinal chord along with ganglionic chain. Pre ganglionic nerve is shorter than post ganglionic nerve.

This nervous system said to be the reverse of adrenergic nervous system. It shows effects on physiology of various functions like-

Effect on eye-

- **Pupil is dilated or mydriasis occurs.**
- **There is decrease in the secretion of lacrimal gland causing dryness.**
- **IOT or intra ocular tension is decreased , there is a decrease in overall glandular secretion.**

Effect on heart-

- **Tachycardia or increased heart rate occurs due to increase force of contraction which causes increase in the blood pressure i.e Hypertension.**

Effect on blood vessels-

- **Dilation of larger blood vessels and cutaneous vasoconstriction in small or fine blood vessels.**

Effect on lungs-

- **The sympathetic nervous system shows dilation in bronchioles (Bronchodilation) of lungs which increases the rate of respiration.**

Effect on salivary gland-

- **Decrease in the secretion of salivary gland as mostly the secretion is decreased due to adrenergic neurotransmitter.**

Effect on digestive system-

- **There is a decrease in peristaltic movement or bowel movement.**
- **There is decrease in gastric acid secretion and other glandular secretion in stomach.**

Effect on integumentary system-

- **Adrenaline increases or show excitatory actions on sweat glands and sebaceous glands.**
- **Adrenaline also stimulates contraction causing goose flesh of arrector pili muscle.**

Effect on urinary bladder-

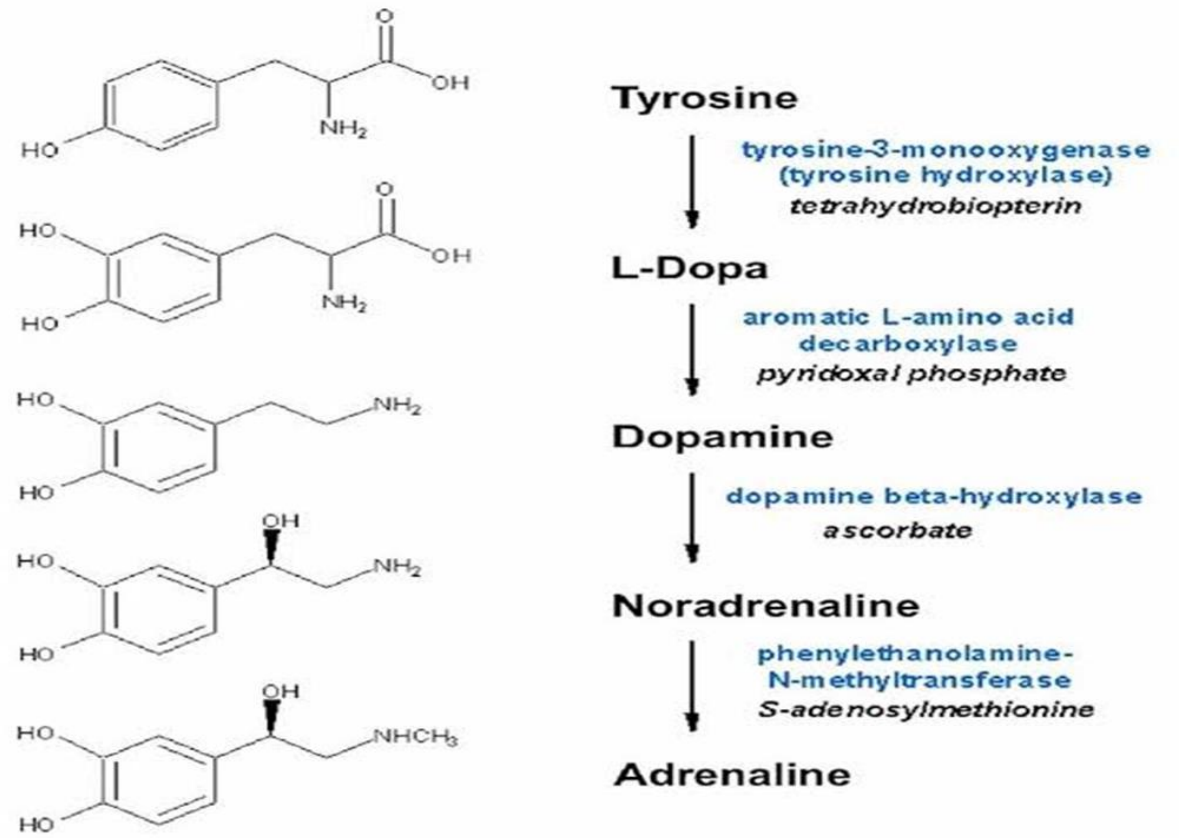
- **In this system when the neurotransmitter is secreted it shows relaxation in muscles present in urinary bladder. Due to which micturition is sustained.**

Effect on adrenal gland-

- **It increases the secretion of adrenaline from adrenal gland.**

Effect on the rest of the physiology-

- **There are many more effect on the body's physiology like in external genitilia in male there is decrease in erection and increase in ejaculation rate.**
- **This system increases basal metabolic rate of metabolism .**
- **It increases blood sugar level and glycogenolysis.**
- **It deals with the stressful situations.**



Receptors of adrenergic neurotransmitter-

1) **α1 Receptors found on blood vessels of all types.**
   Agonists- phenylephrine Antagonists- Prazosin

2) **α2 Receptors found on CNS or spinal and cranial nerves.**
   Agonist- Oxymetazoline Antagonist- Atenolol

3) **β1 Receptors found on heart, kidney (on JGA or juxta glomerulus apparatus cells).**
   Agonist- Dobutamine Antagonist- atenolol

4) **β2 Receptors found on lungs , uterus and gastro intestinal tracts.**
   Agonist- Terbutaline.

5) **β3 Receptors found in adipose tissue.**
   Agonist – BRL37344.

Drugs that mimics the action of adrenergic neurotransmitter were said to be sympathomimetic and are classified as-

EPINEPHRINE-

Also known as adrenaline and binds to α and β receptors. It shows action by binding to it and shows various physiological effects on-

Effect on CVS-

- **Myocardium contraction.**
- **Positive ionotropic effect.**
- **Increase in renal renin release.**
- **Arteriolar contraction in skin.**
- **Vasodilation of blood vessels taking part in Renin Angiotensin system.**
- **Increase in systolic blood pressure and slightly decrease in diastolic pressure.**

NOTE:-

DALES VASOMOTOR REVERSAL PHENOMENON-

- **IF Adrenaline is administered via I.V there is α1 action i.e increase in B.P which is gradually followed by β2 action prolonged fall of B.P.**
- **If administered after giving α - blockers , only fall in B.P is seen.**

Effect on Respiratory system-

- **Direct stimulation of β2 receptors on smooth muscles.**
- **Powerful bronchodilation.**

Effect on metabolism-

- **Increased release of glucagon.**
- **Decreased release of insulin due to α2 effect.**
- **There is an increase in energy demand.**
- **It shows agitated action in which body works more.**
- **There is increase in glycogenesis in liver.**
- **Increases activity on adipose tissue due to presence of β3 receptor resulting in lipolysis.**

Action-

- **Epinephrine shows rapid onset of action but brief duration of action due to rapid degradation.**
- **Epinephrine cannot be given orally as it is inactivated or metabolized by the intestinal enzymes.**
- **Epinephrine administered via I.V and only its metabolites get excreted in urine.**

Therapeutic uses-

- **This medication acts as treatment of type 1 hypersensitivity reaction.**
- **It relieves bronchospasm when used as a nebulizer and induces bronchodilation.**
- **Epinephrine restores cardiac rhythm in patients with cardiac arrest in case of drowning or electrocution.**
- **It can sometimes act as local anesthetic in which case the solution contains 1ppm parts epinephrine which greatly increases the duration of local anesthetic and causes local vasoconstriction.**
- **To control epistaxis very weak solution is used topically to vasoconstrict mucous membrane to control oozing of blood capillary.**

Adverse effects-

- **In CNS , it can cause spontaneous actions like – anxiety , fear , tension , headache and tremor.**
- **It can cause cerebral hemorrhage marked with elevated blood pressure.**
- **Epinephrine can trigger cardiac arrhythmias particularly if the patient is receiving Digoxin.**
- **It induces pulmonary oedema.**

Contraindications-

- **It is contraindicated to prescribe epinephrine in hyperthyroidism.**
- **It should not be administered when the patient is diabetic.**

Note- it can not be given if the patient is on cocaine as it may leads to cardiovascular effects. It cannot be given with β-blockers or with inhalation anesthetics which may leads to tachycardia.

NOREPINEPHRINE-

- **It shows similar effects as epinephrine.**
- **It is administered by slow i.v infusion.**
- **It can cause necrosis in the local tissues.**
- **Rapid alkalization of NE or NA occurs at alkaline pH. It is used as a strong vasoconstricting agent. NORAD,VASCUE.**

PHENYLEPHRINE-

- **This is a selective α1 agonist. It raises BP by vasoconstriction. It reduces IOT by constricting ciliary body. It does nor shows central effects with normal doses. FRENIN 10mg in 1ml inj , PHENIL eye drops0.12%.**

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