# Nervous System-Neurotransmitters

Neurotransmitters are the language of the nervous system one type of **chemical signaling** = is the main way cells talk to each other. Many different kinds of chemicals can be used for signaling:

**a. paracrine regulators** (tissue hormones)
effects only on neighboring cells, distributed by simple diffusion through interstitial fluids don't enter blood
rapidly inactivated by enzymes after triggering receptor protein on target cell, eg. histamine

**b. neurotransmitters (NT)**
secreted by neurons in response to electrical stimulus
very short range _ cell to cell across synapse

**c. neurohormones**
released into blood by neurons

**d. hormones**
long range, secreted into blood by endocrine gland
specific chemicals bind to receptors on or in cell to cause change in cell function
_some receptor proteins are enzymes that cause reactions
_some open and close gated membrane channels
cell only responds to a chemical if it has the correct receptor protein
= **target cell** for that chemical

Neurotransmitters are released at most **synapses (**100's of neurotransmitters have been identified**)** some are excitatory **,** inhibitory
some neurons produce and release a single NT, most make 2 or more and can release one or all at the same time
different cells respond in different ways to same chemical
eg. ACh _ stim skeletal muscle cells
_ inhibits heart muscle cells
the same NT may have different effects in different parts of body
eg. excitatory one place, inhibitory another

**The effect of a NT on a postsynaptic neuron depends on:**
the properties of the **receptor protein *not on*** the nature of the NT
a variety of different kinds of chemicals have been found to act as neurotransmitters:

1. **acetylcholine**
2. **protein & peptides**
3. **amino acid derivatives**
4. **Inorganic gasses**
5. **ATP**

synapses in Peripheral Nervous System ( PNS ) release only a few different neurotransmitters
eg. Somatic Motor Neurons _ ACh,
eg. Autonomic Motor Neurons _Epinephrine, NE
most of the diversity is in the CNS, especially the brain

**Neuromodulators (NM)**
other chemicals can be released at synapse in addition to neurotransmitters:

**neuromodulators =**neuromodulators can influence the release of NTs or the post synaptic neuron's response to the NT
NM are usually peptides = **neuropeptides,** a chemical may be both a NT and NM

neuromodulators function in 2 different ways:
1. have **direct effect** on membrane potential by opening and closing chemical gates
2. have **indirect effect** on membrane potential through "second messenger" inside the cell
eg. receptor on cell membrane : adenylate cyclase , cyclic AMP

**Effects of Drugs on Nervous Transmission**
many drugs have their effects on the body because they either mimic or somehow modify the action of neurotransmitters or neuromodulators at synapses, knowing receptor types is clinically important = allows selection of drugs that can affect specific organs in ways desired
The end result of these actions:
**A. enhance** the action of the neurotransmitter
1. drugs mimic specific neurotransmitters
2. speed up the rate of NT synthesis or release
3. prevent neurotransmitter inactivation
**B. inhibit (block)** the action of neurotransmitter
1. reduce synthesis of the NT in axonal end bulbs
2. prevent binding of NT to receptor
3. slow down rate of synthesis or release

## PNS Neurotransmitters
few NT are found in PNS, most diversity is in CNS. Two main Neurotransmitters in PNS:
**Acetylcholine**
**Nor Epinephrine**
_neurons that release ACh are called **cholinergic**
_neurons that release NE are called **adrenergic**

PNS synapses occur in **somatic** and in **autonomic** branches
**Somatic Neurotransmitters = acetylcholine** at all NM junctions was the 1st NT to be identified
always stimulatory _ causes muscle contractions ,removed from synapse by enzyme **acetylcholinesterase**
in ACh can be affected at these NM junctions by:
**1. Botulism Toxin =**blocks release of ACh_ paralysis
**2. Black Widow Toxin =**stimulates massive release of Ach  intense cramping and muscle spasms
**3. Nicotine =**mimics ACh: binds to receptor and activates it but no enzyme to remove it prolonged hyperactivity
**4. atropine, curare =**binds to receptor but does not induce muscle contractions
since ACh cant bind, muscle cells cannot be stimulated = paralysis
**5. nerve gas, malathione =**block the breakdown of ACh (=cholinesterase inhibitors)
_ extended, extremely strong contractions

**Autonomic Neurotransmitters**
autonomic synapses produce **Acetylcholine** or **Norepinephrine**
synapses at ganglion and at effector organ:

at ganglion (preganglionic fibers), neurons secrete **acetylcholine**
synapses at end organs
in parasympathetic branch, most fibers also secrete **ACh** at effector organ
in sympathetic branch most fibers secrete **NE** at effector organ
different neurotransmitters of post synaptic neurons are responsible for each branches'
different effects on same target organ:
but same NT can have **excitatory** effect on some organs and **inhibitory** effect on other organs

**Acetylcholine (Cholinergic Fibers)**
secreted by all autonomic preganglionic fibers_ always excitatory
secreted by most parasympathetic postganglionic fibers_ usually excitatory
a few are inhibitory due to two major kinds of NT receptors:
**1. Nicotinic ACh Receptors**
(named for drug that binds to receptor and mimics ACh)
most ACh receptors in body:
a. Neuromuscular junctions of somatic motor neurons
b. all ganglionic receptors (sym & parasym)
c. also secreted by sym branch at adrenal medulla
*always causes stimulation*

**2. Muscarinic ACh Receptors**
( = "mushroom" named from source of drug that binds to these receptors) can cause stimulation or inhibition of effector organs
**stimulatory**
all parasympathetic effectors except the heart
a. parasympathetic synapses stimulate glandular secretion
b. parasympathetic synapses stimulate bronchial constriction
c. parasympathetic synapses constrict iris circular muscle to constrict pupil
d. in sym branch _ACh activates sweat glands
eg. **Atropine** blocks stimulatory muscarinic effects:_ used in pre-operations to suppress salivation and respiratory secretions, _ used to dilate pupils
**inhibitory**
a. parasympathetic synapse at heart decreases force and rate of heart beat
b. in sym branch _ ACh inhibits (dilates) blood vessels in skeletal muscles

**NorEpinephrine (Adrenergic Fibers)**
secreted by most sympathetic postganglionic fibers at effector organ can be excitatory or inhibitory depending on receptor type:

**1. Alpha Receptors** (alpha 1 & alpha 2)
usually **stimulatory** in sym branch, NE:
_constrict blood vessels of skin and visceral organ sphincters
_causes contraction of radial muscles in iris to dilate pupils
**eg. Ephedrine**
in cold, cough & allergy medications _ stimulate alpha receptors to cause:
constriction of blood vessels serving skin, mucosa, salivary glands, etc
**eg. Alpha blockers** (drug=Celebrex)
_ dilates blood vessels to lower blood pressure

**2. Beta Receptors** (ك1, ك2, ك3)
usually **inhibitory**: dilation or relaxation of effector muscles,
stops glandular secretion
in sym branch, NE:
_relaxes muscles to dilate coronary arterioles (ك1)
_relaxes muscles to dilate bronchioles (ك2)
_relaxes muscles in walls of digestive and urinary organs (ك2)
a few are **stimulatory**: constriction, glandular secretion in sym branch, NE:
_increases heart rate (ك1)
_stimulates renin release by kidneys (ك1)
_stimulates secretion of insulin by pancreas (ك2)
_stimulates lipolysis of fat cells (ك3)
**eg. Beta blockers**
_ reduce heart rate without interfering with other sympathetic functions

## CNS Neurotransmitters

most of the diversity is in the CNS, esp the brain several hundred neurotransmitters & neuromodulators have been identified so far. Many hormones act as neurotransmitters in the brain, a variety of different chemicals have been found to act as neurotransmitters in the CNS:
**1. acetylcholine**
**2. proteins & peptides**
**3. amino acid derivatives** biogenic amines (=catecholamines)**,** amino acids
**4. Inorganic gasses**
**5. ATP**

1. **Acetylcholine (ACh)**
also at all NM junctions and in Autonomic NS
**in CNS:**
1. inadequate amt ACh _ correlated with Alzheimer's
2. ACh receptors destroyed in Myasthenia gravis
an autoimmune disease

**2. Proteins & Peptides**
broadly distributed in brain, affect behavior, moods, sleep, thought
some examples:
**Substance P**
peptide (chain of amino acids) mediates pain transmission in PNS
in CNS affects mood
also involved in respiratory and cardiovascular control
**endorphins & enkephalins**
peptides in limbic system and related structures natural opiates reduces pain perception "runners high"
1. **morphine, heroin, methadone**
binds to enkephalin receptors_ mimicks effecs of endorphins
eg. **Cholecystokinin** peptide may be related to feeding disorders

**3. Amino Acid Derivatives**
unaltered amino acids or modified ones, eg. catecholamines
eg. **Aspartate** amino acid only in CNS excitatory
eg. **Glutamate** amino acid only in CNS excitatory

important in learning and memory
1. released in large quantities after stroke= increases damage to nervous tissue
eg. **Glycine** amino acid in spinal cord inhibitory
1. strychnine blocks receptors _ causes convulsions
eg. **Histamine** produced in hypothalamus in immune system is powerful vasodilator
eg. **GABA** modified amino acid most abundant inhibitory NT in brain(~1/3rd of all)_inhibits skeletal movements
1. deficiency: Huntington's disease_ jerky movements
2. **alcohol**
enhances its inhibitory effects
_ slowed reflexes
_ reduced coordination
3. **tetanus toxin** blocks CNS synapses that release inhibitory NT such as GABA and glycine
_ results in overstimulation of muscles also affects mood
excess: less anxiety, deficiency: more anxiety
1. **Valium** binds to GABA receptors mimics or enhances its effects _ less anxiety

eg. **Dopamine** a catecholamine synthesized from tyrosine esp in substantia nigra of basal ganglia (midbrain) affects coordination of skeletal muscles also a "feel good" NT
1. **Parkinson's Disease**
deficiency_tremors (no inhibition of basal nuclei)
2. **schizophrenia**
correlated with excess of dopamine
3. **amphetamines**
enhance its "feel good" effects
4. **cocaine**
blocks its uptake_ enhances "feel good"
eg. **norepinephrin**
also released by some neurons in autonomic NS esp in brain stem another "feel good" NT
affects mood: arousal, dreaming
1. generally: excess _ mania
deficiency _ depression
2. **Cocaine & amphetamines**
prevents inactivation of norepinephrin _enhances its effect (amphetamines and cocaine have similar effect as on dopamine)
eg. **serotonin**
indolamine, synthesized from tryptophan or histidine ,in brain stem (reticular system)
induces sleep, temp regulation, appetite also affects mood and aggression

**4. Inorganic Gasses**
eg. **NO (nitric oxide)** toxic gas
short lived is synthesized on demand not stored in axonal vesicles
in CNS may be involved in learning and memory
in PNS causes relaxation of smooth muscle
eg. **CO (carbon monoxide)** in CNS similar physiology as NO

**5. ATP**
now recognized as a major neurotransmitter in both CNS and PNS produces fast excitatory response at certain receptors