# Ch 4: Neurotransmitter Substances & Psychopharmacology

Neurotransmitters
NTS are chemical messengers
Through their structure they bind to receptor sites
Through process we get nervous system function

Ligand: Capacity to bind
all have a unique biosynthetic pathway
however, because of commonalities between their synthesis, NTS fall into three different classes
1. Acetylcholine
2. Monoamines
3. Amino Acids

# Acetylcholine (ACh)

It gets it own class
nothing else like it base on its chemical composition
first discovered- PNS
    Vagusschuft- associated with the vagus nerve
Predominantly an excitatory NTS (EPSP)
Synthetic Pathway
    Enzyme called choline acetyltransferase takes acetylcoenzyme  A and Choline
widely implicated in movement, especially in the voluntary nervous system
also has some learning and memory functions
AChE-- ensymatic degradation

# two major ACh receptors have been identified:

1. Muscarinic
    found in the brain stem and autonomic NS
    cholinergic
    anticholinergic
    there are subtypes M1 through M5
    metabotropic receptors
    excitatory
    smooth muscle regulation, gut motility, cardiac contractions
    block muscarinic receptors: block gastric secretion and slow gut motility
    stimulating the receptors: can speed up heart rate, dilate pupils, and raise blood pressure

2. Nicotinic

These receptors are the primary mechanism for neurons to talk to muscle cells

Excitatory

Neuromuscular junction

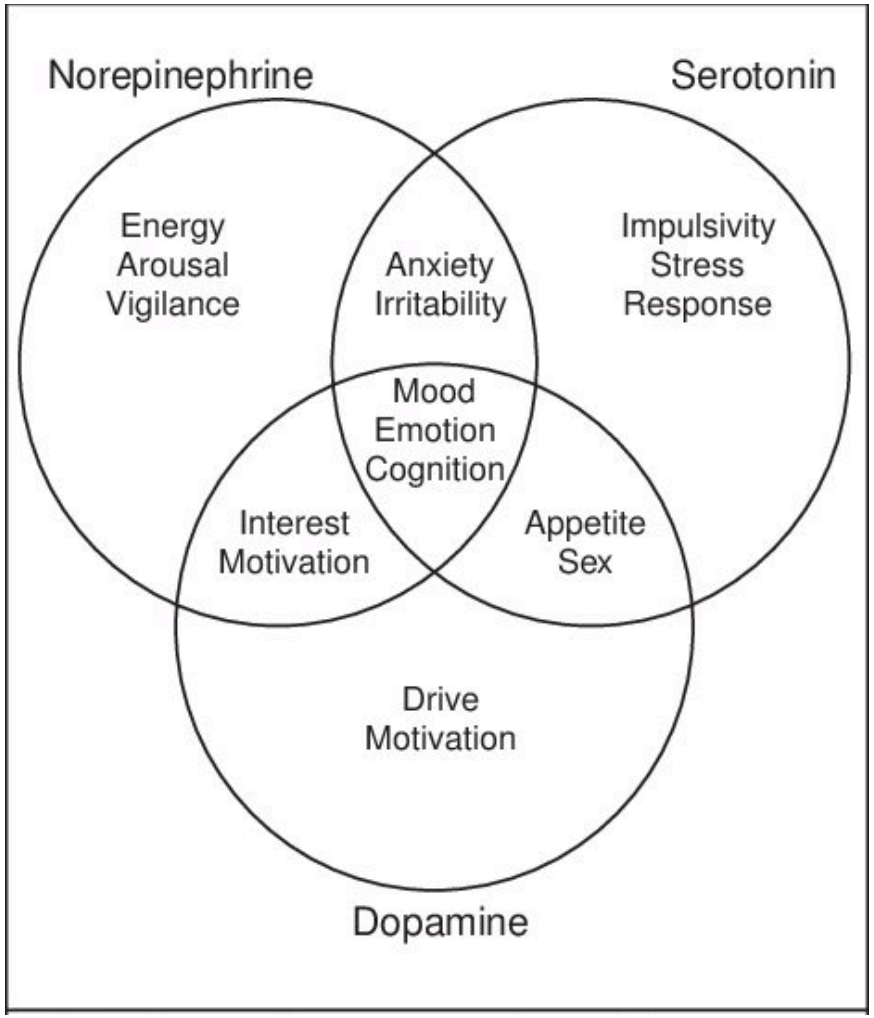
Ionotropic and excitatory

Also find nicotinic receptors in the frontal lobe of the brain- attention and concentration mediated by these receptors

Blocking these receptors: can cause paralysis

# Second major class of NTS is known as the Monoamines

2. Monoamines
   1. Indolamines
      serotonin
      melatonin
   2. Catecholamines
      norepinephrine
      epinephrine
      dopamine



# Metabolism

# 1. Indolamines: serotonin (5-Ht)

over 15 subtypes of 5- Ht receptors
5-Ht sub 1A
EPSP's
Ionotropic receptors
5-Hydroxytryptamine into Tryptophan into 5-HTP into 5-Ht
Mood, emotion, appetite, sleep and dreaming

# Indolamines: Melatonin

Hormone
pineal gland- you only have one that controls a lot, however it helps produce melatonin
5-Ht into Melatonin
pineal gland is tied to the visual system, when it gets dark the pineal gland starts to release melatonin
helps prepare the brains for sleep
sleep/wake cycles, circadian rhythms

# 2b. Catecholamines: norepinephrine (NE)

Ne
Noradrenergic
Excitatory NTS
stimulus  receptors ephinephine
autonomic NS
    Pons, medulla, as well as other regions
mood, emotion, cognition
tyrosine into L-DOPA into dopamine into  NE

catecholamines: epinephrine

Highly involved in the sympathetic NS
But released from adrenal glands
    sit on top of the kidneys
Arousal
Alpha 2 and 2
Beta 1 and 2 (betablcokers)
Cardiovascular drugs treating psych issues

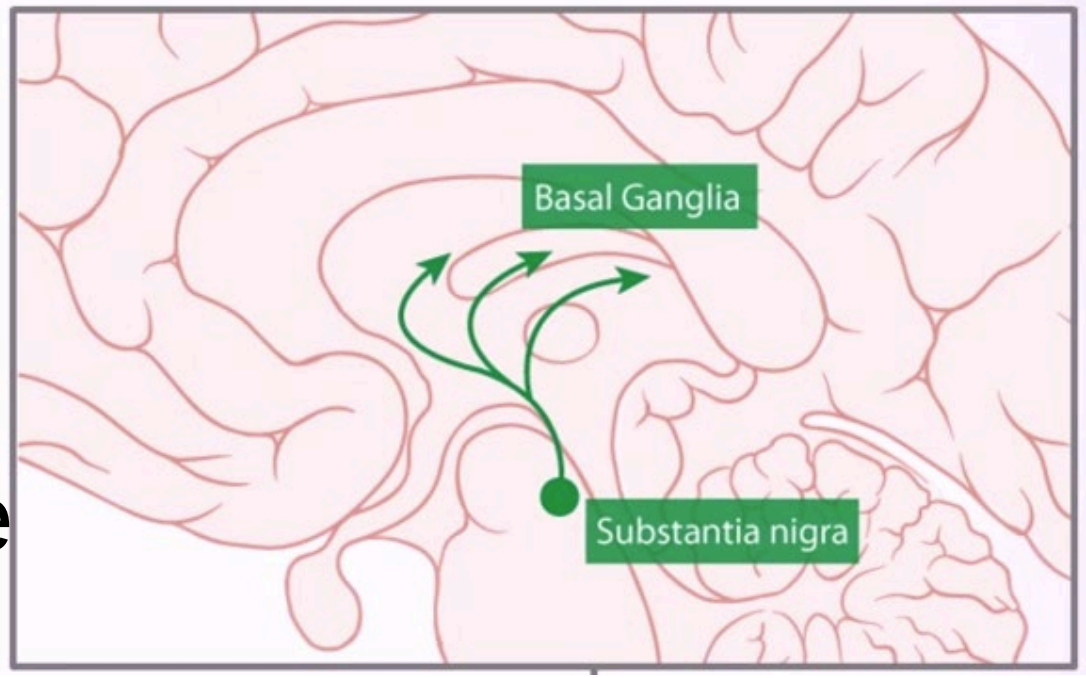
# Catecholamines: Dopamine (DA)

Both inhibitory and excitatory
D1-D5
Learning, movement, attention, reward, perception
Dopaminergic

# Dopamine: **Nigrostriatal System**

70% of the brains goes into the basal ganglia

DA is in this system coordinating movement that is affect in parkinsons disease where these neurons stop producing

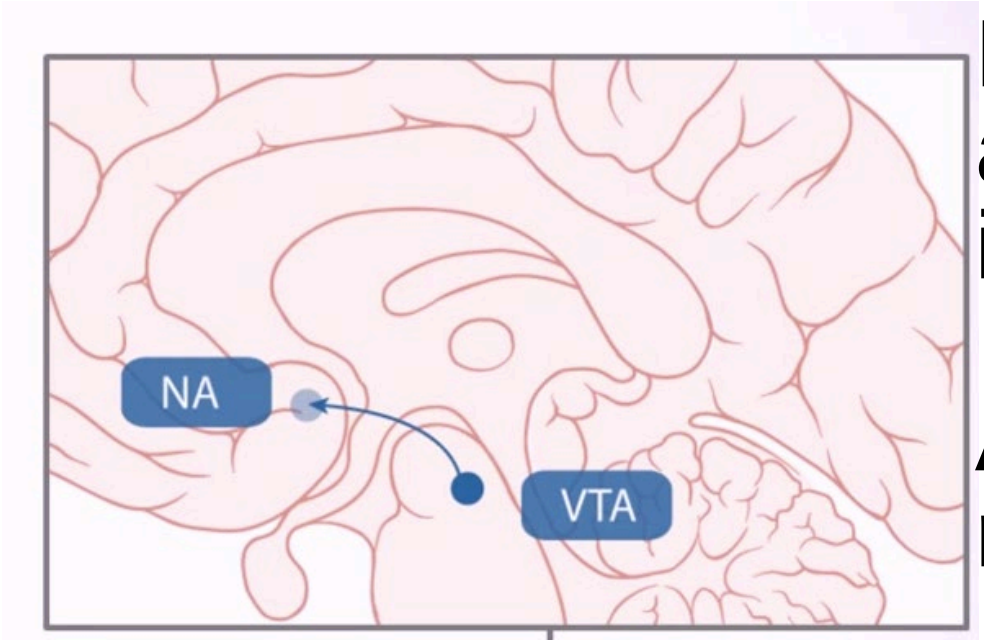



D2 receptors is mostly movement cant mess with these

# Dopamine: **Mesolimbic System**

DA cells in

Ventral tegmental area project to the limbic system highly implicated in reinforcement

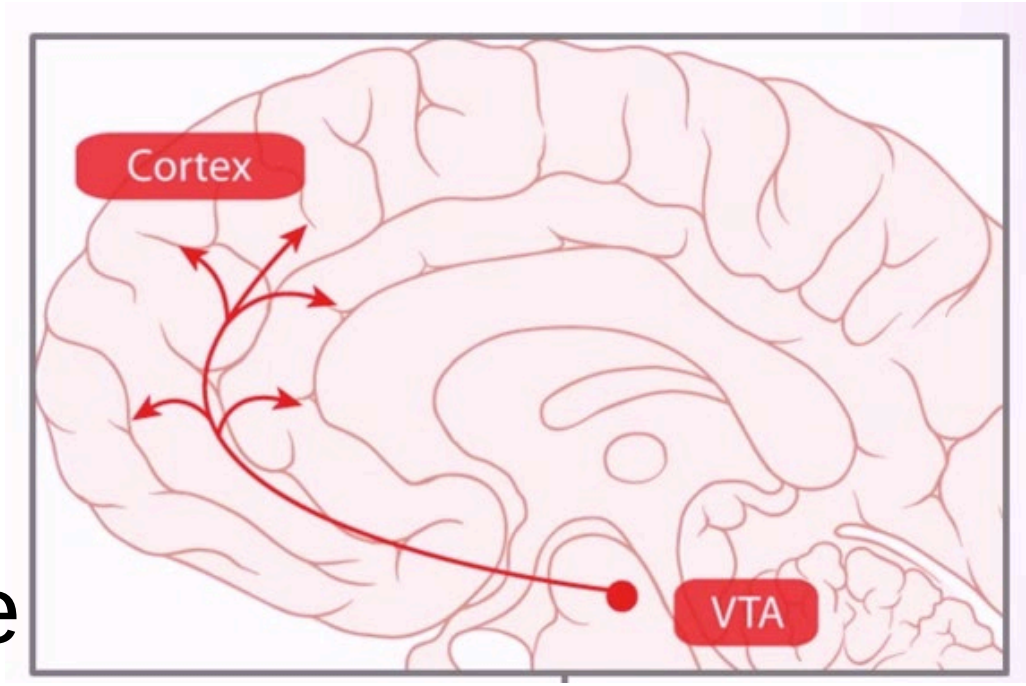



Learning, memory, addictions seem to involve this system

Again a lot of D2 receptors

# Dopamine: **Mesocortical System**

Starting from the VTA again but going to the frontal lobe
Executive functions
D4 receptors here
Overactivity: schizophrenia



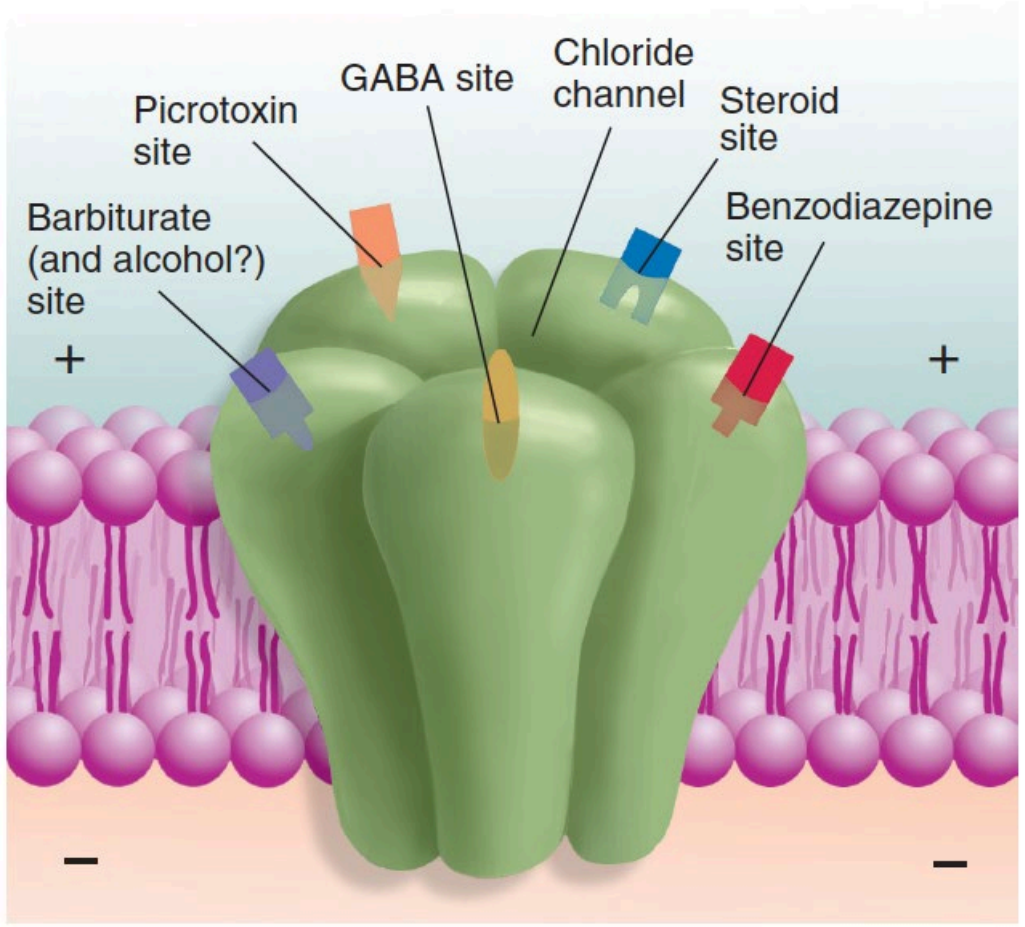
# AMino acids

Chains of proteins
consider 2
- GABA
- Glutamate

these are among the oldest NTS

# 3. Amino Acids: **GABA**

Widely distributed throughout the NS
Highly Inhibitory
GABA sub A: ionotropic lets Cl-
GABA sub B: metabotropic K+



# Amino acids: Glutamate

It is the most common NTS
Principal Excitatory NTS
It increases the efficacy of NTS
Primes neurons so when the neuron gets just a little bit of excitation it will fire faster
Ionotropic receptors
    NMDA, AMPA, kinate
Metabotropic glutamate receptor

# Amino acid: Glycine

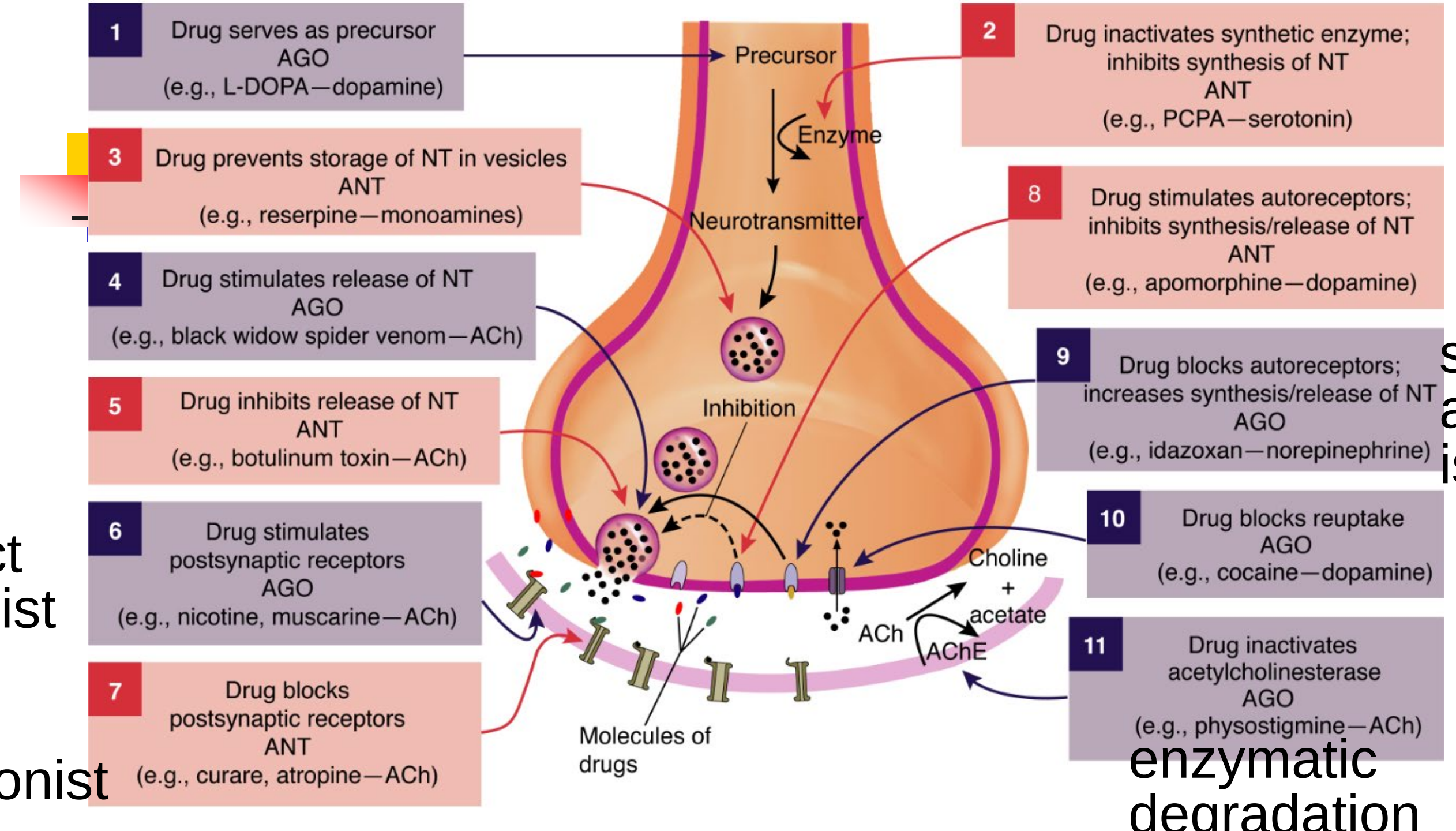
Stimulate a ionotropic Cl- channel in the lower spinal cord
Tetnus- locks muscles,
Inhibits Glycine

otheer potential NTS

Peptides- opioids-poppy
Lipids- cannabis sits in a thc receptor
nucleosides- neuromodulator called adosine
soluble gasses- that can break down to liquids

**most of psychopharmacology is manipulating NTS or their receptors**

psychopharmacology is the science of manipulating either NTS or its receptors
-mechanism of action- refers to the biochemical process through which a drug produces its effect.
-site of action
-agonists (more serotonin the it would be an agonist)
-antagonists (narcan is an opioid antagonist which negates)


1 Drug serves as precursor
AGO
(e.g., L-DOPA—dopamine)
2 Drug inactivates synthetic enzyme; inhibits synthesis of NT
ANT
(e.g., PCPA—serotonin)
3 Drug prevents storage of NT in vesicles
ANT
(e.g., reserpine—monoamines)
4 Drug stimulates release of NT
AGO
(e.g., black widow spider venom—ACh)
5 Drug inhibits release of NT
ANT
(e.g., botulinum toxin—ACh)
6 Drug stimulates postsynaptic receptors
AGO
(e.g., nicotine, muscarine—ACh)
7 Drug blocks postsynaptic receptors
ANT
(e.g., curare, atropine—ACh)
8 Drug stimulates autoreceptors; inhibits synthesis/release of NT
ANT
(e.g., apomorphine—dopamine)
9 Drug blocks autoreceptors; increases synthesis/release of NT
AGO
(e.g., idazoxan—norepinephrine)
10 Drug blocks reuptake
AGO
(e.g., cocaine—dopamine)
11 Drug inactivates acetylcholinesterase
AGO
(e.g., physostigmine—ACh)
Precursor
Enzyme
Neurotransmitter
Inhibition
Choline
+
acetate
ACh
AChE
Molecules of drugs

**Pharmacokinetics**

**- getting the drugs in, how they move around, what jobs they do**

**- how the drug affects the body**

**Pharmacodynamics**

**- this is how drugs are metabolized and eliminated**

**- body's affect on the drug**

**drug routes: absorption**

- getting to the circulatory system
- Direct Access
  - -Intravenous (IV)
  - Intraperitoneal (IP)
- Intramuscular (IM)- create biohazard which is now called a sharp and also once you give it you cannot take it back.
- PO (by mouth)- most people are okay with putting foreign things in their mouth
- PR (per rectum)- by asshole
- IN (intranasally)- get it in the nose
- Inhalation
- epidural- into the brain stem
- intracranial- in the head
- IO- intraosseous
- Sub Q- under the skin
- Transdermal- a patch
- Sub Lingual - a couple antipsychotic that is early disintegratin that goes under the tongue

# Distribution of drugs in the body

-Any psych drug has to be able to diffuse across the blood brain barrier
    - lipid soluble (fat)
-Drugs need to have sufficient quantities so that they are present in blood plasma
-They may target unintended systems

# Drug Effectiveness

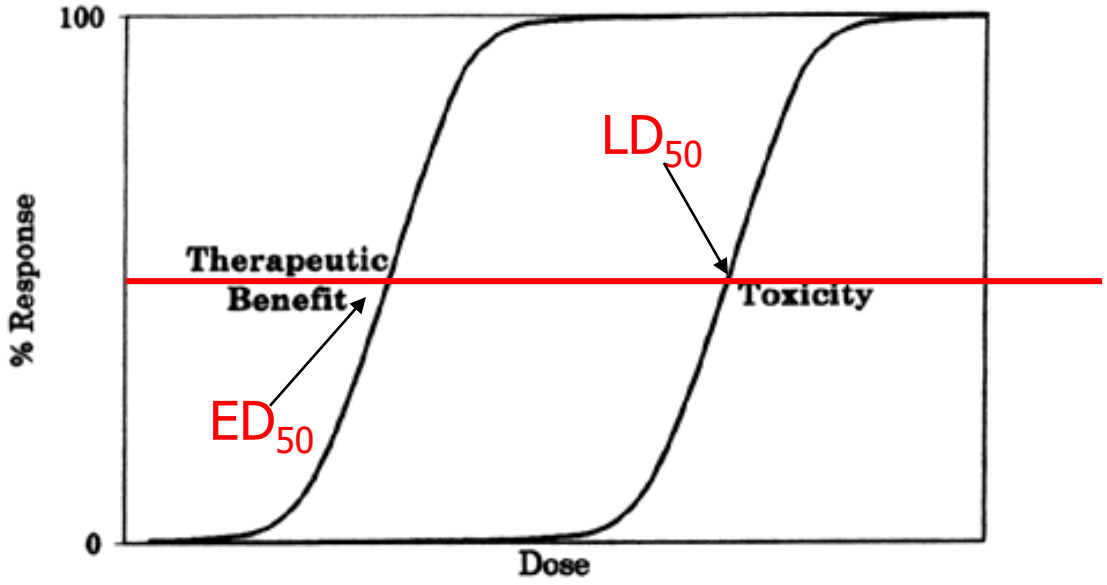
Dose-response curve

-ED50 which is the effective dosage

-LD50 which is the toxic effects or the lethal dose

- morphine is respiration issues

- Therapeutic window- you want the LD to be as afar away from the ED as best as you can

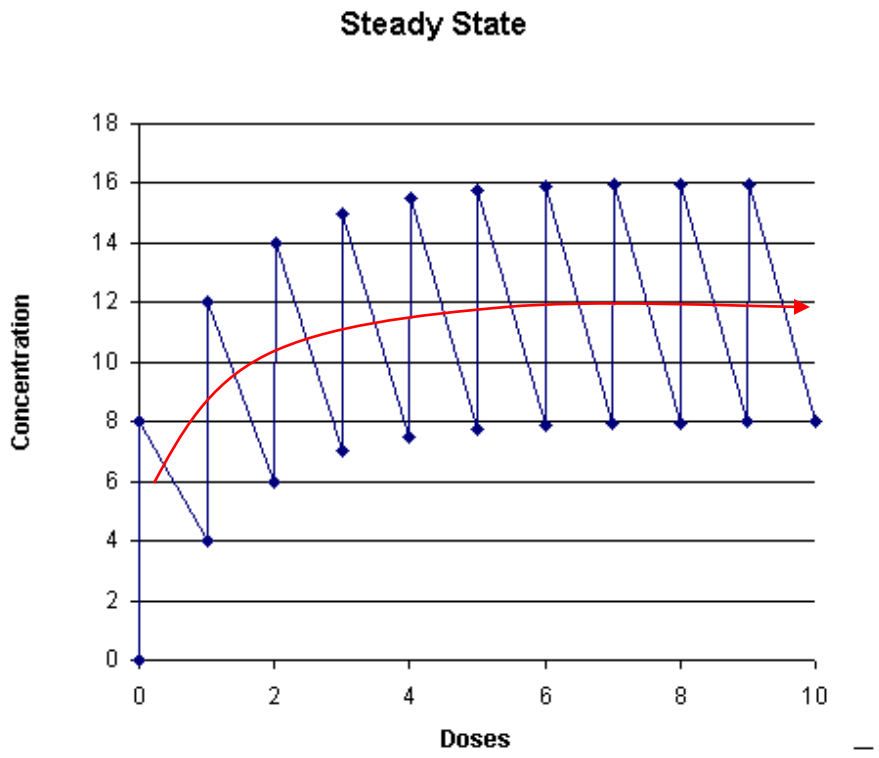



Dose-response curve for Morphine

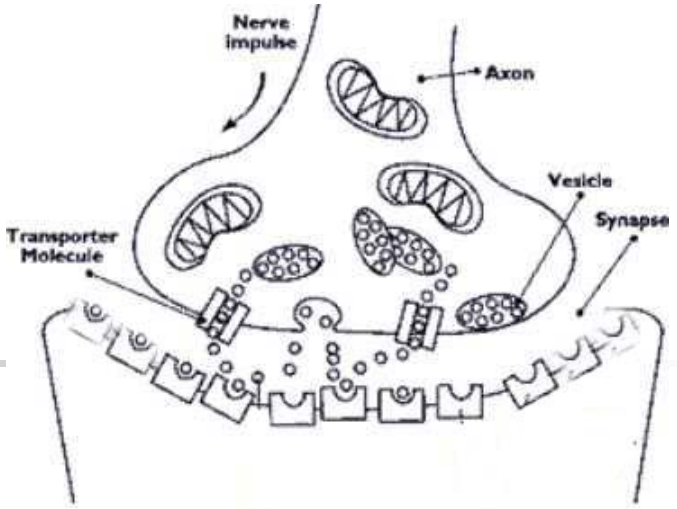
# Drug inactivation and excretion

- Drugs can last only so long in the boyd
- Enzymes will eventually start working on them and -pulling them apart
- Metabolism
- Metabolites- active metabolites- activate the drug/ substance formed in or necessary for metabolism.
- Get rid of wates: Excretion
    - Urine
    - Respiration

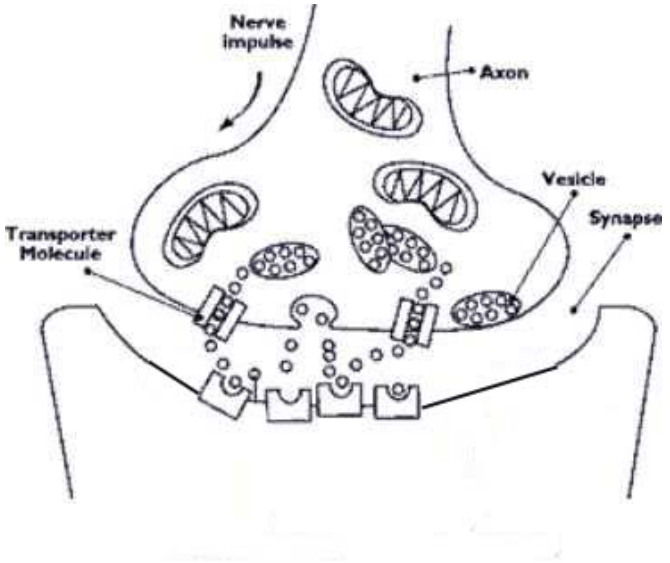
# Half Life and Accumulation



# Effects of Repeated Administration

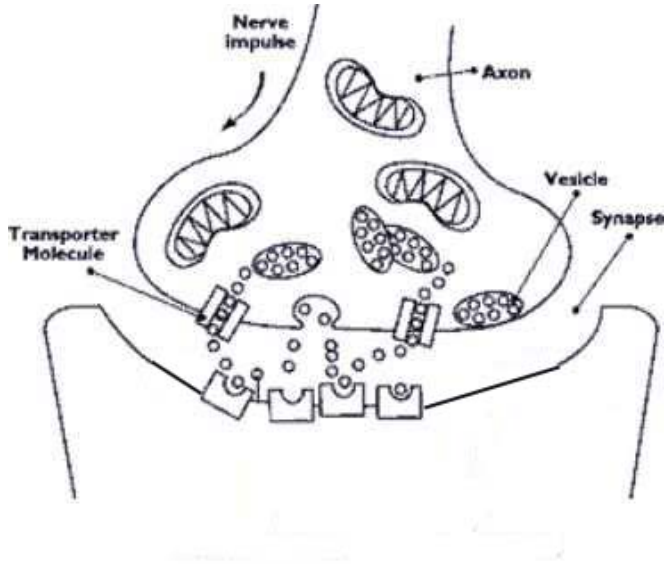



Before repeated administration




After repeated administration

# Effects of Repeated Administration




Cranky synapse needs to up regulate: no NTS