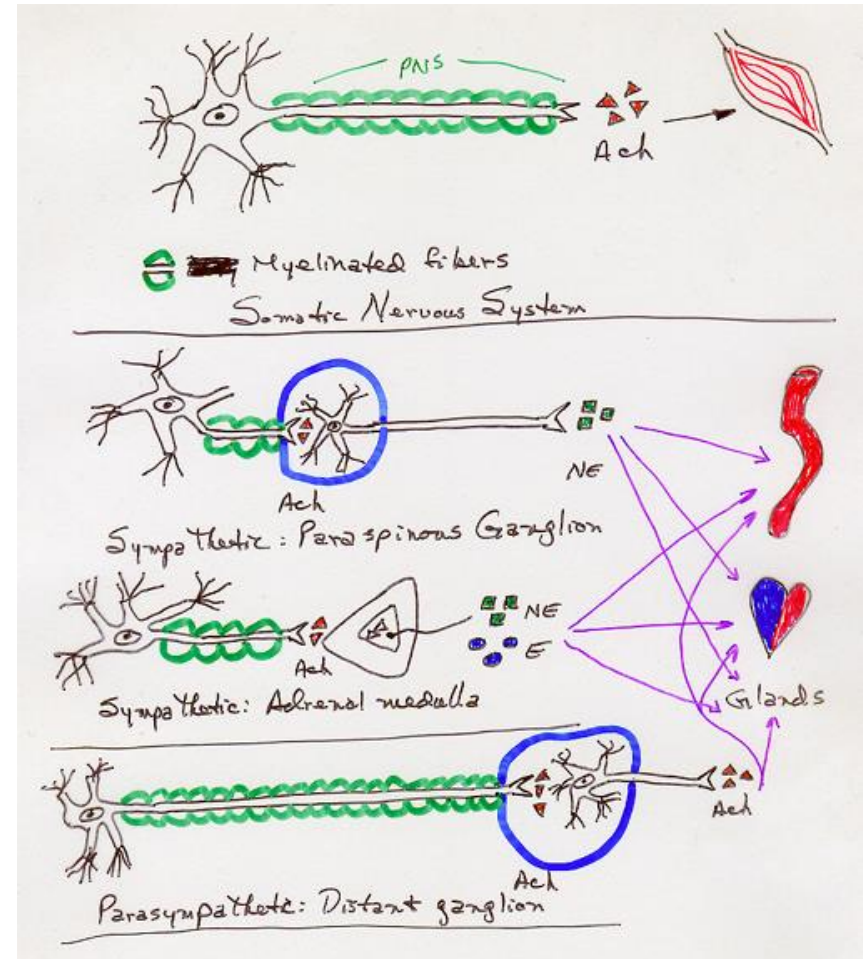
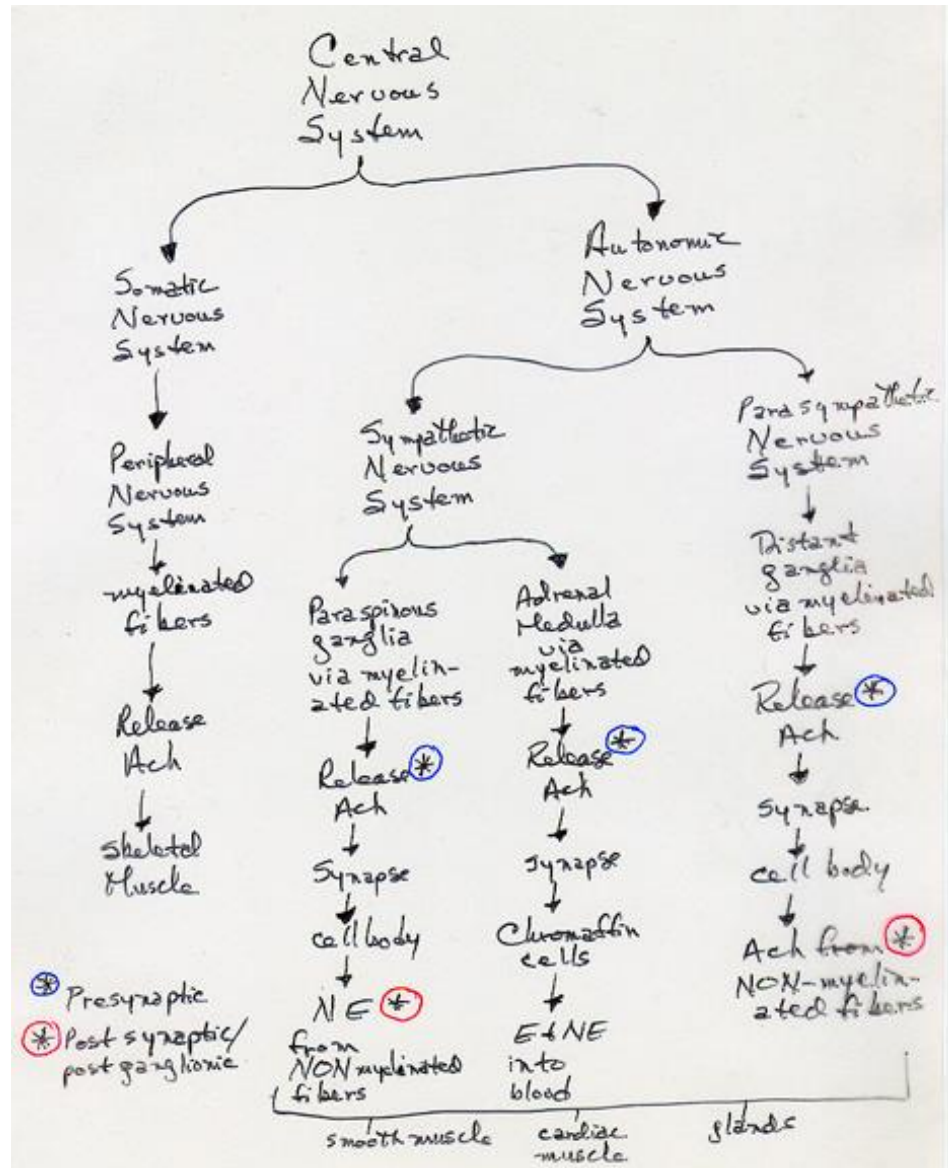


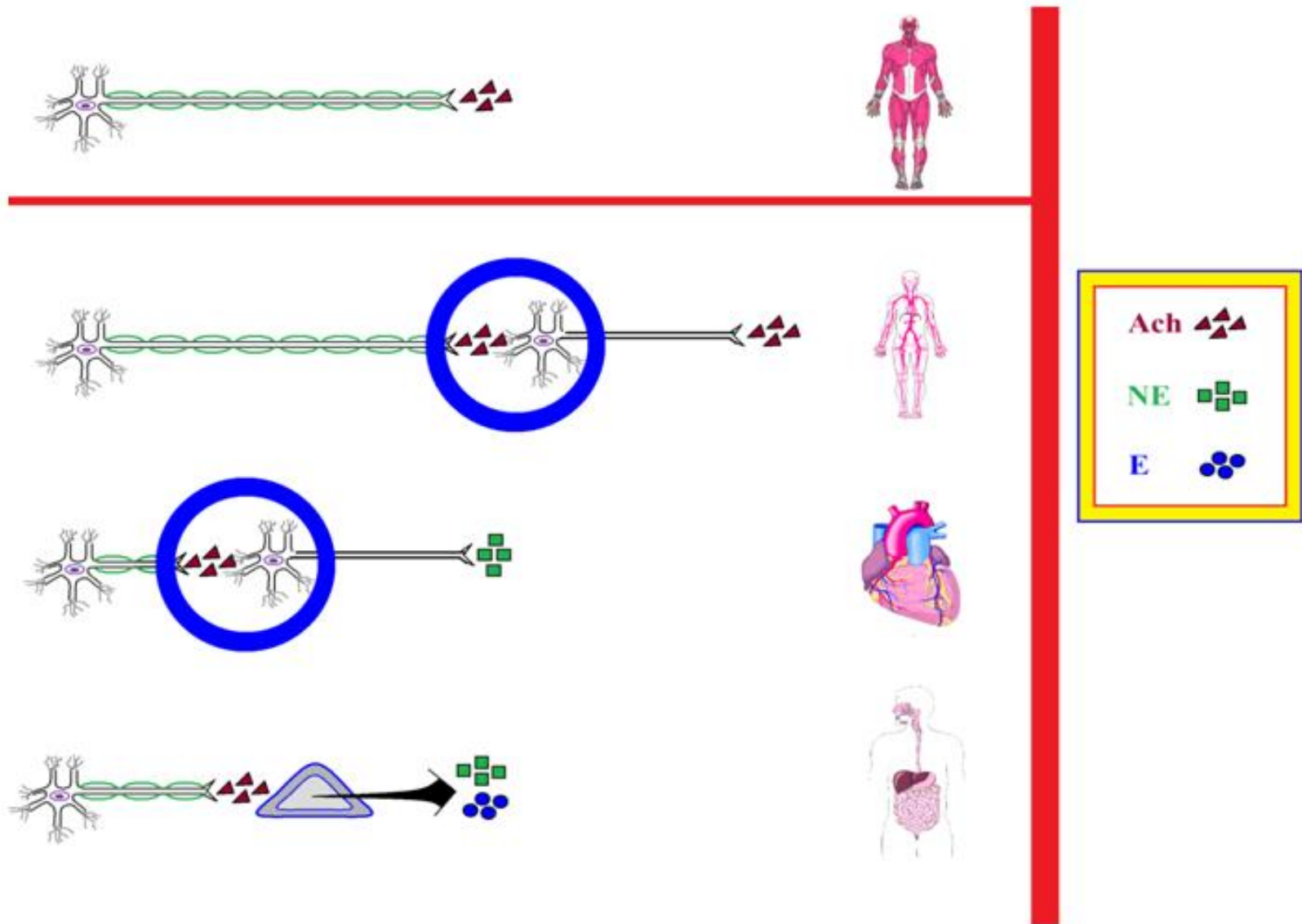
Nervous System and Neuroceptors

Subdivisions

Overview



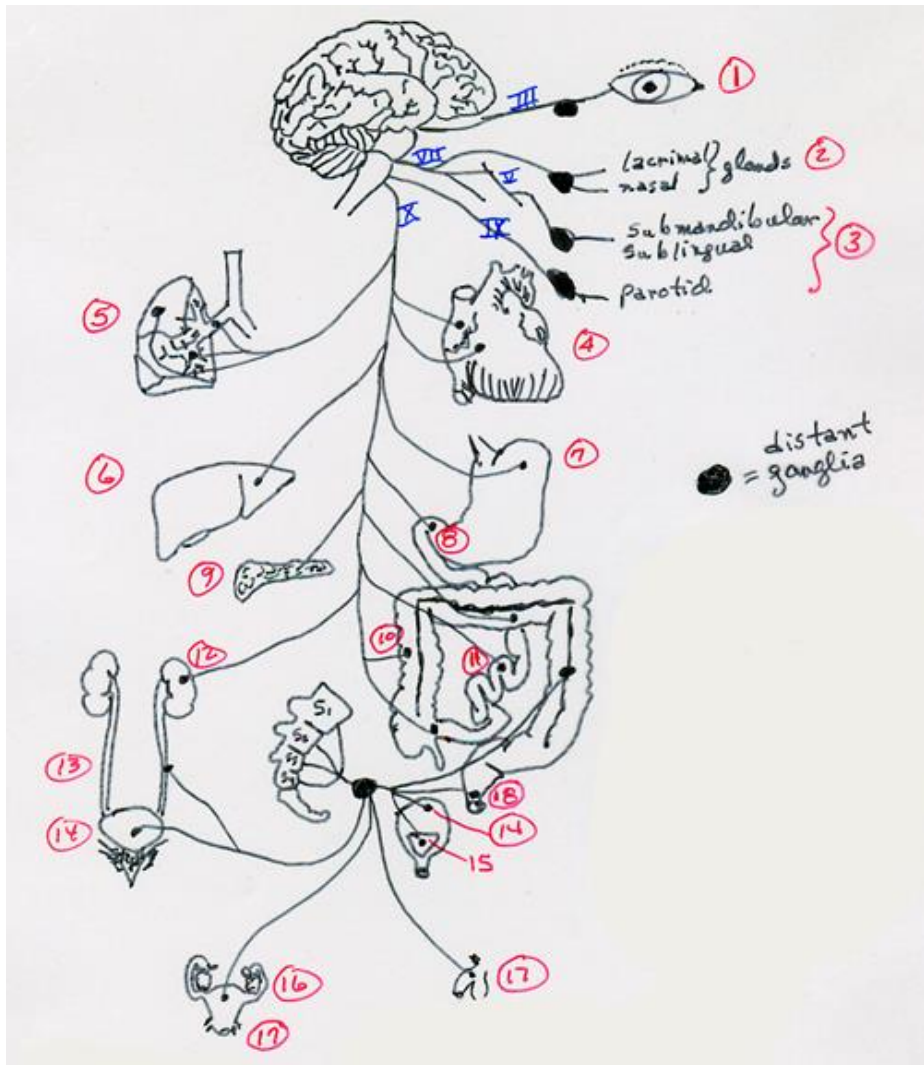
Another Way to Look at It



NOT Innervated by the Parasympathetic Nervous System

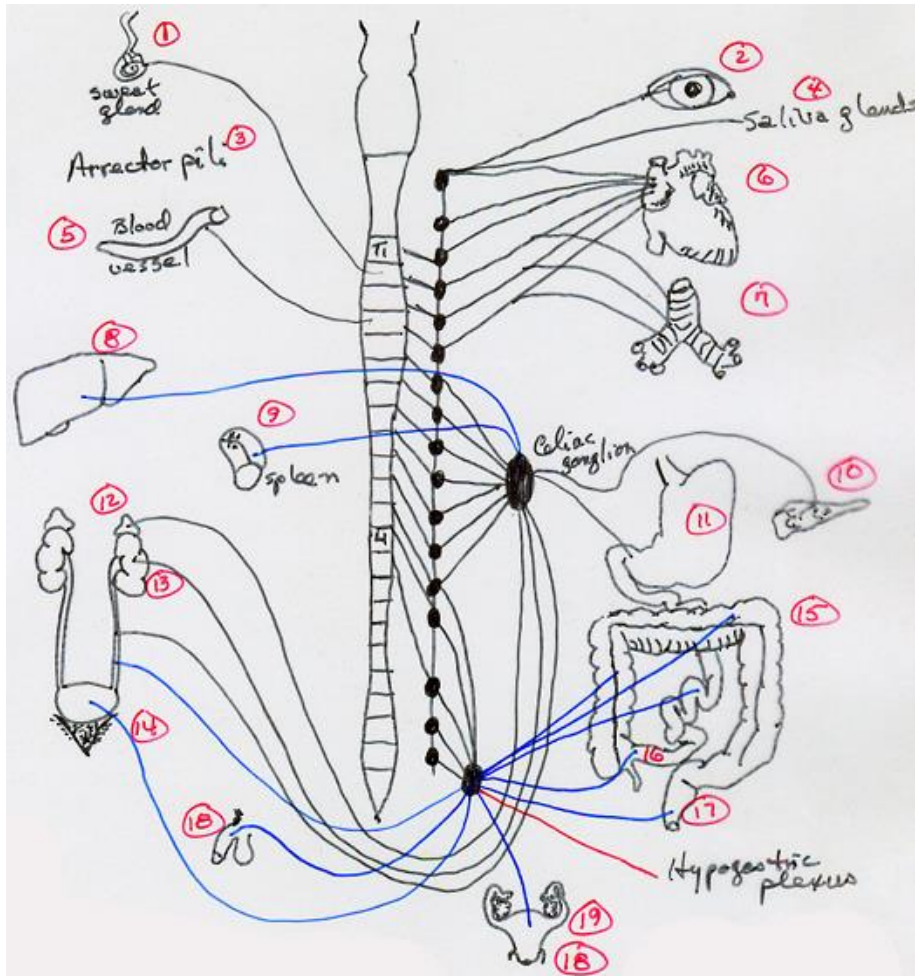
- Sweat glands
- Adrenal medulla
- Skin blood vessels
- Visceral organ vessels – except heart and lungs
- Skeletal muscle vessels
 - Spleen
- Arrector pili
- Fight or Flight or Freeze Response Is PURELY SYMPATHETIC!!!!

Parasympathetic System



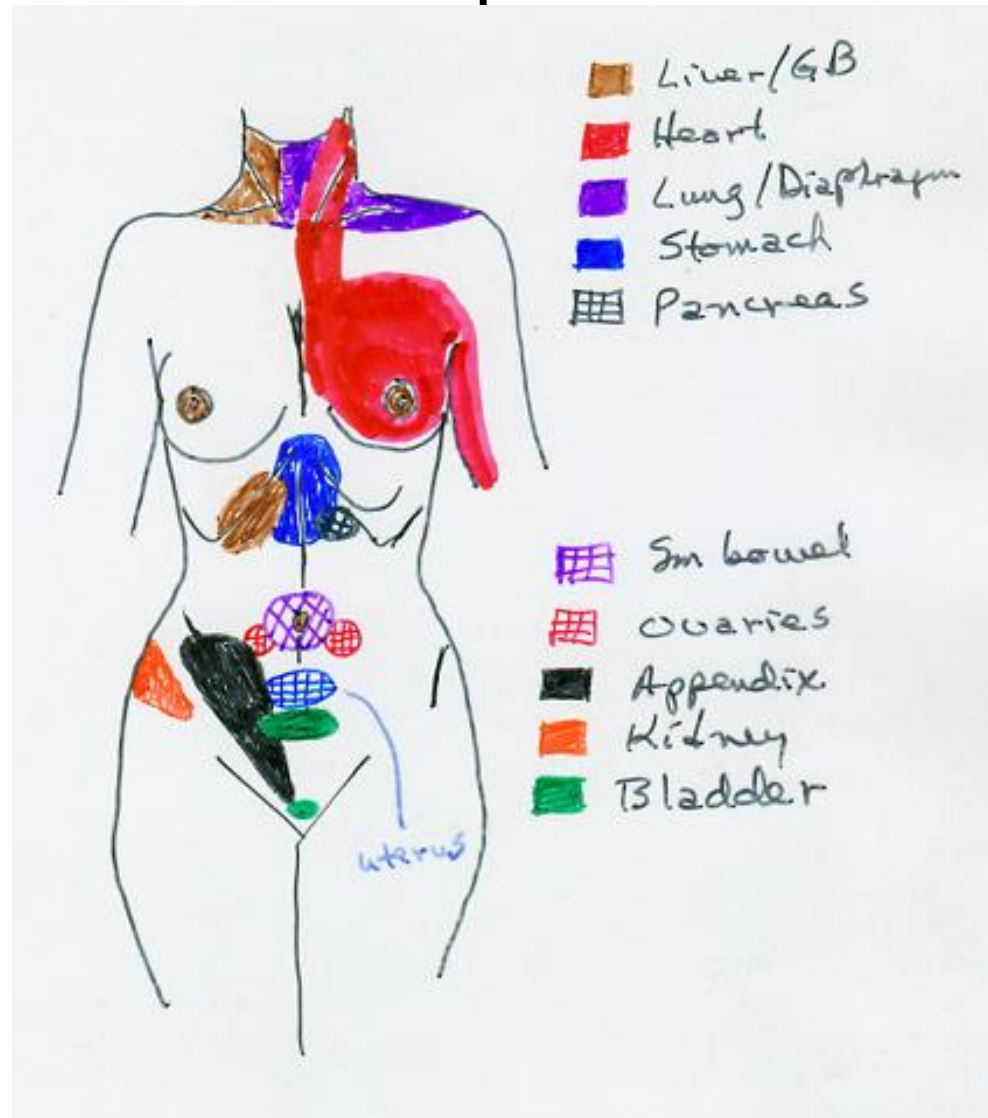
1. Accomodation/constriction
2. Excessive secretion
3. Stimulates salivation
4. ↓HR and strength; constricts coronary arteries
5. Constriction
6. ↑bile secretion; ↑glycogenesis
7. Stimulates secretion; ↑ motility
8. Pylorus
9. ↑secretions
10. Stimulates secretion; ↑ motility
11. Ibid
12. No effect
13. Minimal effect
14. Contracts detrusor
15. Trigone
16. Minimal effect
17. Vasodilation and erection
18. Constriction

Sympathetic System

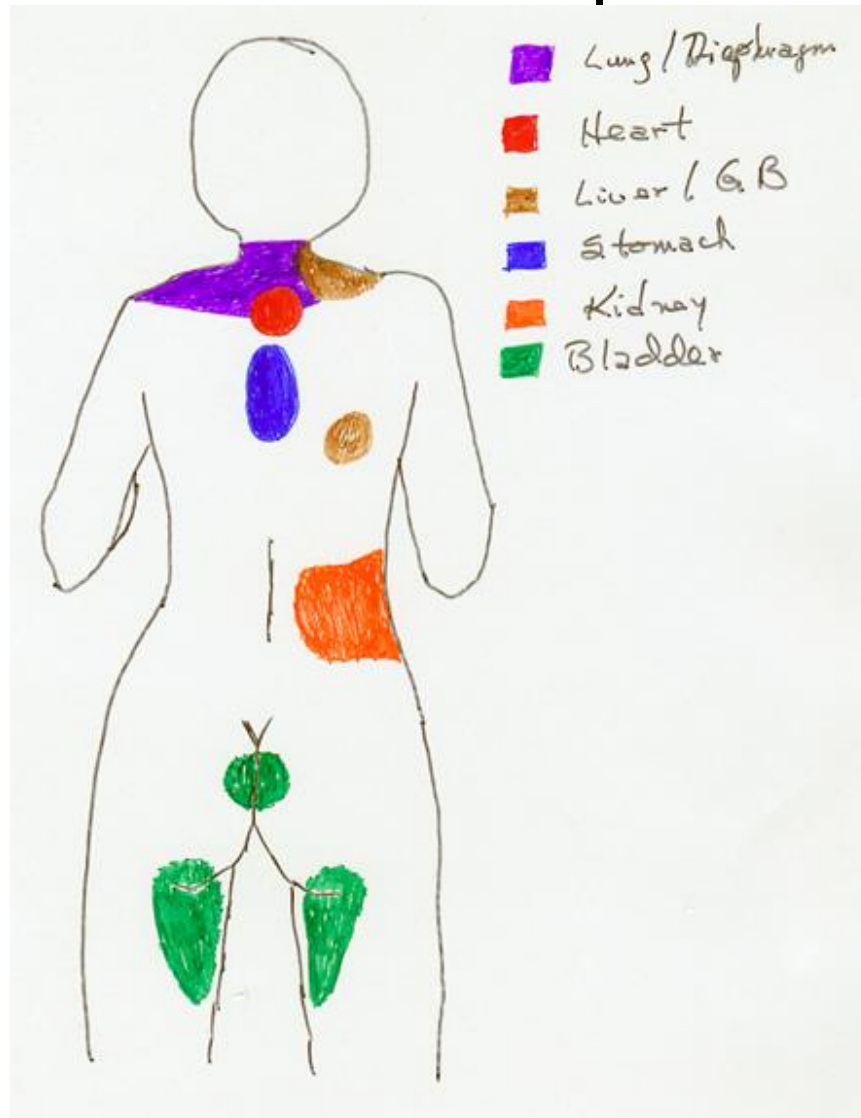


1. Secrete
2. Dilate
3. Contract
4. ↓ secretion
5. Skin: constrict; skeletal muscle: dilate; viscera: constrict; heart and lungs: dilate
6. ↑HR; ↑strength of contraction; dilates coronary arteries
7. Dilate
8. ↑glycogenolysis; ↓bile secretion
9. Contracts
10. ↓ secretion
11. ↓ motility
12. E and NE secretion
13. ↓urine volume
14. Relaxes detrusor
15. ↓ motility
16. Ileocecal valve
17. Relaxation
18. Vasoconstriction of ductus deferens, seminal vesicle, prostate → ejaculation/climax
19. ↓contraction (non-pregnant); ↑ contraction (pregnant)

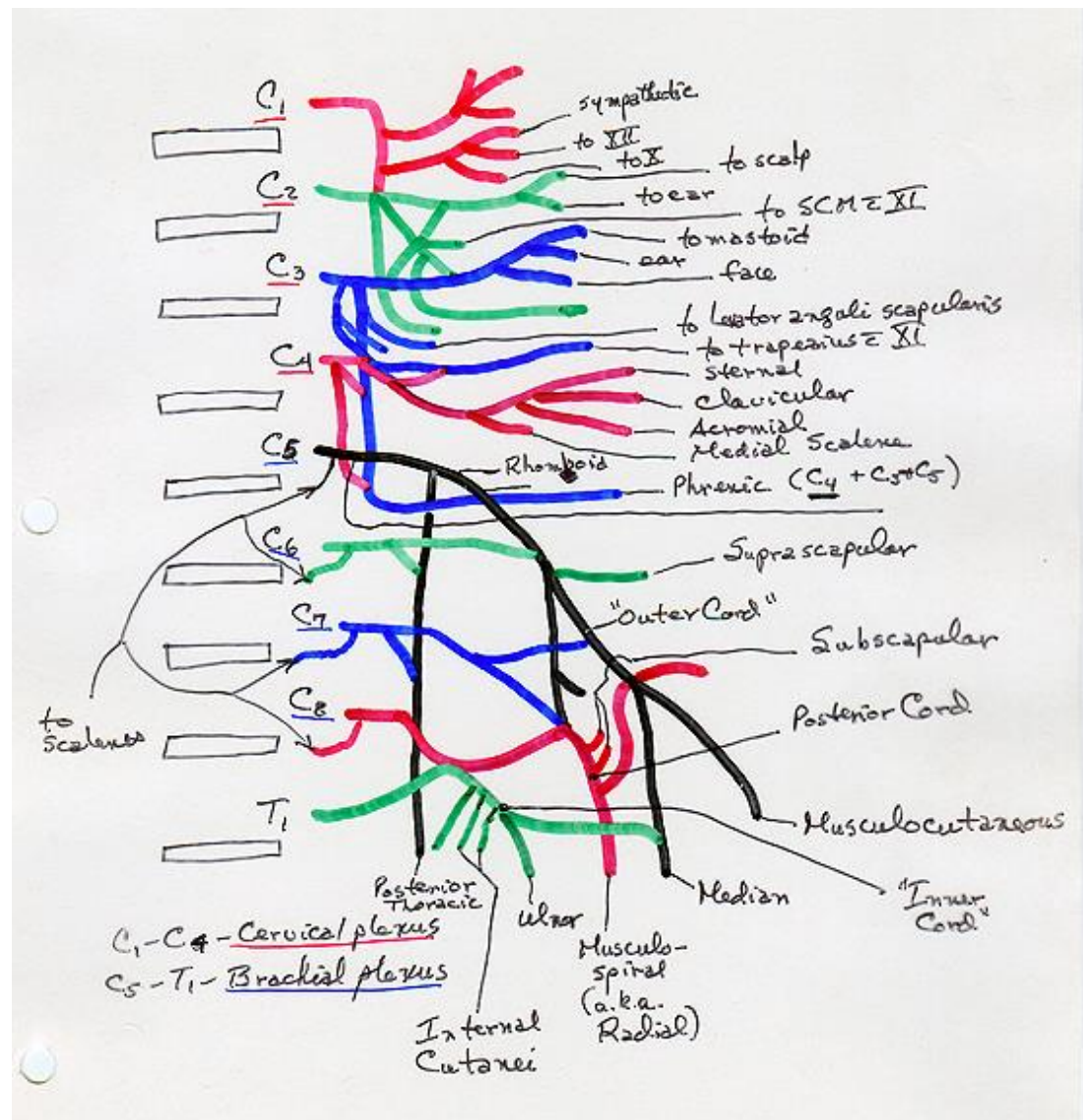
Referred Pain – Visceral to Cutaneous – Anterior Aspect



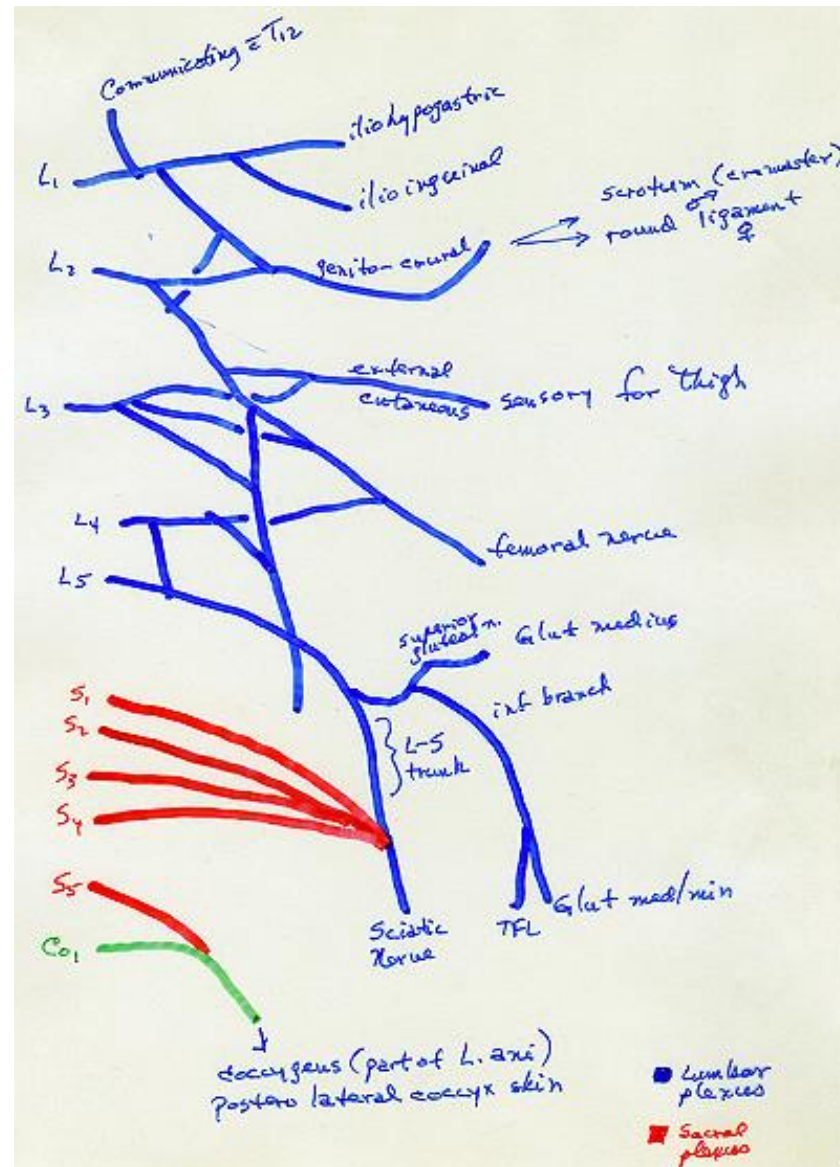
Referred Pain – Visceral to Cutaneous – Posterior Aspect



Cervical and Brachial Plexi



Lumbar and Sacral Plexi



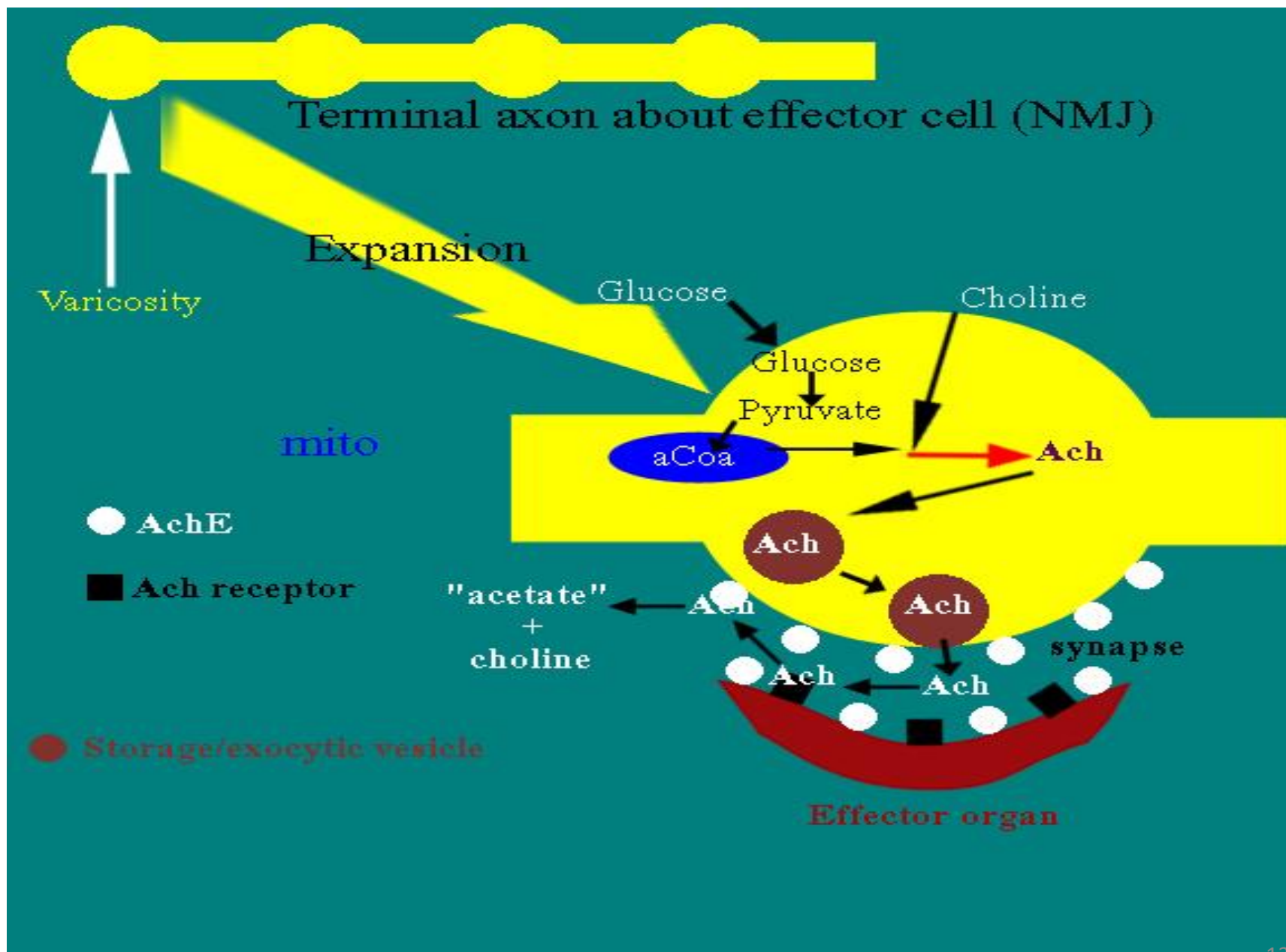
Neurophysiology

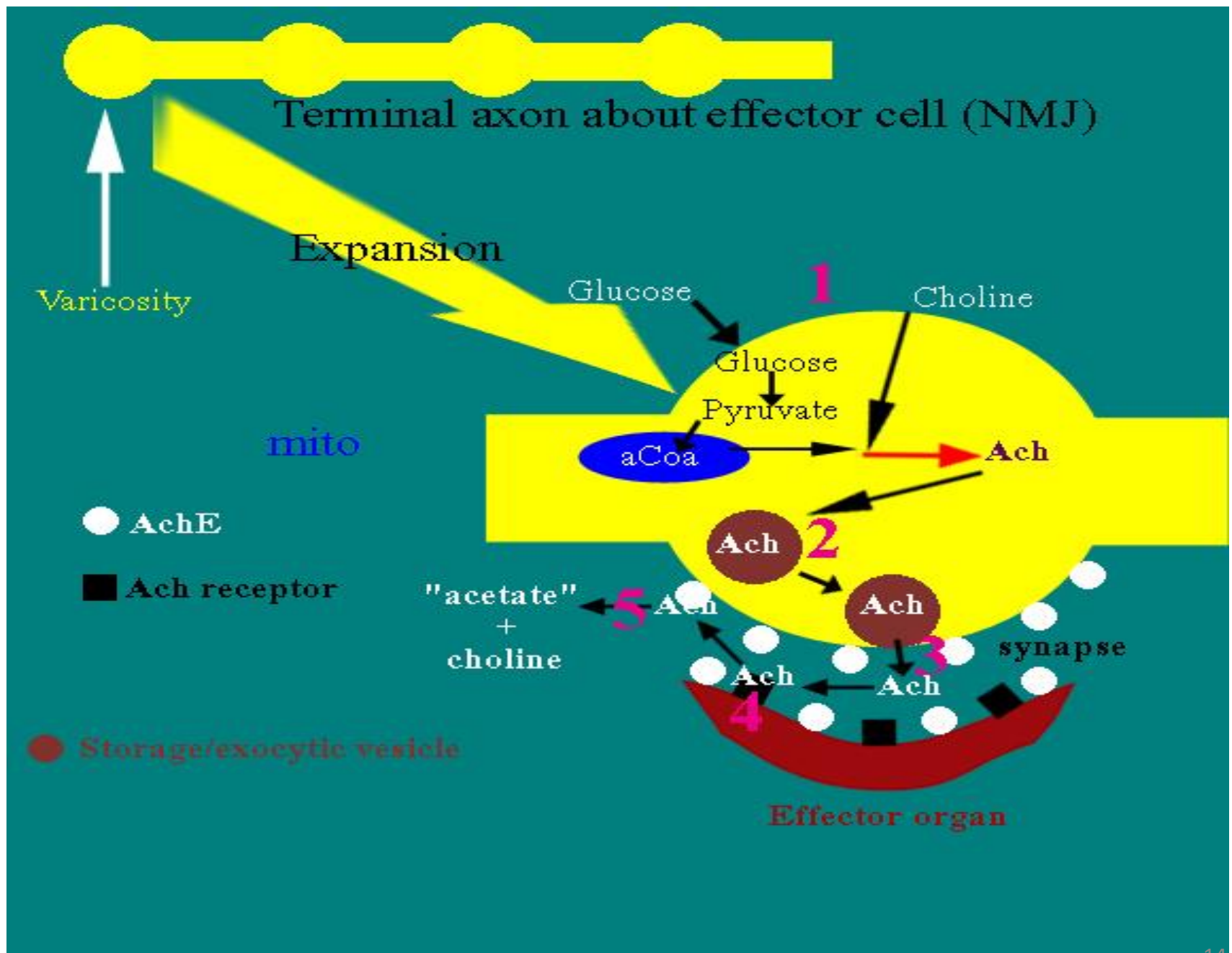
Neuroceptors

Neurochemical Transmission

Steps in Neurochemical Transmission

1. Synthesis of transmitter
2. Storage of the transmitter
3. Release of transmitter by a nerve action potential
4. Receptor binding on effector cell membrane → effect
5. Rapid removal of transmitter from vicinity of receptors
6. Recovery of effector cell to the state that preceded transmitter action





Muscarinic Acetylcholine Receptors (MAchR's) in Brain

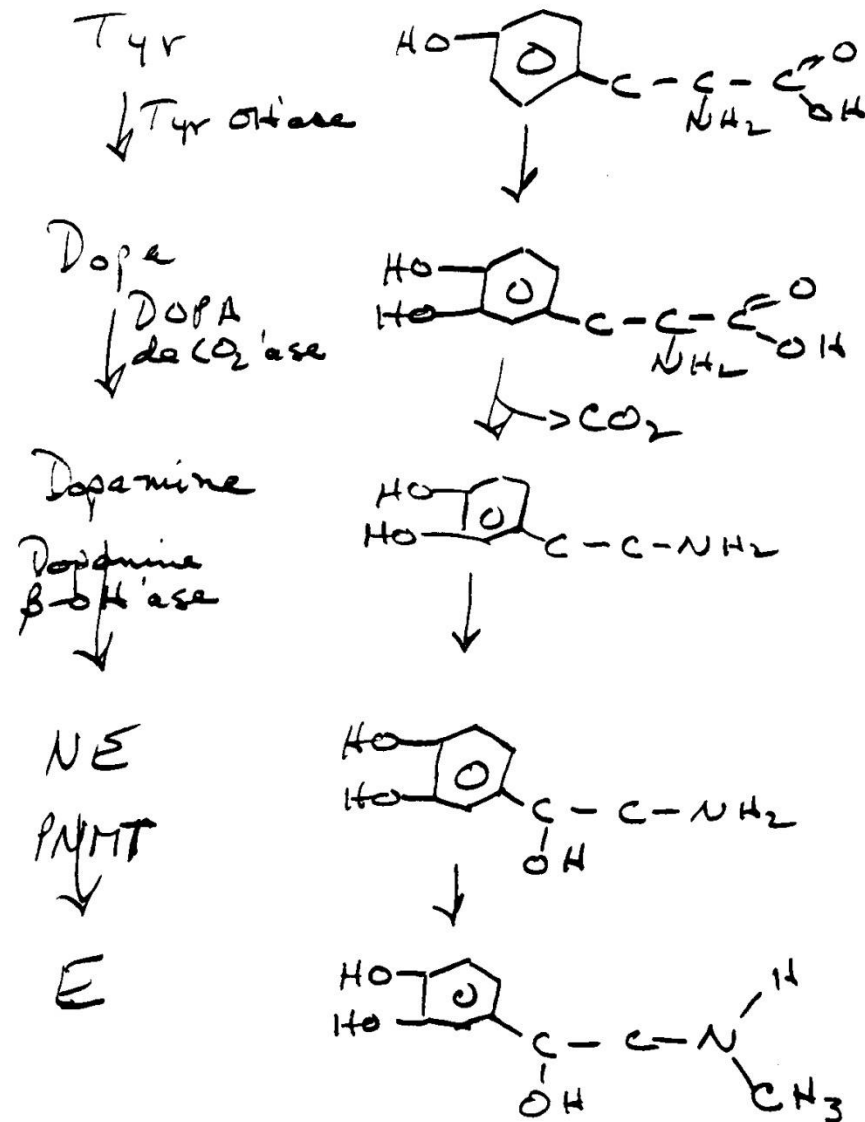
MAchR's are slow excitatory/inhibitory responses

Muscarinic Acetylcholine Receptors (AChR's) in Brain				
M ₁	M ₂ (“cardiac”)	M ₃ (“M ₂ glandular”)	M ₄	M ₅
High affinity for pirenzipine (tricyclic antidepressant that blocks HCl secretion in stomach, without any cardiovascular effect)	High affinity for AF-DX (a benzodiazepine similar to Valium, xanax, librium, ativan)	High affinity for 4-DAMP	Limited information on these receptors	
?	Coupled with G proteins			
IP ₃ with Ca ²⁺ α cAMP (?)	G _I = ↓cAMP	IP ₃ with Ca ²⁺ α cAMP (?)	G _I = ↓cAMP	IP ₃ with Ca ²⁺ α cAMP (?)
↑IP ₃	↓cAMP	↑IP ₃	↓cAMP	↑IP ₃
High AND low affinities for carbachol (used to treat glaucoma to reduce IOP)			Low affinity for carbachol	??????
Greatest generic affinity for pirenzipine (antagonist)				??????
May be related to M ₄	??????	??????	May be related to M ₁	??????
2 glycosylation sites on Asn of N terminus	3	5	3	3
Reduced glycosylation leads to reduced numbers of MAChR's in the cell membrane.				
Exocrine glands	Heart (M2 _A – used to be)	Smooth muscle {(M2 _B – used to be)}	Adrenal medulla	No evidence at this date
Cerebral cortex	V, VII	Cerebral cortex	?	?

Muscarinic Acetylcholine Receptors (MAchR's) in General

- ☞ Regulates parasympathetic function of, e.g., heart, bladder, lungs, GI tract
- ☞ When M_{1,3,5} receptors are stimulated, IP₃ is increased through G regulatory proteins
- ☞ When M_{2,4} receptors are stimulated, cAMP is reduced, BUT paradoxically, IP₃ is weakly increased
- ☞ involved in spontaneous locomotor activity
- ☞ involved in teaching passive avoidance (reduces punishment by shock)
- ☞ involved in memory retention in retaining newly learned task material ()

Catecholamine Biosynthesis

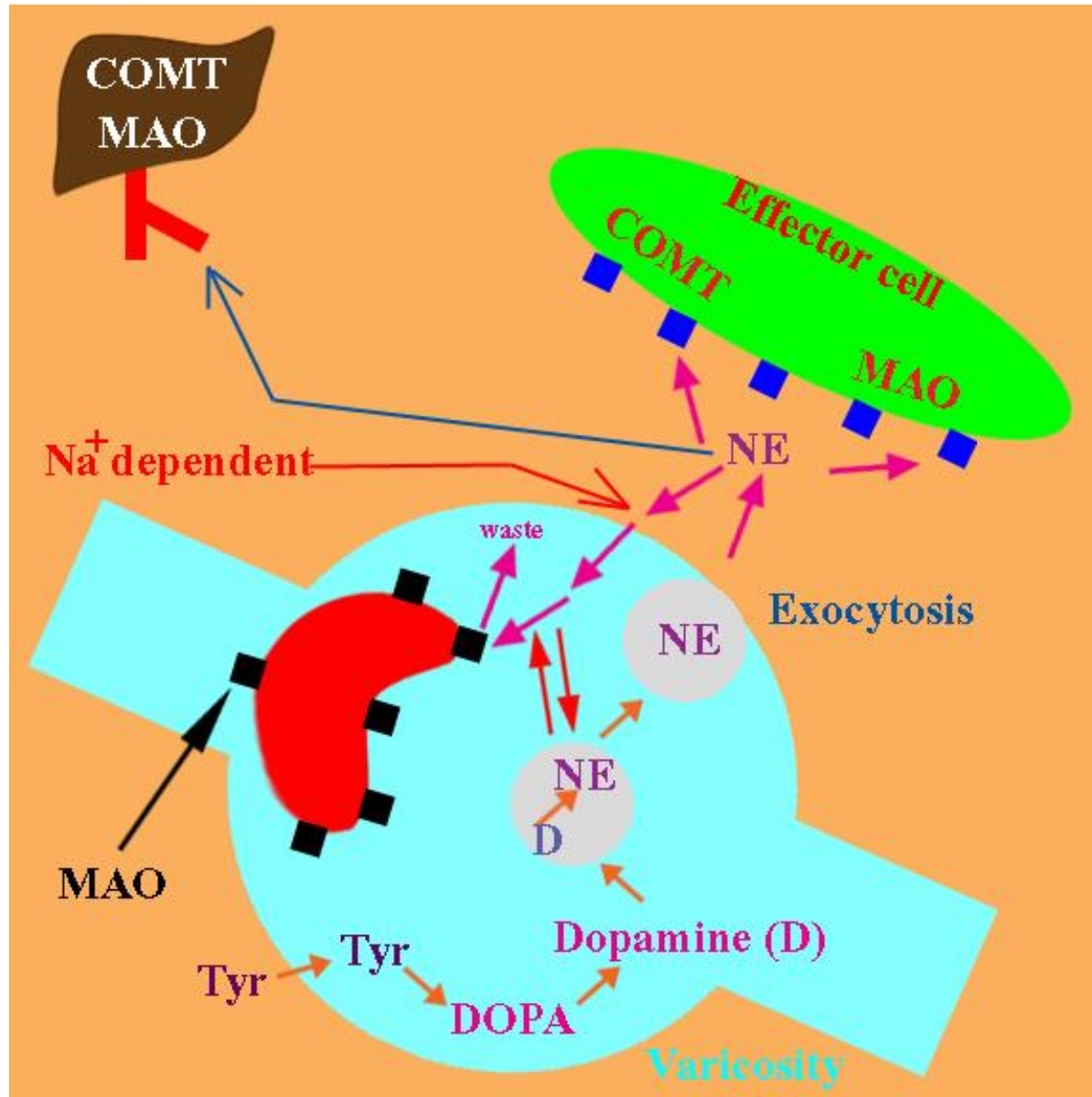


1. Starts with Tyr
2. Requires Cu and Vitamin C
3. Is one reason why Tyr becomes essential in PKU

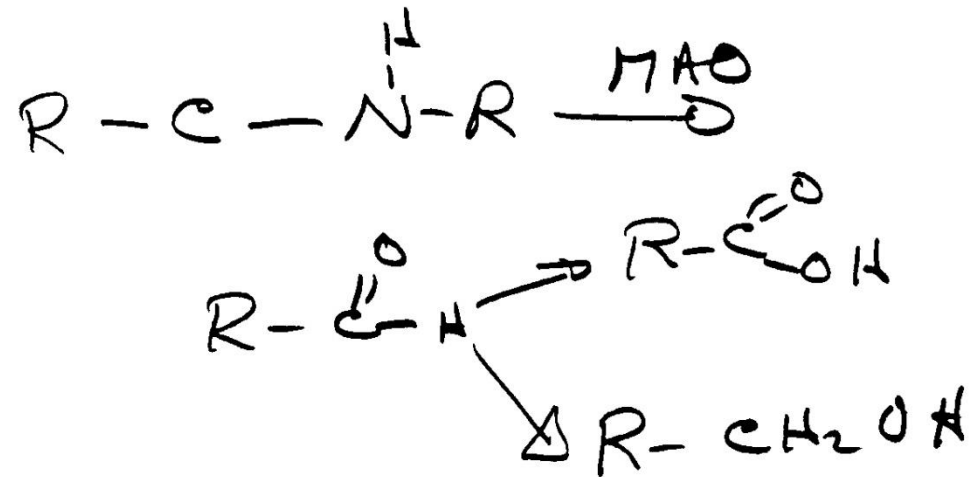
Processes for NE (E) Synaptic Removal

1. Na^+ -dependent re-uptake to neuron of origin
 - a. For vesicular storage – re-cycling OR
 - b. Mitochondrial MAO inactivation
2. Diffusion from synapse into the blood for hepatic (extra-neuronal) uptake and enzymatic destruction
3. Active transport into effector cells (extra-neuronal uptake) followed by either COMT or MAO inactivation

Steps in Nor-adrenergic (Adrenergic, too) Metabolism – Neuronal and Extra-Neuronal

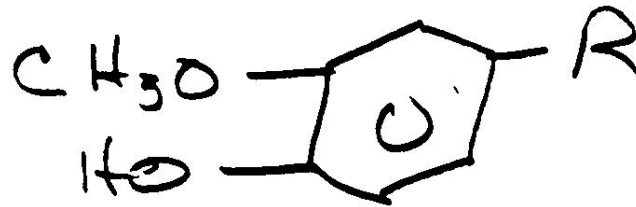
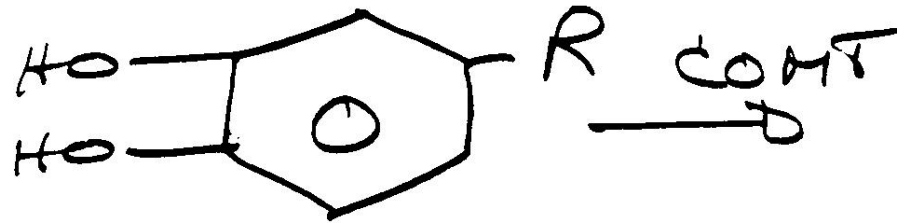


What Mono-Amine Oxidase (MAO) Does



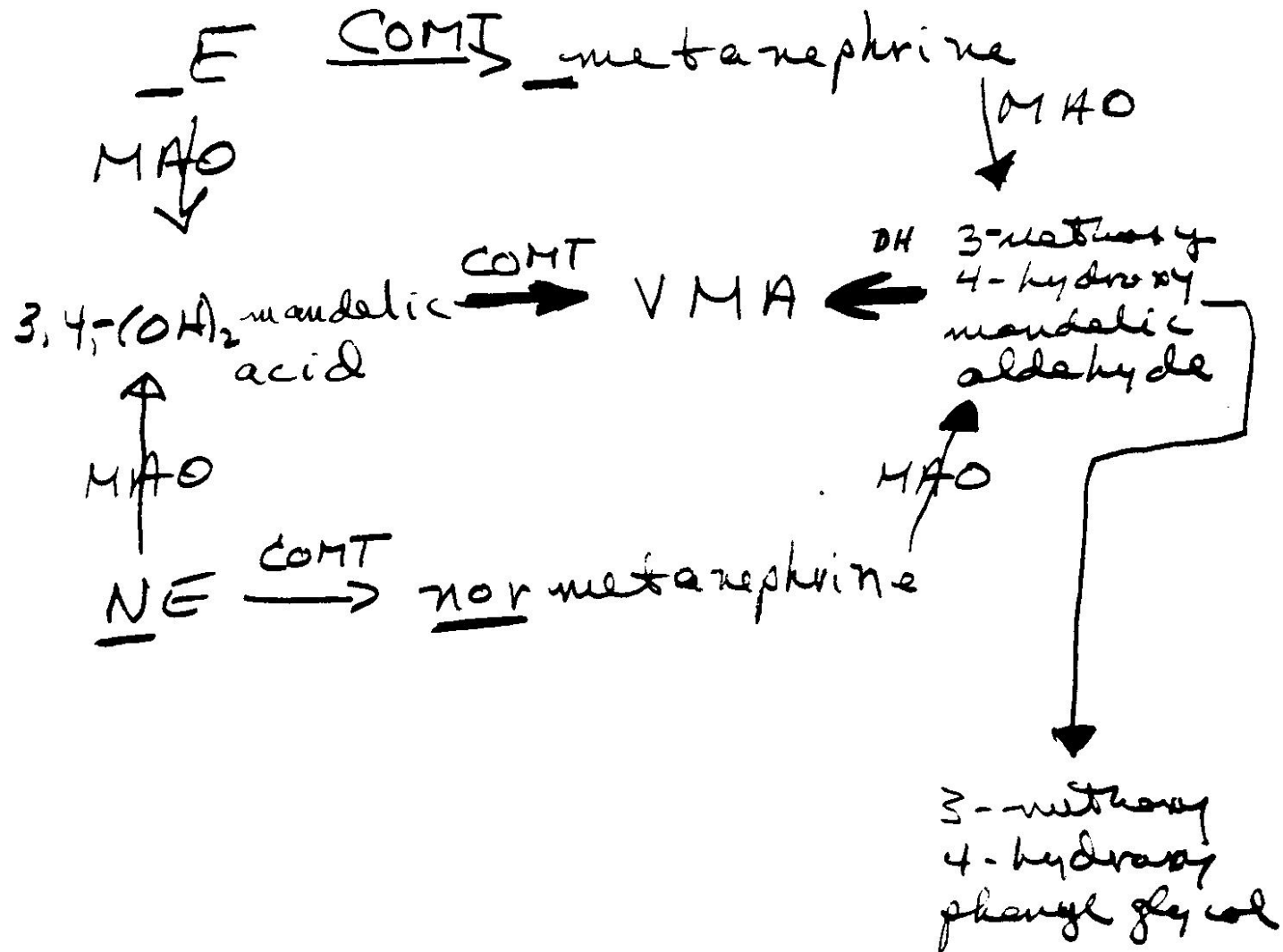
NE, E, Dopamine, Tyramine,
Serotonin

What Catechol-O-Methyl Transferase (COMT) Does

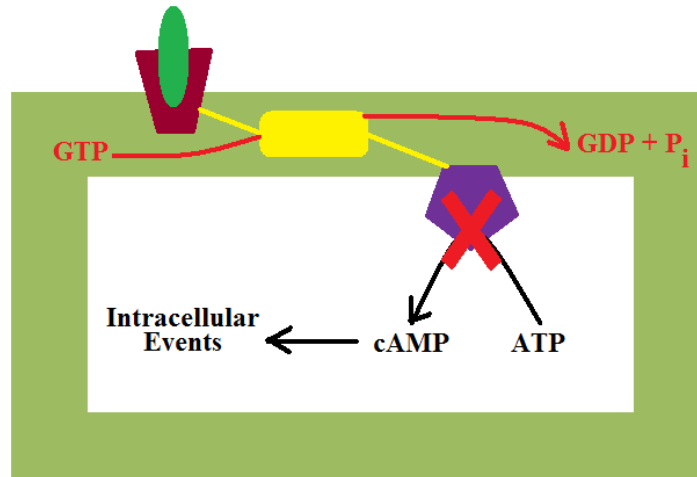
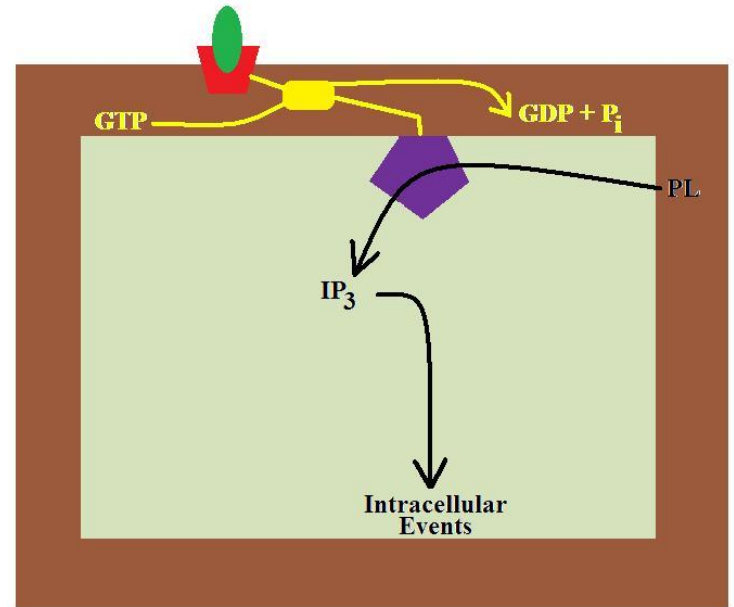
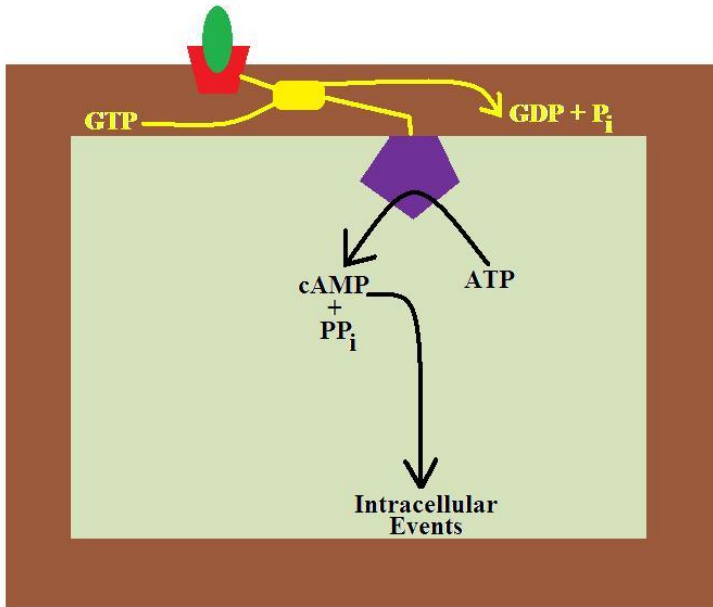


NE, E
↓ Q X $\frac{1}{100}$

E and NE Catabolism



G Proteins



Alpha (α)-Adrenergic Receptors: α_1 and α_2

Generic α -Receptor Locations & Functions

Functions

- Generally excitatory (contractions of smooth muscle cells or increased secretory activity of glandular cells)
- Dilator muscles of iris
- Constricts most blood vessels
- Contracts GI sphincters
- Contracts muscle fibers of trigone, vas deferens, uterus
- Sweat glands, arrector pili
- Contracts spleen
- Decreased salivary secretion

Location

1. Iris, ileocecal valve, uterus, sphincter vesiculi, salivary glands, spleen, arrector pili
2. Pyloric valve, kidney, GI tract
3. Arterioles, coronary, cerebral and pulmonary arteries, skin mucosa
4. Pregnant uterus
5. Male sex organs

α_1 and α_2 Receptors

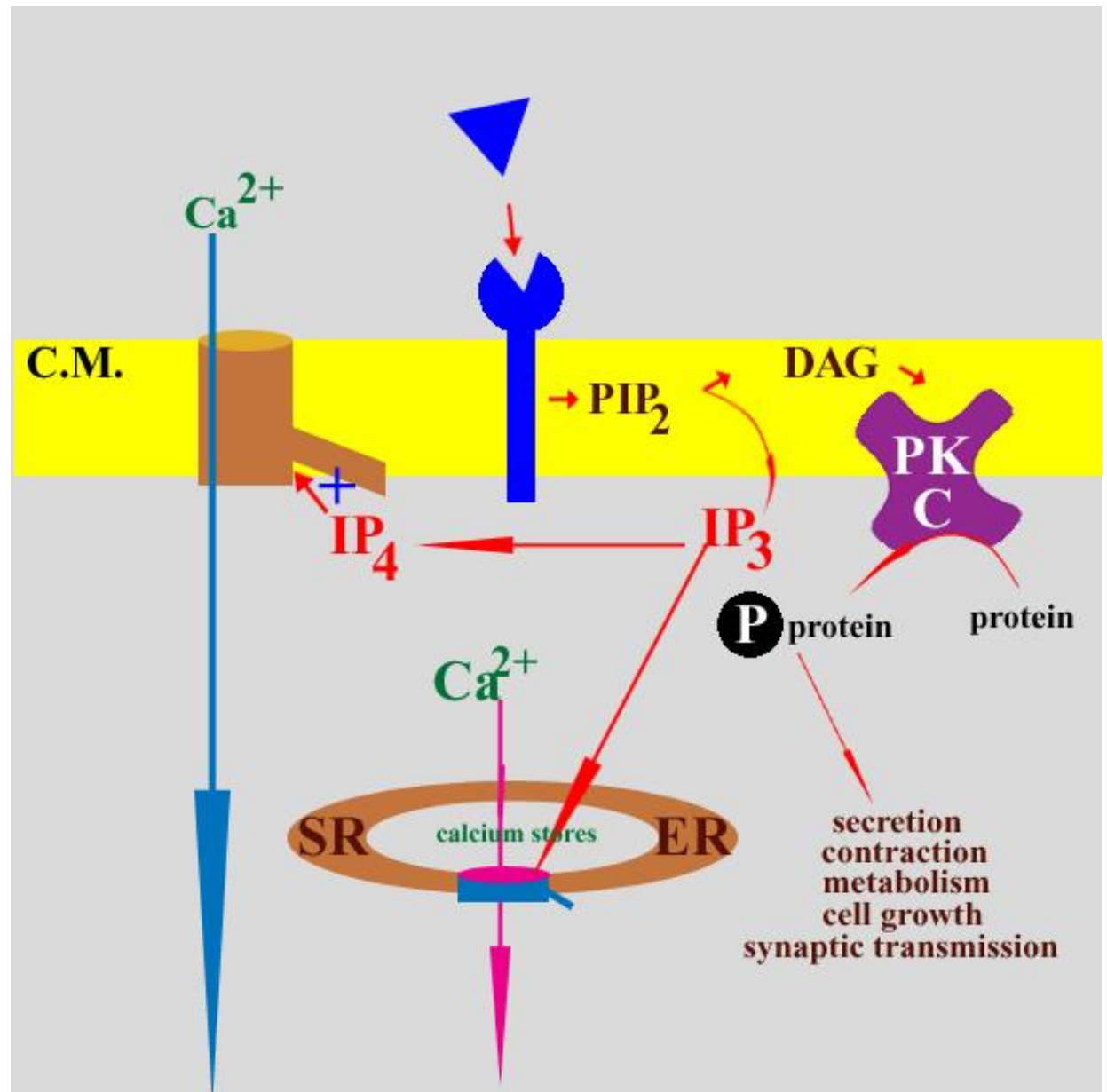
α_1

- phenylephrine (α_1 -selective **agonist**)
- prazosin (α_1 -selective **antagonist**)

α_2

- B-HT 933 (α_2 -selective **agonist**)
- yohimbine (α_2 -selective **antagonist**)

α_1 Receptors



α_1 Receptors – Locations & Functions

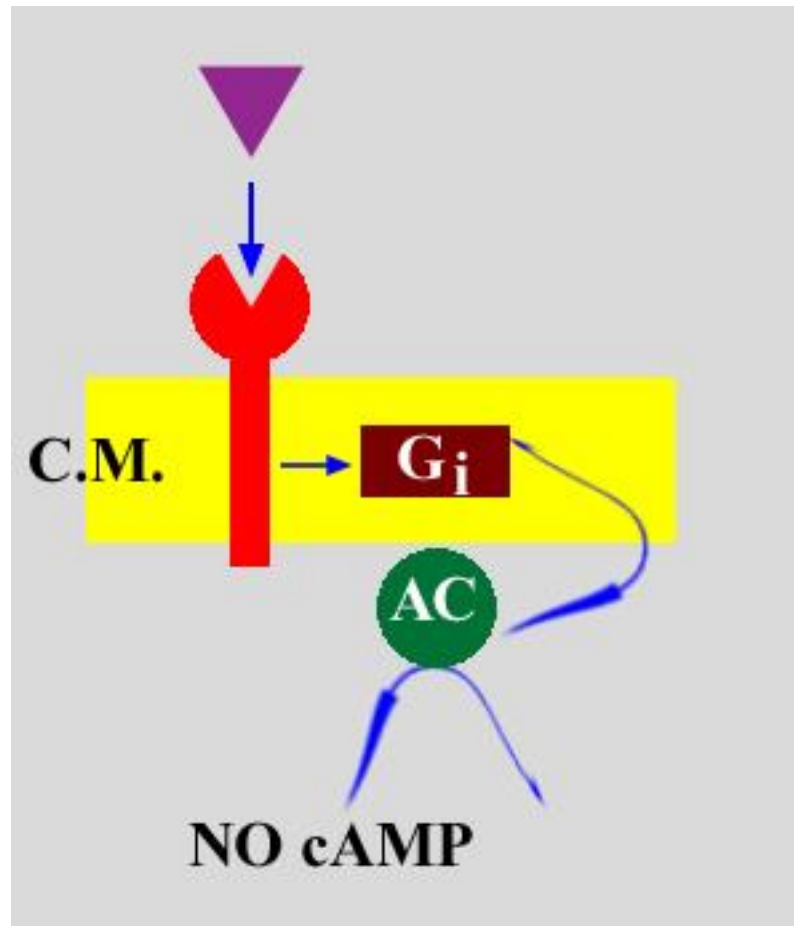
Locations

- Veins, bronchial glands, iris of eye, frontal cortex, hypothalamus, trigone, uterus, sphincter vesiculi, splenic capsule, liver

Functions

- \uparrow Glycogenolysis, contracts smooth muscle of blood vessels and GU tract

α_2 Receptors



α_2 Receptors – Locations & Functions

Locations

- GI sphincters, adipocytes, pancreas, platelets, sympathetic baroreceptors in brain stem, GI tract

Functions

1. Post-synaptic vascular smooth muscle contraction in some vascular beds,
2. smooth muscle relaxation in GI tract,
3. inhibits
 - a. lipolysis, renin release, platelet aggregation, insulin secretion

NE Aside -- α Receptors ???

- Excessively high levels of norepinephrine lead to a manic state.
- Exceedingly low levels of norepinephrine lead to depression.

Involvement in Bipolar Disorder???

Beta (β)-Adrenergic Receptors: β_1 and β_2

Generic β -Receptor Locations & Functions

Functions

1. Generally Inhibitory – 2 exceptions:
 - A. Stimulates SA node, atrial and ventricular β 's which increases HR
 - B. Stimulates bowel β 's which reduce GI motility and tone
2. Constricts pupil
3. Dilates blood vessels to heart, muscle, lungs
4. Relaxes bladder muscles and uterus

Location

1. Heart
2. Lungs
3. Smooth muscle

Generic β Receptors

Agonist

- Isoproterenol

Antagonist

- Propranolol

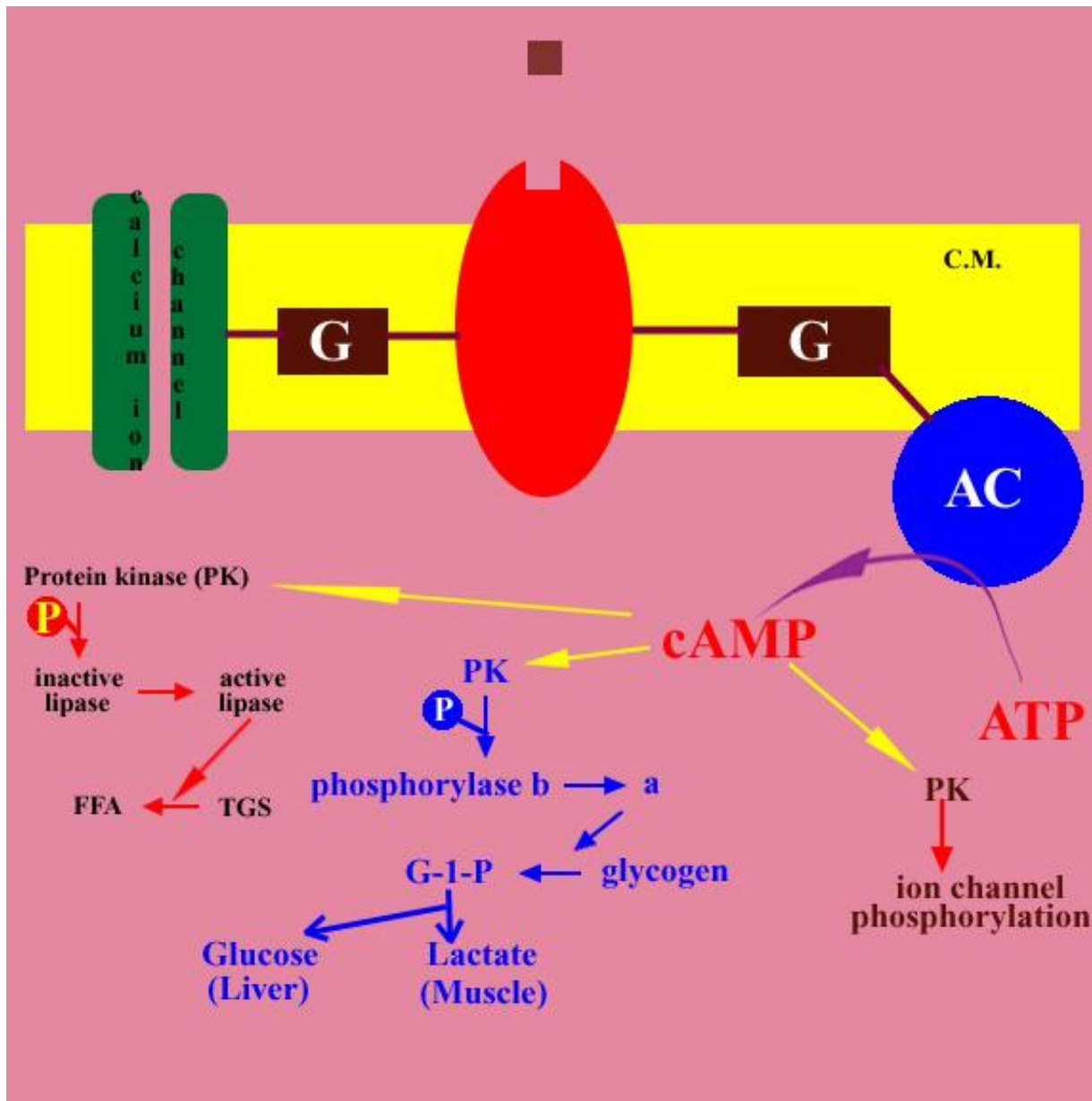
β_1 and β_2 (β_3) Receptors

β_1

- dobutamine (β_1 -selective **agonist**)
- metoprolol, atenolol (β_1 -selective **antagonists**)

β_2

- terbutaline, albuterol, procaterol and zinterol (β_2 -selective **agonists**)
- ICI 118551 (β_2 -selective **antagonist**) -- limited info – not useful clinically?
- **ASIDE:** β_3 receptors are also present in adipose tissue – not much known about them



- β_1 : Activation of the β_1 receptor leads to increases in contractile force and heart rate (cAMP and via G protein coupling with Ca²⁺ ion channel).
- β_2 : Activation of the β_2 receptor leads to calcium pathway **inhibition** in smooth muscle leading to relaxation (ion channel phosphorylation; NO G protein coupling).

β_1 Receptors – Locations & Functions

Locations

- Heart
- Small bowel

Functions

- \uparrow lipolysis (really β_3 receptors? – unclear in literature – could be both!)
- Increases rate and force of myocardial contraction

β_2 Receptors – Locations & Functions

Locations

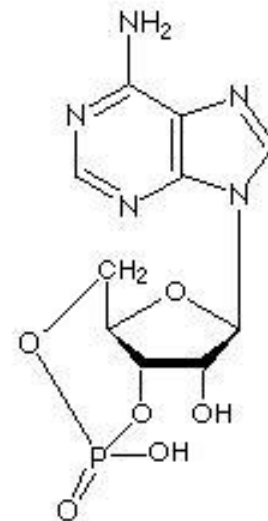
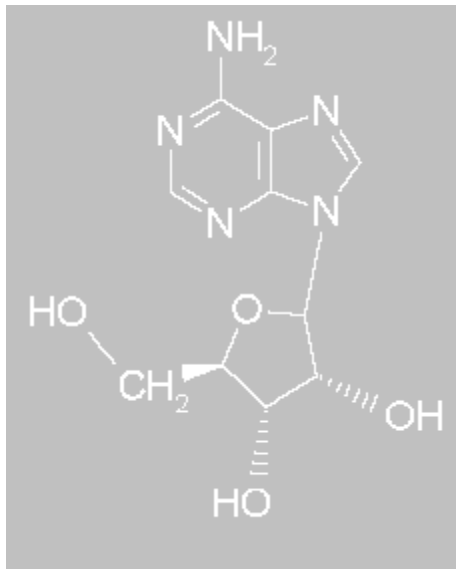
- Bronchi
- Vascular beds
- Uterus

Functions

- Increased hepatic gluconeogenesis, glycogenolysis, muscle glycogenolysis
- Increased release of insulin, glucagon, renin
- Relaxes smooth muscle of bronchi, blood vessels, GI tract and GU tract

Adenosine Receptors

Neuromodulators



Introduction

- Adenosine is not a usual hormone or neurotransmitter.
- Adenosine is probably the most important neuromodulator in the CNS and PNS.
- A neuromodulator is a compound which has a modulatory effect on neuronal activity, increasing or decreasing the rate at which a nerve cell fires.
- Neuromodulators are distinct entities from neurotransmitters, which are stored in presynaptic end-bulbs, released into the synaptic cleft, then bind with post-synaptic receptors and are then either neuronally internalized for re-cycling or metabolized.
- A neuromodulator, such as adenosine, is more likely to be either constitutively released (constitutive release occurs at a reasonably constant rate), or released at times of high or low metabolic activity – i.e., pretty much whenever.
- Neuromodulators may act pre- or post-synaptically, and may then be either neuronally internalized for re-cycling or metabolized.

Adenosine Receptors

- There are 4 types of adenosine receptor known at this time:
 - A1 ,
 - A2A ,
 - A2B and
 - A3
- Adenosine receptors are coupled to G-proteins and mediate stimulation (G_s -- A2 family) or inhibition (G_i or G_o – A1 and A3) of adenylyl (adenylate) cyclase and cyclic AMP (cAMP) levels.
- The stimulant properties of the methylxanthine antagonists of adenosine receptors (caffeine, theophylline - found in tea, coffee and cocoa) are very well known.

The Human A1 Adenosine Receptor

- This subtype inhibits adenylate cyclase.
- Is also good evidence for coupling (via G-proteins) to ion channels, and phospholipase C.
- A1 receptor antagonism in the heart leads to the rapid, pronounced "pounding" observed after consuming large amounts of potent coffee (due to the caffeine & theophylline).
- Adenosine is used in the treatment of supraventricular tachycardia (causes 'pharmacological cardioversion'), and may also be used as a diagnostic tool in the investigation of cardiac abnormalities.
- It is thought that adenosine accumulation in the brain inhibits cholinergic cells and induces sleep.
- A1 receptor antagonists cause diuresis and natriuresis without significantly impacting GFR.
- A1 receptors promote vasoconstriction.

The Human A2A Adenosine Receptor

- This subtype stimulates adenylate cyclase.
- Distribution in the CNS is very discrete:
 - concentrated in the caudate and putamen bodies,
 - the nucleus accumbens and
 - the olfactory tubercle
- There is growing interest in this receptor as a means of influencing dopamine-mediated responses in these brain regions.
- In the periphery the A2A receptor is found on platelets and is anti-aggregatory.
- Stimulation is anti-inflammatory.
- Agonists may also inhibit psychosis

The Human A2B Adenosine Receptor

- The function of the A2B adenosine receptor remains poorly understood, although it mediates the largest observed stimulation of cAMP levels in human brain slices.
- Found on the human mast cell
- One possible mechanism of action of aminophylline in asthma may be by way of inhibiting A2B receptors (receptor blockade or receptor antagonism).

ASIDE

- **Fredholm BB: On the mechanism of action of theophylline and caffeine.**
Acta Med Scand. 1985;217(2):149-53.
- ***ABSTRACT:*** Important developments in our understanding of the mechanism of action of methylxanthines have taken place in the last 10 years. A brief overview of these developments is provided below and the author concludes that the common view that theophylline (and caffeine) acts by raising the levels of cyclic AMP is generally untenable. Instead, many of the actions of the methylxanthines can be explained on the basis of their being antagonists of endogenous adenosine. However, the mechanism behind the antiasthmatic effects of xanthines still remains unknown and further research is necessary.

The Human A3 Adenosine Receptor

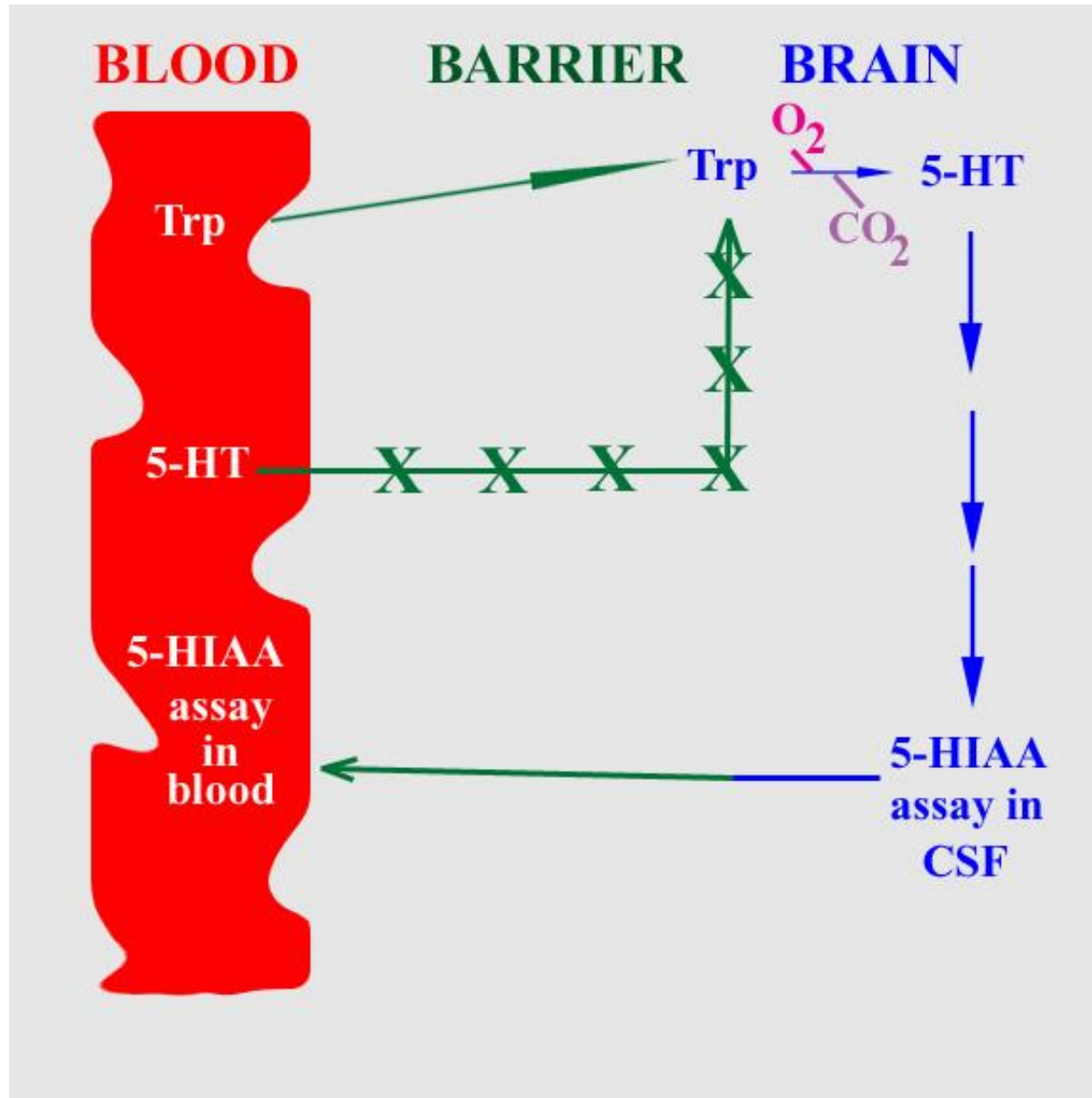
- The A3 adenosine receptor is the most recently cloned of the adenosine receptors, and still awaits conclusive proof of its involvement in physiological processes, although a potential role in mast cells has been proposed.
- This subtype is coupled to inhibition of adenylate cyclase.
- This receptor has provided many conflicting scientific reports – has been called the “Janus” of the A receptors because of that.
- Seems to play a role in apoptosis
 - **Apoptosis** is a tightly regulated form of cell death, aka programmed cell death, cellular suicide.
 - Apoptosis is an important process during normal development.
 - It is also involved in aging and various diseases such as cancer, AIDS, Alzheimer's disease and Parkinson's disease.

Sources

1. <http://www.ccc.nottingham.ac.uk/~mqzwww/adenosine.html>
2. <http://www.anaesthetist.com/icu/manage/drugs/adenosine/>
3. <http://www.web-books.com/MoBio/Free/Ch6G.htm>
4. http://en.wikipedia.org/wiki/Cyclic_AMP
5. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=2986418&dopt=Abstract
6. http://care.diabetesjournals.org/cgi/content/full/25/2/364?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Keijzers&searchid=1053002817613_1149&stored_search=&FIRSTINDEX=0

Serotonin

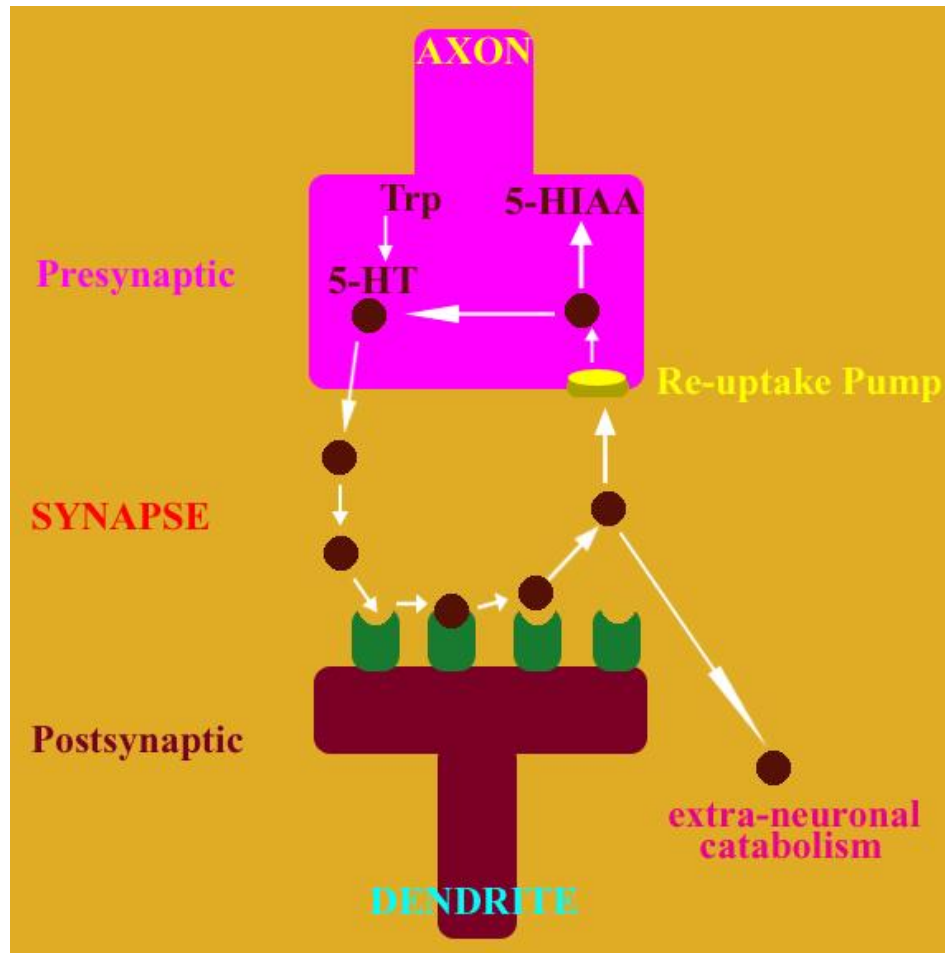
Neuronal Source and
Neurophysiological Chemistry



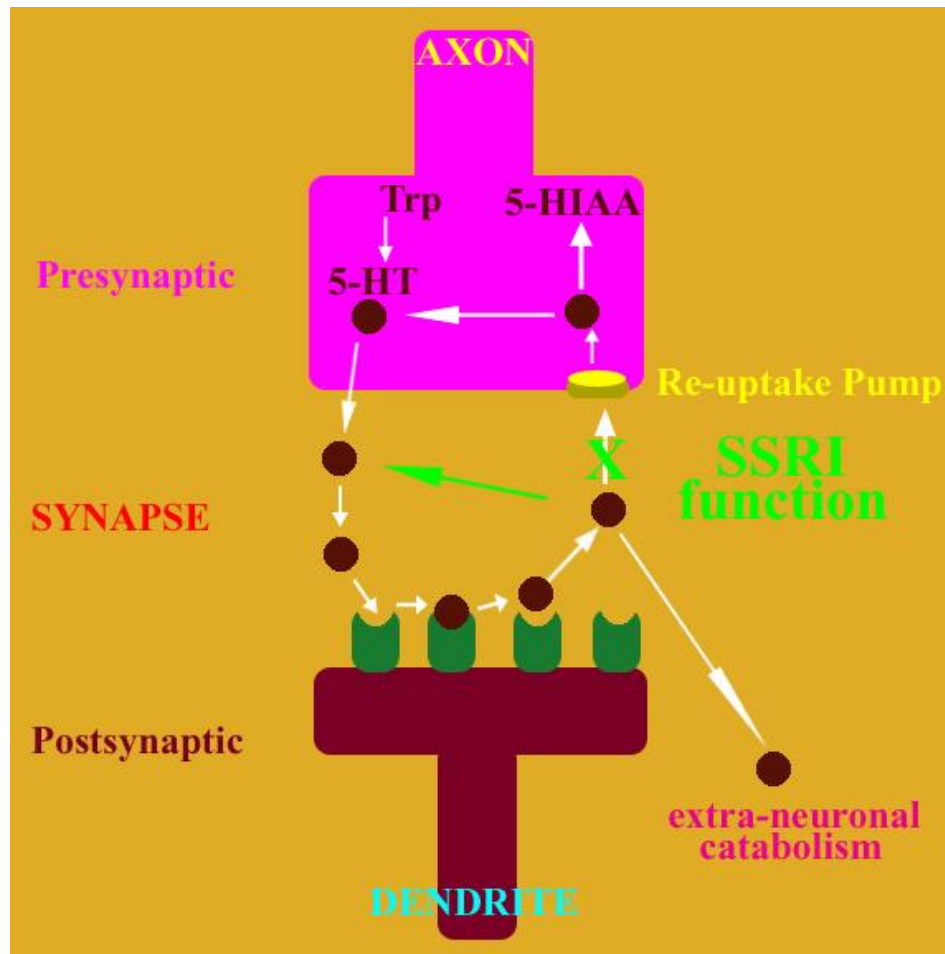
5-HIAA Levels – “Balancing Act”

1. 5-HIAA levels found in the CSF of patients who died from violent suicide were incredibly low.
2. 5-HIAA levels were also low in murderers and other violent offenders.
3. 5-HIAA levels were elevated in obsessive compulsive disorders, sociopaths and those with “guilt complexes”.
4. In each case, these levels (too low or too high) cause clinical depression.

General Neurophysiological Chemistry



SSRI's – Selective Serotonin Re-Uptake Inhibitors



Serotonin Comments

Phen-Fen

1. MAOI's and SSRI's are useful as antidepressants.
 2. SSRI's enhance morphine analgesia.
 3. 5-HT (S) release may be increased with p-chloroamphetamine (pCA) or **fenfluramine** which reduces food intake.
 4. pCA causes insomnia, too.
- Combination of **fenfluramine** or **dexfenfluramine** with phentermine.
 - Caused heart valvular disease.
 - Removed from market due to lawsuit after 1999.

Serotonin Comments

Cocaine

1. Blocking 5-HT (S) uptake with fluoxetine or zimelidine lowers body weight in NON-depressed obese people.
 2. Correlation of obesity with depression ~ 85%
- Increases 5-HT (S) release.
 - Blocks re-uptake pump, too.
 - Blocks Na^+ channel.
 - Reduces vasoconstrictive activity of 5-HT in peripheral tissues.
 - Cocaine hydrolase

Putative Mechanism (per Wurtman and Wurtman, et al) of Carbo Auto-Treatment of Depression (CAT-D)

DISCLAIMER:

This synopsis has been pulled from numerous sources. It is not intended to be used as either diagnostic or therapeutic tools. It is intended as part of academics and as an educational tool for the central nervous system.

For your best care, seek assistance from a qualified mental health care practitioner.

S..E..R..O..T..O..N..I..N

- This is the putative mechanism as to why some people who have depressive types of disorders, e.g., PMS, SAD, chronic depression, self-medicate with carbohydrates.



Depressed?

PMS?

S.A.D.?

Numb?

S..E..R..O..T..O..N..I..N

- It does not explain the mechanism of self-medicating with chocolate -- while that seems to be partially through the release of phenylethylamine (PEA; the "in love" chemical), there are some simple sugars that are generally in the chocolate product that may give a "double-whammy" effect, so to speak.
- The former (simple carb's) appears to work by increasing CNS serotonin release into synapses; the latter (chocolate) seems to act via beta-adrenergic receptors to relieve depression.
- Remember, too, that exercise (e.g., walking, hiking, running, cycling, weight lifting, basket ball, soccer, martial arts) plays a role in recovering from depression, as well.



Depressed?

PMS?

S.A.D.?

Numb?

- Depression is one of the most common mental health problems.
- It appears that there are biological depressions and situational depressions.
- Often both factors are involved.
- Treatment can include antidepressant medications such as Prozac, Zoloft, Paxil, Celexa, Welbutrin and St. John's Wort - and it can also include psychotherapy.
- Dysthymia refers to a milder depression than "major depression" or "major affective disorder."

DEPRESSION Symptomatology

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being "slowed down"
- Difficulty concentrating, remembering, or making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain

PMS

- A recent NIMH study showed that in the case of premenstrual syndrome (PMS), women with a preexisting vulnerability to PMS experienced relief from mood and physical symptoms when their sex hormones were suppressed (? what about oral contraceptives?). Shortly after the hormones were re-introduced (? oral contraceptives?) , they again developed symptoms of PMS. Women without a history of PMS reported no effects of the hormonal manipulation.

Side Effects of Anti-Depressants

- Antidepressants may cause mild and, usually, temporary side effects (sometimes referred to as adverse effects) in some people.
- Typically these are annoying, but not serious.
- However, any unusual reactions or side effects or those that interfere with functioning should be reported to your healthcare provider immediately.

The most common side effects of tricyclic antidepressants, and ways to deal with them, are:

- Dry mouth--it is helpful to drink lots of water; chew sugarless gum; clean teeth daily.
- Constipation--bran cereals, prunes, fruit, and vegetables should be in the diet.
- Bladder problems--emptying the bladder may be troublesome, and the urine stream may not be as strong as usual; the doctor should be notified if there is any pain.
- Sexual problems--sexual functioning may change; if worrisome, it should be discussed with the physician. Periactin.
- Blurred vision--this will pass soon and will not necessitate new glasses.
- Dizziness--rising from the bed or chair slowly is helpful.
- Drowsiness as a daytime problem--this usually passes soon. A person feeling drowsy or sedated should not drive or operate heavy equipment. The more sedating antidepressants are generally taken at bedtime to help sleep and minimize daytime drowsiness.

The newer antidepressants have different types of side effects:

- Headache--this will usually go away.
- Nausea--even when it occurs, it is transient after each dose.
- Nervousness and insomnia (trouble falling asleep or waking often during the night)--these may occur during the first few weeks; dosage reductions or time will usually resolve them.
- Agitation (feeling jittery)--if this happens for the first time after the drug is taken and is more than transient, the physician should be notified.
- Sexual problems--the physician should be consulted if the problem is persistent or worrisome (the powerful anti-histamine Periactin taken just before intercourse will "stop" the effects of SSRI's for successful intercourse -- the drawback is that the person will fall asleep very rapidly after successful intercourse, minimizing "cuddling time").

- Depressive disorders make one feel exhausted, worthless, helpless, and hopeless. Such negative thoughts and feelings make some people feel like giving up. It is important to realize that these negative views are part of the depression and typically do not accurately reflect the situation. Negative thinking fades as treatment begins to take effect.



Depressed?

PMS?

S.A.D.?

Numb?

In the meantime:

- Set realistic goals and assume a reasonable amount of responsibility.
- Break large tasks into small ones, set some priorities, and do what you can as you can.
- Try to be with other people and to confide in someone; it is usually better than being alone and secretive.
- Participate in activities that may make you feel better.
- Mild exercise, going to a movie, a ballgame, or participating in religious, social, or other activities may help.
- Expect your mood to improve gradually, not immediately. Feeling better takes time.
- It is advisable to postpone important decisions until the depression has lifted. Before deciding to make a significant transition--change jobs, get married or divorced--discuss it with others who know you well and have a more objective view of your situation.
- People rarely "snap out of" a depression. But they can feel a little better day by day.
- Remember, positive thinking will replace the negative thinking that is part of the depression and will disappear as your depression responds to treatment.
- Let your family and friends help you.
- Know that everyone makes mistakes every day and survives.

- Many people attempt to self medicate (CAT-D) their depressive disorder by eating products containing refined sugars, e.g., candy and other "junk food" and/or complex carbohydrates, e.g., pasta, rice, breads.
- As the carbohydrates are digested in the small bowel, glucose is taken up across the gut into the blood.
- While a person is ingesting food, his/her insulin levels are increasing as the pancreas prepares to "drive" glucose into the cell.
- As the glucose enters the blood stream, insulin levels continue to increase.
- The increase in insulin levels in the blood is believed to increase the uptake of tryptophan into the blood.

The brain increases its uptake of the tryptophan from the blood. It is believed that this increased uptake is due to one or more of the following elevated insulin mechanisms:

- Increases the sensitivity of the blood-brain barrier to tryptophan (by reducing the resistance to its uptake?),
- Increases the uptake of tryptophan at the expense of the branched chain amino acids, or
- Increases the uptake of tryptophan as a natural extension of amino acid uptake with/by growth hormone.

The brain increases its uptake of the tryptophan from the blood. It is believed that this increased uptake is due to one or more of the following elevated insulin mechanisms:

- The increased tryptophan is taken up by the brain. The brain then synthesizes serotonin from the tryptophan. Serotonin, BTW, does NOT go across (into) the blood-brain barrier -- tryptophan has to be taken up for serotonin synthesis to occur in the neurological tissue. Once serotonin is synthesized, it is released following the release of a neurotransmitter or neurotransmitters and the resulting action potential[s].

The brain increases its uptake of the tryptophan from the blood. It is believed that this increased uptake is due to one or more of the following elevated insulin mechanisms:

- When serotonin is released into the synapses, the person's mood is elevated. The major drawback to this CAT-D is that unless one exercises regularly, one will accumulate excessive weight. On the other hand, exercise practiced regularly and with moderation will cause the release of endorphins (a whole different category of "feel good" neurotransmitters) into that person's brain and will cause the person's mood to lift. In addition, the person will develop a healthier level of physical conditioning which will improve his or her quality of life. Couple that with the sense of well-being from the exercise and that person will soon experience a new level of self-confidence which will improve his or her self image and self value and the depression will slowly lift.

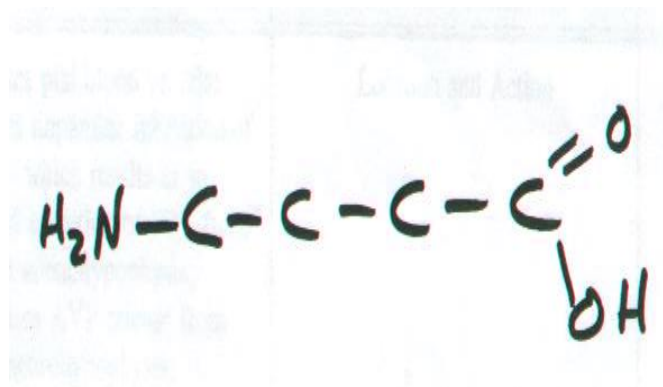
- The bottom line is that with moderation in all things and prudent, healthy self-care and self-respect, the depression will slowly lift.
- It takes time and it takes effort and it takes a desire/commitment to resolve the depression, as well.



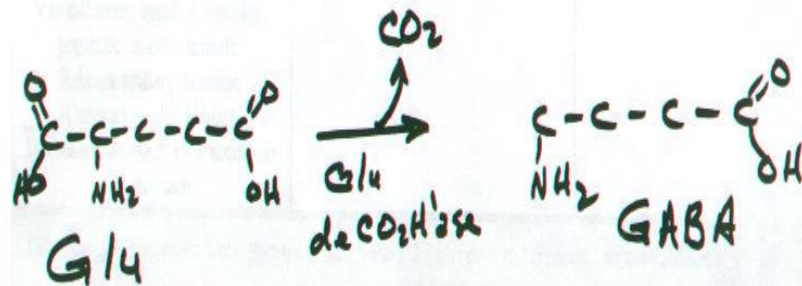
Happy!
Alive!
Feeling good!

Chemical Structure of GABA: gamma-aminobutyric acid

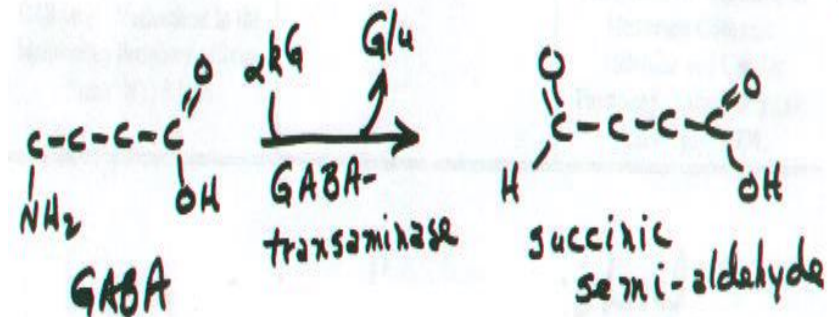
- In CNS = Primarily Inhibitory; All data coming up for GABA receptors is for peripheral receptors



Biosynthesis of GABA



Initial Degradation of GABA



GABA _A	Characteristic	GABA _B
Muscimol, isoguavicine, homotaurine	Agonists	Baclofen
Bicuculline	Antagonists	delta-aminovaleric acid
Cl ⁻ channel OR K ⁺ channel	Coupled with	Ca ²⁺ movement OR K ⁺ movement
Benzodiazepines and barbiturates	Binds also	
Enhances binding of GABA to receptors	Absence of Divalent Cations	Inhibits binding of GABA to receptors
Inhibits binding of GABA to receptors	Presence of Divalent Cations	Required for binding of GABA to receptors

GABA _A	Characteristic	GABA _B
<p>Relaxes pial blood vessels; Decreases dopamine inhibition of PRL which results in an increased secretion of PRL from the adenohypophysis; Increases AVP release from the neurohypophysis; Pineal gland; Increases E and NE secretion from the adrenal medulla; Female reproductive tract and placenta; Contracts ileum smooth muscle; Contracts all other gut smooth muscle; Vas deferens, seminal vesicles, prostatic smooth muscle; Relaxes urinary bladder; Contracts gall bladder; Decreases stomach HCl secretion in stomach</p>	<p>Location and/or action</p>	<p>Reduces HR and BP at level of atria; Increases contractility of female reproductive tract; Smooth muscle; β-cells in pancreas; Relaxes urinary bladder; Contracts gall bladder; Decreases stomach HCl secretion; C fibers and A-delta fibers are activated by GABA</p>
<p>GABA_{generic}: increases liver glycogenolysis with a secondary increase in BS; seems to also increase bile flow from the liver</p>		