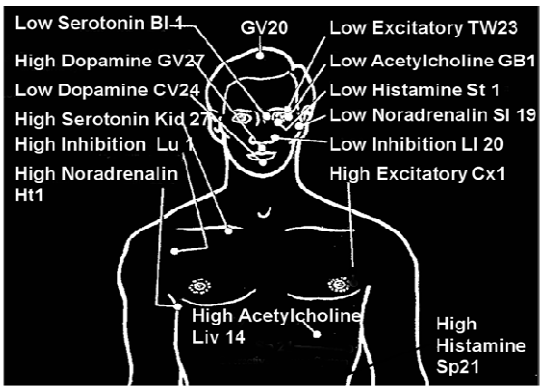
Neurotransmitters and Perception

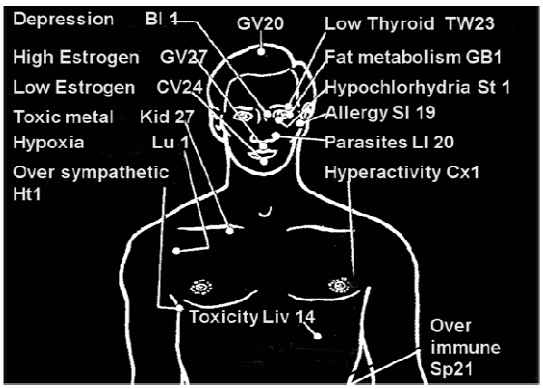
Mother Nature writes some things in pen and some things in pencil. Things written in pen you cannot change. That's DNA. But things written in pencil you can. That's Epigenetics.

"simply ingenious"

Meridians B&E Points



A meridian should be thought of reflecting its physiological function rather than just the organ its named after.



How the Nervous System Communicates

Nerves talk to each other by secreting specific chemicals called neurotransmitters.

The message is transmitted by electricity just like a telephone.

Neurotransmitters are chemicals made by neurons and used by them to transmit signals to the other neurons or non-neuronal cells

(e.g., skeletal muscle, myocardium, pineal glandular cells etc) that they innervate.

The neurotransmitters produce their effects by being released into synapses when their neuron of origin fires (i.e., becomes depolarized)

and then attaching to receptors in the membrane of the post-synaptic cells.

This causes changes in the fluxes of particular ions across that membrane, making cells more likely to become depolarized, if the neurotransmitter happens to be excitatory,
or stimulatory
or less likely if it is inhibitory.

Neurotransmitters can also produce their effects by modulating the production of other signal-transducing molecules ("second messengers“ such as cAMP, cGMP, Phosphatidylinositol)
in the post-synaptic cells.

Ten compounds -- belonging to three chemical families -- are generally believed to function as neurotransmitters somewhere in the central nervous system or periphery.

Excitatory	**Aspartic acid** **Glutamic acid**
Stimulatory	**Acetylcholine** **Noradrenalin** **Dopamine** **Serotonin** **Histamine**

Inhibitory GABA, Glycine, Taurine

In addition, certain other body chemicals, for example
adenosine,
enkephalins,
endorphins,
nitric oxide

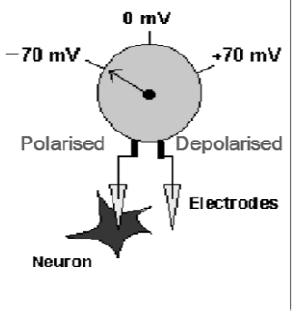
have neurotransmitter-like properties.

Glutamic acid and GABA are the most abundant neurotransmitters within the central nervous system, particularly in the cerebral cortex; glutamic acid tends to be excitatory and GABA inhibitory. Aspartic acid and glycine subserve these functions in the spinal cord.

Once released into the synapse, each neurotransmitter combines chemically with one or more highly specific receptors;

these are protein molecules which are imbedded in the post-synaptic membrane.

This interaction can affect the electrical properties of the post-synaptic cell, its chemical properties, or both.



When a Neuron is in its resting state, it sustains a voltage of about
- 70 milli volts
as the consequence of differences between the concentrations of certain ions at the internal and external sides of its bounding membrane.

Stimulatory neurotransmitters either open protein-lined channels in this membrane, allowing extracellular ions, like

Sodium (Na+)

to move into the cell, or close channels for potassium.

This raises the neuron's voltage towards zero, and makes it more likely that the cell will become depolarized. If the postsynaptic cell happens also to be a neuron (i.e., as opposed to a muscle cell), this depolarization will cause it to release its own neurotransmitter from its terminals.

Inhibitory neurotransmitters like GABA , Glycine and Taurine activate receptors that cause chloride (Cl-) to pass through the membrane;

this usually hyperpolarizes the postsynaptic cell, and decreases the likelihood that it will become depolarized.

The excitatory neurotransmitter glutamic acid, acting via its NMDA receptor, can also open channels for calcium ions (Ca++).

Excessive activation of these receptors in neurological diseases can cause toxic quantities of calcium to enter the cells, and kill them.

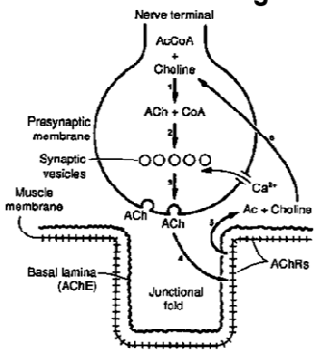
Once neurotransmitters have been secreted into synapses and have acted on their receptors, they are metabolised from the synapse either by enzymatic breakdown - for example acetylcholine, which is converted to choline and acetate, neither of which has neurotransmitter activity.

For neurotransmitters like

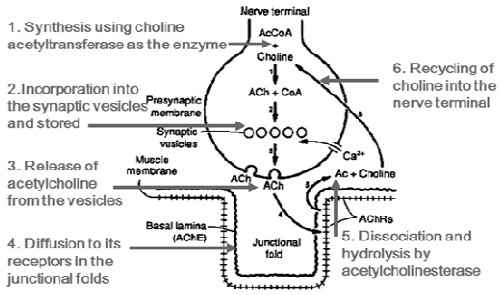
Dopamine
Serotonin
GABA

a physical process called reuptake takes place.

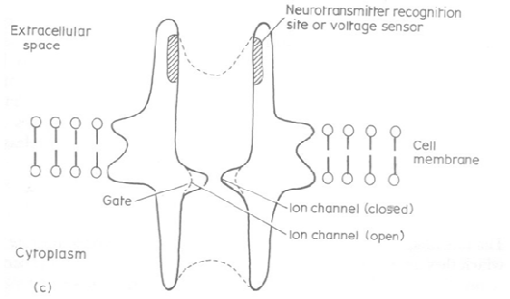
Terminal end of a cholinergic neuron



Neurotransmitter synthesis



Receptors are like molecular ears



Neuronal membranes

The lipid portion of cell membranes is just 3 nanometres thick.
If you were to stack sheets of them one upon the other – it would take 10,000 membranes to make up the thickness of a piece of paper.

Lipids are classified as

1. **Simple lipids – oils and fats**
2. **Complex lipids**
   a) Phospholipids
   b) Glycosphingolipids containing a fatty acid, sphingosine and a CHO
   c) Lipoproteins

Simple lipids are

a) Saturated (no double bonds)
   CH3 ----------COOH

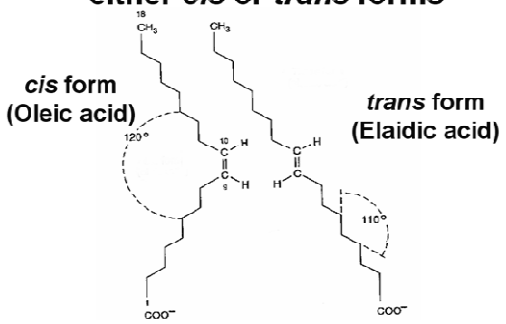
b) Unsaturated (mono or poly double bonds)
   CH3 ----=---------- COOH
   (Methyl (w) end Carboxyl end)

Saturated fatty acids

Name	Number	
Formic	1	Bee stings
Acetic	2	Rumen fermentation
Proprionic	3	Rumen fermentation
Butyric	4 (-8°C)	Rumen fermentation
Valeric	5	Rumen fermentation
Caproic	6 (-3°C)	Coconut

Caprylic	8 (17°)	Coconut
Nonanoic	9	Licorice root
Capric	10 (32 °)	Coconut
Undecanoic	11	Castor bean oil
Lauric	12 (44 °)	Breast milk, Coconut
Myristic	14 (54 °)	Nutmegs, Coconut
Palmitic	16 (63 °)	Animal and plant fats
Stearic	18 (70 °)	Animal and plant fats
Arachidic	20 (75 °)	Peanuts
Behenic	22 (80 °)	Seeds
Lignoceric	24 (84 °)	Cerebrosides, Peanuts

Unsaturated fatty acids can be in either *cis* or *trans* forms



Monoenoic acid (one double bond)

Number	Series	Common Name	Systematic Name	Source
16:1:9	w7	Palmitoleic	Cis-9-hexadecenoic	All fats
18:1:9	w9	Oleic	Cis-9-Octadecenoic	Olive
18:1:9	w9	Elaidic	Trans-9-Octadecenoic	Hydrogenated fats
22:1:13	w9	Erucic	Cis-13-Docosenoic	Rapeseed
24:1:15	w9	Nervoic	Cis-15-Tetracosenoic	Cerebrosides Honesty seed

Dienoic acids (two double bonds)

18:2:9,12	**w6**	**Linoleic**	**all-cis-9,12-Octadenenoic**	**Corn, peanut, soybean**

Trienoic acids (three double bonds)

18:3:6,9,12	**w6**	**γ-Linolenic**	**all-cis-6,9.12-Octadecatrienoic**	**EPO, BSO, Borage**
18:3:9,12,15	**w3**	**α-Linolenic**	**all-cis-8,12,15-Octadecatrienoic**	**Flax, walnut, pumpkin**

Tetraenoic acids (four double bonds)

20:4:5,8,11,14	w6	Arachidonic	all-cis-5,8,11,14-Eicotetraenoic	Peanut

Pentaenoic acids (five double bonds)

20:5:5,8,11,14,17	w3	Timnodonic (EPA)	all--cis-5,8,11,14,17-Eicosapentaenoic	Fish oil, Canola, Eggs
22:5:7,10,13,16,19	w3	Clupanodonic (DPA)	all-cis-7,10,13,16,19, Docosapenaenoic	Fish oil

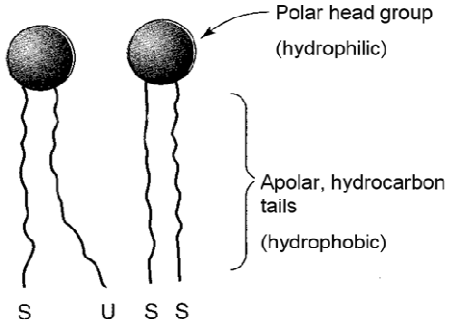
Hexaenoic acids (six double bonds)

22:6:4,7,10,13,16,19	**w3**	**Cervonic (DHA)**	**all-cis-4,7,10,13,16,19-Docosahexaenoic**	**Fish oil Algae, Eggs**

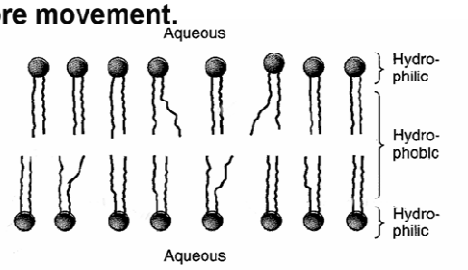
Fatty Acid Properties

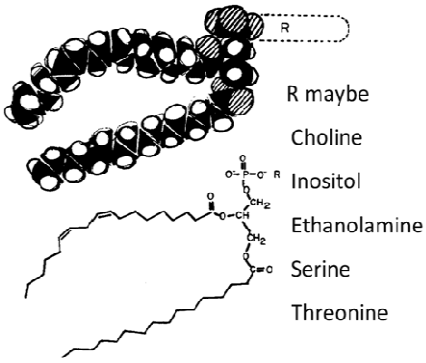
Stacking (acid end / fatty end)	18:0	18:1 w9 c	18:1 w9 t	18:2 w6 c,c	18:3 w3 c,c,c
Saturation	Saturated	Unsaturated 1 double bond cis-configuration	Unsaturated 1 double bond trans-	Unsaturated 2 double bonds cis,cis-	Unsaturated 3 double bonds cis,cis,cis-
Melting Point	70°c sfs sticky	13°c cis-single slightly anti-sticky	44°c trans-single slightly sticky	-5°c cis,cis-double anti-sticky	-12°c cis,cis,cis-triple very anti-sticky
Repelling Charges	no charge	1 neg. charge	1 neg. charge	2 neg. charges	3 neg. charges

A Phospholipid

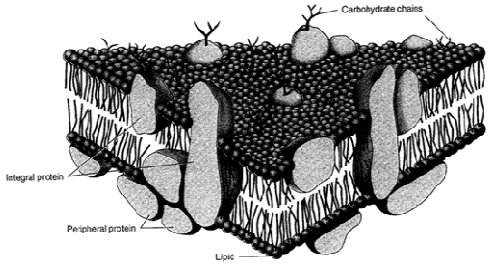


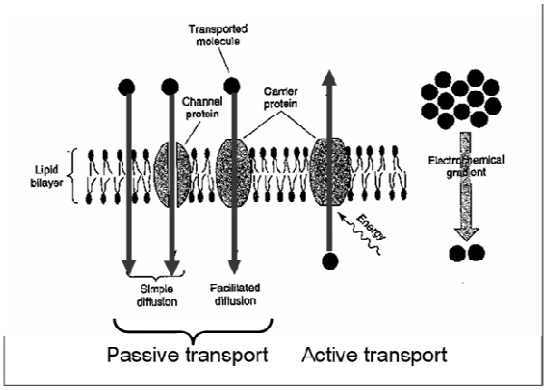
The unsaturated fatty acid tails are kinked and lead to more spacing between the polar heads and hence more movement.



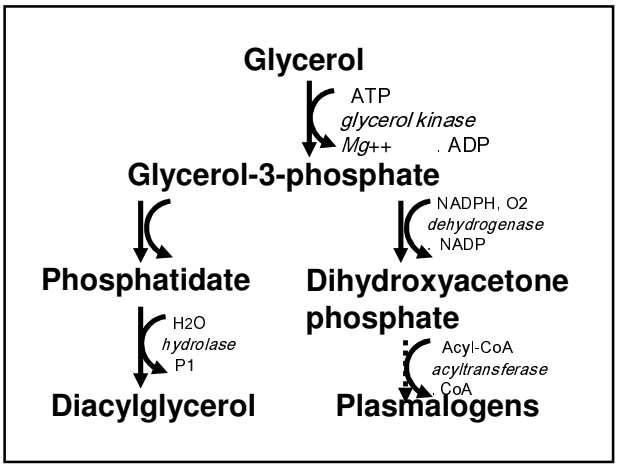


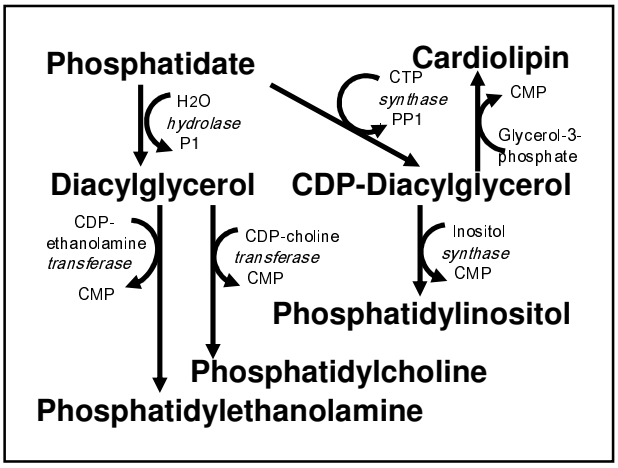
Cell Membranes

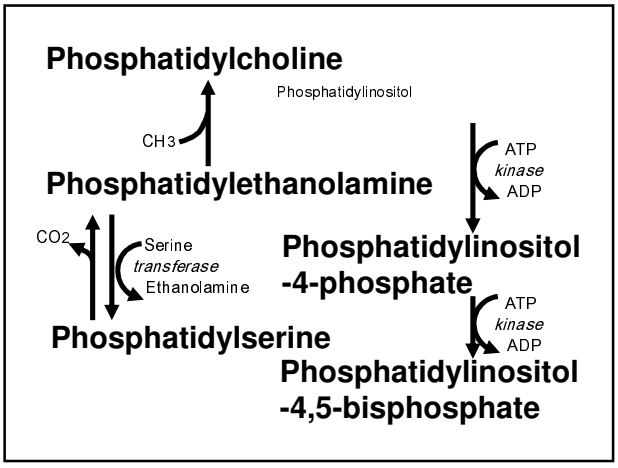




Neuronal cell membranes
Glial cells – the C1 position is taken by a saturated fatty acid and C2 by an unsaturated fatty acid
Neurones – in many neurones the C1 position is taken by Arachidonic acid and C2 by DHA.
Retina – both C1 and C2 positions are taken by DHA.


Glycerol
ATP
glycerol kinase
Mg++
ADP
Glycerol-3-phosphate
NADPH, O2
dehydrogenase
NADP
Phosphatidate
Dihydroxyacetone phosphate
H2O
hydrolase
P1
Acyl-CoA
acyltransferase
CoA
Diacylglycerol
Plasmalogens


Phosphatidate
Cardiolipin
CTP
synthase
PP1
CMP
Glycerol-3-phosphate
H2O
hydrolase
P1
Diacylglycerol
CDP-Diacylglycerol
CDP-ethanolamine transferase
CMP
CDP-choline transferase
CMP
Inositol synthase
CMP
Phosphatidylinositol
Phosphatidylcholine
Phosphatidylethanolamine

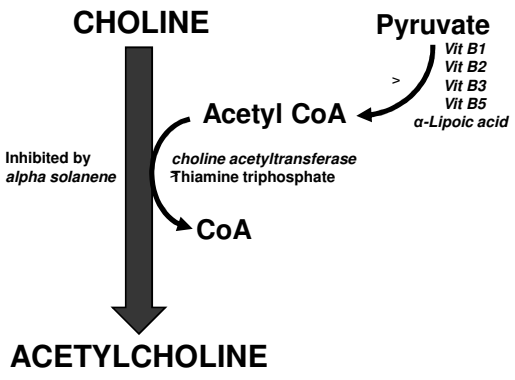

Phosphatidylcholine
Phosphatidylinositol
CH3
Phosphatidylethanolamine
ATP
kinase
ADP
CO2
Serine transferase
Ethanolamine
Phosphatidylinositol -4-phosphate
ATP
kinase
ADP
Phosphatidylserine
Phosphatidylinositol -4,5-bisphosphate

Key nutrients for synthesising the phospholipids

Acetyl CoA (Vit B5)
NAD, NADPH (Vit B3)
Mg, Zn, SAM (Mg, B6, Folates, B12)
Choline
Ethanolamine
Serine
Inositol
Saturated fatty acids C16-18 (palmitic – stearic)
Unsaturated fatty acids C18-24

Regulatory Neurotransmitters

open Na_+ channels causing depolarisation or stimulation.



ACETYLCHOLINE

H_20

acetylcholinesterase

B2

B3

Mn++

Zn++

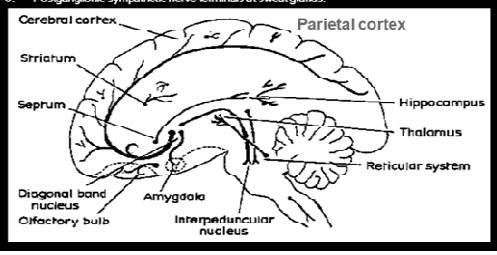
Recycled

Inhibited by
chemicals – pesticides
toxic metals
radiation
galantamine

Acetate + Choline

Acetylcholine is the transmitter at

1. All preganglionic nerve terminals (both parasympathetic and sympathetic) of the autonomic nervous system
2. All postganglionic parasympathetic nerve terminals
3. The neuromuscular junction of voluntary muscles
4. The adrenal medulla
5. Parts of the central nervous system especially the hippocampus
6. Postganglionic sympathetic nerve terminals at sweat glands.



Acetylcholine Receptors

1. Muscarine from the fungus Amanita muscaria. The effect of muscarine is tearing eyes, pupillary constriction, profuse sweating, drooling saliva, faecal dribbling or explosion from the anus. Painful peristalsis, low blood pressure and bradycardia.

Acetylcholine Receptors

1. Muscarine receptor stimulation occurs physiologically when the parasympathetic nervous system is active during rest and sleep.

i) Slows the heart rate

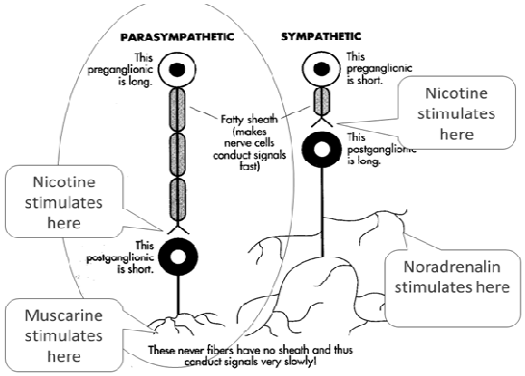
ii) Stimulates the release of NO in blood vessels and so vasodilates

iii) Stimulates the secretion of saliva, mucous, HCl, digestive enzymes and skin sweat glands.

iv) Stimulates intestinal tone and peristalsis.

v) Stimulates ureter and bladder contraction.

vi) Stimulates cilary muscle contraction in the eye causing relaxation of the lens, which is then focused for near vision. Stimulates contraction of the iris circular muscles causing constriction of the pupil. Stimulates reduction of the intra ocular pressure by better drainage through the canal of Schlemm.



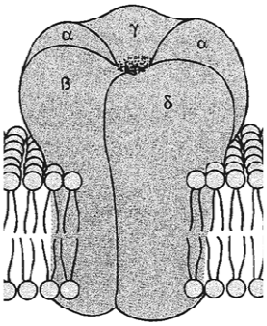
2. Nicotinic (antagonised by curare) receptors occur at

i) CNS especially in the hippocampus.

ii) The neuromuscular junctions

Acetylcholine is possibly the most widely used neurotransmitter in the body, and all axons that leave the central nervous system (for example, those running to skeletal muscle, or to sympathetic or parasympathetic ganglia) use acetylcholine as their neurotransmitter.

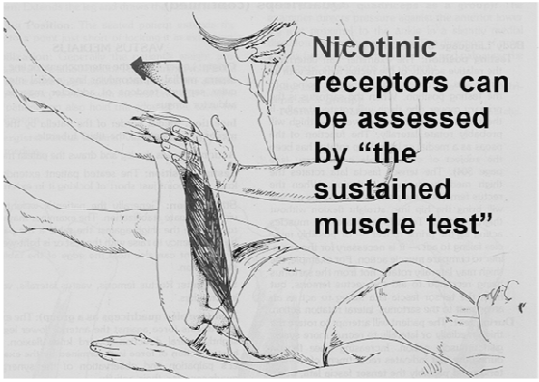
Acetylcholine Receptors



1. **Muscarine receptors occur in the parasympathetic nervous system**

2. **Nicotinic receptors occur at**
   i) CNS especially in the hippocampus.
   ii) The neuromuscular junctions

Muscarinic receptors can be assessed by "the looking into a bright light" test.



Natural sources of Acetylcholine

Shepherds purse	Fennel
Coriander	Black pepper
Hawthorn	Spinach
Carrot	Fenugreek
Cardamom	Stinging nettle

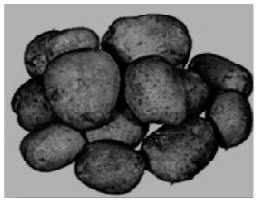
Acetylcholine is contained in

Egg yolks, peanuts, wheat germ, liver, meat, fish, milk, cheese and vegetables (especially broccoli, cabbage and cauliflower), legumes, organ and muscle meat, milk, and whole-grain cereals.

Anticholinergics

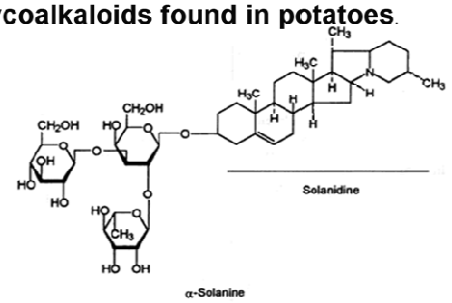
Solanacea family

- **Tomatoes**
- **Potato**
- **Tobacco**
- **Jimsonweed (Thorne apple)**



<u>Alpha-Solanine</u>

Solanine is one of the main glycoalkaloids found in potatoes.



Natural Acetylcholinesterase Inhibitors

Galantathine (Galanthamine)	Snowdrops Daffodils Lemon balm

In a study done in 2003 at Nottingham University researchers investigating the use of Lemon balm for both mood elevation and cognitive performance in healthy volunteers aged18-22 years, found that a low dose of 500mg a day was much more effective than taking either 800mg and suggested best taking the dose twice a day.

Lemon balm

Tincture low dose	↑Calmness
Tincture high dose	↑ Memory
Powder low dose	↑ Memory
Powder high dose	↑ Calmness

High dose Powder also increased secondary memory.

Limonene – a powerful ACh-E inhibitor

Rosemary	Caraway seed
Black walnut	Oranges
Cardamom	Fennel
Tangerine	Spearmint
Lemon	Lime
Corn	

Recent research has shown that Sage (Salvia) oil (50-150mg) can inhibit acetylcholinesterase improving memory recall by 8%. (Probably due to a high limonene concentration).

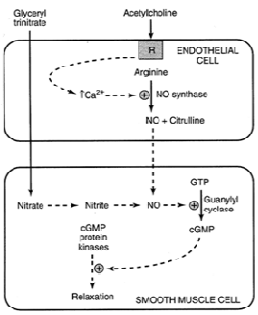
Medicinal Plant Research Centre, University of Newcastle and Northumberland August 2003

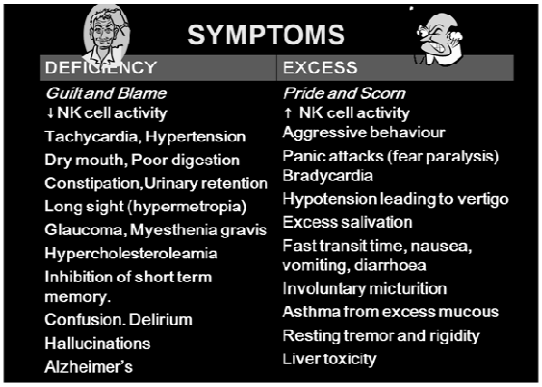
Many of the current drugs that inhibit acetylcholinesterase such as "Donepezil" have unpleasant side effects.

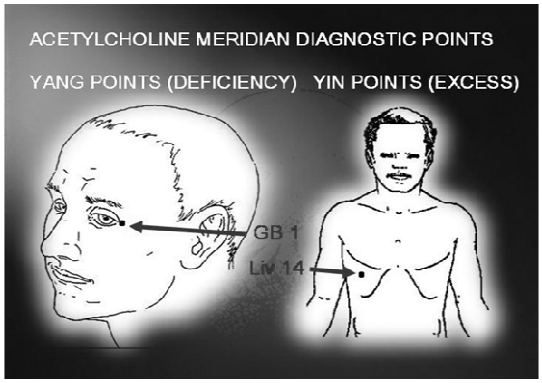
No side effects were noted in the sage trial, details of which are published in the journal

"Pharmacology and Biochemistry".

Possible mechanism by which lemon balm and sage may improve memory by increasing cerebral circulation.



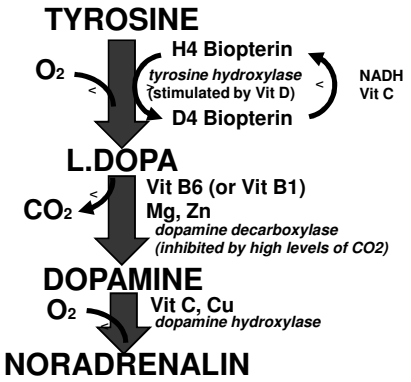


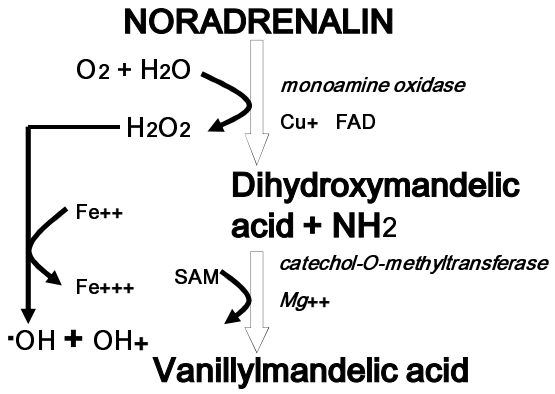


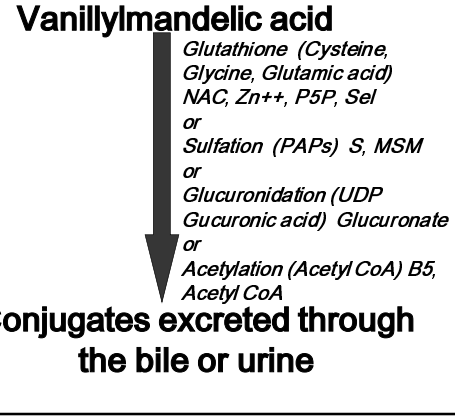
Exercises to stimulate Acetylcholine
Resistance / Weight training

Exercises to inhibit Acetylcholine
Yoga, stretching tight muscles to loosen up.

NORADRENALIN
(NOREPINEPHRINE)

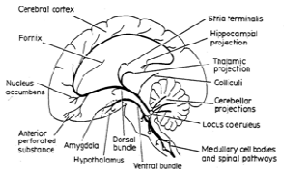

TYROSINE
H4 Biopterin
O2
tyrosine hydroxylase
(stimulated by Vit D)
NADH
Vit C
D4 Biopterin
L.DOPA
Vit B6 (or Vit B1)
Mg, Zn
CO2
dopamine decarboxylase
(inhibited by high levels of CO2)
DOPAMINE
O2
Vit C, Cu
dopamine hydroxylase
NORADRENALIN


NORADRENALIN
O2 + H2O
monoamine oxidase
H2O2
Cu+ FAD
Dihydroxymandelic acid + NH2
Fe++
Fe+++
SAM
catechol-O-methyltransferase
Mg++
·OH + OH+
Vanillylmandelic acid


Vanillylmandelic acid
Glutathione (Cysteine, Glycine, Glutamic acid)
NAC, Zn++, P5P, Sel
or
Sulfation (PAPs) S, MSM
or
Glucuronidation (UDP Gucuronic acid) Glucuronate
or
Acetylation (Acetyl CoA) B5, Acetyl CoA
Conjugates excreted through the bile or urine

Noradrenalin is a neurotransmitter @

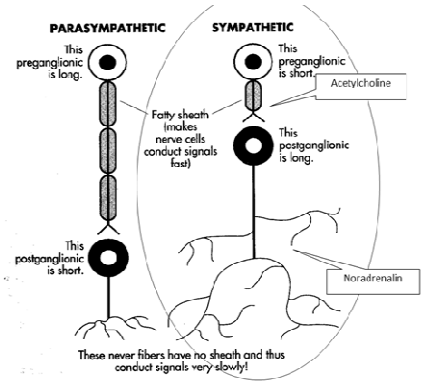
1. **Postganglionic sympathetic nerves**
2. The Brain stem
3. Some spinal pathways
4. The Pontine – thalamic, hypothalamic, limbic, hippocampus and neocortex tracts.



Adrenoreceptors

Two sub-types designated alpha and beta.

Alpha 1 receptors are found postsynaptically.
Alpha 2 receptors are found in presynaptic autoreceptors, postsynaptically and in the CNS.
Post synaptic effects
i) Contraction of the radial muscles of the iris leading to papillary dilation. Also keeps the eyelid open.
ii) Vasoconstriction.
iii) GI smooth muscle relaxation but sphincter contraction.
iv) Seminal vesicle and vas deferens contraction.
v) Constriction of trigone and bladder sphincter



Beta 1 receptors are found in the heart and increases force and contraction.

Beta 2 receptors cause

i) Skeletal muscle and liver vasodilation

ii) Brochodilation.

iii) GI smooth muscle relaxation.

iv) Relaxation of the uterus in pregnancy.

v) Relaxation of the bladder detrusor muscles.

vi) Release of renin causing hypertension

vii) Stimulates glycogenolysis, lipolysis and hypoinsulinism.

Noradrenalin enhances

Alertness,

Arousal

and Mood

Noradrenaline (NA) is secreted by many neurones in the brain stem and hypothalamus. Neurones in the locus ceruleus in the pons send fibres to many areas of the brain and help to regulate the overall activity and mood of the *mind*.

NA has both stimulatory and inhibitory actions.

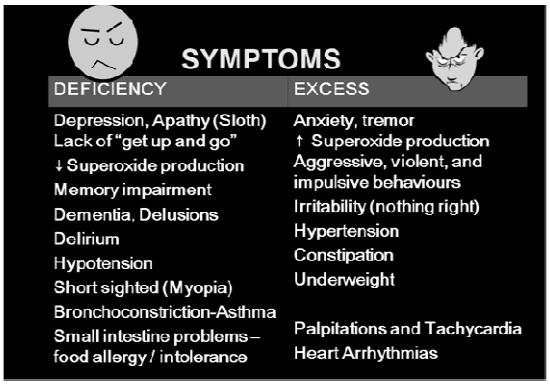
Noradrenalin is the neurotransmitter released by sympathetic nerves

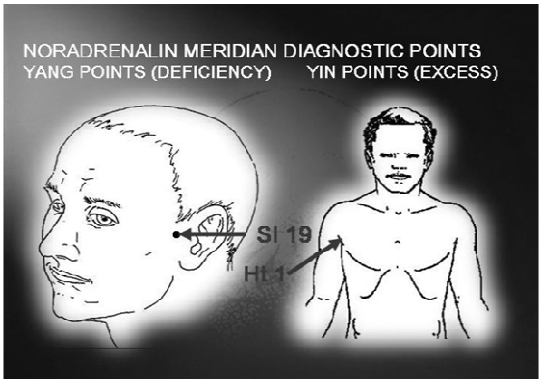
(e.g., those innervating the heart and blood vessels)

and, within the brain, those of the locus ceruleus, a nucleus activated in the process of focusing attention.

Sources of Noradrenalin

Banana,
Orange,
Plum,
Sweet potato,
Potatoes,





Exercises to stimulate Noradrenalin – Aerobics class – build heart rate up.

Exercises to inhibit Noradrenalin –Sprinting anaerobically to burn up noradrenalin.

Tyramine is an indirect acting catcholaminergic amine found in Bananas and Avocados, Barley grass, Mandarin, Tangerine, Orange, Lemon, Grapefruit, Tomato, Pea, Plum, Aubergine, Cacao, Potato Cheese, Sour cream, Pizzas, Chocolate.

***Pickled Herrings,* Caviar, Liver, *Salamis,* Broad Beans pods.**

Fermented dairy products such as Yoghurt, Sauerkraut

Yeast extracts* including Beer and Wine, Bovril, Oxo, Marmite, MSG and all *fermented Soya Bean products.

Normally tyramine is completely inactivated by MAO when taken in the diet. Thus inhibition of MAO enzymes will lead to excess sympathetic activity. When these foods are eaten in the evening they often cause disrupted sleep and nightmares if high dopamine.

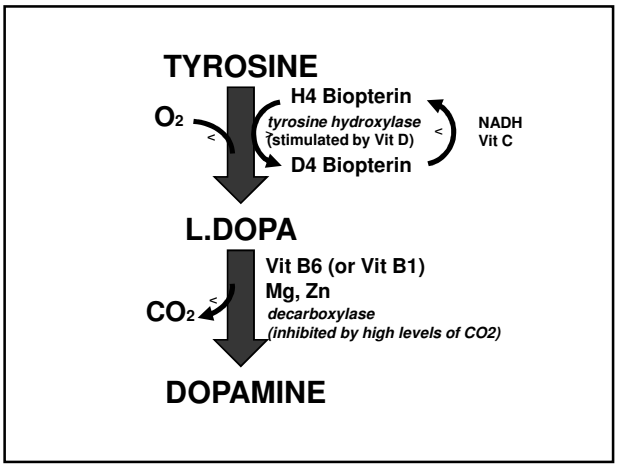
We know these foods because they are not permitted to be ingested when patients are taking monoamine oxidase inhibitor drugs such as

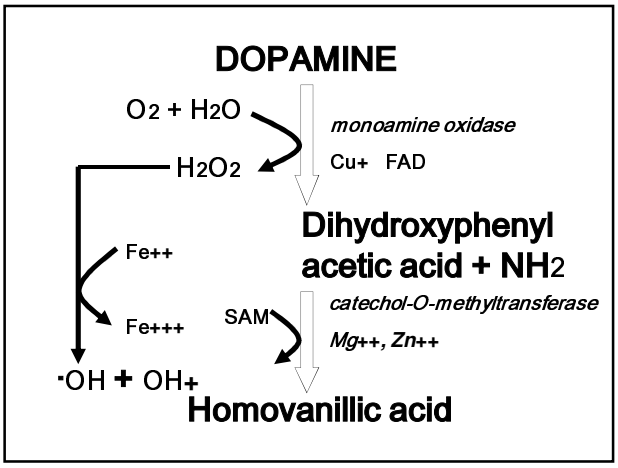
"Marplan",
"Nardil",
"Parnate".

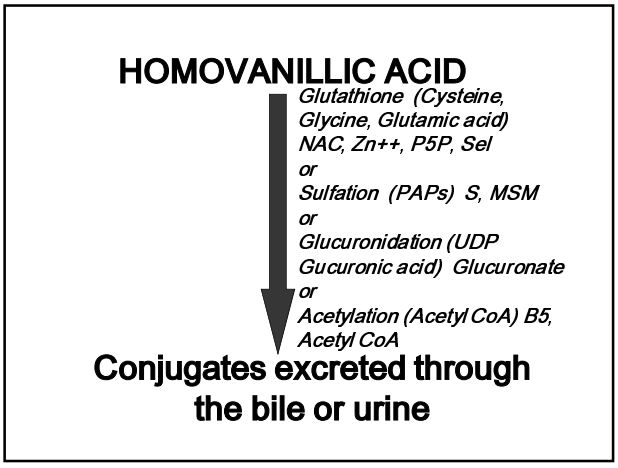
SLEEP DISTURBANCES

1. Difficulty in going to sleep. Check for high Noradrenalin and Tyramine excess.
2. Nightmares. Check for high Dopamine and Tyramine.
3. Awakes in the middle of the night. Usually a liver problem. Check for high Acetylcholine and detoxification defects.
4. General sleep disturbances maybe due to low serotonin leading also to low melatonin. Check especially for magnesium.

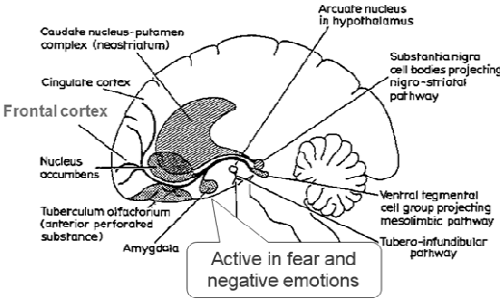
DOPAMINE


TYROSINE
O2
H4 Biopterin
tyrosine hydroxylase
(stimulated by Vit D)
D4 Biopterin
NADH
Vit C
L.DOPA
Vit B6 (or Vit B1)
Mg, Zn
decarboxylase
(inhibited by high levels of CO2)
CO2
DOPAMINE


DOPAMINE
O2 + H2O
monoamine oxidase
Cu+ FAD
H2O2
Dihydroxyphenyl
acetic acid + NH2
Fe++
Fe+++
SAM
catechol-O-methyltransferase
Mg++, Zn++
·OH + OH+
Homovanillic acid


HOMOVANILLIC ACID
Glutathione (Cysteine,
Glycine, Glutamic acid)
NAC, Zn++, P5P, Sel
or
Sulfation (PAPs) S, MSM
or
Glucuronidation (UDP
Gucuronic acid) Glucuronate
or
Acetylation (Acetyl CoA) B5,
Acetyl CoA
Conjugates excreted through
the bile or urine

Dopamine circuits



Dopamine is a neurotransmitter @

1. some sympathetic ganglion.
2. some exocrine glands.
3. the gastrointestinal tract.
4. mesenteric and renal arteries causing vasodilation.
5. carotid body controlling respiratory reflexes. Hypoxia decreases dopamine release in the carotid body and reflexly stimulates respiration.

6. the dopaminergic nigro-neostriatal (extrapyramidal) pathway.
7. dopaminergic midbrain mesolimbic forebrain system associated with cognitive, reward and emotional behaviour.
8. dopaminergic tubero-infundibular system associated with neuronal control of the hypothalamic-pituitary endocrines.
9. retina and is associated with photophobia and illumination.

Dopamine Receptors

Mainly are located in the CNS but many peripheral tissues such as the gut, blood vessels and the heart respond to exogenously applied dopamine indicating their sensitivity.

Receptors are sub-typed as

- **D1 located in post synaptic structures.**
- **D2 located pre and post synaptically.**
- **D3 located mainly in the mesolimbic pathways.**

Some dopaminergic (i.e., dopamine-releasing) neurons run from the substantia nigra to the corpus striatum; their loss gives rise to the clinical manifestations of Parkinson's Disease; others, involved in the rewarding effects of drugs and natural stimuli, run from the mesencephalon to the nucleus accumbens.

Dopaminergic neurons involved in the actions of most antipsychotic drugs (which antagonize the effects of dopamine on its receptors) run from the brain stem to limbic cortical structures in the frontal region, while the dopamine released from hypothalamic cells travels via a private blood supply

the pituitary portal vascular system, to the anterior pituitary gland, where it tonically suppresses release of the hormone prolactin.

(Drugs that interfere with the release or actions of this dopamine can cause lactation as a side-effect, even in men.)

Dopamine enhances

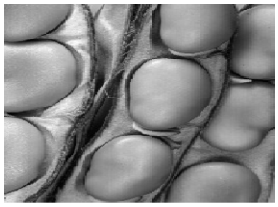
Sex drive

Mood

Alertness

Movement

L.DOPA is contained in
Avocado,
Banana,
Beans especially broad beans.



Natural sources of Dopamine

Hawthorn

Banana

Poppy seeds

Avocado

All proteins (meat, milk products, fish, beans, nuts, soy products).

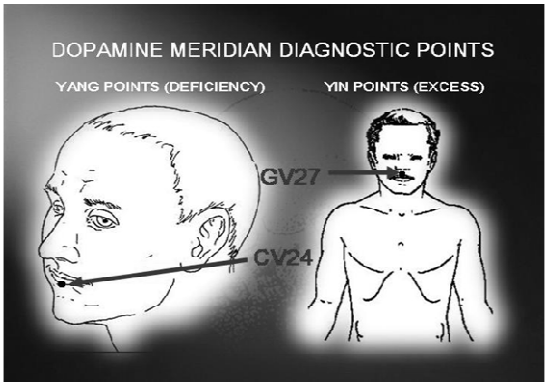
Dopamine facilitates critical brain functions when present in normal amounts. It is associated with the feeling of pleasure and pain, and helps to mediate the reinforcing effects of natural rewards such as food, water, and sex. It is associated with emotional responses and subconscious skeletal muscle movements.

Dopamine is used to communicate between the hypothalamus and the pituitary gland, in the control of movement, and in the communication between the limbic system and frontal cortex.

SYMPTOMS

Bipolar manic depression

DEFICIENCY	EXCESS
Grief and Regret	*Craving and Desire*
↓TH2 production	↑TH2 production
Indecision	Anxiety
Poor concentration	Aggression
Irrational behaviour	Confusion
A world without pleasure.	Nightmares
Clumsiness, Photophobia	Psychoses
Dendritic growth inhibition	Schizophrenia
Depression / Manic depression	
Loss of smell, Tremor	
Rigidity , Pains	

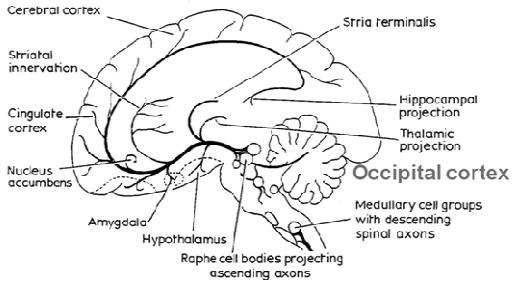


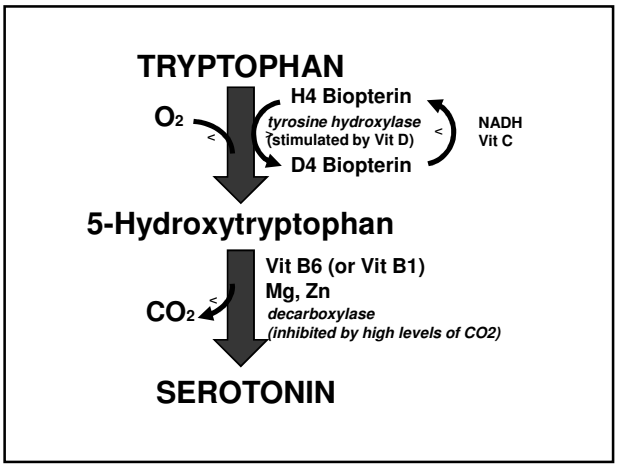
Exercises to stimulate Dopamine
Running - aerobically

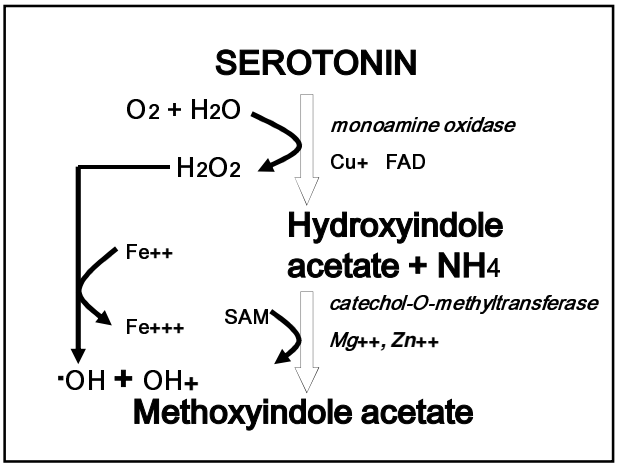
Exercises to inhibit Dopamine
Sailing or any sport that they can achieve in

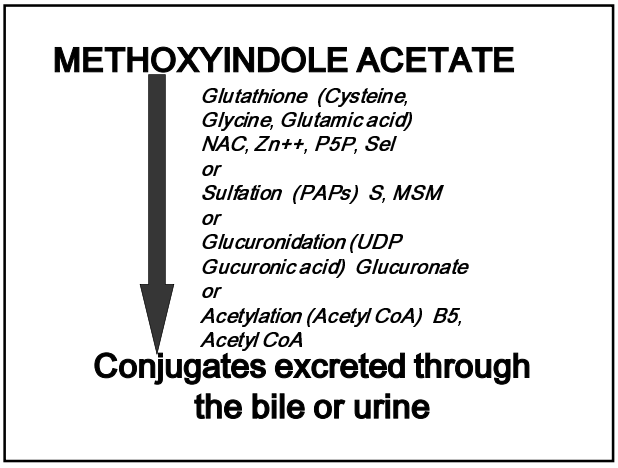
SEROTONIN

The Gin of the Neurotransmitters




TRYPTOPHAN
O2
H4 Biopterin
tyrosine hydroxylase
(stimulated by Vit D)
D4 Biopterin
NADH
Vit C
5-Hydroxytryptophan
Vit B6 (or Vit B1)
Mg, Zn
decarboxylase
(inhibited by high levels of CO2)
CO2
SEROTONIN


SEROTONIN
O2 + H2O
monoamine oxidase
H2O2
Cu+ FAD
Hydroxyindole acetate + NH4
Fe++
Fe+++
SAM
catechol-O-methyltransferase
Mg++, Zn++
·OH + OH+
Methoxyindole acetate


METHOXYINDOLE ACETATE
Glutathione (Cysteine, Glycine, Glutamic acid)
NAC, Zn++, P5P, Sel
or
Sulfation (PAPs) S, MSM
or
Glucuronidation (UDP Gucuronic acid) Glucuronate
or
Acetylation (Acetyl CoA) B5, Acetyl CoA
Conjugates excreted through the bile or urine

Serotonin is a neurotransmitter at

1. **the midline raphe nuclei of the rostral pons**
2. **basal ganglion**
3. **hypothalamus**
4. **thalamus**
5. **hippocampus**
6. **limbic forebrain**
7. **areas of the cortex**
8. **brain stem to the medulla and spinal cord**

The cell bodies, of serotoninergic neurons reside in the brain stem; their axons can descend in the spinal cord (where they "gate" incoming sensory inputs and also decrease sympathetic nervous outflow, thus lowering blood pressure) or ascend to other parts of the brain.

Brains of women produce only about two-thirds as much serotonin as those of men; this may explain their greater vulnerability to serotonin-related diseases like depression and obesity.
Within the pineal gland serotonin is also the precursor for the sleep - inducing hormone melatonin.

Serotoninergic nerve terminals are found in virtually all regions, enabling this transmitter to modulate

mood; sleep; total food intake and macronutrient (carbohydrate vs. protein) selection; aggressive behaviors; and PAIN sensitivity.

Experiments using Prozac showed initially an increase in transit time in the gut motility. As the dose increased the motility slowed until it stopped. This indicated a loss of receptor activity due to over saturation. This may occur in the brain and it may predispose to an acute depressive crisis leading in severe cases to suicide.

Migraines and Serotonin

Serotonin is systemically a vasoconstrictor, but a vasodilator of the mid meningeal artery.

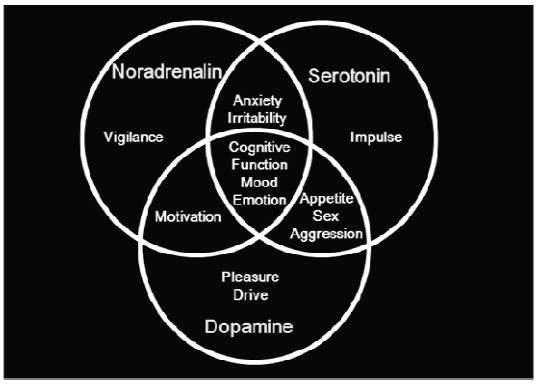
SEROTONERGIC RECEPTORS

5-HT release either from nerves or from platelets causes vasoconstriction of all large blood vessels.

Currently there are fifteen different receptor subtypes.

Natural sources of Serotonin

Sallow thorn,	Avocado
Stinging nettle	Banana
English walnut	Cocoa
Pineapple	Chocolate
Dates	Plum
Tomato	Turkey



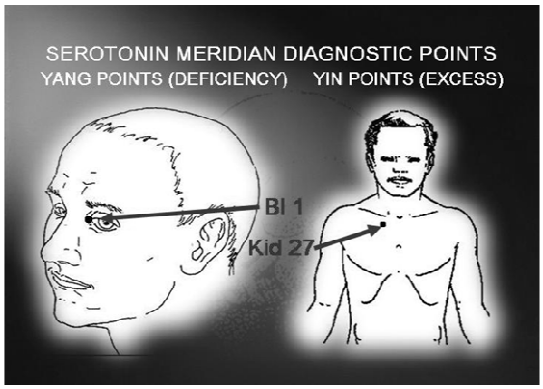
The neurotransmitters serotonin, noradrenaline and dopamine are involved in the control of many of our mental states, sometimes acting on their own and other times acting together. These, and other neurotransmitters, are likely to play a pivotal role in the pathological basis of mental illness and brain disease.

Understanding the numerous neurotransmitters, their receptors, their location, and their interactions with one another has been central to the design of medicines for mental illness and has led to the development of successful products for many brain disorders.

Any activity in a garden such as weeding, pruning, cultivating and harvesting has been shown to increase low levels of serotonin.

Dr Roger Ultrich Texas A&M University August 2003

DEFICIENCY	EXCESS
Shame and Humiliation	*Anxiety and Fear*
↓ B cell production	↑ B cell production
Depression (the blues)	Migraine
Suicide, Sleep disorders	Depression
Compulsive disorders	Pains
Obsessive behaviour	Anorexia
such as Anorexia nervosa, Bulimia, weight gain	Masked aggression
Decreased libido	Obsessive compulsion
Impulsive aggression	Shyness
Alcoholism, Sexual deviance	Lack of self confidence
Explosive rage	Low sex drive
Low blood pressure	Hypertension
Low body temperature	High body temperature
Bladder problems-Toxic metal	Kidney problems-Toxic metal
	Need for more water



Exercises to stimulate Serotonin
Waliking outside in daylight, Gardening

Exercises to inhibit Serotonin
Tai Chi (calm and relaxing)

HISTAMINE

Histamine is most often thought of as a bad guy, associated with irritation.
In fact it is associated with arousal.

HISTADINE

Vit B6 (or Vit B1)
Mg, Zn
decarboxylase
(inhibited by high levels of CO2)

CO_2

HISTAMINE

HISTAMINE

methyltransferase
SAM (Mg++, Zn++, P5P)
Methylcobalamin
Methyltetrahydrofolate

diamine oxidase
O2
(adenosylcobalamin)
Vit C
Fe++
P5P

aldehyde oxidase
O2
(adenosylcobalamin)
NAD, FAD
Mol, Fe++
K, Thiols

Methylhistamine

Imidazole acetic acid

monoamine oxidase
O2
(Fe++,
Adenosylcobalamin)
FMN / FAD
Cu

(systemic histamine)
Natural anti histamines -
Vit E, Zn, Mg,
Bioflavonoids

Methyl imidazole acetic acid

Low stomach acid (hypochlorrhydria) causes the morning nausea and sickness often associated with pregnancy

Histamine activates cAMP.

cAMP stimulates a Protein kinase which phosphorylates carbonic anhydrase.

Carbonic anhydrase forms HCl in the stomach and NaHCO3 in the pancreas.

Low stomach HCl leads to nausea.

Histamine stimulates
Hydrochloric acid
Pepsinogen
Secretin
Nitric Oxide (from iNOS)

So stimulating
Alertness
Sexuality
Motor activity

Histamine is a neurotransmitter at CNS pathways involved in
1. Arousal
2. Nausea and vomiting
3. Control of blood pressure
4. Control of water metabolism

Natural sources of Histamine

Prickly pear
Cabbage
Shepherds purse
Celendine
Melon
Sunflower
Stinging nettle
Milk thistle

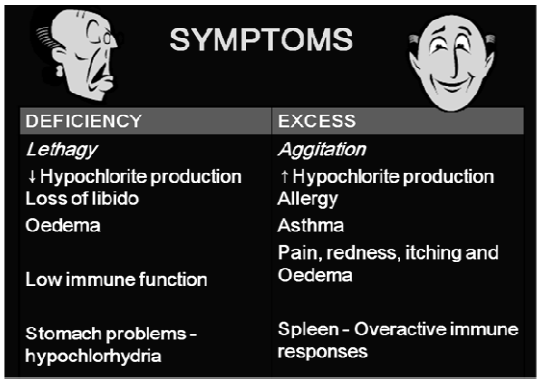
Histamine is contained in Bass, Beer, Chicken, Cocoa, Chocolate, Cod, Crab, Haddock, Ham, Lobster, Milk (cow and goat), Mutton, Oyster, Salmon, Scallop, Shrimp, Trout, Tuna, Turkey, Yeast.

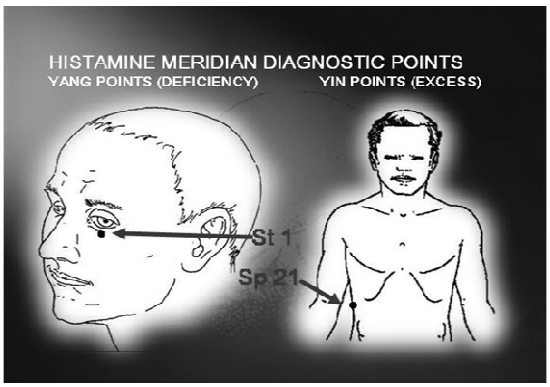
Histamine receptors in the CNS

Ligand binding studies have shown H1, H2, H3 receptors in the CNS of uneven distribution.

Histamine receptors outside the CNS

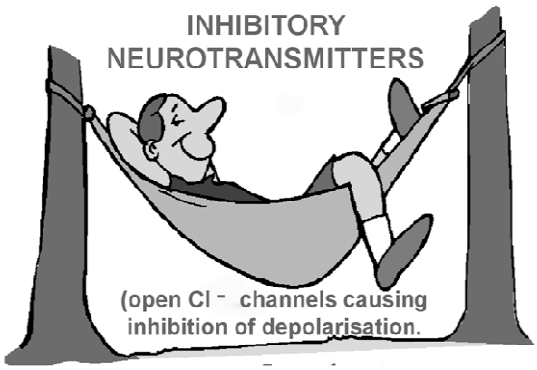
- H1 receptors stimulation induces
- Brochoconstriction.
- Constriction of intestinal smooth muscle.
- Constriction of large arteries and veins.
- Relaxation of arterioles, small veins and capillaries especially in the brain.
- Increased capillary permeability
- H2 receptor stimulation induces gastric acid secretion.



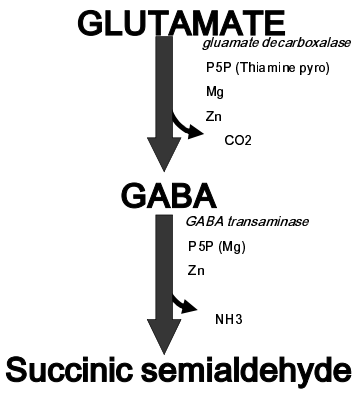


Exercises to stimulate Histamine Dancing

Exercises to inhibit Histamine Stretching, Mobility exercises, Flexibility, Oxygenation.


INHIBITORY
NEUROTRANSMITTERS
(open Cl⁻ channels causing
inhibition of depolarisation.

GABA


GLUTAMATE
gluamate decarboxalase
P5P (Thiamine pyro)
Mg
Zn
CO2
GABA
GABA transaminase
P5P (Mg)
Zn
NH3
Succinic semialdehyde

GABA is an inhibitory neurotransmitter in parts of

1.The brain especially the cortex, hypothalamus, basal ganglia, cerebellum and hippocampus

2. Substantia gelatinosa of the dorsal horn of the spinal cord

3. Retina- It is not present in peripheral nerves

GABA receptors

GABA A receptor stimulation leads to an increase in chloride ion permeability.

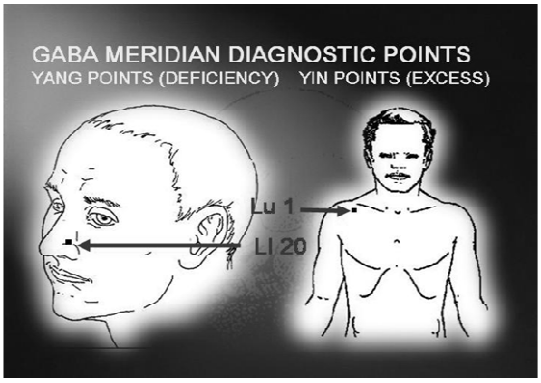
They are present mainly in the cerebral cortex and the hippocampus.

GABA B receptor stimulation leads to changes in potassium conduction. They are present mainly in the cerebellum and spinal cord.

GABA C receptor for *benzodiazepine and ?Barbiturate*

Symptoms

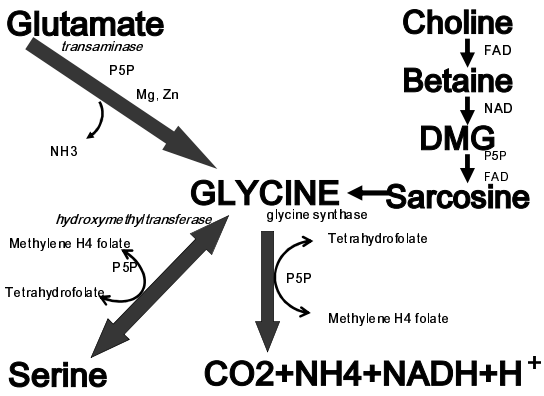
DEFICIENCY	EXCESS
Apathy and Despair	*Anger and Hate*
↓TH1 production	↑TH1 production
Symptoms of Glutamate excess	Muscle relaxation.
Convulsions such as epilepsy.	Stuttering (Phosserine)
Tetany and spastic disorders such as torticollis.	Lung problems
Decreased cerebellar reflexes.	
Extrapyramidal disorders such as dyskinesis.	
Lateral inhibition of the retina.	
Thalamic sensory disorders.	
Large intestine problems such as parasites / fungi	



Exercises to stimulate GABA
Golf

Exercises to inhibit GABA
Skipping, opens up, improves oxygenation, coordination.

GLYCINE



Glycine is an inhibitory neurotransmitter at some pathways in the

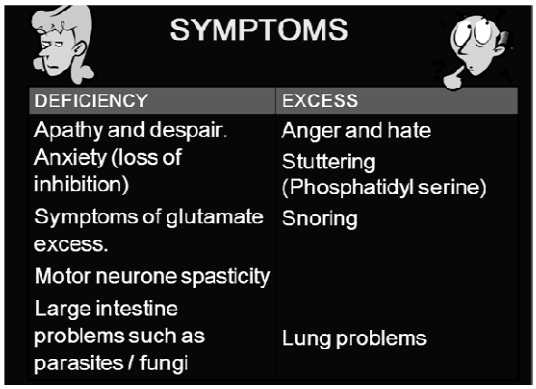
1. spinal cord

2. retinal

3. brainstem and forebrain

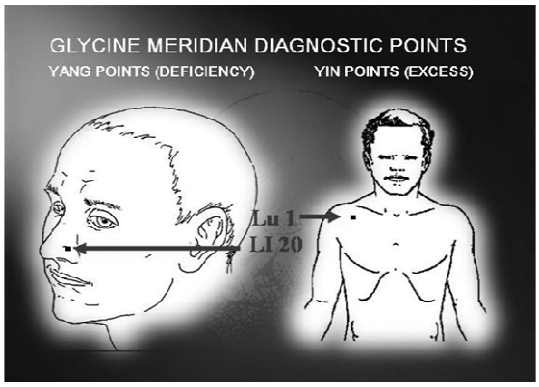
Glycine is a free form amino acid found in protein foods and can be synthesised from glutamate, alanine, serine, choline via DMG and from carbohydrates.

Glycine receptors are blocked by strychnine.



SYMPTOMS

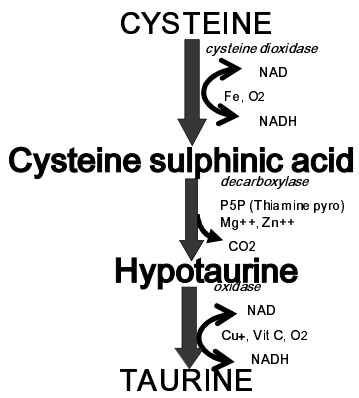
DEFICIENCY	EXCESS
Apathy and despair. Anxiety (loss of inhibition)	Anger and hate Stuttering (Phosphatidyl serine)
Symptoms of glutamate excess.	Snoring
Motor neurone spasticity	
Large intestine problems such as parasites / fungi	Lung problems

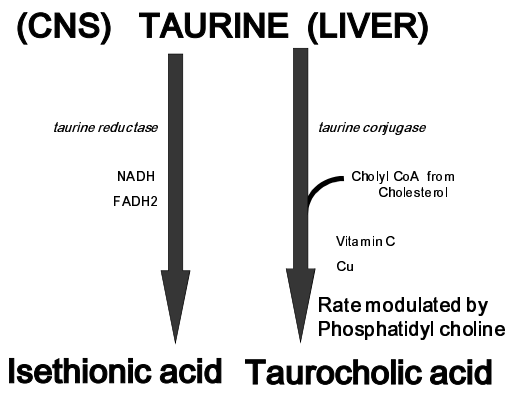


Exercises to stimulate Glycine
Golf

Exercises to inhibit Glycine
Skipping, opens up, improves oxygenation, coordination.

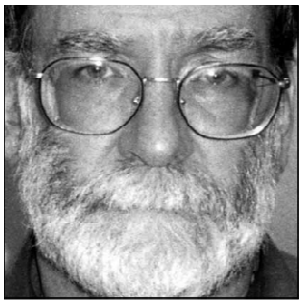
TAURINE


CYSTEINE
cysteine dioxidase
NAD
Fe, O2
NADH
Cysteine sulphinic acid
decarboxylase
P5P (Thiamine pyro)
Mg++, Zn++
CO2
Hypotaurine
oxidase
NAD
Cu++, Vit C, O2
NADH
TAURINE

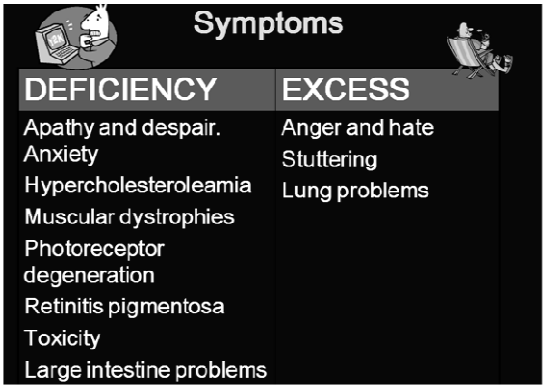

(CNS) TAURINE (LIVER)
taurine reductase
NADH
FADH2
taurine conjugase
Cholyl CoA from Cholesterol
Vitamin C
Cu
Rate modulated by Phosphatidyl choline
Isethionic acid
Taurocholic acid

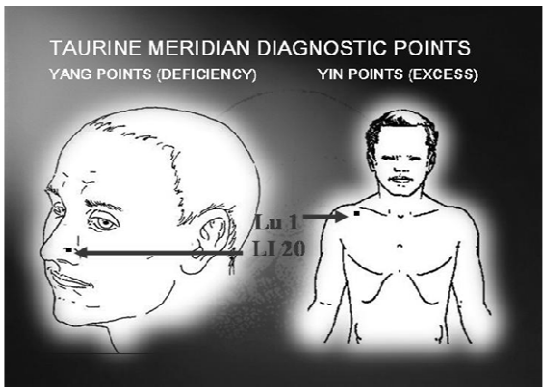
Taurine is the most abundant amino acid in the body and acts as an inhibitory or neuro-modulatory neurotransmitter at some pathways in the
1. Brainstem
2. Retina at the inner plexiform layer
3. Striated muscles

Taurine receptors are blocked by strychnine.



Died whilst eating an apple





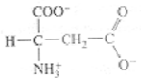
Exercises to stimulate Taurine
Golf

Exercises to inhibit Taurine
Skipping, opens up, improves oxygenation, coordination.

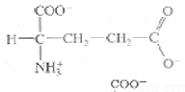
EXCITATORY NEUROTRANSMITTERS (open Na_+, K_+ and / or Ca_{++} channels causing multiple depolarisation or stimulation

EXCITATORY NEUROTRANSMITTERS

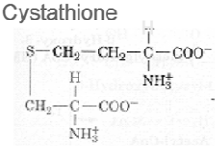
Aspartic acid



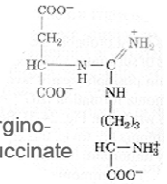
Glutamic acid



Cystathione



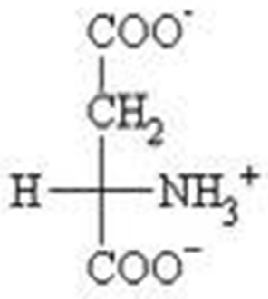
Argino-succinate

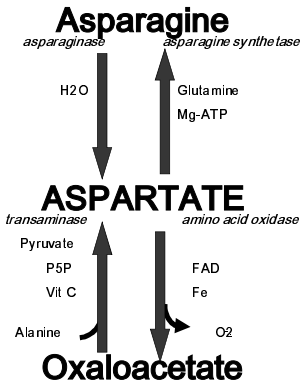


Excitatory Neurotransmitters

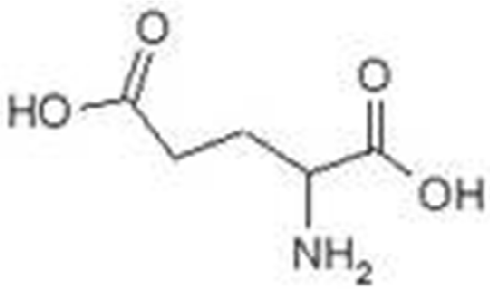
Glutamic acid	Salt taste
Aspartic acid	Sweet taste
Cystathione *(blocked by AMP)*	Bitter taste
Arginosuccinate	Sour taste

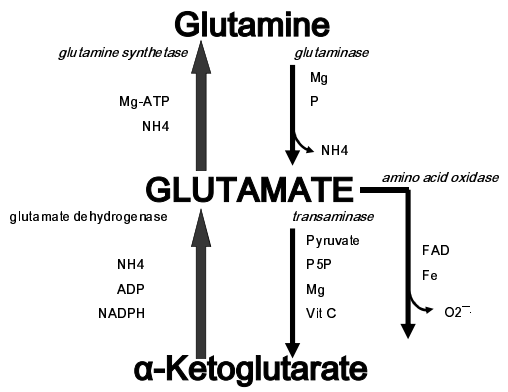
ASPARTATE (ASPARTIC ACID)

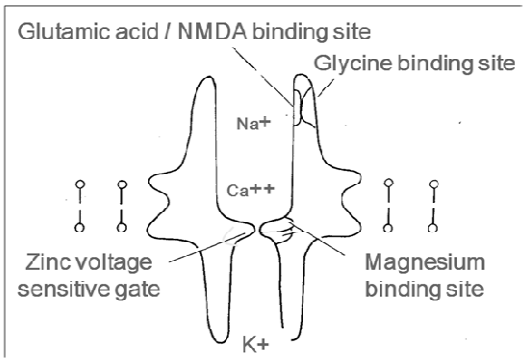




GLUTAMATE (Glutamic Acid)







RECEPTORS

Aspartate and Glutamate receptors occur throughout the CNS.

Glutamate receptors
In the spinal cord glutamate receptors are most concentrated at the primary afferent fibres in the dorsal roots and may serve to relay sensory information and to regulate motor activity and spinal reflexes.

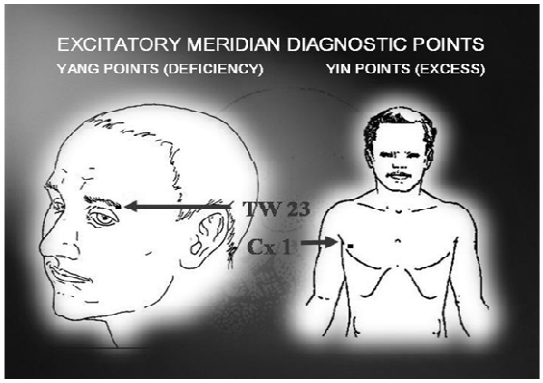
In the brain glutamate receptors are found in high concentration in the cortex, hippocampus, neostratum and cerebellum with lower levels in the hypothalamus. They are also present in the retina of the eye.

ASPARTATE RECEPTORS

Aspartate receptors are located in the dorsal and ventral grey matter where they cause excitation of spinal excitatory interneurones where it may regulate motor and spinal reflexes and in the retina of the eye.

SYMPTOMS

DEFICIENCY	EXCESS
Aimless	Manic
↓NO production	↑NO production
	High libido due to high NO
Learning disorders	Hyperactivity
Weight gain	ADDH / Dyslexia / Amnesia
	Muscle spasm, Restless legs
Loss of libido due to low NO	Nystagmus and Tinnitus
	Irritable Bowel Syndrome
Memory loss	Chronic Fatigue Syndrome
	Fibromyalgia
Hypothyroidism	Convulsions / Epilepsy
	Hyperthyroidism



Exercises to stimulate Excitatory Skating – ice skating, roller blading, scooting.

Exercises to inhibit Excitatory
Interval training (fast / slow to break up hyper states.)

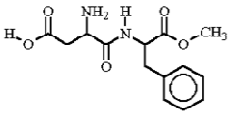
ASPARTAME and DEPRESSION

Aspartame decreases the availability of Tryptophan to the brain.

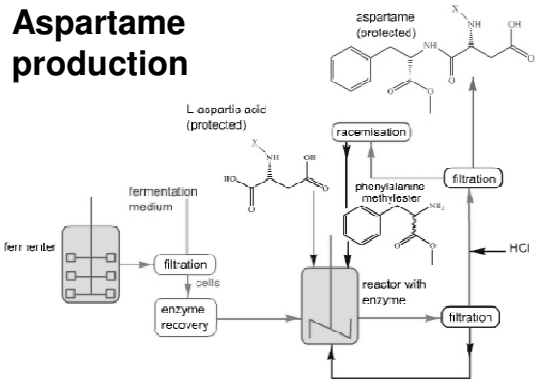
Tryptophan is the essential amino acid building block to serotonin, which when present in the brain in low amounts leads to depression and compulsive disorders.

ASPARTAME DEGREDATION

ASPARTAME
is
ASPARTIC ACID
+
PHENYLALANINE



Aspartame production



INGESTED AND WARMED TO BODY TEMPERATURE 37° C IT IS ACTIVATED UPON BY

CHYMOTRYPSIN

WITH THE CREATION OF METHANOL IN THE ILEUM.

METHANOL IS OXIDISED TO FORMALDEHYDE AND FORMIC ACID

The Physiology of Learning

The learning and remembering of such an event involved its
1. INTENSITY, FREQUENCY and DURATION

2. Coupled with the optimal synthesis of the appropriate neurotransmitter chemicals.

The Most Memorable Event in Living British History

LEARNING

Can be divided into three phases

1. **Input**
2. **Storage**
3. **Output**

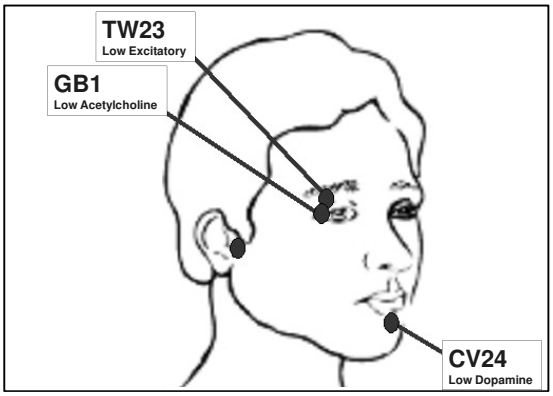
1. Input information is through our excitatory senses mediated by Glutamate.

2. We store our memories in the cortex and the hippocampus mediated by Dopamine.

3. Output is by recalling our memories via the hippocampus mediated by Acetylcholine.

Learning difficulties must therefore be due to either
1. Insufficient sensory stimulation or insufficient glutamate synthesis.
2. Insufficient dendritic connection or insufficient dopamine synthesis.
3. Insufficient cortical / hippocampal connections or insufficient acetylcholine synthesis.

1. **A deficiency in the excitatory neurotransmitter *glutamate* can be challenged for at TW23.**
2. **A deficiency of the neurotransmitter *dopamine* can be challenged for at CV24.**
3. **A deficiency of the neurotransmitter *acetylcholine* can be challenged for at GB1.**



Learning is a process that can be stopped, slowed or speeded up.

All that is necessary to speed up learning is stimulation to the 5 senses of vision, hearing, smell, taste and touch with increasing frequency, intensity and duration.

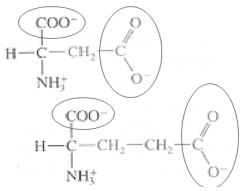
Glen Doman – Institutes of Human Potential

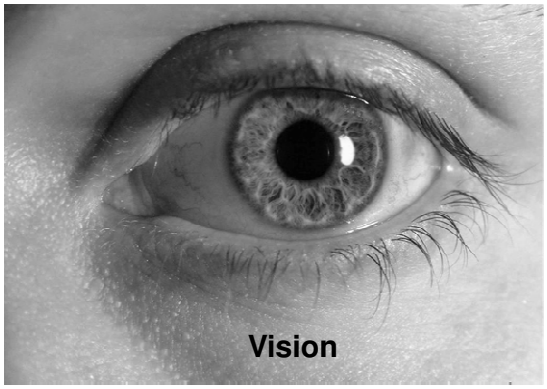
The sensory neurones of the 5 senses are all mediated by excitatory neurotransmitters. That is that they depolarise by permitting Ca++ ions to influx in addition to Na+.

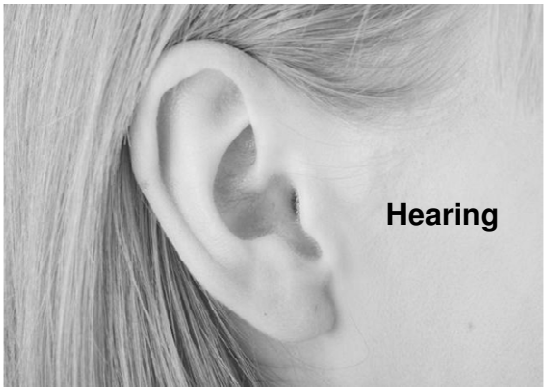
Excitatory Neurotransmitters

Aspartic acid
(aspartate)

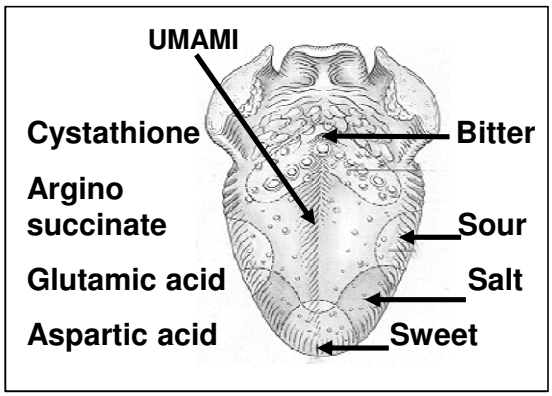
Glutamic acid
(glutamate)



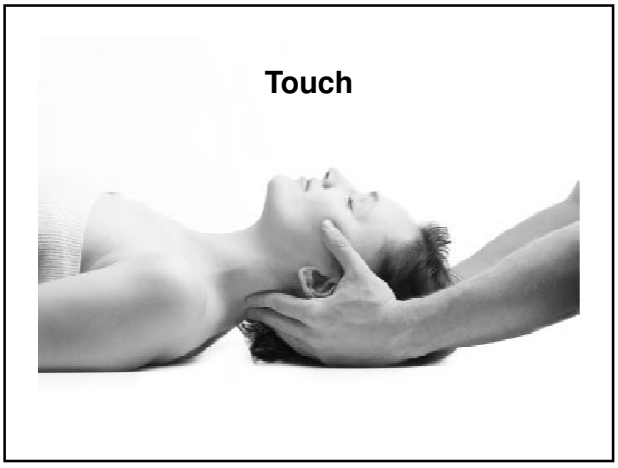

Vision


Hearing


Taste
seleneriverpress


UMAMI
Cystathione
Argino succinate
Glutamic acid
Aspartic acid
Bitter
Sour
Salt
Sweet

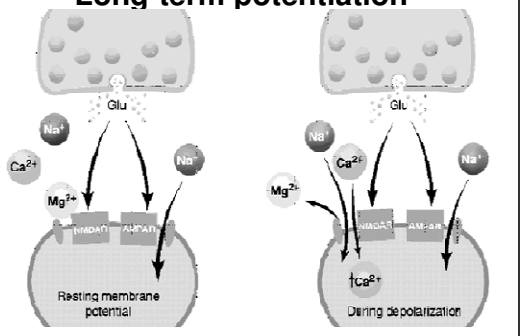

Smell

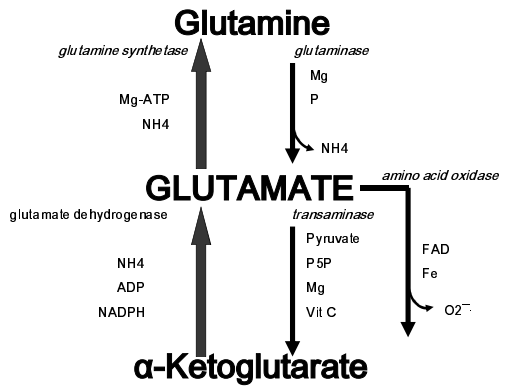

Touch

The NMDA glutamate sensitive receptor activation and the induction of long-term potentiation are thought to be necessary substrates for learning.

Glutamate receptors are also thought to play a critical role in the hippocampal long-term potentiation and the memory processes.

Long-term potentiation





Nutrients to consider for optimal GLUTAMATE synthesis

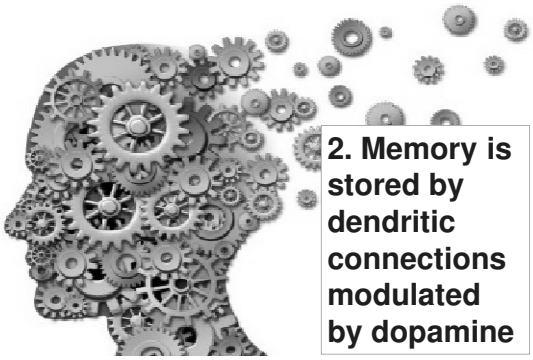
Glutamine
Mg++ and Phosphorus

NADPH (Vit B3)

Aspartic acid / Glycine / Mg++ (N.Methyl D. Aspartate 1000x times more active than glutamate)

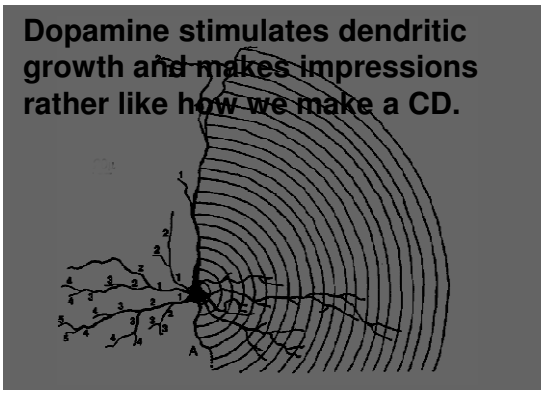
Challenge for 5 Senses Input

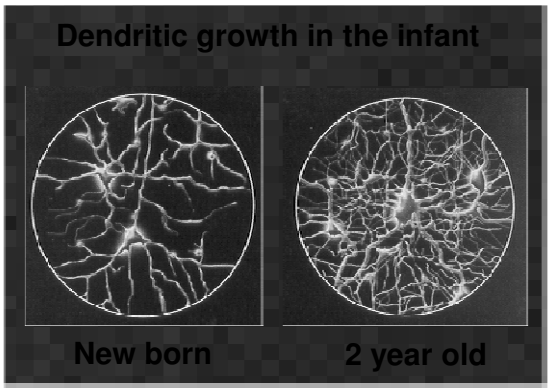
1. **Challenge each of the 5 senses right to left and then left to right.**
2. **Maintain positive TL and treat with Miron light in umbilicus for 1 minute.**
3. **Re-challenge remaining 4 senses etc.**

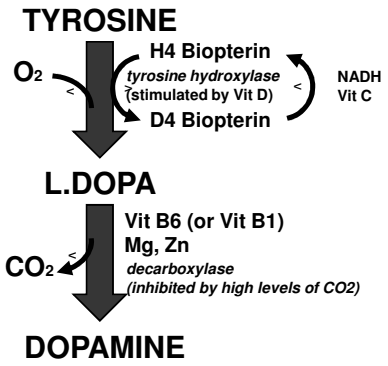


2. Memory is stored by dendritic connections modulated by dopamine

Dopamine stimulates dendritic growth and makes impressions rather like how we make a CD.





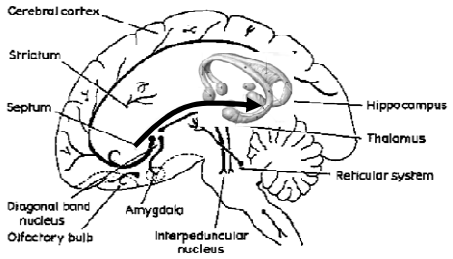


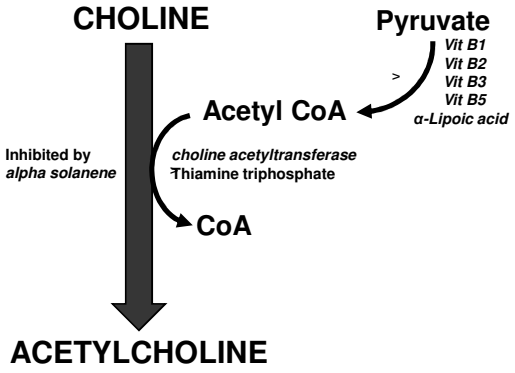
Nutrients to consider for optimal DOPAMINE synthesis

Tyrosine
O2, H4Biopterin (P5P, Folate, NADPH (Vit B3), Fe++), Vit D

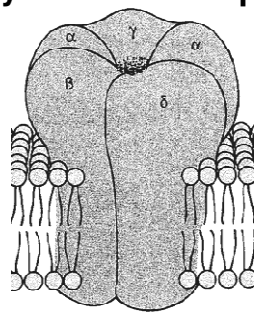
P5P (Vit B6) or Thiamine pyrophosphate (Vit B1), Mg++, Zn++

3. Memory recall involves adequate communication between the septum and the hippocampus



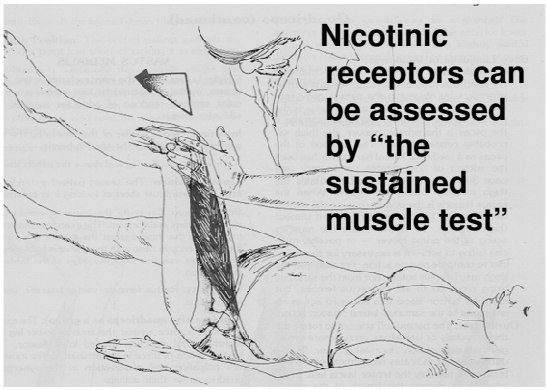


Acetylcholine Receptors



1. Muscarine receptors occur in the parasympathetic nervous system

2. Nicotinic receptors occur at
   i) CNS especially in the hippocampus.
   ii) The neuromuscular junctions



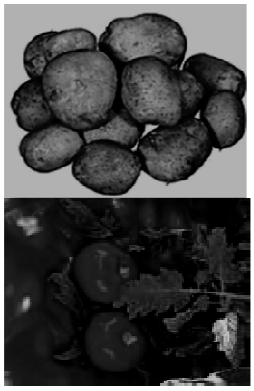
Natural sources of Acetylcholine

Fennel
Coriander
Black pepper
Hawthorn
Fenugreek
Cardamom
Stinging nettle

Anticholinergics

Solanacea family

Tomatoes
Potato
Bell peppers
Aubergine
Chili
Tobacco



Nutrients to consider for optimal ACETYLCHOLINE synthesis

Choline
Acetyl CoA (Vit B5, Mg, Vit B6)
Thiamine triphosphate (Vit B1)
Mn++

No Potatoes, Tomatoes, Peppers, Aubergine, Chili

Non-threatening Learning / Remembering Challenges
Long term memory

Remember the first day at college.

Remember your 16th birthday.

Remember the first girl / boy you kissed.

What coloured eyes did he/she have

Whilst maintaining the challenge if positive

1. **Cross therapy localise to TW23**
2. **Cross therapy localise to CV24**
3. **Cross therapy localise to GB1**

Challenge for negating nutrients.

Dr. Williams, in collaboration with Dr. Warren H. Meck, associate professor in the Department of Experimental Psychology, opted to build an improved cholinergic system by adding choline to the diet when the cholinergic cells are being formed and making the synaptic connections in the brain.
Cholinergic cells are special because they need choline to make acetylcholine but cholinergic cells, like all cells, also require choline to maintain their cell membranes. "Thus, cholinergic cells doubly require choline," said Dr. Williams. So, Dr. Williams supplemented pregnant rats with choline in their drinking water.
This task taps into working and reference memories.
"Amazingly enough, the rats which had pre-natal or post-natal or both pre- and post-natal supplementation of choline made fewer mistakes on the first day of training and the choline animals continually perform better than control rats even as adults," said Dr. Williams. In fact, rats which had both pre- and post-natal supplementation of choline demonstrated the greatest amount of permanent improvement in their memory capacity and precision.
"Since those experiments were completed, the sensitive periods for choline administration have been determined to be prior to birth on days 12 to 17 in development and also days 15 and 30 after birth," said Dr. Williams.
The former period occurs when all the cholinergic neurons in the basal forebrain form. The latter period also seems to be highly significant because it is when these developing rats are being weaned and synaptic connections are being made in the hippocampus and cortex that are critical in visuospatial learning and memory.

In Human Terms
First 4 months of pregnancy
First 3 months of neonatal life

Prescribe 1500mg Choline bitartrate (delivering 600mg Choline)