Excitotoxins

The Taste that Kills

Russell L. Blaylock, MD

Russell L. Blaylock, MD, has written *Excitotoxins: The Taste that Kills* in which he explains that certain amino acids when overly abundant in the brain can cause neurons to die.

- Many biochemicals can act as neurotransmitters in the brain—some excite our neurons; others calm them.

Three acidic amino acids

- That excite our neurons so called "excitotoxins."
- **Glutamate, Aspartate, and Cysteine**

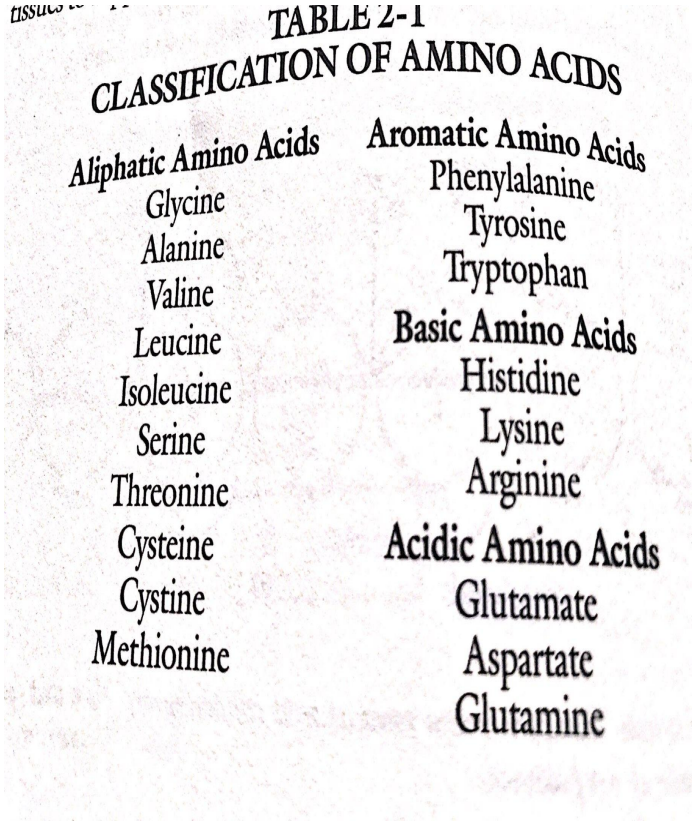


TABLE 2-1
CLASSIFICATION OF AMINO ACIDS

Aliphatic Amino Acids	Aromatic Amino Acids
Glycine	Phenylalanine
Alanine	Tyrosine
Valine	Tryptophan
Leucine	**Basic Amino Acids**
Isoleucine	Histidine
Serine	Lysine
Threonine	Arginine
Cysteine	**Acidic Amino Acids**
Cystine	Glutamate
Methionine	Aspartate
	Glutamine

Why Toxic to our body?

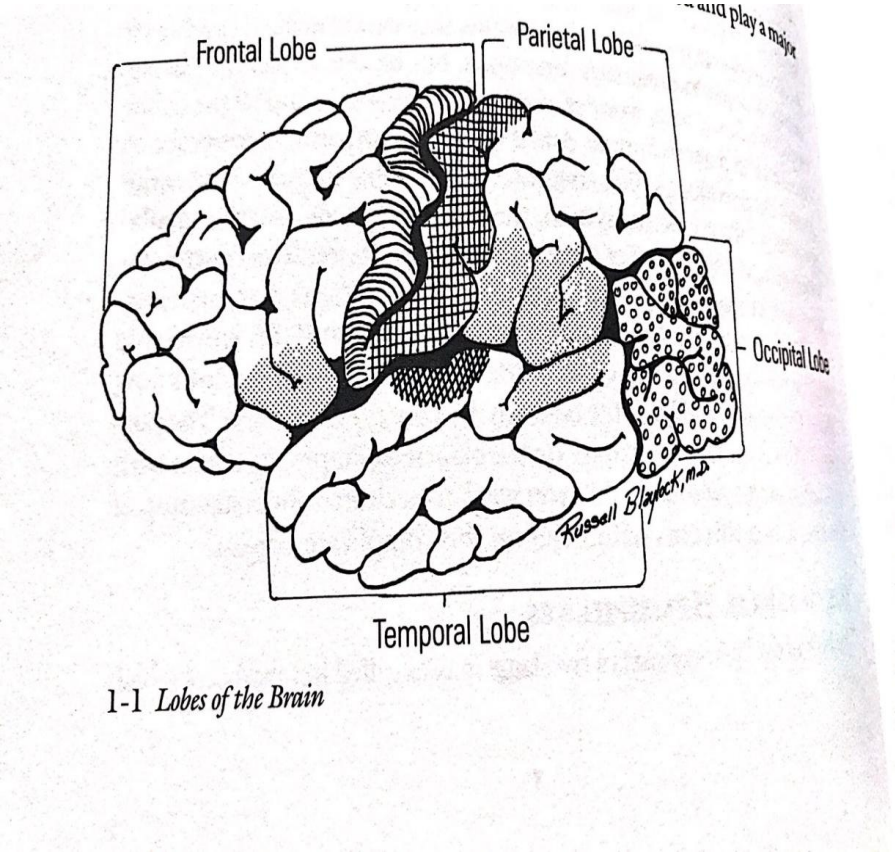
Glutamate, as a neurotransmitter, exists in the extracellular fluid very small concentrations --- no more than 8 to 12uM.

- When the concentration of this transmitter rises above this level, the neurons begin to fire abnormally
- The cells undergo this specialized process of delayed cell death, excitotoxicity. That is, they are excited to death.
- For example, the food labelled as 'hydrolyzed vegetable protein,' 'vegetable protein,' 'natural flavorings,' and 'spices.' Each of these may contain from 12 per cent to 40 per cent MSG."

Brain

Brain is a living computer, made of billions of cells and pathways and trillions of neural connections.

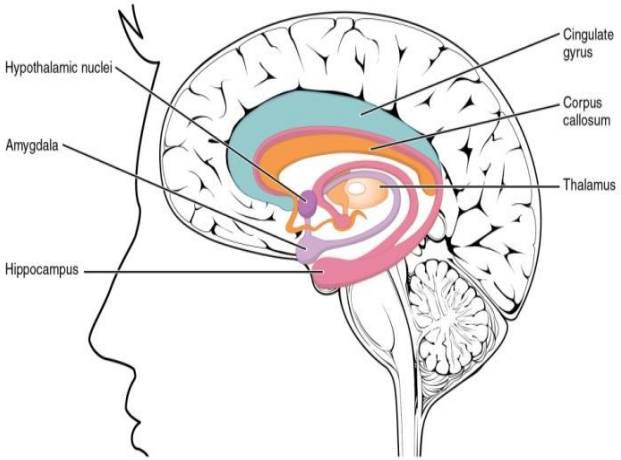
- Frontal lobes-decision making, planning thinking and premotor areas
- Parietal Lobes-Association Cortex
- Occipital Lobes-Visual cortex
- Temporal Lobes- Memory lobes or interpretive cortex

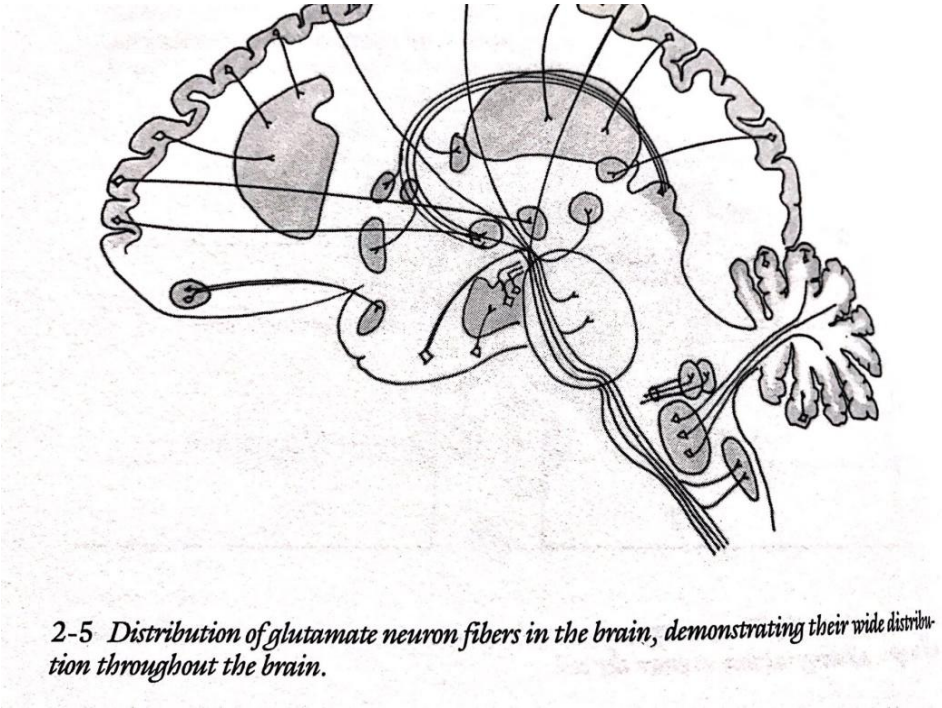


1-1 *Lobes of the Brain*

The hippocampus

- short-term memory to long-term memory and
- spatial-memory
- In diseases such as Alzheimer's disease, the hippocampus is one of the first regions affected.





2-5 *Distribution of glutamate neuron fibers in the brain, demonstrating their wide distribution throughout the brain.*

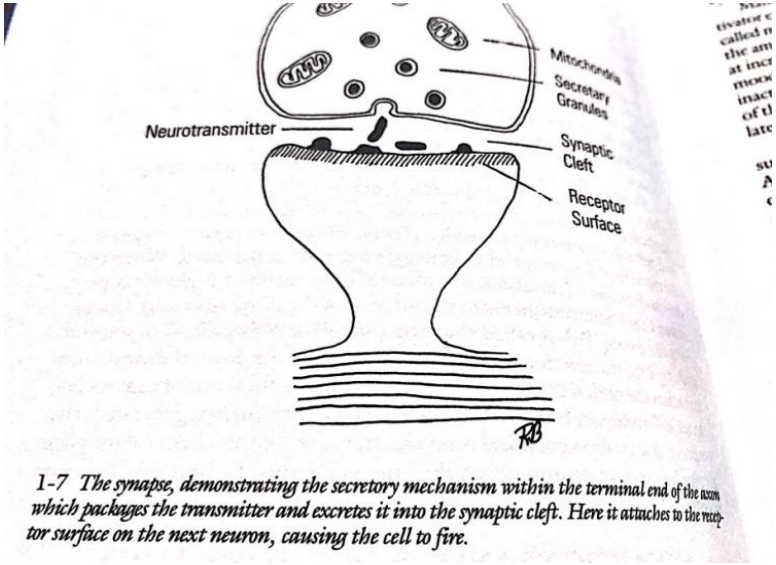
Wide Distribution of the glutamate neuron fibers throughout the brain

How Excitotoxins Were Discovered?

(Experiments with newborn of MSG exposed mice)

- In 1957, two ophthalmology residents, Lucas and Newhouse demonstrated widespread destruction of the inner nerve layer of the retina ,(published in the *Archives of Ophthalmology)*
- 1969, Dr. John Olney, a neuroscientist and neuropathologist repeated Lucas and Newhouse's experiment.- newborn of MSG exposed mice were grossly obese and short in stature, hypo plastic organs and damage to widespread areas in the brain.

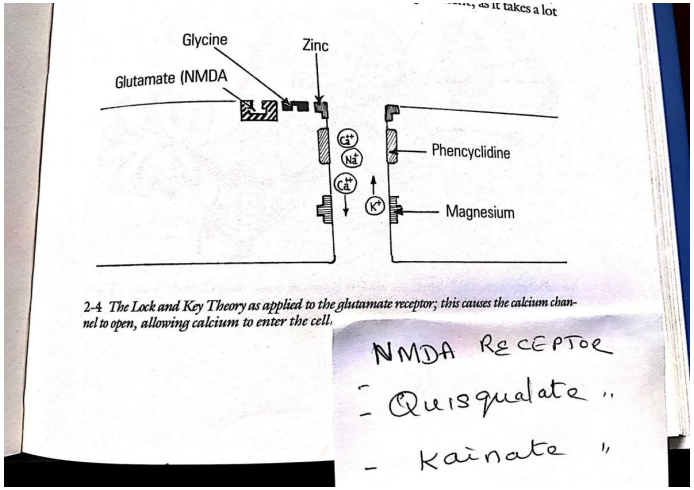
Mechanism of this destruction



1-7 The synapse, demonstrating the secretory mechanism within the terminal end of the axon which packages the transmitter and excretes it into the synaptic cleft. Here it attaches to the receptor surface on the next neuron, causing the cell to fire.

The synapse, demonstrating the secretary mechanism within the terminal end of the axon which holds the neurotransmitter packages and excretes into the synaptic clefts. Here it attaches to the receptor surface on the next neuron causing the cell to fire.

- **With calcium triggered stimulation, the neuron becomes very excited, firing its impulses repetitively until the point of cell death, hence the name excitotoxin.**



2-4 The Lock and Key Theory as applied to the glutamate receptor; this causes the calcium channel to open, allowing calcium to enter the cell.

- **The Lock and Key theory as applied to the glutamate receptor, this cause the calcium channel to open allowing Ca enter into the cell.**

Failure of Protective Mechanisms

Energy, Magnesium, and Antioxidants

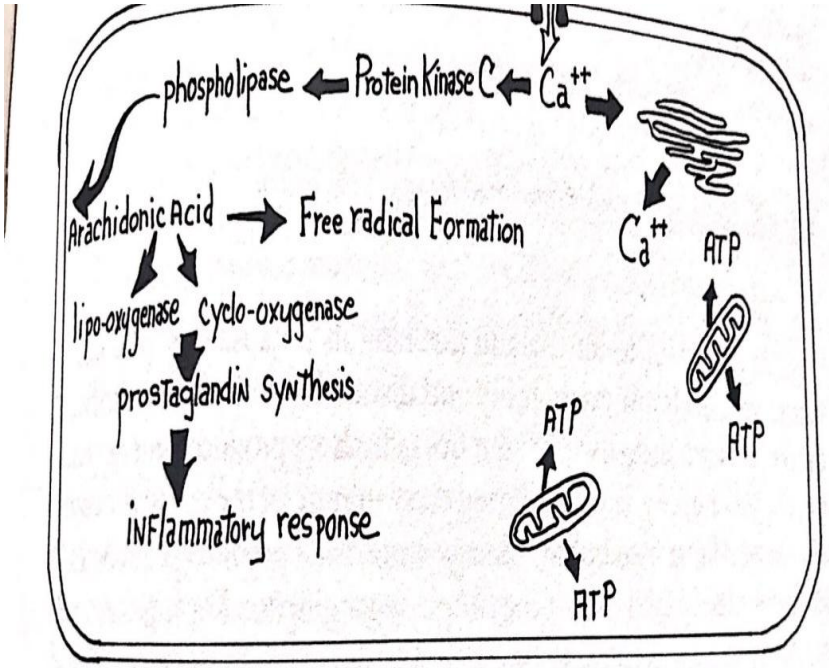
- Brain has many protective mechanisms against these toxins.
- Reducing excess glutamate (or glutamic acid) at the special glutamate receptors
- Storing the extra glutamate in nearby glia cells
- Magnesium to block the uptake of glutamate

Other protective processes

- The powerful antioxidant glutathione (formed from these amino acids when magnesium, potassium, and sufficient energy are all present)
- **Vitamin C or ascorbic acid:**
  Adequate ascorbate levels for CNS function and neural protection against excitotoxicity.

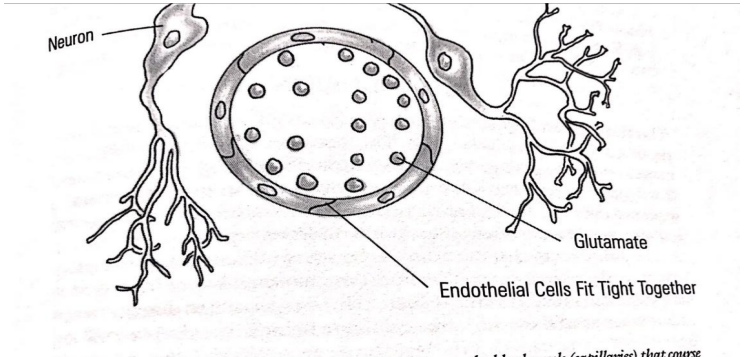
Free Radicals and Calcium

- First, the excitatory amino acids attached to specialized family of receptors (NMDA, kainate, AMPA and metabotrophic) cause calcium entry into the cells controlled by the "calcium pump," which requires much energy.
- Lack of protective mechanisms with excitotoxins, too much calcium enters the neuron through special channels in the cell membrane.
- This calcium will trigger a cascade of reactions, including free radical generation, eicosanoid production, and lipid peroxidation, which will destroy the cell



3-5 *How calcium activates destructive reactions within the neuron by triggering prostaglandin synthesis and free radical formation.*

Blood-Brain Barrier



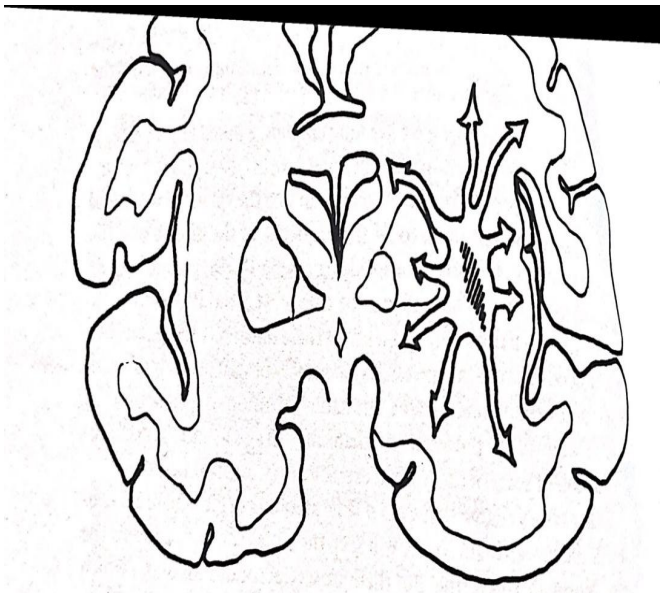
1-8 *The Blood–Brain Barrier: The barrier exists between the blood vessels (capillaries) that course throughout the brain tissue and the extracellular space within the brain. It prevents certain molecules in the blood from entering the tissue space of the brain itself. It is thought that the major portion of the "barrier" lies in the tight junction between the cells (endothelial cells) that line the capillary walls. Blood vessels in other parts of the body have relatively large spaces between the cells that allow passage of even large molecules.*

Blood vessel walls in the brain that allow certain chemicals to enter the brain while excluding others—the so-called blood-brain barrier.

Defects in Blood brain barrier

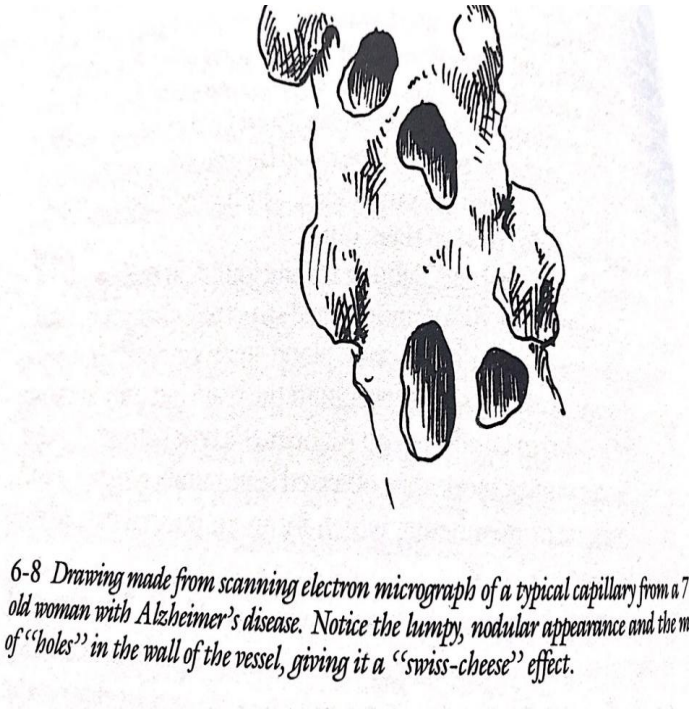
Temporarily broken down by

- Heat stroke,
- Brain trauma
- Encephalitis
- Strokes,
- Hypertension,
- Severe hypoglycemia and also in Aging



5-2 *This cross section of the brain demonstrates how a small silent stroke can act as a point of seepage for glutamate and other excitotoxins to by-pass the blood-brain barrier. In this way normally excluded excitotoxins from food can endanger the brain.*

A small silent stroke can act as a point of seepage for excitotoxins to bypass the barrier

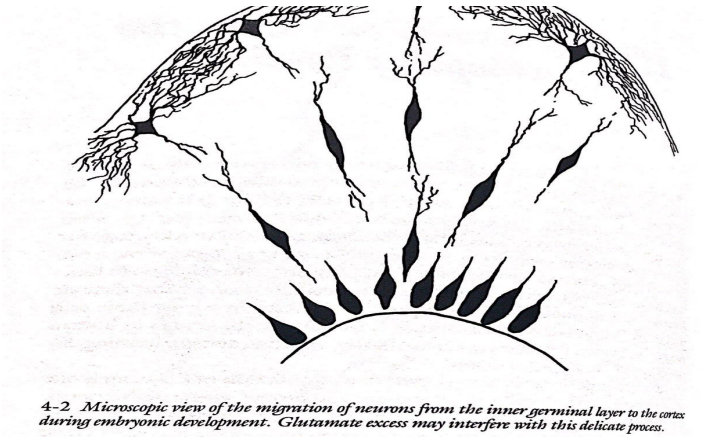


6-8 *Drawing made from scanning electron micrograph of a typical capillary from a 7 old woman with Alzheimer's disease. Notice the lumpy, nodular appearance and the m of "holes" in the wall of the vessel, giving it a "swiss-cheese" effect.*

- In Alzheimer's disease the vessels have the appearance of "Swiss cheese.
- In children is exposure to excess lead from the environment, such as old lead paint can easily disrupt the blood-brain barrier

Fetal effect

Dr. Blaylock points out that this barrier is not well developed in the very young and it may even be still developing in the adolescent.



4-2 Microscopic view of the migration of neurons from the inner germinal layer to the cortex during embryonic development. Glutamate excess may interfere with this delicate process.

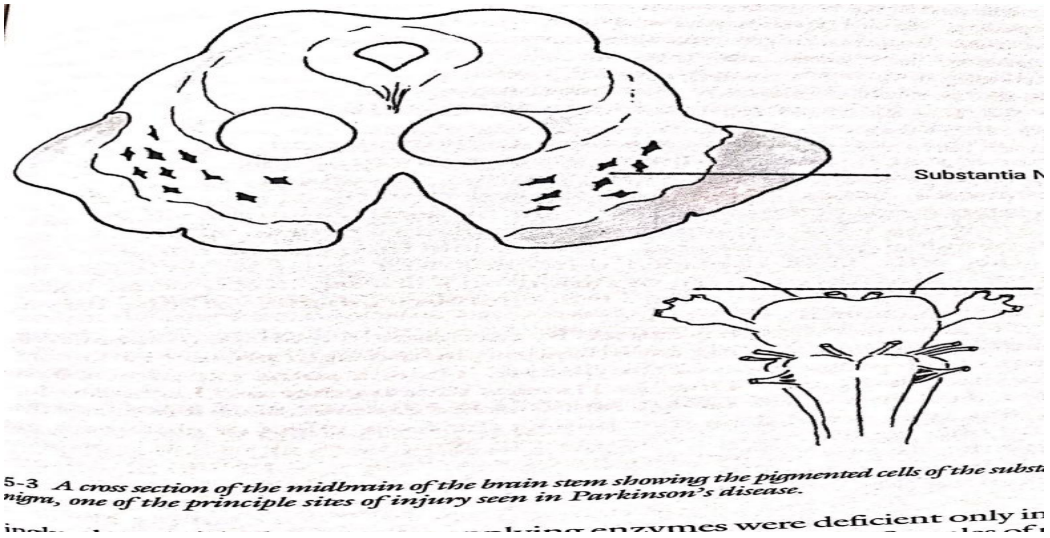
ants search for food, they first send out a scout. After the scout finds the food he makes his way back to the nest. On his way back he will leave a chemical trail for the other ants to follow. It appears that within the brain there are special cells that also secrete a molecular "trail" for the axon fiber of the neuron to follow. The neuron's dendrite has specialized "growth cones" at the tips of its spines that act as a sensor used in following this trail. These growth cones are critical to the normal development and ultimate wiring of the brain.

Often the neuron's first attempt at wiring its pathways is rather crude and inaccurate. To correct this the growth cone will continuously fine tune the process. This fine tuning depends on just the proper amount of stimulation of the neurons. It is known that timing of these events is critical, that

Migration of neurons from the germinal layer to the cortex during embryonic development. Glutamate excess may interfere with this delicate process.

Neurodegenerative Diseases

Dr. Blaylock explains in detail and with excellent illustrations exactly which areas of the brain are involved in the neurodegenerative diseases: amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), Parkinson's, and Alzheimer's.

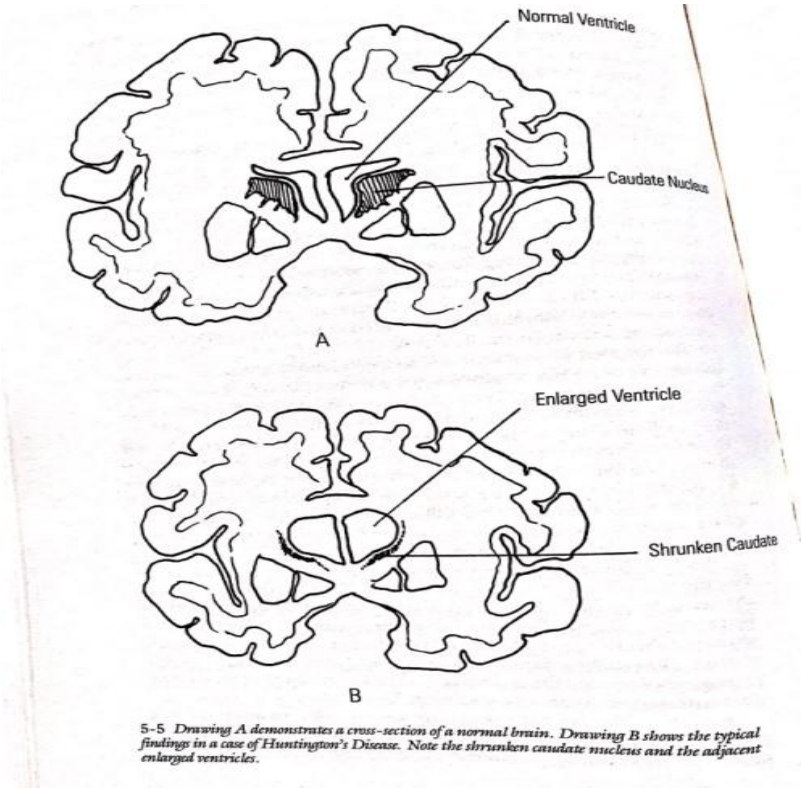


5-3 *A cross section of the midbrain of the brain stem showing the pigmented cells of the substa nigra, one of the principle sites of injury seen in Parkinson's disease.*

enzymes were deficient only in

A cross section of the mid brain of the brain stem showing the pigmented cells of the Substantia nigra one of the principle sites of injury seen in Parkinson's. By using selective glutamate blocking drugs or nutrients, one may be able to alter some of the more devastating effects of Parkinson's disease.

Huntington Chorea

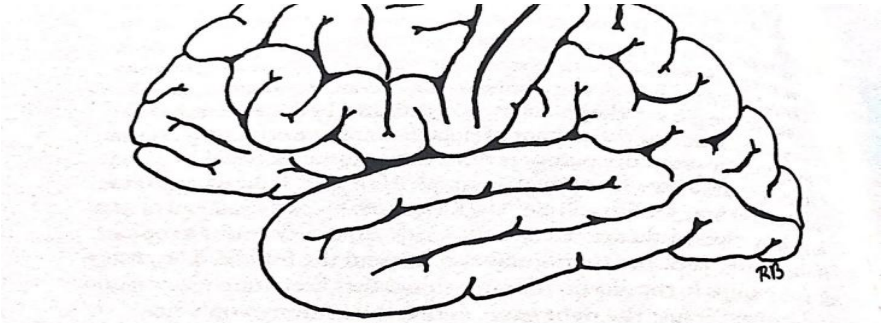


5-5 *Drawing A demonstrates a cross-section of a normal brain. Drawing B shows the typical findings in a case of Huntington's Disease. Note the shrunken caudate nucleus and the adjacent enlarged ventricles.*

Drawing A – Normal brain

Drawing B – Shrunken caudate nuclei and adjacent enlarged ventricles

Other factors



6-5 *The brain requires enormous amounts of energy to survive.*

The brain requires enormous amount of energy to survive.

- When the neurons have abundant energy supplies they are resistant to glutamate toxicity; when the energy deficiencies exits the neurons become vulnerable even as low doses of glucose.

Avoiding Excitotoxins

- In summary, Dr. Blaylock recommends that we avoid the dietary excitotoxins so prevalent in prepared foods—the MSG and the aspartame –NutraSweet.
- Over 100 million Americans now consume aspartame products and a greater number consume products containing one or more excitotoxins.
- Remember also that the powerful excitotoxins, aspartate and L-cysteine, are frequently added to foods and according to FDA rules require no labeling at all.

Additives that always contain MSG:

- Monosodium Glutamate
- Hydrolyzed Vegetable Protein
- Hydrolyzed Protein
- Hydrolyzed Plant Protein
- Plant Protein Extract

We need to concentrate on whole, and unprocessed food.