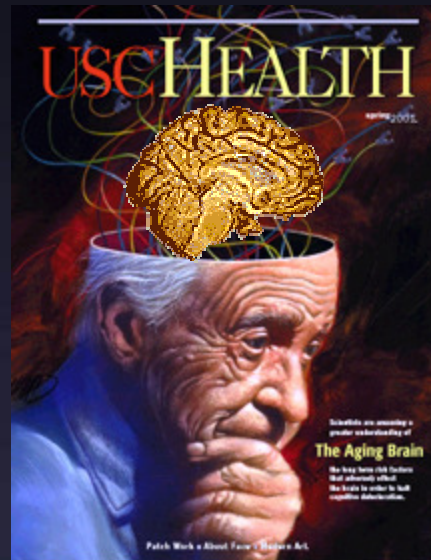
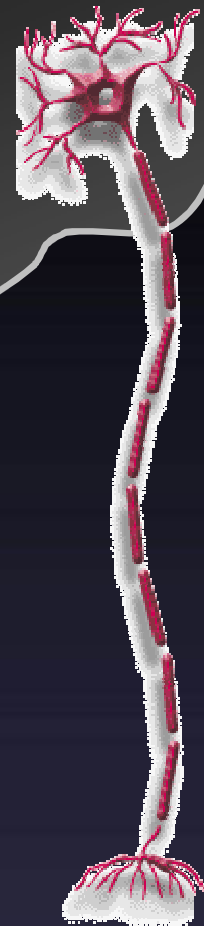


AGEING AND CHANGES IN THE BRAIN



Objectives

1. *Definition of Aging*
2. *Theories and terms Used*
3. *Body Changes in Aging*
4. *Brain Changes in Aging*
5. *Memory Changes in Aging*
6. *Carotid Hypersensitivity*

AGING

Aging is the progressive, universal decline first in **functional reserve** and then in **function** that occurs in organisms over time

*Aging is not a disease; however, the **risk** of developing disease is increased, often dramatically, as a function of age.*

Aging is characterized by

- Changes in appearance (gradual reduction in height and weight loss due to loss of muscle & bone mass)
- A lower metabolic rate
- Longer reaction times
- Declines in certain memory functions
- Declines in sexual activity and in women menopause
- A functional decline in audition, olfaction, and vision
- Declines in kidney, pulmonary, and immune functions, declines in exercise performance, and multiple endocrine changes

(Craik and Salthouse, 1992; Hayflick, 1994, pp. 137-186; Spence, 1995)

THE TERM AGEING

- **UNIVERSAL AGEING**: age changes that all people share)
- **PROBABILISTIC AGEING**: age changes that may happen to some (eg type two diabetes).
- **CHRONOLOGICAL AGEING**: referring to how old a person is
- **SOCIAL AGEING**: society's expectations of how people should act as they grow older
- **BIOLOGICAL AGEING**: an organism's physical state as it ages

Some Theories of Aging

Hypothesis	How It May Work
Genetic	Aging is a genetic program activated in post-reproductive life when an individual's evolutionary mission is accomplished
Oxidative stress	Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses
Mitochondrial dysfunction	A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change

Some Theories of Aging

Hypothesis	How It May Work
Hormonal changes	The decline and loss of circadian rhythm in secretion of some hormones produces a functional hormone deficiency state
Telomere shortening	Aging is related to a decline in the ability of cells to replicate
Defective host defenses	The failure of the immune system to respond to infectious agents and the overactivity of natural immunity create vulnerability to Inf..
Accumulation of senescent cells	Renewing tissues become dysfunctional through loss of ability to renew

OXYGEN - free radicals (FR) and reactive oxygen species (ROS)

Cell metabolism

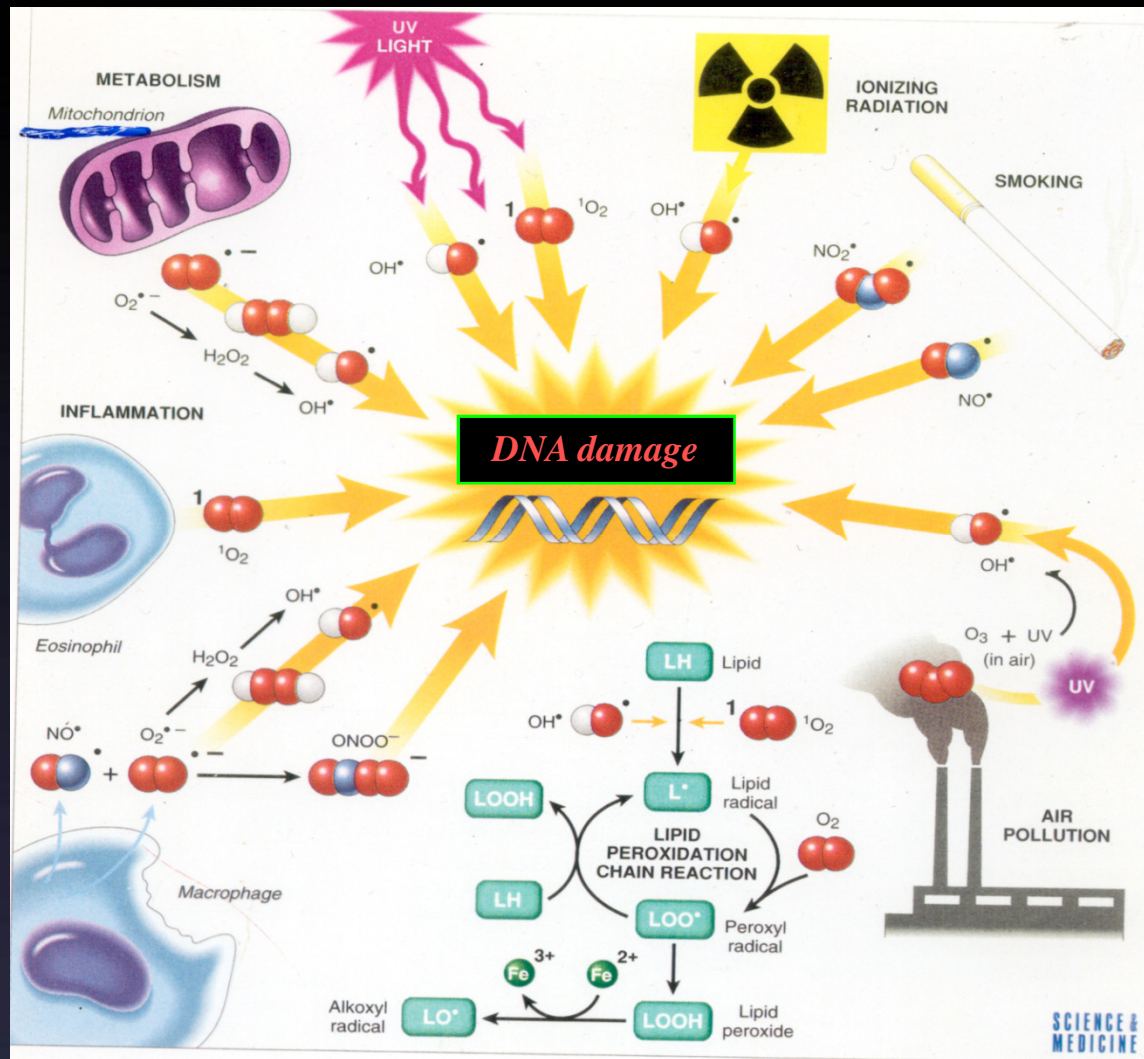
environment

Infection

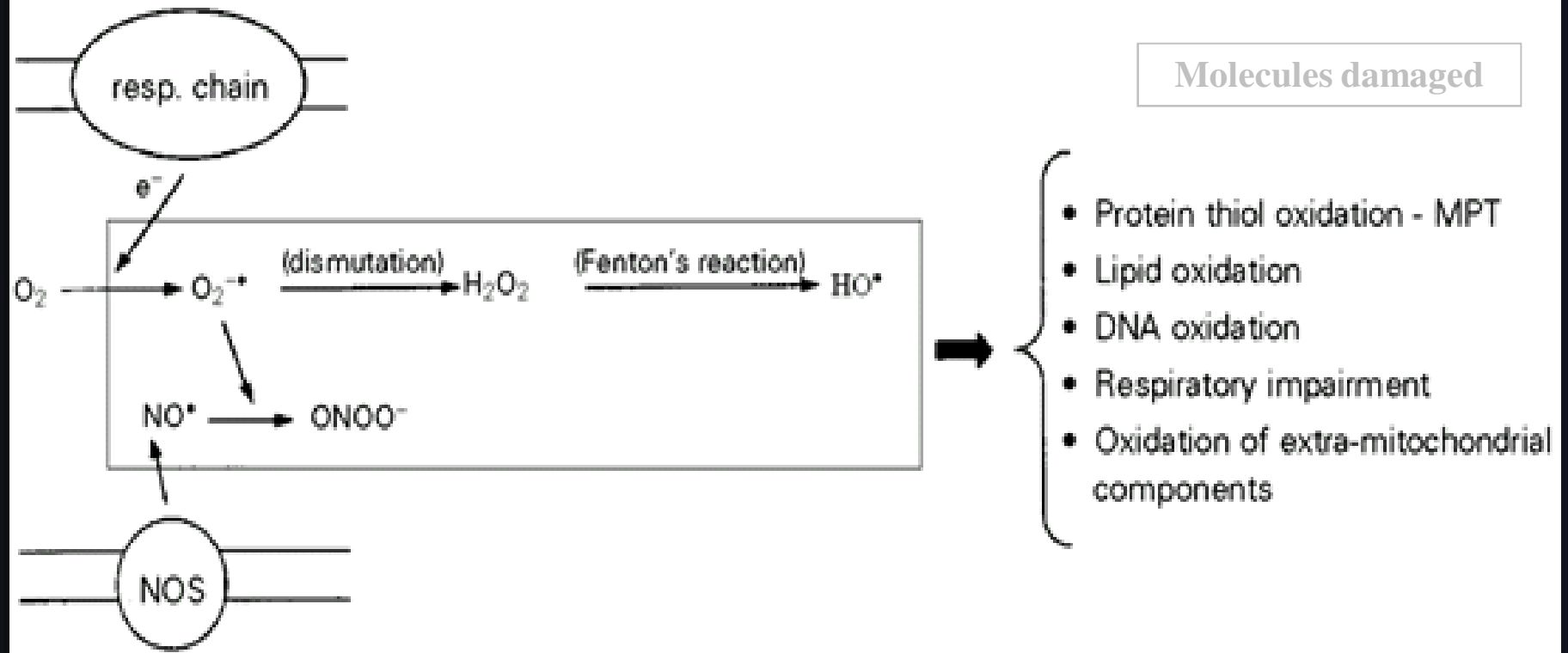
diet

lifestyle

pollution



Mitochondria produce ROS:

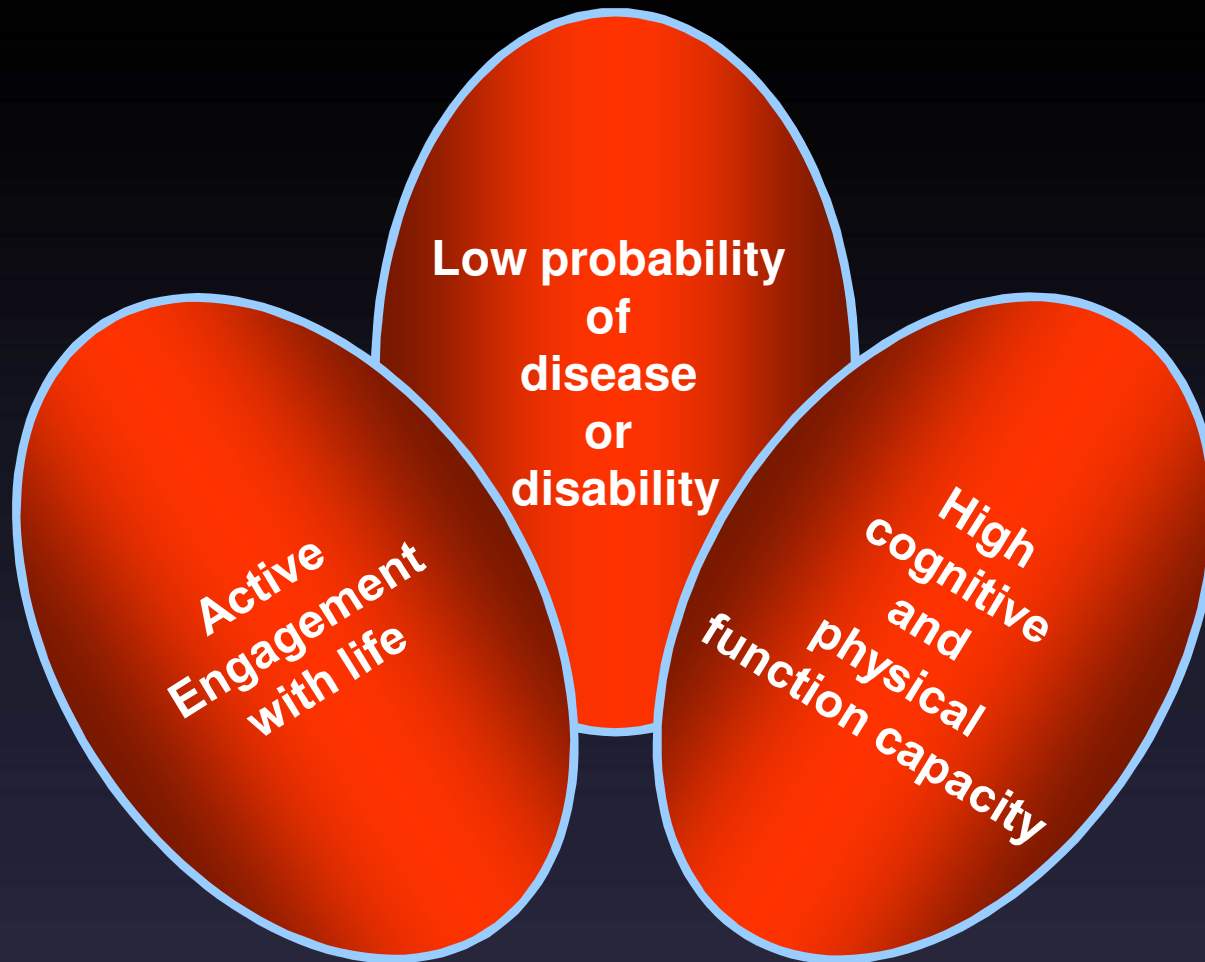


The respiratory chain (resp. chain) produces superoxide radicals ($O_2^{\cdot-}$), which generate hydrogen peroxide (H_2O_2) and hydroxyl radicals (HO^\bullet). Mitochondrial nitric oxide synthase (NOS) produces nitric oxide (NO^\bullet), which combines with $O_2^{\cdot-}$ to generate peroxynitrite ($ONOO^-$). All these ROS may cause mitochondrial and cellular damage if present in excess.

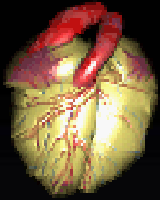
MPT, Mitochondrial permeability transition.

Kowaltowski 2002

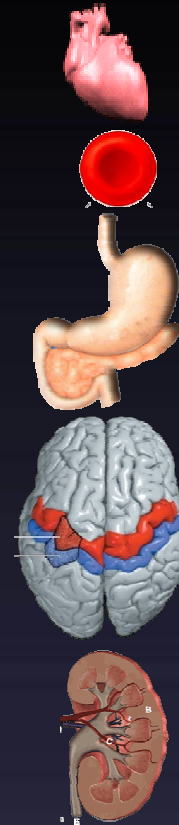
SUCCESSFUL AGEING



Leading Causes of Death Age 65+ “Medical Diagnoses”



- | | |
|------------------------------|------------|
| • Heart Disease | 32% |
| • Cancer | 22% |
| • Stroke | 8% |
| • Chronic respiratory | 6% |
| • Flu/Pneumonia | 3% |
| • Diabetes | 3% |
| • Alzheimer's | 3% |



State of Aging and Health CDC/NCHS Health US, 2002

Brief Geriatric Assessment Instruments

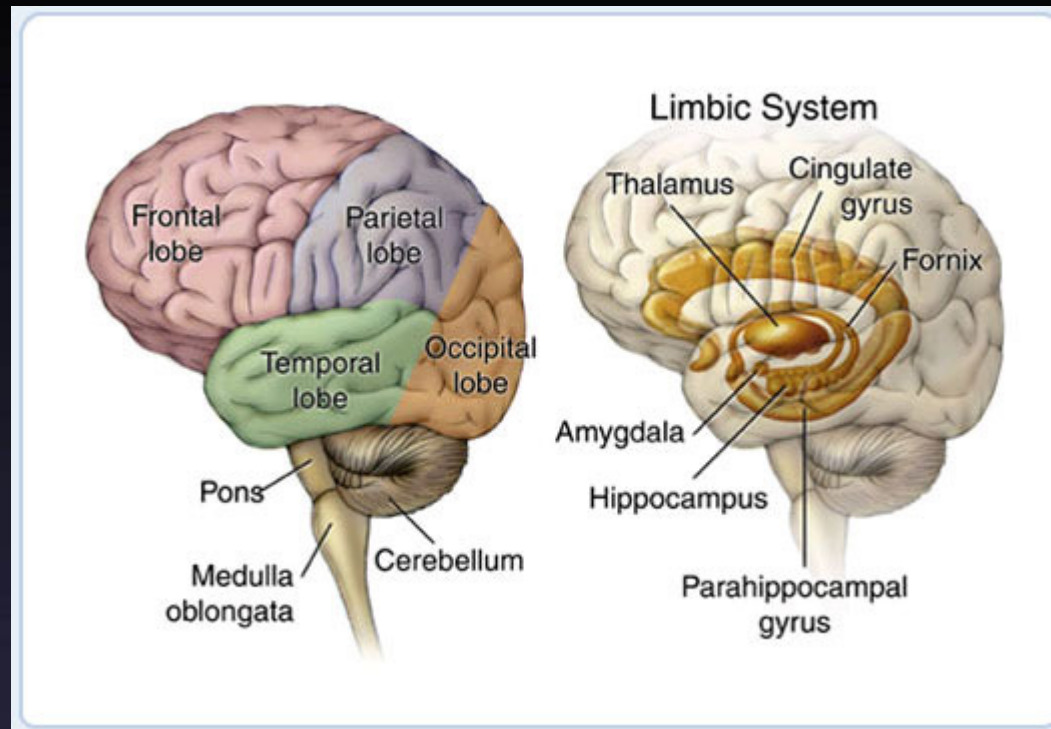
Domain	Instrument	Comments
Cognition		
Dementia	MMSE	Widely studied and accepted
	Timed time and change test	Sensitive and quick
Delirium	CAM	Sensitive and easy to apply
Affective disorders	GDS 5-question form	Rapid screen
Visual impairment	Snellen chart	Universally used
Hearing impairment	Whispered voice	No special equipment needed
	Pure tone audiometry	Can be performed by trained office staff
Dental health	DENTAL ^c	
Nutritional status	Weight loss of >4.5 kg (>10 lb) in 6 months or weight <45 kg (<100 lb)	
Gait and balance	"Timed Get Up and Go" test	Requires no special equipment

Age Related Changes

- Decreased height, lean body mass and body water
- Increased body fat
- Consequence Changes in pharmacokinetics



Aging nervous system



Brain Changes

- **Enlargement of the ventricular system:** as people get older, the volume of the ventricles increases. It is thought that this enlargement occurs because cells surrounding the ventricles are lost.
- **Widening of sulci (the grooves) on the surface of the brain.**
- **Reduced brain weight and brain volume:** these changes are probably caused by the loss of neurons. Reductions in the size of many areas of the cerebral cortex have been reported.
- **Neurological disorders:** brain disorders such as Alzheimer's disease, Parkinson's disease and stroke are more common in the elderly.

Aging nervous system

Changes

- Decreased brain weight
- Cerebral blood flow
- memory
- Alteration in CNS neurotransmitters
- Decreased vibratory sense

Consequences

- Drug toxicities
- delirium
- Altered mood
- Decreased IQ scores
- “Benign senile forgetfulness”
- Increased postural instability
- Altered gait
- Falls, accidents

Neurological System

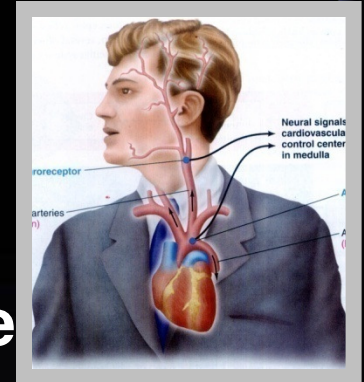
- **Neuronal loss is normal in the aging brain but the ability to learn remains generally unchanged**
- **There is loss of dendritic arborization**
- **Recall memory is affected more than cognitive function in normal aging**
- **Cerebral atrophy shows up on CTs and MRI scans**
- **Lowered seizure threshold**
- **Reduced Sympathetic nervous system activity**
- **Reduced Neurotransmitter levels**
- **Changes in sleep patterns**
- **Abnormalities in EEG tracings**
- **Increased risk of stroke**

Nervous System

- **Aging leads to increased cerebral amyloid**
- **Average amount of brain protein is reduced with a marked loss in multiple enzymes (carbonic anhydrase and the dehydrogenases) but with a relative increase in abnormal proteins such as amyloid in tangles and plaques.**
- **Loss of RNA (messenger and transcription) but not DNA**
- **Loss of lipids, and lipid turnover rate, and a decrease in catabolism and synthesis.**

Carotid sinus hypersensitivity

- Carotid sinus syncope occurs when there is an exaggerated vagal response to carotid sinus stimulation,
- Provoked by wearing a tight collar, looking upwards or turning the head
- Carotid sinus syndrome occurs in the elderly and mainly results in bradycardia.
- Most common etiologies of atrioventricular block
- Do not massage both carotids simultaneously.





The diagram is set within a dark blue frame with a double border. At the top is a large red 3D ring containing the text 'Control of blood pressure'. Below this ring are two spheres: a green one on the left and a purple one on the right. The green sphere is labeled 'Short-term Control (Rapid)' and sits on a dark blue rectangular base labeled 'Baroreceptor reflex'. The purple sphere is labeled 'Long-term control' and sits on a light blue rectangular base labeled 'Renal compensation'.

Control of blood pressure

**Short-term
Control
(Rapid)**

**Baroreceptor
reflex**

**Long-term
control**

**Renal
compensation**

Baroreceptor Reflex

Quick operation
(within few
seconds)

Mediated
through
autonomic nerves

Adjusts CO & TPR
to restore BP
to normal

Influences
heart &
blood vessels

Baroreceptor Reflex Arc

Receptors

Baroreceptors in carotid sinuses aorta

Afferents

Vagus Nerve

Center

Vasomotor Center in medulla oblongata

Efferents

Sympathetic & parasympathetic nerves

Effectors

Heart and blood vessels

**Pressure on the carotid sinus,
produced by the
tight collar or carotid massage**

**can
cause**

vasodilatation

**marked
bradycardia**

**Fainting
or syncope**

Touch

Age-related changes in the ability to perceive tactile stimuli may be due to:

- **Loss of various receptors (for example, Meissner's and Pacinian corpuscles) in the skin.**
- **Reductions in the number of sensory fibers innervating the skin.**

Vision

- **Lens:** proteins in the lens change with age and the elasticity of the lens is reduced. Therefore, many elderly individuals have trouble focusing their eyes.
- **Cornea:** the cornea may become less transparent and more flat. This may cause images to appear distorted or blurred. There may also be a loss of color sensitivity to green, blue and violet shades.
- **Pupil:** changes in the autonomic nervous system alter the ability of older people to dilate the pupil. By age 70, the pupil may not dilate easily in low lighting conditions (Hampton, 1997).

Vision

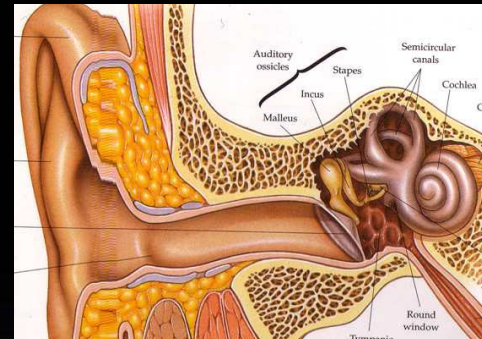
- **Cataracts:** cloudy areas of the lens. Cataracts decrease the amount of light that passes through the lens and can bend light abnormally. The National Eye Institute estimates that more than 50% of Americans age 65 years and older have a cataract.
- **Retina:** the peripheral retina is thinner and contains fewer rods in older individuals.
- **Other disorders of the eye common in the elderly:** glaucoma, macular degeneration, presbyopia.

Olfaction

- **Changes in the nasal mucosa, cribriform plate and air passages may contribute to impaired odor recognition.**
- **The amygdala and other brain areas involved with smell may be damaged in older individuals.**



Hearing Loss



- Ear wax build up.
- Stiffening of the tympanic membrane (eardrum).
- Atrophy of small ear muscles.
- Degeneration of hair cells and support cells in the cochlea.
- Stiffening of basilar membrane.
- Loss of nerve fibers leading from the cochlea to the brain.
- Loss of neurons in auditory areas of the brain.

Disorders of the Sense of Taste

- Medications that the elderly need.
- Reductions in the number of taste buds.
- Dentures that cover taste buds on the soft palate.



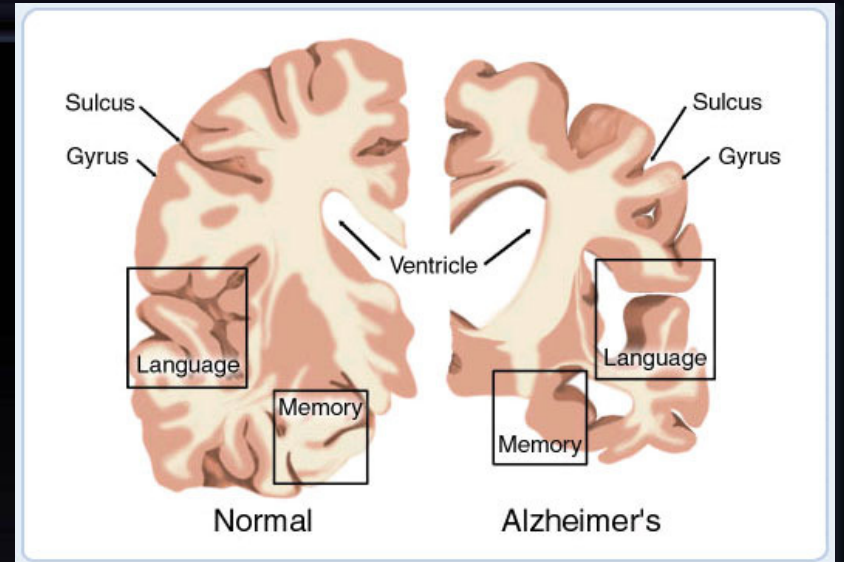
Geriatric Syndromes

- ***Dementia and Delirium***
- ***Falls***
- ***Urinary Incontinence***
- ***Pressure Ulcers***
- ***Functional Decline***

Dementia and Delirium

- Dementia is a syndrome of progressive decline in which multiple intellectual abilities deteriorate, causing both cognitive and functional impairment.
- Delirium is an acute state of confusion
- Delirium may be the only manifestation of a life-threatening illness in the older adult.

Alzheimer's Disease



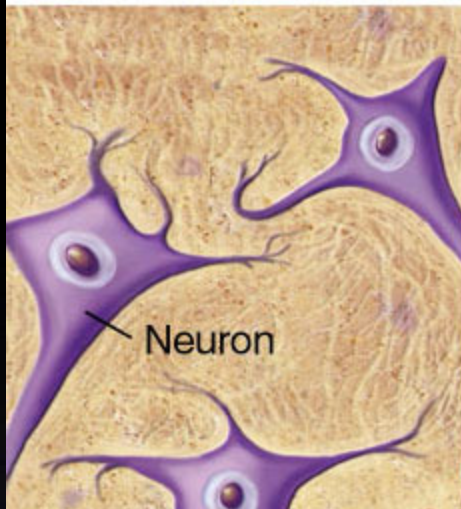
- Alzheimer's disease is defined as premature aging of the brain, usually beginning in mid-adult life and progressing rapidly to extreme loss of mental powers similar to that seen in very, very old age.

Alzheimer's Disease (Features)

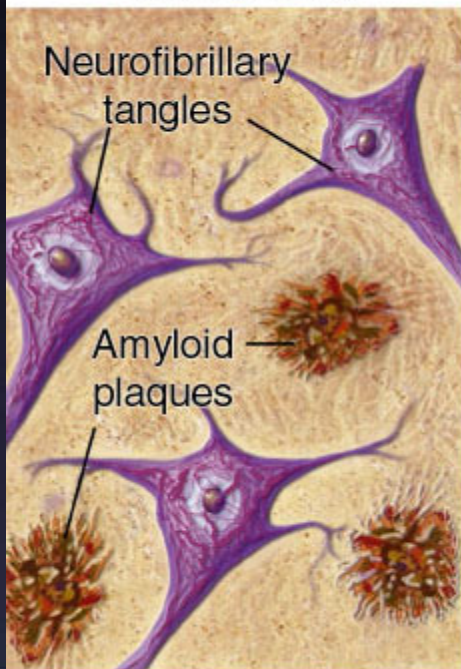
- (1) an amnesic type of memory impairment
- (2) deterioration of language
- (3) visuospatial deficits.

Motor and sensory abnormalities, gait disturbances, and seizures are uncommon until the late phases of the disease.

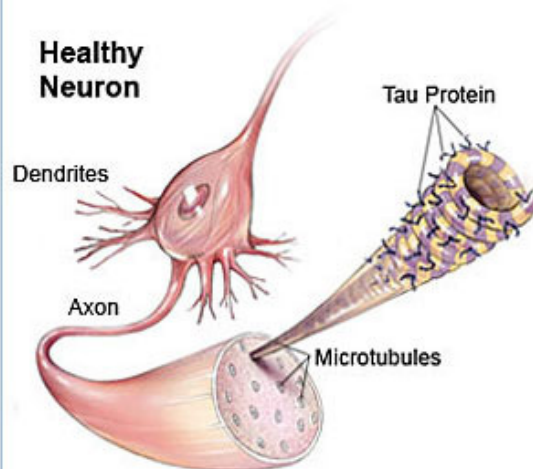
Normal



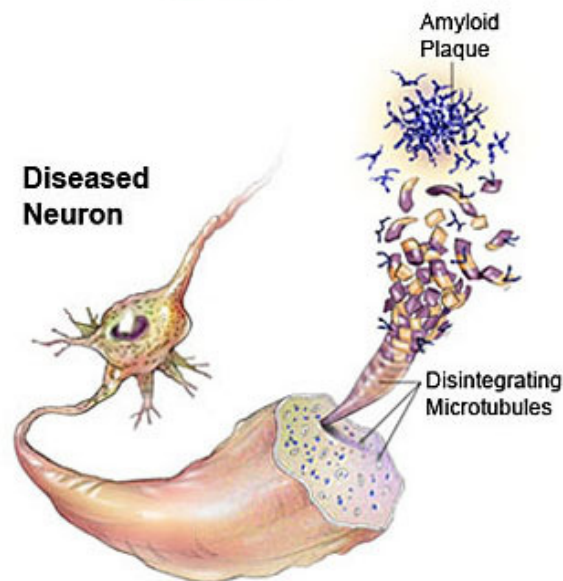
Alzheimer's



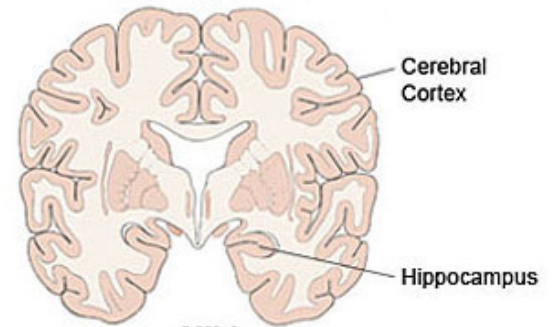
Healthy Neuron



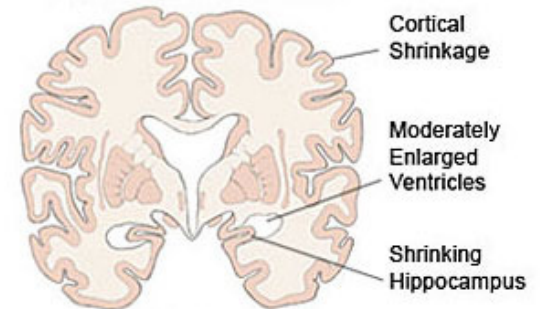
Diseased Neuron



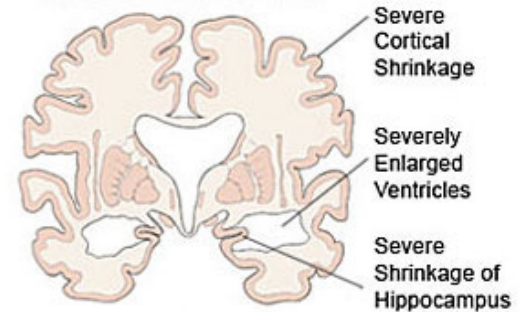
Healthy Brain



Mild Alzheimer's Disease



Severe Alzheimer's Disease



Amyloid Plaques

- **It is hallmark of Alzheimer's disease**
- **There is accumulation of amyloid plaques between nerve cells (neurons) in the brain.**
- **Amyloid is a general term for protein fragments that the body produces normally. Beta amyloid is a protein fragment snipped from an amyloid precursor protein (APP).**
- **In a healthy brain, these protein fragments are broken down and eliminated. In Alzheimer's disease, the fragments accumulate to form hard, insoluble plaques.**

Neurofibrillary Tangles

- **These are insoluble twisted fibers found inside the brain's cells.**
- **Consist primarily of a protein called tau, which forms part of a structure called a microtubule. The microtubule helps transport nutrients and other important substances from one part of the nerve cell to another.**
- **In Alzheimer's disease, however, the tau protein is abnormal and the microtubule structures collapse.**

Sexual Dysfunction

Erectile dysfunction (ED) is not considered a normal part of the aging process. Nonetheless, it is associated with certain physiologic and psychological changes related to age.

In the Massachusetts Male Aging Study (MMAS), a community-based survey of men between the ages of 40 and 70, 52% of responders reported some degree of ED. Complete ED occurred in 10% of respondents, moderate ED occurred in 25%, and minimal ED in 17%.

THANKS



- *The American Psychiatric Press Textbook of Geriatric Neuropsychiatry*, edited by C. E. Coffey, J. L. Cummings, Washington, DC: American Psychiatric Press, 2000.
- Hampton, J.K., Craven, R.F., and Heitkemper, M.M. *The Biology of Human Aging*, Dubuque: Wm. C. Brown, 1997.
- Hooper, C.R., Sensory and sensory integrative development, in *Functional Performance in Older Adults*, edited by B.R. Bonder and M.B. Wagner, Philadelphia: F.A. Davis Company, 2001, pp. 121-136.