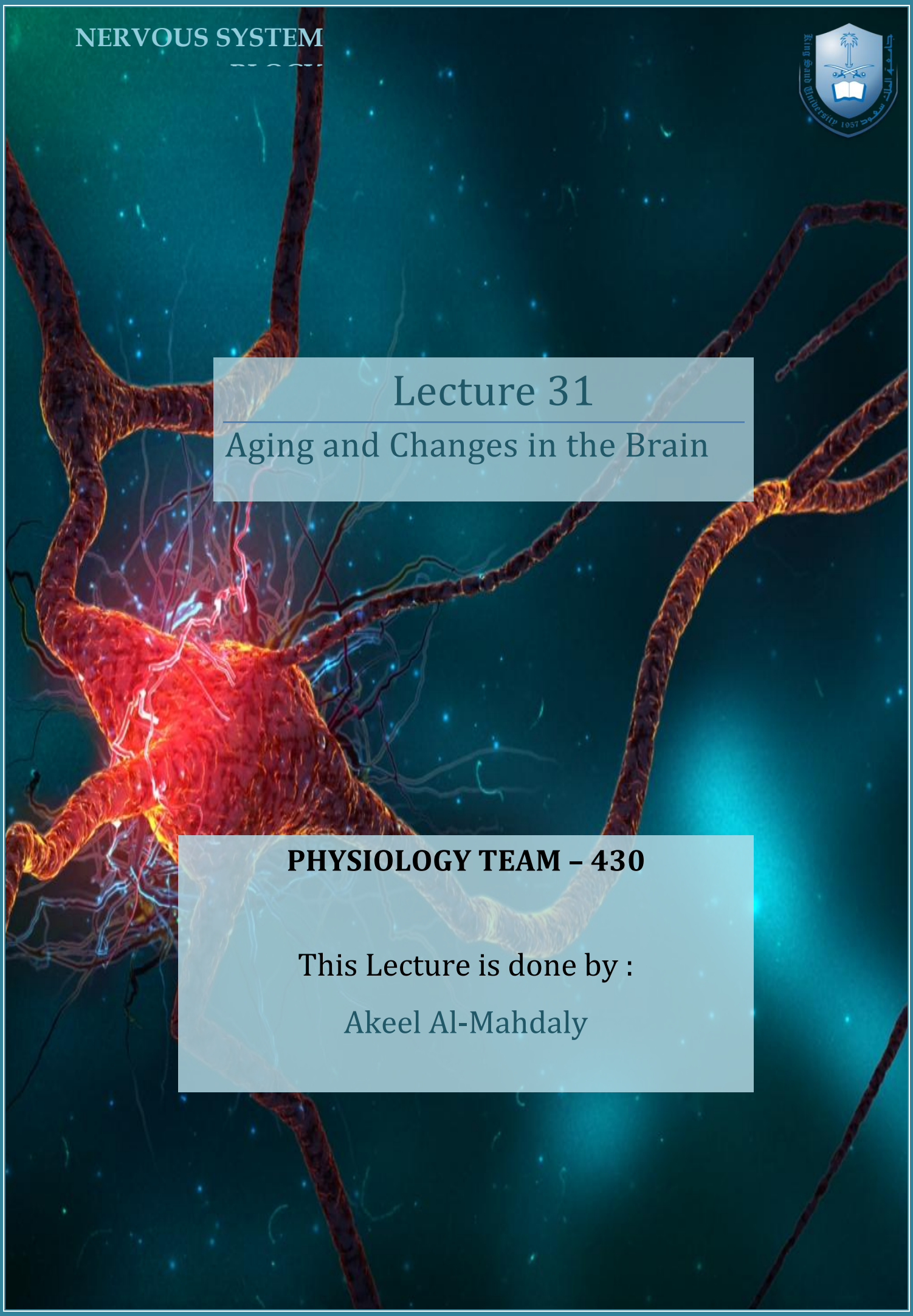
NERVOUS SYSTEM



Lecture 31

Aging and Changes in the Brain

PHYSIOLOGY TEAM – 430

This Lecture is done by :

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– 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.

With aging → destructive of tissues (not disease) → losing their functions.

– 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 → Slow response
- 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.

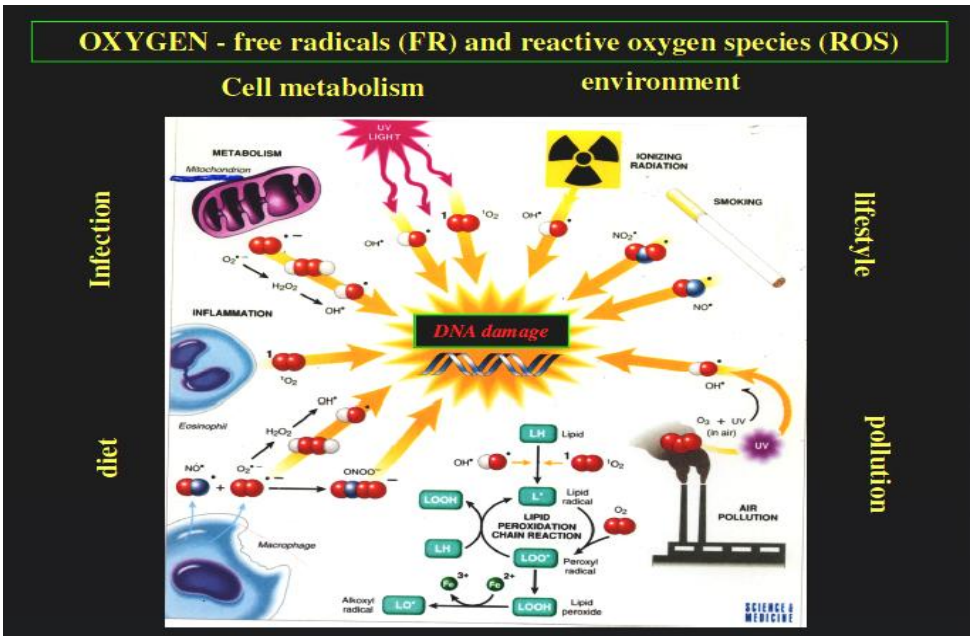
Also, it's characterized by ***Carotid Hypersensitivity***

– The Term Ageing (very important)

- **UNIVERSAL AGEING:**
  age changes that <u>all people</u> share.
- **PROBABILISTIC AGEING:**
  changes that <u>may happen to some and some may not</u> (e.g. type2 diabetes).
- **CHRONOLOGICAL AGEING:**
  referring to <u>how old</u> a person is. (age number)
- **SOCIAL AGEING:**
  <u>society's expectations</u> of how people should act as they grow older.
- **BIOLOGICAL AGEING:**
  an organism's physical state as it ages.

- **Theories of Aging** (not Important) (Just for reading)

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 Infections
Accumulation of senescent cells	Renewing tissues become dysfunctional through loss of ability to renew
Genetic	Aging is a genetic program activated in post-reproductive life when an individual's evolutionary mission is accomplished
Mitochondrial dysfunction	A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change
Oxidative stress *(very important)*	Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses



Oxidative Stress → less in relaxed life (DNA Damage)

Mitochondria produce ROS (Just for reading)

- The respiratory chain produces superoxide radicals (O_2-), which generates Hydrogen peroxide (H_2O_2) and hydroxyl radicals (HO).

- Mitochondrial nitric oxide synthase (NOS) produces nitric oxide (NO), which combines with O_2- to generate peroxinitrite ($ONOO^-$).

All these ROS may cause mitochondrial and cellular damage if present in excess.

– Leading Causes of Death Age 65+ "Medical Diagnoses"

- **Heart Disease 32% → Most common**
- Cancer 22%
- **Stroke 8% → (CNS) at the third level**
- Chronic respiratory 6%
- Flu/Pneumonia 3%
- Diabetes 3%
- Alzheimer's 3%

MPT = Mitochondrial permeability transition.

Delirium is sudden severe confusion and rapid changes in brain function that occur with physical or mental illness.

– Brief Geriatric Assessment Instruments

What is the geriatric assessment? (Just for reading)

The geriatric assessment is a multidimensional, multidisciplinary diagnostic instrument designed to collect data on the medical, psychosocial and functional capabilities and limitations of elderly patients. Various geriatric practitioners use the information generated to develop treatment and long-term follow-up plans, arrange for primary care and rehabilitative services, organize and facilitate the intricate process of case management, determine long-term care requirements and optimal placement, and make the best use of health care resources.

Domain(imp)	Instrument(not imp)
Dementia	MMSE = *Mini Mental State Examination* or Timed time and change test
Delirium	CAM = Confusion Assessment Method
Affective disorders	GDS 5-question form = *Geriatric Depression Scale (GDS)*
Visual impairment	Snellen chart
Hearing impairment	Whispered voice and Pure tone audiometry
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

– Age Related Changes

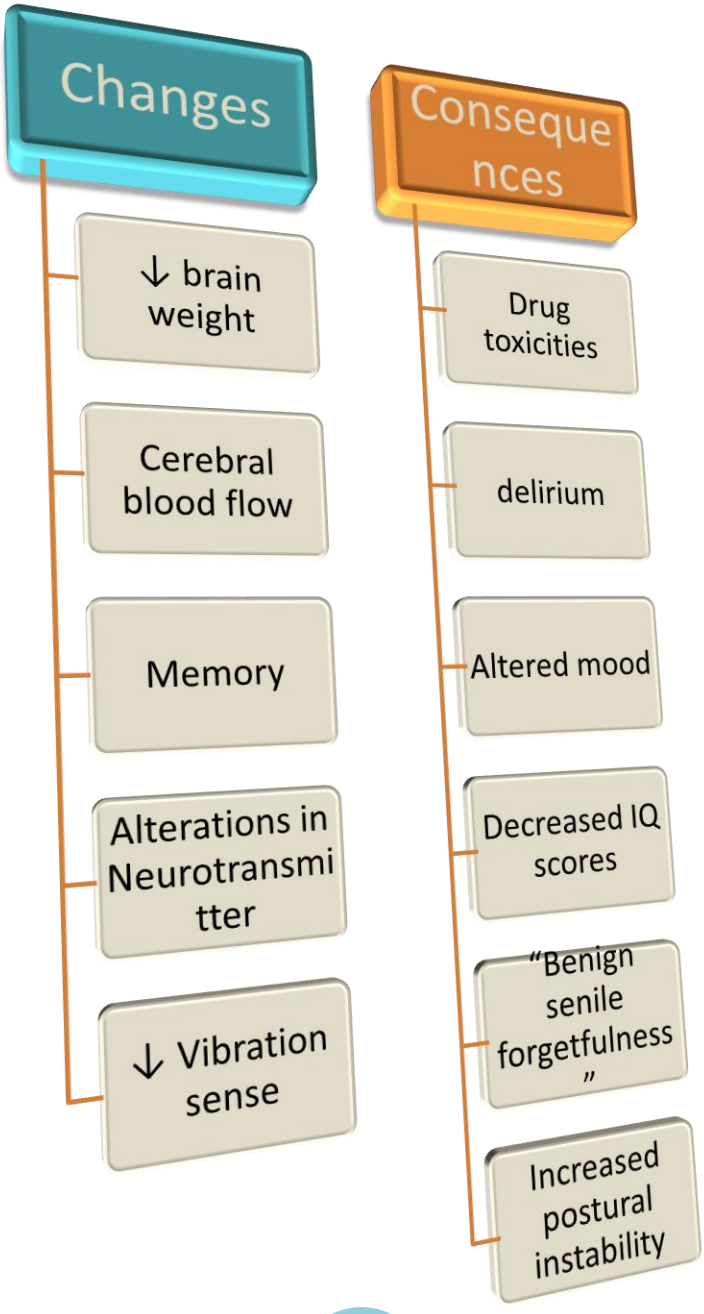
- Decreased height, lean body mass and body water
- Increased body fat
- Consequence Changes in pharmacokinetics
- ↓ Neurons → ↓ Brain weight
- ↓ Dendrites → ↓ Connections → ↓ Memory and learning

old people metabolizes drugs slowly → accumulating → Toxicity

– 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 (by the loss of neurons.)
- Reductions in the size of many areas of the cerebral cortex.
- Neurological disorders
  (Alzheimer's disease, Parkinson's disease and stroke)

- **Aging nervous system**

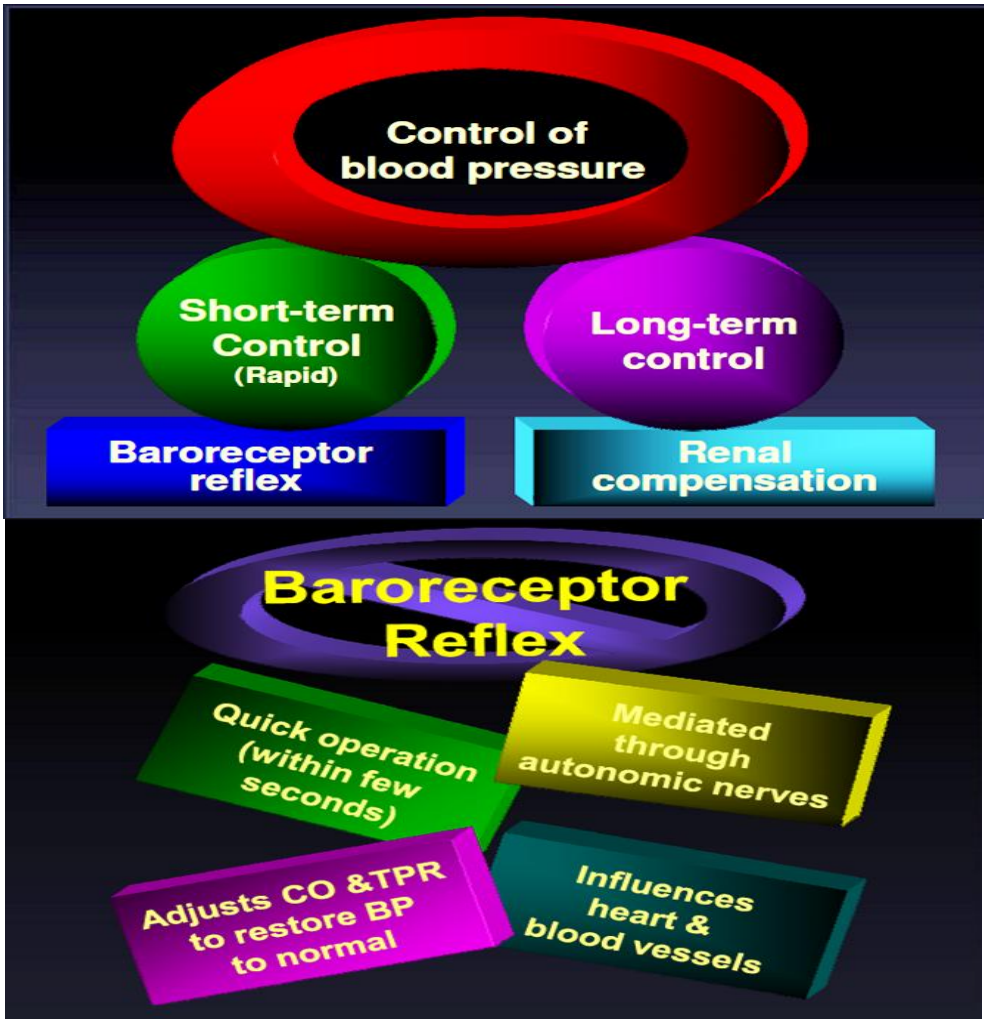


- **Neurological System**

- Neuronal loss is normal in the aging brain but the ability to learn remains generally unchanged
- 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
- 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.

Cognitive function: is what mental processes does a person go through to retrieve a long-lost memory. Or, what differentiates between the cognitive process of recognition (seeing hints of something before remembering it, or memory in context) and recall (retrieving a memory, as in "fill-in-the-blank").

- **Carotid sinus hypersensitivity (very Important)**

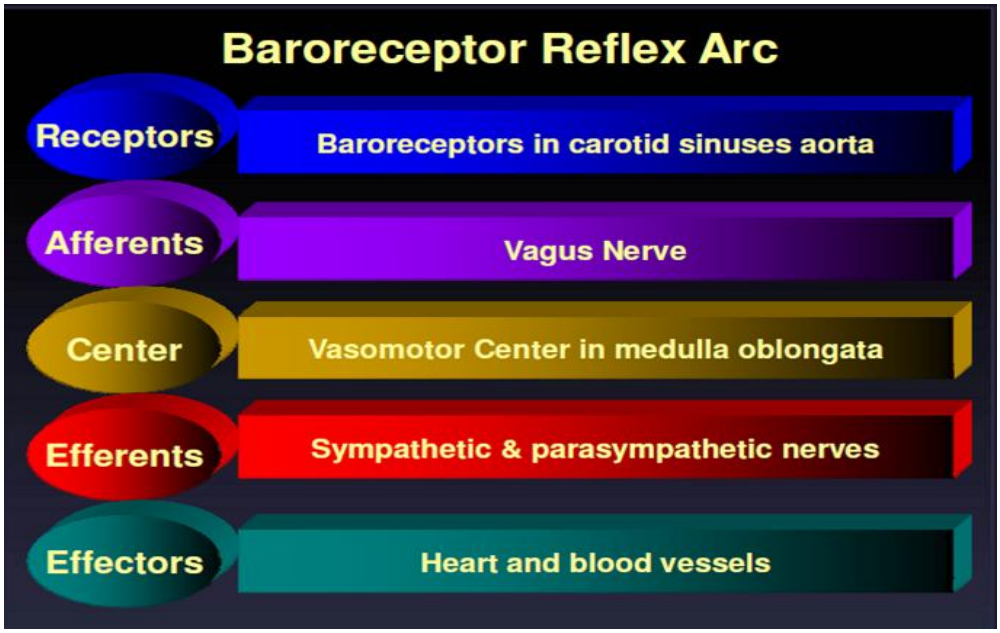


Carotid sinus syncope occurs when there is an exaggerated vagal response to carotid sinus stimulation, provoked by wearing a tight collar, looking upwards or turning the head

- Carotid sinus syndrome occurs in the elderly and mainly results in Bradycardia.
- Most common etiologies of Atrioventricular block

- **Examination:**
  It's when you are pressing on the carotid arteries, the pressure of the brain increases → baroreceptors → sympathetic inhibition and parasympathetic stimulation.

  ** Do not massage both carotids simultaneously. (Never examine both of the arteries at the same time)



(Very Important)

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. 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. Cataracts: cloudy areas of the lens. Cataracts decrease the amount of light that passes through the lens and can bend light abnormally. 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.

Hearing	• Conductive deafness: ▪ Ear wax builds 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.
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.
Taste	Medications that the elderly need. Reductions in the number of taste buds. Dentures that cover taste buds on the soft palate

Dementia (Syndrome of progressive decline) – Slow

→ Physically and mentally

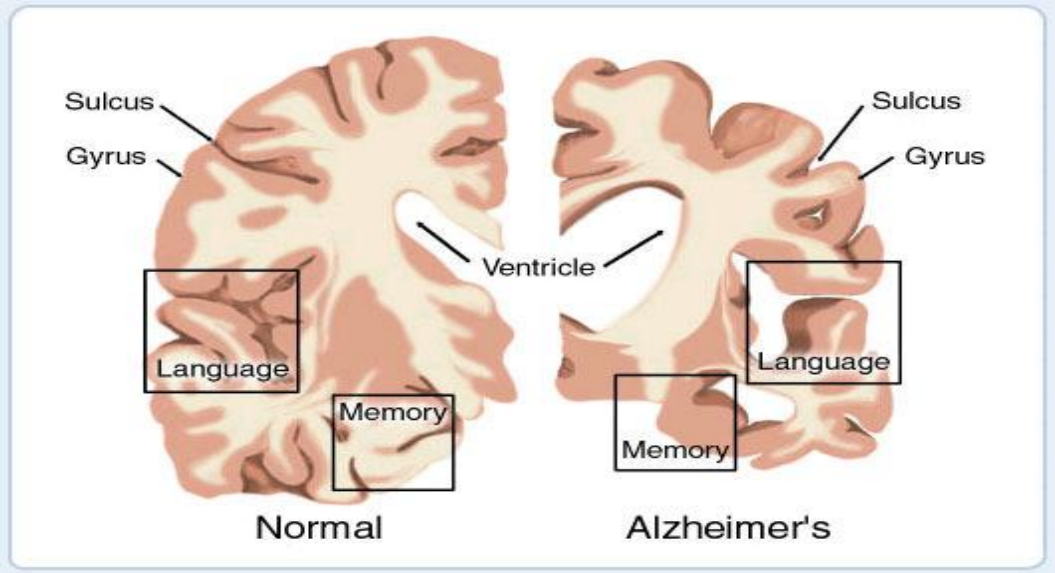
Delirium (Acute state of confusion) – Sudden

– Geriatric Syndromes

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

Old people don't hear low voices but they hear loud sounds as louder as it is. Because, the loss is patchy

– Alzheimer's disease

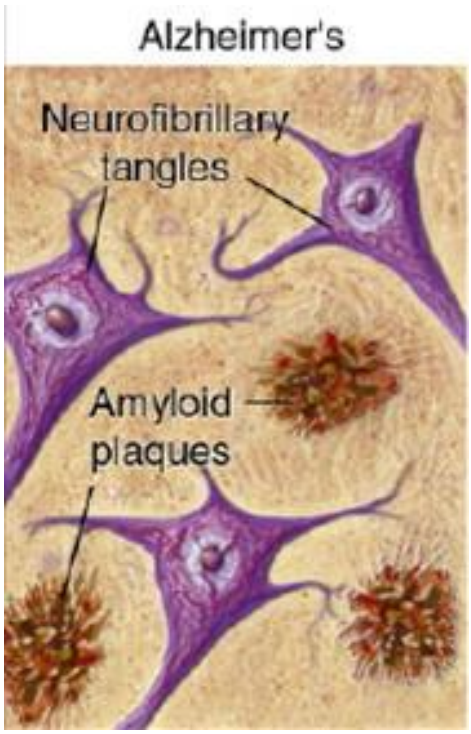


- Alzheimer's disease is defined as premature aging of the brain, usually beginning in mid-adult life and progressing rapidly to extreme loss of mental powers similar to that seen in very, very old age.

- 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.

1) 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.

2) 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.**
- **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.