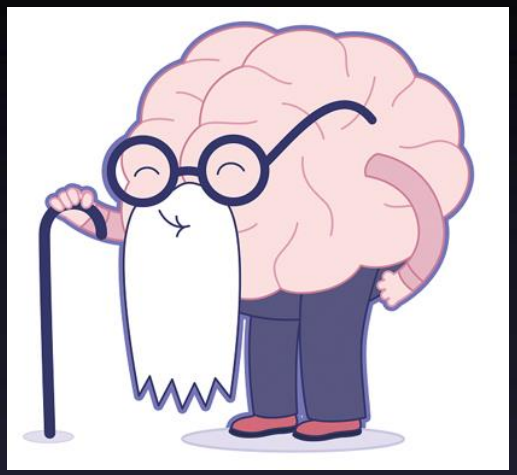
# AGING & CHANGES IN THE BRAIN

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# Objectives

***At the end of this session you should be able to:***

1. Define Aging and its consequences
2. Describe the theories of aging and terms Used
3. Name some Brief Geriatric Assessment Instruments
4. Describe brain changes associated with healthy aging related to structure, chemical, neuropsychological and genetic
5. Describe Important clinical conditions eg; geriatric syndrome, Alzheimer, 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.***

**Elderly ------ Age 65 to 74**
**Aged -------- Age 75 to 84**
**Very Old ---- Age 85 and more**

**Young old (65–74),**
**The middle old (75–84)**
**Oldest old (85+)**

# 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 ($O_2^{-\cdot}$, $H_2O_2$, $HO^-$) and reactive oxygen species (ROS) are produced in Mitochondria ($NO+O_2 \rightarrow ONOO^-$)

CELL METABOLISM

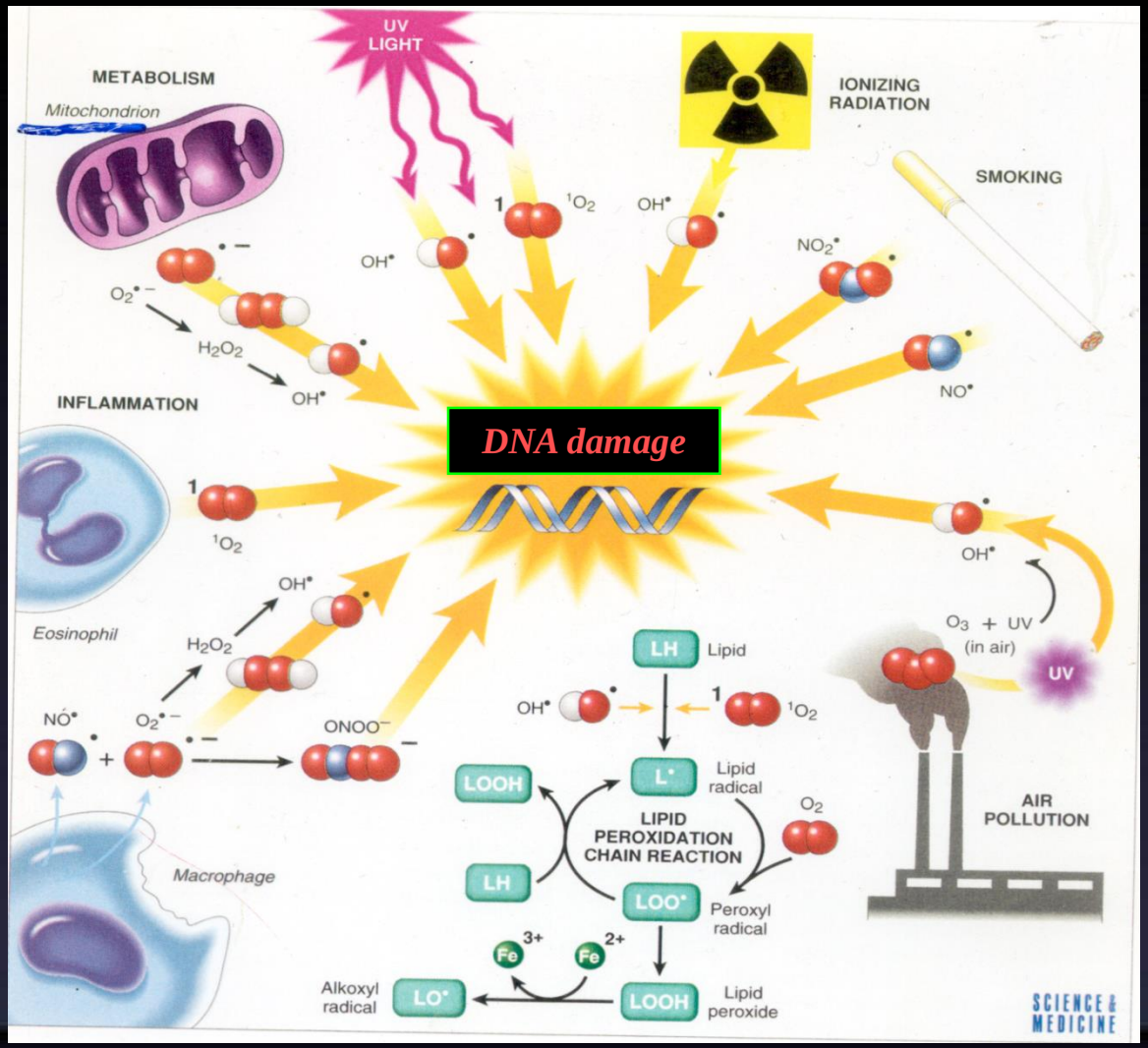
ENVIRONMENT

INFECTION

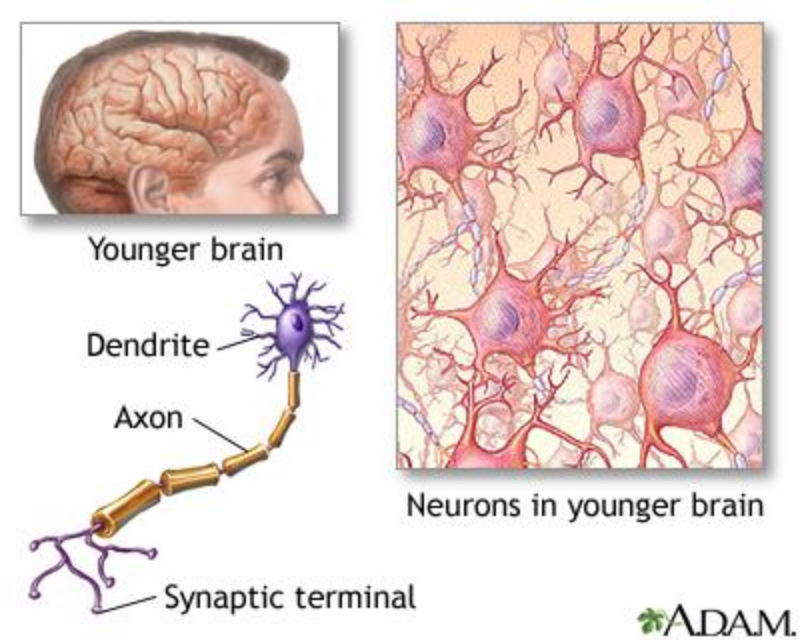
LIFESTYLE

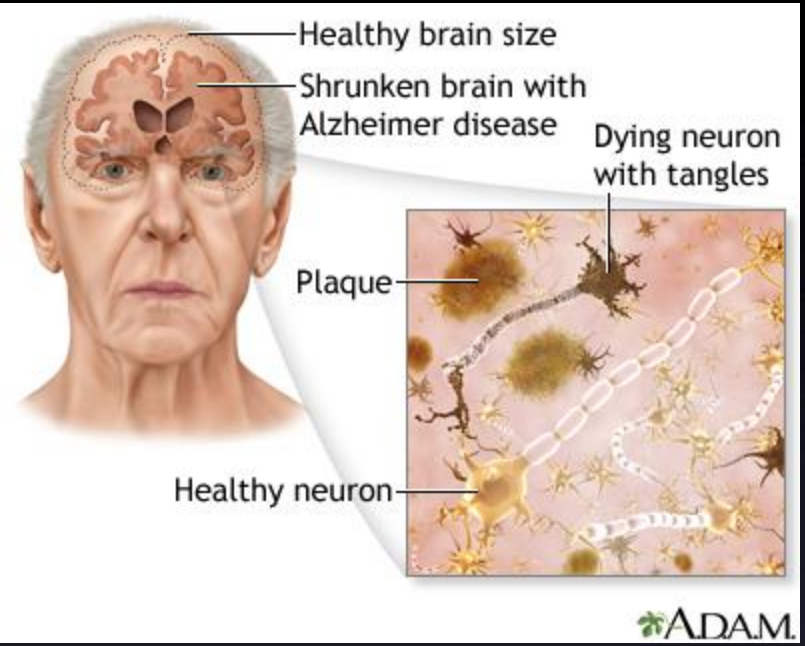
DIET

POLLUTION



# AGING NERVOUS SYSTEM



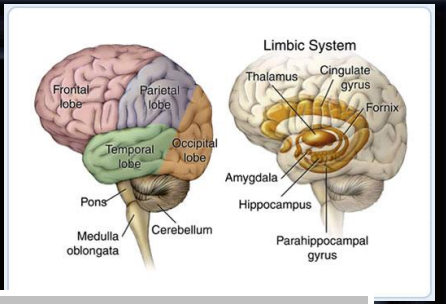




## "Use it or lose it!"

**Individuals who remain mentally active perform better on cognitive tasks than those who engage in mental activity less often**

- **Accelerated rate of brain shrinkage after age 50.**
- **Loss of 100,000 neurons in the cortex per day.**
- **Irreversible process of brain dysfunction.**

# Aging & Brain Regions




| Structure | Regional function |
|---|---|
| Basal ganglia | Becomes bright in appearance due to iron accumulation (movements affected) |
| Subarachnoid space | Increase in size due to brain shrinkage |
| Hippocampus | Reduction in size due to cell loss in the structure.<br>Par of limbic system Involved in learning & long term memory |
| Ventricles | Increase in size due brain shrinkage. |
| White Matter | Reduction in size due to neuronal atrophy in the deep brain.<br>Involved in information transmission. |

**The cerebellum is the youngest brain region least affected by aging**

# Aging Nervous system Changes & its Consequences in General

| Changes | Consequences |
| --- | --- |
| • Decreased brain weight<br>• Cerebral blood flow<br>• memory<br>• Alteration in CNS neurotransmitters<br>• Decreased vibratory sense | • Drug toxicities<br>• delirium<br>• Altered mood<br>• Decreased IQ scores<br>• “Benign senile forgetfulness”<br>• Increased postural<br>• instability<br>• Altered gait<br>• Falls, accidents |

# Aging Nervous 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
- Lowered **seizure threshold**
- Reduced Sympathetic nervous system activity
- Reduced **Neurotransmitter levels** (Dopamine, Serotonin, Glutamate
- Changes in sleep patterns
- Increased risk of stroke

**Intellectual functioning defined as "Stored" memory increases with age**
**Problem solving skills increase with age**

# 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 |

MMSE, Mini-Mental Status Examination; CAM, confusion assessment method; GDS, geriatric depression scale.

# Aging Changes in Nervous System

Aging is a major risk factor for most common neurodegenerative diseases, including mild cognitive impairment, dementias including Alzheimer's disease, cerebrovascular disease, Parkinson's disease and Lou Gehrig's disease.

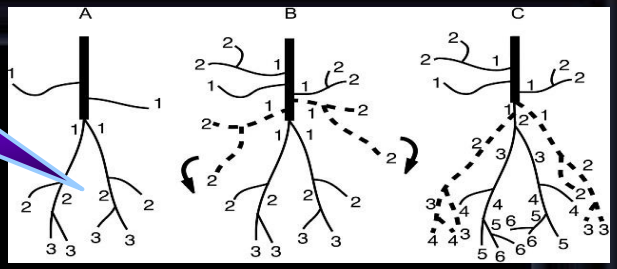
While much research has focused on diseases of aging, there are few informative studies on the molecular biology of the aging brain in the absence of neurodegenerative disease or the neuropsychological profile of healthy older adults.

This Lecture will focus on reviewing the brain changes associated with healthy aging

- Structural changes
- Chemical changes
- Neuropsychological
- Genetic changes

# Structural changes

**Dendrtic Arborization in new and experienced**




## Loss of neural circuits and brain plasticity

- Some areas would be more vulnerable to aging eg: hippocampus and neocortical circuits
- Age-related cognitive decline is due in part not to neuronal death but to synaptic alterations
- This cognitive deficit is due to functional and biochemical factors such as changes in enzymatic activity, chemical messengers (calcium), or gene expression in cortical circuits

## Thinning of the cortex

There is a decrease in grey matter volume between adulthood and old age, whereas white matter volume was found to increase from age 19-40, and decline after this age

## Age-related neuronal morphology

- Dendritic arbors and dendritic spines of cortical pyramidal neurons decrease in size and/or number in specific regions and layers of human and non-human primate cortex as a result of age
- A 46% decrease in spine number and spine density has been reported in humans older than 50 compared with younger individuals

## Neurofibrillary tangles

One of the important differences between normal aging and pathological aging is the location of neurofibrillary tangles. In normal, non-demented aging, the number of tangles in each affected cell body is relatively low. However, unlike tangles, plaques have not been found to be a consistent feature of normal aging.

# Chemical changes

**Dopamine**

Significant age-related **decline** in dopamine synthesis → notably in the striatum and extrastriatal regions Significant age-related decreases in all dopamine receptors $D_1$, $D_2$, and $D_3$ → The loss of dopamine with age is thought to be responsible for many neurological symptoms that increase in frequency with age, such as decreased arm swing and increased rigidity. Changes in dopamine levels may also cause age-related changes in cognitive flexibility.

**Serotonin**

**Decreasing levels** of different serotonin receptors and the serotonin transporter, 5-HTT, have also been shown to occur with age. → in the caudate nucleus, putamen, and frontal cerebral cortex, decline with age.

**Glutamate**

Glutamate is another neurotransmitter that tends to **decrease with age**.→ lower glutamate concentration in the motor cortex compared to younger subjects → especially in the parietal gray matter, basal ganglia, and to a lesser degree, the frontal white matter, → glutamate may be useful as a marker of brain diseases that are affected by aging

# Neuropsychological

## Changes in orientation

Deficits in orientation are one of the most common symptoms of brain disease, hence tests of orientation are included in almost all medical and neuropsychological evaluations.→ Results of studies are somewhat **inconclusive.** So although current research suggests that normal aging is not usually associated with significant declines in orientation, **mild difficulties** may be a part of normal aging and not necessarily a sign of pathology.

## Changes in attention

Many older adults notice a decline in their attentional abilities → Results suggest that sustained attention increases in early adulthood and then remains relatively stable, at least through the seventh decade of life.→ It is worth noting that there are factors other than true attentional abilities that might relate to difficulty paying attention. **For example, sensory deficits like hearing or vision may make attention it more difficult.**

## Changes in memory

•Memory functions, more specifically those associated with the medial temporal lobe are especially vulnerable to age-related decline. **(↓ working & explicit memory but not implicit)**

**Changes in language**

**Changes in performance** on verbal tasks, vary in predictable patterns with age. For example, behavioral changes associated with age include compromised performance on tasks related to word retrieval, comprehension of sentences with high syntactic and/or working memory demands, and production of such sentences

# Genetic changes

Research focused on discovering the genetic component in developing AD has also contributed greatly to the understanding the genetics behind normal or "non-pathological" aging.
The human brain shows a **decline in function and a change in gene expression** → This modulation in gene expression may be due to oxidative DNA damage at promoter regions in the genome.

**Genes that are down-regulated over the age of 40 include:**

- GABA-A receptor gene
- Genes involved in long-term potentiation e.g. calmodulin
- Calcium signaling genes
- Synaptic plasticity genes
- Synaptic vesicle release and recycling genes

**Genes that are upregulated include:**

- Genes associated with stress response and DNA repair
- Antioxidant defense

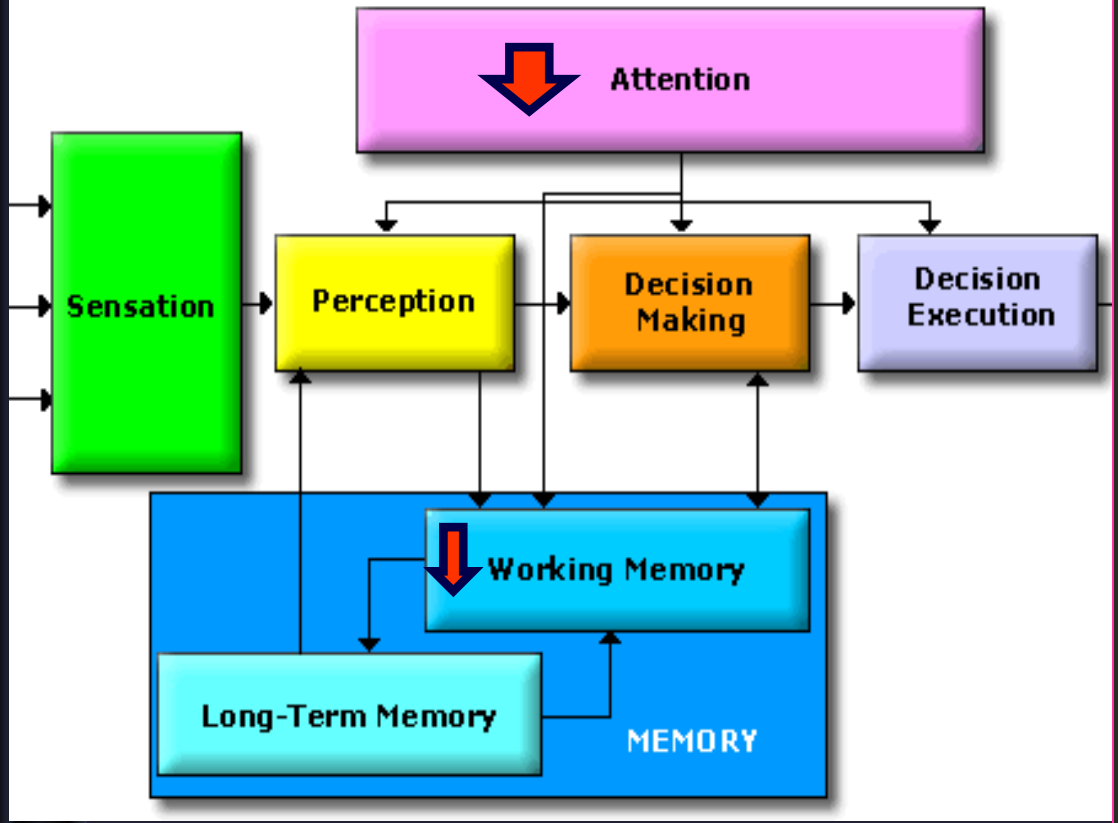
# CONGITIVE CHANGES IN AGING: MEMORY & MENTAL PROCESSING

## SHORT TERM MEMORY

20 to 30 seconds

IMMEDIATE RECALL ↓

WORKING MEMORY ↓




## LONG TERM MEMORY

**DECLARATIVE MEMORY OR EXPLICIT MEMORY** (stored in hippocampus and you retrieve it after consciously thinking about it)

- Semantic memory (Words, language) is retained & late to ↓
- Episodic memory (events): start to ↓ from middle age.

**SKILL MEMORY OR IMPLICIT MEMORY** (Involves cerebellum, motor cortex, sensory cortex, visual areas and does not involve awareness)

- Procedural memory is retained

There is decline in mental processing via reduction of attentional ability and decline in ability in forming **working memory** (mainly includes short term memory)

There is **decline in explicit memory** but **implicit memory is retained** (eg; driving a car, tying a shoe).

# Hearing

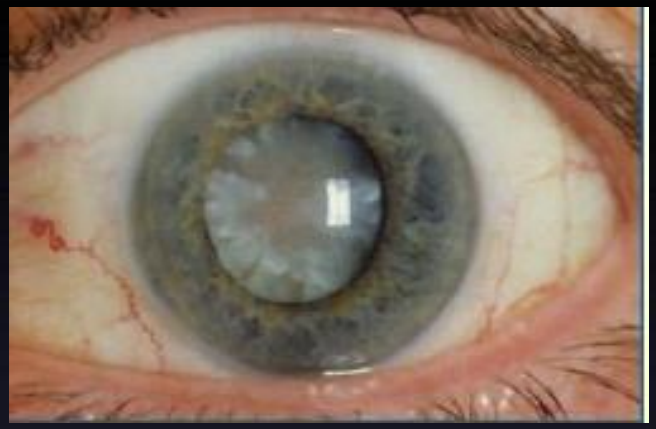
- **Presbycusis:** Part of normal aging (35% people over 60 years of age have bilateral, symmetric & progressive impairment for high pitched sounds sensorineural hearing loss)
- **Cerumen impaction:** is one of the most common reversible cause of conductive hearing loss in elderly

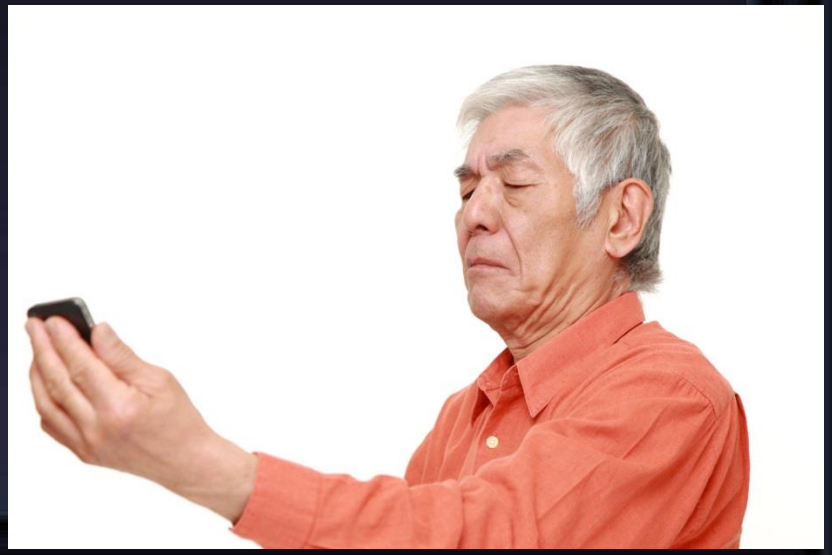
- Paradoxical hypersensitivity to loud sounds
- Exacerbated in the presence of competing background noise

Slow, persistent decline in hearing with age. The hearing loss begins in the sixth decade and is typically symmetrical, beginning in the high-frequency range.

# Vision

- Loss of ability to see items that are close up begins in the 40's (**Presbyopia**)
- Size of **pupil** grows smaller with age: focusing becomes less accurate
- Pupil less sensitive to light
- Opacaification of lens (**Cataract**)
- Lens of eye yellows making it more difficult to see red and green colors
- **Night vision** not as acute
- **Arcus Senilis**





# Disorders of the Sense of Taste

- Dorsum surface shows loss of filiform papilla
- Foliate papillae more prominent.
- Fissures increase
- Dryness of the mouth
- The ventral surface of the tongue shows the presence of nodular varicose enlargement also known as caviar tongue
- Loss of taste buds with age

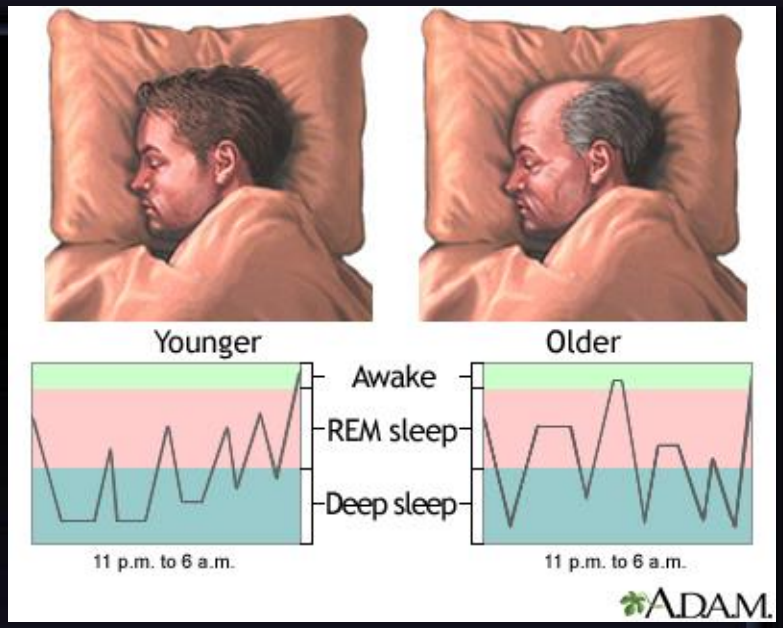
**Sensory gustatory losses are caused by inflammatory and degenerative diseases in the oral cavity; a vast number of drugs, such as antithyroid and antineoplastic agents; radiation therapy to the oral cavity and pharynx; viral infections; endocrine disorders; neoplasms; and aging**

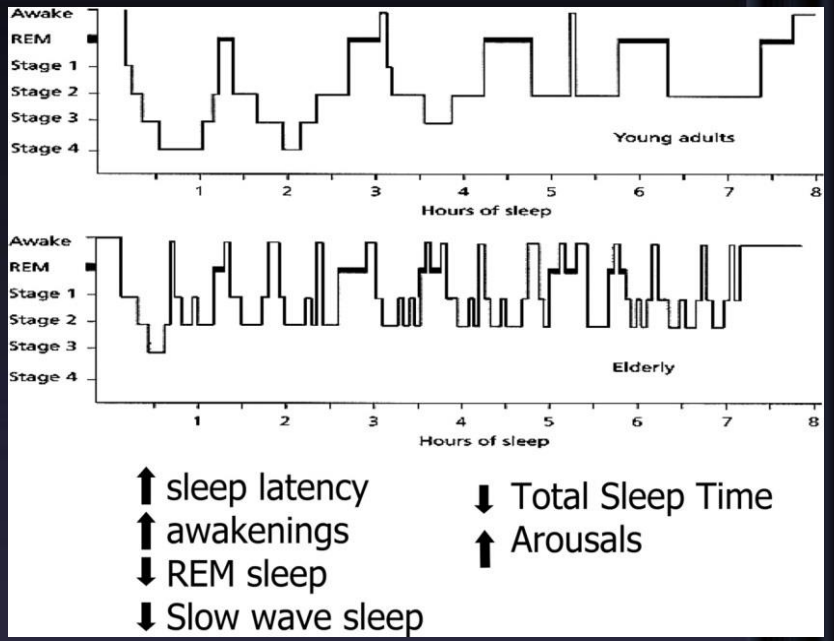
# Pain and Sense of Touch

- With age, skin is not as sensitive as in youth
  - Contributing factors include:
    1. Loss of elasticity
    2. Loss of pigment
    3. Reduced fat layer
- Safety Implications:
  1. Lessened ability to recognize dangerous levels of heat
  2. Lessened ability of body to maintain temperature
  3. Tendency to develop bruises, skin tears more easily

# SLEEP PATTERNS

- It tends to become more **fragmented**, with more awakenings during the night.
- Total sleep time stays the same or is slightly decreased (6.5 to 7 hours per night).
- The transition between sleep and waking up is often abrupt, which makes older people feel like they are a lighter sleeper than when they were younger.
- **Three or four awakenings** each night
- The **proportion** of slow wave sleep decreases relative to total sleep time, but the proportion of sleep that is REM sleep ↓ or is unchanged




**⬇High Quality Sleep**

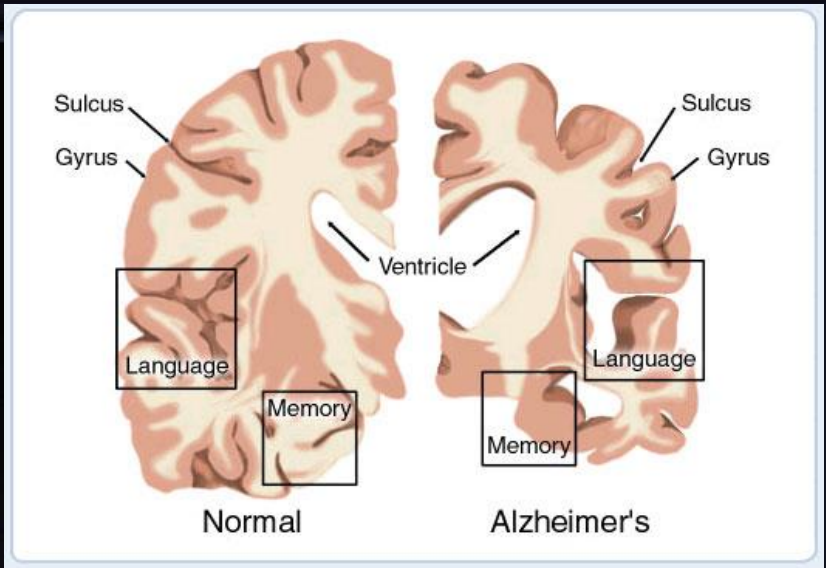
# *Geriatric Syndromes*

- ***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.

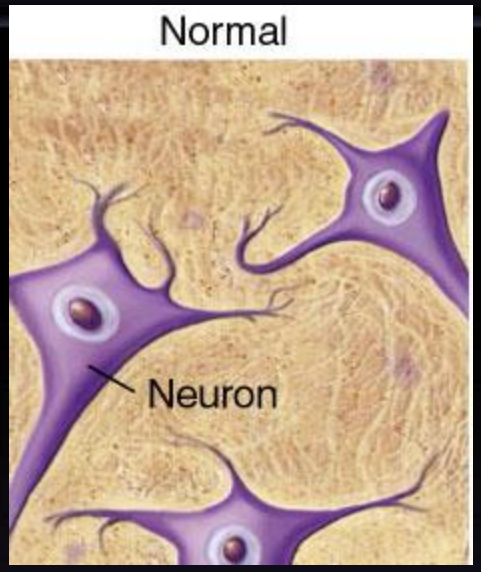
**Features**

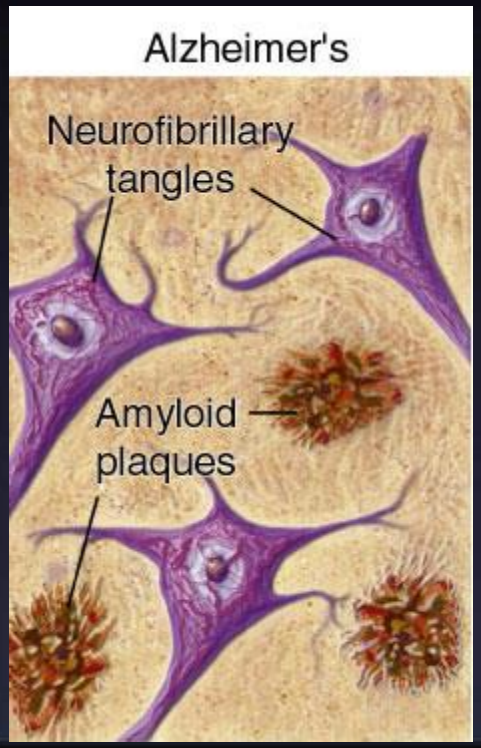
(1) An amnesic type of memory impairment

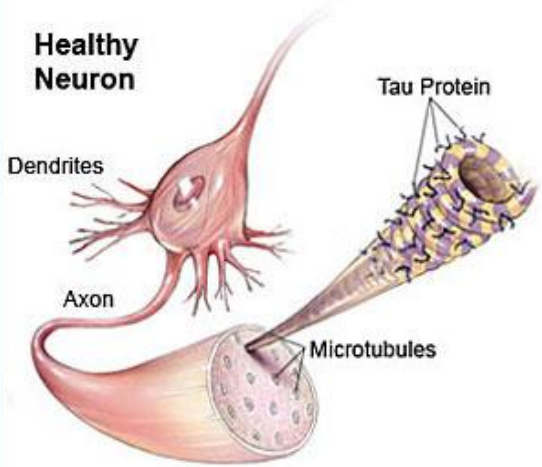
(2) Deterioration of language

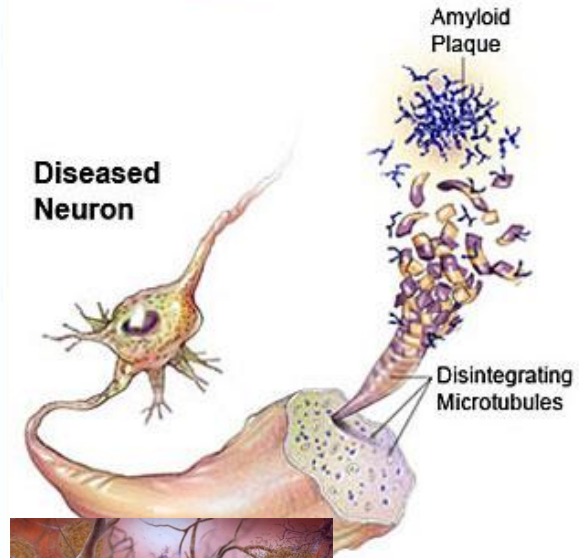
(3) Visuospatial deficits.

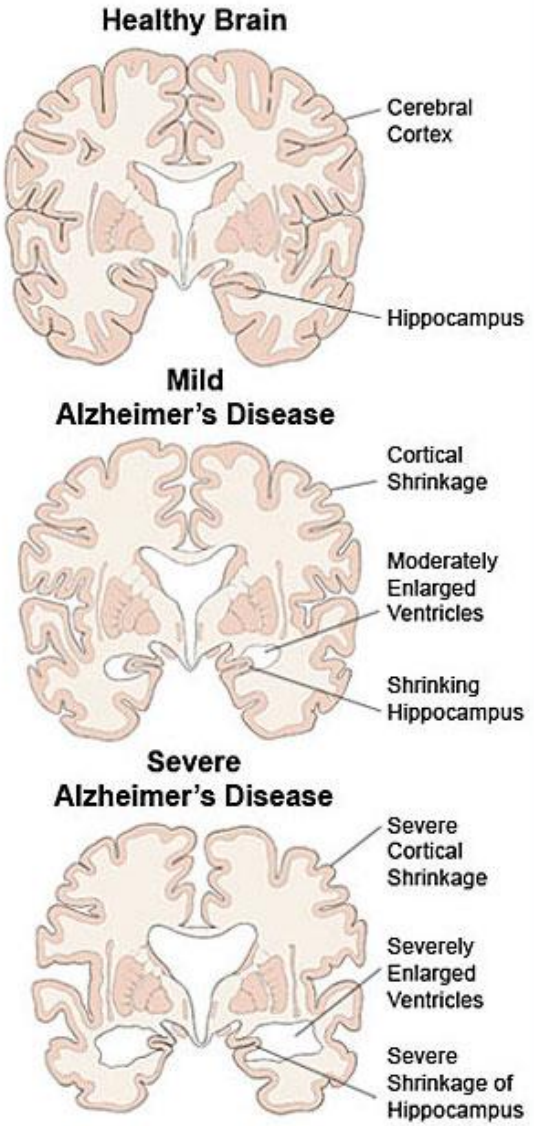
**Motor and sensory abnormalities, gait disturbances, and seizures are uncommon until the late phases of the disease.**


Normal
Neuron


Alzheimer's
Neurofibrillary tangles
Amyloid plaques


Healthy Neuron
Tau Protein
Dendrites
Axon
Microtubules


Amyloid Plaque
Diseased Neuron
Disintegrating Microtubules


Healthy Brain
Cerebral Cortex
Hippocampus
Mild Alzheimer's Disease
Cortical Shrinkage
Moderately Enlarged Ventricles
Shrinking Hippocampus
Severe Alzheimer's Disease
Severe Cortical Shrinkage
Severely Enlarged Ventricles
Severe Shrinkage of Hippocampus

# 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 normal, non-demented aging, the number of tangles in each affected cell body is relatively low
- In **Alzheimer's disease**, however, the tau protein is abnormal and the microtubule structures collapse.

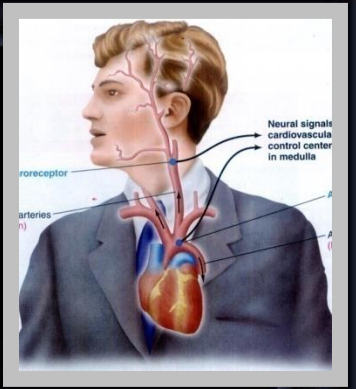
# Amyloid Plaques

- **Plaques have not been found to be a consistent feature of normal aging**
- **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.**

# Decline in Autonomic Functions

- **Aging is associated with decreased Heart rate variability which is associated with increased mortality.**
- **For eg: Changing position from supine to standing may trigger dizziness more frequently with ageing reflect the diminished cardiovascular sympathetic modulations and significant decline in overall autonomic functions**
- **Variation in heart rate response to deep breathing and valsalva manoeuvre is decreased because of impaired vagal control of heart rate with increasing age.**

# 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
- **Remember:** Do not massage both carotids simultaneously.


THANKS