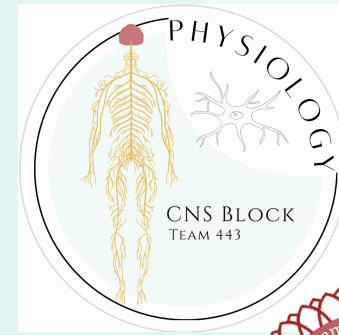




Aging and Brain



Color Index:

- Main text
- **Important**
- Girls Slides
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- Notes
- Extra

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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.
- 7 Sensory changes.

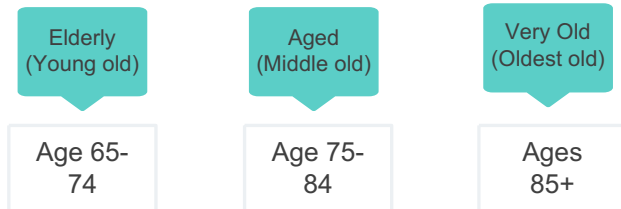


Aging

Definition

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

- In USA, life expectancy has increased from 47 years in 1900 to 75 years in 2000.
- Classification: Each nation, government and non-governmental organization have different ways of classification and (nomenclature) of age.



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

2 Gerontology: a relatively new discipline dealing with old adults.

Aging terminology

Chronological Ageing

Referring to how old a person is.

Biological Ageing

An organism's physical state as it ages.

Universal Ageing

The age changes that all people share.

Probabilistic Ageing:

The age changes that may happen to some people (Ex.: **Type Two Diabetes Mellitus**).

Social Ageing

Society's expectations of how people should act as they grow older.

Proximal aging

Age-based effect due to factors in recent past (Ex: **stroke**).

Distal aging

Age-based effect due to factors in early past (Ex: **poliomyelitis**).



Theories Of Aging

Apoptosis: Programmed cell death (genetic programming) vs.
Necrosis: Cell death due to damage.

Hypothesis	How It May Work
Genetic	Aging is a genetic program activated in post-reproductive life when an individual's mission is accomplished (mutations could lead to changes of the DNA of somatic cells).
Oxidative stress	Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses (Longer life species produce more superoxide dismutase).
Mitochondrial dysfunction	A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change
Hormonal changes	The decline and loss of circadian rhythm in secretion of some hormones produces a functional hormone deficiency state (DHEA, Melatonin, Estrogen, GH).
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 Infection.
Accumulation of senescent cells	Renewing tissues become dysfunctional through loss of ability to renew (Hormonal or material deficiencies).



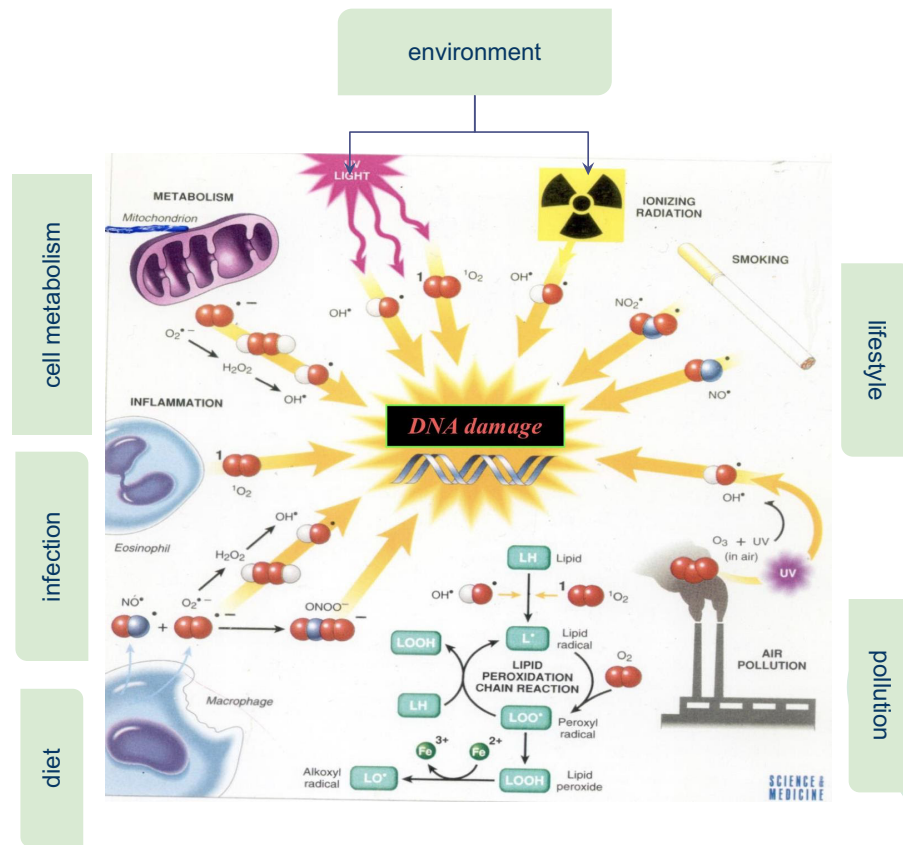
Free radicals (FR) & reactive oxygen species(ROS)

- Mitochondria produce ROS:
1-produces superoxide radicals which generate H₂O₂ and OH.
- 2-Mitochondria NOS produces NO and peroxynitrite ions ONOO⁻.
- NO is rapidly broken down to give oxidative end products (nitrite and nitrate), excreted by the kidneys.

From team 439 :

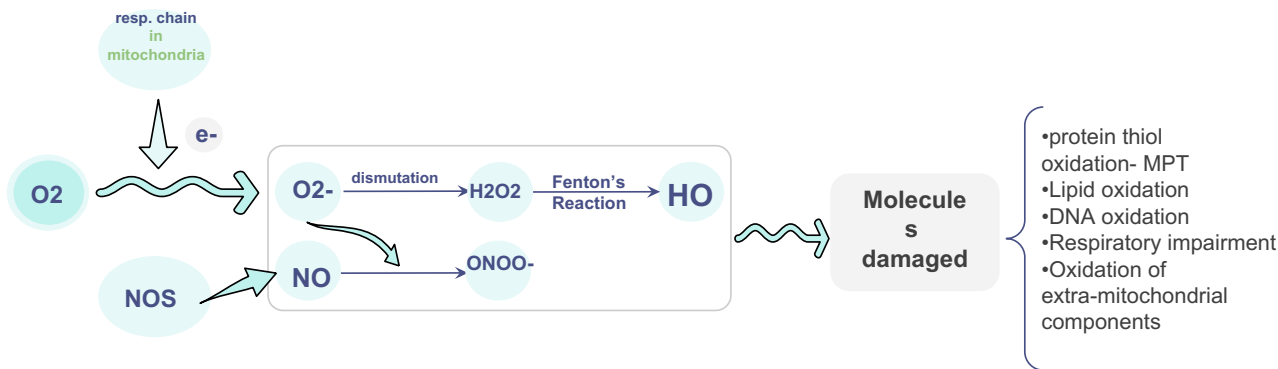
❖ oxidative stress comes from a group of oxygen derivatives. and **normally** oxygen is used in mitochondria to oxidise nutrients and produce energy, as a byproduct of these oxidative processes some oxygen free radical release.

❖ other sources for oxygen radicals to be "released" not normal": exposure of ionizing radiation, smoking/inhale smoke, exposure to atmospheric pollution, multiple previous infections(autoimmunity by macrophages and neutrophils during their action release FR) , diets with a lot of preservatives or genetically modified foods.

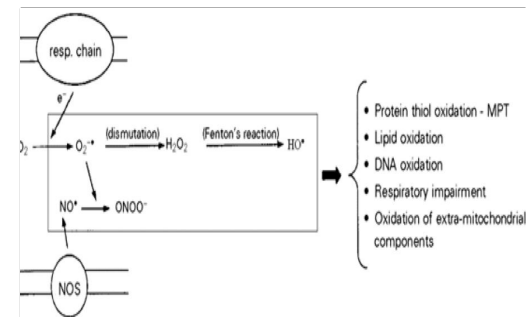




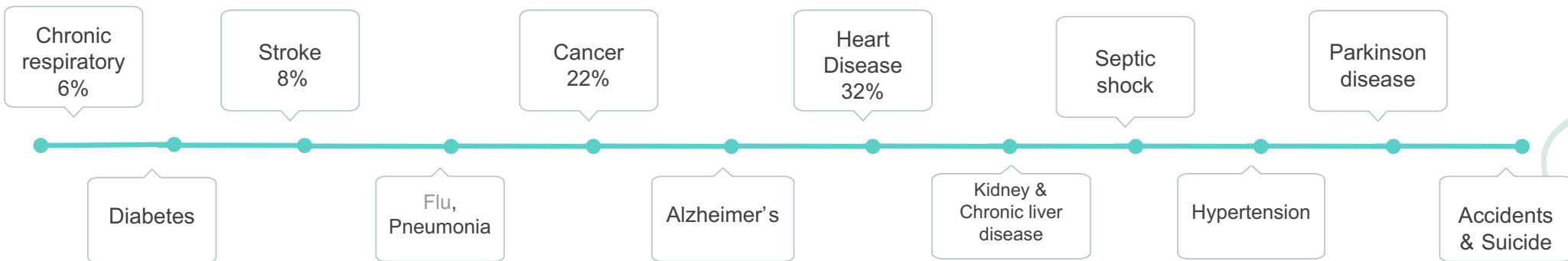
Mitochondria produce ROS



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



Leading Causes of Death Age 65+ "Medical Diagnoses"





Age related changes

1

Decreased height (**kyphosis**), lean body mass and body water, increased body fat.

2

Cardiac output decrease: 50 % decrease between ages of 18 and 80 years.

3

Lower metabolic rate,
Longer reaction times.

4

Declines in certain memory functions (**especially short term memory**)

5

A functional decline in audition , olfaction, and vision

6

Decline in kidney, pulmonary (max. breathing capacity), and immune functions, declines in exercise performance, and multiple endocrine changes

7

Consequence Changes drug in pharmacokinetics

8

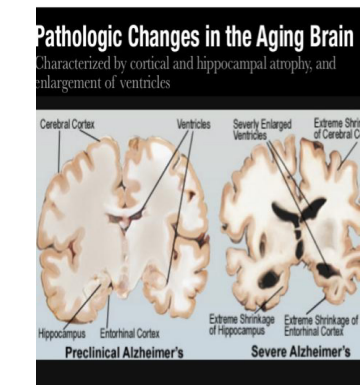
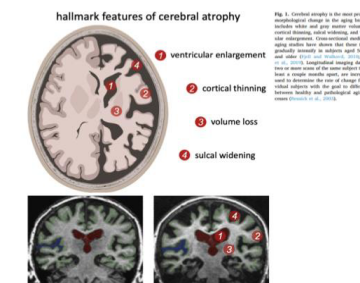
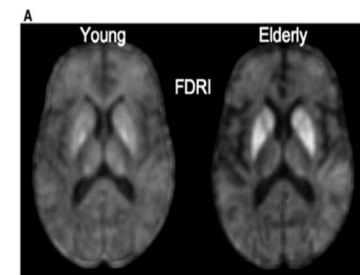
Declines in sexual activity and women menopause



Aging and Brain regions

The cerebellum is the youngest brain region least affected by aging.
the hippocampus and neocortical circuits are more affected

Structure	Regional function
Basal ganglia	Becomes bright in appearance/ MRI 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 (long term memory) Part of limbic system Involved in learning
Ventricles	Increase in size due brain shrinkage.
Grey matter	Decreases in size leading to thinning of the cortex (1% per year in some area while some areas are stable).
White Matter	Reduction in size due to neuronal atrophy in the deep brain. Involved in information transmission.
Brain weight	Decreased.
Cerebral blood flow	Decreased.





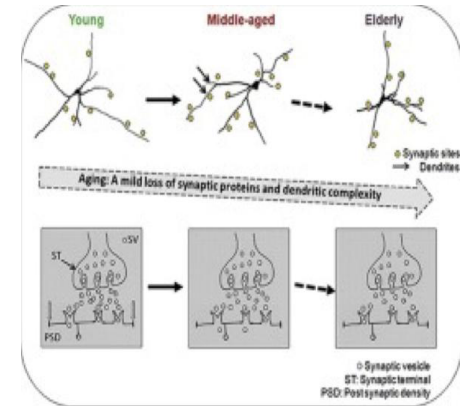
Aging changes in Nervous System

1-Structural changes:

Loss of neural circuits and brain plasticity:

- ❖ **Loss of the dendritic arborization:** Dendritic arbors and dendritic spines of cortical pyramidal neurons decrease in size and/or number in specific regions and layers of the brain.
- ❖ 50% decrease in spine number and density has been noticed in humans >50 years.
- ❖ **Neuronal loss** is normally expected in the aging brain but the ability to learn remains generally unchanged.
- ❖ **Age-related cognitive decline is not due to neuronal death only but also to synaptic alterations, functional and biochemical factors such as changes in enzymatic activity, chemical messengers (calcium), or gene expression in cortical circuits.**
- ❖ Intellectual functioning defined as (stored) memory increase with age
problem solving skills increase with age

438 team: Dendritic arborization also called dendritic branching, describes the tree-like branching out of dendrites to make new synaptic connections, the branches themselves are called spines.





Aging changes in Nervous System

2-Chemical changes:

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

1

Dopamine: decrease in the synthesis and receptors D1, D2, and D3 (could be responsible for the rigidity).

2

Serotonin: decrease in the synthesis, decrease in the receptor (5-HTT), and decrease in the transporter, **especially in the frontal lobe.**

3

Glutamate: Low glutamate concentration in motor cortex especially in the parietal gray matter and basal ganglia.



Aging changes in Nervous System

3-Psychological changes:

❖ Changes in attention:

- ❖ Many older adults notice a decline in their attentional abilities. This might not be due to neuronal dysfunction but could be related to **sensory deficits like hearing or vision that may make attention more difficult.**

❖ Changes in orientation (awareness of self in relation to one's surroundings):

- ❖ Mild difficulties in orientation may be a part of normal aging and not necessarily a sign of pathology.
- ❖ Could cause increased postural instability, altered gait and frequent falling (Matrix and minerals of bone are lost; growth hormone and growth factors diminish with decrease in protein anabolism).

❖ Altered mood

❖ Decreased IQ scores

❖ Benign senile forgetfulness

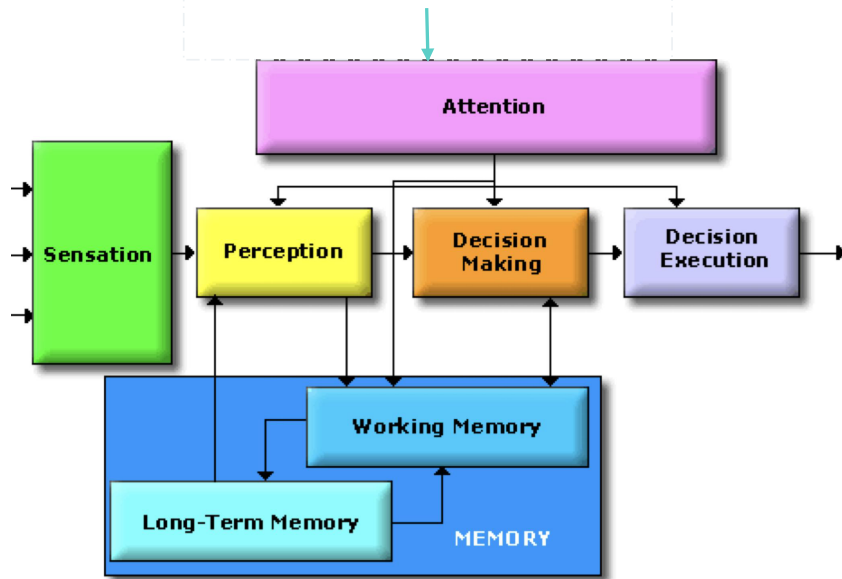
❖ Decreased vibratory sense.

❖ Delirium (fast onset serious change in mental abilities).



Aging changes in Nervous System

Cognitive changes in aging: memory & mental processing



Example of working memory:
Doing a task that involves multitasking such as Typing during a lecture, where you will be 1)typing 2)listening 3)lookin at the screen.

Short term memory
20 to 30 seconds

1. Immediate recall ↓
1. Working memory ↓ due to ↓
in processing speed and attention.

Which type of explicit memory is affected more? Episodic

let's say for example you 'perceive' someone knocking at the door by your 'sensory' ear. You pay 'attention': oh, my friend is at the door. Now you're pondering weather to open the door or not. And your 'memory' knows, as it recalls if you like this person enough to get up and open the door. And you 'decide' and finally 'execute' & open it



Aging changes in Nervous System

Long term memory



1. Declarative memory or explicit memory (in hippocampus and you retrieve it after consciously thinking about it)

- Semantic memory (words, language) is retained but decreased lately.
- Episodic memory (events) : start to decrease from middle age.



2. Skill memory or implicit memory (involves cerebellum, motor cortex, sensory cortex, visual areas and does not need awareness)

- Procedural memory is retained (driving).

Age Changes:

- 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 that involves hippocampus (surroundings & Skills) and is associated with awareness & attention unlike implicit memory but implicit memory is retained (eg; driving a car, tying a shoe).



Extra from Gyton

Gyton

MEMORY & ITS TYPES

Memory is the retention of learned information, in other words, the storage of information is the process we call memory. This is a function of synapses. That is each time a sensory signals reach the brain it passes through a series of synapses, the ability of the brain to recreate the same synapses without the presence of the stimulus is memory. This is done by long-term potentiation as we explained earlier in the lecture, long-term potentiation allows a signal to persist after cessation of stimulus.

- Memory for facts and events is called **declarative memory**, this is generally what we mean in everyday life when we mention memory, since it can be accessed by conscious control. For example information like “The capital of Saudi Arabia is Riyadh”, “I had scrambled eggs for breakfast” can be accessed by declarative memory.
- But we actually remember many other things, called **nondeclarative memories** fall into several categories. The type we are most concerned with here is *procedural* memory, or memory for skills, habits, and behavior, as the saying goes “You never forget how to ride a bicycle”, you may not remember the day you first rode the bicycle (declarative) but your brain knows what to do once you’re on one (non-declarative) Generally, *declarative* memories can be accessed for conscious recollection, and *nondeclarative*(implicit) memories cannot. However, the tasks we learn, as well as the reflexes and emotional associations we have formed, operate smoothly without conscious recollection.



Geriatric Syndromes

Dementia

Dementia is a syndrome of **progressive decline** (premature aging of the brain) in which multiple intellectual abilities deteriorate (worsen), causing **both cognitive and functional impairment**. dementia is a state of chronic confusion.

Delirium

Delirium is an **acute state** of confusion.

- Both dementia and delirium are characterised by:



Disorientation



Memory impairment



Paranoia and hallucination



Emotional lability



Sleep-wake cycle reversal

- **It's important to differentiate delirium and dementia.** Early identification and treatment of the underlying causes of delirium can improve outcomes.
- Delirium causes loss of independence, prolonged hospitalisation and increased health care costs and can be life threatening .
- It is often due to illnesses that are not related to the brain. Infections, medications and **organ failure** can cause an older person to become severely confused.



Alzheimer's Disease

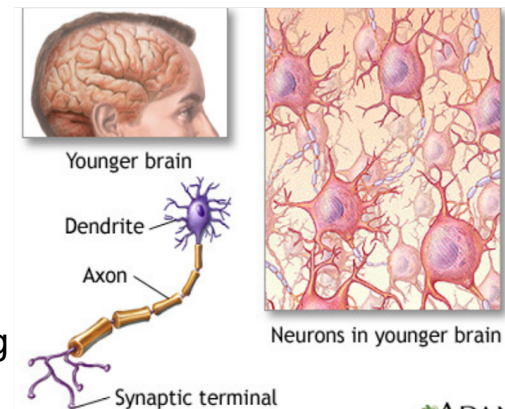
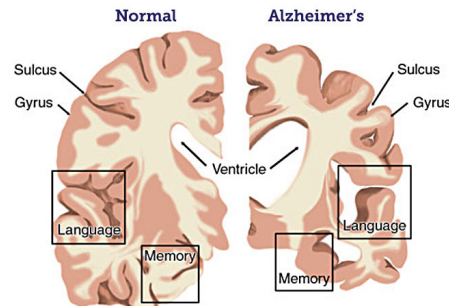
Definition

- Dementia and severe memory loss are not a normal part of aging (**remember: premature and severe**).
- They can be caused by brain diseases such as Alzheimer's disease, which scientists believe is associated with **amyloid plaques, tangles, neurofibrillary and the buildup of lipofuscin**; fine yellow-brown granules composed of lipid-containing residues of lysosomal digestion (a genuine marker for aged cells).
- Usually beginning in mid-adult life and progressing rapidly to extreme loss of mental powers similar to that seen in very very old age.

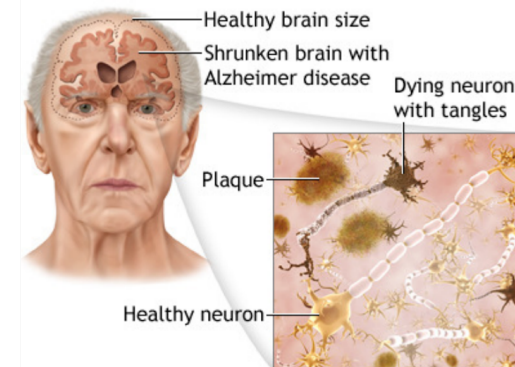
Features:

1	An amnesiac type of memory impairment
2	Deterioration of language
3	Visuospatial deficits.
4	Motor and sensory abnormalities, gait disturbances and seizures are uncommon until the late phases

Brain Cross-Sections



ADAM





Amyloid plaques

1 Plaques have not been found to be a consistent feature of normal aging. It is **hallmark of Alzheimer's disease**.

2 There is accumulation of **amyloid plaques between and in nerve cells** (neurons) in the brain.

3 Amyloid is a general term for protein fragments that the body produces normally (bone marrow). Beta amyloid is a protein fragment snipped from an amyloid precursor protein (APP); a Lagrange membrane protein.

4 In a healthy brain, these protein fragments are broken down and eliminated. Therefore, plaques have not been found to be a consistent feature of normal aging.

5 In Alzheimer's disease the fragments accumulate to form hard, insoluble plaques.

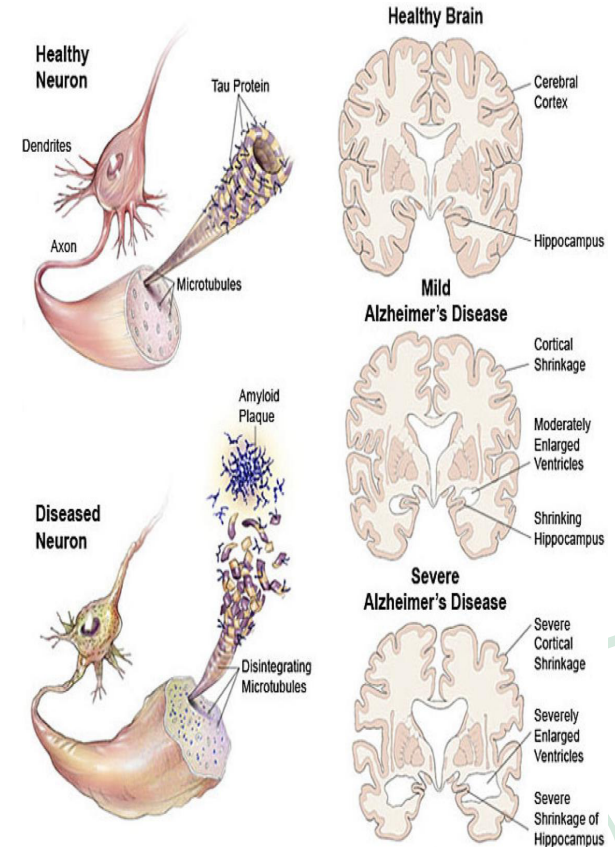
6 Healthy food, vitamin D, antioxidants, hormones and dark chocolate might help to clear the brain from amyloid beta.

Amyloid plaques are seen in very old age 80 but if we find it in a person who is 40 this is due to Alzheimer's disease



Neurofibrillary Tangles

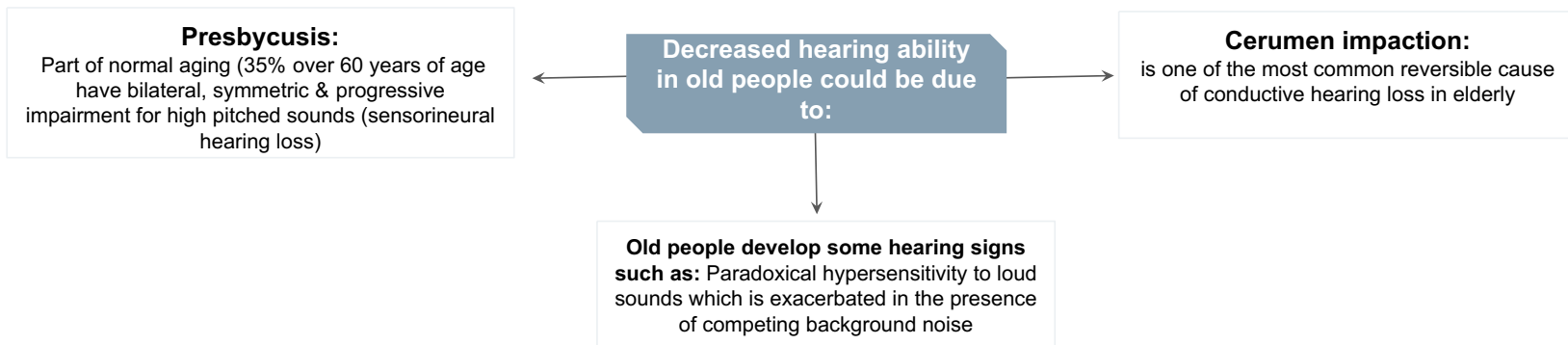
- These are insoluble twisted fibers found inside the brain's cells (paired helical filaments (PHF)).
- Consist primarily of a protein called **tau**, which forms part of a structure called a microtubule. The microtubule helps transport nutrients and other important substances from one part of the nerve cell to another.
- In normal, non-demented aging, the number of tangles in each affected cell body is relatively low and restricted to the olfactory nucleus, parahippocampal gyrus and amygdala
- In **Alzheimer's disease**, the tau protein is abnormal and the microtubule structures collapse.
- 10-15% over age of 65 and 50% over age of 85.
- Mutations of presenilin 1 and 2 (Down's syndrome similar mutations).
- Estrogen slows the progress of Alzheimer.





Disorders of senses associated with aging

Hearing



- The hearing loss begins in the sixth decade and is typically symmetrical, beginning in the high-frequency range (carry the consonant sounds)
- Perform quite well in one-on-one communication in a quiet room.



Disorders of senses associated with aging

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.

Lens of eye become yellows making it more difficult to see red and green colors.

Opacification of lens (**Cataract**) Cloudy lens

Night vision not as acute.

Pupil less sensitive to light.

Sensitivity to glare increases. (**Photophobia**).

Pain and sense of touch

Safety Implications:

- ❖ **Lessened ability to recognize** dangerous levels of **heat**.
- ❖ **Lessened** ability of body to **maintain temperature**.
- ❖ Tendency to **develop bruises, skin tears more easily** .

With age, skin is not as sensitive as in youth due to:

Loss of elasticity

Loss of pigment

Reduced fat layer



Disorders of senses associated with aging

Sleep patterns



It tends to become more **fragmented**, with more awakenings during the night. (**Three or four times** each night.)



Total sleep time 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 (the average elderly person takes 18 minutes to fall asleep)



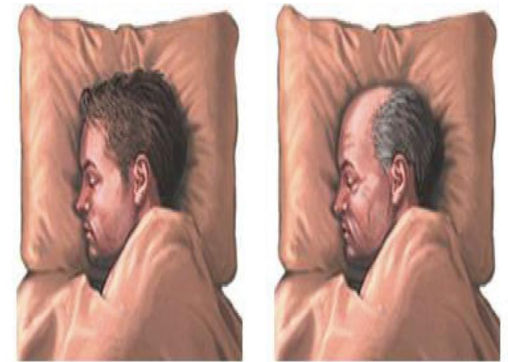
The amount of time that the aging brain spends in deep sleep decreases from 20-25% for a 30 years old to only 5-10% for most 70 years old but the proportion of sleep that is REM sleep remains largely unchanged.



Sleep disturbances include: staying asleep, leg movements, problems with breathing and awaking in the middle of the night.

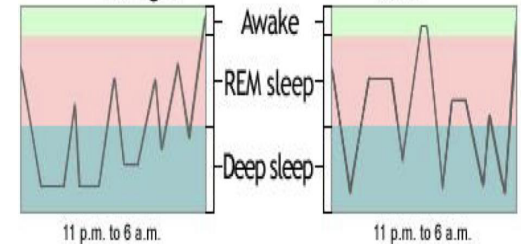


Alcohol also contributes to sleeping disturbances. Alcohol reduces or can possibly even eliminate REM and dreaming. Tobacco use has been linked to causing daytime drowsiness for women and unpleasant dreams for men.



Younger

Older





Disorders of senses associated with aging

Decline in Autonomic function

- Aging is associated with **decreased Heart rate variability** which is associated with increased mortality (Normal HRV ranges in adults between 20-200 milliseconds which is a slight fluctuation of heartbeats upon the time).
- For example:
 - Changing position from supine to standing may trigger dizziness more frequently with ageing which reflects **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.
 - Systolic BP increases due to (decrease distensibility of arteries) **pressure rises with age**. Diastolic pressure also rises with age but it starts to decrease **in middle age** as the stiffness of arteries increases. **Consequently/ Therefore**, pulse pressure increases with age.
 - Total body water tend to decrease with age 46-52%



Disorders of senses associated with aging

Carotid sinus hypersensitivity

1

Carotid sinus syncope occurs when there is an exaggerated vagal response to carotid sinus stimulation.

2

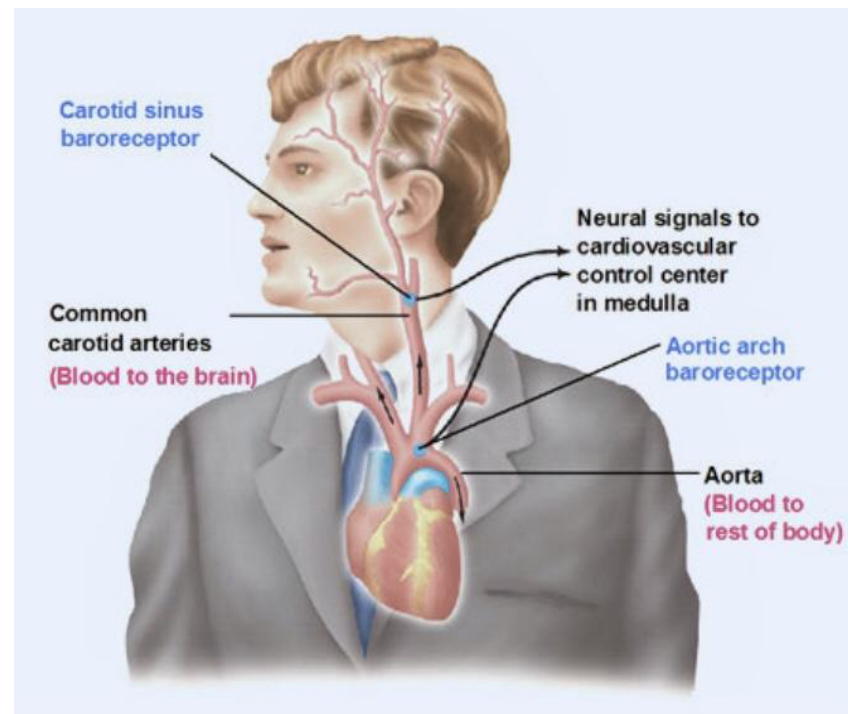
Provoked by wearing a tight collar, looking upwards or turning the head.

3

Carotid sinus syndrome occurs in the elderly and mainly results in bradycardia.

4

could be a cause of atrioventricular block(do not massage carotids simultaneously)



Touching the carotid artery > Pressure increases > Sends signals to the brain > The brain tells the heart to slow down > Bradycardia > Syncope (collapse).



How not to speed the process of aging?

1

Decrease caloric intake (Decrease free radicals)

2

Physiological status (Decrease cortisol)

3

Hormone replacement therapy.

4

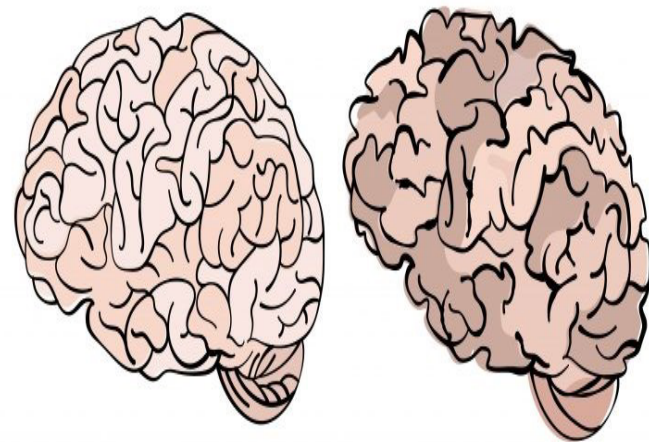
Physical activity.

5

Regular bedtime routines would improve sleeping problems in the elderly

6

Family and society support.





TEST YOURSELF !

1) All the following are neurological symptoms caused by loss of dopamine with age EXCEPT:

A) Increased rigidity

B) Changes in cognitive flexibility

C) Increased dendritic arborization

D) Decreased arm swing

2) Oxygen free radicals & reactive oxygen species are produced in

A) Golgi apparatus

B) Mitochondria

C) rER

D) Environment

3) increases in size during aging due to brain shrinkage.

A) Subarachnoid space

B) Ventricles

C) Hippocampus

D) Both A & B

4) During aging, there is a in grey matter and in white matter.

A) Increase - decrease

B) Decrease - increase

C) Increase - increase

D) Decrease - decrease

1) C
2) B
3) D
4) B



Team Leaders



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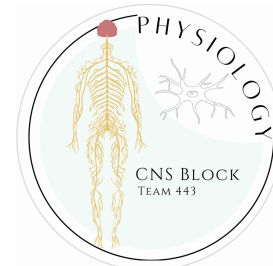
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Abdullah alzamil

Mohammed Alqutub

Salmam Althunayan

faisal alzuhairy

Mohammed Alarfaj

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Nazmi Adel Alqutub

Faisal Alshowier

Ziad Alhabardi

Osamah almubbadel

Abo owayed

💡 Special Thanks to Physic logy **Team441**
💡 Team logo and design was done by **Rafan Alhazzani**
💡 Thanks to **ALEEN ALKULYAH** for Helping with the design!



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