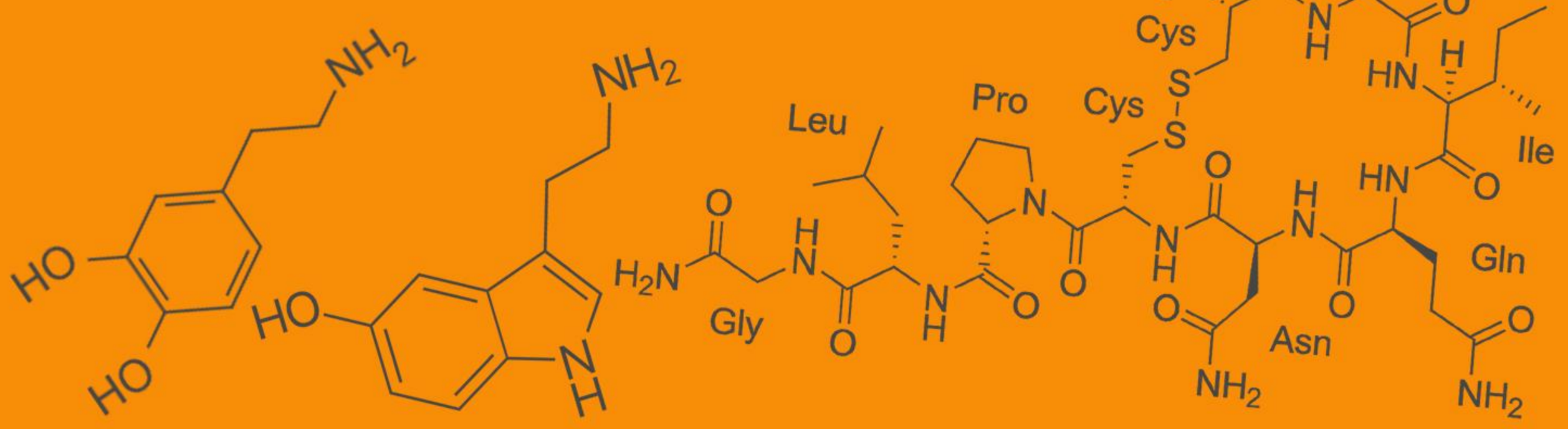
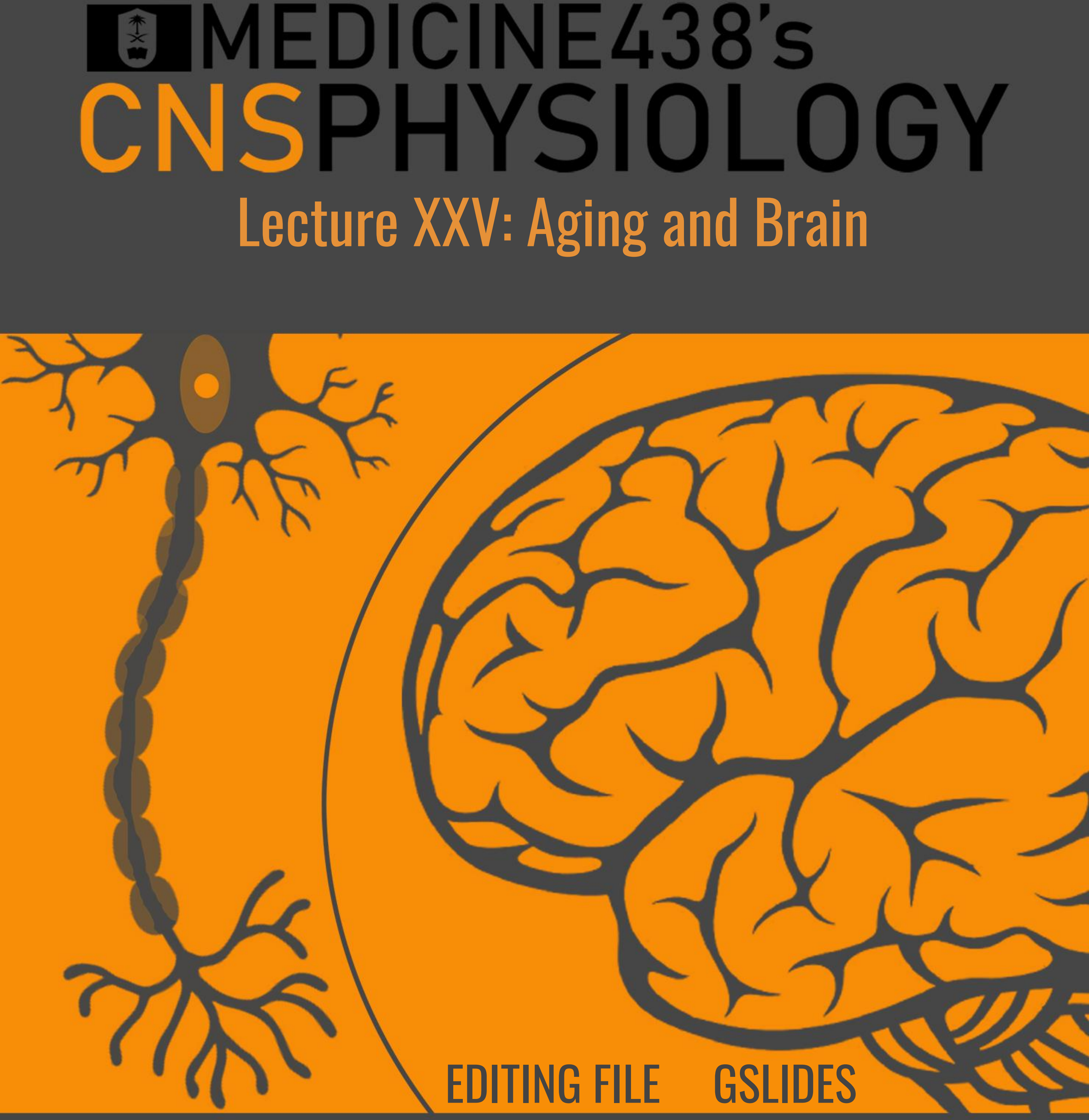


MEDICINE438's CNSPHYSIOLOGY

Lecture XXV: Aging and Brain



EDITING FILE GSLIDES

IMPORTANT MALE SLIDES EXTRA FEMALE SLIDES LECTURER'S NOTES

1 AGING AND BRAIN

Lecture Twenty Five

OBJECTIVES

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 AND DEVELOPMENT

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. *We have two kidneys, one functions while the other acts as a reserve.*

- AGING IN THE DEVELOPMENT AGENDA *"Ageing is a development issue. Healthy older persons are a resource for their families, their communities and the economy."* — WHO Brasilia Declaration on Ageing, July, 1996
- KEYS TO SUCCESSFUL AGING (1) Low probability of a disease or a disability (2) Active engagement with life. (3) High cognitive and physical functional capacity.

THE TERM AGING AND ITS TYPES

UNIVERSAL AGING Age changes that all people share Eg: graying of the hair, wrinkles.

PROBABILISTIC AGING Age changes that may happen to some (an example is: type two diabetes).

CHRONOLOGICAL AGING Referring to how old a person is.

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

BIOLOGICAL AGING An organism's physical state as it ages. Eg: the liver tissue of an alcoholic 27-year-old appears older than it actually should.

MITOCHONDRIA AND FREE RADICALS

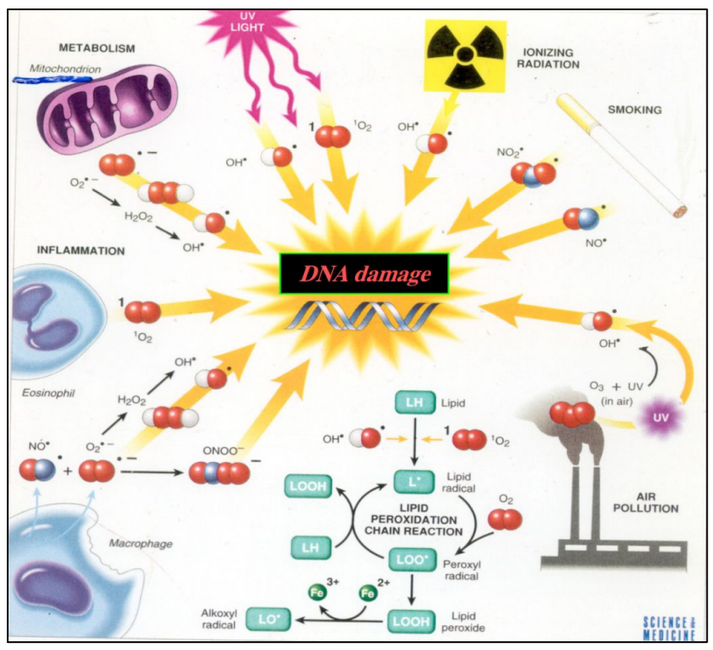


Figure 25-1

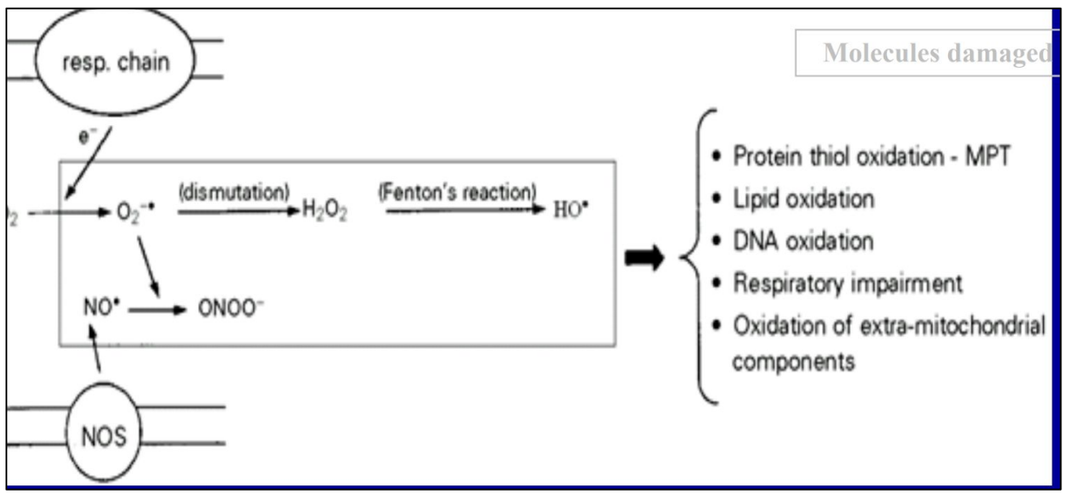


Figure 25-2

Oxygen - free radicals (O_2^-, H_2O_2, HO^-) and reactive oxygen species (ROS) are produced in Mitochondria ($NO + O_2 \rightarrow ONOO^-$).

"The respiratory chain (resp. chain) produces superoxide radicals (O2 -·), which generate hydrogen peroxide (H2O2) and hydroxyl radicals (HO·). Mitochondrial nitric oxide synthase (NOS) produces nitric oxide (NO·), which combines with O2 - · to generate peroxinitrite (ONOO-). All these ROS may cause mitochondrial and cellular damage if present in excess. MPT, Mitochondrial permeability transition." — Kowaltowski 2002

"Leading Causes of Death Age 65+: *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

PRESENT ONLY IN FEMALE SLIDES

THEORIES OF AGING

Divided based on the name of hypothesis, and how it may work:

1. **GENETIC** Aging is a genetic program activated in postreproductive life when an individual's evolutionary mission is accomplished. (BOX 25-1)
2. **OXIDATIVE STRESS** Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses.
3. **MITOCHONDRIAL DYSFUNCTION**[1] A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change.
4. **HORMONAL CHANGES**[2] The decline and loss of circadian rhythm in secretion of some hormones produces a functional hormone deficiency state.
5. **TELOMERE SHORTENING** Aging is related to a decline in the ability of cells to replicate (BOX 25-2)
6. **DEFECTIVE HOST DEFENSES**[3] The failure of the immune system to respond to infectious agents and the overactivity of natural immunity create vulnerability to Infection.
7. **ACCUMULATION OF SENESCENT CELLS** Renewing tissues become dysfunctional through loss of ability to renew

BOX 25-1: EXTRACURRICULAR: BIOLOGY

The meaning of this theory is that our age is largely determined by our genes, and that evolution molded our genes through successful generation to trigger self-destruction whenever our evolutionary mission, reproduction, was accomplished. Therefore, a shorter lifespan for each individual favored survival of the whole species by keeping our numbers in check.

AGE-RELATED CHANGES

Decreased height(collapse of vertebrae), lean body mass and body water(d.t:increased fat), increased body fat, consequential changes in pharmacokinetics.

- A lower metabolic rate
- Longer reaction times
- Declines in certain memory functions especially short term memory
- 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

BOX 25-2: CLINICAL RELEVANCE

TELOMERES

Telomeres are short repeated sequences of non-coding DNA present at end of chromosomes and are gradually lost with each cell division, they act to protect DNA, they also bind protein to prevent DNA damage. Telemorase can synthesize telomeres, but is inactivated in most cells. Some think activation of telomerase in some cells can help prolong life and delay aging.

FOOTNOTES

1. It really shouldn't come as a surprise that mitochondria govern even our lifespan in some extent, after all, an accepted theory for the **origin of mitochondria is that it's a remnant of a bacterium** belonging to a group called alphaproteobacteria,which includes Rickettsia, the pathogen that causes typhus fever, the primordium mitochondria got integrated into an archaea during the early origins of life. Gradually the bacteria lost most of its genes, and the essential ones were made transferred to the nucleus of archaea, the genes of that old bacteria still remain within our genome. However, some genes are still retained within the mitochondria, around 37 genes. Mutations in these genes can adversely affect the cell by production of free radicals.
2. Aging is associated with **decreased production of melatonin,** melatonin acts as a free radical scavenger and an antioxidant as well. It is produced by the circadian rhythm during low exposure to light.
3. **Defective proliferation of T-cells and B-cells in aging** causes difficulties in mounting an immune response, remember an antigen presenting cell must activate T-cells, if there is defective proliferation then we can expect that the natural immunity will increase in activity until a more specific response can be mounted.

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.

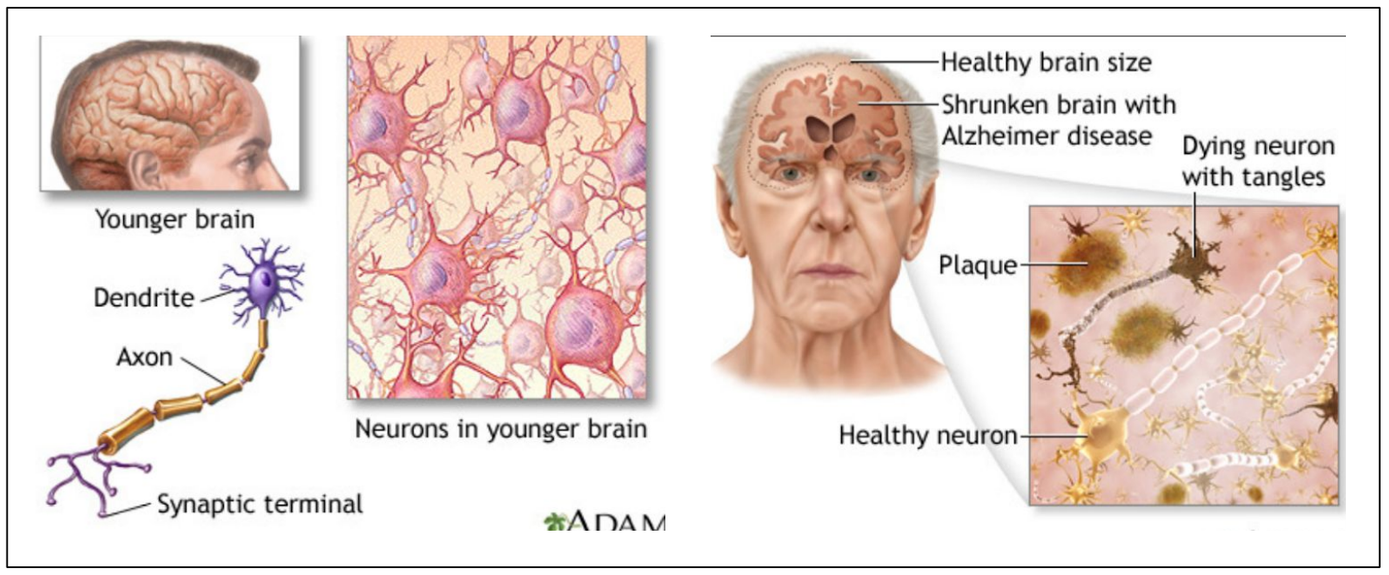


Figure 25-3

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** (BOX 25-3).

- 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.

BOX 25-3: ROBBINS AND COTRAN PATHOLOGIC BASIS OF DISEASE

LOU GEHRIG'S DISEASE

Other names include Amyotrophic lateral sclerosis (ALS), and Motor neurone disease (MND).
ALS is a progressive disorder in which there is loss of upper motor neurons in the cerebral cortex and lower motor neurons in brain and spinal cord.

- Loss of these neurons causes weakness of denervated muscles. It affects males more than females, and commonly emerges in the fifth decade or later.
- The anterior roots of the spinal cord are thin due to loss of anterior horn cell fibers, and the motor cortex may be atrophic in especially severe cases. The number of AHCs is decreased throughout the spinal cord, with reactive gliosis (in reactive gliosis we frequently encounter gemistocytic astrocytes instead of fibrillary. Gemistocytic astrocytes have a prominent nucleolus, indicating that the process of gene transcription is active, with the cell release the products of its genes)
- Degeneration of corticospinal tracts due to loss of UMNs (therefore we can expect a positive babinski sign)

REGIONAL CHANGES IN AGING NERVOUS SYSTEM

STRUCTURE	REGIONAL FUNCTION
Basal Ganglia	Becomes bright in appearance due to iron accumulation (movements affected)
Hippocampus	Reduction in size due to cell loss in the structure. Par of limbic system Involved in learning & long term memory
Ventricles	Increase in size due brain shrinkage.
Subarachnoid Space	Increase in size due brain shrinkage.
White Matter	Reduction in size due to neuronal atrophy in the deep brain, Involved in information transmission.

Table 25-1 The cerebellum is the youngest brain region least affected by aging.

BOX 25-4: CROSSMAN NEUROANATOMY & GUYTON AND HALL & NEUROSCIENCE: EXPLORING THE BRAIN

THE HIPPOCAMPUS

We're gonna be mentioning this structure numerous times throughout this lecture, it would be remiss of us if we didn't give a brief overview on this important structure. It is the most medial portion of temporal cortex, it has a lot of roles including memory storage, almost any type of sensory stimulus causes an activation of a part of the hippocampus, the hippocampus in-turn send many outgoing signals through a specialized structure called the fornix to other parts of the brain, as seen in the figure. For people who had their hippocampus surgically removed for epilepsy treatment, they still retained their stored memory. (mainly way we specify the medial portion of temporal lobe to be important in memory) However these people were not able to store new memories, (this is called anterograde amnesia) most importantly declarative type of memory in long-term memory, or even intermediate memory lasting more than a few minutes. (memory types discussed in BOX 25-6)

- Stimulation of the hippocampus can cause pleasure, rage, passivity. An important feature of the hippocampus is that it is easily excited by weak electrical stimuli, after the stimulus ends, the hippocampus remain active for several seconds, this is called long-term potentiation (the ability of signals to continue to fire after cessation of stimulus). A reason for this is that the hippocampus has a different type of cortex, having only three nerve cell layers! Unlike the rest of the cerebrum that has six nerve cell layers.

CHANGES ASSOCIATED WITH HEALTHY AGING

STRUCTURAL CHANGES

Loss Of Neural Circuits And Brain Plasticity Age-related plasticity deficits in animals is the result of age-induced alterations in calcium regulation.

- Some areas would be more vulnerable to aging eg: **hippocampus and neocortical[1] 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, 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 Changes In Neuronal Morphology Dendritic arbors and dendritic spines[2] 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[3] One of the important differences between normal aging and pathological aging is the location of neurofibrillary tangles.[3] 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.

BOX 25-5: CLINICAL RELEVANCE

PLASTICITY

Whenever we learn a new skill, acquire a new memory something must change within our brain to permanently save these changes. The ability of the brain to modify its own structure in response to experience is called plasticity. Memories, skills, and thoughts are merely the result of sequence of maintained synapses that exist in the brain, we recognize these maintained synapses as memories or thoughts. These maintained synapses create circuits, like the reverberatory circuits from earlier lectures, which manifest as memories. Therefore with age when we lose white matter, we can naturally expect loss of synapses and consequently the circuits maintaining our memories as well as the ability of the brain to mold itself due to loss of plasticity.

FOOTNOTES

1. There are two types of cortices in the cerebrum, the more evolved and commonest, the neocortex 90%, which is composed of **six** layers, the other type is the allocortex, 10%,, which is made only of **three** layers, like the **hippocampus**.
2. 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.
3. Definition of neurofibrillary tangles and further explanation can be found later in the lecture.

CHANGES ASSOCIATED WITH HEALTHY AGING (CONTINUED)

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** D1, D2, and D3.
- 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.

Glutamate is another neurotransmitter that tends to **decrease** with age.

- Lower glutamate concentration in the motor cortex, **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

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.

- Small number of studies have examined whether there is a normal decline in orientation among healthy aging adults.
- Results have been 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.

- A large review of studies on cognition and aging suggest that this hypothesis has not been wholly supported.
- 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** (like *hippocampus*) are especially vulnerable to age-related decline.

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[1] and/or working memory demands[2], and production of such sentences

GENETIC CHANGES

Research focused on discovering the genetic component in developing alzheimer's disease has also contributed greatly to the understanding the genetics behind normal or "nonpathological" 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[3] in the genome.**

FOOTNOTES

1. Syntax: the arrangement of words to create a meaningful sentence, in contrast, semantics (next page) refers to meaning of sentences or the logic behind it rather than pure linguistics.
2. Working memory is a temporary type of memory that requires rehearsal, like when someone tells you their phone number, you can retain it for a limited period of time by repeating the number to yourself, therefore working memory is information "held in mind".
3. Where gene transcription starts.

AGING NERVOUS SYSTEM

Changes

1. Decreased brain weight
2. Decreased cerebral blood flow
3. Decline in memory
4. Alteration in CNS neurotransmitters
5. Decreased vibratory sense.

Consequences

1. Drug toxicities
2. delirium
3. Decreased IQ scores
4. "Benign senile forgetfulness"
5. Altered mood
6. Increased postural instability
7. Altered gait, falls, accidents

Table 25-2

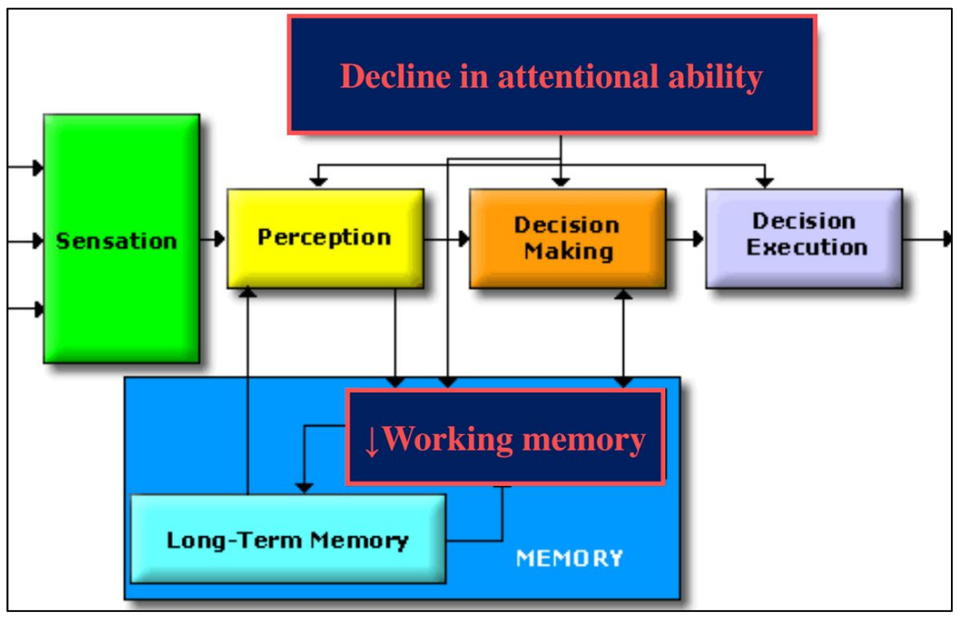


Figure 25-4, let's say for example you 'perceive' someone knocking at the door by your 'sensory' ear. You pay 'attention': oh, my friend is at the door. Now you're pondering weather to open the door or not.
And your 'memory' knows, as it recalls if you like this person enough to get up and open the door. And you 'decide' and finally 'execute' & open it.

COGNITIVE CHANGES IN AGING: MENTAL PROCESSING

1. DECLARATIVE MEMORY OR EXPLICIT MEMORY

A. Episodic Memory (Events), B. Semantic Memory (Late to decrease) (Words, language)

- **Hippocampus** is involved in this type of memory and is associated with consciousness.

2. SKILL MEMORY OR IMPLICIT MEMORY OR NON-DECLERATIVE MEMORY: It does not involve awareness. involves cerebellum, motor cortex, sensory cortex, visual areas

AGE CHANGES

1. There is decline in mental processing via reduction of attentional ability and decline in ability in forming working memory (mainly includes short term memory).
2. There is decline in explicit memory that involves hippocampus (surroundings & Skills) and is associated with awareness & attention unlike implicit.

BOX 25-6: NEUROSCIENCE: EXPLORING THE BRAIN & GUYTON AND HALL

MEMORY AND 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.

NERVOUS SYSTEM CHANGES

Molecular

- Loss of RNA(messenger and transcription) which is responsible for protein and neurotransmitter synthesis. While the DNA is spared.
- Loss of lipids, and lipid turnover rate, and a *decrease* in catabolism and synthesis(which decreases brain mass).
- Aging leads to **increased** cerebral amyloid[1](Protein fragments).
- Average amount of brain protein is *reduced* with marked loss in multiple enzymes (*carbonic anhydrase* and the *dehydrogenases*)[2] but with a relative *increase* in abnormal proteins such as *amyloid in tangles and plaques.*

Clinical

- Cerebral atrophy shows up on CTs and MRI scans.
- Reduced Sympathetic nervous system activity.
- Reduced neurotransmitter levels(Dopamine,serotonin, glutamate)
- Abnormalities in EEG tracings[3].
- Increased risk of stroke.
- Lowered seizure threshold

Functional

- Neuronal loss is normal in the aging brain but the *ability to learn remains generally unchanged.*
- OBJ There is **loss of dendritic arborization**(branching) which leads to loss of function.
- **Recall memory is affected more** & cognitive function in normal.intellectual functioning defined as "stored" increase.
- problem-solving skills increase.
- Changes in sleep pattern, interrupted sleep at night leading to feeling sleepy all day (More frequent naps).

Table 25-3 Showing changes that occurs with age in the nervous system.

GERIATRIC SYNDROME

1. Dementia (gradual) and Delirium (sudden).
2. OBJ Falls, due to loss of vibratory receptor..
3. Pressure ulcers [4] in bedridden elders which could lead to septicemia and death.
4. Urinary Incontinence due to reduced sympathetic activity on bladder and sphincter.
5. Functional Decline

CLINICAL RELEVANCE

Cholinesterase inhibitors have been shown to be effective in slowing the progression of the Dementia by potentiating the action of available acetylcholine. These drugs—donepezil, rivastigmine and galantamine— inhibit acetylcholinesterase, preventing the metabolism of endogenous acetylcholine, and are used in the early stages of the disease for mild cognitive impairment. Especially, Alzheimer.

BARORECEPTOR REFLEX

One of the Quick operations (within few seconds). when we suddenly stand, we develop **postural hypotension**, so baroreceptor in in the carotid sinus and in the aortic arch send impulses to cardiovascular center via autonomic (**sympathetic**) reflexes which leads to vasoconstriction & increasing heart rate-adjusting cardiac output and peripheral resistance- in order to restore normal BP.

CAROTID SINUS HYPERSENSITIVITY[5]

Carotid sinus syncope occurs when there is an exaggerated vagal response to carotid sinus stimulation. Carotid sinus syndrome occurs in the elderly and mainly results in bradycardia.

- Most common etiologie is an *atrioventricular block.*
- Provoked by wearing a tight collar, looking upwards or turning the head
- **Do not massage both carotids simultaneously.**

FOOTNOTES

1. **Amyloids** are aggregates of proteins that become folded into a shape that allows many copies of that protein to stick together, forming fibrils.
2. Carbonic anhydrases (**CA**) are enzymes involved in the reversible conversion of carbon dioxide and water into bicarbonate and protons. Which also plays a role in the regulation of Aβ-induced neuronal and microvascular toxicity
3. Guyton and Hall: **Theta** waves also occur in many brain disorders, often in degenerative brain states.
4. injuries to the skin and underlying tissue, primarily caused by **prolonged pressure** on the skin.
5. To understand carotid sinus hypersensitivity, an increase in pressure on the carotid sinus in the neck sends strong discharge through CN X and CN IX to the vasomotor centers, those centers respond by inhibiting the sympathetic system. In contrast, when pressure is decreased, the firing of the cranial nerves is reduced, and the vasomotor center activates the sympathetic nervous system.

8 AGING AND BRAIN

Lecture Twenty Five

DEMENTIA	DELIRIUM
A syndrome of **progressive** decline in which multiple intellectual abilities deteriorate, causing both cognitive and functional impairment.	An **acute** state of confusion Delirium may be the only manifestation of a life-threatening illness in the older adult (infection, drugs).
ALZHEIMER'S DISEASE	Example: 1. Hyperactive delirium, may include restlessness, agitation, rapid mood changes or hallucinations, and refusal to cooperate with care. 2. Hypoactive delirium, may include inactivity, sluggishness, abnormal drowsiness, or seeming to be in a daze. 3. Mixed delirium.
Dementia of Alzheimer type 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.	

Table 23-2

FEATURES OF ALZHEIMER

1. An **amnesic** 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 of the 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.

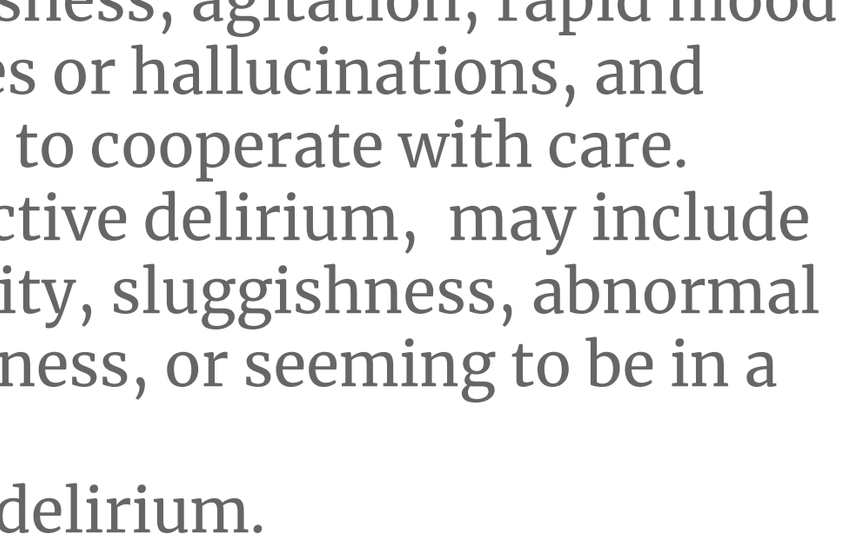


Figure 23-5

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.

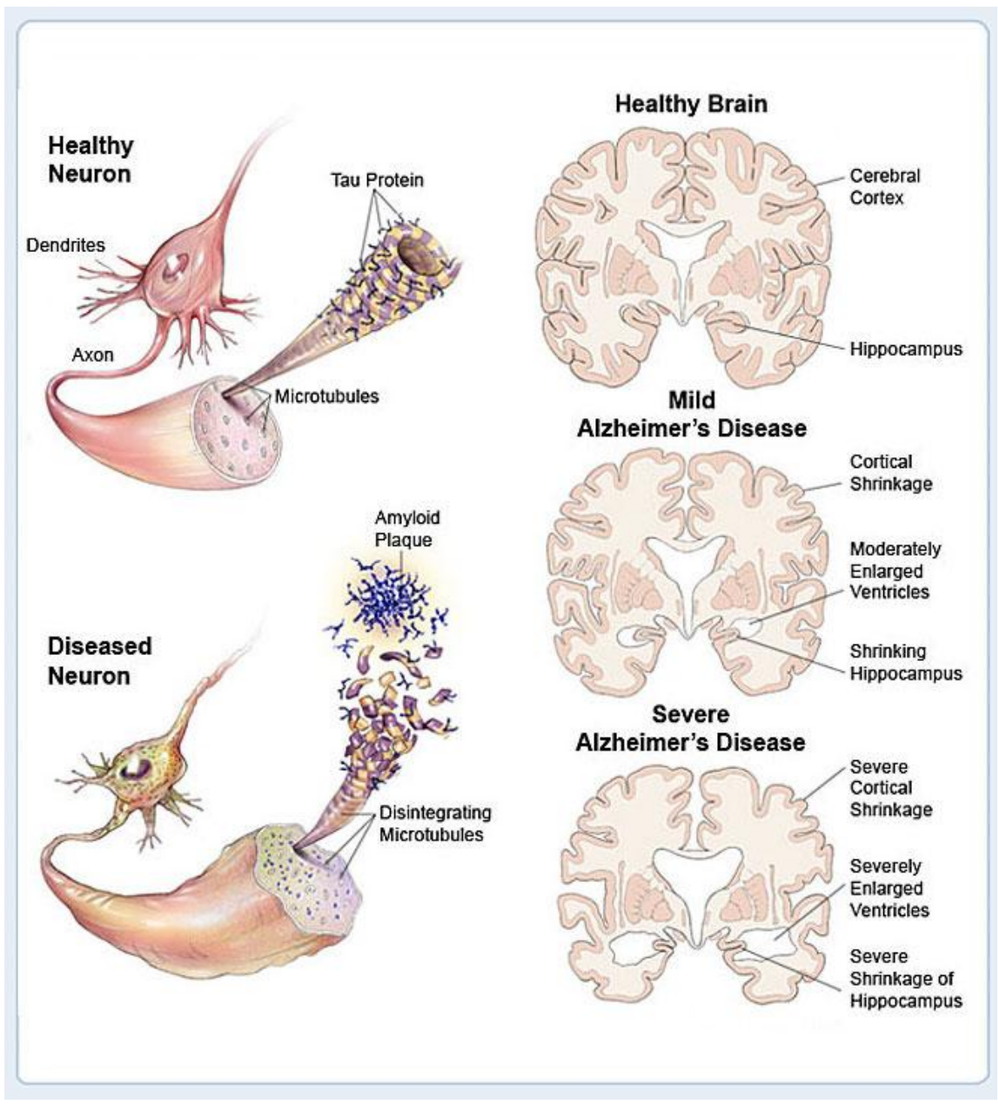


Figure 23-6

BOX 25-7: ROBBINS BASIC PATHOLOGY

ALZHEIMER'S

Alzheimer's disease (insidious onset of impaired higher intellectual function) is the most common cause of dementia in the elderly population. Death usually occurs from intercurrent pneumonia or other infections. A peptide called beta amyloid, or A β, accumulates in the brain over time, initiating a chain of events that result in AD. Mutations in APP(transmembrane protein amyloid precursor protein) or in components of enzymatic components lead to familial AD by increasing the rate at which Aβ is generated.

- The APP gene is located on chromosome 21, and the risk of AD also is higher in those with an extra copy of the APP gene, such as patients with trisomy 21 (Down syndrome).

The presence of Aβ also affects the protein tau leading to its redistribution from axons into dendrites and cell bodies, where it aggregates into tangles, which also contribute to neuronal dysfunction & cell death.

- Keep in mind that tangles are not specific to AD, being found in other degenerative diseases as well.

9 AGING AND BRAIN

Lecture Twenty Five

DISORDERS OF SENSES THAT ARE 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 *yellows*** making it more difficult to see red and green colors.
- Sensitivity to glare increases (Photophobia).
- Opacification of lens (cataracts)
- Pupil less sensitive to light.
- Night vision not as acute.
- Arcus Senilis (a white, grey, or blue opaque ring in the corneal margin (peripheral corneal opacity), or white ring in front of the periphery of the iris)

Sensorineural hearing loss

Damage to the hair cells of the organ of Corti may be caused by:
- intense noise
- viral infections
- ototoxic drugs (example: salicylates, quinine[1] and its synthetic analogues, aminoglycoside antibiotics, loop diuretics such as furosemide and ethacrynic acid, and cancer chemotherapeutic agents such as cisplatin)
- fractures of the temporal bone
- meningitis
- cochlear otosclerosis
- Ménière's disease[2]
- aging.

-**Presbycusis**: Part of normal aging (35% of people over 60 years of age have bilateral symmetrical progressive impairment or high-pitched sound **sensorineural** hearing loss)

-**Cerulean impaction**: is one of the most common reversible causes of **conductive** hearing loss in elderly.

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

Basically, slow persistent decline in hearing with age. The hearing loss begins in the six decades and is typically symmetrical, beginning in the high frequency range.

Taste

Disorders of the sense of taste are caused by:
- transport loss
- sensory loss
- neural loss
- Sensory gustatory losses are caused by:
  - -inflammatory and degenerative diseases in the oral cavity.
  - -A vast number of drugs, particularly those that interfere with cell turnover[3] such as antithyroid and antineoplastic agents.
  - -radiation therapy to oral cavity and pharynx.
  - -viral infections.
  - -endocrine disorders.
  - - neoplasms.
  - -aging.

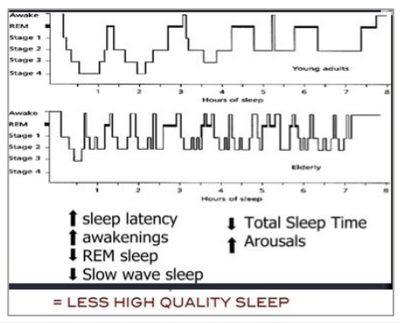
- Dorsum surface shows loss of filiform papilla.
- Foliate papillae more prominent.
- Fissures increase.
- Dryness of the mouth.
- Ventral surface shows nodular varicose enlargement (caviar tongue).
- Loss of taste buds.

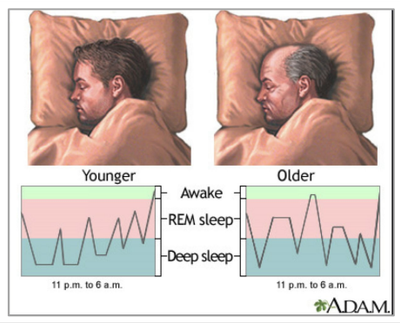
Pain and touch

With age, skin is not as sensitive as in youth due to:
- Loss of elasticity
- Loss of pigments
- Reduced fat layer

Safety Implications:
- **Decreased ability to recognize** dangerous levels of **heat**.
- **Decreased** ability to **maintain temperature**.
- Tendency to **develop bruises, skin tears**.

Sleep





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

Autonomic

Ageing is the associated with **depressed heart rate for variability** which is associated with increased mortality. For example changing position from supine to standing may trigger dizziness more frequently with ageing reflect the **diminished cardiovascular sympathetic modulation** and significant decline in overall autonomic function. Variation in heart rate response to deep breathing and Valsalva manoeuvre(forceful attempted exhalation against a closed airway) is decreased because of impaired vagal control of heart rate with increasing age.

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 from the ages of 40-70, 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%

FOOTNOTES

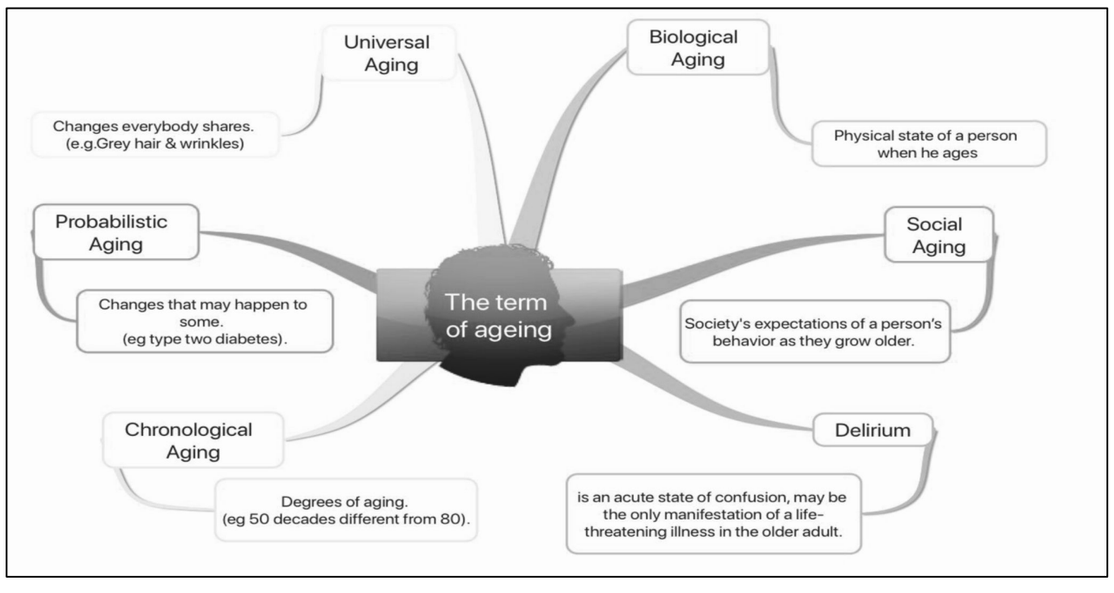
1. Quinine used to treat malaria or nocturnal leg cramps can cause temporary hearing loss.
2. Mainly due to: Endolymphatic hydrops is a disorder of the inner ear. It consists of an excessive build-up of the endolymph fluid
3. A term used to describe the constant shedding of dead skin cells and subsequent replacement with younger cells.

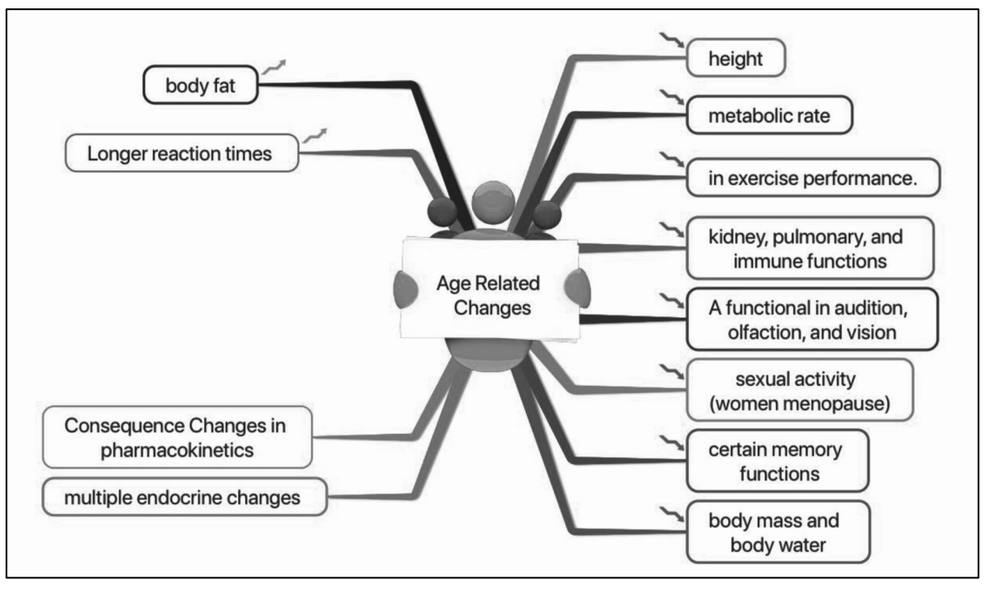
BRIEF GERIATRIC ASSESSMENT INSTRUMENT

DOMAIN	INSTRUMENT	COMMENT
Cognition	IQ	
Dementia	MMSE (mini-mental state examination).	Widely studied and accepted.
	Time and change (T&C) test. How much time he takes to do a specific task to move to the other one.	Sensitive and quick.
Delirium	CAM (confusion assessment method).	Sensitive and easy to apply.
Affective disorders (also called mood disorders)	GDS 5-question form (Geriatric depression scale) Qs to evaluate the depression	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	
Nutritional status	Weight loss of >4.5 kg (>10 lb) in 6 months or weight <45 kg (<100 lb) in general.	We fear if they lose massive weight in short time
Gait and balance	"Timed Get Up and Go" test	Requires no special equipment.

SUMMARY

- Cerebellum is the youngest brain region least affected by aging
- Recall memory is affected more than cognitive function in normal aging Amyloid plaques is hallmark of Alzheimer's disease.
- Carotid sinus syndrome occurs in the elderly and mainly results in bradycardia.
- 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.





QUIZ

MEDICINE438's CNSPHYSIOLOGY

1. Which one of the following parts of the brain is most vulnerable to aging?

A) Hippocampus
B) Archeocerebellum
C) Spinal cord
D) Hypothalamus

2. Which of the following statement is true regarding the neocortix:

A) It's composed of six layers
B) It's more evolved than the allocortex
C) Both A and B
D) None of the above

3. Which of the following neurotransmitters decrease with age?

A) Serotonin
B) Dopamine
C) Neoasprin
D) Both A and B

4. Sensorineural hearing loss that occurs with age:

A) Presbycusis
B) Wax impaction
C) Homonymous hemianopia
D) Acute labyrinthitis

5. A change that occurs in the oral cavity with aging:

A) Increased number of taste buds
B) Umami taste buds become stimulated by nitric oxide
C) Caviar tongue
D) None of the above

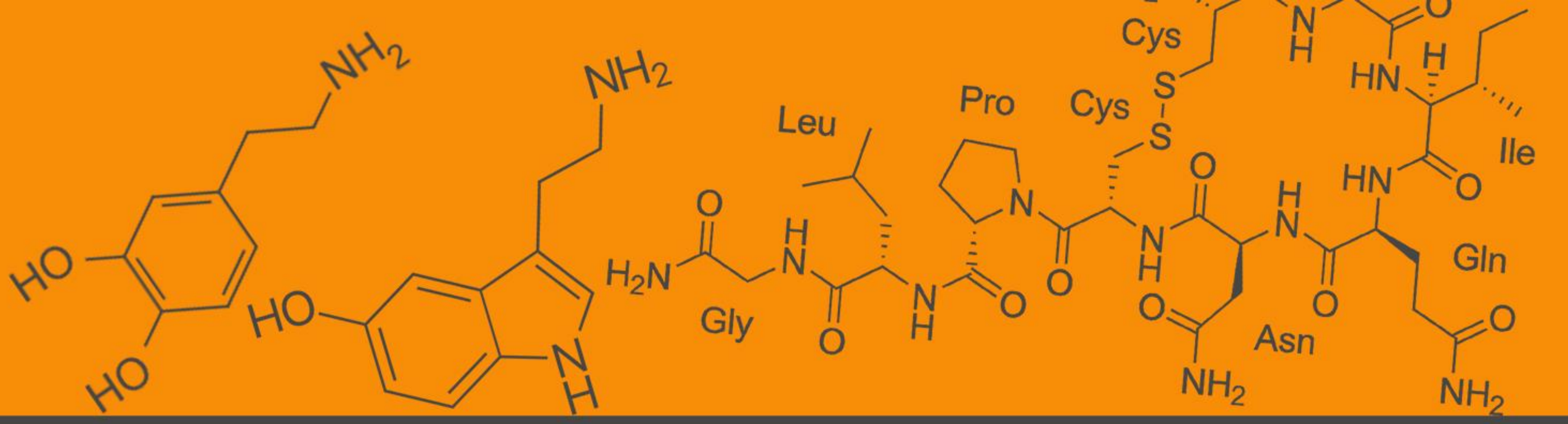
SHORT ANSWER QUESTIONS

1. List three neurotransmitter systems that become impaired with aging.
2. Describe what happens to the following structures with aging
   A. Ventricles, B. Subarachnoid space, C. Basal ganglia

ANSWERS

1. Serotonin, Dopamine, Glutamate.
2. Ventricles and subarachnoid space: Increase in size due to brain shrinkage.
   Basal ganglia: Becomes bright in appearance due to iron accumulation.

ANSWER KEY: A, C, D, A, C



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REFERENCES

- Guyton and Hall Textbook of Medical Physiology
- Ganong's Review of Medical Physiology