

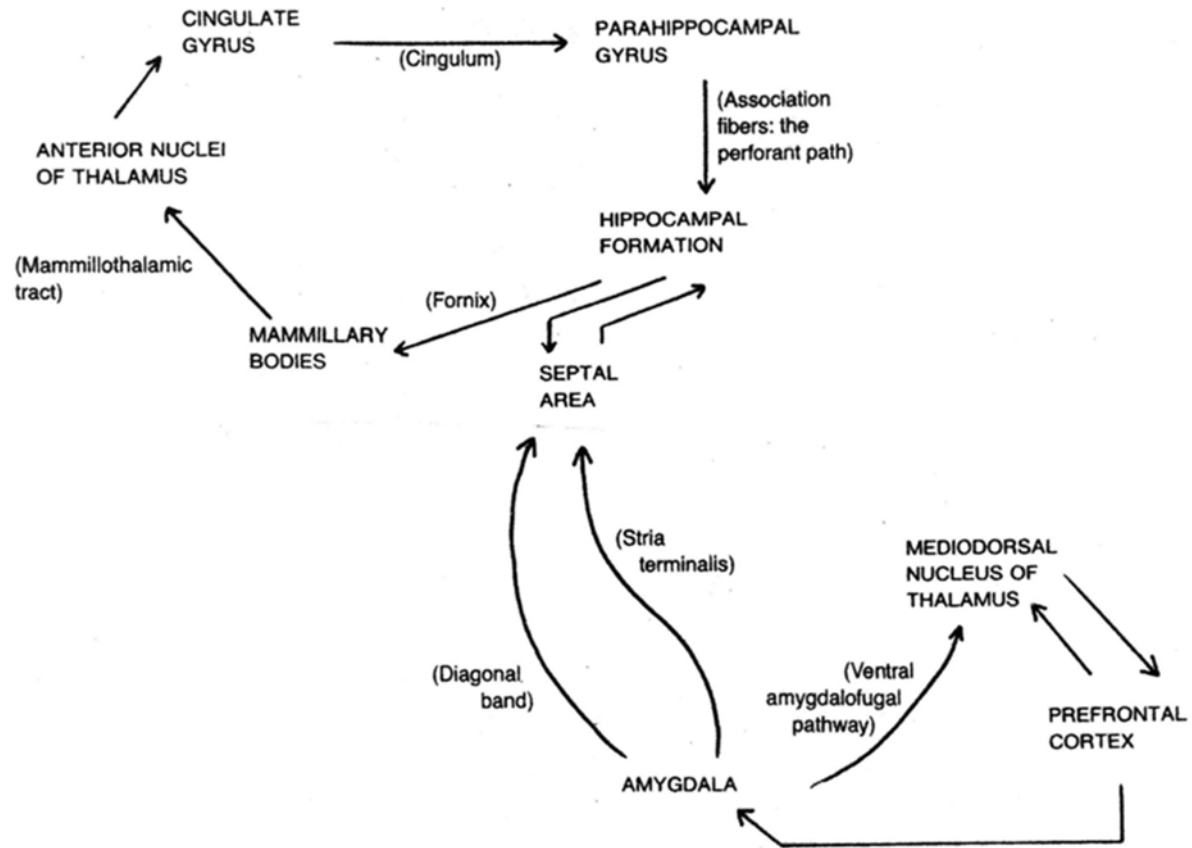
Disorders that affect Memory

Jeanette J. Norden, Ph.D.

Professor Emerita

Vanderbilt University School of Medicine

REVIEW (😊)



What can cause Memory Loss?

- *Any* disorder or damage which affects areas of the brain that are involved in memory – or the pathways that connect these areas - can cause some type of memory loss
- Here we will discuss only a few of the possible causes of memory loss
 - Contusions and concussions
 - Vascular events
 - Seizures
 - Hippocampal sclerosis
 - Psychiatric illness; abuse
 - Neurodegenerative disorders (Alzheimer's disease)

Contusions & Concussions

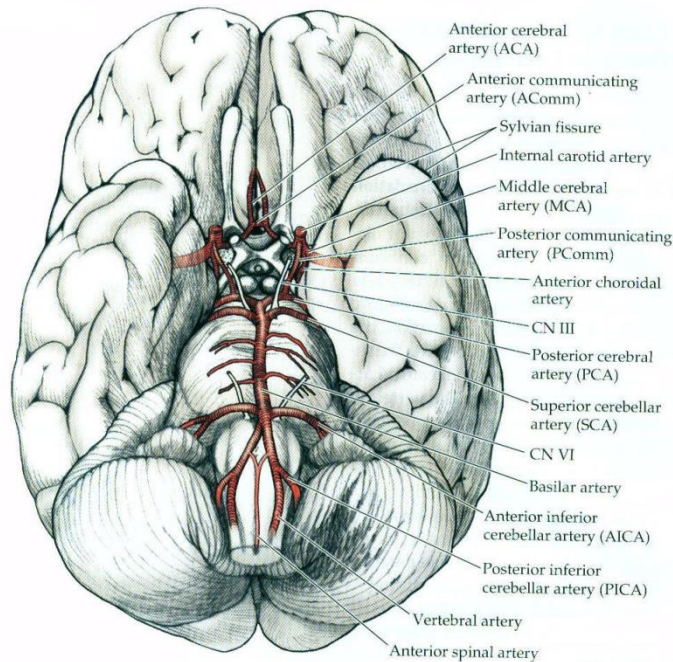
- A contusion is a “bruise”, generally on the surface of the brain; occurs from rupture of surface vessels
- A concussion is a transient disruption of electrical activity in the brain from trauma; now called “mild traumatic brain injury” (mild TBI)
- Even a single mild TBI increases risk (slightly) for Alzheimer’s disease; repeated mild or severe TBIs are a significant risk factor for the development of Chronic Traumatic Encephalopathy (CTE) and for development of neurodegenerative disorders (Alzheimer’s, Amyotrophic Lateral Sclerosis [ALS], Parkinson’s, other)

Vascular Events

- Many of the areas we have discussed are supplied by branches of the same artery (the posterior cerebral artery or PCA); for example, the hippocampus is supplied (in part) by the PCA. Other arteries supply other areas involved in memory.
- Even unilateral strokes (either ischemic [decreased blood supply due to blockage of an artery] or hemorrhagic [rupture of a vessel]) can produce memory loss (e.g., L hippo – words/facts; R hippo – spatial)
- The two PCAs arise from a single artery (called the basilar artery); thus, bilateral loss of blood supply can occur from blockage of the superior portion of the basilar artery (for ex., from atherosclerosis or an aneurysm)

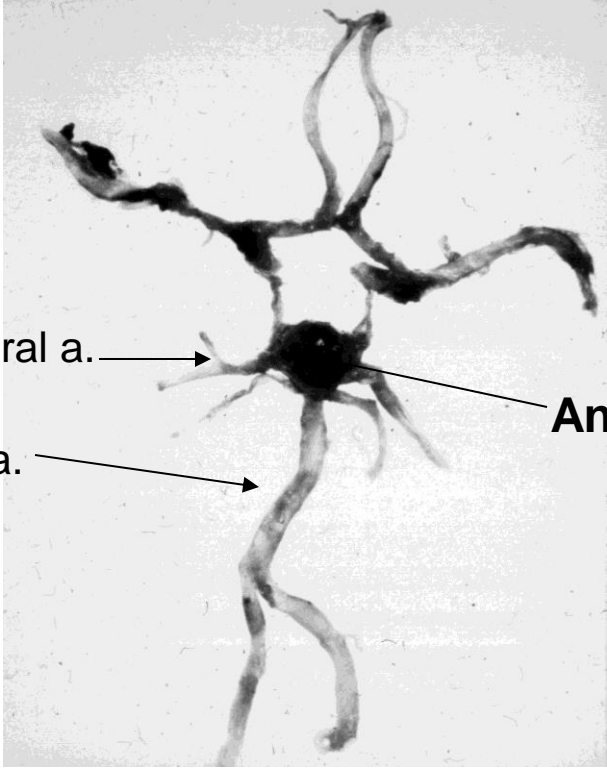
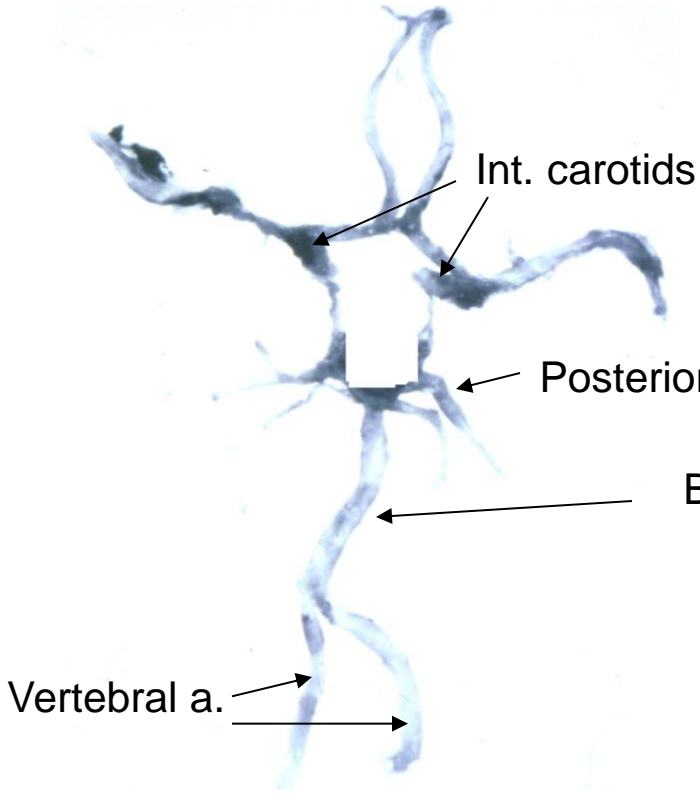
Circle of Willis

- The internal carotid and vertebral arteries supply the entire brain with blood; they join on the underside of the brain to form a circle of vessels called the Circle of Willis



While the brain constitutes only 2% of the body mass, it requires 20% of the oxygen – which is carried by blood; the brain has NO mechanisms for storing either oxygen or glucose

Circle of Willis



Global Cerebral Anoxia

- A vascular episode that can occur following events such as cardiac arrest; due to decreased brain perfusion (decreased oxygenation of the brain)
- Within minutes of decreased brain perfusion, neurons start to die – thus, memory and other functions will be lost
- The hippocampus is one of the most vulnerable areas of the brain to decreased oxygen (or hypoxia)!

Seizures

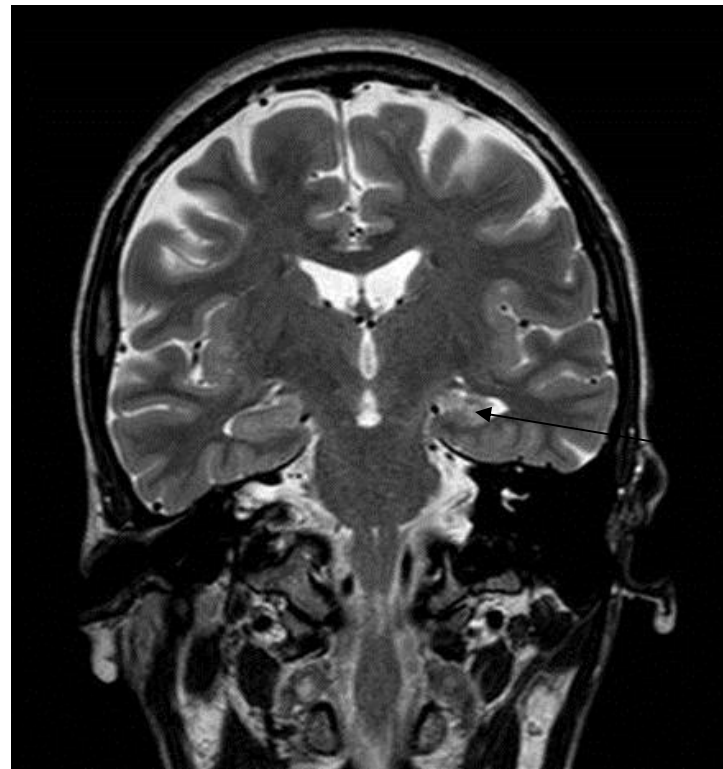
- A seizure is an abnormal electrical discharge of neurons
- Seizures involving the hippocampus (temporal lobe seizures) are common – and may present with “déjà vu” – and other “memory” phenomena; after a seizure, the individual may suffer from “post-ictal” (post-seizure) amnesia or loss of memory for some time surrounding the seizure; repeated seizures can impair memory
- All generalized seizures (seizures involving both hemispheres) - except the most brief - cause some memory impairment

Hippocampal Sclerosis

- Hippocampal sclerosis (“scarring”) may be both the result or cause of repeated temporal lobe seizures – or both; may be unilateral (one-sided) or bilateral (both sides of the brain)

Note that in MRIs, right is on the left, and left is on the right!

R



L

L hippocampal sclerosis

Psychiatric Disorders

- Many different psychiatric disorders are associated with memory impairment
- May be primary in the disorder, for example, in schizophrenia (psychosis)
- May also be secondary, for example in depression, because of activation of the system (hypothalamic-pituitary-adrenal axis) that responds to “stress” – either psychological or physical and results in a “fight or flight” response); occurs in depression, PTSD (post-traumatic stress disorder), and other psychiatric conditions

Abuse

- Memory impairment is present in adults who were emotionally, physically or sexually abused as children
- Involves primarily L hippocampus, amygdala
- Decreased hippocampal volume, increased amygdala and HPA activation
- These brain changes are believed to underlie both the memory impairment – and emotional “hyper-vigilance” seen in these adults

Neurodegenerative Disorders

- **A number of neurodegenerative disorders (disorders in which neurons of the brain degenerate or die) can cause memory loss**
- **Alzheimer's disease is the prototypical neurodegenerative disorder which results in memory loss**

ALZHEIMER'S DISEASE

HISTORICAL LOOK

- **“Dementia” is a general term meaning “progressive mental deterioration/decline”; it can be primary or secondary to another disorder**
- **Alzheimer’s disease is a primary “dementia” which is both progressive and irreversible**
- **Early onset and late onset forms**
- **Alzheimer’s disease is the most common primary dementia and the most common neurodegenerative disease in the U.S., currently ~5 million people have been diagnosed**

There are two major forms of Alzheimer's Disease

- **Early onset familial Alzheimer's disease**
 - Autosomal dominant inheritance (you get the gene, you get the disease)
 - Accounts for a very small number of cases (~5%)
- **Late onset sporadic Alzheimer's disease (what we will focus on)**
 - May be multiple causes or etiologies (**Current top etiology is that it is secondary to cerebrovascular dysregulation!)
 - Associated with various “risk” factors which change the “probability” of developing Alzheimer's Disease

BEHAVIORAL CHANGES IN ALZHEIMER'S DISEASE

- **COMMON EARLY CHANGES**
 - **MEMORY LOSS (primarily short-term memory)**
 - **DECREASED INITIATIVE**
 - **DEPRESSION**
 - **FAULTY JUDGMENT, LOSS OF INSIGHT, AND OTHER "HIGHER-ORDER" FUNCTIONS**

BEHAVIORAL CHANGES IN ALZHEIMER'S DISEASE

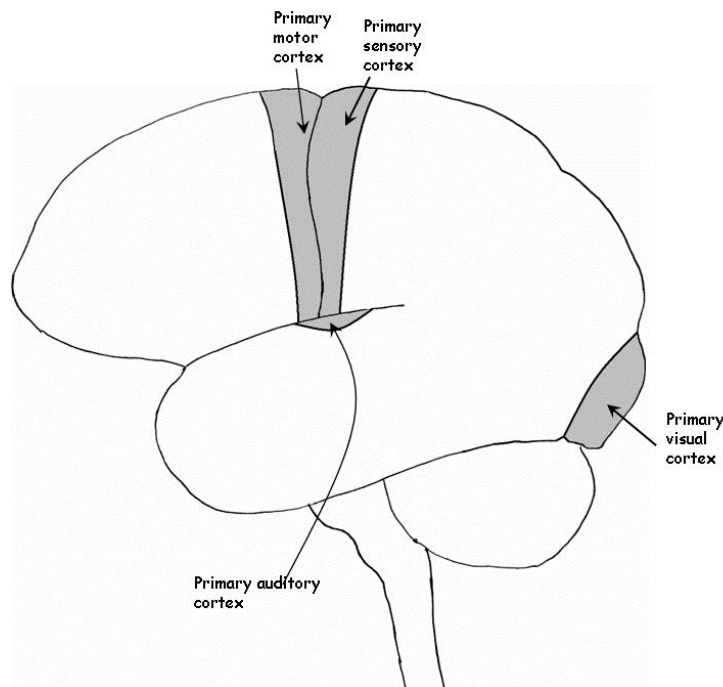
- ***AS THE DISEASE PROGRESSES***
 - **PROFOUND MEMORY LOSS (working and short-term memory)**
 - **ADDITIONAL CHANGES IN HIGHER-ORDER FUNCTIONING**
 - **BEHAVIORAL AND MOOD DISTURBANCES**
 - **“SUNDOWNING”; HYPERSEXUALITY**

BEHAVIORAL CHANGES IN ALZHEIMER'S DISEASE

- ***LATE IN THE COURSE OF THE DISEASE***
 - COMPLETE LOSS OF “SELF” AND MEMORY (including long-term memory)
 - PARANOIA; EMOTIONAL LABILITY/INSTABILITY; LITTLE IMPULSE CONTROL
 - SEVERE LANGUAGE DEFICITS OR MUTENESS
 - CACHETIC AND INCONTINENT
- **DEATH GENERALLY OCCURS SECONDARY TO PNEUMONIA OR FROM CEREBRAL HEMORRHAGE**

WHAT HAPPENS IN THE BRAIN IN ALZHEIMER'S DISEASE TO PRODUCE MEMORY LOSS AS WELL AS THE OTHER BEHAVIORAL CHANGES?

- **Many different changes occur in cortex**
 - **Loss of cortical neurons, especially cortical neurons involved in “higher-order” functions**



Note: “Unshaded areas are the most affected in Alzheimer’s Disease

Degeneration of Neurons within Specific Cortical Areas results in Loss of Memory in Alzheimer's Disease

- The first area to undergo degeneration is an area called the Entorhinal Cortex – it is the “higher-order” cortical area that processes information across all of the sensory systems and communicates this information to the Hippocampus**
- The Hippocampus also degenerates early in the disorder which results in loss of Short-term Memory and inability to consolidate new memories**
- Prefrontal cortex degenerates resulting in the loss of Working Memory**
- And finally, late in the disorder, degeneration of large areas of the cortex results in the loss of Long-term Memory as well**

Loss of Cortical Neurons is PROFOUND

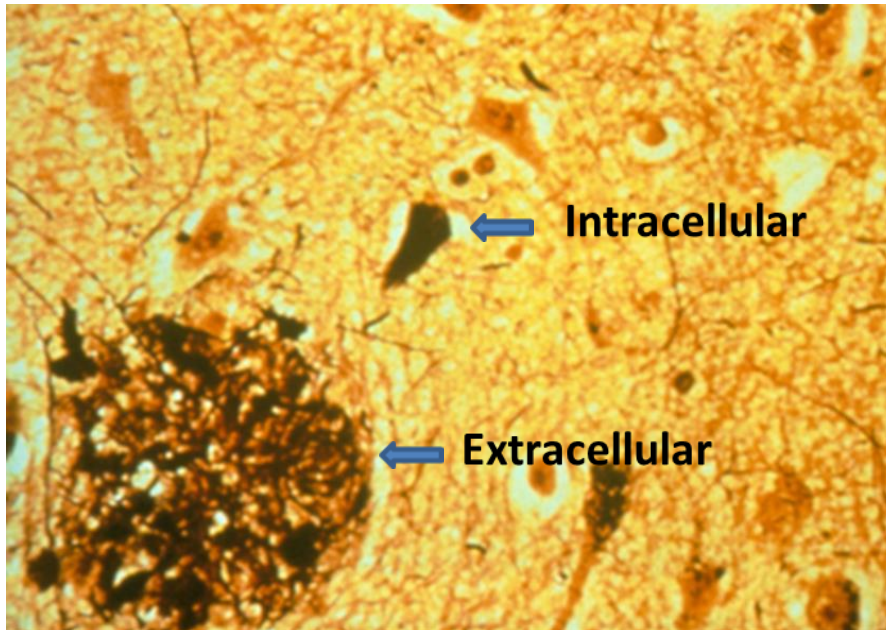


Alzheimer's Disease

Normal age-matched Control

Changes also occur at the cellular & molecular levels

- Loss of neurons, especially within the cortex (previous slide)
- Loss of synapses and connections between these neurons (remember, a single neuron can receive 10,000 synapses – if the neuron is lost – all of the synapses are lost as well)
- Accumulation of altered proteins within remaining neurons (intracellular (tau protein); neurofibrillary tangles) and deposition of β -amyloid protein within the brain (extracellular; plaques)



These changes can be identified at autopsy

To keep your memory sharp, if possible

- **Avoid head injury**
- **Keep your arteries healthy**
- **Be compliant (with meds) to avoid seizures if you have a seizure disorder**
- **Treat psychiatric illness; if you were abused as a child, seek help; decrease stress; practice mindfulness meditation**
- **Decrease “factors” which increase risk for Alzheimer’s disease (to be discussed next week)**