Disorders that affect Memory

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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.

From Blumenfeld, 2010
Circle of Willis

Int. carotids

Posterior Cerebral a.

Basilar a.

Vertebral a.

Aneurysm
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!
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)