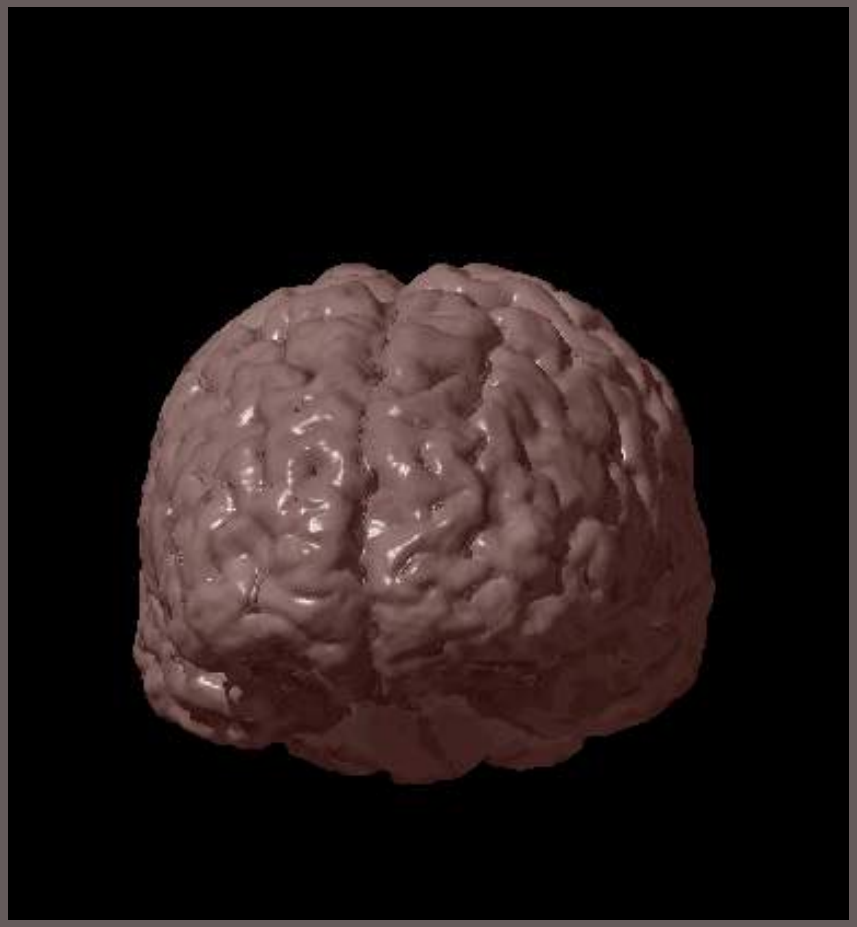
DON'T *MIND* THIS OLD THING: THE AGING BRAIN

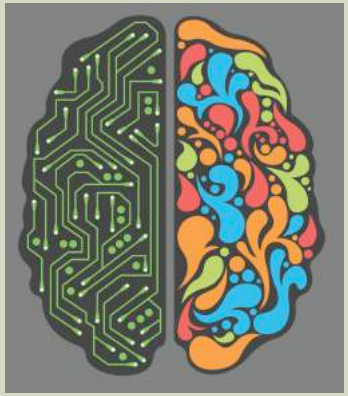


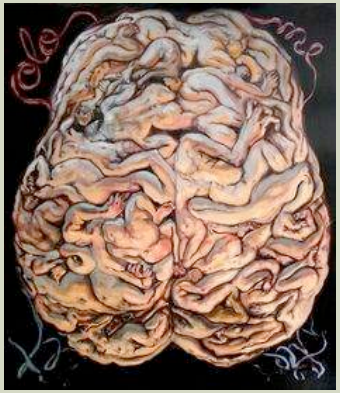
Sara Gombash Lampe, Ph.D.

Lecture 1

Sept. 13, 2016

THE BRAIN IS ALWAYS CHANGING. ALWAYS.







Aging is just a continuation of the brain's evolution.

TODAY'S LECTURE

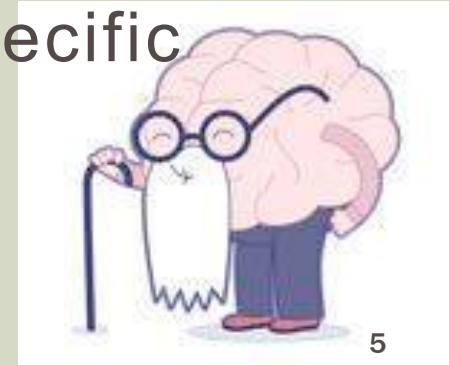
1. What cognitive changes occur in the healthy aging brain?
2. How does brain structure change as we age?
3. How does brain function change as we age?

WHAT IS AGING?

- To US: increase in chronological years
- To SCIENTISTS: age related effects of those years on your body
- SENESCENCE: accumulation of harmful effects that makes us much more fragile and vulnerable to disease and death

THE BRAIN AGES LIKE THE BODY

- Just like our physical bodies are affected by aging, so is our brain
- Brain cells (neurons) accumulate insults like any other cell type
- Certain neurons are more susceptible to age-related deterioration
- Cell-specific deterioration impacts specific brain regions



COGNITION

- As we age, we experience cognitive changes

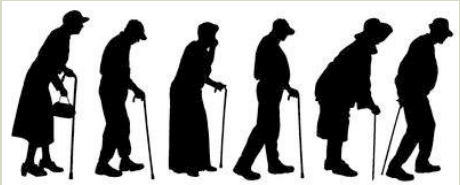
COGNITION:

the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses

- Brain function determines our personality, emotions, and intellect—the attributes that make us unique

AGING COGNITION STUDIES

- University of Michigan- Denise Park 2000
- 350+ volunteers
- Ages 20-92 years old

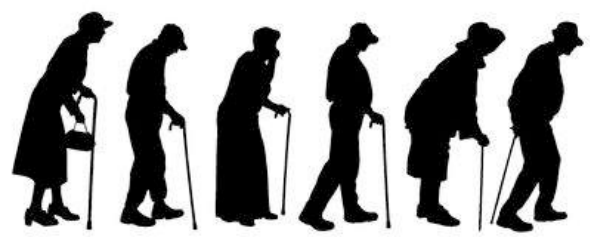


Cognitive Tests → Vocabulary
Cognitive Tests → Types of Memory
Cognitive Tests → Processing Speed

Compared performance on tests in each decade of life….

AGING COGNITION STUDIES

- Some aspects of cognitive function decline, but others did not
- 3 specific areas of decline in aged population



1. Processing speed
2. Executive function
3. Episodic Memory

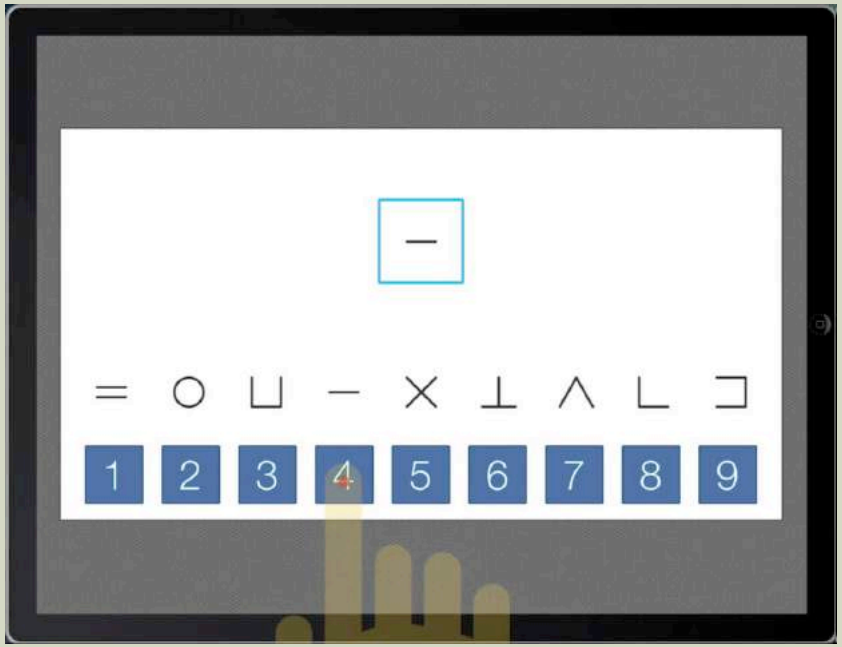
- Let's examine each….

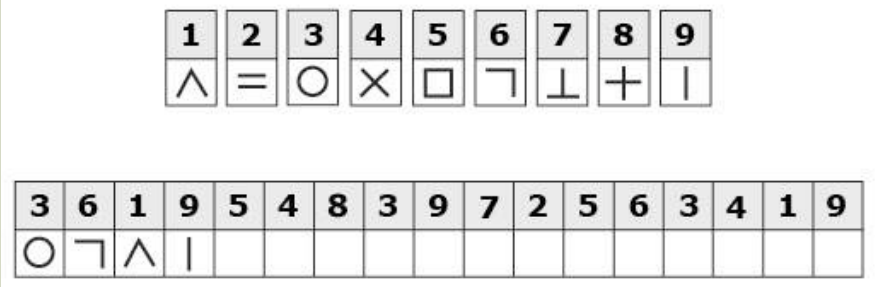
1. PROCESSING SPEED

PROCESSING SPEED

- Rate at which we accomplish cognitive tasks
- The amount of time it takes to
  1. perceive information,
  2. process information, and
  3. formulate or enact a response
- Cognitive tasks include problem solving, making judgments, learning new tasks

PROCESSING SPEED TESTS





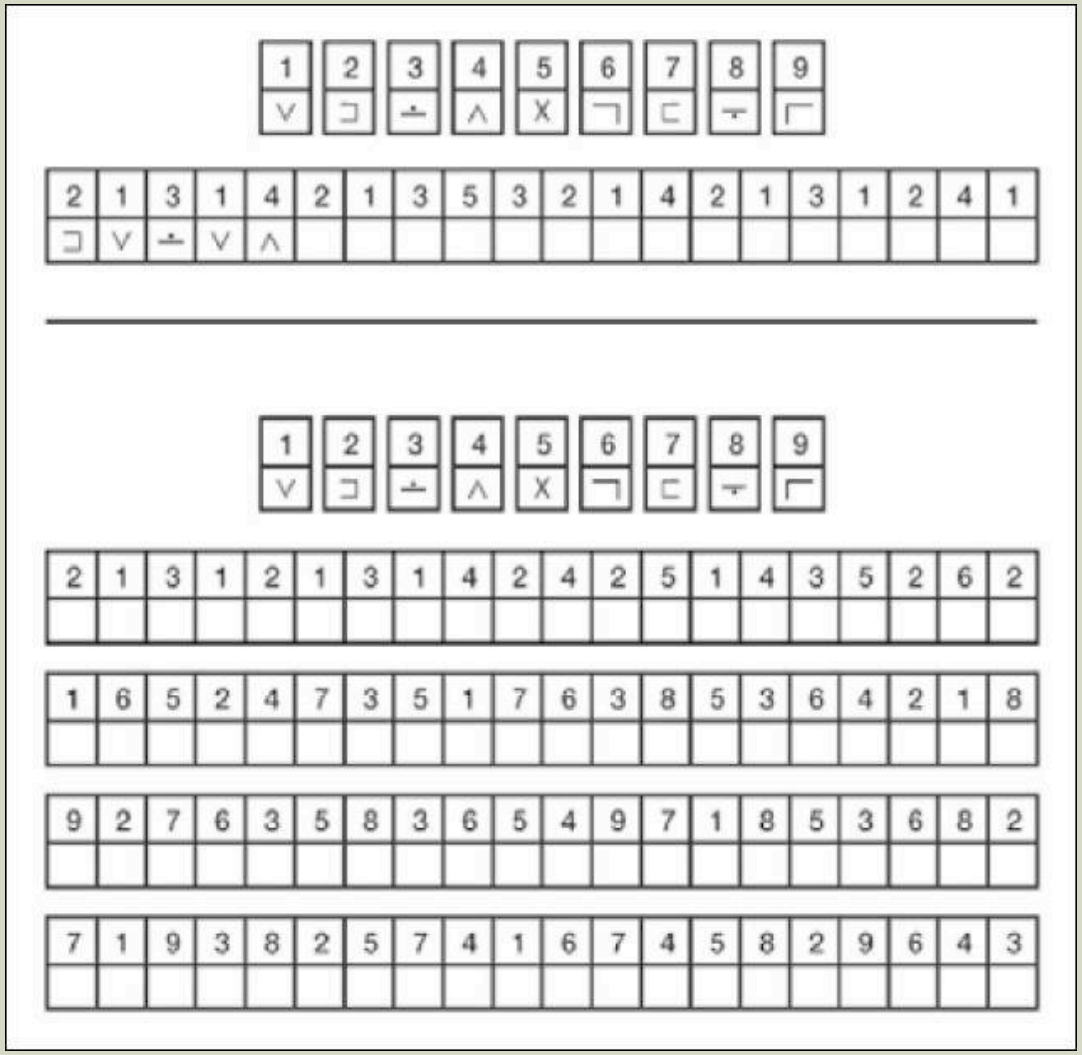
1	2	3	4	5	6	7	8	9
∧	=	○	×	□	⅂	⊥	+	|

3	6	1	9	5	4	8	3	9	7	2	5	6	3	4	1	9
○	⅂	∧	|													

Digital-Symbol Task

1. Each digit (1-9) has a corresponding geometric picture
2. Participants given a sequence of numbers with blanks next to them
3. Fill in the shapes with as many blanks as they could in 90 seconds

DIGIT-SYMBOL TASK: YOUR TURN



1	2	3	4	5	6	7	8	9
V	⊐	⊥	∧	X	⊓	⊏	⊤	⊓

2	1	3	1	4	2	1	3	5	3	2	1	4	2	1	3	1	2	4	1
⊐	V	⊥	V	∧															

1	2	3	4	5	6	7	8	9
V	⊐	⊥	∧	X	⊓	⊏	⊤	⊓

2	1	3	1	2	1	3	1	4	2	4	2	5	1	4	3	5	2	6	2

1	6	5	2	4	7	3	5	1	7	6	3	8	5	3	6	4	2	1	8

9	2	7	6	3	5	8	3	6	5	4	9	7	1	8	5	3	6	8	2

7	1	9	3	8	2	5	7	4	1	6	7	4	5	8	2	9	6	4	3

PROCESSING SPEED TESTS

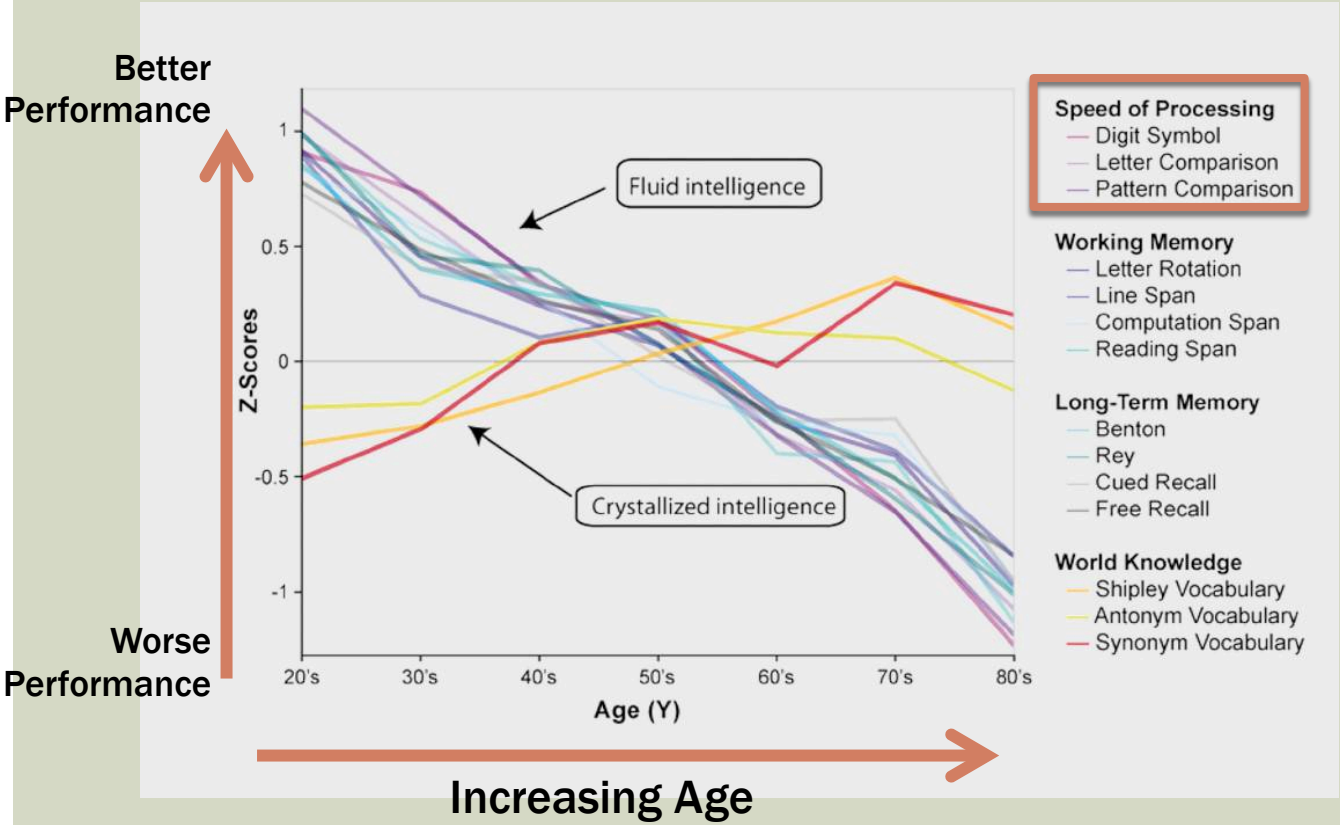
A	G	Y	F
D	O	B	N
L	L	P	S
K	Y	F	E
G	V	K	J
G	V	K	J
U	Q	M	Z
R	G	A	D

Letter-Pattern Matching

1. Given pairs of letter strings
2. Asked if each pair of strings was identical or different as fast as possible
3. Counted numbers of correct answers

PROCESSING SPEED DECLINES WITH AGE

- Processing speed declined by a constant amount with each passing decade



- Decline begins in 20's
- Aging makes us physically and mentally a little slower
- We can still perform, just slower then before

BRAIN STRUCTURES AND FUNCTIONS IMPACTED IN AGING

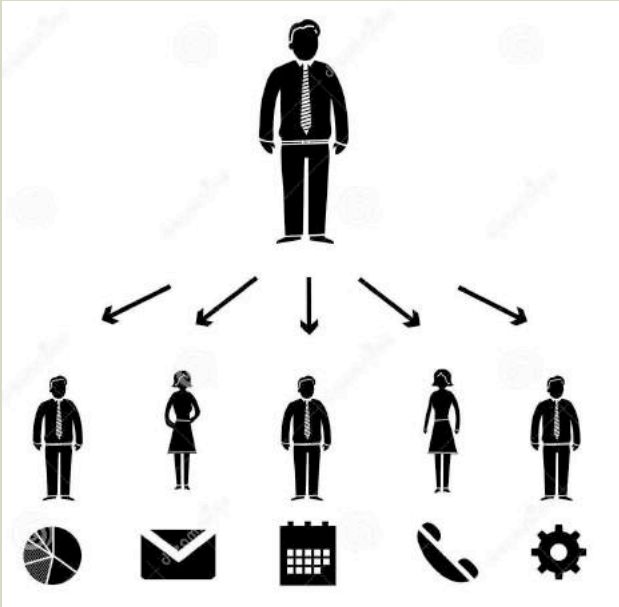
Function Name	Action
Processing Speed	Rate at which we can accomplish cognitive tasks
Executive Function	
Episodic Memory	

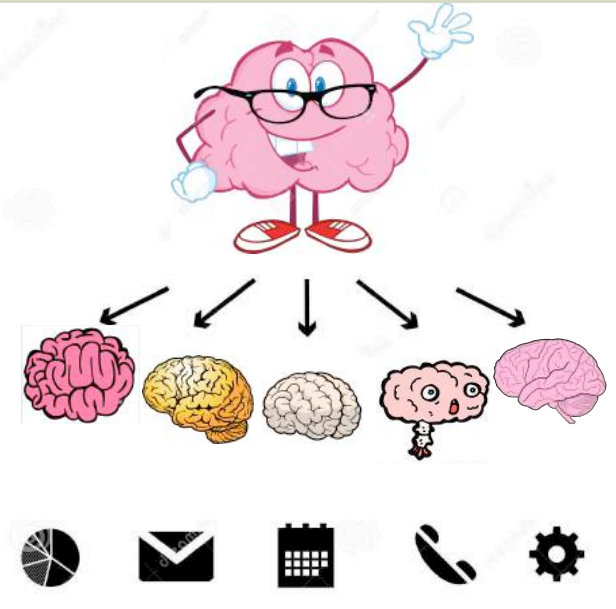
2. EXECUTIVE FUNCTION & WORKING MEMORY

EXECUTIVE FUNCTION

- Functions like an executive of a company
- Executives DON'T usually..
  - Sort mail
  - Pay the bills
  - Design the advertising
- Executives DO…
  - Set goals
  - Delegate responsibilities
  - Allocate resources
  - Monitor progress

EXECUTIVE FUNCTION





- Executive functions in the brain are higher order functions
  - Decisions
  - Planning
  - Setting goals
  - Monitoring progress during mental tasks

WORKING MEMORY

Working memory is a sticky-note that keeps track of short-term information

Working Memory

1. Store information temporarily
2. Maintain information over brief time
3. Retrieve information for use

Requires executive control over your memory system

WORKING MEMORY TESTS

Expert performance depends on extreme adaptations, accomplished through life-long efforts in well-defined domains.

Great things are not done by impulse, but by a series of small things done together.

Hard work always pays off, but it is helpful to have good intuition.

Answer: domains, together, intuition

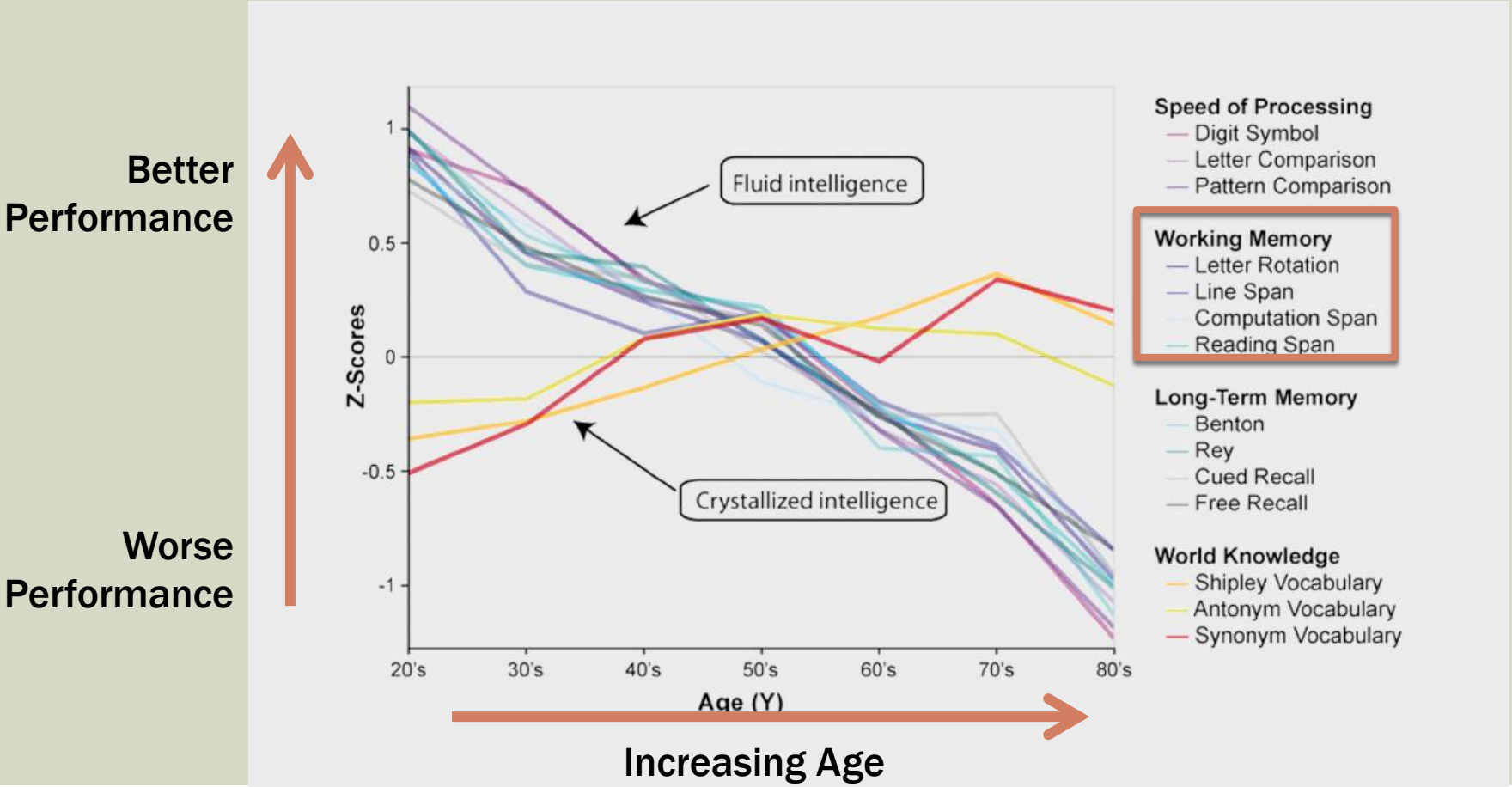
Reading Span Task

- Read each sentence
- Recall the last word from each sentence
- Record the words, in order, at the end of the task

- Line Span Task – asked spatial locations of lines while they are connected to dots
- Computational Span Task- remember numbers while computing

WORKING MEMORY DETERIORATES WITH AGE

- With each passing decade, working memory capacity deteriorates

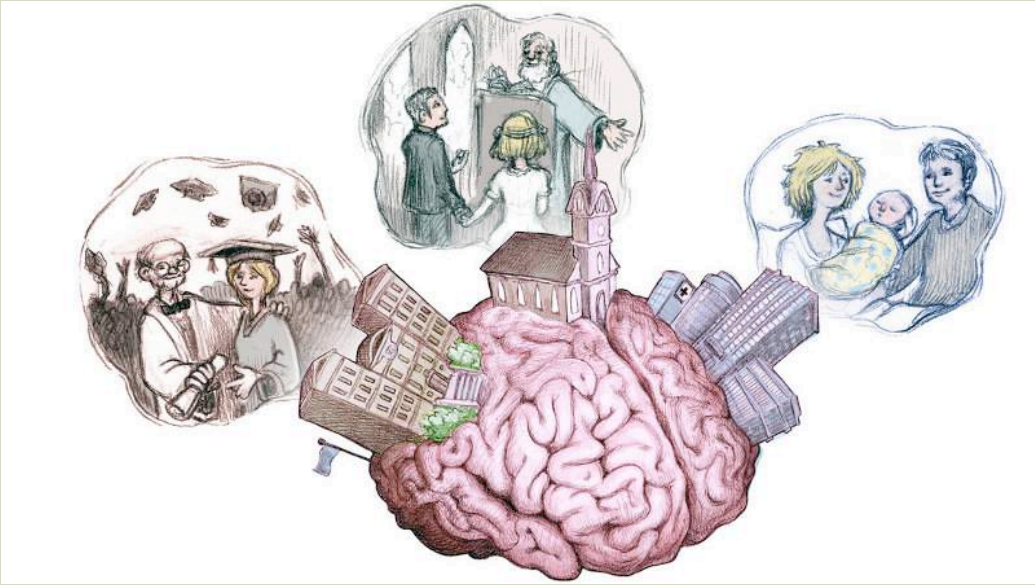


BRAIN STRUCTURES AND FUNCTIONS IMPACTED IN AGING

Function Name	Action
Processing Speed	Rate at which we can accomplish cognitive tasks
Executive Function (Working Memory)	Our ability to oversee and manage our most basic cognitive processes
Episodic Memory	

3. EPISODIC MEMORY

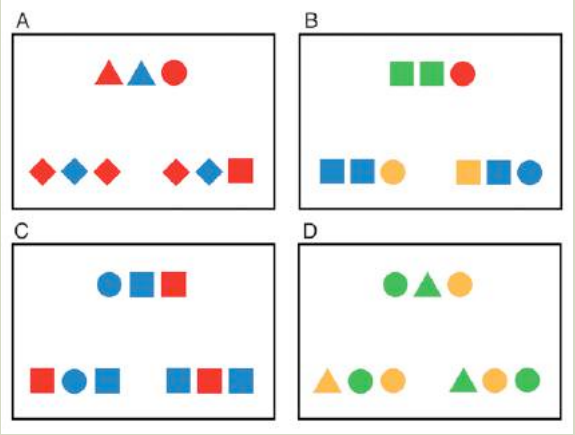
EPISODIC MEMORY



- Memories for specific episodes in your life
  - Ex: conversation you had, vacation you took, what you did last night
- Tied to a specific time and place
- Remembered from your own perspective
- Can be short or long-term

EPISODIC MEMORY TESTS

1. Visuospatial tests – person views a collection of shapes, then is asked to recall those shapes at a later time



2. Verbal tests- **<u>Free recall task</u>**
   - Participants given a list of words to look over
   - Participants asked to recall as many of the words as they could in any order

21. season	41. lady
22. boys	42. hear
23. older	43. vassal
24. forbear	44. think
25. by	45. sunder

EPISODIC MEMORY TEST: YOUR TURN

Free Recall Task

Page 2 of your handouts

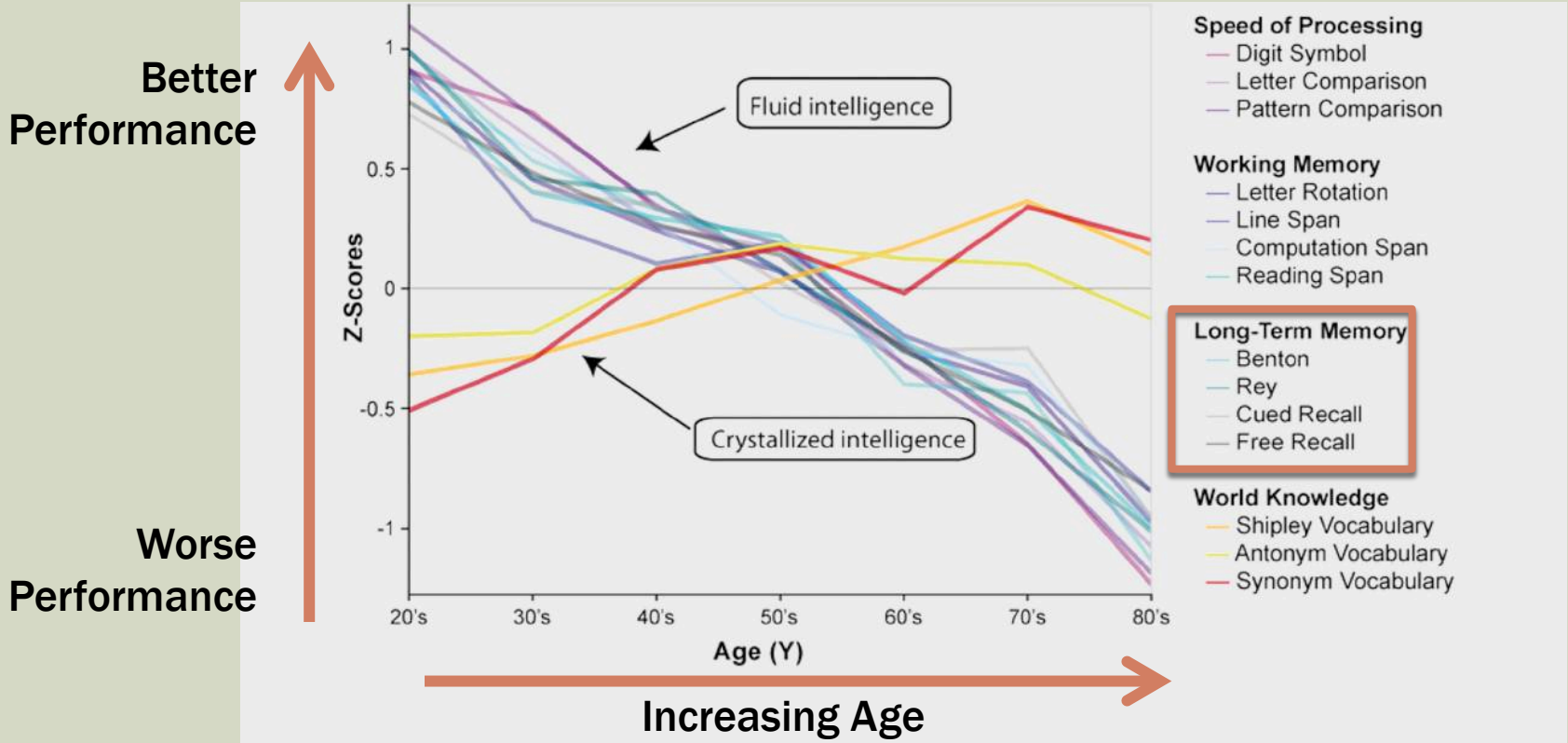
Study this list of words for 30 seconds.

swing		laughter	
feast		Thursday	
tempted		relative	
rainbow		wild	
pants		doctor	
avoid		war	
wink		wildlife	
juvenile		wolves	
sword		baby	

After 30 seconds, write down as many words as you can remember.

EPISODIC MEMORY DETERIORATES WITH INCREASING AGE

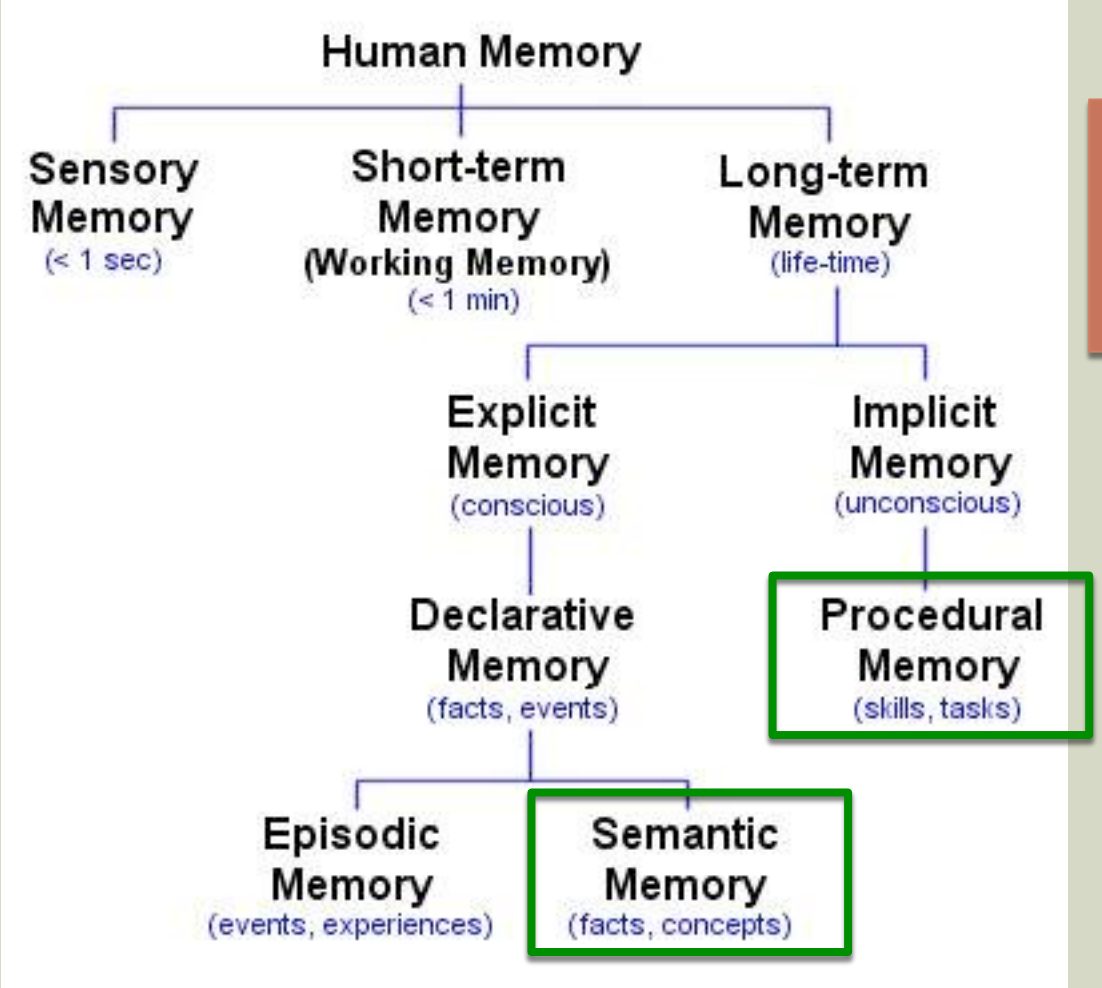
- Results for episodic memory tests looked very similar to the results for working memory and processing speed
- Steady decline in episodic memory with each decade



BRAIN STRUCTURES AND FUNCTIONS IMPACTED IN AGING

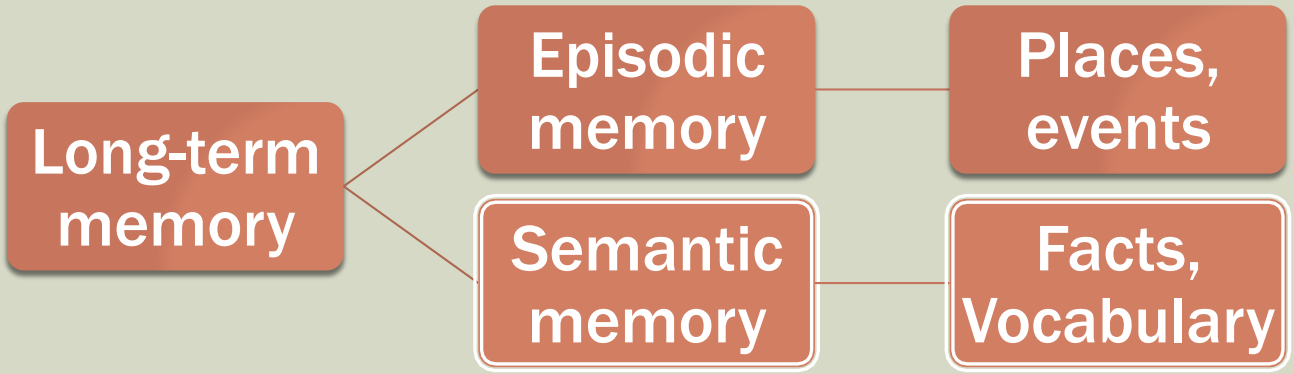
Function Name	Action
Processing Speed	Rate at which we can accomplish cognitive tasks
Executive Function (Working Memory)	Our ability to oversee and manage our most basic cognitive processes
Episodic Memory	Short and long-term memories for episodes

MEMORY SYSTEMS PRESERVED IN AGING



- Semantic Memory
- Procedural Memory

SEMANTIC LONG-TERM MEMORY



- Long-term memory for <u>facts</u> is called <u>semantic memory</u>
  - 2+2=4
  - Birds have wings
- Not tied to a specific time and place
- Not remembered from a first person perspective

SEMANTIC MEMORY TESTS

Synonym Vocabulary task

- Participants given a word with four word choices below
- Must pick the word closest in meaning to the given word

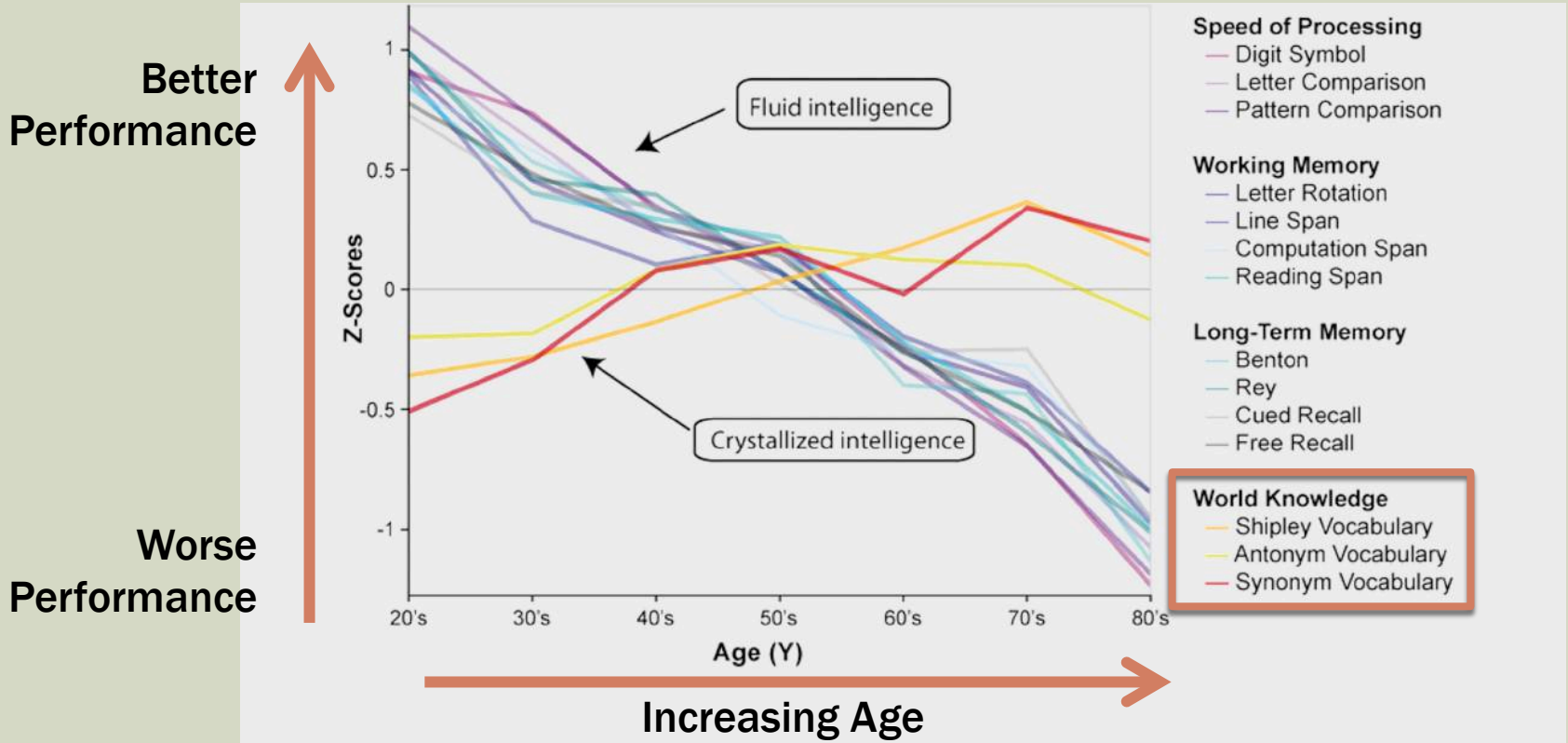
Strange	Believable
a) Funny	a) Interesting
b) True	b) Convincing
c) Weird	c) Surprising
d) False	d) Implausible

Antonym Vocabulary task

- Pick the opposite meaning word

Strange	Believable
a) Weird	a) True
b) Unusual	b) Convincing
c) Normal	c) Likely
d) Opposite	d) Implausible

SEMANTIC MEMORY IMPROVES WITH AGE



- Older participants performed better then younger
- Older participants knew more words
- Better at choosing synonyms and antonyms

PROCEDURAL MEMORY

- Memory for skills and habits
  - Ex: Knowing how to read, cook, play an instrument or speak a language
- Difficult to explain how you perform these skills
- Unconscious memory for how to do these skills
  - Ex: muscle memory for riding a bike or tying your shoe
  - Ex: cognitive skills like reading
- Procedural memory doesn't decline in healthy aging

Not everything declines with age, and many mental processes remain stable. Some even improve.

More then just cognitive processes improve with age.

- *Emotional life improves with age.*
- *Older people report greater life satisfaction and fewer negative emotions then younger counterparts.*
- *Better at solving interpersonal problems and conflicts.*

TAKE HOME POINT

A lot of our mental life is not adversely affected by age.

Age related declines are restricted to a few cognitive processes during healthy aging.

Why do some systems stay intact and some deteriorate?

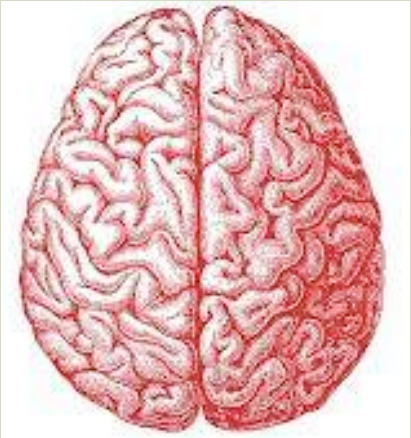
AGING AND BRAIN STRUCTURE

WHY DO SOME SYSTEMS STAY INTACT WHILE SOME DETERIORATE?

- Over a lifetime, cells in our brain accumulate damage and begin to malfunction
- Certain brain regions are more susceptible to damage
- Some regions regions are spared

Decline

Executive function
Processing
Episodic memory



Stable or Improve

World Knowledge
Procedural memory
Emotional processing

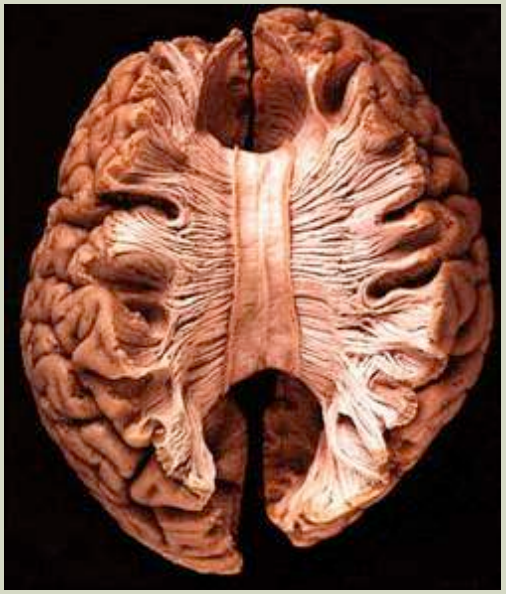
- The brain regions that support executive function, processing, and episodic memory are the SAME brain regions that deteriorate

THREE MAJOR STRUCTURAL BRAIN CHANGES

1. Prefrontal cortex

2. Hippocampus

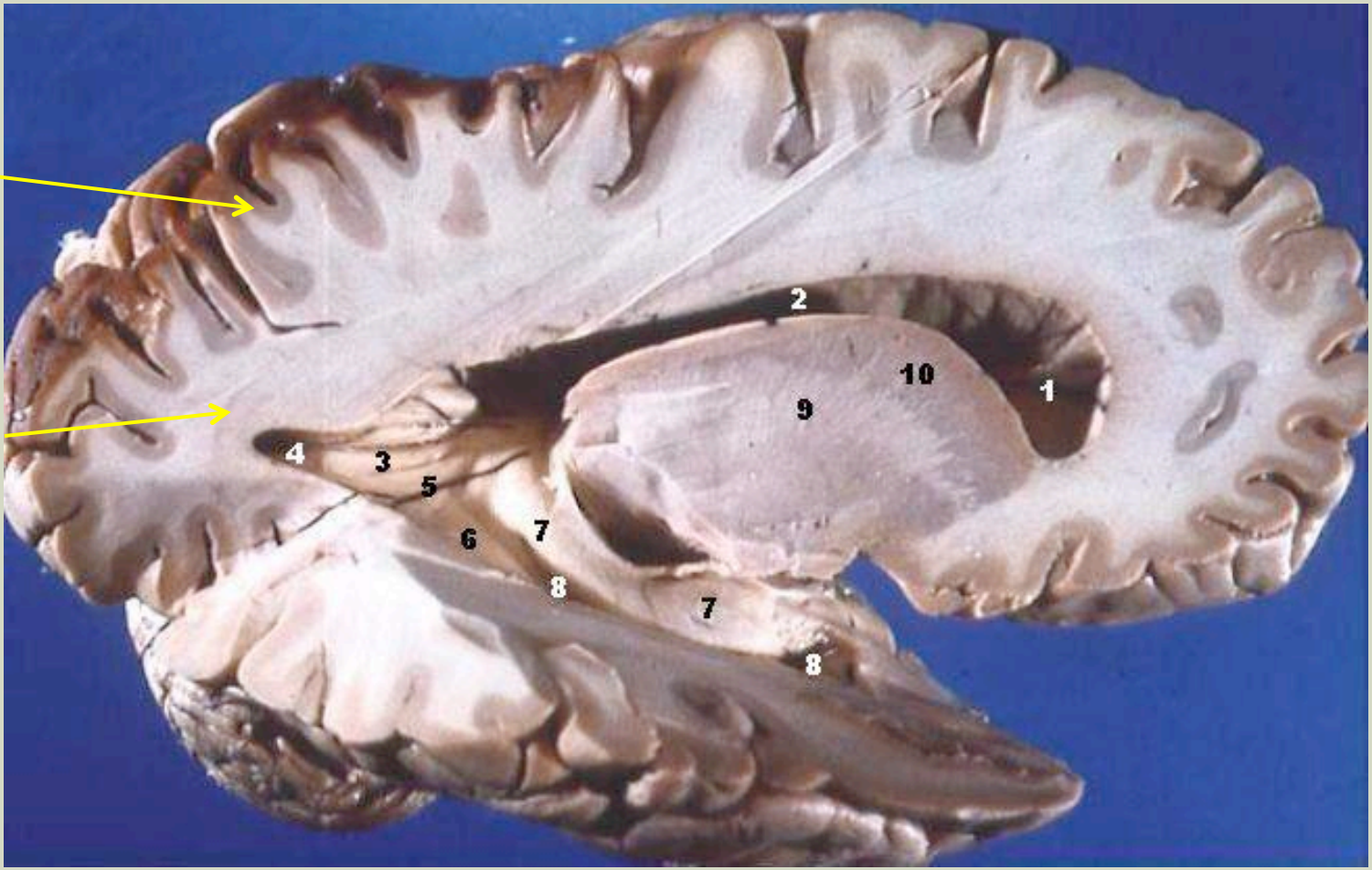
3. White Matter Pathways



BRAIN ANATOMY: GRAY AND WHITE MATTER

Grey Matter

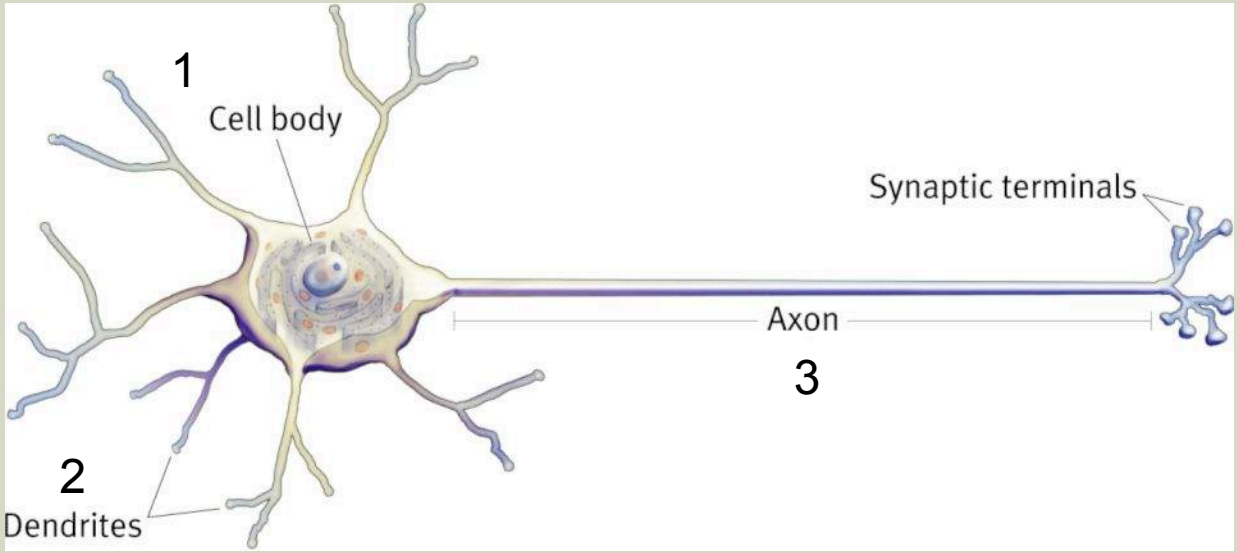
White Matter



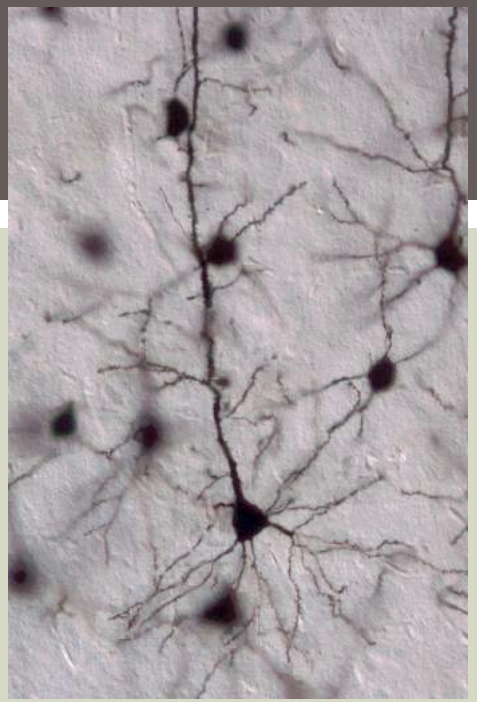
THE PARTS OF A NEURON

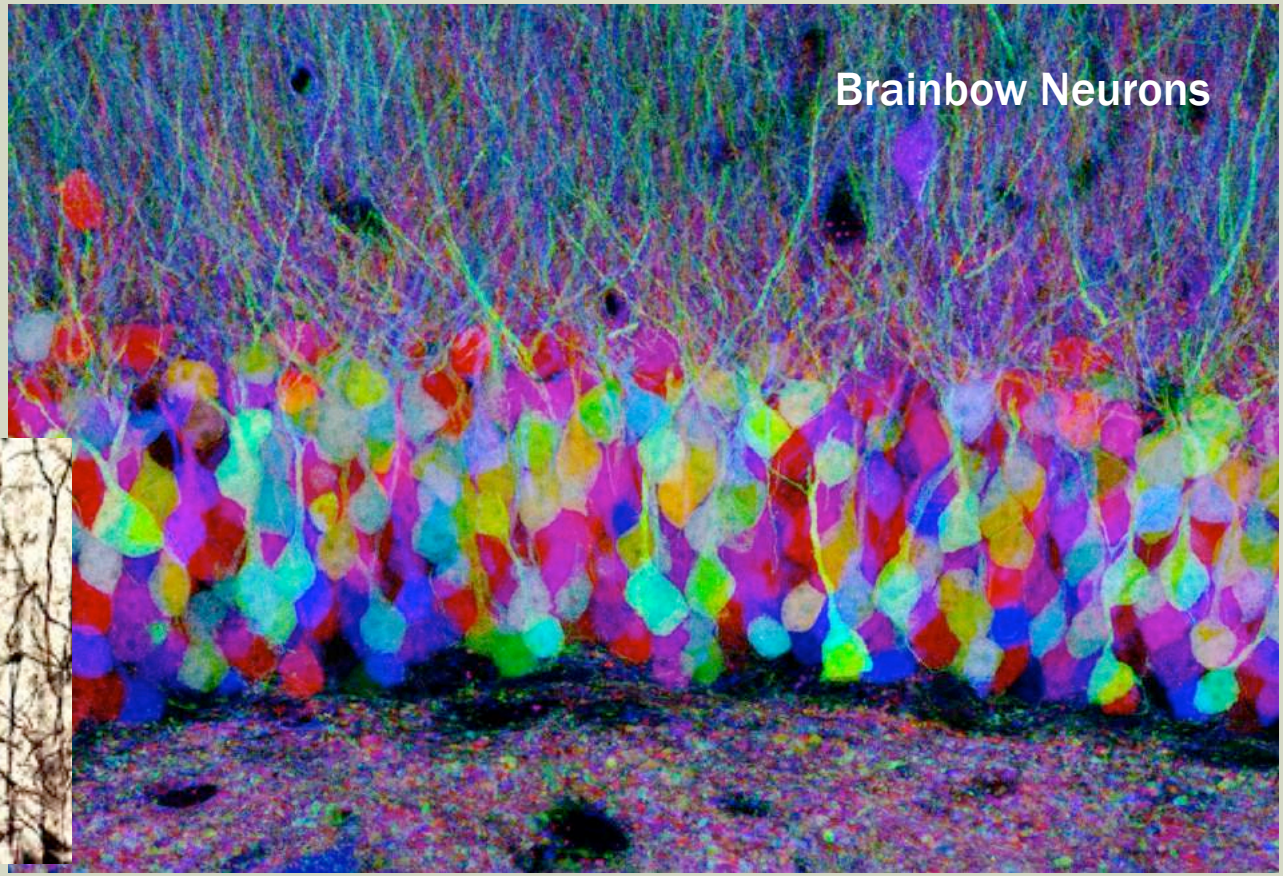
- Gray matter and white matter correspond to different parts of neurons
- Neurons are specialized cells in the nervous system that can send and receive communication using electrical and chemical signals

Three major parts:
1. Cell body
2. Dendrites
3. Axon



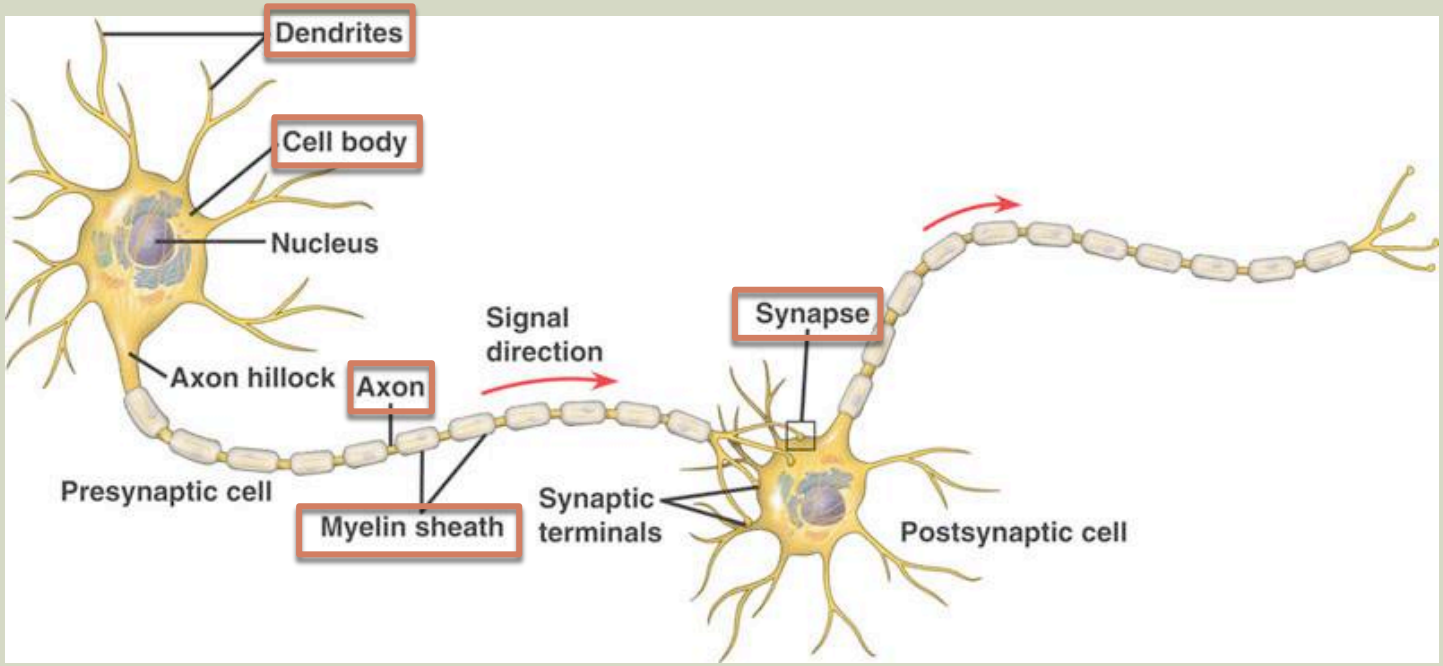
NEURONS





- Human nervous system made of billions of linked neurons

THE PARTS OF A NEURON



1. Cell body - holds the DNA
2. Dendrites – receive signals from other neurons (chemical or electrical)
3. Axon - sends message to next neuron
   - Myelin sheath – fatty insulating layer to help signals travel far and fast
   - Synapse – connections between neurons

MYELIN SHEATH

- Axons can run almost the entire length of your body
- Messages sent over that distance can be slow
- Requires faster transmission (ex: burning skin)
- Fatty insulation allows for speedy transmission

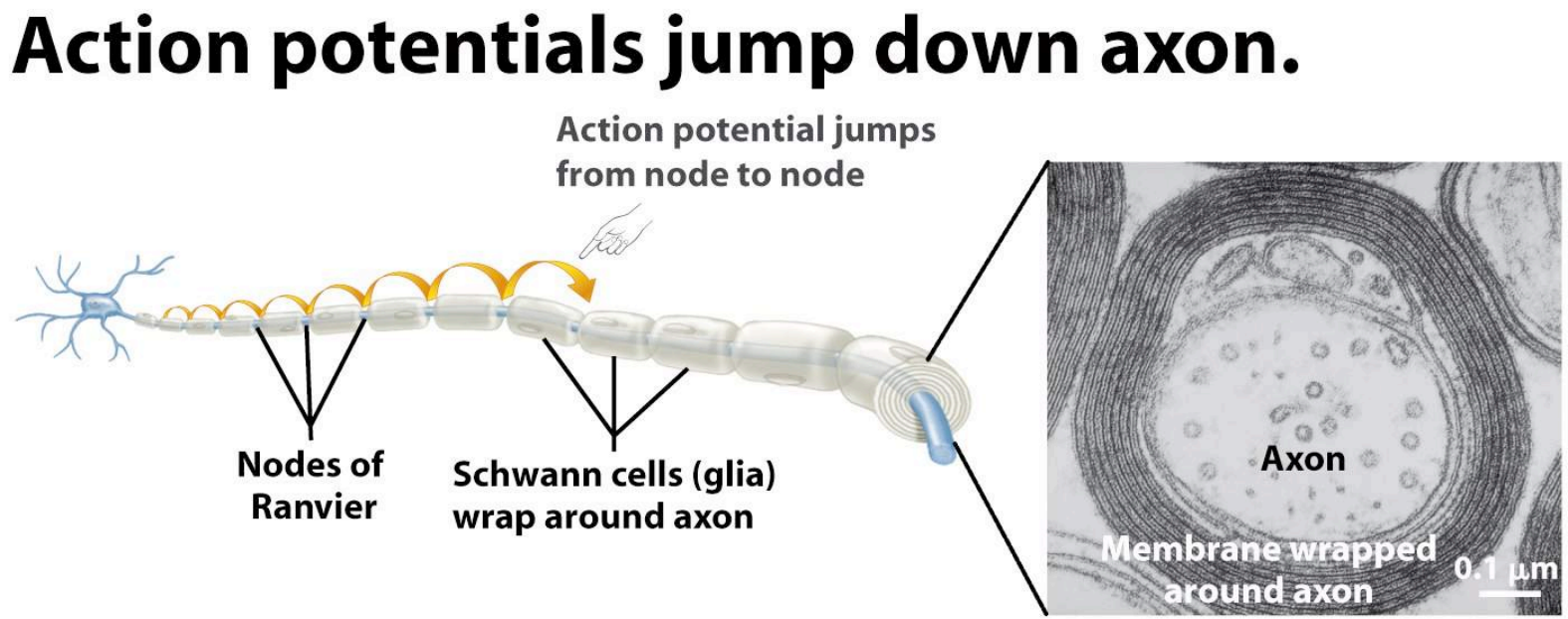
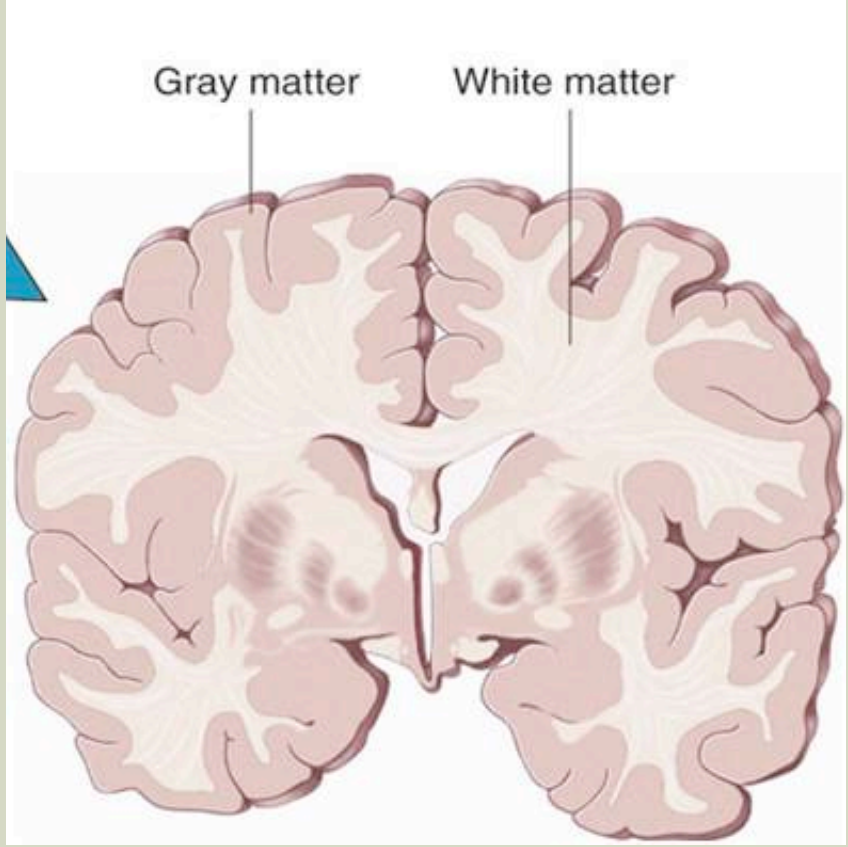


Figure 45-12a Biological Science, 2/e

BRAIN ANATOMY: GRAY AND WHITE MATTER

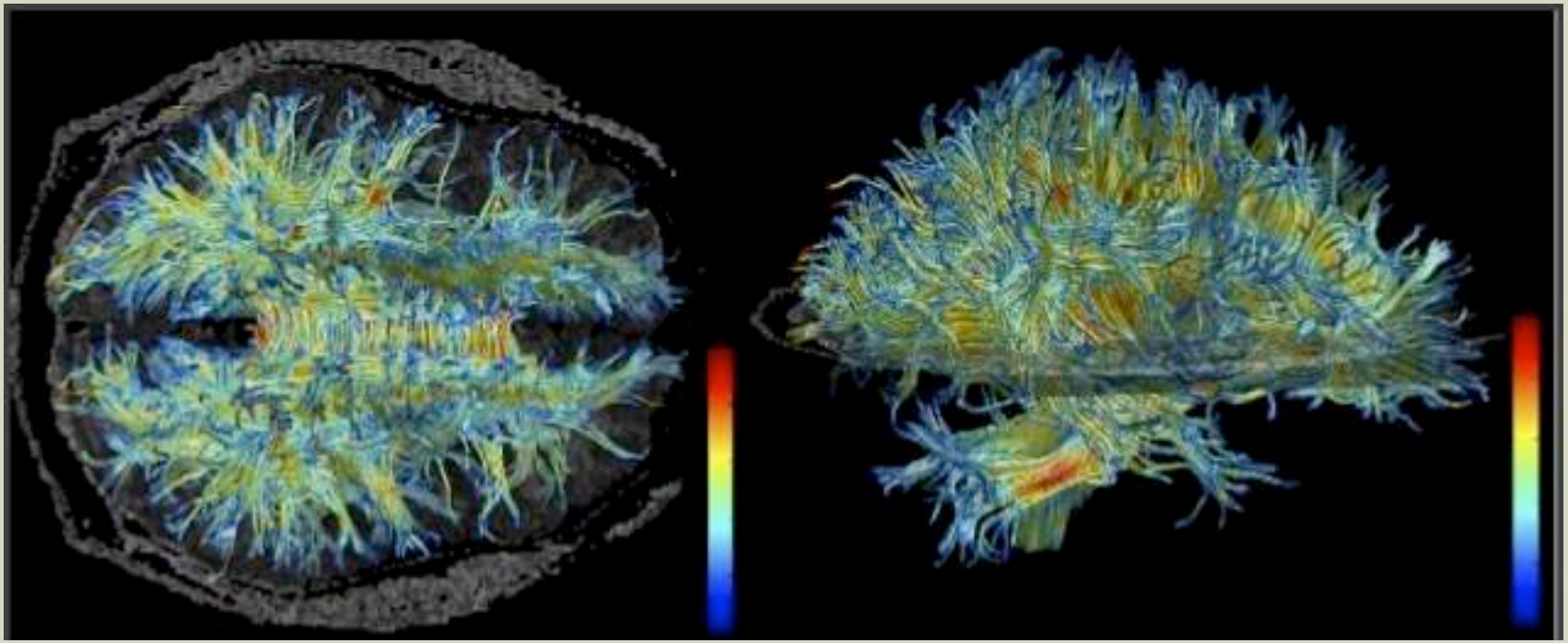
<u>Gray Matter</u>
Neuron Cell Bodies
Few Axons



<u>White Matter</u>
Myelinated Axons
Few cell bodies

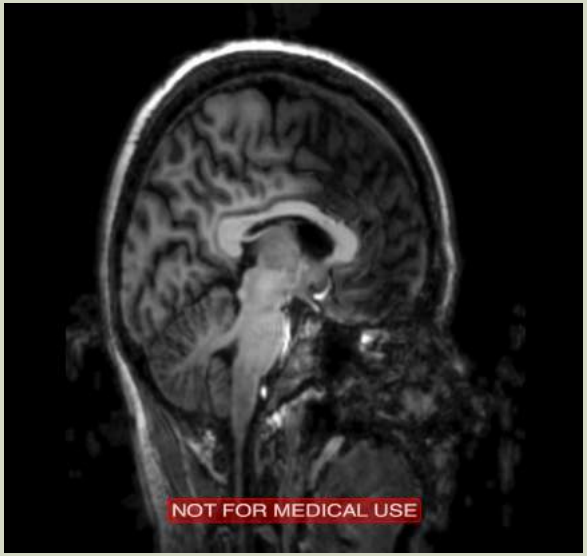
WHITE MATTER FIBER TRACTS

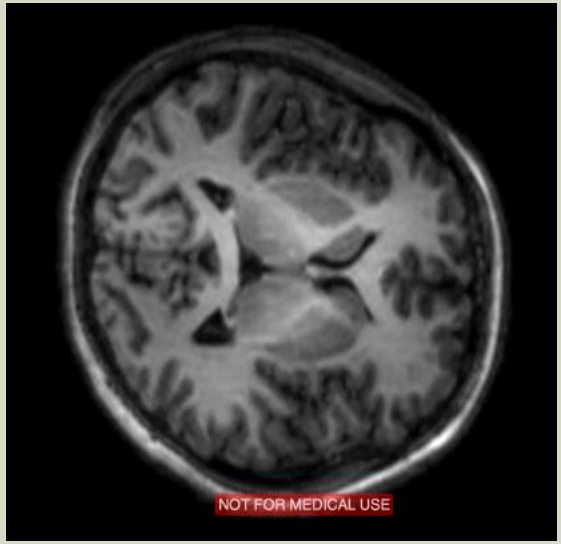
- White matter fiber bundles send messages from one brain region to another
- Neuroimaging techniques can map fiber tracts

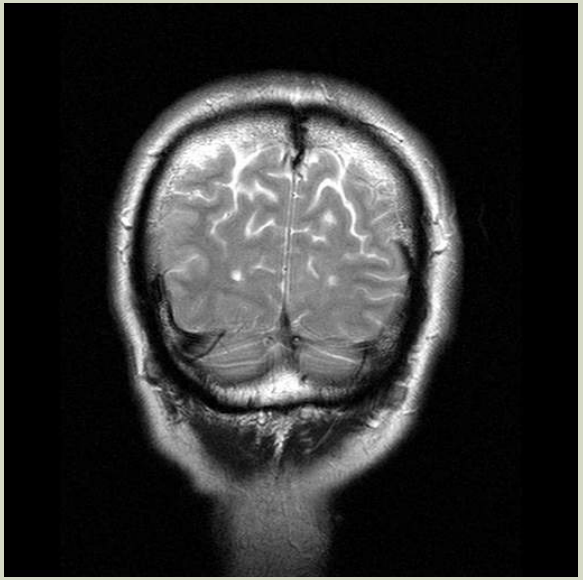


NEUROIMAGING TECHNIQUES

- Non-invasive methods for looking at the live human brain
  - Magnetic Resonance Imaging (MRI)
  - Computerized tomography (CT)
  - Positron emission tomography (PET)
  - Electroencephalogram (EEG)



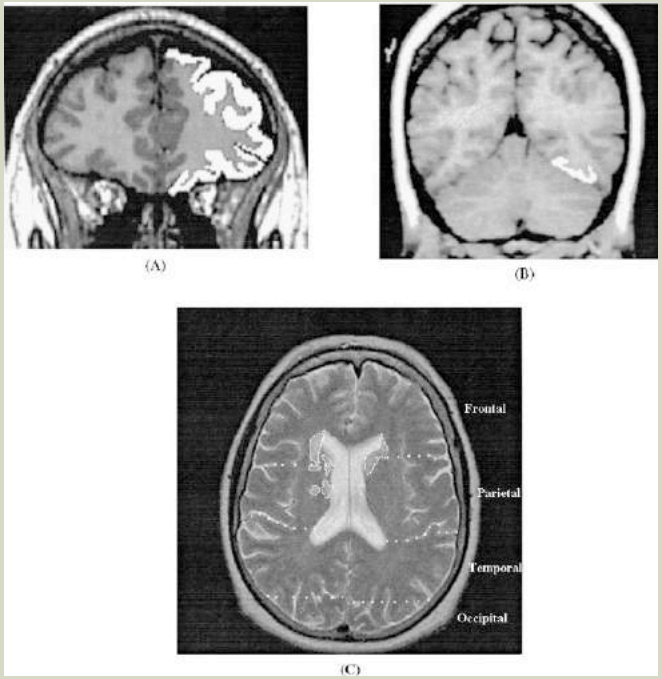




MRI Images

MEASURING BRAIN CHANGES IN AGING

- Naftali Raz- Wayne State University
- Charted changes in brain volume over time using MRI images

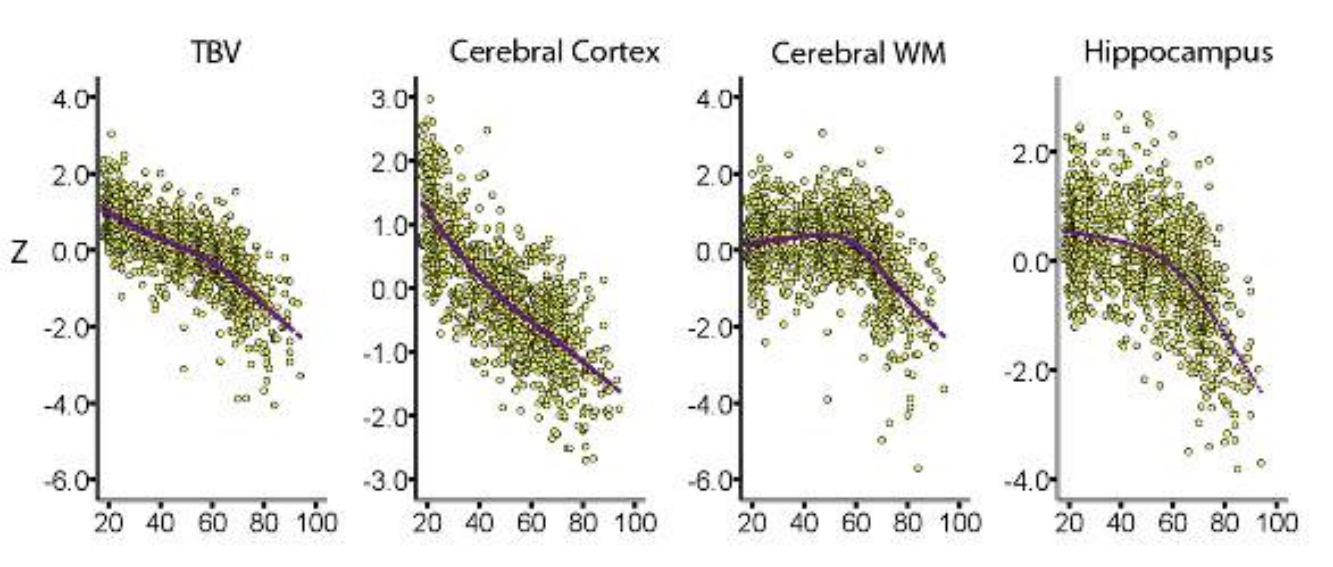


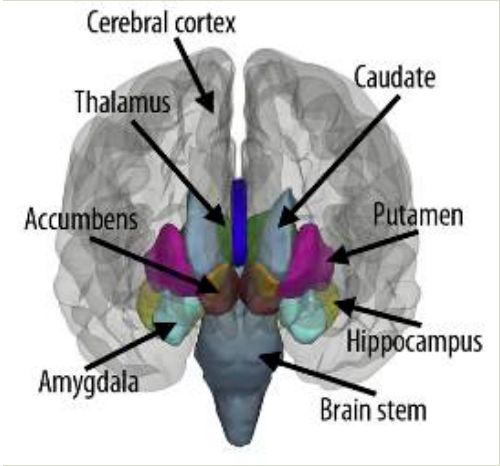
- Collected MRI brain scans from people ages 18-82
- Traced specific brain regions
- Recorded volume of those regions

1) Compared brain volume *between people* of different ages
2) Compared brain volume in the *same person* over time

PREFRONTAL CORTEX AND HIPPOCAMPUS SHRINK

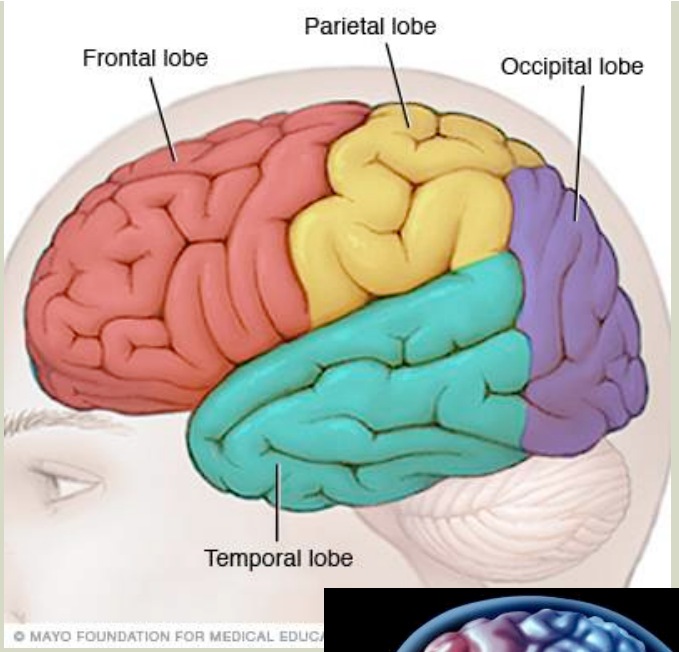
- Overall volume of GRAY matter declines with age
- Shrinkage is NOT uniform
- Some brain regions shrink, while others do not
- Prefrontal cortex and hippocampus shrank most





Fjeli et al., 2013

CORTICAL ANATOMY



- Cortex is the outside layer of gray matter on the brain
- Cortex divided into 4 major lobes
  1. Frontal lobe
  2. Temporal lobes
  3. Occipital lobe
  4. Parietal lobe
- The front-most parts of the frontal lobe = <u>prefrontal cortex</u>

PREFRONTAL CORTEX VOLUME SHRINKS WITH AGE

- Prefrontal cortex volume is 50% smaller in 80 vs. 20 year olds
- PFC volume shrunk by ½

What are the consequences of PFC shrinkage?

↓

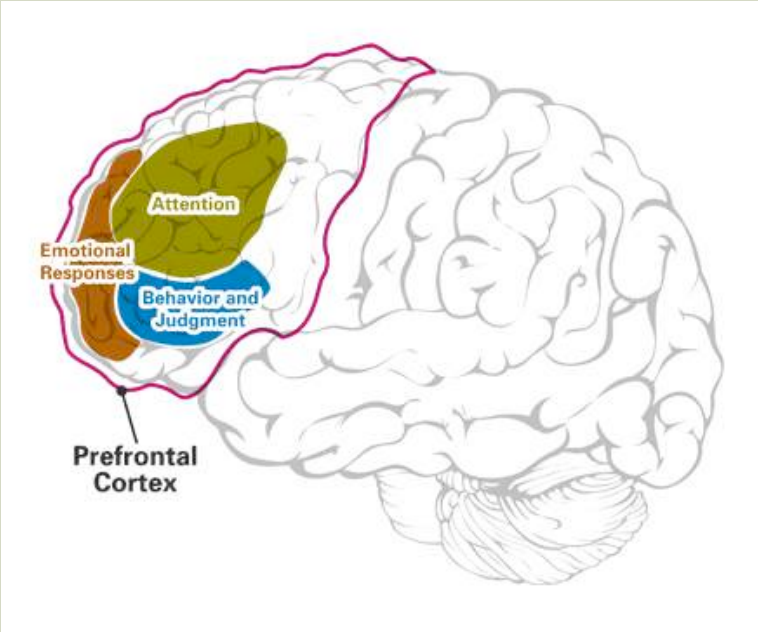
What is the function of the PFC?

PREFRONTAL CORTEX FUNCTION

- Supports our executive functions
  - Company executive- delegation, monitor progress, sets goals, etc.

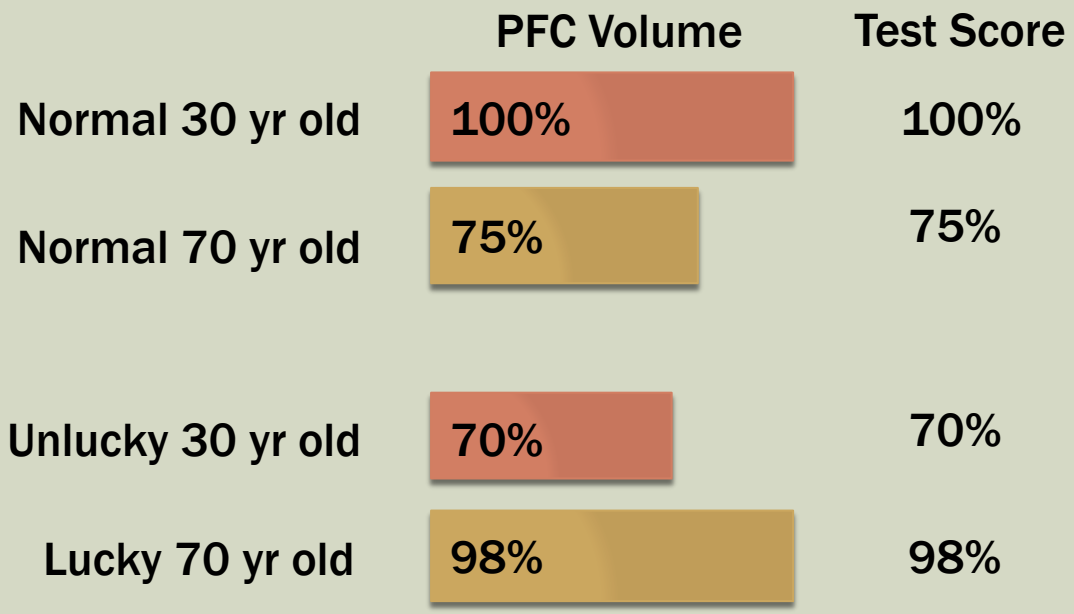
- PFC is our brain executive
  - Controls:
    - Emotions
    - Learning
    - Working memory
    - Social behavior
    - Planning
    - Problem solving
    - Monitors brain activity in lower regions
    - Focus and attention

  - <u>PFC shrinkage impacts</u>:
    - Multitasking
    - Attention and focus
    - Short-term recall



PREFRONTAL CORTEX VOLUME CORRELATES WITH FUNCTION

- People who have greater PFC volume perform better on tests of executive function
- Not everyone experiences PFC shrinkage at the same rate



Greater PFC volume correlates with greater performance on tests of executive function, regardless of age.

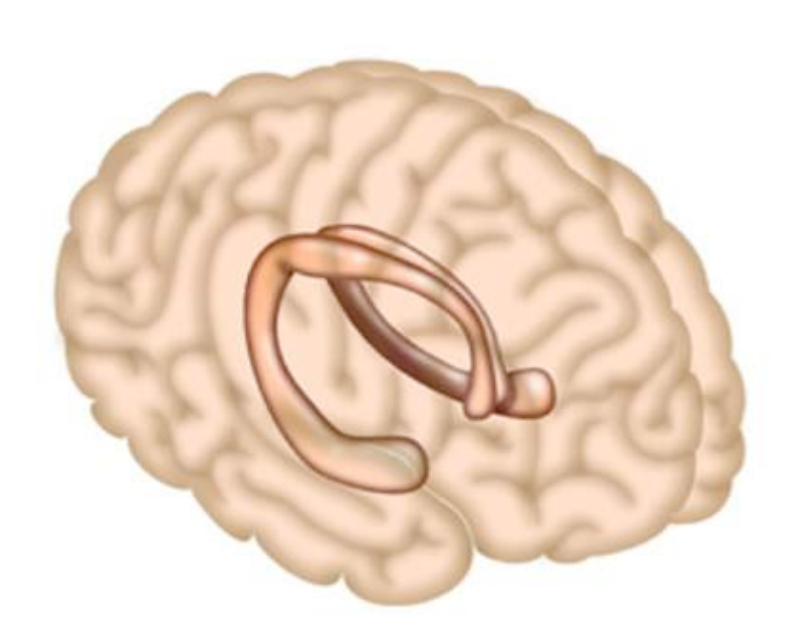
PFC controls executive function. → PFC shrinks with age. → Executive function deteriorates with age.

Structural changes → Functional consequences

Function Name	Action	Brain Region Affected
Processing Speed	Rate at which we can accomplish cognitive tasks	
Executive Function (Working Memory)	**Our ability to oversee and manage our most basic cognitive processes**	**Prefrontal cortex**
Episodic Memory	Short and long-term memories for episodes	

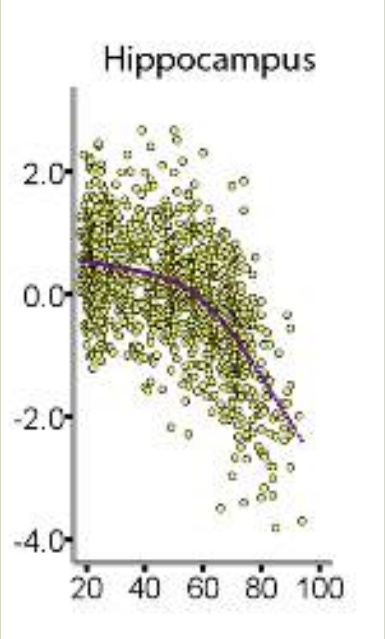
HIPPOCAMPAL ANATOMY

- 2 hippocampi – right and left hemispheres
- Hippocampus = “seahorse” in Greek
- Located under the medial temporal lobes



HIPPOCAMPUS SHRINKAGE DURING AGING

- Hippocampi also shrink with age
- 30% smaller in 80 year olds compared to 20 year olds

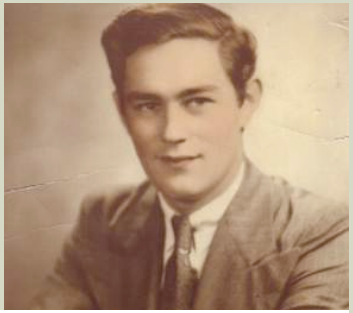


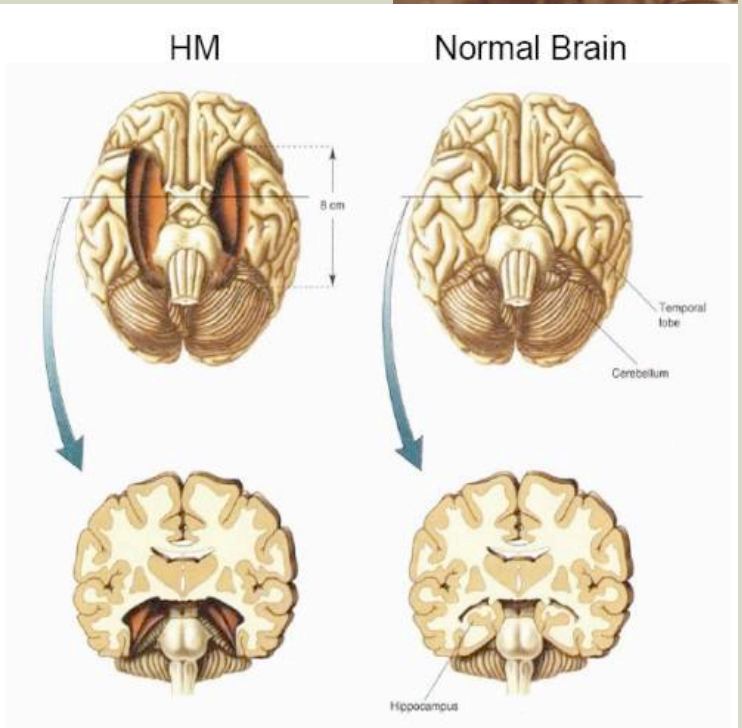
- *What are the consequences of hippocampal shrinkage on cognition?*
- *What functions are the hippocampi responsible for?*

HOW WE DISCOVERED HIPPOCAMPAL FUNCTION

- **Henry Molaison (HM)**
- Suffered from epilepsy since childhood
- Epilepsy = electrical storm in the brain that results in seizures
- Surgery to isolate and remove area of brain where the storm begins
- HM's electrical storms began in his medial temporal lobes
- 1953 HM had his hippocampi removed
- Relieved his seizures,

  however…..





HIPPOCAMPUS IS THE CENTER OF MEMORY

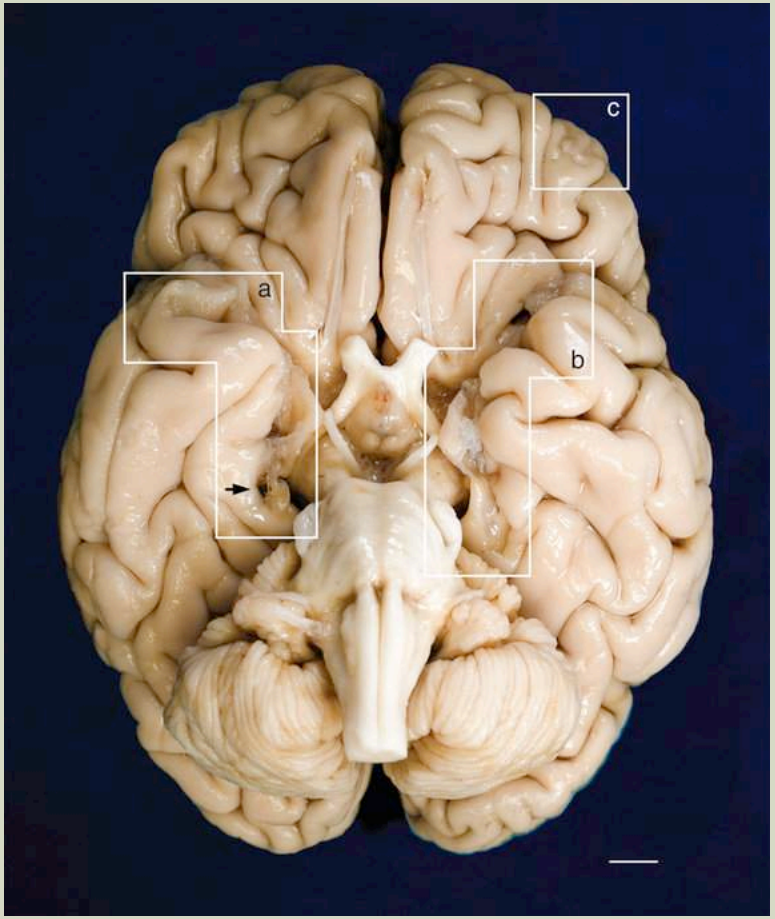
- HM's episodic memory dramatically impaired
- He could not longer remember personal episodes in his life, events in his life were no longer tied to a specific time or place
- He could not remember what he did last month, last week, or even 5 minutes before
- He could not remember anything that occurred since or a few years before his operation

HM in his 80's
2007, family released interviews
3 voices
    Female- Dr. Brenda Milner, scientist
    Older Male – HM
    Younger Male – Brian Newhouse, reporter

http://www.npr.org/templates/story/story.php?storyId=7584970

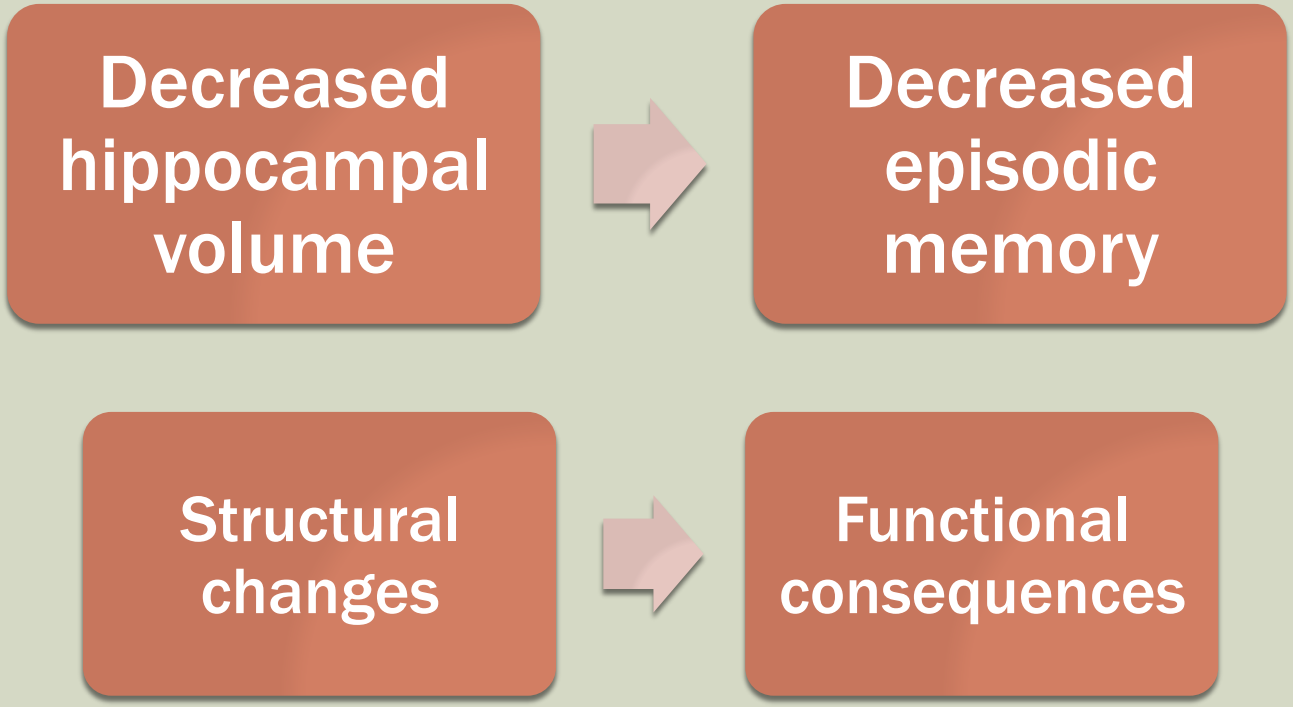
HM'S FINAL CONTRIBUTION

- HM's died on December 2, 2008
- Brain was donated to science



HIPPOCAMPUS IS CRUCIAL FOR EPISODIC MEMORY

- HM's case sheds light on the neuroscience of aging
- Demonstrates why hippocampal shrinkage impacts our episodic memory



SUPPORTIVE RESEARCH

- Karolinska Institute Stockholm, Sweden
- Measured hippocampal volume in the SAME individual at time points years apart
- Individuals who experienced the most hippocampal shrinkage had the greatest decline in episodic memory

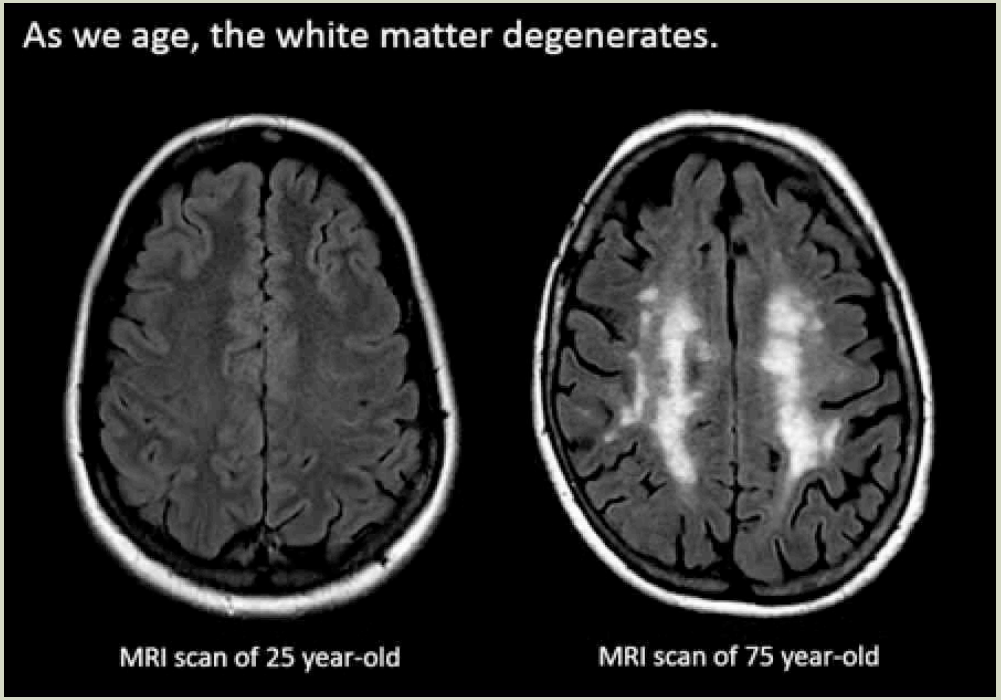
Function Name	Action	Brain Region Affected
Processing Speed	Rate at which we can accomplish cognitive tasks	
Executive Function (Working Memory)	Our ability to oversee and manage our most basic cognitive processes	Prefrontal cortex
Episodic Memory	**Short and long-term memories for episodes**	**Hippocampus**

WHITE MATTER HYPERINTENSITIES

The Aging Brain: Week by Week Time Lapse

https://www.youtube.com/watch?v=J3fb0CaDpEk

- Compared MRI images of older and younger individuals
- Older people have decreased white matter
- “Spots” on their white matter – areas of damage
- Termed hyperintensities
- Appear ~ age 55 in healthy people



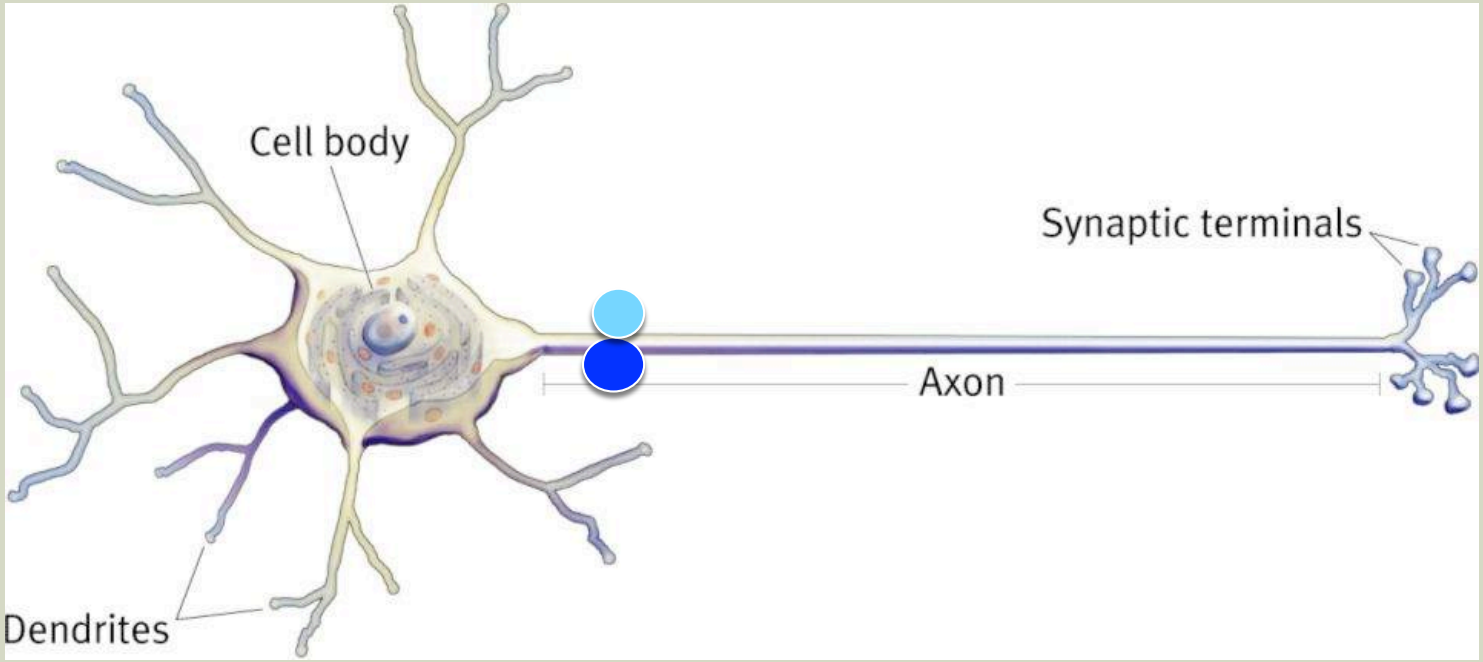
MAPPING WHITE MATTER HIGHWAYS

- Diffusion tension imaging (DTI)
  - Measures movement or diffusion of molecules in the body (water)
  - Detects which direction water molecules can and can not move
  - Uses directional information to construct and image of structural pathways

- Using headlights to map roads at night

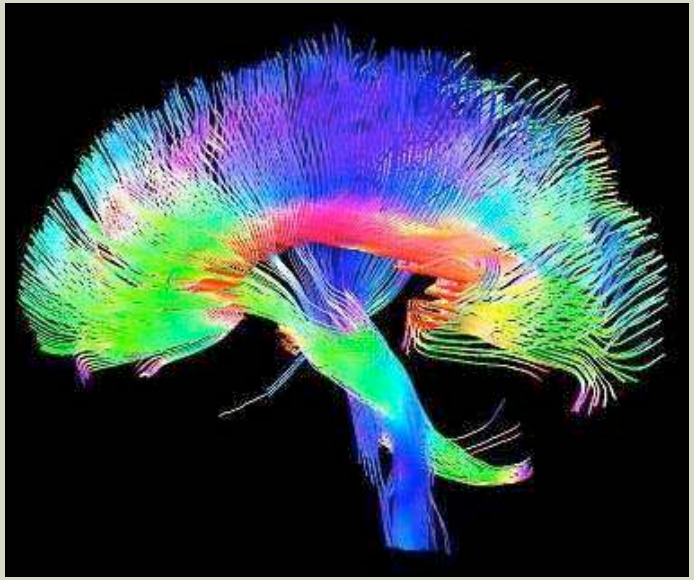
MAPPING WHITE MATTER HIGHWAYS

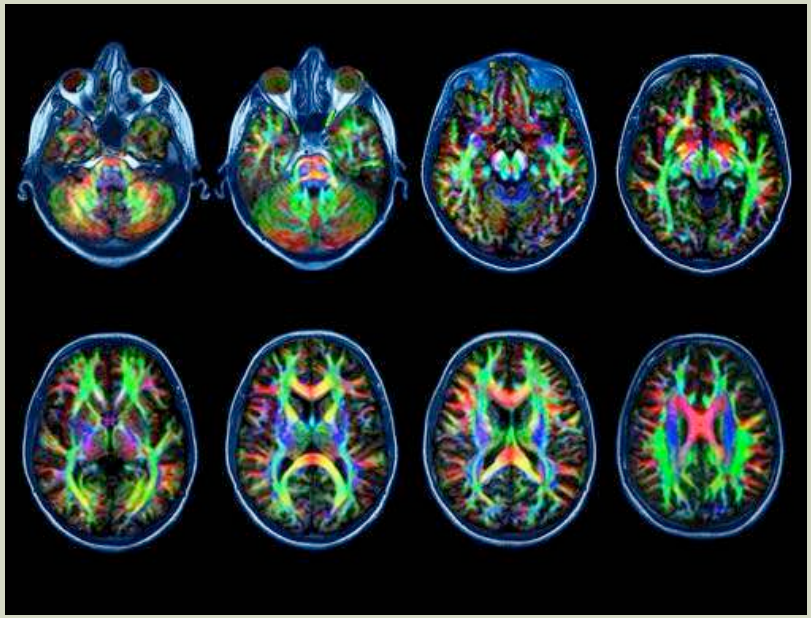
- Water molecules in the brain can only move down a neuron's axon
- Cannot move right, left, or back toward the cell body



MAPPING WHITE MATTER HIGHWAYS

- DTI
- By following the water, we can see where the axons go in white matter tracts
- Strong signals = more well myelinated axons in a pathway
- Weak signals = less myelinated axons in the pathway



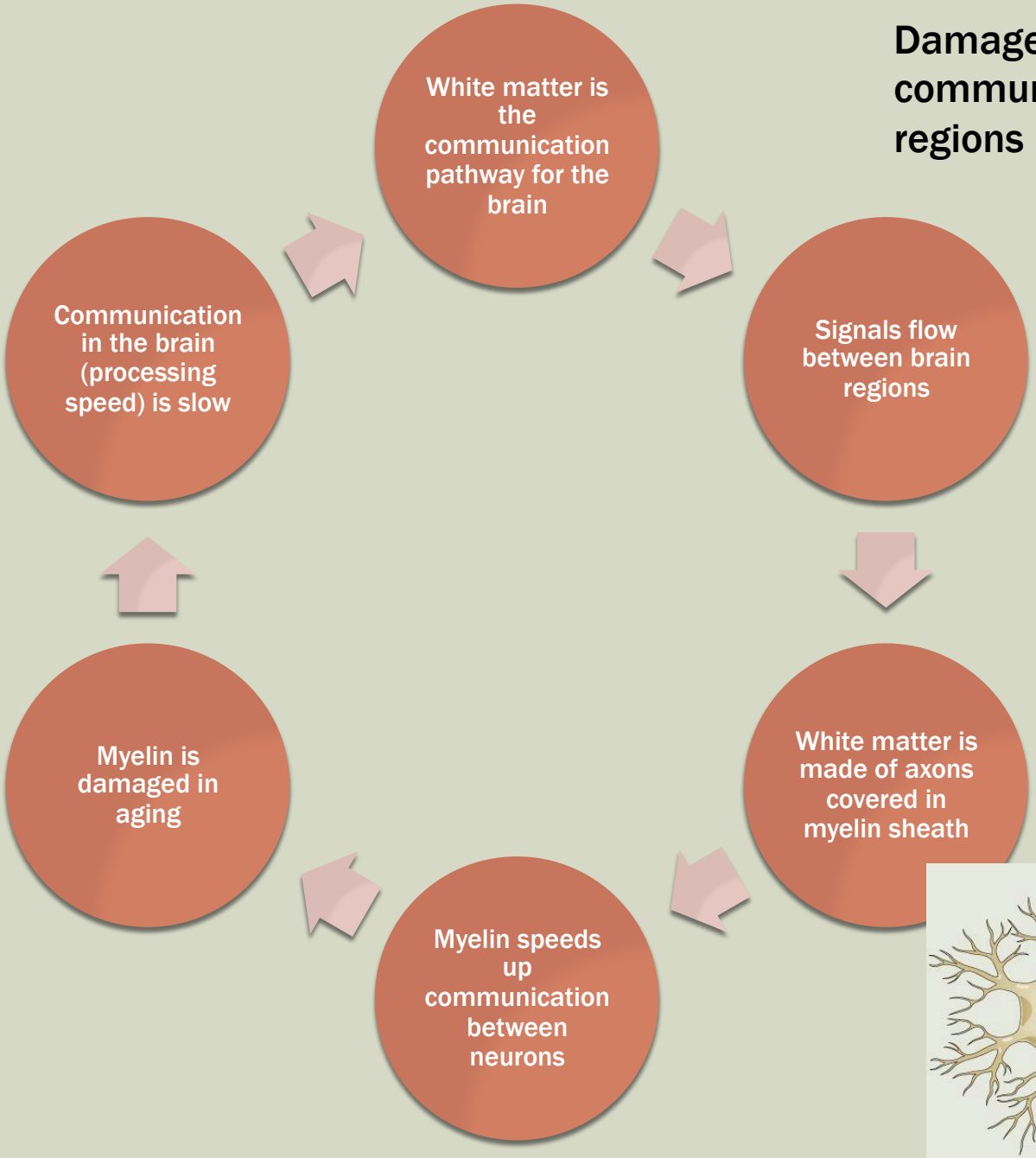


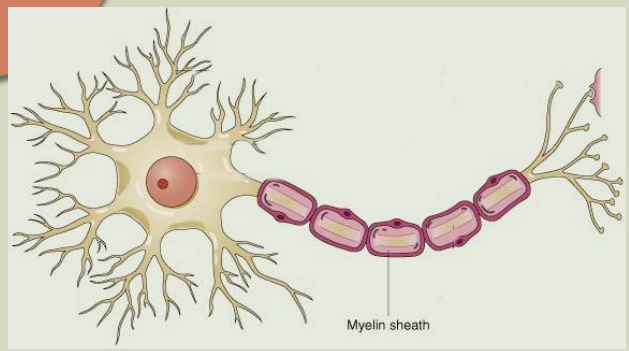
WHITE MATTER DAMAGE IN AGED BRAIN

- DTI studies demonstrate that white matter coherence and myelination decreases with age
- Weaker signals in aged brains
- Prevalent in the frontal lobe of the brain

What are the consequences for white matter hyper-intensities and decreased coherence on cognition?

Damage to white matter slows communication between brain regions in the aged brain.





Function Name	Action	Brain Region Affected
Processing Speed	**Rate at which we can accomplish cognitive tasks**	**White matter tracts**
Executive Function (Working Memory)	Our ability to oversee and manage our most basic cognitive processes	Prefrontal cortex
Episodic Memory	Short and long-term memories for episodes	Hippocampus

Structural changes → Functional consequences

SUMMARY

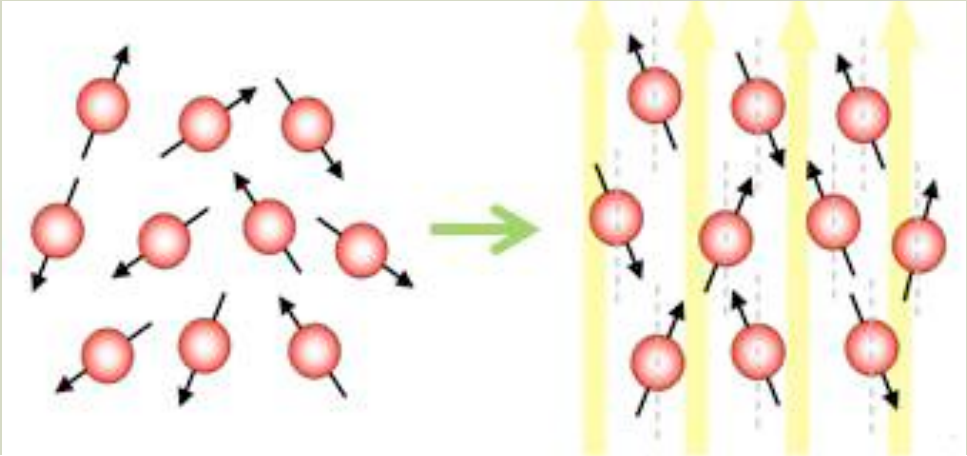
- Reviewed some of the brain's structural changes that occur in healthy aging
  - Prefrontal cortex shrinks
  - Hippocampi shrink
  - White matter becomes less efficient
- Changes in brain structure may explain some cognitive deficits that occur in aging
  - Executive function
  - Episodic memory
  - Processing speed
- Changes in the brain's structure only tell part of the story…
- **Does the brain's function change? Do older people use the same regions of the brain as younger people? How does activity change in the aged brain?**

AGING AND BRAIN FUNCTION

THE AGED BRAIN ADAPTS TO CHANGES

- Brain structural deterioration means corresponding deterioration in neural function
- Our brains don’t take structural deterioration lying down
- The brain is able to reorganize itself to compensate for structural deterioration
- Allows us to perform significantly better as we age

- To study the brain in action, we need to be able to see the brain in action
- **Functional Magnetic Resonance Imaging (fMRI)**
  - Create images of the inside of your body
  - Based on a very strong magnetic field
  - Protons in hydrogen atoms of water molecules act as tiny magnets
  - Hydrogen protons line up with magnetic field
  - Scanner then uses radio frequency pulses to kick those protons out of alignment
  - When pulse stops, protons realign and give off energy that can be detected by the scanner

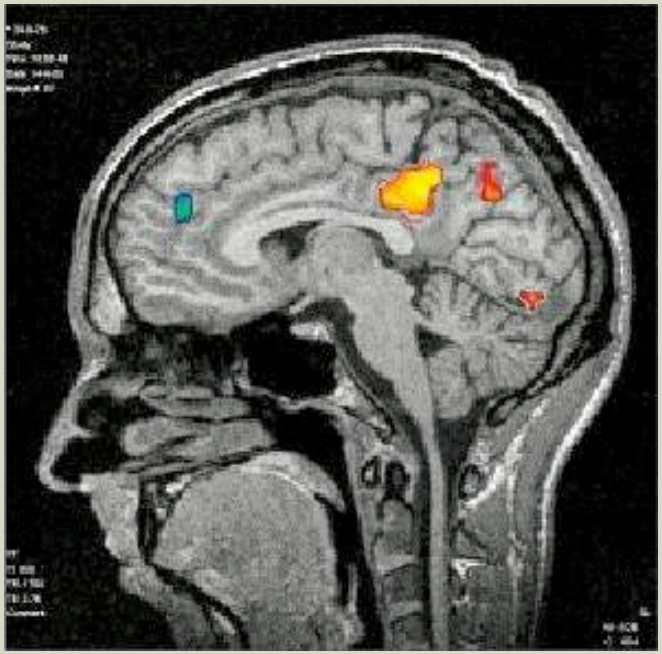


MRI PURPOSE IN BRAIN HEALTH

- MRI – different magnetic properties in different tissues gives us a picture of bone, brain, cartilage, etc.

Structural Image

- fMRI – blood carrying and not carrying oxygen has different magnetic properties; follow oxygenated blood to see active brain areas



Functional Image

AGE RELATED ALTERATIONS IN BRAIN FUNCTION

Decline

- Neural specificity
- Communication between brain areas

Increase

- Brain reorganization and compensation

NEURAL SPECIFICITY

- Different areas of our brain, different neurons, perform specific functions
  - Example:
    - Reading letters and numbers- different parts of the brain react when we are reading letters versus digits
    - Identifying faces or body parts – different parts of the brain are activated when asked to identify a face versus a leg
  - Selective areas of neural response
  - Different stimuli are processed in different areas
- Identified in the brains of young people
- Does neural specificity change in the aged brain?

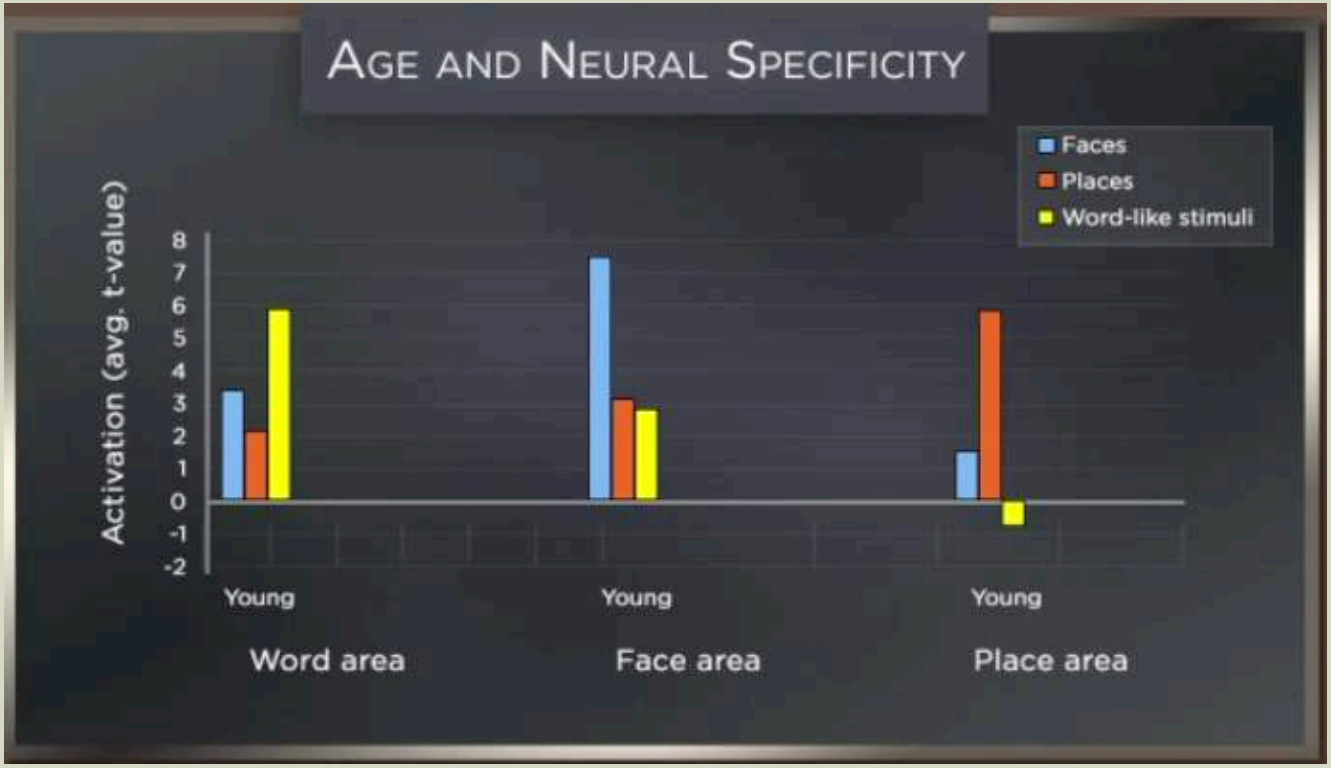
fMRI of a harpist listening to Bach

NEURAL SPECIFICITY STUDIES

Neural Specificity ↑↓ = ?

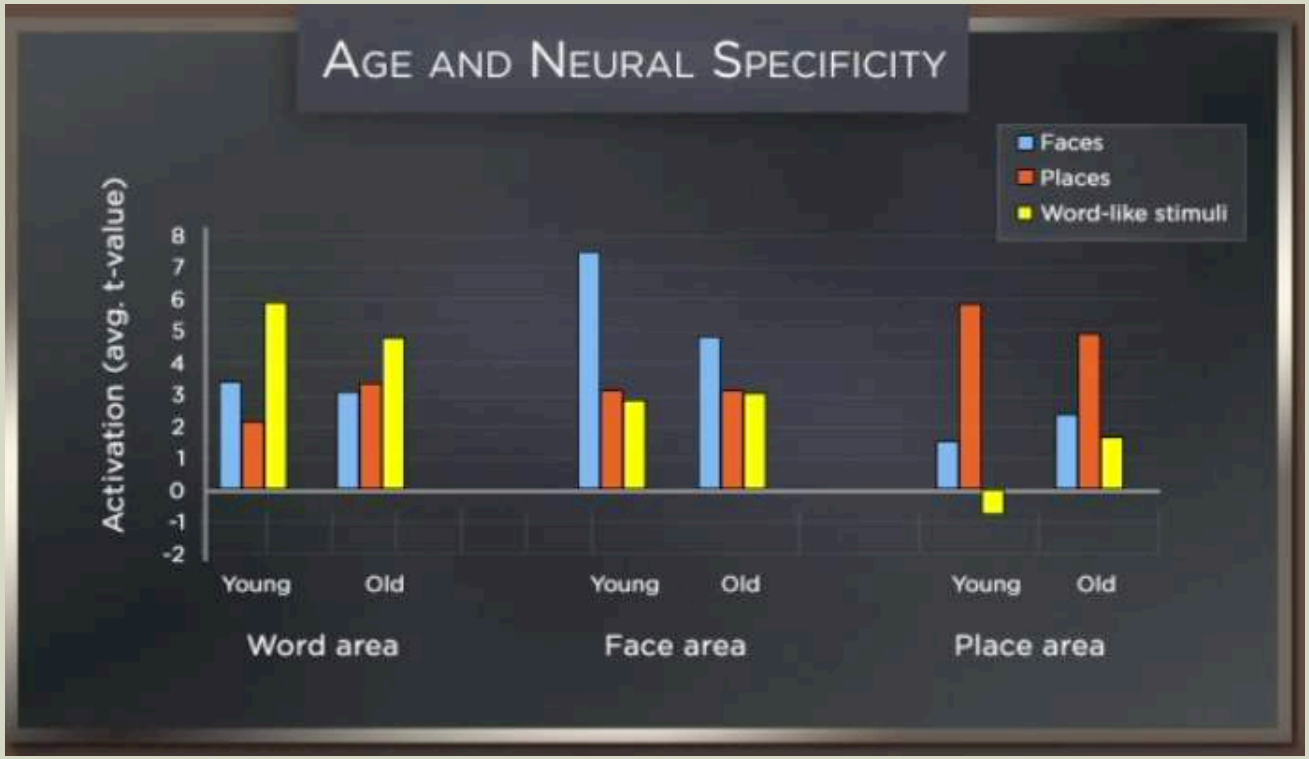
- Polk and Park – University of Michigan
- fMRI scans of college age and older (~70 years old) adults
- During fMRI scans, participants looked at
  1. Words
  2. Pictures of places
  3. Pictures of faces

NEURAL SPECIFICITY STUDIES



- Young adults have high neural specificity
- Areas that selectively respond to words, places, and faces

NEURAL SPECIFICITY IS REDUCED IN AGED PATIENTS



- Neural specificity was reduced in the older participants
- Multiple regions were highly activated during each task
- The differentiation between neural responses was reduced in the older people
- “Age-related neural dedifferentiation”

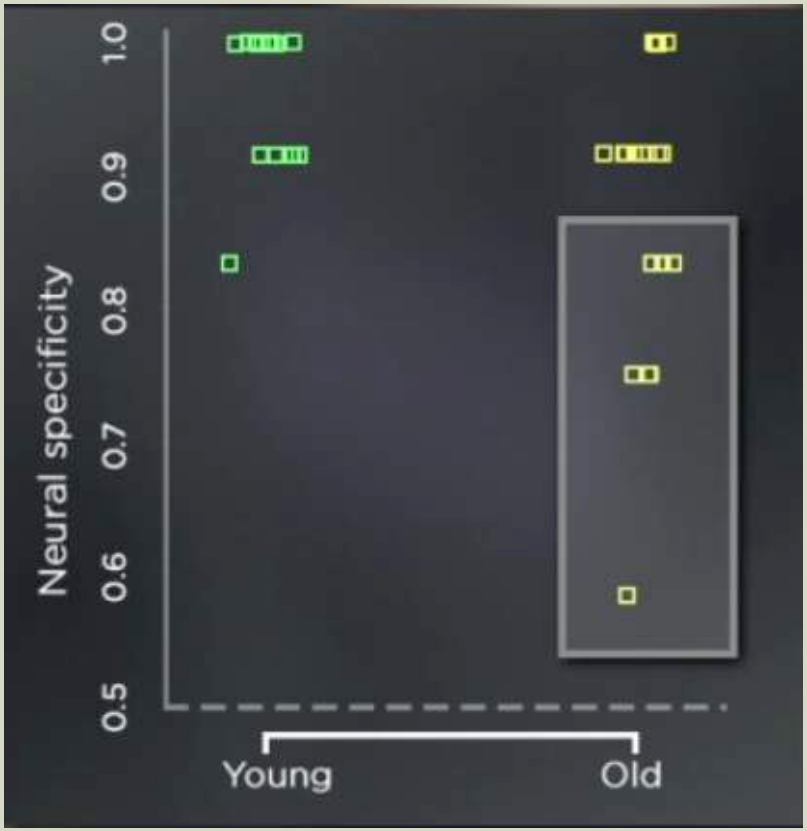
DOES REDUCED NEURAL SPECIFICITY MATTER?

- Neural representations get less distinctive as we age
- Does that matter?

- Park and Carp- University of Michigan
- fMRIs on of participants in 20's and 60's
- Performed a visual matching tasks on pictures of faces and buildings
- Measured the distinctiveness of neural activation patterns in the brains associated with either task

NEURAL SPECIFICITY IS DIVERSE

- Levels of neural specificity is diverse within older populations
- Some older participants had less neural specificity
- Some had neural specificity similar to the 20 year olds



NEURAL SPECIFICITY AND COGNITIVE PERFORMANCE ARE RELATED

- The older people in that study were all given a battery of cognitive tests
  - Executive function (declines with age)
  - Processing speed (declines with age)

- Those with the <u>most</u> neural specificity had the <u>least</u> impairments in executive function and processing speed
- Changes in age-related neural distinctiveness may be linked to age-related changes in cognitive decline

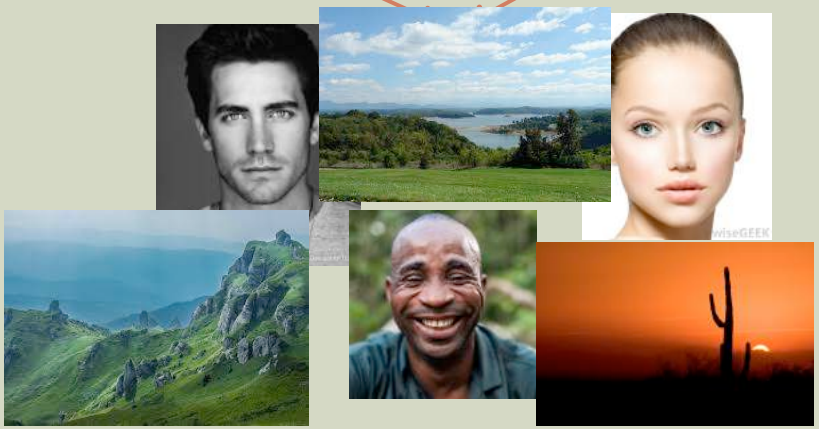
COMMUNICATION BETWEEN BRAIN REGIONS CHANGES WITH AGE

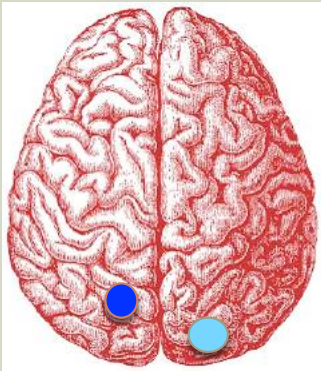
- UC Berkley

Groups

fMRI

Asked to remember names OR faces





Active region for scenes
Active region for faces

Brain Activity

	Remember scenes	Ignore scenes
Young	+++	-
Old	+++	+

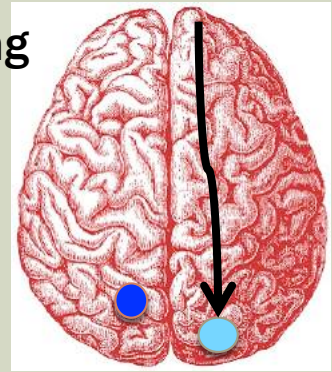
- When asked to remember scenes, the scene region of the brain was highly active in BOTH groups.

- When asked to ignore scenes, the scenes region of the brain was INACTIVE in YOUNG brains, but ACTIVE in AGED brains

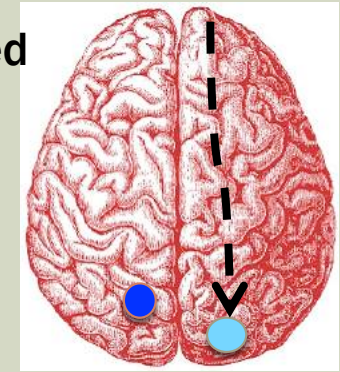
COMMUNICATION BETWEEN BRAIN REGIONS CHANGES WITH AGE

- Why did the scene brain region not turn off when asked to ignore the scene images?
- In older adults, the scene region was never told to turn 'off' – or was never inhibited
- What type of brain region in involved in making executive decisions- PREFRONTAL CORTEX!

young



aged



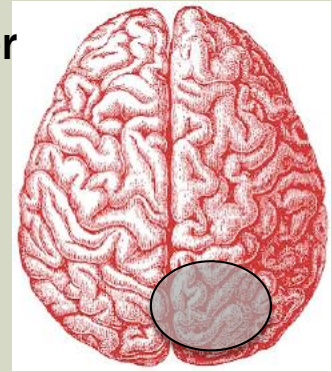
REORGANIZATION AND COMPENSATION WITH AGE

- Brain changes and evolves through life time
- Brain has built in mechanisms to compensate for age-related changes

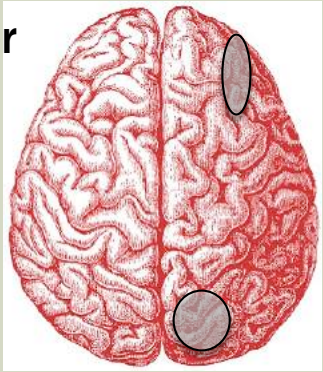
- Haxby and Grady study
- fMRI to examine activation areas during a matching task

Younger

1 posterior area



Older



1 posterior and 1 anterior area

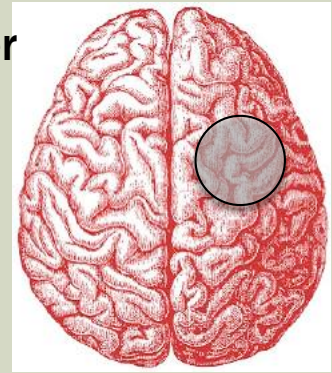
Posterior to anterior reorganization common in aged brain

REORGANIZATION AND COMPENSATION WITH AGE

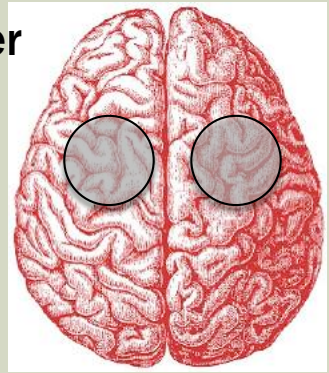
- Lateralization of brain activity- activity usually in a single hemisphere moves to both hemispheres

Younger

Lateral



Older



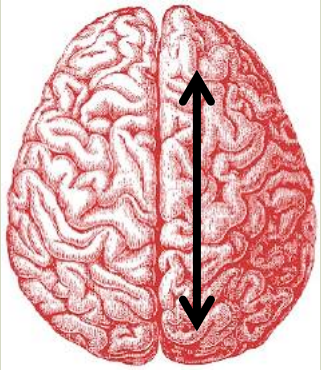
Bilateral

Cognitive tasks that evoke activity in a <u>SINGLE</u> hemisphere in <u>young</u> adults, evoke activity in <u>BOTH</u> hemispheres in <u>aged</u> adults.

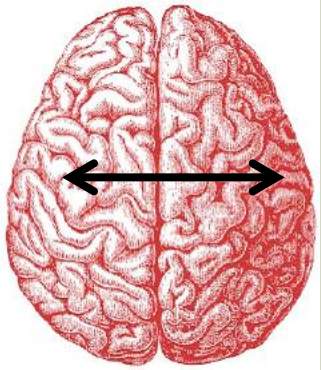
Ex: episodic memory retrieval, working memory tasks

REORGANIZATION AND COMPENSATION WITH AGE

Summary of aged brain functional shifting:



Posterior to Anterior



Lateral to Bilateral

- Aged brain can activate additional areas of the brain
- Compensatory mechanism
- Brain can adapt and compensate for impaired function in a single region by increasing function in another
- Results in increased cognitive abilities

SUMMARY

- The aged brain experiences undesirable changes in brain function
  - Neural distinctiveness
  - Communication between brain regions
- Changes in function impact our cognitive ability as we age
- Compensatory changes, recruiting new brain region for function, is our brain's way of adapting to change
- Compensatory mechanisms can maintain or even enhance our cognitive abilities as we age

TODAY'S LECTURE

1. What cognitive changes occur in the healthy aging brain?
2. How does brain structure change as we age?
3. How does brain function change as we age?

GOOD READS

- **Patient H.M.: A Story of Memory, Madness, and Family Secrets** by Luke Dittrich
- **In Search of Memory** by Eric Kandel
- **The Brain That Changes Itself: Stories of Personal Triumph from the Frontiers of Brain Science** by Norman Doidge
- **The Scientific American Healthy Aging Brain: The Neuroscience of Making the Most of your Mature Mind** by Judith Horstman
- **Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging** by Robert Cabeza, Lars Nyberg, and Denise Park