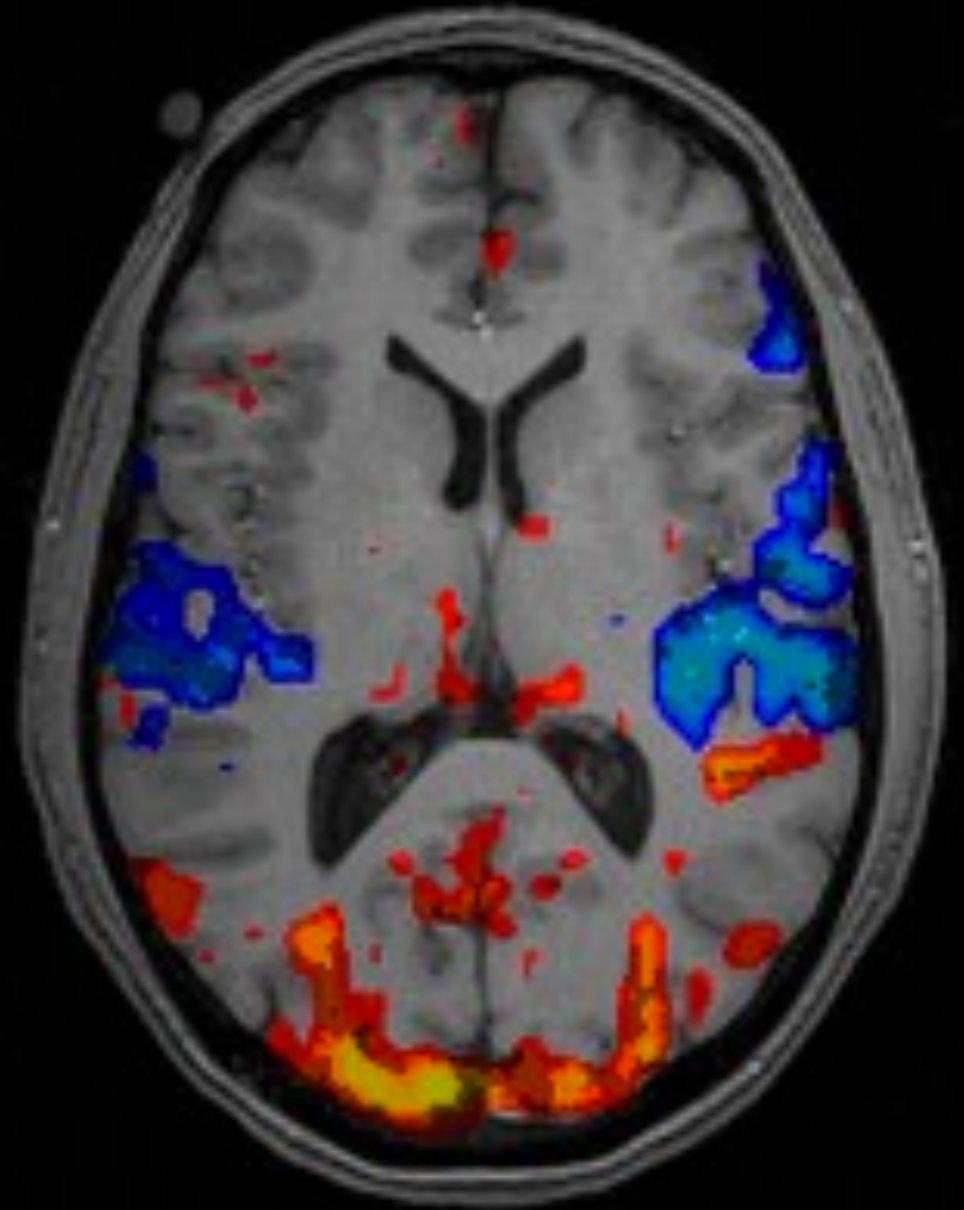


ASHI691:

Why We Fall Apart:  
The Neuroscience and  
Neurophysiology of Aging

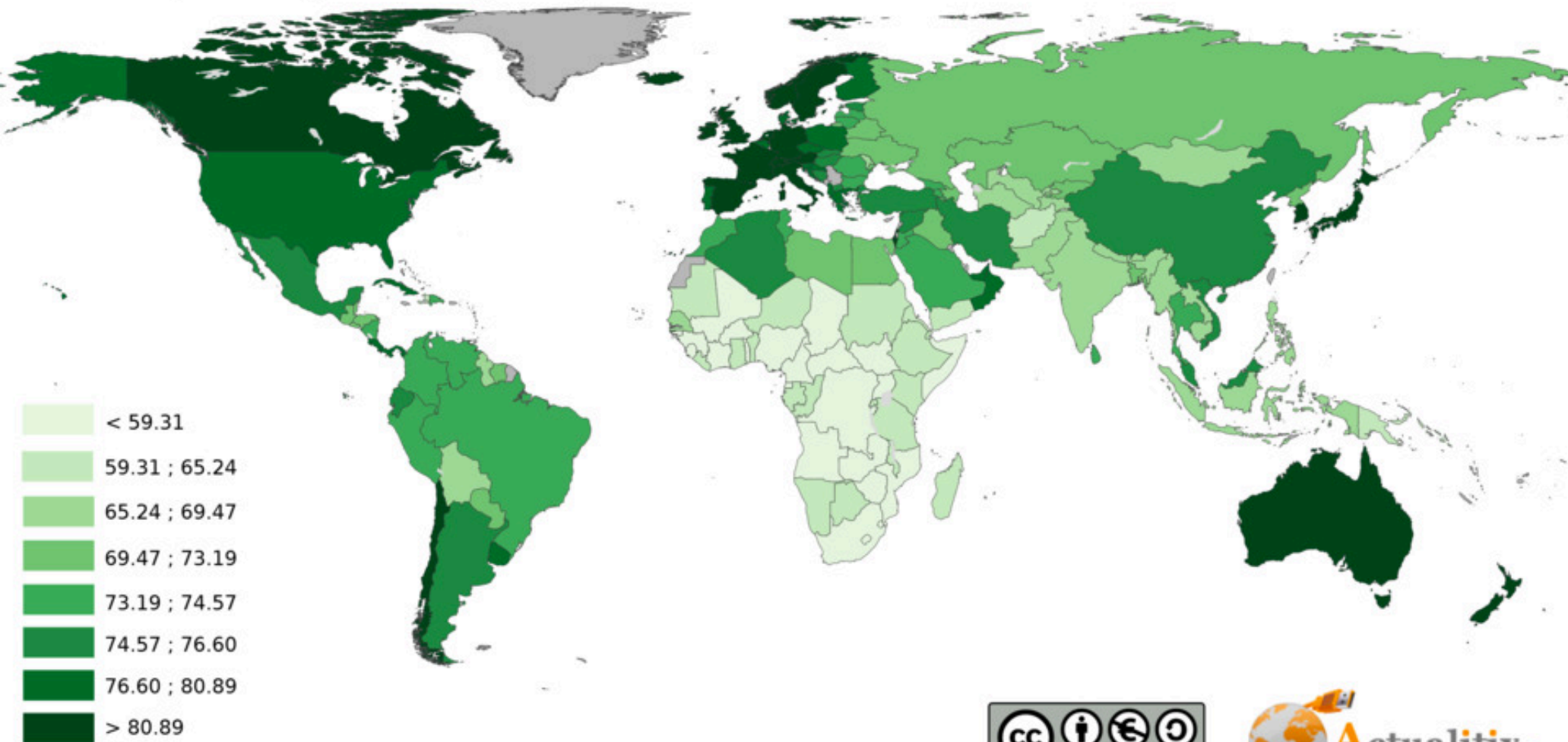
DR. OLAV E. KRIGOLSON  
krigolson@uvic.ca

LECTURE 2:  
THE AGING BRAIN



Relatively few people die of old age.

## Life expectancy at birth (years)



Source : The World Bank - 2013  
Copyright © Actualitix.com All rights reserved

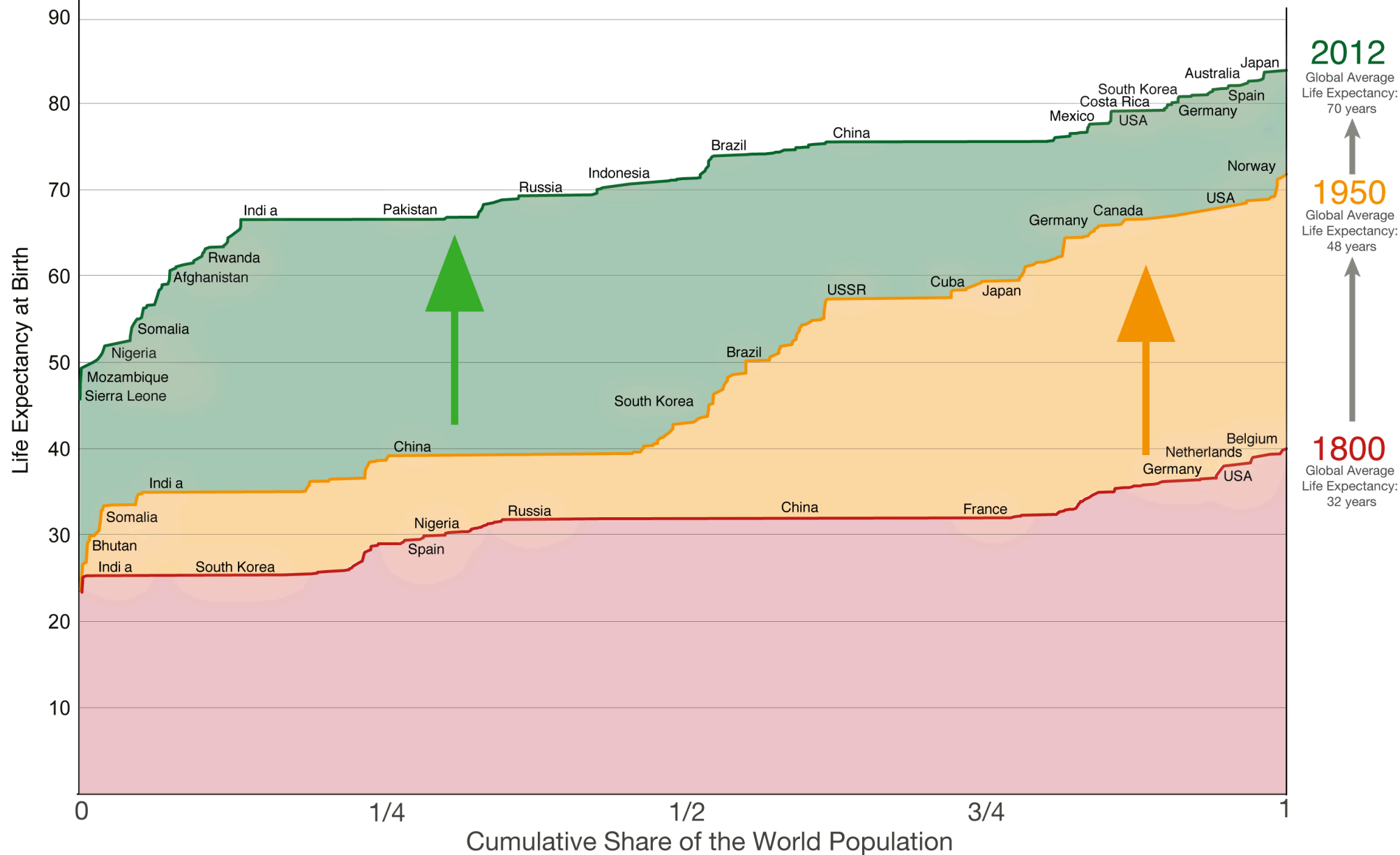


Male		Female	
Country	Years	Country	Years
<b>Highest</b>		<b>Highest</b>	
Switzerland	81.3	Japan	86.8
Iceland	81.2	Singapore	86.1
Australia	80.9	Spain	85.5
Sweden	80.7	Republic of Korea	85.5
Israel	80.6	France	85.4
Japan	80.5	Switzerland	85.3
Italy	80.5	Australia	84.8
Canada	80.2	Italy	84.8
Spain	80.1	Israel	84.3
Singapore	80.0	Iceland	84.1
<b>Lowest</b>		<b>Lowest</b>	
Lesotho	51.7	Chad	54.5
Chad	51.7	Côte d'Ivoire	54.4
Central African Republic	50.9	Central African Republic	54.1
Angola	50.9	Angola	54.0
Sierra Leone	49.3	Sierra Leone	50.8



# Life Expectancy of the World Population in 1800, 1950 and 2012

Countries are ordered along the x-axis ascending by the life expectancy of the population. Data for almost all countries is shown in this chart, but not all data points are labelled with the country name.

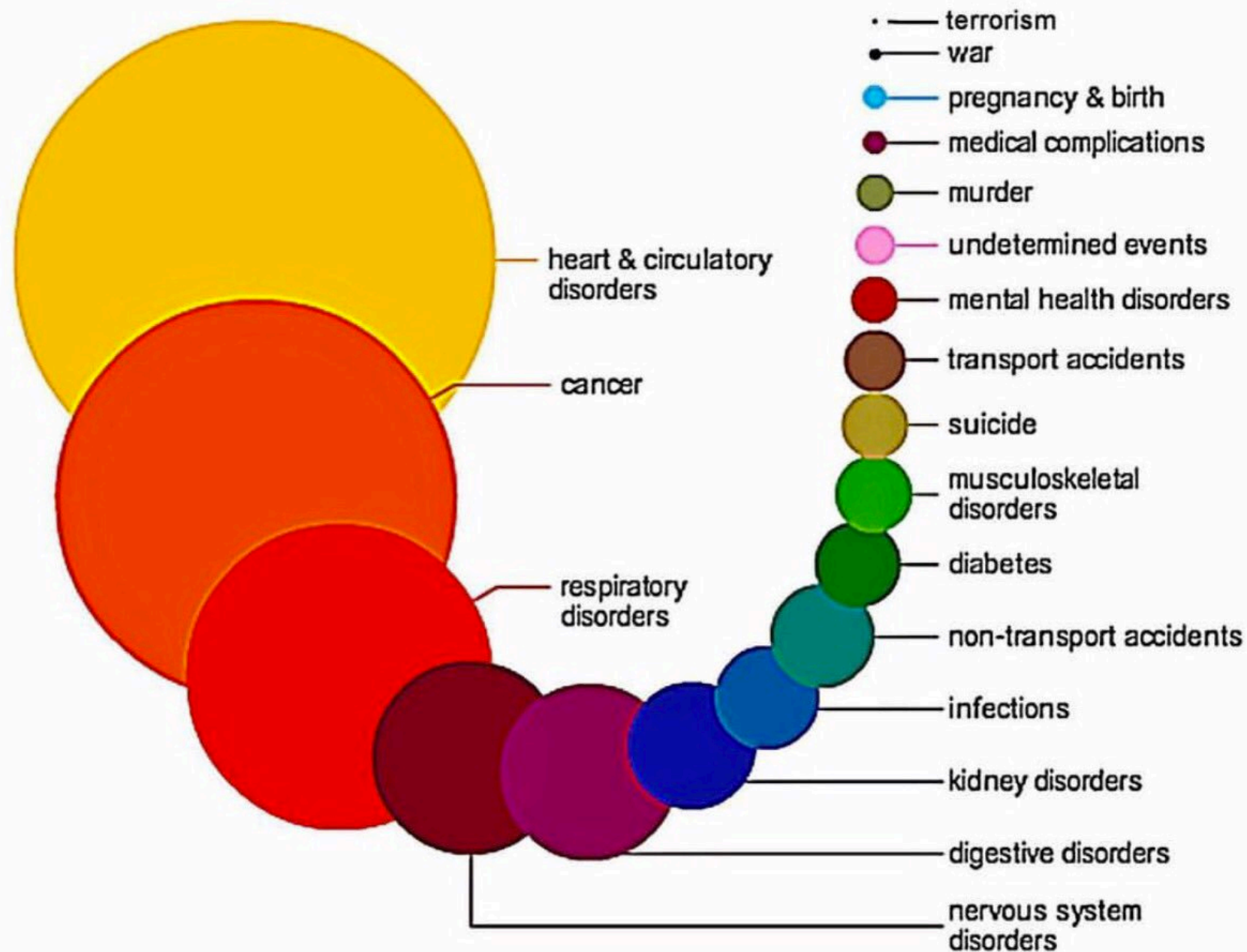


Data source: The data on life expectancy by country and population by country are taken from [Gapminder.org](https://Gapminder.org).

The interactive data visualisation is available at [OurWorldinData.org](https://OurWorldinData.org). There you find the raw data and more visualisations on this topic.

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# Leading causes of death in perspective



# Definition of Normal Biological Aging

“the decline and deterioration of functional capability at the cellular, tissue, organ, and systems level”

AGING leads to:

1. Loss of ability to maintain homeostasis
2. Decreased ability to adapt to internal and external stress
3. Damage to body systems

Loss of functional properties and decrease in ability to adapt to stress results in increased vulnerability to disease and mortality

1. Loss of ability to maintain homeostasis

# **Homeostasis**

**Important functions that must be maintained by body  
(amongst others)**

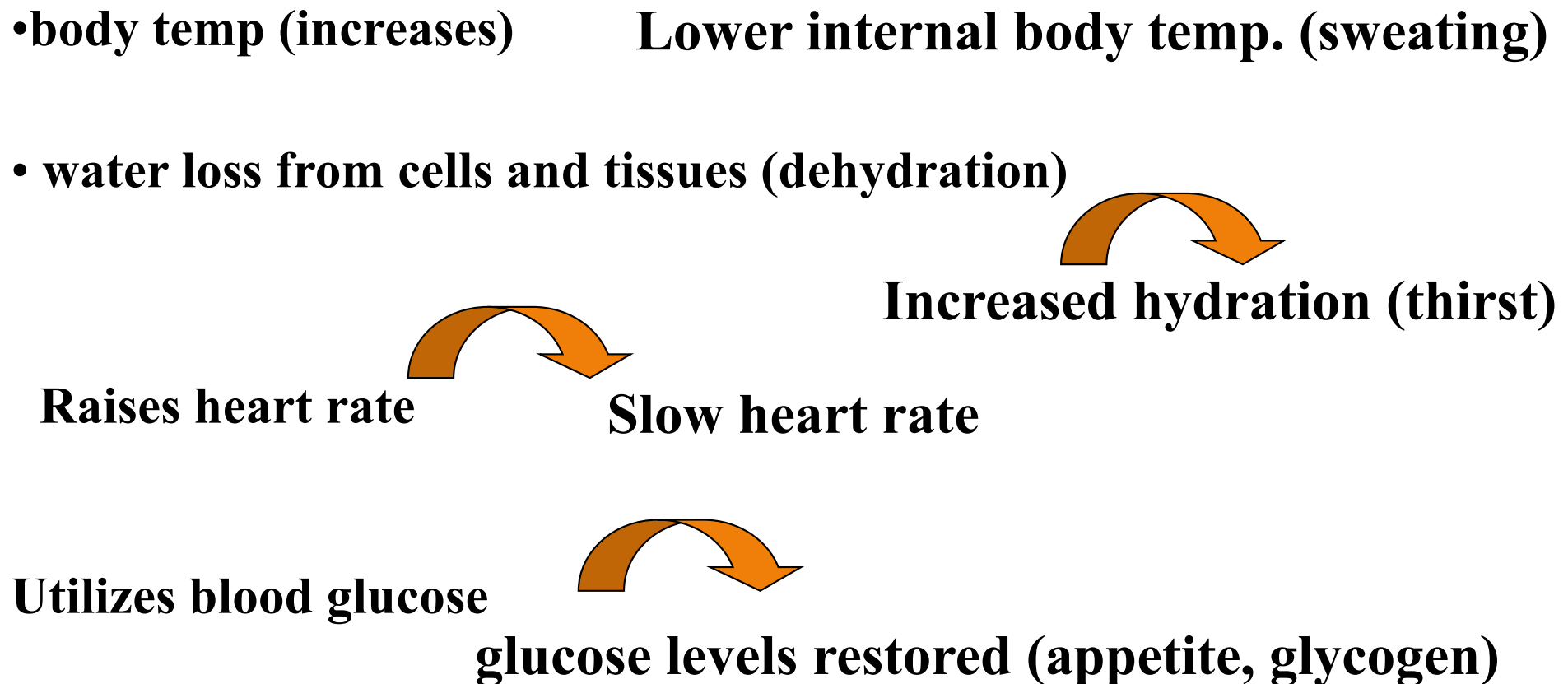
- 1. blood sugar levels (glucose)**
- 2. water content (dehydration)**
- 3. pH (gas exchange of CO<sub>2</sub> and O<sub>2</sub>)**
- 4. body heat (body temperature)**
- 5. nutrient levels**



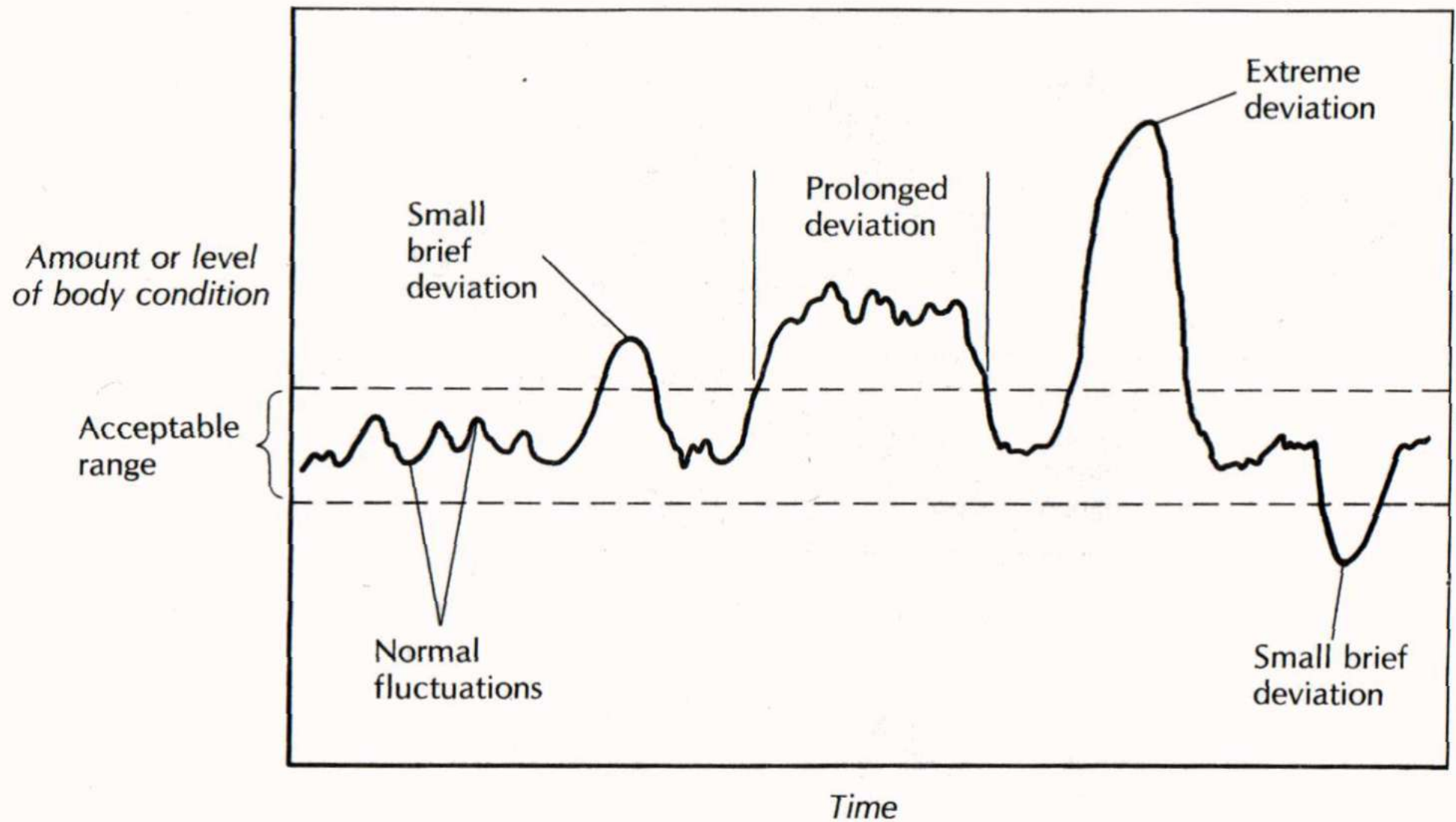
## **Examples of Homeostasis:**

- **Conditions in the body change from time/time**
- **Every time we alter body conditions, we alter homeostasis**

### **Running or walking:**



**FIGURE 1.9** Homeostasis and unacceptable alterations in body conditions.



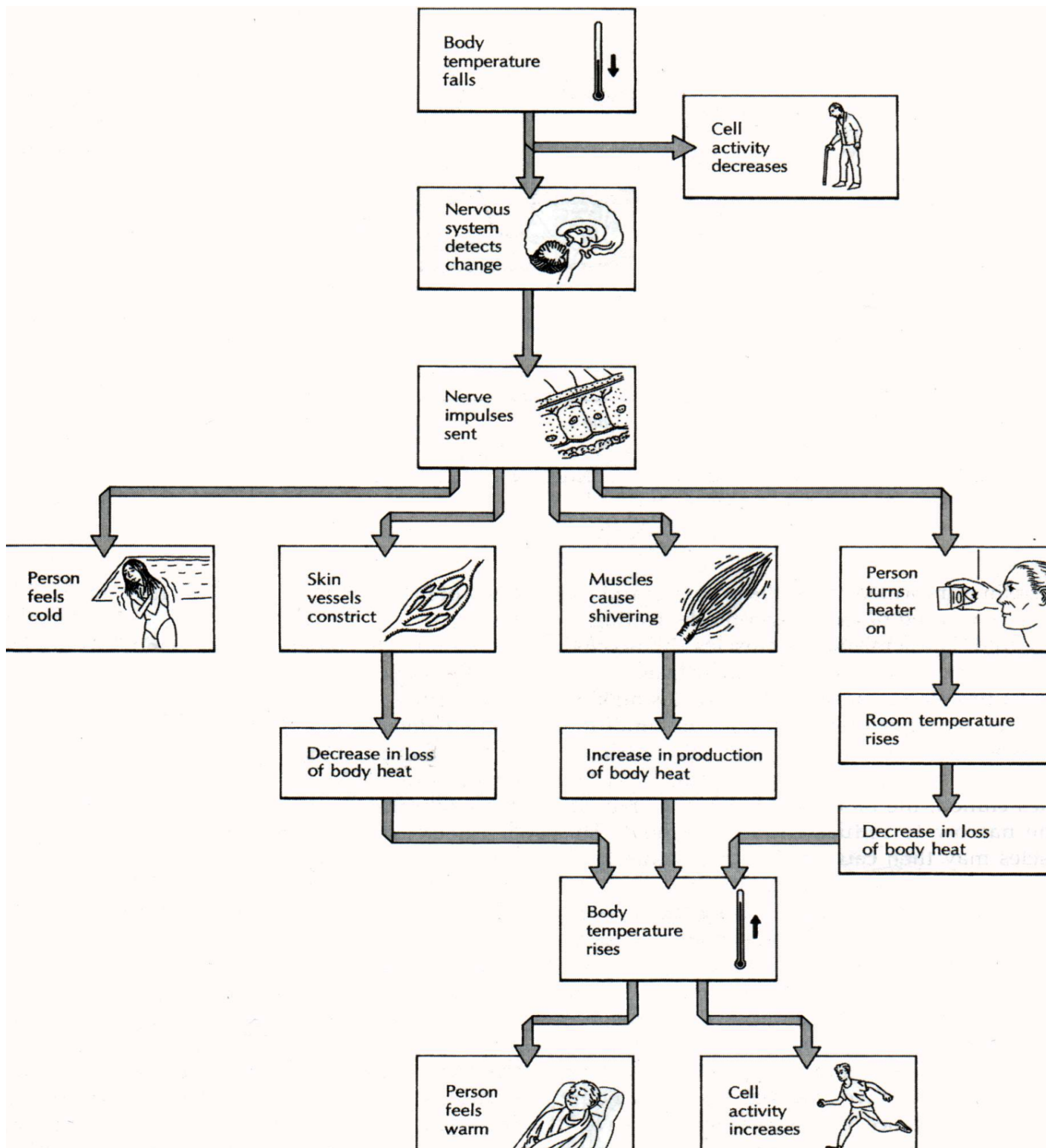
# **How do cells of body maintain homeostasis?**

## **Negative feedback systems (control of brain-nervous system)**

**Monitors homeostasis by 3 basic steps:**

- 1. Detecting presence of deviations from homeostasis**
- 2. Informing part(s) of body that some condition is unacceptable, and how to correct the problem**
- 3. Making necessary adjustments to restore conditions to normal level**

# A Normal Negative Feedback System For Thermoregulation



## Aging Can Affect Homeostasis in 2 Possible Ways:

Biological age changes to structures that allow more rapid or extreme alteration in body conditions (i.e. body temp)

- loss of fat in elderly
- thinning of skin
- loss of sweat glands
- decreased # of blood vessels and blood flow to skin surface
- decrease in muscle mass

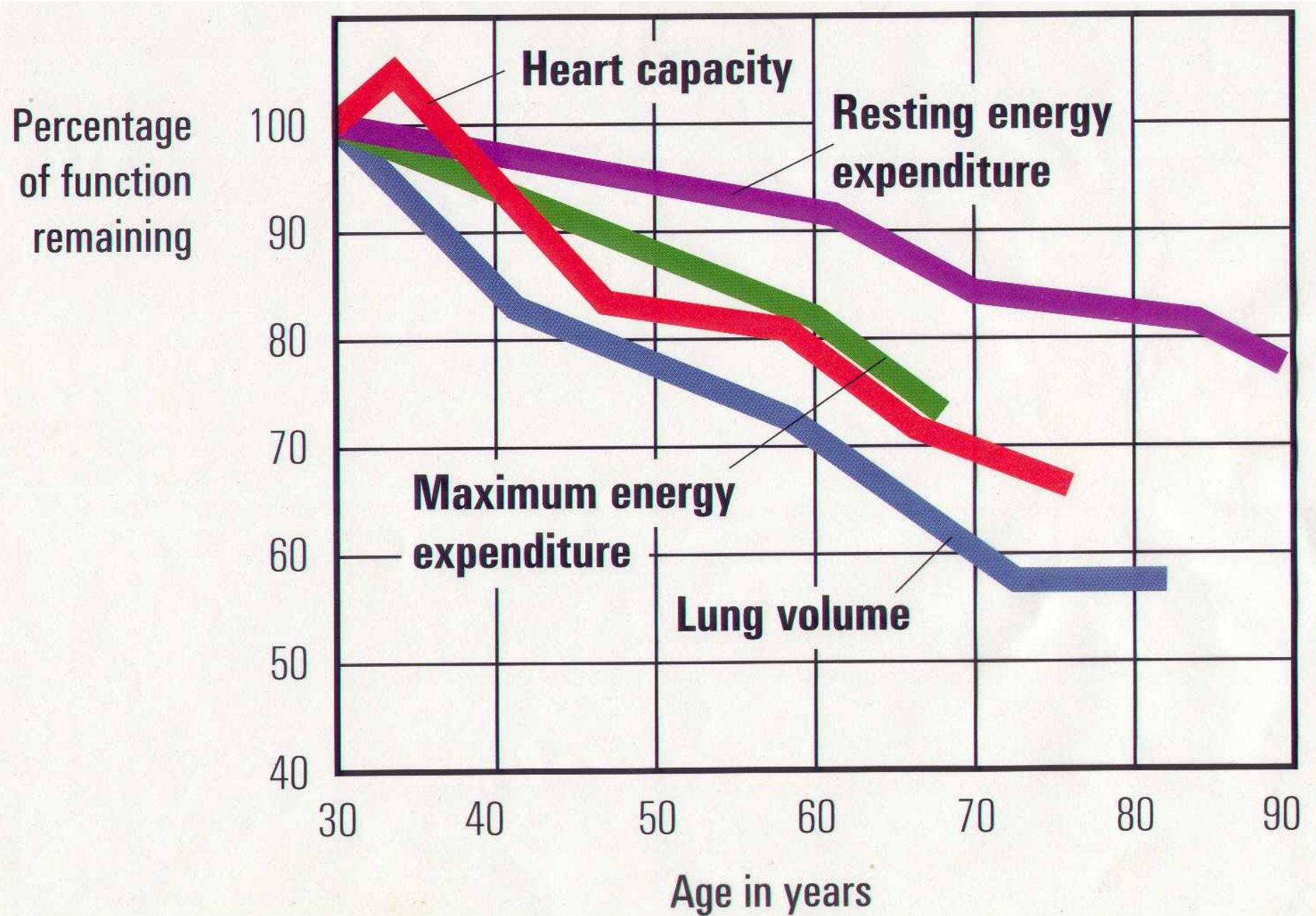
Biological age changes to negative feedback that allow more rapid or extreme alteration in body conditions (i.e. body temp)

- Nervous system changes with age
  - ↓ # of nerve cells that monitor condition
  - nerve cells left function weakly
  - results in a decreased in detection + response



2. Decreased ability to adapt to internal and external stress

# Physical Decline with Aging



### 3. Damage to body systems

# Damage to body systems

1. Muscle deterioration and damage
2. Damage to skeletal system (e.g., osteoporosis)
3. Damage to internal organs
4. Damage to nervous system

# But why do we age?

1. Error Theories
2. Programmed Theories



# Error Theories

1. Wear and tear theory
2. Rate of living (cells burn out more quickly the more work they do)
3. Cross linking theories (cross linked proteins damage organs)
4. Free radical theories (atoms with unpaired electrons)(do damage to what they encounter)
5. DNA Damage theories

# Programmed Theories

1. Programmed Longevity (its in the genetic code)
2. Endocrine Theory (its in the hormones)
3. Immunological Theory (our immune system is programmed to shut down)

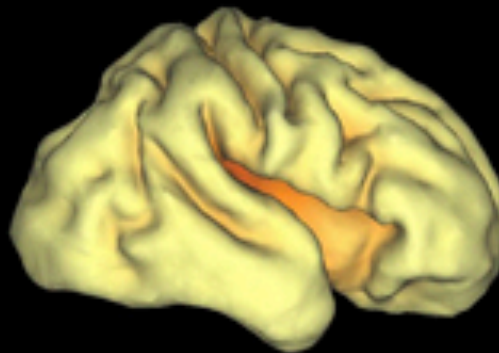
The simple truth is scientists are still not  
sure why we age

# Age-related changes in the nervous system

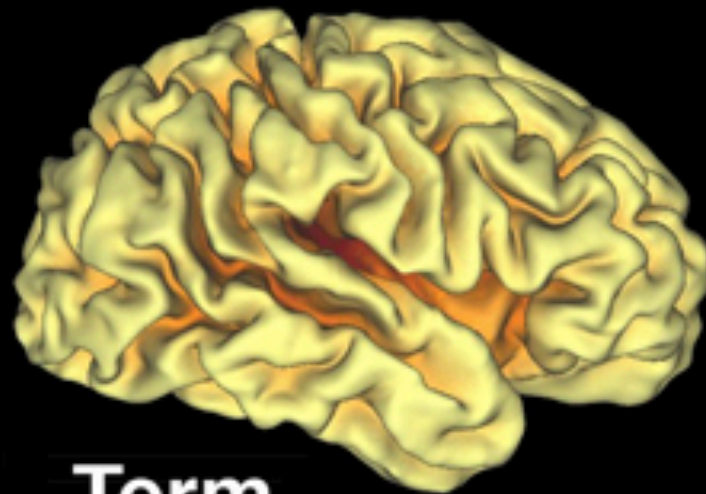
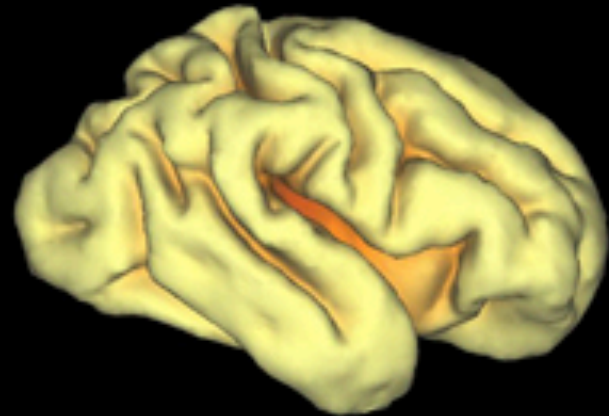
**25 week**



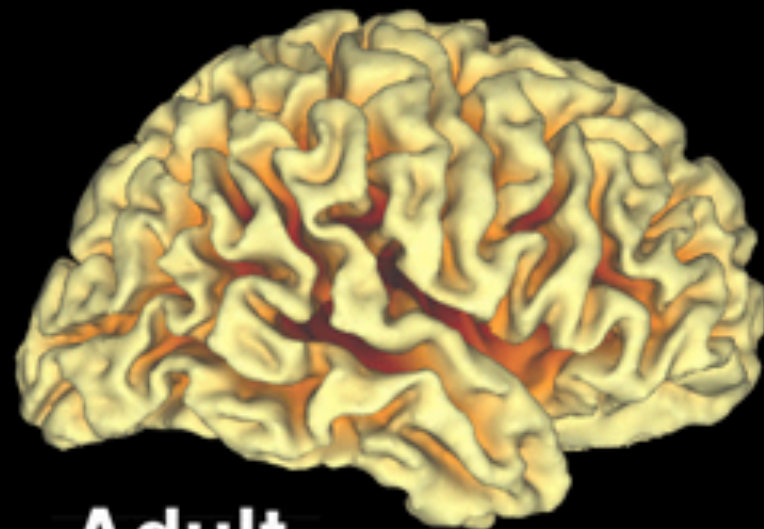
**30 week**



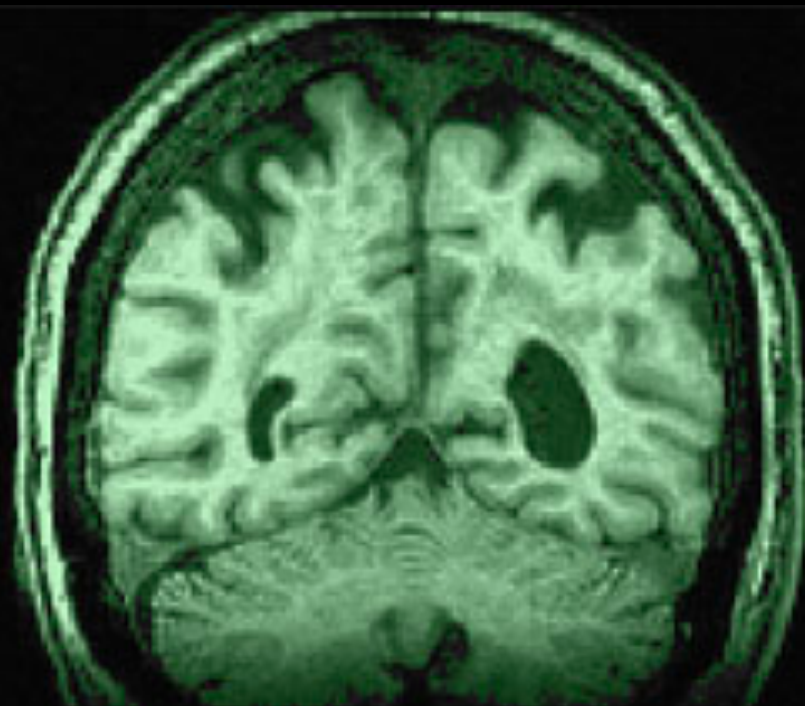
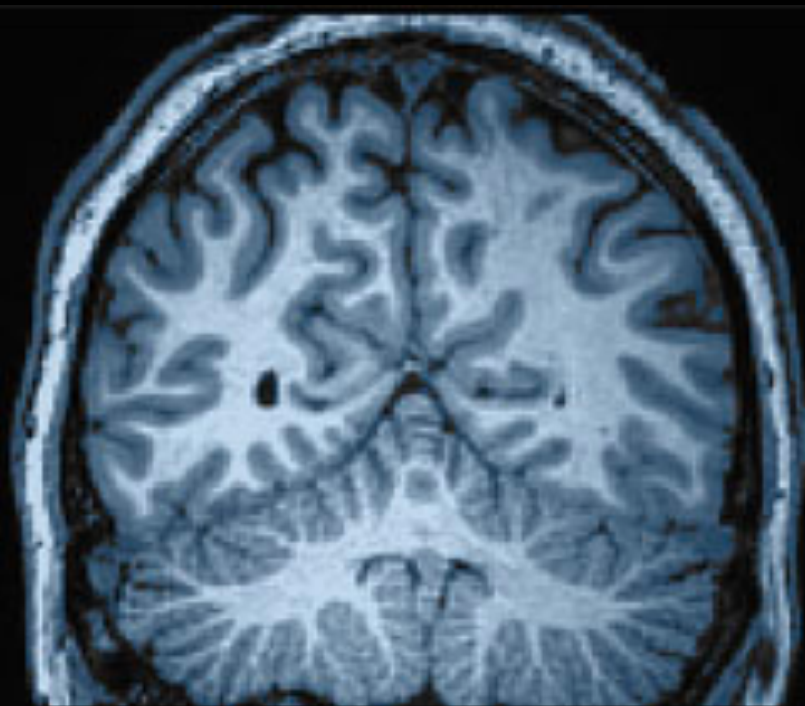
**33 week**



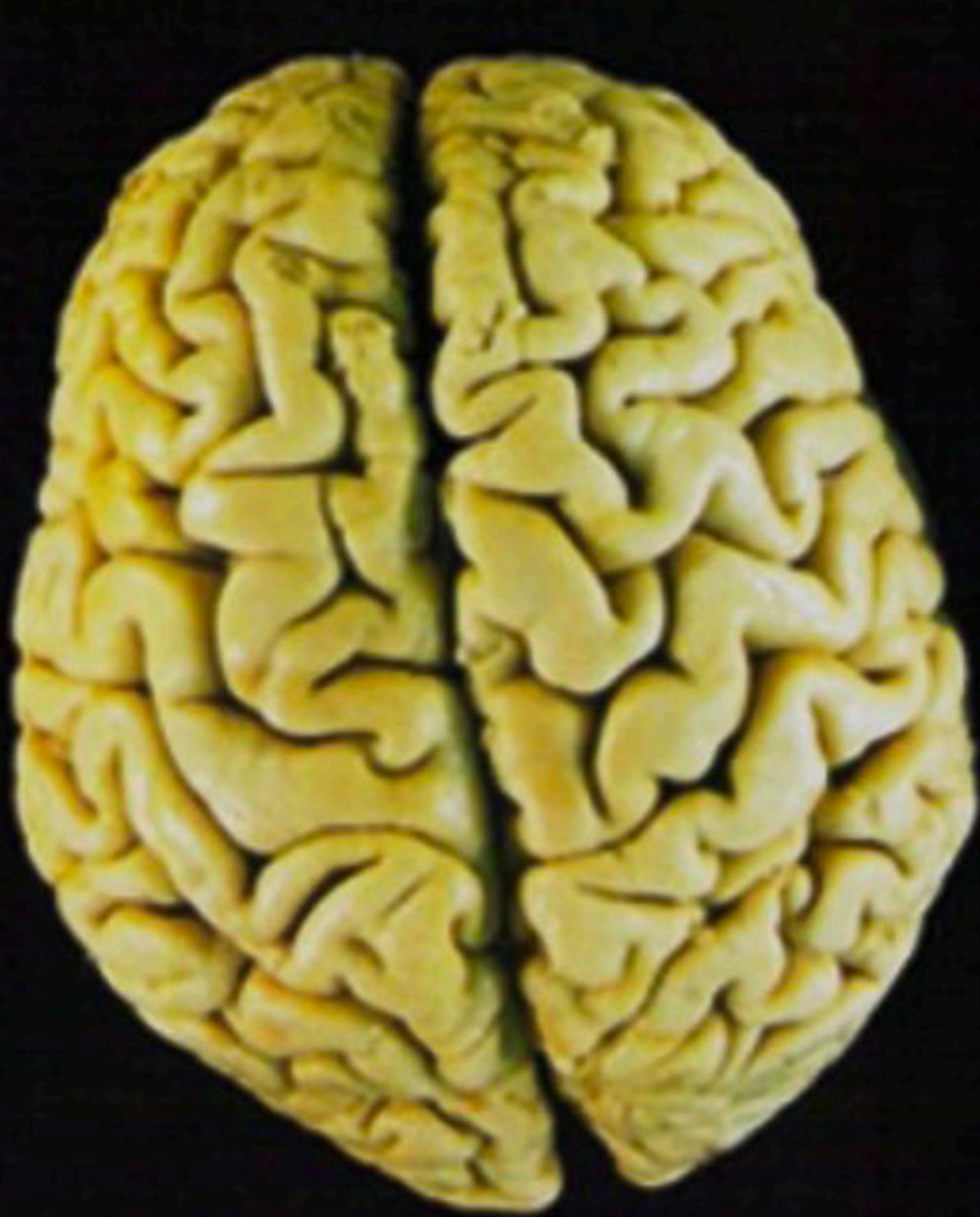
**Term**



**Adult**

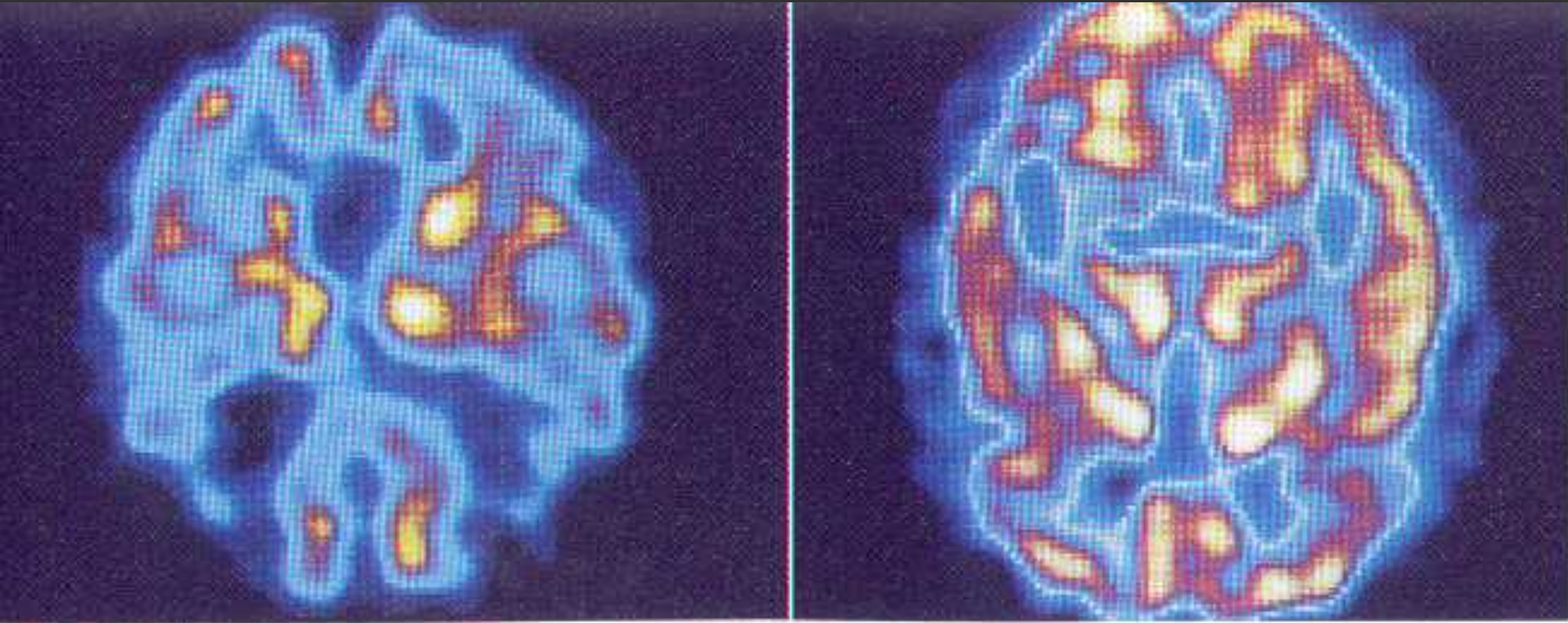








# DECREASED CEREBRAL METABOLISM

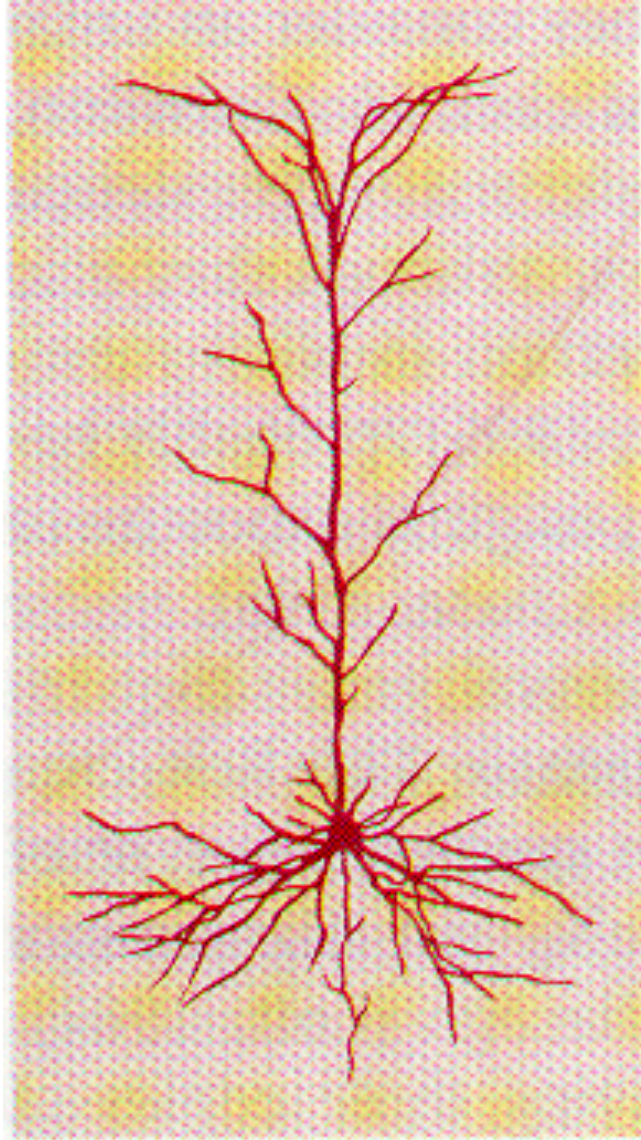


Alzheimer's

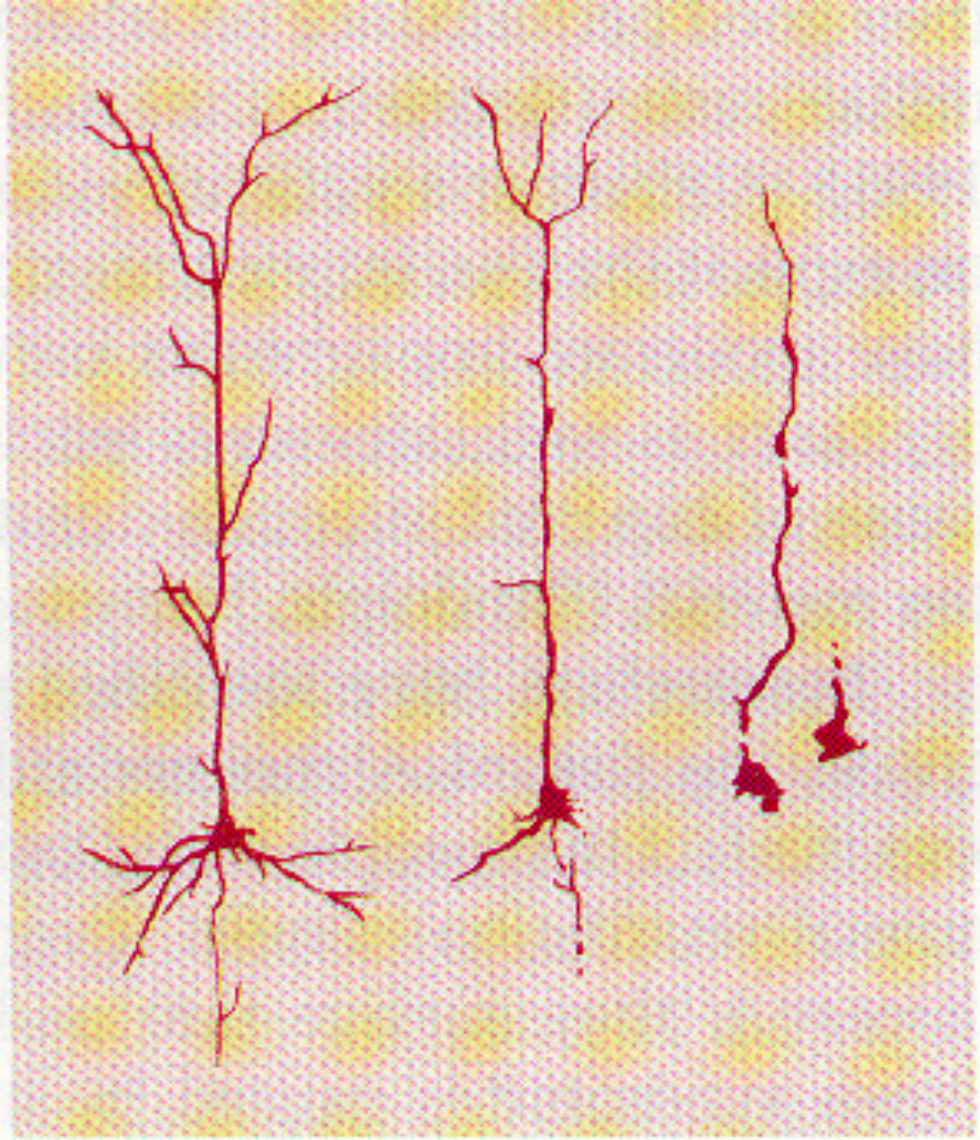
Normal



# Neuronal Degeneration



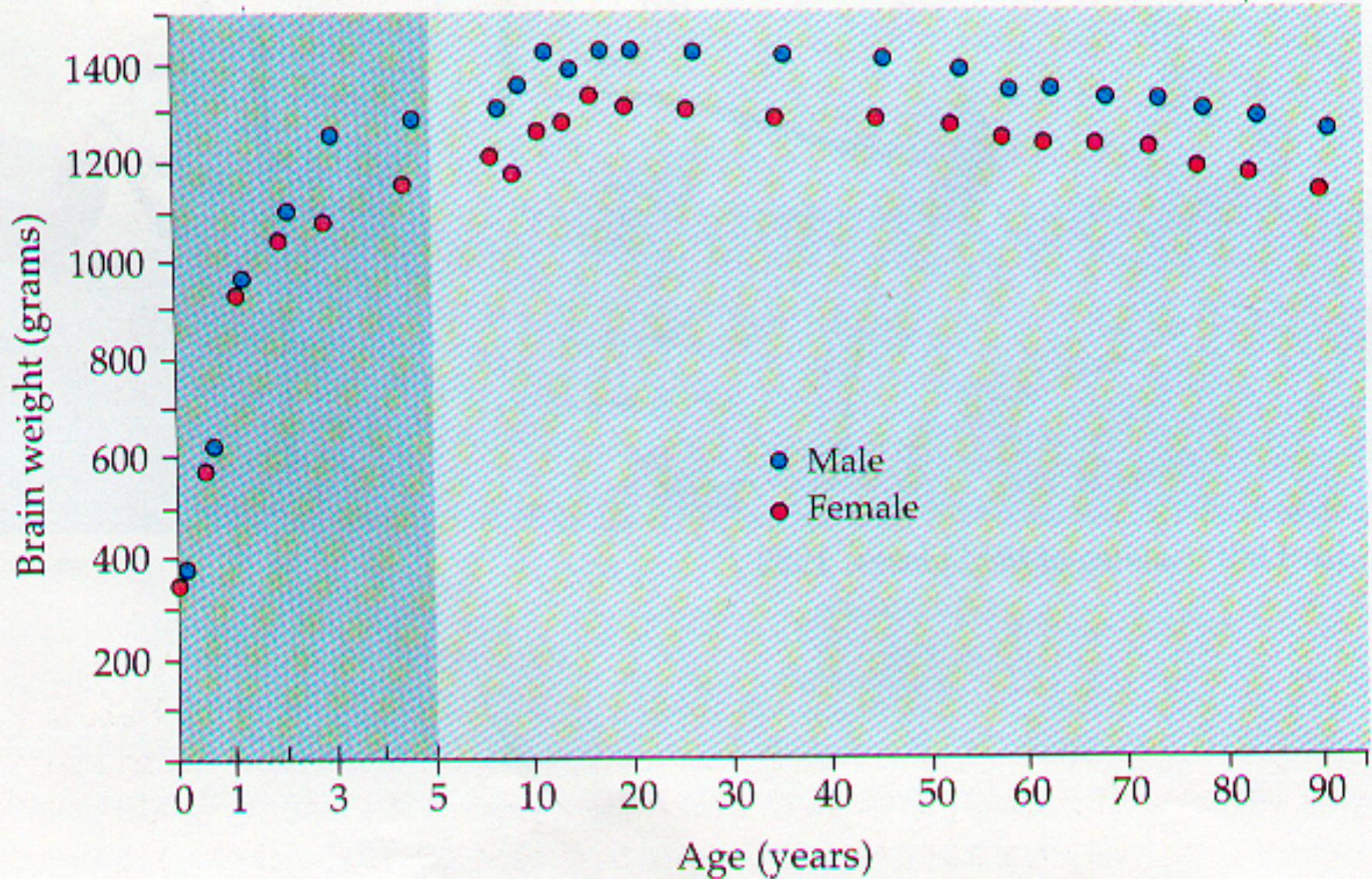
**Normal**



**Alzheimer's**



# Brain Weight and Aging



Nerve cells diminish with age

~ 10000 are lost per day

WHY?

- lost neurons are not replaced
- nervous tissue is gradually reduced

But why?

Theories on neuronal death have changed a lot over the past decade. Now, it is believed that most neuronal death is due to non age related factors:

1. damage from external causes
2. neurodegenerative disease





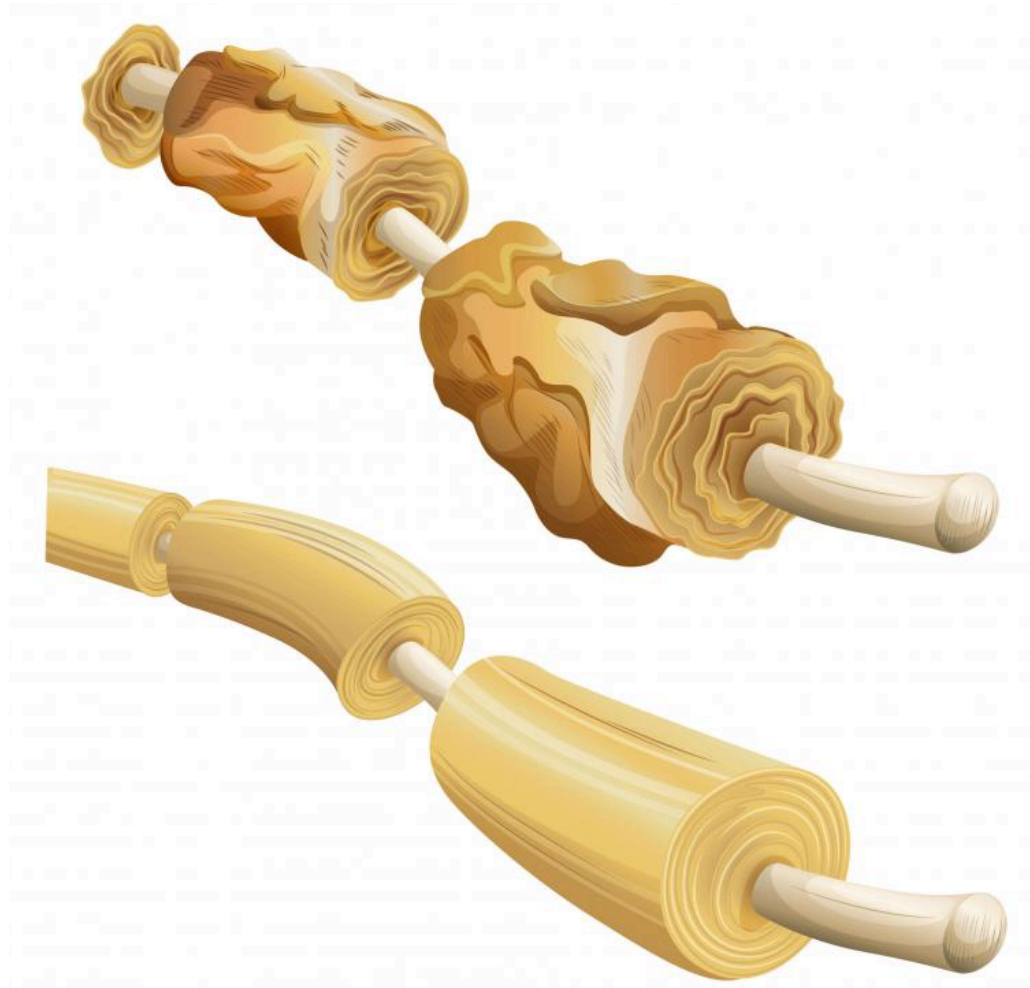
Alzheimer's



Healthy Senior

However,

Maybe the neurons themselves do change. For example, there may be a loss of myelin which results in a reduction in neural function.

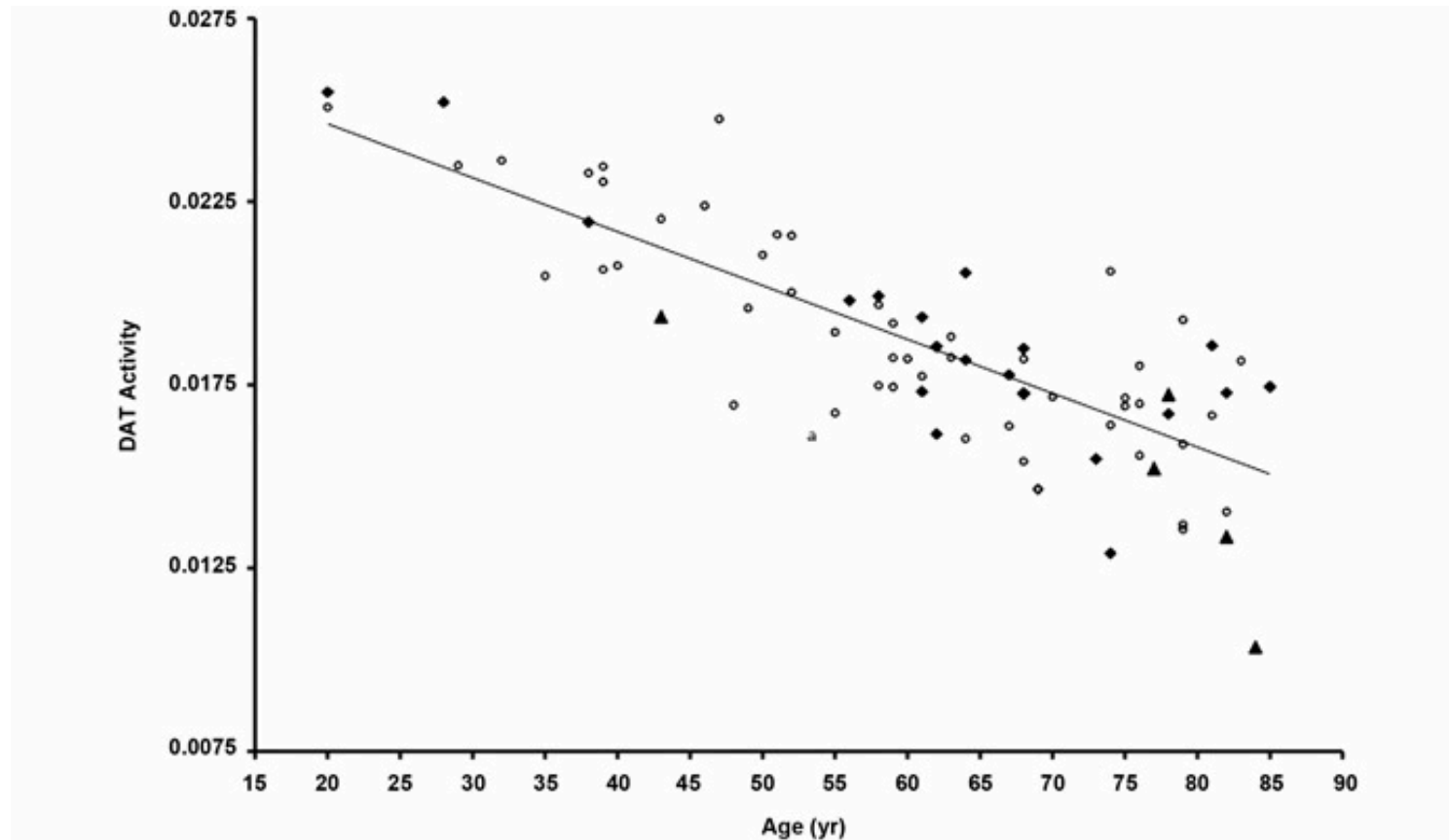


But

“It is suggested that such degenerative changes lead to cognitive decline because they cause changes in conduction velocity, resulting in a disruption of the normal timing in neuronal circuits. Yet as degeneration occurs, other changes, such as the formation of redundant myelin and increasing thickness suggest of sheaths, suggest some myelin formation is continuing during aging.”



## What about neurotransmitters?



**Figure.**

Striatal dopamine transporter (DAT) activity versus age and fall status: Nonfaller = open circles, single-time faller = black rhombus, recurrent faller = black triangle. Plot shows significant age-associated nigrostriatal dopaminergic denervation. Linear regression line is presented. No overall significant difference was noted in nigrostriatal dopaminergic activity between fallers and nonfallers.

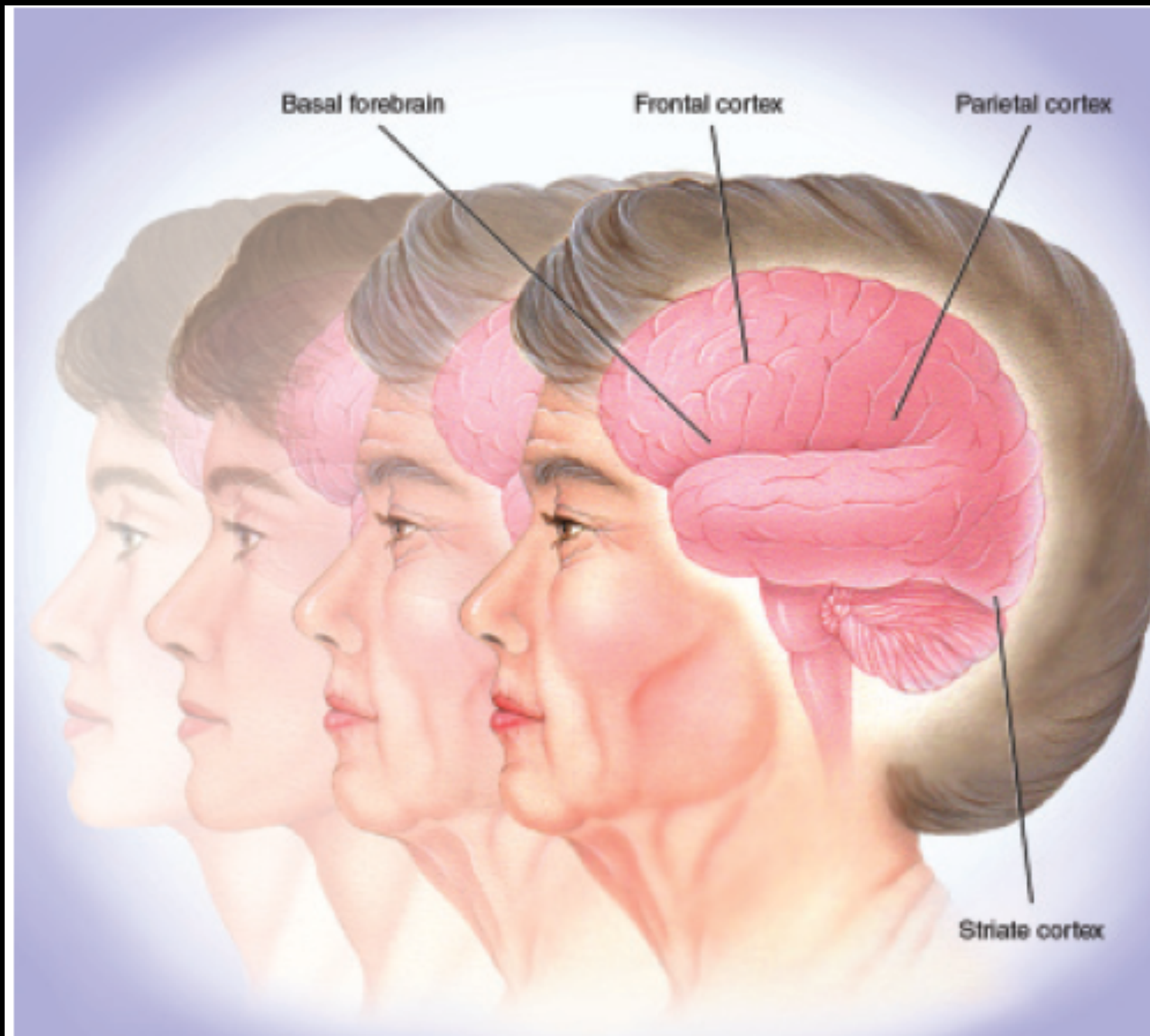
Loss of neurons + loss of myelin =  
decreased brain mass



Note – loss is not uniform across the  
brain

# **Changes in Brain Tissue**

Max weight at 20 (3 lbs): loss of 10% over lifetime



No widespread  
loss of neurons

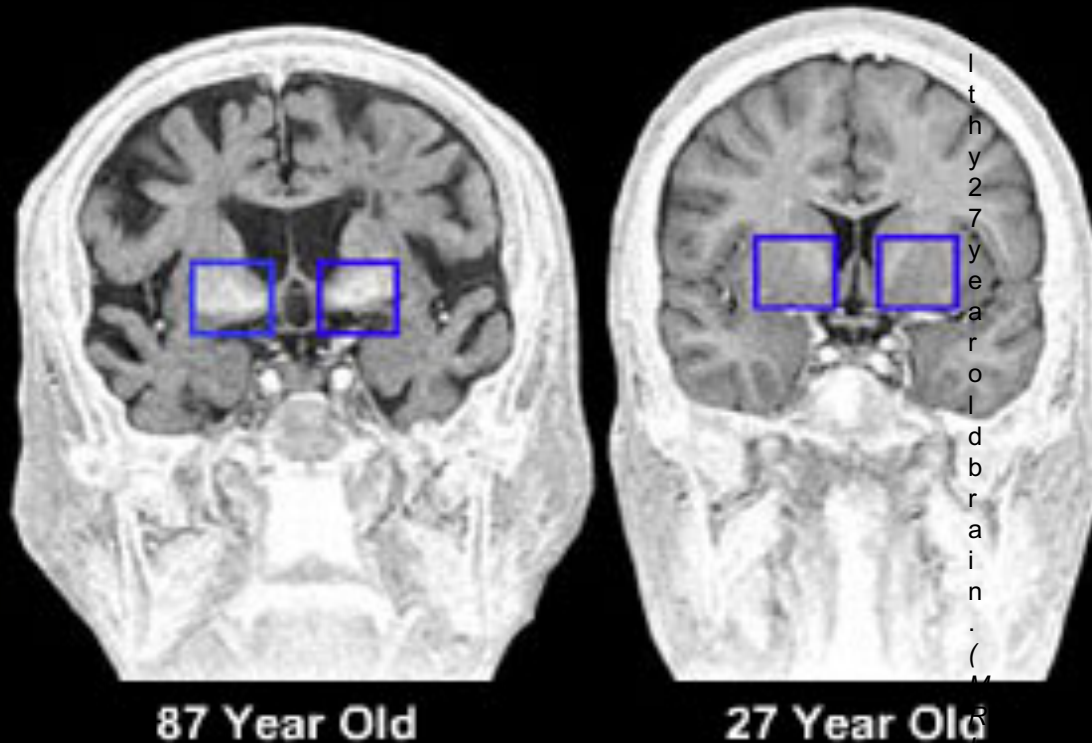
Brain maintains  
most  
neurons

Some regions do  
experience loss

Loss in nucleus  
basalis

↓  
acetylcholine

↓  
memory

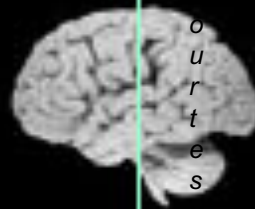


## Basal Ganglia

Hub of motor activity:  
responsible for initiating  
and integrating movements

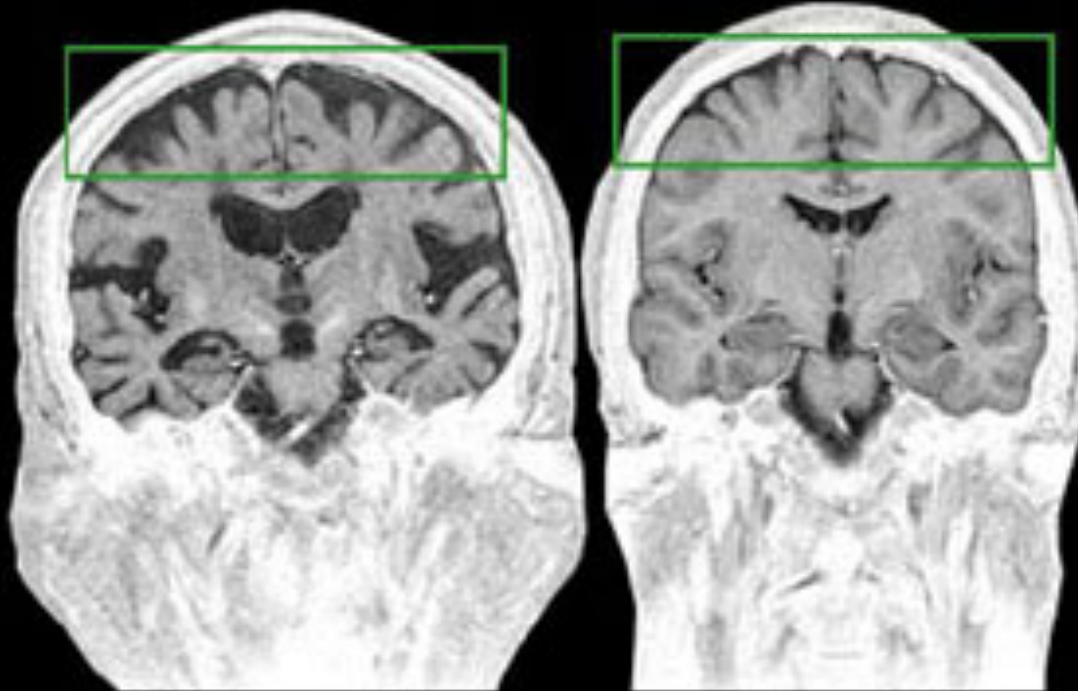
- become bright with age due to iron accumulation
- No health problems are associated with this change

Location of  
these scans  
in the brain



MRI of healthy 87 year old brain, next to a healthy 27  
(MRIs courtesy of the Oregon Brain Aging Study.)





87 Year Old

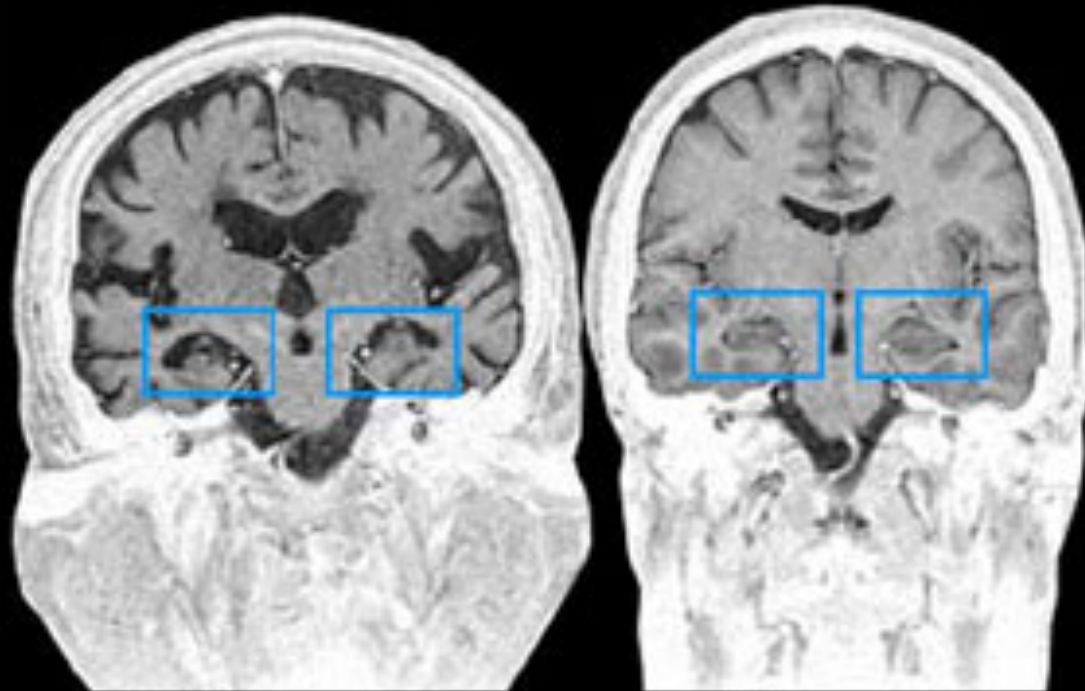
27 Year Old

## Subarachnoid

As the brain becomes smaller as a result of the gradual, life-long loss of brain cells, this area increases in size to fill the space

Location of  
these scans  
in the brain





87 Year Old

27 Year Old

## Hippocampus

Memory center of the brain

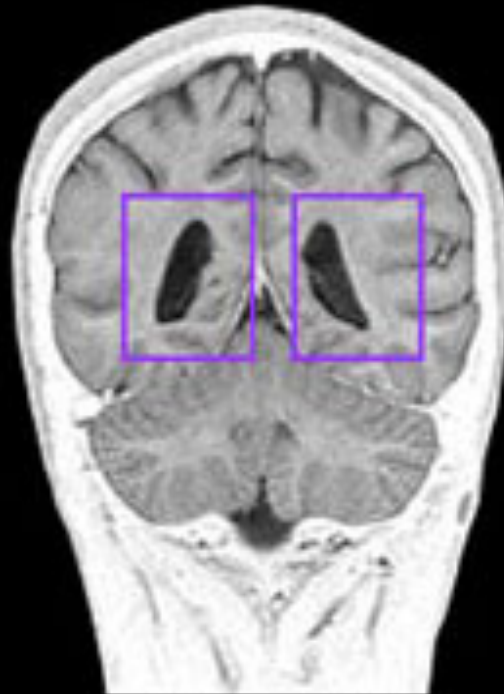
There is some cell loss associated with healthy aging, but this by itself does not indicate significant memory loss

Location of  
these scans  
in the brain





87 Year Old



27 Year Old

## Ventricles

Hollow spaces filled with CSF

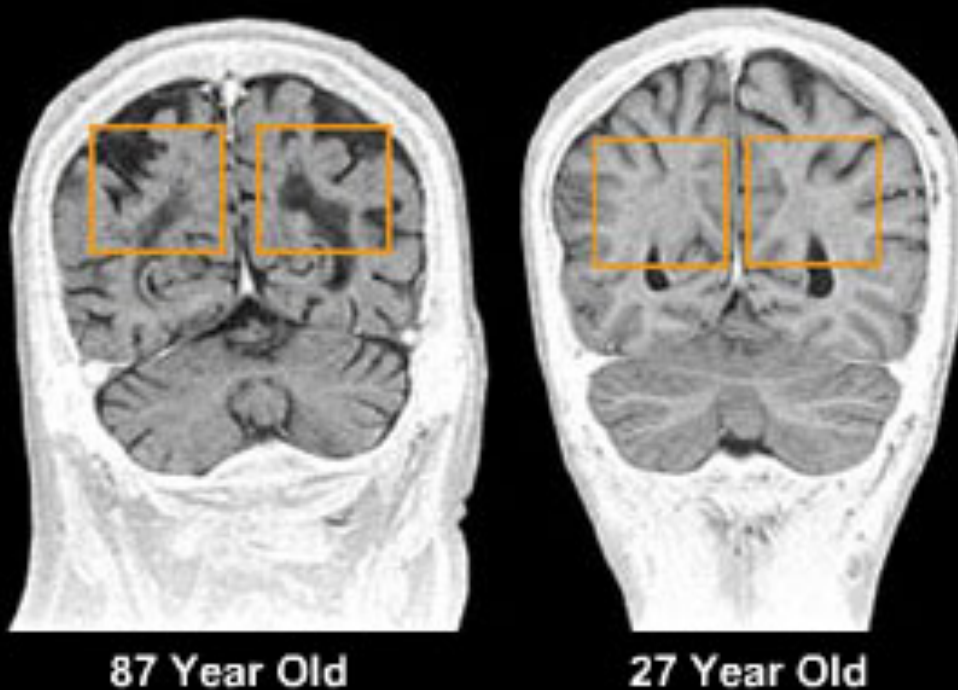
Like the subarachnoid space, these spaces increase in size as the brain becomes smaller with age

Location of  
these scans  
in the brain

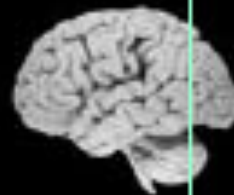




## White Matter

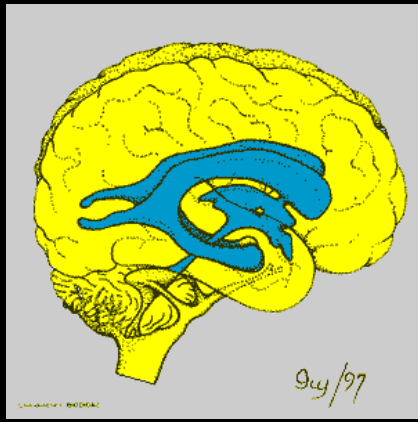


Location of  
these scans  
in the brain




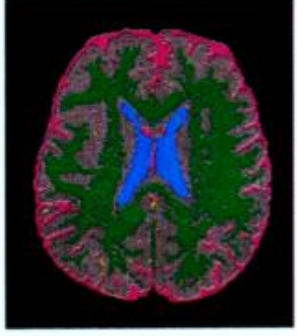
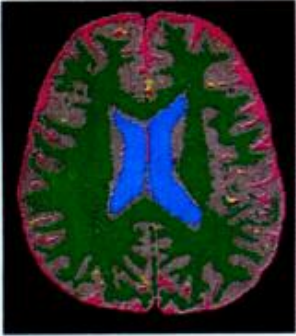
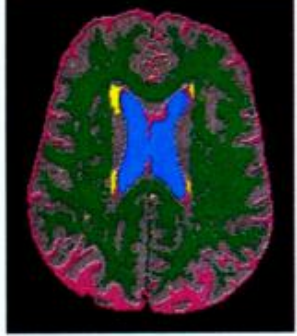
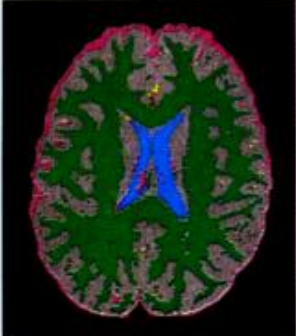

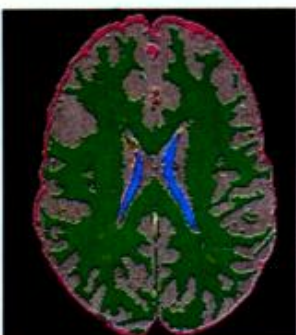
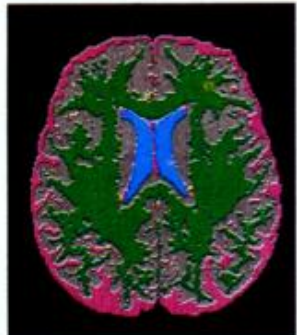
Myelination: communication channel for the brain's information processing gray matter

White matter changes in appearance with aging. The reason for these changes is unclear, but it may be related to the normal slowing of information processing in the brain with age



- white matter decrease
- increase in ventricles
- increases in CSF

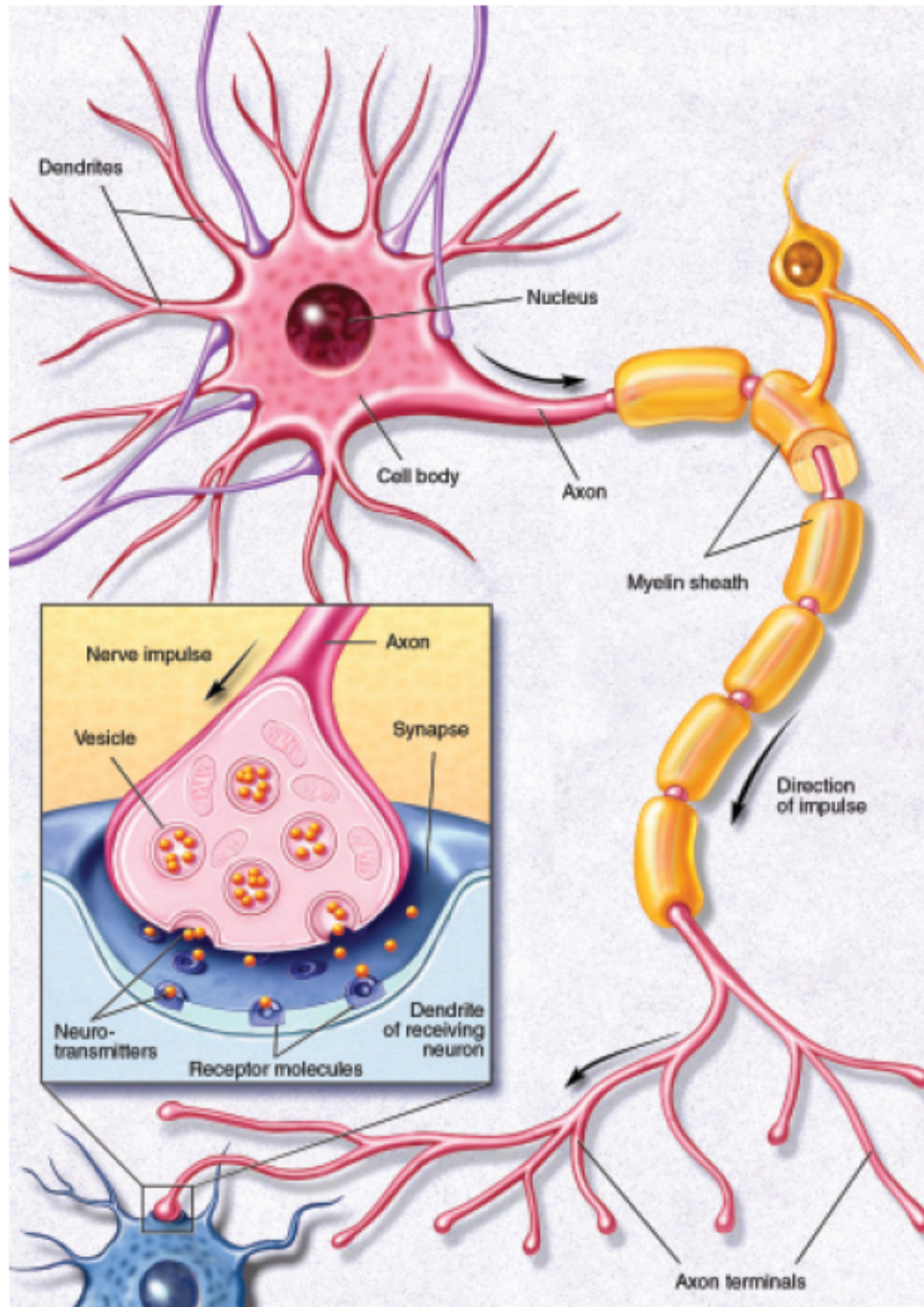
Gray matter okay!

YOUNG			OLD		
	Gender/Age	WM%		Gender/Age	WM%
	M 18	41.1		F 72	25.0
	F 19	34.6		F 77	33.3
	M 19	40.1		M 74	32.1
	F 19	43.8		F 80	32.9

However, in most instances the large and obvious changes are brought about by neurodegenerative disease.

# The Course of Physical Development in Late Adulthood

- The Aging Brain
- The Adapting Brain
  - As the brain ages, it adapts in several ways:
    - Neurogenesis: the generation of new brain cells
    - Dendritic growth can occur in human adults
    - Older brains rewire to compensate for losses
    - Hemispheric lateralization can decrease; may improve cognitive functioning



Aging brain → plasticity

Dendrites!!

So, assuming your brain is healthy...



# Biological Myths of Aging

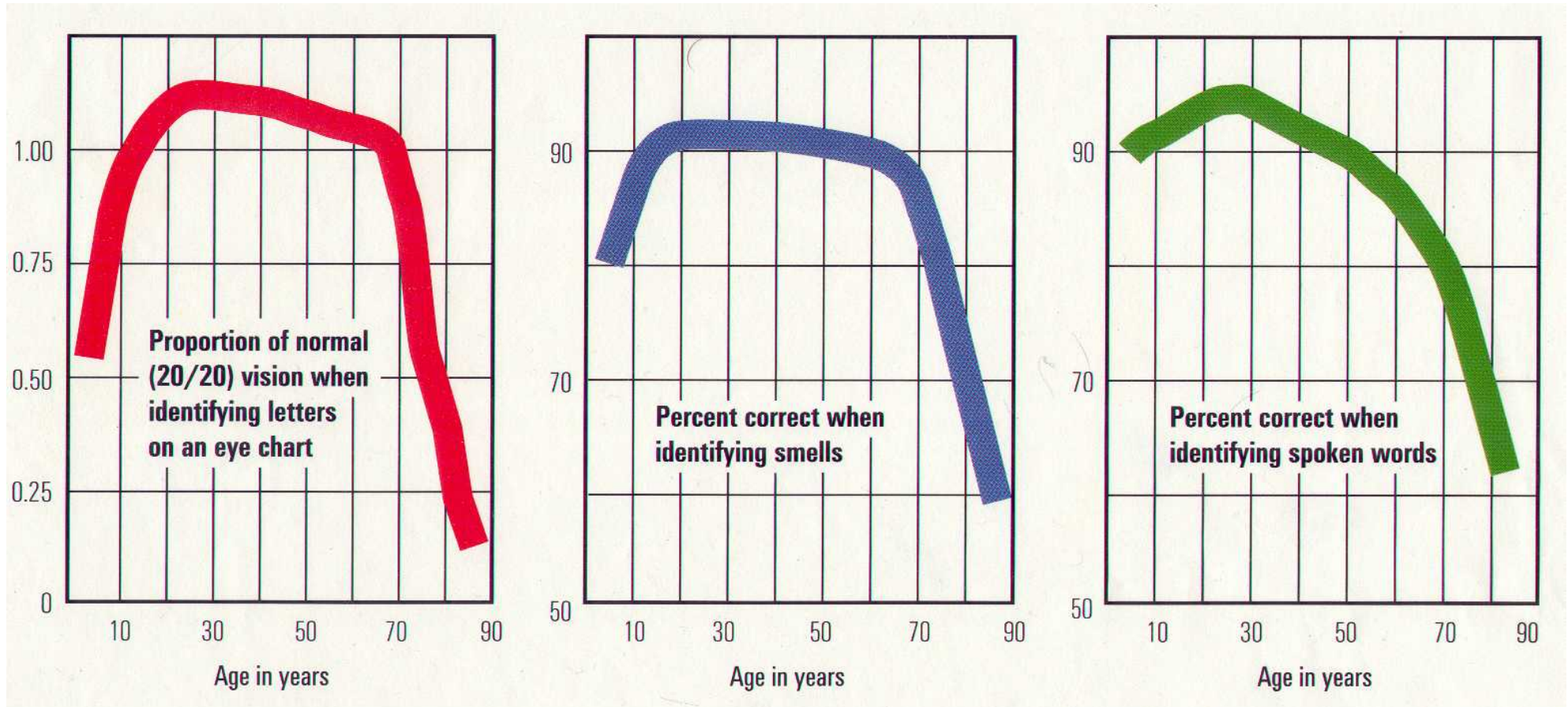
Memory declines drastically with age for all people.

IQ declines drastically with age in all people.

Learning becomes more difficult as we get older.

There is nothing you can do counter these aging deficits.

# Senses Decline with Aging



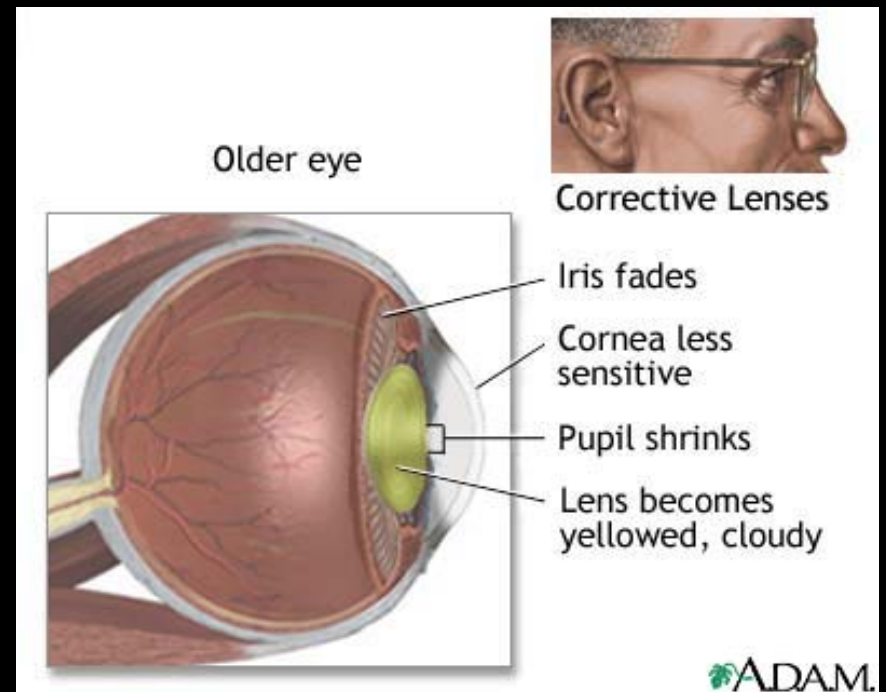
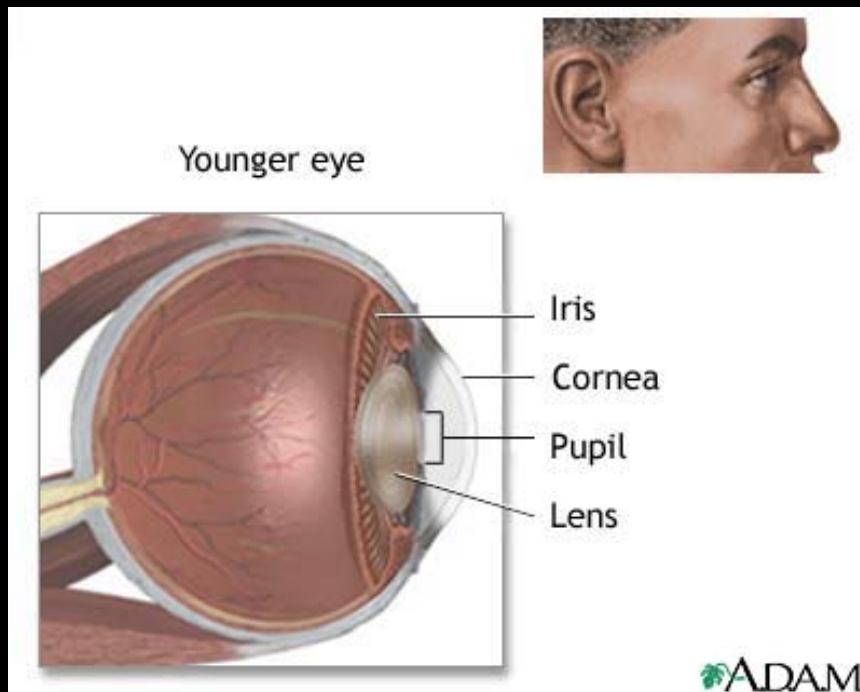


# Changes in Sensory Input

# Vision

Visual impairment: most common sensory problem

- 95% wear glasses (across cultures)
- pupil 1/3 size (iris more rigid) (by 60 vs 20)
- 5% cannot read
- 20% cannot drive





## Normal Vision

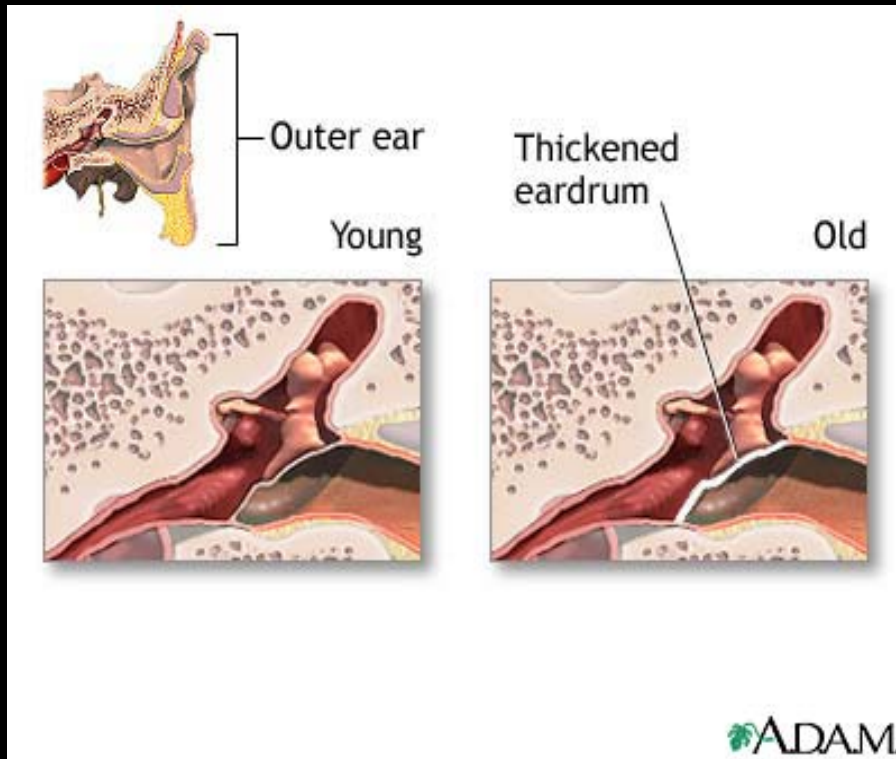


Problem in lens → Cataracts  
protein clumping together



Problem in the macula (fovea)  
Macular Degeneration: loss of  
acuity and center vision

# Hearing



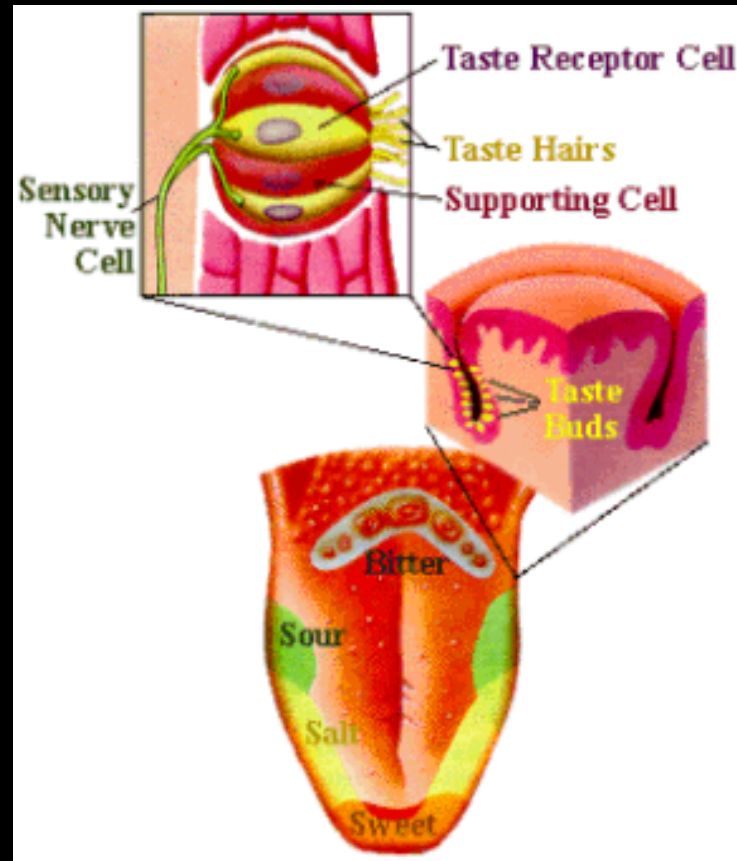
- ear structures deteriorates
- eardrum often thickens
- inner ear bones and other structures are affected
- Earlobes increases  $\frac{1}{4}$  longer (↑ cartilage) & fatter

- 30%: 65 & up significant hearing impairment
- 25%- between 65 and 74
- 50%- 75 & up difficulty hearing
- 10dB reduction in hearing sensitivity each decade after 60
- older men more likely to have hearing loss than older women

# Taste

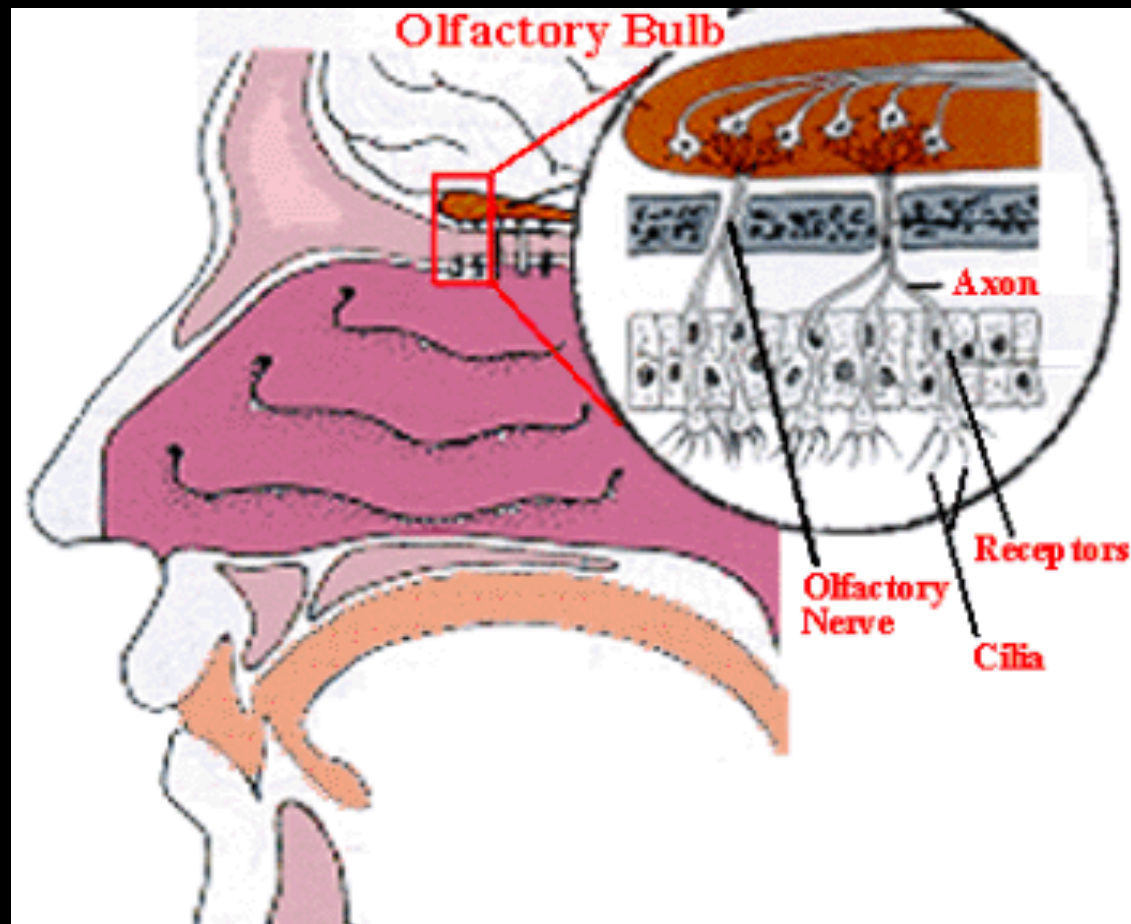
9,000 taste buds  
↓ 40 to 50 in women  
↓ 50 to 60 in men

After 60 loss of sensitivity: sweet & salty 1<sup>st</sup> to go





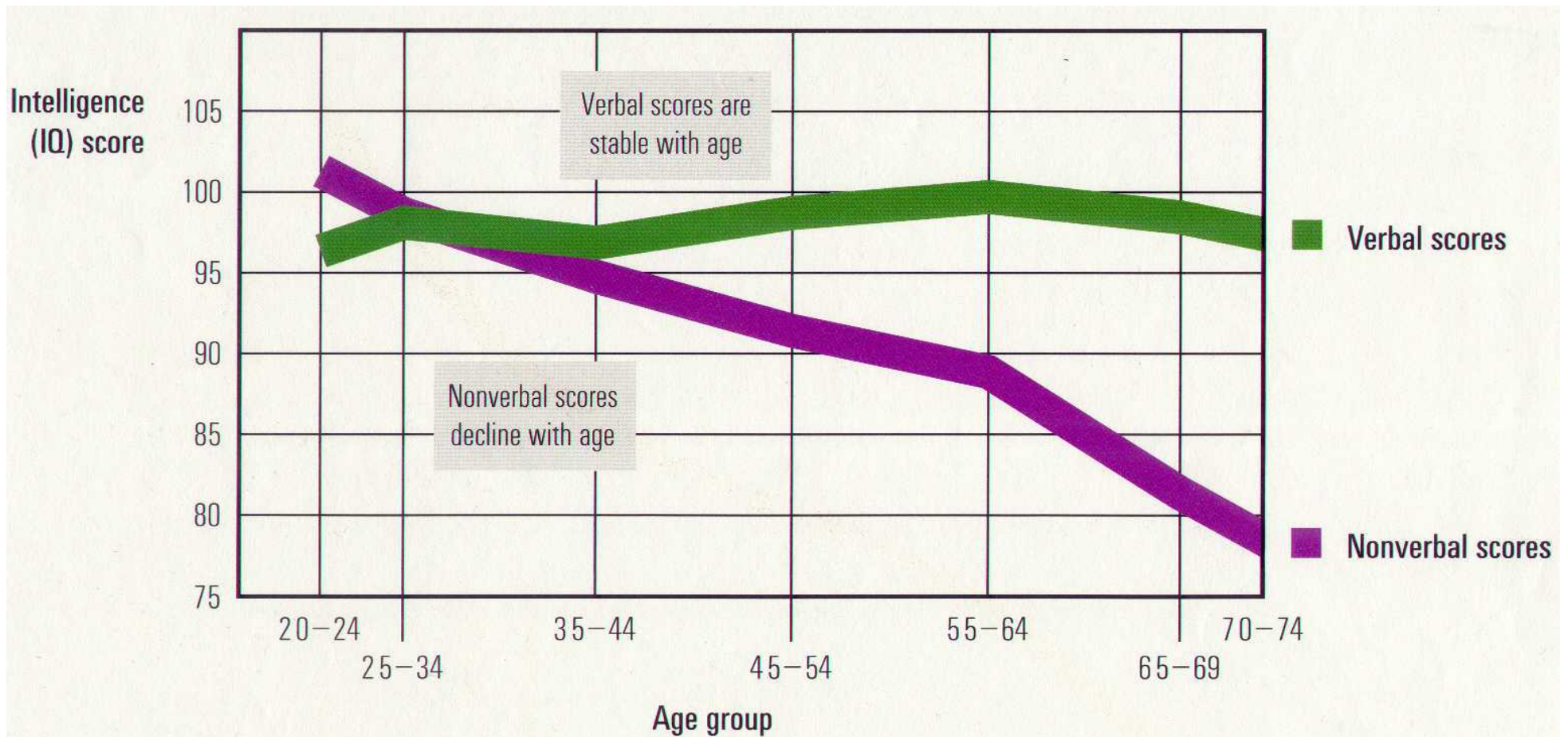
# Smell

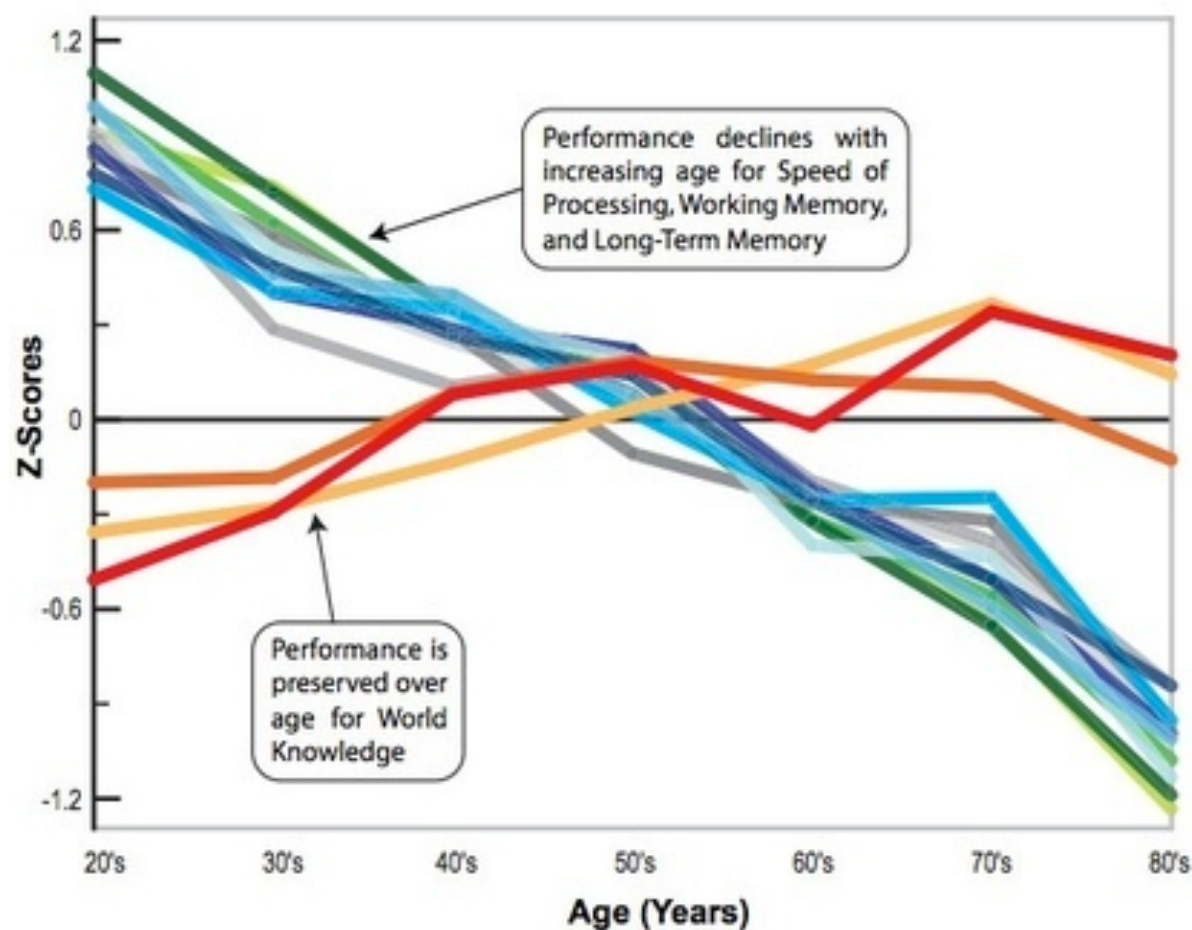


- smell receptors decreases increases the threshold for smell
- after 50 the sense of smell decreases rapidly
- 80: reduced by about half
- Size increases  $\frac{1}{2}$  in wider &  $\frac{1}{2}$  in longer (↑ cartilage)

# Changes in Cognitive Function

# Intelligence and Aging





### Speed of Processing

- Digit Symbol
- Letter Comparison
- Pattern Comparison

### Working Memory

- Letter Rotation
- Line Span
- Computation Span
- Reading Span

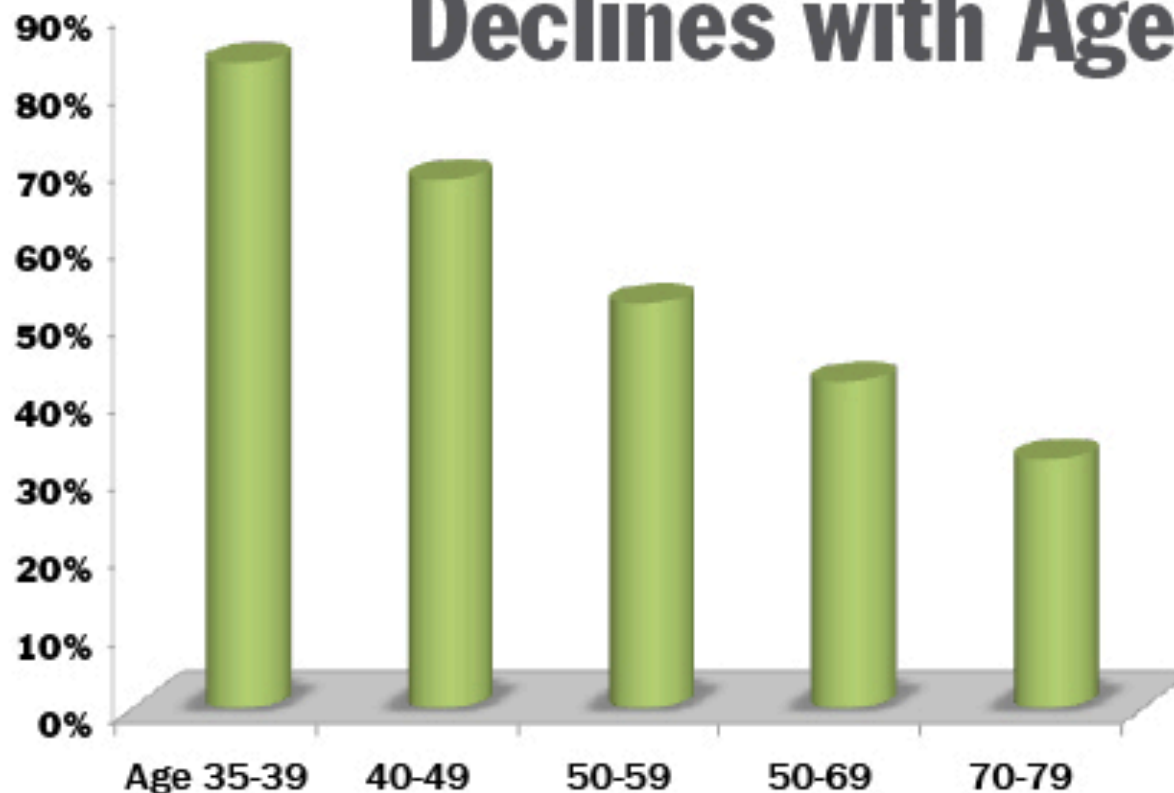
### Long-Term Memory

- Benton
- Rey
- Cued Recall
- Free Recall

### World Knowledge

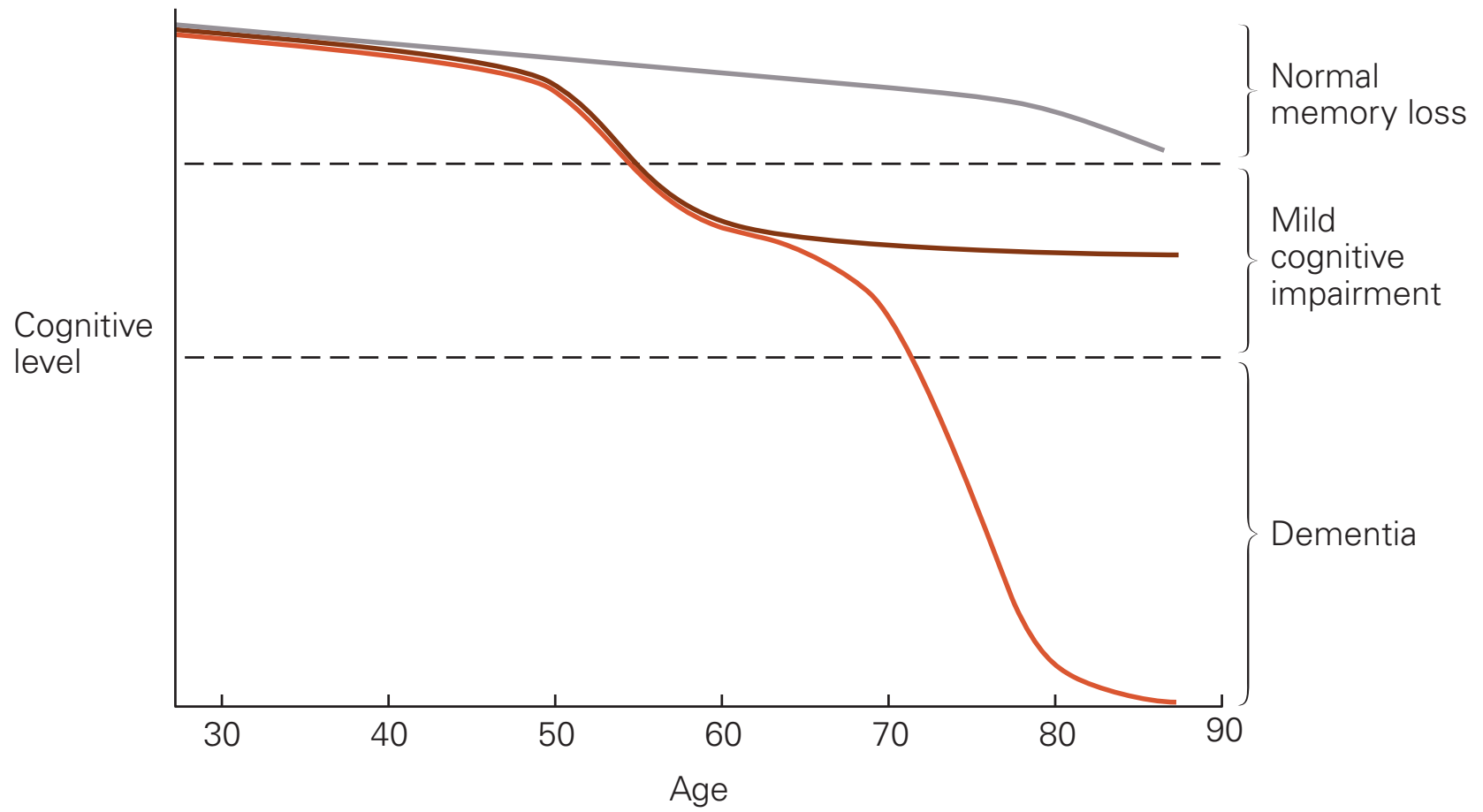
- Shipley Vocabulary
- Antonym Vocabulary
- Synonym Vocabulary

## **Normal Memory Recall** **Declines with Age**



Crook, T.H. et. al. (1993): Recalling names after introduction: Changes across lifespan in two cultures. *Developmental Neuropsychology*, 9, 103-113.





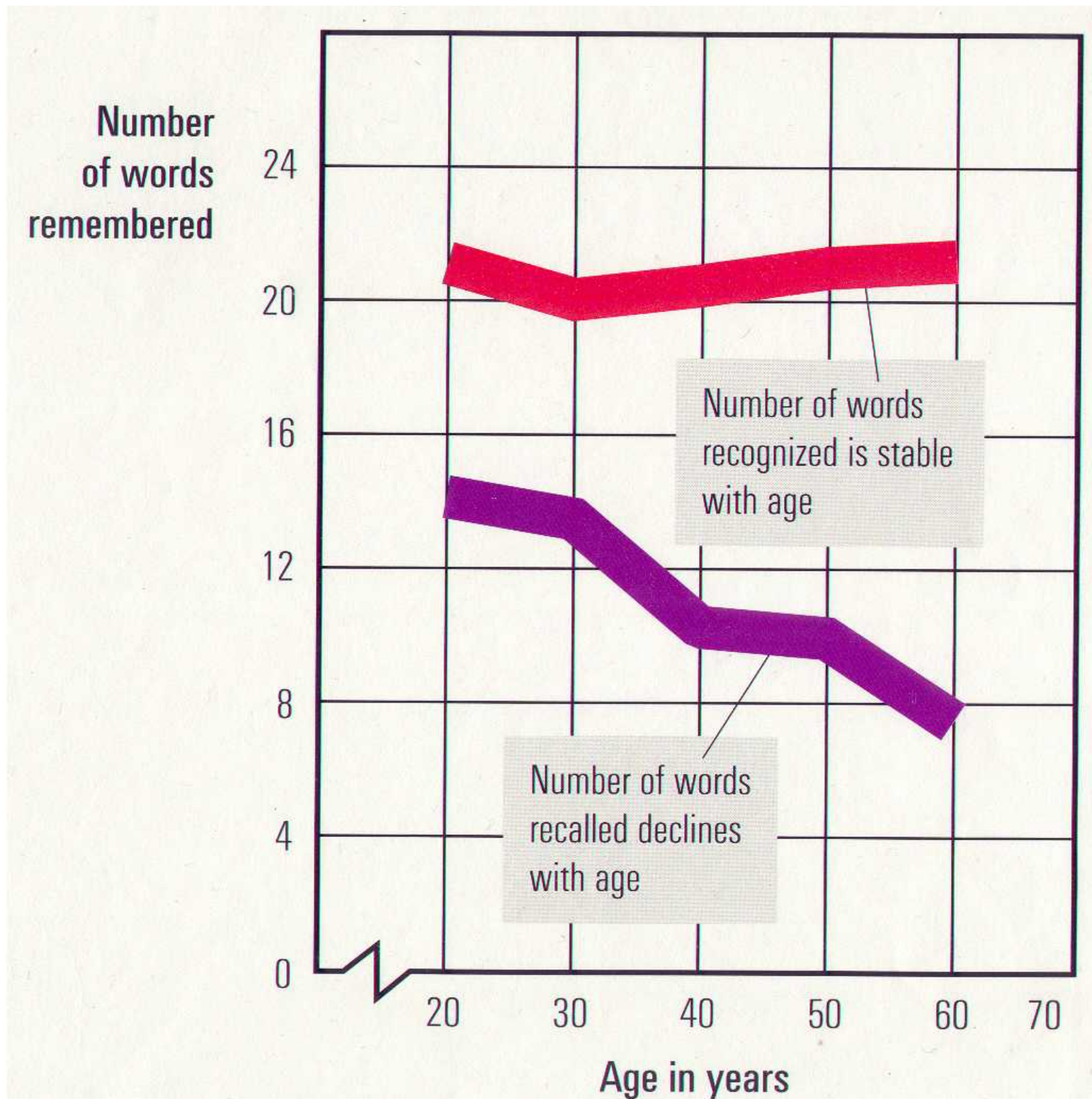
# Recall and Recognition in Adulthood

- **Recognition**

- stable

- **Recall**

- declines



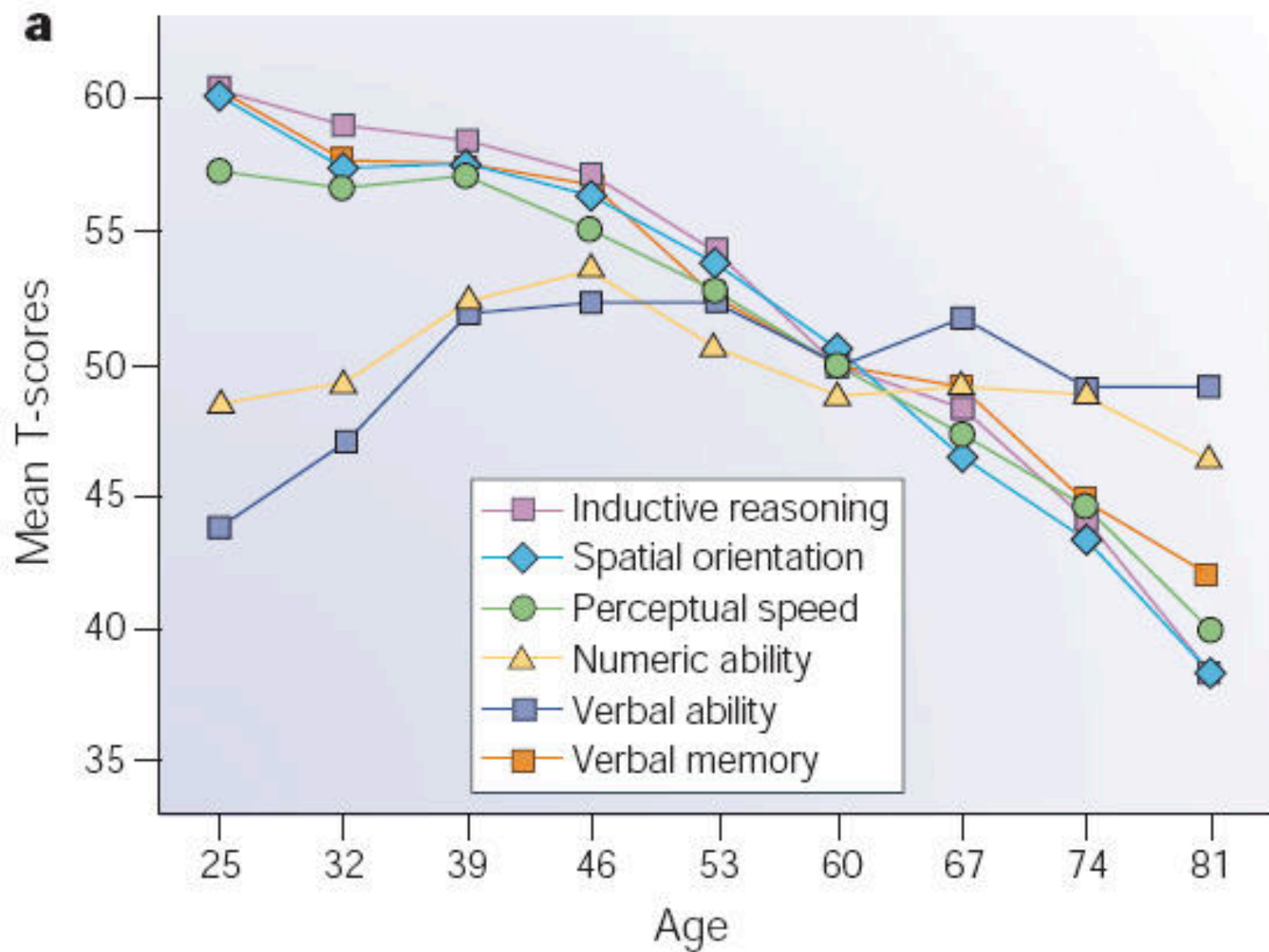
# Memory Decline with Aging

## **Age-Related Deficits:**

- long-term memory
- physical-motor tasks
- free recall learning
  - requiring conscious recollection and effort

## **No Age-Related Deficits:**

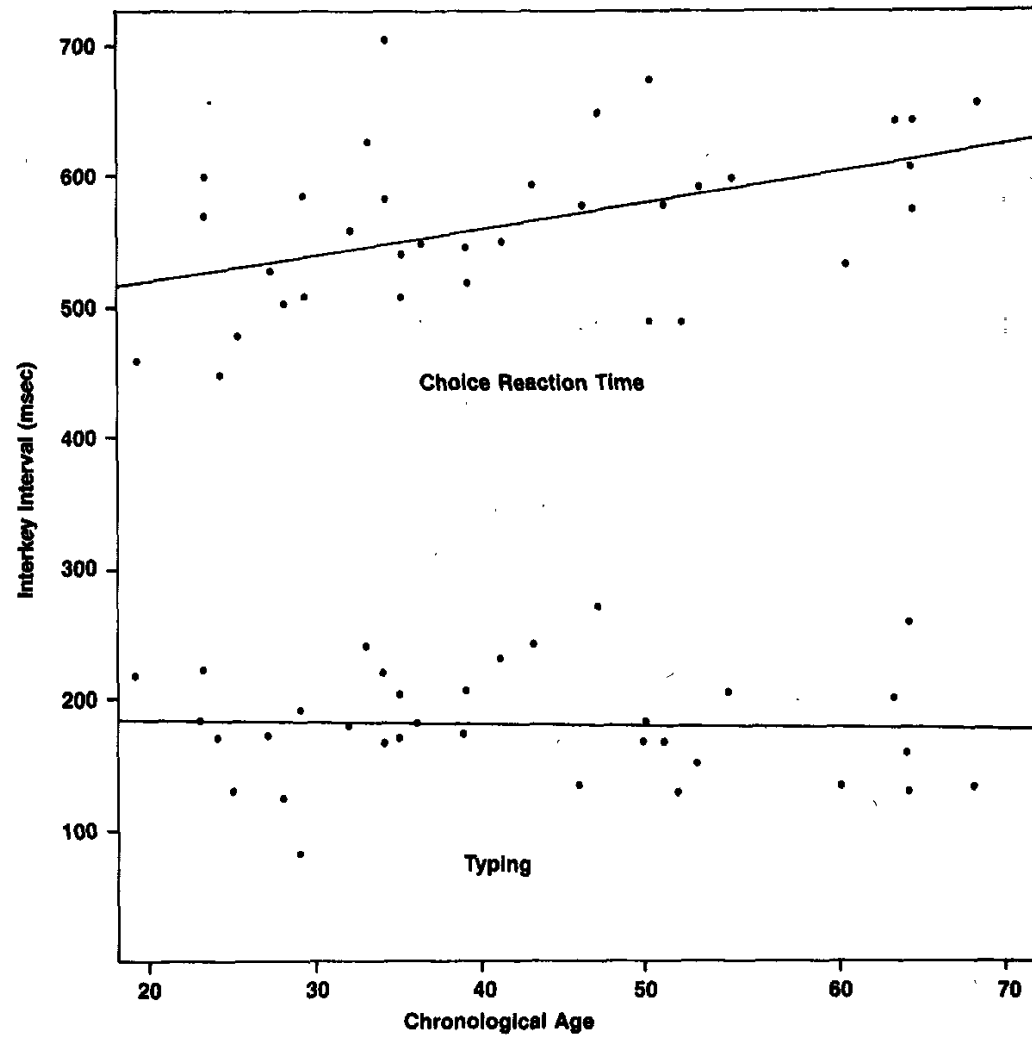
- short-term memory
- non physical-motor tasks
- recognition learning
  - easily organized task structures or cues



# Effects of Age and Skill in Typing

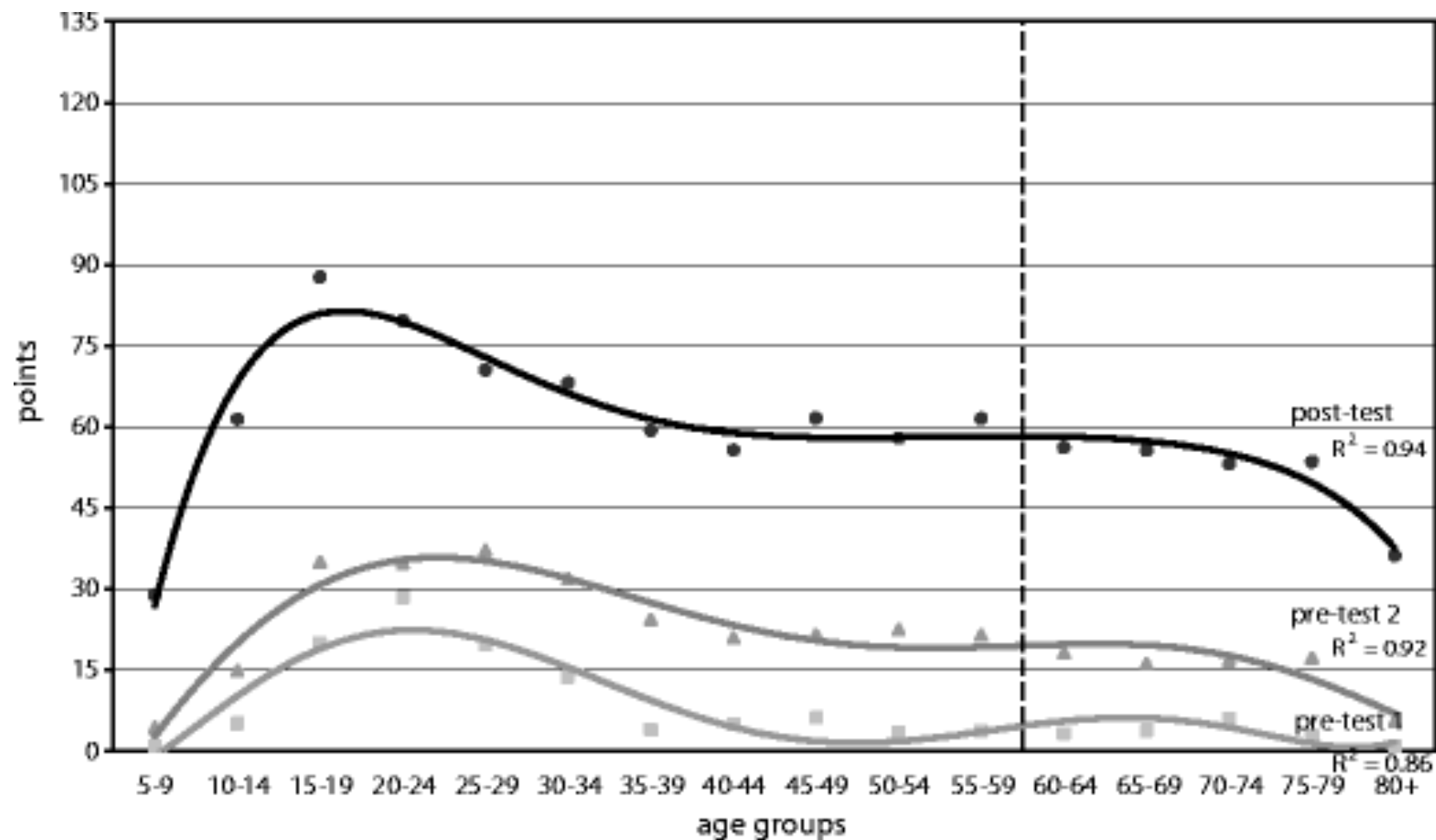
Timothy A. Salthouse

Andrus Gerontology Center, University of Southern California and University of Missouri





# Skill Learning



# Reducing Cognitive Decline

# Reducing Cognitive Decline

## **1. Live in Favorable Environmental Circumstances**

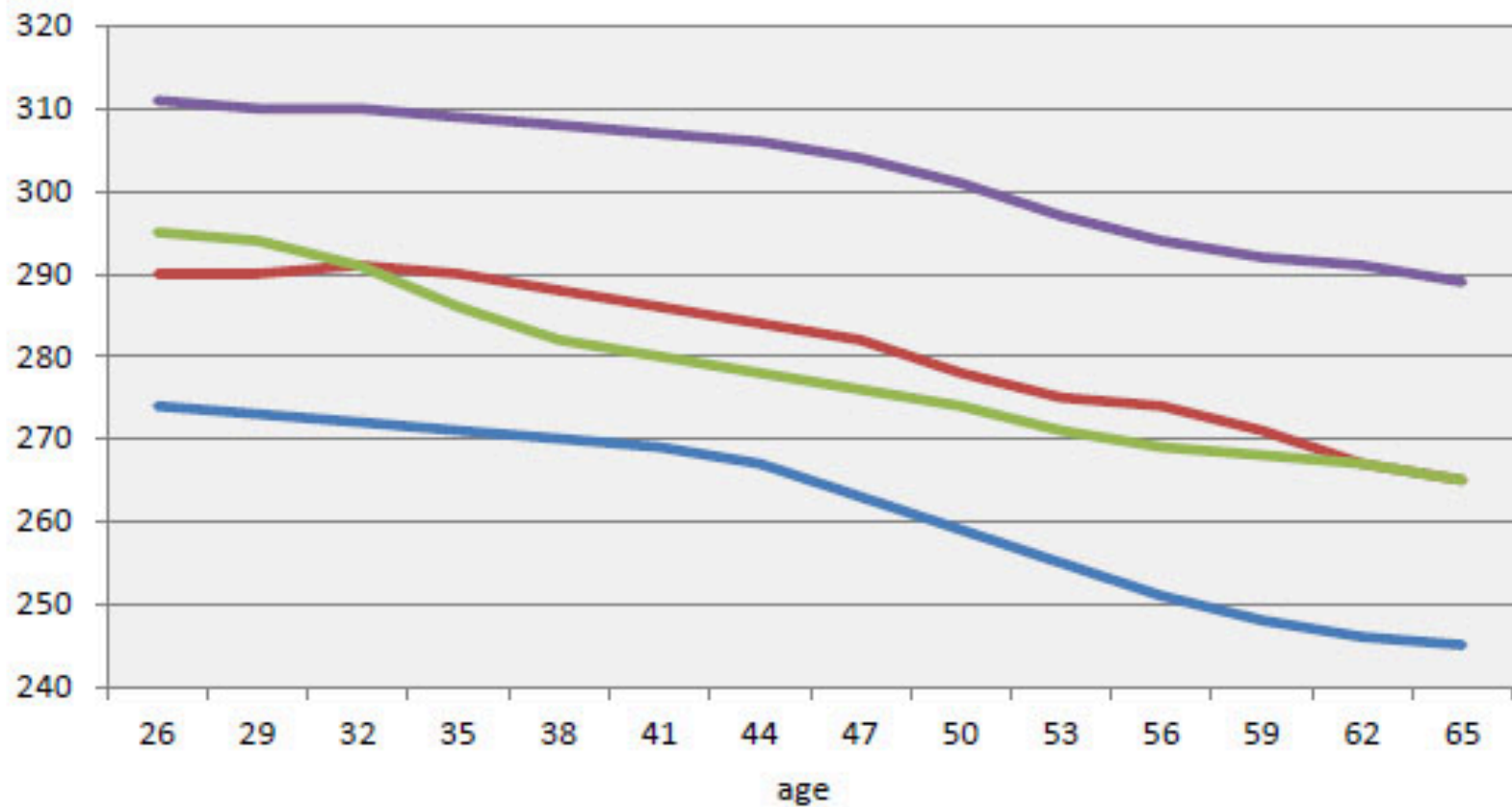
above-average education

high complexity occupations

above-average income

maintaining intact families

problem solving score



Low education; low knowledge occupation

Low education; high knowledge occupation

High education; low knowledge occupation

High education; high knowledge occupation

# Reducing Cognitive Decline

## **2. Be involved in activities typical of complex and intellectually stimulating environments**

extensive reading

travel

attending cultural events

continuing education activities

participation in clubs and professional associations



# Reducing Cognitive Decline

**3. Be married to a spouse with high cognitive status**

# A few more things...

**JNeurosci**  
THE JOURNAL OF NEUROSCIENCE

An Official Journal of



**SOCIETY for  
NEUROSCIENCE**



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Research Articles, Behavioral/Cognitive

## No Effect of Commercial Cognitive Training on Brain Activity, Choice Behavior, or Cognitive Performance

Joseph W. Kable, M. Kathleen Caulfield, Mary Falcone, Mairead McConnell, Leah Bernardo, Trishala Parthasarathi, Nicole Cooper, Rebecca Ashare, Janet Audrain-McGovern, Robert Hornik, Paul Diefenbach, Frank J. Lee, and Caryn Lerman

Journal of Neuroscience 2 August 2017, 37 (31) 7390-7402; DOI: <https://doi.org/10.1523/JNEUROSCI.2832-16.2017>

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


# What is the association between sedentary behaviour and cognitive function? A systematic review

Ryan S Falck,<sup>1</sup> Jennifer C Davis,<sup>1</sup> Teresa Liu-Ambrose<sup>1,2</sup>

Br J Sports Med. 2015 Feb;49(4):248-54. doi: 10.1136/bjsports-2013-093184. Epub 2014 Apr 7.

**Aerobic exercise increases hippocampal volume in older women with probable mild cognitive impairment: a 6-month randomised controlled trial.**

ten Brinke LF<sup>1</sup>, Bolandzadeh N<sup>2</sup>, Nagamatsu LS<sup>3</sup>, Hsu CL<sup>2</sup>, Davis JC<sup>4</sup>, Miran-Khan K<sup>5</sup>, Liu-Ambrose T<sup>6</sup>.

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# Long-Term Effects of Resistance Exercise Training on Cognition and Brain Volume in Older Women: Results from a Randomized Controlled Trial

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# Conclusions

- All things being equal, assuming you are healthy, your brain is fine
- IQ does not show a drastic decline with age.
- Only certain types of memory show declines with aging.
- The ability to learn does not deviate much as we get older.
- There is plenty you can do counter aging deficits.
  - Exercise regularly
  - Eat properly
  - Engage in learning activities
  - Stop smoking
  - Stay in touch with friends, families, communities