



Brain Fitness

What we know about keeping your brain
Healthy

CHARLES J. VELLA, PHD

CONSULTANT, NEUROPSYCHOLOGY

FEBRUARY 17, 2016

Brain Fitness

HOW TO KEEP YOUR BRAIN HEALTHY



The Facts

- ▶ Life expectancy is rising as a result of advances in medical science and the availability of better healthcare services;
- ▶ The proportion of elderly persons in the general population is therefore rising.
- ▶ As the risk of dementia increases with increasing age, the number of persons with dementia in the general population is also rising.

How to Live a Brain Healthy Lifestyle

- ▶ Information is based on science and current research.
- ▶ We do not know how to prevent Alzheimer's disease.
- ▶ We do know some of risk factors that contribute to AD development.
- ▶ How to be proactive regarding brain health and potential risk reduction.
- ▶ While genetics drives vulnerability to Alzheimer's, the way we live earlier in life will determine how normal our brain remains, and for how long.

What do you know?

- ▶ Does being overweight increase your risk of AD?
- ▶ Does being socially active protect you from developing cognitive decline?
- ▶ Does being physically inactivate increase your risk of AD?
- ▶ Does getting more education protect you from developing cognitive decline?

Lifestyle Risks and Protective factors

- ▶ We know **lifestyle risk and protective factors** as things that:
 - ▶ reduce the risk of heart attack and dying from a stroke
 - ▶ but they also protect the brain

Roman poet Juvenal:

“A healthy mind in a healthy body.”

Current Science:

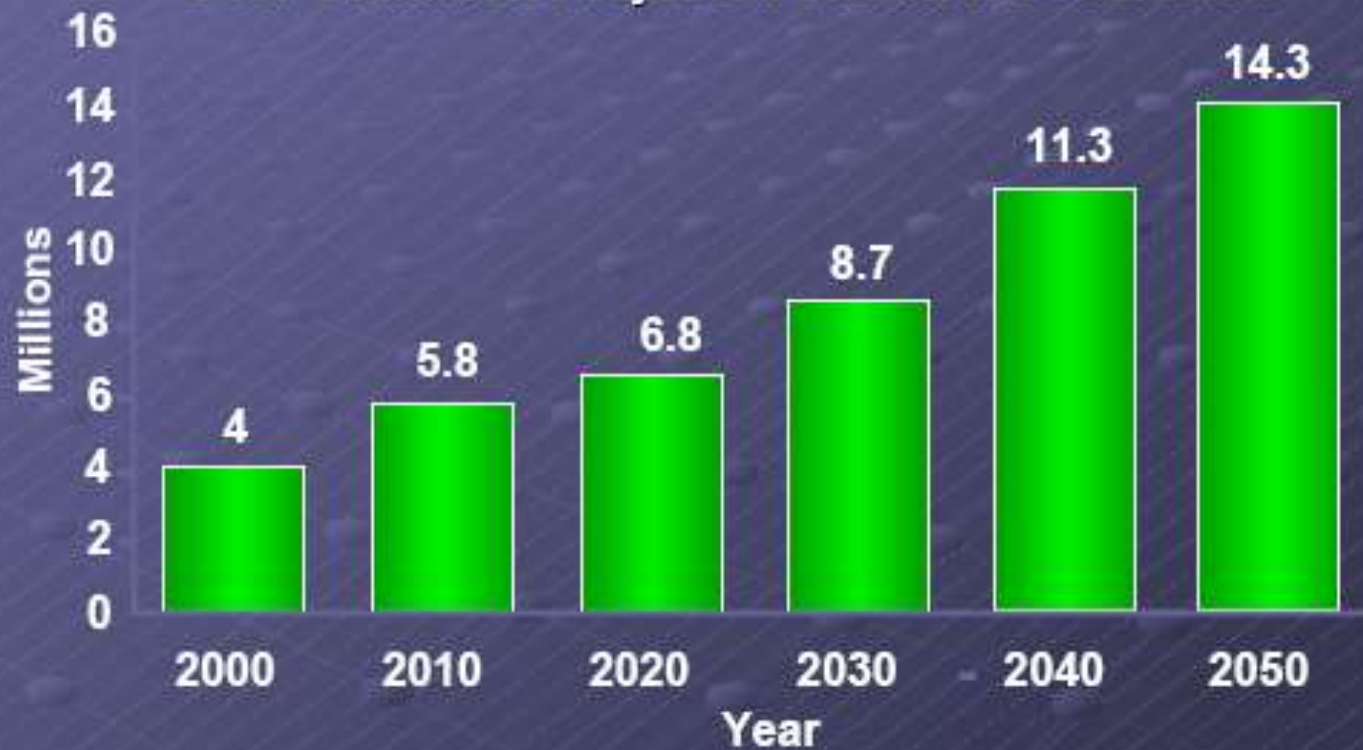
Staying physically fit isn't just good for your health.
It's also the single best way to keep your brain fit.

Getting Major Neurocognitive Disorder (Dementia) is partially a lifestyle decision

- ▶ You cannot change your age or the genes you are born with.
- ▶ Major NCD depends on lifestyle choices
- ▶ Santiago Ramon y Cajal: "Every man can, if he so desires, become the sculptor of his own brain."

Projected Prevalence of AD

4 Million AD Cases Today—
Over 14 Million Projected Within a Generation

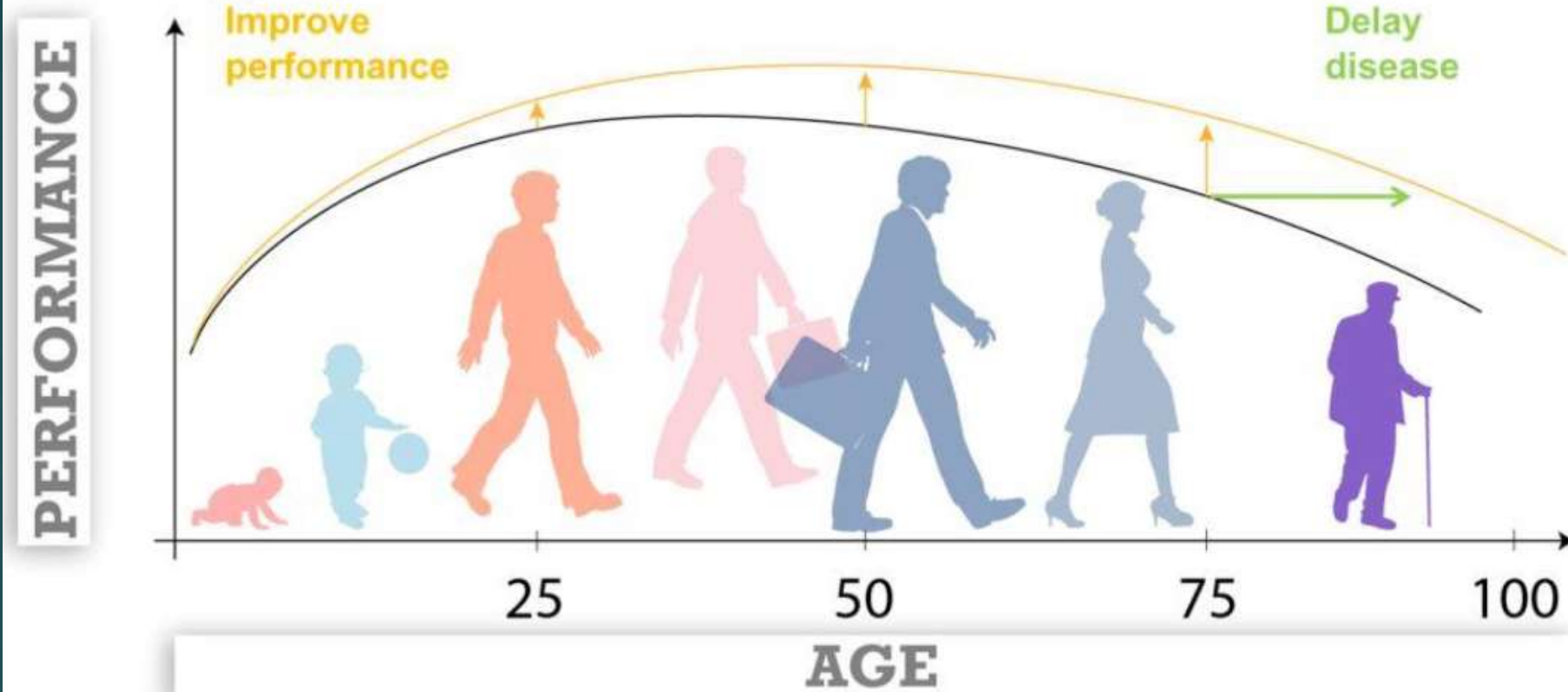


Evans DA et al. *Milbank Quarterly*. 1990;68:267-289

Our Health is modifiable

- ▶ Between 1969 and 2013, the death rate for all causes declined 43% in US
- ▶ Five of the six leading causes of death declined during the study period: 77% for stroke, 68% for heart disease, 40% for unintended injuries, 18% for cancer, and 17% for diabetes.
- ▶ Due to reductions of:
 - ▶ Tobacco use
 - ▶ high blood pressure
 - ▶ heart disease
 - ▶ cancer

Why brain fitness matters



- ▶ Nothing has been shown to prevent Alzheimer's pathology, but there are evidence-based ways to improve and prolong brain functionality, and to reduce the probability of manifesting brain disease



Dear God,
My prayer for 2016 is for a fat bank account & a thin body.
Please don't mix these up like you did last year.

Three Characteristics of Successful Aging

- ▶ 1 Lowering the risk of disease & disease-related disability
- ▶ 2 High cognitive and physical functioning
- ▶ 3 Active social and productive engagement with life

You become what you believe

- Endorsing negative stereotypes about aging and holding negative attitudes toward your own aging is correlated with:
 - Poorer memory performance
 - Slower walking speed
 - Slower recovery from disability
 - Less engagement in preventative health behaviors
 - And reduced longevity (earlier death)



My advice.

Don't give in to fatalistic thinking about ageing.

Factors Influencing How Well You Age Cognitively

- ▶ Age
- ▶ Genetics
- ▶ Early life environment
- ▶ Nutrition
- ▶ Education
- ▶ Medical co-morbidities
- ▶ Cardiovascular health
- ▶ Beta Amyloid increase
- ▶ Social networks
- ▶ Exercise

Key points to remember

- ▶ Brain fitness is a critical part of overall health.
- ▶ Cognition is more than just memory.
- ▶ Alzheimer's is not the only dementing disorder.
- ▶ The 2 biggest threats to brain health are stroke and Major NCD.
- ▶ What is bad for the heart is bad for the brain.
- ▶ Brain fitness can be nurtured.
- ▶ Middle age is when you should begin practicing good habits.



Do you...

- ▶ Misplace your keys?
- ▶ Miss an appointment?
- ▶ Forget the names of people you know well?
- ▶ Believe your memory is fading?
- ▶ Is there something you can do about this?

Retirement Home Test

During a visit to the retirement home, I asked the director, "How do you determine whether or not a person should be institutionalized?"

'Well,' said the Director, ' we fill up a bathtub, and then we offer a ½ teaspoon, a teacup and a bucket to the patient and ask him or her to empty the bathtub.'

'Oh, I understand,' I said.. 'A normal person would use the bucket because it's bigger than the spoon or the teacup.'

'No.' said the Director, 'A normal person would pull the plug.
Do you want a bed near the window?'

Old Age has Negative Press

- ▶ Brain damaged theory of old age:
 - ▶ Aging as inevitable process of brain damage and decline
 - ▶ You can't teach an old dog new tricks.
- ▶ Elderly are often described as:
 - ▶ Cranky
 - ▶ Eccentric
 - ▶ Lonely
 - ▶ Afraid of change
 - ▶ Depressed
 - ▶ Forgetful or Senile
 - ▶ Unable to keep up with technology
 - ▶ Dependent
 - ▶ Physically infirm



The Cat In The Hat On Aging

I cannot see
I cannot pee
I cannot chew
I cannot screw
Oh, my God, what can I do?
My memory shrinks
My hearing stinks
No sense of smell
I look like hell
My mood is bad -- can you tell?
My body's drooping
Have trouble pooping
The Golden Years have come at last
The Golden Years can kiss my ass

Dynamic Old Brains

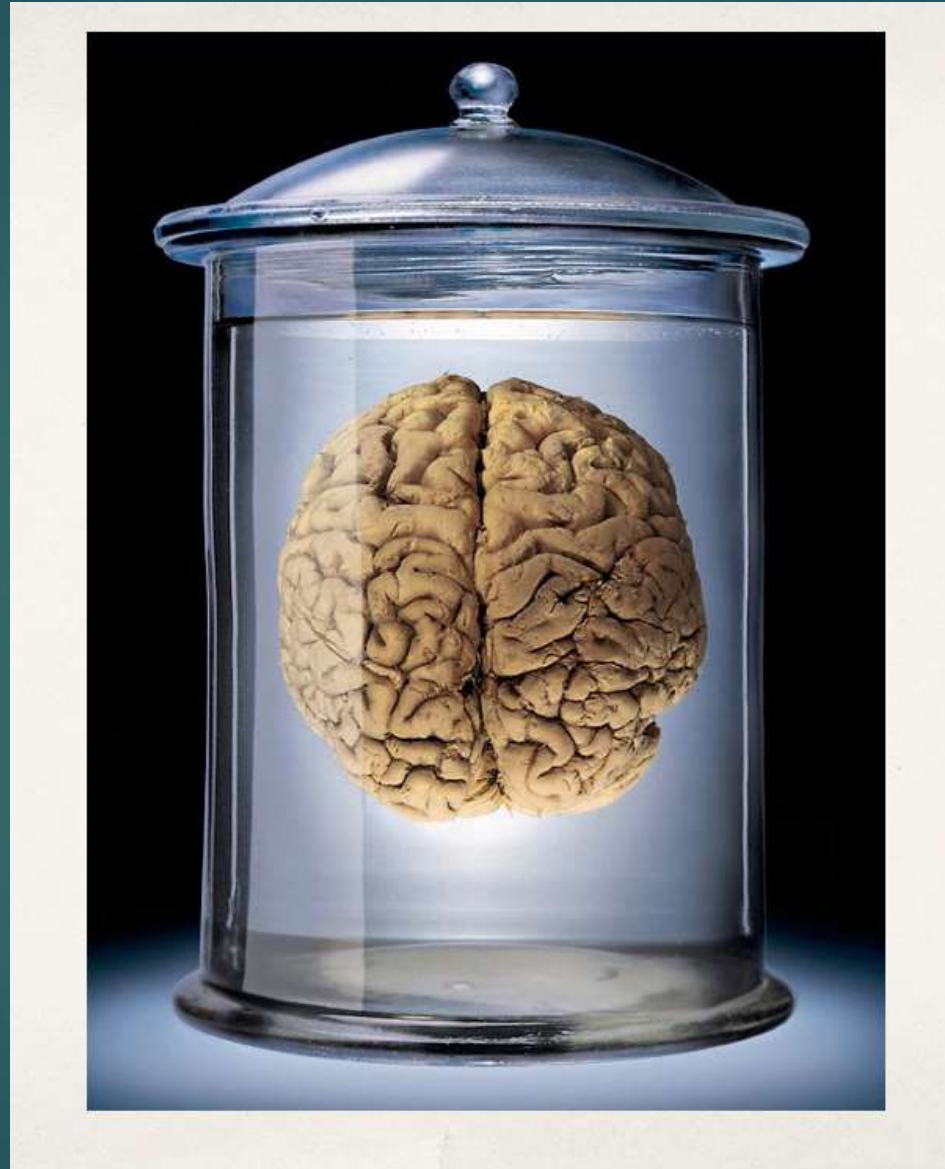
- ▶ The advent of functional neuroimaging has demonstrated that the aging brain is:
 - ▶ an adaptive structure
 - ▶ responds dynamically to cognitive challenge and structural deterioration
 - ▶ with compensatory mechanisms related to brain plasticity and reorganization of function
 - ▶ This fundamentally changes our view of cognitive aging.

Chill Out

- ▶ Aging glitches do not necessarily mean you have Alzheimer's disease
- ▶ There's a difference between not remembering where you put the car keys today...
- ▶ And not remembering that you own a car.
- ▶ Young people lose their keys and they just think they lost their keys.

- ▶ Daniel Dennett:
- ▶ “The brain is the only organ where it is preferable to be the donor than the recipient.”
- ▶ We always want to keep our own brain healthy.

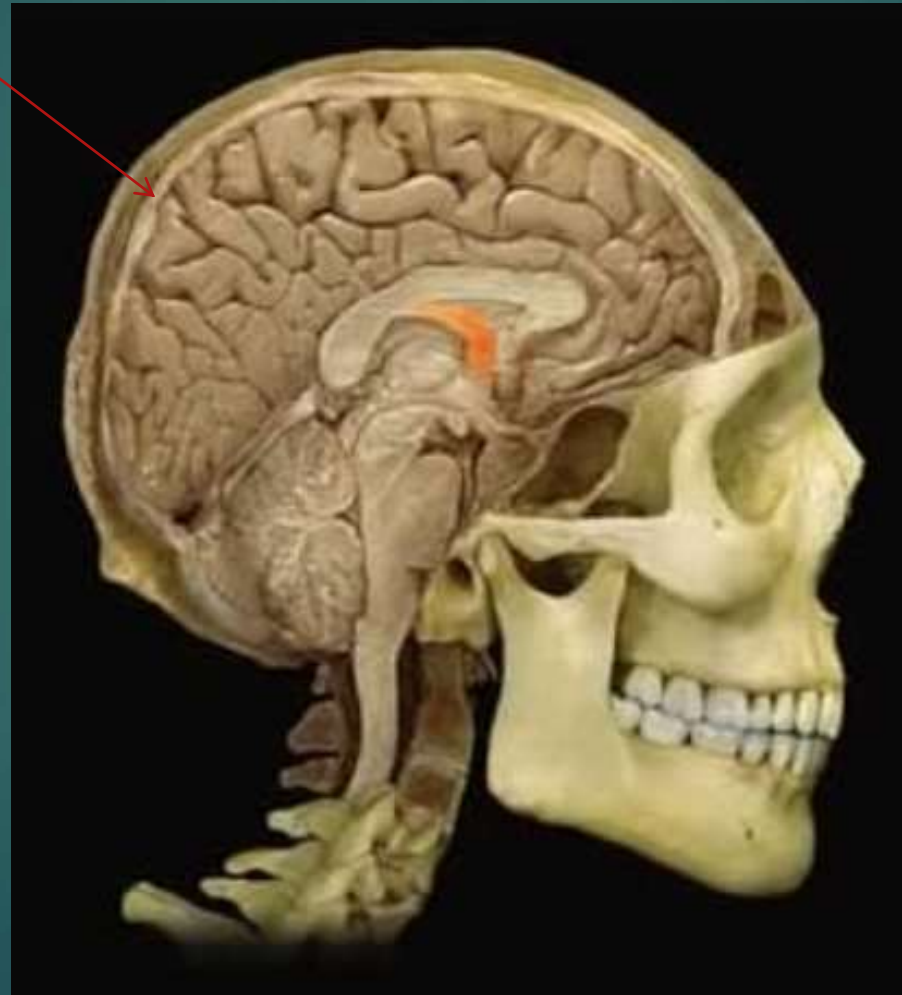
The Brain



3 pounds

Always buckle up or wear helmet!!

Thin skull



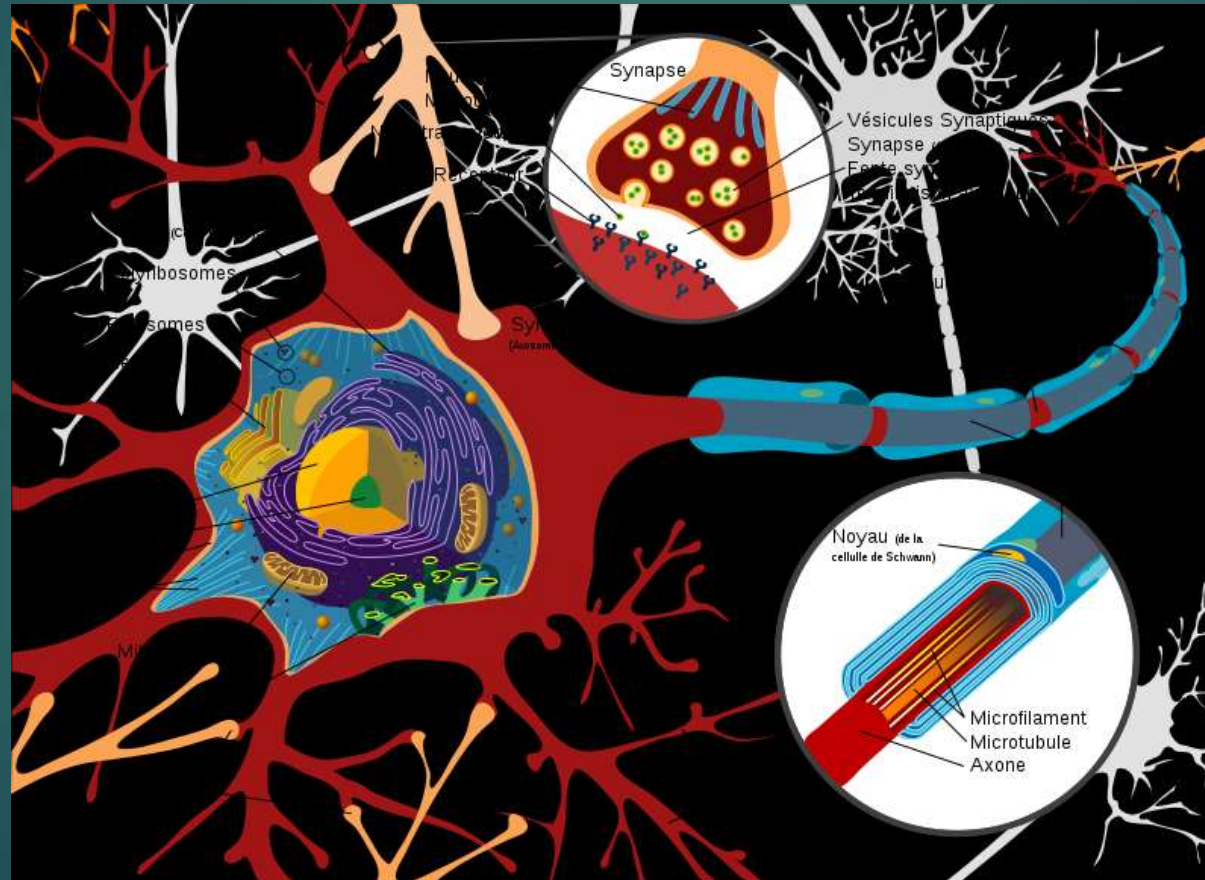
1 grain of rice



Would hold 10,000 neurons

Neurons: We have 86 billion brain cells with 10,000 synapses each (10 trillion connections)

Neuron



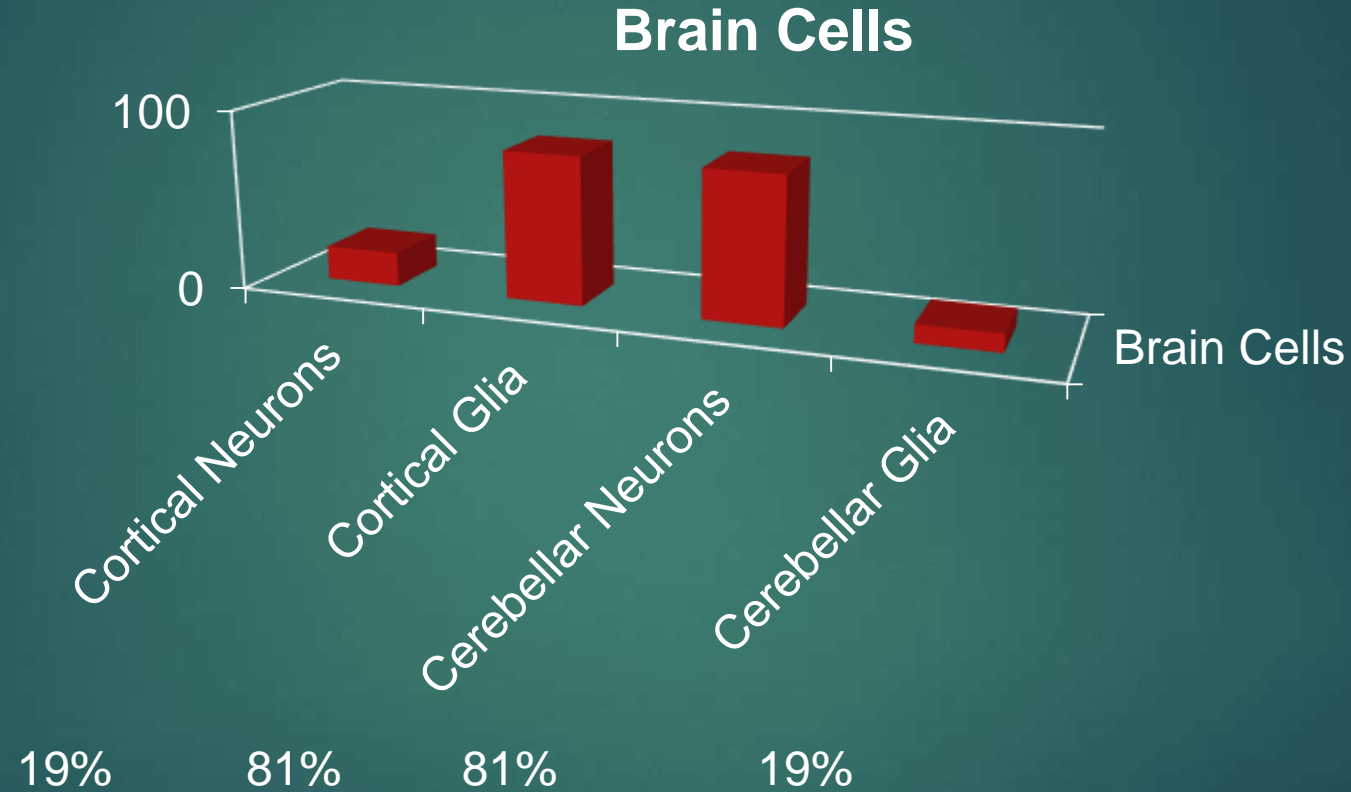
Axon

Dendrites

Brain

- ▶ 86 Billion neurons, 85 billion glial cells
- ▶ 1 neuron can fire 200 x per second
- ▶ 10000 connections
- ▶ 13 ms to process a visual image
- ▶ 1000s of networks of neurons

Cortical Brain Cells: 170 Billion



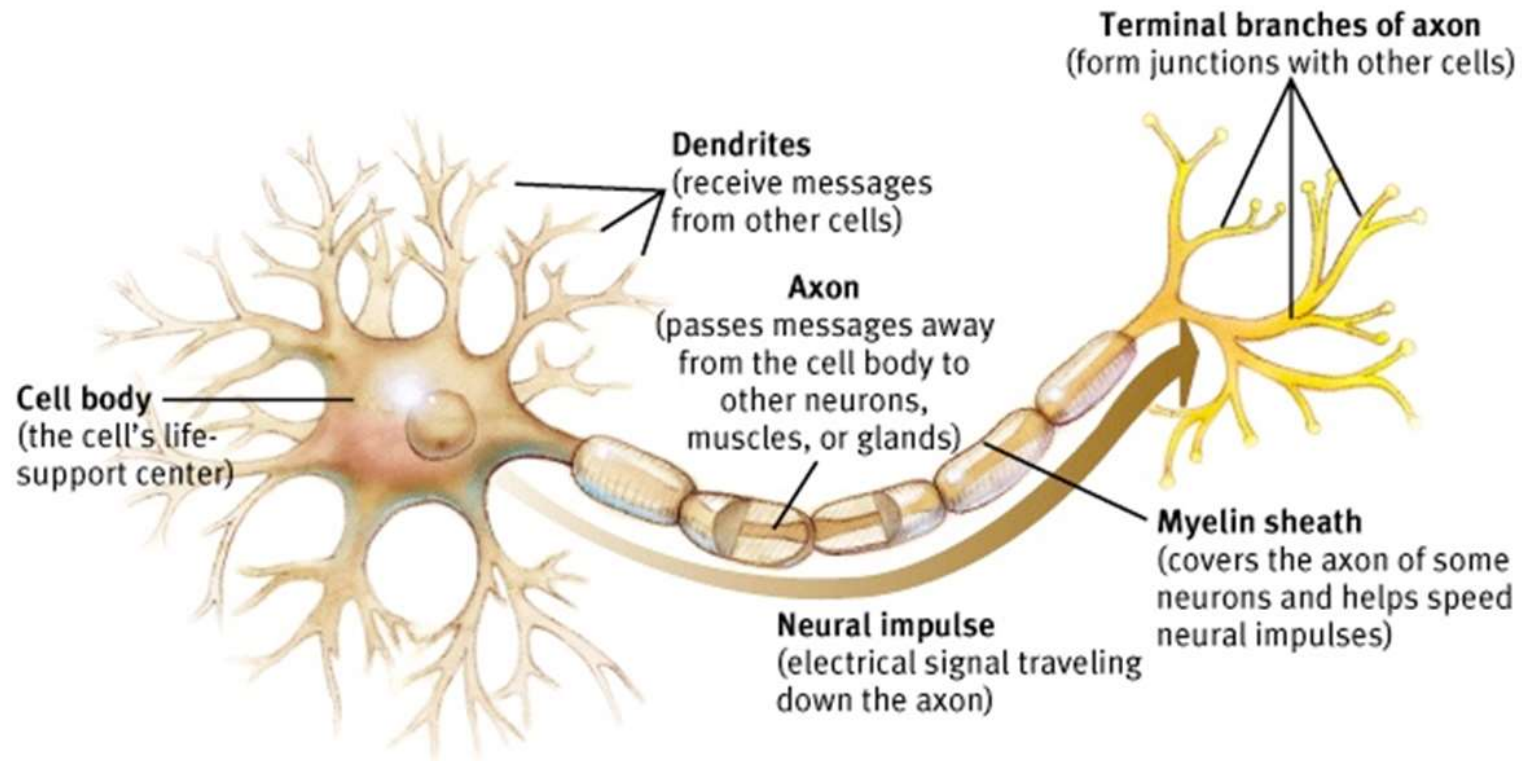
Adult male human brain contains on average:

86 ± 8 billion neurons

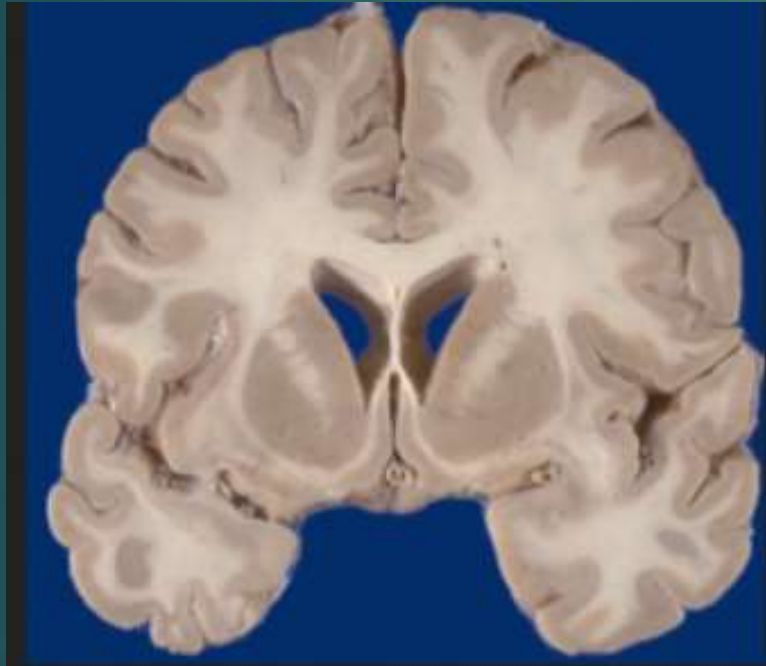
85 ± 10 billion glial cells.

Neuron

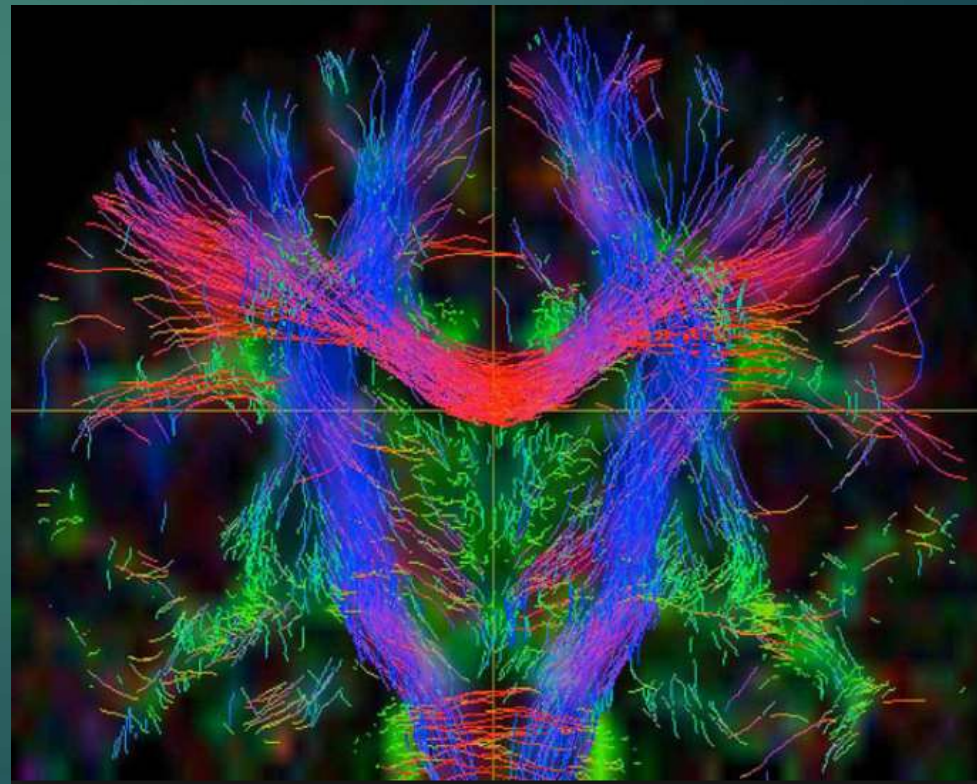
Neuronal Structure



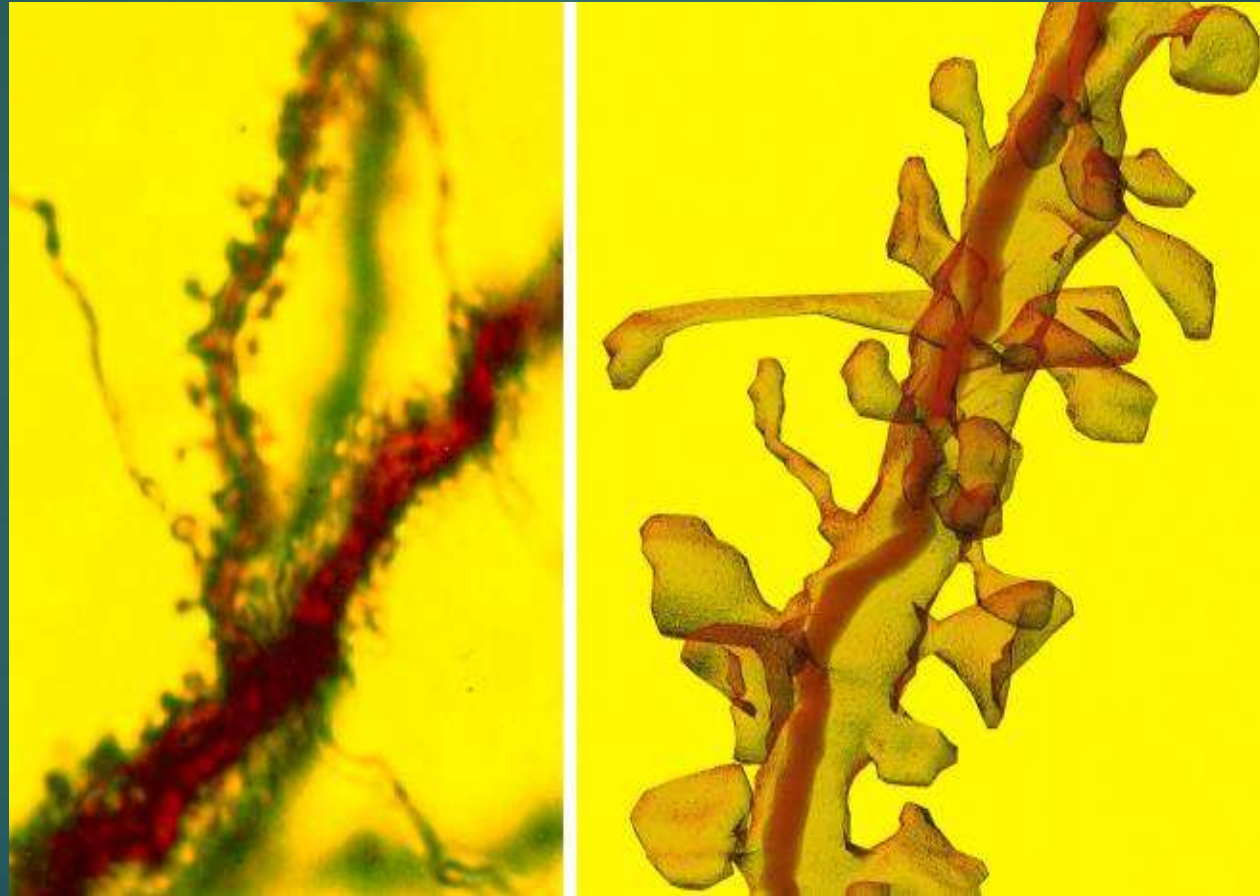
White Matter: Insulation on your Neuronal axons



The Internet of your brain:
How fast you process information

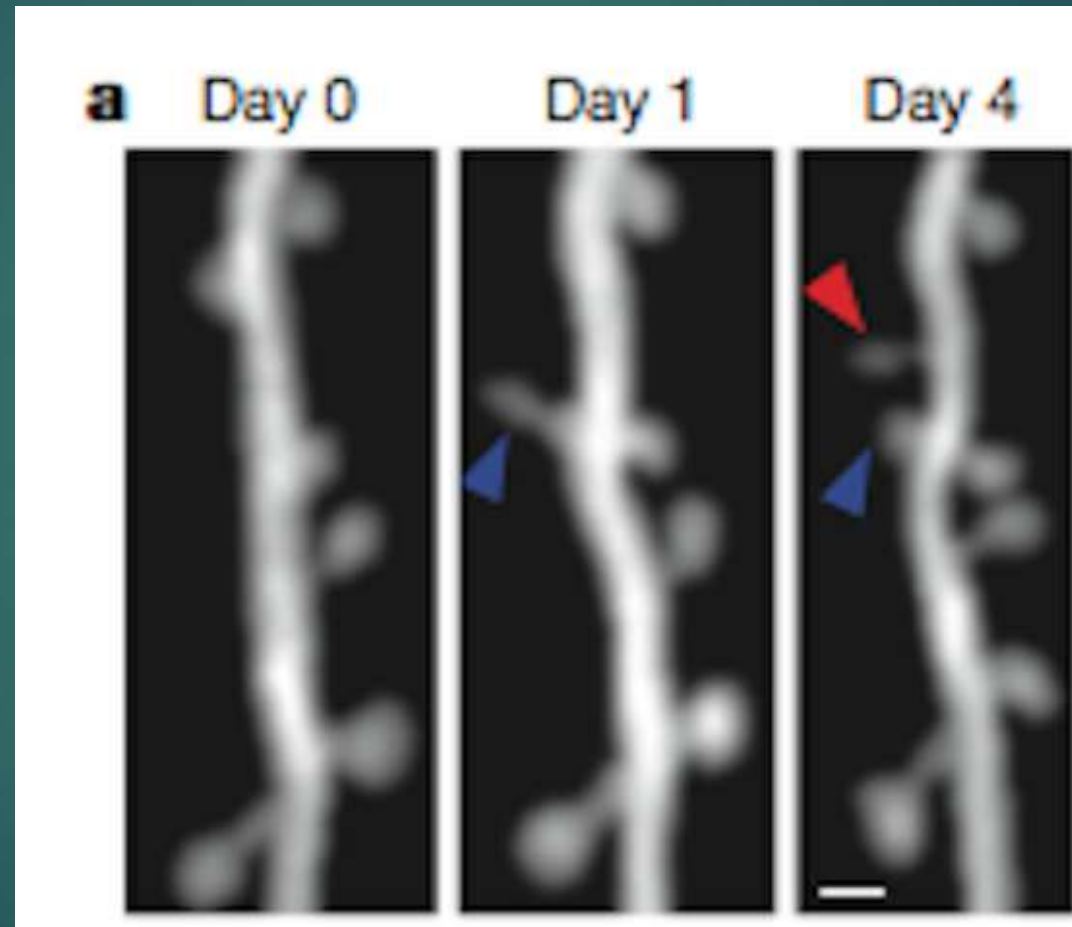


Dendrites: Electron Microscope



Dendrites are dynamic: can change in hours or over weeks

Physical basis of Neuroplasticity

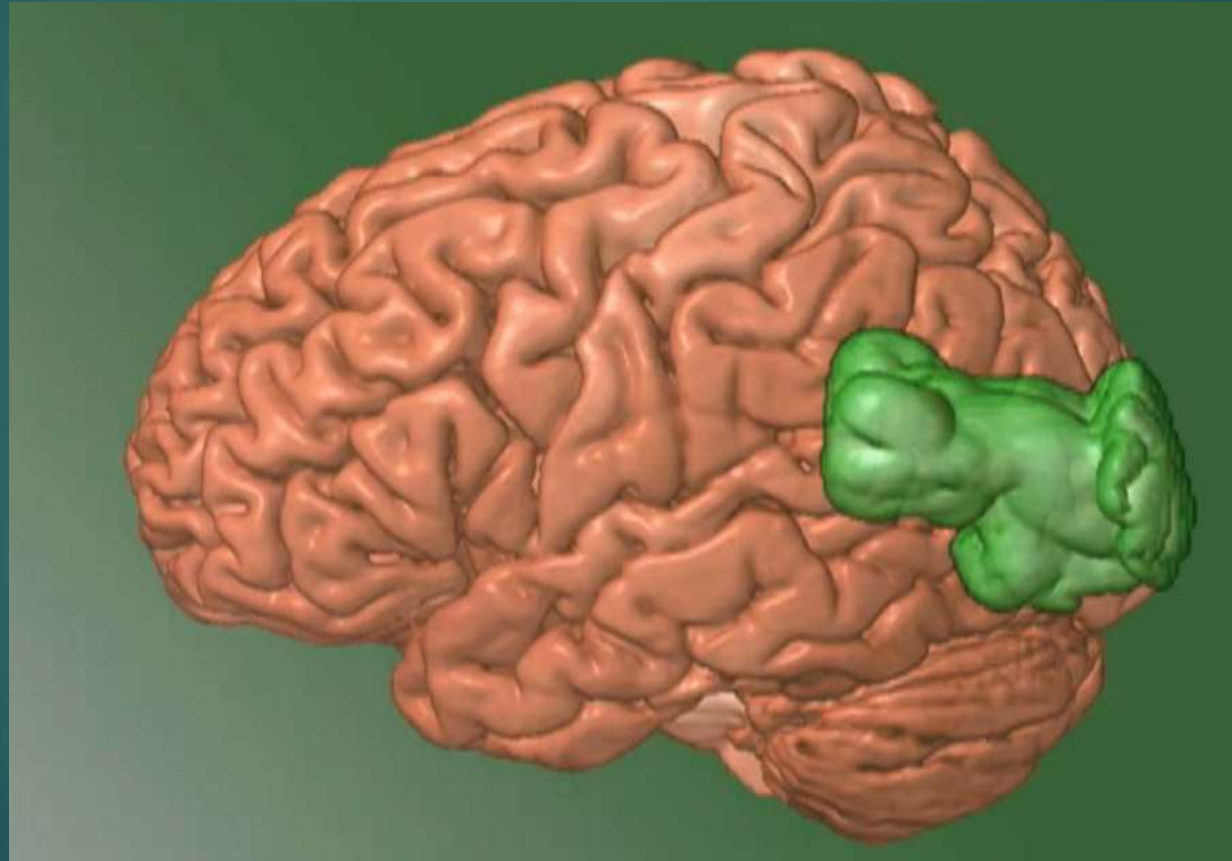


2 dendrites grow in a mouse after 4 days of reaching for a seed

Brain: Consistency of room temperature butter



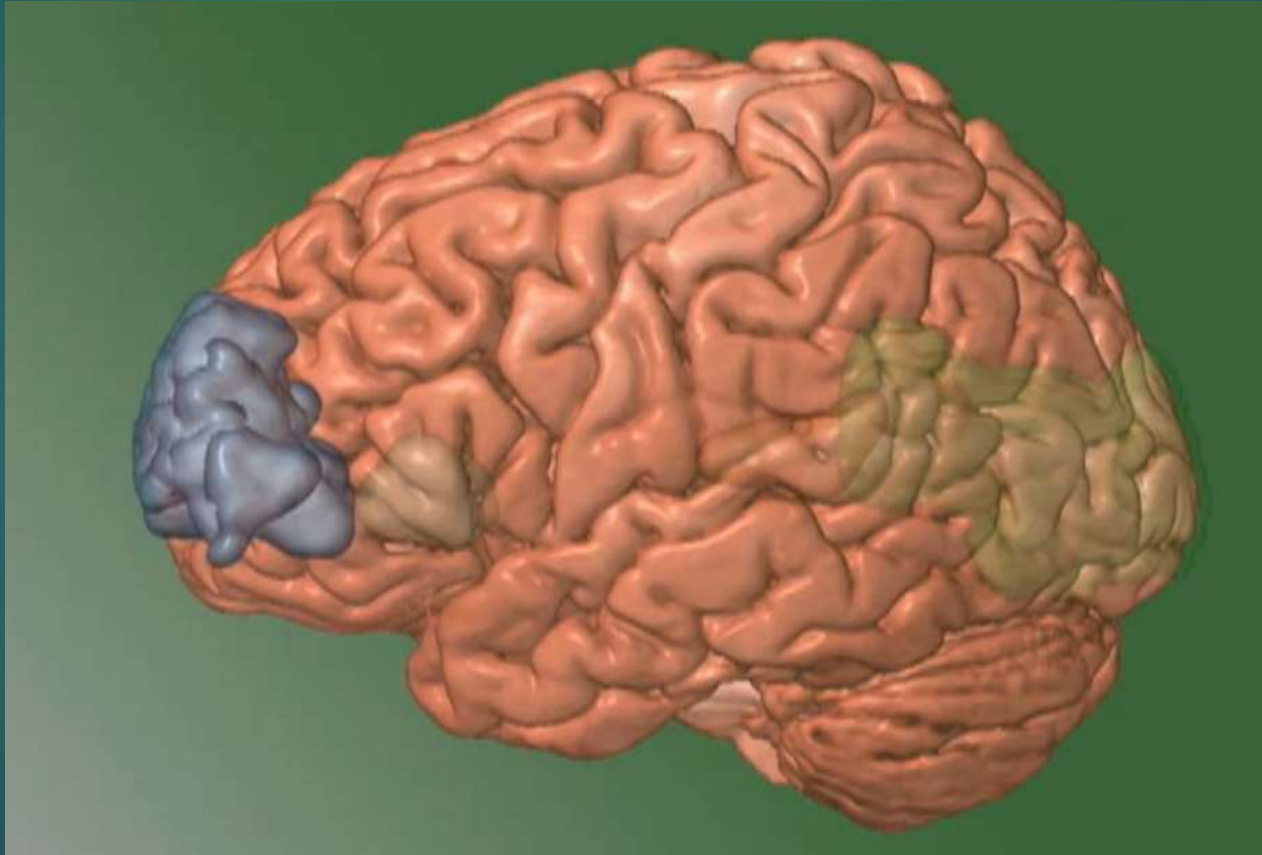
Damage to Occipital area: Blindness



Damage to Broca's or Wernicke's: Language disorders



Damage to Prefrontal area:
Personality & decision making changes

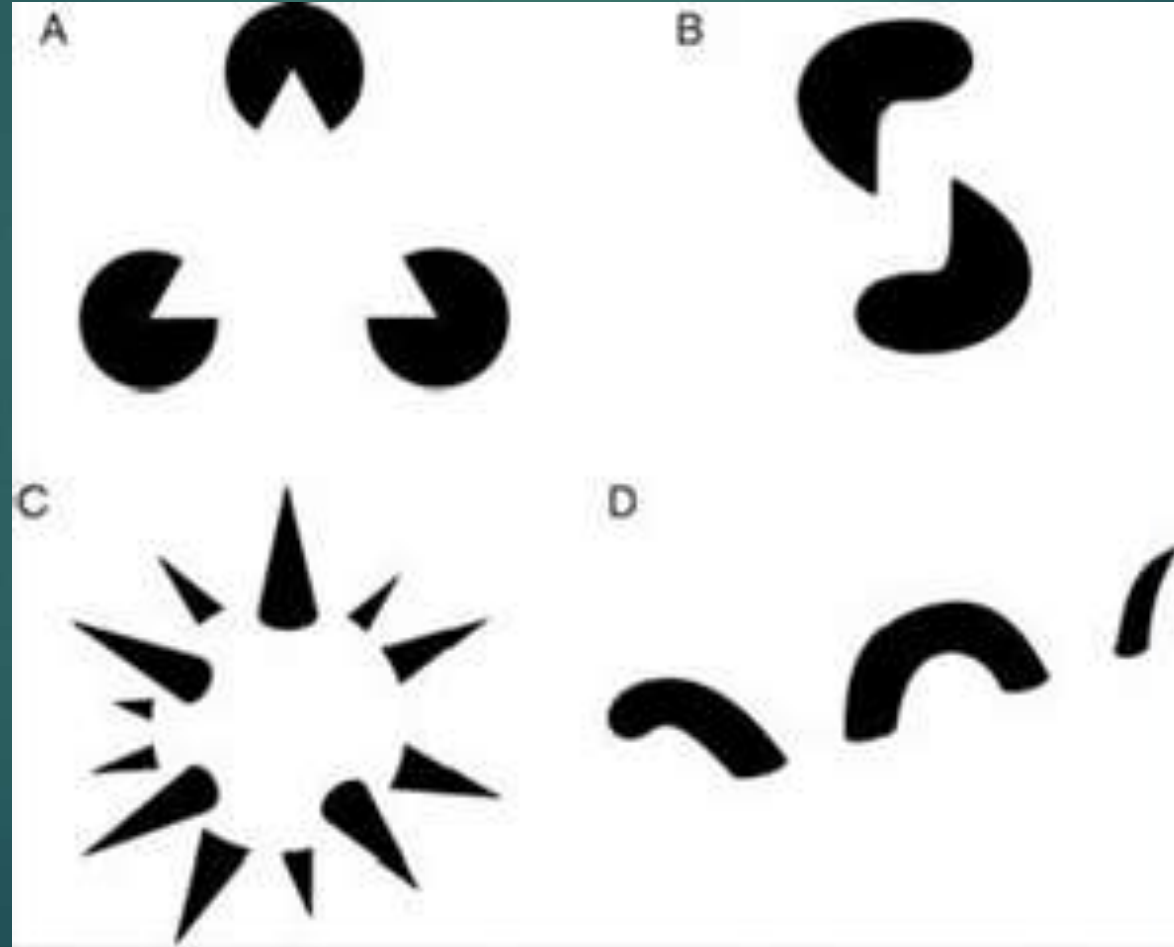


But we can be fooled:
Which is male vs. female?

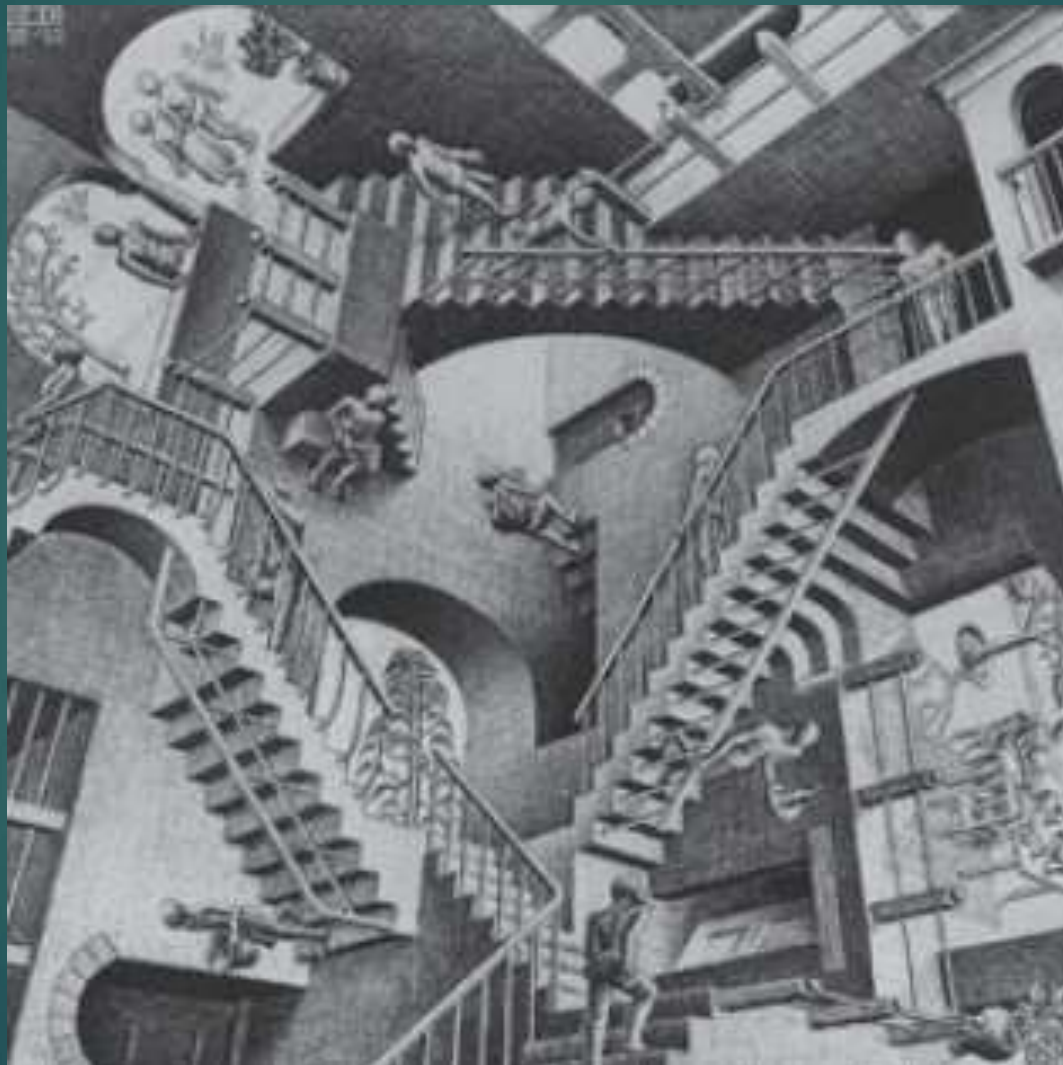


The contrast between the eyes and mouth and the rest of the face is higher for the face on the left.

The Brain often tricks us:
You don't see *exactly* what is there



We can see the impossible: Escher



Done in Origami

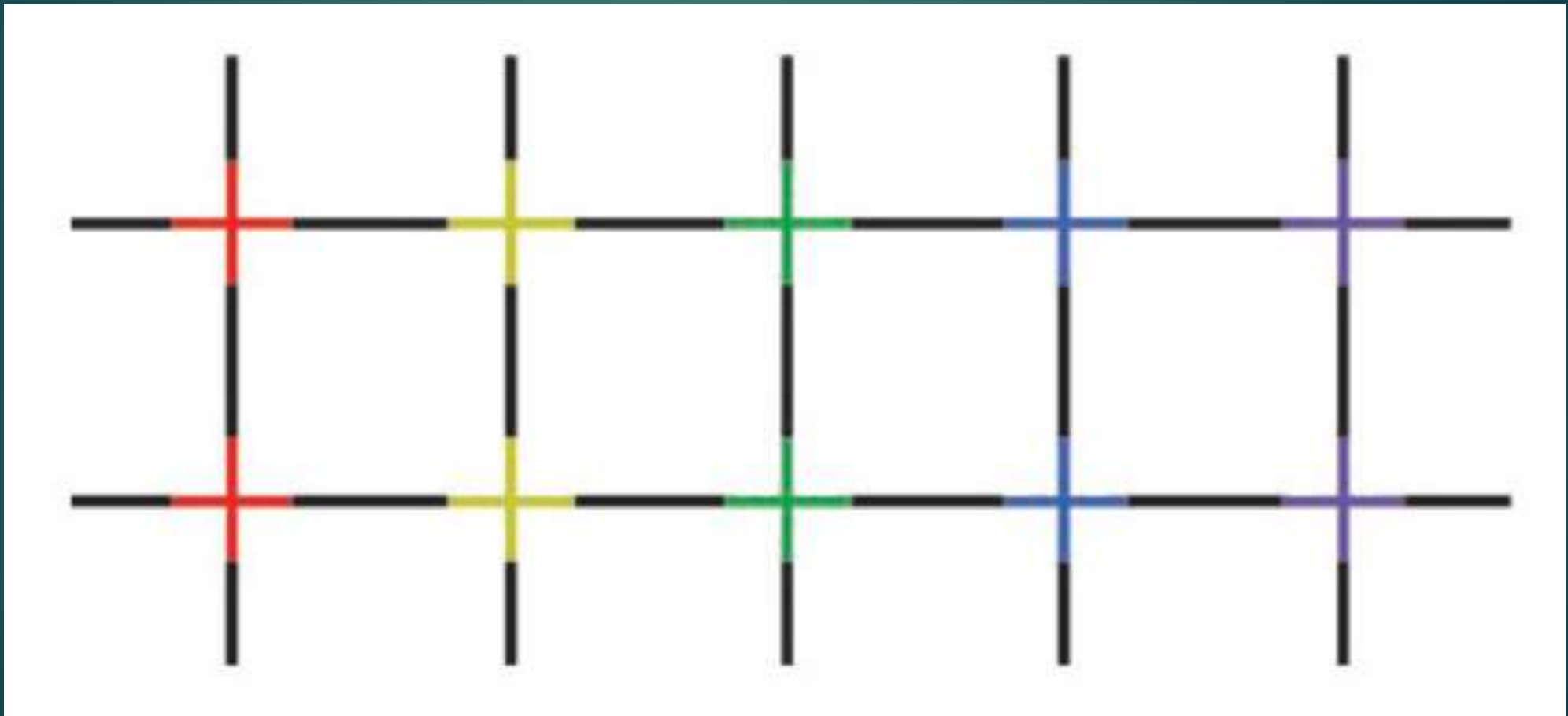


Even with Legos...



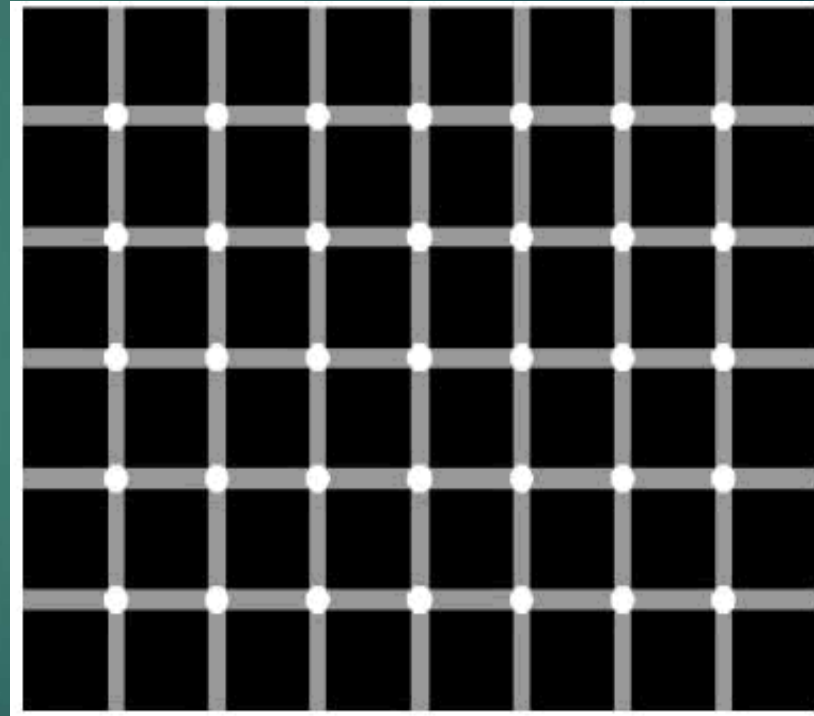
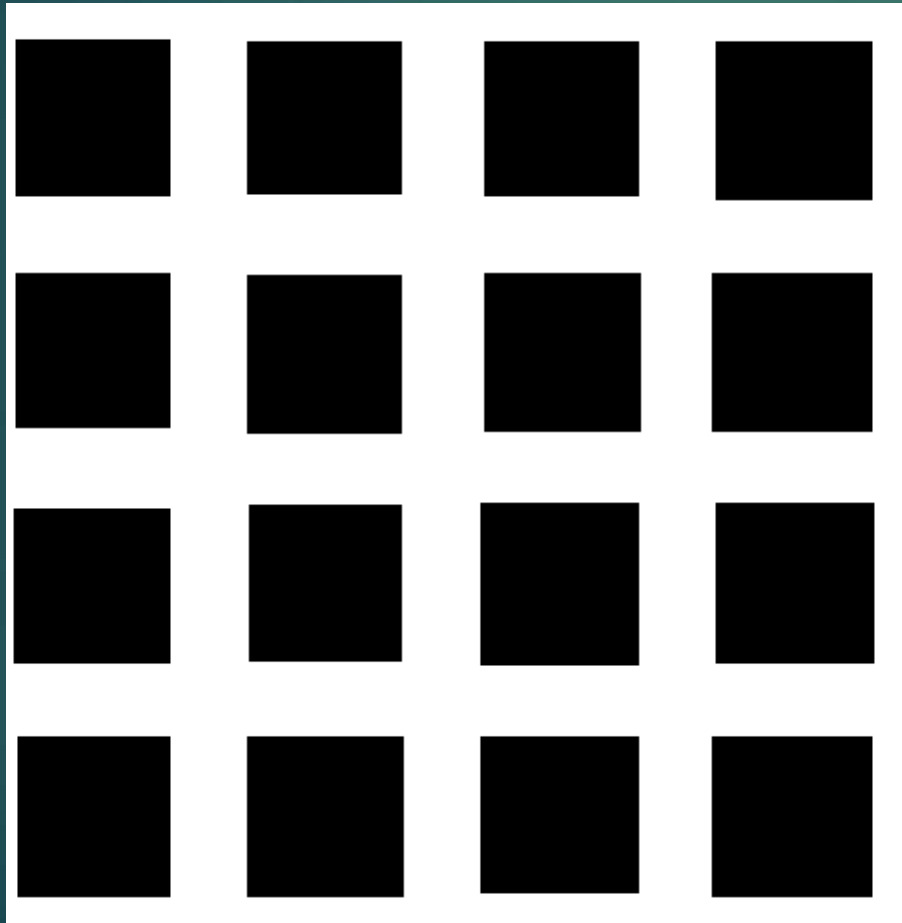
Our Brain Can Trick Us:

Neon Effect: We see colors where they do not physically exist

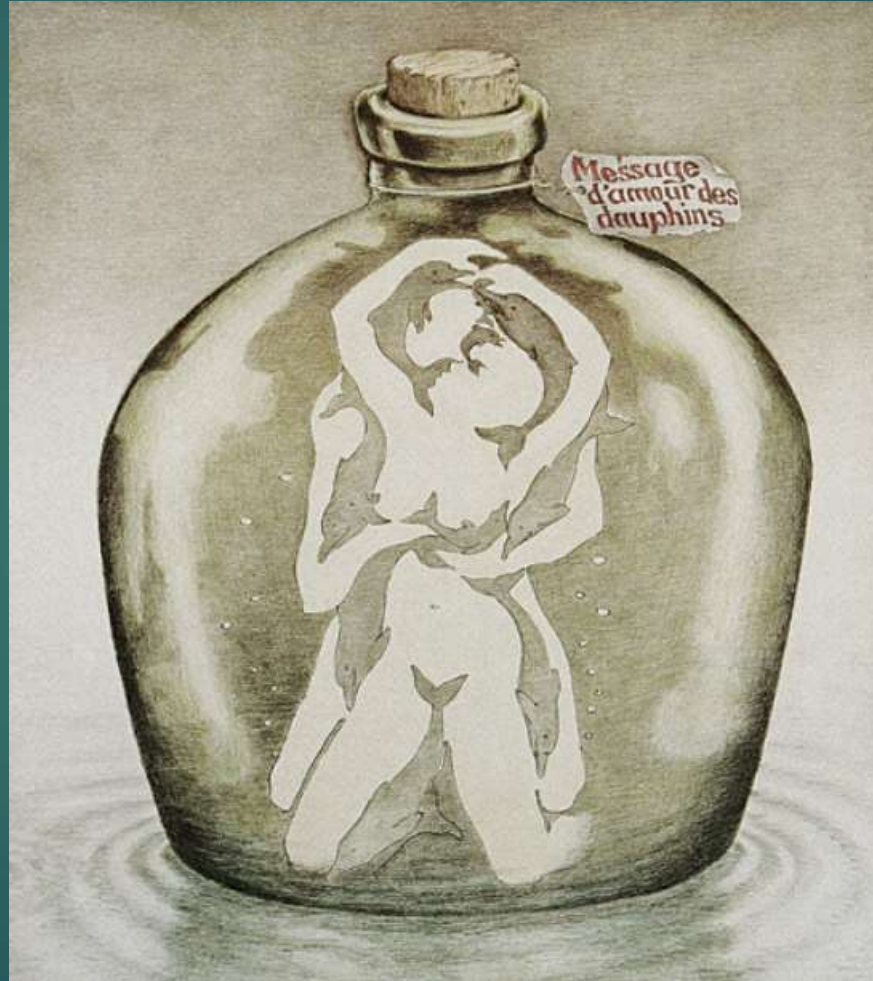


Contrast Effects:

Are there really grey balls or black dots?



Effect of Experience on Vision: 2 Nudes or 10 Dolphins



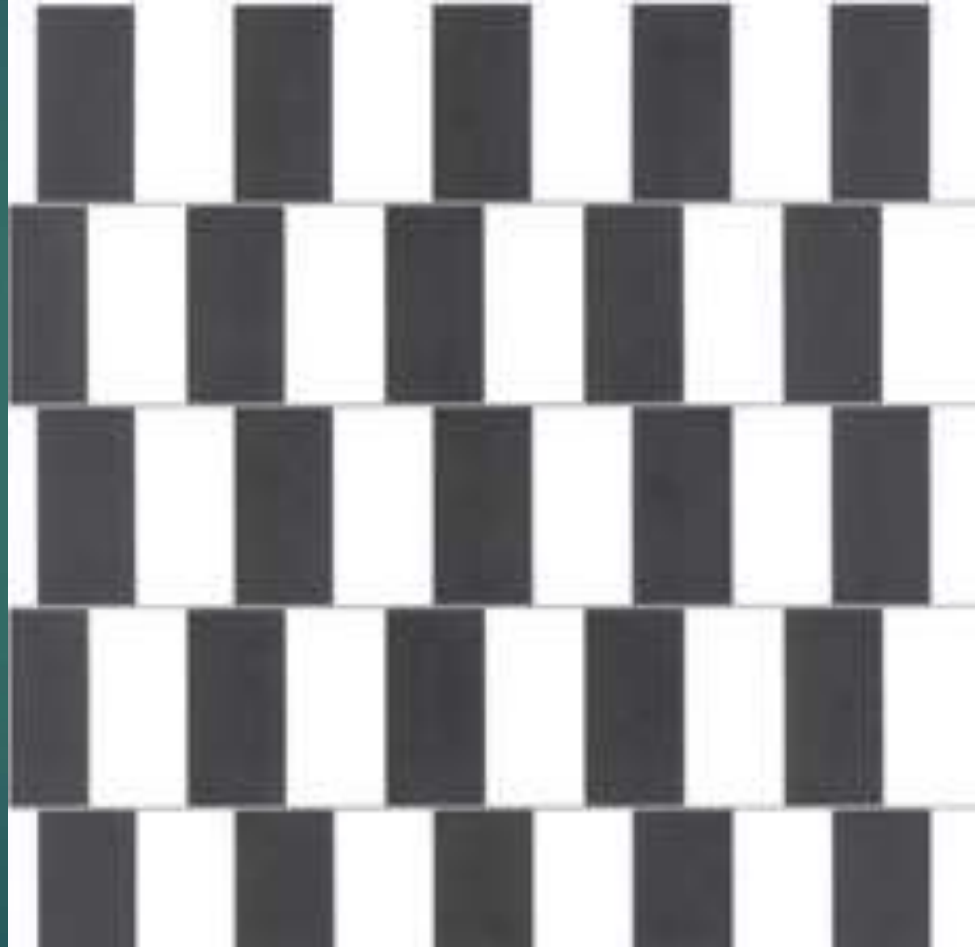
Young children see only 10 dolphins. Adults see two nude lovers embracing.

Effect of Cultural Experience on Visual Interpretation



Westerners see people inside a room; African villagers see family outside

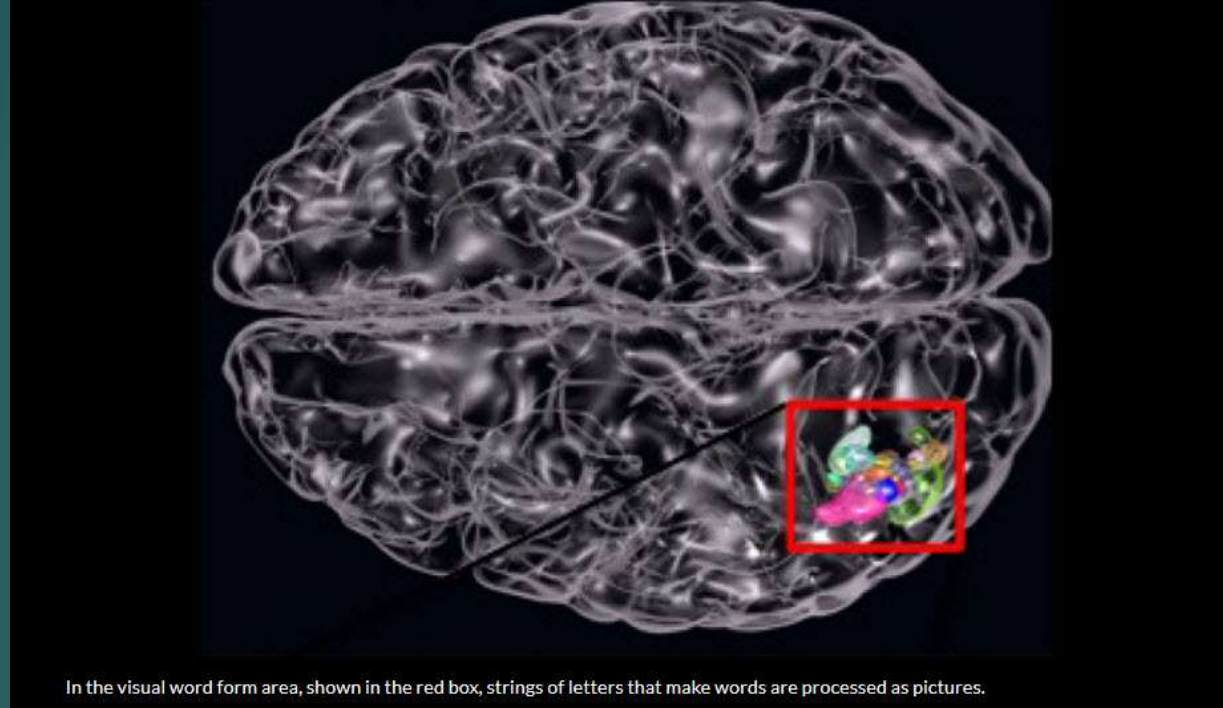
Actually lines are straight



Only when the contrasting black and white “tiles” are offset and when every tile is surrounded by a border of gray “grout.”

Words as Pictures:

Does the brain not read every letter by itself, but the word as a whole?



VWFA makes pictures out of words. Left ventral occipitotemporal cortex (specifically the "visual word form area," VWFA) contains a representation based on neurons highly selective for individual real words

Where is the human face?



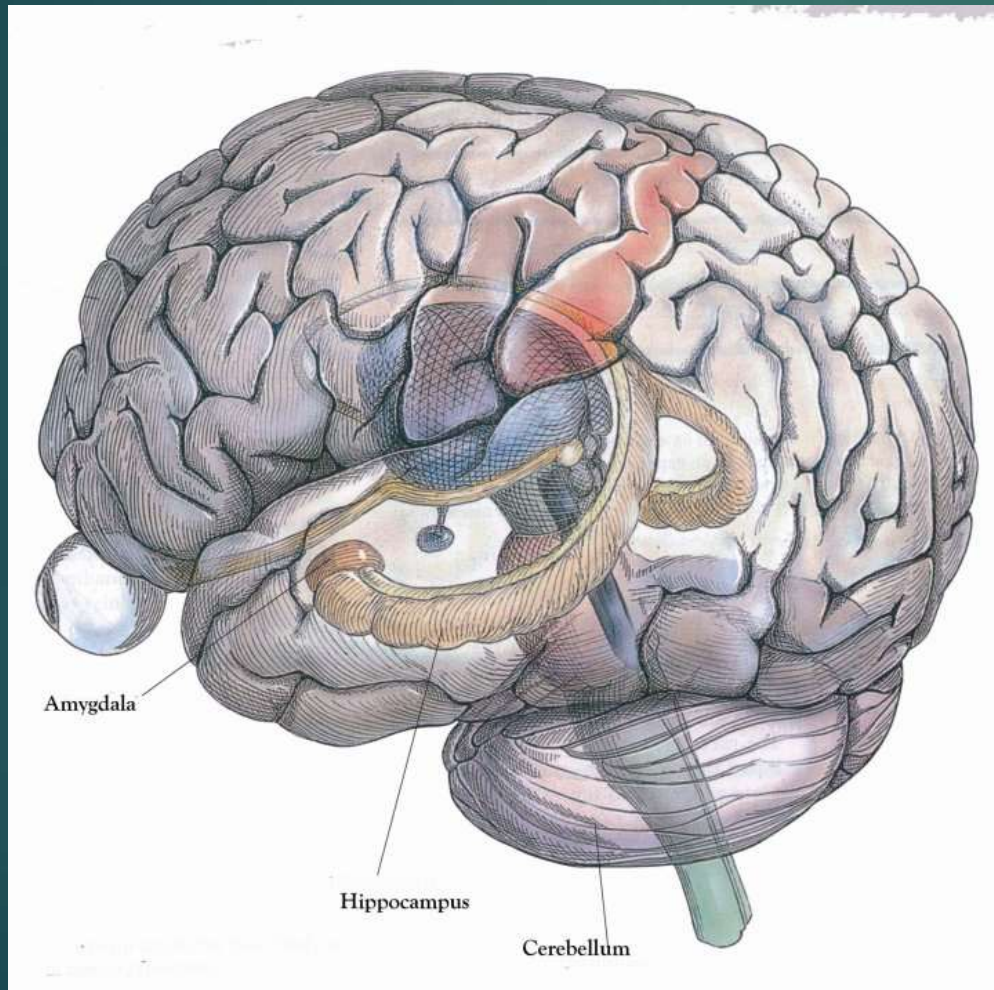
Test for the Sharp Minded

Even the sharpest mind can be fooled.

There are certain things that the average reader will overlook. Even if you are paying extra attention, you may not notice simple mistakes.

What are the 2 mistakes?

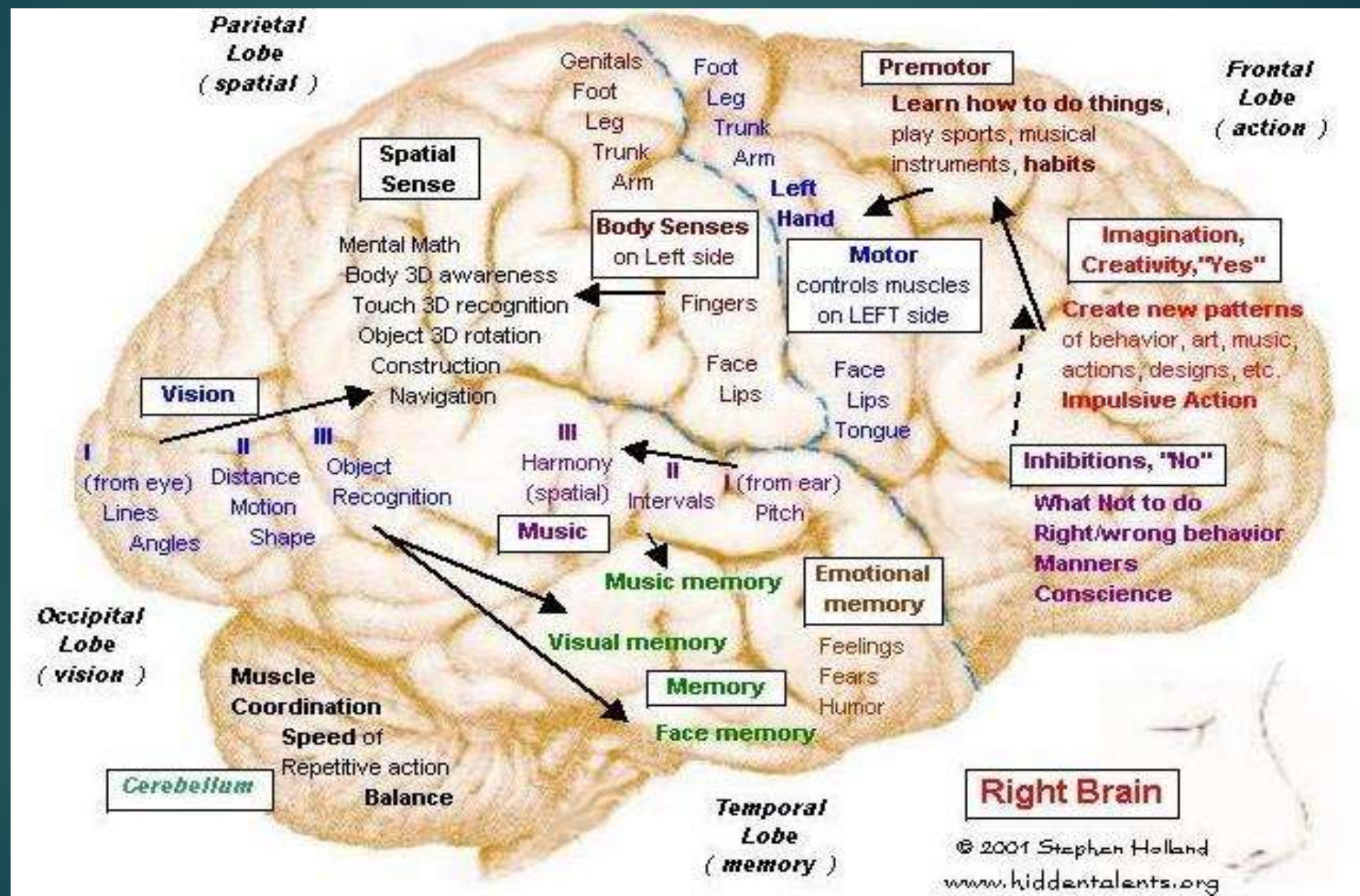
Hippocampus, Amygdala, & Prefrontal Cortex



Hippocampus is index to your memory database. It connects anything new you experience to what you already know.

Amygdala is your fear response center. It reminds you that you need to run away from tigers. It underlies PTSD.

Prefrontal Cortex is what makes us rational adults. Gives us the ability to inhibit behavior.



Erroneous Brain Beliefs

No basis in research:

- ▶ We use only 10% of our brain
- ▶ The notion that we have specific learning styles, that some are "visual learners" and others are auditory; some are "left-brain" students, others "right-brain."
- ▶ Creativity is a right brain phenomenon: different hemispheres differ on how they process same function (declarative vs. connotative language)

Brain has ability to change: Neuroplasticity

- ▶ Neuroplasticity = Physical and chemical brain changes based on experience
- ▶ It is the brain's ability to rewire itself or change itself based on new experience

Neuroplasticity

- ▶ **Neuroplasticity** is the ability of the brain to change and adapt in response to:
 - ▶ changes in its input,
 - ▶ by an alteration in the number of neurons or glia via cell division or apoptosis,
 - ▶ by formation of new circuits,
 - ▶ by strengthening or weakening specific synapses,
 - ▶ by changing the number of dendritic spines,
 - ▶ and/or by other mechanisms

Real Life Changes

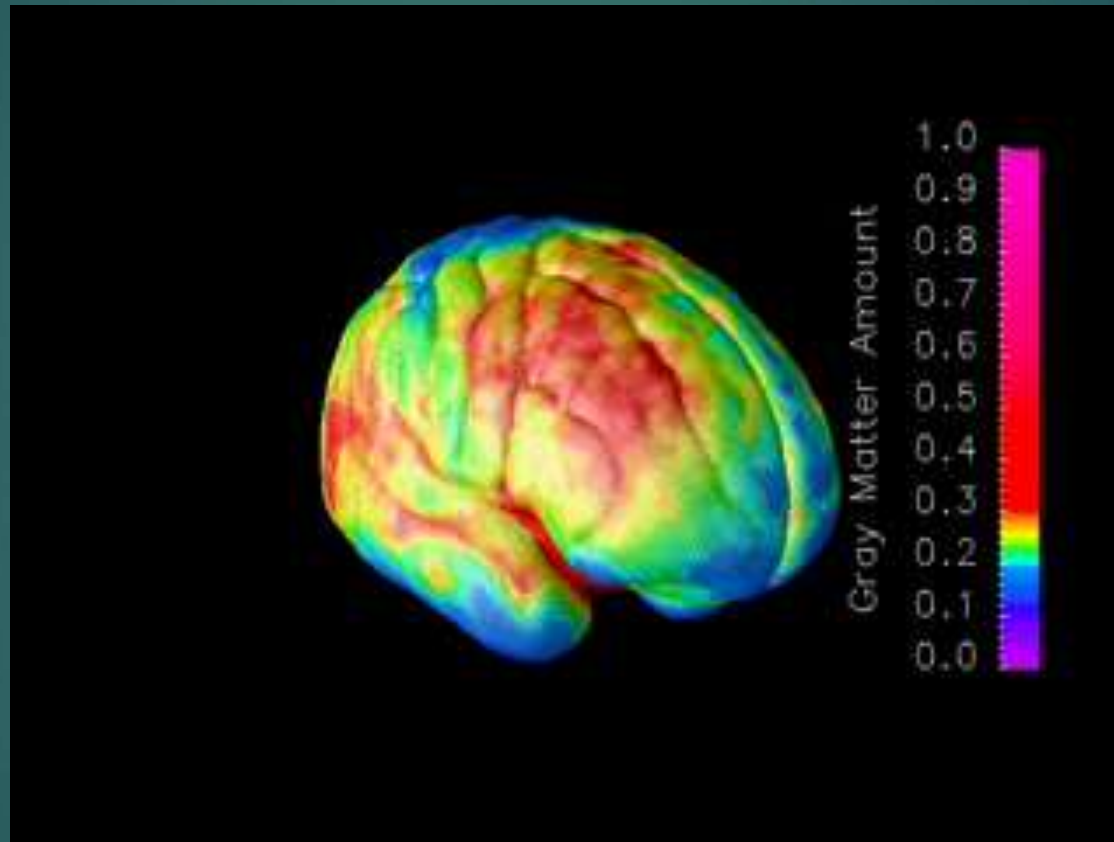
1993:



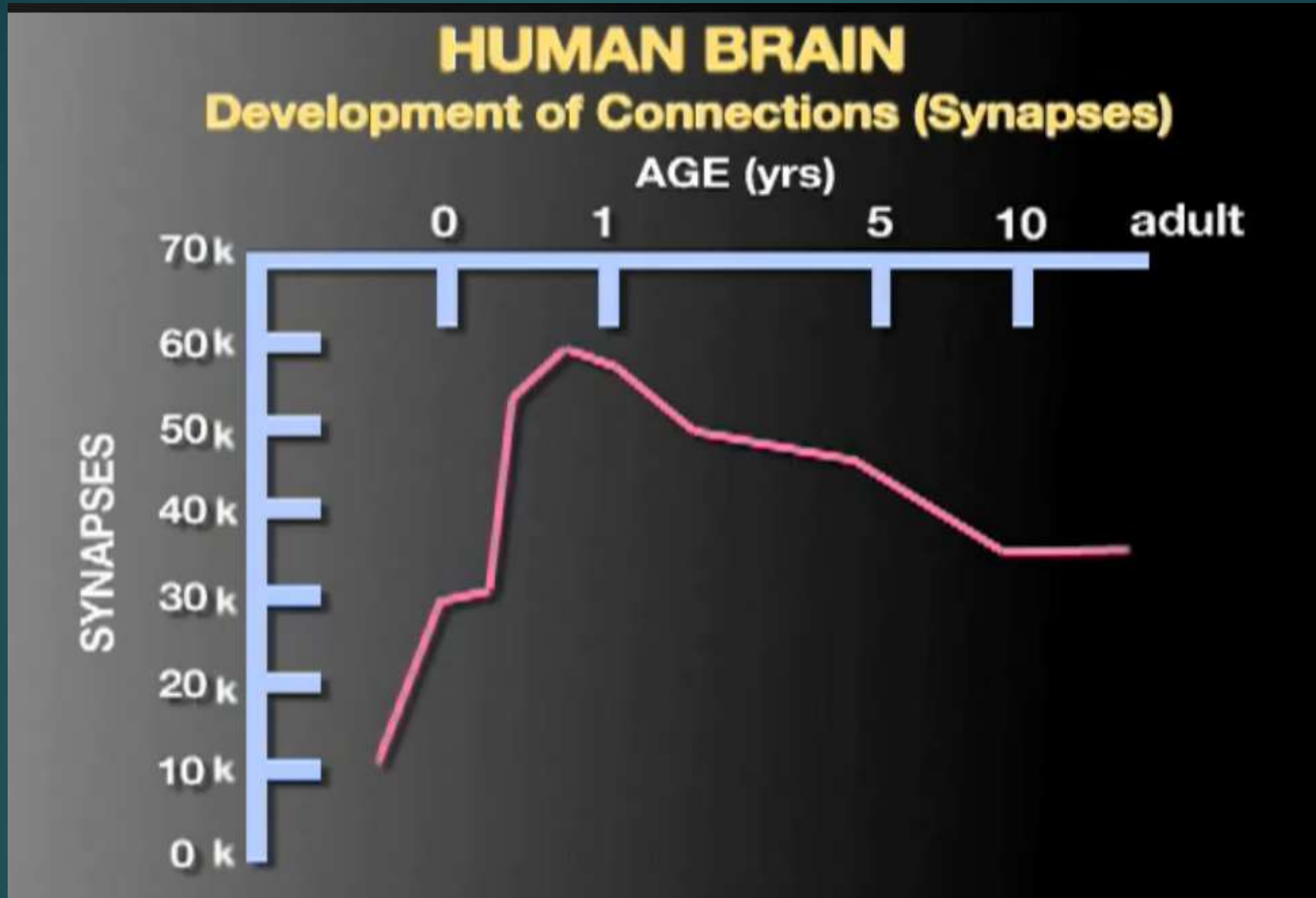
Life is simpler & more powerful



Teen Brain: age 5 to 21

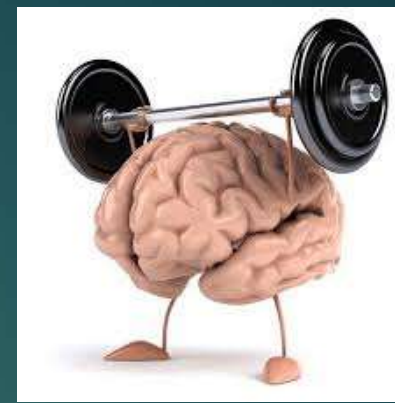


Lose 50% of all synaptic connections.
(Blue is thinner brain.)



2 year old child has twice as many synaptic connections as her mother/father

Use it or lose it theory



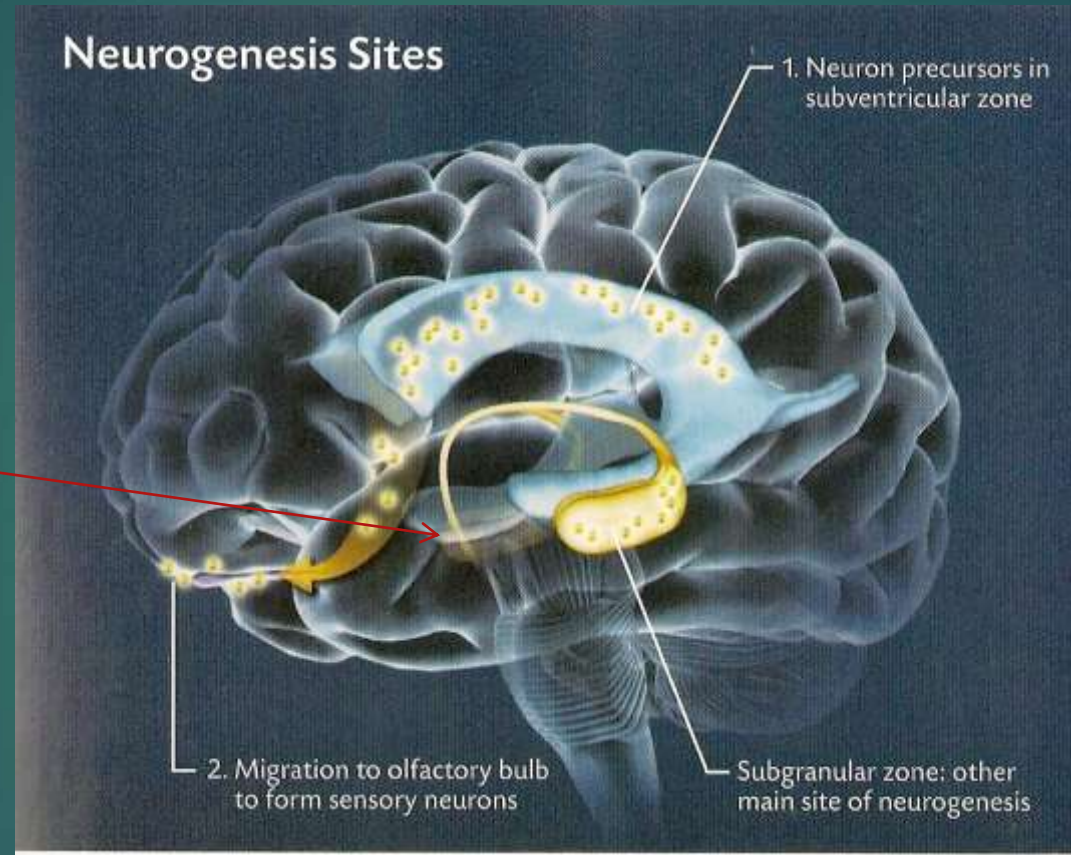
- ▶ People who use their brain cells protect these cells from wear and tear
- ▶ Without use, neuron is signaled that it is no longer needed
 - ▶ Dendrites atrophy
 - ▶ Synaptic connections weaken
- ▶ With no new input, brain synapses begin to weaken.

Cognitive Activity in old age

- ▶ High levels of mental activity can potentially decrease an individual's risk for developing Major NCD (dementia) by approximately 50%
- ▶ There is a dose response relationship between declining Major NCD risk and extent of mental activity in the later years of life in healthy elderly.

Neurogenesis: 3 major sites

Interneurons
in Striatum



1400 new neurons per day, enough to replace all the neurons in the dentate gyrus of the hippocampus over a lifetime; needed for new memories

Brain Changes with Aging

- ▶ Brains shrink 2 % per decade; especially in frontal and hippocampal region
- ▶ Cells/dendrites die – 150 grams loss
- ▶ Neurotransmitters change – lose half of dopamine
- ▶ Age-related increase in free radical injury in the human brain; greater in women than in men.
- ▶ Increase in beta amyloid plaques
- ▶ But great variability in aging in brain; not wholesale neuron loss

Brain shrinks with age

- ▶ Big Question: Is brain atrophy normal or pathological?
- ▶ Does brain shrink due to normal processes due to age, due to pathology, or because we stop challenging it?
- ▶ Can we stay cognitively OK even with atrophy?

Neuroplasticity can also have negative consequences

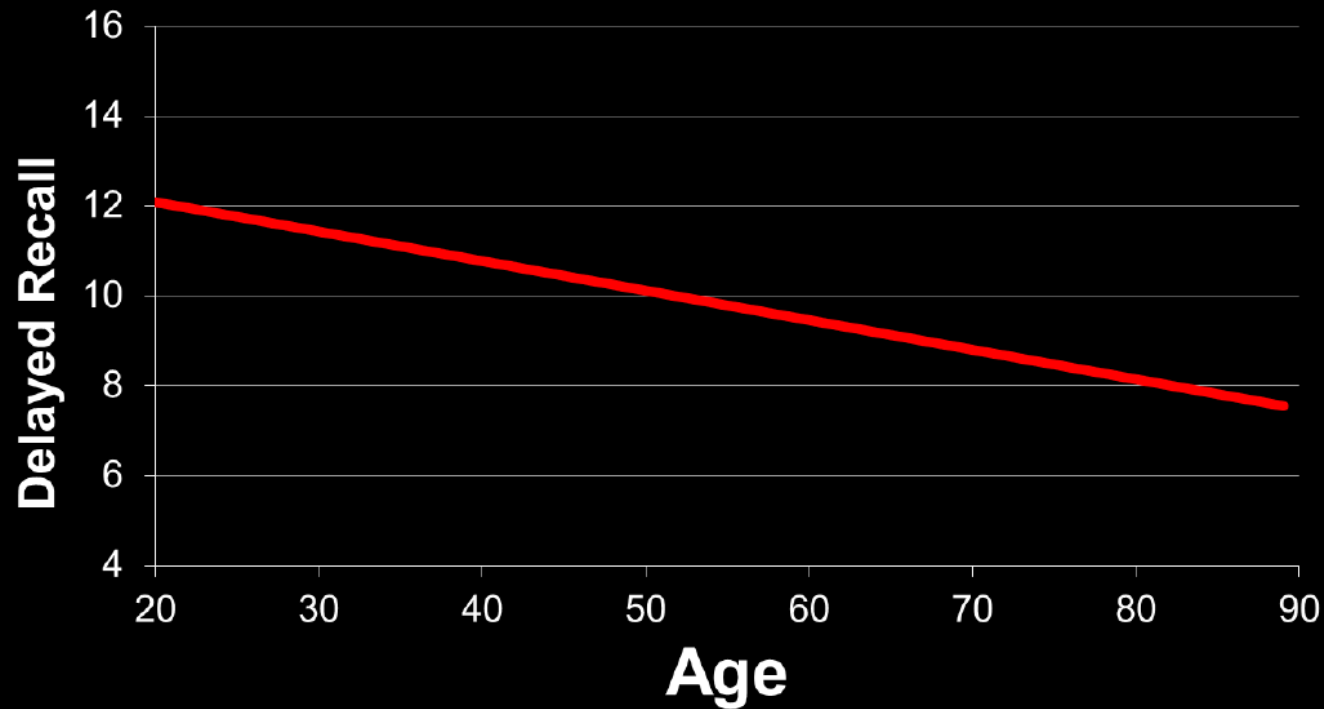
- ▶ Negative neuroplasticity in older adults:
 - ▶ Reduced brain activity - “Brain disuse” and sedentary lifestyles
 - ▶ Negative learning (loss of skills) due to non practice
 - ▶ Example: sitting all day in front of TV

Intellectual Ability Declines
in Normal, Non-pathological Aging

But functional independence is maintained

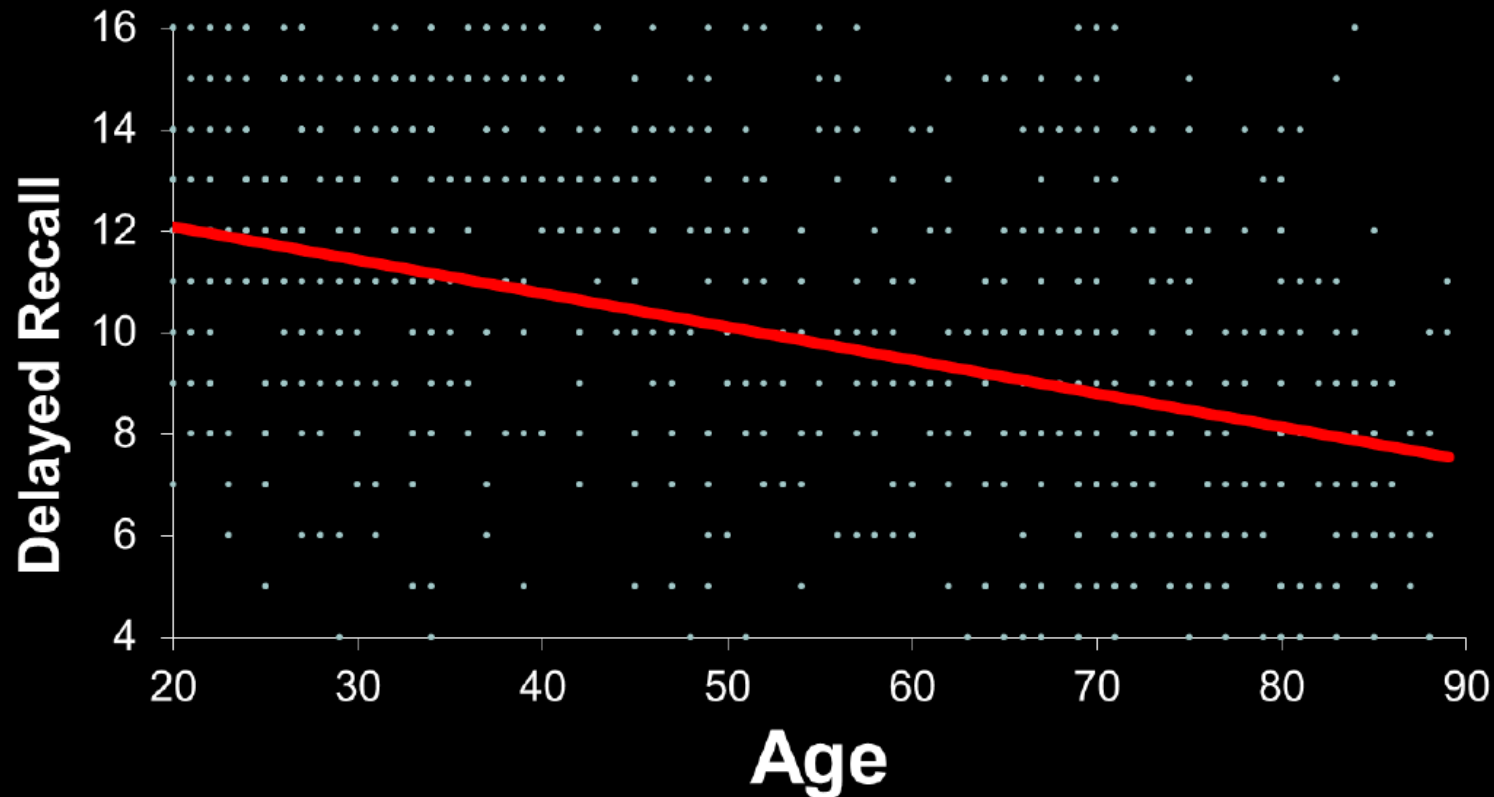
Public Perception of Normal Aging: Major Decline with Age

The myth of cognitive decline



Actual Delayed Memory Scores by Age

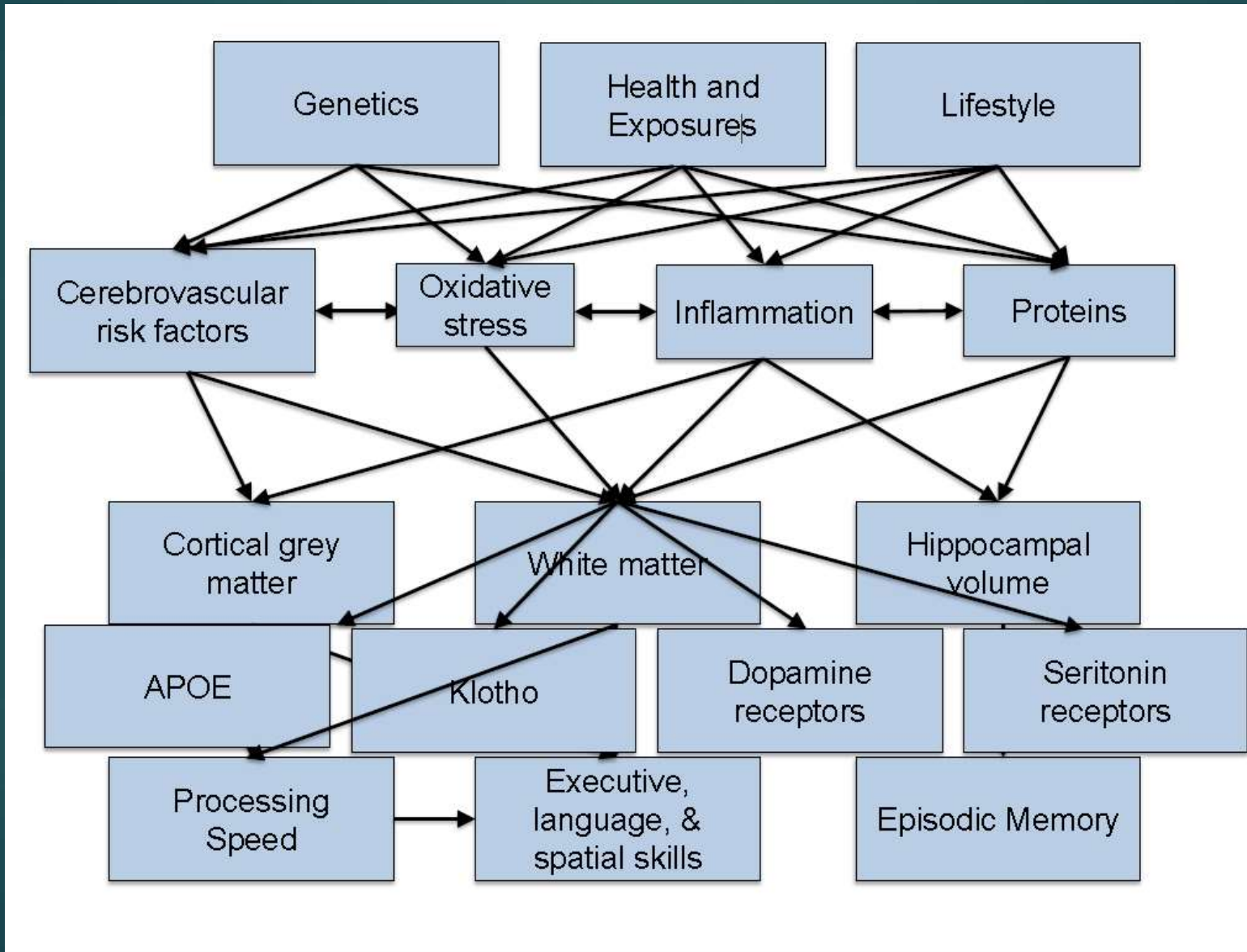
The myth of cognitive decline



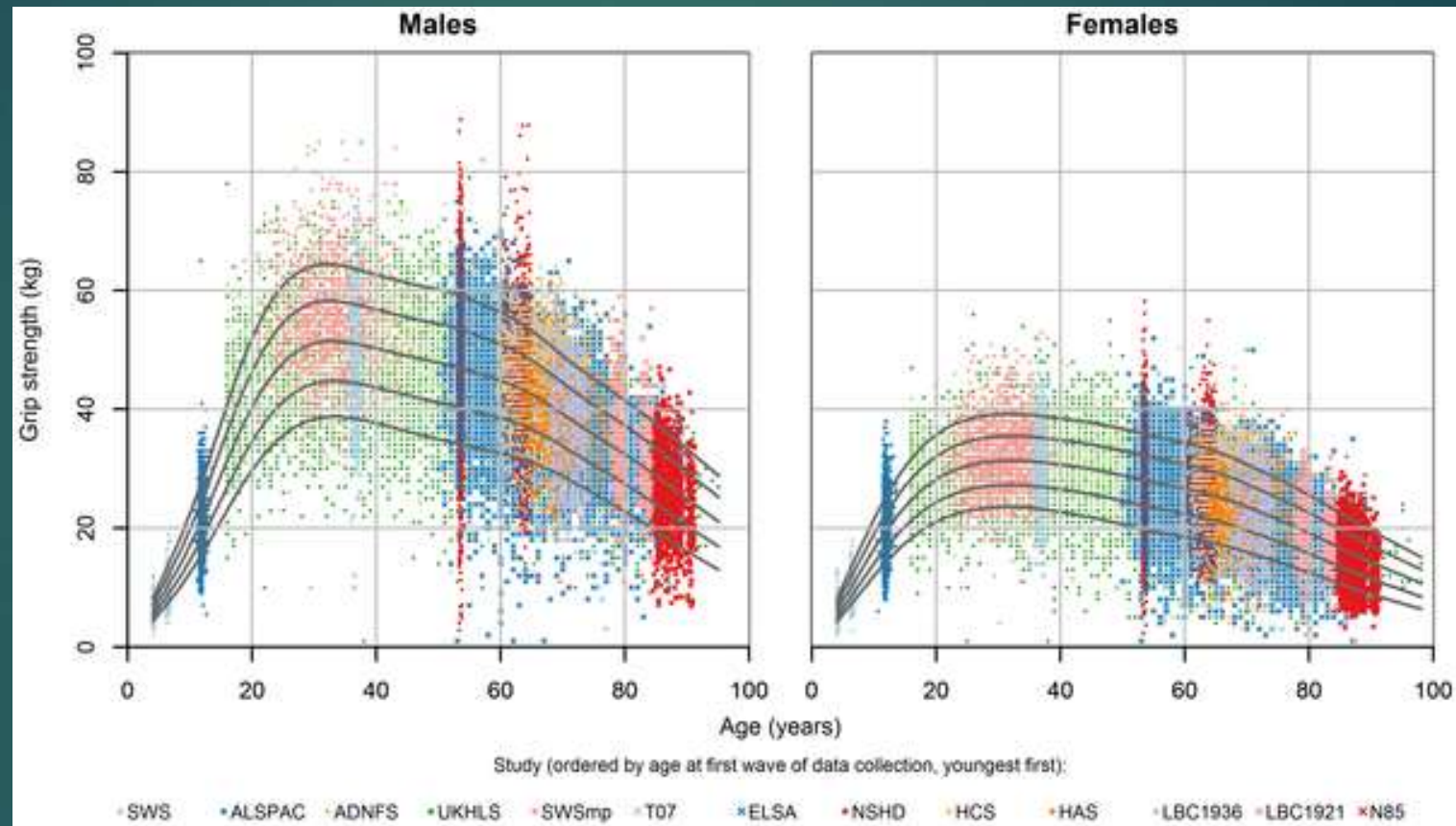
Age and cognitive decline

- Decline in cognition with age and brain structure is not inevitable; there is considerable variability in how much and how fast.
- Age-related declines in cognition and brain structure and function are the result of pathological processes.
- The better we understand these processes, the better equipped we are to do something about them

Complex Picture



Grip Strength in 50,000 people



Grip strength: an increase to peak in early adult life, & decline from midlife onwards.

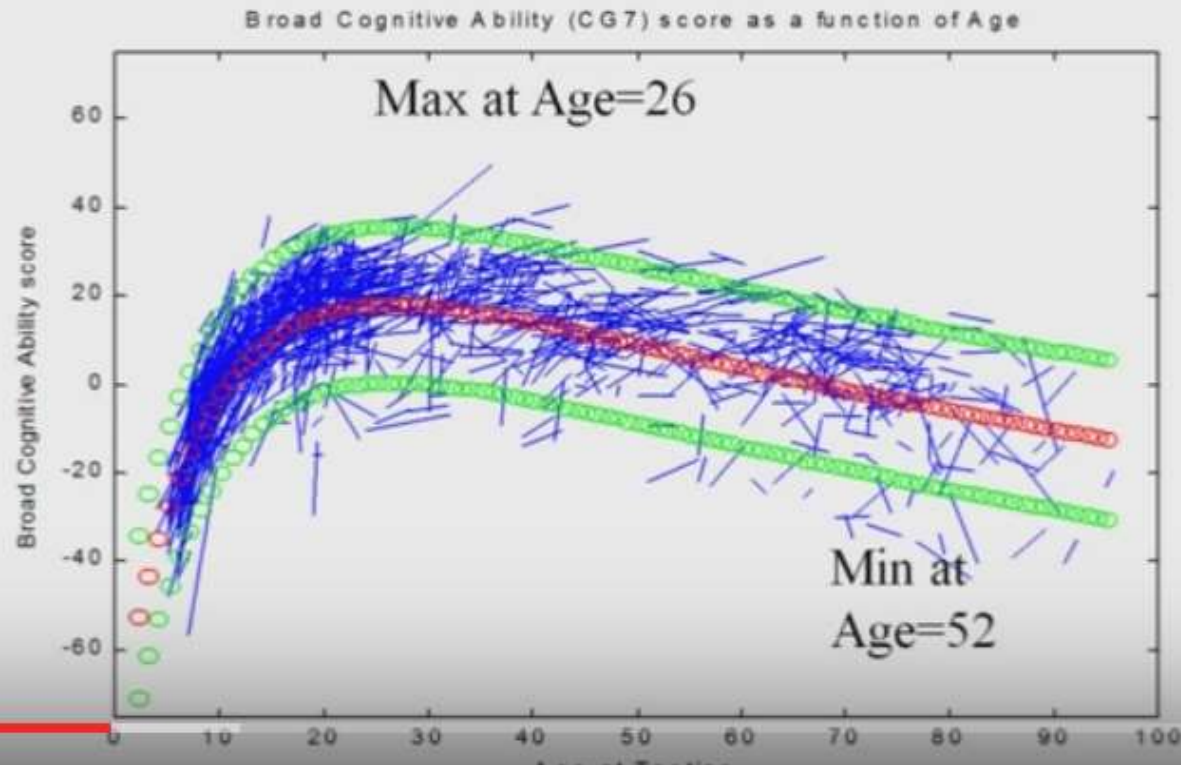
Males were on average stronger than females from adolescence onwards:

Cognitive capacity peaks between 25 to 30; then ½ to 1% per year decline

Broad Cognitive Ability peaks before 30 in US

John McArdle, USC Dept Psychology

Finch Neurobiol Aging 2009



Brain Aging

1. Normative aging changes begin <30 years
2. Independent of neurological disease
3. No gross neuron loss or slowing of axonal wave
4. Cell changes:
 1. Synaptic atrophy
 2. Slowing of polysynaptic functions
 3. Myelin deterioration
 4. Astroglial hyperactivity
5. Brain aging is plastic and manipulable; is open to interventions
6. Most decline is in speed of processing

Risk: ApoE4

- ▶ ApoE4 is the only gene proven to be linked to the common form of non-autosomal-dominant, late-onset AD
- ▶ 25% of population have 1 or 2 alleles (1 from Mom, 1 from Dad).
- ▶ Strongest genetic risk factor for late-onset Alzheimer disease (AD).
- ▶ One ApoE4 allele = 4x risk; 2 alleles =12-15x.
- ▶ It is a risk factor for earlier AD onset, and general brain decline .

Klotho: aging regulator & cognitive enhancer

▶ Klotho (KL):

- ▶ A protein; hormone
- ▶ Circulates throughout body & brain

▶ Klotho: F352V & C370S (KL-VS)

- ▶ 20-25% heterozygosity
- ▶ Carrying 1 copy of KL-VS is associated with:
 - ▶ Greater Longevity: protection against age-related diseases
 - ▶ More Cognitive enhancement (better EF) & right DLPFC cortical volume in aging humans

Eye-blink conditioning declines during middle-age in normal humans

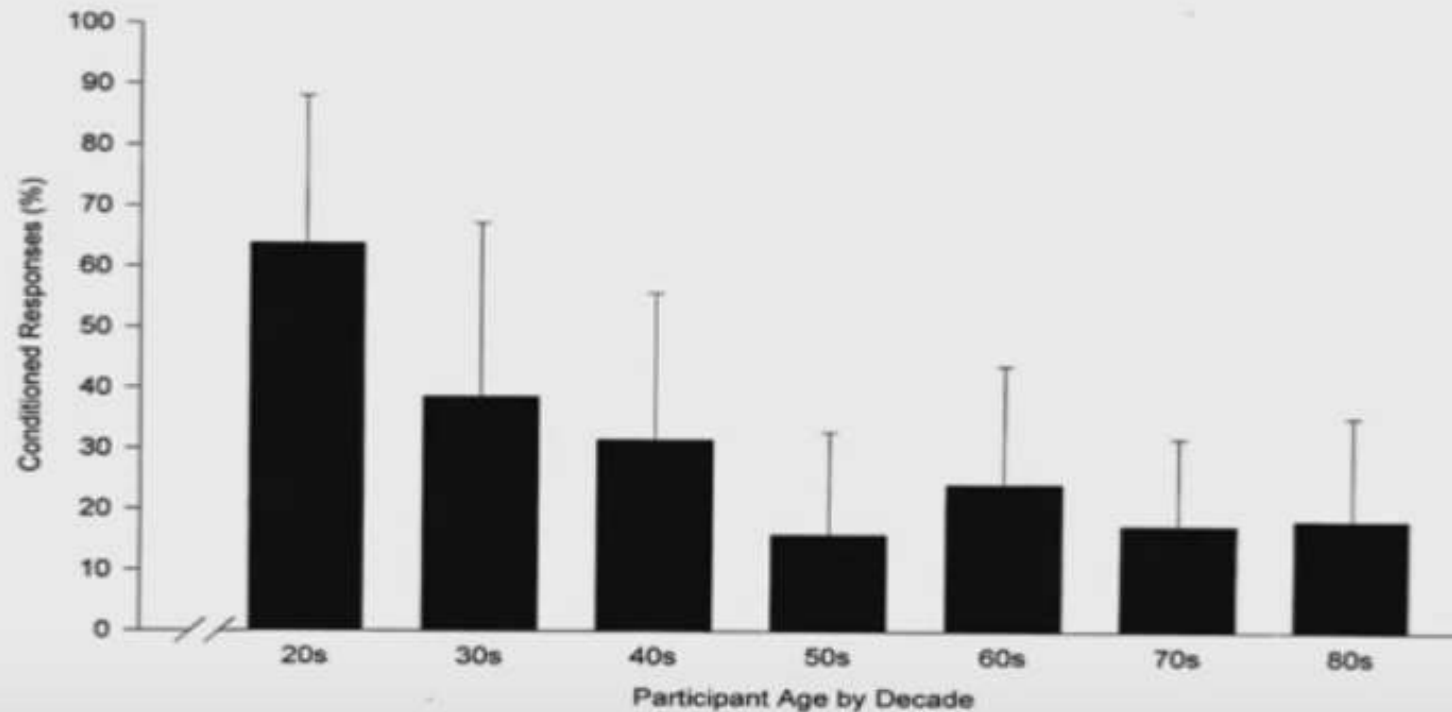


Figure 1. Mean total percentage of conditioned responses by decade in the 400-ms CS-US interval delay eyeblink classical conditioning paradigm for 150 participants ages 20–89 years by decade. Error bars are standard deviations. CS = conditioned stimulus; US = unconditioned stimulus.

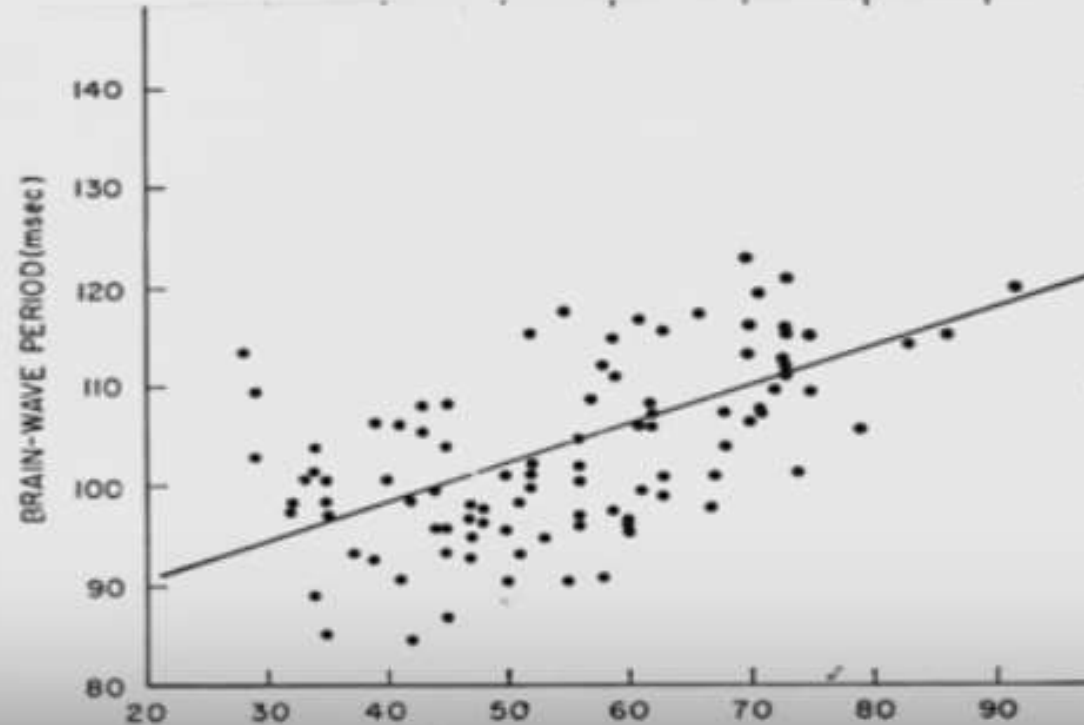


19:56 / 1:09:33



EEG responses slow in middle-aging

EEG response delay time to auditory stimulus :
progressive delay beginning in middle-age
(Surwillo 1963)



Brain response to flash of light or click of sound – longer delay time to response

Six Longitudinal Studies

- ▣ K. Warner Schaie and Sherry Willis's Seattle Longitudinal Study
- ▣ Whitehall Study of British Civil Servants
- ▣ The Nun Study
- ▣ The Religious Order Study
- ▣ Rush Memory and Aging Study
- ▣ Lothian Scottish Study

Normal Age-Related Changes in Cognitive Abilities

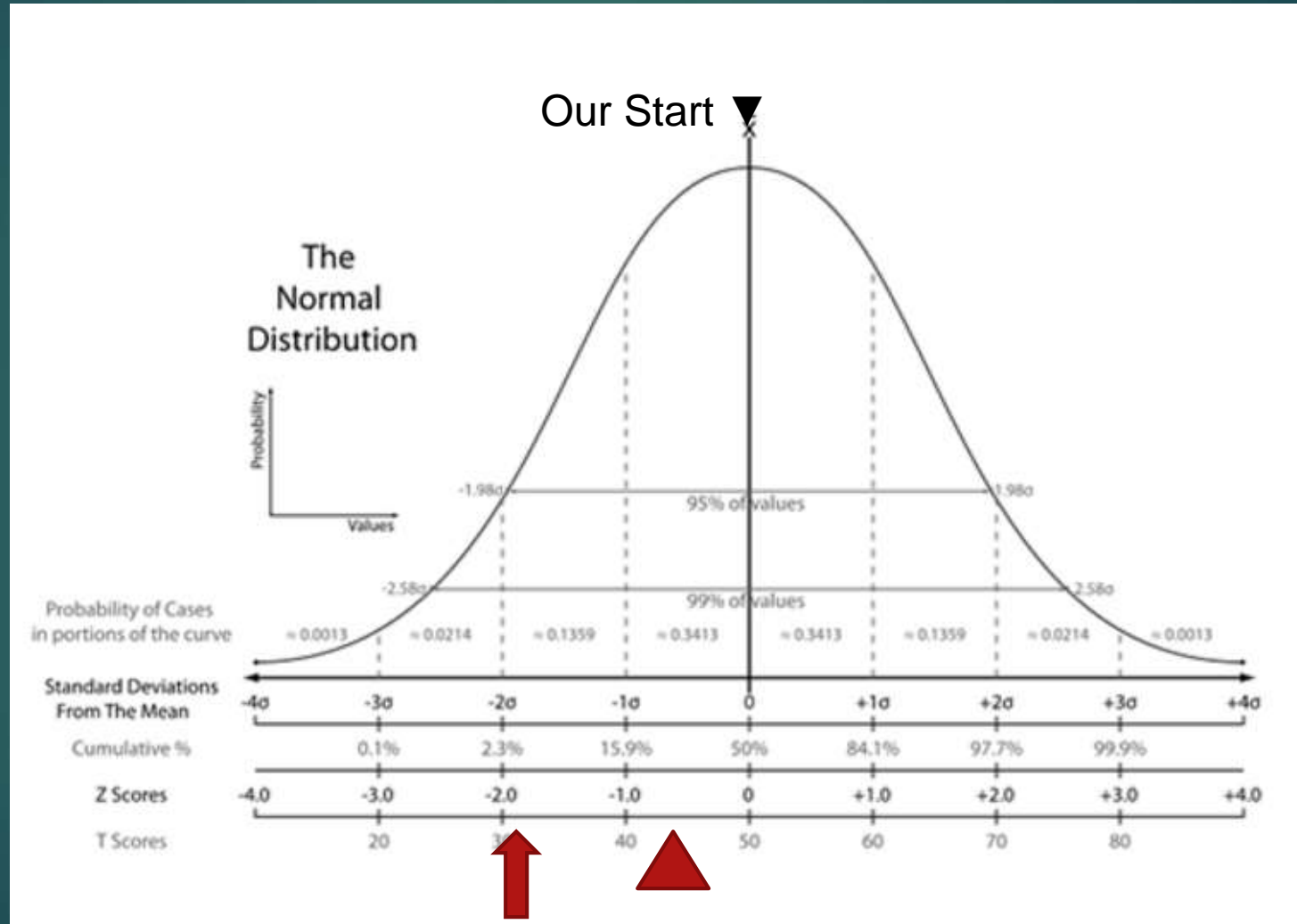
- ▣ K. Warner Schaie and Sherry Willis's Seattle Longitudinal Study:
- ▣ Cognitive better from age 40-65 than in our 20s for:
 - ▣ Vocabulary
 - ▣ Verbal Memory
 - ▣ Spatial Orientation
 - ▣ Inductive reasoning (Drawing a general conclusion based on a limited set of observations)

Normal Age-Related Changes in Cognitive Abilities

Seattle Longitudinal Study: After age 65:

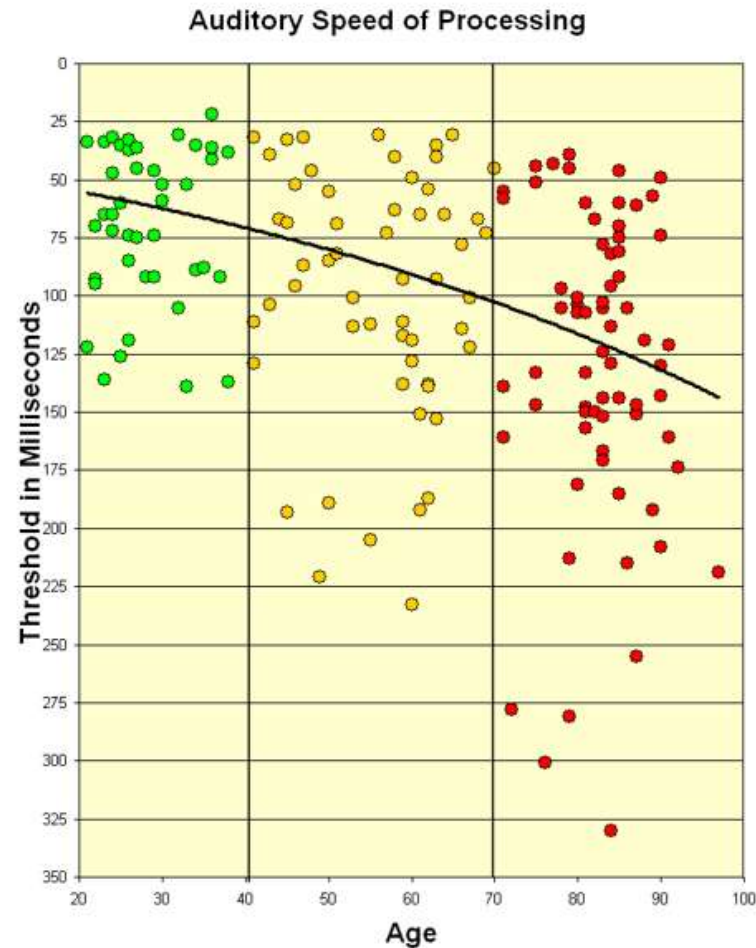
- ▶ Verbal Knowledge intact; difficulty with name retrieval, particularly the names of those we've not seen in a while
- ▶ Memory Ability = $\frac{1}{2}$ s.d. decrease ↓
- ▶ Spatial Ability = 1 s.d. decrease ↓ ↓
- ▶ Perceptual speed = $1 \frac{1}{2}$ s.d. decrease ↓ ↓ ↓

Normal Distribution



Processing Speed & Free Recall

The Brain Changes *Functionally* With Age – Encoding and Processing Speed

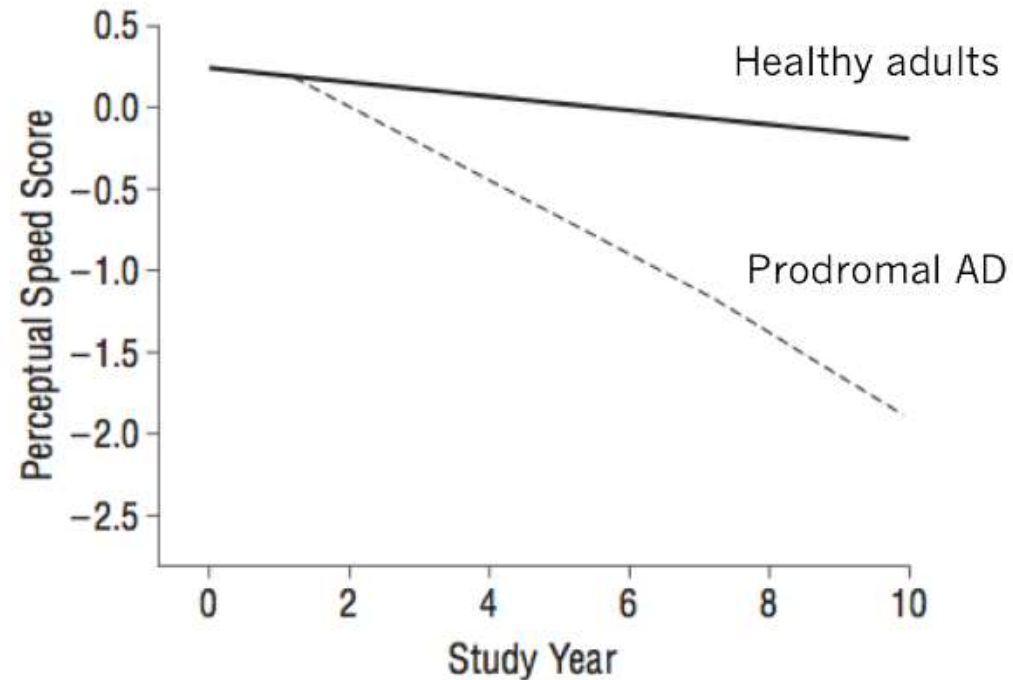


At age 75, it takes us more than twice as long to process information than when we were age 20

3 ms per decade decline

Processing Speed decline is worse in Alzheimer's

Age-related decline in cognitive processing parsing healthy from those who develop Alzheimer's Disease or Related Disorders



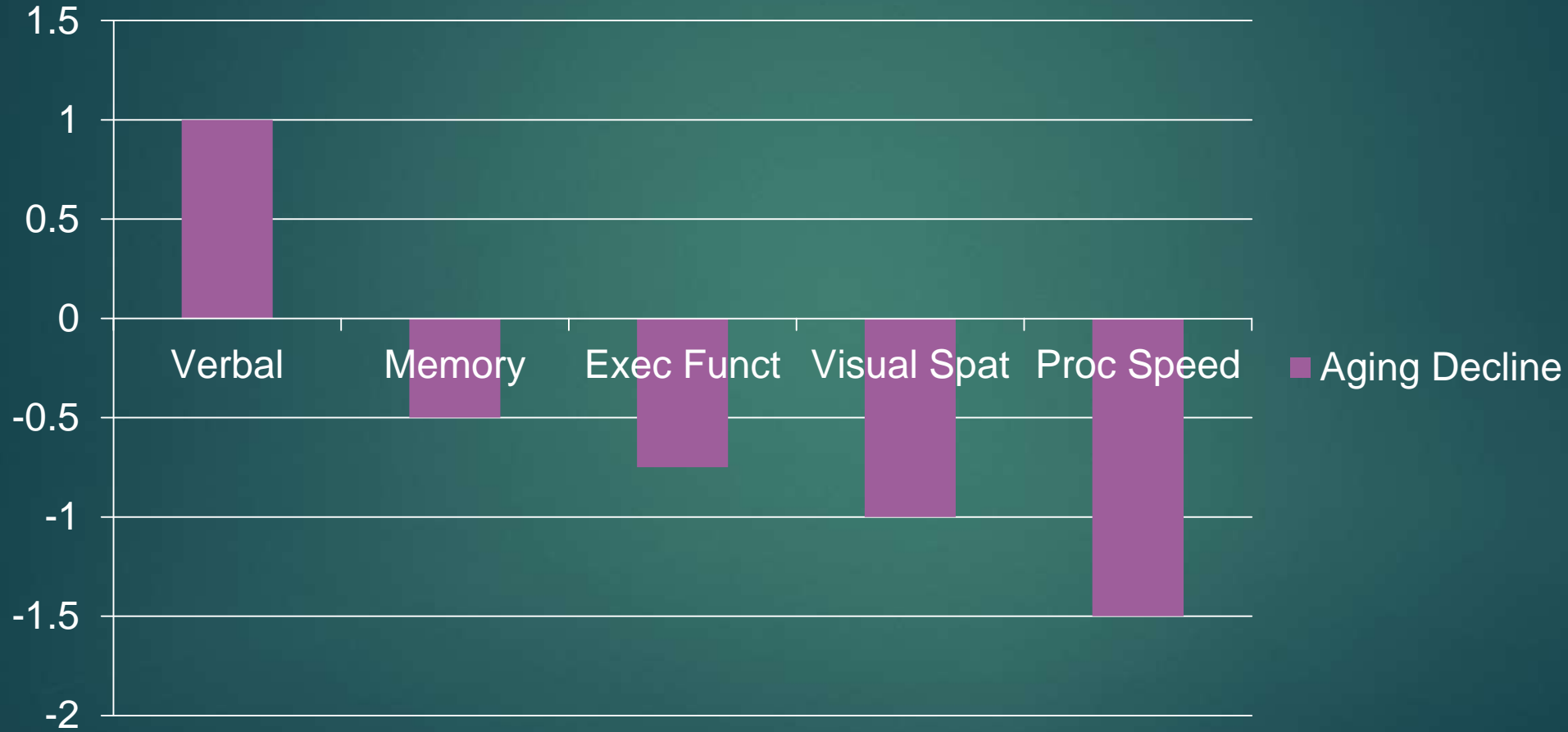
Wilson, R.S., Leurgans, S.E., Boyle, P.A., Bennet, D.A. (2011) Cognitive Decline in Prodromal Alzheimer Disease and Mild Cognitive Impairment. [Arch Neurol](#).

And this is why we all need
to work on keeping our brain sharp...

Click to add text



Normal Aging Cognitive Decline in the absence of brain pathology



Based on Schaie and Salthouse

Tale of Two Computers: Speed ↑↑↑



1982 IBM Computer
Intel 8088 chip @ 4.77 MHz

After age 65, we return to this speed!



Lenovo W5307
Intel Core i72. @ 2.70GHz

2500 times faster

Normal Age-Related Changes 2

- ▶ Cognitively better with age with:
 - ▶ higher education
 - ▶ higher occupation
 - ▶ better cardiovascular status
- ▶ Spouse's cognitive ability was protective: lower IQ spouse gets the benefit (lower risk of AD); merges toward higher

Two Different Aging Populations

▶ Age Unimpaired:

- ▶ Optimally healthy and higher SES:

- ▶ Fewer cognitive changes

▶ Age Impaired:

- ▶ Typically health (DM↑, HTN↑, obesity↑, cardiac↓):

- ▶

- ▶ More cognitive deficits

Increasing medical burden with age

- ▶ Number of chronic health conditions increases with age; 75% of 65+ have multiple chronic medical conditions
- ▶ Most common: HTN, DM, CV, arthritis, COPD
- ▶ 25% have multiple chronic conditions; 6% of women & 4 % of men have 5 or more conditions; 67% of Medicare pts have 2+, 14% have 6+
- ▶ Medical burden is associated with concurrent increase in risk of hospitalizations, functional limitations, disability, mortality, and neuropsychological decline
- ▶ Increase in polypharmacy and its effects, esp. anticholinergic drugs (bladder control meds, Lopressor, Coumadin, Benadryl, Flexaril, Paxil, Haldol, Valium); 90 day use of these meds are 3 x more likely to be diagnosed with MCI & had more beta amyloid

Whitehall Study, 2012:

Cognitive decline begins at age 45

- ▶ 10,308 (67% men) **British civil servants**
- ▶ Evidence of cognitive decline at all ages between 45 and 70
- ▶ All cognitive scores (reasoning, memory, verbal fluency, vocabulary), except vocabulary, declined in all five age categories (ages 45-49, 50-54, 55-59, 60-64, and 65-70)
- ▶ Evidence of faster decline in older people.

Whitehall Conclusions:

Take care of your heart

- ▶ Importance of healthy lifestyles and cardiovascular risk factors.
- ▶ Mid-life levels of obesity, hypertension, and high cholesterol seem to be more important than at older ages.
- ▶ What is good for your heart is good for your brain
- ▶ Need aggressive control of behavioral and cardiovascular risk factors as early as possible

What to do?

- ▶ Medical school professor says to his medical class:
- ▶ Imagine you begin to lose your memory and your thinking begins to become more clouded.
- ▶ What would you do?

Medical student responds:

I guess I would have to transfer to law school.

Age and Memory Decline

▶ Preserved:

- ▶ Semantic memory (factual and conceptual knowledge),
- ▶ procedural memory
- ▶ language abilities

▶ Begin to decline in your 20s:

- ▶ Episodic memory (recall of experiences and events)
- ▶ spontaneous recall (of names)
- ▶ working memory
- ▶ processing speed
- ▶ selective attention
- ▶ ability to multitask

What is dementia (now Major Neurocognitive Disorder)?

Major NCD:

- ▶ Not a disease
- ▶ A diagnosis
- ▶ A set of cognitive symptoms
- ▶ Caused by a variety of illnesses and injuries.
- ▶ Not the same as a neurological disease.

What is Major NCD? 2

Major NCD due to a neurodegenerative disease is an:

- ▶ Acquired
- ▶ Long-lasting
- ▶ Global **deterioration** of cognitive and emotional functions and personality.
- ▶ Can be caused by AD, TBI, over-medication, etc.

Alzheimer's ≠ Major NCD

- ▶ **Alzheimer's Disease** = neurodegenerative disease due to increased beta amyloid presence in your brain
- ▶ **Major NCD** = cognitive decline due to anything that affects the brain (neuropathological disorder, TBI, medications, etc.)
- ▶ You do not have NCD while you develop Alzheimer's.
- ▶ Major NCD is the most common final sign of Alzheimer's
- ▶ They are not same thing

Souls go to God; Brains to Lab



Sister Matthia from
the Nun Study

- ▶ 1986, N=677, School Sisters of Notre Dame; 40 left
- ▶ Age 75-103, 85% teachers, half got NCD
- ▶ Despite lots of BA, many nuns = no sxs;
without Major NCD
- ▶ Nun who had severe beta amyloid pathology, but no Major NCD: had 10 x social networks of others

Which sentence from a **1 page autobiography, at age 22,** predicts dementia & AD ~60 years later?

- ▶ Sister Helen: I was born in Éclair, Wisconsin on May 24, 1913 and was baptized at St. James Church.
- ▶ Sister Emma: It was about half past midnight between February 28 and 29 of the leap year 1912 when I began to live and to die as the third child of my mother whose maiden name is Hilda Hoffman and my father Otto Schmidt.
- ▶ **Early life language skills are related to late life cognitive functioning; Idea density and grammatical complexity; Idea density predicted AD in 60 years with 80% accuracy.**
- ▶ The fewer the number of ideas expressed in those autobiographies the greater the severity of Major NCD later in life

Read to your kids & grandkids!

- ▶ Idea density depends on vocabulary & reading comprehension; best way to increase both is to read to your children starting early in life
- ▶ Pre 4 language & SES:
- ▶ Quantity:
 - ▶ Low SES: 600 words spoken to child per day
 - ▶ High SES: 2100 words spoken to child per day

Hart, B. & Risley, T.R. "The Early Catastrophe: The 30 Million Word Gap by Age 3" (2003, spring). *American Educator*, pp.4-9..

Reading More at any Age

- ▶ Use it or lose it applies no matter what your age
- ▶ More frequent cognitive activity leads to slower late-life cognitive decline that is independent of common neuropathologic conditions
- ▶ Cognitive workouts at any age delays effects of age related lesions.

The Nun Study Findings

- ▶ Nuns: income is not a factor, all the subjects are nonsmokers, and all have similar access to diet, healthcare, and housing.
- ▶ Higher education
 - ▶ Longer survival with good function
 - ▶ Lower risk of death at every age
 - ▶ Less assistance with age
- ▣ Optimists live longer.
- ▣ APOe4: 4 x risk of AD.
- ▣ Exercise reduces CV disease: Walk!!

The Nun Study Findings

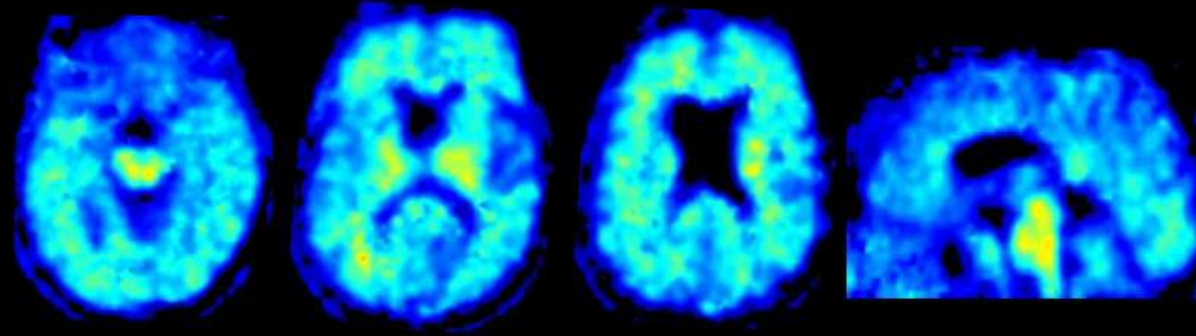
- ▶ Lower rate of Alzheimer's with:
 - ▶ Higher education
 - ▶ Lower rates of stroke and heart diseases
 - ▶ Higher linguistic ability
 - ▶ Regular exercise
 - ▶ More social networks

Alzheimer disease without dementia:

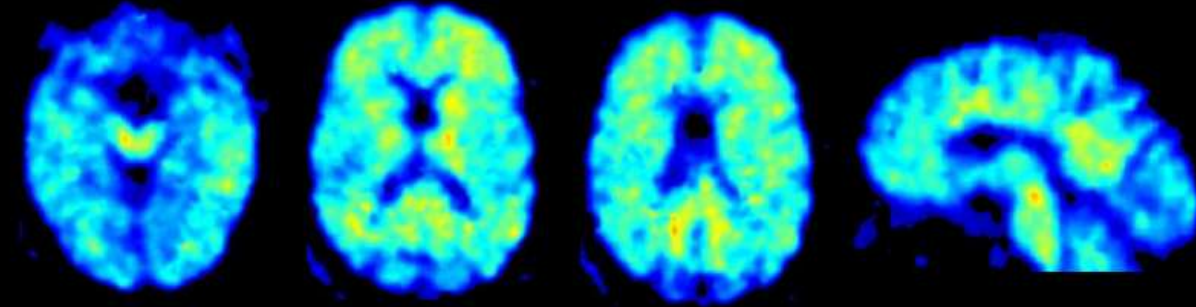
Sister Bernadette

- ▶ Died at 85 of heart attack; MA, teacher for 40 years; double APOe4
- ▶ One of brightest nuns; died “sharp as a tack” with no signs of dementia; MMSE = 30 at 3 testings
- ▶ On autopsy, had massive Alzheimer’s pathology (Braak stage 6)
- ▶ Had more grey matter than 90% of other nuns on original MRI (better brain to begin with)
- ▶ A testament to resistance to genetics and pathology of AD

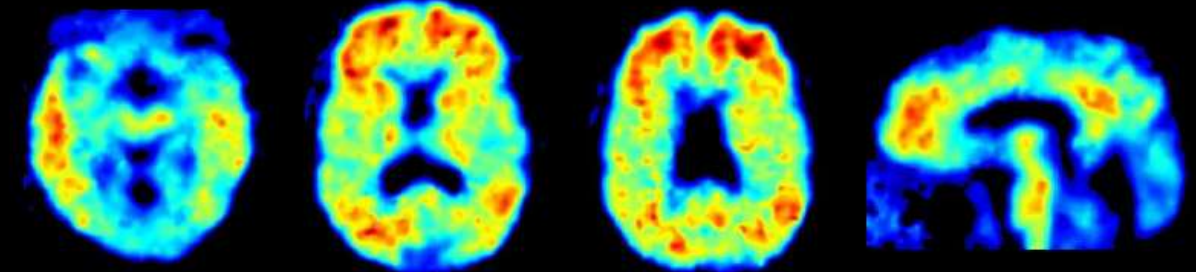
**Cog normal:
low amyloid**



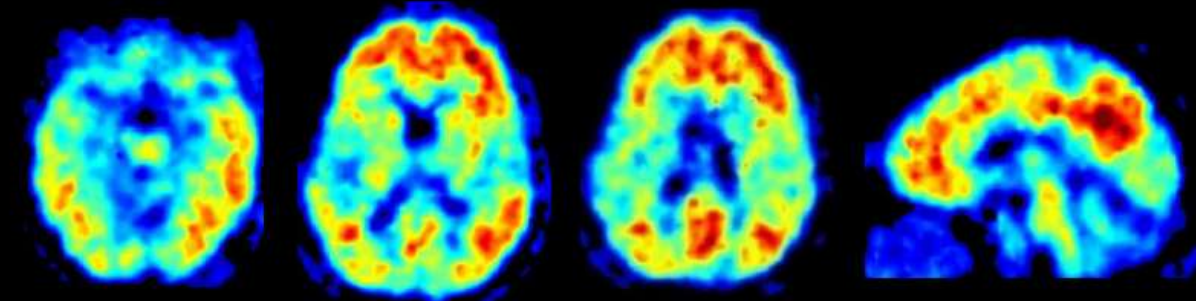
**Cog normal:
intermediate
amyloid**



**Cog normal:
high amyloid**



**Alzheimer's
disease**

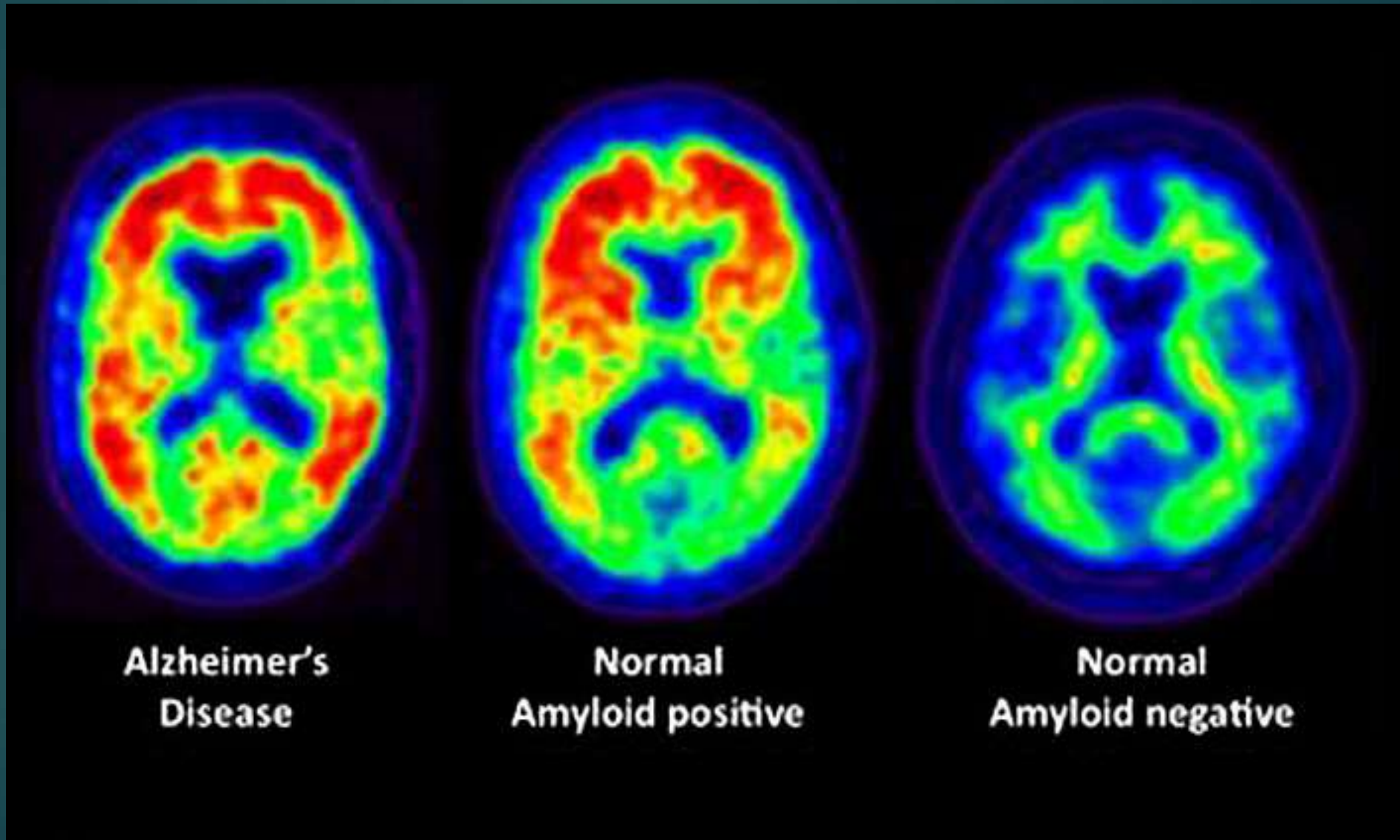


DVR
2.5
0.4



Normal

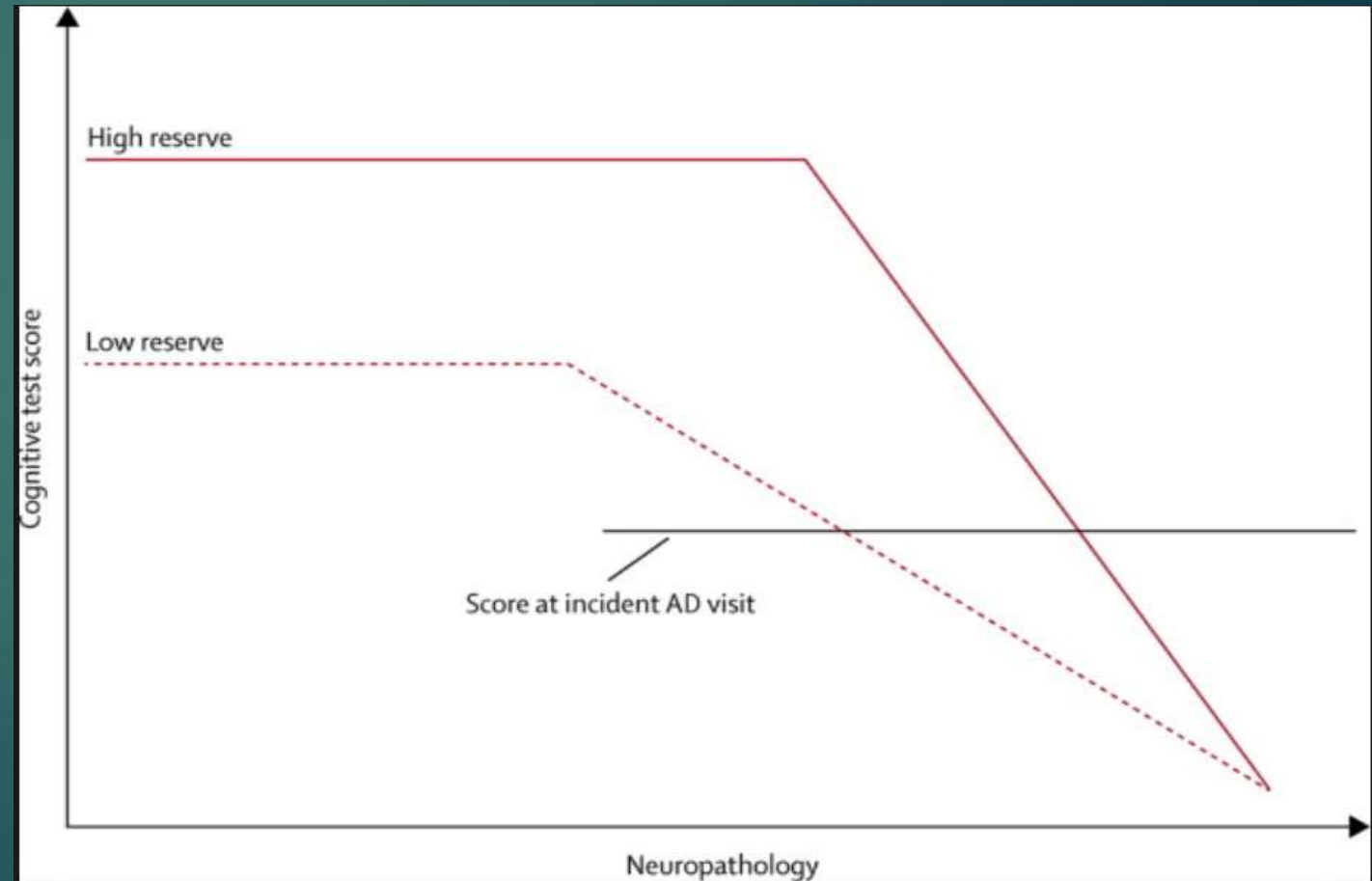
You can be cognitively normal and have a lot of Beta Amyloid



Cognitive Reserve

CR: the capacity that helps people withstand greater brain pathology without cognitive decline symptoms; a preventive factor vs. NCD

Patients with greater Cognitive Reserve may handle a larger amount of brain damage before showing the same level of impairment



Cognitive Reserve

- ▶ Cognitive reserve: brain's ability to cope with increasing brain damage or age-related degeneration while still functioning appropriately.
- ▶ The difference between amount of brain pathology & actual cognitive function
- ▶ Benefit: Protective (can have more pathology before cognitive decline):
 - ▶ Bigger brain/head circumference
 - ▶ Higher IQ
 - ▶ Higher education
 - ▶ Higher occupation
 - ▶ More leisure activity
 - ▶ Higher literacy
- ▶ Cost: Once cognitive decline begins, brain decline goes faster & die sooner

Does Brain Development in Childhood Set the Stage for Dementia?

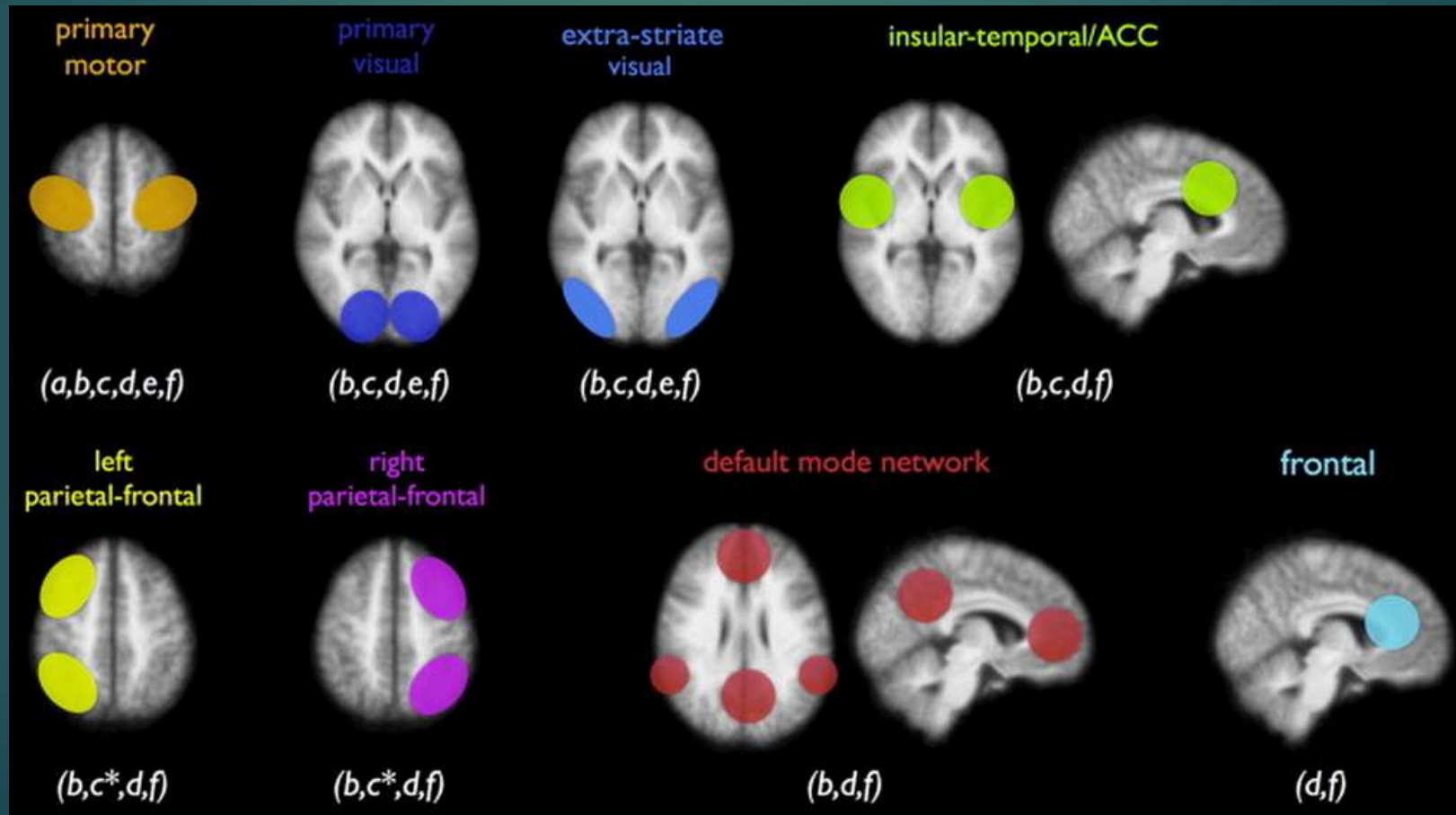
- ▶ If you are going to get some form of dementia, then the brain area where it presents first, or the 'locus of least resistance,' might be determined by how your brain has developed
- ▶ There is a connection between learning problems and dementia. People with learning disabilities, particularly dyslexia, are over-represented among patients with primary progressive aphasia (PPA) and dyscalculia with right hem. posterior cortical atrophy (PCA).
- ▶ This dementia was five times higher in learning disabled than that in the general population

Brain's developmental history

- ▶ Early learning patterns might subtly influence the course of sub-types of dementia.
- ▶ Swedish education & dementia study: those who were in the lowest quintile for academic test scores at around age 10 had a 20-50 percent greater risk of developing dementia later in life.

Brain networks

- ▶ Multiple brain networks have been found
 - ▶ all show activity during rest and during tasks
 - ▶ The **default mode network (DMN)** shows a decrease in activity during cognitive tasks



Brain networks in Cognitive Reserve

- ▶ Brain networks with more alternative routes between nodes provide more ability of compensation or resilience to brain damages; ability of network reorganization to secure the information flow within the brain network
- ▶ Education & other social activities help the development of alternative routes and facilitate functional compensation if needed later on.
- ▶ White matter network connectivity changes with education levels; people with higher cognitive reserve have higher maximum flow in WM brain networks;

Education and brain networks

- ▶ **Education strengthens brain network reliability in normal aging**
- ▶ **In AD, less education correlates with more brain network unreliability**
- ▶ The left hemisphere is clearly more correlated with education levels.
Indeed, the node with the greatest number of connections was the left middle frontal gyrus,
- ▶ Highly educated subjects with normal cognition had more brain volume than poorly educated subjects

Experience changes brain structure: Cognitive Reserve Theory (CR)

- ▶ The more educated live longer
- ▶ Individuals resist effects of NCD who have:
 - ▶ Higher education: a college degree appears to slow the brain's aging process by up to a decade
 - ▶ Higher social economic status
 - ▶ Higher occupational achievement
 - ▶ Better cardiovascular status
- ▶ A form of neuroplasticity or born with better brain?

Dr. Vella's Water tank hypothesis of CR

- ▶ Best current science:
- ▶ The better your brain is to start with (due to good genes & early environment & better IQ), the more cognitive reserve you have to lose to neurodegeneration.
- ▶ The more you start out with in your tank, the longer it takes to empty it.
- ▶ Original brain is 50% of whole amount; your lifestyle choices control the other 50%.

Education makes you more Major NCD Resistant

- ▶ More education does not protect you from developing Alzheimer's and vascular neuropathology before you die.
- ▶ Lowers the impact of pathology on your cognitive abilities before death.
- ▶ More education is associated with:
 - ▶ decreased Major NCD risk
 - ▶ greater brain weight
- ▶ But there is no relationship to neurodegenerative or vascular pathologies.

2015 studies: Education & Occupation

▶ Study 1:

- ▶ 65+, dementia risk was 21% higher in people who were in the lowest 20 percent of childhood school grades
- ▶ Dementia risk was 23% lower in individuals in occupations characterized by high complexity with data and numbers.

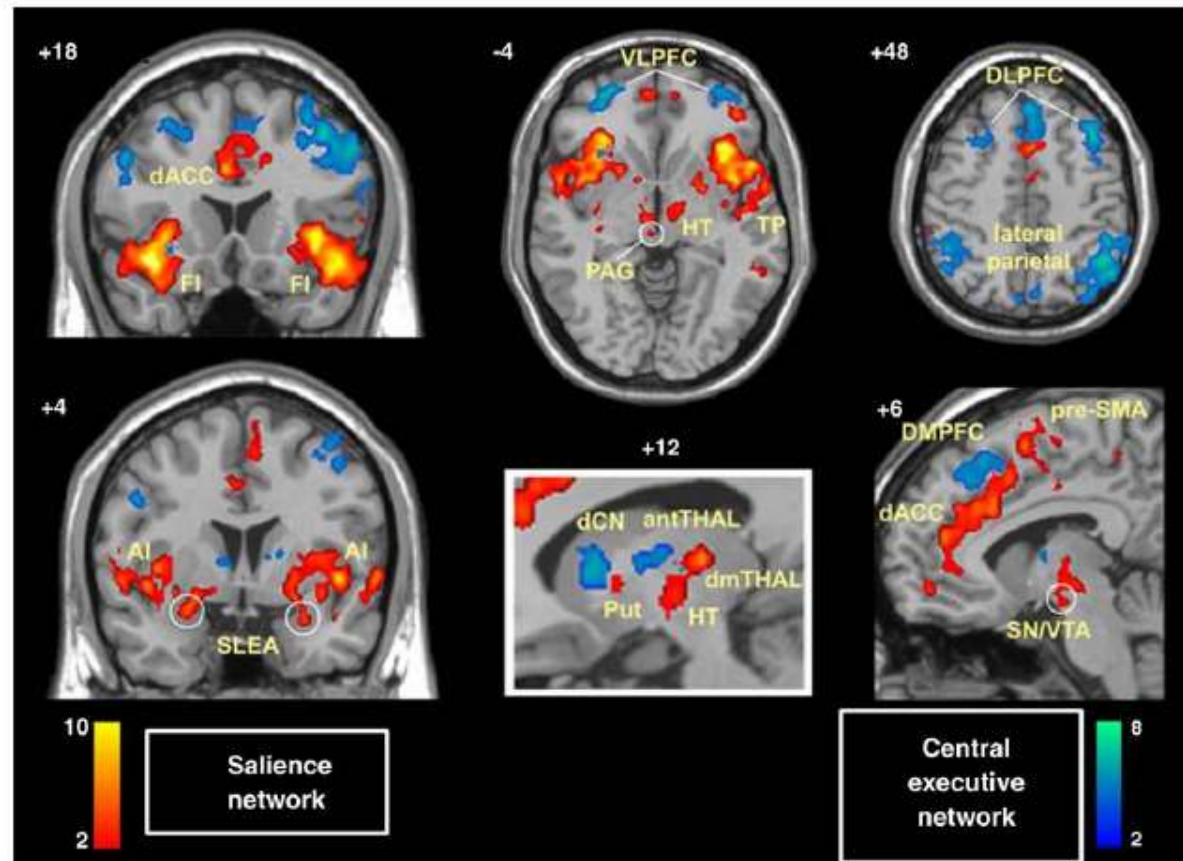
▶ Study 2: dementia risk was 50% higher in people over 75 with the lowest 20% of early-life school grades, even if they had more formal education or a job was associated with significant complexity

▶ Study 3: Sending Your Grandparents to University Increases Cognitive Reserve: The Tasmanian Healthy Brain Project -- Taking college courses when aged 50-79: 92 % displayed a significant increase in cognitive capacity after 4 years

Connectome: How your brain is wired

- ▶ 2015: Human Connectome Project (HCP), an international effort to map active connections between neurons in different parts of the brain: Scanning the brain networks, or connectomes, of 1,200 adults. Among its goals is to chart the networks that are active when the brain is idle;
- ▶ People with more 'positive' variables, such as more education, better physical endurance and above-average performance on memory tests, shared the same connectivity patterns.
- ▶ Their brains seemed to be more strongly connected than those of people with 'negative' traits such as smoking, aggressive behavior or a family history of alcohol abuse.

Saliency & Executive Network



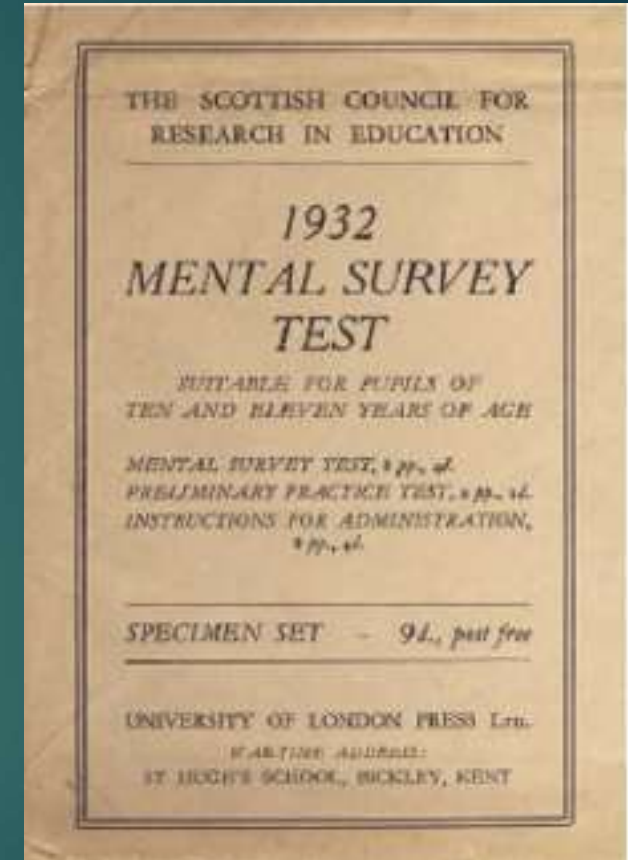
TRENDS in Cognitive Sciences

Figure 5. Two core brain networks identified using intrinsic physiological coupling in resting-state fMRI data. The saliency network (shown in red) is important for monitoring the saliency of external inputs and internal brain events, and the central-executive network (shown in blue) is engaged in higher-order cognitive and attentional control. The saliency network is anchored in anterior insular (AI) and dorsal anterior cingulate cortices (dACC), and features extensive connectivity with subcortical and limbic structures involved in reward and motivation. The central-executive network links the dorsolateral prefrontal and posterior parietal cortices, and has subcortical coupling that is distinct from that of the saliency network. (Reproduced with permission from [107].)

Lothian Study Scotland: all of Scotland's 1921-born population, 87,498 children, were IQ tested in 1932



Study participants alive in 2011



Data rediscovered
in 1990s: **took test at
ages 11, 79, 87 & 90**

Scottish IQ study: **Brain you are born with**

- ▶ Scottish Mental Survey: 1932 & 1947: all 160,000 (now 697) eleven year olds in Scotland took IQ test; the 1947 group scored on average higher than their predecessors (Flynn effect)
- ▶ 50% of the variance at age 77 is explained by IQ at age 11
- ▶ Early IQ is more powerful predictor of good cognition at age 77 than: alcohol, coffee, BMI, diet, social & intellectual ability
- ▶ But lifestyle matters: those who did not smoke, were physically fit, bilingual, more educated had higher IQ scores at age 77
- ▶ Abstract problem solving, fast thinking & reaction time declined in all.

Scottish Lothian Study Findings

- ▶ People with thinner brains in old age had a lower IQ in childhood & adulthood; they started out with less grey matter
- ▶ Facial symmetry is linked to successful cognitive ageing
- ▶ Personality traits are stable over time
- ▶ IQ is very stable: intelligence in childhood is strongly correlated with intelligence in old age; genes more important than environment
- ▶ Double APOe4 gene is a risk factor for faster cognitive decline (lower abstract reasoning and verbal memory)
- ▶ Avoiding CV illness will reduce cognitive decline

Scottish Lothian Study Findings

▶ At age 70:

▶ Physical exercise correlates with better IQ & Processing speed

▶ Higher cognitive scores are

▶ positively associated with coffee and alcohol consumption (1-2 glasses of wine)

▶ negatively associated with BMI, inflammation, and beer drinking.

▶ Smoking lowers IQ by 6 points by age 70: quitting at any age helps

▶ Speaking more than one language & having a more professional occupation correlates with better cognition at age 70

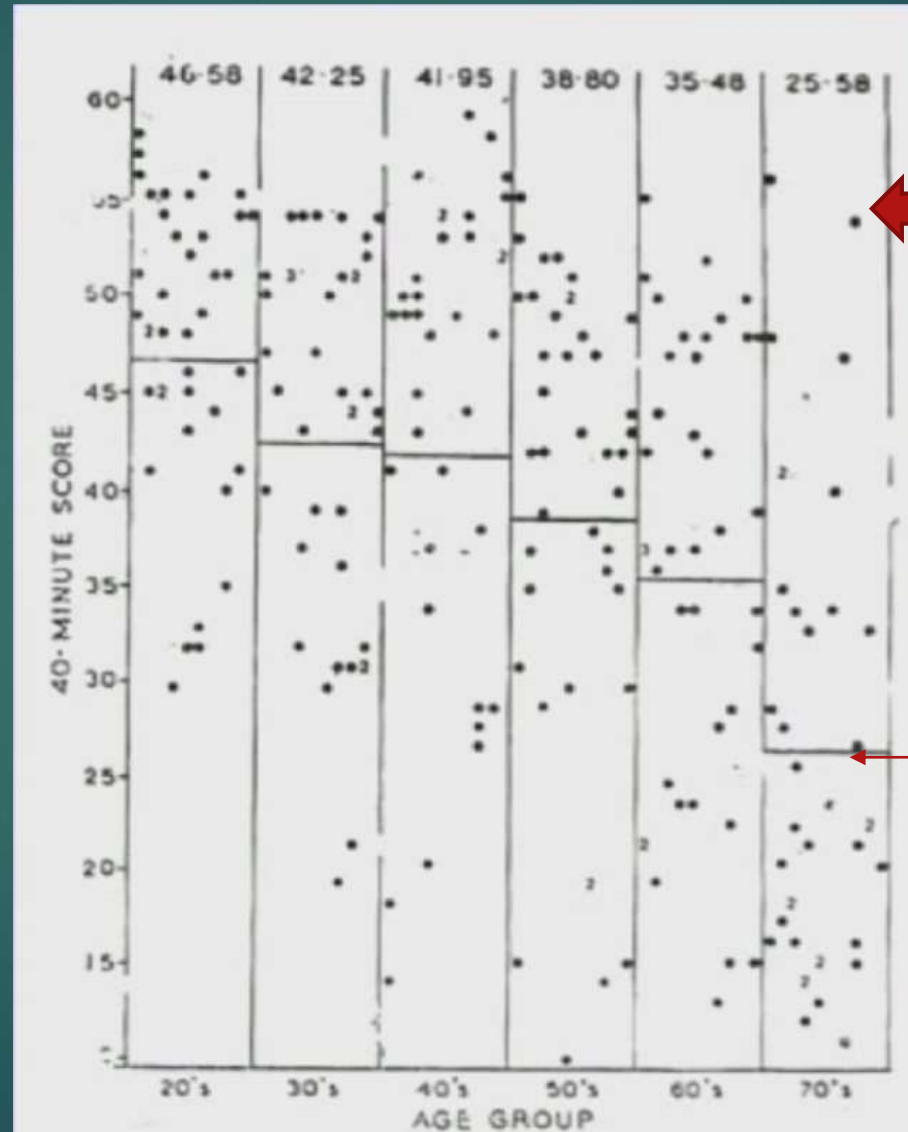
Two other Studies

- ▶ Religious Order Study, 1993; n = 1200; PI = David Bennett, MD
- ▶ Rush Memory & Aging Study, 1997, n = 1700
- ▶ Cognitive decline with aging shows significant individual variability

Great Cognitive Variability: Each dot is a subject

Higher Scores

Lower Scores



Note these
70 yo scorers

Average score line

AGE

What is the most common cause of cognitive decline with aging?

- ▶ 1 – Alzheimer's Disease (AD)
- ▶ 2 – Cardiovascular Disease (CV)
- ▶ 3 – Lewy Body Dementia (LBD)
- ▶ 4 – Mixed causation

Cognitive Decline with Age: Heterogeneity of Pathology

- ▶ In diagnosed Dementia/NCD: 90% of causation = AD, CVD, LBD
- ▶ In all cognitive decline:
 - ▶ AD (34%), CVD, LBD = **only 41%**
 - ▶ Residual decline = 59%

Causes of other 59% of Residual Cognitive Decline

- ▶ Much of late life cognitive decline is not due to common neurodegenerative pathology
- ▶ Causation in 59% residual:
 - ▶ Soluble AB
 - ▶ A-synuclein
 - ▶ TDP-43
 - ▶ Hippocampal sclerosis
 - ▶ Chronic macro/micro infarcts
 - ▶ GSTPI
 - ▶ Other pathologies
- ▶ GSTPI protein (Glutathione S-transferase) (an antioxidant toxic cleanser in the cells) = 5% of all variability of residual cognitive decline

Religious Order Study

- ▶ Cognitive decline in Diabetes: caused by infarcts not AD pathology
- ▶ Lack of Purpose in life significantly related to cognitive decline:
 - ▶ What is important to you? What gives your life meaning? What is your reason for living?
 - ▶ Do things you enjoy
 - ▶ Have a hobby
 - ▶ Find a way to give back
 - ▶ Volunteer

Brains don't want to be demented

▶ Decline predictors:

- ▶ Depression ↓
- ▶ Loneliness ↓
- ▶ Anxiety ↓
- ▶ Neuroticism ↓
- ▶ Kidney disease ↓

Resilience markers:

- Education ↑
- Social networks ↑
- Conscientiousness ↑
- Harm avoidance ↑
- Good sleep ↑
- Purpose in life ↑
- Late life cognitive activity ↑

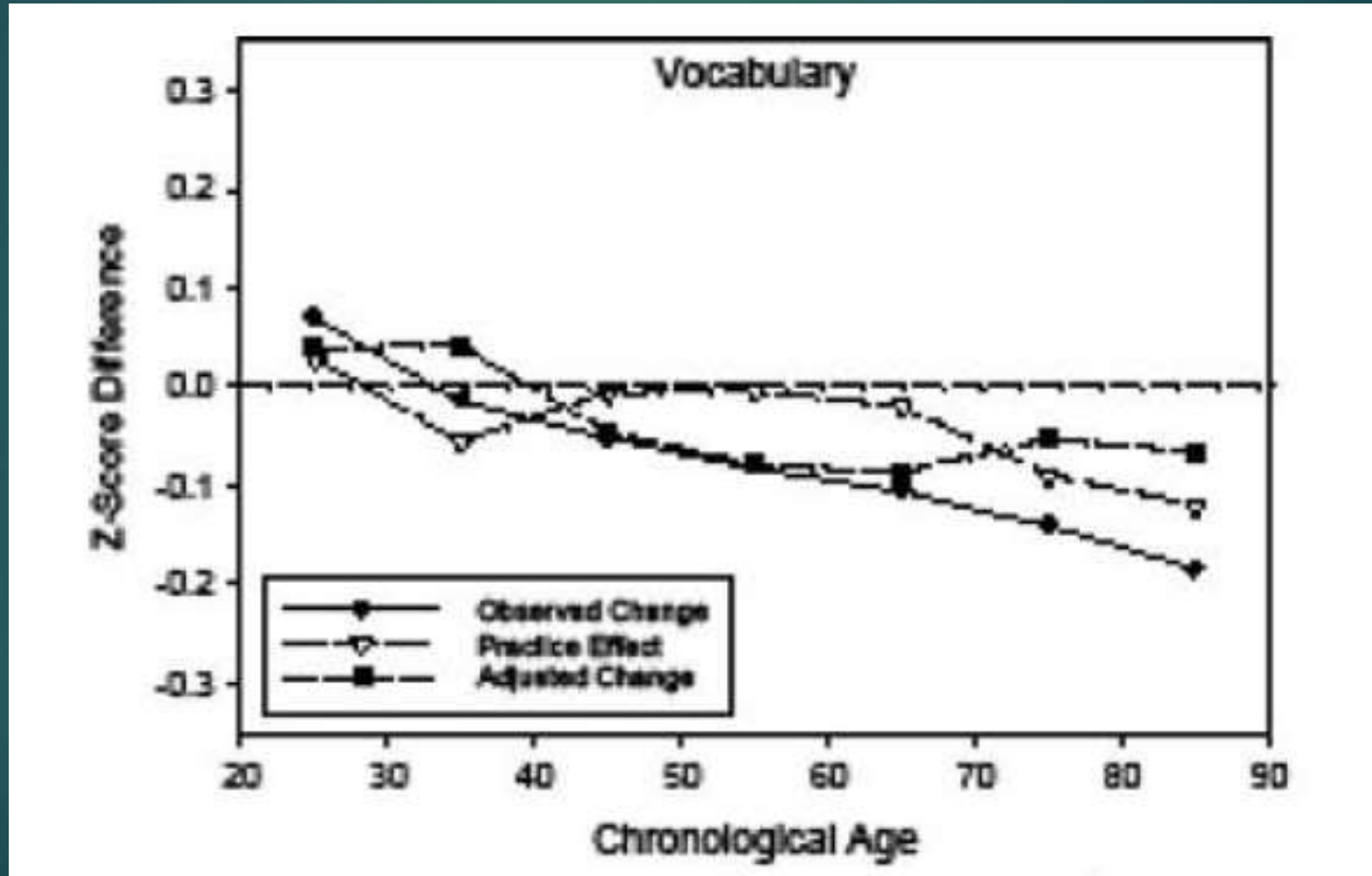
Plato

- ▶ “In order for man to succeed in life, God provided him with two means, education and physical activity. Not separately, one for the soul and the other for the body, but for the two together. With these two means, man can attain perfection.”
- ▶ Juvenal: “A sound mind in a sound body.”

Language ability

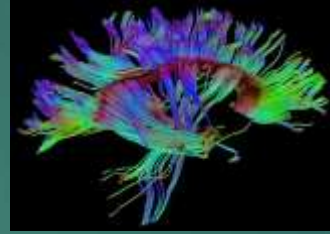
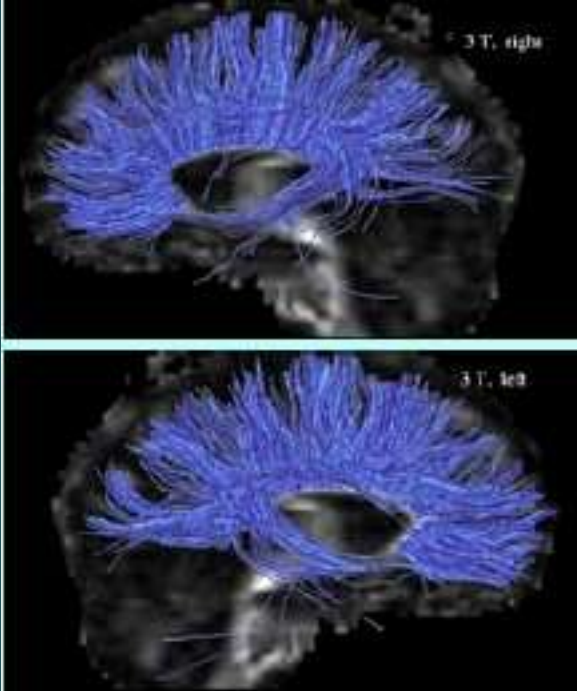
- ▶ Advise to Post Docs: Do not necessarily believe what pt tells you; all older patients want to leave hospital.
- ▶ Many language functions well preserved
- ▶ Vocabulary continues to increase (or may decline slightly)
- ▶ Word finding declines (longer to search; due to processing speed)
- ▶ But all other abilities may be impaired.

Vocabulary stays relatively intact



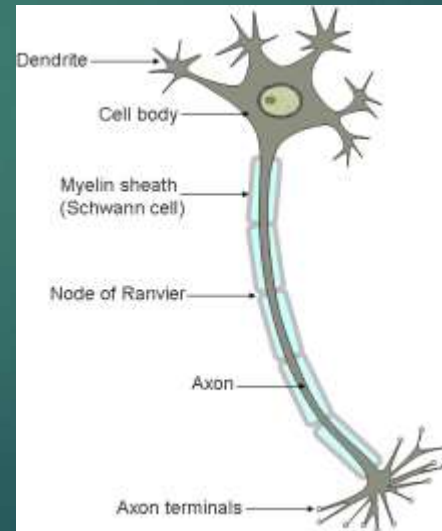
Squares = less than .05 change

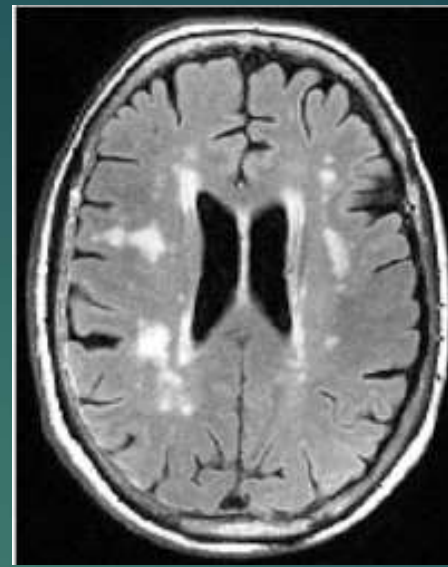
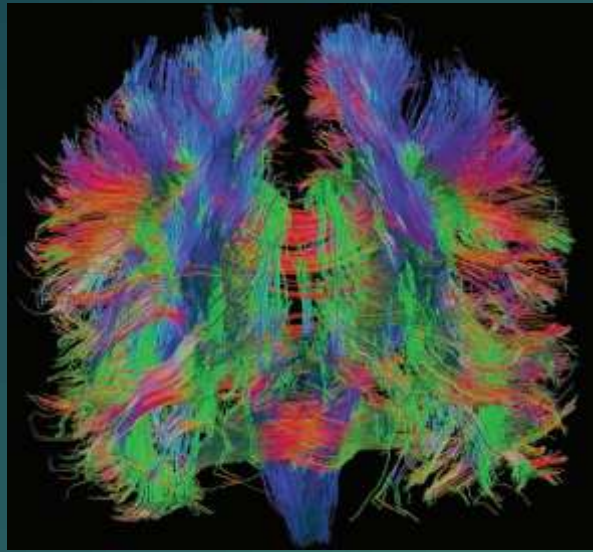
Older are Centrally Slowed: Processing Speed Decreases (3 ms per decade)



Diffuse Tensor Images of axonal tracts

One of reasons naming
ability decreases

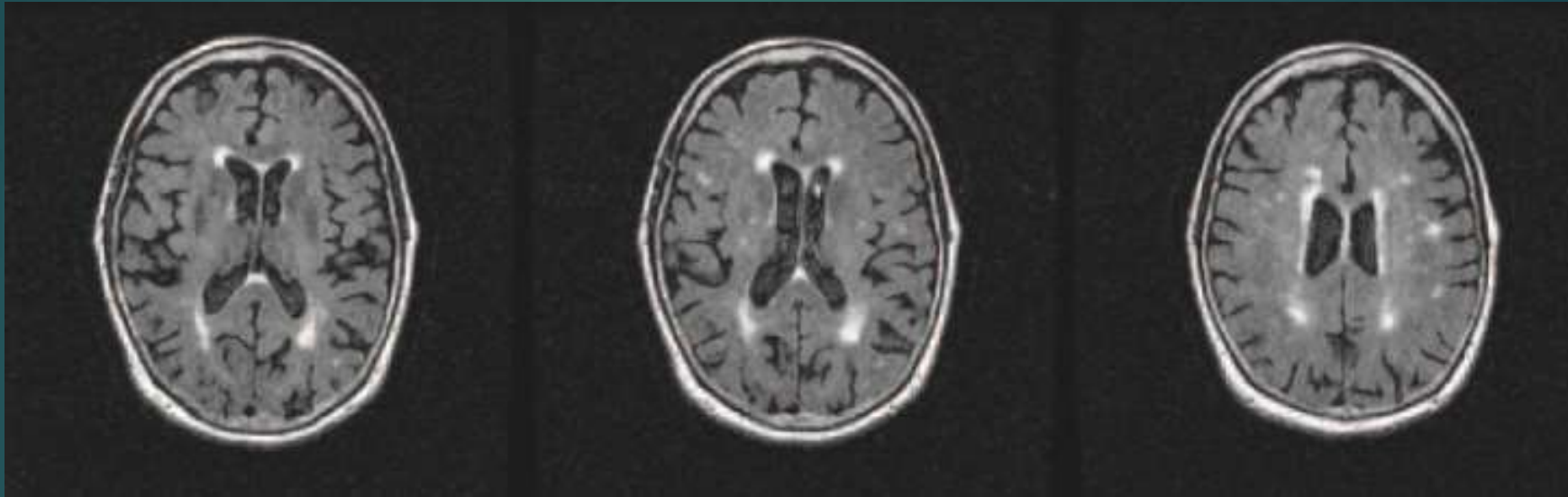




▶ White Matter Matters:

- ▶ Better neuronal wiring (white matter) in old age is linked to higher cognitive function
- ▶ Fewer UBOs associated with higher general cognitive ability and faster processing speed at age 73
- ▶ Greater brain atrophy correlates with more white matter lesions
- ▶ Hyperintensities closely linked to high levels of cortisol (stress) and hypertension

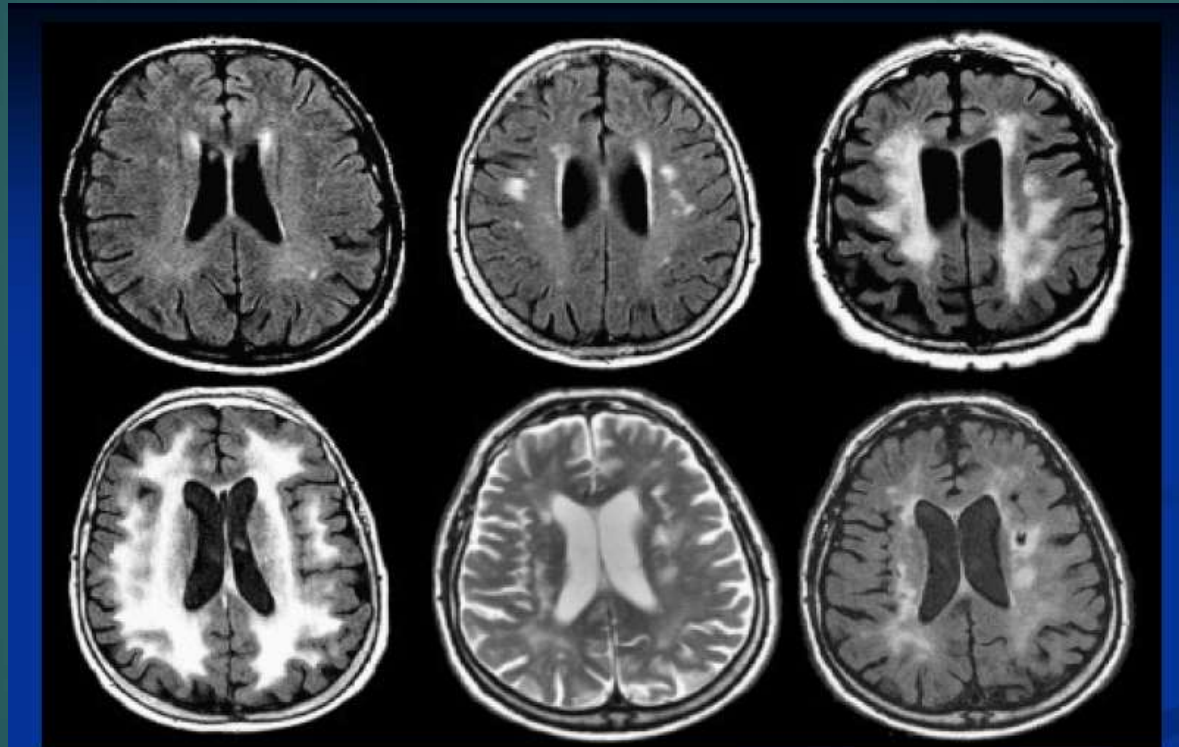
White Matter Hyperintensities on MRIs: Small blood vessel damage



Processing speed declines as white matter hyperintensities increase

Strong associations between vascular risk factors and vascular disease when WMH volumes are extensive.

Mild to Extensive Vascular Hyperintensities: Slower Processing Speed



The spectrum of small vessel disease–related brain changes in MRI: white matter lesions ranging from punctate foci (*upper left*) to extensive confluent abnormalities (*lower left*) and lacunar infarcts (*lower right*).

Samuel Johnson

“The true art of memory is the art
of attention”

Ninety percent of remembering is
paying attention

Attention

- ▶ Slight decline in simple attention (i.e. “remember” phone #)
- ▶ Decline in divided and sustained attention
 - ▶ On road, don't use cell phone, but it's ok to talk to your partner

Texting for 5 seconds:
Driving length of football field blindfolded



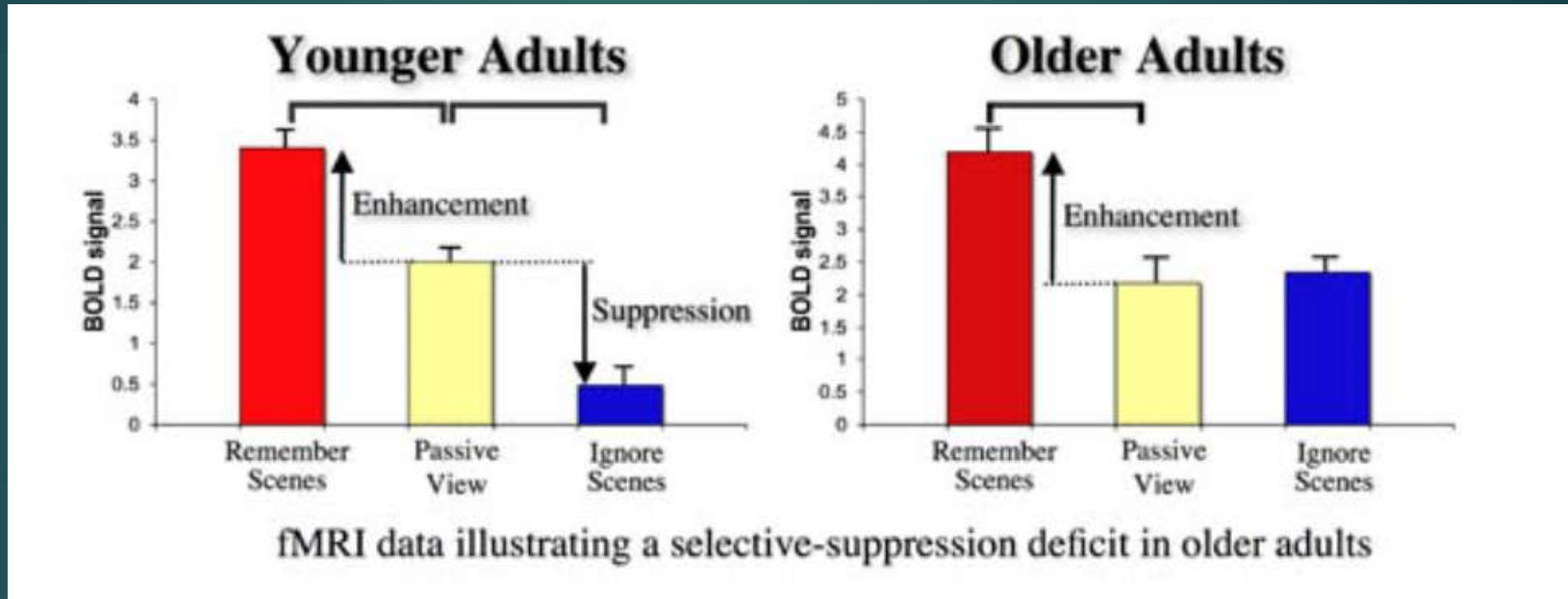
=



Age related Attention Deficit Disorder

- ▶ Attention is like a football team:
 - ▶ need quarterback for focus
 - ▶ and a defensive line against distractions.
- ▶ As we get older, we lose our defensive line
- ▶ Older people are able to pay attention, but have more difficulty inhibiting distractions.
- ▶ Older people get age-activated “ADD”

Older Adults are more distractible



While healthy older adults (above 60 y.o.) were as effective at enhancing activity for relevant information in visual brain regions as young adults, they were unable to successfully suppress activity for irrelevant information;

Some older have normal suppression; are less distractible.

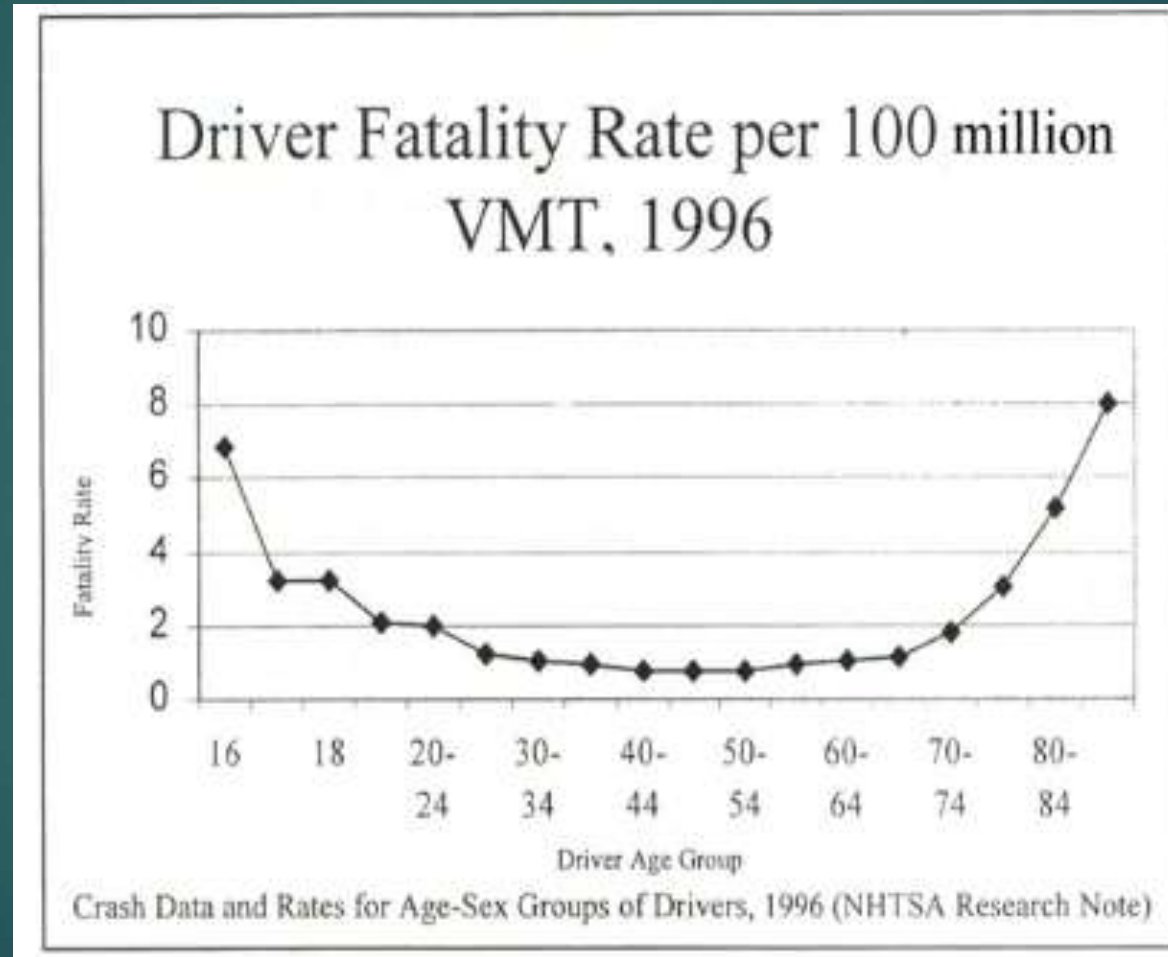
Age Activated Attention Deficit Disorder

- ▶ I walk into the kitchen to make coffee.
- ▶ I see the paper towel holder is empty.
- ▶ I go to get paper towel and notice clothes that need to be watched. So I do a load of clothes.
- ▶ On my way back to the coffee, I see that the garbage is full, so I go out and empty it.
- ▶ So I have done the garbage.
- ▶ I have done a load of clothes
- ▶ I have my paper towels filled.
- ▶ But where is my coffee?

Cautionary tale...

- ▶ When I die I want to go peaceably in my sleep, like my grandfather did...
- Not screaming like the other passengers in his car.

Driving: Seniors are more fatal than Teenagers



Teens: Impulsivity & Alcohol ↑↑

Seniors: Sensory & Processing Speed Declines

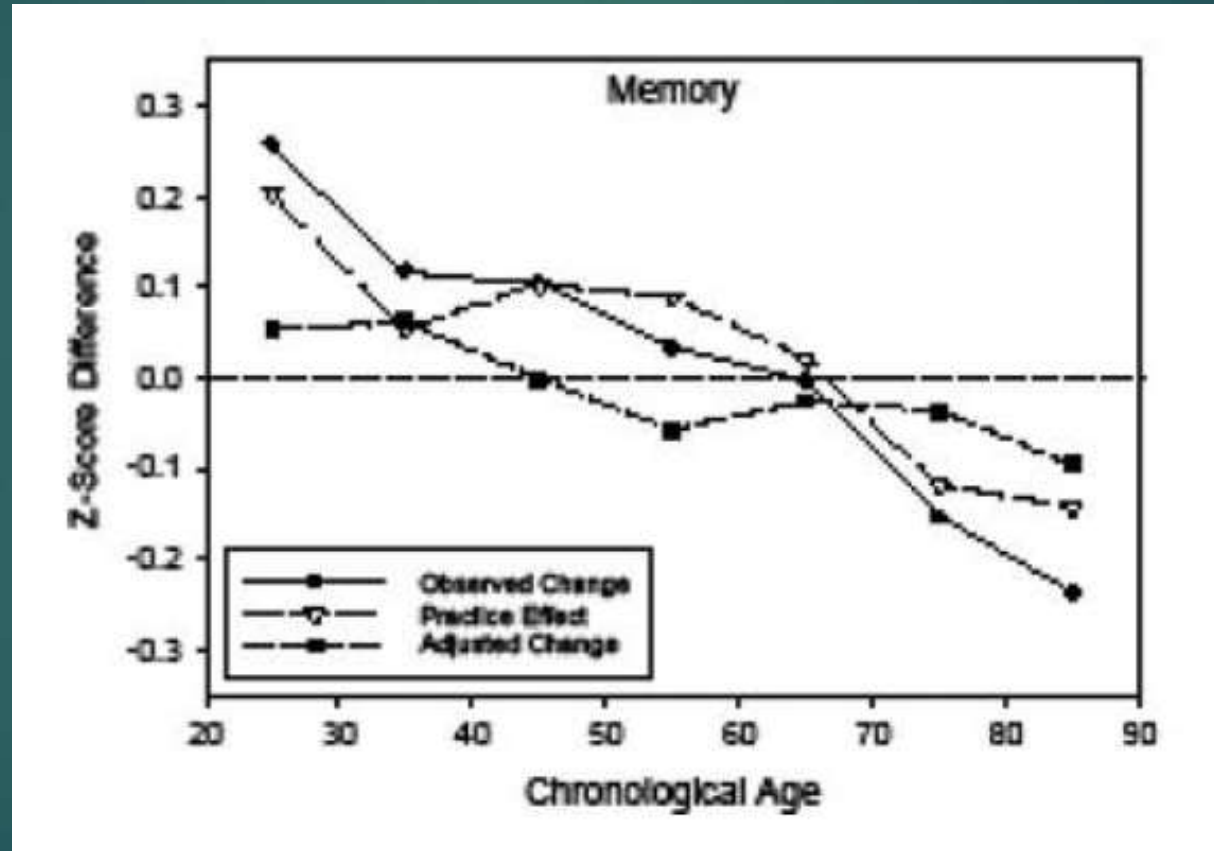
Don't text or use cell phone while crossing the street



Memory: 2 Women

- ▶ Two very old friends sitting together
- ▶ One says “I feel so embarrassed, but could you tell me your name. I just seem to have forgotten it. I must be getting old.”
- ▶ Friend answers, “Do you need to know the answer now or can I have a day or two.”

Factual Memory Declines



Decline in Spontaneous Verbal Free Recall: 12 items at age 20, 7 items at 80



Number of items learned in 1 attempt

Word memory in elderly: **Keep playing word games**

- ▶ Normal 65+ experience slight but reliable difficulties in retrieving lexical information learned decades earlier, difficulties that become progressively more severe with aging.
- ▶ Words become irretrievable if these words are rarely spoken, seen or heard.
- ▶ Reason to play Scrabble & crossword puzzles.

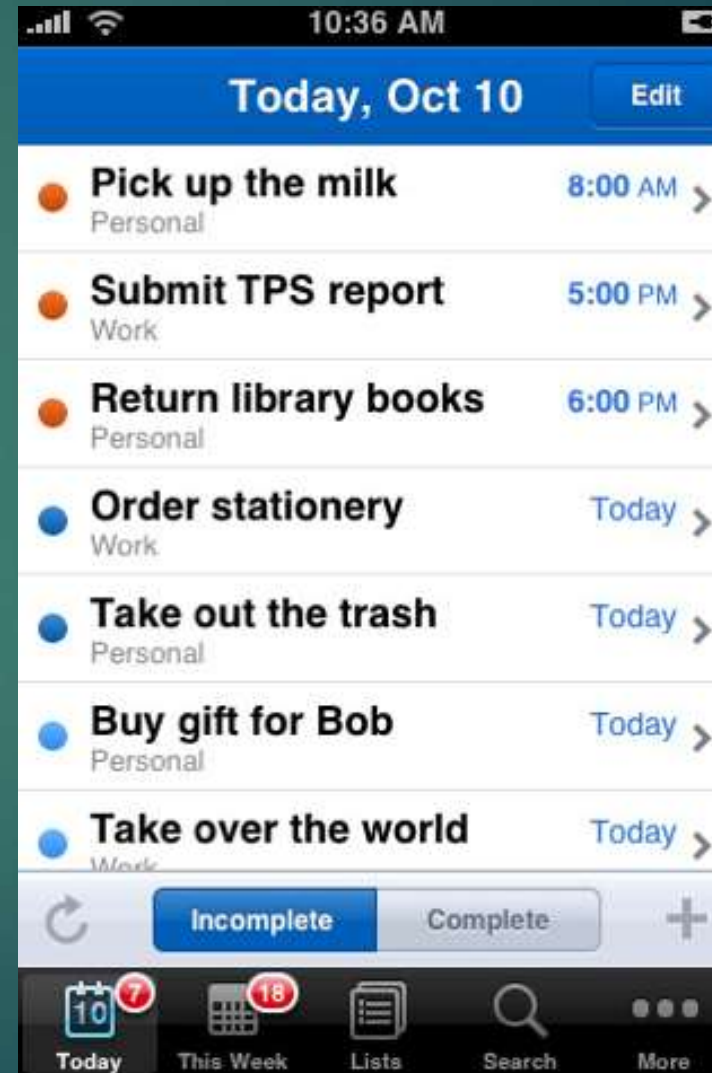
Language memory issues

- ▶ The ability to recall pronunciations of familiar but rarely used words declines systematically: “a type of interlocking fastener made of nylon”:
- ▶ The ability to spell familiar but irregularly written words such as “rhythm,” “physicist” and “yacht” declines with aging. Older misspell more.
- ▶ Frequent use or recent exposure to a word strengthens those connections and prevents forgetting. Older people show no deficits in understanding, spelling or recalling words they often use, hear or write.

Prospective Memory

remains normal in real world

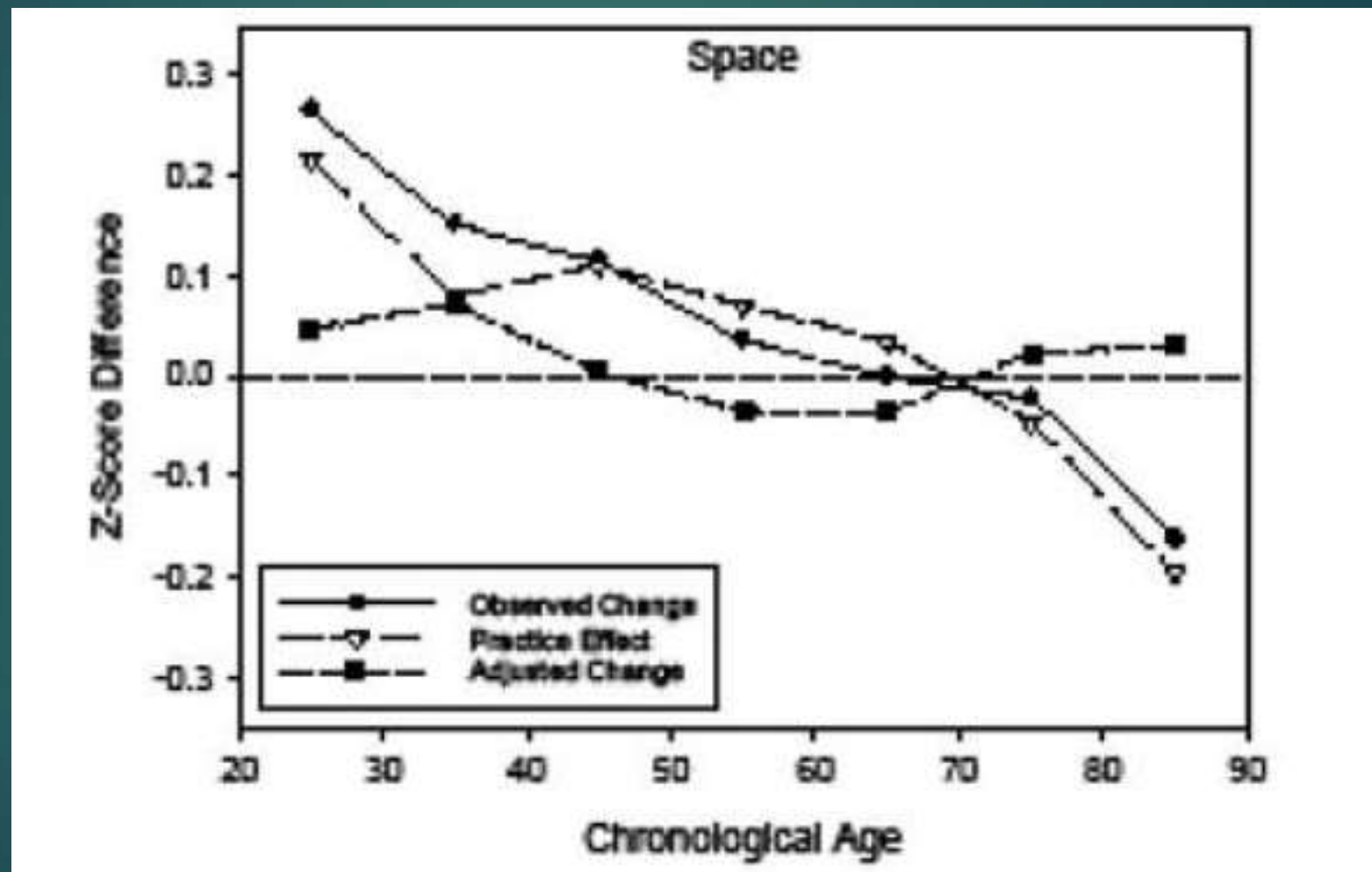
- ▶ Remembering to remember
- ▶ Intention



Medication/drug/alcohol = negative effects on Cognition

- ▶ Alcohol: Memory, EF, motor decline
- ▶ Benzodiazepines : all produce sedative, psychomotor, concentration, and memory deficits
- ▶ Opioids/Pain Meds: impaired attention, memory and motor
- ▶ Sedative antihistamines: negatively impact psychomotor function, vigilance, adaptive measures, such as driving and memory,
- ▶ When doing NP testing, 3 week ban for: alcohol, benzos, pain meds, stimulants

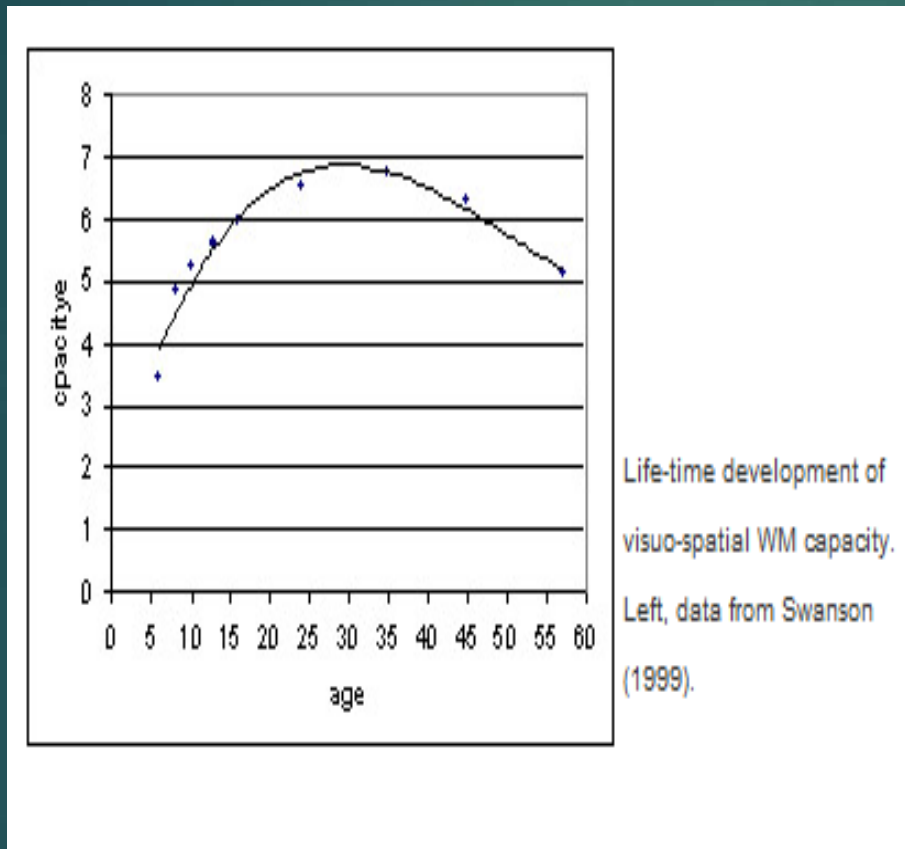
Spatial Decline



Spatial Ability Declines

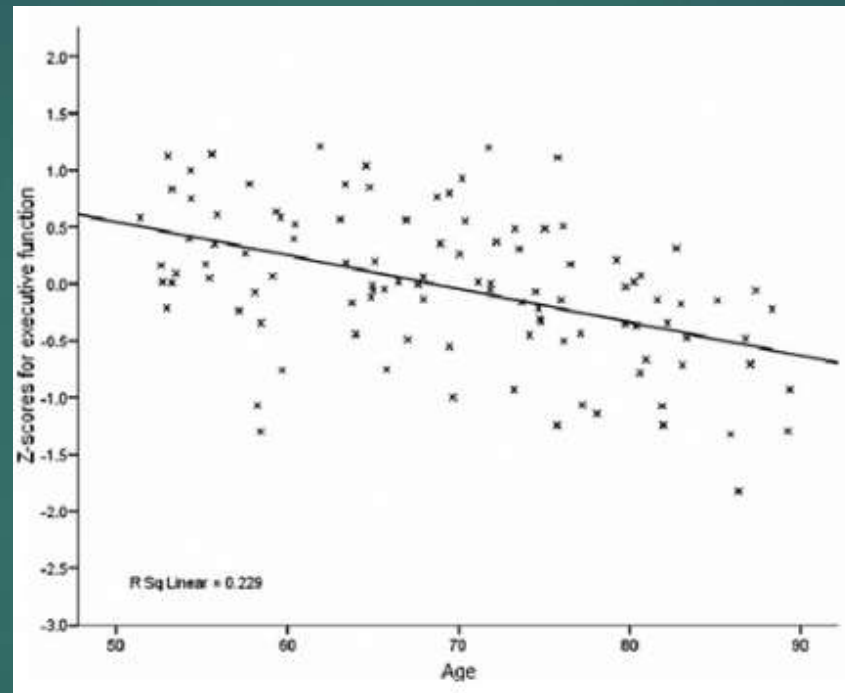
- ▶ Visual acuity declines with age
- ▶ Spatial abilities decline
 - ▶ Directions
 - ▶ Map reading
 - ▶ Longer processing time

Working Memory (holding a phone number in mind) declines



Need to use calculator for math

Executive Functioning (new problem solving, fluid IQ) declines



In old age, be prepared to know more than younger people, but not to be as fast in working out new stuff quickly.

Intelligence Applied

▶ Intact: Crystallized abilities: Your Knowledge and Expertise

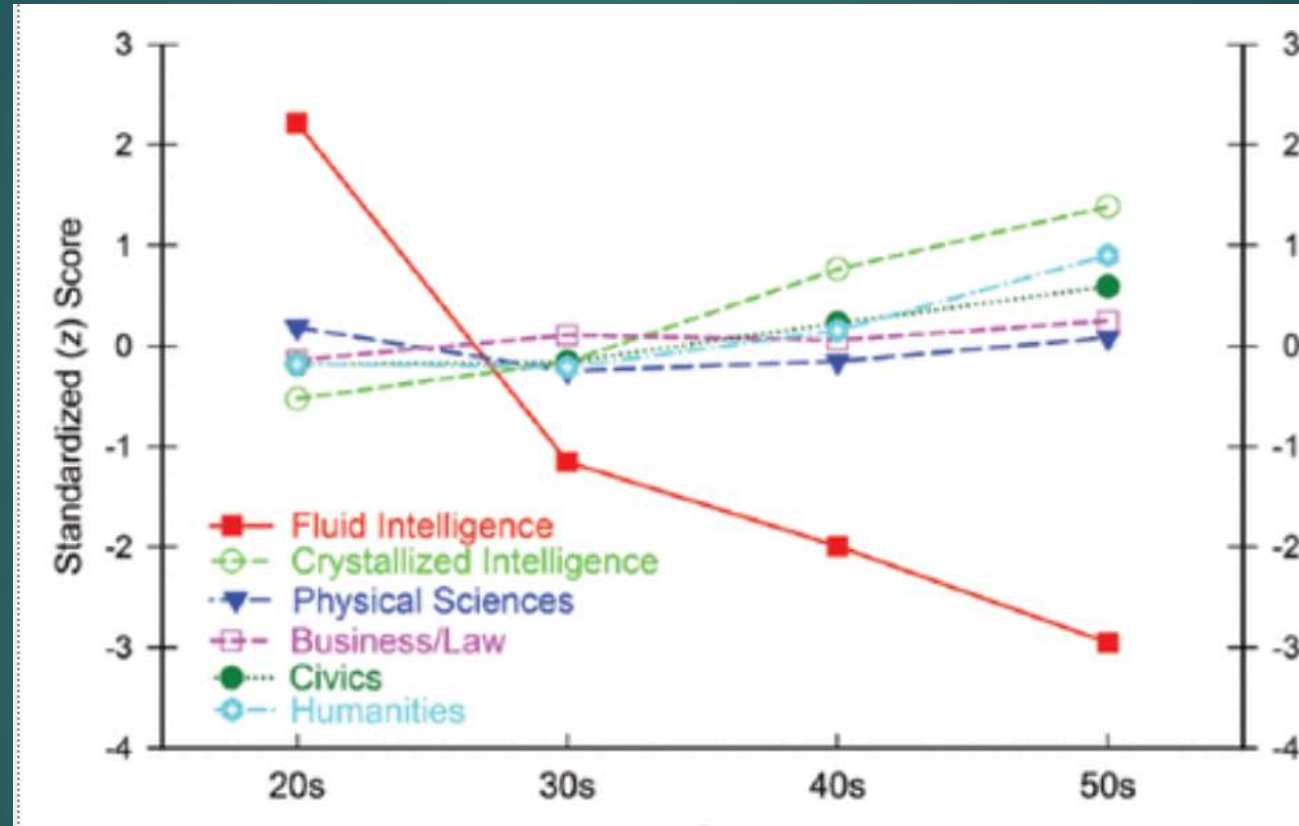
- ▶ Vocabulary
- ▶ Your fund of knowledge: occupational, avocational
- ▶ Product (of earlier processing)
- ▶ i.e. you are good at Trivial Pursuits or Jeopardy

▶ Declines: Fluid ability: Your Problem Solving Ability

- ▶ Solving new problems
- ▶ Ability to generate and manipulate information
- ▶ New processing ability

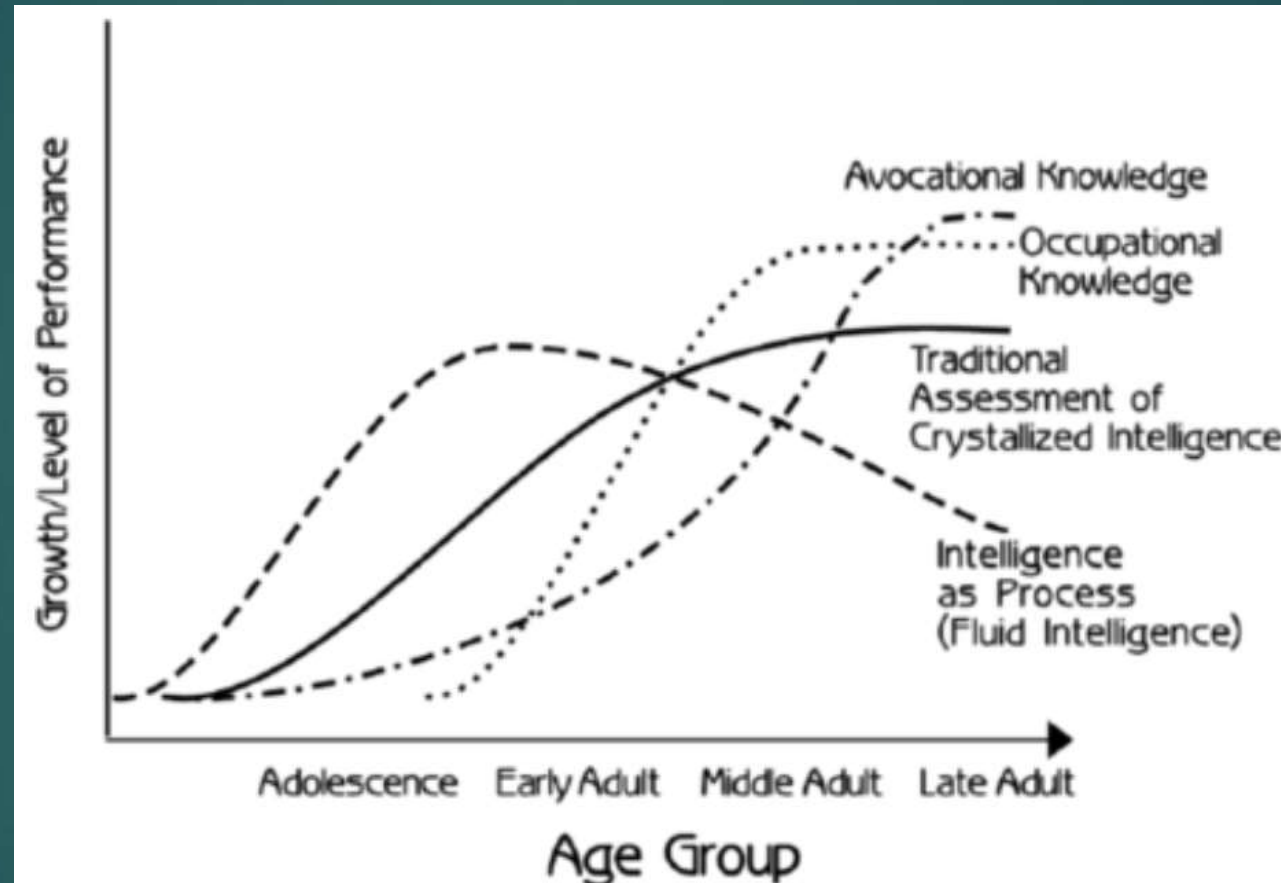
Fluid IQ (Problem Solving) declines, Experience Knowledge does not

All had
a B.A.



In contrast to performance on fluid IQ measures, middle-aged adults performed as well as or better than young adults on nearly all domain-knowledge tests

Knowledge Sticks



Avocational interests: hobbies, reading, other skills and areas of expertise

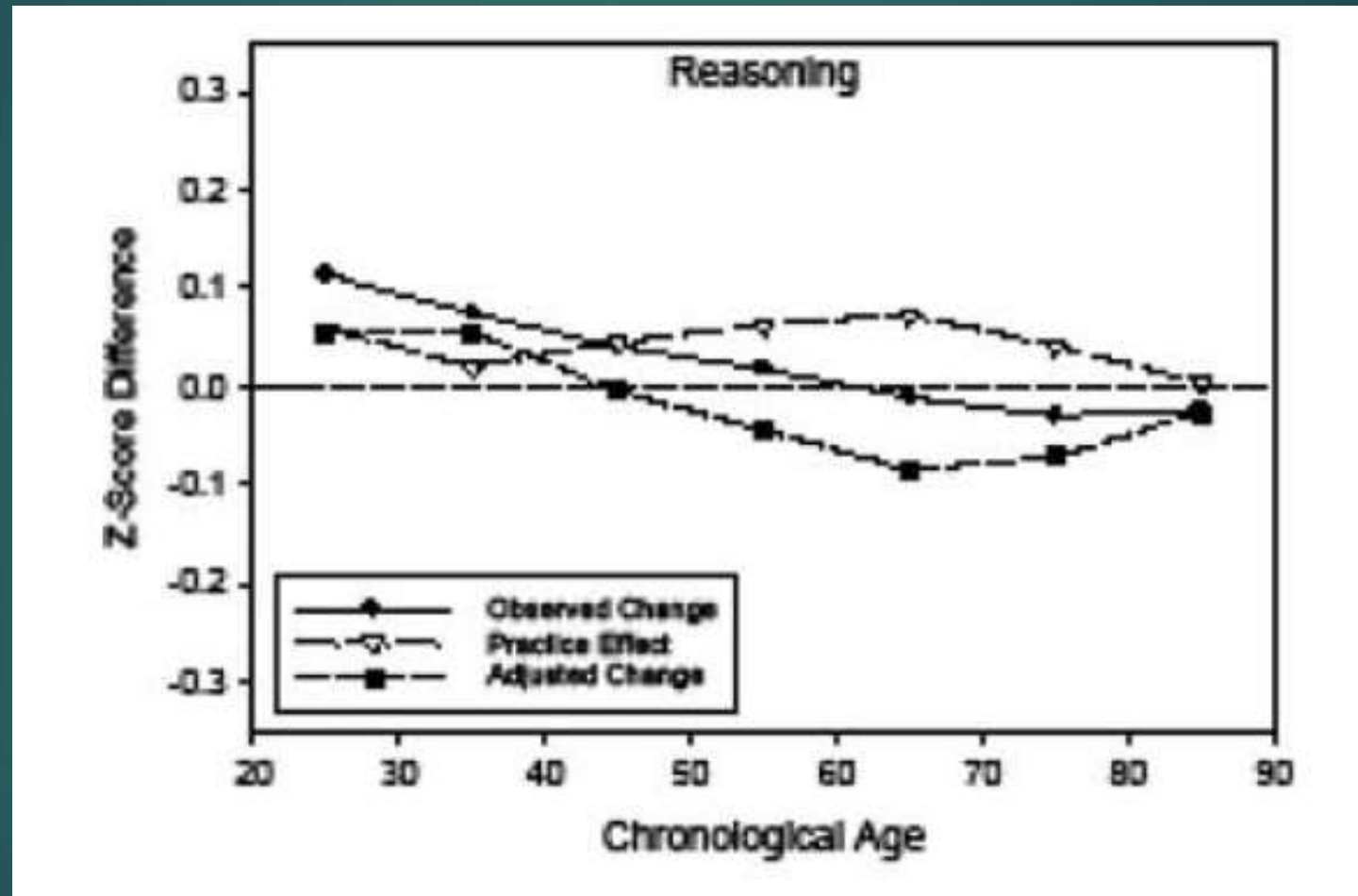
after Horn, 1965

Advantage of Bilingualism?: Stick with the evidence

Better Executive Function?

- ▶ Regularly speaking more than one language appears to strengthen skills that boost cognitive reserve
- ▶ Bialystok, 2010: Major NCD delayed by four years in bilingual people.
- ▶ Bilingual subjects were better able to block out distracting information; Better executive functioning
- ▶ Kenneth Paap, SFSU, 2015: not true
- ▶ New metaanalysis: comparing executive functions between bilinguals and monolinguals published since 2011, finding that **83 percent of them found no difference between the two groups.** There was also a tendency for studies with positive results to have used smaller samples, whereas those using larger study populations were more likely to find no effect.
- ▶ Publication bias: 68% of positive studies published (in reproducibility crisis in psychological science)
- ▶ Claudia von Bastian, 2015: **no language effect on EF**

Reasoning



Square = .1 change

Stroop Test 1: Read the words

▶ red white green brown

▶ green red brown white

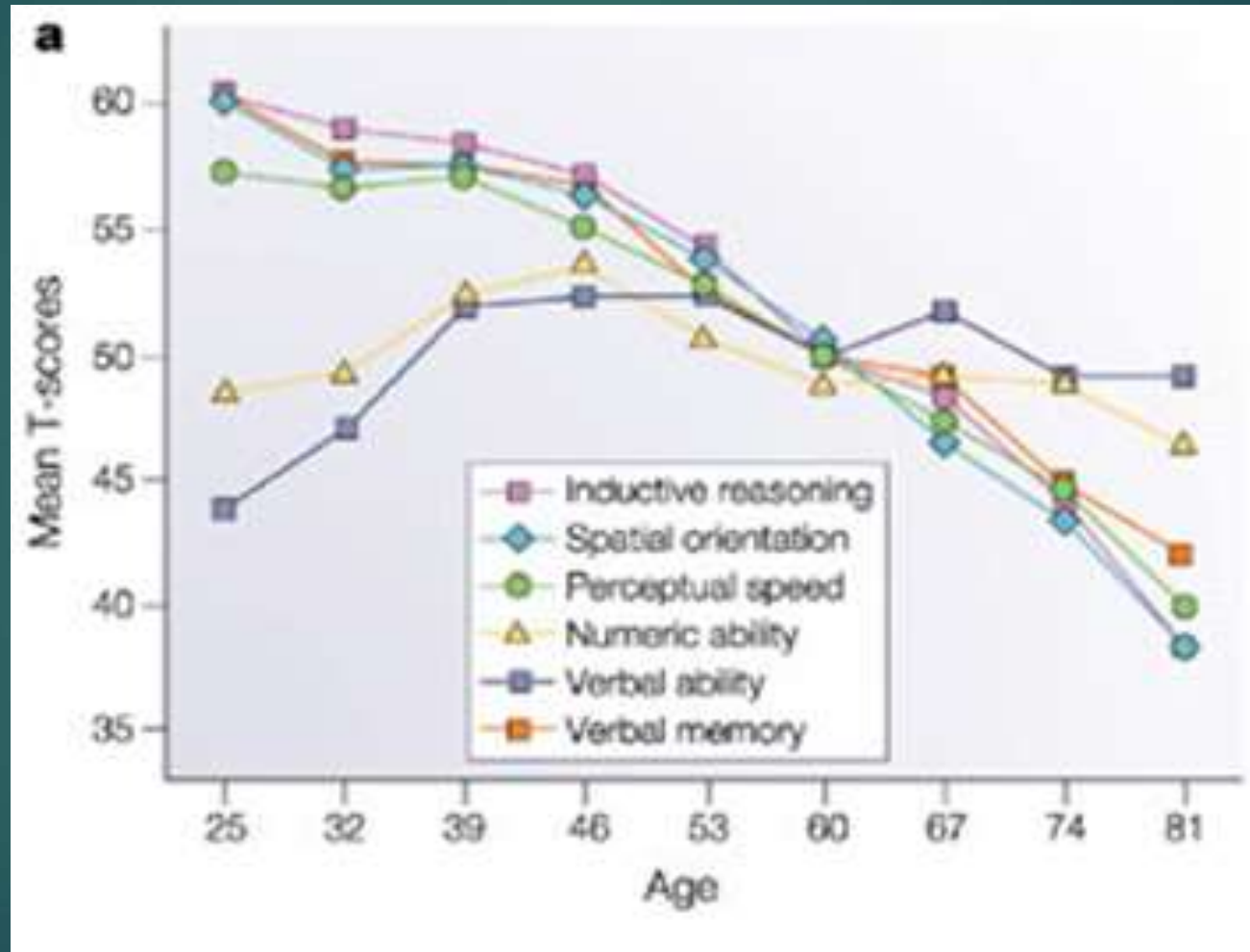
▶ white brown green red

Please read color of print not word

Green red brown white
white brown green red
Red white green brown
brown green white red

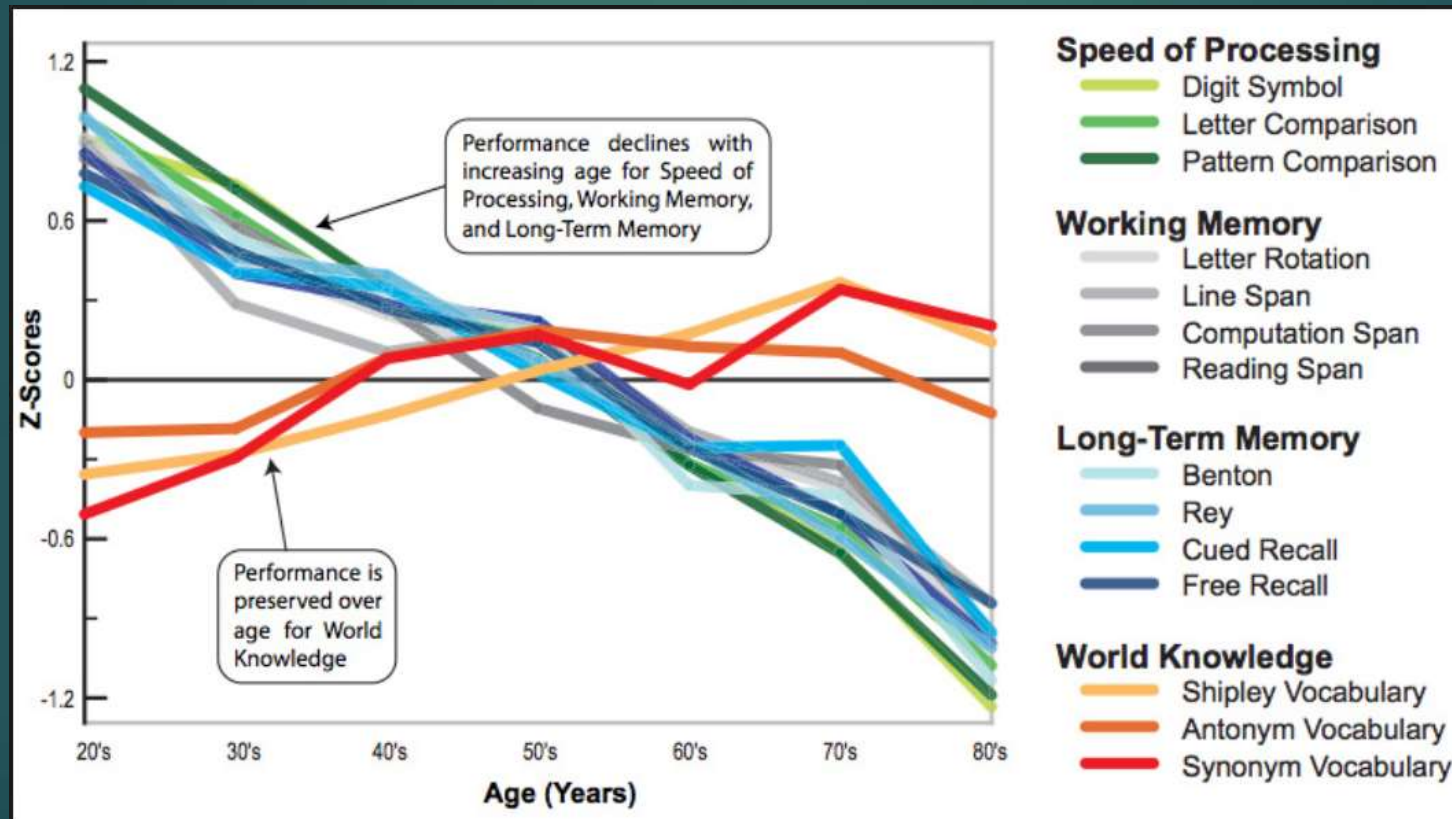
This measures prefrontal lobe functioning: inhibition

Verbal Ability ok vs. All Else ↓↓



Seattle Longitudinal Study; no practice effect correction

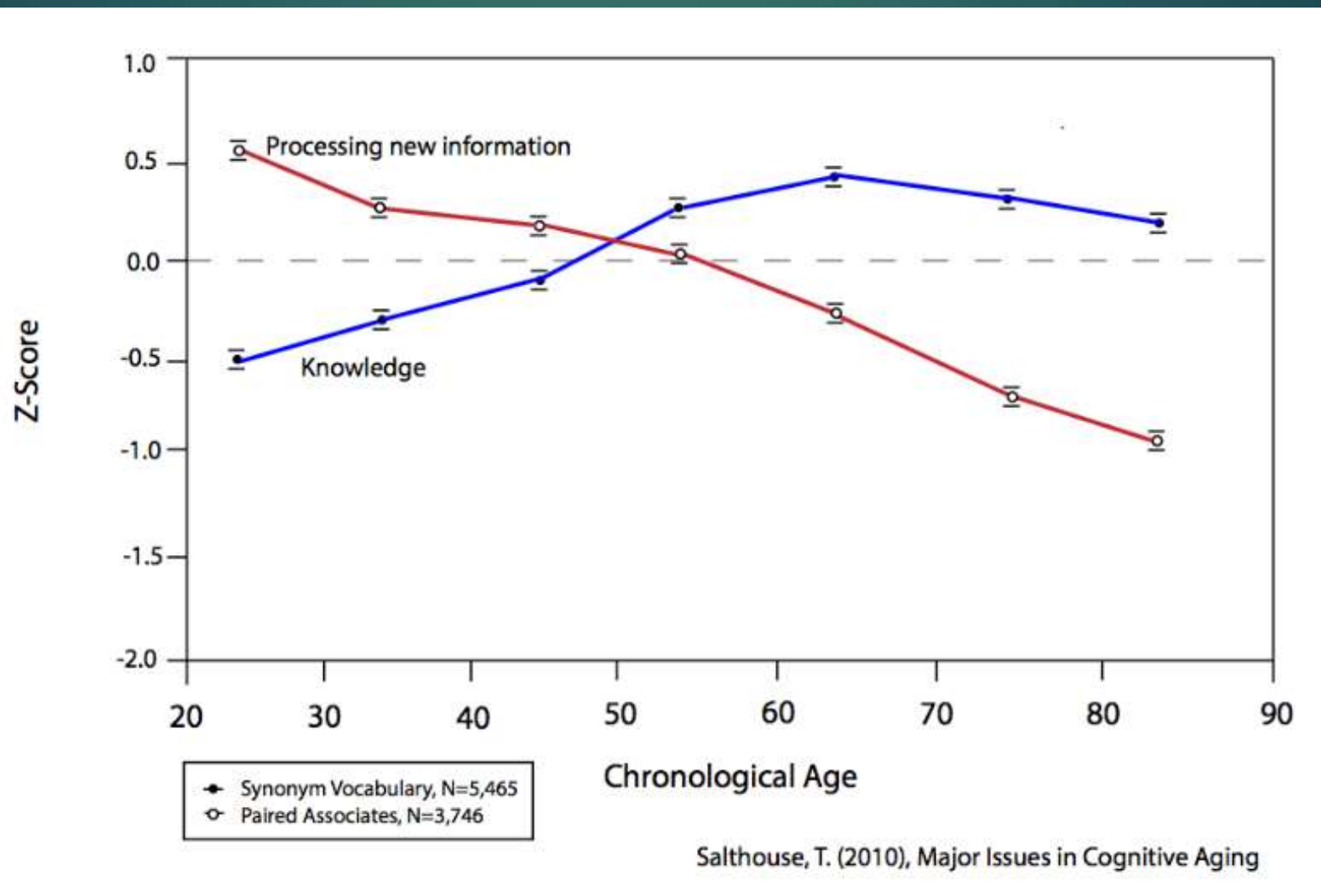
Knowledge and Experience stays normal with age



Best preserved with age...

- ▶ Verbal ability
- ▶ Behavioral memory
- ▶ Prospective memory in naturalistic settings

Processing speed declines Knowledge Increases with Age



Real World Complexity



Do you want a young or older pilot?
“Sully” Sullenberger & Hudson River, age 59



Brain Characteristics of Individuals Resisting Age-Related Cognitive Decline over Two Decades

- ▶ Neural correlates of successful cognitive aging:
 - ▶ Preservation of hippocampal function
 - ▶ high frontal responsivity is key.

- ▶ Predictors of better performance:
 - ▶ Being brighter to begin with,
 - ▶ living with somebody,
 - ▶ being physically active
 - ▶ having lower decline rate

Don't Retire or have a good cognitive replacement

- ▶ 2013 French study: n = 500K
- ▶ People who delay retirement have less risk of developing Alzheimer's disease or other types of Major NCD
- ▶ For each additional year of work, the risk of getting Major NCD is reduced by 3.2 percent
- ▶ People should work as long as they want because it may have health benefits.

Advanced age is accompanied by
mild deterioration of cognitive processes.

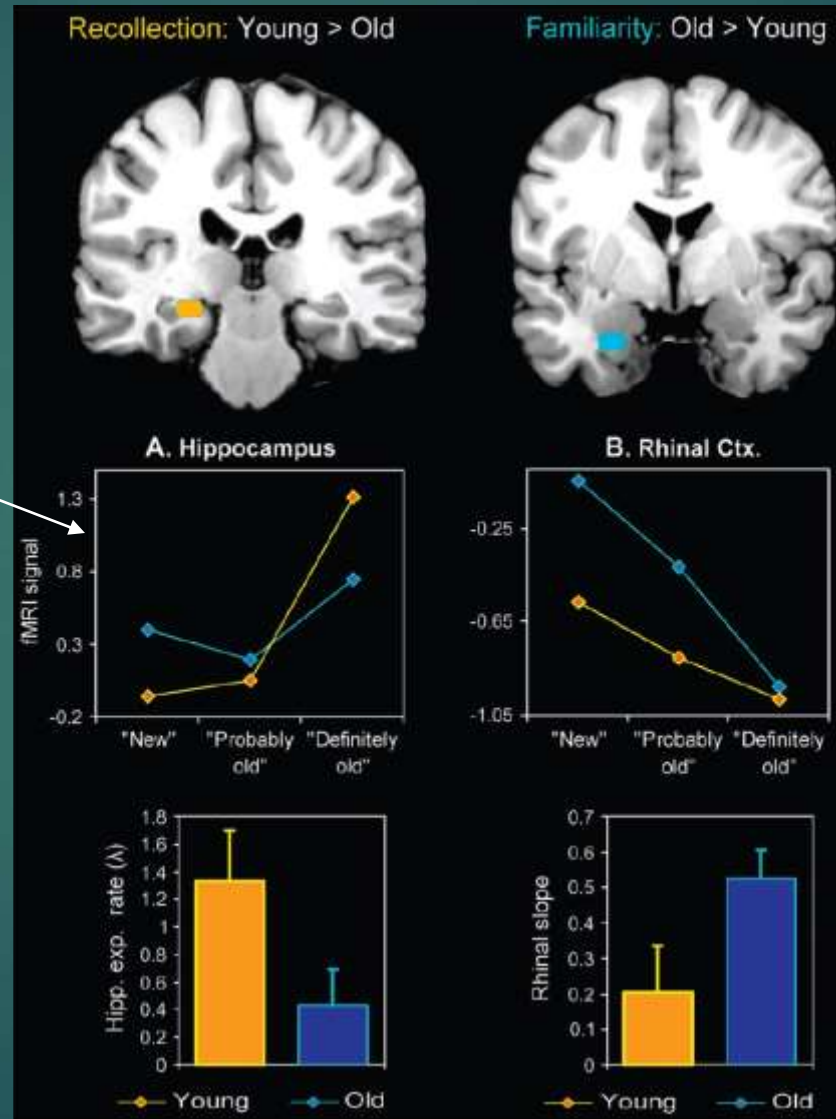
How does brain fight back?

It nonconsciously recruits and reorganizes.

Selective Deficits: Memory

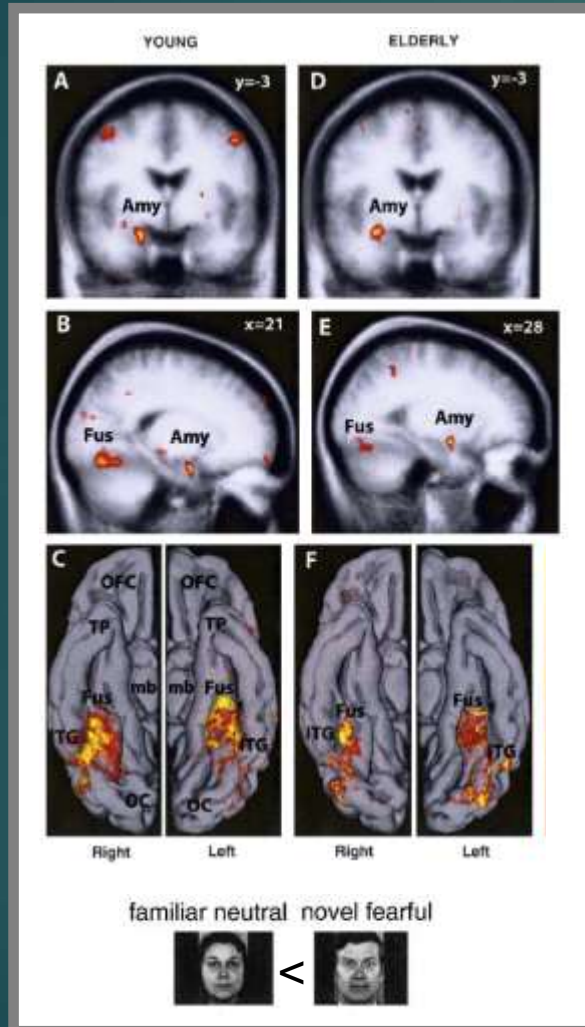
Aging has greater effects on recollection (hippocampally mediated)

Elderly: Recollection worse-based activation in hippocampus.

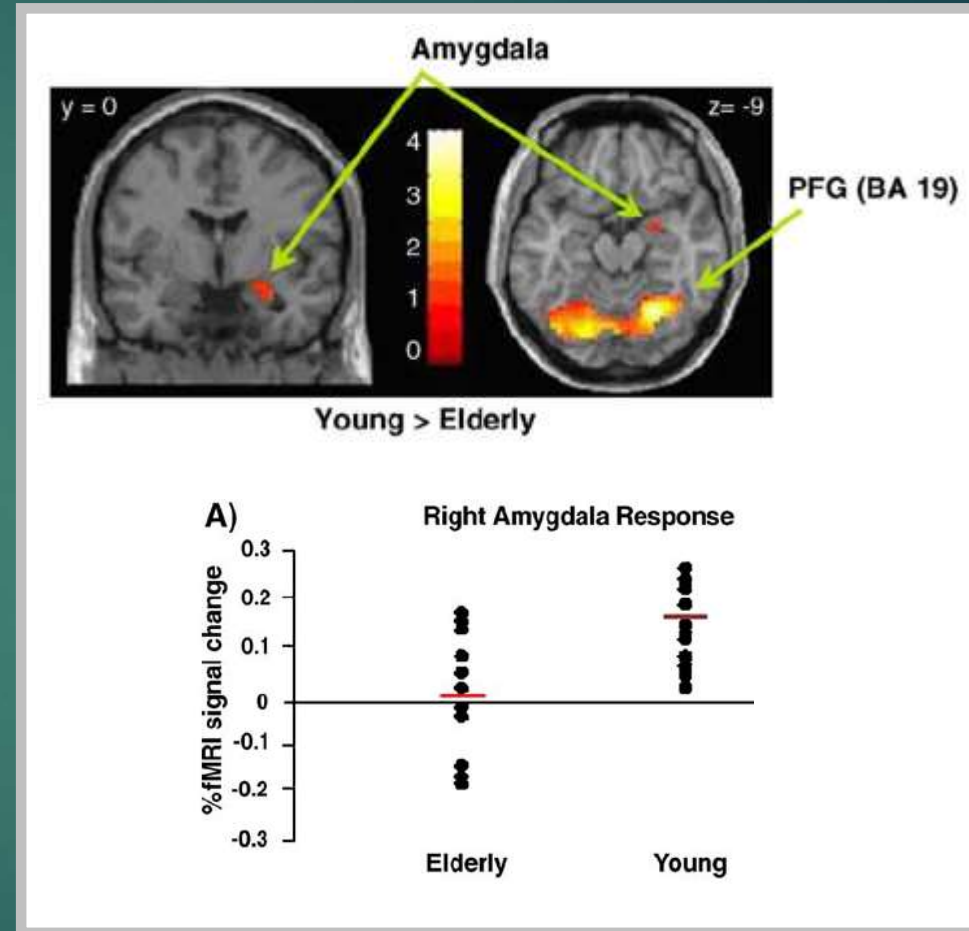


Elderly: Better familiarity-based activation in rhinal cortex.

Emotion: Less extensive activation of amygdala in the elderly



Wright et al., 2006

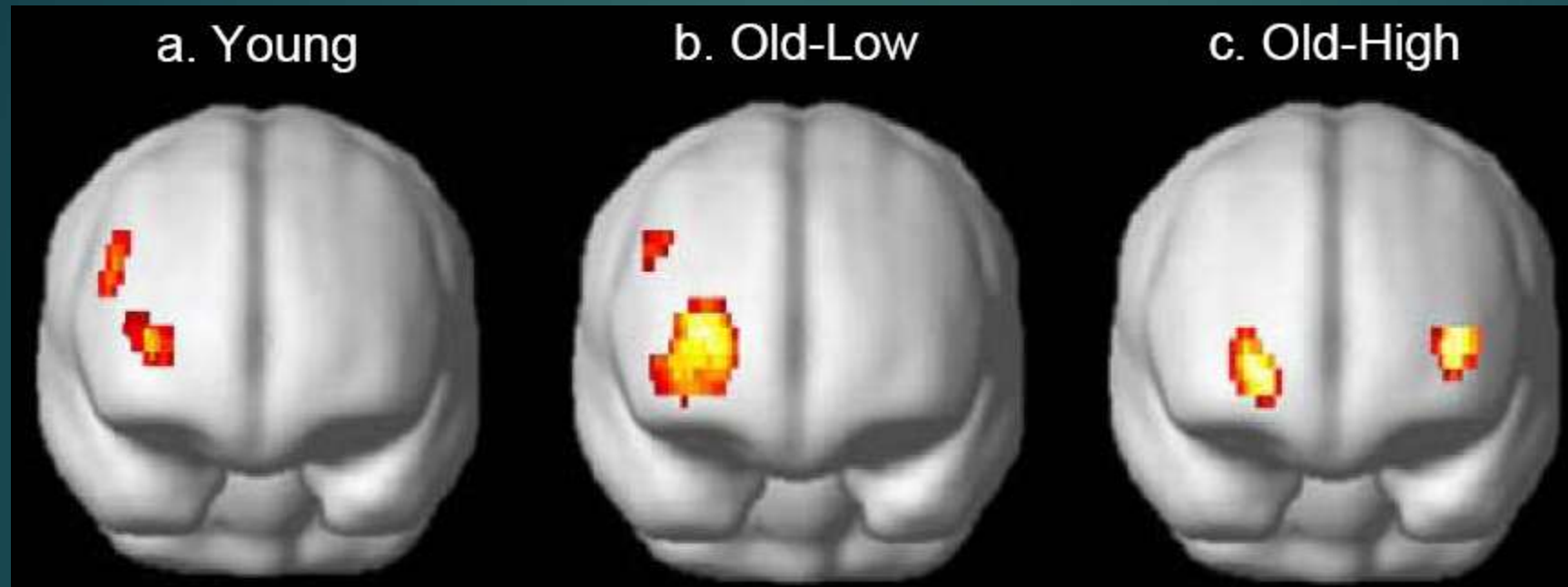


Tessitore et al., 2005

Less negative emotional reactions

Compensation: Memory

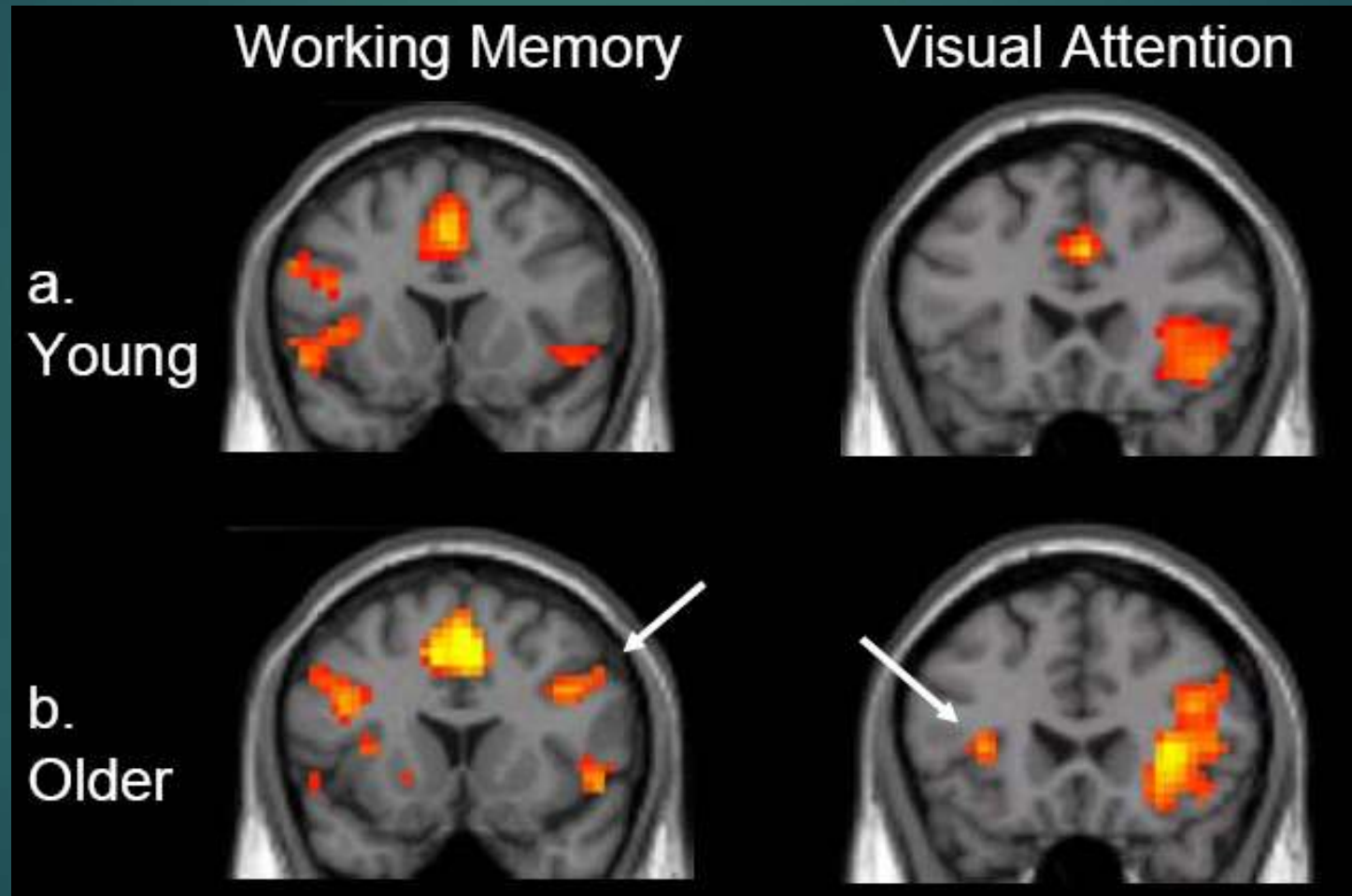
Elderly adults recruit additional regions to maintain performance



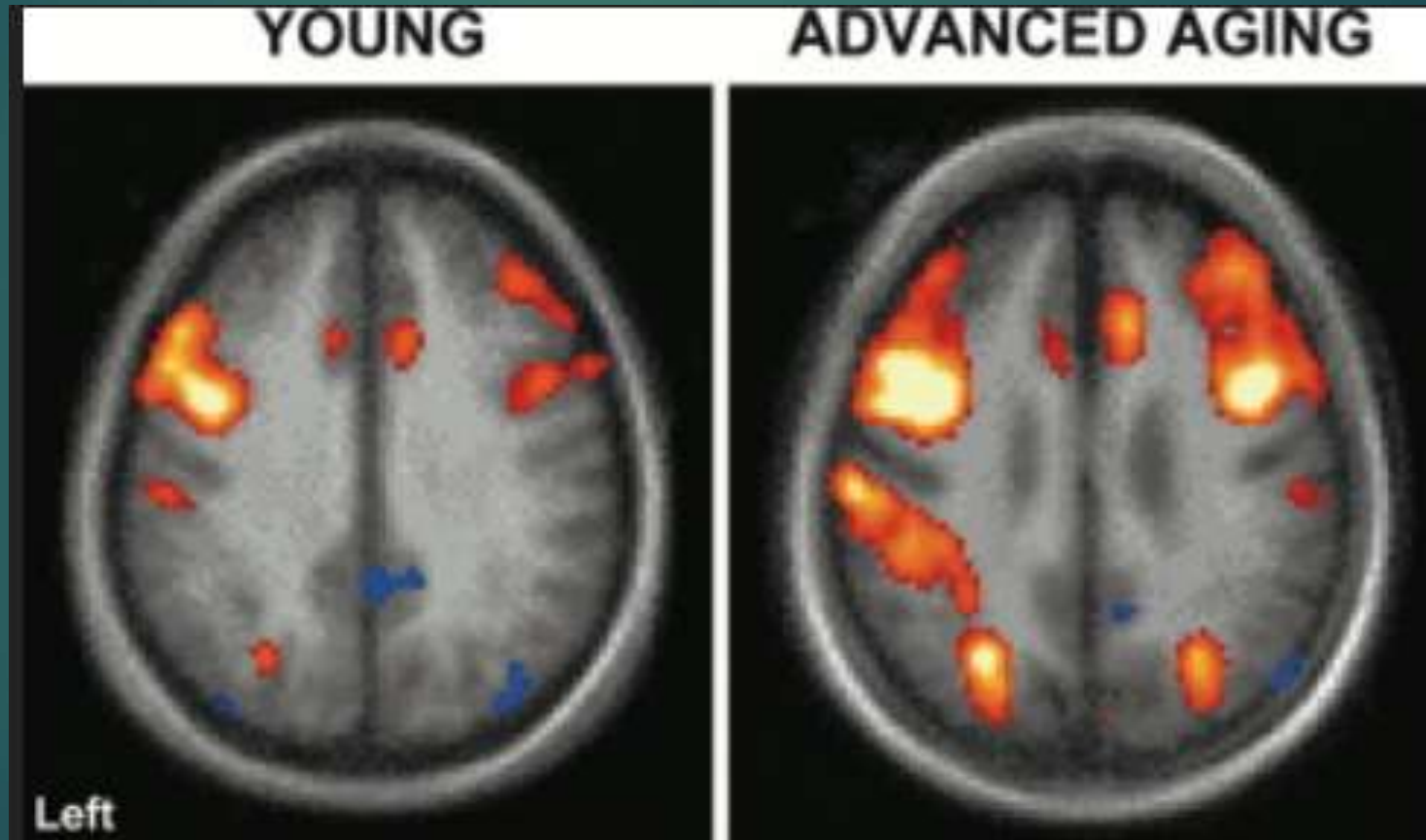
In a memory retrieval task, elderly adults who perform similarly to young adults (Old-High) show increased activation in left PFC, compared to elderly adults with impaired performance.

Compensation: Memory & Attention

Older use more Frontal regions.



Older work harder on same task



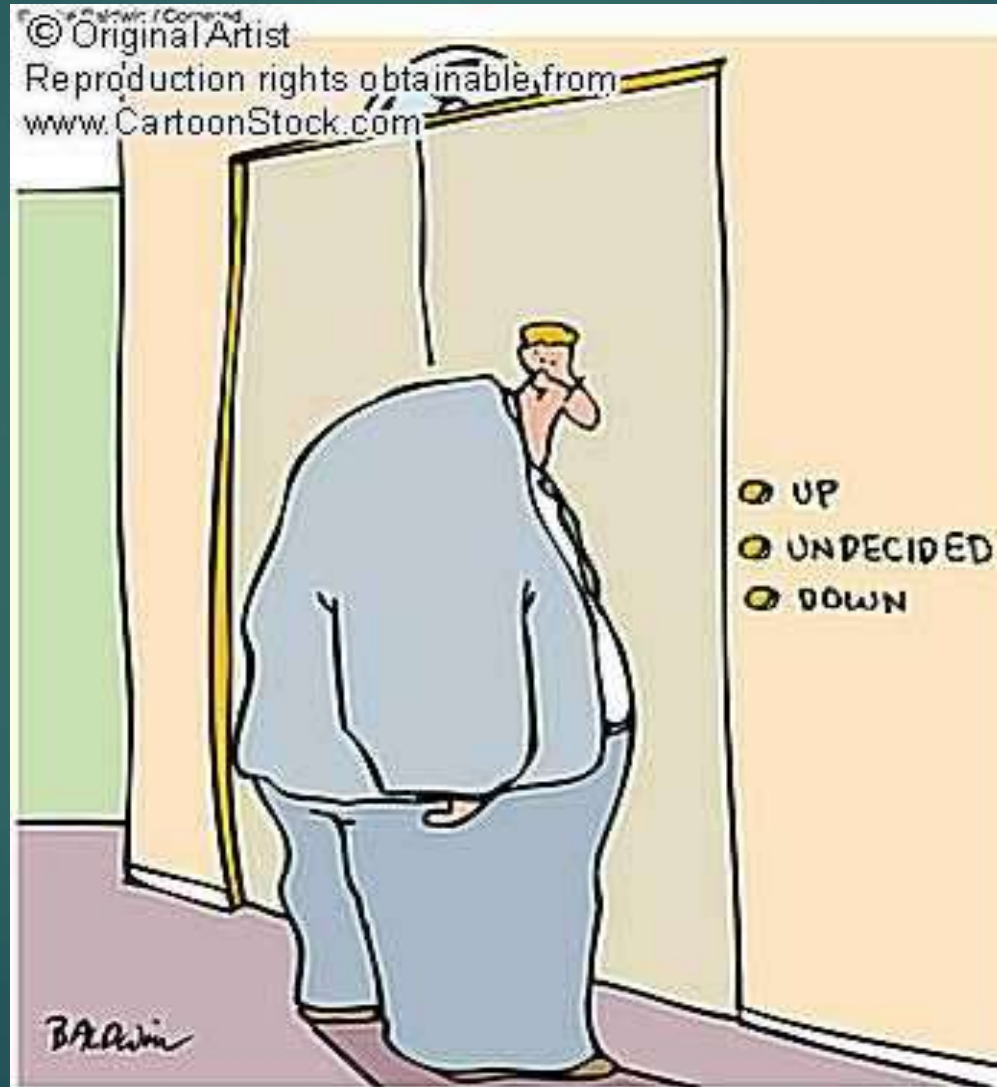
Older people use more frontal lobe resources

- ▶ Older adults often show:
 - ▶ bilateral prefrontal activations on both working memory and long-term memory tasks
 - ▶ whereas younger adults show primarily left-lateralized prefrontal activations

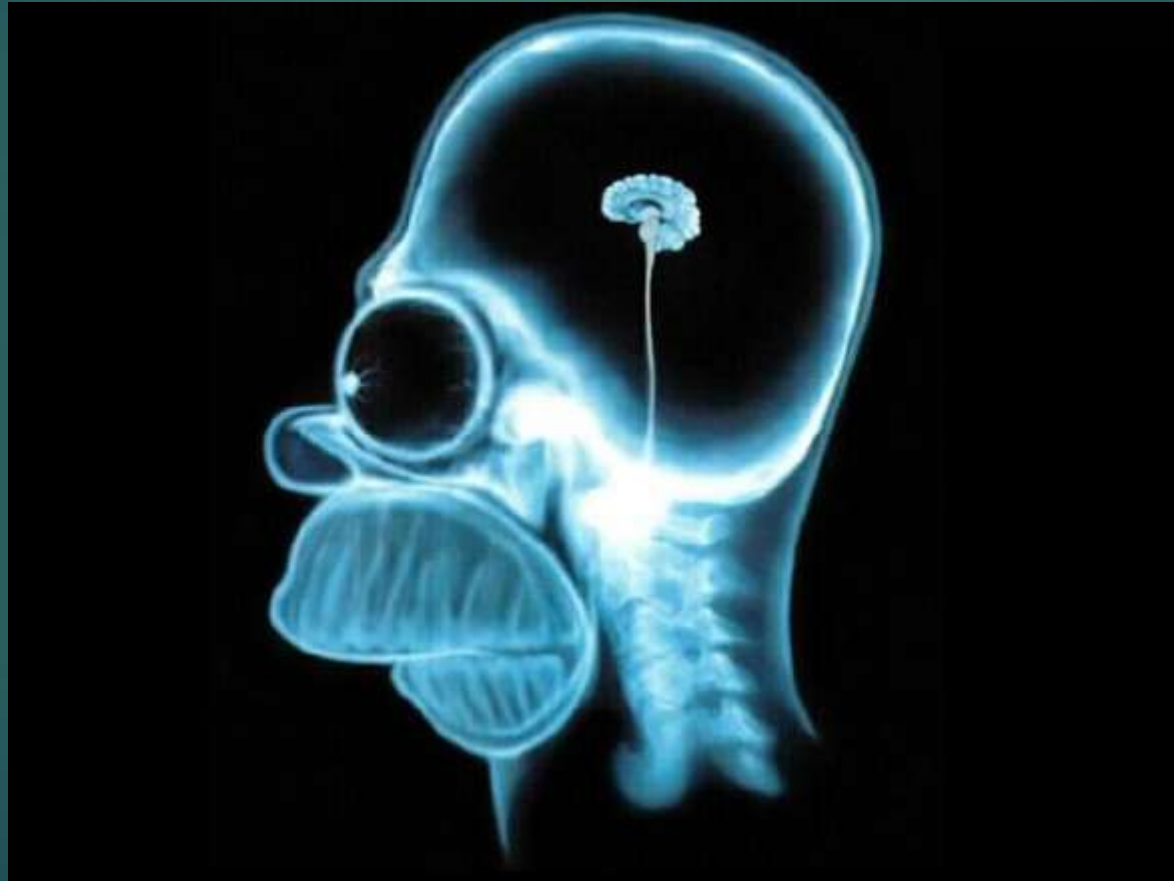
Age & Happiness: Older look at brighter side

- ▶ **Positivity effect**—an increasing focus on positive events and happy feelings. **Brightest seniors show most effect.**
- ▶ Older people **look longer at upbeat images and away from upsetting ones.** **Look away faster from pictures depicting negative situations** (funerals, plane crashes, angry faces), but **fix their gaze longer on images of good stuff:** smiling kids, cute kittens, happy faces.
- ▶ The **memory of older people is skewed toward the positive.**
- ▶ Over 23 years, the **older people got, the less they experienced negative feelings.** There is an increasing tendency to concentrate on sources of happiness while downplaying negative information.

Decision Making



Does this individual have the capacity to make decisions?



The Fly Problem

- ▶ Two bicyclists start twenty miles apart and head toward each other, each going at a steady rate of 10 mph. At the same time a fly that travels at a steady 15 mph starts from the front wheel of the southbound bicycle and flies to the front wheel of the northbound one, then turns around and flies to the front wheel of the southbound one again, and continues in this manner till he is crushed between the two front wheels.
- ▶ Question: what total distance did the fly cover?
- ▶ John Von Neumann = 2 seconds to solve

Executive Functioning

- ▶ EF is distinct from more automatic memory processes that have been overlearned by repetition.
- ▶ Ability to respond flexibly to the environment
- ▶ Impairments in EF thus have serious functional consequences

Executive Functioning

- ▶ EF = Applying knowledge toward real world goal directed behavior
- ▶ Executive functioning examples:
 - ▶ Self monitoring behavior
 - ▶ Anticipate consequence of action
 - ▶ Disregard erroneous strategies
 - ▶ Inhibit automatic but inappropriate response
 - ▶ Comply with treatment
 - ▶ Do something when needed (not just know how to do it)

Majority of the elderly have Normal Decision Making

- ▶ If free of disease that impairs thinking, older adults are just as good or even better at decision-making than someone younger.
- ▶ Healthy older adults show no decline in decision-making.

Executive Dysfunction in Major NCD

- ▶ Executive dysfunction is associated with impairment of prefrontal and frontal-subcortical circuits
- ▶ Executive ↓ can be independent of Memory ↓
- ▶ New changes in behavior:
personality changes, disinhibition, hypomania, apathy

Executive Dysfunction in Major NCD 2

- ▶ Neurogenic denial of deficit: Do not know we have the problem (“I can drive; I can live alone”)
- ▶ Executive dysfunction associated with:
 - ▶ Functional decline
 - ▶ Increased need for care
- ▶ Executive ↓ correlates with decline in IADLS (inability to use phone, letter, finances, meal prep)

Executive Deficit Predicts:

- ▶ Functional autonomy decline:
 - ▶ Can't live independently
 - ▶ Money management decline
 - ▶ Medication management decline
- ▶ Poor geriatric orthopedic & stroke rehabilitation outcome

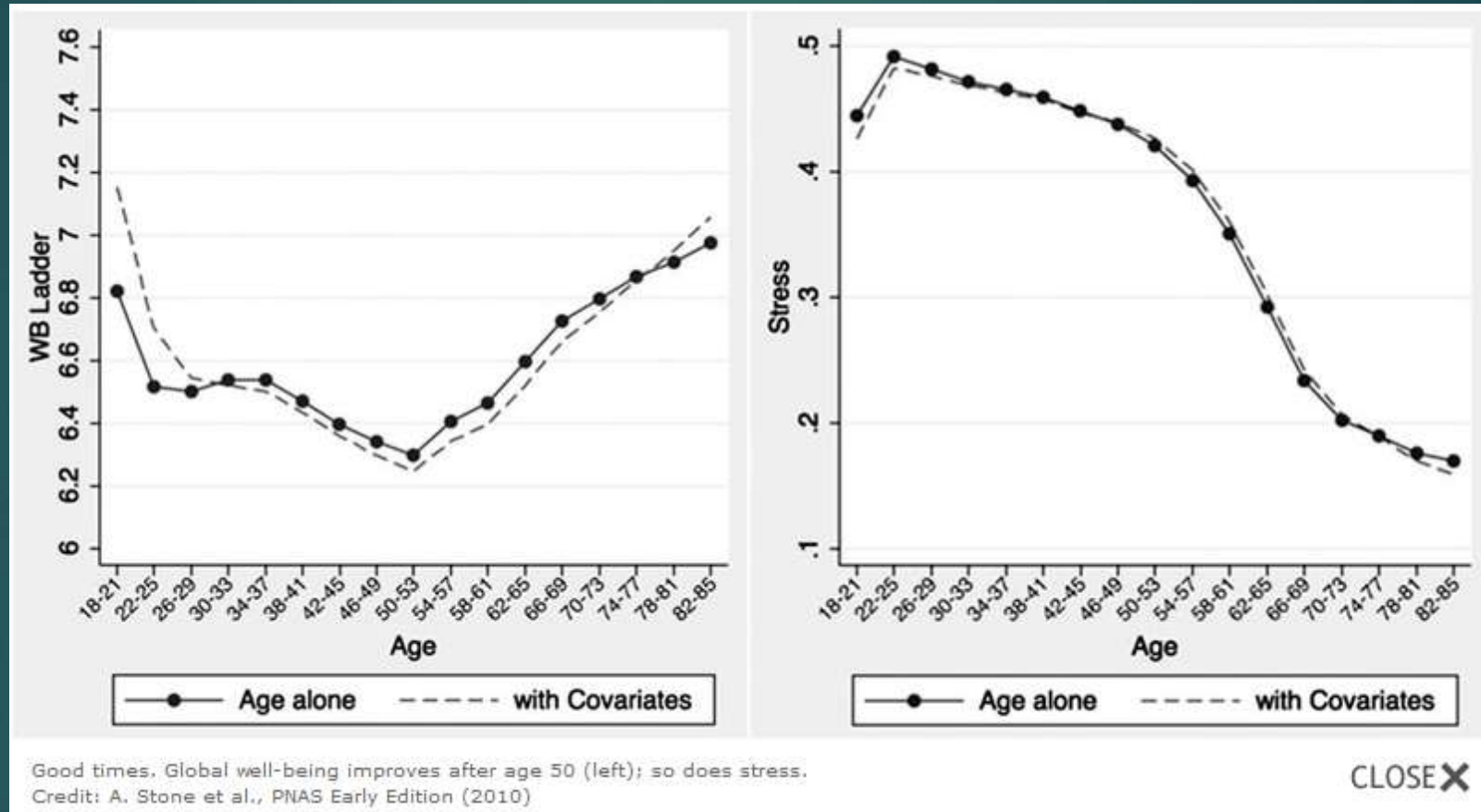
Reasoning about social conflicts improves into old age

- ▶ Older people have **better social reasoning**:
 - ▶ Use multiple perspectives,
 - ▶ allow for compromise,
 - ▶ recognize the limits of knowledge.
- ▶ Complicated reasoning that relates to people, moral issues or political institutions improves with age.

Senility (or Neurodegeneration) Prayer

- ▶ God, Grant me the senility to forget the people I never liked anyway
- ▶ The good fortune to run into the ones I do
- ▶ And the eyesight to tell the difference.

Aging is not all bad news...



Sense of well being increases and stress decreases after age 50

Benefits of Aging

- ▶ You are not dead!
- ▶ More life experience
- ▶ Wisdom, hopefully
- ▶ Verbal ability intact
- ▶ Prospective memory better than younger
- ▶ Better at making connections, seeing patterns
- ▶ Older adults rely more heavily on gut emotional responses in making decisions than on reasoned, detailed analysis.

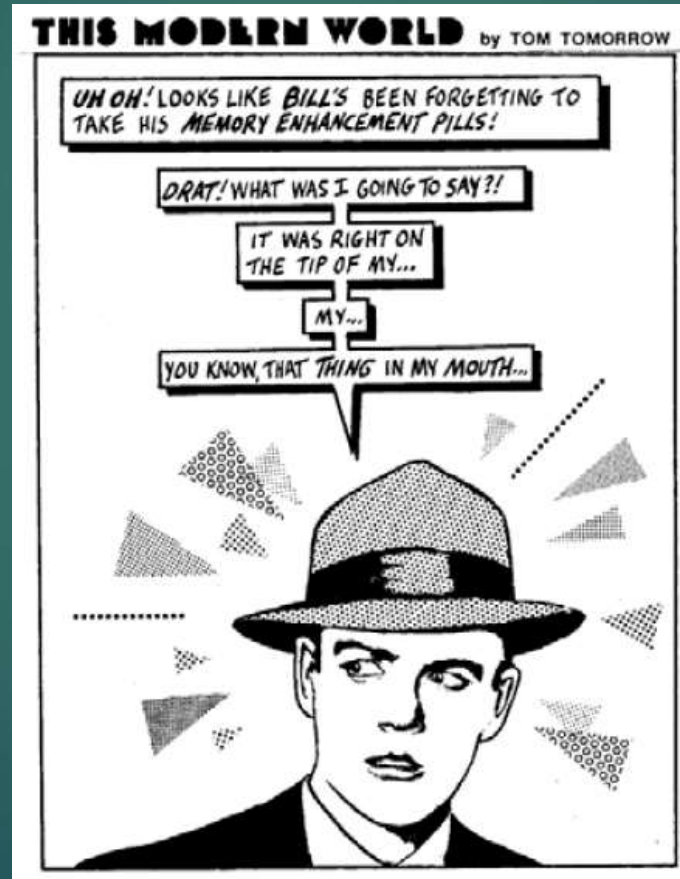
Seven Most Common “Memory” Problems

1 – Namensia (Coming up with right name)



**Hi. I'm, I'm, I'm..... You'll have to forgive me.
I'm terrible with names.**

2 – Wordmnesia (Tip of Tongue)



3 - Roomnesia



Increased Distractibility

The Hereafter

“Doc... The older I get, the more experience I have with the hereafter.

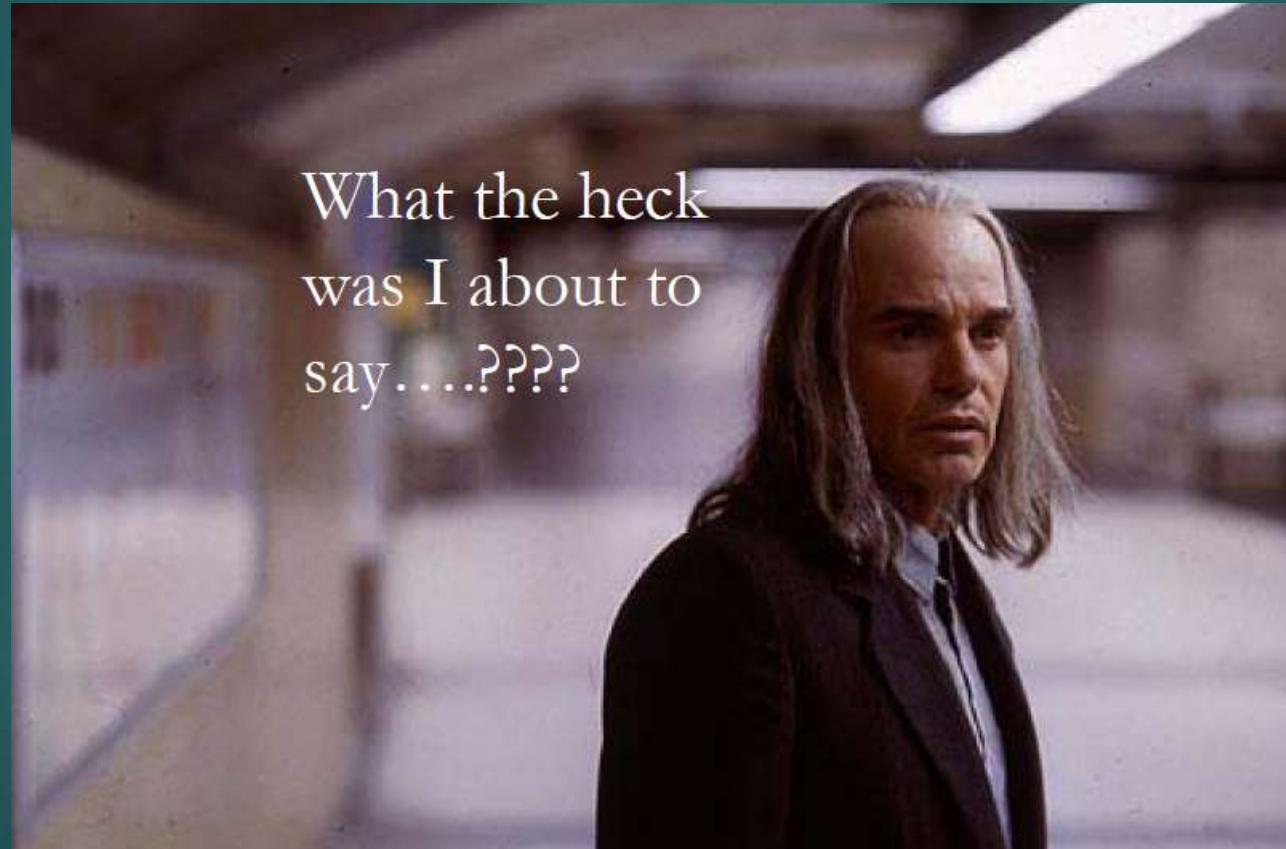
Every time I walk into a room, I wonder “what am I here after?!”



4 - I can never remember where I put things



5 - Episodic Fleeting Thought Syndrome



6 – Parkingmnesia (Shopping Mall type)



I think it was in Section GG-17... or was it DD-71?

7 - Paroxysmal A-Navigationalism (Missing the Exit Syndrome)

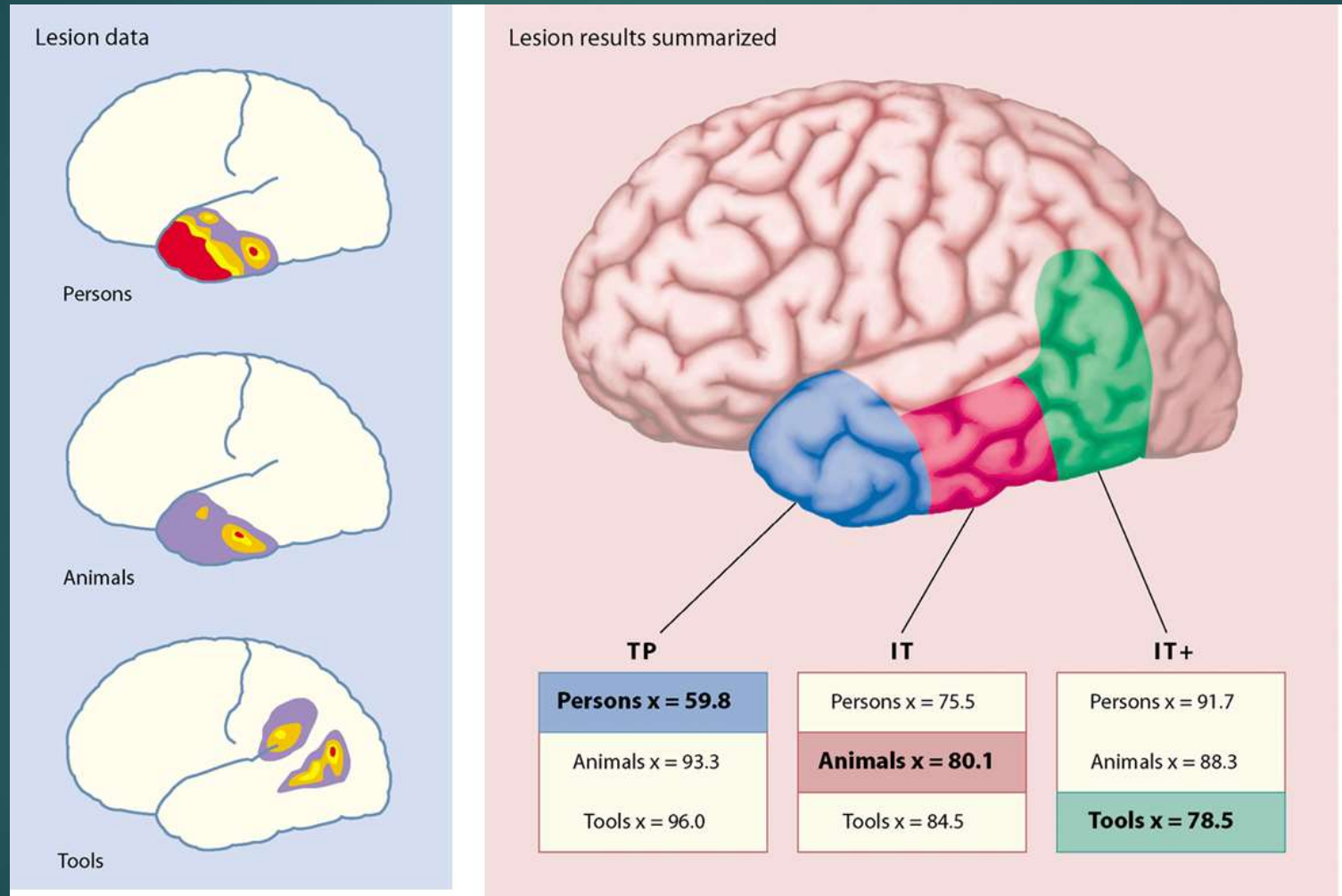


Actual Memory Worries in a Mental Aerobics Class

- ▶ Forgetting names
- ▶ Sudden spelling blanks
- ▶ Train of thought: Lose point of what I am saying
- ▶ Memory for words, keys, movies, novels
- ▶ Tip of tongue
- ▶ Why am I in this room
- ▶ Driving directions
- ▶ Distraction
- ▶ Turning off stove, water; locking door

That Naming Problem

Where the brain stores Persons, Animals, Tools



Location of brain lesions that are correlated with selective deficits in naming persons, animals or tools (Damasio et al., 1996).

Processing Speed and Rapid Naming

Visual-Verbal Connection: aka “see-it/say-it”
Arcuate and/or inferior longitudinal fasciculus?

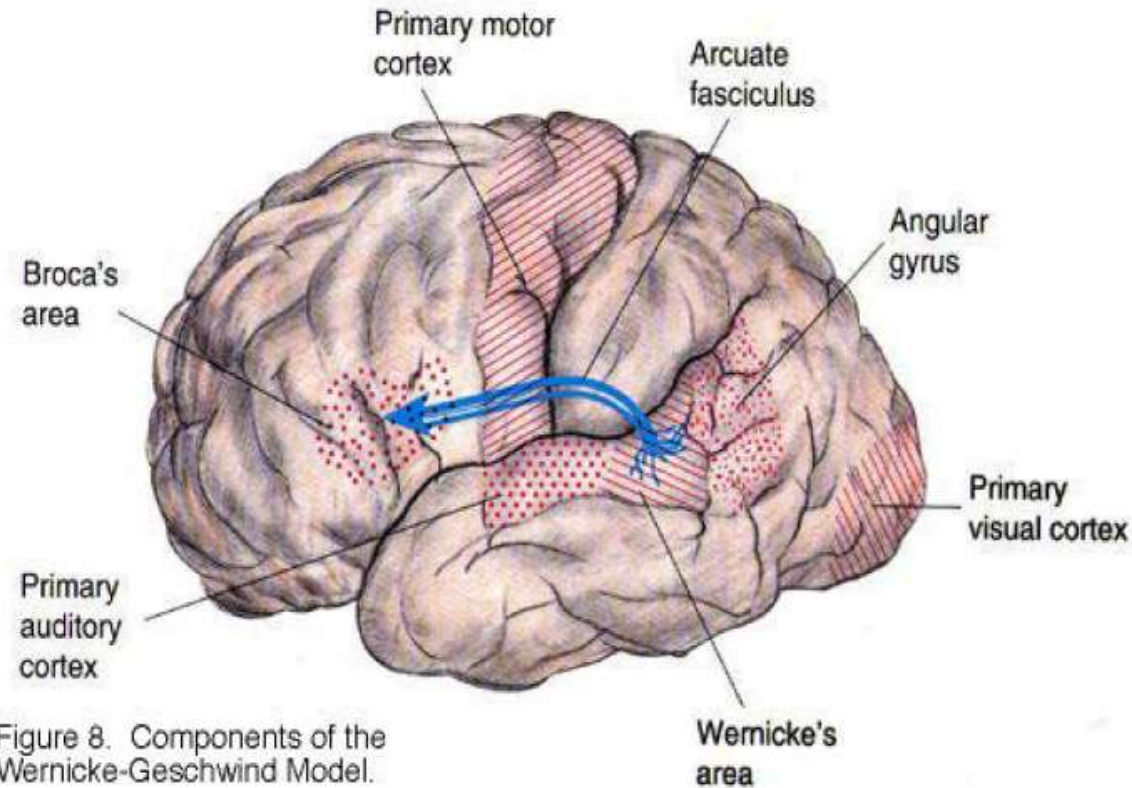
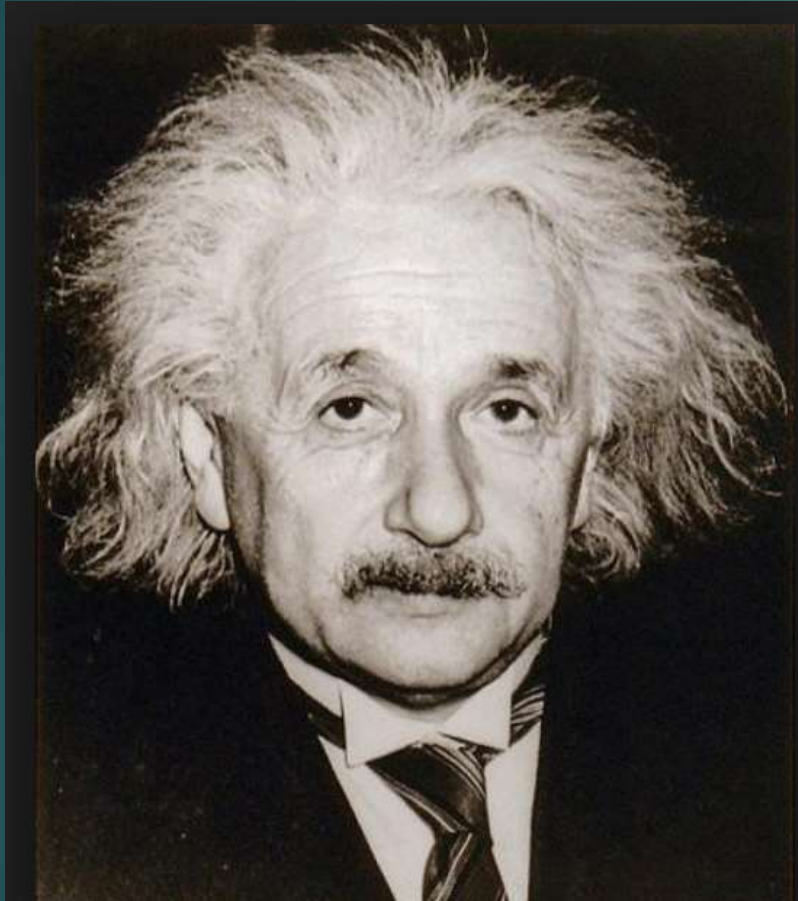


Figure 8. Components of the Wernicke-Geschwind Model.

TOTS: **Tip-of-the-tongue** =
recall of proper nouns

- ▶ Tip-of-the-tongue experiences (TOTs): a name is known but cannot be immediately retrieved from memory
- ▶ The age-related increase in TOTs (semantic memory) and age-related declines of episodic memory (episodic memory) are only weakly related.

Name & Memory



- ▶ Who is this?
- ▶ Albert Einstein

- ▶ Facts about him?
- ▶ $E=MC^2$
- ▶ Physicist
- ▶ Flunked algebra
- ▶ Married twice

The Nature of Memory

Superman in his later years



Things People Normally Forget

“Forgetting Symptom”	Percentage
Telephone numbers	58%
People’s names	48%
Where car is parked	32%
Lose car keys	31%
Groceries	28%
Reason for entering room	27%
Directions	24%
Appointments	20%

Memory & Insurance Claims: behavioral memory

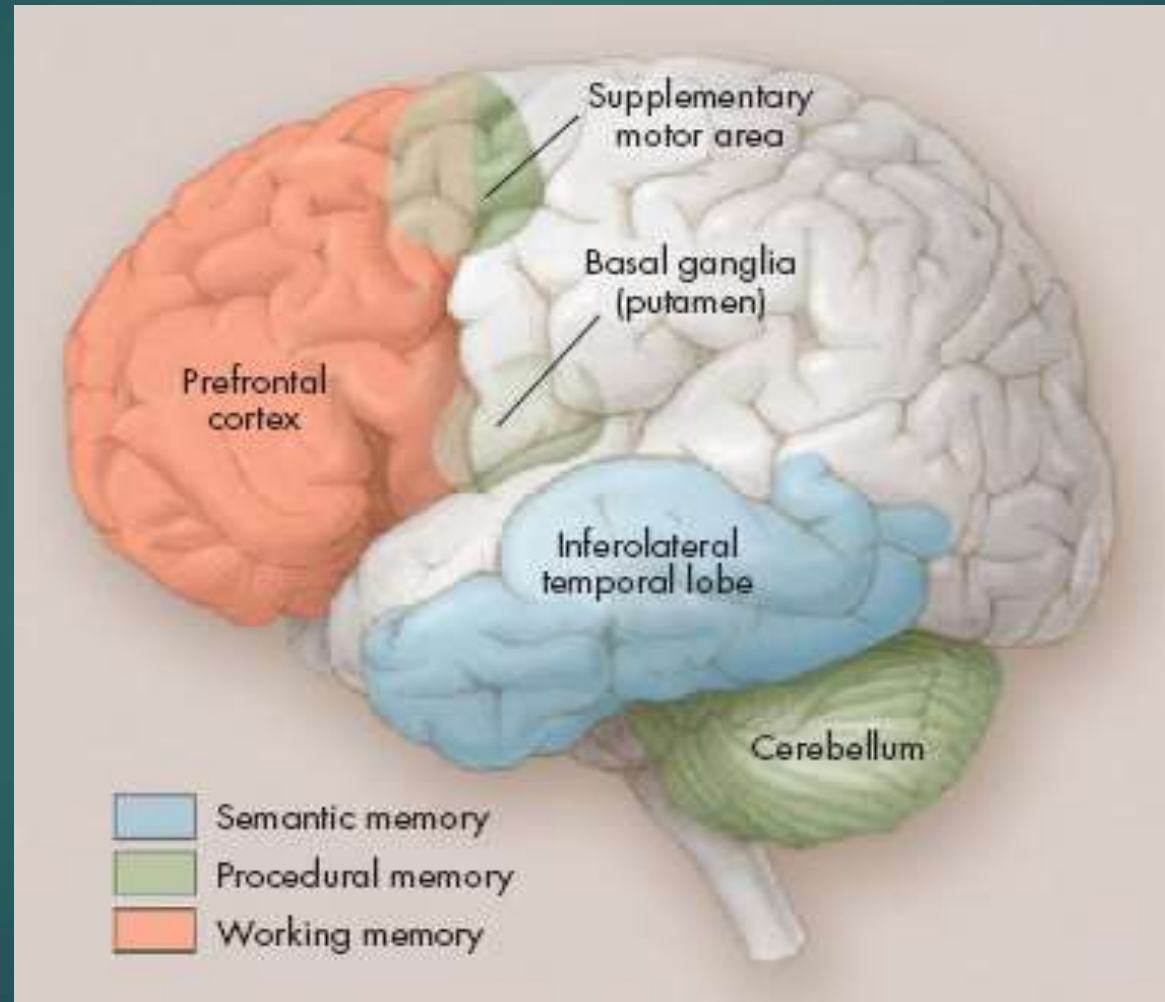
▶ Most common insurance claims based on acts of forgetfulness
(commonalities = very repetitive behaviors or distraction):

- ▶ Leaving stove on
- ▶ Leave garage door open
- ▶ Leave water on
- ▶ Leave car door open
- ▶ Leave keys in front door
- ▶ Leave house unlocked
- ▶ Left candle burning
- ▶ Left heater on
- ▶ Distracted while driving

5 Types of Memory

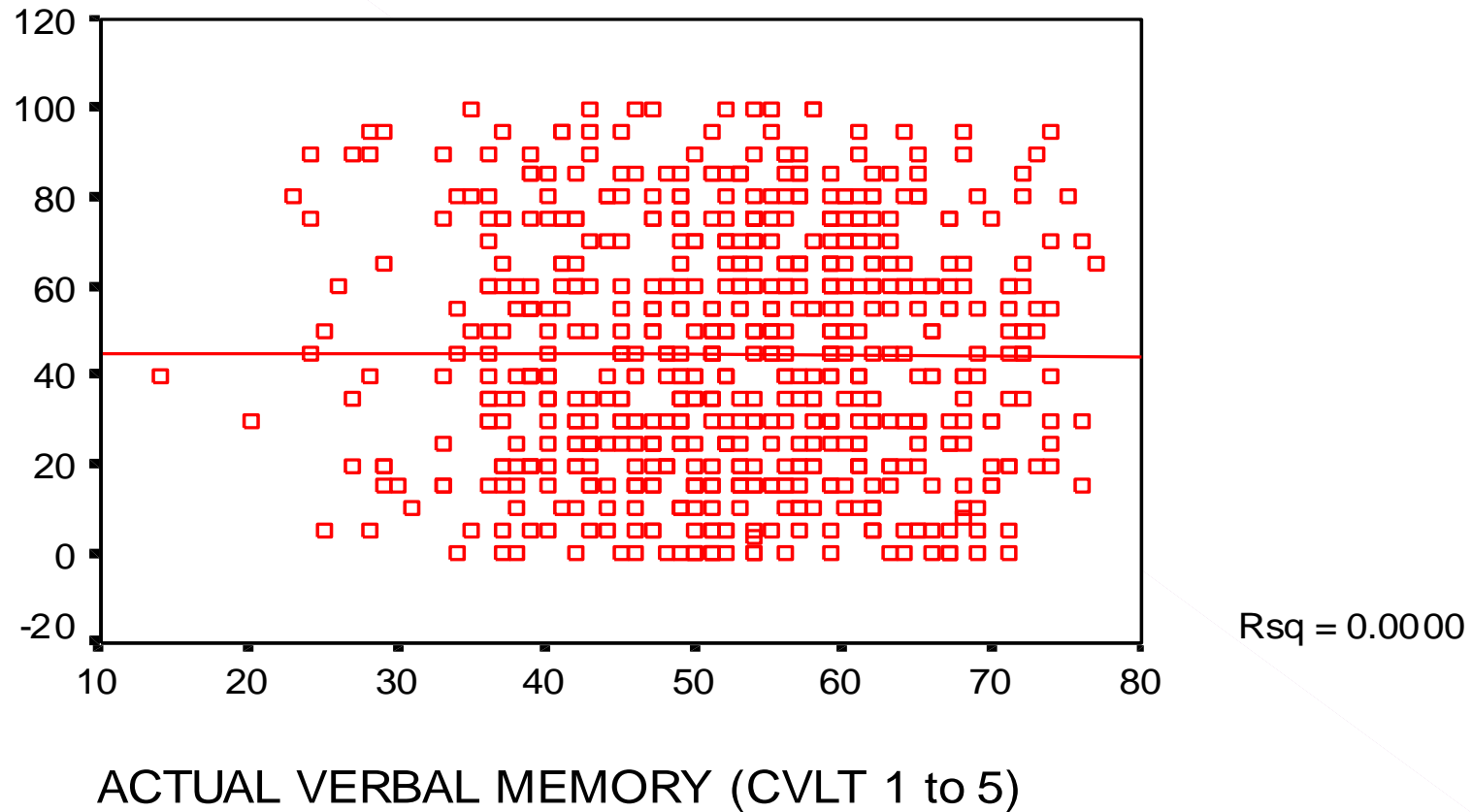
- ▶ Explicit (Factual) Memory
- ▶ Episodic (Personal) Memory
- ▶ Working (Brief, Temporary) Memory
- ▶ Prospective Memory
- ▶ Procedural (How to...) Memory

Location of Memory in the Brain: Everywhere



Verbal memory complaints versus verbal memory test scores

Zero correlation in 995 cases



Not Major NCD

- ▶ If you remember that you forgot something
- ▶ If you complain about memory problem
- ▶ If you forget something that is unimportant to you (name, appt.)
- ▶ If you forget a fact you used to know (i.e. 1066)
- ▶ If you forget details of about places you've been and things you have done
- ▶ If you forget exactly how to get somewhere (we have GPS!)

Memory Worry

- ▶ A memory glitch does not mean you have a memory disorder
- ▶ Most memory glitches are attentional issue.
- ▶ Most Alzheimer's patients rarely know they have a memory disorder; due to its insidious onset
- ▶ If you or a partner are concerned about your memory, tell your doctor; get tested by a neuropsychologist

Normal Memory vs. Real Memory Deficit Types

- ▶ Normal:
- ▶ Tape recorder works fine for input & output
- ▶ Given 16 new words 5 times, you recall 12 at half an hour
- ▶ New & old memories are equally accessible

Encoding Failure: Tape recorder is off

- ▶ Tape recorder: no new input or output
- ▶ Poor spontaneous recall and recognition
- ▶ Cueing does not help
- ▶ Types: TBI, Alzheimer's, Down's

Retrieval Failure: Trouble finding your memory

- ▶ Tape recorder works fine; output of memories that exist is slower
- ▶ Poor spontaneous recall: poor 1-3 items on spontaneous recall,
- ▶ Normal recognition (cueing helps)
- ▶ Some normals, depression, subcortical Major NCDs (Korsakoff syndrome, chronic alcohol abuse, Parkinson's, HIV)

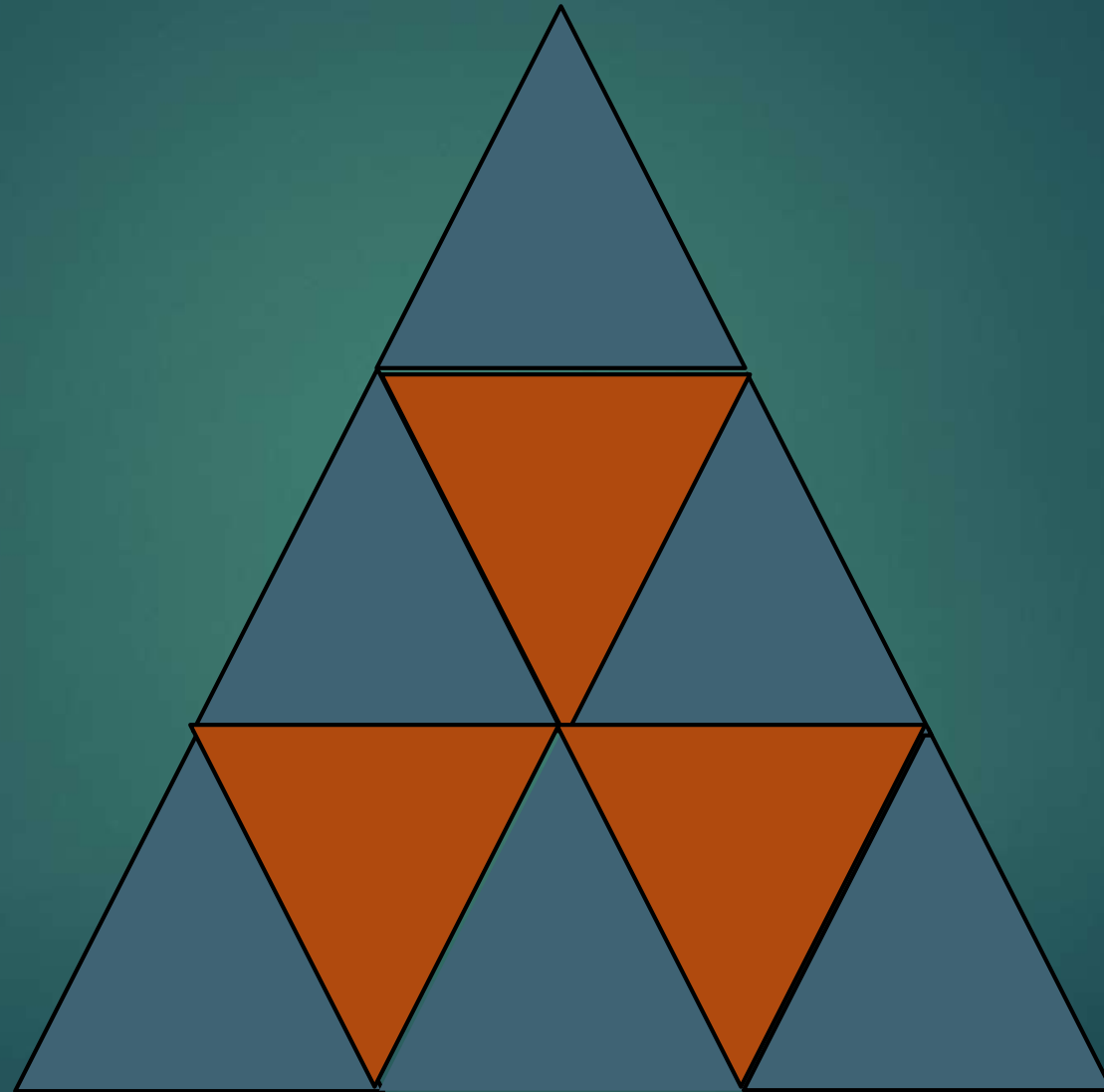
Reasons we forget

- ▶ Distraction, inattention, information overload: inattention causes lack of encoding
- ▶ Stress: when you're stressed, you're preoccupied, and if you're preoccupied, you're not paying attention.
- ▶ Too much alcohol
- ▶ Fatigue and lack of sleep
- ▶ Aging
- ▶ Neurodegenerative disease.

Reasons we remember

- ▶ Something emotionally arousing will be remembered after a single experience.
 - ▶ If we get embarrassed, we will remember.
- ▶ Sleep is essential for learning and retention.

Try This: How many triangles?



13 Triangles

Ranking of **MOST-FEARED** Disabling Diseases – 14 country study

1. Quadriplegia
2. **Major NCD**
3. Active psychosis
4. Paraplegia
5. Blindness
6. Major depression
7. Drug dependence
8. HIV infection
9. Alcoholism
10. Total deafness
11. Mild mental retardation
12. Incontinence
13. Below-knee amputation
14. Rheumatoid arthritis
15. Severe migraine
16. Infertility
17. Vitiligo on the face

Major Neurocognitive Disorders (NCD)

How many major forms of Major NCD
are there?

Protein aggregation: Neurodegenerative diseases

- Insidious onset; gradual progression
- Abnormal accumulation of a protein
- Focal vulnerability: regions & network

Neurodegenerative Disorders (Major NCDs)

- ▶ All have abnormal protein aggregate that kills cells
- ▶ All have rare genetic and more common sporadic (unknown reason) forms
- ▶ All have
 - ▶ Preclinical phase
 - ▶ Early symptom phase, i.e. mild NCD
 - ▶ Symptomatic phase, i.e. dementia/major NCD
- ▶ Major NCDs often do not come in pure form
 - ▶ Vascular & Alzheimer's
 - ▶ Parkinson's develop AD features and vice versa

Mild NCD: Mild Cognitive Impairment

1. Memory or Cognitive Complaint severe enough to be noticeable to others
 2. Normal everyday functioning
 3. Normal General Cognitive Function
 4. Abnormal Memory or Cognitive change for age on testing
 5. Not major NCD
- ▶ Some with MCI go on to develop Major NCD.
 - ▶ Some with MCI do not progress to Major NCD,
 - ▶ Some with MCI at one point in time later revert to normal cognitive status.

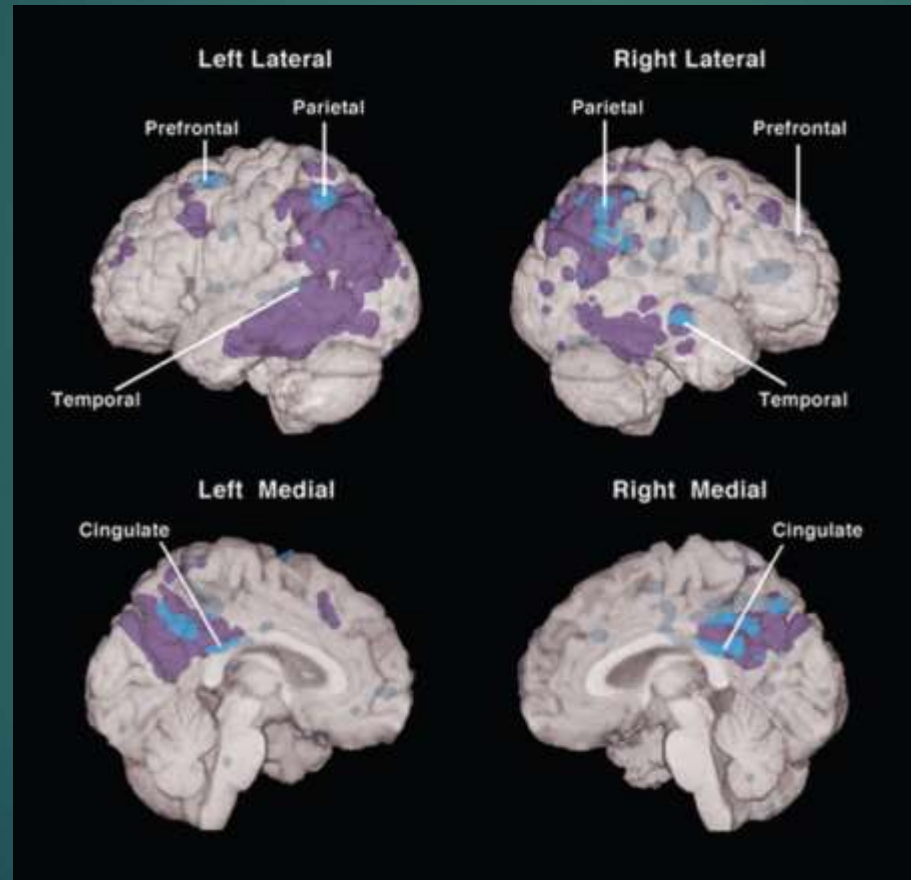
2012 Mayo Clinic MCI study

- More men than women develop mild NCD
- Amnestic mild NCD is 2x greater.
- Those less educated or not married had higher rates of mild NCD.

Known Culprits: Molecular Bases of Major NCDs

<u>Type</u>	<u>Molecule/Abnormal Proteins</u>
Alzheimer's	AB42, Tau
FTD	Ubiquitin, Tau, TDP-43
ALS	Ubiquitin inclusion, TDP-43
Parkinson's	α -synuclein
Huntington's	Intranuclear inclusion, Huntington's protein
JCD	Prion, spongiosis
CTE	Tau, TDP-43

FMRI abnormalities in cognitively normal 20-39 y.o. with double APOE4

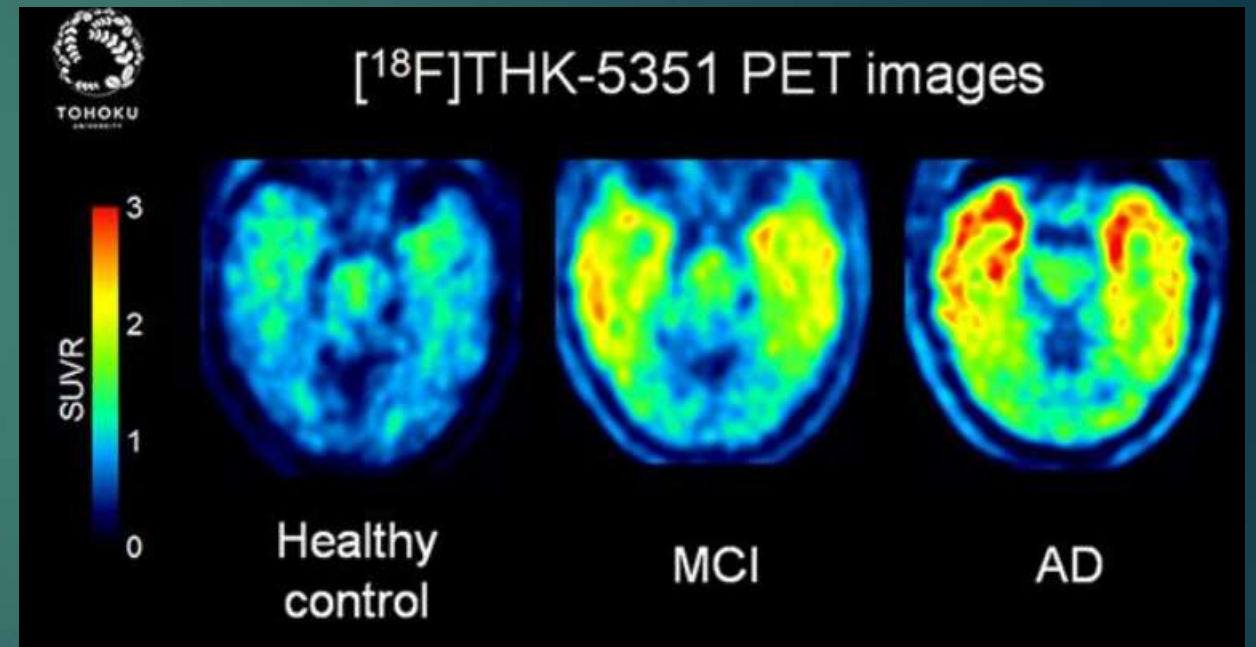
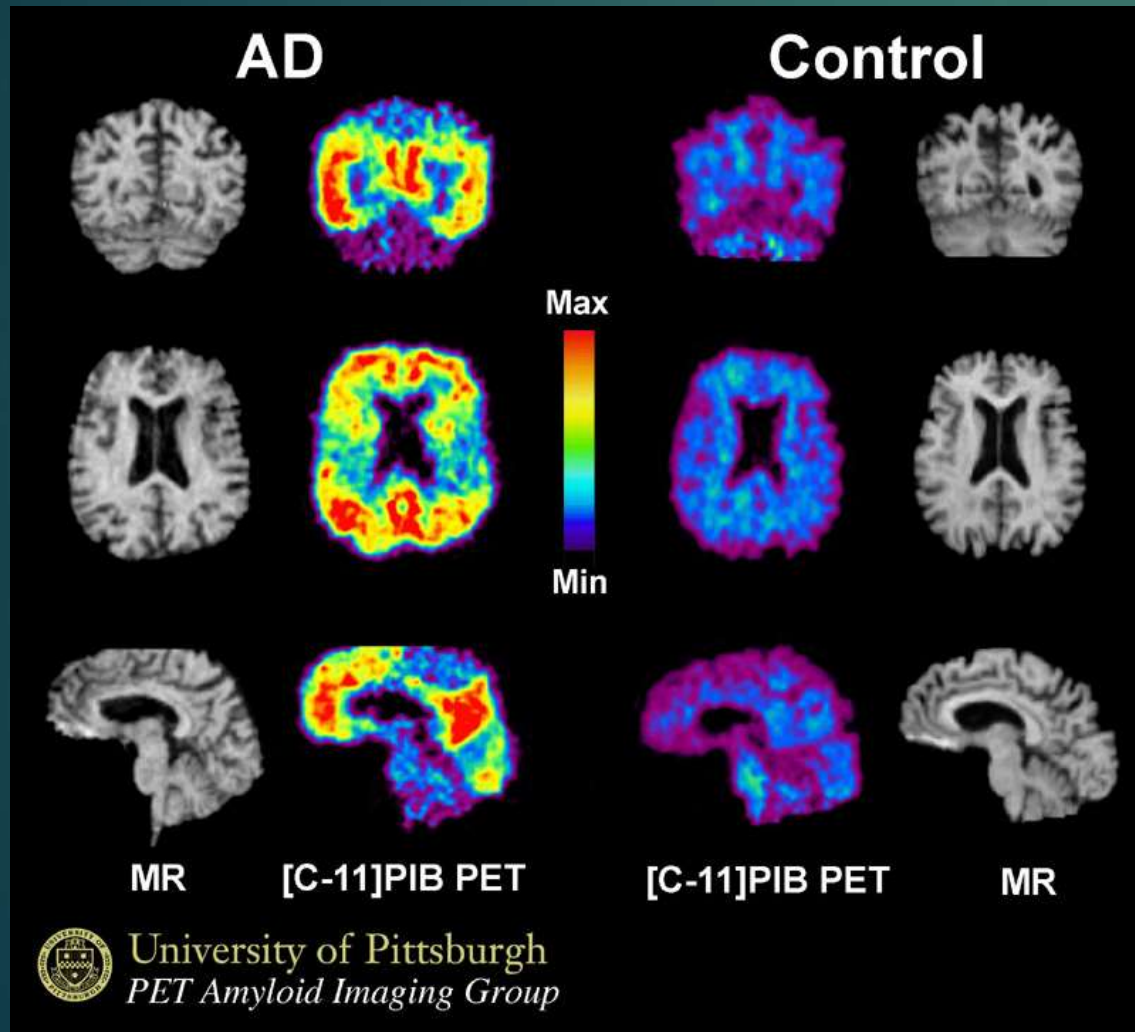


Cerebral metabolic rate for glucose declines; hypometabolic Parietal & Temporal lobes

Biomarkers: AD Tests of future

- ▶ 1 for **Tau deposition**:
 - ▶ PET AV1451
- ▶ 2 for brain A β plaque deposition: how much abnormal protein
 - ▶ CSF A β 42
 - ▶ PET amyloid imaging, using Pittsburgh Compound B (PIB)
- ▶ 3 for neurodegeneration
 - ▶ CSF tau
 - ▶ deficits in glucose uptake on FDG-PET
 - ▶ and **structural MRI (most predictive of Major NCD)**

Pittsburg B Compound (& Amvid) labels Amyloid Plaques on PET & 18 F-THK-5361 Tau : AD vs. Normals



Best Biomarker Conversion to AD Predictors

- ▶ APOE 4 allele frequency
- ▶ CSF proteins (AB-42, total tau)
- ▶ Glucose metabolism (FDG-PET)
- ▶ Hippocampal volume via MRI: best predictor of cognitive decline

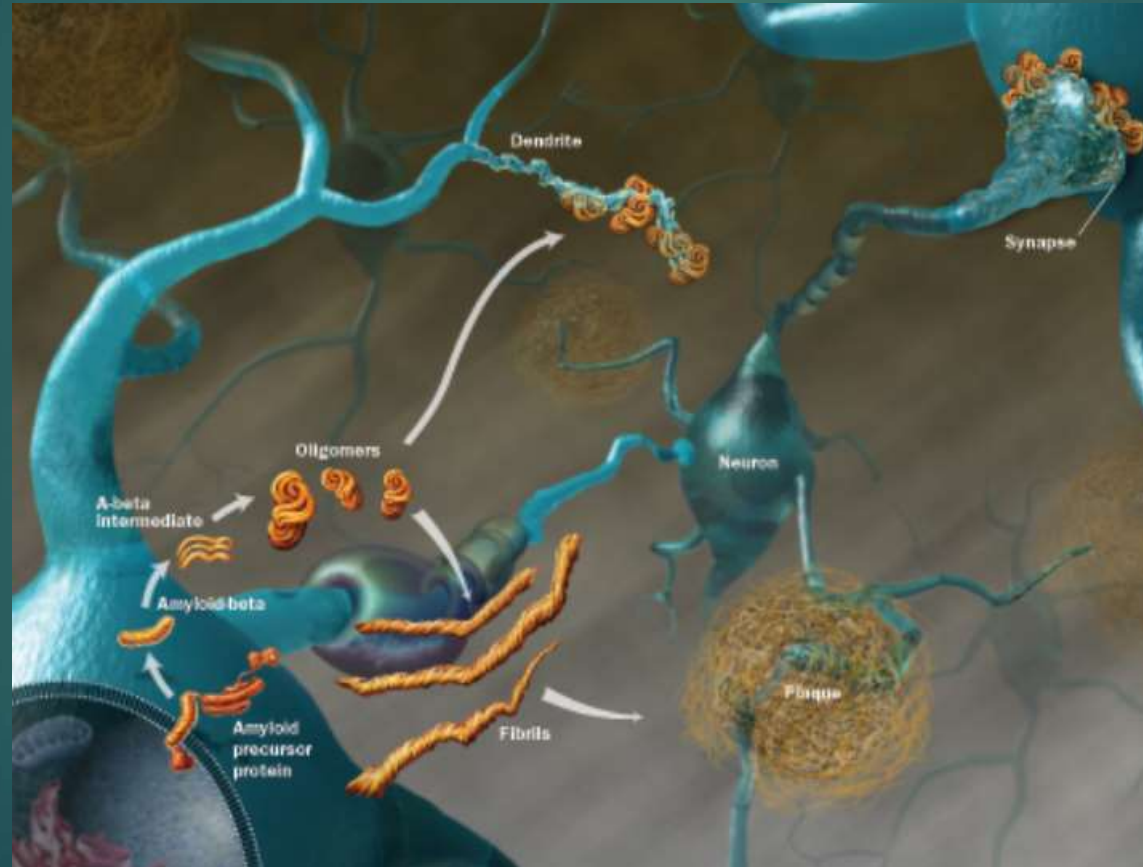
Agatha Christie
(1890 –1976)



Agatha Christie

- ▶ 80 novels in 85 years
- ▶ Novel # 73, at age 81:
 - ▶ 20% fewer words
 - ▶ 18% more repeated phrases
 - ▶ 3 x greater indefinite words (thing, something, anything)
- ▶ Her novel *Elephants Can Remember* (1972)
 - ▶ Aging female novelist suffering memory loss calls in Hercule Poirot to solve murder

Current AD Culprits: abnormal protein Beta Amyloid & Tau

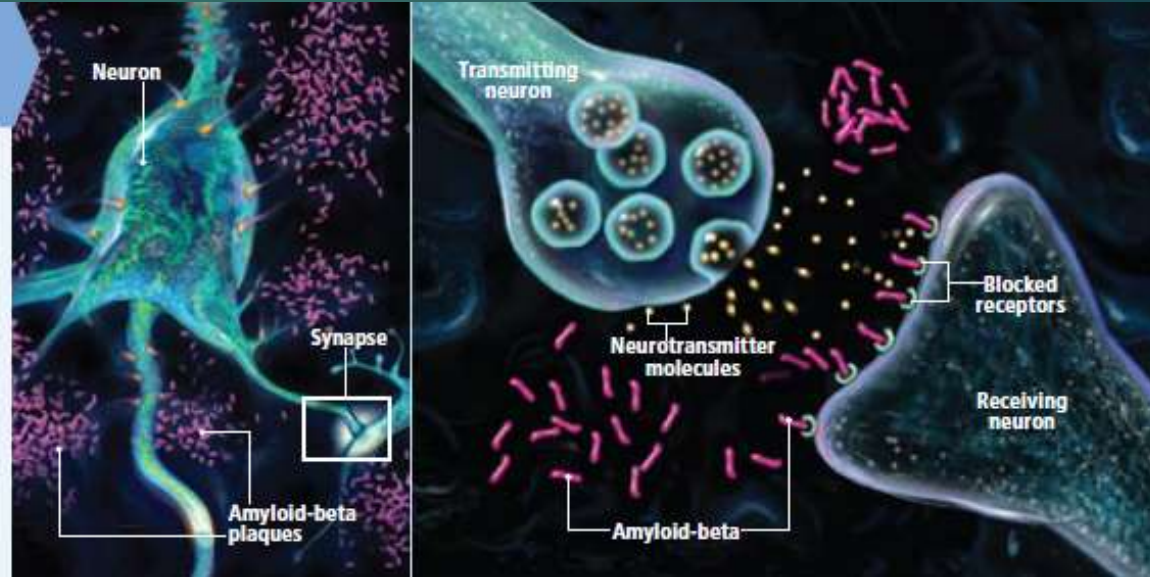


Step 1: Increasing amounts of Beta Amyloid starting 25 years before diagnosis

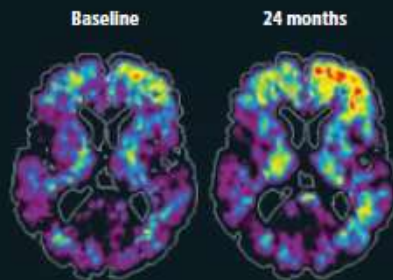
AMYLOID ACCRETION

5–20 years before diagnosis of Alzheimer's dementia

Early on, a protein fragment called amyloid-beta aggregates in the brain centers that form new memories. The amyloid buildup, a biomarker detected by the presence of plaques, results in damage to synapses, the interface between neurons (*detail*). Amyloid blocks chemical signals (neurotransmitters) from reaching receptors on receiving neurons. This buildup can be captured by various forms of neuroimaging, including positron-emission tomography (PET), that detect a radioactive compound, Pittsburgh imaging compound-B (PIB), able to bind specifically to amyloid. A spinal tap can also be used to gauge the amyloid biomarker.



BIOMARKER TECHNOLOGIES



PET scans show increasing retention in the brain's frontal lobes of the amyloid-beta tracer PIB over the course of two years in a 74-year-old, even while the subject remained cognitively normal.

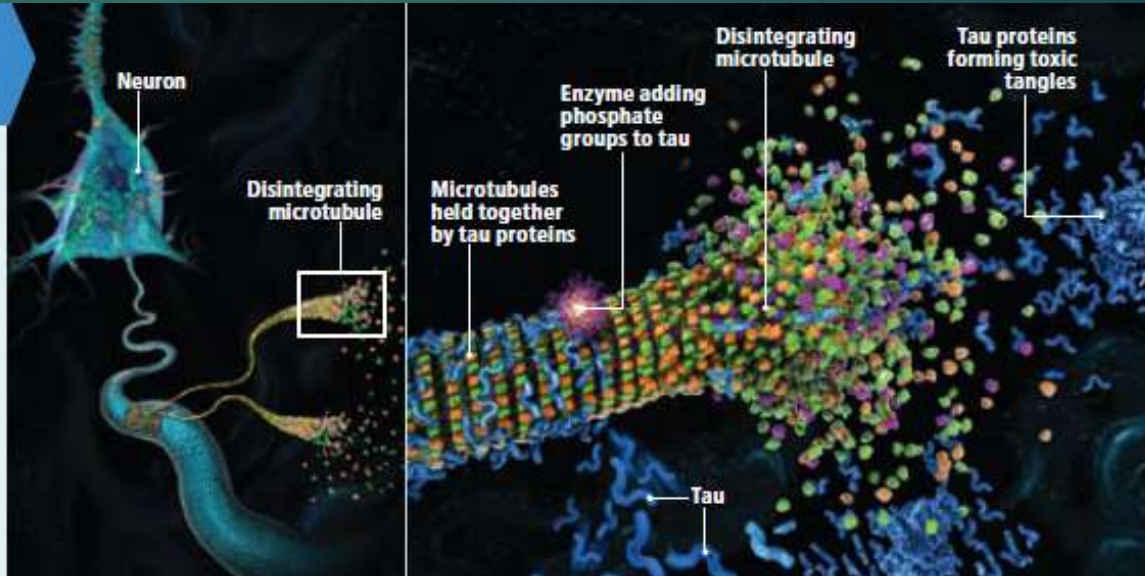
30-40% of cognitively normals have significant levels of Beta Amyloid

All Alzheimer's patients have significant levels

Step Two: Tau Buildup – 15 years before

TAU BUILDUP 1–5 years before diagnosis

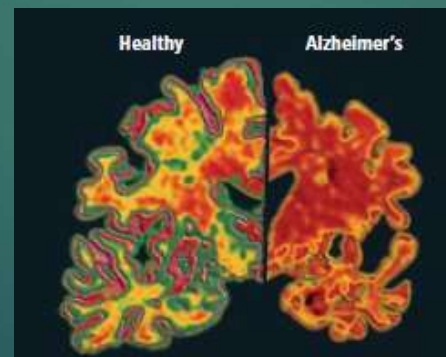
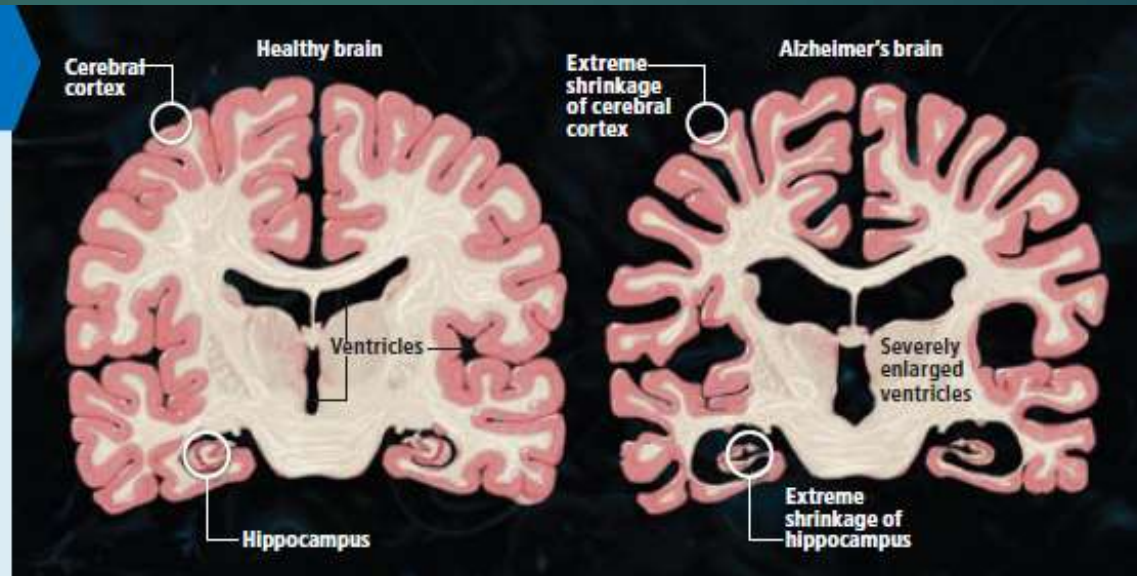
Before symptoms would justify an Alzheimer's diagnosis, a protein called tau inside neurons begins misbehaving. Normally tau helps to maintain the structure of tiny tubes (microtubules) critical to the proper functioning of neurons. But now phosphate groups begin to accumulate on tau proteins (*detail*), which detach from the microtubules. The tubules go on to disintegrate, and tau then aggregates, forming tangles that interfere with cellular functions. A sample of spinal fluid can detect this process.



Step Three: Atrophy (Neuron death)

BRAIN SHRINKAGE 1–3 years before diagnosis

As the underlying disease process advances, nerve cells start to die, and patients and family notice memory and other cognitive lapses. Cell death shrinks the brain in areas that involve memory (the hippocampus) and higher-level brain functions (the cortex) and thus can be tracked with a form of magnetic resonance imaging that measures brain volume. Such shrinkage accelerates and ultimately involves many areas of the brain.



Computer graphic of slices through a normal brain and an Alzheimer's brain, derived from volumetric magnetic resonance imaging, shows considerable shrinkage (*right*) from degeneration and death of nerve cells.



Normal



Alzheimer



Alzheimer's Disease = Amyloid-facilitated tauopathy

- ▶ AD as 2 punch disease: BA 1st, then Tau along DMN network
- ▶ AD is an “amyloid-facilitated tauopathy,” in which the accumulation of tau tangles is more closely correlated with synapse loss, neurodegeneration, and the development of cognitive decline than the accumulation of amyloid beta.

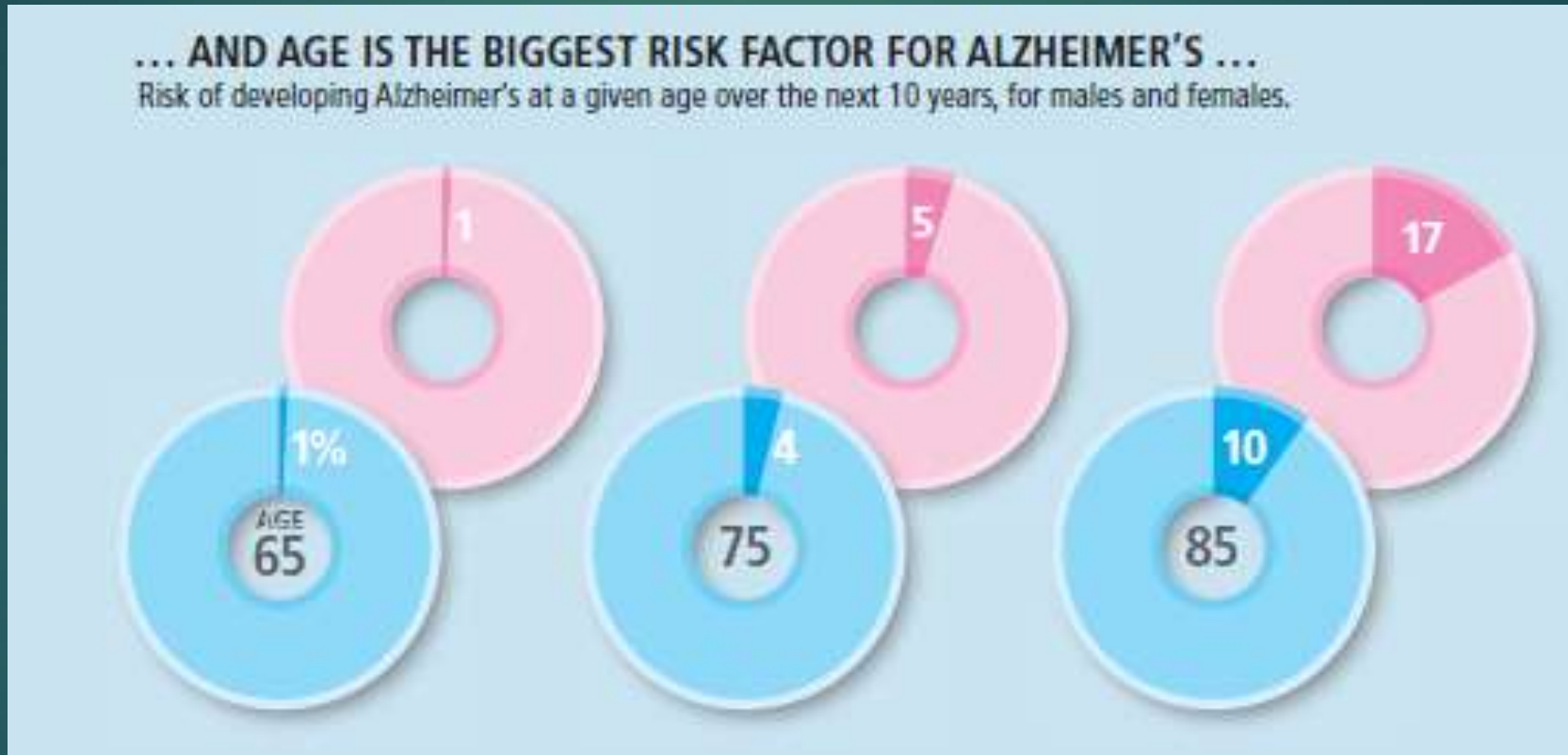
AD Timeline to Major NCD

- ▶ 25 years before, beta-amyloid protein levels in the CSF
- ▶ 15 years before, beta-amyloid can be detected in the brain. (the earliest sure sign of the disease).
- ▶ 15 years before, the brain begins to shrink. Neurons begin to die.
- ▶ 10 years before, brain metabolism slows down & episodic memory is impaired.
- ▶ 5 years before, cognitive impairment sets in.
- ▶ Year 0, diagnosis of Major NCD

Cognitive Decline in Elderly

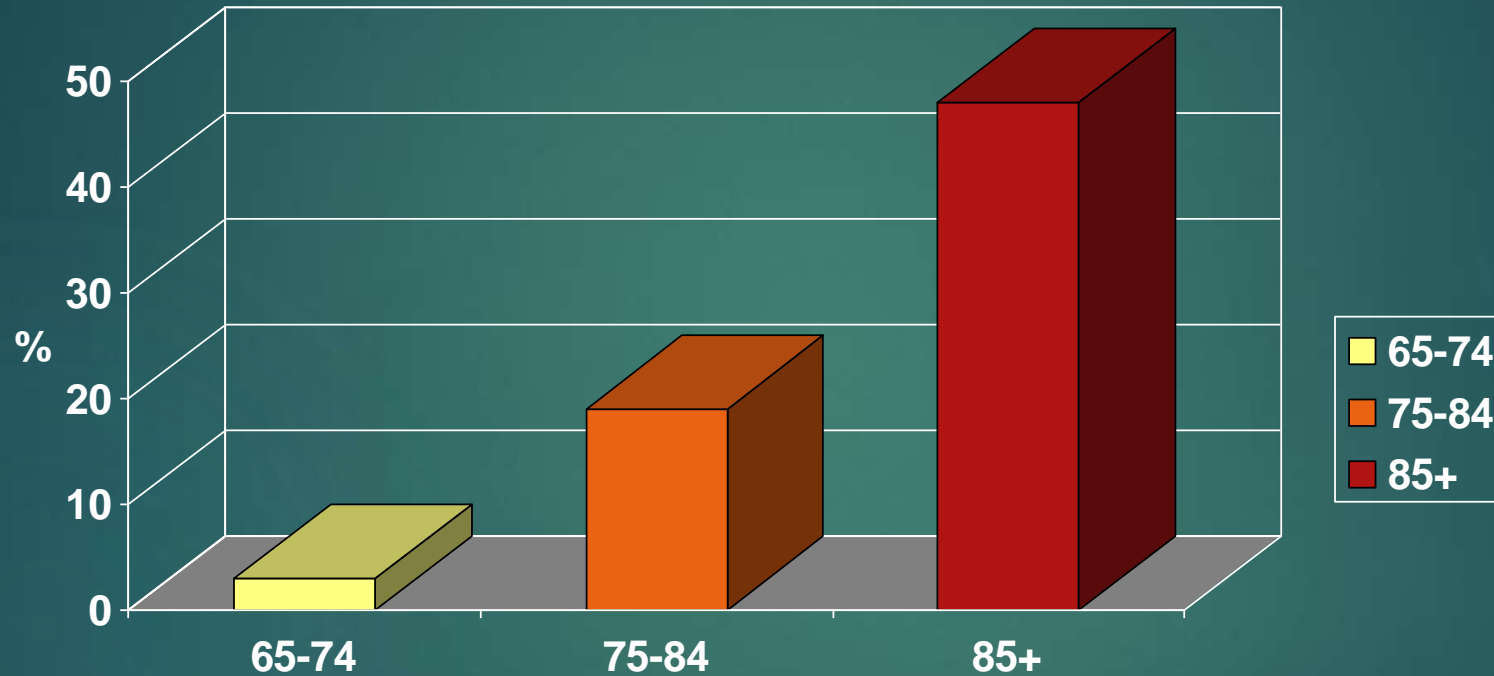
- Of all Americans in 2002, aged 71+:
- 65% were cognitively normal
- 21 % had some mild NCD
- 14% had dementia/major NCD

Age is greatest risk factor;
Major NCD doubles every 5 years after 65



Prevalence of Alzheimer's Disease by Age

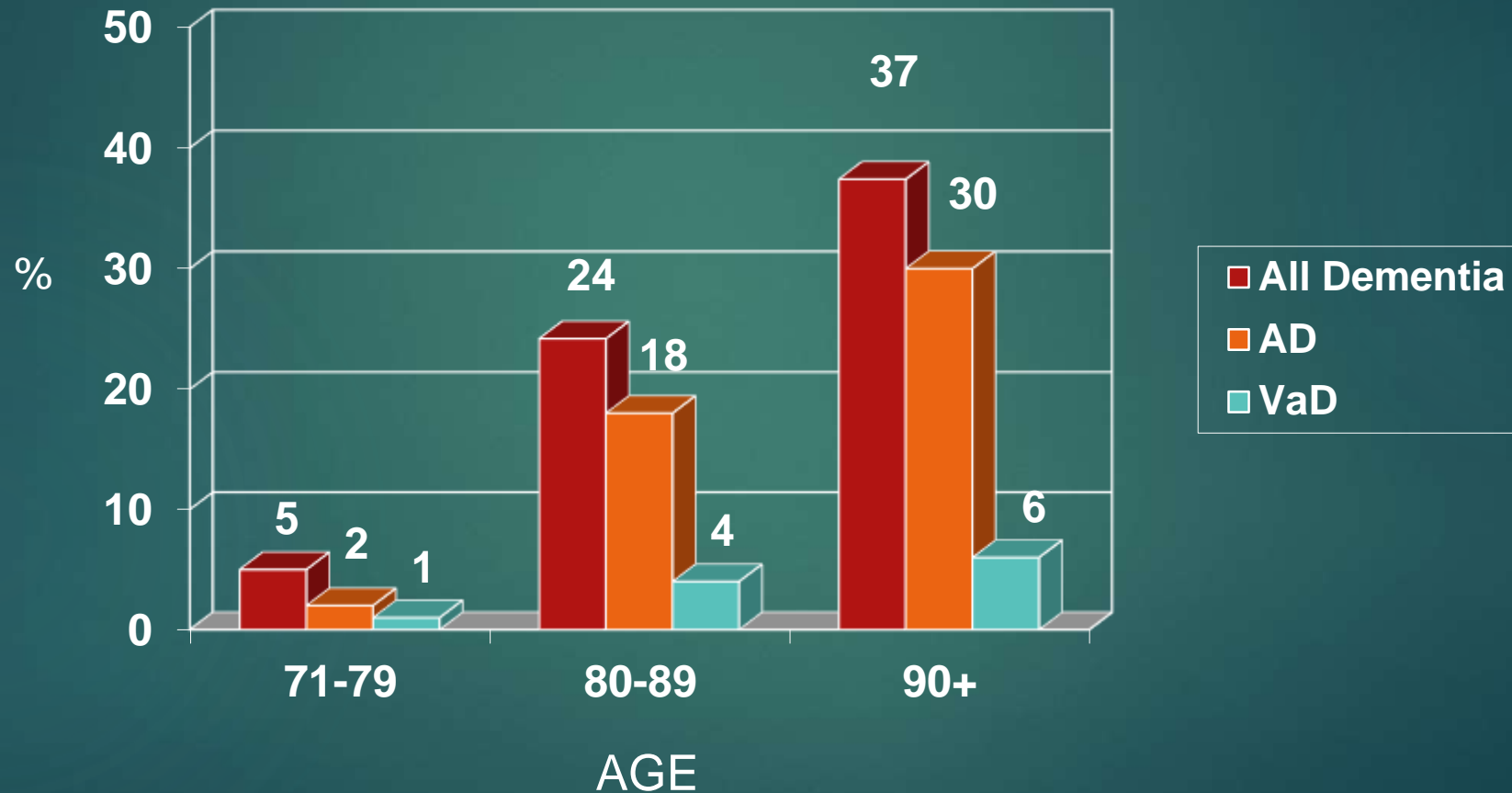
1% at age 60, doubles every five years.



Evans, D.A. et al. (1989). Journal of the American Medical Association. Vol. 262: 2251-2256.

1 in 7 (14%) after 70:

Prevalence of Major NCD in 2002 in USA



Executive measures: TMT, COWAT

Plassman, et. Al., 2007

Over 65: 1 in 9 have Alzheimer's

2010 AD Data:

AD = Most common type of dementia;
60-80 % of cases; ~ 50% of these
cases involve solely Alzheimer's
pathology

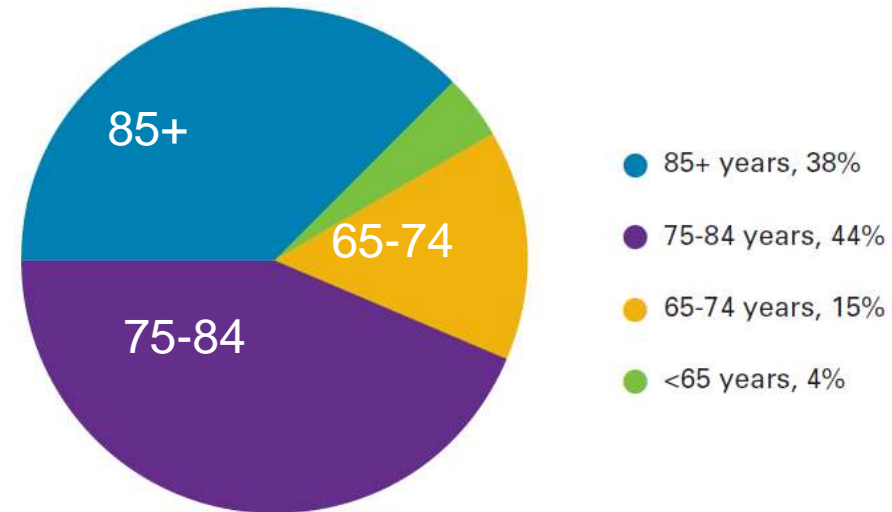
82 percent with AD = age 75+

14 % of people age 71+ in the USA
have dementia

50% of the estimated 5.2 million
Americans with Alzheimer's may not
know they have it.

figure 1

Proportion of People With Alzheimer's
Disease in the United States by Age



Percentages may not total 100 because of rounding.
Created from data from Hebert et al.^{(114), A3}

Higher NCD Risk & Ethnicity:

Life experience factors

- ▶ Original Studies: Age 65+ African Americans & Hispanics had 2 x higher rate of AD
- ▶ Higher rates of hypertension, diabetes?
- ▶ Higher rates of low education, low quality of education, low income, rural living (all risk factors for AD)
- ▶ Newer Studies: Higher dementia risk accounted for, not by race, but by low childhood SES, low adult literacy, and low exercise

Women are the epicenter of AD crisis

- ▶ A woman's AD risk at age 65 is 1 in 6, compared with nearly 1 in 11 for a man; women with early sx's decline at twice the rate as men (2 pts per year on cognitive tests)
- ▶ Women in their 60s are twice as likely to develop AD as they are to develop breast cancer.
- ▶ More likely to be caregivers of those with Alzheimer's: More than 3 in 5 unpaid Alzheimer's caregivers are women

Kaiser & UCSF 2016 study

- ▶ 274,000 Northern California Kaiser Permanente members over 14 years encompassing six racial or ethnic groups; included virtually every Kaiser member in Northern California who was at least 64 when the study began in January 2000; nearly 22 percent were diagnosed with dementia by 2013
- ▶ African Americans had the highest incidence of dementia-related disease. Their risk was 65 percent higher than that of Asian Americans, who had the lowest rates
- ▶ American Indians and Alaska Natives also had a higher dementia risk, followed by Latinos, Pacific Islanders and whites.
- ▶ These are large differences in people who have equal access to care. The next big question is why; age, sex, cardiovascular disease, hypertension, depression, & hypertension did not account for difference;
- ▶ But no education or APOE4 data

Women get worse AD

- ▶ One study of about 400 people with mild cognitive impairment (141 women, 257 men), mostly in their mid-seventies, showed that **women deteriorate twice as fast as men with the condition in both cognitive and functional abilities.**
- ▶ Additionally, women declined much more dramatically than men in cognition, function and brain size following surgery with general anesthesia,

Good News: Less Major NCD

- ▶ Incidence of dementia has declined gradually over the past 40 years in higher income developed nations
- ▶ Better education and CV health effects
- ▶ These incidence declines will be overwhelmed by increases in NCD brought on by population aging and negative health trends such as diabetes and obesity.

The Neurodegenerative Disorders

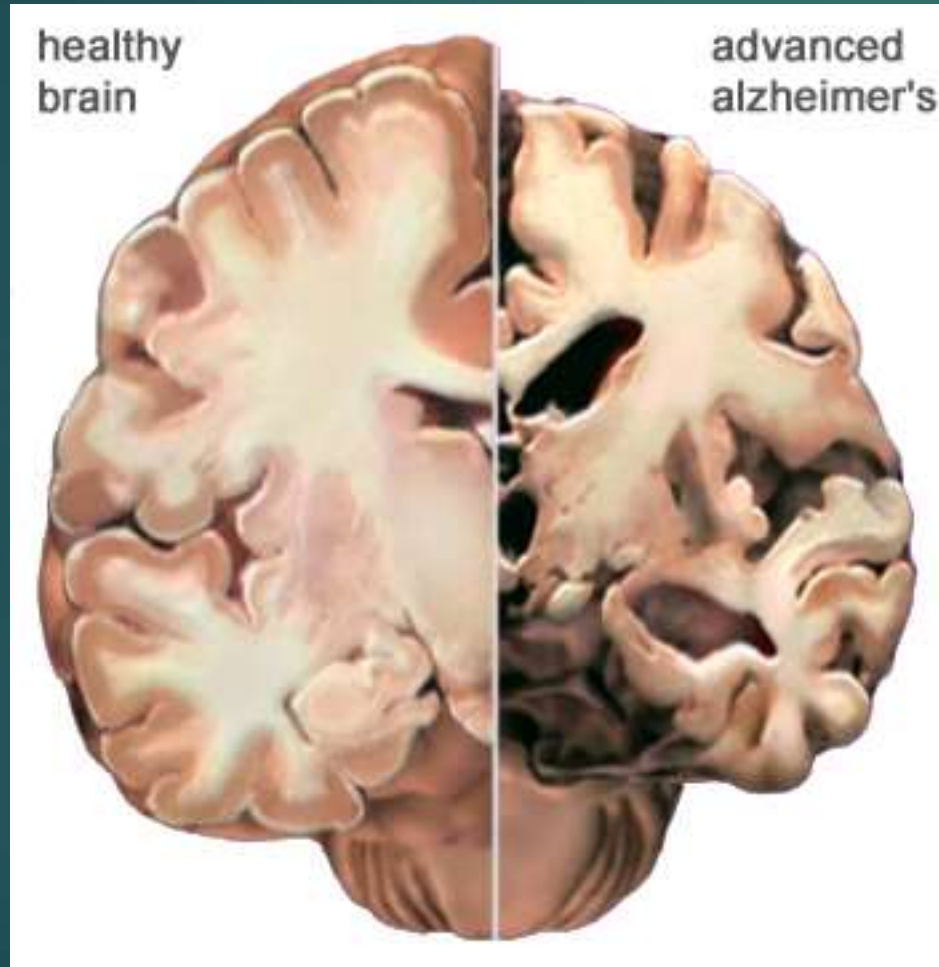
- ▶ Alzheimer's Disease
- ▶ Lewy-Body Disease
- ▶ Vascular Disease
- ▶ Frontal Temporal Disease
- ▶ Chronic Traumatic Encephalopathy
- ▶ Creutzfeldt-Jakob Disease (CJD)

Alois Alzheimer, 1864-1915: In 1901,
First diagnosed patient with Alzheimer's, Auguste Deter.



51 y.o.. woman;
1st sx of pathological jealousy of husband,
“I have lost myself,” then rapid decline with amnesia

Neuropathology of Alzheimer's



1 Atrophy

2 Enlarged
Ventricles

3 Reduced
Hippocampal
Volume

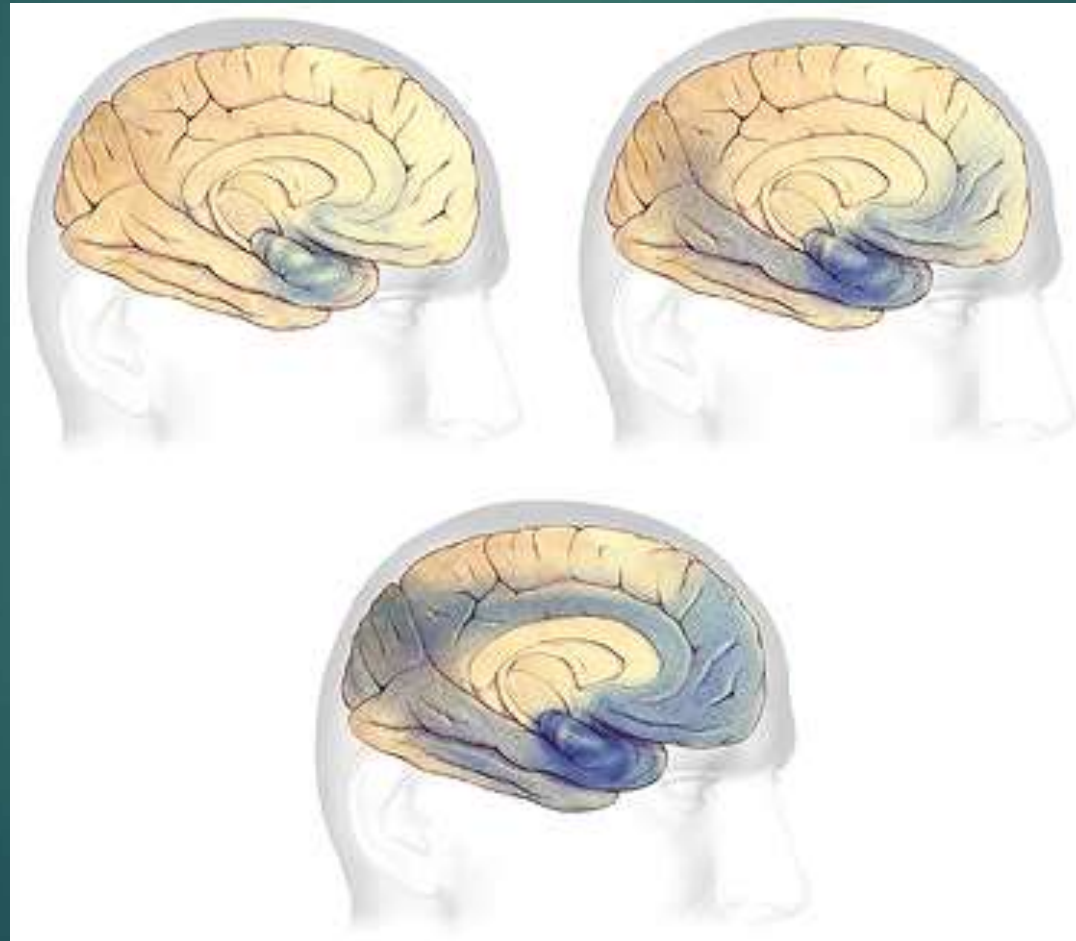
Core AD issue: No tape/CD recorder

- ▶ Encoding Deficit: tape recorder does not work
- ▶ People with AD no longer have the ability to remember what's new now; they do not have the ability to remember new life experiences.
- ▶ Their brain has stopped recording
- ▶ The record machine is permanently broken.

Alzheimer's Disease: 70% of ND disease

- ▶ Insidious gradual decline
- ▶ Hallmark is memory loss: Encoding deficit; rapid rate of forgetting; poor delayed recall
- ▶ Hippocampal loss first: 5% ↓↓ per year
- ▶ >67% of pts are at moderate level NCD at first diagnosis
- ▶ AD is a fatal disorder, inevitably progressive and terminates in cognitive and functional incapacity and death.

AD Progression in the Brain



AD Symptoms 1

Proportion of First Symptoms:

Memory 55%

Language 15%

Visual Spatial 13%

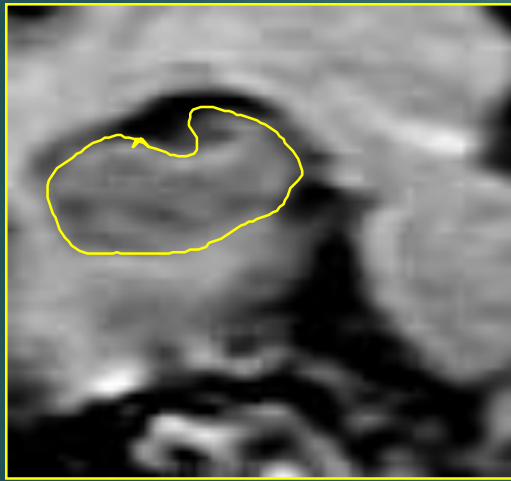
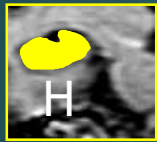
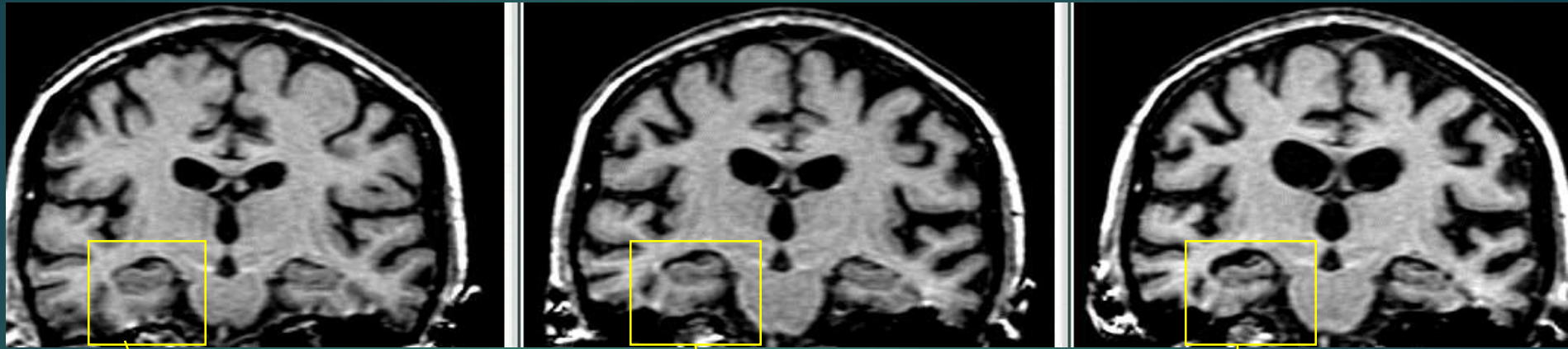
Executive 13%

Behavioral 4%

AD Symptoms 2

▶ Family Home behavior description:

- Question Repetitions 70%
- Agitation 66%
- Dependent 56%
- Incontinence 43%
- Dressing difficulty 41%
- Wandering 40%



Time 0



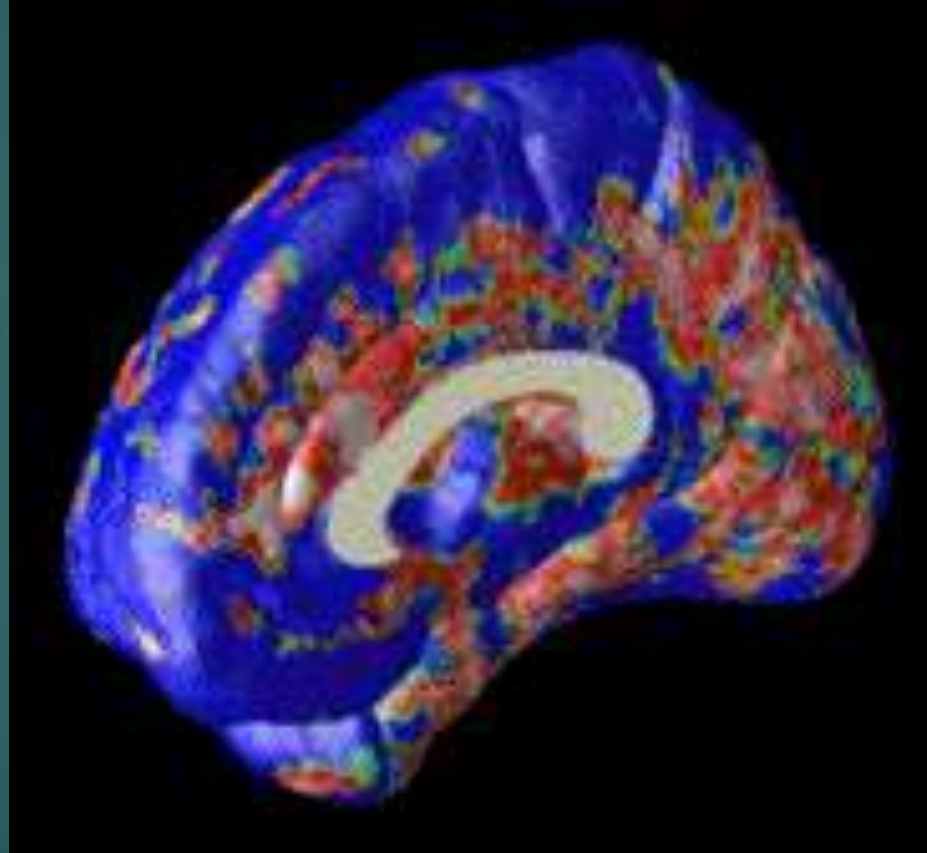
18 months



36 months

Hippocampal Atrophy: Serial coronal MRI of an individual with initially mild AD

Alzheimer's: 18 months of atrophy

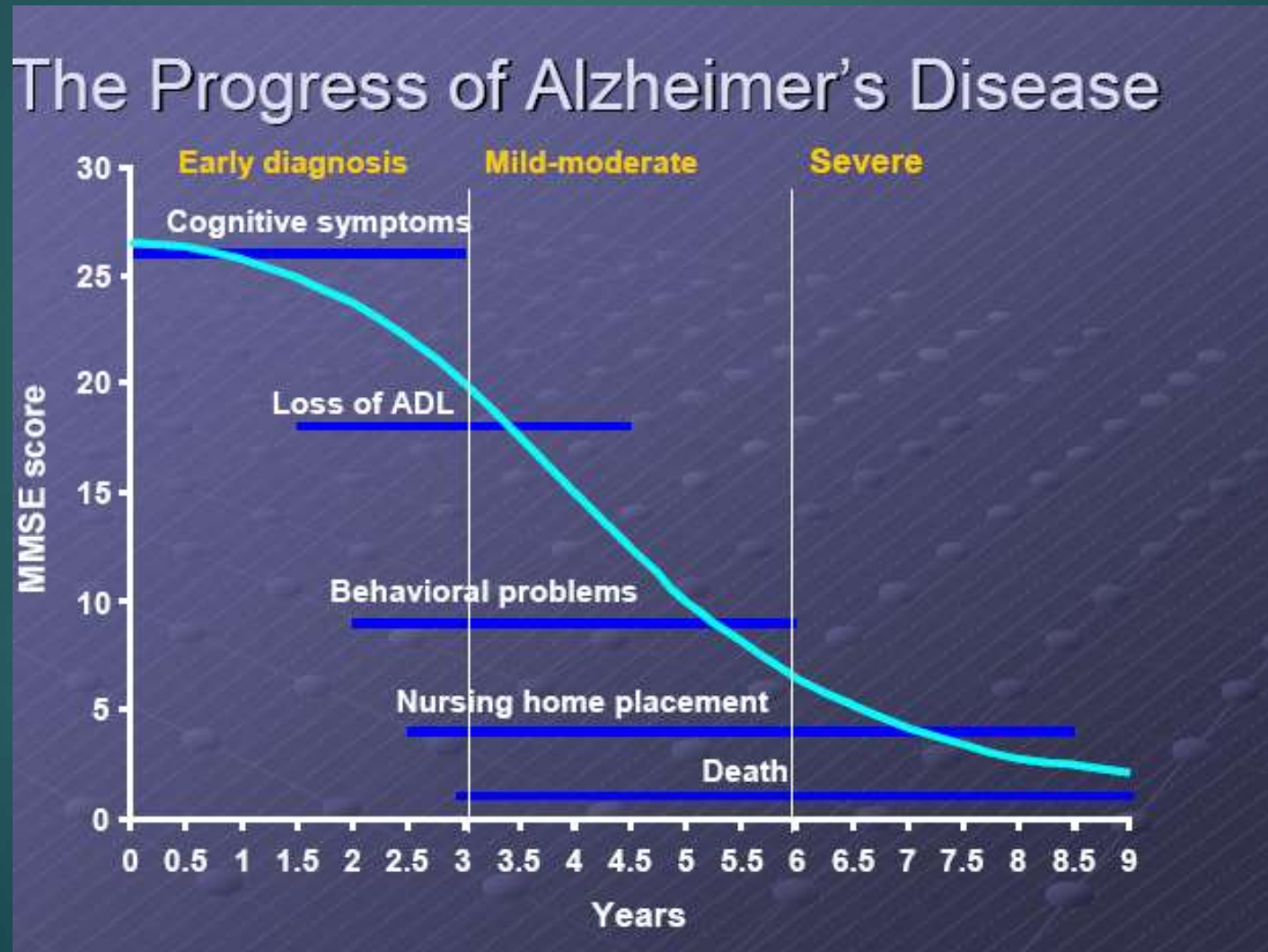


Neuron death & atrophy in White areas

Alzheimer's = Most are Not Diagnosed

- ▶ Not Diagnosed: Three-quarters of the 36 million people living with Major NCD
- ▶ 50% of people with AD do not know they have it.

Alzheimer's Progress by Cognitive Decline (MMSE score)



3 stages of Alzheimer's

▶ Preclinical –

- ▶ 25 years or more; asymptomatic beta amyloid (BA) accumulation
- ▶ Evidence of abnormal biomarker patterns, but without signs of cognitive impairment.
- ▶ No clinical dx, may not progress.

▶ Mild NCD:

- ▶ BA increase + neurodegeneration (dead neurons) + cognitive ↓
- ▶ Diagnosis is made clinically and by exclusion of other causes.

▶ Alzheimer's Major NCD

- ▶ Significant neurodegeneration (severe neuron death)

Older AD less aggressive

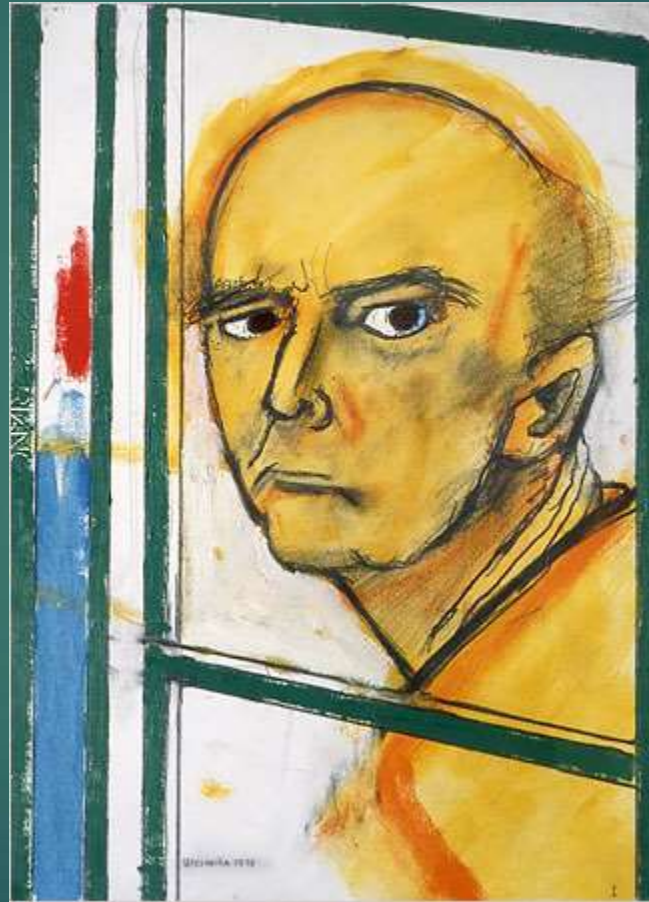
- ▶ The greatest risk factor for Alzheimer's disease (AD) is advancing age.
- ▶ AD hits hardest among the “younger elderly” – age 60-70s – show faster rates of brain tissue loss and cognitive decline than AD patients 80 years and older.

A picture is worth a 1000 words:
Painter **William Utermohlen's self-portraits**; age 61, AD dx



1967

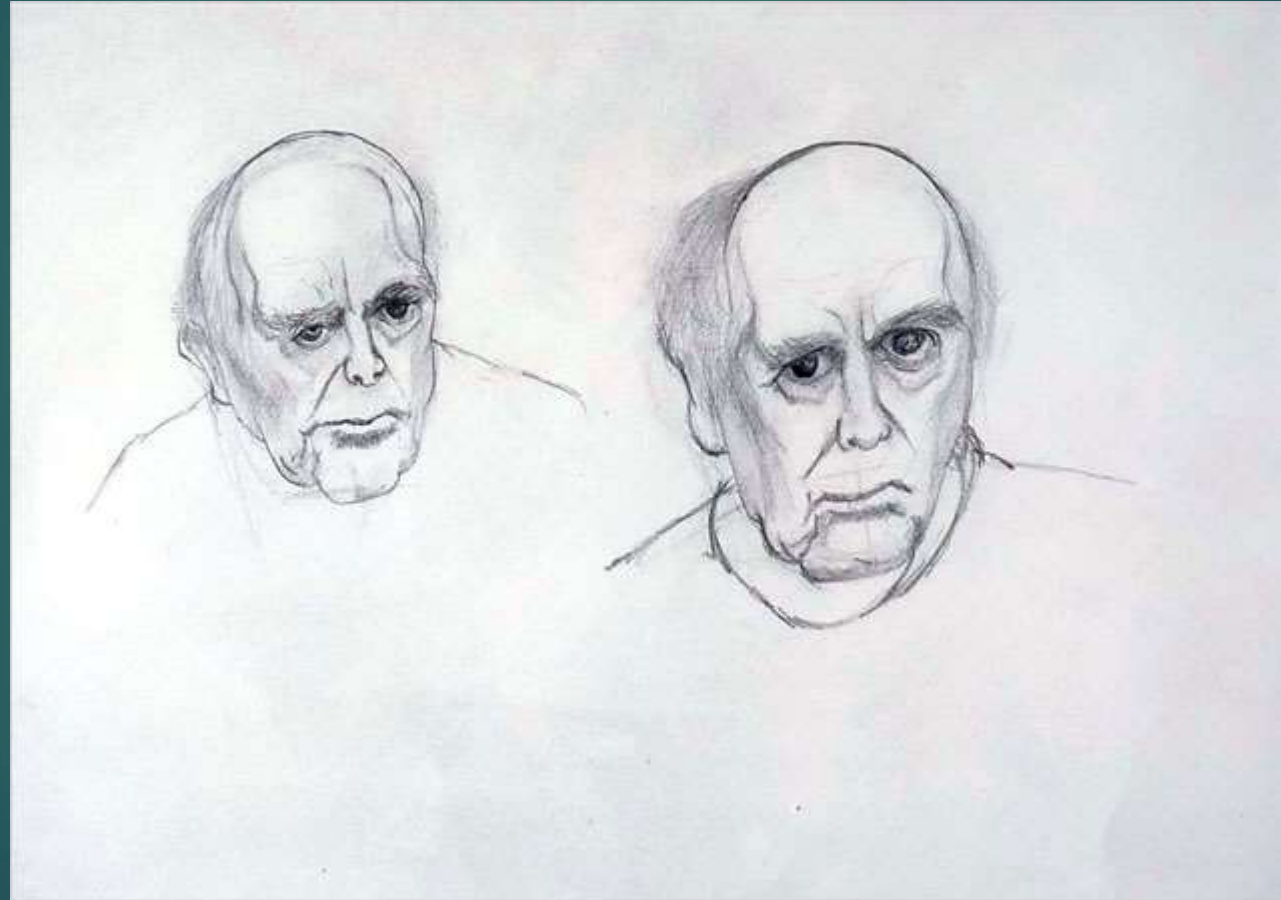
Self Portrait: 1996



Self Portrait: 1996



Self Portrait: 1996

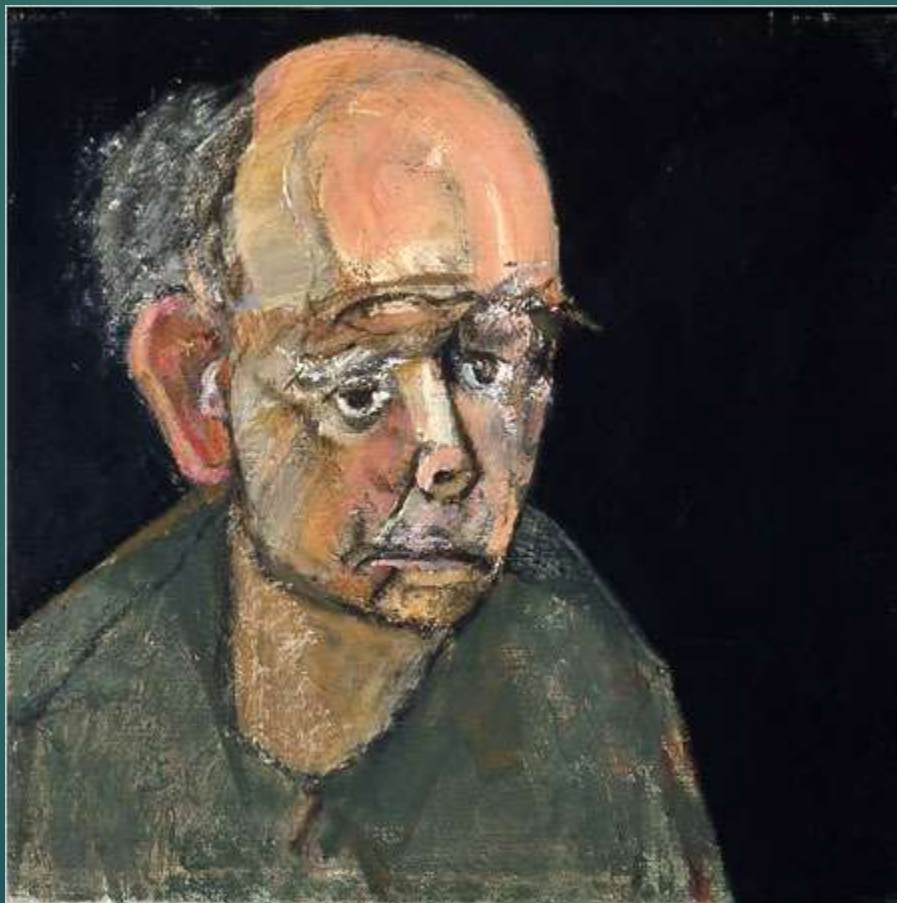


Self Portrait: 1997



Decides to donate his body to science

Self Portrait: 1997



Self Portrait: 1998



Self Portrait: 1999



2 years to complete

Self Portrait: 2000



Self Portrait 2000+



Self Portrait 2000+



William Untermyer – self-portraits correlate with cognitive decline

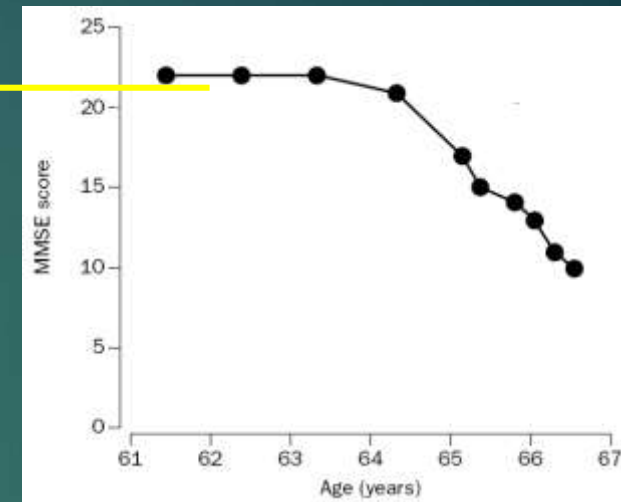
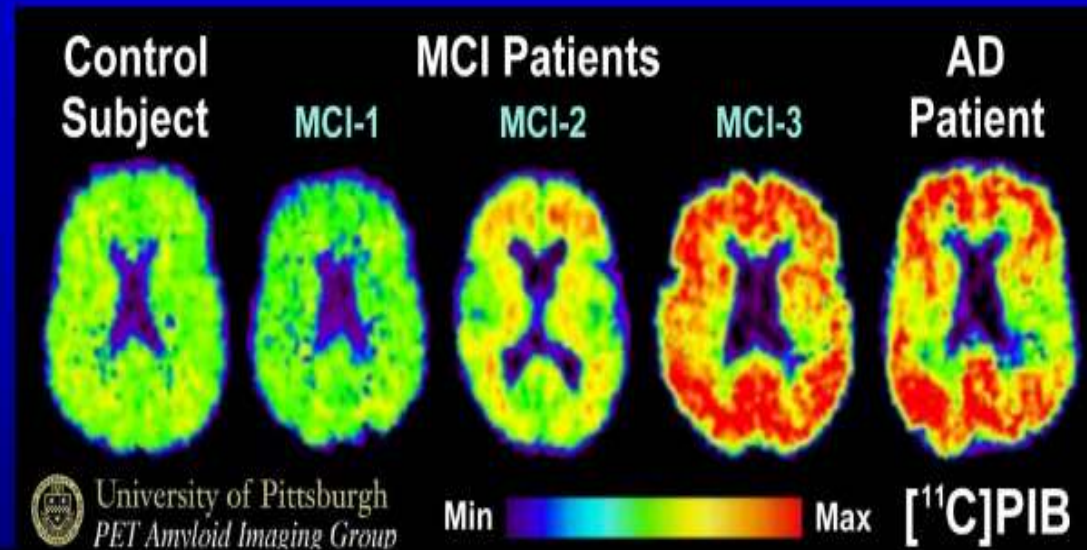


Figure 3: Self-portrait series
Painted at age 60 years (A), at 62 years (B), at 63 years (C), and at 64 years (D). Pencil drawing at age 66 years (E). Abstract self-portrait painted at age 65 years (F).

Crutch SJ, Isaacs R, Rossor MN. Some workmen can blame their tool: artistic changes in an individual with Alzheimer disease. *Lancet*, 2001, 357:2129

PIB-PET (radioactive): Beta Amyloid in Normal to AD

PIB in Controls, MCI, AD



Some MCI's have control-like PIB retention, some have AD-like retention, and some have intermediate retention

Price et al., JCBFM 2005
Lopresti et al., J Nucl Med, in press

100+ Disease Modifying Treatment Trials: 99.6% Failure Rate

- ▶ AN1792 vaccine: 2003 (Eliminated BA; still NCD)
 - ▶ Tramprostate
 - ▶ Flurizan: 2008
 - ▶ Bapineuzumab: 2009
 - ▶ Semagacestat: 2010
 - ▶ Etc.
-
- ▶ Right TX?, wrong stage of disease

Hope for near future: Columbian Prevention Study

- ▶ Eventually treat AD like HTN and heart disease preclinically
- ▶ Columbian study: extended clan of 5,000 people who live in Medellín, Colombia with early onset AD
- ▶ Family members with a presenilin 1 gene mutation begin showing cognitive impairment around age 45, and full Major NCD around age 51; disease they call La Bobera — the foolishness.
- ▶ N = 300; 5 year trial; Roche (Genentech) drug, Crenezumab injection every 2 weeks; massive pre and post testing
- ▶ Also Dominantly Inherited Alzheimer Network (DIAN)
- ▶ Data in 2 years

Lewy Body Variant Disease: 10-15%

- ▶ Alzheimer's cognitive + Parkinson's motor systems (no tremor)
- ▶ Presenting with visual hallucinations (fully formed), lucid periods, movement disorders, falls or syncope
- ▶ Visual Spatial deficits
- ▶ Fluctuations in functioning: confusion, sleepiness, inattention, incoherent speech, task difficulty

Heyman A et al. *Neurology*. 1999;52:1839-1844.

Ballard CG et al. *Dement Geriatr Cogn Disord*. 1999;10:104-108.

Visual Hallucinations in LBD

- Small Animals
- Little People
- Dwarves
- Odd Creatures
- Animals with hats
- Well-formed landscapes



Cases with well-formed visual hallucinations had high densities of LB in the amygdala and parahippocampus, with early hallucinations relating to higher densities in parahippocampal and inferior temporal cortices.

Dendritic, not neuronal, loss in LBD

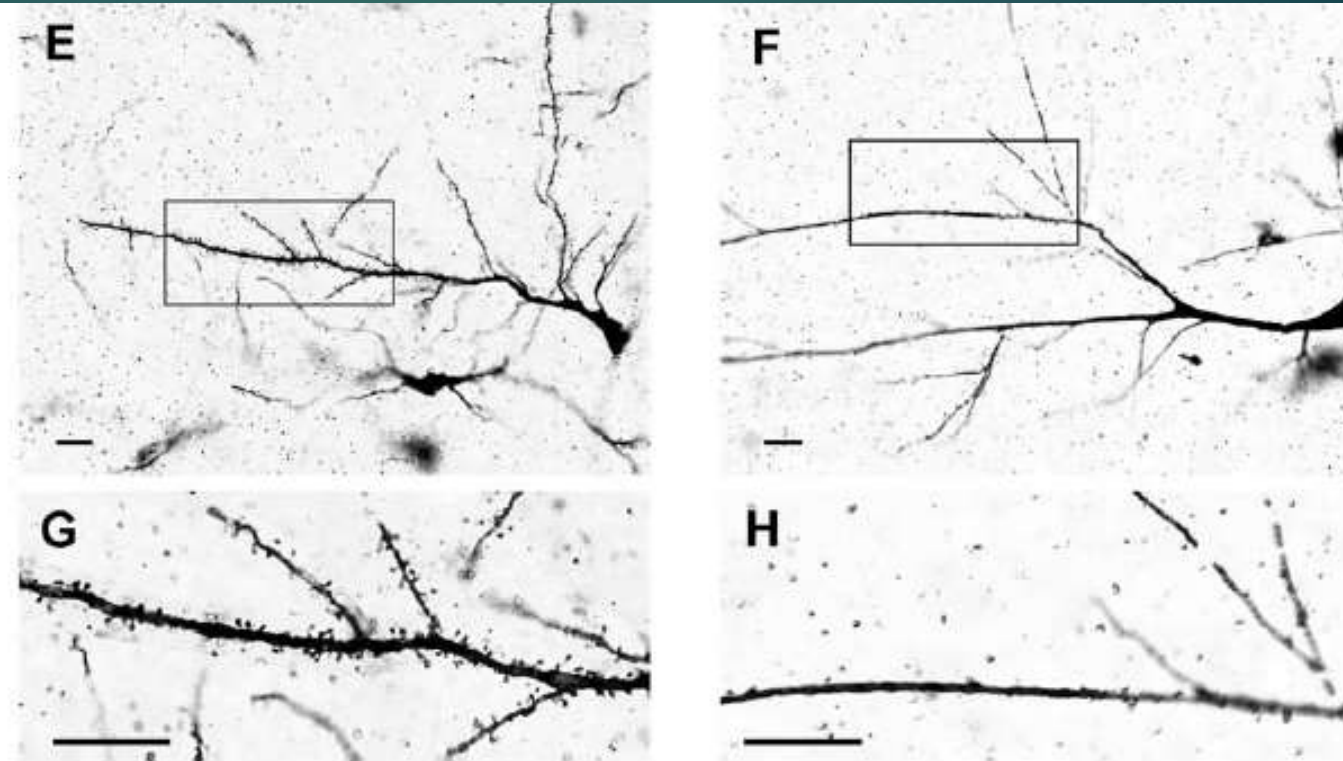
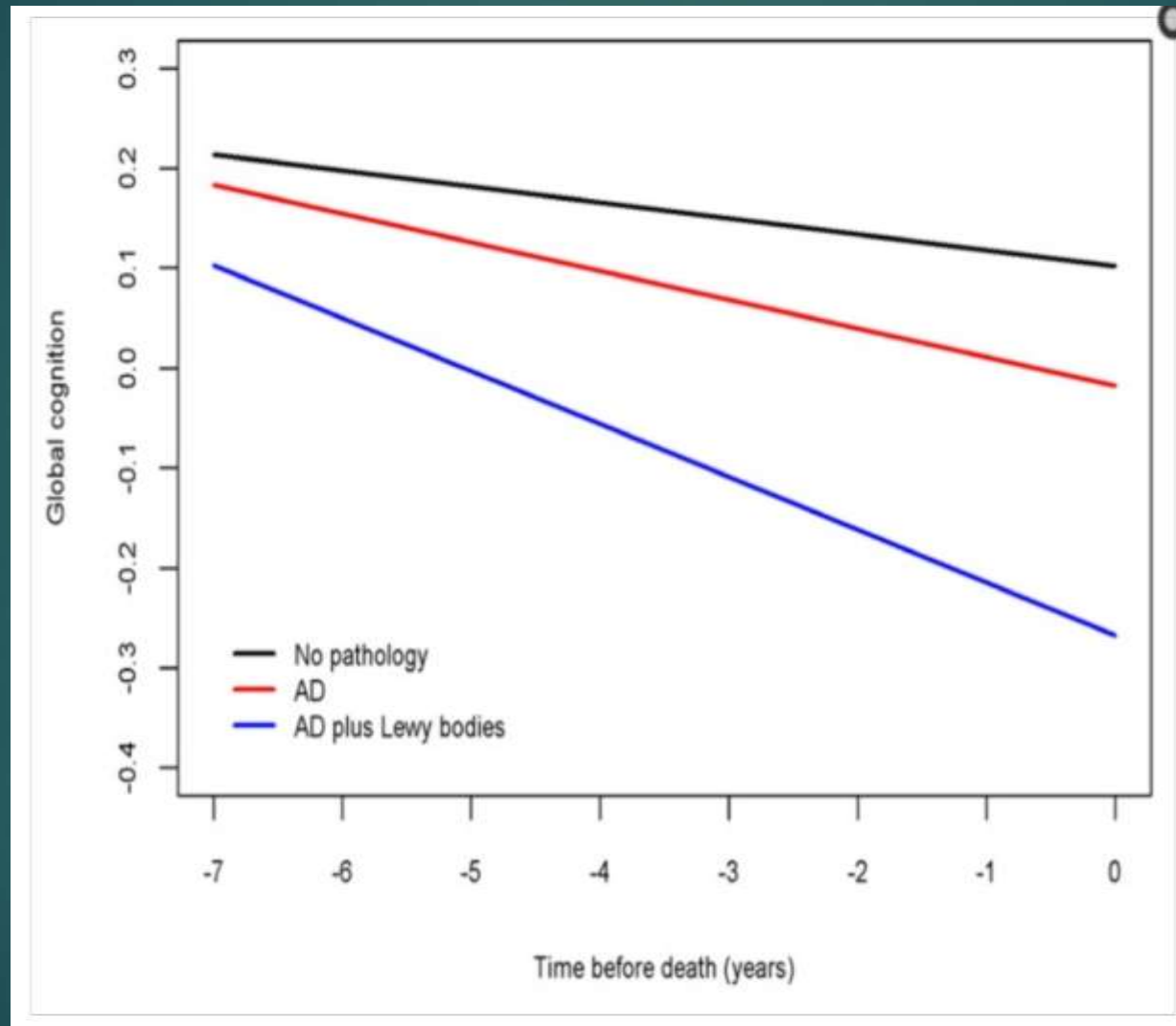


Figure 4. Pathophysiological changes at synapses in DLB. *A–D*, Brain homogenates of six confirmed DLB cases (D1–D6) are compared with age-matched non-dementia controls (C1–C6). *A, C*, Western blot analysis for presynaptic markers (*A*) synaptophysin (SPH; SY38) and syntaxin (STX; HPC-1) and postsynaptic markers (*C*) postsynaptic density protein (PSD95, rabbit anti-PSD95) and drebrin (Dreb.; M2F6), including the loading control β -actin (β -Act.). *B, D*, Plot of the β -actin normalized average intensities for presynaptic marker (*B*) and postsynaptic marker (*D*) proteins of non-dementia controls (black bars) and DLB cases (gray bars) \pm SE. *E–H*, Golgi–Cox–Davenport staining of brain slices for visualization of dendrites and their spines in non-dementia control (*E, G*) and DLB (*F, H*). *G* and *H* show the magnification of the black boxes in *E* and *F*. Scale bars, 50 μ m.

Cognitive Decline: AD + Lewy bodies worse than AD



Normals

Alzheimers

AD + Lewy body

Young men's dreams become old men's fate

- ▶ Rapid Eye Movement (REM) Behavior Disorder
- ▶ Loss of normal motor paralysis during REM sleep: physically act out while asleep
- ▶ Average 25 (15-50) year onset of REM Behavior Disorder
- ▶ 50% develop Parkinson's or Lewy Body Major NCD

Bizket: REM Sleep Disorder



Why “what is good for the heart is good for the brain”



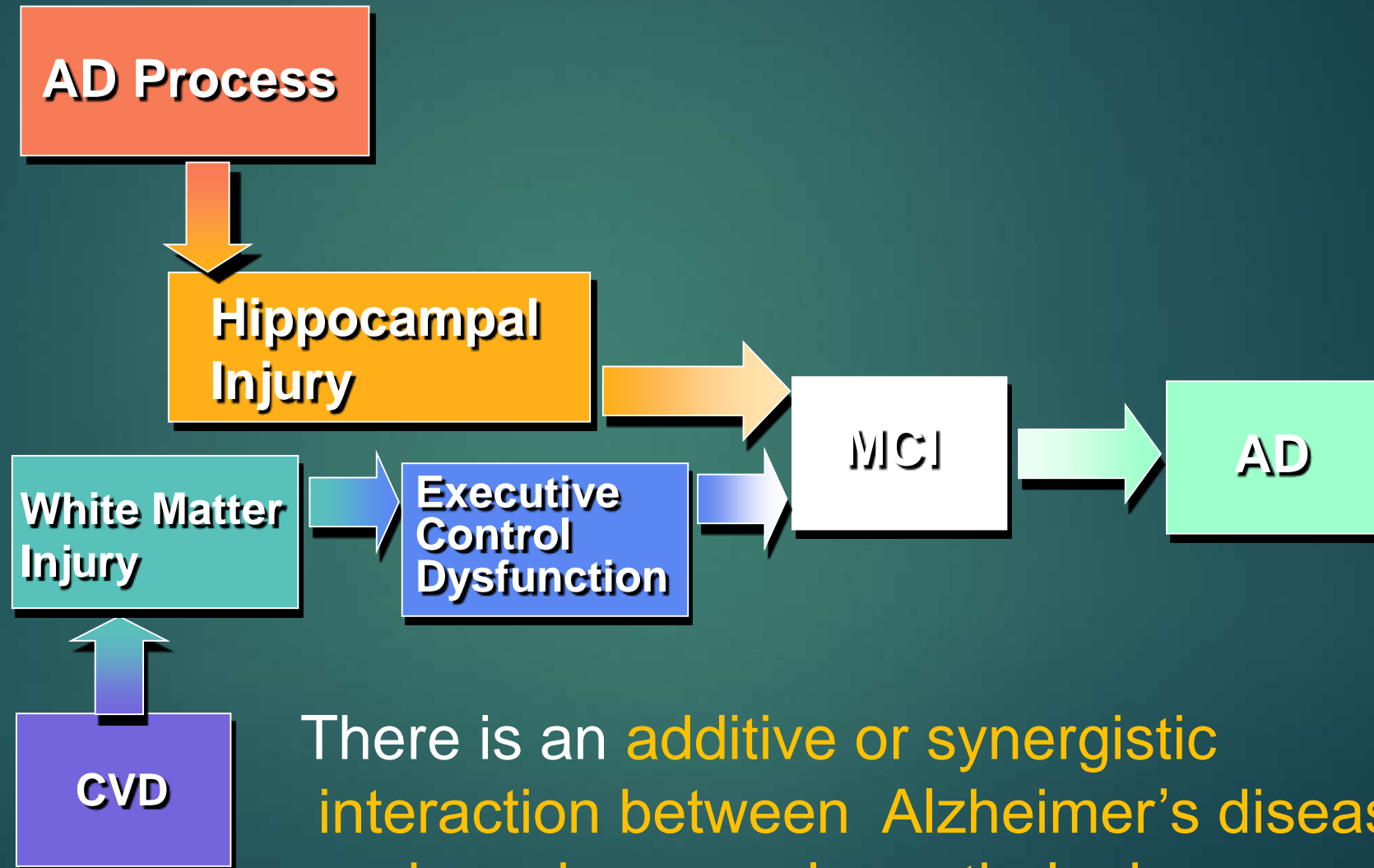
400 miles of blood vessels in human brain.

A plastic emulsion was injected into brain vessels and brain tissue was dissolved.

NCD due to Vascular Disease: 15-25%

- ▶ Series of mini strokes, HTN, blood vessel auto-regulation impaired
- ▶ Abrupt onset, stepwise course
- ▶ Focal neurological and neuropsychological deficits
- ▶ May or may not include memory deficit
- ▶ Major NCD: onset with presence of Alzheimer's

Combined Role of AD and CVD in MCI and Major NCD Risk



There is an **additive or synergistic** interaction between Alzheimer's disease and cerebrovascular pathologies

Vascular Dementia is declining

- Framingham Heart Study (Caucasian and educated population): since 1975
- Incidence of dementia declined by 22%, 38%, and 44% during the second, third, and fourth decades, respectively
- Progressive decline in the incidence of dementia over time, esp. in vascular dementia; a parallel improvement in cardiovascular health; but only in high school education or beyond
- Decreases in their heart health risk factors -- cholesterol, smoking, hypertension.
- If heart risk factors are controlled, a person is probably less likely to develop dementia as they age.

Frontal Temporal Disease: 5-10%

- ▶ FTD: Psychiatric Sxs precede Neurological presentation
- ▶ Personality/Behavioral changes precede memory deficit: loss of empathy, disinhibition, agitation, delusion, hallucinations, apathy
- ▶ Executive dysfunction: poor judgment, loss of impulse control/disinhibition
- ▶ Language Variant: semantic, non-fluent aphasia
- ▶ 4 x greater in men; average age: 53

FTD: Proportion of First Symptoms

<u>Behavior</u>	62%
Memory	11%
Language	12%
Executive	11%
Motor	4%

First Symptoms of FTD to appear commonly

Symptom

Examples

▶ Behavioral Disinhibition

▶ Rudeness, hypersexuality, hoarding

▶ Apathy

▶ New “coach potato” habit

▶ Loss of empathy

▶ Insensitivity to others

▶ Perseveration

▶ New obsessions, grinding teeth, humming

▶ Craving for sweets

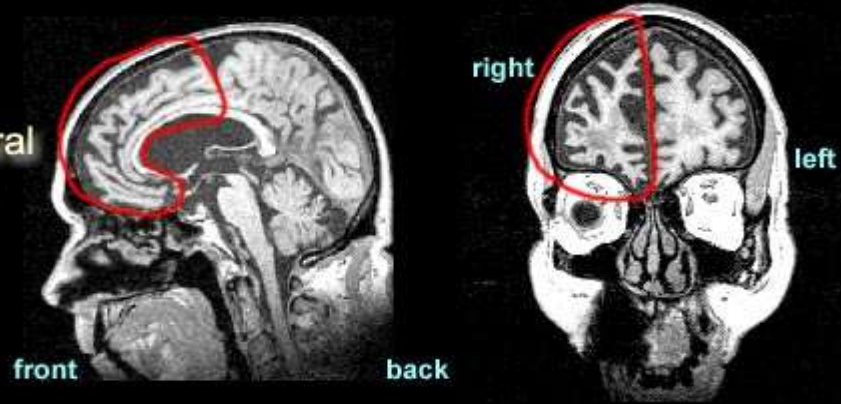
▶ Hyperorality

▶ Disorganized at work

▶ EF deficits

Notice that the areas circled in red have less white area compared with the other areas. This indicates loss of brain tissue (atrophy).

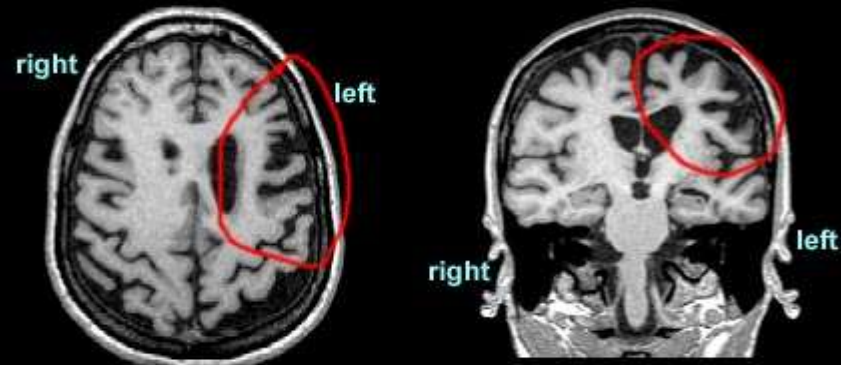
Frontotemporal
Dementia
(FTD)



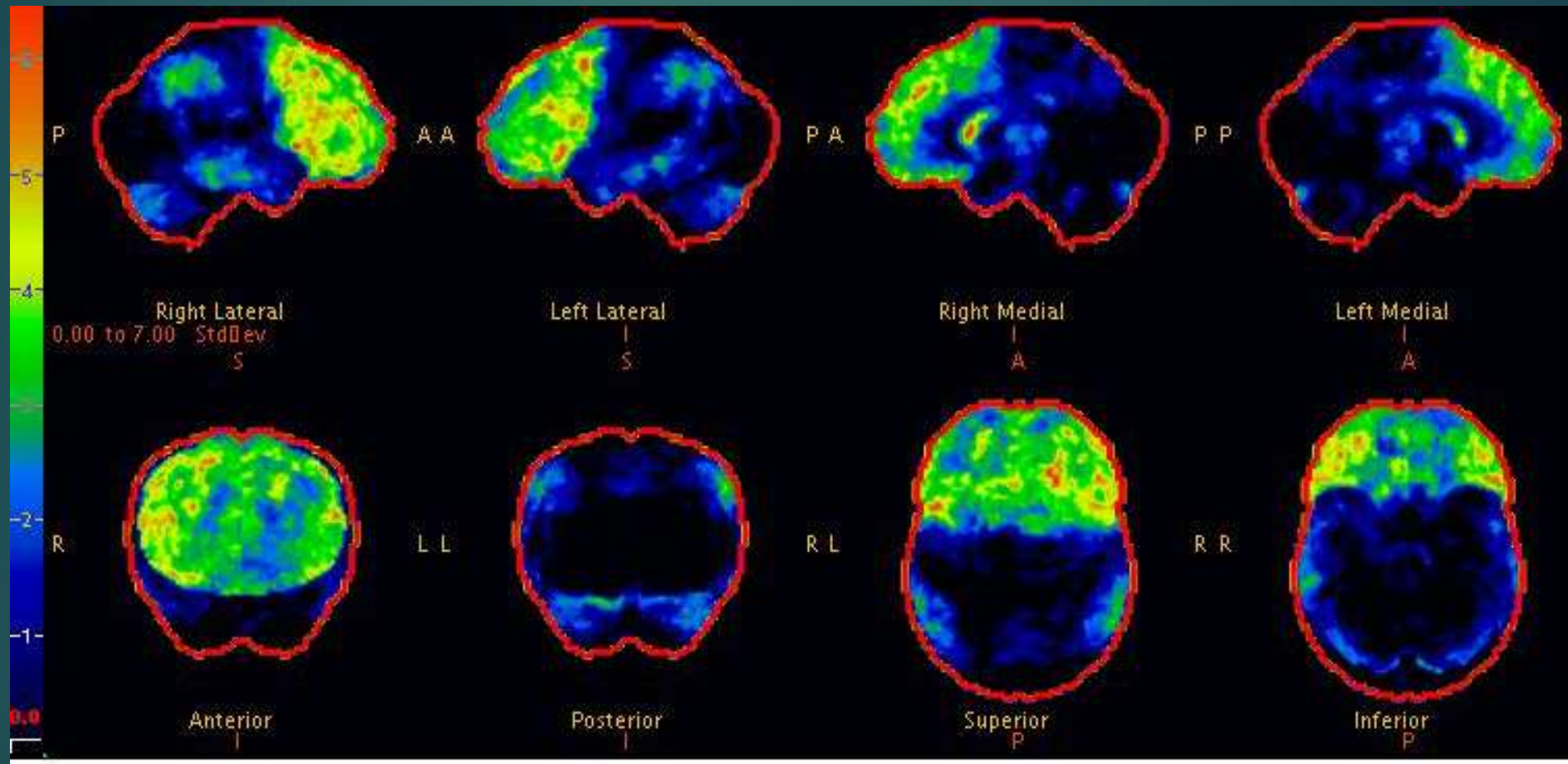
Semantic
Dementia
(SD)



Progressive
Non-Fluent
Aphasia
(PNFA)



bvFTD Imaging (FDG PET)



FTD and Art



Dr. Adams: Pi (each number colored)

FTD and Art




Dr. Adams: Pebbles

A. A. : Unraveling Bolero

A "The colored, treble parts are embellished with geometric shapes in black and also engraved into the paper to represent the quality of tone of each note. When the modulation finally does occur I use gaudy fluorescent colors to make the few #'s in the piece. The music soon collapses and dies in the final two bars.
I find Bolero an exciting experiment in sound, one which Ravel didn't really consider true 'music'."

B



Musical notation for Bolero, measures 321-340. The notation is presented in three staves. The first staff contains measures 321-327, the second staff contains measures 328-334, and the third staff contains measures 335-340. The notes are decorated with various geometric shapes and colors, including black, blue, orange, and pink. A small red box is visible on the right side of the second staff.

C



Decorative graphic for Bolero, measures 321-340. The graphic consists of a series of vertical panels, each corresponding to a measure of the music. Each panel is filled with intricate, colorful geometric patterns and shapes, including triangles, squares, and circles. The colors used include blue, orange, pink, and purple. The patterns are highly detailed and vary significantly from measure to measure.

Dr. Adams was Obsessed with Ravel's Bolero, who also had Progressive Primary Aphasia

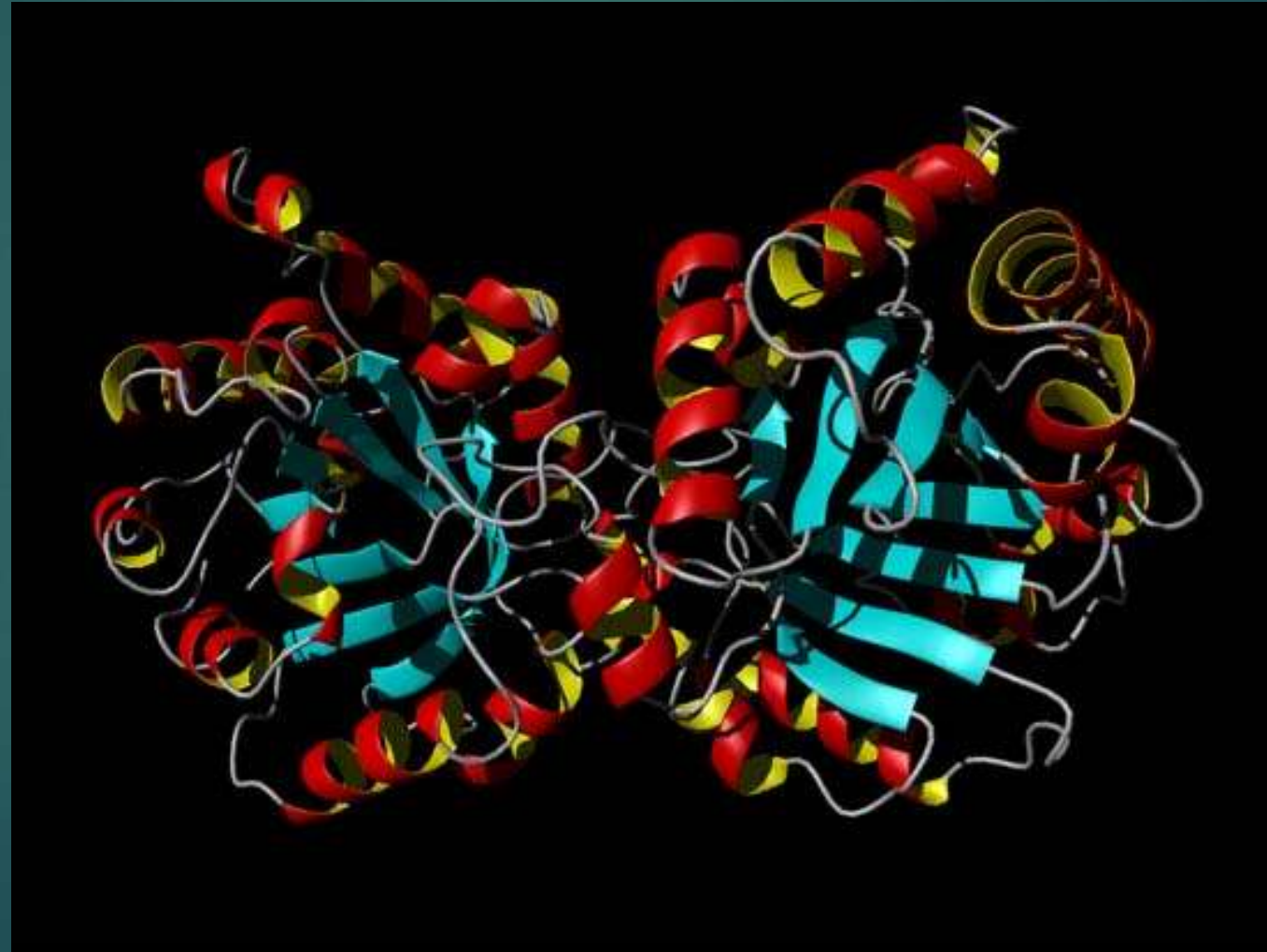
FTD and Art



Subcortical Diseases: Parkinson's, Huntington's, HIV, MS

- ▶ White Matter & Prefrontal Disorders
- ▶ Slow processing speed
- ▶ Motor problems
- ▶ Memory Retrieval:
 - ▶ Impaired free recall, but normal recognition
 - ▶ Cueing helps
- ▶ Executive Dysfunction
- ▶ Sustained attention decline
- ▶ Visual spatial/PIQ decline

Prion: abnormally folded protein



Creutzfeldt-Jakob Disease (CJD)

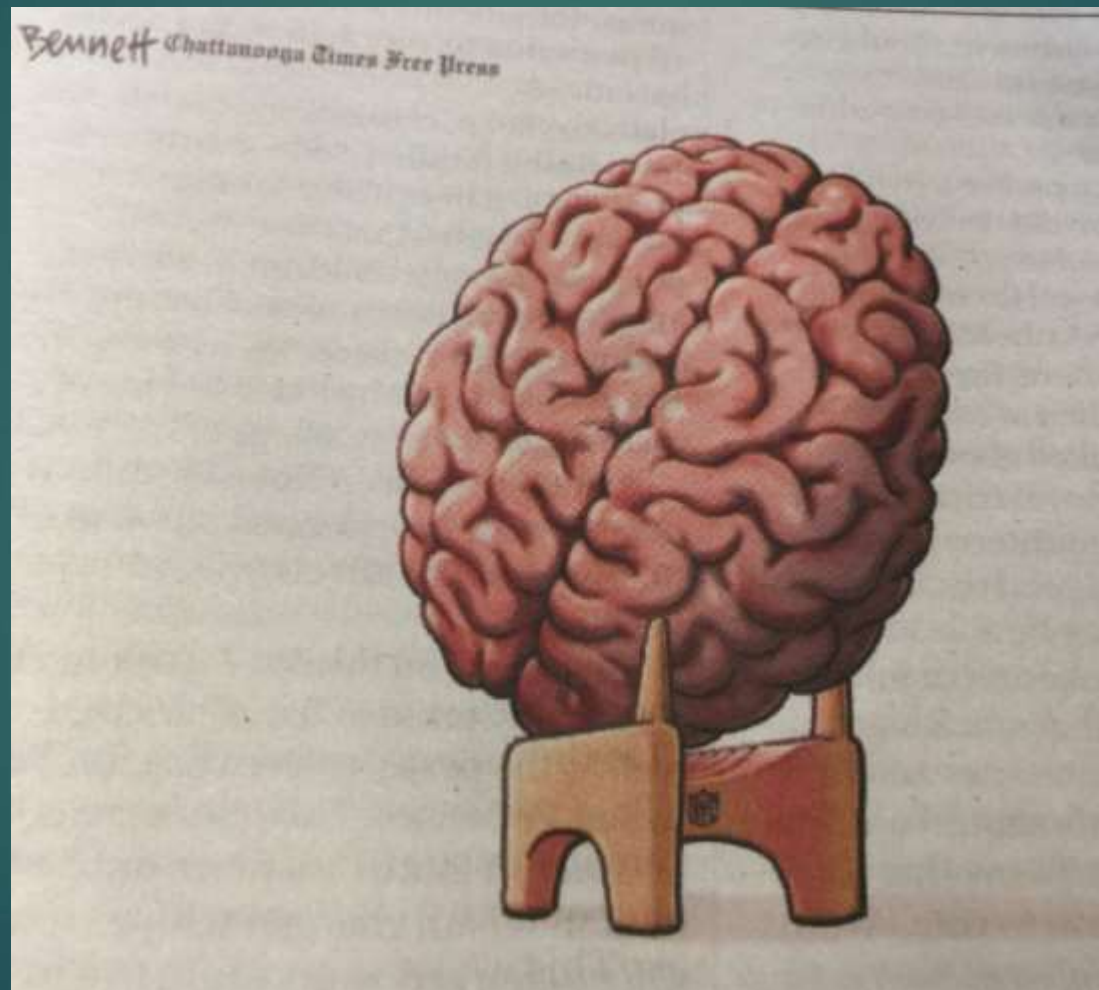
- ▶ Prevalence: 1% of Major NCD; most rapidly fatal ND
- ▶ Causation: infectious prion disorder (abnormal shape changing protein) (Posner, UCSF); **very infective** (heat does not kill; corneal transplant, human growth factor transmission); Gaba ↓
- ▶ Creutzfeldt-Jakob: Historically Eastern European Jewish disorder, in 50's, very rapid (1 year); any age (40-60); 5-15% familial
- ▶ Mad Cow Disease (Bovine Spongiform encephalitis): CJD in humans; meat consumption; related, younger (in England: 2 million cows; 156 human cases currently)

Symptoms of CJD

- ▶ Triad of symptoms: Major NCD, involuntary movements (esp. myoclonus), specific EEG wave)
- ▶ Prodromal: fatigue, anxiety, appetite/sleep/concentration ↓; then incoordination, altered vision, abnormal gait, rapid Major NCD
- ▶ Proportion of First Symptoms:

<u>Motor</u>	30%
Memory	25%
Executive	15%
Language	10%

Don't Kick Your Brain



NFL Football & Concussions





CONCUSSION

A Must Read for NFL Players
Let's Take Brain Injuries Out of Play



Concussion Facts

Concussion is a *brain injury* that alters the way your brain functions

Concussion can occur from a blow to the head/body:

- following helmet to helmet contact, and / or
- contact with the ground, object or another player

Most concussions occur without being knocked unconscious

Severity of injury depends on many factors and is not known until symptoms resolve and brain function is back to normal

All concussions are not created equally. Each player is different, each injury is different and all injuries should be evaluated by your team medical staff

Concussion Symptoms

Different symptoms can occur and may not show up for several hours. Common symptoms include:

- Confusion
- Headache
- Amnesia / Difficulty remembering
- Balance problems
- Irritability
- Dizziness
- Difficulty concentrating
- Nausea
- Feeling sluggish, foggy or groggy
- Sensitivity to noise
- Sensitivity to light
- Double / fuzzy vision
- Slowed reaction time
- Feeling more emotional
- Sleep disturbances
- Loss of consciousness

Symptoms may worsen with physical or mental exertion (e.g. lifting, computer use, reading)

Why Should I Report My Symptoms?

- Practicing or playing while still experiencing symptoms can prolong the time to recover and return to play.
- Unlike other injuries, there may be significant consequences of "playing through" a concussion. Repetitive brain injury, when not treated promptly and properly may cause permanent damage to your brain.

What Should I Do If I Think I've Had a Concussion?

Report it. Never ignore symptoms even if they appear mild. Look out for your teammates. Tell your Athletic Trainer or Team Physician if you think you or a teammate may have had a concussion.

Get Checked Out. Your team medical staff has your health and well being as its first priority. They will manage your concussions according to NFL / NFLPA Guidelines which include being fully asymptomatic, both at rest and after exertion, having a normal neurologic examination, normal neuropsychological testing, and clearance to play by both the team medical staff and the independent neurologic consultant.

Take Care of Your Brain. According to the CDC*, "traumatic brain injury can cause a wide range of short- or long term changes affecting thinking, sensation, language , or emotions". These changes may lead to problems with memory and communication , personality changes, as well as depression and the early onset of dementia. Concussions and conditions resulting from repeated brain injury can change your life and your family's life forever.

Work smart. Use your head, don't lead with it. Help make our game safer. Other athletes are watching...



*for more information about traumatic brain injury and concussion, go to <http://www.cdc.gov/concussion>

Chronic Traumatic Encephalopathy

- ▶ Long term effects of repetitive sports related brain trauma
- ▶ Historically dementia pugilistica among boxers
- ▶ Caused by Tau & TDP-43 abnormal proteins
- ▶ Professional football players, 50% of boxers, wrestlers, military veterans (blast injuries)
- ▶ Repeated trauma early in life, end of career; 8 year latency period, then personality & mood & cognitive changes over 17 years, then Major NCD
- ▶ Motor neuron disease (ALS) in some i.e. Lou Gehrig ?

Differential Diagnosis of Neurodegenerative Disorders: First Symptom

- ▶ AD – Memory (no encoding) (70%)
- ▶ FTD – Behavior, executive loss, language
- ▶ VaD – Apathy, executive deficits
- ▶ LBD – Visual hallucinations, Visual Spatial deficits, Parkinsonism, delirium
- ▶ CTE - Behavior
- ▶ CJD – Involuntary motor

Apathy = Sign of Brain Atrophy

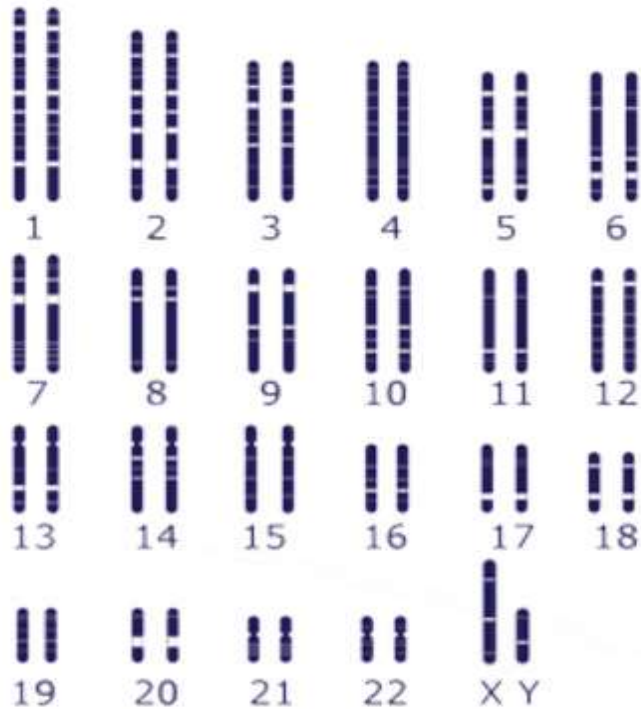
- ▶ N = 4,354 older persons without NCD, aged 76 +/- 5 years, 49% had apathy (no depression)
- ▶ Had significantly smaller gray matter volumes, particularly in the frontal and temporal lobes; smaller white matter volumes, mainly in the parietal lobe;
- ▶ In this older population without NCD, apathy symptoms are associated with a more diffuse loss of both gray and white matter volumes, independent of depression.

Aging is more risky than having a Parent with AD

- ▶ The risk to a person who has a first-degree relative (parent or sibling) with late-onset Alzheimer disease is just slightly higher than the risk in the general population
- ▶ Risk for AD doubles every 5 years post age 65
- ▶ 95 % will reach the age of 75 without developing Major NCD

4 Major Genes Implicated in Alzheimer's:

3 in only 450 families in whole world



Amyloid precursor protein (APP), discovered in 1987, is the first gene with mutations found to cause an inherited form of Alzheimer's.

Presenilin-1 (PS-1), identified in 1992, is the second gene with mutations found to cause early-onset of Alzheimer's. Variations in this gene are the most common cause of early-onset Alzheimer's.

Presenilin-2 (PS-2), 1993, is the third gene with mutations found to cause early-onset Alzheimer's.

Apolipoprotein E-e4 (APOE4), 1993, is the first gene variation found to increase risk of Alzheimer's and remains the risk gene with the greatest known impact. Having this mutation, however, does not mean that a person will develop the disease.

Youngest
Onset: 40s

Onset: 58-59

Onset: 60-70s

Alzheimer's Genetics

- ▶ 95 %: Sporadic (unknown cause) age related AD with onset later than 65 yo
- ▶ 5%: Familial genetic AD, onset 40-50s
- ▶ Sporadic: Many genes + age + environment/lifestyle
- ▶ **No family hx:**
 - ▶ Lifetime risk = 15%
 - ▶ ApoE4 neg = 9%;
 - ▶ ApoE4+ = 30%
- ▶ **One parent with AD:**
 - ▶ ApoE3/E3: 30%
 - ▶ ApoE3/E4: 45%
 - ▶ ApoE4/E4: 60% (& telomere shortening)

23andMe: \$99



My genetic study: double APOE 3; 2.7% Neanderthal

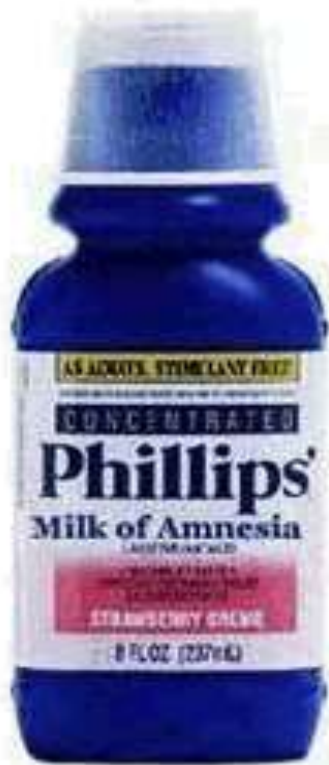
Remember:

- No current treatment for AD

BDNF: Brain-derived neurotropic factor

- BDNF: involved in learning and memory and is released in response to neural activity; **encourages new neuron growth** and support the formation of synapses; protect neurons from dying; slower cognitive decline in face of brain pathology
- Higher BDNF levels appear to be protective against Alzheimer disease and dementia
- What increases BDNF: exercise, low caloric diet, social interaction, behavioral activities, statins, antidepressants

Latest Memory Cure



Phillip's Milk of Amnesia



for people
who can't
remember shit.

Anti-Major NCD Medications ?

- ▶ **The Question:** Are there medications that prevent Major NCDs like Alzheimer's disease?
- ▶ **The Verdict:** No Major NCD disease prevention medications.
- ▶ **Symptomatic versus Disease-Modifying Treatments:** Symptomatic treatments simply relieve symptoms associated with a disease. They do not affect the underlying cause of the disease; i.e. Aricept.
- ▶ But...There are Major NCD modifying behaviors.

Risk Factors for Cognitive Decline:

Need to begin fighting them in your 20's

- ▶ Hypertension
- ▶ Heart Disease
- ▶ Diabetes
- ▶ Poor Nutrition
- ▶ Chronic Stress
- ▶ Poor hearing
- ▶ Recurrent Major Depression
- ▶ Low education
- ▶ No physical exercise
- ▶ Long term Benzodiazepine use.

Brain fitness is a critical part of overall health.



Research Caveat

- ▶ Majority of studies are observational & correlational, i.e. people who eat chocolate have less CV disease
- ▶ Correlation is not causation: gum disease does not cause CV disease, higher plaque in blood vessel does.
- ▶ Most studies are cross-sectional (same age cohort), not longitudinal: alcoholics who have cirrhosis
- ▶ There are few double blind, randomized, control studies of factors that reduce risk factors for Alzheimer's and cognitive decline.

2015: Meta-analysis of modifiable risk factors for Alzheimer's disease

16,906 articles were identified of which 323 with 93 factors met the inclusion criteria for meta-analysis

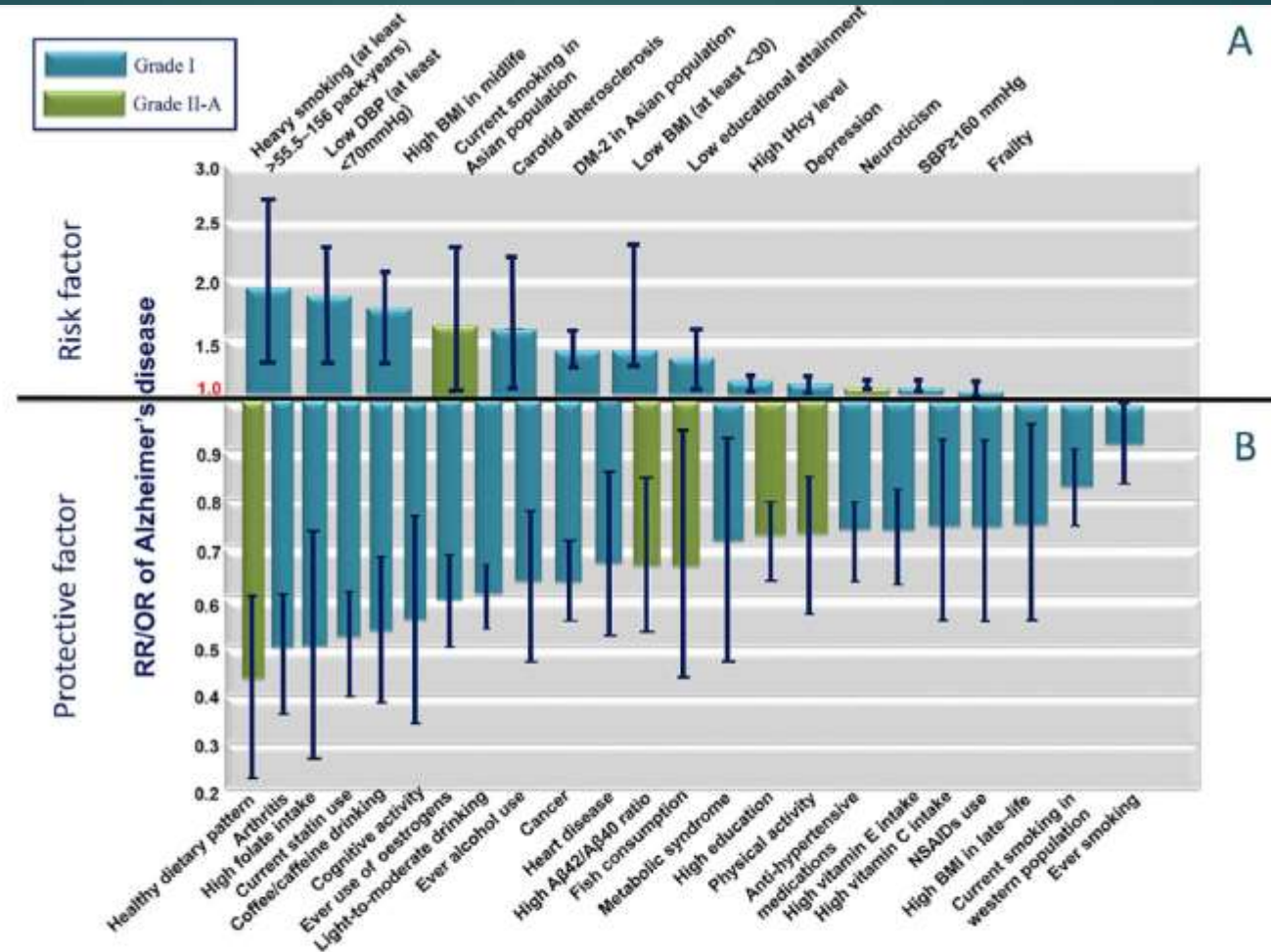


Figure 2 Factors showing significant positive (A) and negative (B) association with AD. With a relatively large pooled population ($n > 5000$), (A) a total of 13 (11 with grade I evidence and 2 with grade II-A evidence) factors showed a trend of increasing risk of AD while (B) a total of 23 (18 with grade I evidence and 5 with grade II-A evidence) factors showed a trend of decreasing risk of AD. The height of the strip is representative of the effect size. The length of the longitudinal line is representative of the range of 95% CI (AD, Alzheimer's disease; BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; NSAIDs, non-steroidal anti-inflammatory drugs; RR, relative risk; SBP, systolic blood pressure; tHcy, total homocysteine).

32 AD risk factors (orange = 66% of modifiable risk)

- ▶ Hyperhomocysteine (red meat)
- ▶ depression
- ▶ Physical frailty
- ▶ carotid atherosclerosis
- ▶ dysfunctional gait speed
- ▶ poor self-rated health status
- ▶ Obesity
- ▶ hypertension,
- ▶ hypotension
- ▶ low diastolic blood pressure,
- ▶ type 2 diabetes mellitus (Asian)
- ▶ Current smoking (Asian); heavy smoking for all
- ▶ history of stress
- ▶ low education <6-8 years (worse than low level ≤10–16 years)

high body mass index (BMI) in mid-life
low BMI in late life

Neuroinflammation

high-sensitivity C reactive protein levels at mid-life

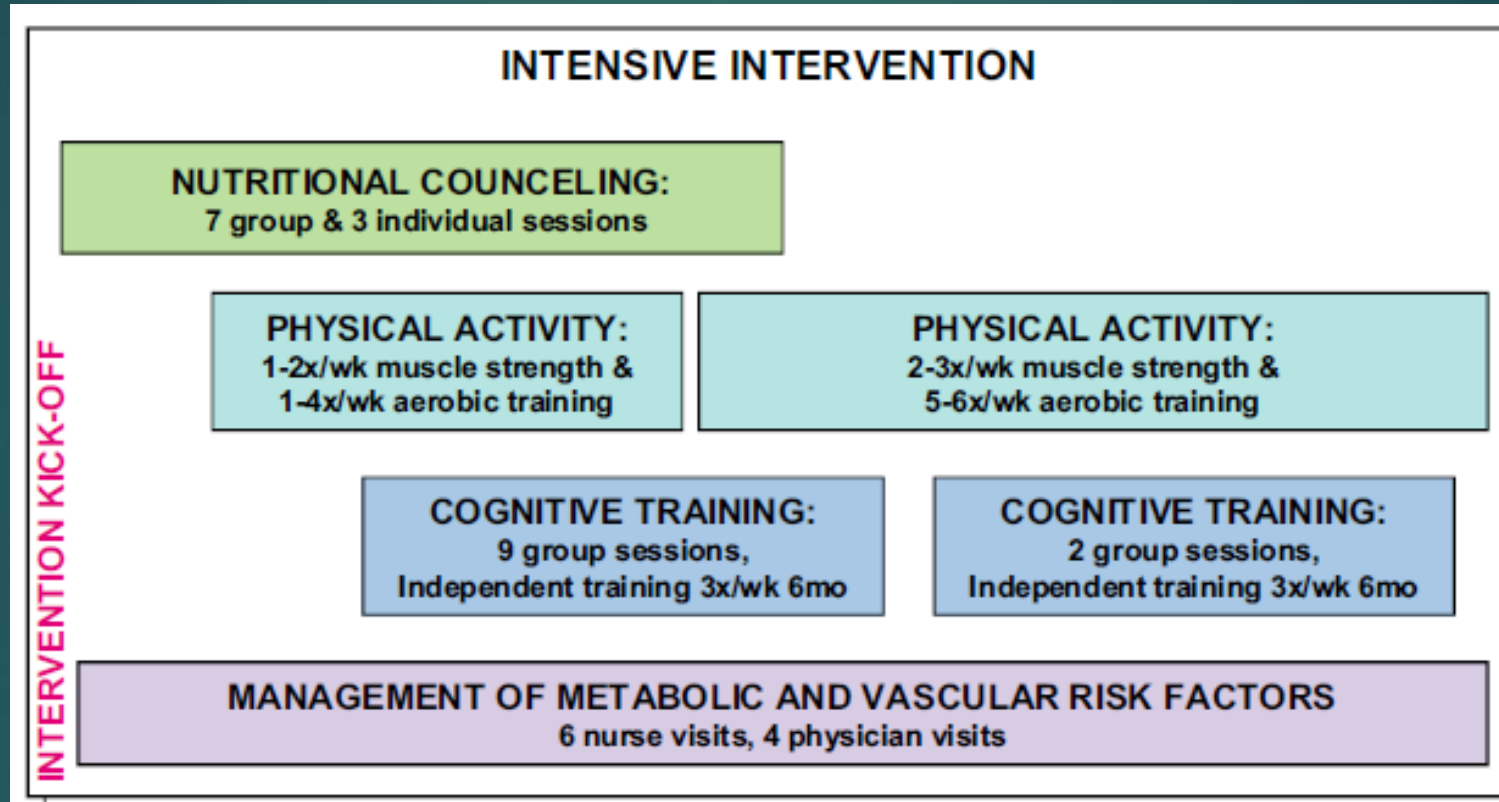
neuroticism and conscientiousness

less physical activity,
Less cognitive activity
less purpose in life

2015 *Lancet* first RCT study

- ▶ N = 1650; 2 year (2009-2011) Finnish study of ages 60-77
- ▶ FINGER is the first large-scale, longer-term randomized controlled trial to assess a multidomain approach to prevent cognitive decline in at-risk elderly people (nutritional guidance, physical exercise, cognitive training, social activities, and management of heart health risk factors) (control group received regular health advice);
- ▶ Would this lead to a protective effect on cognition?
- ▶ There were significant intervention effects on the outcome (overall cognition, executive functioning and processing speed, complex memory tasks), and other secondary outcomes (BMI, dietary habits, and physical activity).
- ▶ Outcomes were 25% to 150% better in the intervention group.
- ▶ Now 7-year follow up study

FINGER Interventions



Nutrition: high consumption of fruit and vegetables; whole grain in all cereal products; low-fat options in milk and meat products; sucrose intake, 50 g/day; using vegetable margarine and rapeseed oil instead of butter; and at least two portions of fish per week. Vitamin D supplementation (10–20 mg/day) and , and fish oil supplements are recommended .

You can change 30% of risky AD behaviors

- ▶ 30% of the risk factors for Alzheimer's disease are potentially changeable
- ▶ Most negative risk factors: Tackling seven risk factors could reduce the prevalence of Alzheimer's disease in 2050 by 8% worldwide:
- ▶ Low education 19% of cases
- ▶ **Vascular Risk Factors:**
 - ▶ Physical inactivity 21%
 - ▶ Smoking 14%
 - ▶ Midlife hypertension 5%
 - ▶ Midlife obesity 2%
 - ▶ Diabetes 2%
 - ▶ Depression 11%

Twenty Six Tips for Protecting Your Brain:

2 Red Tips are RCT proven

Join UCSF's Brain Registry

- ▶ If you have a computer, join this new research program:
 - ▶ <http://www.brainhealthregistry.org/>
- ▶ Answer some health questions and play some Lumosity games, which gives them info on your brain functioning.
- ▶ They check in with you every 6 months.
- ▶ It's easy and you contribute to a very large brain research project. They are building a large pool of potential participants in clinical trials to find cures for brain disorders.
- ▶ Join it!!

Tip #1: **Protect your head!**

- ▶ Blows to the head increase odds of Major NCD years later.
- ▶ Pro football players have 19 times the typical rate of memory-related diseases.
- ▶ Alzheimer's risk is 4x more common in elderly who suffer a head injury,
- ▶ Wear seat belts and helmets, fall-proof your house, and don't take risks.

Tip #2: Protect your Heart

What is bad for your heart
is bad for your brain.

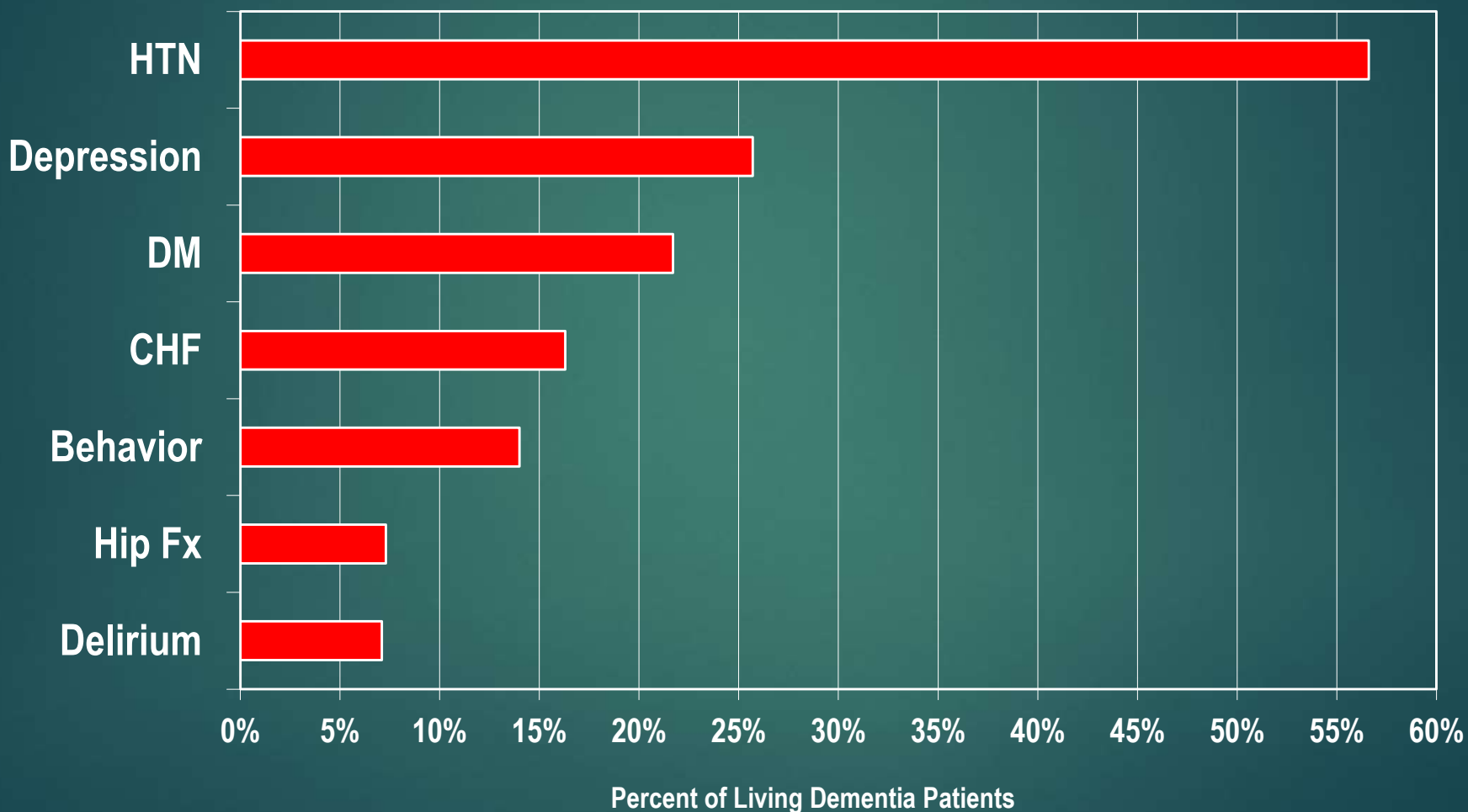


Maintain healthy blood pressure, cholesterol, weight, and activity levels;
take your heart meds!

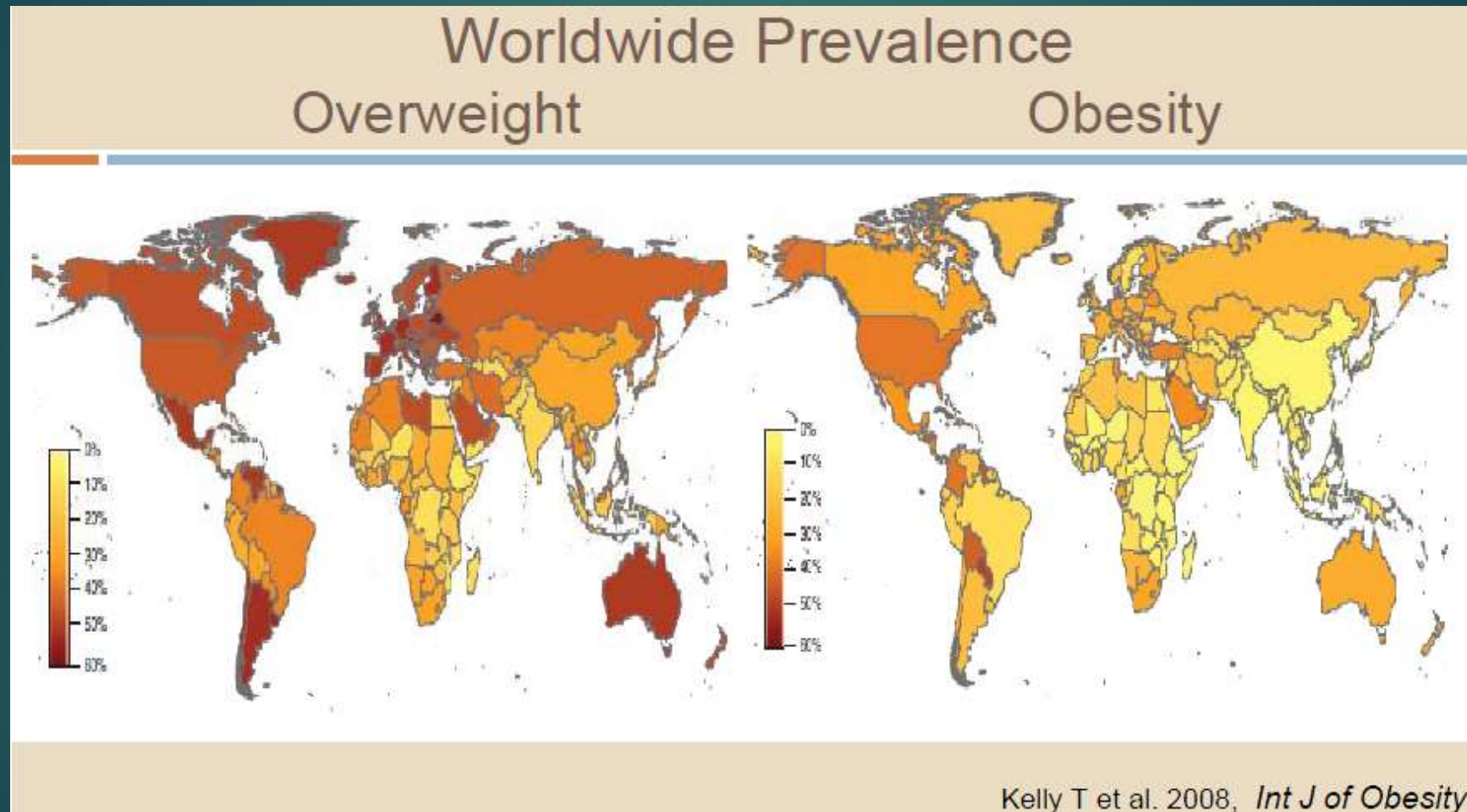
Cardiovascular Risk Factors

- ▶ AD has a vascular component
- ▶ Major NCD is often “mixed” with both AD and vascular pathology
- ▶ CVD risk factors are all “modifiable”

Co-Morbidities of Northern Cal KP Dementia NCD Pts



Tip #3: Stay at a normal weight



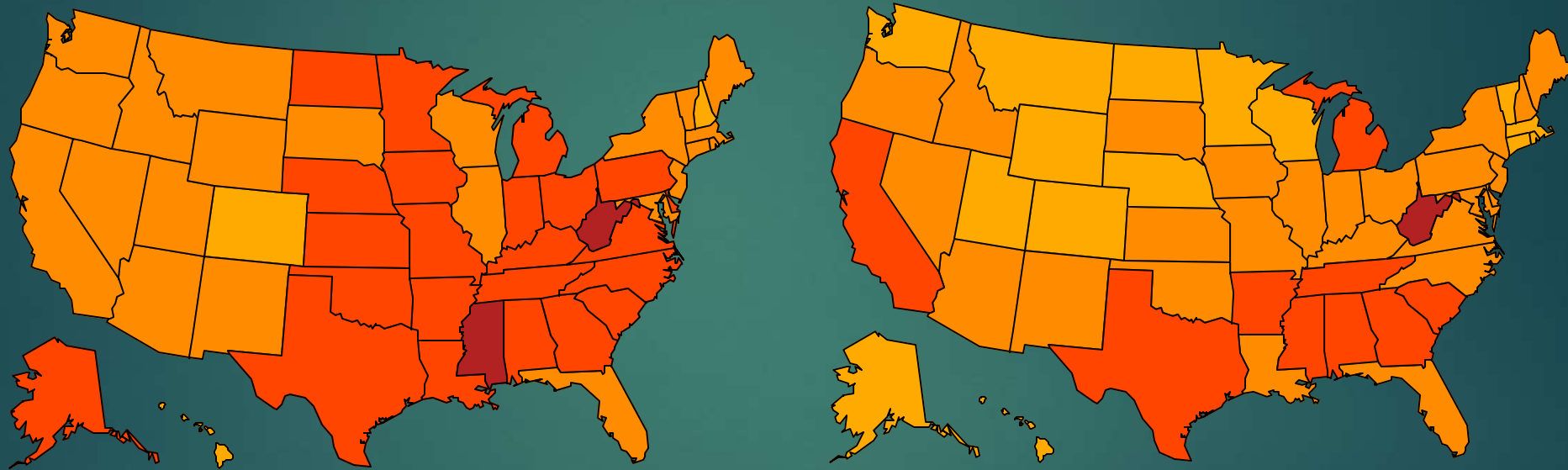
We are overweight

- 75% of U.S. Men & 67% of Women Are Overweight
- 35% of US adults are obese (>30 lbs.)

Run 1 mile = 100 calories

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

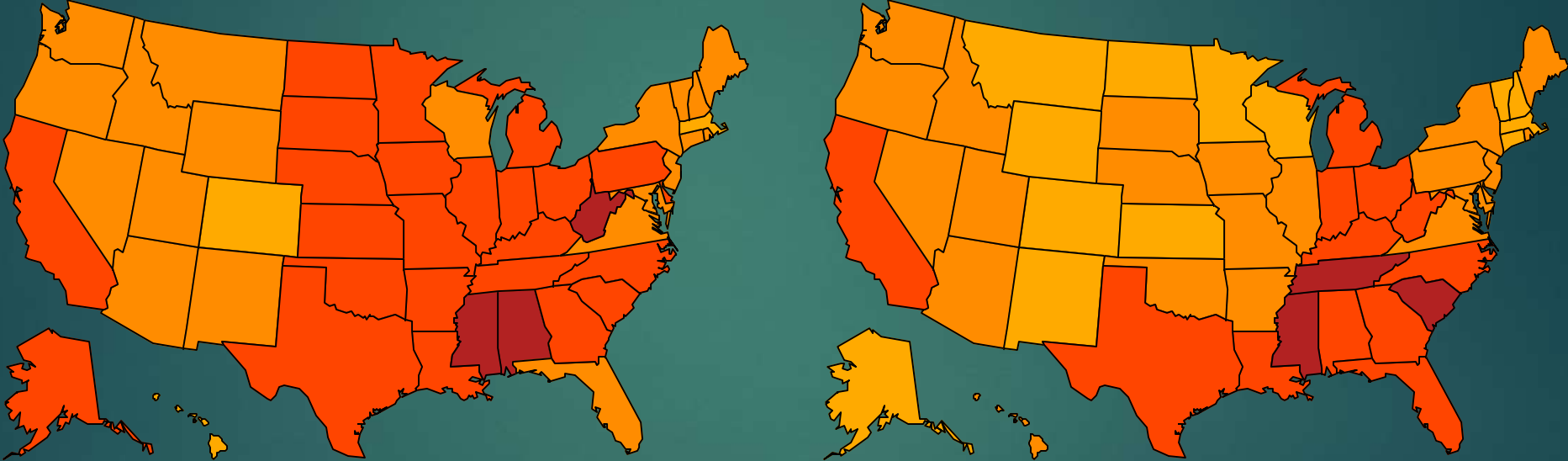
2002



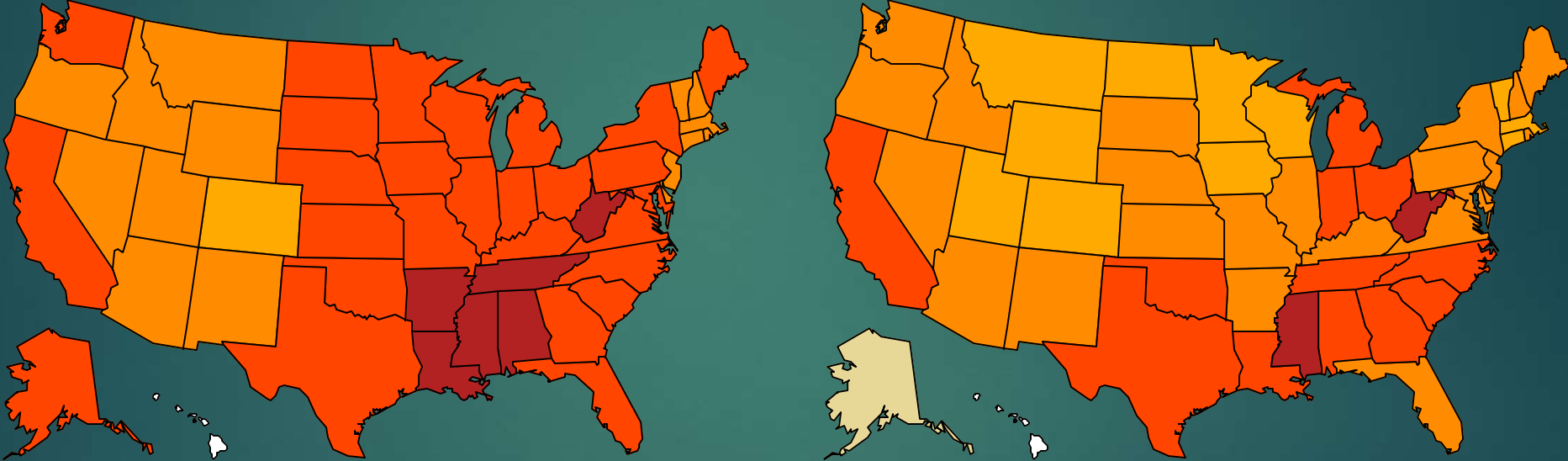
Obesity

Diabetes

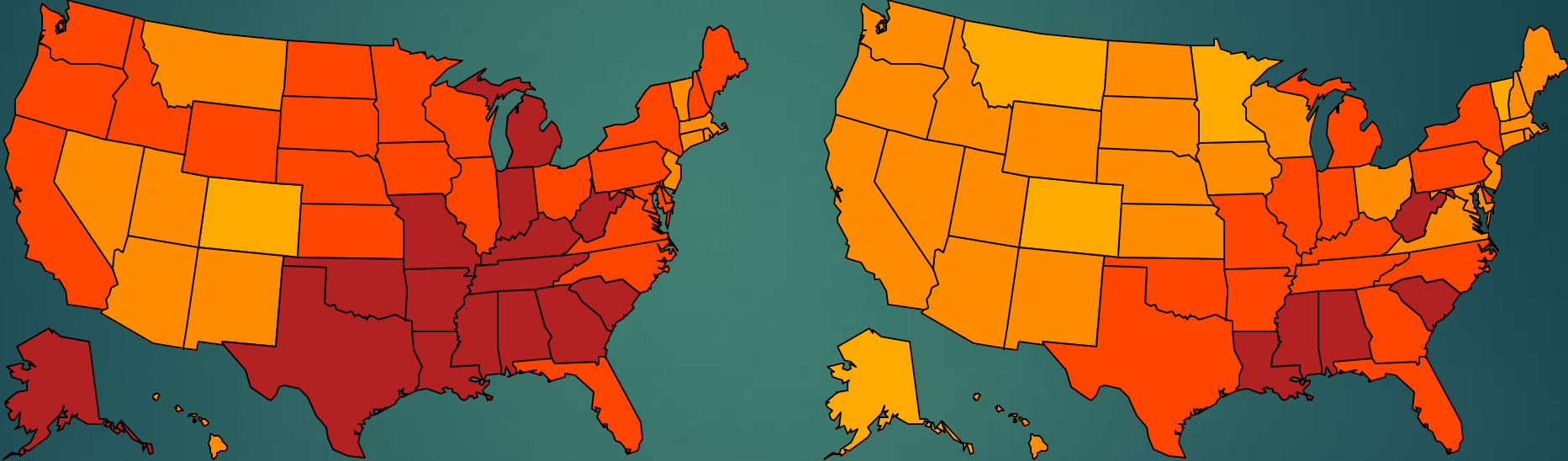
2003



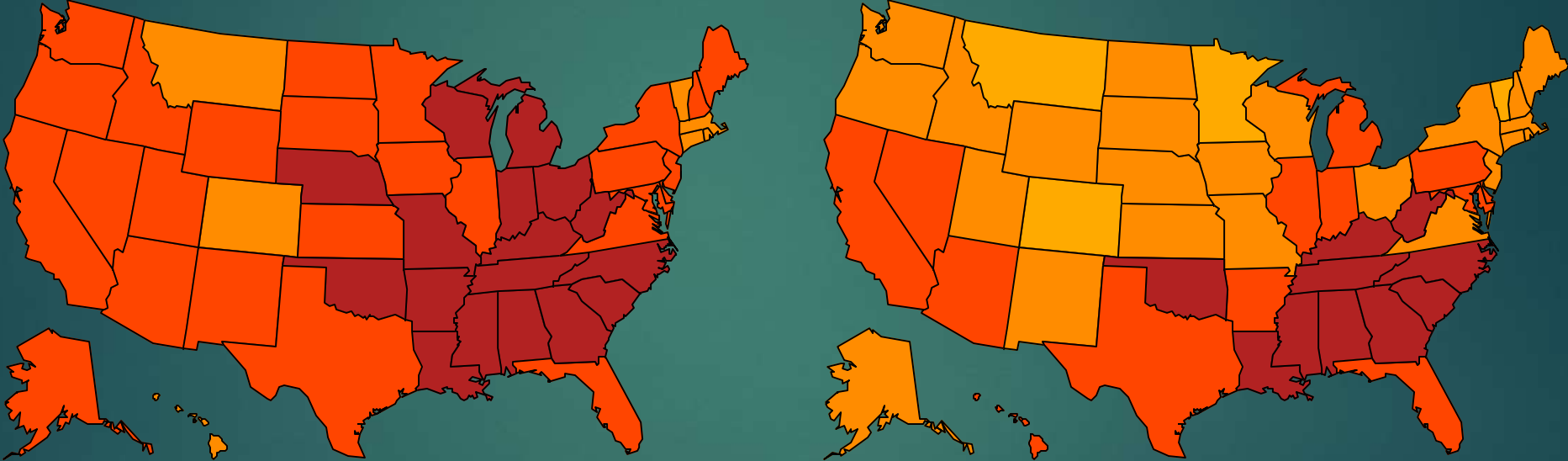
2004



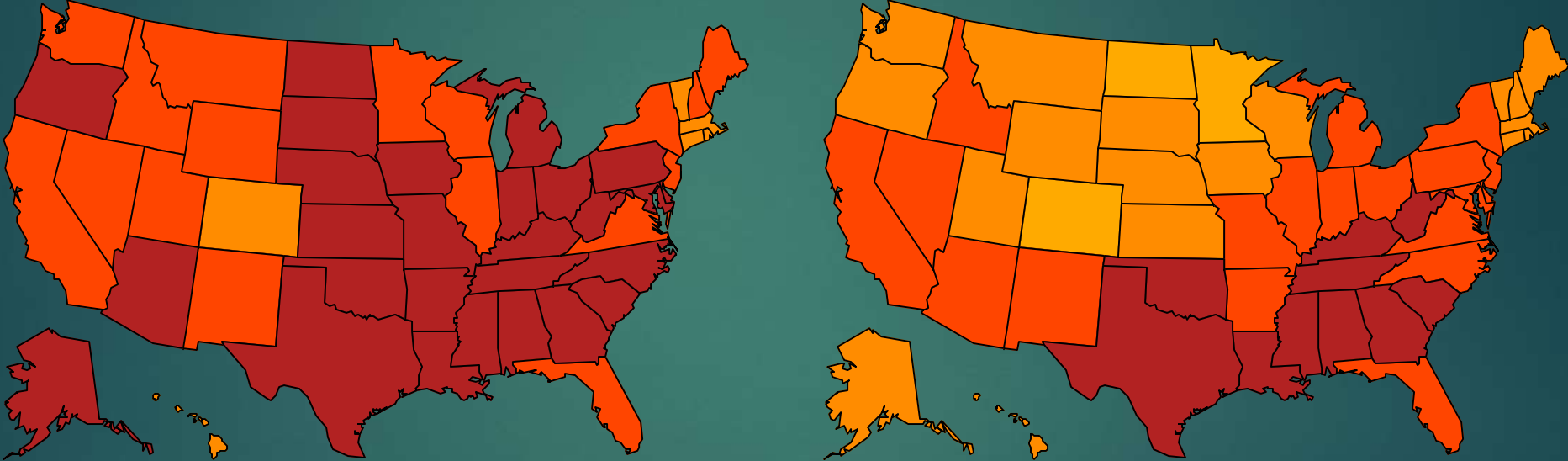
2005



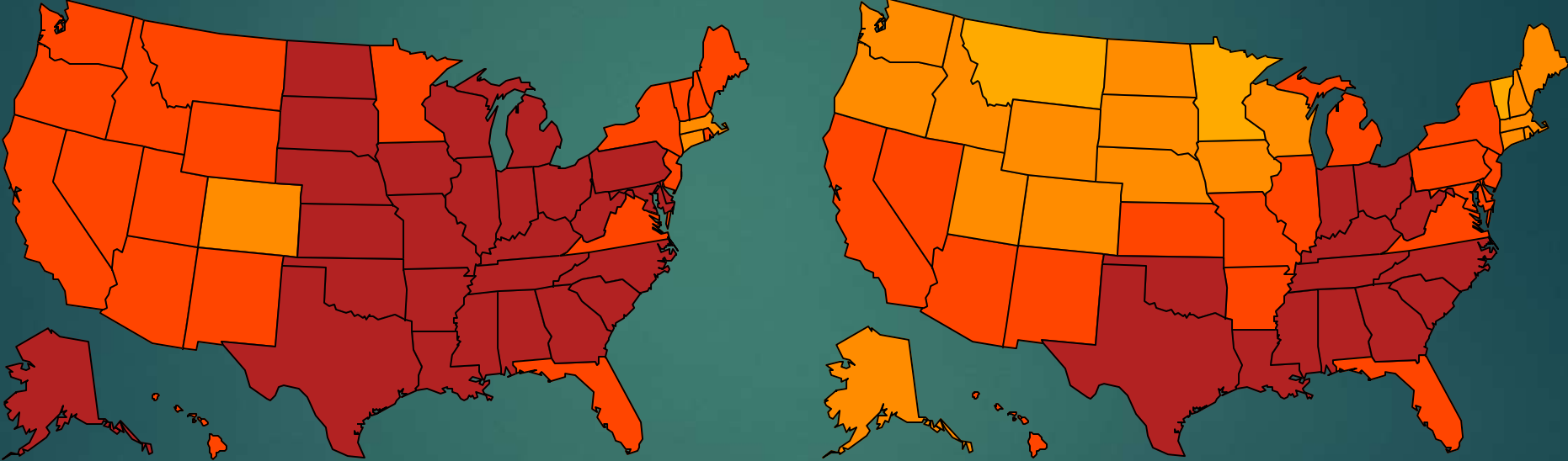
2006



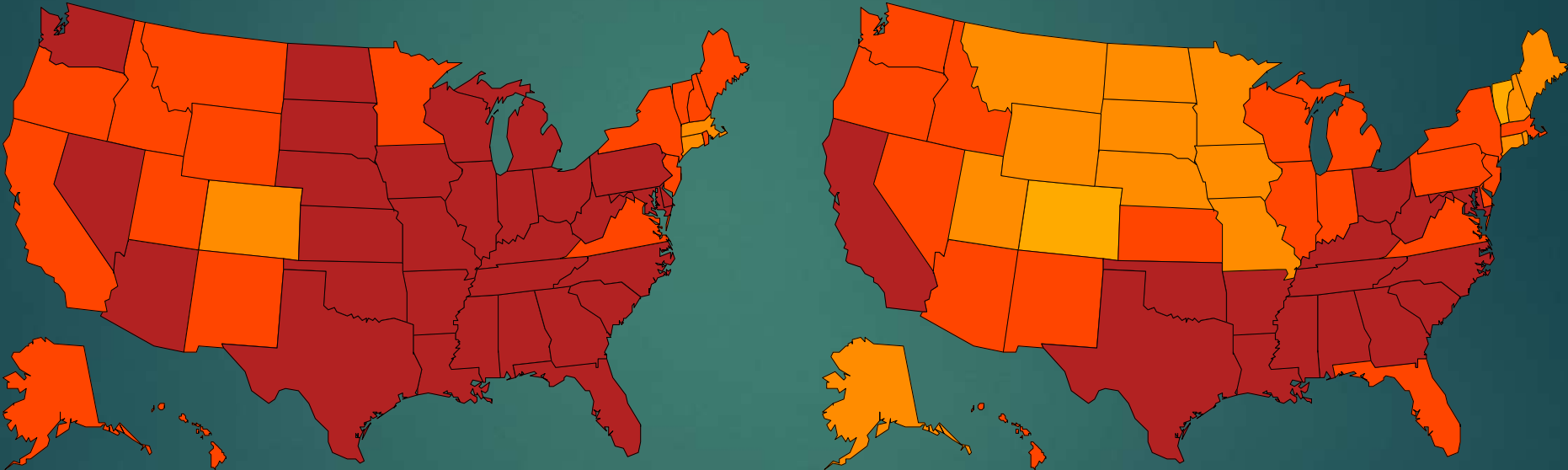
2007



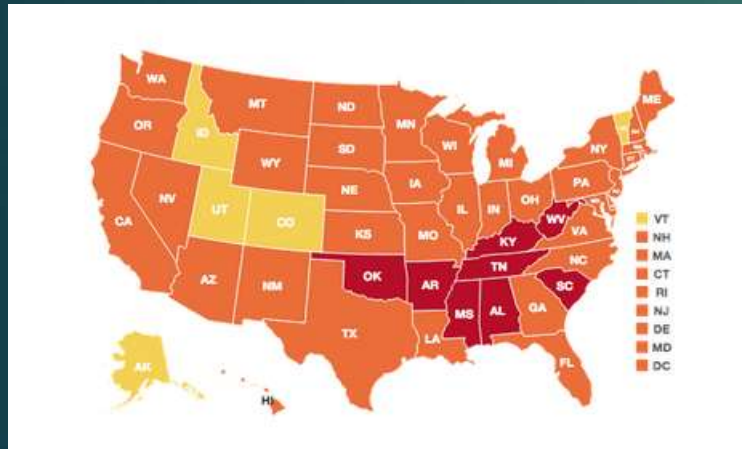
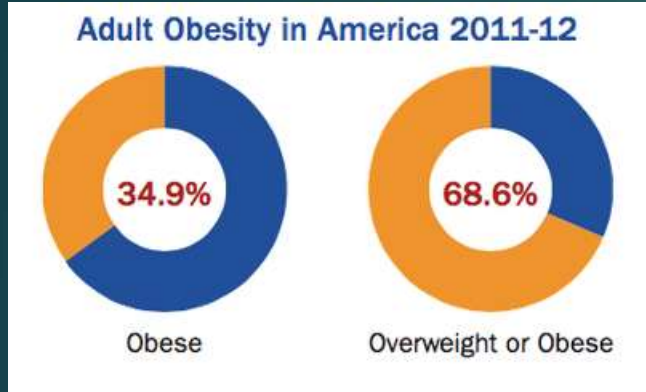
2008



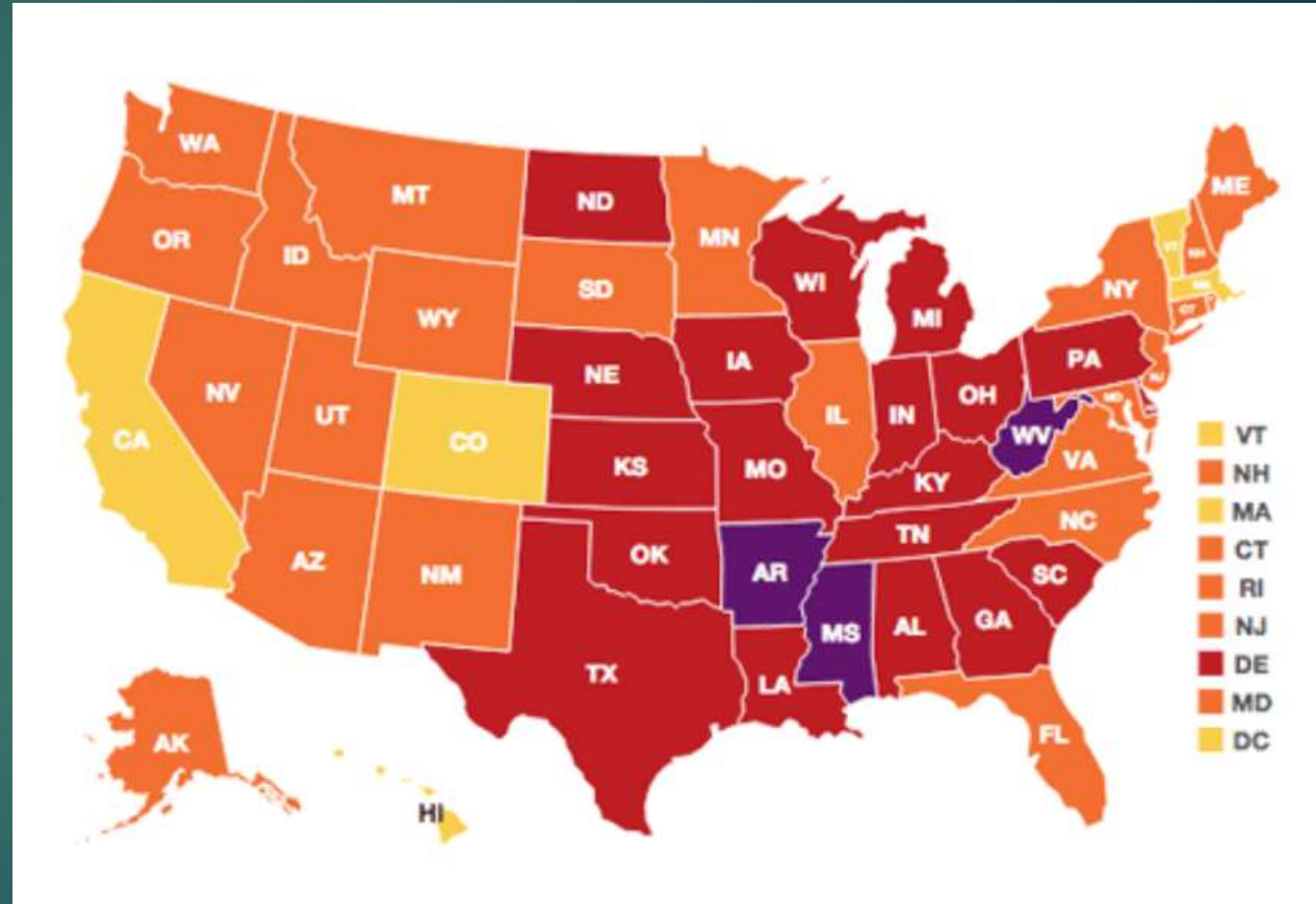
2009



2015: Obesity in US



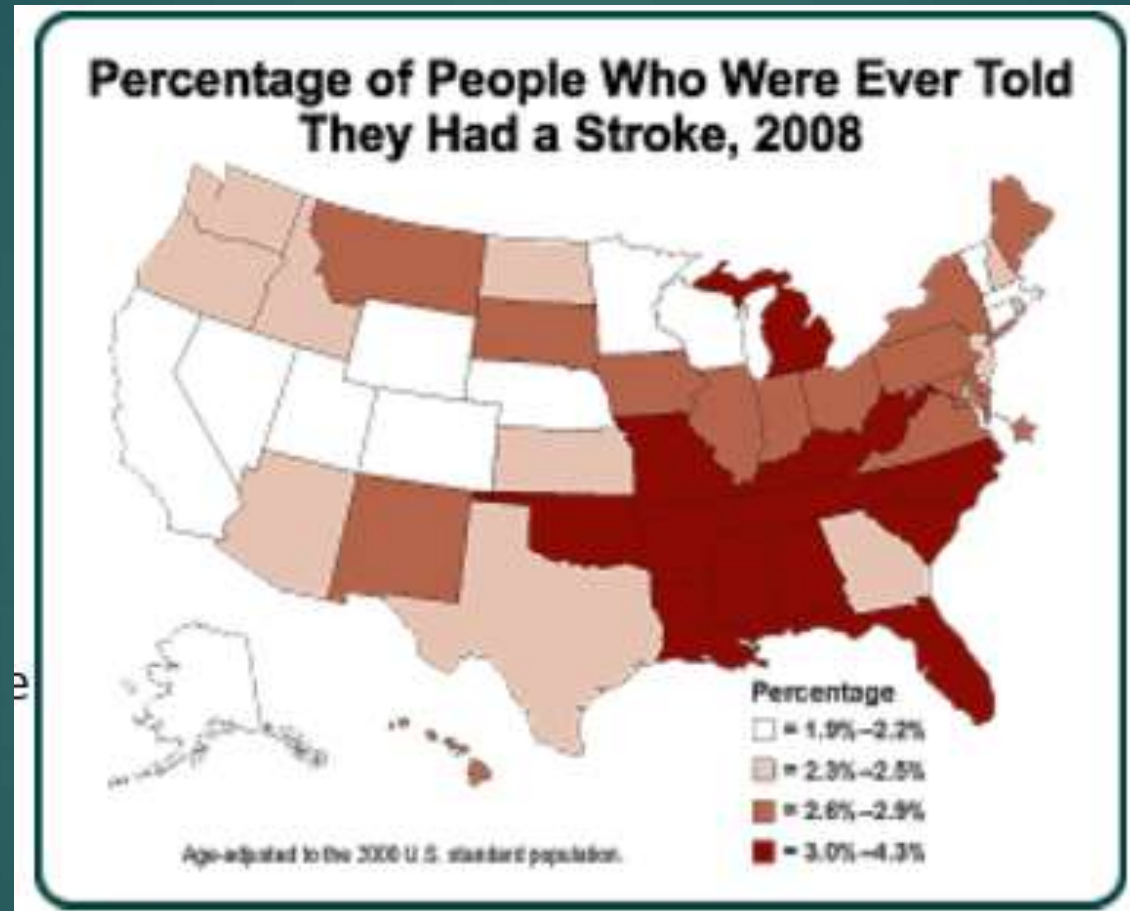
Diabetes



Arkansas: 35%

Colorado: 21%

CDC: % Strokes by State



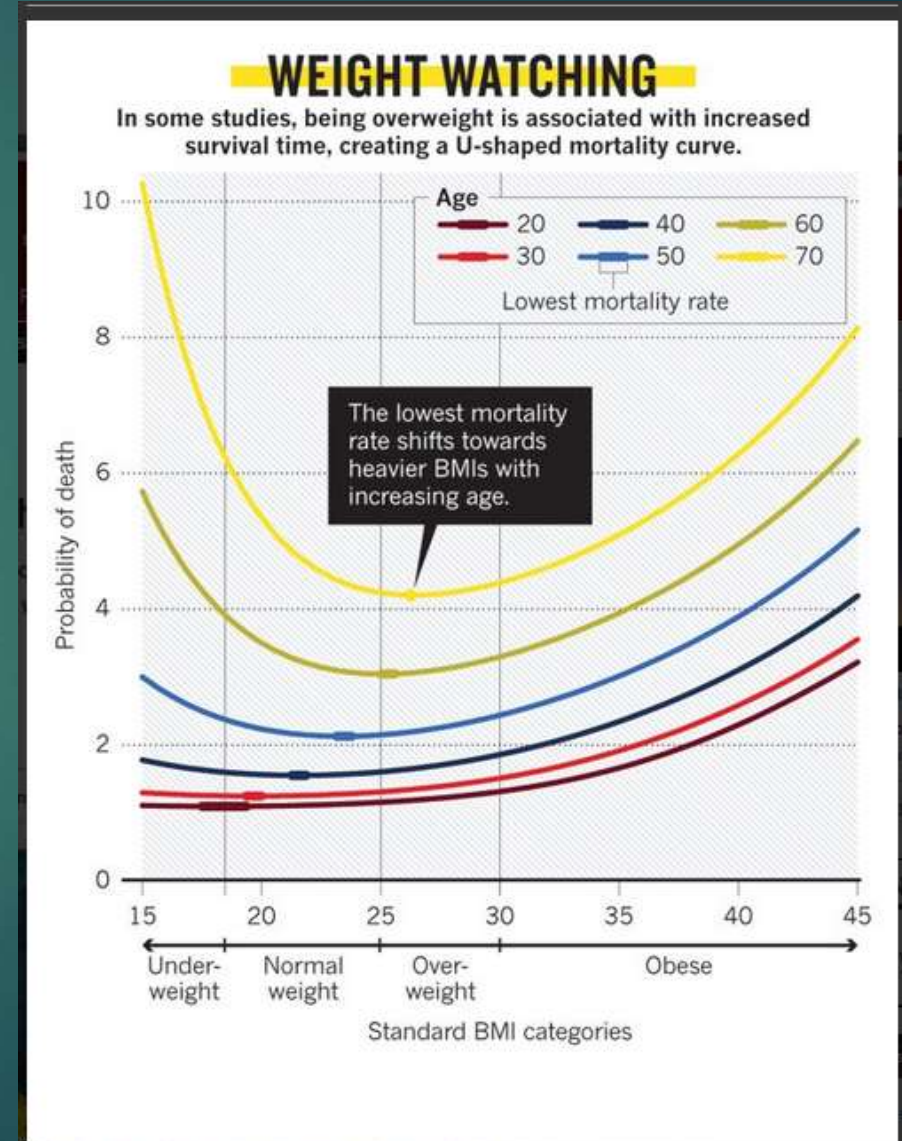
Highly tied to high consumption of fried and processed foods

The obesity paradox:

With age, lower death rates with higher BMIs

- ▶ Paradox: Being overweight increases a person's risk of diabetes, heart disease, cancer and many other chronic illnesses.
- ▶ But for those who are middle-aged or older, or already sick — a bit of extra weight - but not obesity - is not particularly harmful.
- ▶ Metabolic reserves could be important as people age.

Katherine Flegal, et al. 2014



The 2 biggest threats
to brain health are
stroke and Major NCD.



Preventable Cardiovascular Risk Factors:

Stop Strokes, Heart attacks, Heart failure & Vascular NCD

- ▶ Cigarette smoking
- ▶ Poor nutrition
- ▶ Physical inactivity
- ▶ Excessive alcohol use

- ▶ High blood pressure
- ▶ High cholesterol
- ▶ High blood sugar (Diabetes)
- ▶ Metabolic Syndrome (Insulin resistance)
- ▶ Obesity
- ▶ Atherosclerosis → Impaired cerebral blood flow → Brain infarction (stroke)

Keep your heart fit

- ▶ 1 - Get moving: People who exercise regularly have a 30 to 40 percent lower risk of heart disease
- ▶ 2 - Eat more plants: 17 percent lower risk of heart disease ; Make plant foods and fish the centerpiece of your meals.
- ▶ 3 - Replace saturated fat, such as butter, with canola, olive oil, and other unsaturated oils.

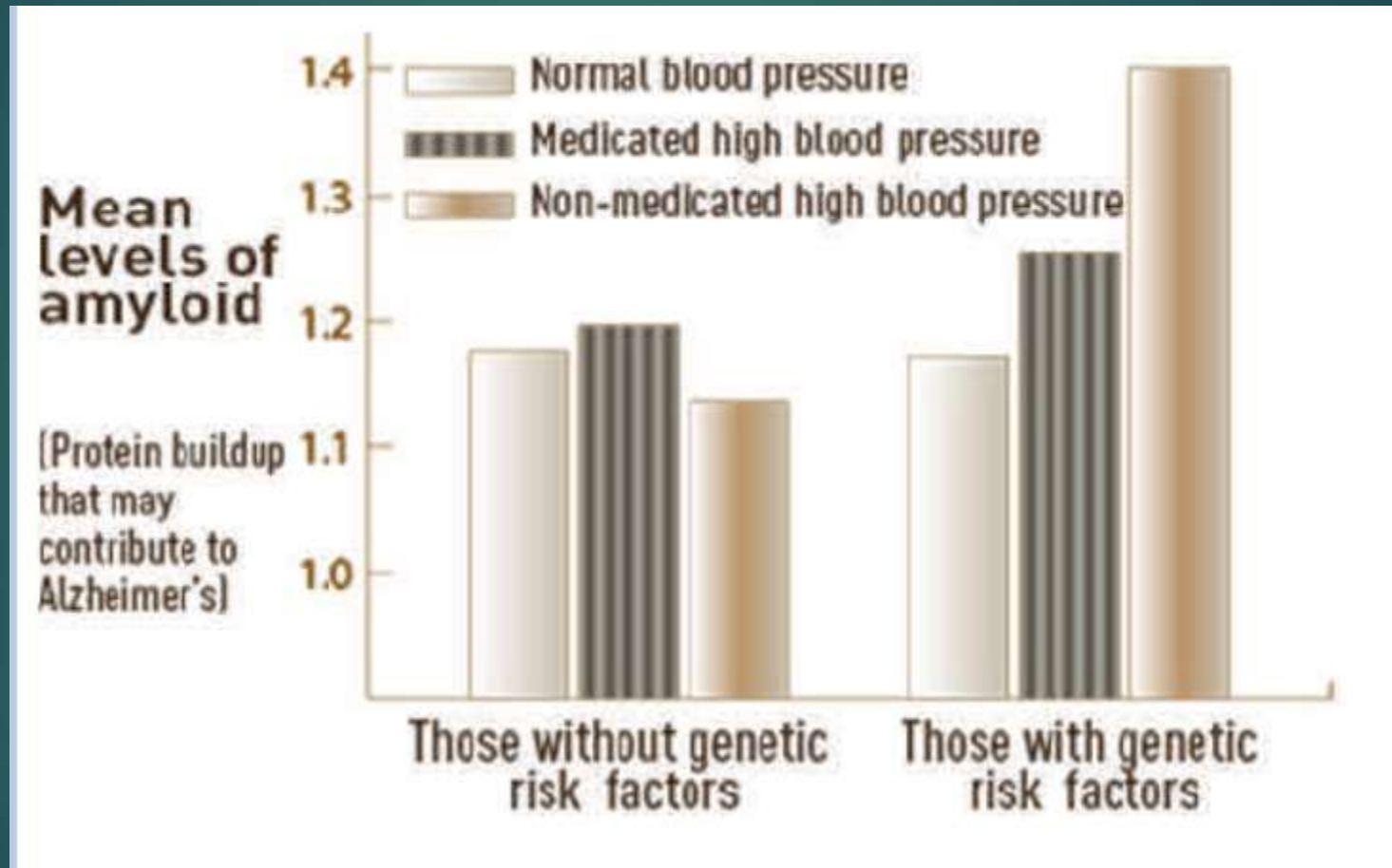
Keep your heart fit 2

- ▶ 4 - Relax
- ▶ 5 - Drink alcohol (a little)
- ▶ 6 - Quit smoking: Smokers are 2 to 4 times more likely to develop heart disease than nonsmokers.
- ▶ 7 – Take your heart medications

We need to prevent Hypertension

- ▶ Hypertension-related changes in White Matter is detectable in middle age.
- ▶ Individuals with long-standing hypertension (> 6 years) show WM tract damage, esp. if ApoE4
- ▶ Better blood pressure control among hypertensive individuals did not lessen the adverse effects.
- ▶ **Need to prevent HTN**

Hypertension Increases Beta Amyloid



Bad news: APOE4 & non-medicated hypertension

Strokes

- ▶ 800,000 strokes in US every year
 - ▶ On average, one stroke every 45 seconds
- ▶ Age is greatest risk factor.
- ▶ Women 3x greater risk in 45 to 54 age
- ▶ Related to abdominal fat

Why stroke prevention is important

- ▶ Stroke is the leading cause of disability
 - ▶ Only 50-70% re-gain functional independence
- ▶ 3rd leading cause of death (after Heart Disease & Cancer)
- ▶ 80% of strokes are preventable

Usual Suspects:

Conditions that **increase risk of stroke**

▶ Ischemic (blocking) stroke

- ▶ Obesity
- ▶ Diabetes
- ▶ High blood pressure
- ▶ High cholesterol
- ▶ Smoking
- ▶ Sleep apnea

• Hemorrhagic (bleed) stroke

- High blood pressure
- High Alcohol use

Most Strokes Can Be Prevented; 1 in 6 People Will Have a Stroke

- ▶ Know your personal risk factors: high blood pressure, diabetes, and high blood cholesterol.
- ▶ Take your medications faithfully.
- ▶ Be physically active and exercise regularly.
- ▶ Avoid obesity by keeping to a healthy diet.
- ▶ Limit your alcohol consumption.

FAST



Warning signs:

Sudden numbness, especially at one side of the body;
sudden trouble speaking or seeing;
loss of balance or sudden vertigo;
sudden severe headache with no apparent cause

Each hour lost: 120 million neurons, 830 billion synapses, and 447 miles of myelinated fibers are lost

Tip #4: Meditate!

Get longer telomeres

- ▶ People who meditate regularly have less cognitive decline and brain shrinkage
- ▶ 12 minutes a day for two months = improved cognition in seniors with memory problems.
- ▶ More mind wandering = shorter telomeres; being present in the moment = longer telomeres

Tip # 5: Do not Smoke

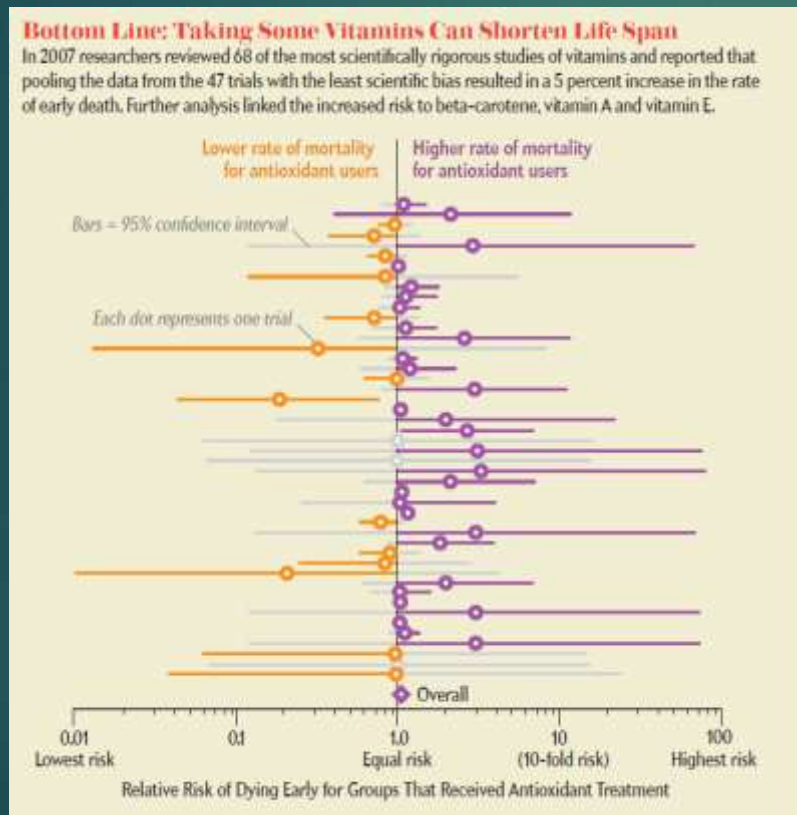
- ▶ Cigarettes kill more people than: AIDS, drugs, alcohol, murder, & car crashes combined
- ▶ Cigarettes are **lethal**: 400,000 deaths per year
- ▶ Increases **stroke risk**
- ▶ **Five times faster decline in cognition/Major NCD** in smokers compared to non-smokers

Tip #6: Take Vitamin D

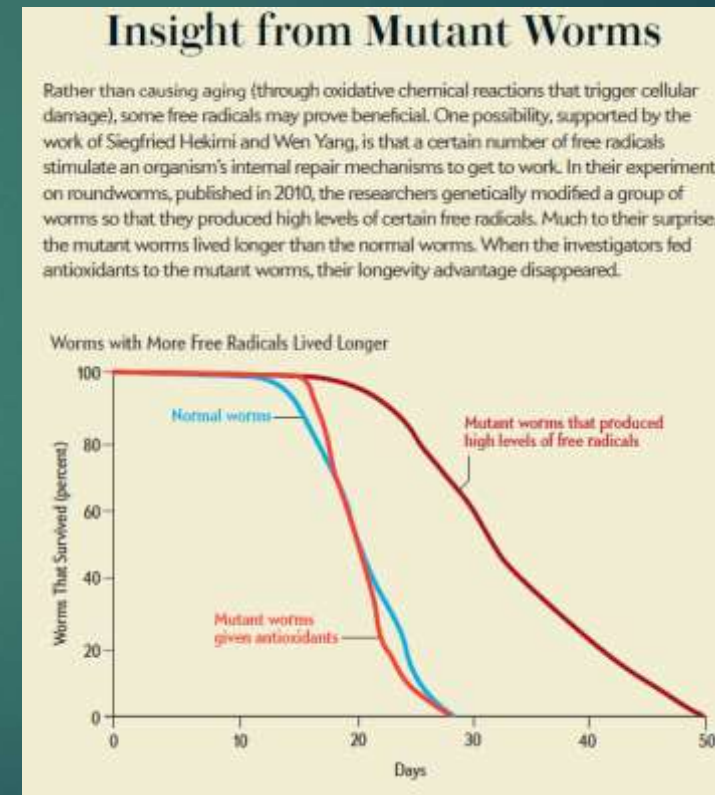
- ▶ Older do not get enough sunlight
- ▶ Low Vitamin D increases cognitive decline
- ▶ Older need 1000 IUs/day (eat with a fat); Eat fish regularly
- ▶ Stroke: The lower the vitamin D level, the more severe the stroke and the poorer the recovery
- ▶ Higher Vitamin D associated with a decreased risk of developing:
 - ▶ cardiovascular disease (33% reduction)
 - ▶ type 2 diabetes (55% reduction)
 - ▶ metabolic syndrome (51% reduction).

Anti-oxidants: Beware

People should not take antioxidant supplements/vitamins except to treat a diagnosed vitamin deficiency. Especially megadoses of Vitamin E



5% risk of early death:
Beta-carotene, Vitamins A & E



More free radicals = more cellular repair, longer life; vs. anti-oxidants, earlier death

New Miracle Drug



Tip #7: Drink Coffee

- ▶ People who drink coffee have:
 - ▶ 36% less strokes; less heart disease
 - ▶ reduced risk of NCD/dementia (reducing inflammation & beta amyloid); reduces Alzheimer's risk by 20%
 - ▶ reduced cancer risk (50% less recurrent breast cancer, prostate cancer, 72% less liver cancer)
 - ▶ lower risk of tinnitus in women; lower risk of liver disease
 - ▶ lower type 2 diabetes (21-33% less)
 - ▶ less depression (15% less), Parkinson's (25% less)
 - ▶ More muscle force
 - ▶ live longer, 10% less mortality
- ▶ 1 to 4 cup per day effect.
- ▶ Not for: pregnant women, those with sleep problems

Drinking three to five cups of coffee a day carries no chronic disease risk.

Benefits of Coffee

▶ Caffeine

- ▶ Reduces liver fibrosis (tamps down enzyme alanine aminotransferase)
- ▶ Slows heart and liver damage
- ▶ May counter Parkinson's, dementia, depression
- ▶ Boosts feel-good dopamine

▶ Polyphenols (chlorogenic acids, caffeic acid)

- ▶ Reduce liver fibrosis
- ▶ Boost DNA repair
- ▶ May fend off blood clots
- ▶ Boost metabolic efficiency
- ▶ Lower blood pressure (offsetting caffeine's fleeting blood pressure-boosting effect)
- ▶ Act as demethylating agents
- ▶ Lessen intestinal injury from free radicals

Diterpenes (cafestol and kahweol)

Fight certain carcinogens

Reduce liver DNA adducts (bits of DNA bound to carcinogens)

Boost levels of glutathione, an antioxidant that prevents liver damage

Target and kill mesothelioma cells in lung tissues

Kahweol is anti-inflammatory and cuts blood flow to tumors

But both can also lead to higher levels of bad cholesterol (LDL)

Trigonelline

Antioxidant

Lowers blood sugar

May have brain benefits

Green Tea & Stroke

- ▶ 13 year Japanese study, 2013:
- ▶ The more green tea or coffee people drink, the lower their stroke risks.
- ▶ Green tea drinkers in the study were more likely to exercise
- ▶ Red wine and Green Tea: may reduce beta amyloid

Tip #8: Brush and Floss

- ▶ Gingival inflammation is associated with cognitive decline.
- ▶ Periodontal disease before age 35 quadrupled the odds of Major NCD years later.
- ▶ Elderly people who reported brushing their teeth less than once a day were up to 65 percent more likely to develop Major NCD than those who brushed daily.

Tip #9: Google! Use the Internet.

- ▶ Doing an online search can stimulate your aging brain even more than reading a book
- ▶ UCLA's Gary Small: Novice Internet surfers, ages 55 to 78, activated key memory and learning centers in the brain after only a week of Web surfing for an hour a day.

Tip #10: Get Enough Sleep

▶ Brain during sleep:

- ▶ It cleans our brain cells: removes beta amyloid during sleep
- ▶ consolidate our memories: we sleep to learn. Sleep is crucial to memory functioning

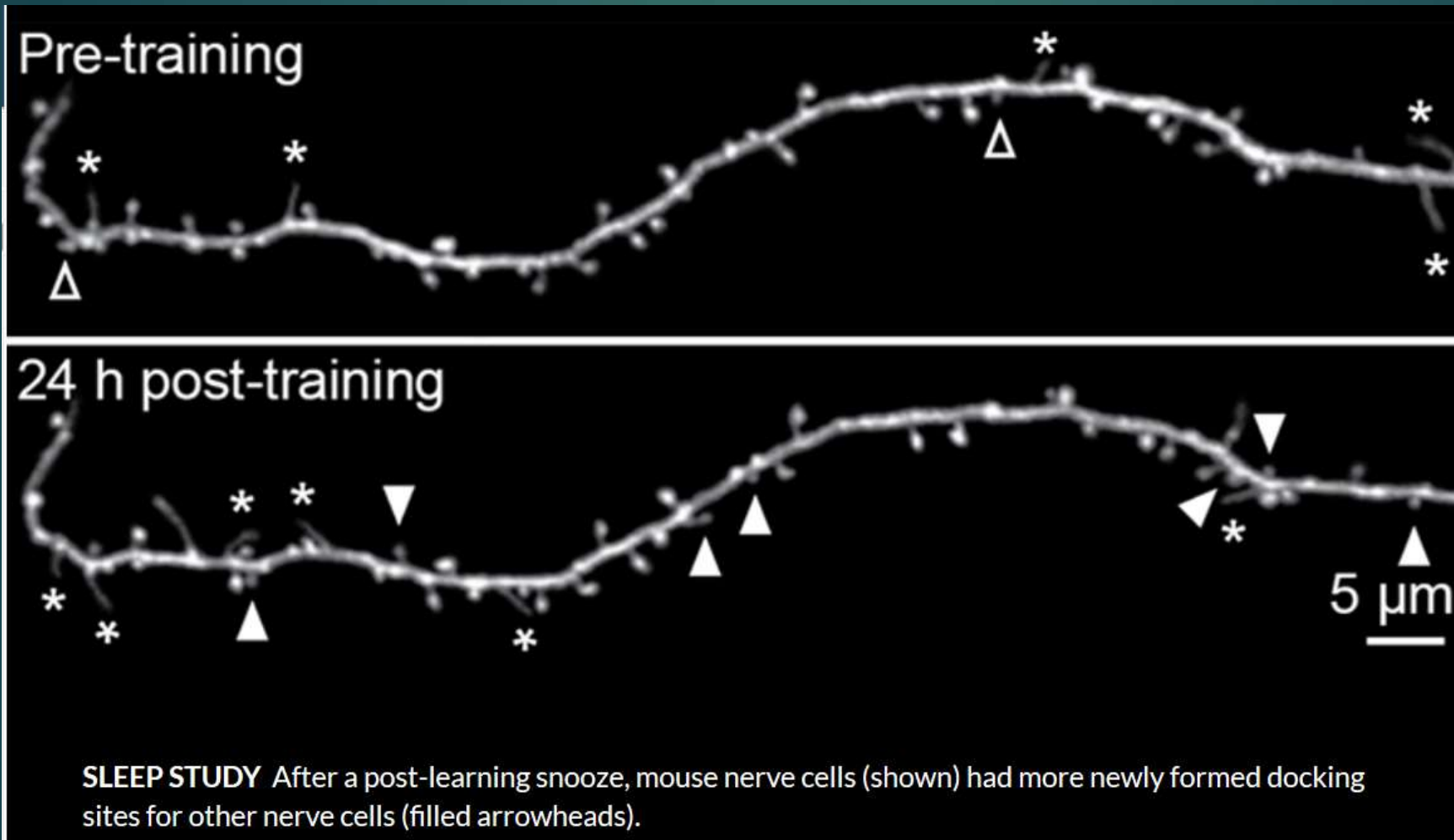
▣ Lack of sleep:

- ▣ poorer response inhibition, executive function, & task-switching
- ▣ poorer attention & processing speed
- ▣ makes us dangerous drivers
- ▣ can make us eat too much.
- ▣ poorer declarative, behavioral, spatial, & working memory

Deep Sleep and Memory

- ▶ Slow brain waves during deep sleep enhance strengthens newly formed memories
- ▶ Brain deterioration, bad memory and bad sleep are significantly interrelated.
- ▶ Least slow-wave activity in deep sleep = worst on memory testing.

Sleep strengthens synapses and memory



Sleep Problem Treatment

- ▶ Avoid or cut down on having daytime naps.
- ▶ Don't lie in bed trying to get to sleep.
- ▶ Minimize the amount of time you spend in bed awake.
- ▶ Do **Cognitive Behavioral Therapy for Insomnia** (80% successful)

Sleep apnea increases stroke, cancer, dementia & death risk



- ▶ Sleep-disordered breathing is very common among the elderly (53% of men & 26% of women)
- ▶ Moderate to severe sleep apnea triples risk of stroke, cancer, and earlier death
- ▶ Sleep apnea = temporary blockage of air flow by “floppy muscles” during sleep
 - ▶ Causes short drop in oxygen level in blood & raises blood pressure at night
 - ▶ 1 in 10; 3x higher stroke rate; 2x higher death rate if no C-PAP Tx
 - ▶ Sleep deprivation: increased appetite, increased diabetes, insulin resistance
- ▶ There is treatment for apnea: C-pap & B-pap machines

Sleep apnea

- ▶ As sleep apnea increases, so does Major NCD risk
- ▶ Begin experiencing cognitive decline 10 years earlier than those without the disorder, or those who use a breathing machine to treat their apnea
- ▶ MCI at average age of 77, compared to age 90
- ▶ Due to oxygen deprivation or to sleep fragmentation

Tip #11: 15 minutes of laughter and smiling

- ▶ Laughter & smiling are good for the heart.
- ▶ Benefits:
 - ▶ blood vessel relaxation
 - ▶ Lower blood pressure
 - ▶ Less pain
 - ▶ Longer life



Smiling: 250 baseball players photos of 1950s: smile intensity in photographs was linked to longevity.

Smilers lived 7 years longer.

Tip #12: De-stress!

- ▶ Chronic stress increases risk of Major NCD
- ▶ Increases levels of “stress hormones” (adrenaline, cortisol)
 - ▶ Increases blood sugar and blood pressure
 - ▶ High cortisol levels kill hippocampal cells
 - ▶ Impairs neuron functioning
 - ▶ Affects cognitive abilities



Tip #13: Eat a little dark chocolate

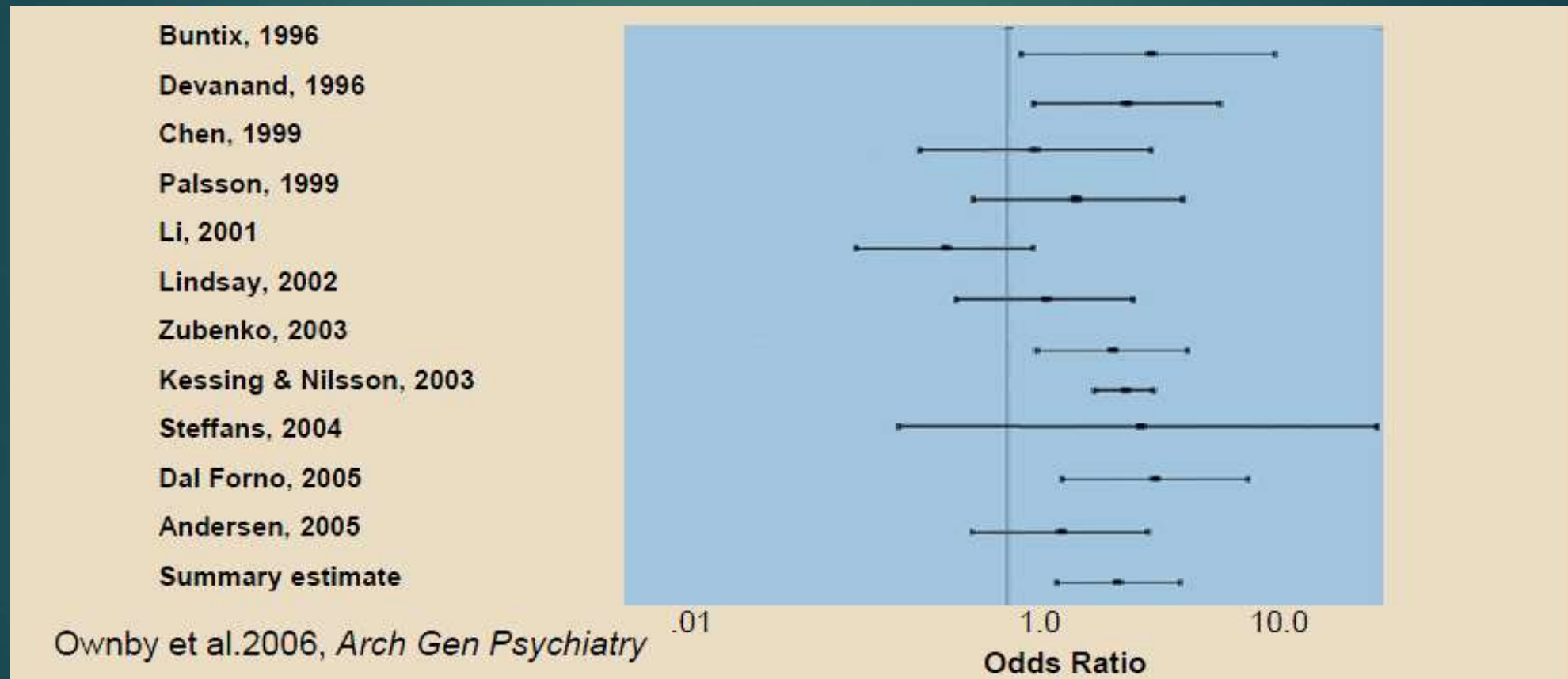
- Chocolate, red wine, cocoa, and coffee are major dietary flavonoids (polyphenols) sources found in plant-derived foods.
- A high-flavanol intervention was found to enhance memory functioning.
- Increases Dopamine (reward neurotransmitter) in brain for several hours.
- But correlation between depression and increased chocolate consumption



Tip #14: Treat Depression

- ▶ Depression is a risk factor for Major NCD
- ▶ Depression turns off neurogenesis
- ▶ Anti-depression TX (either medication or Cognitive Behavioral Therapy or ECT) turns on neurogenesis and reduces risk of Major NCD

Depression Associated with a Doubling in Risk of Major NCD



Antidepressants: Increase Hippocampal Volume



Most Important Tip #15: Exercise

Keep moving and Keep your wits

- ▶ Exercise is the single most powerful and best way to reduce the risk of cognitive decline.
- ▶ Aerobic exercise keeps your heart fit and increases the size of hippocampus
- ▶ Increases BDNF and VEGF in your brain

★ Get Moving!

- Exercise daily!
- Walk with a friend or a dog
- Join a health club
- Get physical!



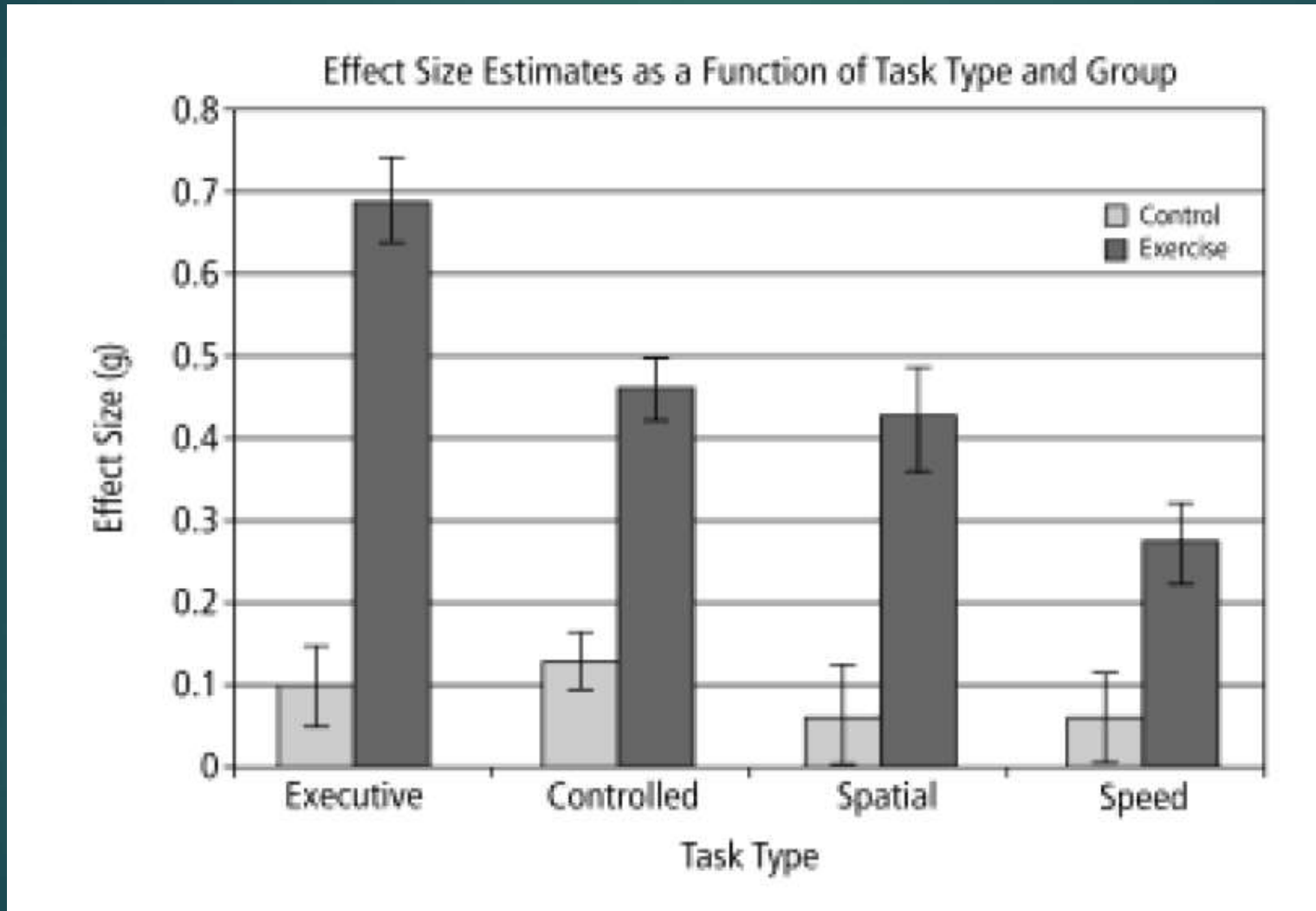
Benefits of Exercise

- ▶ Reduces risk of cardiovascular disease, stroke, diabetes; increases large LDL molecules, less small LDL; increases HDL
- ▶ Prevents certain cancers (breast, colon)
- ▶ Improves mood and reduces anxiety/stress
- ▶ Builds bones and muscles; less falls
- ▶ Expands lung capacity
- ▶ Reduces inflammation
- ▶ Reduces fall and fracture risk
- ▶ Keeps weight normal; reduces metabolic syndrome
- ▶ Boosts cognitive ability (executive function)

Benefits of Exercise

- ▶ Reduces major NCD risk
- ▶ Increases size of dentate gyrus of hippocampus by 2% (reversing normal yearly loss)
- ▶ Increases new synapses and dendritic branches
- ▶ more neurogenesis
- ▶ more BDNF
- ▶ Better executive functioning

Cognitive performance in elders who do aerobic exercise vs. who do not



Current Recommendations

- ▶ A – 150 minutes of aerobic exercise (AHA) per week
 - ▶ 30 minutes of moderate activity (brisk walk; can still talk) 5 times a week
 - ▶ Or 75 minutes of vigorous activity (jogging)
- ▶ B - 20 minutes of muscle strengthening (resistance) activity 2 x a week
- ▶ Only 52% meet A
- ▶ Only 29% meet B

2013 Meta-analysis: Exercise reduces risk of AD

- ▶ People over age 65 who were physically active were about 38 per cent less likely to develop the degenerative brain disease than those who were physically inactive.
- ▶ Moderate to vigorous activity makes breathing harder while still allowing a person to sing.
- ▶ Brisk walking, running, swimming, dancing

Sitting kills you sooner; even if you exercise

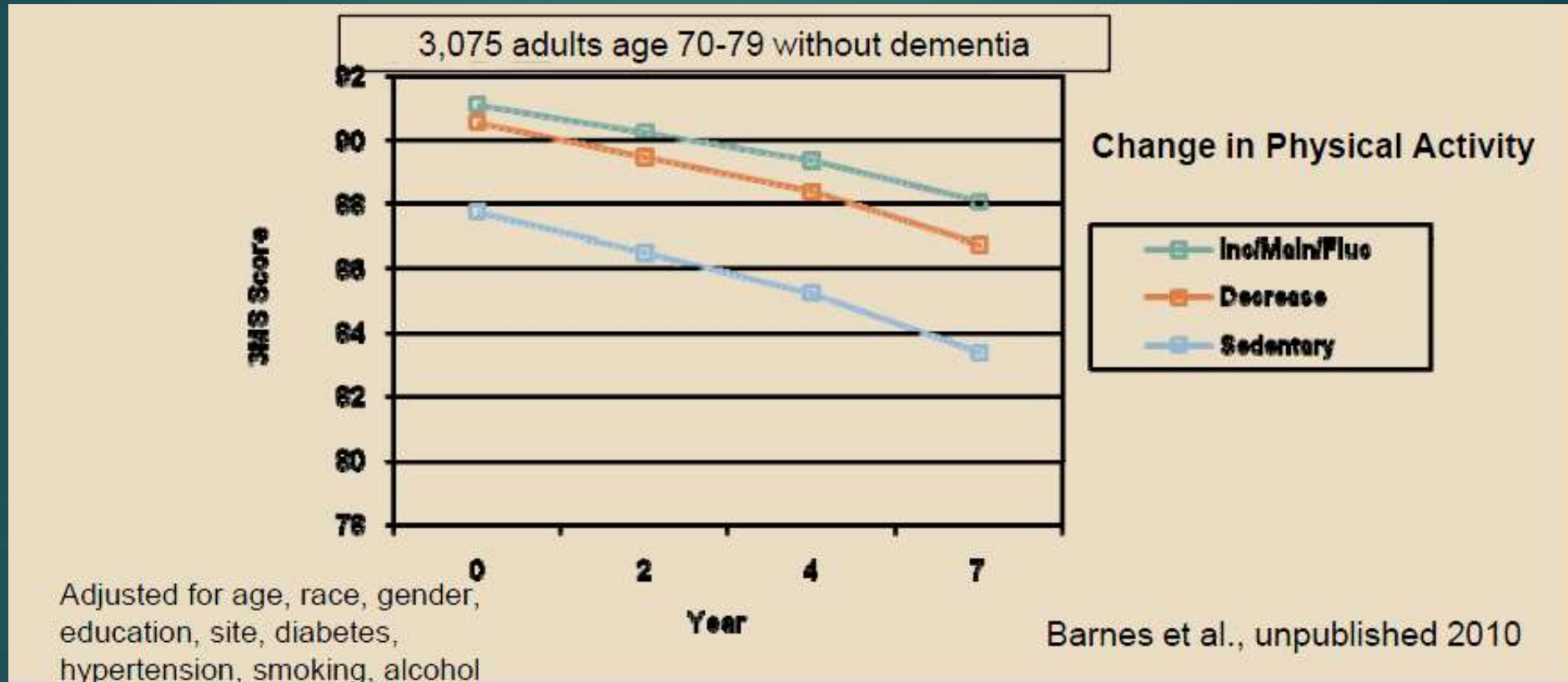


- ▶ Adults = 55% of their day engaged in sedentary pursuits
- ▶ Link between extended sitting &/or watching TV to poor health: significantly higher risk of heart disease, diabetes, obesity, cancer, and depression, as well as muscle and joint problems.
- ▶ Metabolism slows down 90 percent after 30 minutes of sitting. After two hours, good cholesterol drops 20 percent. Just getting up for five minutes is going to get things going again

Sitting is the new smoking unless you fidget

- ▶ Americans **sit for an average of 13 hours every day**. Sitting for more than half the day doubles the risk of diabetes and cardiovascular problems
- ▶ **Increases:**
 - ▶ high blood sugar spikes
 - ▶ abnormal glucose metabolism for example, and an increased risk of metabolic syndrome.
- ▶ **Sitting for seven plus hours a day correlates to a 30 percent higher risk of death**—regardless of how active study subjects were at other times.
- ▶ **Fidgeting counteracts negative effects.**

Sedentary/Decreasing Activity → → Faster Cognitive Decline



To counteract sitting effects:

- ▶ Remember to stand once an hour.
- ▶ Get about 30 minutes of activity per day.
 - ▶ Can be broken up into 5-10 minutes of activity
- ▶ Set an hourly standing alarm to remind you to stand (or use computer program WorkRay to remind you)
- ▶ Use TV commercial breaks as a chance to stand and stretch.

Exercise causes Neurogenesis



- Neurogenesis declines with age; declines with early Major NCD
- Number of new hippocampus neurons is twice that of mice living in standard cages.

-

Exercise: **Best is one you will do**

- ▶ Exercise ↑, Cognitive ↑
- ▶ Strength + aerobic better
- ▶ 30 minutes per day
- ▶ Find an “exercise partner”

Walk a Hound, Lose a Pound

- ▶ Dogs can be powerful motivators to get people moving.
- ▶ Dog owners more likely to take regular walks

Muscles: Use em or lose em



- ▶ For our muscles, it's a case of 'Use em or lose em'.
- ▶ Strength training (lifting weights; 20 minutes, 3x a week) is as important as anaerobic exercise
- ▶ You can use cans of beans to lift

90+ Cohort: What helps you live longer

- ▶ Alcohol - 1 glass daily
- ▶ Caffeine (coffee, cola, chocolate): U shape relationship, 1-2 cups daily
- ▶ Weight: your BMI: if 70+, normal or slightly overwgt better; thin in 80's, higher mortality
- ▶ Exercise: minimum of 15 minutes daily; 45 minutes best
- ▶ Active leisure & social life: up to 8 hrs a day

General Correlates of Living longer

- ▶ Don't smoke: 56% lower risk of dying
- ▶ Exercise: 47%
- ▶ Healthy (Mediterranean) Diet: 26%
- ▶ Have a Higher IQ: a person with an IQ of 115 is 21% more likely to be alive at age 76 than a person with an IQ of 100 (the average for the general population)
 - ▶ SES accounts for only 30% of this
 - ▶ it's mostly genetic;
 - ▶ higher IQ contributes to optimal health behaviors, such as exercising, wearing a seatbelt, and not smoking.
 - ▶ Highly correlated to processing speed
 - ▶ IQ predicts outcomes such as job performance, academic achievement, and, as it happens, mortality, better than any psychological factor that we know of.

Tip #16: Drink a little Alcohol

- ▶ If you drink 5 drinks in 2 hours on any day of the week, you are alcoholic! Increases the risk for death by 31% to 54%; cancers by 51%.
- ▶ Drinking one drink per day correlates with positive health outcomes
- ▶ Latest 2014 British Study: 2.5 drinks per day produces memory impairment 10 years later
- ▶ 2014 study: light and moderate alcohol consumption in older people is associated with higher episodic memory and is linked with larger hippocampal brain volume.

Tip #17: Socialize: Longer life & less cognitive decline



Go dancing



Socialize

- Remain actively engaged with other people
- Being social: more BDNF

Real source of happiness



Harvard Study of Adult Development: Longest Prospective Study

- ▶ **75 year prospective study** (every 2 years reexamined)
 - ▶ Group 1 (724 sophomores at Harvard; JFK's class); 60 still alive
 - ▶ Group 2 (456 disadvantaged Boston teenagers); 120 alive

Harvard Study results

- ▶ **Good relationships** keep us happier and healthier
- ▶ **Quality of vacations younger in life (ability to play) is a better indicator of late-life happiness than income.**
- ▶ Importance of a **healthy, stable marriage** to late-life happiness
- ▶ **Negative effects of alcohol** on marital and lifetime success; **57 % of all divorces in men involved alcoholism.** AA works best
- ▶ **Main developmental task for younger couples is managing conflicts. The main task for older couples is mutual support.**

Be social

- ▶ Social relationships (family, friends, community) are really good for us
- ▶ Loneliness kills: isolation is toxic (less happy, health declines earlier in midlife, brain declines sooner, die sooner); 1 in 5 Americans
- ▶ Quality of close relationships count; living in conflict with no affection is toxic, & worse than divorce; warm relationships are protective
- ▶ Those who were **most satisfied in their relationship at age fifty were most healthy at age 80**
- ▶ Physical pain is magnified if in unhappy relationships
- ▶ Being in securely attached relationship (can depend on the other, even if bicker a lot) in your 80s is protective of brain and memory functioning

Possibilities

- ▶ Do as much people time as screen time
- ▶ Reach out to old friends and family
- ▶ Revitalize stale relationships: do something new (walk together; date nights)
- ▶ **Mark Twain**: “There isn’t time, so brief is life, for bickerings, apologies, heart burnings, callings to account. There is only time for loving; and but an instance, so to speak, for that. The good life is built with good relationships.”

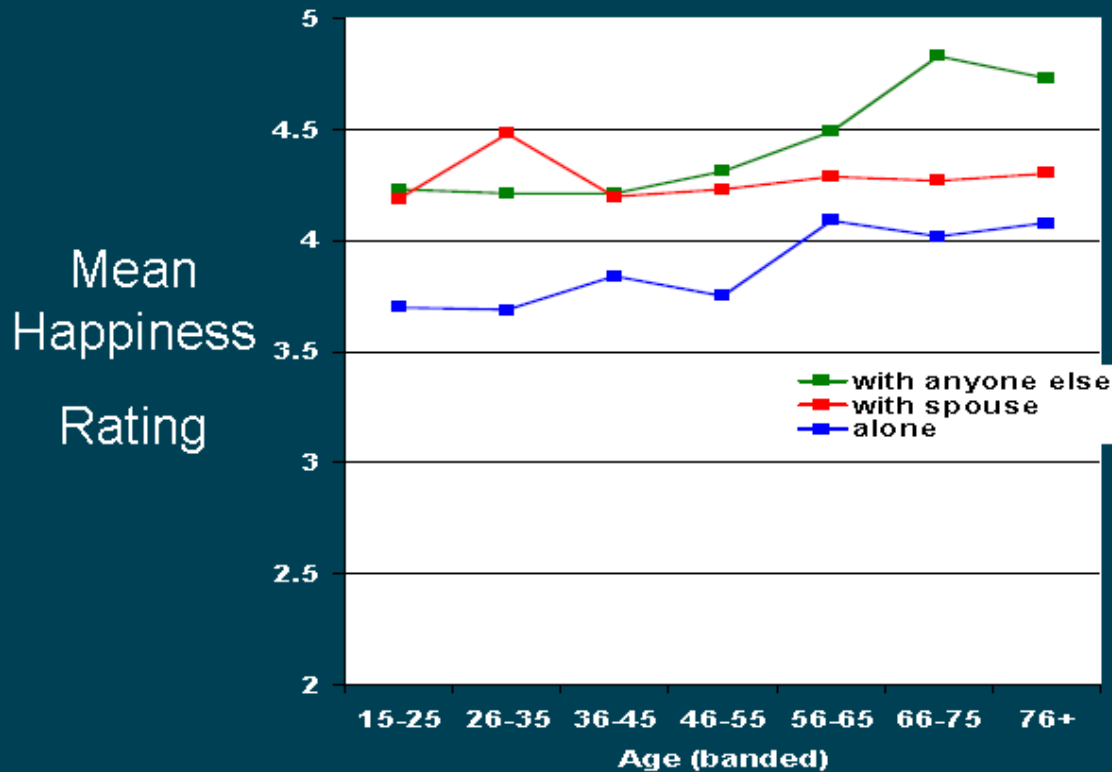
★ Get Social!

- Meet with friends
- Join a club
- Volunteer your services
- Meet someone new and chat...



Stay in Touch: More positive feelings when time spent with others

Positive Emotion by Time Spent Alone, with Spouse or with Others



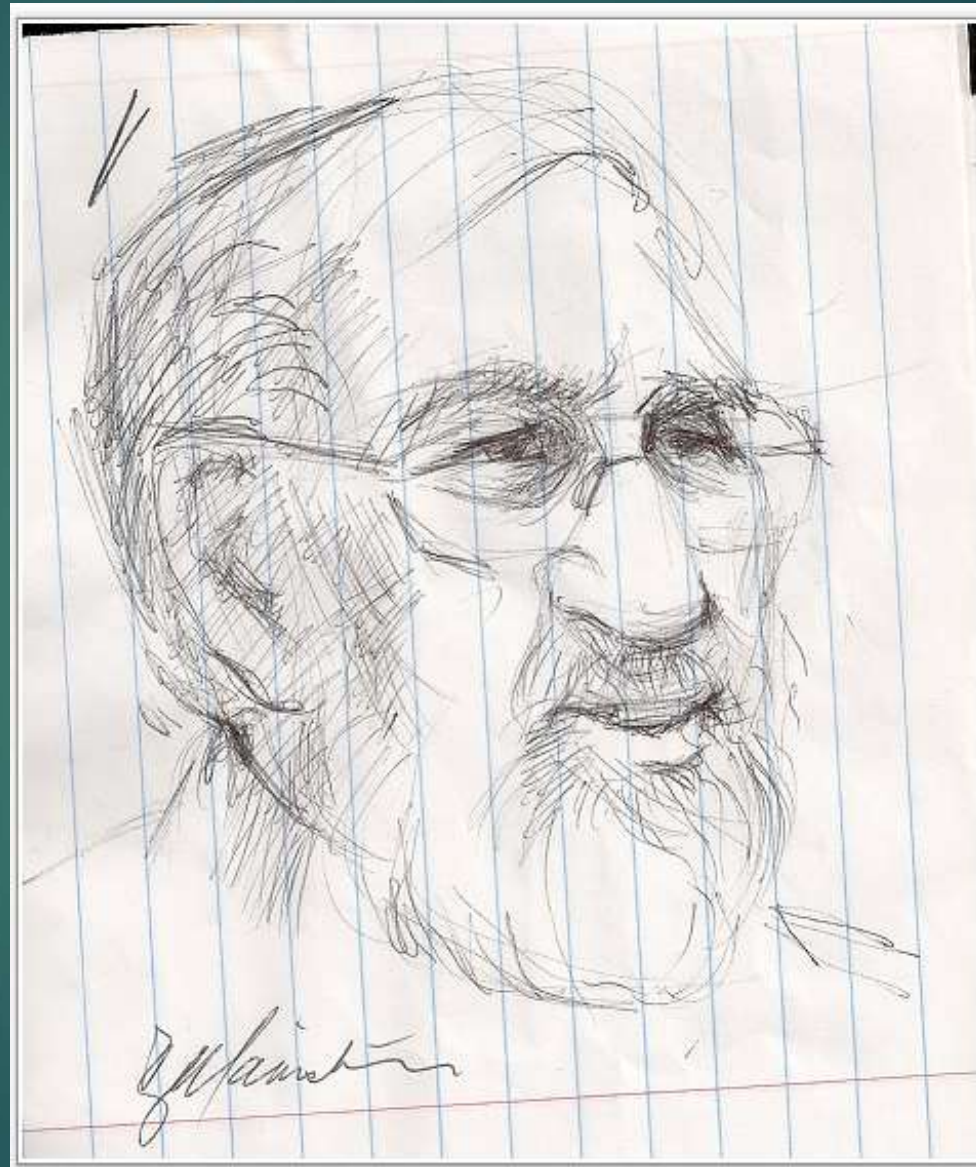
Depp et al.,
Unpublished;
Data from Princeton
Affect and Time Use
Survey

Playing Bridge: Better immune system



M. Diamond: 1.5 hours of bridge playing increased T lymphocytes immune cells

Paint your lecturer



Social relationships predict longer life

- ▶ Adults with adequate social relationships have a 50% greater likelihood of survival.
- ▶ Magnitude of this effect is comparable with quitting smoking.
- ▶ The greater the extent of the relationships, the lower the risk of mortality.

Loneliness kills

- ▶ Loneliness = 2 packs of cigarettes per day effect
- ▶ Socially isolated people have shorter life spans and increased risk of a host of health problems,
- ▶ Subjective experience of loneliness is harmful, not the actual number of social contacts a person has.
- ▶ Need one intimate friend
- ▶ Seniors who are "housebound" have nearly double the risk of developing Alzheimer's disease or MCI

Tip #18: Stay Cognitively Active

- ▶ Risk of Major NCD is lower with:
 - ▶ More education; college courses at any age
 - ▶ Higher IQ
 - ▶ Greater occupational achievement
 - ▶ More mentally stimulating activities
 - ▶ More leisure activities

What doesn't kill you, makes you smarter.

"One should not pursue goals that are easily achieved. One must develop an instinct for what one can just barely achieve through one's greatest efforts."

Albert Einstein

Do any of following (or see my website)

- ▶ Visit a museum
- ▶ Memorize a song
- ▶ Exercise your peripheral vision
- ▶ Learn a new musical instrument
- ▶ Do jigsaw puzzles
- ▶ Turn down the TV (listen better)
- ▶ Throw & catch a ball; learn to juggle
- ▶ Increase difficulty level of crossword/sudoku
- ▶ Use your other hand
- ▶ Walk on cobblestones
- ▶ Learn a new dance or a new language

Tip #19: Dance

- ▶ Increased socialization and improved physical functioning
- ▶ Improves balance and gait in older adults.
- ▶ There is a significantly reduced risk of Major NCD in older adults who dance frequently.



Pumpkin carving, belly dancing,
UCSF med school grad, daughter
Dr. Maya Vella

Tip #20: Play a Musical Instrument

- ▶ 10 years of musical experience = better nonverbal memory, naming, and executive functioning in advanced age relative to nonmusicians.
- ▶ It is never too late to be musically active.

Tip #21: You are what you eat: Eat like a Greek



- ▶ Mediterranean diet:
 - ▶ high plant foods (vegetables, fruits, legumes, and cereals)
 - ▶ high intake of olive/canola oil; low intake of saturated fat, butter
 - ▶ moderate intake of fish and poultry twice a week
 - ▶ red meat to no more than a few times a month
 - ▶ low dairy products
 - ▶ using herbs and spices instead of salt to flavor foods
 - ▶ wine in moderation, normally with meals.
- ▶ Associated with more exercise & sociability

Mediterranean Diet: many benefits

- ▶ Associated with:
 - ▶ longer survival,
 - ▶ reduced obesity,
 - ▶ reduced diabetes,
 - ▶ reduced risk of CV or cancer death,
 - ▶ reduced risk of neurodegenerative disease
- ▶ 36% fewer strokes
- ▶ Significantly reduces Metabolic Syndrome

Type of Fat affects Memory

- ▶ **2012 Harvard study:** women >65
- ▶ **Worse memory:** red meat, butter (food high in saturated fats); transfats
- ▶ **Better memory:** olive oil, sunflower oil, seeds, nuts and avocados (monounsaturated fats)
- ▶ Link between high cholesterol and a higher risk of developing Alzheimer's

Tip #22: Eat Fish twice a week: Omega 3 & Vitamin D



Fish twice a week better at reducing heart attacks & strokes than dietary supplements of Omega 3 fish oil

Algae/green grass source crucial

Preserves telomere lengths in (best longevity predictor)

Omega 3: Positive & Negative

- ▶ Omega 3 Fish Oil: lower levels of Beta amyloid & Major NCD risk
- ▶ But DHA 1000mg 2x/day had no effect on AD
- ▶ Caution for men: High intake of omega-3 fats linked to 40% increased prostate cancer risk in men



Omega 3 alternatives

▶ Green leafy vegetables such as, spinach, broccoli, kale, and Brussels sprouts.

Legumes such as, pinto beans, kidney beans, black beans, and split peas.

Walnuts

Pumpkin seeds and flax

Berries such as, raspberries, blueberries, blackberries, and strawberries

Avocados.

Tip #23: Lifelong learning

- ▶ **Local Universities: Fromm Institute at USF, OLLI at SFSU, CLIR**
- ▶ **Hope Levy's Mental Aerobics Class thru SFCC**
- ▶ **Elderhostel/Exploritas: <http://www.exploritas.org/>**
- ▶ **Lifelong Learning Institutes**
 - ▶ **www.exploritas.org/ein/LLIList.asp?state=CA**
- ▶ **Local Senior Centers**
- ▶ **SeniorNet: <http://www.seniornet.org/>**
- ▶ **OASIS Institutes (volunteer)**
 - ▶ **<http://www.oasisnet.org/>**
- ▶ **Shepherd's Centers of America**
 - ▶ **<http://www.shepherdcenters.org/>**
- ▶ **Senior Community Service Employment Program (SCSEP)**



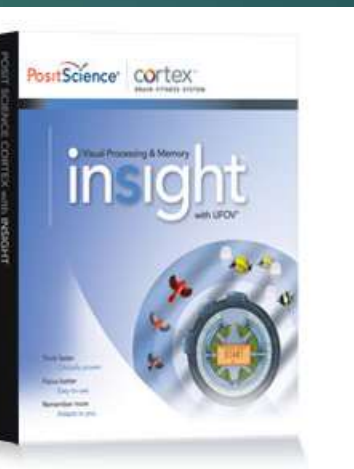
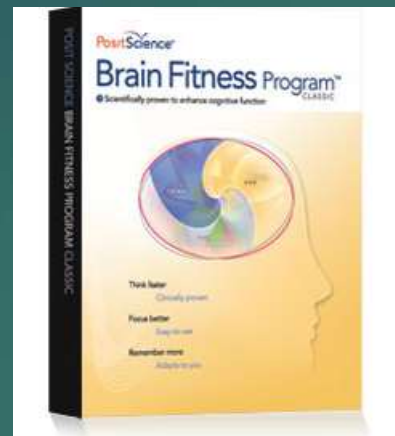
Computer Programs

- ▶ A variety of computer programs claim to reduce the risk of cognitive decline
- ▶ Neurobics: Sales are expected to jump from \$265 million to up to \$5 billion by 2015, according to market-research firm SharpBrains.

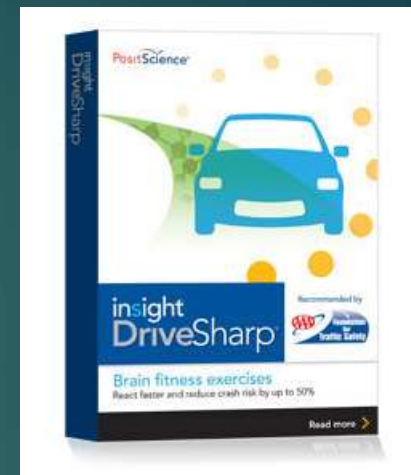
Products (No endorsement Implied)



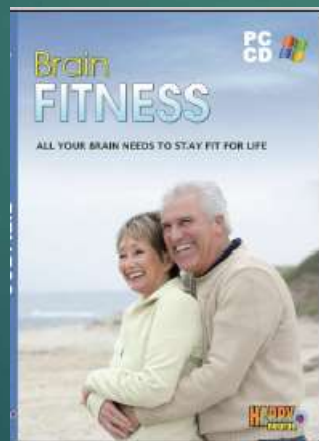
NeuroActive



Posit Science



Mindfit



Happy Neuron



Lumosity

Brain Websites

- ▶ Dakim: <http://www.dakim.com>
- ▶ Brainmetrix: <http://www.brainmetrix.com/mind.htm>
- ▶ Lumosity: <http://www.lumosity.com/k/brain-train>
- ▶ Brain Training Games: www.braintraininggames.net
- ▶ Miniclip: www.miniclip.com
- ▶ Mindsparke: www.mindsparke.com
- ▶ Cambridge Brain Sciences:
www.cambridgebrainsciences.com

Lumosity.com: example of unscientific claims

- ▶ Lumosity to Pay \$2 Million to Settle FTC Deceptive Advertising Charges for Its “Brain Training” Program
- ▶ Deceived consumers with unfounded claims that Lumosity games can help users perform better at work and in school, and reduce or delay cognitive impairment associated with age and other serious health conditions.

BrainHQ: Posit Science

– some research base



The image shows a screenshot of the BrainHQ website homepage. The page has a dark grey header with the BrainHQ logo and 'help' on the left, and 'LOG IN | SUBSCRIBE | SIGN UP' on the right. The main content area has a yellow background with the text 'Brain Training That Works' in the center. Below this text is a circular graphic of a brain with colored lobes. To the right of the brain graphic are two yellow buttons: 'SIGN UP >' with 'FREE EXERCISES' below it, and 'SUBSCRIBE >' with 'FULL ACCESS' below it. At the bottom center, there is a logo for 'brainHQ from Posit Science' and a yellow button that says 'LEARN MORE' with a downward arrow.

brainHQ | help

LOG IN | SUBSCRIBE | SIGN UP

Brain Training That Works

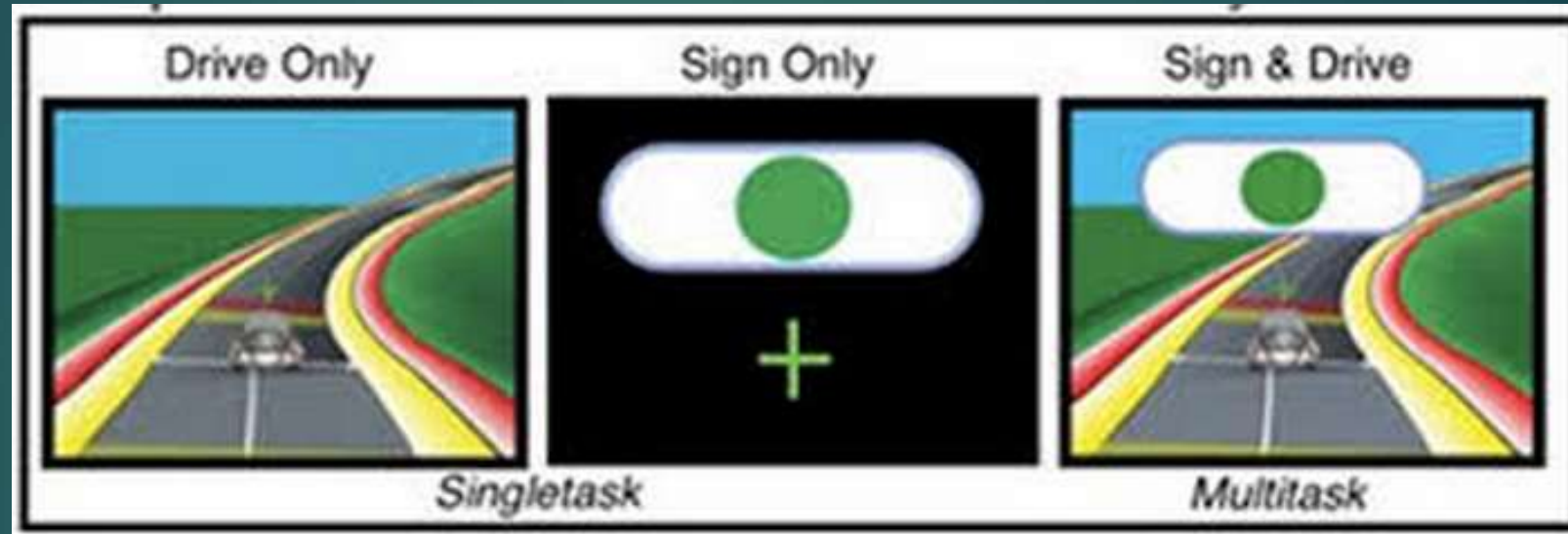
SIGN UP >
FREE EXERCISES

SUBSCRIBE >
FULL ACCESS

brainHQ
from Posit Science

LEARN MORE

NeuroRacer:



- ▶ Adam Gazzaley of UCSF:
- ▶ A game called NeuroRacer can help older people to improve their capacity to multitask — and the effect seems to carry over to tasks in everyday life and is still there after six months.

Project: Evo



Software-based method to measure and improve a key system of executive function known as "interference processing." FDA medical device approach

NIH 10 year study

- ▶ Older adults who engaged in brain training drills retained measurable benefits up to 10 years later.
- ▶ 10 sessions, each lasting about 60 to 70 minutes over five to six weeks: paper-and-pencil tests that honed problem-solving involving letter and number patterns, in addition to computer drills (only 1 on the market – by **Posit Science**)
- ▶ 74% of those who participated in reasoning exercises and information-processing drills & 71 % of speed-trained participants still displayed those abilities a decade later; above the level they displayed at the beginning of the trial.
- ▶ No such difference was observed in memory skills

Brain Training: **Current Conclusions**

- ▶ Brain-training programs do indeed produce short-term, highly specific improvements in the task at hand, but they do not produce generalized improvements to overall real world intelligence, memory, attention, or other cognitive ability.
- ▶ A more real benefit: expose yourself to a variety of problem-solving skills throughout the day--and not necessarily on the computer.

Computer Cognitive Training: Current Conclusions

- ▶ Cannot repair or restore neurons
- ▶ Transfer of computerized training is still controversial and being researched.
- ▶ Not a disease modifying intervention
- ▶ CT is not a substitute for exercise, CV medications, or socializing
- ▶ Every hour spent alone at the computer is an hour not spent hiking, learning a new language, inventing a new recipe, or playing with your grandkids.

2014 Stanford & Max Planck Inst. Scientific Consensus

- ▶ “We object to the claim that brain games offer consumers a scientifically grounded avenue to reduce or reverse cognitive decline when there is no compelling scientific evidence to date that they do. The promise of a magic bullet detracts from the best evidence to date, which is that cognitive health in old age reflects the long-term effects of healthy, engaged lifestyles. In the judgment of the signatories below, exaggerated and misleading claims exploit the anxieties of older adults about impending cognitive decline. We encourage continued careful research and validation in this field.”

2015 Counter Claim

- ▶ Alescio-Lautier, B., et al., 2014. “Open Letter Response to ‘A Consensus on the Brain Training Industry from the Scientific Community.’ ” www.cognitivetrainingdata.org. Retrieved January 15, 2015.
- ▶ “We cannot agree with the part of your statement that says “there is no compelling scientific evidence” that brain exercises “offer consumers a scientifically grounded avenue to reduce or reverse cognitive decline.” We fear that most readers would take this to mean there is little or no peer-reviewed evidence that certain brain exercises have been shown to drive cognitive improvements. There is, in fact, a large and growing body of such evidence.”

Useful field of view training

- ▶ AAA Foundation, now offers free or discounted computerized cognitive training to its 30 million members. The product, which comprises 10–15 hours of training, is specifically linked to the elements of cognition associated with safe driving such as 'useful field of view', which is a predictor of accidents and tends to decline for people in their 50s, 60s and 70s.
- ▶ Trials in several states have shown **fewer auto accidents**

New Online Assessments

- ▶ **BrainBaseline**: A free mobile app with cognitive tests that facilitate self-monitoring; www.brainbaseline.com/.
- ▶ **BrainHQ**: A Web-based cognitive training program that includes Useful Field of View (UFOV) training for safe driving; www.brainhq.com/.

New Online Assessments 2

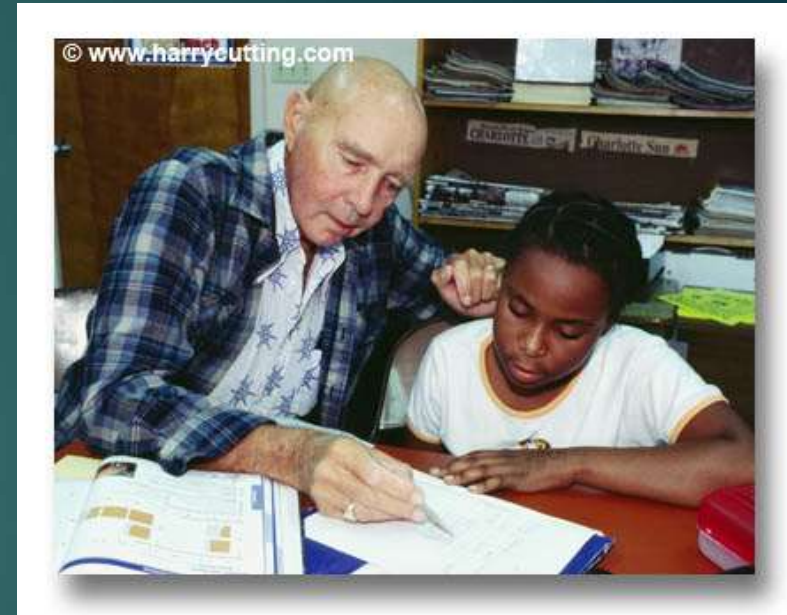
- ▶ Cogniciti: A free Web-based cognitive assessment designed to measure whether the test taker's cognition is within a normal range; www.cogniciti.com/.
- ▶ CogniFit Senior Driver: A Web-based cognitive training program that assesses and trains for ten driving-related cognitive skills<https://lifestore.aol.com/category/online-learning/cognifit-senior-driver>.

Tip #24: Be Passionate!: Have a Purpose in Life

- ▶ Purpose in life (psychological tendency to derive meaning from life's experiences and possess a sense of intentionality and goal directedness)
- ▶ Greater purpose in life is associated with
 - ▶ 2x reduced risk of AD and MCI
 - ▶ exhibit better cognitive function
 - ▶ less disability
 - ▶ have better mental health
 - ▶ live longer.

Tip #25: Volunteering is Win-Win: You live longer

- ▶ Meta-analysis: Helping others yields health benefits for the helper.
- ▶ Volunteering reduces mortality risk by 25%.
- ▶ Seniors who tutor young children in reading and math have **slower cognitive decline**



Tip #26: Hearing and Vision

- Hearing and vision are your primary senses
- Good hearing and vision are primary ways you stimulate your neurons.
- Poor hearing and vision reduce neuroplasticity
- Get good hearing aides and glasses!!

Get Smart Everyday

Get SMART
A 5-Step Program for Successful Aging

EVERY DAY!

Get Social!

Get Moving!

Get Artistic!

Get Responsive!

Get Thinking!

EVERY DAY!

Be An Active Learner!

If you want the 1-step program...

**USE IT
OR
LOSE IT!**



Prevent Major NCD in your child's future

- ▶ Whole milk as infants
- ▶ Prevent head blows.
- ▶ Do lots of physical exercise = play.
- ▶ Encourage language skills & musical instruments. Bilingualism reduces Major NCD risk
- ▶ Support your child going to college. The more years of formal schooling, the lower the odds.
- ▶ Provide stimulation: Keep your child's brain busy with physical, mental and social activities and novel experiences.
- ▶ Spare the junk food: Lab animals raised on berries, spinach and high omega-3 fish have great memories in old age.

General Recommendations

- ▶ Manage your medical “numbers” (cholesterol count, blood pressure level, blood glucose level, and weight)
- ▶ Take blood pressure, cholesterol, and/or diabetes medications as prescribed.
- ▶ Eat a Mediterranean diet rich in leafy and bright-colored vegetables, folic acid, antioxidants, and omega-3 fatty acids. Avoid omega-6 fats like butter and processed oils.
- ▶ Get aerobic exercise at least two to three times per week.

Recommendations 2

- ▶ Cognitive exercise is equally vital -- rather than staying entrenched in a routine; Try new things and do familiar things in novel ways.
- ▶ Maintain social and family relationships: isolation is “a huge risk factor for AD.”
- ▶ Manage mental health issues such as anxiety, stress, and depression -- all of these can adversely affect memory.
- ▶ Avoid excess alcohol, as it can hamper memory formation.

Ten Commandments for Brain Fitness

- I. Exercise daily.
- II. Minimize risk factors for cerebrovascular disease (HTN, Hyperlipidemia, DM, overweight, smoking)
- III. Eat a Mediterranean Diet
- IV. Choose thy parents wisely (For brain genes & IQ)
- V. Maintain intellectual engagement throughout life
- VI. Stay socially engaged with others.
- VII. Get sufficiently good quality sleep
- VIII. Drink 1 drink of alcohol per day
- IX. Manage your stress effectively
- X. Don't text or use cell phone while driving.

Best: Exercise & Socialize



Best Brain Fitness Behavior

- ▶ Go for a 2 mile walk with a smart friend
- ▶ and while walking, talk about what you just heard about in this lecture today,
- ▶ then have a salad.

Exercise



Interact with your friends



Laugh!



George Bernard Shaw

"We don't stop playing because
we grow old;
we grow old because we stop
playing."

Keep a Young Mind:
All is possible



Hang On!



Einstein

“He who can no longer pause to wonder and stand rapt in awe, is as good as dead.”









Major NCD Self Test

- ▶ Johns Hopkins Memory Survey:
- ▶ <http://www.alzcast.org/memorysurvey/>

AARP's Best Books Guide

- ▶ **The Dana Guide to Brain Health**, by Floyd E. Bloom, M. Flint Beal, and David J. Kupfer (Dana Press, 2006).
- ▶ **The SharpBrains Guide to Brain Fitness: 18 Interviews with Scientists, Practical Advice, and Product Reviews, to Keep Your Brain Sharp**, by Alvaro Fernandez and Elkhonon Goldberg. (SharpBrains Inc., 2009).
- ▶ **Save Your Brain: The 5 Things You Must Do To Keep Your Mind Young and Sharp**, by Paul Nussbaum. (McGraw-Hill, 2010).
- ▶ **The Secret Life of the Grown-Up Brain: The Surprising Talents of the Middle-Aged Mind**, by Barbara Strauch (Viking, 2010).
- ▶ **The Memory Bible: An Innovative Strategy for Keeping Your Brain Young**, by Gary Small (Hyperion, 2003).
- ▶ ***Also Recommended:***
- ▶ **The Mature Mind: The Positive Power of the Aging Brain**, by Gene Cohen (Basic Books, 2006).
- ▶ **The Brain That Changes Itself**, by Norman Doidge (Penguin, 2007).
- ▶ **Spark: The Revolutionary New Science of Exercise and the Brain**, by John Ratey and Eric Hagerman (Little, Brown and Co., 2008).
- ▶ **Think Smart: A Neuroscientist's Prescription for Improving Your Brain's Performance**, by Richard Restak (Riverhead, 2010).

Happiness & Wisdom

“Happiness is nothing more than good health
and a bad memory”

Albert Schweitzer (1875-1965)

“Wisdom is the art of knowing what to
overlook.”

William James, 1890

As the Vulcans say...

Live long and prosper!

End is Here



Contact Info

- ▶ Charles J. Vella, PhD
- ▶ www.charlesjvellaphd.com
- ▶ charlesvella@comcast.net
- ▶ 415-939-6175