Neuropsychology of Psychopathology

(Select DSM-5 Disorders)

CHARLES J. VELLA, PHD

NEUROPSYCHOLOGY

MARCH 26, 2015

Bio: Charles J. Vella, PhD

- Neuropsychologist
- 34 years, Kaiser San Francisco, 1975-2009
  - Chief Psychologist/Manager
  - Director, Neuropsychology Service
- Neuropsychology Lecturer: 2009-present
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- All of my lectures in PDF files

- Go to "Neuropsychology Seminar Talks"
  - Logon: Kaiser
  - Password: Kaiser
- "Downloadable NP Tests" Section:
  - Logon: test
  - Password: P@ssW

Agenda

- 1:00 PM Brain and Brain Development
- 2:00 PM Schizophrenia & Alcohol Abuse
- 2:45 PM Break
- 3:00 PM Neuropsychology of ADHD, Depression, Bipolar, OCD
- 4:00 PM Neuropsychology of PTSD, & some Personality Disorders
- 4:45 PM Q & A
- 5:00 PM Adjourn

Brain Basis of Behavior

- Motivation, behavior, & emotions are all by-products of brain activity.
- Focus on neuroscience: neuropsychology, neuropsychiatry, behavioral neurology; on the neurobiological correlates of behavior and cognition.
- 1970 graduate school: differential of "organic" vs "functional"

NP lens

- Looking through a neuropsychological lens allows us to conceptualize neuropsychiatric disorders
  - not just by their behavioral features
  - but also by their central neuropsychological/cognitive and neurobehavioral features.

- **Neuropsychological profile is predictive of level of daily functioning**
- **Cognitive deficits are more predictive of level of functioning than positive psychiatric sxs**

Role of Neuropsychologist

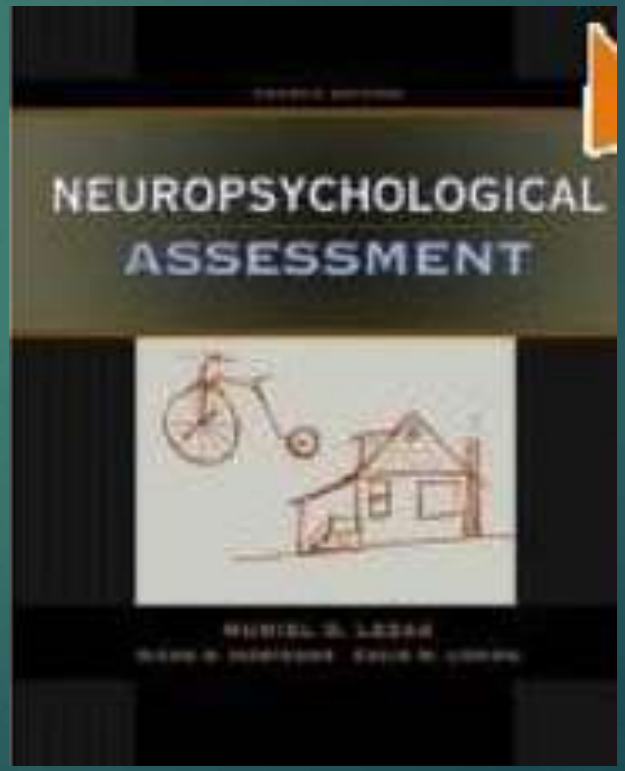
- Neuropsychologist may help in treatment planning
  - Assess for appropriate level of intervention / supervision needed
  - Highlight domains of relative strength and weakness
  - Assess need and level of appropriate cognitive rehabilitation and skill learning to increase independence, vocational training and/or educational goals
    - E.g. patients who perform better on the WCST are able to make use of interventions to increase independence
  - Suggest accommodations to enable patient to return to school/work

My Neuropsychological Premise

- Any psychiatric patient that is more difficult to treat has a neuropsychological deficit of some kind.
- Majority of patients in Psychiatry have a neuropsychological deficit
- Psychiatry needs more NP assessment capability & therefore more neuropsychologists
- Psychiatry needs more groups aimed at cognitive deficit rehabilitation for psychiatric patients.

Muriel Lezak:
The Bible of Neuropsychology

Assessment and rehabilitation of brain injury

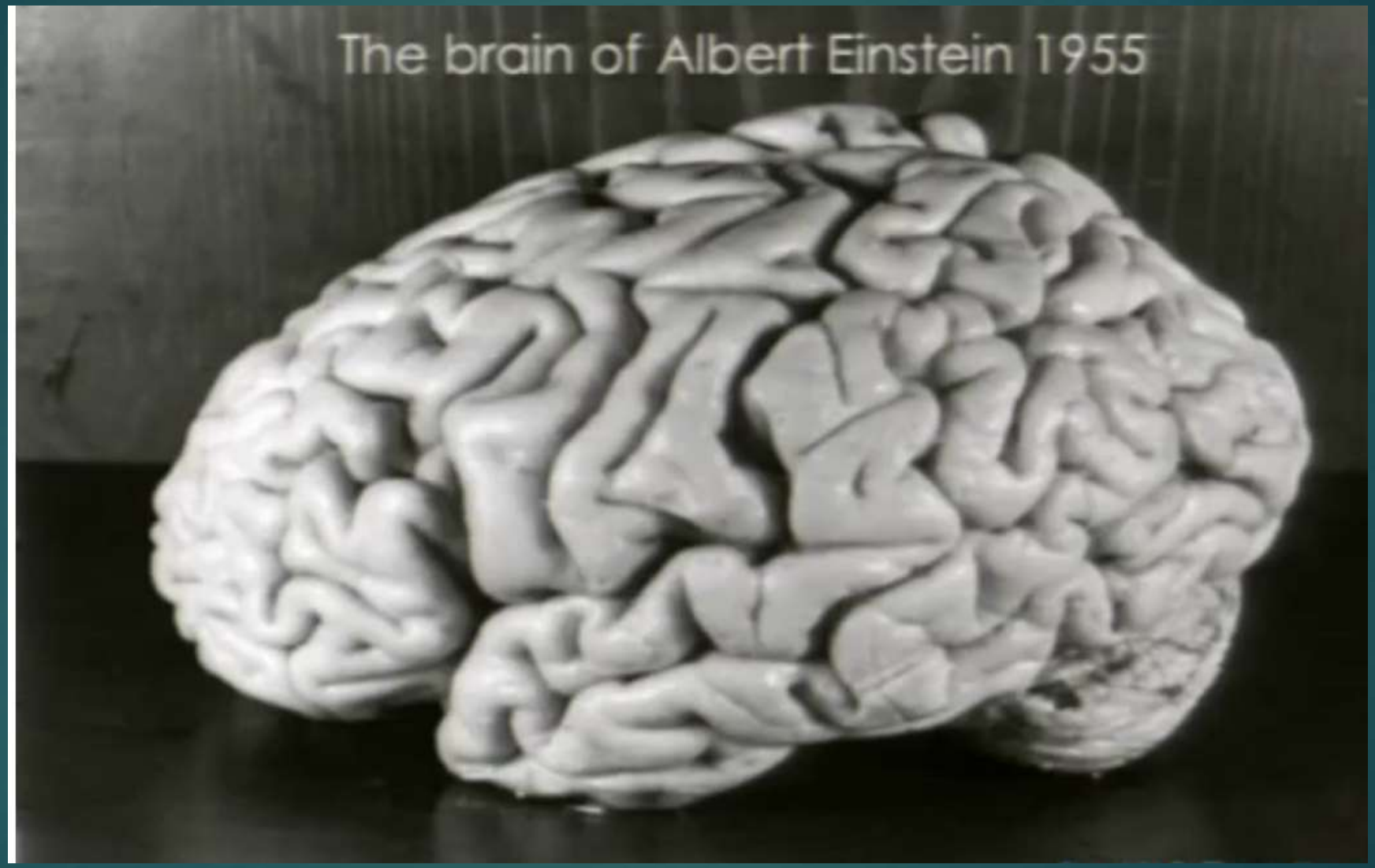


DSM-5 and Neuropsychology

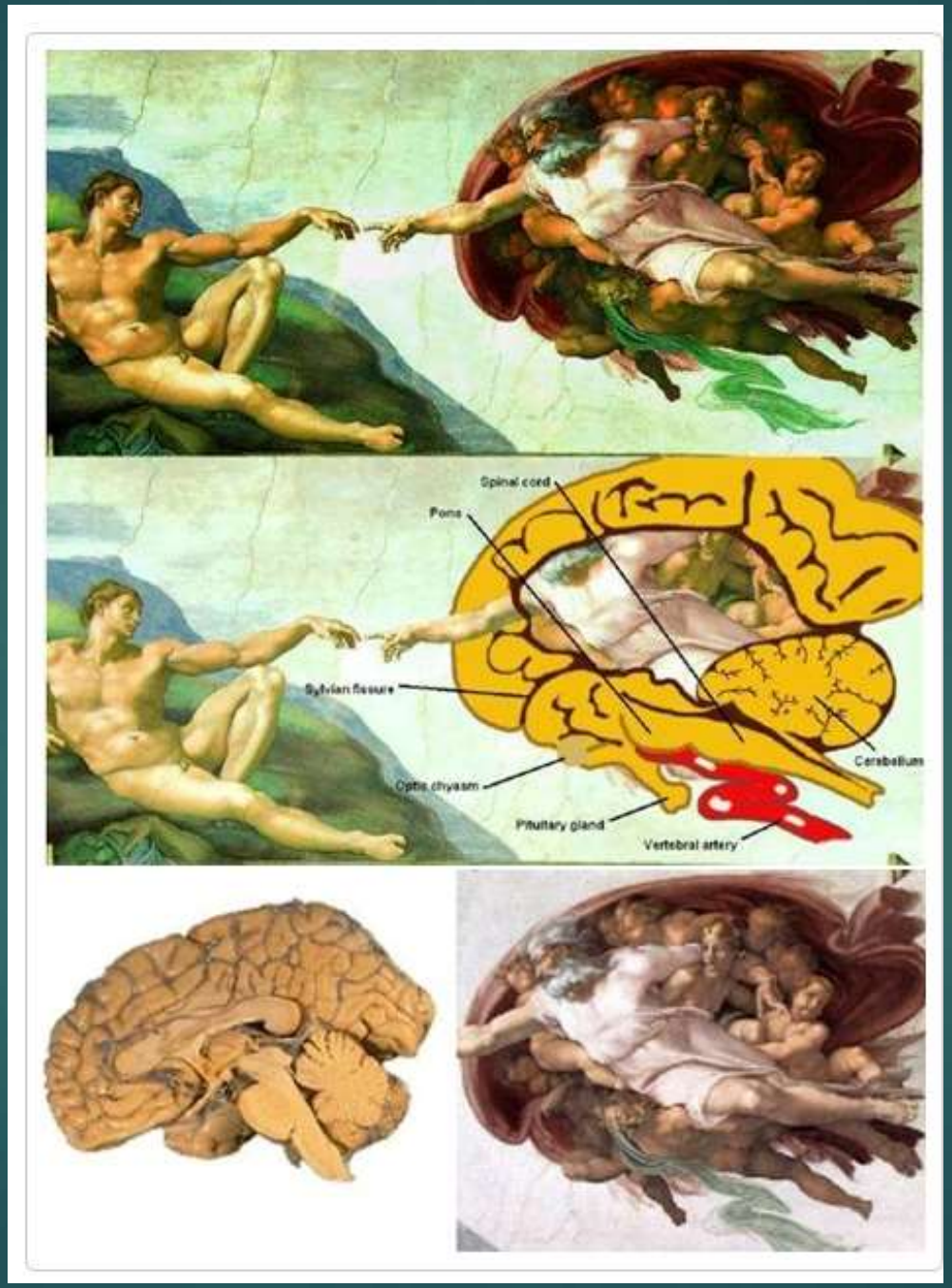
- DSM-5: disorders are conceptualized psychiatrically rather than neuropsychiatrically
- DSM-5 ignores neuropsychological deficits in its psychiatric diagnostic system.
- Only exception to this is in NCD criteria; only place that neurological/biological causation is referenced
- DSM-5 aimed at psychiatrists and insurance.
- Kaiser: NP testing is a covered benefit

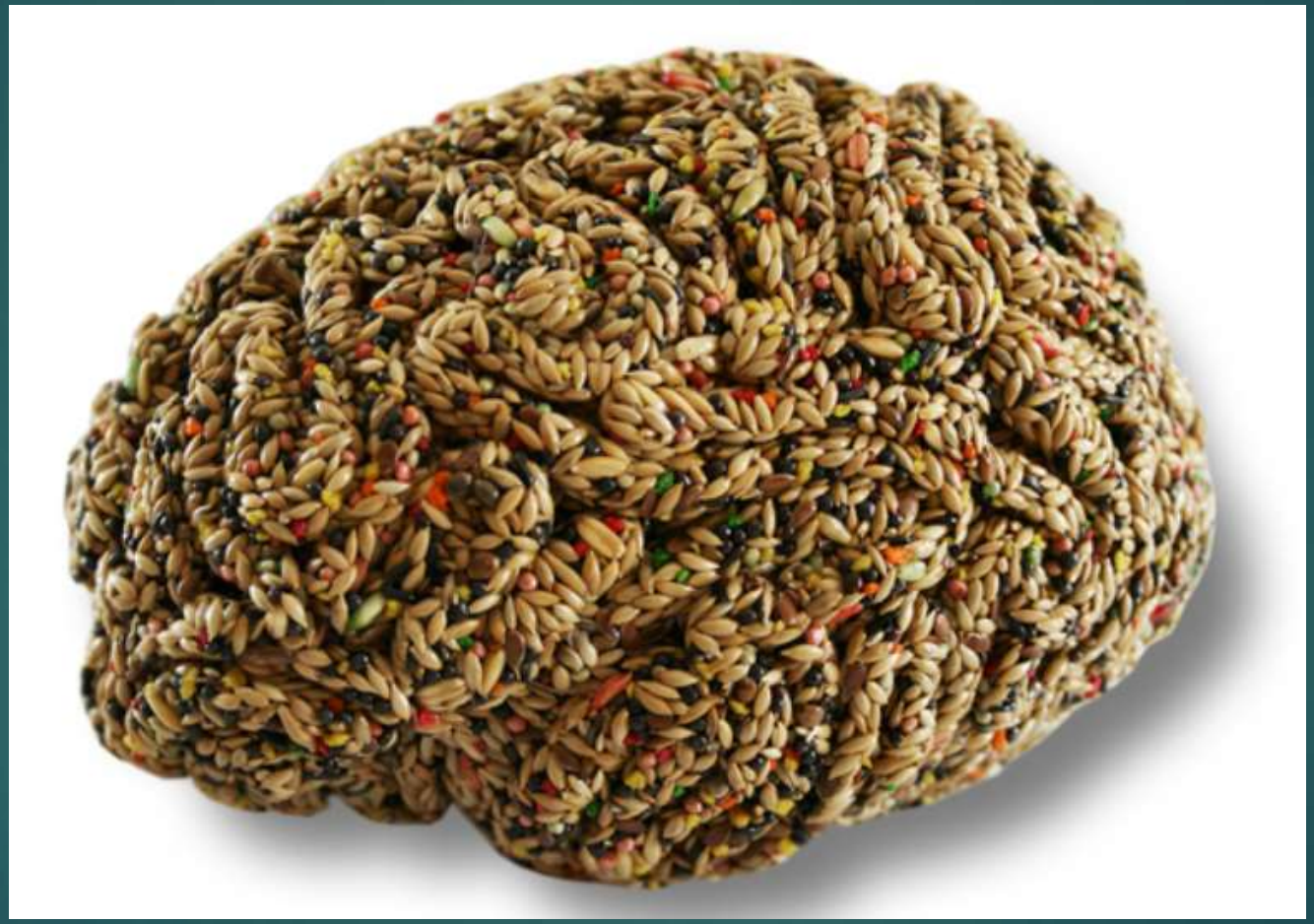
The Human Brain

Your Brain

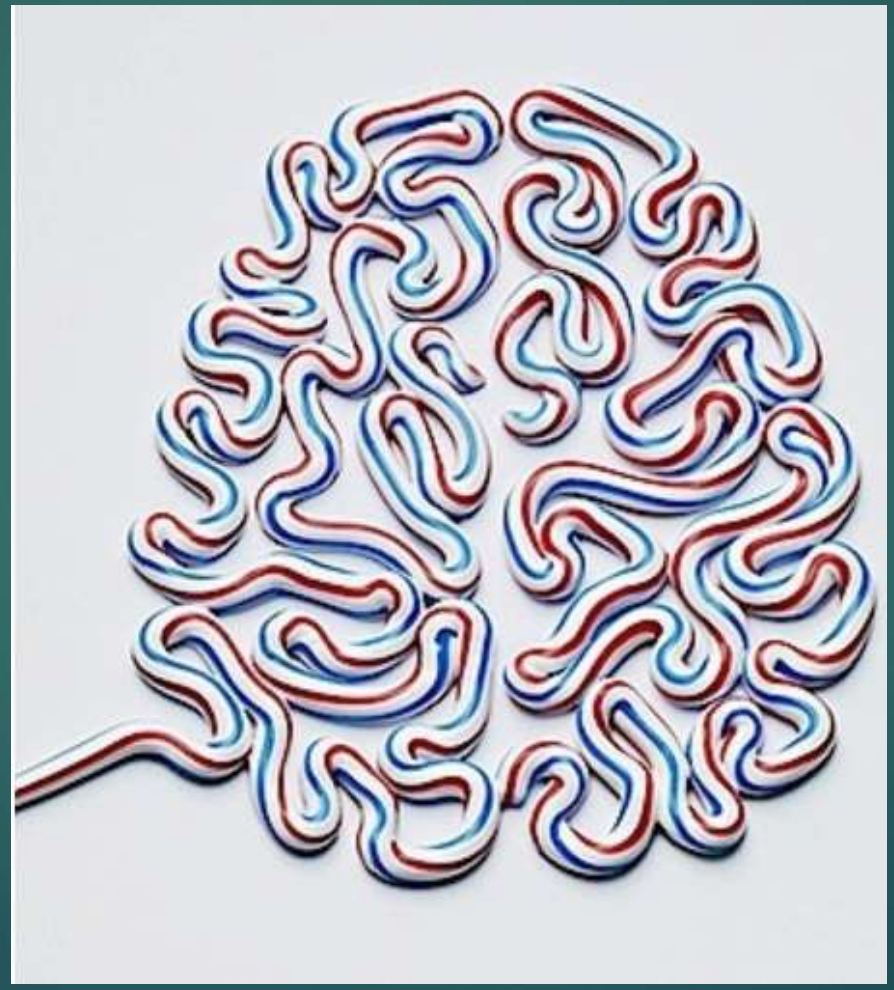

The brain of Albert Einstein 1955

Agyria – a lack of gyri and sulci

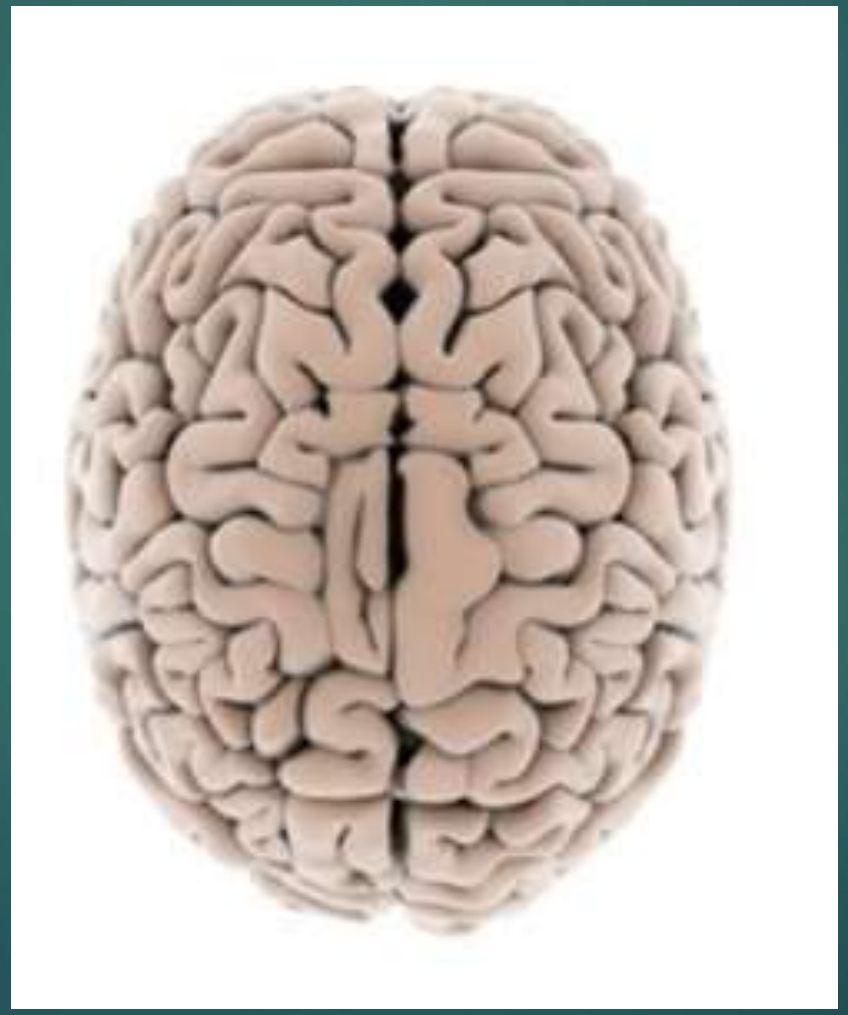

Spinal cord
Pons
Sylvian fissure
Cerebellum
Optic chyasm
Pituitary gland
Vertebral artery



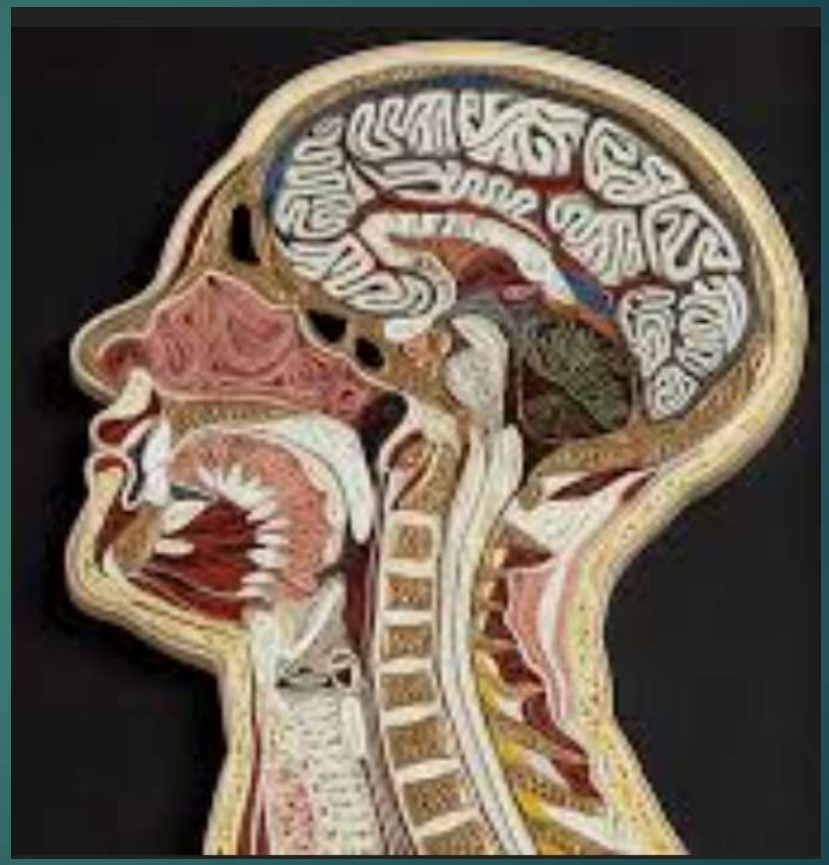
Toothpaste by Kyle Bean



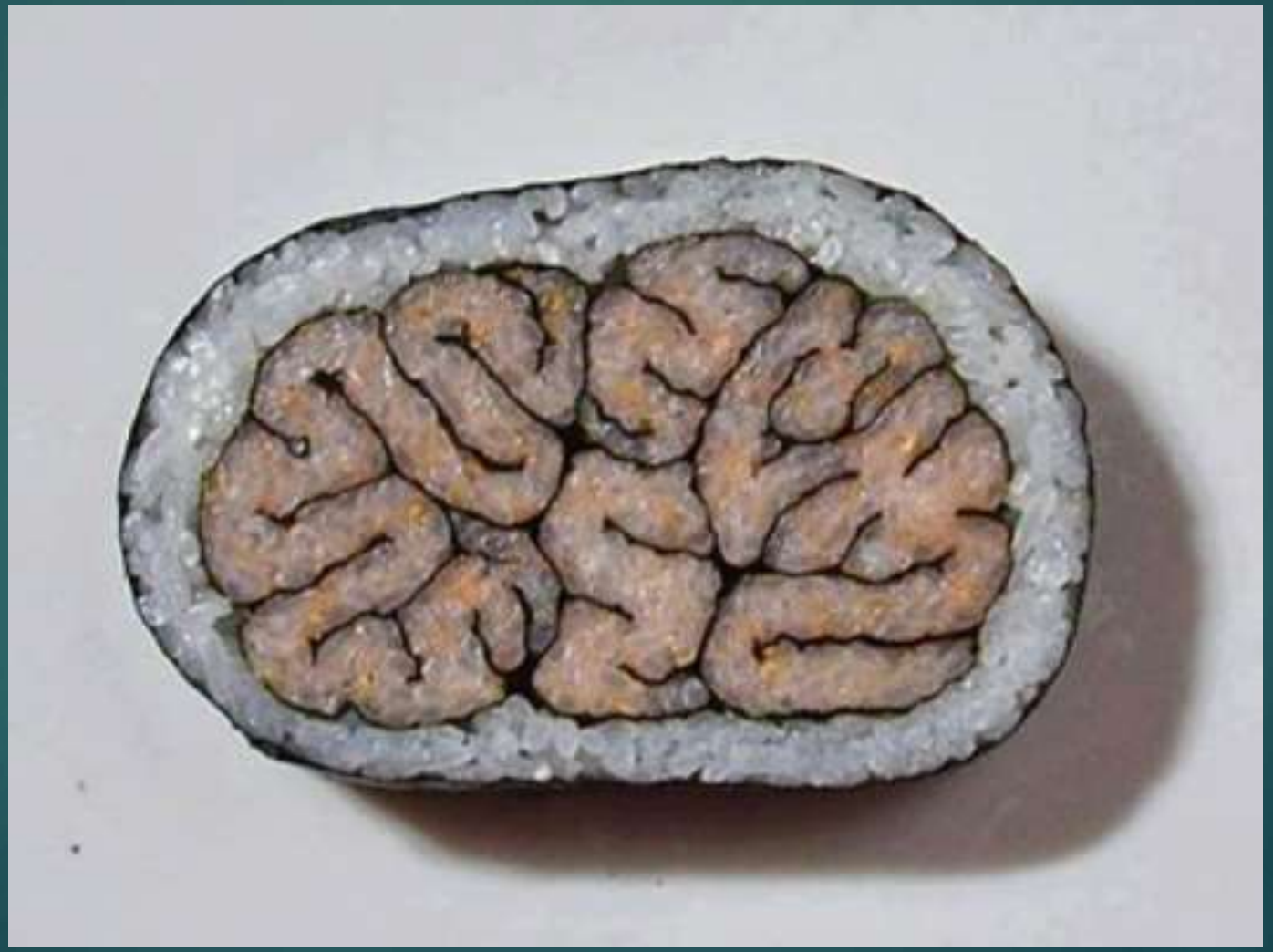
Out of Clay



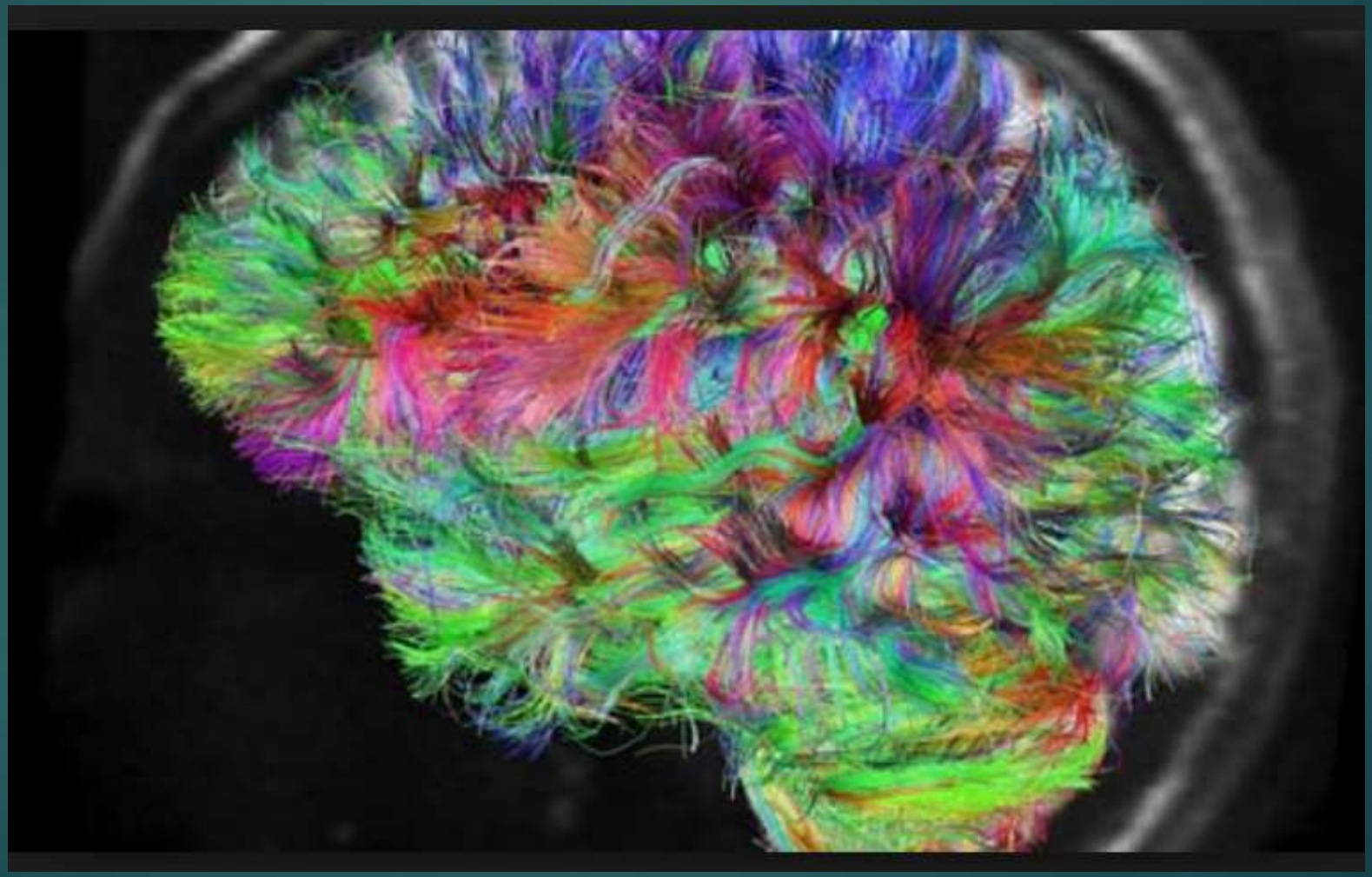
Lisa Nilsson Quilted Paper



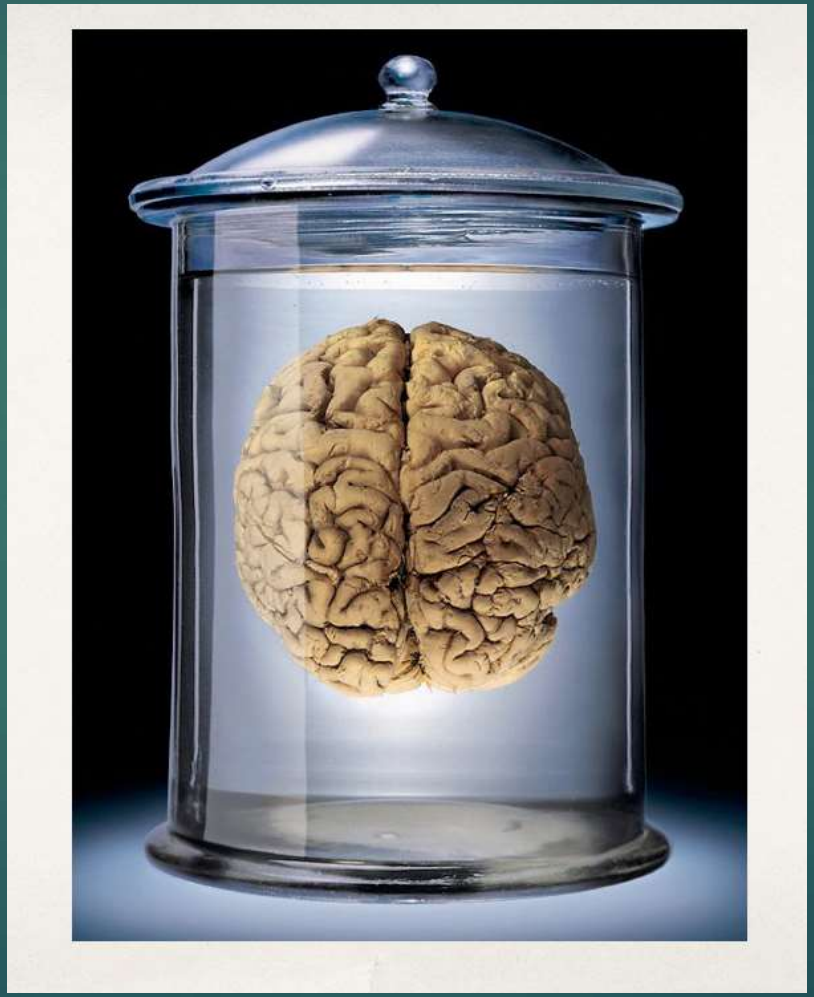
Sushi as Brain



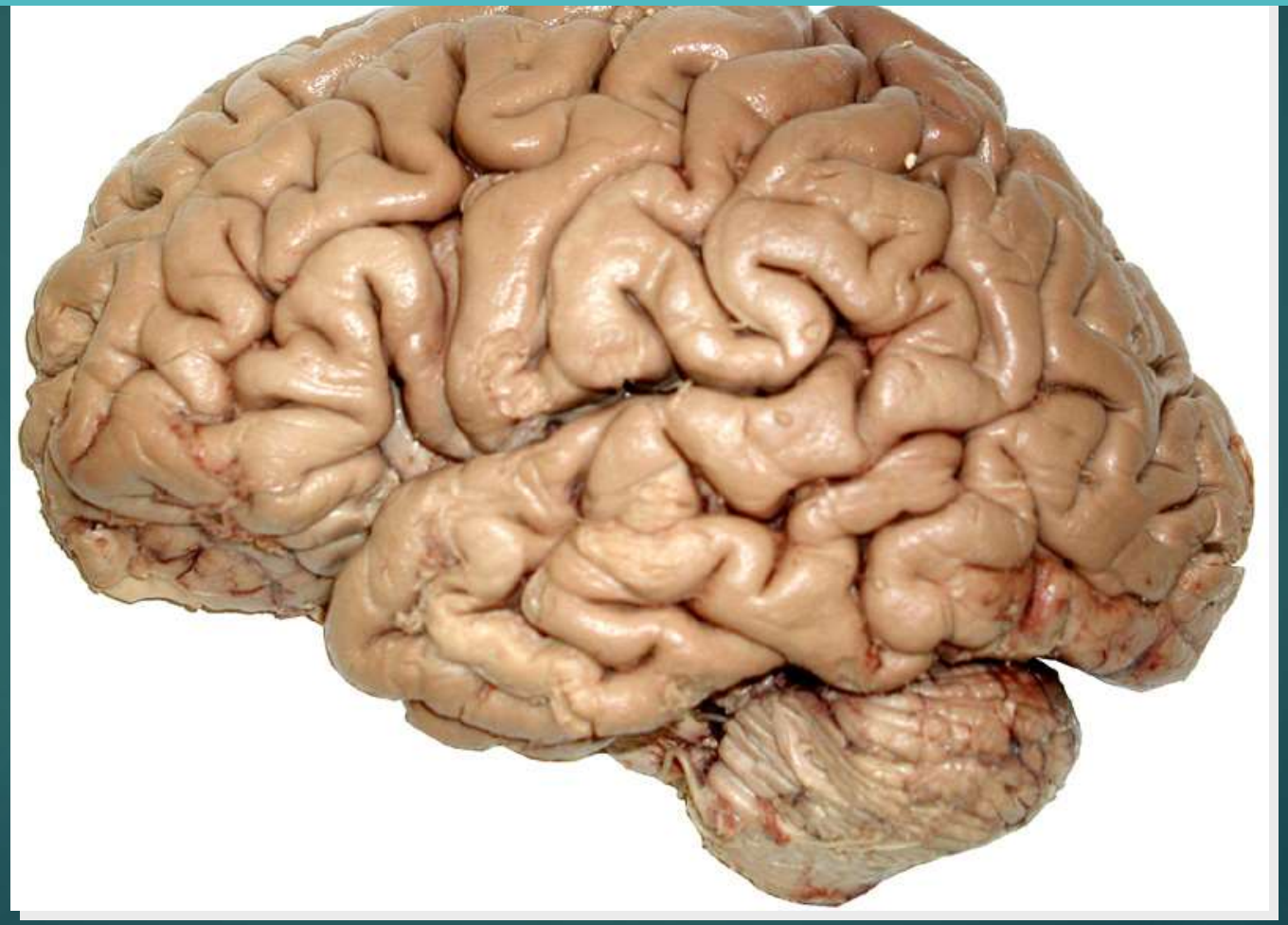
Real: Diffuse Tensor Imaging



The Brain



Human Brain



Imaging the Brain

Advanced Neuroimaging circa 1905:
Phrenology "MRI"

Cautionary Tale: Many "current" theories are eventually discredited

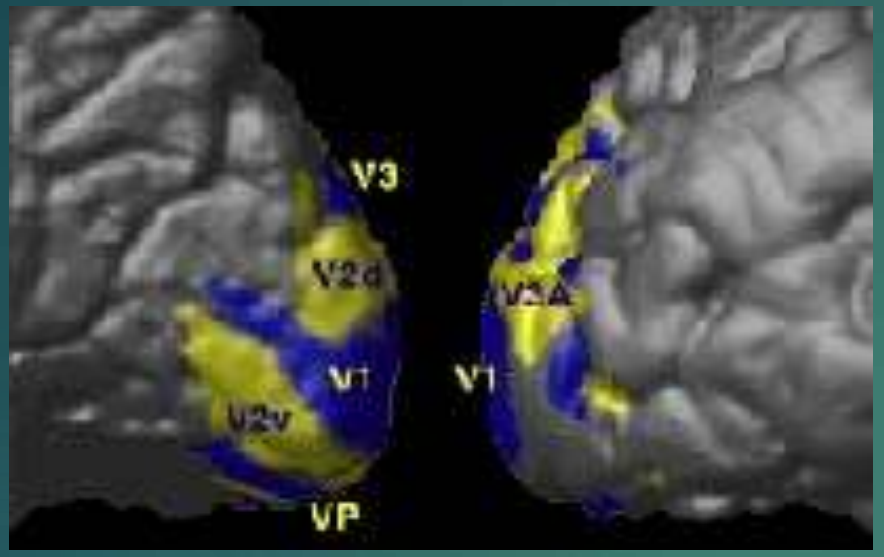
Psychoanalysis Device, 1931

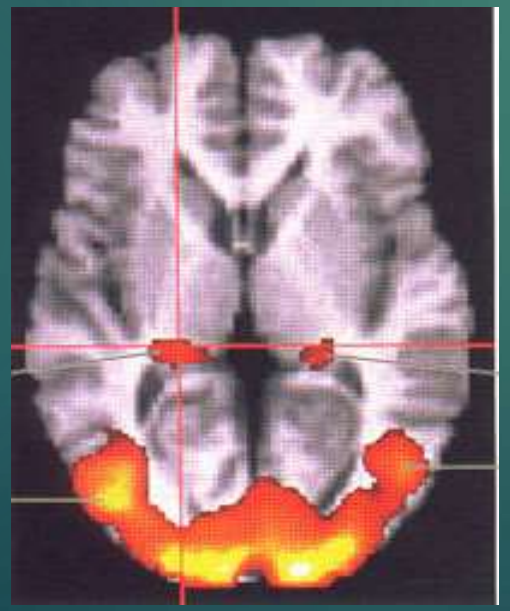
A demonstration of a new “psychoanalyzing apparatus” in 1931

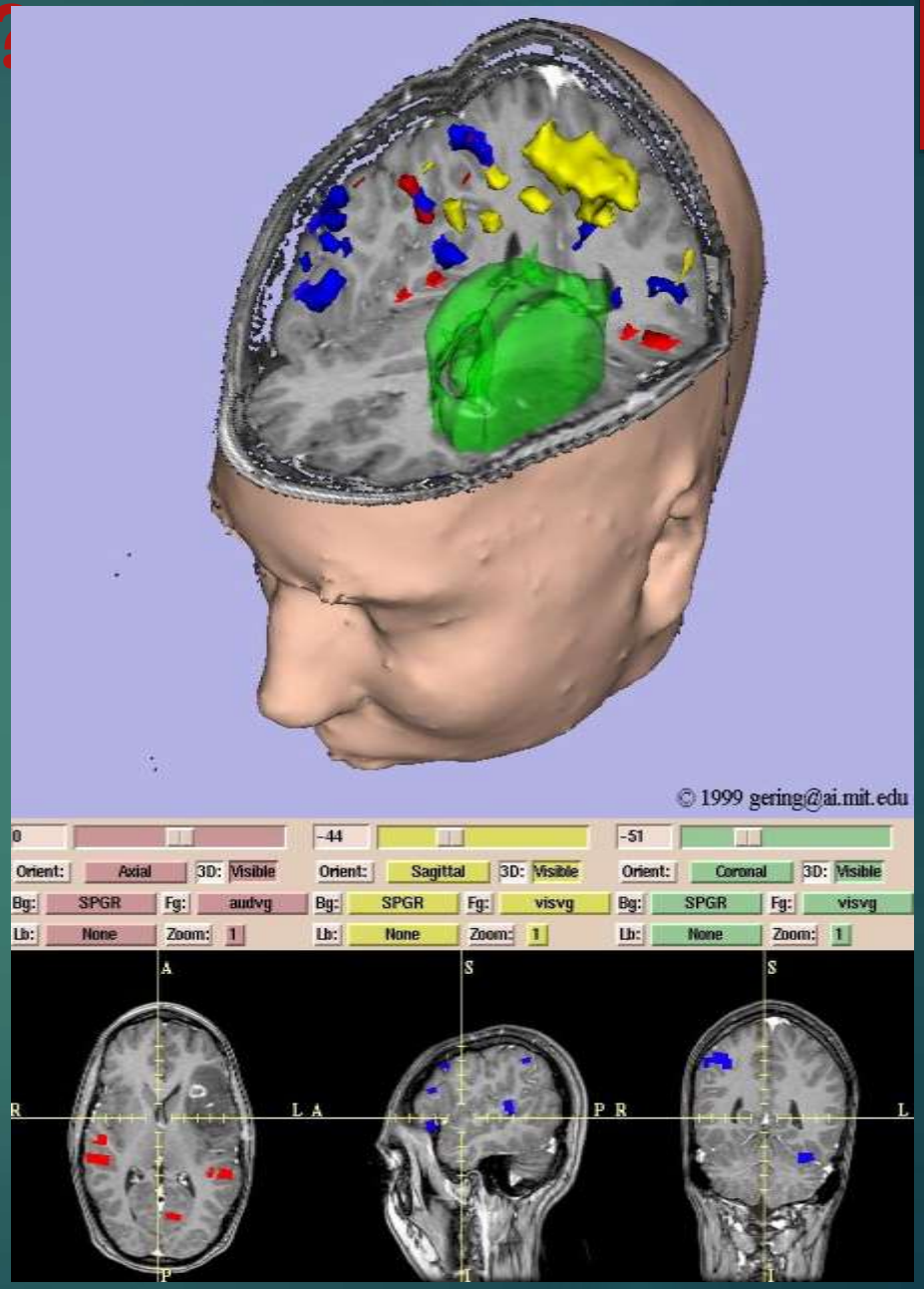
The major brain study methods

- Lesion studies
- 1960s - Single-unit recording
- Neurosurgery-related methods
  - Direct cortical stimulation
  - Split-brain
  - WADA
- Functional imaging
  - 1970s - Electromagnetic: EEG, MEG
  - Hemodynamic: PET, fMRI
- Transcranial magnetic stimulation (TMS)

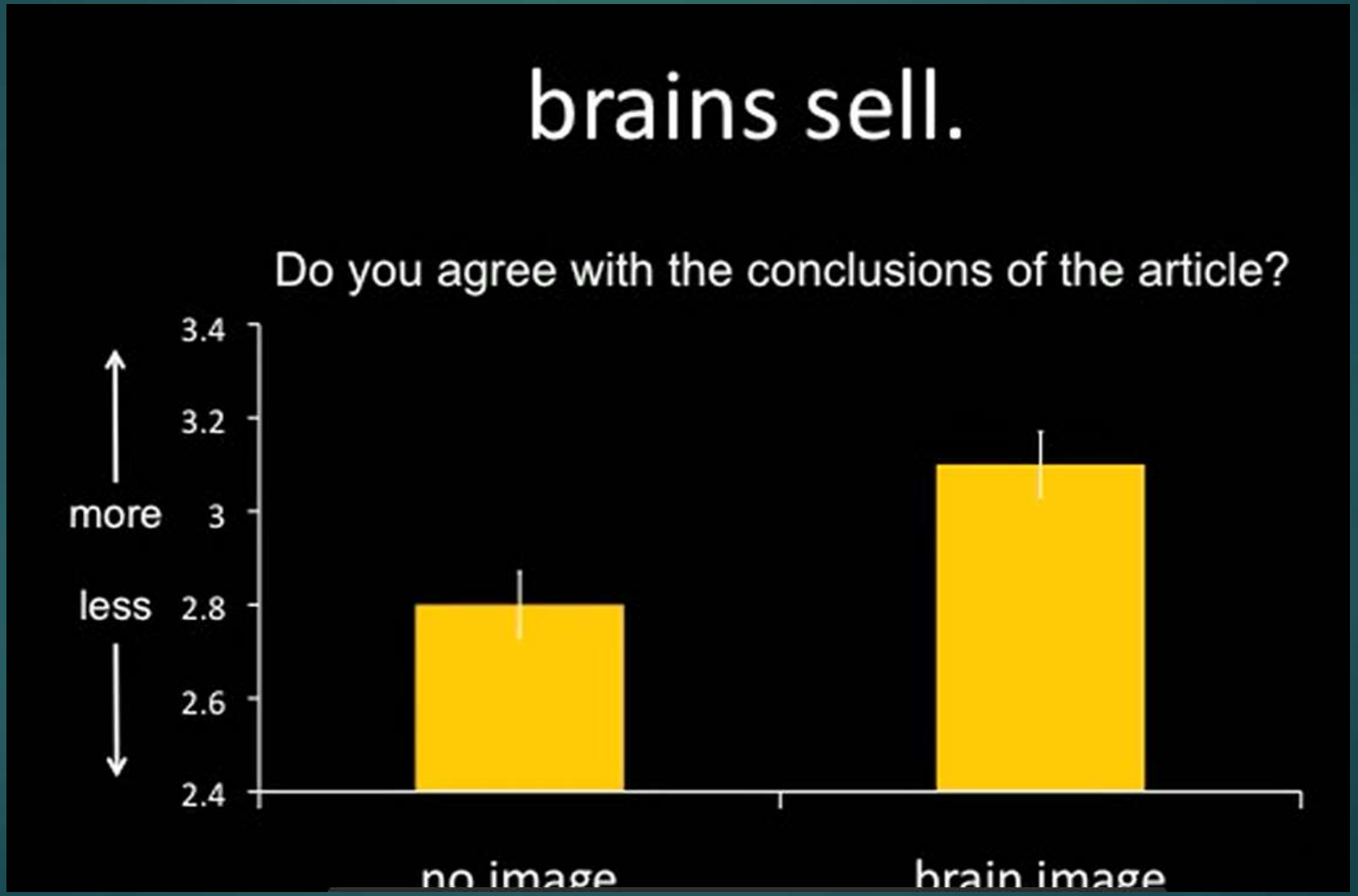
Modern Phrenology ?





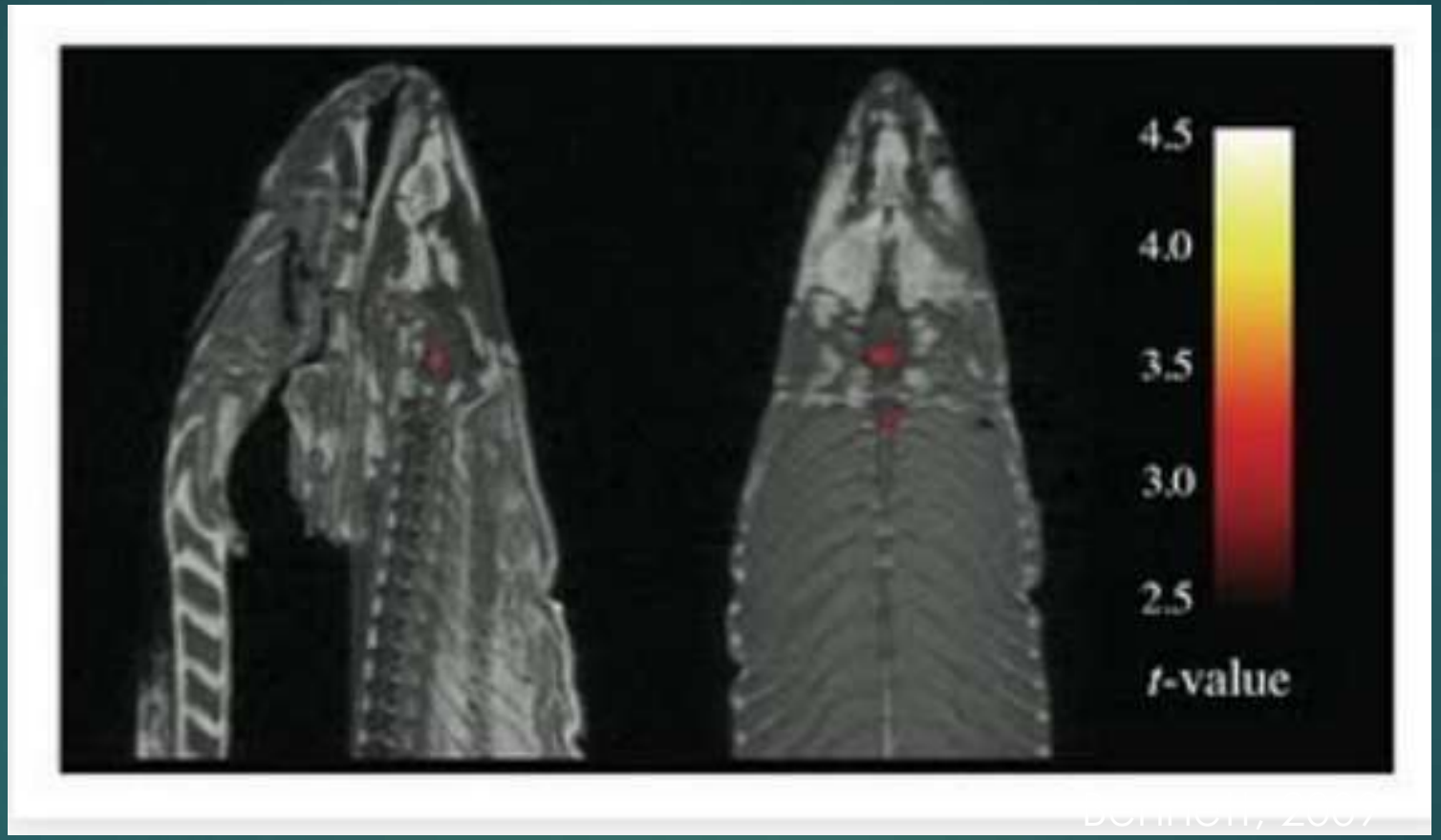


Neurobunk


brains sell.
Do you agree with the conclusions of the article?
more
less
3.4
3.2
3
2.8
2.6
2.4
no image
brain image

Cautionary Tale: Post-Mortem Atlantic Salmon: false positives in MRI phantom data

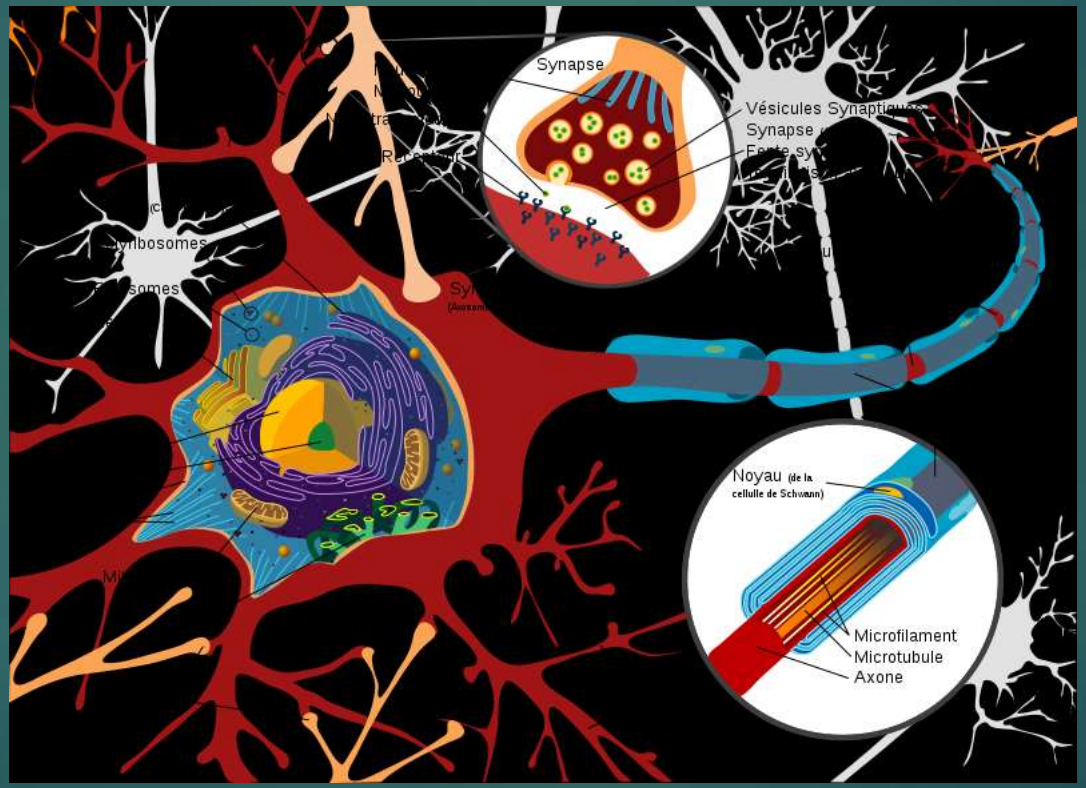
Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction



This is a lesson in statistics, not in fMRI. Which is why this was never published in a peer-reviewed journal. It is a lesson about how probability indicates that you certainly can get activation in a dead salmon by chance, and that if you only have one salmon and no corrected threshold in 2 M samples, you will get about 100,000 false positives.

Neurons: We have 86 billion with 10,000 synapses each

Neuron



Axon

Dendrites

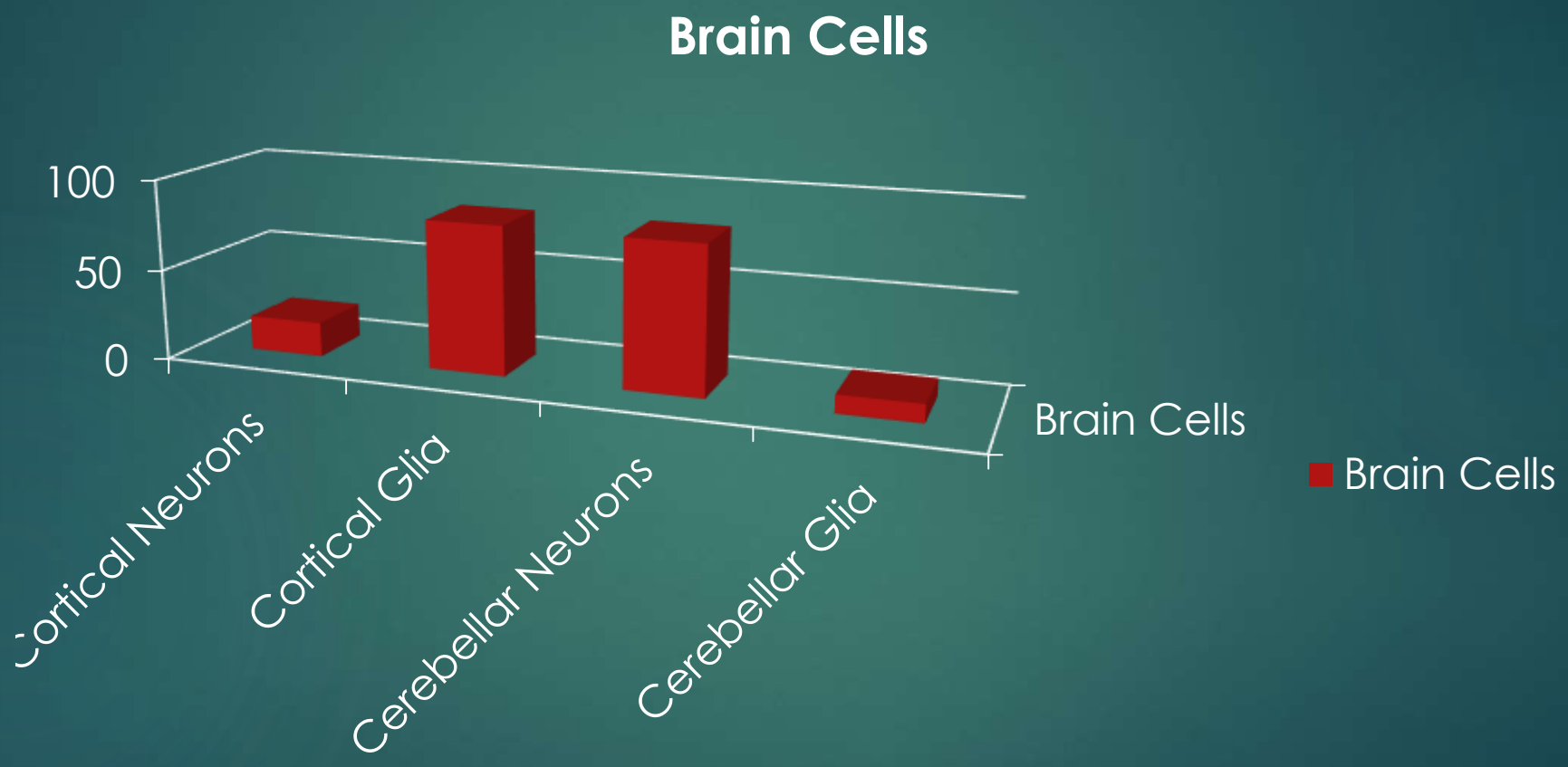
Suzana Herculano-Houzel et al., 2009

170 Billion: First Official Count in 2009

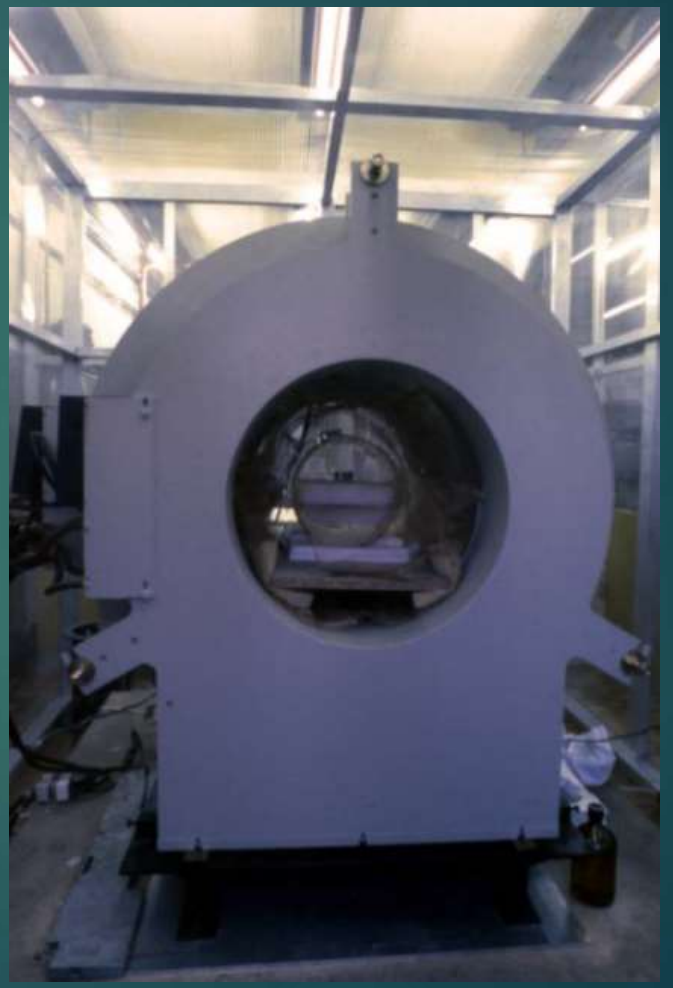
- Adult male human brain contains on average:
  - 86 ± 8 billion neurons
  - 85 ± 10 billion glial cells.
- Cerebral cortex: 16 billion neurons
  - 19% of all neurons
  - 81% of total brain mass.
- Cerebellum: 69 billion cells
  - 81% of all neurons
  - 10% of brain mass
- Glial cells are 50% of all brain cells.

Suzana Herculano-Houzel et al., J. Comp. Neurol. 513:532–541, 2009

Cortical Brain Cells



First NMR of Human Brain 1983, Rome



First NMR image (of a mouse) was in 1974

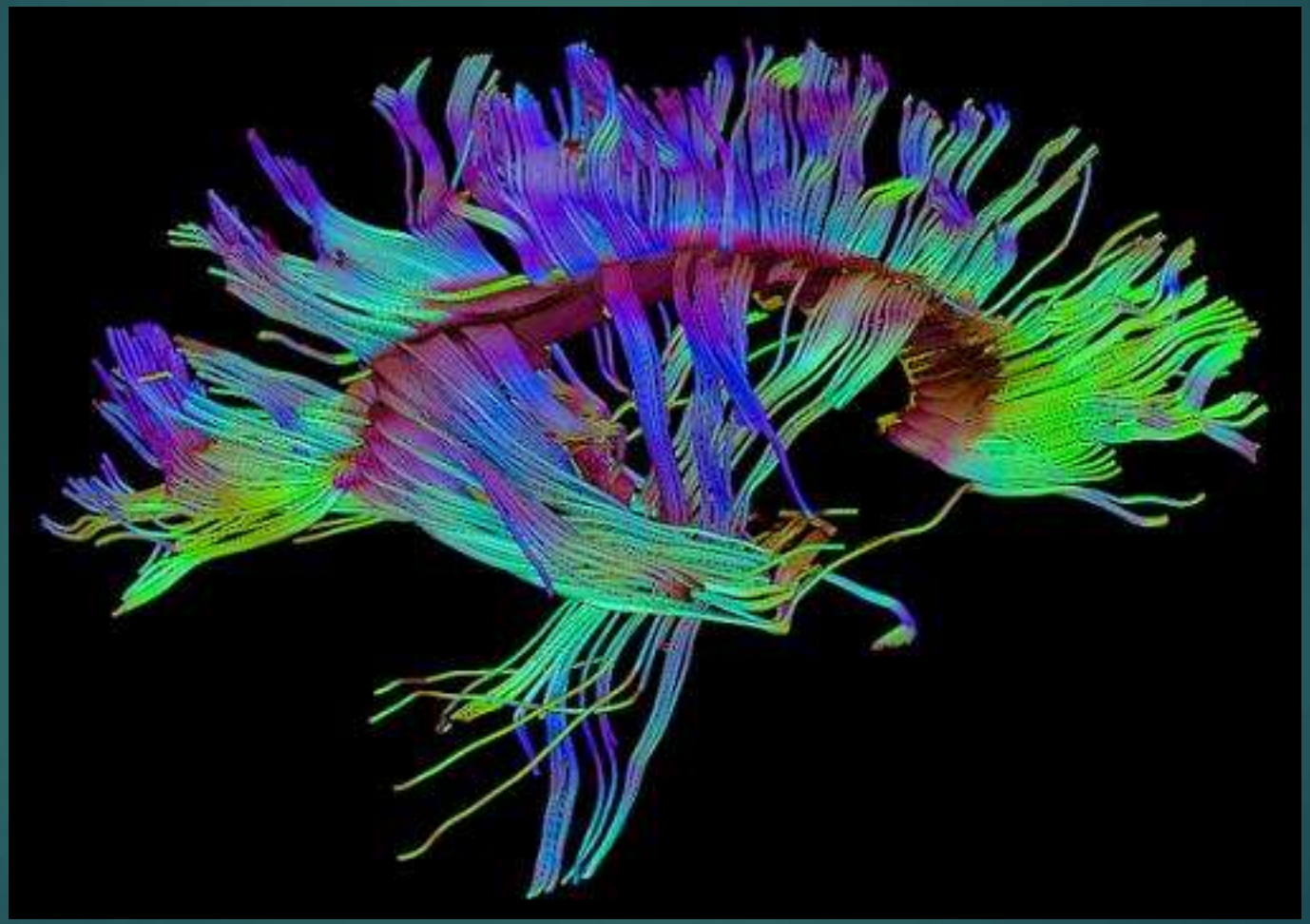
Imaging The Living Brain

- Computed Tomography (CT)
- Magnetic Resonance Imaging (MRI)
- Positron Emission Tomography (PET)
- Functional MRI (fMRI)
- Electroencephalography (EEG)
- Diffuse Tensor Imaging (DTI)
- Magnetoencephalography (MEG)

MRI & fMRI

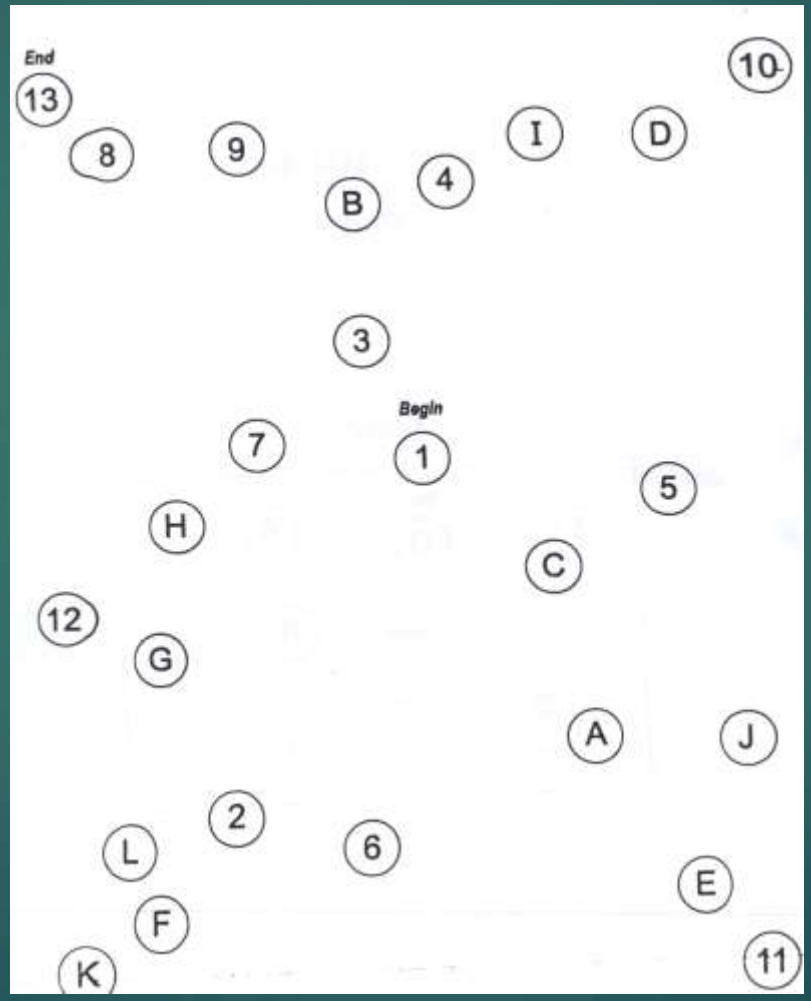
A la Rembrandt's The Anatomy Lesson of Dr. Nicolaes Tulp

DTI: Diffusion Tensor Imaging – Direction of water molecules

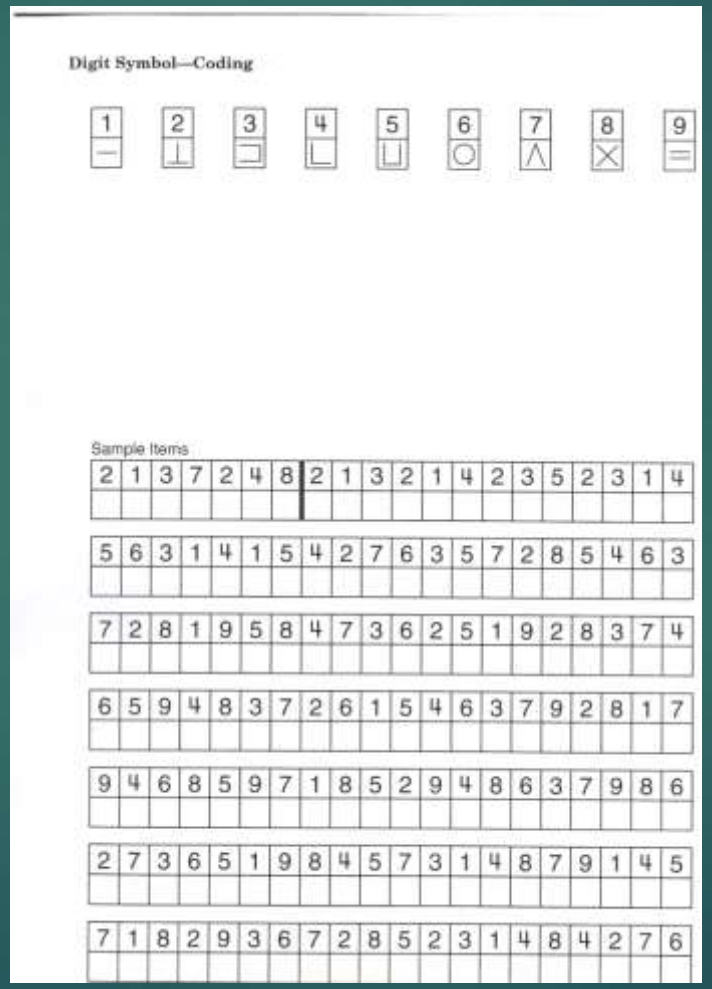


Neuropsychological Testing Measures

Trail Making Test - B



WAIS Digit Symbol



Digit Symbol—Coding

1	2	3	4	5	6	7	8	9
—	⊥	⊐	∟	⊔	○	∧	⊠	=

Sample Items

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

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

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

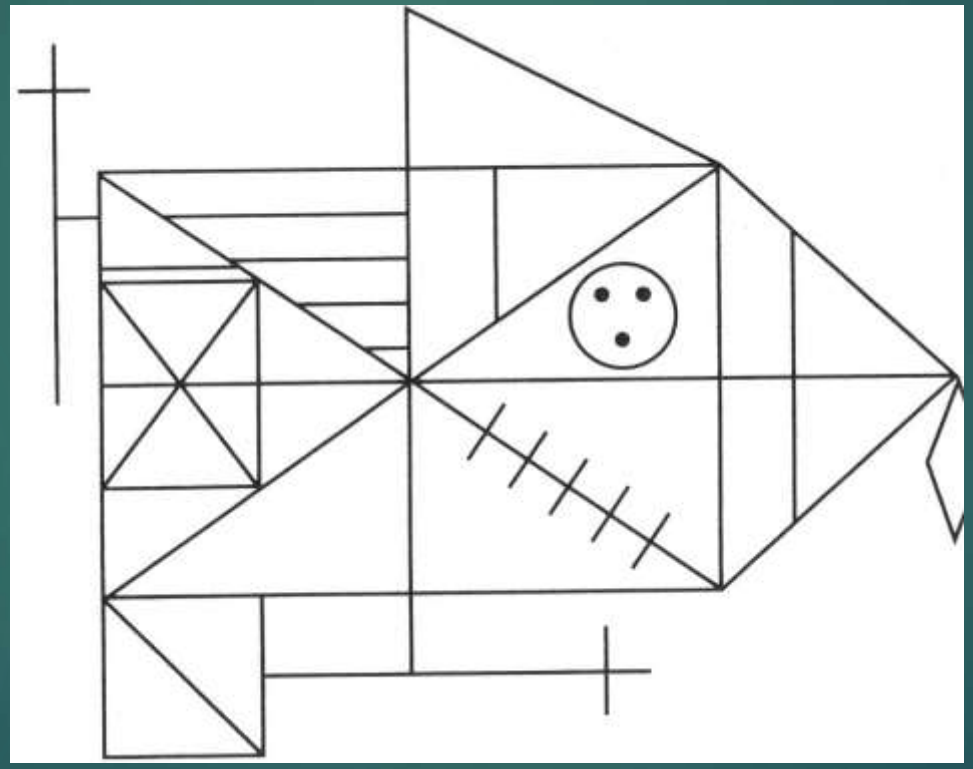
6	5	9	4	8	3	7	2	6	1	5	4	6	3	7	9	2	8	1	7

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

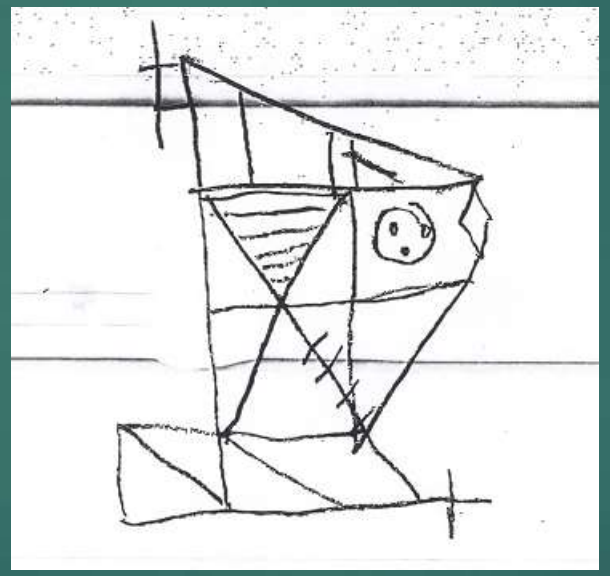
2	7	3	6	5	1	9	8	4	5	7	3	1	4	8	7	9	1	4	5

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

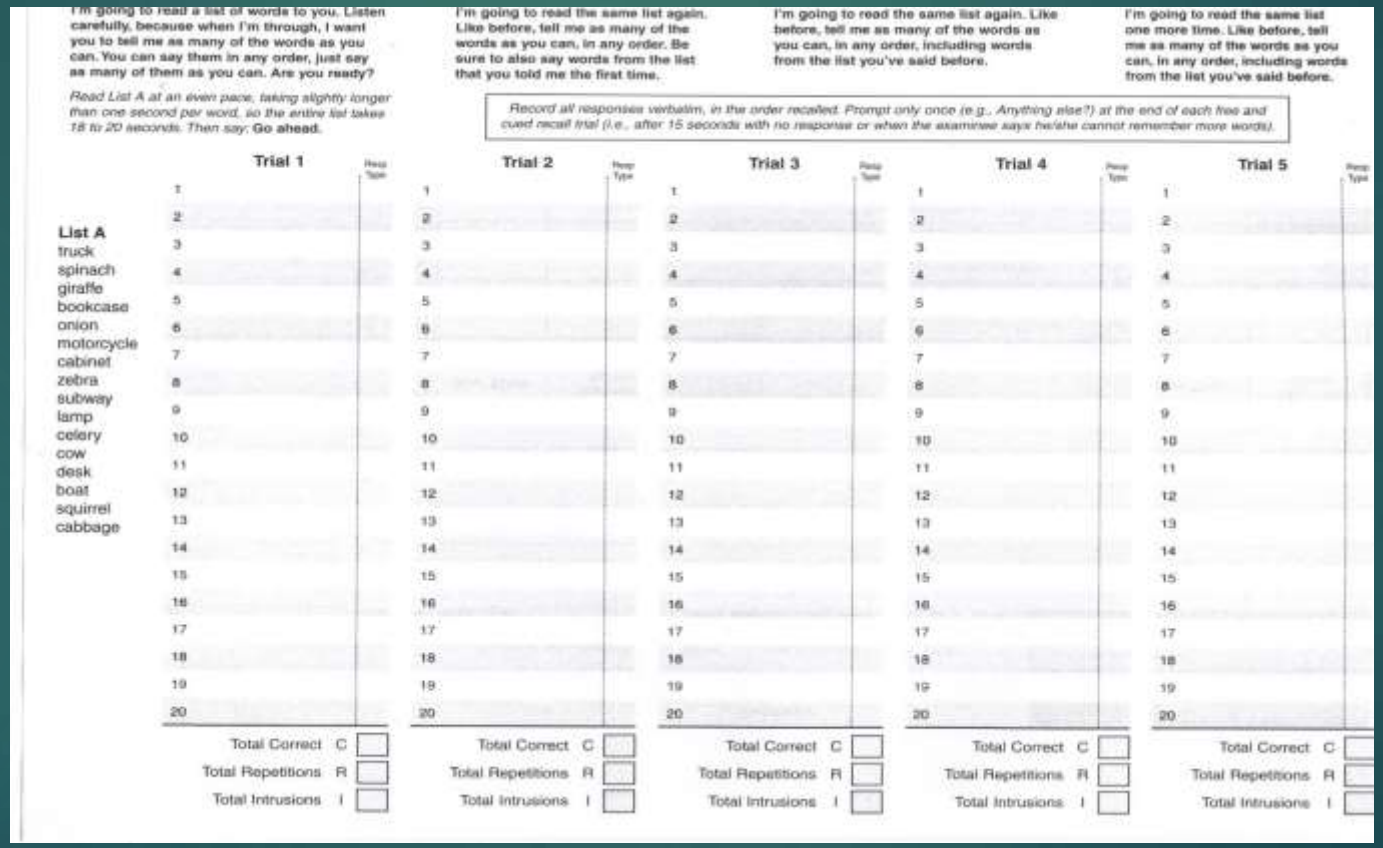
Rey Complex Figure



Rey Complex Figure Example



California Verbal Learning Test II



I'm going to read a list of words to you. Listen carefully, because when I'm through, I want you to tell me as many of the words as you can. You can say them in any order, just say as many of them as you can. Are you ready?

Read List A at an even pace, taking slightly longer than one second per word, so the entire list takes 18 to 20 seconds. Then say: **Go ahead.**

I'm going to read the same list again. Like before, tell me as many of the words as you can, in any order. Be sure to also say words from the list that you told me the first time.

I'm going to read the same list again. Like before, tell me as many of the words as you can, in any order, including words from the list you've said before.

I'm going to read the same list one more time. Like before, tell me as many of the words as you can, in any order, including words from the list you've said before.

Record all responses verbatim, in the order recalled. Prompt only once (e.g., Anything else?) at the end of each free and cued recall trial (i.e., after 15 seconds with no response or when the examinee says he/she cannot remember more words).

List A
truck
spinach
giraffe
bookcase
onion
motorcycle
cabinet
zebra
subway
lamp
celery
cow
desk
boat
squirrel
cabbage

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Prompt Type					
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					
Total Correct C					
Total Repetitions R					
Total Intrusions I					

WCST: Wisconsin Card Sort Test
Gold Standard for Executive Functioning

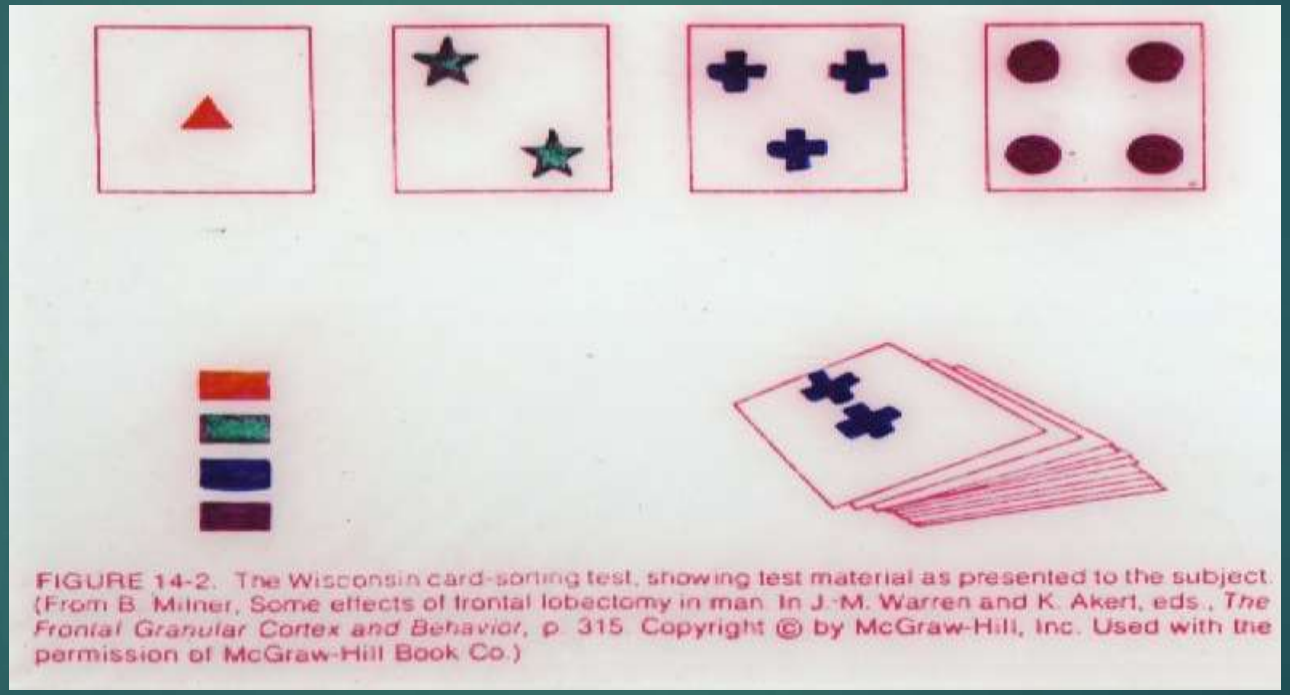
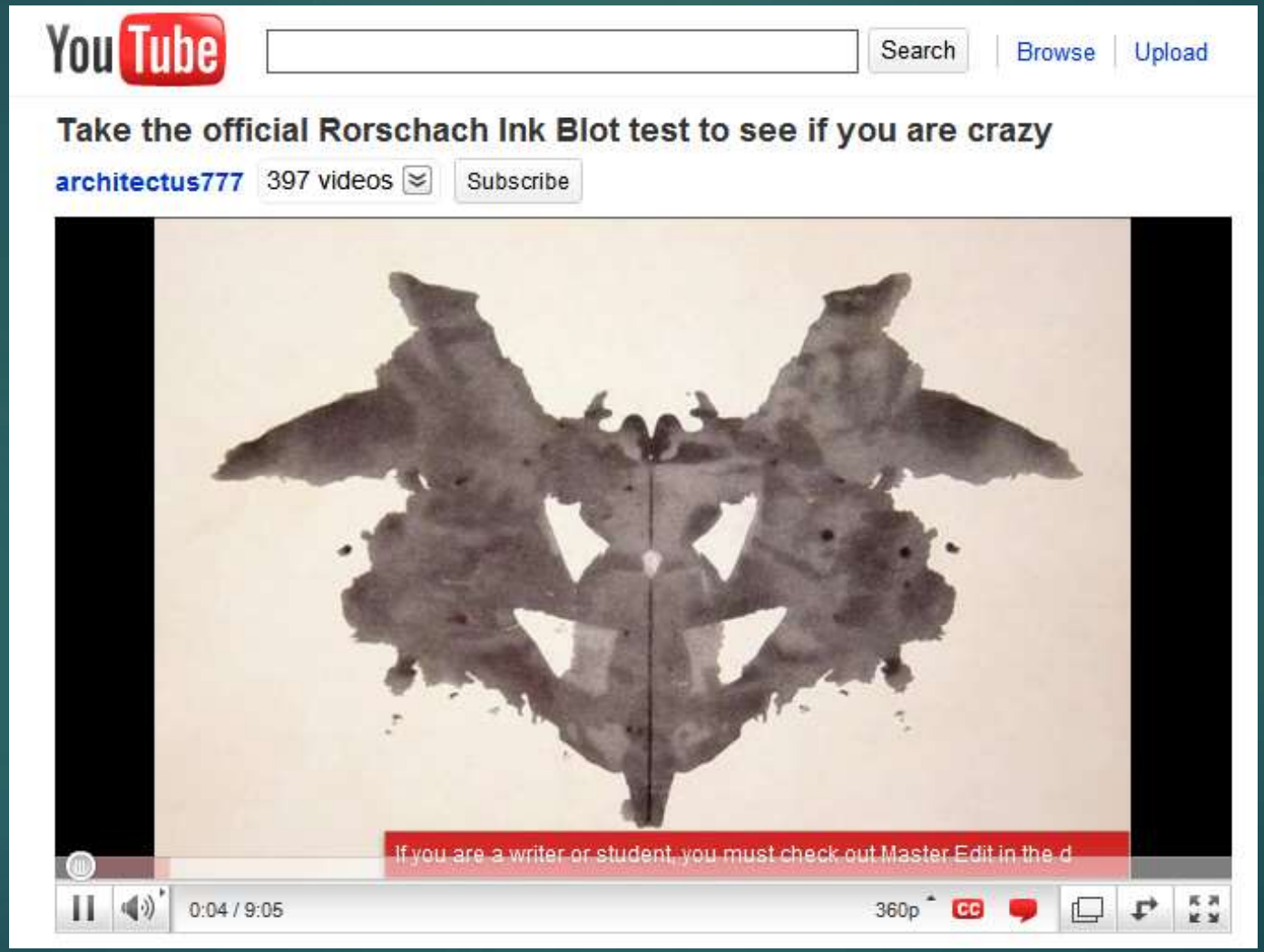


FIGURE 14-2. The Wisconsin card-sorting test, showing test material as presented to the subject. (From B. Milner, Some effects of frontal lobectomy in man. In J.-M. Warren and K. Akert, eds., *The Frontal Granular Cortex and Behavior*, p. 315. Copyright © by McGraw-Hill, Inc. Used with the permission of McGraw-Hill Book Co.)

Opinion: Nonverbal executive function tests are superior to verbal tests in predicting real world independence capability.

Older method, but alas on You Tube…

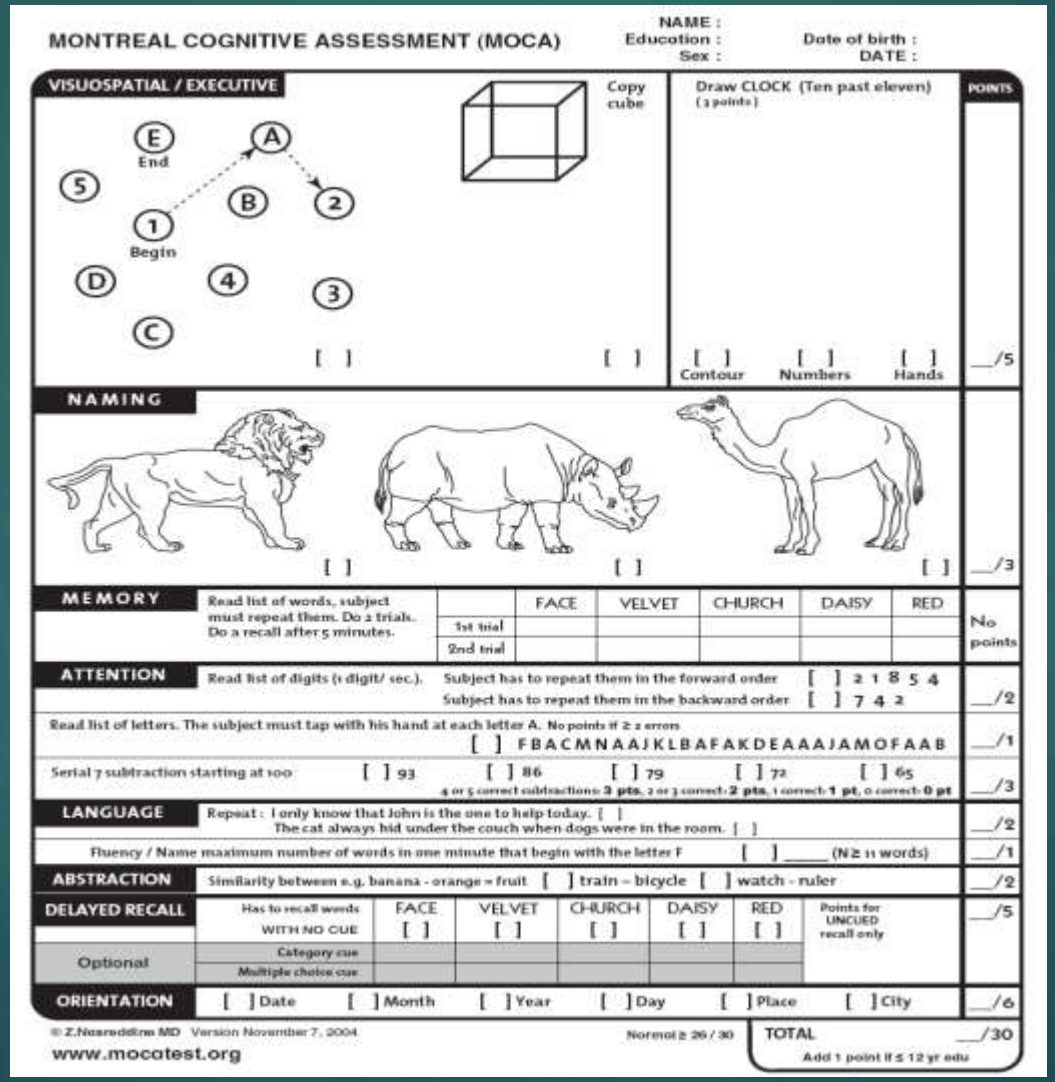


New: Rorschach Performance Assessment System

Your Neurocognitive Assessment Competence

In the last month,
how frequently have you used the following assessment tools?

MoCA:
Montreal Cognitive Assessment



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — POINTS

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

E End · A · 5 · B · 2 · 1 Begin · D · 4 · 3 · C

[ ] [ ] [ ] Contour [ ] Numbers [ ] Hands — /5

NAMING

[ ] [ ] [ ] — /3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2 — /2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B — /1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt — /3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ] — /2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words) — /1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler — /2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

— /5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City — /6

© Z.Nasreddine MD Version November 7, 2004

www.mocatest.org

Normal ≥ 26 / 30

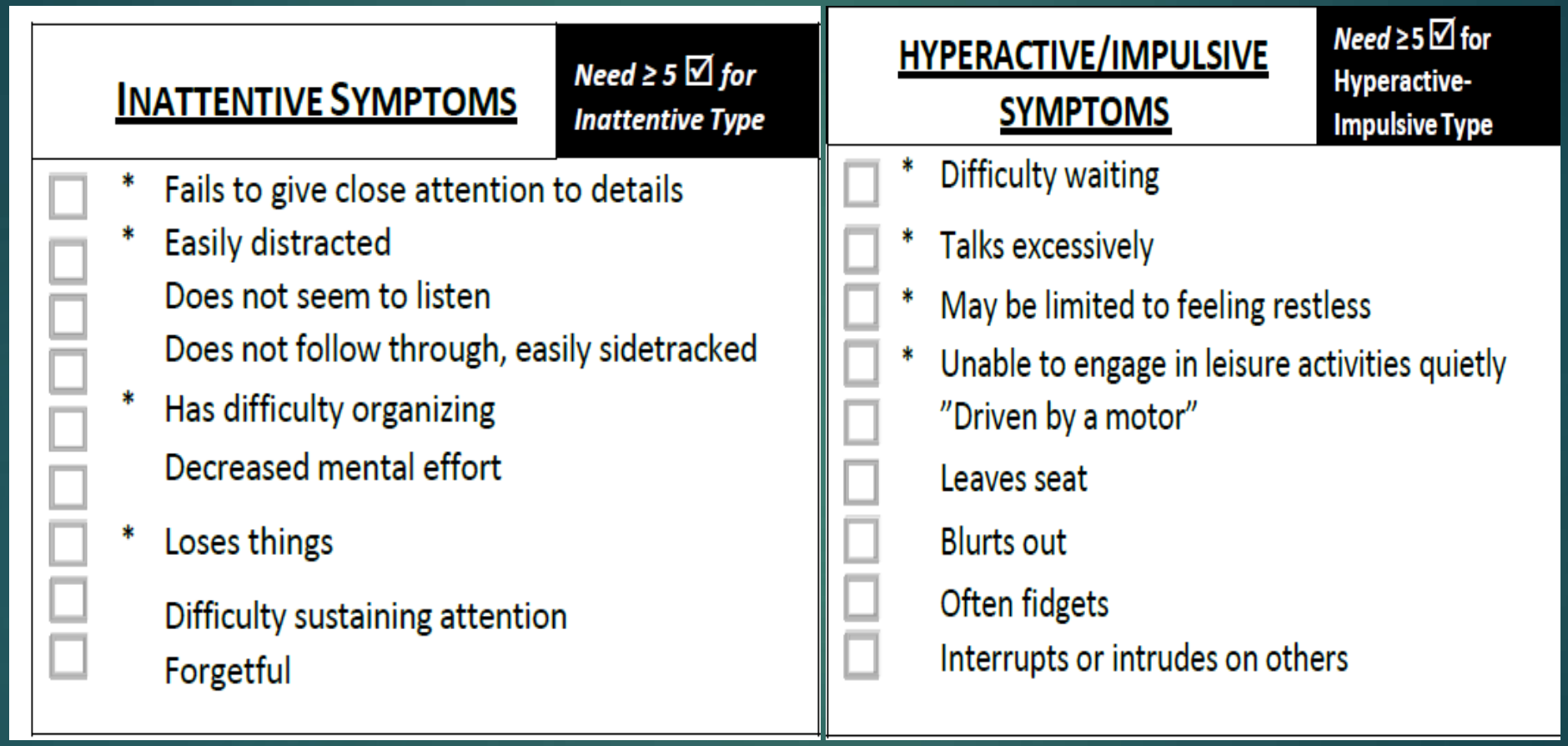
TOTAL — /30

Add 1 point if ≤ 12 yr edu

Alcohol Question

- "How many times in the past year have you had X or more drinks in a day?"
  - X is 5 for men and 4 for women,
  - a response of >1 is considered positive.

ADHD Diagnostic Tool



INATTENTIVE SYMPTOMS — *Need ≥ 5 ☑ for Inattentive Type*

- ☐ * Fails to give close attention to details
- ☐ * Easily distracted
- ☐ Does not seem to listen
- ☐ Does not follow through, easily sidetracked
- ☐ * Has difficulty organizing
- ☐ Decreased mental effort
- ☐ * Loses things
- ☐ Difficulty sustaining attention
- ☐ Forgetful

HYPERACTIVE/IMPULSIVE SYMPTOMS — *Need ≥5 ☑ for Hyperactive-Impulsive Type*

- ☐ * Difficulty waiting
- ☐ * Talks excessively
- ☐ * May be limited to feeling restless
- ☐ * Unable to engage in leisure activities quietly
- ☐ "Driven by a motor"
- ☐ Leaves seat
- ☐ Blurts out
- ☐ Often fidgets
- ☐ Interrupts or intrudes on others

C. Root, C. Vella, E. Miccio, 2008, 2013

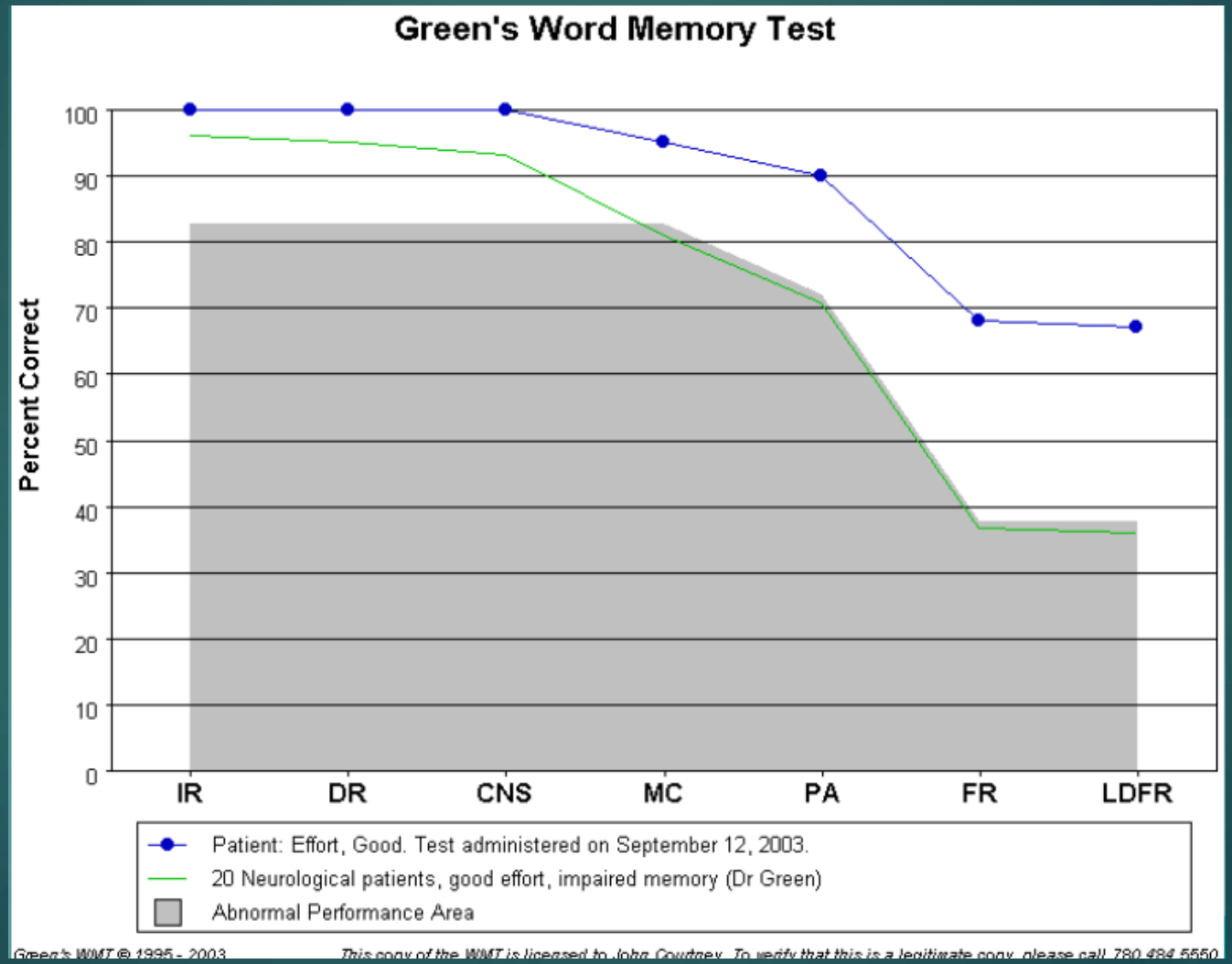
Life Domains Affected by ADHD Symptoms

Circle all that apply:

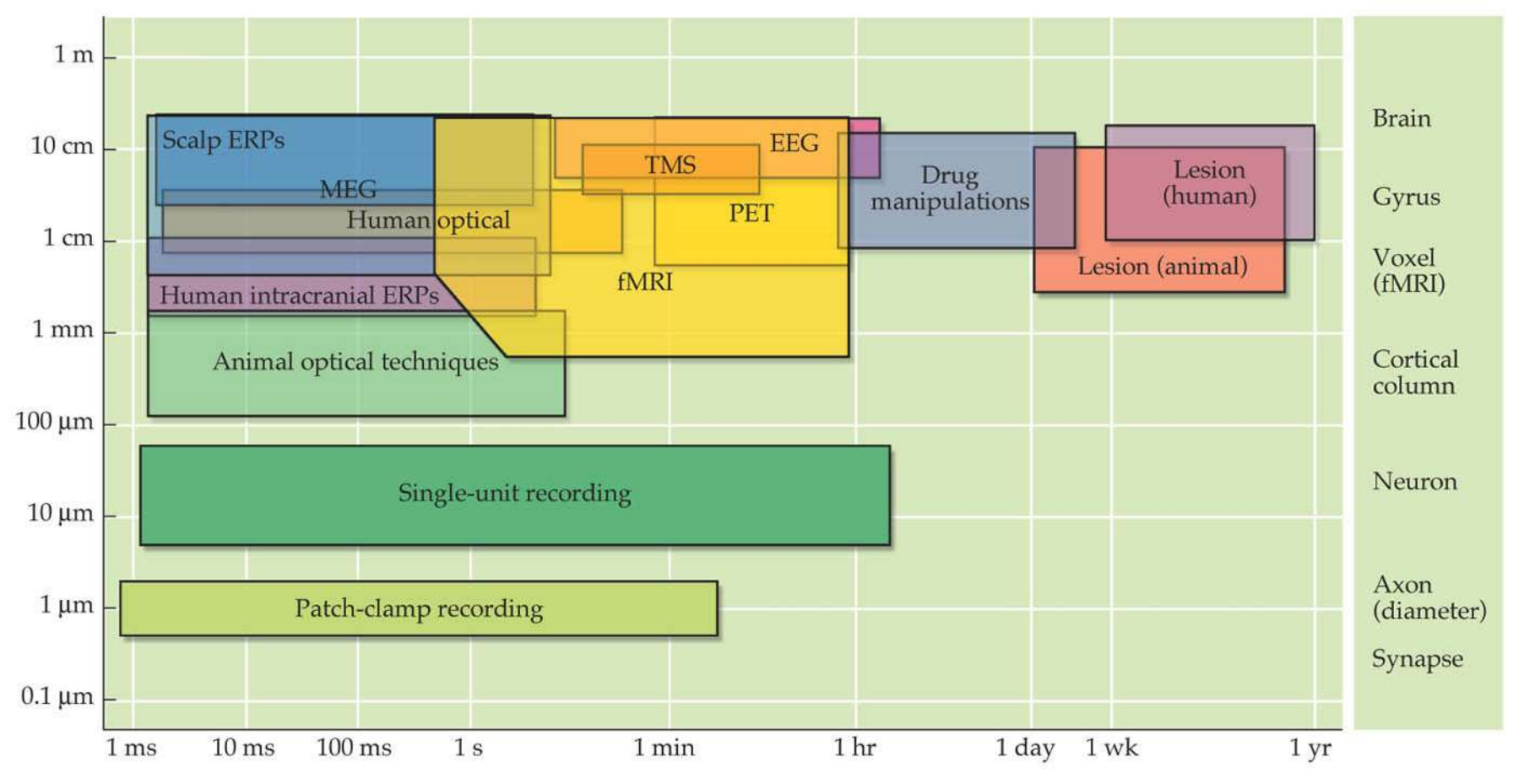
HOME	SCHOOL	WORK	RELATIONSHIPS	LEGAL	HEALTH/HABITS
Poor at money mgmt. (e.g., saving planning ahead)	Failure to turn in projects or complete tasks on time	Often late for mtngs, appointments, etc	Frequently accused of not listening	Hx of shoplifting, truancy, vandalism?	Regular substance use (e.g. Daily MJ use)
Trouble paying bills on time	Trouble organizing/ planning for projects	Difficulty meeting deadlines	Several short-lived relationships	#____of at-fault accidents	Smoking hx? Age began _____ # cigarettes daily____
Often buys items on impulse	Dx (or suspected) learning disability (e.g. diff in sports, learning to tie shoes, buttons)	Frequent job changes/multiple careers or "employment variety"	Impulsive sexual encounters	#____Speeding tickets *Ask about driving in general* (Enjoy it? Reckless?)	Caffeine use? Daily amount _____
Trouble keeping up with routine household chores	GPA lower than likely ability level, Drop out of school/ earned GED	Fired from job(s)	Unprotected sex or unplanned pregnancies	Hx of arrests	Sleep problems-Diff going to sleep, slow to wake up
"Packrat" or likes everything visible bc "out of sight is out of mind"	Failure to complete education, or degree	Quit due to boredom	Hx of STDs	Hx of violent behaviors (e.g., fistfights)	Forget to eat during day

*For items circled above-please explain how this is unique to a formal dx of ADHD (e.g. longevity, degree and impact on fx) versus a mood, personality or substance related disorder.

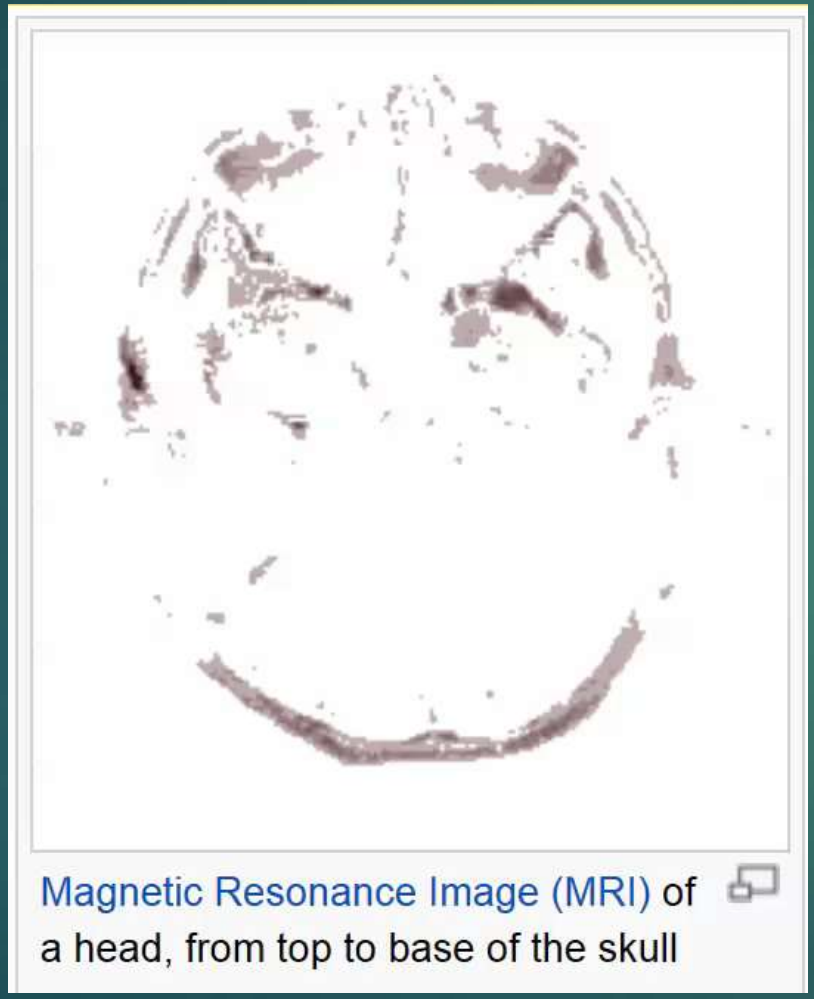
Effort Measure



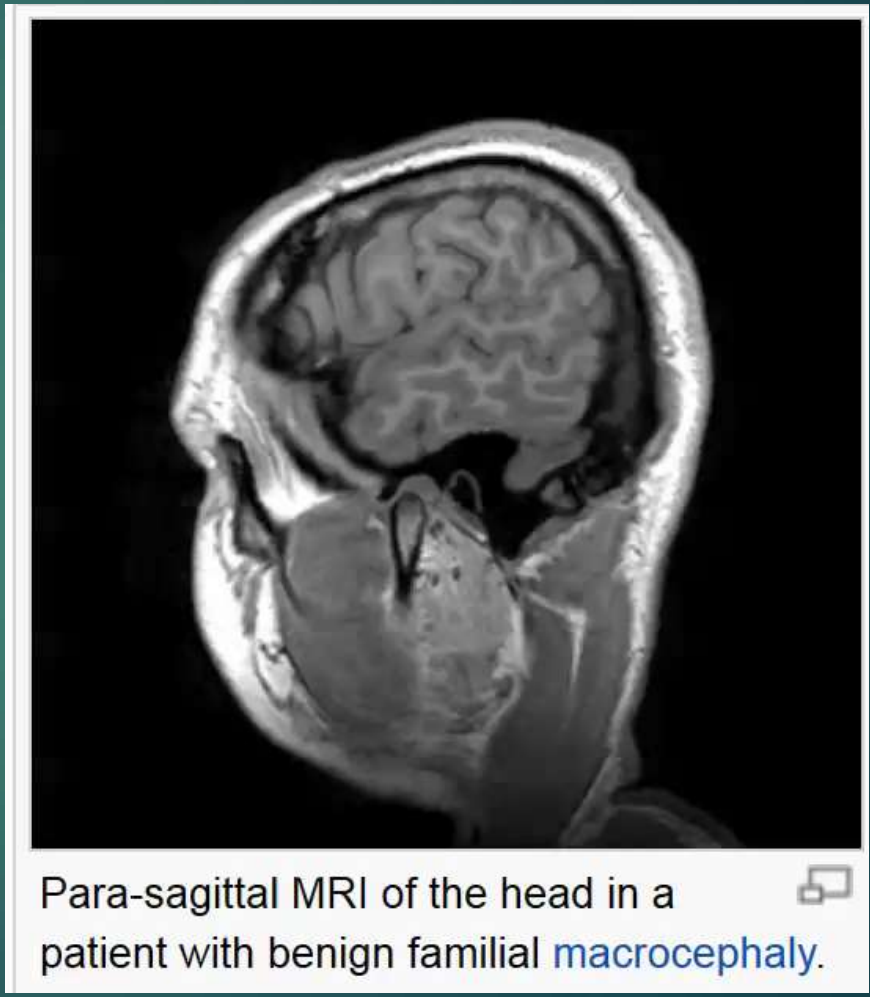
Spatial & Temporal Resolution: Scale in studying the nervous system



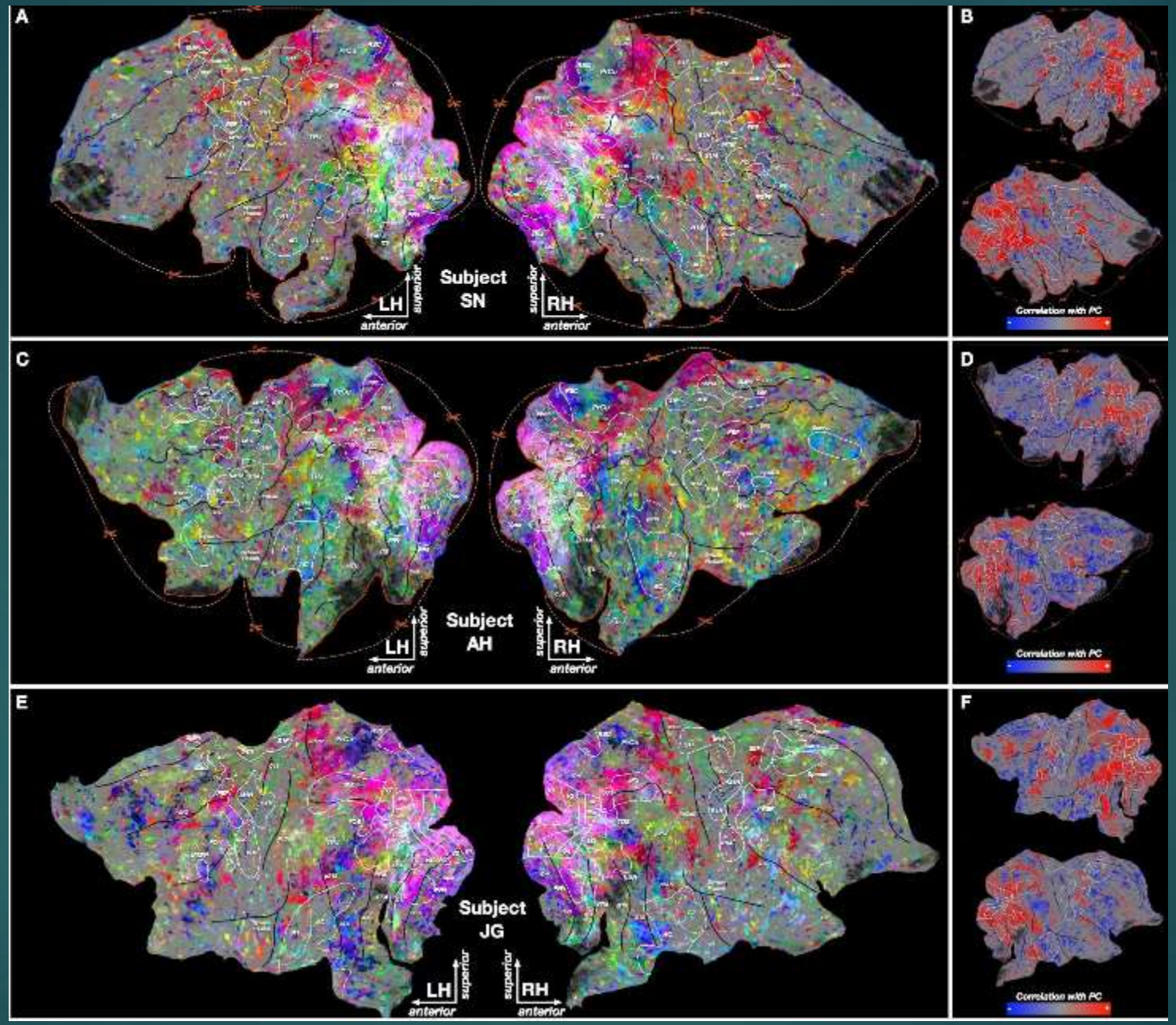
MRI



Magnetic Resonance Image (MRI) of a head, from top to base of the skull



Para-sagittal MRI of the head in a patient with benign familial macrocephaly.

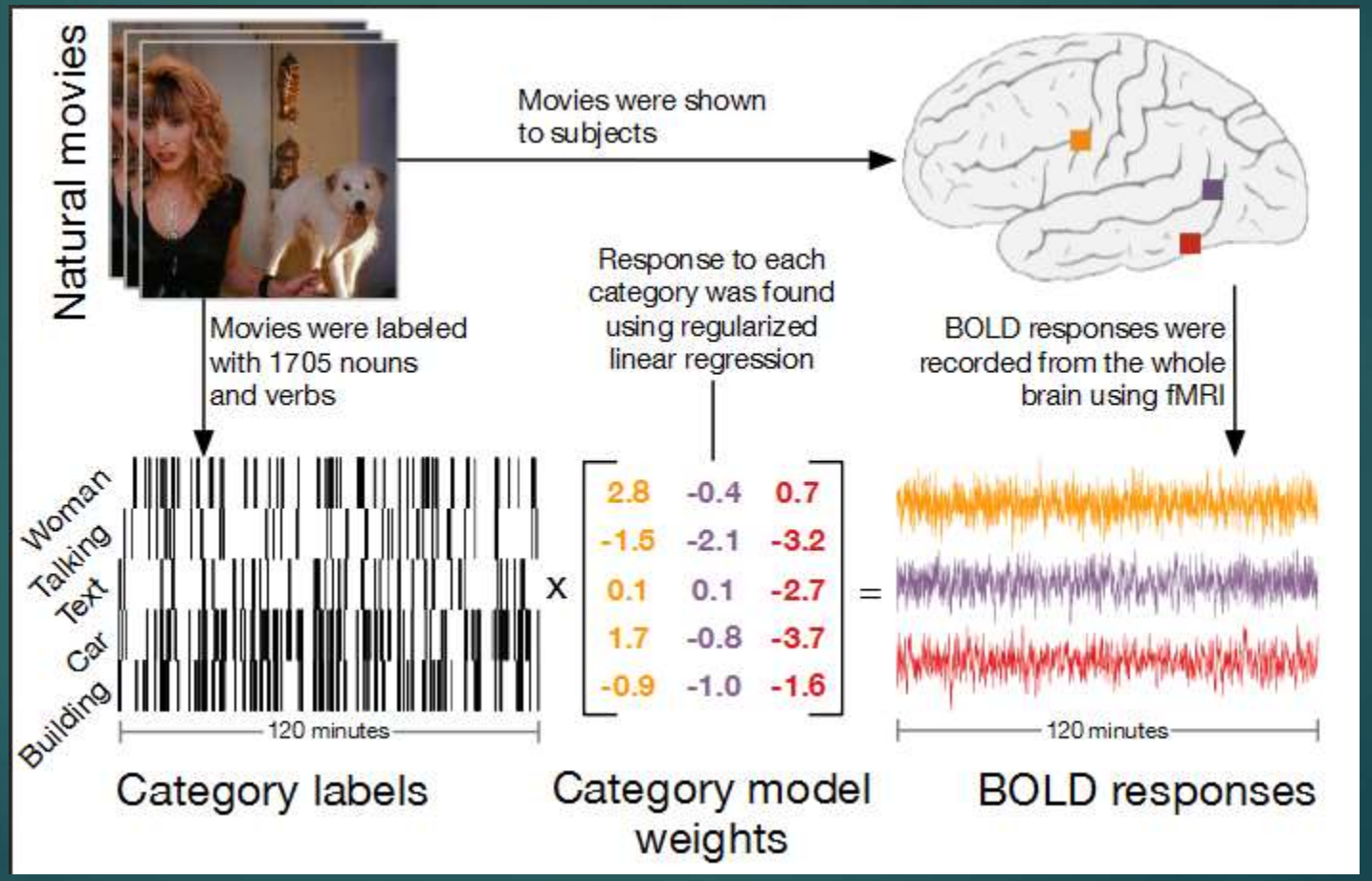


Cortical maps of semantic representation

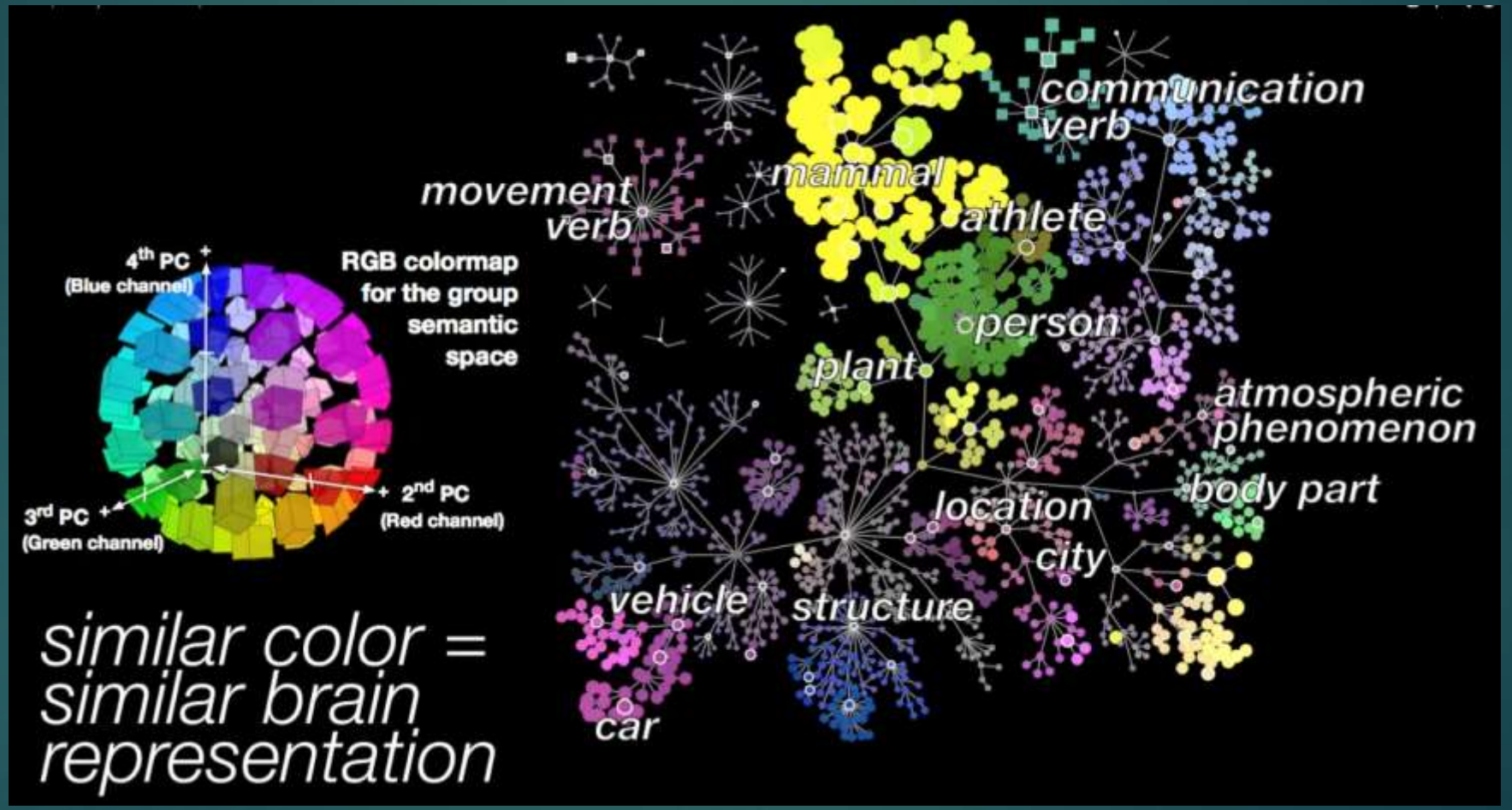
Decoding Brains:
Will know what you think

- J. L. Gallant, UCB: Predictive models of brain activity are the gold standard of computational neuroscience
- Using EEG, fMRI for voxel analysis ; statistical analysis, esp. regression; & theoretical modeling: how each element of the visual system encodes information
- Models can be inverted in order to *decode* brain activity, providing a direct way to do "brain reading", and to build brain-machine interfaces (BMI) and neural prosthetics.
- Lab has been able to make videos of what people see, what people are semantically thinking about

Decoding Brains



Decoding Brains: Words



Brain Visual Decoding: Crude but improving

Presented clip

Clip reconstructed from brain activity

New research

- 3 recent studies:
- Implanted a false memory in a mouse
- Showed that a mouse, via epigenetics, could pass on an aversion to a smell to her child
- Male mouse exposed to 10 days of bullying; Despite having no contact with their depressed fathers, the offspring grew up to be hypersensitive to stress

Optical fibres implanted in a mouse's brain activated memory forming cells

Methodological Issues in this talk

- Medication effects:
  - testing on/off meds i.e. CPT
  - meds causing findings, i.e. processing speed
- Preexisting deficits are cause:
  - Schizophrenia: Seidman & pneumoencephalograms
  - PTSD: Vietnam twin studies
- No effort measures in historical research
- Neuroplasticity issues: is it disease or behavioral practice that changes brain or both

Brief review of functional brain neuroanatomy

Major NP Functions

- Executive Functions
- Working Memory
- Sustained Attention
- Memory
- Social Cognition: Emotional processing, ToM, facial and emotional recognition
- Processing speed
- Visual Spatial Ability
- Language
- IQ

Thinking, Fast and Slow: Daniel Kahnman;

- Most of our behavior is controlled by Type 1 processes running in the background.
- Autonomy is the defining characteristic of Type 1 processes. They do not required "controlled attention"; they make minimal demands on working memory resources.
- Type 1: Rapid execution; they do not put a heavy load on central processing capacity, they tend to be associative.
- Involves implicit learning; and the automatic firing of overlearned associations. Anything learned to automaticity is Type 1 process.
- Neither system is perfect

System 1: The Default

- ***Intuition:*** fast, intuitive, and emotional
- Automatic and unconscious; our autonomous autopilot
- Is wrong as often as it is right; swayed by our emotions.
- Shared by all animals; evolutionarily old. Limbic system.
- The system itself is domain-general
- Based upon our memory of past similar events and our emotions
- Relies on prior knowledge and belief and produces rapid, parallel and automatic processes where only the final product is conscious.

***Thinking, Fast and Slow*, Daniel Kahneman**, antidote to Malcolm Gladwell's Blink.

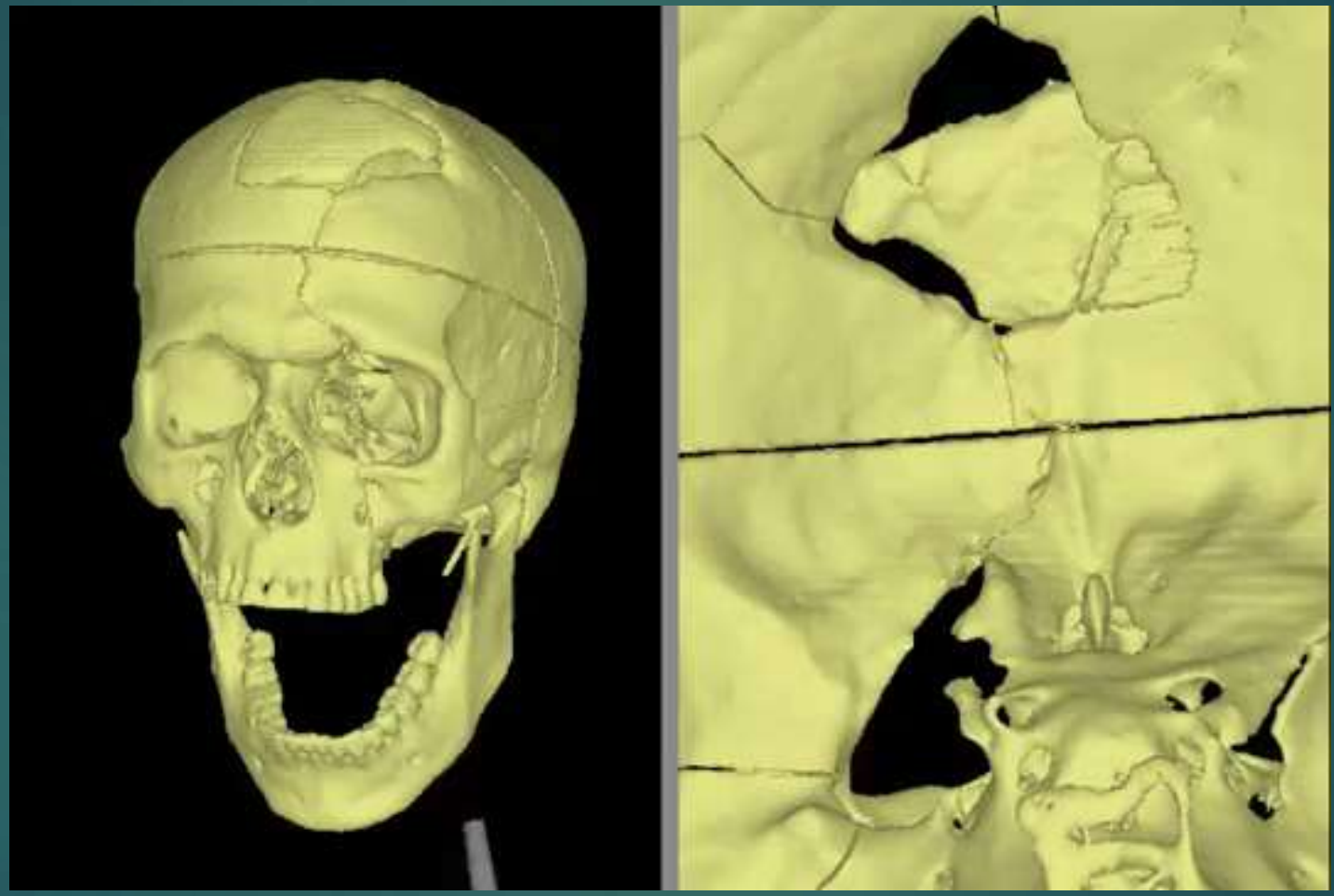
System 2: Reasoning

- ***S***lower, more deliberative, and more logical
- Evolutionarily recent and specific to humans.
- It performs the more slow and sequential thinking; prior appraisal of possible consequences.
- Distracted and hard to engage.
- It is domain-general, performed in the central working memory system. Has a limited capacity and is slower than System 1. Correlates with general intelligence. Frontal.
- Permits the abstract hypothetical thinking that is not permitted in System 1.
- The rational system because it reasons according to logical standards.
- Rule-based, analytic, controlled, demanding of

System 1: Hot (Go) System/Default	System 2: Cool (Know) System
Emotional	Cognitive
Stereotypic	Calculating
Automatic	Effortful
Frequent	Infrequent
Reflexive	Reflective (deliberative, logical)
Nonconscious	Conscious
Fast	Slow
Amygdala & Ventral Striatum	Prefrontal
Develops Early	Develops Later
Accentuated by Stress	Attenuated by Stress
Stimulus Controlled	Self-Control

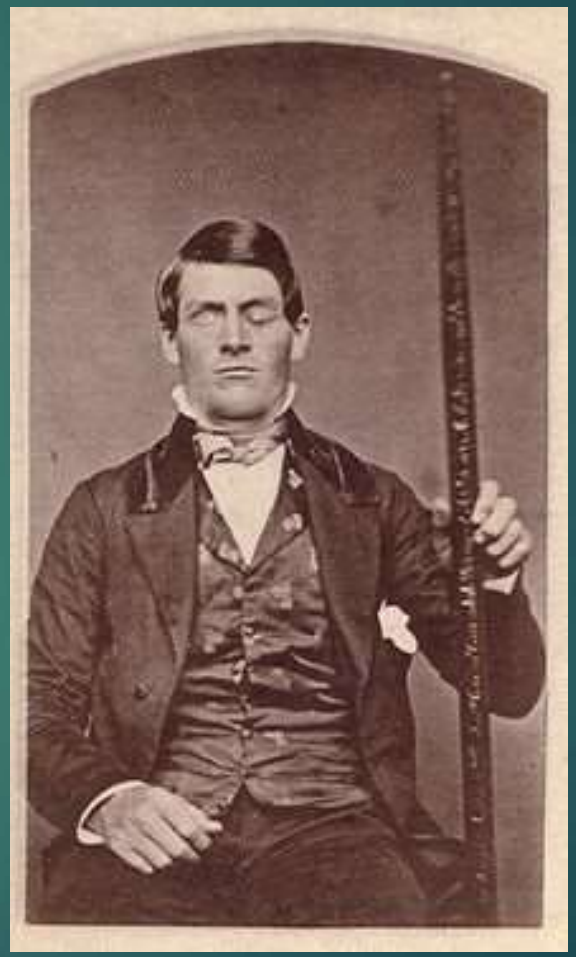
Thinking Fast & Slow - Daniel Kahneman

The Phineas Gage Event



Arrow on picture to start

Phineas Gage, ~ 1848



An Odd Kind of Fame: The Phineas Gage Myth

- According to Malcolm Macmillan, the accounts of Gage's behavioral changes are based largely on anecdotal reports that are not substantiated by the little evidence there is.
- "Phineas' story," Macmilllan writes in his book *An Odd Kind of Fame*, "is worth remembering because it illustrates how easily a small stock of facts becomes transformed into popular and scientific myth."

Evolution of brain

- Evolution of the brain was driven primarily by 3 functions:
  - Movement
  - Social complexity
  - Flexibility

- Current implications for normal brain:
  - Physical Activity !!!
  - Sitting is bad for you: no matter how hard you work out, if you sit for the rest of the day, you are still at greater risk for all the health issues associated with a sedentary lifestyle: obesity, diabetes, heart disease, some cancers, and a shortened life span

Frontal Lobe & Executive Deficits

- DSM-5 rarely mentions cognitive disorders related to EF deficits
- DSM-5 has no index references to Executive Function or Neuropsychology; only references cognition under NCDs
- EF deficits underline a variety of psychiatric disorders:
  - Schizophrenia
  - Substance Abuse
  - ADHD
  - ASD
  - Bipolar
  - PD

Executive Functioning

- EFs allow us to respond flexibly to the environment: to break out of habits, make decisions and evaluate risks, plan for the future, prioritize and sequence actions, and cope with novel situations, among many other things.

- EFs are essential for successfully navigating nearly all of our daily activities.

Executive Functioning: Lezak test

‘‘How or whether to’’ (executive control) vs. ‘‘what or how much’’ (memory, calculation)

- Executive functioning examples:
  - Self monitoring behavior
  - Anticipate consequence of action
  - Ability to give reason for an action
  - Disregard erroneous strategies
  - Inhibit automatic but inappropriate response
  - Modify behavior in response to contextual changes
  - Finish what is started
  - Comply with treatment
  - Do something when needed (not just know how to do it)

Executive Functions

- Goal direction
- Self regulation and impulse control
- Cognitive and Behavioral/response inhibition
- Impulse Control
- Planning
- Working Memory
- Flexibility
- Action monitoring
- Initiation and inhibition of environmental exploration
- ToM

EF predicts…

- Impairments in EF thus have serious consequences:
  - quality of life
  - functional outcomes
  - disability status
  - psychopathology

If EF impaired…

- Viewed as lazy, unmotivated, forgetful
- Can't complete tasks in timely way
- Poor prioritization
- Poor initiation and follow through
- Poor time management and meeting deadlines
- Need reminders
- Difficulty changing behaviors in response to environmental demand
- Live in here and now

Severe EF Consequences

- Lack of capacity to make financial, medical, treatment decisions
- Do not learn from negative feedback
- Inability to live without supervision
- Inability to use psychotherapy
- Need behavioral management

Dorsolateral Prefrontal Functions

- Higher cognitive functions, more complex, strategic thinking
- Fluid IQ, working memory, planning, set shifting, goal directed behavior
- Response selection, inhibition
- DL PFC appears to be critically involved in maintaining goal representation and in anticipating future affectively charged events

Core feature of dlPFC: Working Memory

- Miller's Constant: 7 ± 2 in Psych. 101
- The capacity for online storage and processing of information
- Highly correlated with Fluid IQ; foundation of System 2 Thinking
- Attentional buffer that holds information while we process it
  - Telephone number
  - Mental arithmetic
  - Recall of chess positions, bridge hands, music and baseball klg
  - Delayed response

Stereotype Threat

- Stereotype threat is a disruptive concern that occurs when people know that if they perform poorly, they will confirm a negative self-relevant stereotype
- In response to this threat, people underperform compared with their potential, thereby confirming the stereotype
- When older adults (60+) are confronted with negative stereotypes about age-related cognitive declines, they underperform on memory tests
- Also African Americans, women, etc.

Dorsolateral Damage: NP Tests

- Poor test Performance:
  - Poor TMT
  - Poor WCST
  - Poor Category Test
  - Poor D-KEFS
  - Poor IVA

Orbital Frontal Cortex (OFC): How rewarding is a reward

- Primary functions:
  - analysis of rewards and punishments;
  - rapid evaluation of cost/benefits of behavioral responses to environment, esp. social
    - Behavioral inhibition: can send a 'stop' signal to other brain regions concerned with more automatic behaviors (i.e. OCD)

- Damage in non-human primates: abnormal social behavior, especially social isolation and avoidance

- Damage in humans: severe social deficits (i.e. FTD)

OFC & Stereotyping

- Stereotypes = cognitive "shorthand" for instantaneously decoding social situation for rapid behavioral response; Type 1 process
- Faster Reaction Time to stereotypes
- OFC damage interferes with rapid evaluation of complex social information based on learned associations

Damage to OFC: Alters social behavior

- Abnormal social behavior and violations of social norms
- Cannot see how behavior might be viewed negatively by others & be socially punished
- Bilateral damage: impaired identification of self conscious emotions (embarrassment, shame)
- Unilateral right damage: impaired recognition of anger & disgust

OFC Damage: Emotion Recognition

- Strong evidence for dominance of right hemisphere for emotion perception (facial expression, voice prosody) and emotion expression

- Pts with OFC lesions show:
  - deficits in emotion recognition, both in facial and vocal modes
  - Ventral damage: impaired facial emotion recognition, nonverbal vocal expressions of emotion

Frontal Temporal Disease & OFC

- FTD: all of the OFC social deficits
  - Early decline in social conduct
  - Early impairment in regulation of personal conduct
  - Early emotional blunting
  - Early loss of insight

- Deficits:
  - poor emotion perception,
  - disinhibition,
  - euphoria,
  - apathy,
  - decreased emotional expression,
  - decreased embarrassment,
  - loss of hygiene, increased selfishness

OFC and TBI

- TBI often produces OFC disconnection via axonal shearing
- Emotional recognition deficit common (both emotional face and posture recognition, and lexical naming of emotions)
- Difficulty recognizing faces with negative emotions & interpreting nonverbal vocal emotions

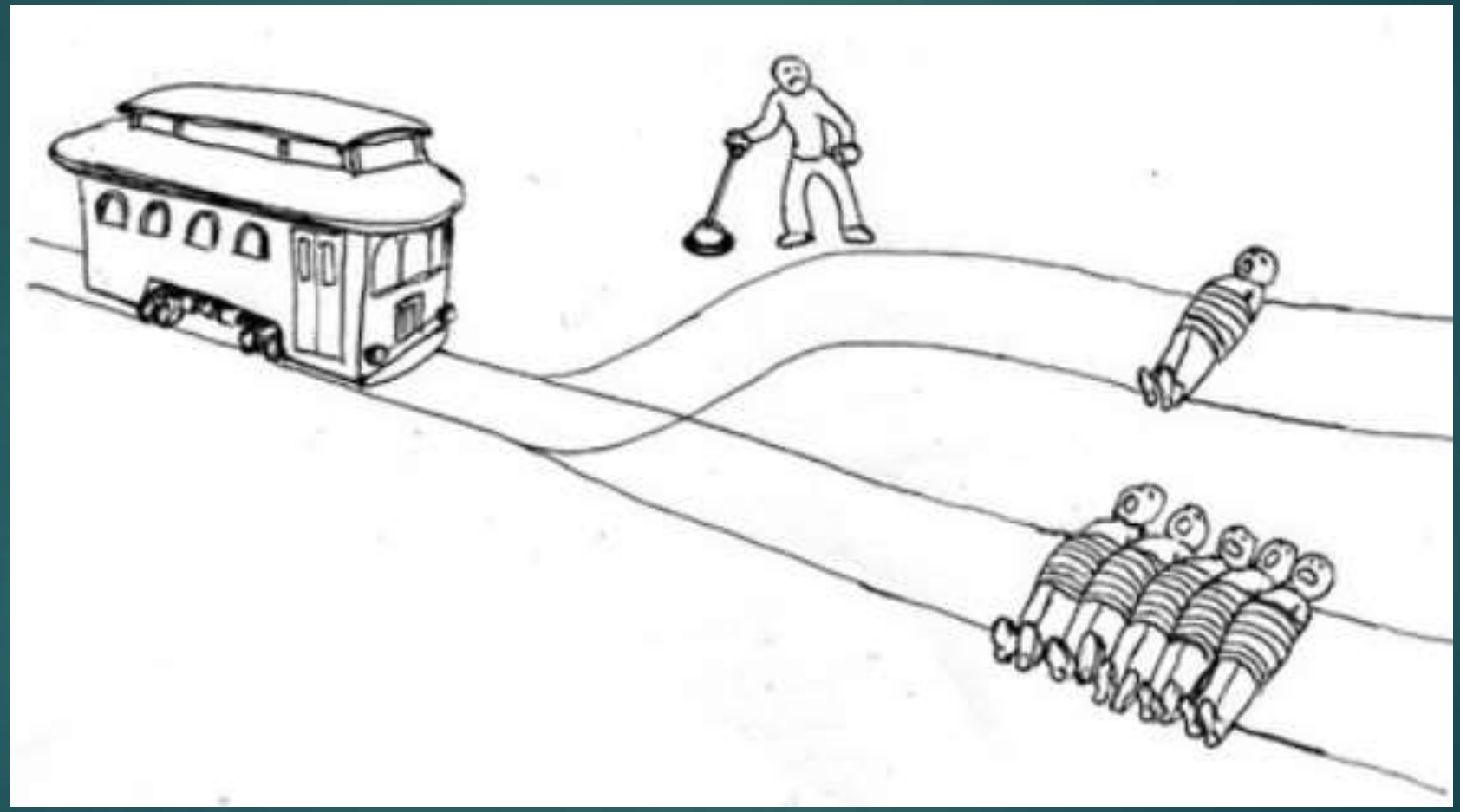
Orbital Damage

- Damage produces:
  - Disinhibition
  - Hyperactivity
  - Emotional lability
  - Aggressiveness
  - Reduce self-awareness
  - Mood disorders
  - Poor Iowa Gambling Test
  - Poor Faux pas test

- Disinhibition:
  - swearing excessively, hypersexuality,
  - poor social interaction, compulsive gambling, drug use (including alcohol and tobacco),
  - poor empathizing ability

- Classic FTD behaviors

Moral Judgment: Trolley Problem 1: DL PFC active

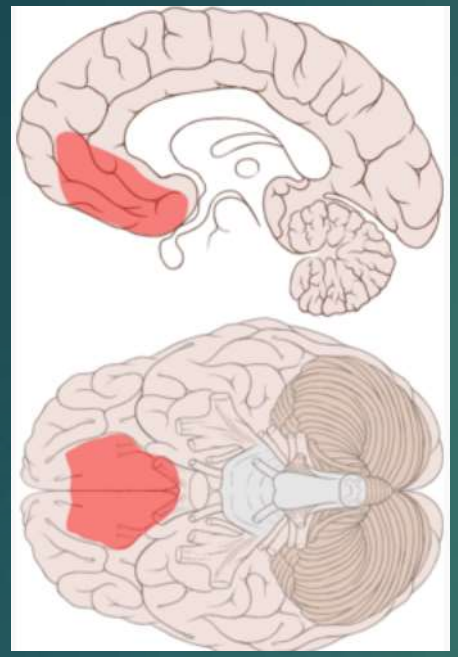


9 of 10 people confronted with this scenario say it's O.K. to hit the switch.

Trolley Problem 2: vmPFC damage

9 of 10 people say it's not O.K. to kill one person to save five;
Individuals with vmPFC damage 3x more likely to push the person off.

Ventromedial PFC



- Evaluation of subjective value of options
- Processing of risk and fear contingencies
- Emotion regulation
- Reactivating past emotional associations (part of pathogenesis of PTSD)
- Natural decision making: System 1
- Processing gender specific social cues.

vmPFC Damage

- VMPFC damage: strongest predictor of empathic deficits

- 3 x more likely to advocate throwing a person to certain death in front of a runaway train to keep it from killing five other people.

- 5 x more likely to advocate smothering one's baby to save others

- Predicts future alcoholism & psychopathy

Damasio, 2007; Amitai Shenhav and Joshua D. Greene, 2010

Medial OFC Tumor: Is Mr. Spock's rationality the ideal

- 1982: Pt. E.: model father, corporate manager, 97%tile IQ
- Then behavior change; considered a "malingerer"; fired from job, wife divorced him.
- He walked into neurologist Antonio Damasio's office: bilateral mOFC tumor diagnosed & removed
- No emotional reaction (no GSR) to scenes of mutilation
- Now: pathological indecision: whether to use a blue or black pen; where to park
- Discovery: human decision making requires emotions to function correctly
- Damasio's Somatic Marker Theory: Iowa Gambling Test

A. R. Damasio, Tranel, & Damasio, 1990; Eslinger & Damasio, 1985

Medial Frontal: Future action & ToM

- Action monitoring: Posterior rostral MFC - Control & monitoring of action, response inhibition, attention, error monitoring; associated with dorsal ACC
- Outcome monitoring: Orbital MFC - Monitoring of outcomes related to punishments and rewards, with OFC
- Social Cognition/ToM – Anterior rostral MFC – emotional region (self referential processing, person perception, inferences about thts of others), with ACC

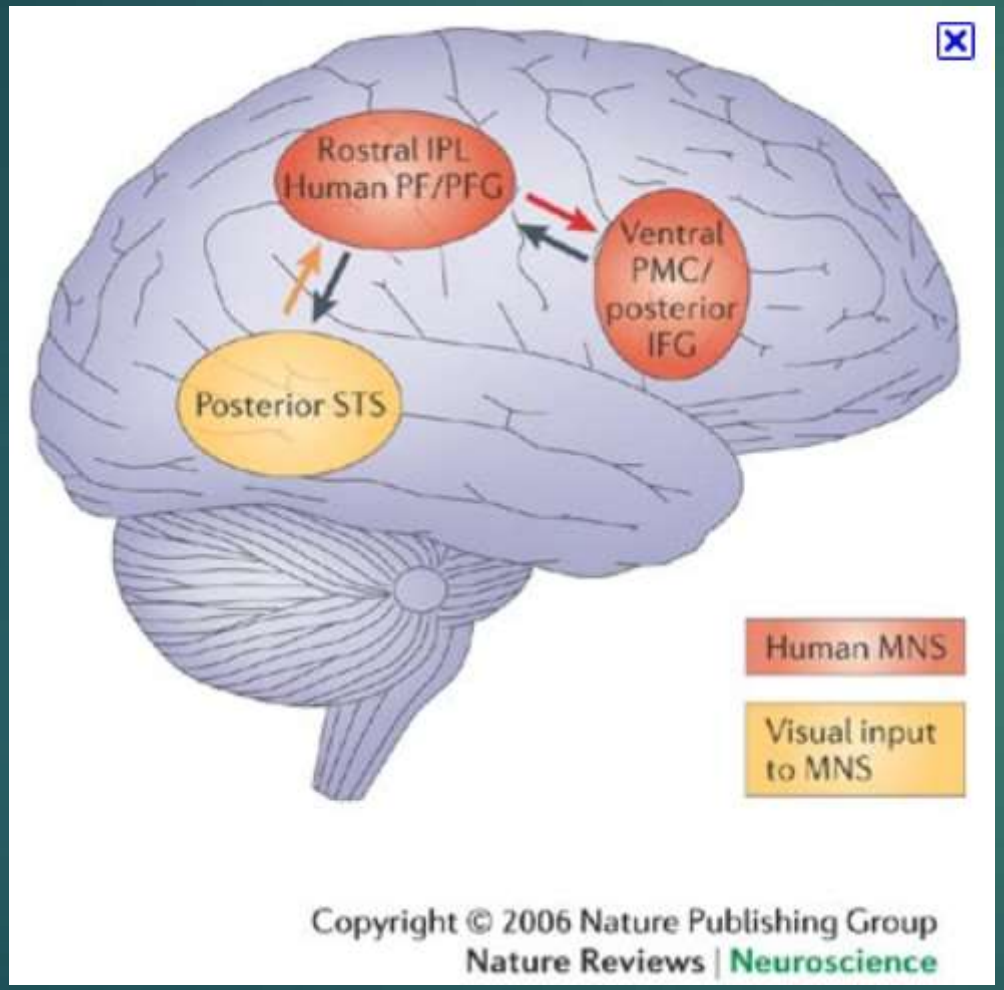
EF Recommendations

- Structurally based EF deficits are forever.
- Classic psychotherapy does not directly address these deficits, but can be undermined by them.
- Given the pervasive presence of EF deficits in psychiatric disorders, it needs to be identified early in the assessment process before setting up a management plan in order to lead to better outcomes.
- Need to identify: Use of EF scales/NP testing

EF Recommendations

- EF deficits are mostly unresponsive to medications.
- Education and Cognitive rehab strategies need to be in place.
- More systematic acknowledgement and use of other people as "surrogate frontal lobes"
- Therapists assume pts need to do everything by themselves; people need collateral help

Mirror Neurons



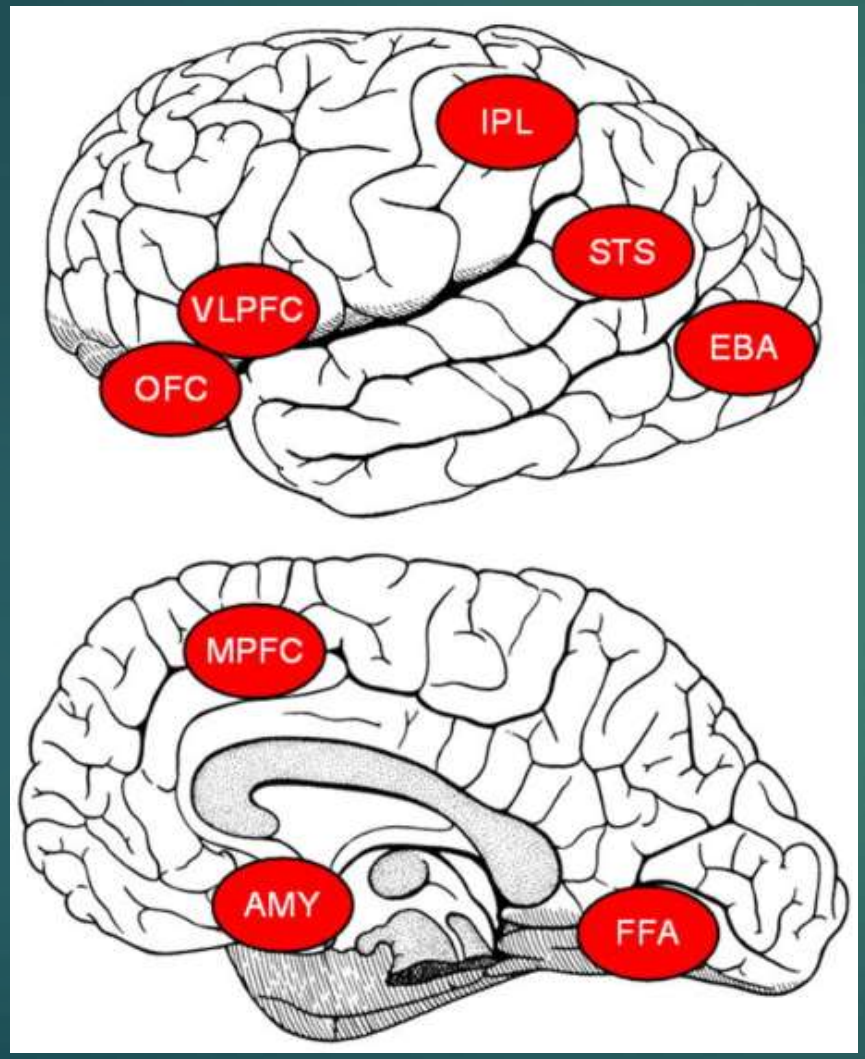
STS: superior temporal sulcus

Monkey who saw researcher lift a banana

Gandhi neurons: dissolve the barrier between you and me

Activation in response to seeing other doing something

Social Cognition:
Brain nodes in social brain



Some of the brain regions involved in various aspects of social cognition and social perception.
VLPFC = ventral lateral prefrontal cortex,
IPL = inferior parietal lobule,
STS = superior temporal sulcus,
OFC = orbital frontal cortex,
MPFC = medial prefrontal cortex,
EBA = extrastriate body area,
AMY = amygdala,
FFA = fusiform face area.

K. Pelphrey & E. Carter, 2008

Social areas of brain: predominantly right

- Social Self Monitoring: right medial & orbital frontal
- Detection of sarcasm: right parahippocampal
- Embarrassment: right pregenual anterior cingulate
- Ability to track dynamically changing emotions: right OFC

Right & Left Hemisphere: counterbalance

- From studies on effects on cerebral lesions on emotions; hemispheres counter balance each other

- Right prefrontal processes negative emotions:
  - Avoidance/withdrawal response
  - Lower activation in mania; release of left hem. containment

- Left prefrontal processes positive emotions:
  - Approach response
  - Lower activation in depression; releases right hem. negative avoidance response

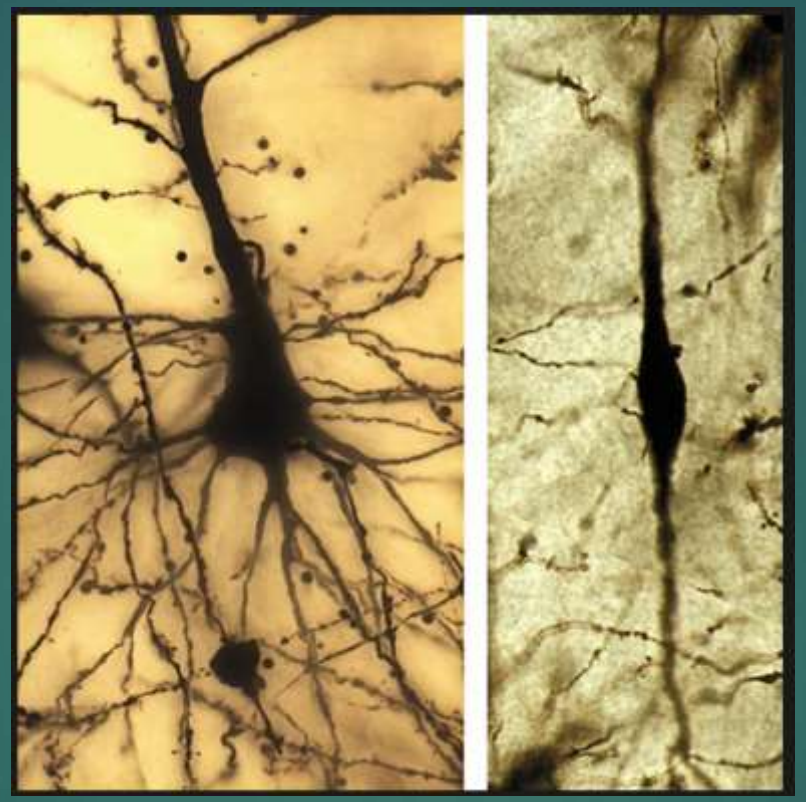
- Atrophy of either region, activates the other

- Depression lowers left PFC activation & increases right PFC activation

Shenal, et al., 2004; Kay, 2009

What is the neuronal commonality in social animals with large brains?

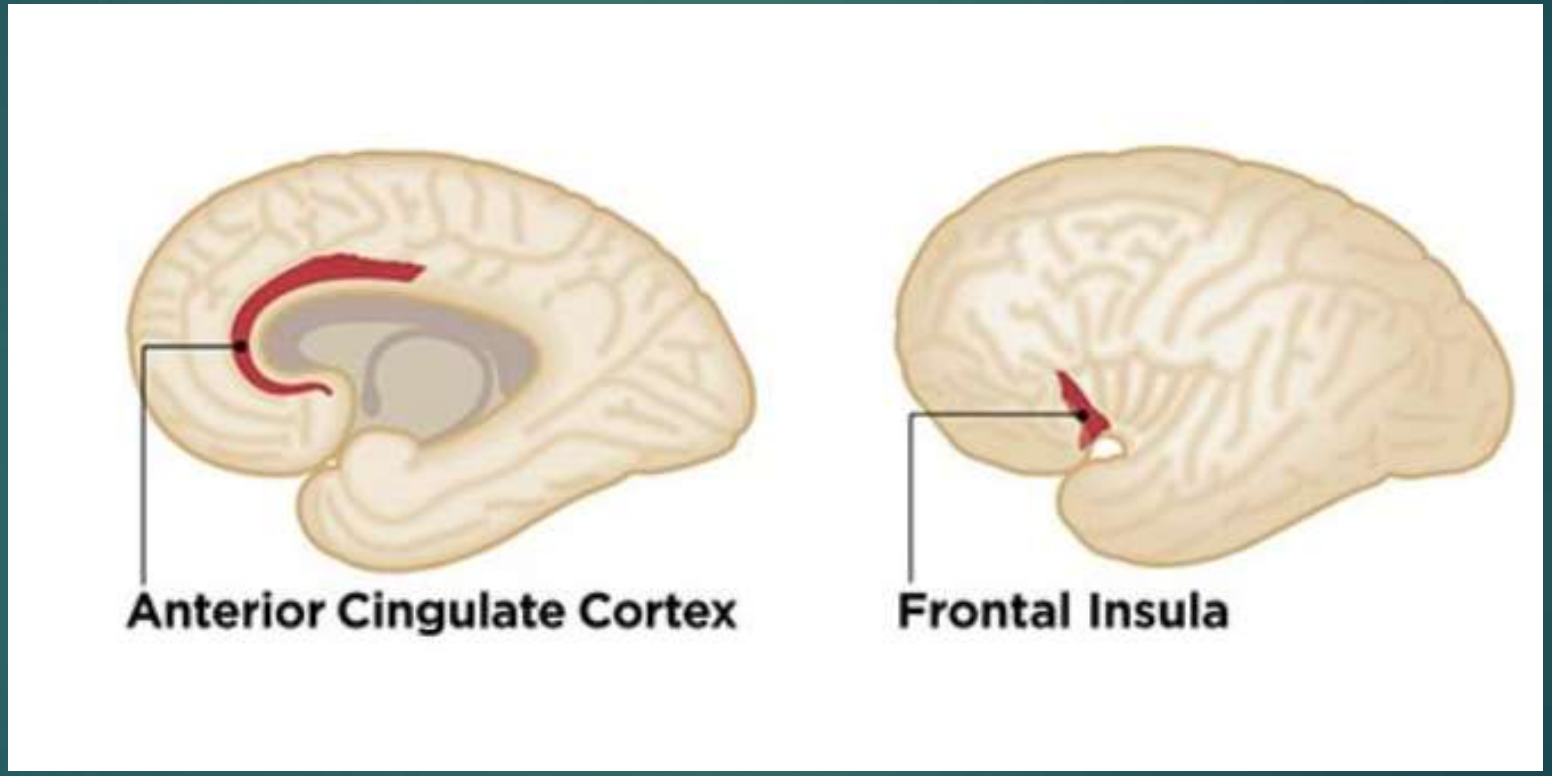
Brain Cells for Socializing?



A focal concentration of VENs in ACC and FI distinguishes large-brained, highly social mammals from other mammals.

(Allman et al., 2010; Hakeem et al., 2009; Hof and Van der Gucht 2007; Nimchinsky et al., 1999; Rose 1928)

Location of VENS: ACC & FI



The FI features the other layer 5 neuron, the fork cell, which is scarcely seen in ACC.

Von Economo Cells

- Fastest, large, bipolar neurons located only in the anterior cingulate and insula (layer Vb), & DLPFC.
- Only 4 species: primates, certain cetacians, elephants and humans. More of them in chimps and human (2x more than chimps).
- The volume of Von Economo neurons is correlated with increased encephalization. Evolved to speed information around a big brain.
- Mirror Test: Ability to recognize oneself in a mirror
- FTD targets ACC and Insula: 70 percent of VENs destroyed
- Abnormally located in autistic brains

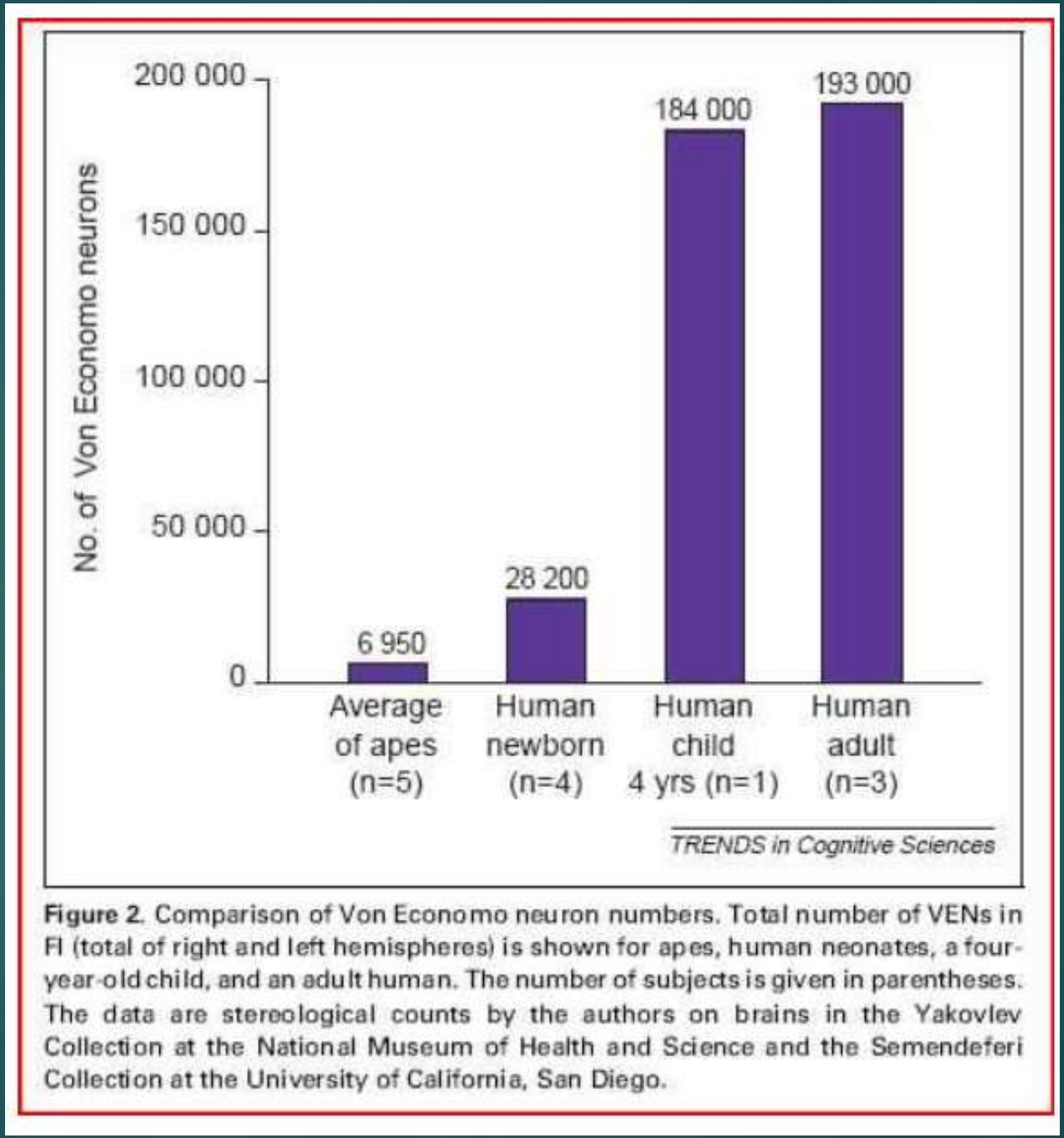


Figure 2. Comparison of Von Economo neuron numbers. Total number of VENs in FI (total of right and left hemispheres) is shown for apes, human neonates, a four-year-old child, and an adult human. The number of subjects is given in parentheses. The data are stereological counts by the authors on brains in the Yakovlev Collection at the National Museum of Health and Science and the Semendeferi Collection at the University of California, San Diego.

Insula

- Frontal insula: generation social emotions such as empathy, trust, guilt, embarrassment, love—even a sense of humor.
- Activation: when a mother hears a crying baby, or when someone scrutinizes a face to determine the other person's intentions.
- **Gut feelings**: from bodily sensations
- Monitoring interactions within a social network
- Empathy for pain of others
- Affective component of physical pain

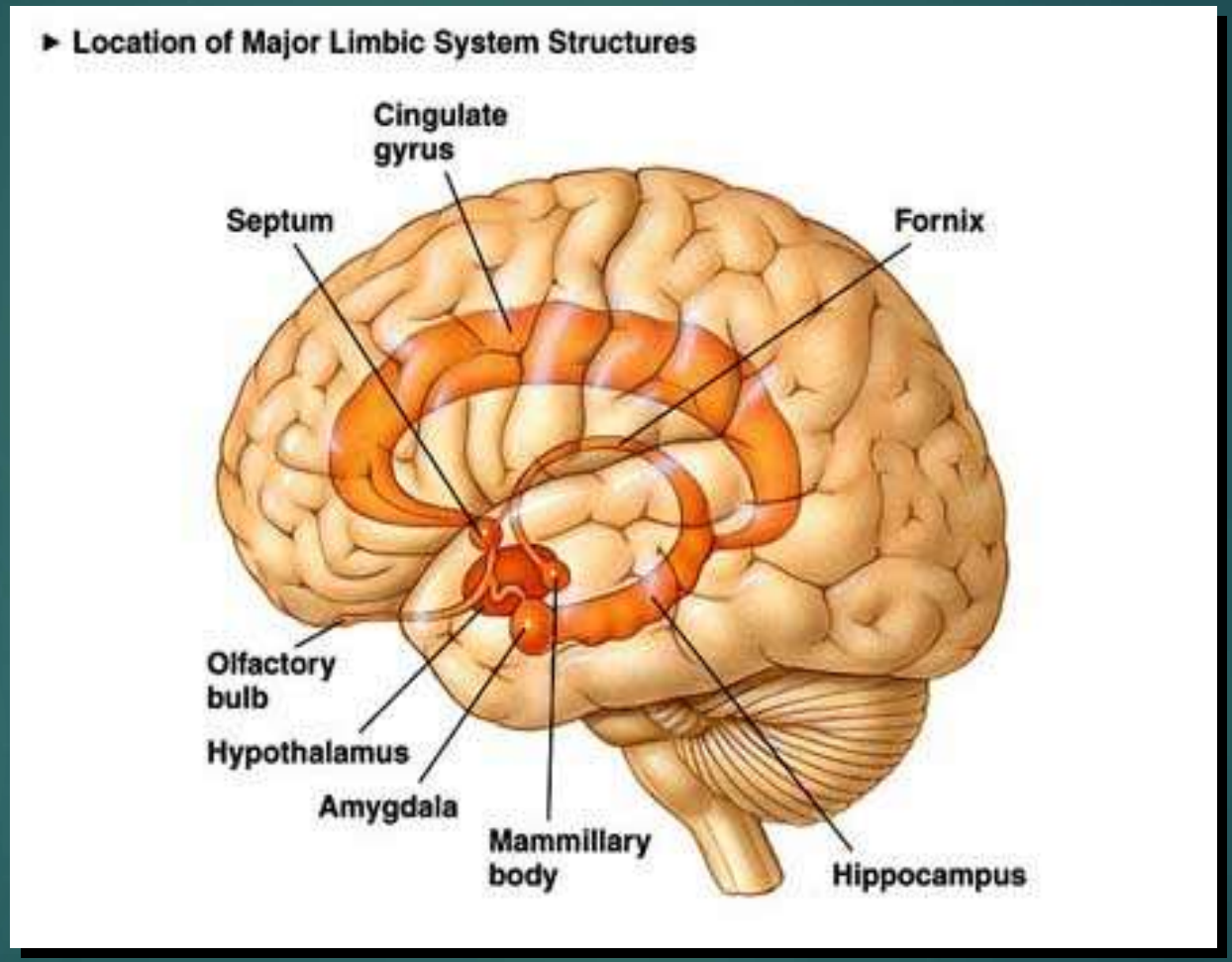
Evidence for Mirror Neuron system for emotions: Disgust

- Insula triggered both for
  - experiencing disgust feelings
  - recognition of disgust in others

- Insula activates
  - if smell rotten odors
  - watch a movie of rotten food (visceral sense of nausea)
  - watch a film of facial disgust in others

- Insula stroke: inability to ID disgust

Cingulate Gyrus



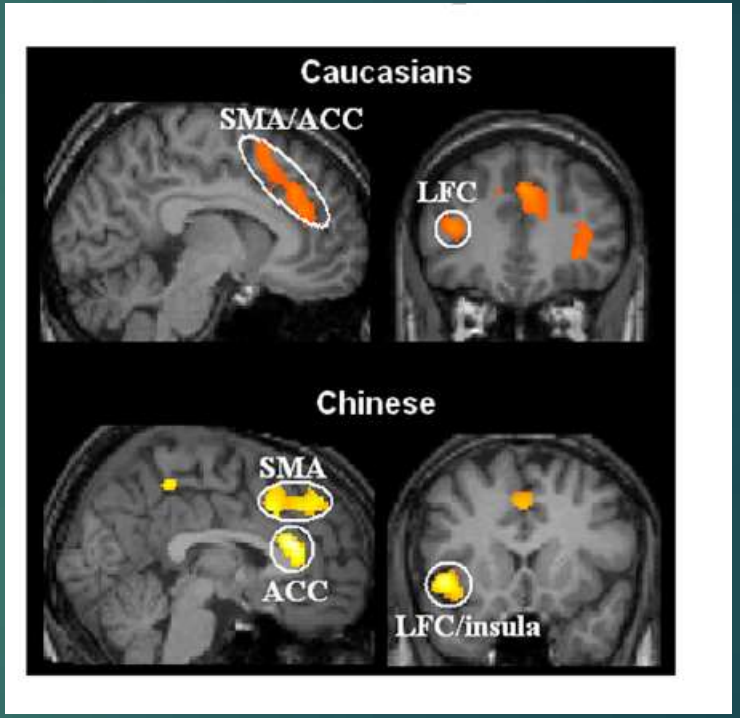
Conflict Resolution circuit; Salience network

Cingulate Gyrus: Conflict & Response

- Location: Collar around Corpus Callosum
- Functions:
  - flags response conflict (incongruent trial on Stroop)
  - error detection (Stroop; error + 1 slower RT)
  - anticipation of tasks
  - motivation
  - modulation of emotional responses (serotonin projections from ACC inhibit amygdala activation)
  - social cognition
  - bravery
- Coactivation with DLPFC (which then corrects behavior)
- Low activation ACC in psychopaths predicts recidivism
- Damage: OCD, akinetic mutism, ADHD, depression, psychopathy

Loyalty & Empathy & Prejudice in the In Group: **Do You Feel My Pain?**

- Inborn Prejudice: People show more empathy to own group.
- ACC mainly contributes to the affective component of empathy
- ACC & FI activate when witnessing someone in pain
- Own-race bias in ACC activity in empathy for pain
- Those with damage in the right ACC were least likely to feel embarrassment.



Rejection Hurts:
Social rejection causes physical pain

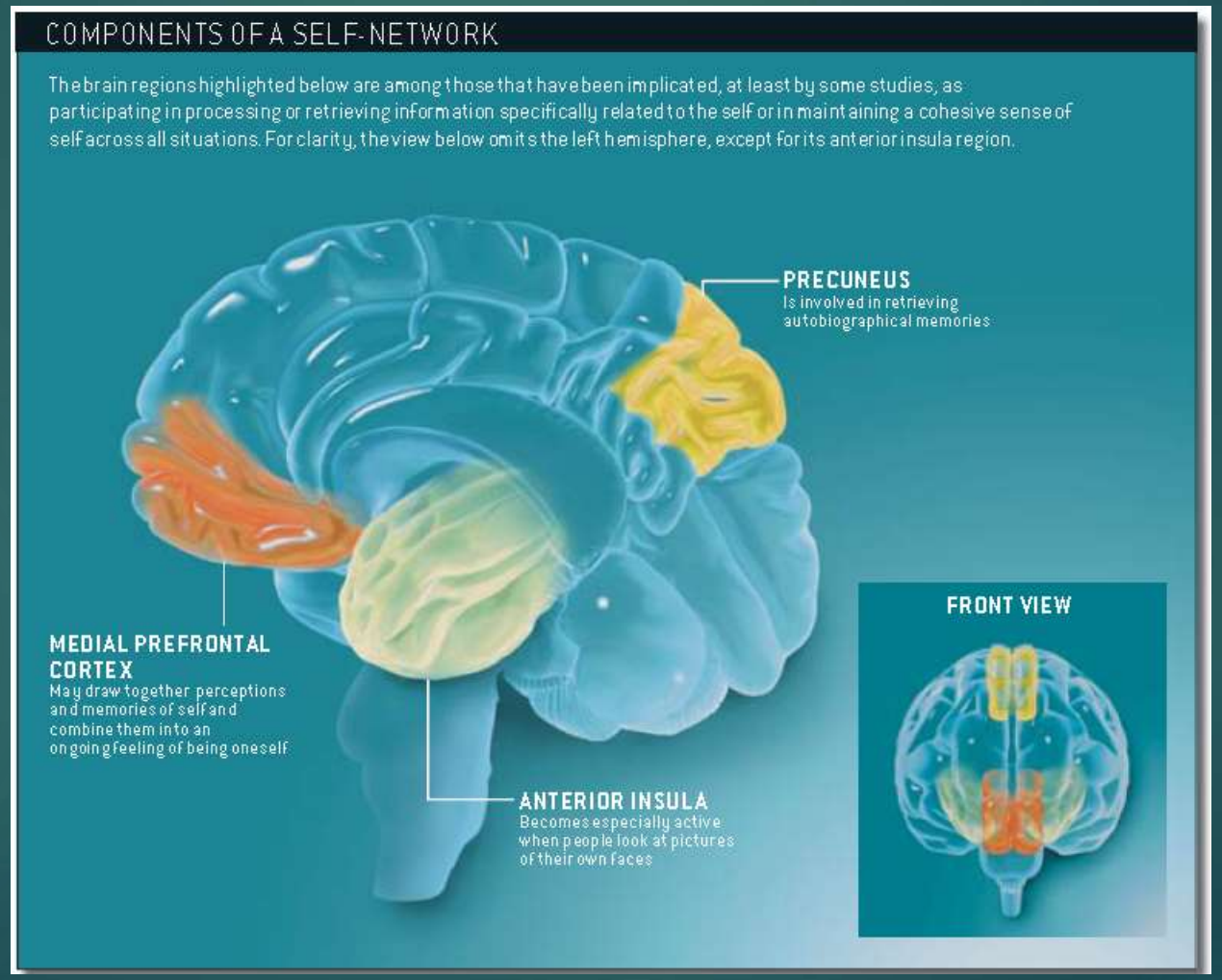
2,000 milligrams daily of acetaminophen for three weeks

Dorsal anterior cingulate cortex & existential dread

- ACC: process many types of negative experiences similarly:
  - Pain: real or social (i.e. rejection)
  - Existential dread: considering your own death

- 1 study: 1000mg of Tylenol decreases real pain, social rejection, & uncertainty

Self Network:
MFC, Precuneus, ACC



Functions of the Precuneus

- Historical research:
- Spatially guided behavior: spatial attention/tracking of different targets in space and between different object features, and in motor imagery tasks

- Mental imagery (visual rotation, deductive reasoning, music processing)
- Recent research:
- Episodic memory retrieval; R - regeneration of contextual autobiographic memory

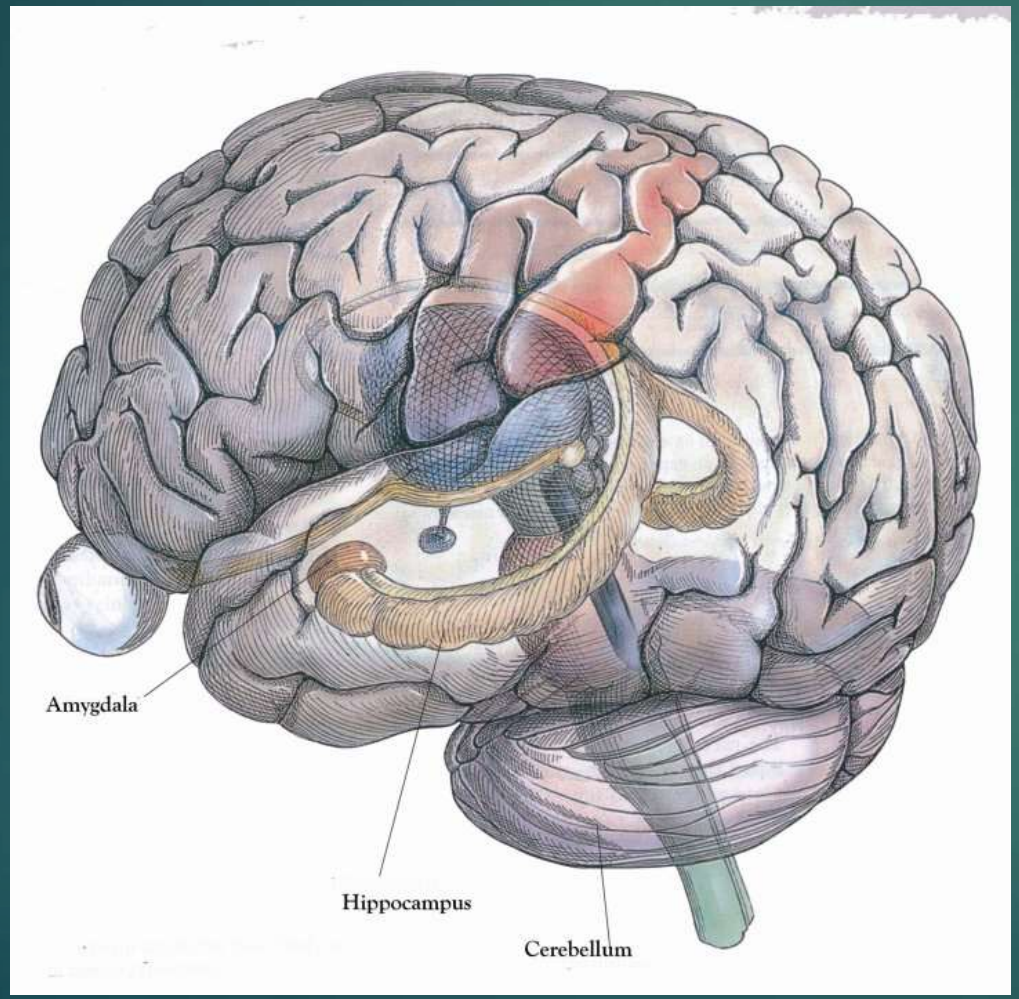
Mid brain: Self Reference

- Self-referential processing: activation of mPFC, pCC/anterior precuneus. Functionally intertwined with episodic memory
- Mental representation of the self: Personal identity via past personal experiences
- The mPFC: support an array of self-related capacities, including memory for self-traits or reflected self-knowledge.
- The pCC and precuneus: relevance or significance of a stimulus for yourself

Eyes Closed, Mind wandering: Precuneus & Consciousness

- Part of the DMN: All of these structures show high activity during rest, mind wandering, and conditions of stimulus-independent thought
- Conscious resting state: baseline processing, the DMN central (35% more glucose)
- Self-awareness and conscious experience.
- Deactivation: Selective hypometabolism in abolished consciousness or altered conscious states:
  - sleep,
  - drug-induced anesthesia

Amygdala & Hippocampus



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.

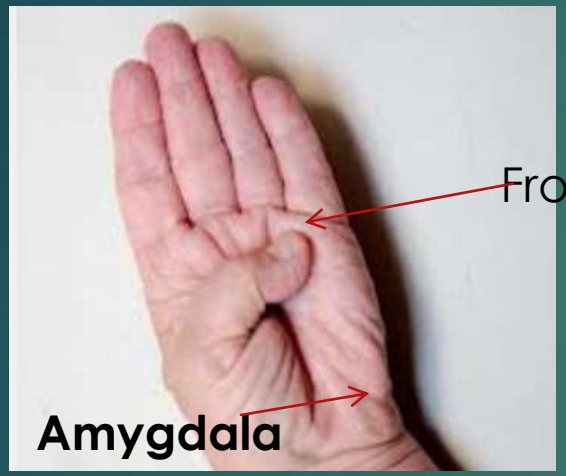
Function of Amygdala

- Amygdala:
  - Alarm system of the brain,
  - "**Fear Center**."
  - Initial emotional responses and reactions
  - "Fight-or-flight" response.

- Emotional recall/fear conditioning:
  - If ok, remember the tiger
  - If impaired, tiger is everywhere

- Stimuli awareness in 50ms vs consciousness of event (600ms)

Correct Frontal-Amygdala Control Pattern



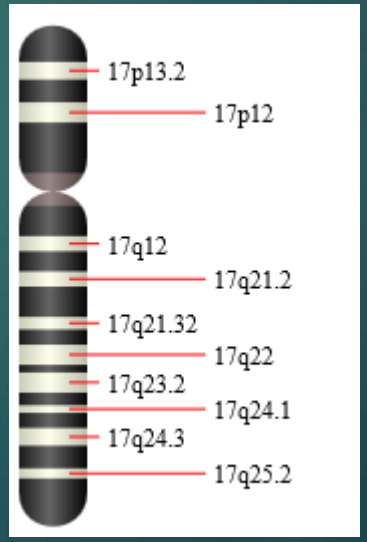
Out of Control Amygdala

Frontal in Charge

Serotonin transporter gene

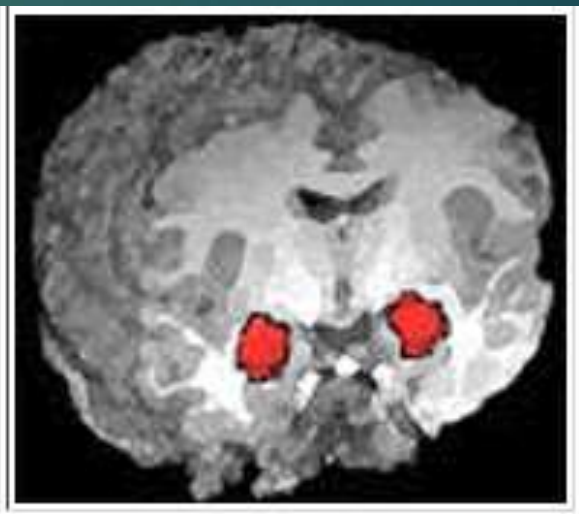
- Serotonin transporter gene (5-HTT) plays a (non-exclusive) role in impulsivity, suicide, and emotional stability
- This suggests a part in hyperactive amygdala activation and dysfunction.

Hariri 2002, Donegan 2003



Amygdala:
Flashbulb/traumatic memory

Challenger Space Shuttle
(NASA)



fMRI of Amygdalae
(NIMH)

Unanticipated, emotionally charged events can create vivid, detailed "Flashbulb Memories."

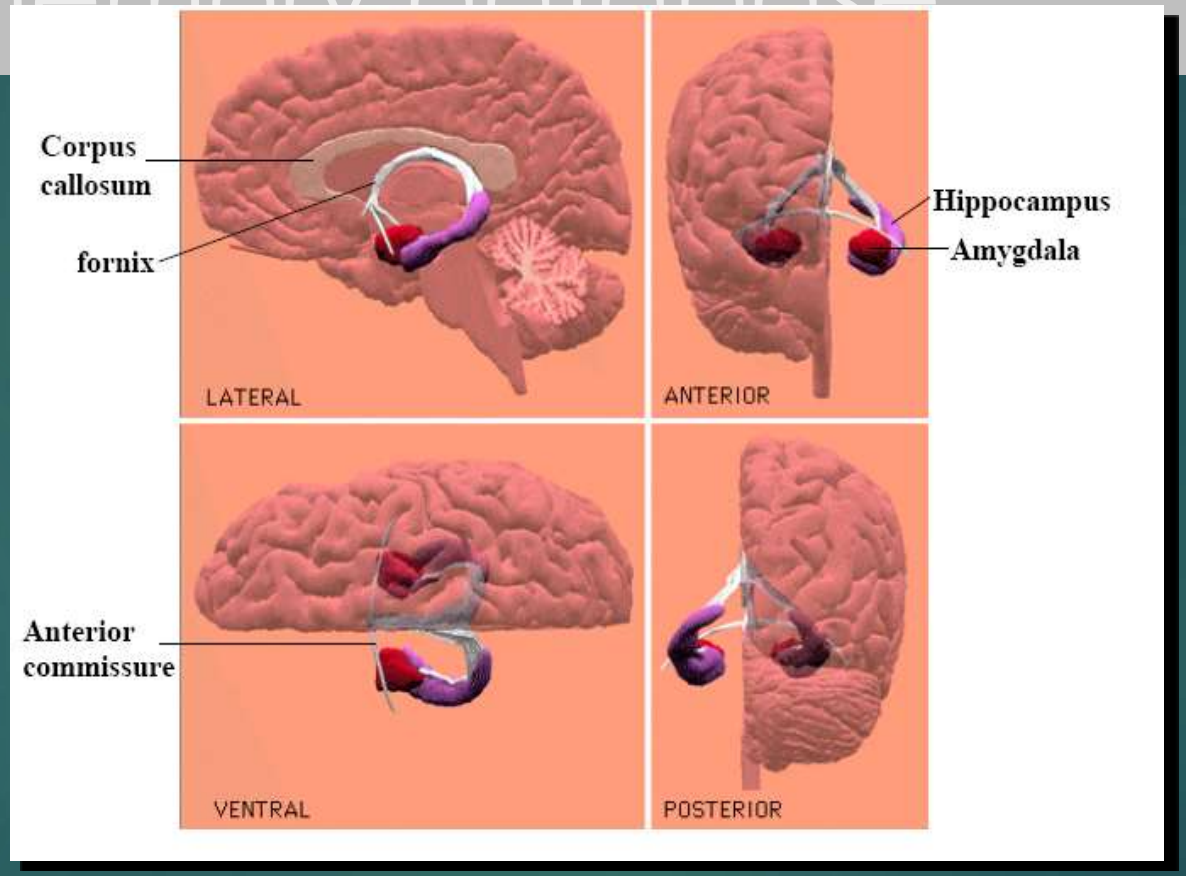
Flashbulb Memory : Nov. 22, 1963

Flashbulb Memory : 1968

Flashbulb Memory : 9/11/2001

Sept 2002: 97% of Americans "can remember exactly where they were or what they were doing the moment they heard about the attacks"

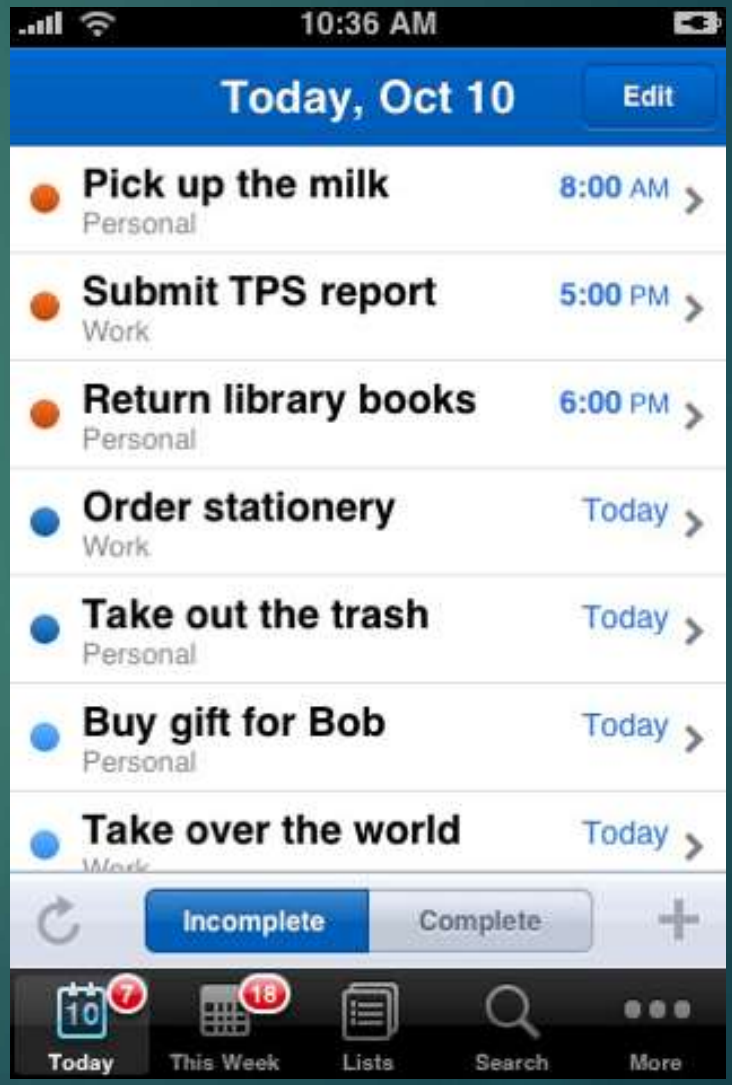
Hippocampus:
Index to memory database



Major site of neurogenesis of stem cells

Prospective Memory

- Remembering to remember
- Intention



Procedural Memory:
Remembering how to…

- Skills, habits, personality
- Playing a musical instrument
- Playing sports
- Riding a bicycle, driving a car
- Reading mirror-reversed word
- Playing Chess, bridge
- Interpersonal Skills, Therapy behavior
- Longest lasting

Coming Up Next: Example of Procedural Memory

- Typewriting skills are procedural memory

Overlearned Memory

Right Hemisphere Language Processes

- Nouns for which image is available (tree)
- Emotional content (love)
- Symbolic or pictorial word form (kanji, logos); pictographic reading
- Distantly related material (journey, life)
- Better at semantic (meaning) than lexical (word or not)
- Metaphor appreciation
- Context processing
- Sarcasm
- Humor
- Prosody

Networks

- Large-scale brain networks: cognitive functioning is the result of *interactions or communication between different brain systems distributed throughout the brain*.
- Different areas of the brain are communicating through a fast-paced synchronized set of brain signals.
- These networks are *preferred neural pathways* for performing a specific set of cognitive or motor behaviors.

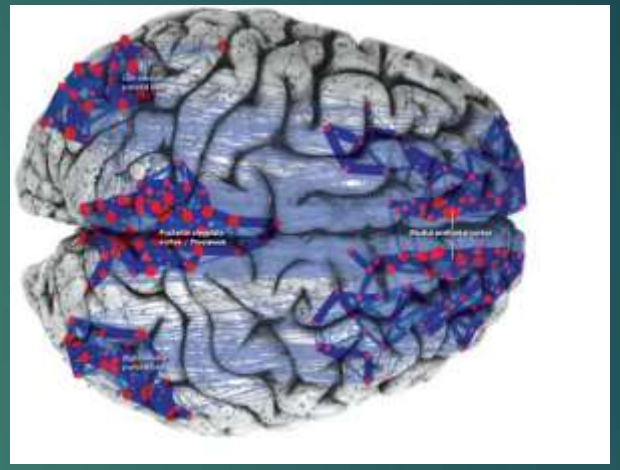
Marcus Raichle: Default Mode Network, 2001

- Marcus Raichle coined "default-mode" in 2001:

  focused thinking increases energy by 5%

- A distributed network that is active when the brain is not doing focused mental tasks.

- Activates during introspection, daydreaming, self-referential thought, and during some kinds of memory retrieval, creativity.

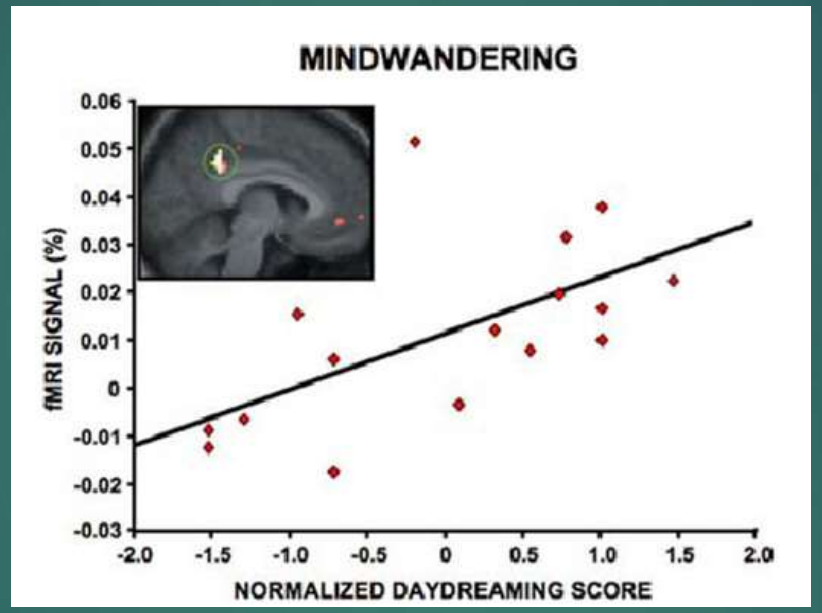


- The network:
  - medial prefrontal cortex,
  - posterior cingular cortex/precuneus,
  - lateral parietal cortex

DMN

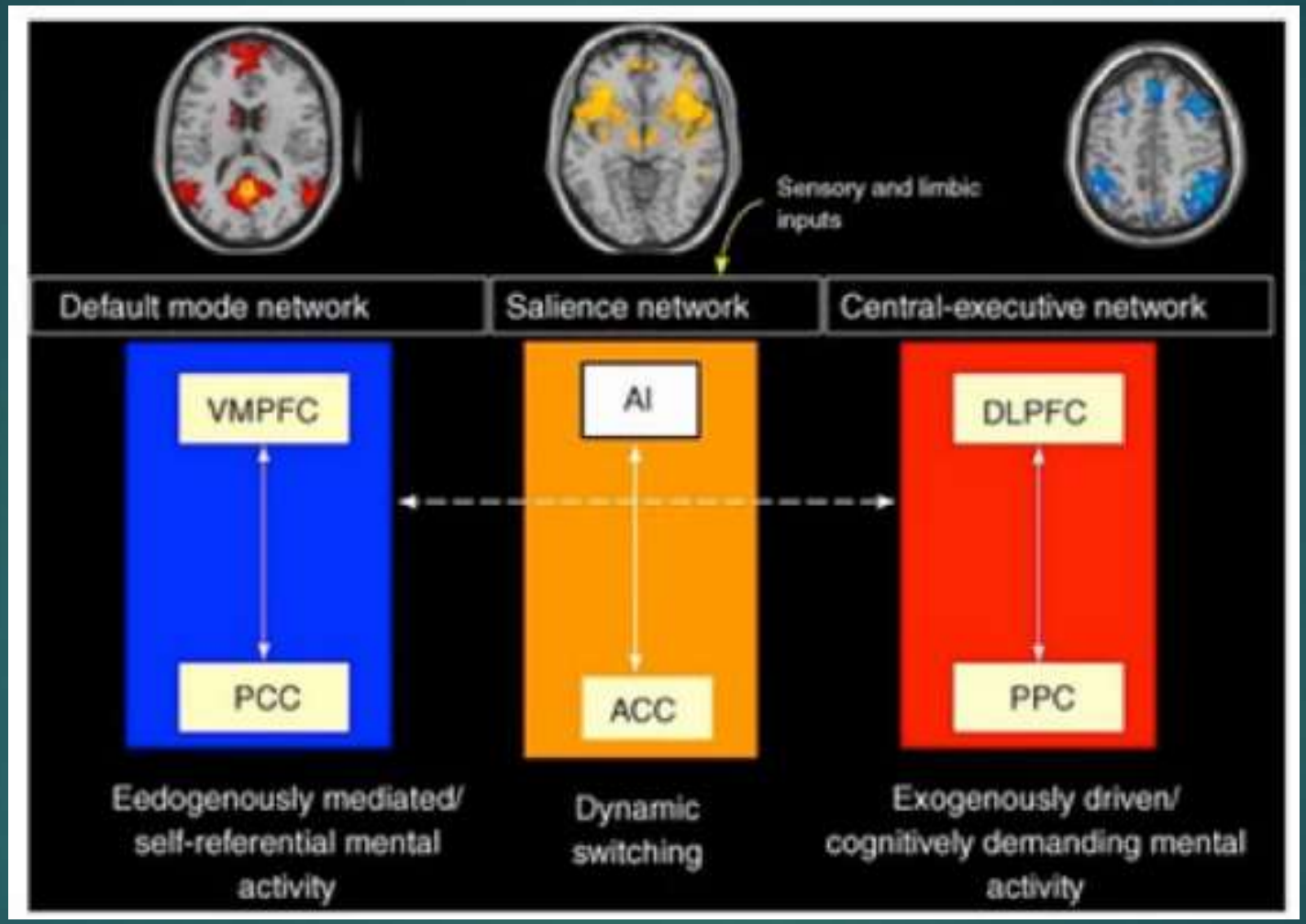
- Alzheimer's atrophied areas exactly match DMN areas
- Autism: Reduced DMN activity
- Schizophrenia: Overactive DMN
- Old age: Impaired control of entering and leaving the DMN.
- Lower connectivity in those with long term trauma experience i.e. child abuse

Frequent mind wandering correlates with most active DMN



- Mind wandering is associated with impaired performance on a wide variety of measures, including WMC, fluid intelligence, and SAT performance
- Mindfulness training reduces DMN activation

Major Networks



- Three major networks: Default, Salience, Executive;
- The central executive network "*is engaged in higher-order cognitive and attentional control*."

Two Opposing Networks: DMN & SN

- Posterior 'Default Mode Network' (Mind wandering; atrophied in AD, but enhanced in bvFTD).
- Anterior 'Salience Network' (Social network; atrophied in bvFTD, but enhanced in AD)
- These networks exhibit an anti-correlated relationship with each other in the healthy brain.

Environmental impact on brain

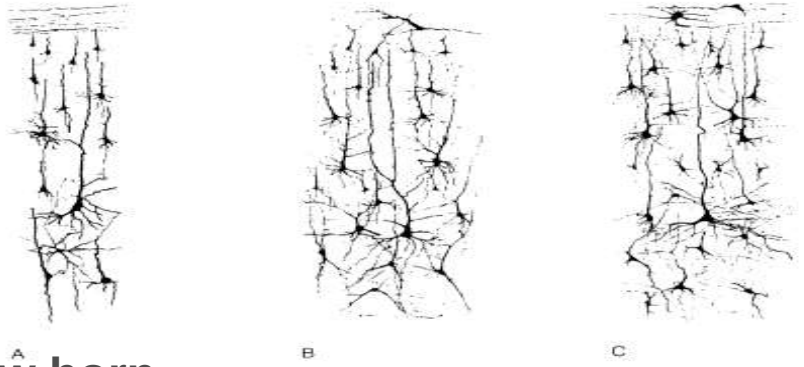
- Hart and Risley (1995) revealed that children in high-income families are exposed to 30 million more words than children from families on welfare.
- Quantity of words heard as a child:
  - Low SES: 600 words spoken to child per day
  - High SES: 2100 words spoken to child per day

- Lower maternal education is linked to poorer processing of auditory information, reading and working memory ability in the adolescent brain

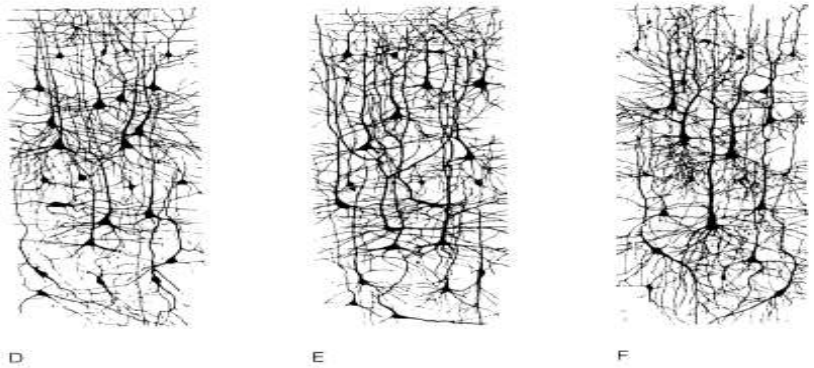
- You are twice as likely to show methylation changes based on family income during early childhood versus economic status as adults.

Brain Development

More Neurons

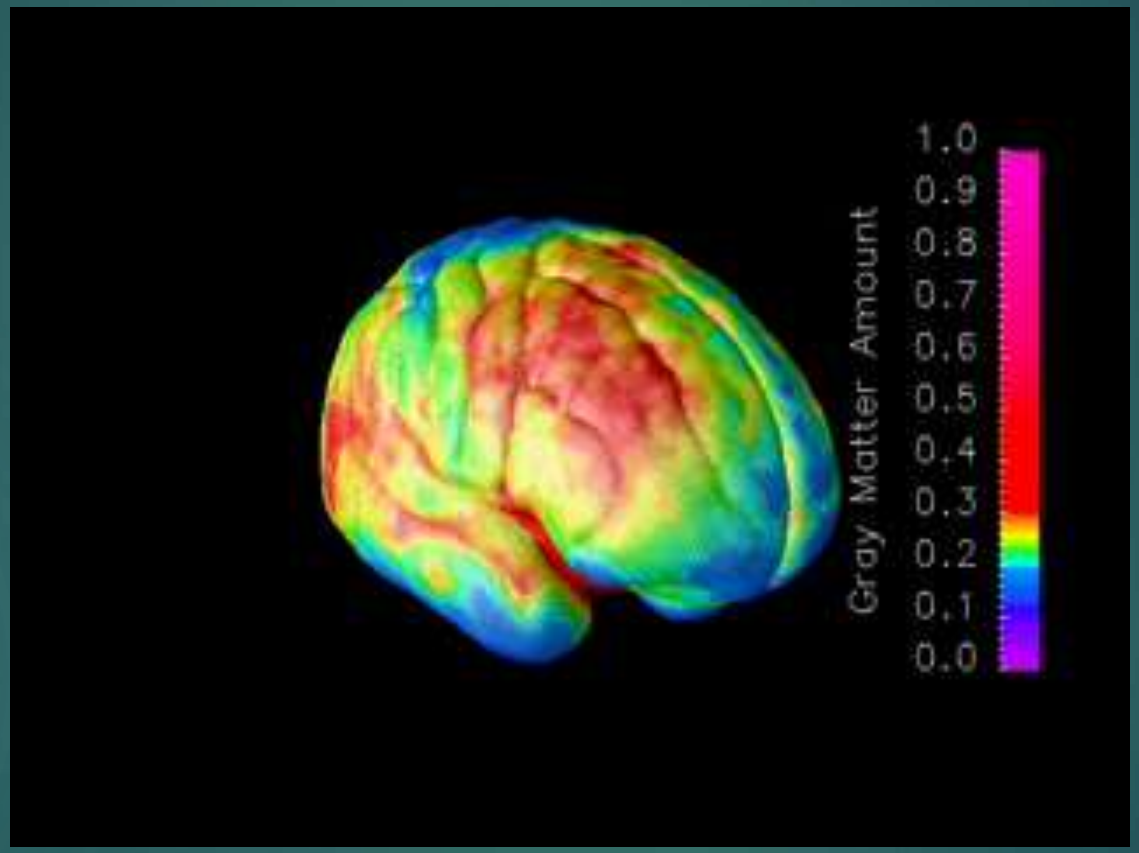


New born



2 years

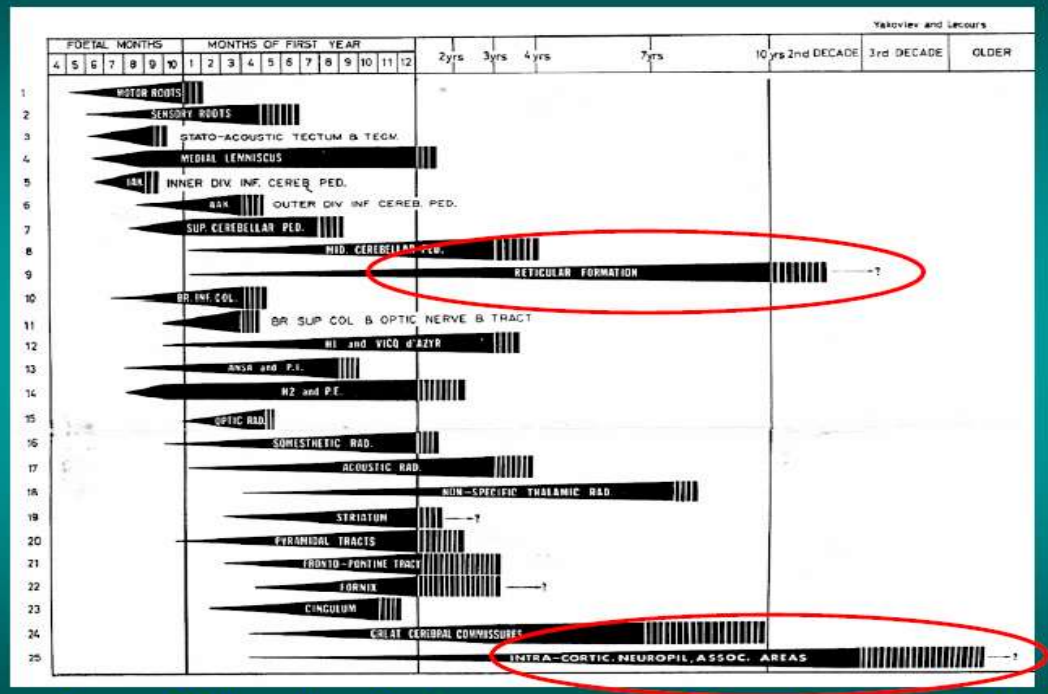
Great Synaptic Pruning: age 5 to 21



Lose 50% of all synaptic connections.

Myelin Sheets on Axons Mature Slowly in Frontal Lobes; may increase into 60s.

Regional Maturation: Myelogenetic Cycles



Taken from Yakovlev & Lecours, The Myelogenetic Cycles

Amount of white matter (axon interconnections) distinguishes us from primates, not size of prefrontal lobes. Creates "greater bandwidth" and processing speed. Einstein had more white matter, not neurons.

Yakovlev & Lecours 1967

White matter matters

- White matter is the subway of the brain:

  long distance speeded connections

- Age 20, the total length of myelinated fibers in males is 176,000 km; at 80, 97,200 km

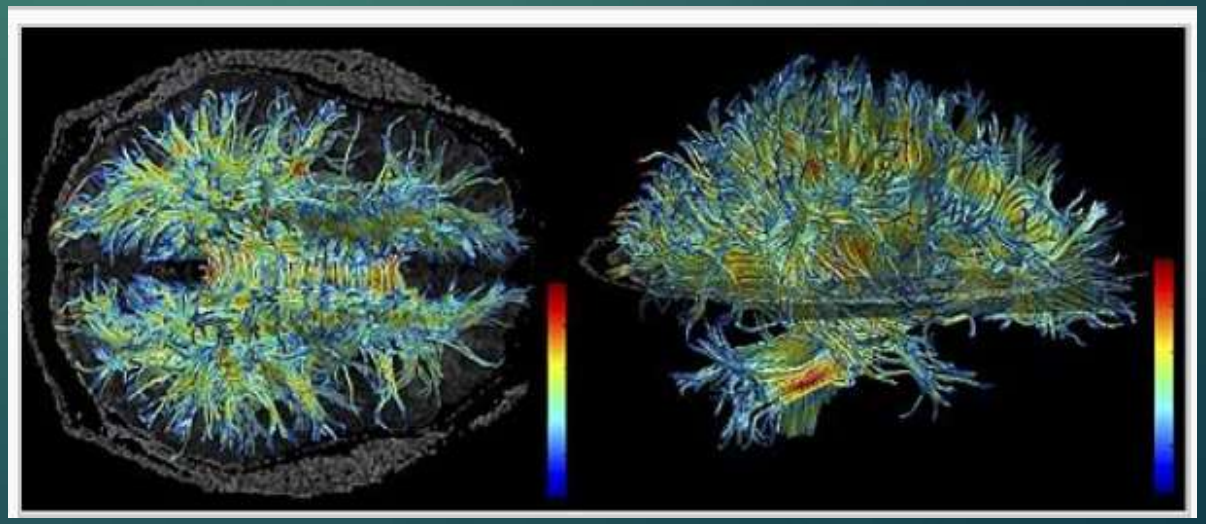
- WM disease targets small blood vessels; Increases risk of having a stroke, vascular dementia or Alzheimer's disease.

- Causes: hypertension, high cholesterol, poorly-managed diabetes, an unhealthy diet, lack of exercise, and smoking.

B P. Vasquez & K K. Zakzanis, , 2014

White Matter

- Metaanalysis of non NCD WM disease (8 deficits in order of effect size):
  - thinking speed (greatest deficit)
  - immediate and delayed memory
  - executive functioning,
  - general functioning,
  - language,
  - working memory
  - visuo-spatial construction.

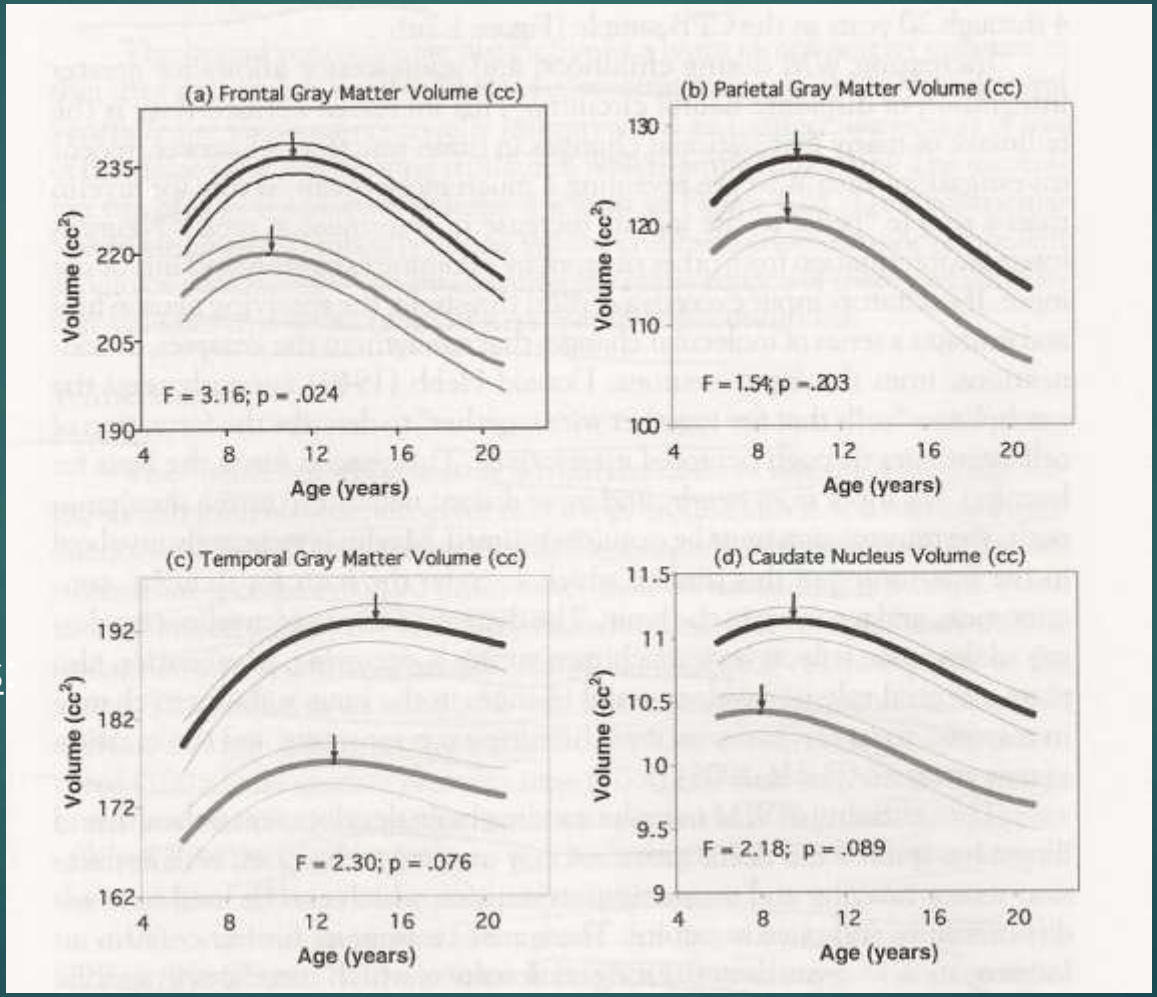


Development: Gray ↓, White ↑

- White matter volume and Corpus Callosum volume increase due to axonal growth and mylenization.
- Gray matter (neurons):
  - increase during preadolescence,
  - peaks in frontal cortex around age 12,
  - and then decreases
- Largest maturational changes between 12-16 and 23-30 is in frontal lobes
- Reduction in gray matter reflects increased myelination (better cognitive processing)

The Great Pruning: Inverted U: GM changes related to synaptic reduction

Frontal Peaks:
9.5 y in girls
10.5 in boys
peaks latest
In prefrontal



Parietal Peaks:
7.5 in girls
9 in boys

Temporal Peaks
10 in girls
11 in boys

Caudate Peaks:
10.5 in girls
14 in boys

R. K. Lenroot, et al. 2007

The Great Pruning: A leaner brain is better

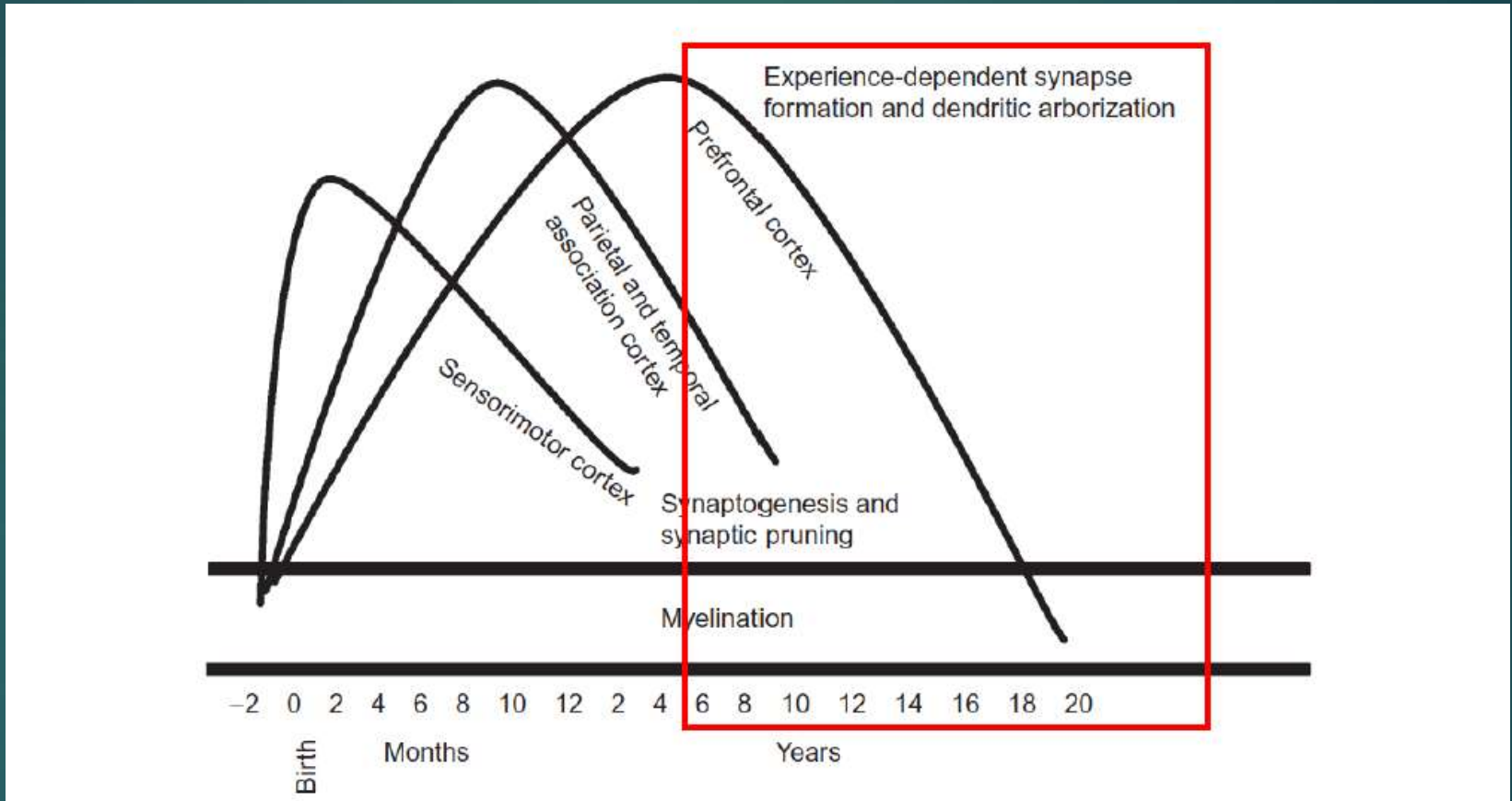
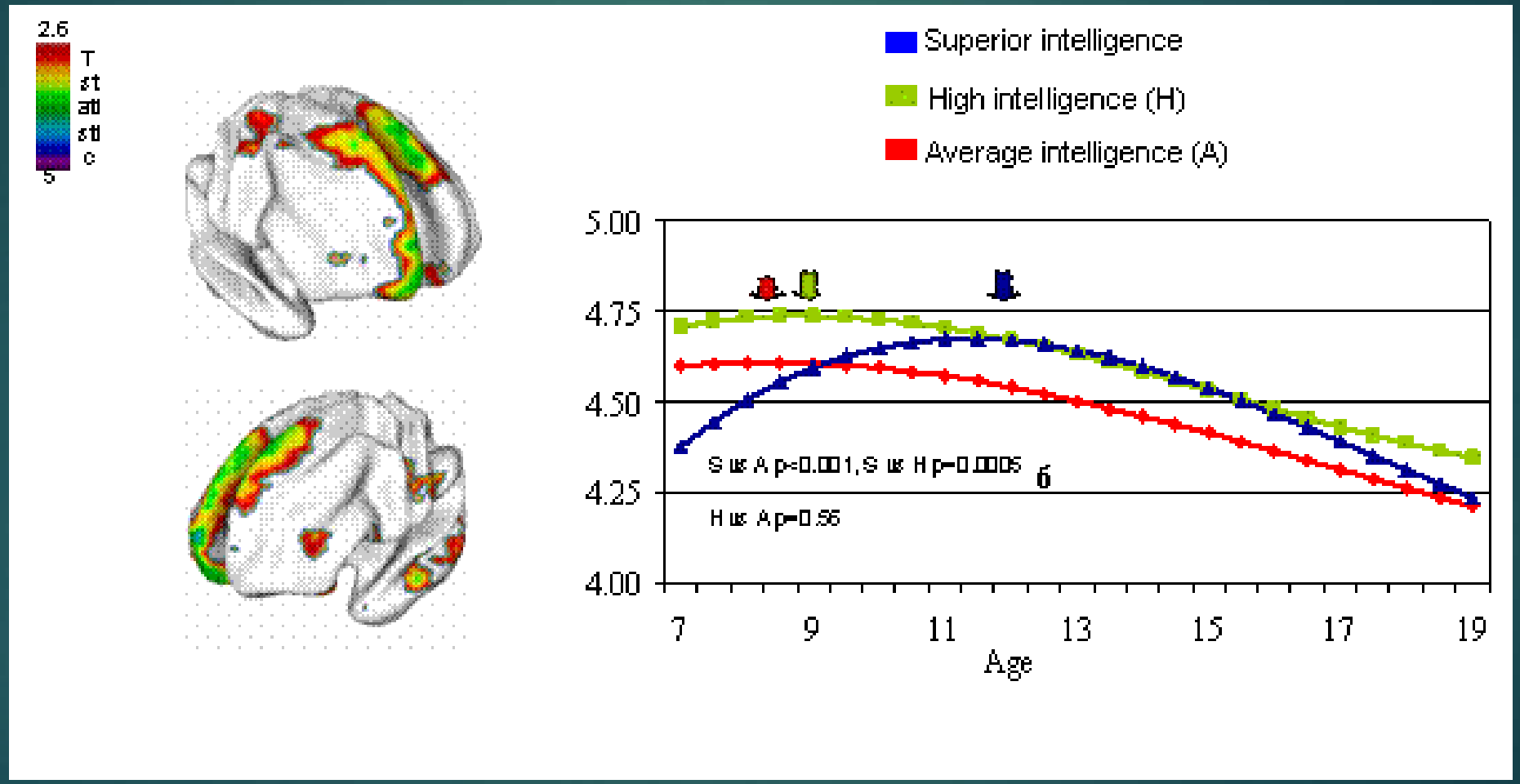


Fig. 2. A depiction of the time course of brain development in human prefrontal cortex, sensorimotor cortex, and parietal and temporal association cortex. Modified from Thompson and Nelson (2001).

Prefrontal last to be pruned

IQ and Brain Development:
N = 11,000 twin pairs
IQs of 100, 120, 140



Superior IQ peaks the latest, before pruning

Brain Maturation ages 5-20

- Pruning away of synapses to neurons that are not used
- Increase in amount of white matter relative to grey neurons
- Increase in myelination of axons, which then can transfer information 1000s of times faster
- This improved connectivity of fewer more specialized neurons creates behavioral maturity
- Crucial decision making frontal lobes are the last to mature
- Females are 2 years ahead in this maturation process.
- High variability: can mature at 13 or 35

Adolescent Brains Have a Missing Part

Why do most 16-year-olds drive like they're missing a part of their brain?

BECAUSE THEY ARE.

Even bright, mature teenagers sometimes do things that are "stupid."

But when that happens, it's not really their fault. It's because their brain hasn't finished developing. The underdeveloped area is called the dorsal lateral prefrontal cortex. It plays a critical role in decision making, problem solving and understanding future consequences of today's actions. Problem is, it won't be fully mature until they're into their 20s.

It's one reason 16-year-old drivers have crash rates three times higher than 17-year-olds and five times higher than 18-year-olds. Is there a way for teens to get their driving experience more safely — giving their brains time to mature as completely as their bodies? **Allstate thinks so.**

STRENGTHEN GRADUATED DRIVER LICENSING (GDL) LAWS.
GDL laws put limitations on teen driving so kids can gain experience safely. Since North Carolina implemented one of the most comprehensive GDL laws in the country, it has seen a 25% decline in crashes involving 16-year-olds.

HAVE THE DRIVING TALK.
75% of teens surveyed said their parents would be the best influence in getting them to drive more safely. The Allstate Parent-Teen Driving Contract can help start the conversation. **Contact an Allstate Agent to get a free copy or visit Allstate.com/teen for the interactive contract.**

Let's help our teenagers not miss out on tomorrow just because they have something missing today.

It's time to make the world a safer place to drive. That's Allstate's Stand.

Allstate. You're in good hands.

Adolescent sex differences in brain

- Robust sex differences in development, with females peaking earlier (related to puberty)
- Rate of cortical thinning more rapid in males; longer for maturity of frontal lobes (testosterone related)
- Amygdala volume increased only in males (higher androgen receptors in Amygdala)
- Hippocampus volume increased only in females (higher number of estrogen receptors in hippocampus)

J. Giedd, et al., 2011; Clark, MacLusky, & Goldman-Rakic, 1988; Morse, Scheff, & DeKosky, 1986

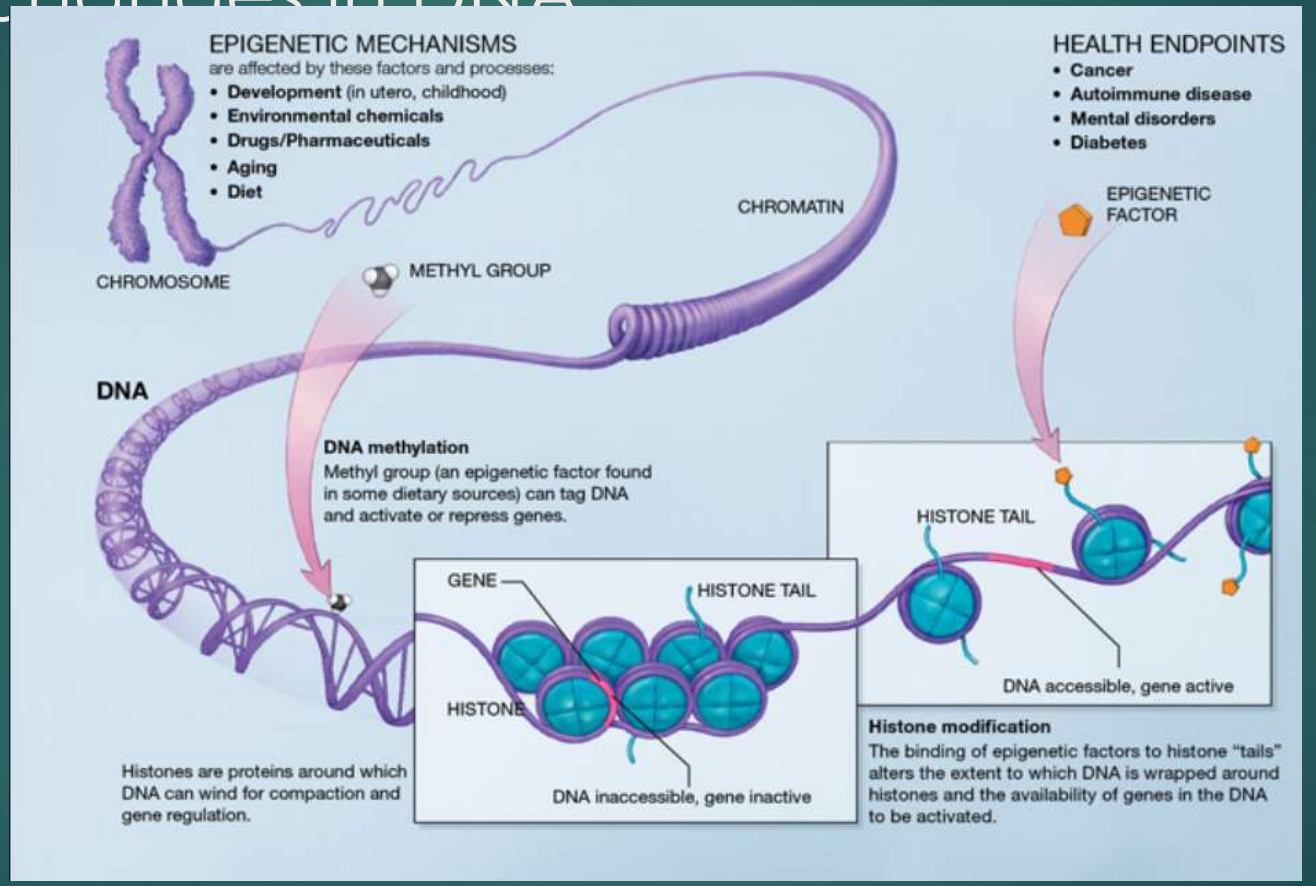
Major Adolescent Brain Changes

- Major synaptic pruning (loss of 50% of synaptic connections in the brain)
- Maturation of frontal and limbic regions
- Increase in mylenization, particularly in frontal region: increase in impulse control
  - In boys, self report of behavioral impulse control
  - In girls, increase in ability to inhibit incorrect answers
- Dopamine distribution changes (risk taking↑↑, reward seeking)

What is cause?

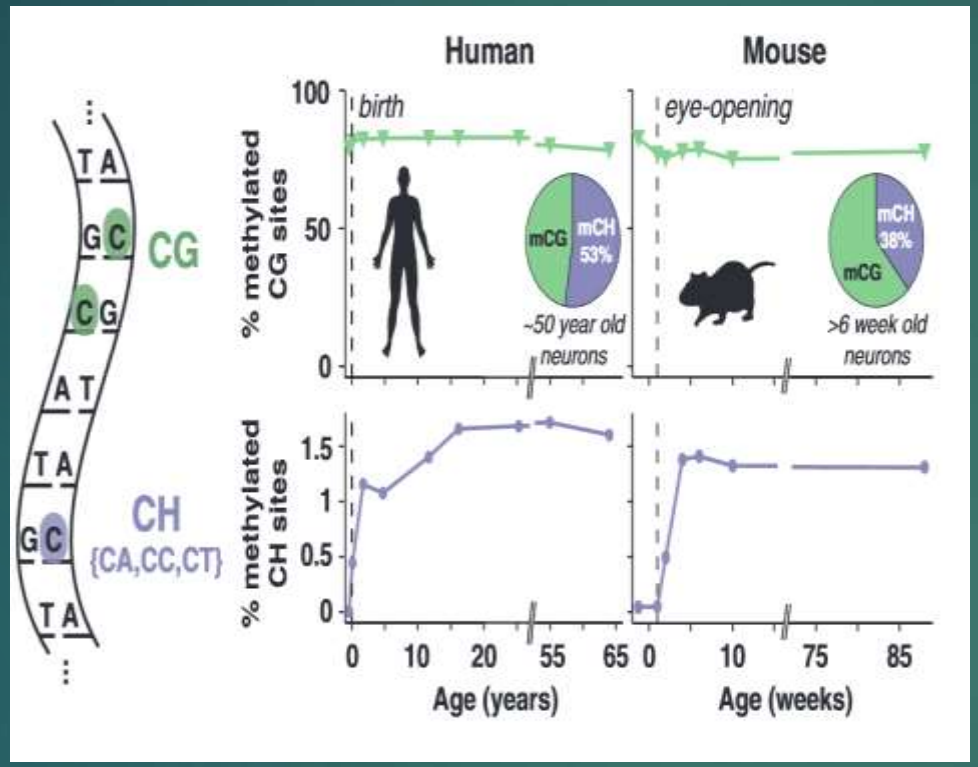
- Mother mouse and her son — sit on two bar stools, lapping gin from two thimbles.
- The mother mouse looks up and says, “Hey, geniuses, tell me how my son got into this sorry state.”
- “Bad inheritance,” says Darwin.
- “Bad mothering,” says Freud.
- But maybe its epigenetics! Experience trumps genes.

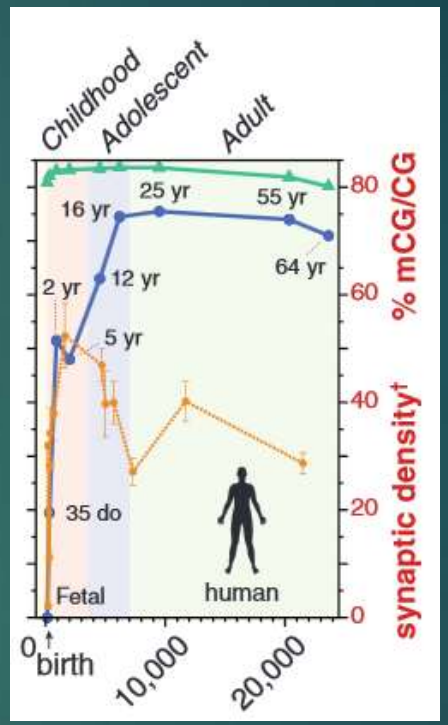
Epigenetics:
heritable changes in gene activity that are *not* caused by changes in DNA



Methyl tags on genes & histone modification control gene expression

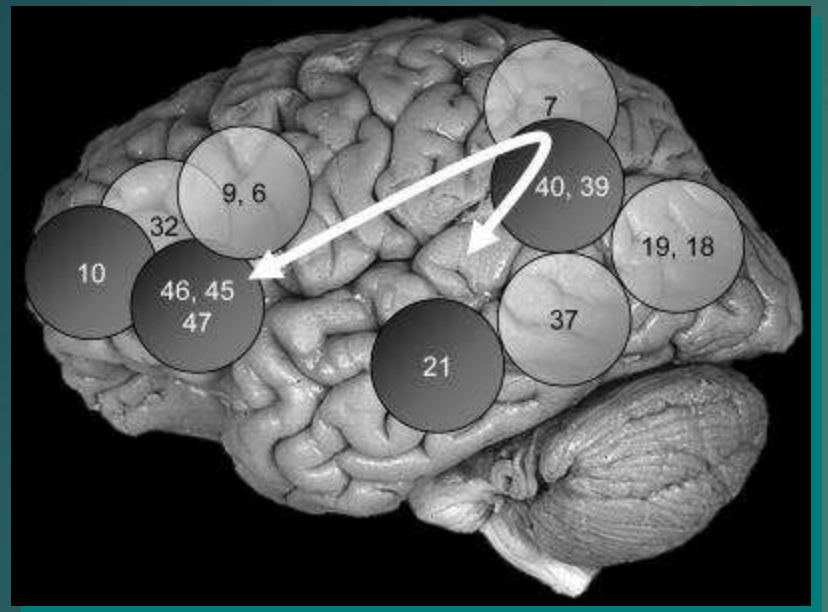
Epigenetics and synatogenesis





- The DNA methylation landscape of human and mouse neurons is dynamically reconfigured through development.
- Neurons accumulate substantial mCH during the early years of life, coinciding with the period of synaptogenesis and brain maturation. (2nd = frontal lobe)

P-FIT: Parieto-Frontal Integration Theory: Biological basis of IQ



Dark Grey: Left Hem

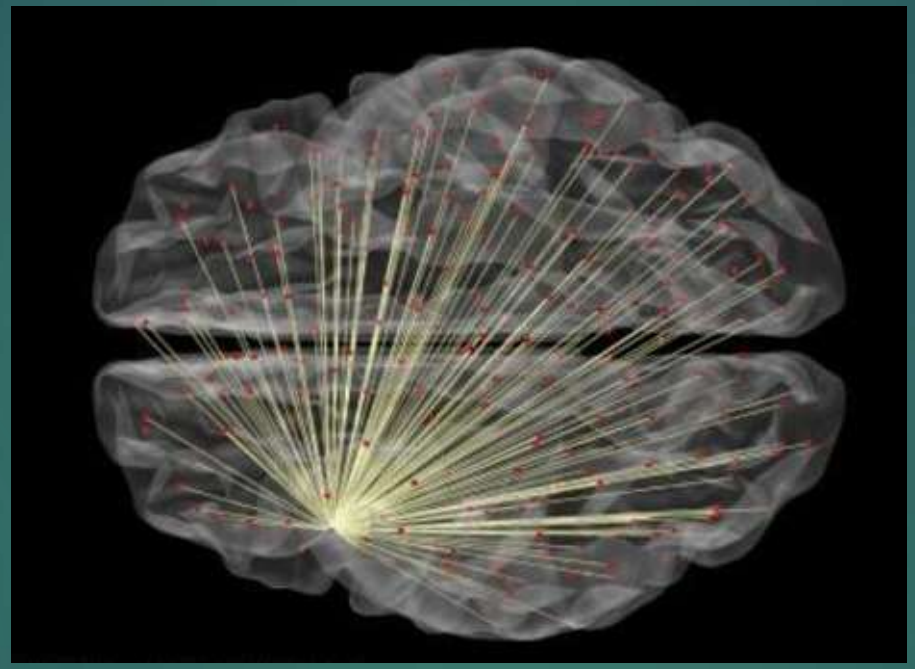
Light Grey: Right Hem

Arcuate Fasiculus: connector

The Parieto-Frontal Integration Theory (P-FIT) identifies a brain network related to intelligence, one that primarily involves areas in the frontal and the parietal lobes:

Jung, Haeir, Colom et al.. (Colom et al., 2009; Jung & Haier, 2007; Deary et al. (2010)

10% of IQ:
Connectivity to Left DLPFC

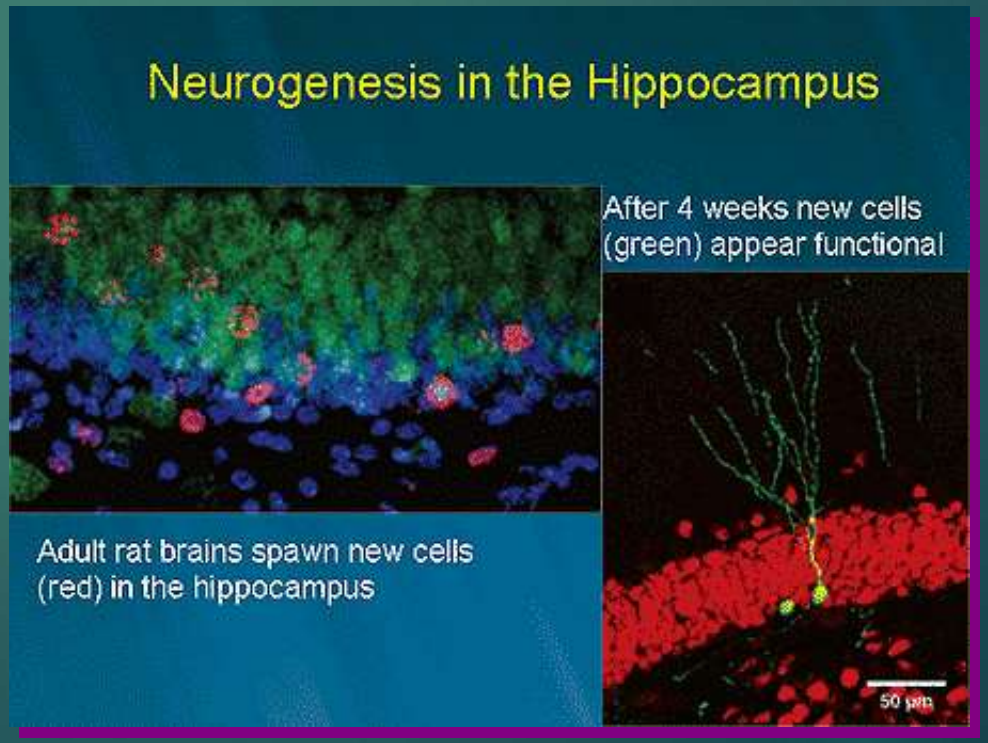


Goal monitor: 10 % of individual differences in IQ can be explained by the strength
of neural pathways connecting the left lateral prefrontal cortex to the rest of the brain.

Strong predictor of both fluid intelligence and cognitive control abilities.

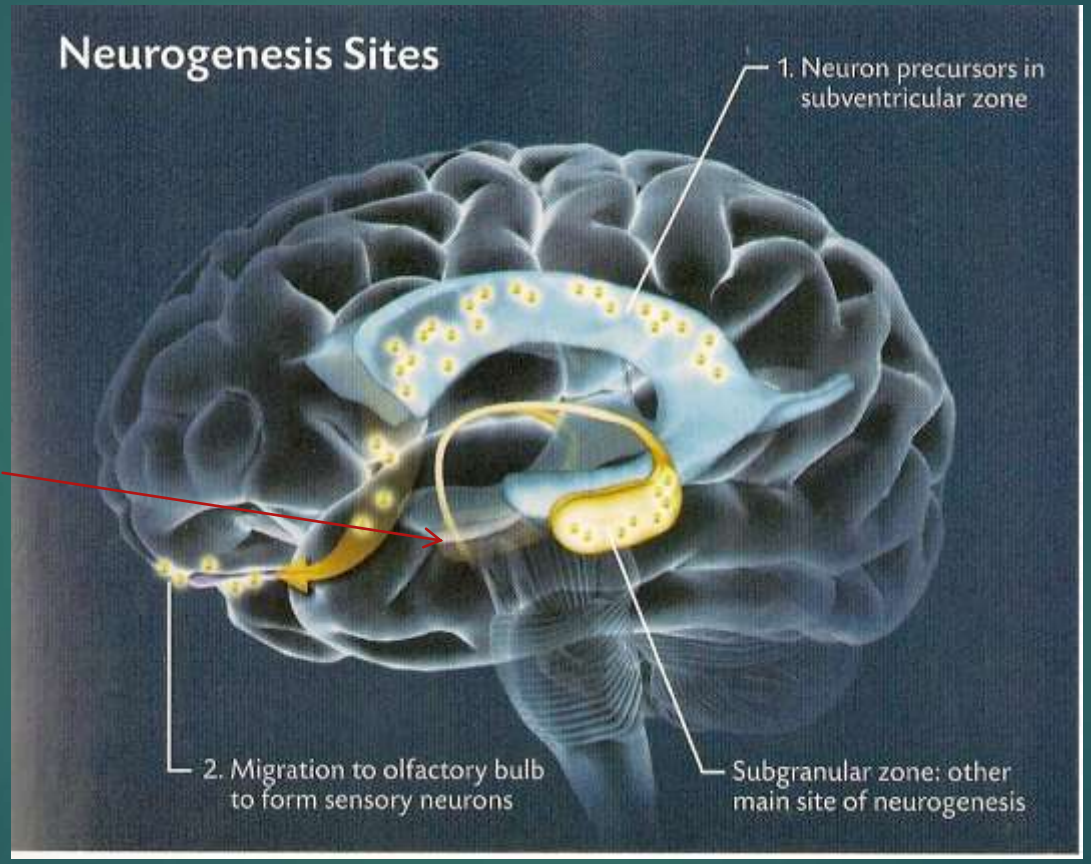
Neurogenesis

- Neurogenesis: growth of new neurons in the adult brain; Stem cells become new adult neurons



Neurogenesis: 3 major sites

Interneurons in Striatum



700 new neurons per day, enough to replace all the neurons in the dentate gyrus of the hippocampus, over a lifetime.

Function of Neurogenesis

- Most stem cells die. Those involved in new learning survive

- Decreased by:
  - Stress (Cortisol)
  - enrichment
  - Depression
  - Aging
  - Alzheimer's

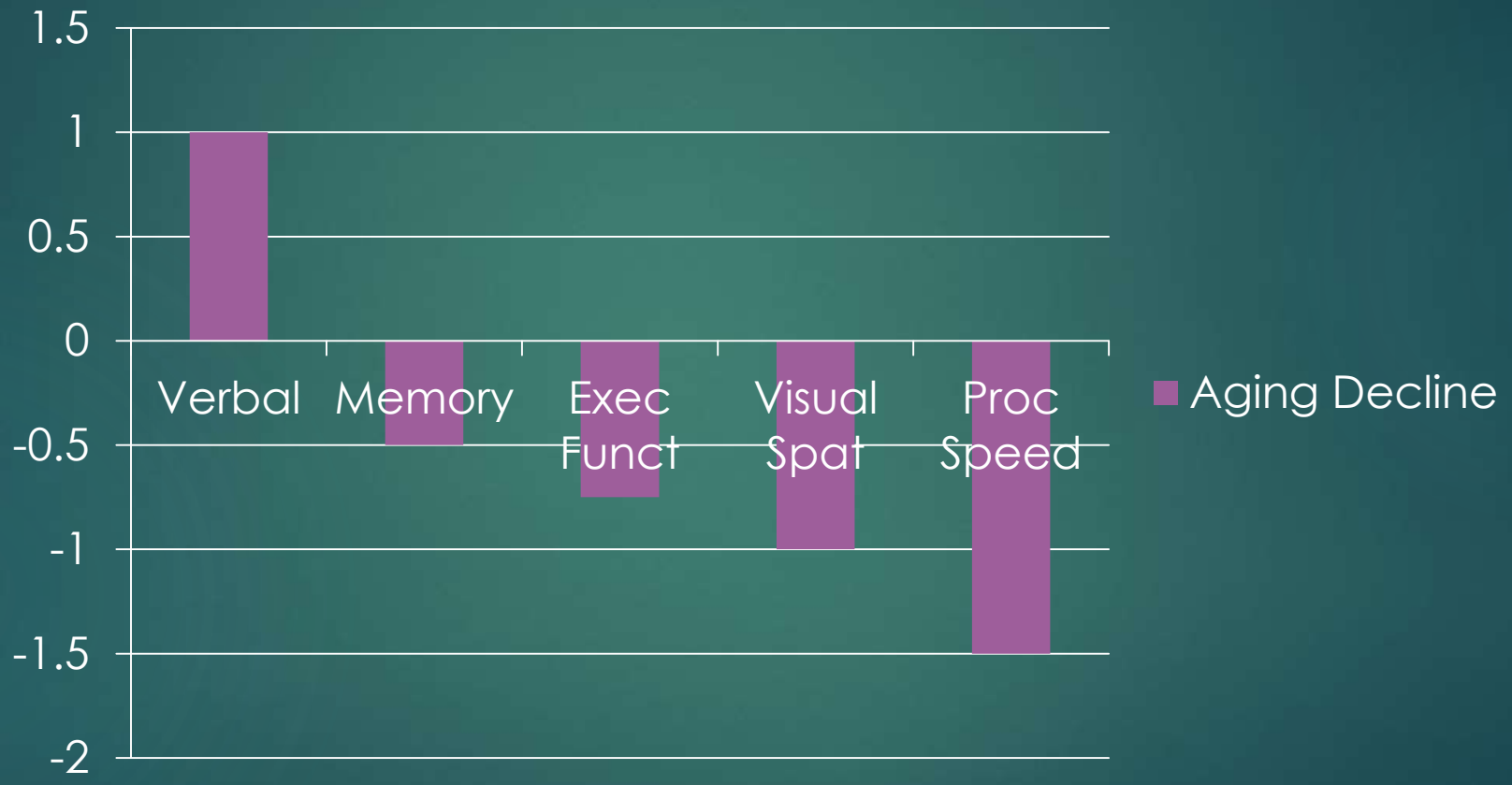
- Increased by:
  - Environmental
  - Exercise
  - Antidepressants
  - Alzheimer's
  - Seizures

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 = ½ s.d. decrease ↓
- Spatial Ability = 1 s.d. decrease ↓ ↓
- Perceptual speed = 1 ½ s.d. decrease ↓ ↓ ↓

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

2013 Lenovo W5307
Intel Core i72. @ 2.70GHz
2400 x faster

Cognitive Reserve

- 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
  - Better cardiovascular function
- Cost: Once cognitive decline begins, goes faster

5 types of brains

- Normal brain/Normal experience → OK
- Developmentally abnormal brain → Down's, ASD, Schiz, PDs, ASPD
- Normal brain, abnormal experience changes brain→ ACES, PTSD
- Normal brain, acquired brain damage →TBI
- Normal brain, acquired neurodegeneration →NCDs

Hardware vs. Software

- Brain = Your hardware
- Experience = Your software
- Experience via neuroplasticity & epigenetics changes your hardware.

Neuroplasticity

- Brain' capacity to rewire itself due to experience
- Experience produces constant neurological changes: neuroplasticity (new synapses, new dendrites)
- Some areas don't rewire
- There are critical periods for experiential exposure in some areas i.e. language, Romanian infants
- Areas unused from birth are rewired for other use i.e. born deaf (Heschel's area rewired for vision & touch)
- Phantom limb

Neuroplasticity:

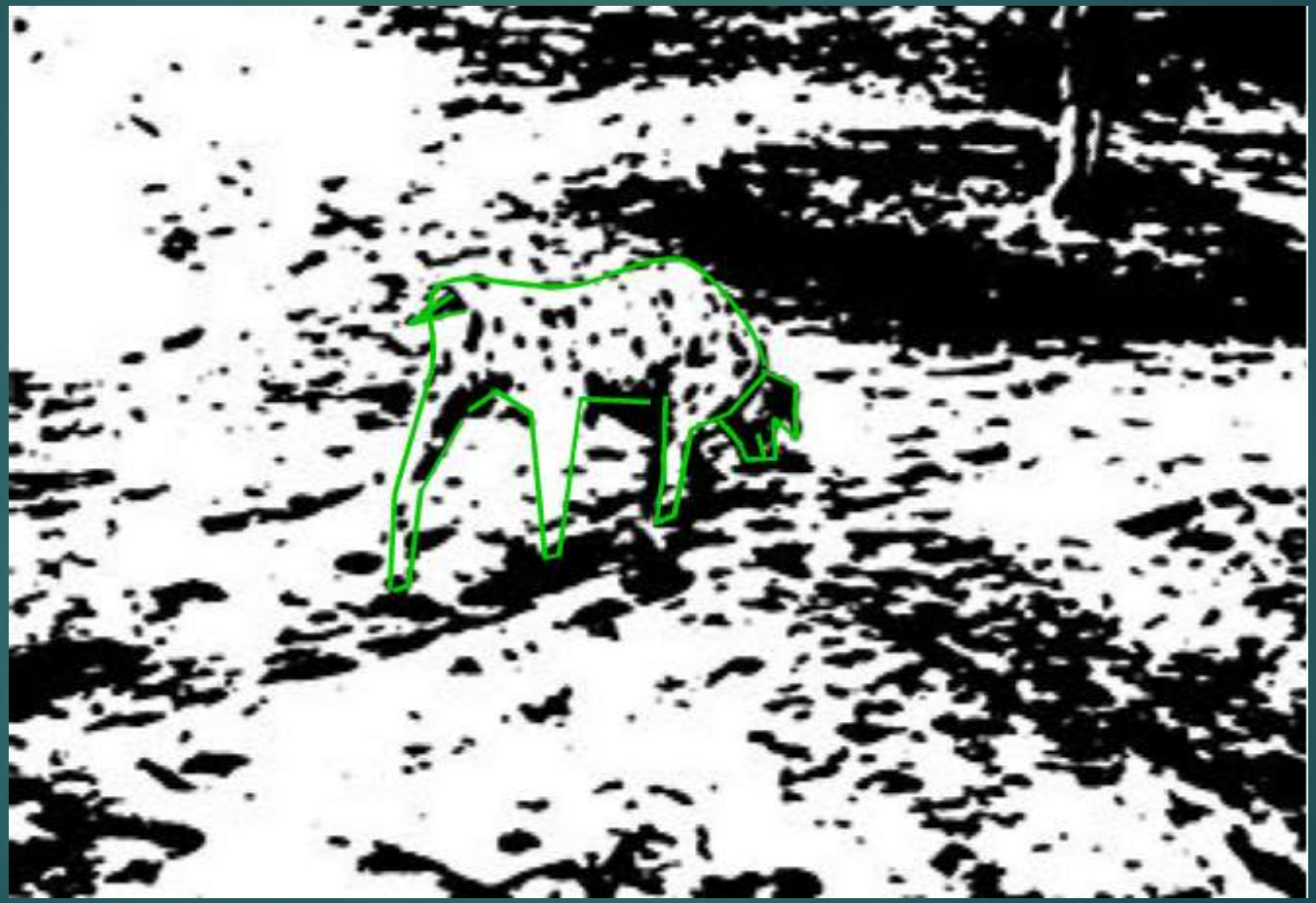
We all have the power to change one another's brain.

On the next slide I will forever change your brain.

R.C. James's Camouflaged Dalmatian

Your brain (perception and memory processes) is permanently changed by each experience

Dalmatian Revealed



Adverse Childhood Experiences: Neurobiology of Abuse

Negative Neuroplasticity

A Traumatized Child Grows Up:
Stress response becomes social culture

• How social interaction becomes neurological:

•A girl grows up in a household where there is domestic violence, which triggers her fight or flight stress response, which affects the way the hormone receptors in her brain develop, and her stress-regulation system goes off track.

• She tends to overreact to confrontation or she doesn’t recognize risky situations and feels comfortable only around a lot of drama.

A Traumatized Child Grows Up 2

- She ends up with an abusive partner, who beats her kids.
- Her son goes to school where 10 of 30 kids come from same background, creating a classroom culture of fighting.
- When they are teenagers, they behave violently, and beat their kids.
- It becomes the cultural norm. The circle starts again

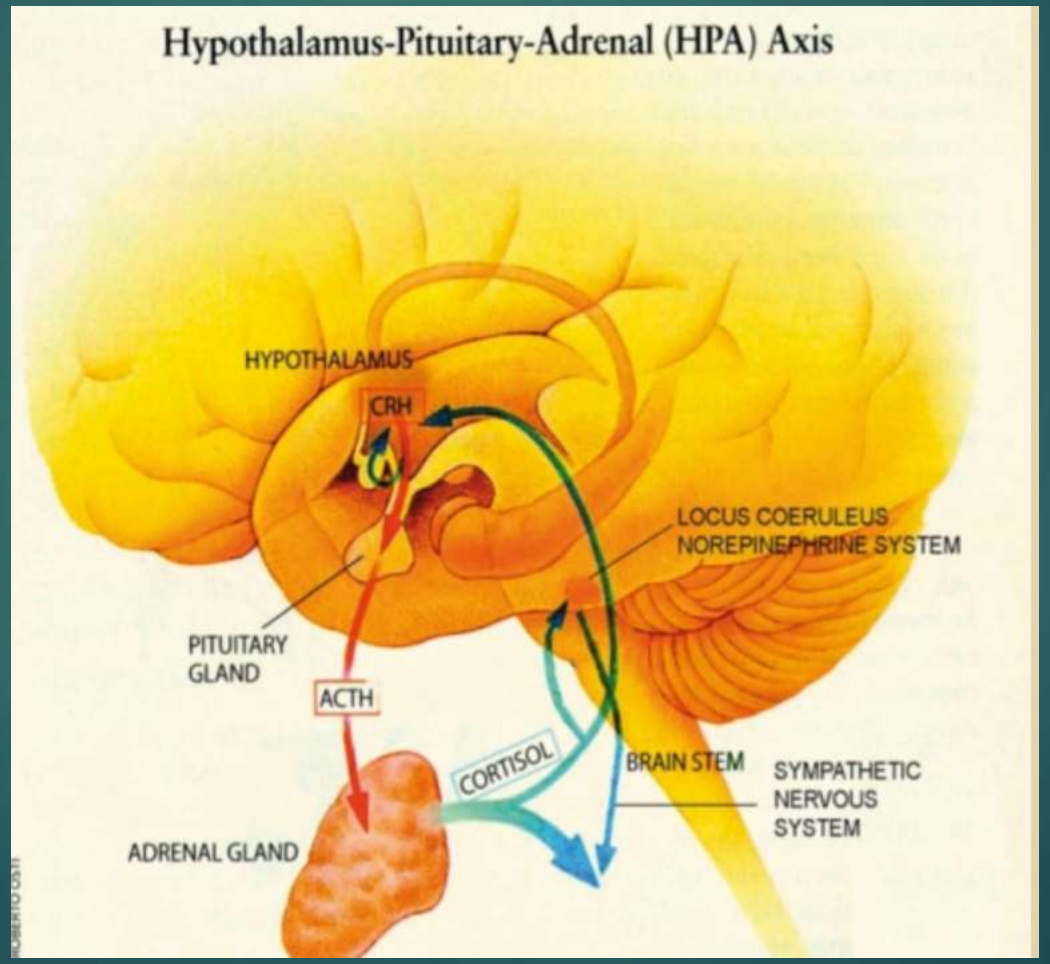
Traumagenic neurodevelopmental model

- Traumagenic neurodevelopmental model:
  - heightened sensitivity to stress
  - originates in neurodevelopmental changes to the brain
  - caused by trauma in the early years.

- Childhood adversity plays a causal role in most mental health problems
  - in childhood (e.g., conduct disorder, ADHD and oppositional defiant disorder)
  - in adulthood (e.g., depression, anxiety disorders, eating disorders, sexual dysfunction, personality disorder, dissociative disorder, PTSD and substance misuse, psychosis).

J. Read, et al., 2014

Hypothalamic-Pituitary-Adrenal (HPA) Axis: Stress Response



Trauma

- Heightened responsivity to stressors:
- Exposure to stressful life events, including childhood adversities, increases emotional reactivity to everyday experiences

Neurological Consequences of trauma

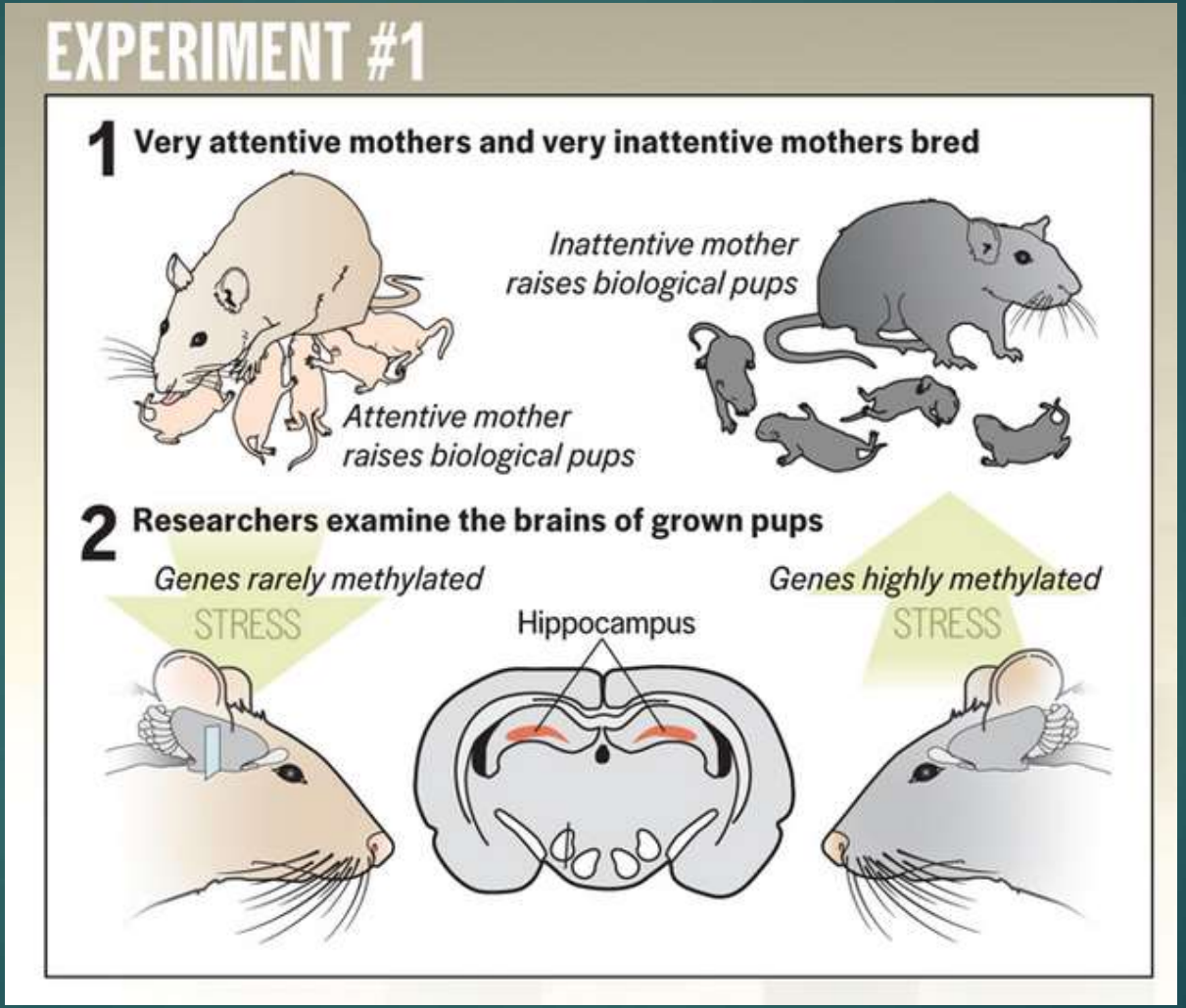
- HPA dysregulation: Severe early social adversity can induce a cascade of long-term disturbances in the HPA axis:
- **O**ver-activity of the hypothalamic–adrenal–pituitary (HPA) axis→→
- Causes dopamine, serotonin and norepinephrine abnormalities →→
- Creates structural differences such as hippocampal damage, cerebral atrophy, ventricular enlargements and reversed cerebral asymmetry.

HPA & Epigenetics: Mother Nurturing

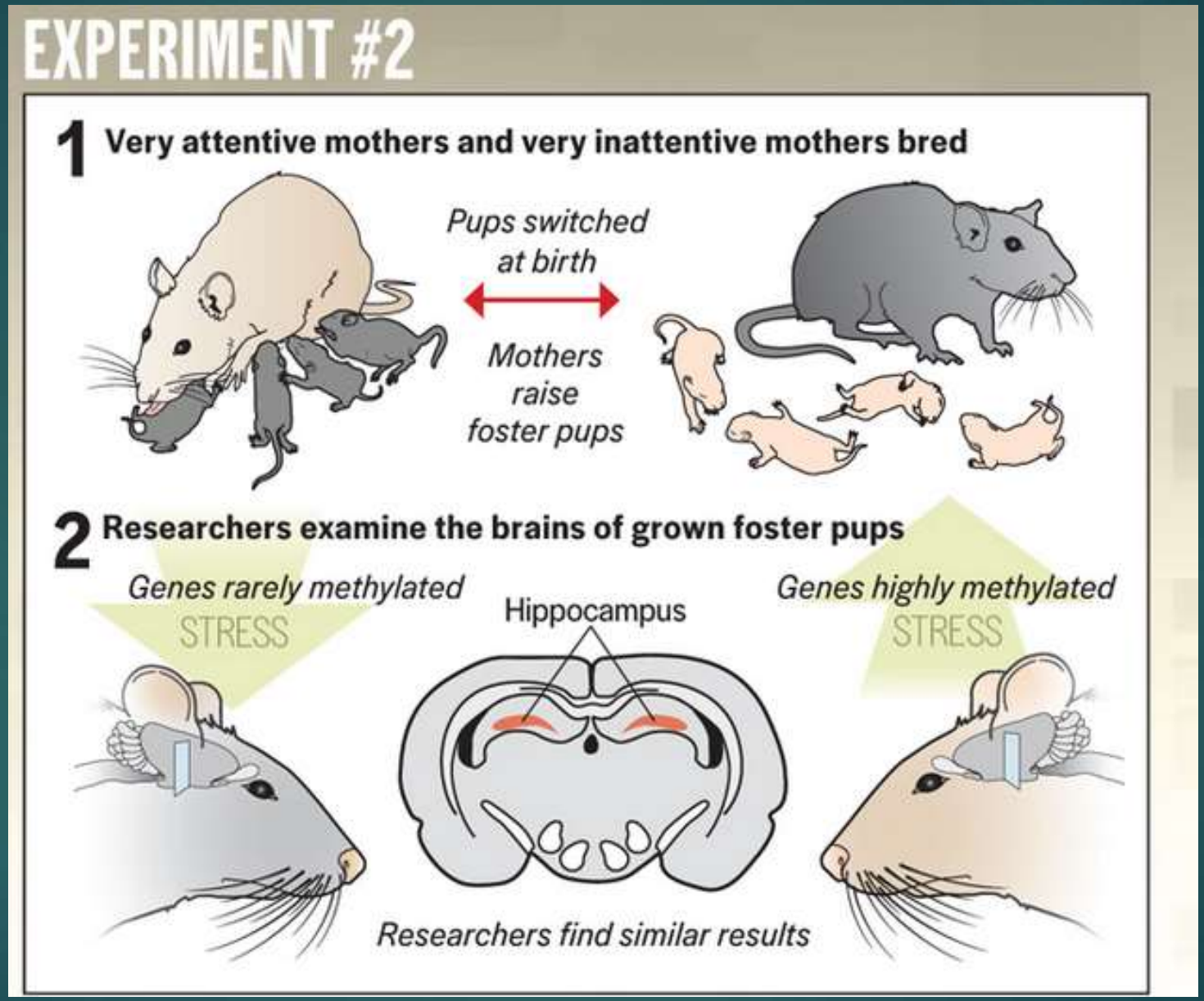
- HPA functions through epigenetic programming of glucocorticoid receptor expression:
- More stress, more methylation tags on genes
- Early adversity alters chemistry of DNA in the brain through methylation:
  - methylation disables stress hormone receptor genes, preventing the brain from properly regulating its response to stress.
  - Mouse mother licking pup; later calmer pup (genes for the glucocorticoid receptors rarely methylated; low levels of glucocorticoid receptors in their hippocampus)
- Variations in maternal care stably influence DNA methylation, gene expression, and neural function in the offspring.

Michael Meaney

Epigenetic programming by maternal behavior

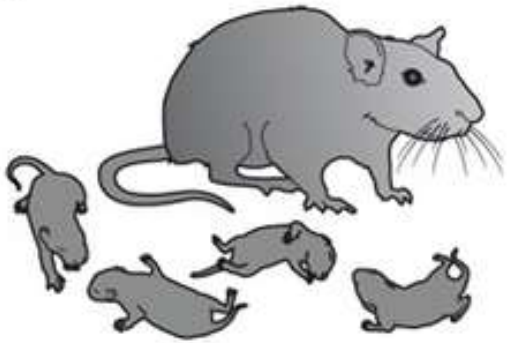


Meaney & Szyf, 1997

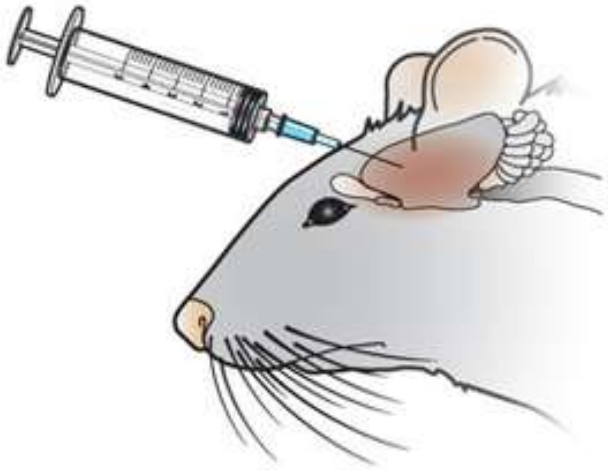

EXPERIMENT #2
1 Very attentive mothers and very inattentive mothers bred
Pups switched at birth
Mothers raise foster pups
2 Researchers examine the brains of grown foster pups
Genes rarely methylated
STRESS
Hippocampus
Genes highly methylated
STRESS
Researchers find similar results

EXPERIMENT #3

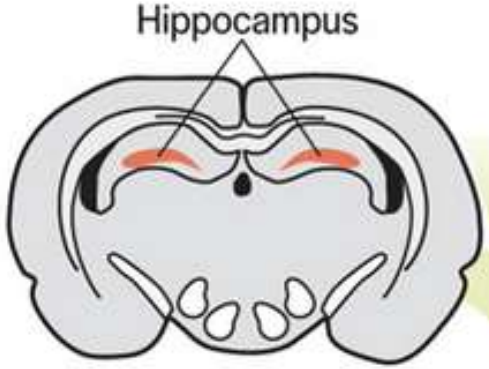
1 **Inattentive mothers bred**



Inattentive mother raises biological pups



2 **Brains of "damaged" pups treated with trichostatin A, a drug that removes methyl groups**



3 **Epigenetic changes disappear**

STRESS

Genes rarely methylated

Stress Decreases Frontal Lobe Volume: less ability to put the brakes on

- Changes following severe stress:
  - dendritic retraction and debranching,
  - reduced volume in vmPFC and mPFC and ACC.

- Gray matter volume losses in the frontal lobes in adults exposed to child adversities/ACEs:
  - dorsolateral and medial prefrontal
  - orbitofrontal regions
  - anterior cingulate

BDNF: You want more

- Brain-derived neurotrophic factor (BDNF) is critical for axonal growth, neuronal survival, and synaptic plasticity, and its levels are affected by stress and cortisol.
- Antidepressant drugs and electroconvulsive therapy increase BDNF levels
- BDNF is the link between:
  - stress,
  - neurogenesis,
  - and hippocampal atrophy in depression.
- Physical exercise increases BDNF

Stress & BDNF

- Severe stress
  - reduces the expression of BDNF
  - excessive glucocorticoids interfere with BDNF signaling.

- Mechanism mediating early-life stress and BDNF reductions in rat studies includes:
  - reduced *BDNF* gene activity, observed in the prefrontal cortex, hippocampus and amygdala,
  - caused by changed epigenetic marking

Neurobiology of Childhood Abuse

- Long term effects of early trauma/stress
- Effects Limbic circuits:
  - Amygdala = increased emotional reactivity (50 ms vs. 600ms for csness = 12 x faster),
  - Hippocampus = higher cortisol levels, stress sensitization, decreased neurogenesis
- Chronic Stress =
  - Smaller frontal regions
  - smaller hippocampus,
  - more reactive amygdala (GABA↓= less inhibition)
  - greater R Hemisphere activation

Trauma and Brain Response

- Evocation of traumatic memory:
  - Right Hemisphere increased activation:
    - limbic
    - amygdala
    - visual centers
  - Decreased Left Broca's area (translating personal experiences into communicable language)

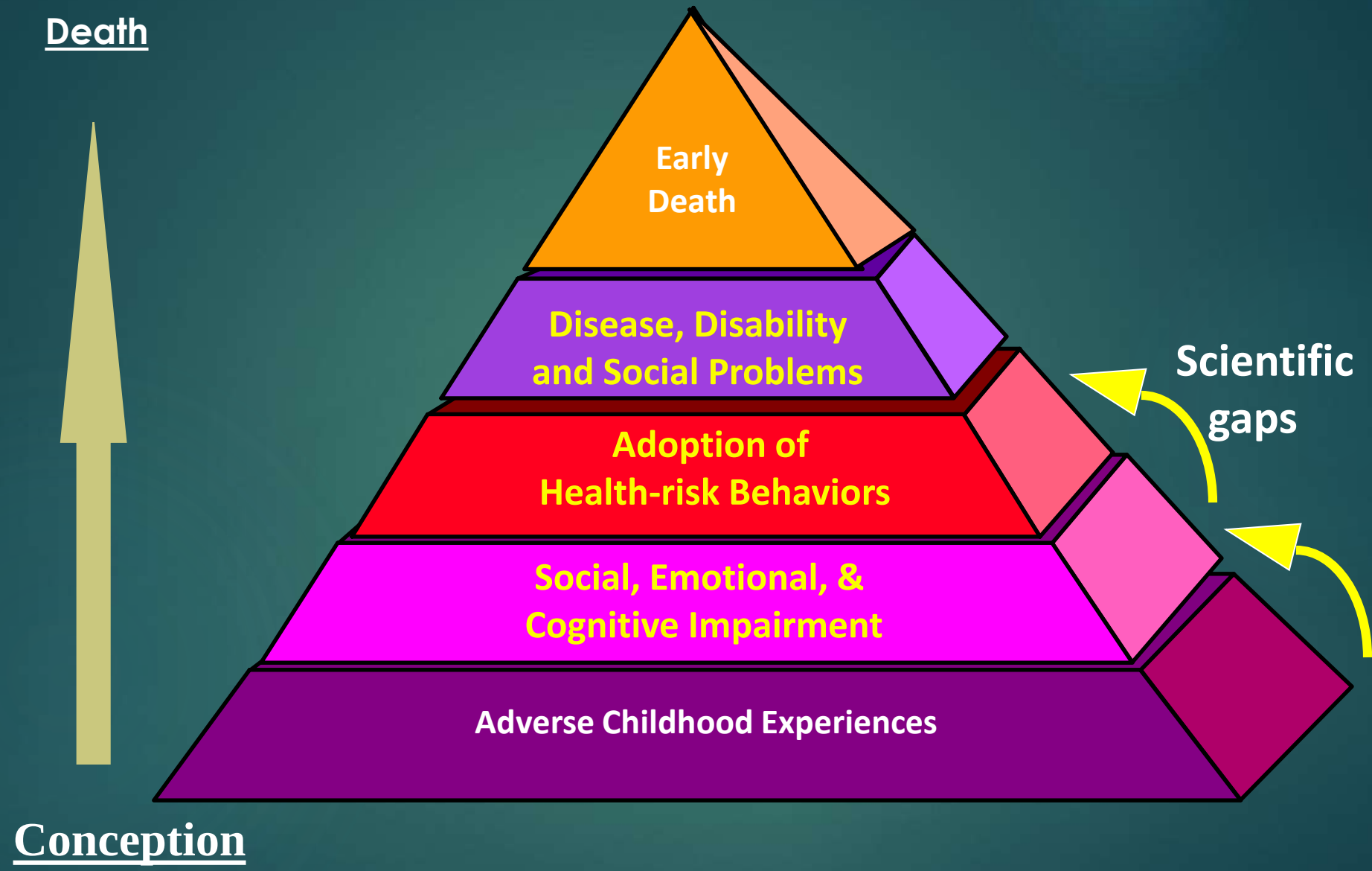
Rauch SL., van der Kolk BA., Fisler RE., et al., 1996

Adverse Childhood Experiences: Felitti and Anda

Growing up (prior to age 18) in a household with:

- Recurrent physical abuse.
- Recurrent emotional abuse.
- Sexual abuse.
- An alcohol or drug abuser.
- An incarcerated household member.
- Someone who is chronically depressed, suicidal, institutionalized or mentally ill.
- Mother being treated violently.
- One or no parents.
- Emotional or physical neglect.

Robert F. Anda, MD, and Vincent J. Felitti, MD,


Death
Early Death
Disease, Disability and Social Problems
Adoption of Health-risk Behaviors
Social, Emotional, & Cognitive Impairment
Adverse Childhood Experiences
Scientific gaps
Conception

Adverse Childhood Experiences Are Common

Household dysfunction:

Substance abuse	27%
Parental sep/divorce	23%
Mental illness	17%
Battered mother	13%
Criminal behavior	6%

Abuse:

Psychological	11%
Physical	28%
Sexual	21%

Neglect:

Emotional	15%
Physical	10%

Prevalence (%) of Early Trauma (ACEs)

ACE Score	Women	Men	Total
0	31	34	33
1	24	27	26
2	15	16	16
3	10	9	10
4	7	5	6
≥≥ 5	13	8	11

Two thirds had at least one ACE; -More than one third had 2 or more ACEs

15-20% of all of your patients will have a significant traumatic background

ACE Scores predict adult medical outcome

- 1 in 6 had 4 or more traumas
- High correlation between Ace score and negative adult medical outcome
- Linear dose-response model: the higher the ACE score, the worse the outcome on almost every medical illness

Adult Outcomes

Ace of 4 +: 2x more likely to smoke
7x more alcoholism
6x more likely to have sex before age 15
2x more Cancer
2x more heart disease
4x more emphysema or bronchitis
260x more COPD
12x more suicide attempts
51 % have school problems

Ace of 6+: 46x more likely to inject drugs

The ACE Study uses the ACE Score, which is a count of the total number of ACE respondents reported. The ACE Score is used to assess the total amount of stress during childhood and has demonstrated that as the number of ACE increase, the risk for the following health problems increases in a strong and graded fashion:

- Alcoholism and alcohol abuse
- Chronic obstructive pulmonary disease (COPD)
- Depression
- Fetal death
- Health-related quality of life
- Illicit drug use
- Ischemic heart disease (IHD)
- Liver disease
- Risk for intimate partner violence
- Multiple sexual partners
- Sexually transmitted diseases (STDs)
- Smoking
- Suicide attempts
- Unintended pregnancies
- Early initiation of smoking
- Early initiation of sexual activity
- Adolescent pregnancy

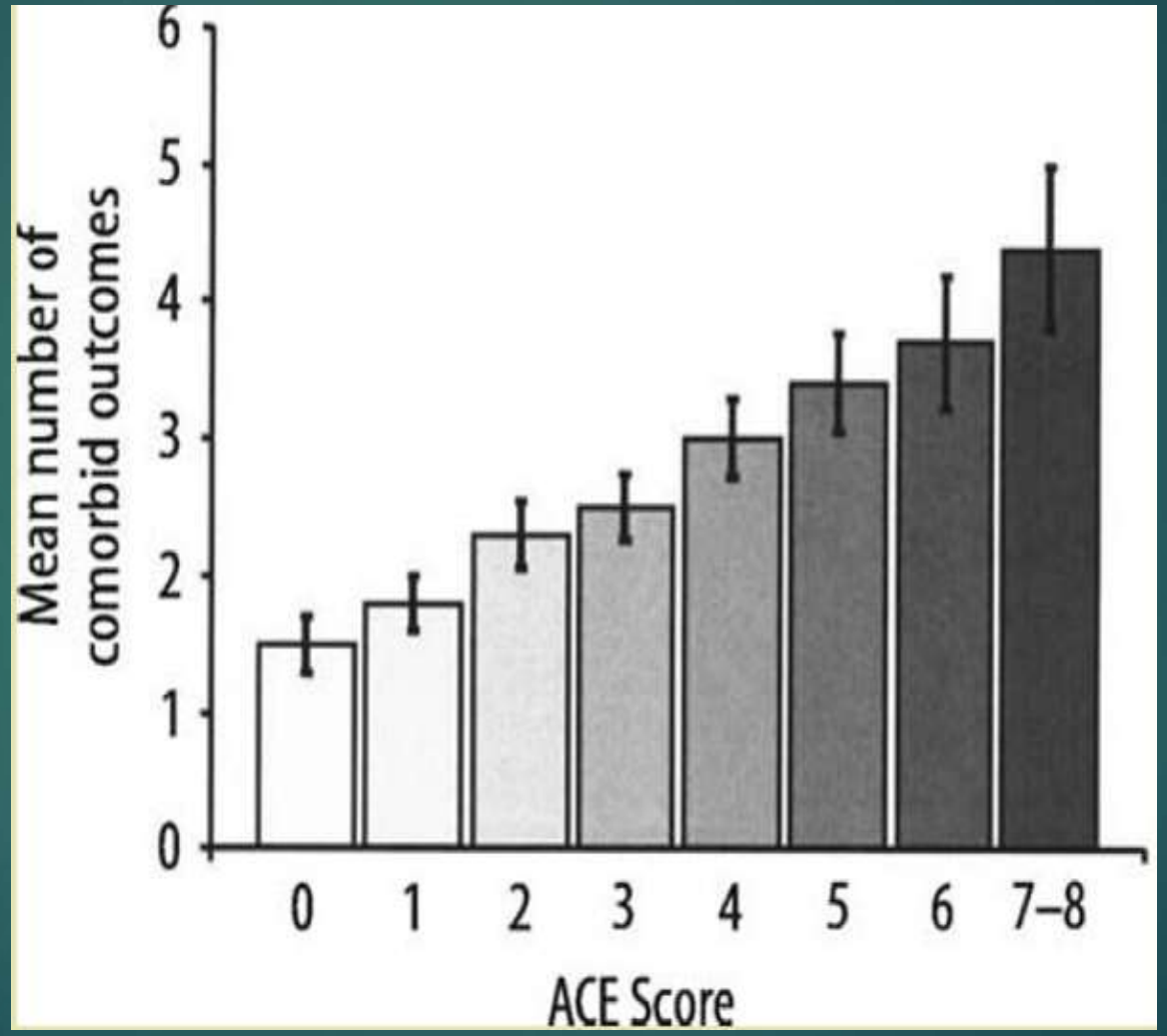
Linear dose-response increase

Adult Outcomes 2

- Felitti's 1st theory: negative outcomes via "bad" behaviors,
  i.e. smoking, heavy drinking, overeating

- Data indicated ACEs had profound negative impact even when no "bad" behaviors were present:
  pts with 7+ who did not smoke, drink, or overeat, had ischemic heart disease 360x higher than 0 scorers

Higher the Ace score, greater the negative outcome

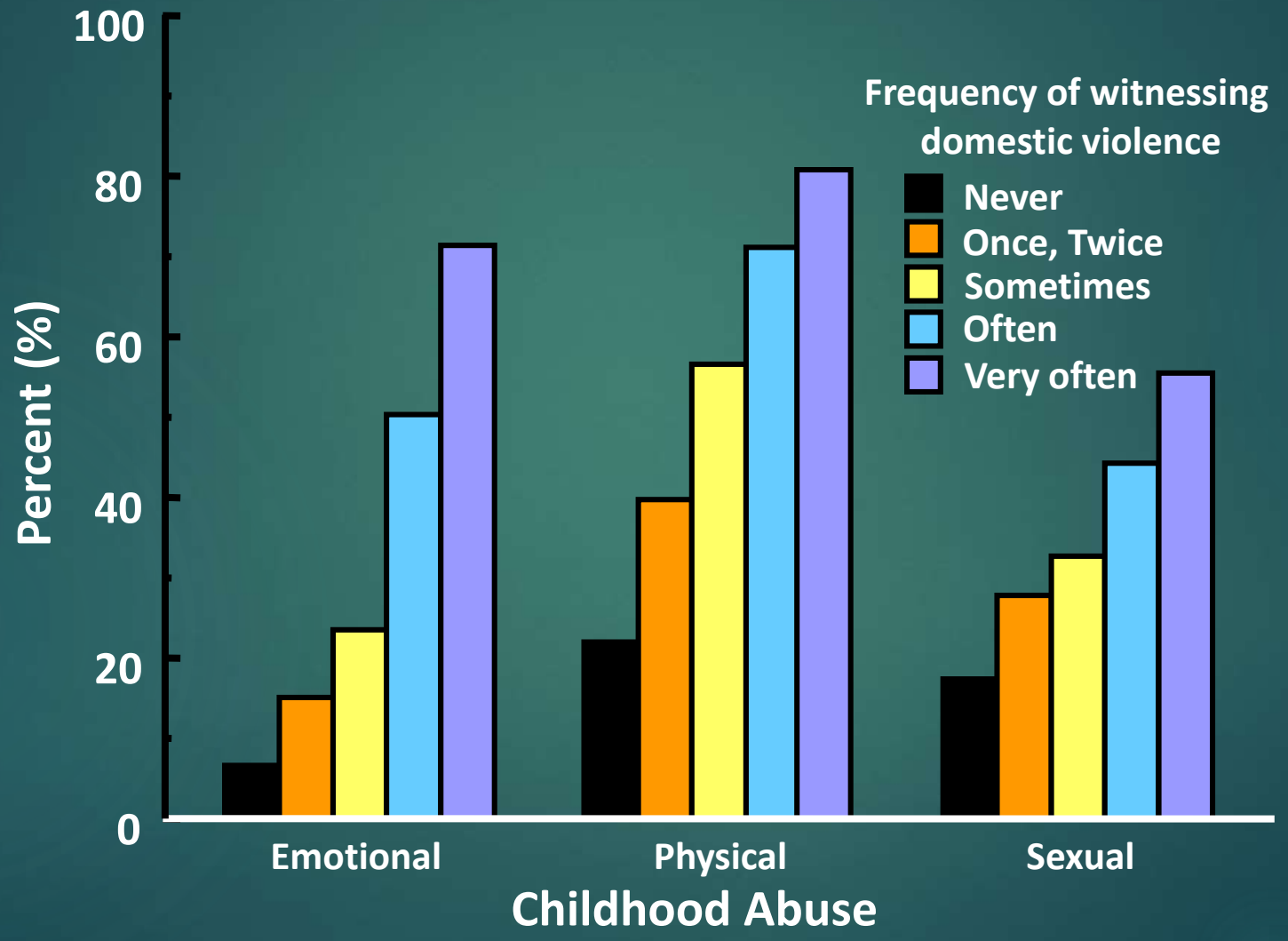


Adverse Childhood Experiences Rarely Occur in Isolation…

They come in groups.

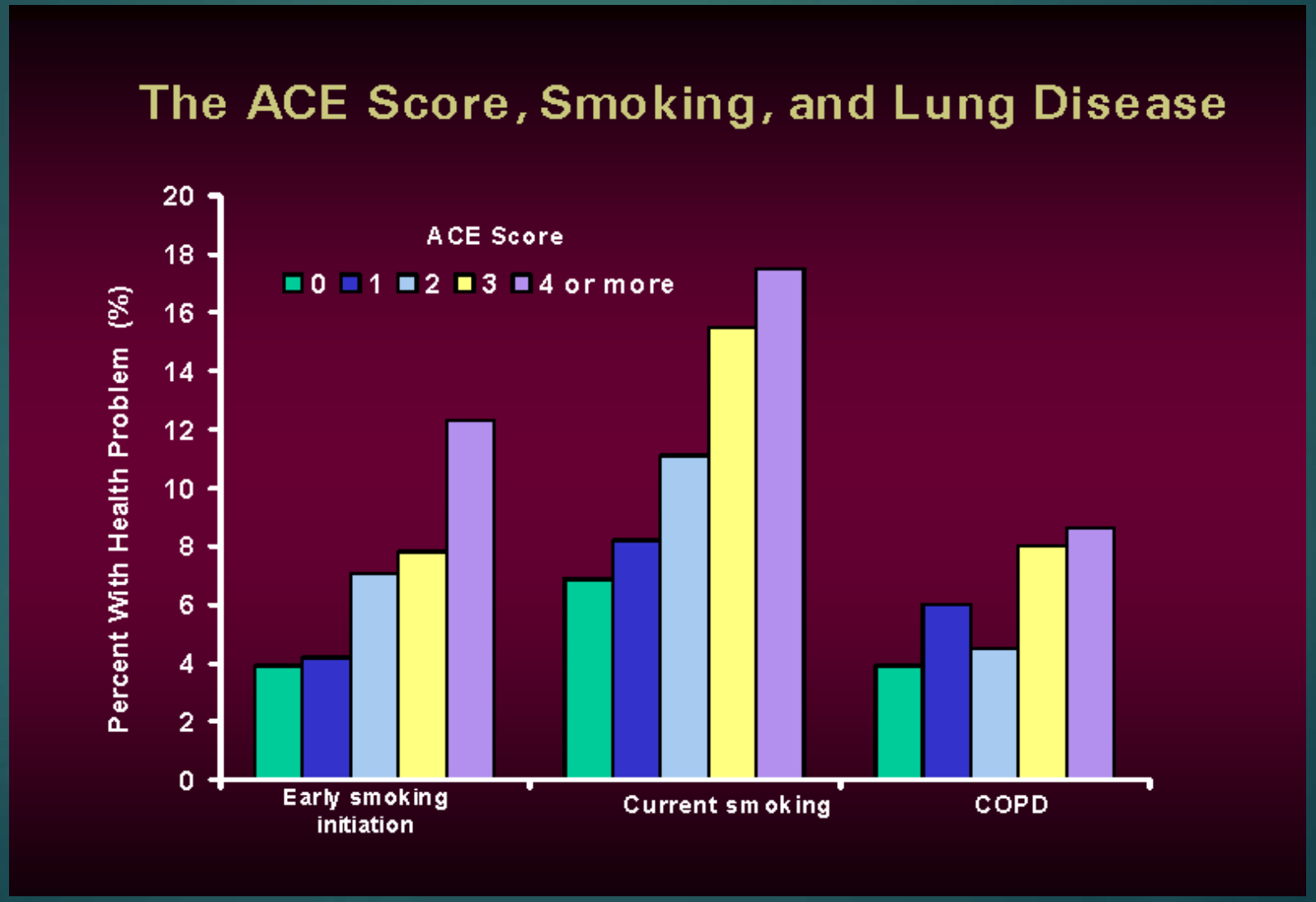
The Occurrence of One ACE Should Evoke a Search for Others

Prevalence of Childhood Abuse by Frequency of Witnessing Domestic Violence

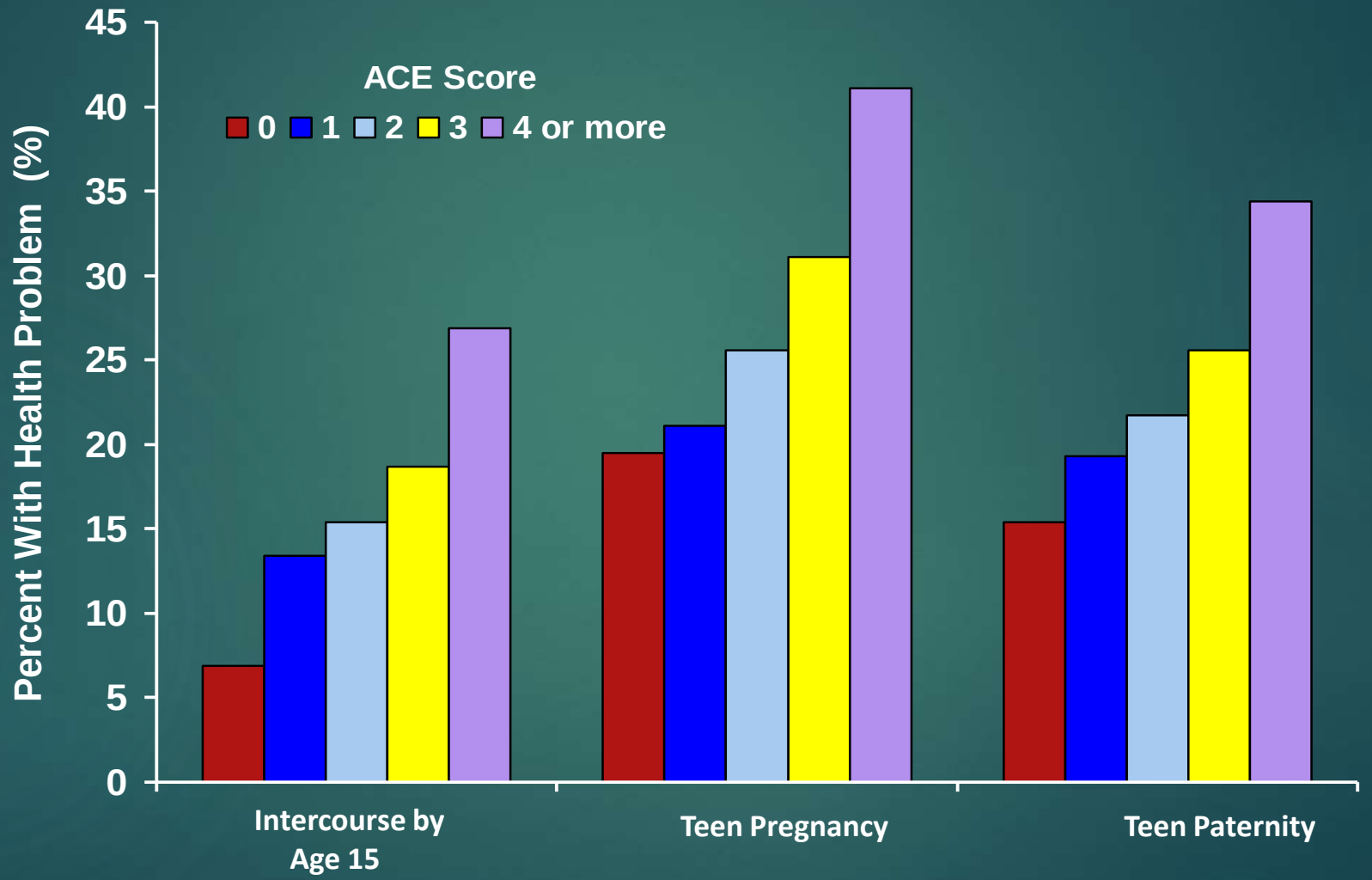


Domestic violence predicts child abuse

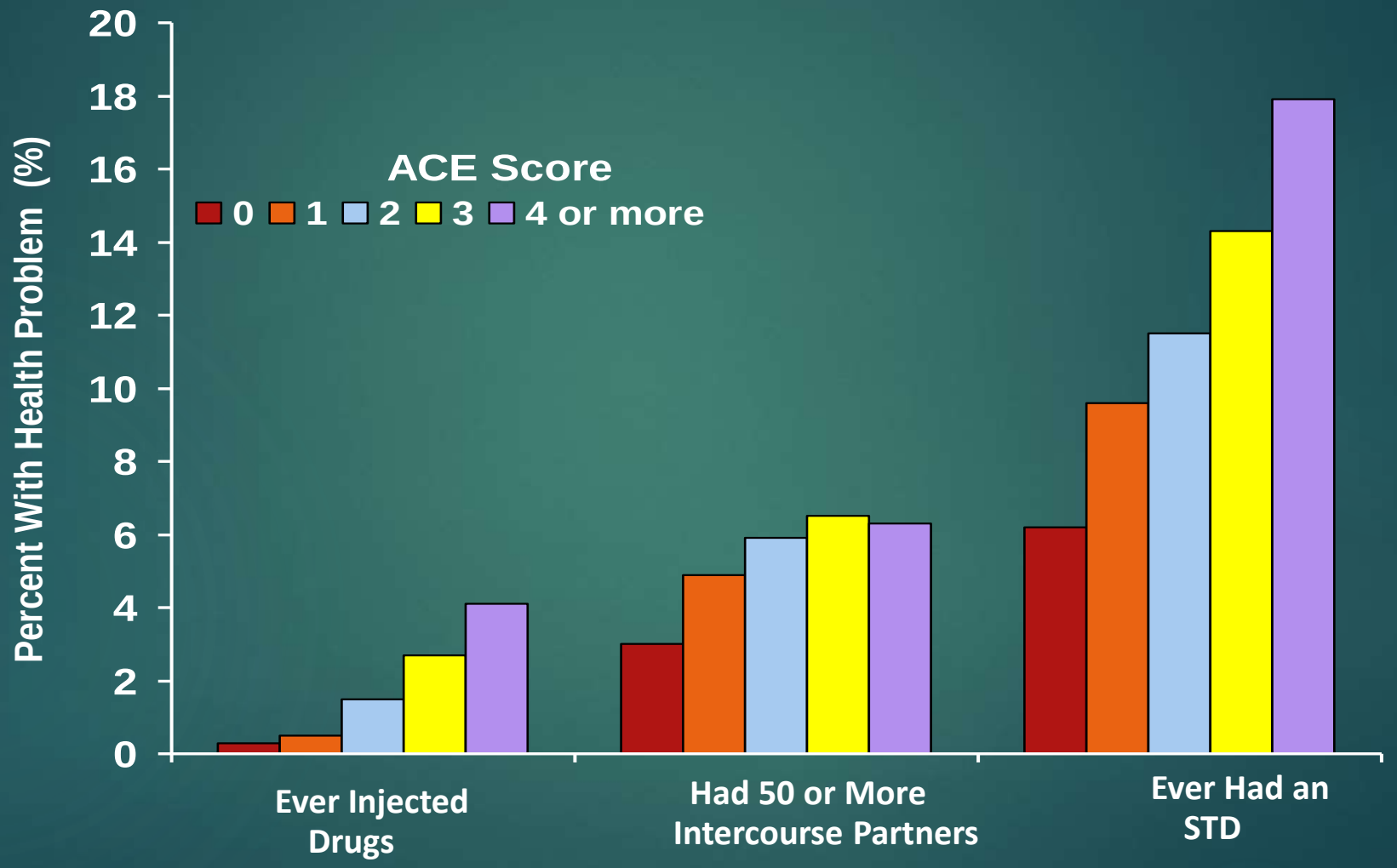
Smoking & COPD



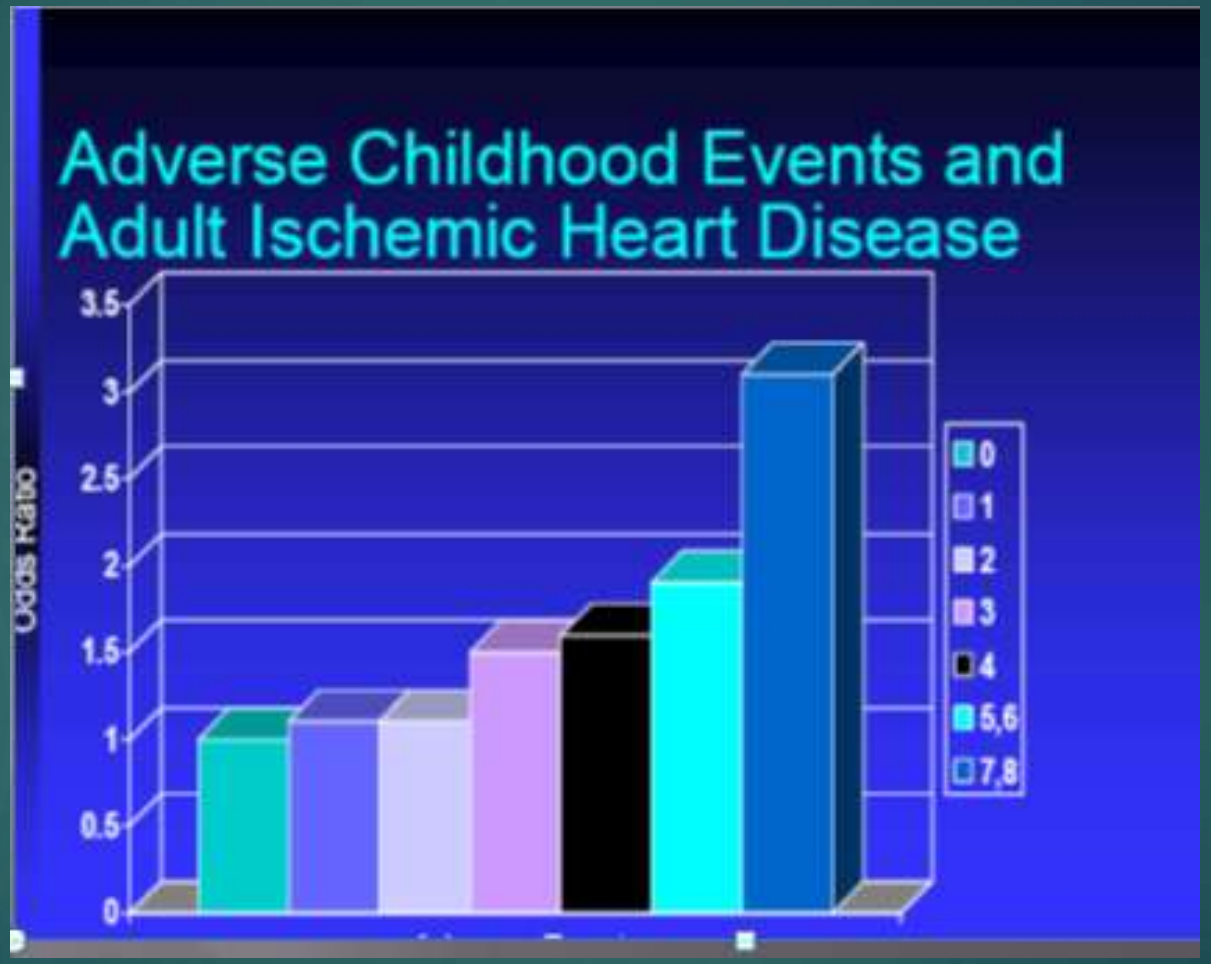
Teen Sexual Behaviors



Injected Drugs, Sex, STDs = HIV Risks

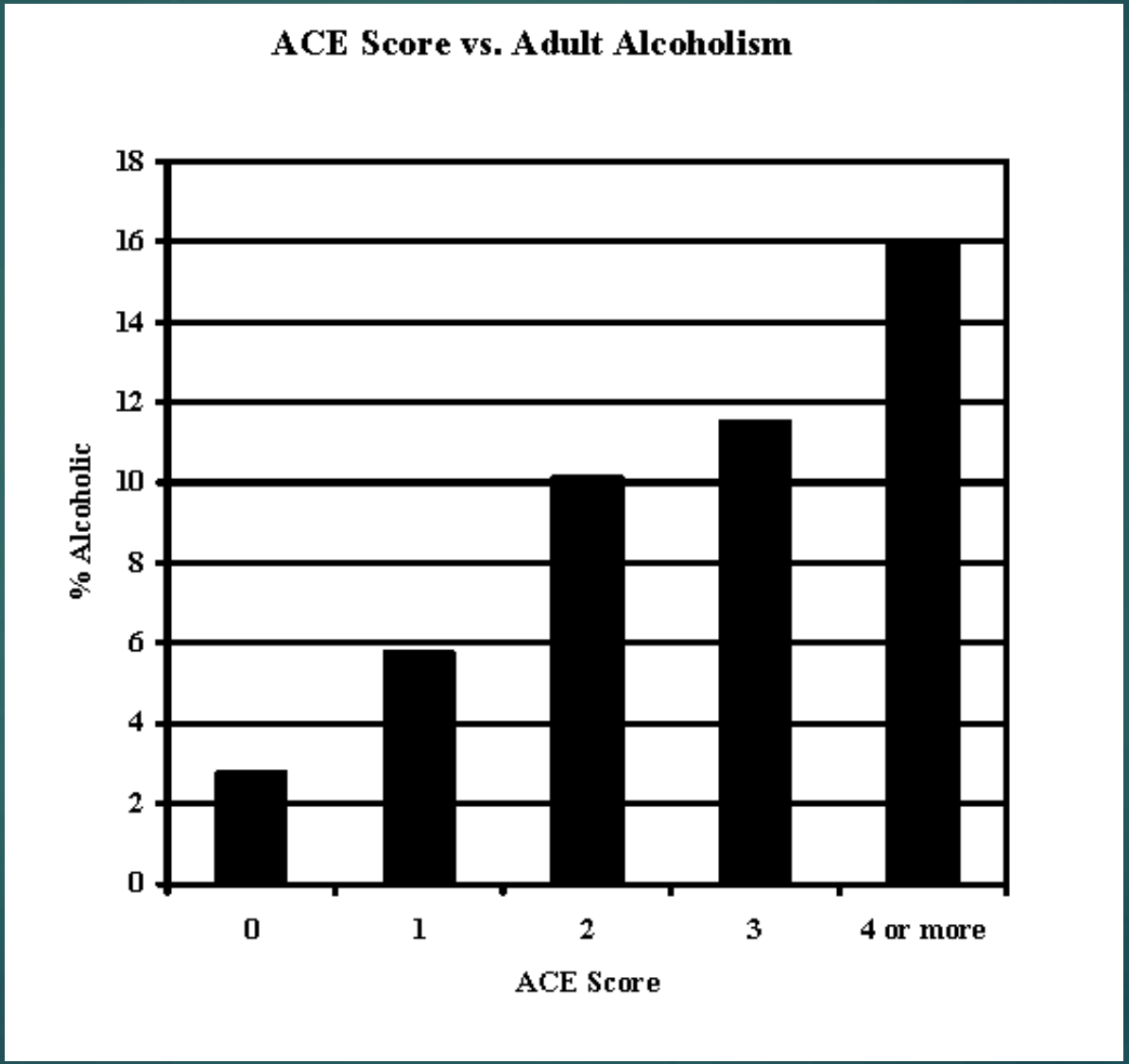


Adult Heart Disease

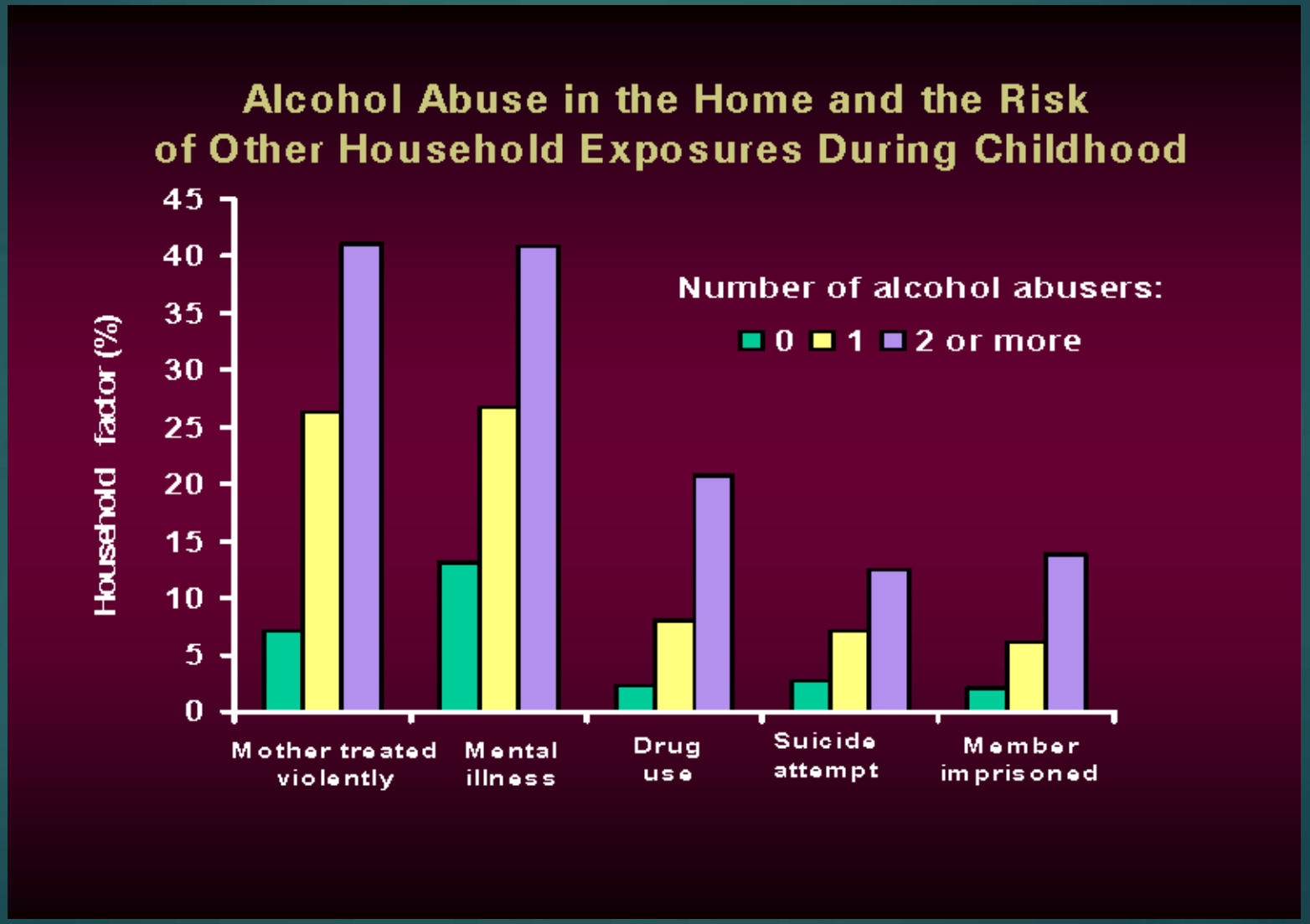


Having 6 or more ACES reduces life expectancy down to age 60.

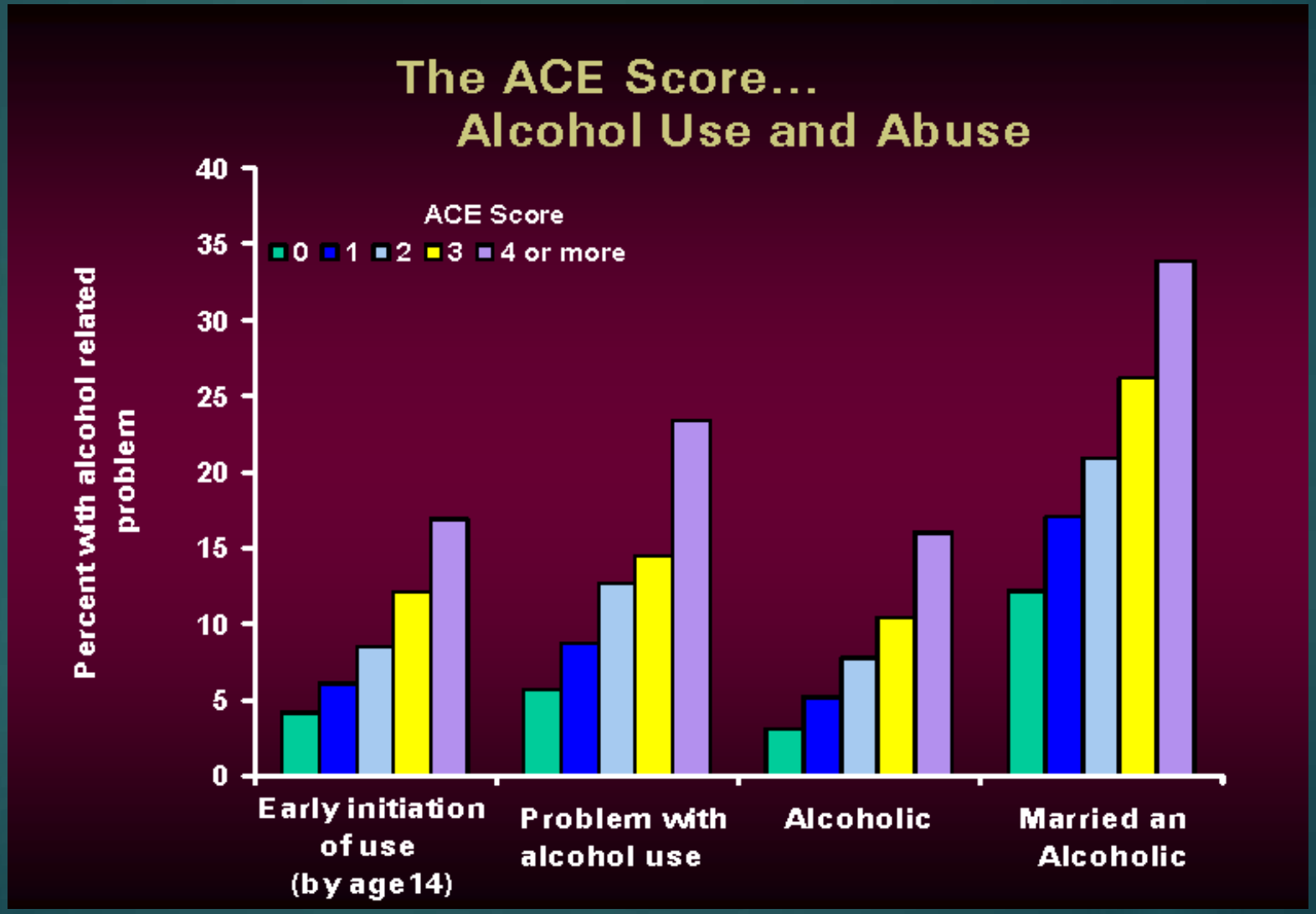
Alcoholism


ACE Score vs. Adult Alcoholism
% Alcoholic
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4 or more
ACE Score

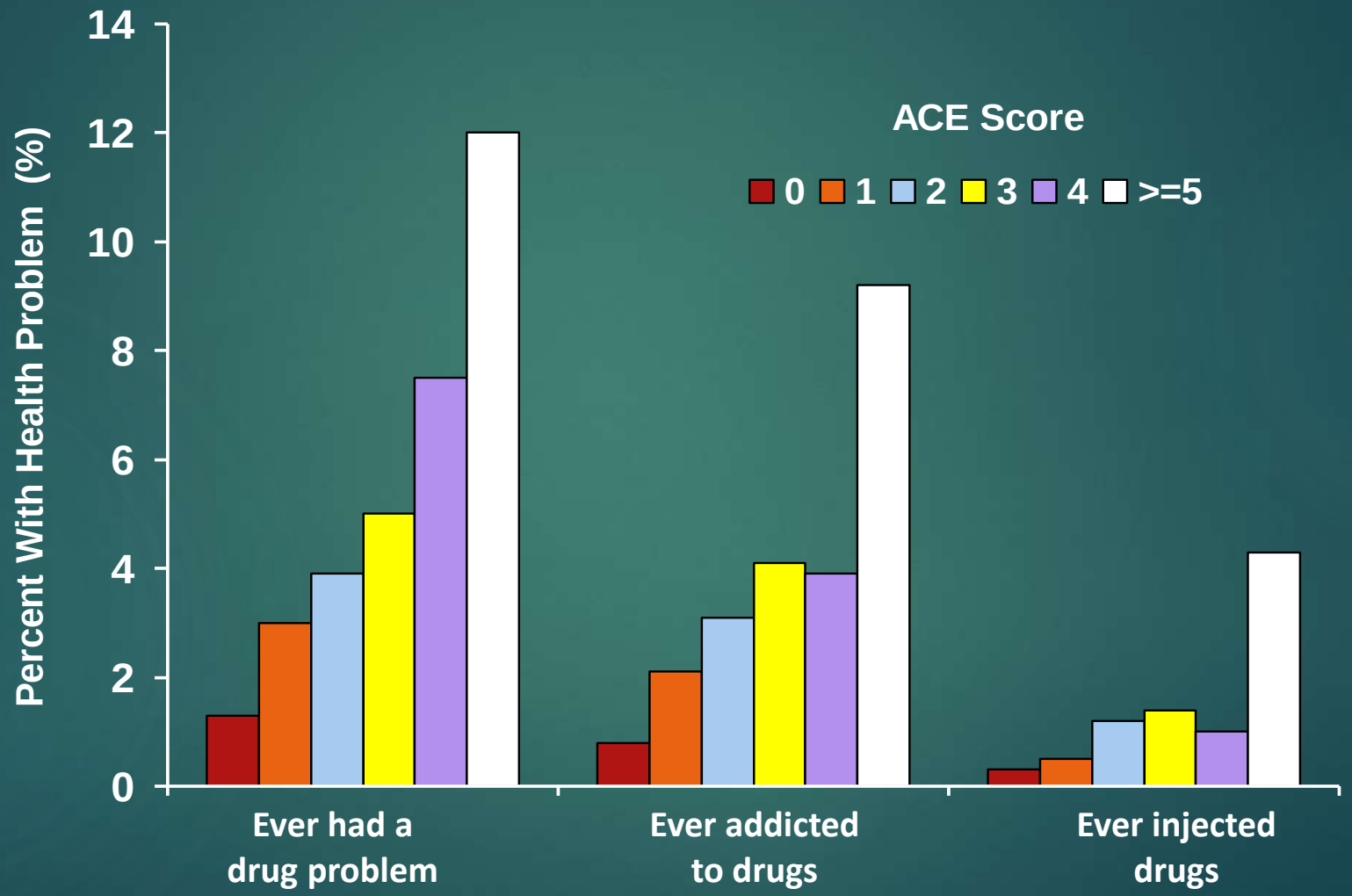
More alcoholism at home, the more abuse factors



More alcoholism at home, more future alcohol problems

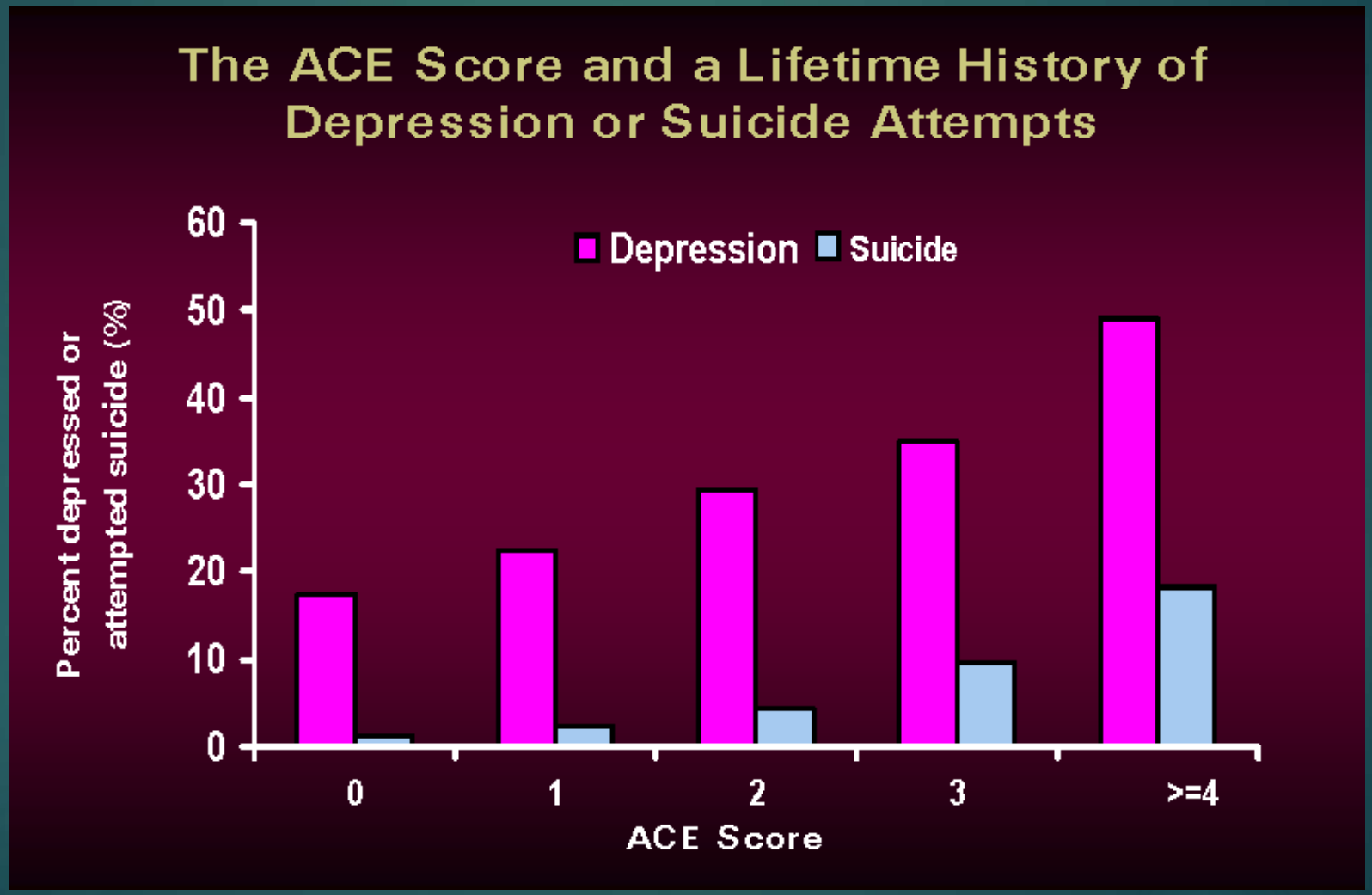


Drug Abuse

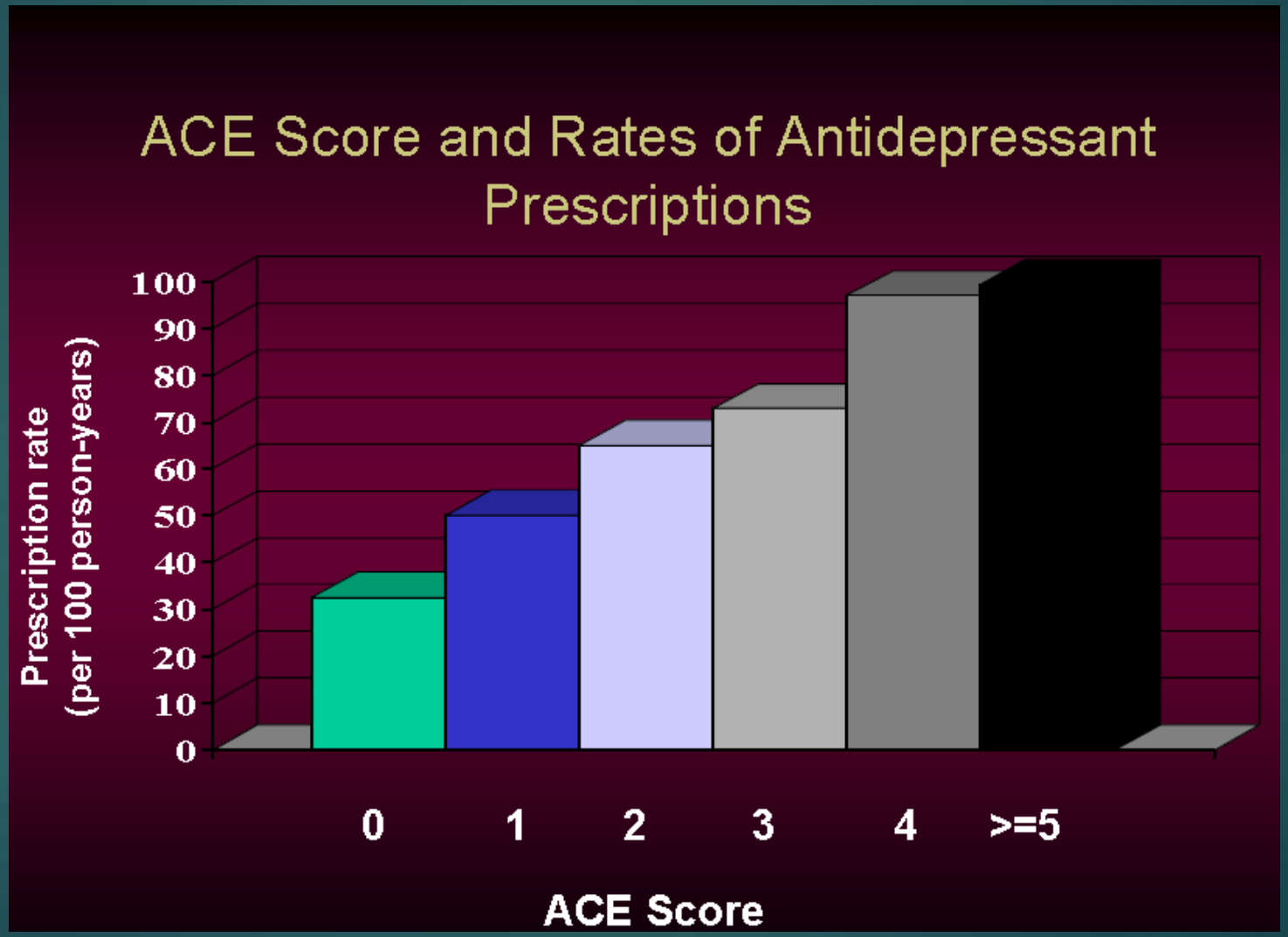

Percent With Health Problem (%)
14
12
10
8
6
4
2
0
ACE Score
0
1
2
3
4
>=5
Ever had a drug problem
Ever addicted to drugs
Ever injected drugs

Lifetime History of Depression

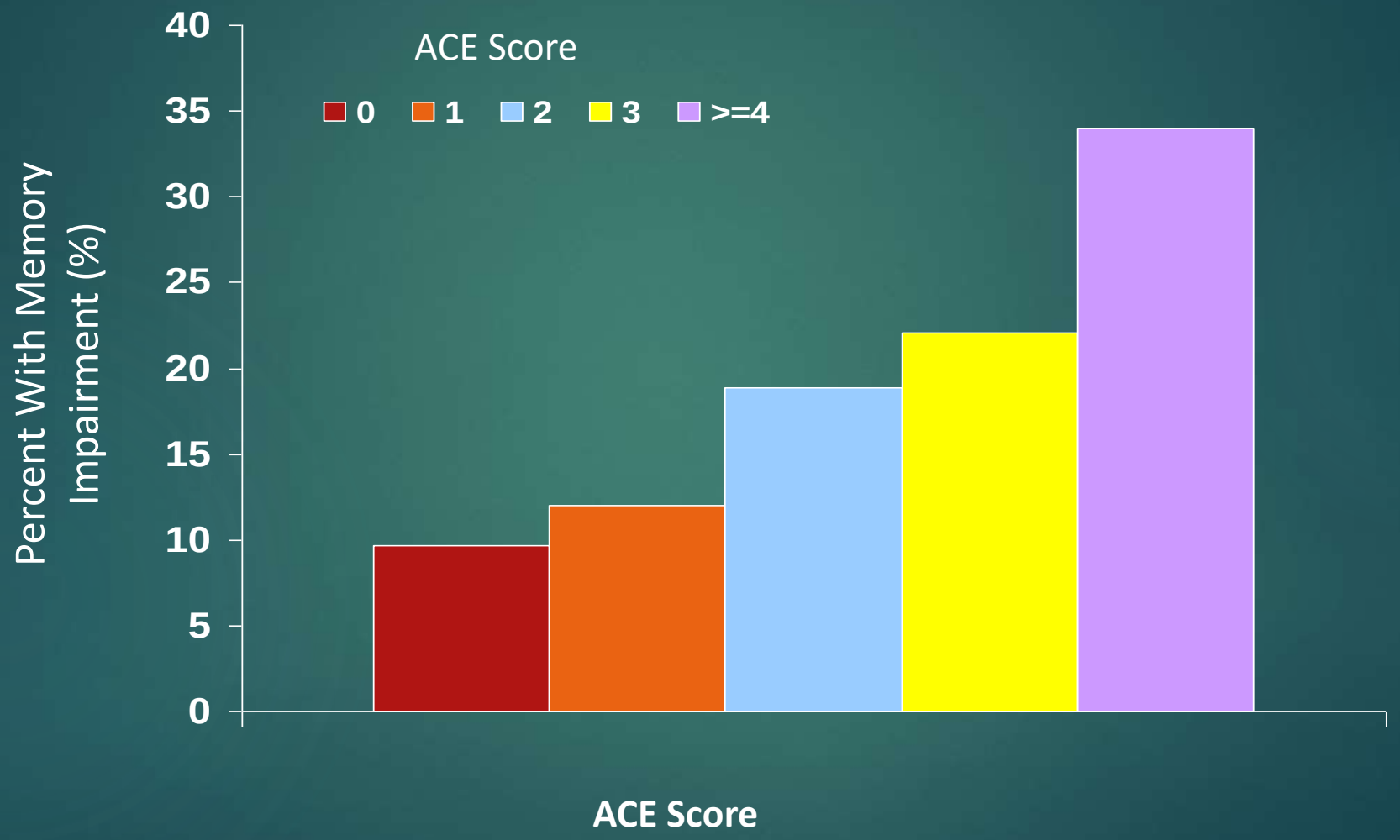
Lifetime History of Depression & Suicide Attempts



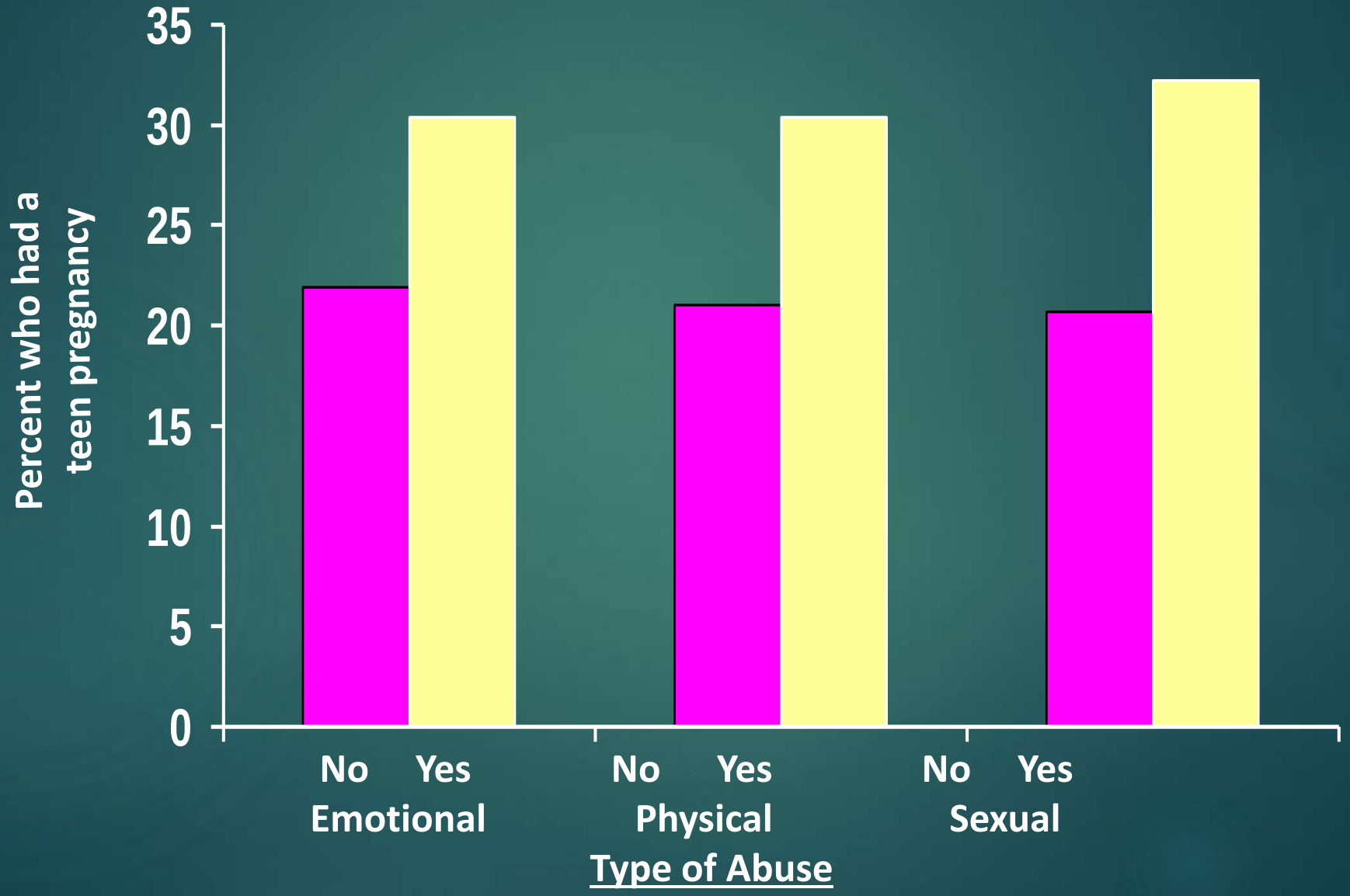
Antidepressant Prescriptions



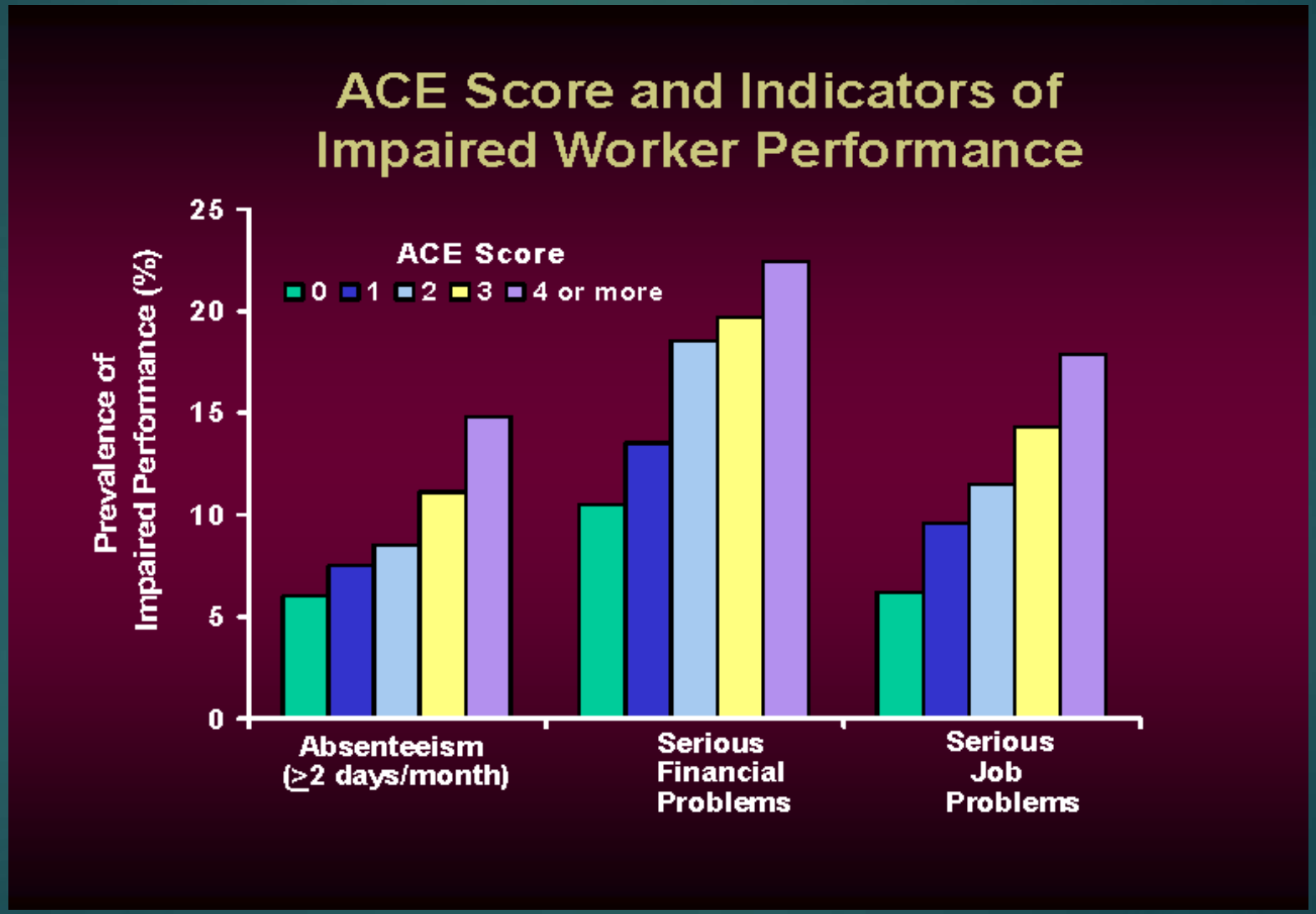
Impaired Memory of Childhood



Prevalence of Teen Pregnancy



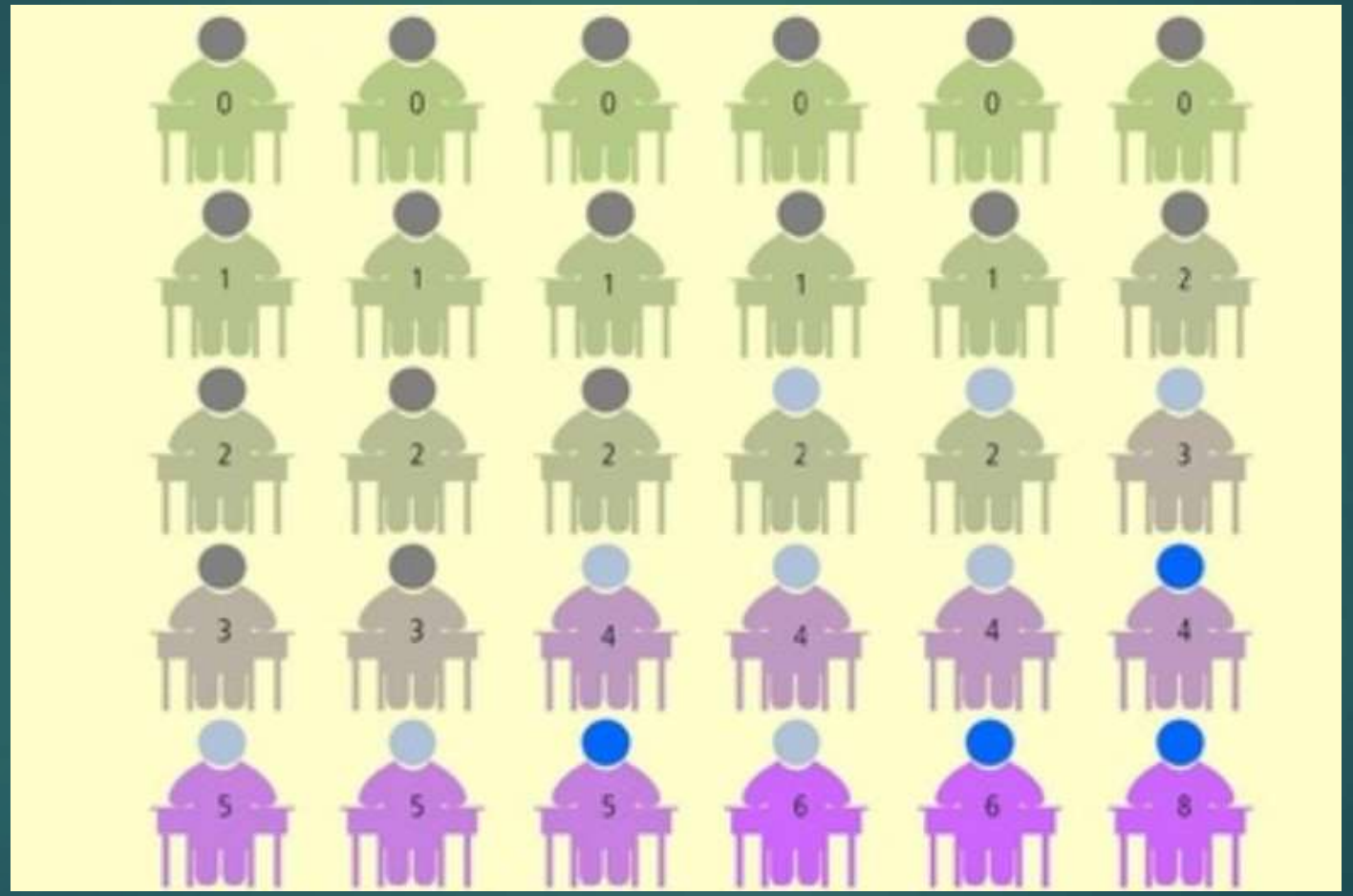
History of Impaired Work Performance



4 vs 0 Aces

RISK FACTOR	% INCREASE
Smoking	242%
Obesity	222%
Depression	357%
Illicit drug use	443%
Injected drug use	1,133%
STD	298%
Attempted suicide	1,525%
Alcoholism	555%

30 Students in a WA state classroom



30% of students in a typical classroom have four or more ACEs.

Bridging The Chasm

Child health as it stands today

Routine screening for trauma is needed

Child health as it could be

The Bilingual Advantage

- Brain activates both languages when speaking one (more EF choice):
- Children:
  - Increased levels of self-control
  - better at learning abstract rules
  - Better at ignoring irrelevant information.
- Better decision making in second language
- Less impact of emotion on thinking
- Tourette's also have better self control

Bilingual advantage

- Dementia 4 years later than monolingual
- Left inferior frontal cortex becomes thicker and the right inferior frontal cortex becomes thinner.
- The later in childhood that the second language is acquired, the greater are the changes in the inferior frontal cortex

Impulse Control

- Ability to delay gratification/Impulse control is more important than IQ in predicting:
  - Academic performance
  - SES success
  - Marital stability
  - Staying out of prison

Marshmallow Test

Marshmallow Resistance at age 4

- Walter Meschel, 1968: 4 year olds, get 2 marshmallows if wait 15 minutes; ring bell and get to eat, but no 2nds; 2 minute wait was average; 25% made it to 15 min; n = 653

- Children who rang the bell within a minute:
  - more likely to have behavioral problems, both in school and at home
  - struggled in stressful situations
  - had trouble paying attention in class
  - had serious problems with their temper
  - significantly higher BMI
  - more drug problems

Marshmallows

- At age 4, ability to wait 15 minutes before eating a marshmallow predicts
  - SAT scores 210 points higher at age 18
  - better adjusted
  - less likely to abuse drugs
  - higher self-esteem
  - better relationships
  - better at handling stress
  - obtained higher degrees
  - earned more money.

- At age 45, delayers better at go/nogo task;
  - increased activity in the inferior frontal gyrus
  - low ventral striatum activation.

Key: Pay attention to something else

- Crucial skill was the "strategic allocation of attention". All wanted the marshmallow.
- "The key is to avoid thinking about it in the first place."
- Working memory and directed attention ability crucial
- Brain involved:
  - Dorsolateral prefrontal cortex
  - anterior prefrontal cortex
  - anterior cingulate
  - bilateral inferior frontal gyri.

Marshmallow Test 2012

- C. Kidd: Children lasted on ave. for 6 minutes
- New procedure: Half dealt with unreliable experimenter who failed to deliver on promises; rest had reliable experience
- Those with unreliable experience lasted 3 minutes (only 1 of 14 lasted 15 min.), others 12 minutes (9 of 12)
- Consistent with Mischel, 1961: 8 y old boys without Fathers went for immediate reward

Multitasking: incompetence breeds over-confidence

- How good are you at multi-tasking?
- The better people *think* they are at multitasking, the worse they actually are at it.
- Higher self estimate of multitasking ability, the more likely you are to multi-task when driving.
- Those most likely to use their cell phones while driving scored highest on measures of impulsivity and thrill-seeking.

David Sanbonmatsu , 2013

Neuropsychology of Psychopathology

- Neurocognitive disorders
- Schizophrenia
- Alcoholism
- ADHD
- Depression
- Bipolar
- OCD
- PTSD
- Anxiety
- Personality Disorders

Neurocognitive Disorders

New category

Deficits in cognitive functioning as a core feature; underlying pathology and etiology can be determined

DSM-5 NCDs

- "Dementia" is replaced by "major NCD
- NCD: The primary clinical deficit is in cognitive function.
- These are the only disorders whose core features are cognitive (not Schiz, bipolar)
- Acquired, not developmental: a decline from previous functioning
- These are only DSM-5 diagnoses with known pathologies
- Cognition, not Memory, central

DSM-5 NCD

- Delirium
- Mild neurocognitive disorder (old MCI, Cog Disorder NOS)
- Major neurocognitive disorder (old dementia)

NCD: 6 Cognitive Domains

- Complex Attention (Sustained, selective divided)
- Executive Function (Planning, decision making, working memory, feedback/error utilization, overriding habits/inhibition, cognitive flexibility
- Learning and memory

NCD: Cognitive Domains 2

- Language (expressive, grammar/syntax, receptive)
- Perceptual-motor (visual, visoconstructional, perceptual-motor, praxis, gnosis)
- Social cognition (recognition of emotions, theory of mind)

Major Neurocognitive Disorder

1. Significant Cognitive decline from previous level of performance in 1 or more cognitive domains
    1. Concern of individual, informant, or clinician of a significant cognitive decline
    2. Substantial cognitive impairment on NP testing (NP Testing: - 2 s.d. (3rd %tile)
2. Deficits interfere with capacity for independence in everyday activities

Mild or Major NCD – Specify due to:

- Alzheimer's disease
- Frontotemporal lobar degeneration
- Lewy boy disease
- Vascular disease
- Traumatic brain injury
- Substance/medication use
- HIV infection
- Prion disease
- Parkinson's disease
- Huntington's disease
- Another medical condition
- Multiple etiologies
- Unspecified

Mild Neurocognitive Disorder

1. Modest Cognitive decline from previous level of performance in 1 or more cognitive domains

    1. Concern of person, informant, or clinician of a mild cognitive decline
    2. Modest cognitive impairment on NP testing NP Testing: - 1-2 s.d. (3 to 16th %tile)

2. Deficits do not interfere with capacity for independence in everyday activities

DSM-5: Possible Dx

- Probable AD diagnosed if evidence of causative AD genetic mutation from family hx or genetic testing
- Possible AD if no genetic evidence and all 3 of following present:
  - Memory decline
  - Progressive gradual decline in cognition
  - No evidence of mixed etiology
- Possible Dx will become the new NOS Dx

DSM-5: New Categories

- Intellectual Disability:
  - Decreased emphasis on IQ;
  - increased emphasis on adaptive fxn
  - (Concern about effect on death penalty of intellectually disabled)

- Social (Pragmatic) Communication Disorder:
  - difficulties in social use of verbal and nonverbal communication;
  - but no repetitive behaviors

Ensuring Validity of Test Data

- Use of SVTs is required in testing
- Patients often put forth suboptimal effort and/or have response bias even with not external secondary gain
- Many seem to lack the motivation to "do their best" but may be responsive to encouragement