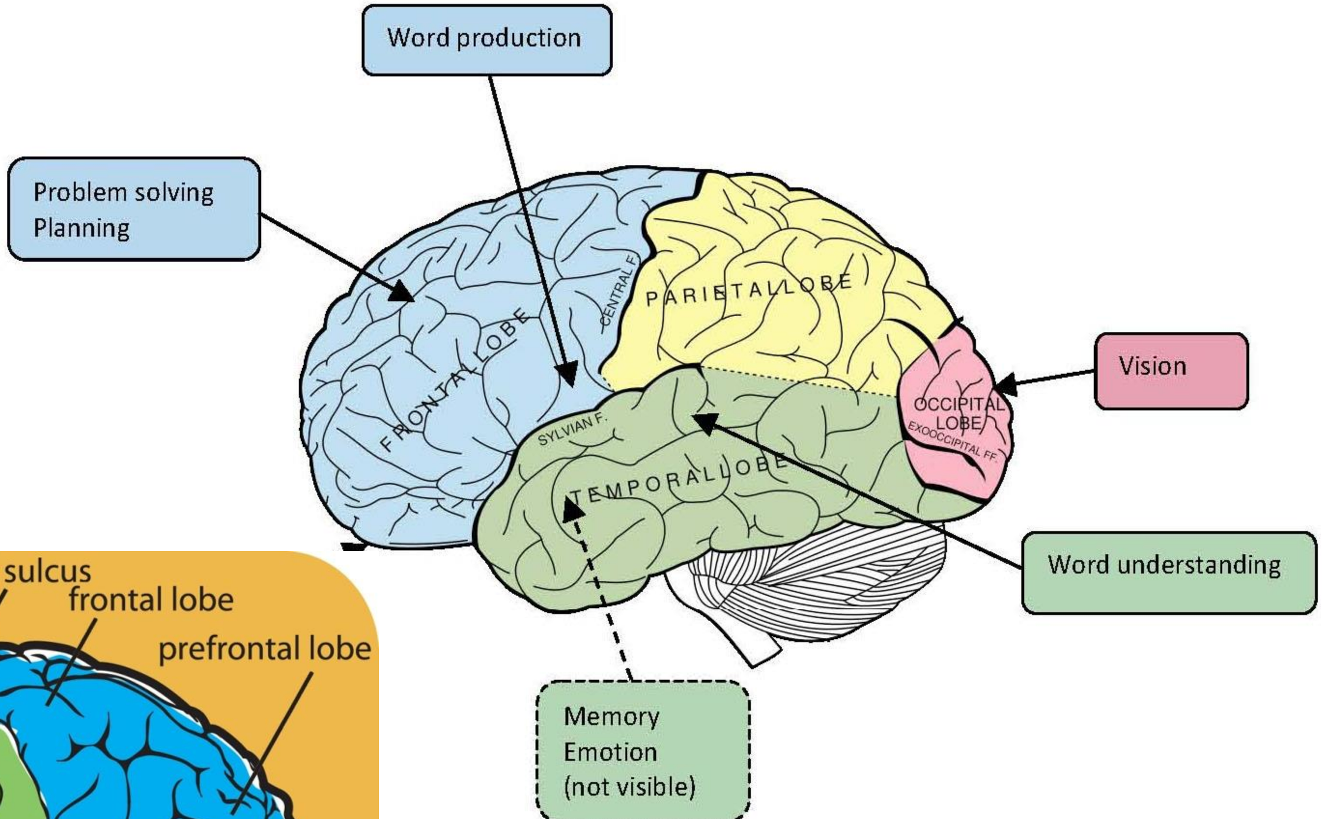
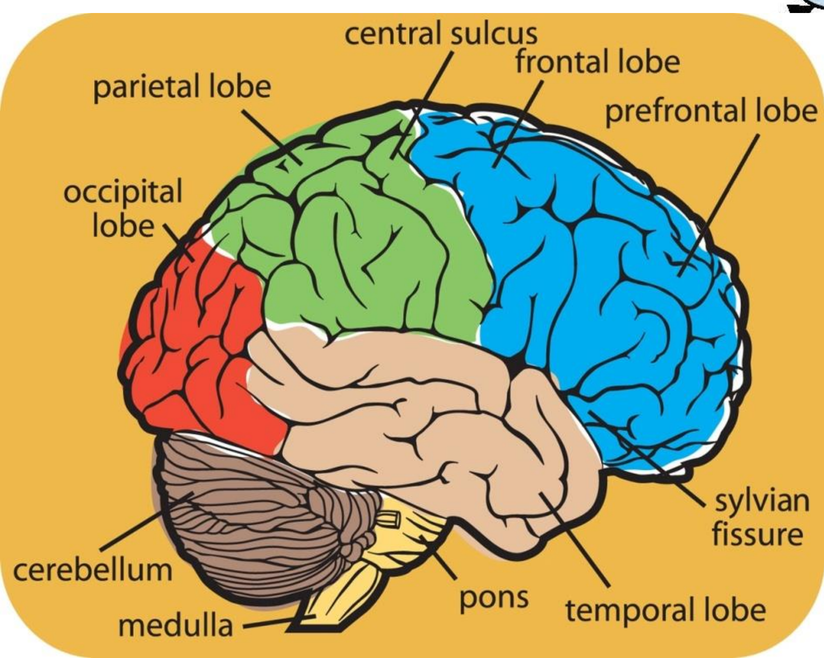
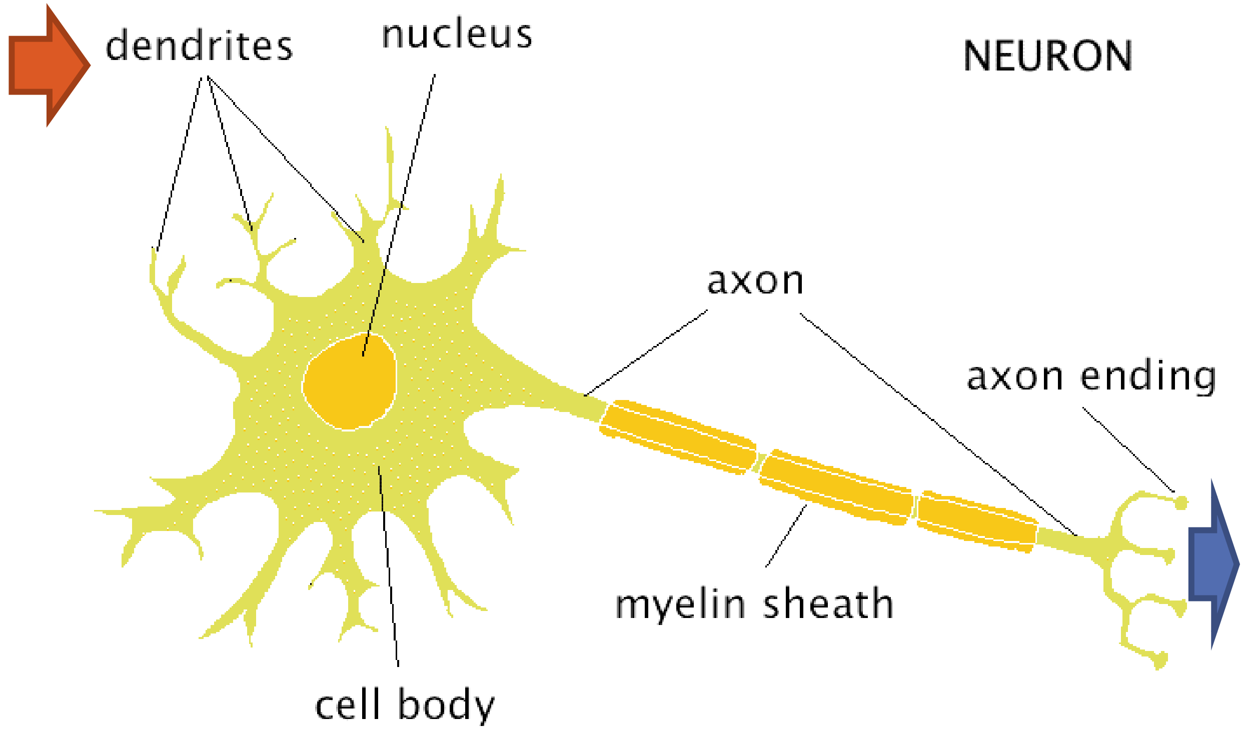
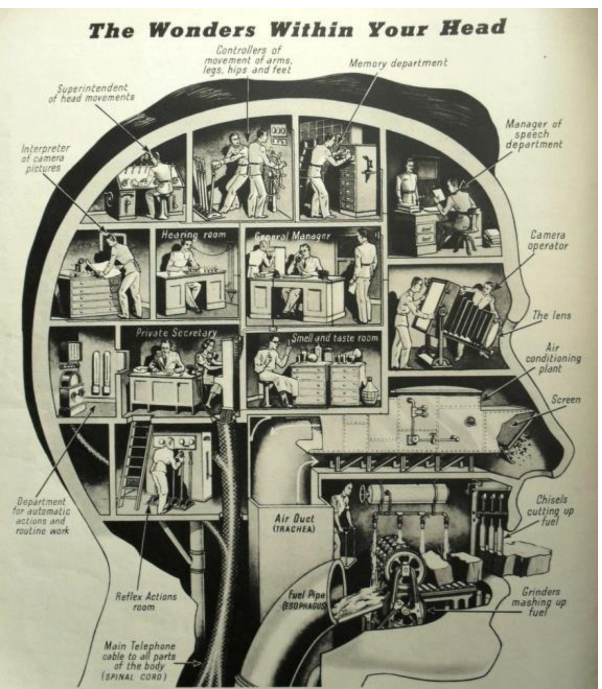

Word production
Problem solving
Planning
CENTRAL F.
PARIETAL LOBE
FRONTAL LOBE
OCCIPITAL LOBE
EXOOCCIPITAL FF.
Vision
SYLVIAN F.
TEMPORAL LOBE
Word understanding
Memory
Emotion
(not visible)


central sulcus
frontal lobe
parietal lobe
prefrontal lobe
occipital lobe
sylvian fissure
cerebellum
pons
temporal lobe
medulla

<u>NEURON</u>:





Glia cells = nerve cells that <u>don't carry nerve impulses (Action Potentials)</u>. Include: Immune system, support, nutrients (Astrocytes..)..

IS THE HUMAN BRAIN IS UNIQUE?

“We have brains that are bigger than expected for an ape, we have a neocortex that is three times bigger than predicted for our body size, we have … *areas* of the neocortex and cerebellum that are larger than expected..” (Gazzaniga, 2008).

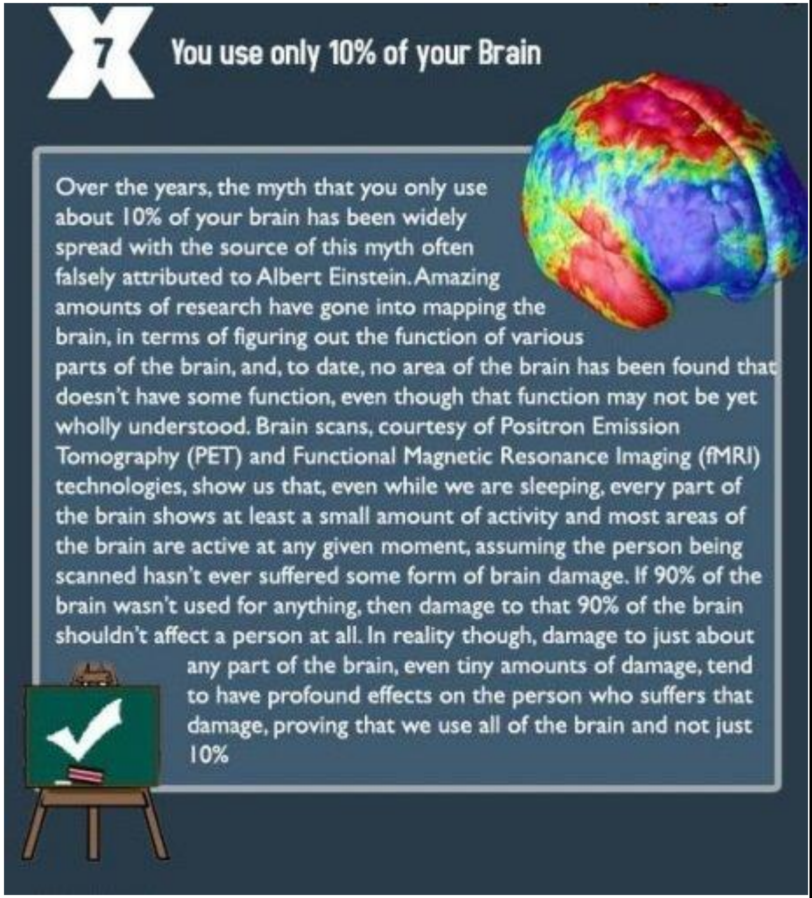
“The only brain that studies brains”

5 BRAIN MYTHS: #1 YOU ONLY USE 10 % OF YOUR BRAIN.

NO!

Evidence:

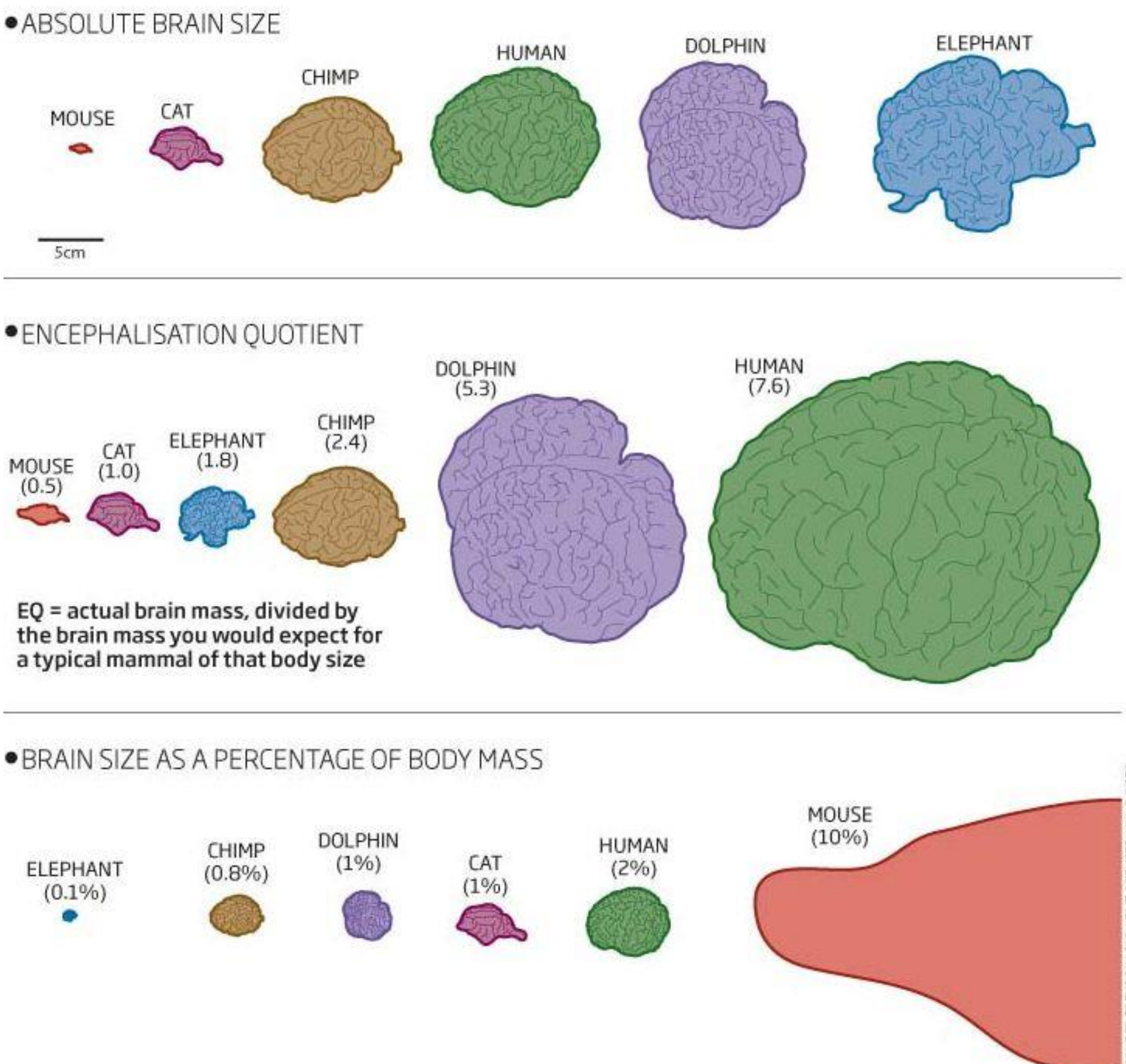
1. fMRI. PET scans.
2. Effects of Damage.
3. Evolution. (Wasted space)



Who's the cleverest of them all?

©NewScientist

Inferring intelligence from brain size is questionable, not least because the relative sizes of brains change dramatically depending on how they are measured

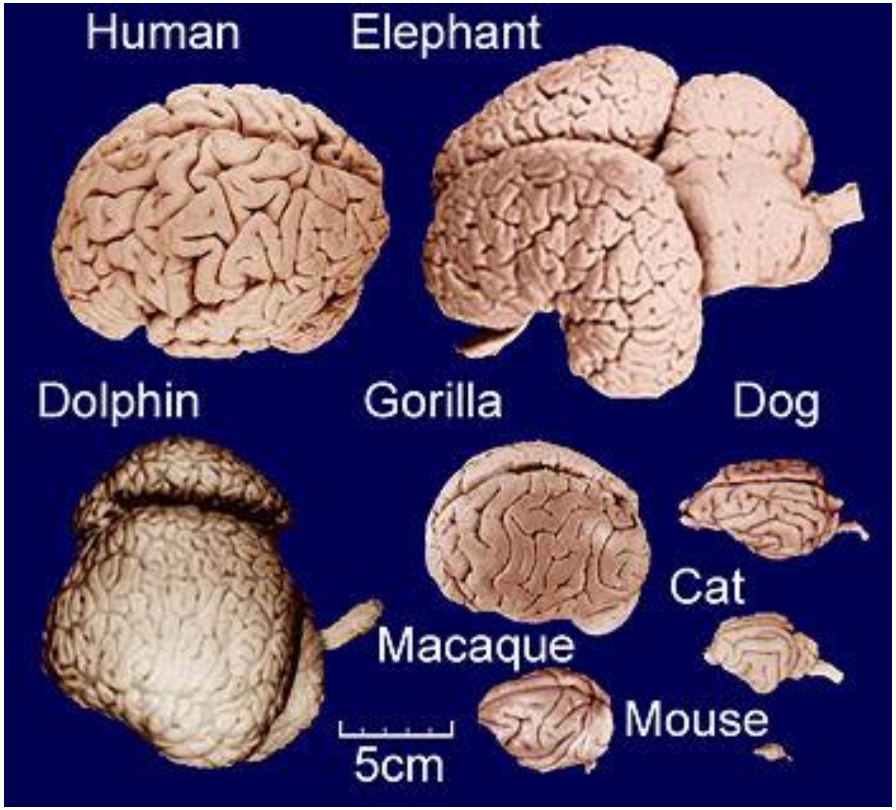


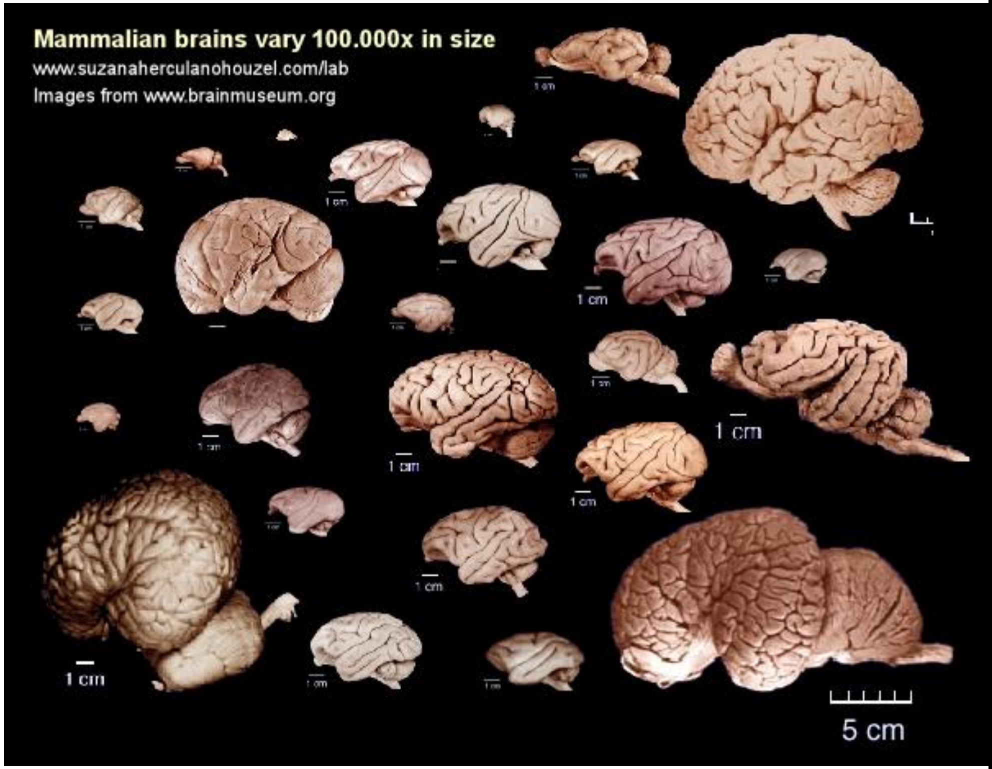
SOURCE: TRENDS IN COGNITIVE SCIENCES, VOL 9, P 250

MYTH #2: BIGGEST BRAINS?

Absolute Size?

BIGGER = BETTER BRAIN?





MYTH #2: BIGGEST BRAIN?

We Do NOT have the biggest brains !

The bigger = better relationship collapses, when comparing **species across orders .**

•Cows have larger brains than just about any species of monkey..

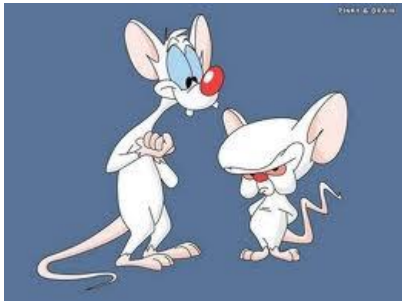
•Capybara & Capuchin monkey..

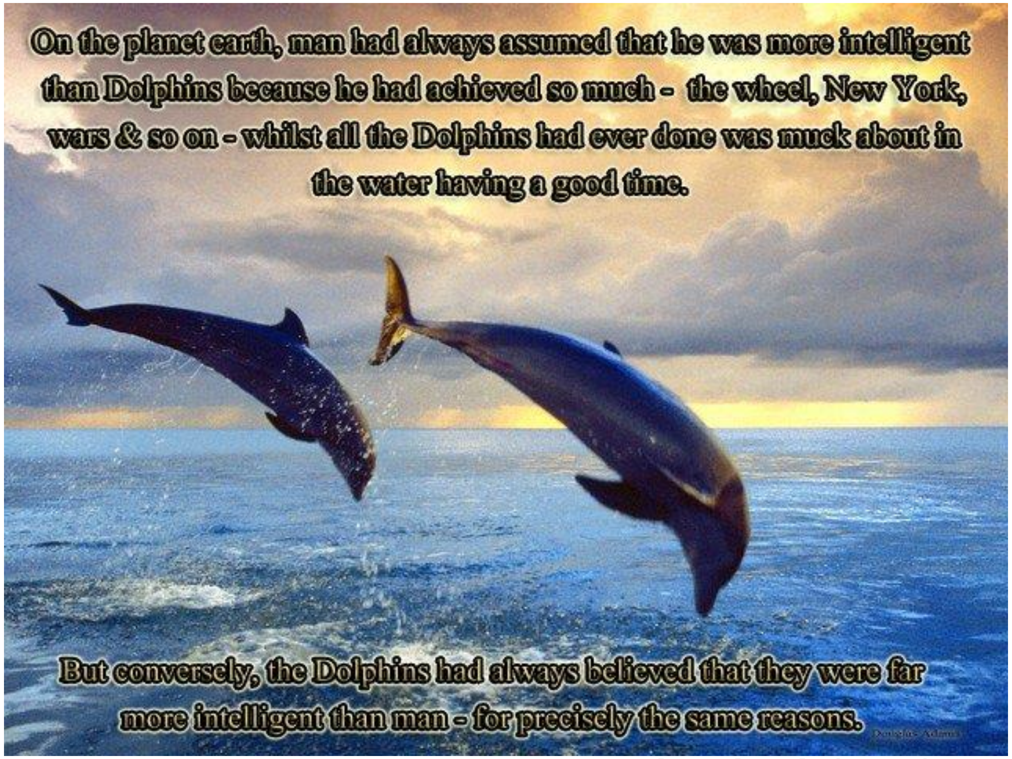
Humans	**1.5kg**
Elephants	5.6kg
Whales	7.8 kg

Species	Name	Weight (kg)	Brain (grams)	EQ
Human	*Homo sapiens*	75.00	1400.00	6.56
Whale dolphin	*Lissodelphis borealis*	73.00	1162.00	5.55
Bottlenose dolphin	*Tursiops truncatus*	119.96	1535.00	5.26
Commerson's dolphin	*Cephalorhynchus commersonii*	43.00	732.00	4.97
Macaque	*Macaca nemestrina*	4.89	108.87	3.15
Baboon	*Papio hamadryas*	9.88	155.44	2.81
Chimpanzee	*Pan troglodytes*	45.00	398.60	2.63
Capuchin	*Cebus capucinus*	3.10	66.94	2.63
Gorilla	*Gorilla gorilla*	120.50	512.92	1.75
Coyote	*Canis latrans*	8.51	84.24	1.69
African gray parrot	*Psittacus erithacus*	0.33	5.70	1.00
Lion	*Felis leo*	142.82	240.60	0.73
Tiger	*Felis tigris*	184.50	263.50	0.68
Hippopotamus	*Hippopotamus amphibius*	1351.00	732.00	0.50
Blue whale	*Balaenoptera musculus*	58059.00	6800.00	0.38

MYTH #3: RELATIVELY LARGEST BRAIN TO BODY MASS RATIO?

Humming bird: 1/25
Squirrel monkeys: 1/20
Mice: 1/40
Humans: 1/49
Dolphins: ~1/80
Cats: 1/100
Dogs: 1/125
Lions: 1/500
Elephants: 1/560
Horses: 1/600
Sharks: 1/2500





Kuhlenbeck (1973)

MYTH #3: HUMAN BRAINS ARE THE RELATIVELY LARGEST ?
- ENCEPHALIZATION

"A brain 7 times too large for a mammal of its size…"

(Marino, 1998)

Species	*EQ*	*Species*	*EQ*
Man	7.44	**Cat**	1.00
Dolphin	5.31	**Horse**	0.86
Chimpanzee	2.49	**Sheep**	0.81
Rhesus Monkey	2.09	**Mouse**	0.50
Elephant	1.87	**Rat**	0.40
Whale	1.76	**Rabbit**	0.40
Dog	1.17	(Macphail, 243)	

(Jerison, 1973).
(Macphail, 243)

CLAIMS OF HUMAN UNIQUENESS: **ENCEPHALIZATION QUOTIENT**

Expected body–brain ratio dependant on <u>Species</u> compared.

- **Compared to Primates: E.Q of <u>3</u>**
- **Compared to small monkeys: E.Q <u>1.1</u>!**

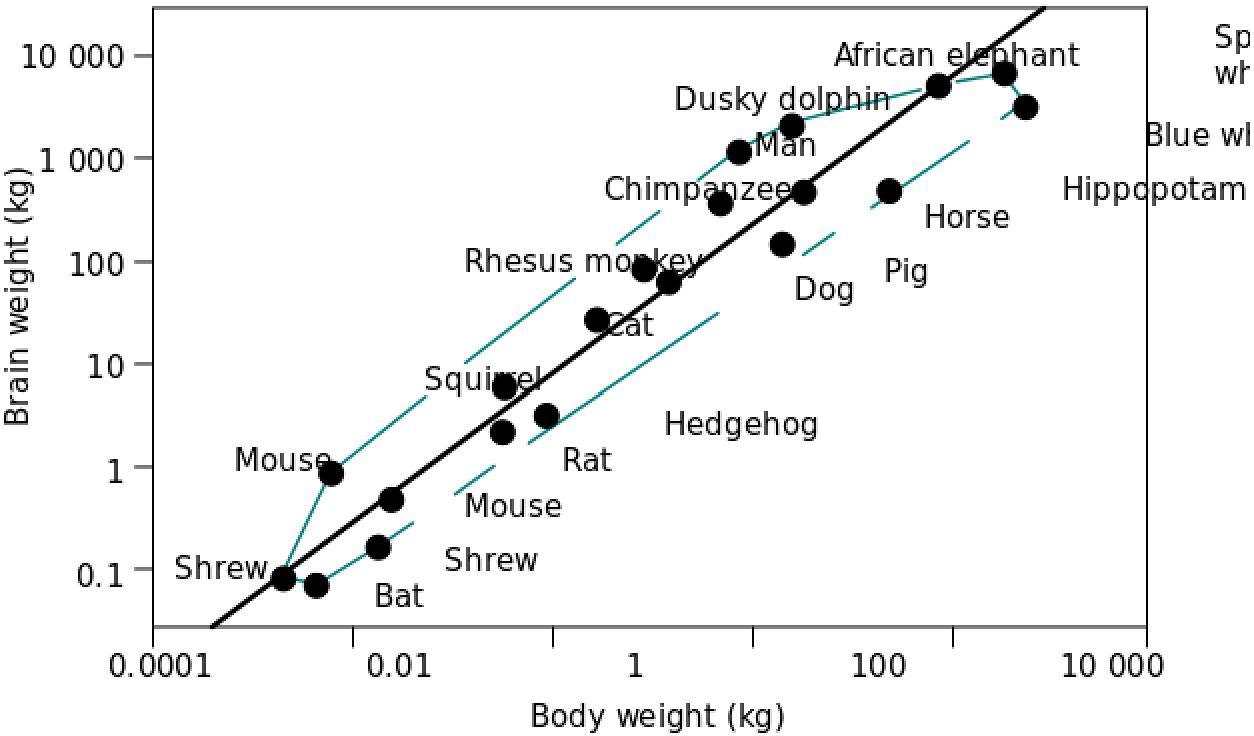
“gorillas and orangutans, rather than humans, are outlier species in terms of body size” {Brain: 1% vs 2% of body mass}

(Semendeferi and Damasio, 2000)

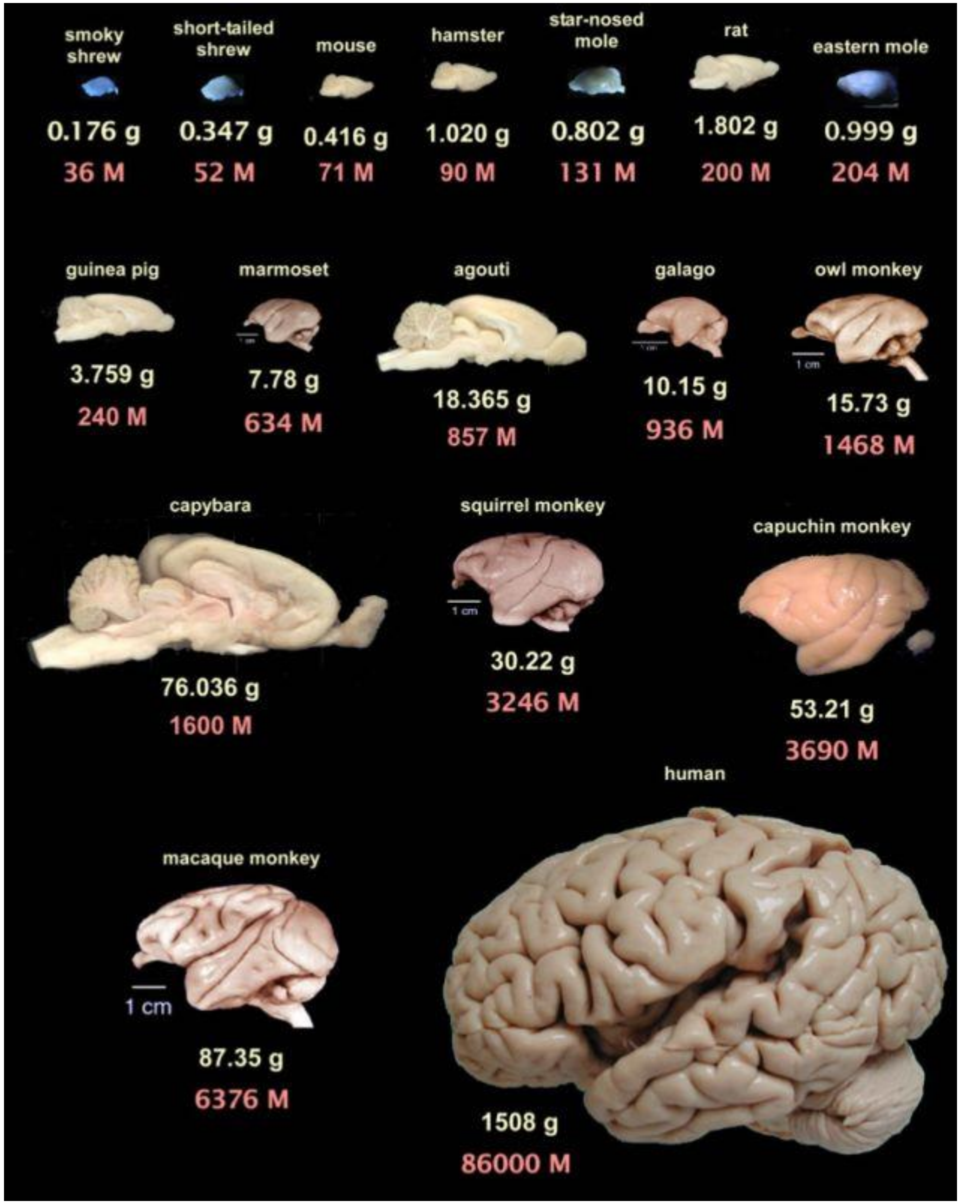
(Barton, 2006; Herculano-Houzel et al.,2007).
The human brain in numbers: a linearly scaled-up primate brain; Herculano-Houzel, 2009

MYTH #3: HUMAN BRAINS ARE THE RELATIVELY LARGEST ?

NO!



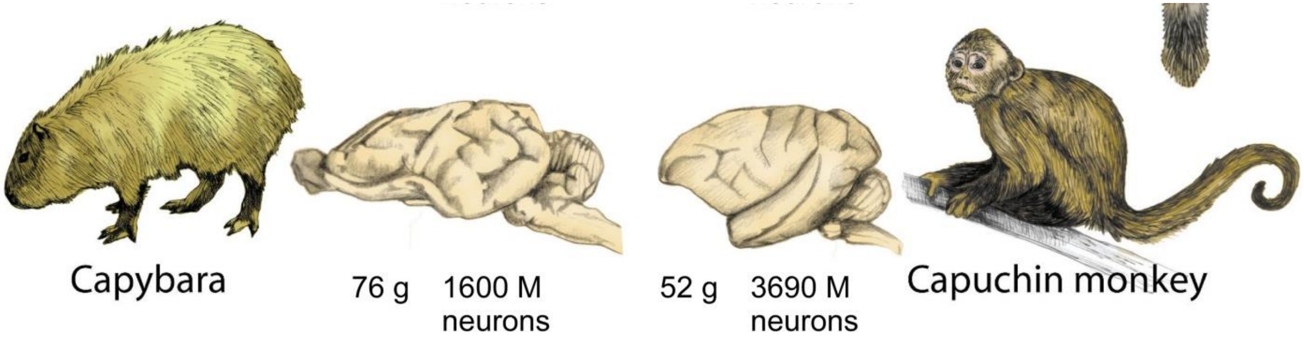
MYTH #4: BIGGER = BETTER

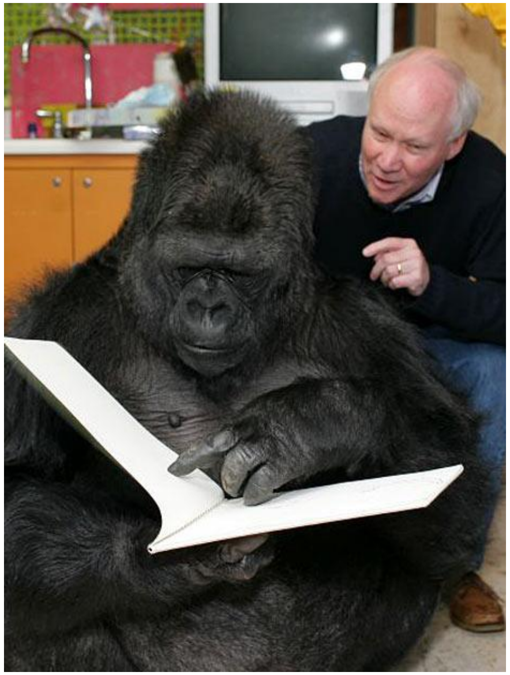


BIGGER BY RATIO OR ABSOLUTE SIZE?

Absolute?

Capybara vs Capuchin Monkey:





Relative?

Gorilla Vs Capuchin

(Roth and Dicke, 2005)

DEAR BAYESIANS, WHO CAN GUESS: HOW MANY **CELLS** IN THE BRAIN?

- 50 Billion? 500 billion? 60,000,000?
  - **% Neurons**? 10%? 25%?
- **% Glia**? 90%? 1%?

MYTH #5: 100 BILLION NEURONS

Azevedo, Herculano-Houzel, Lent et al. (2009). Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. *The Journal of comparative neurology*, *513*(5), 532-41.

“There was, to our knowledge, no actual, direct estimate of numbers of cells or of neurons in the entire human brain until 2009” [HH].

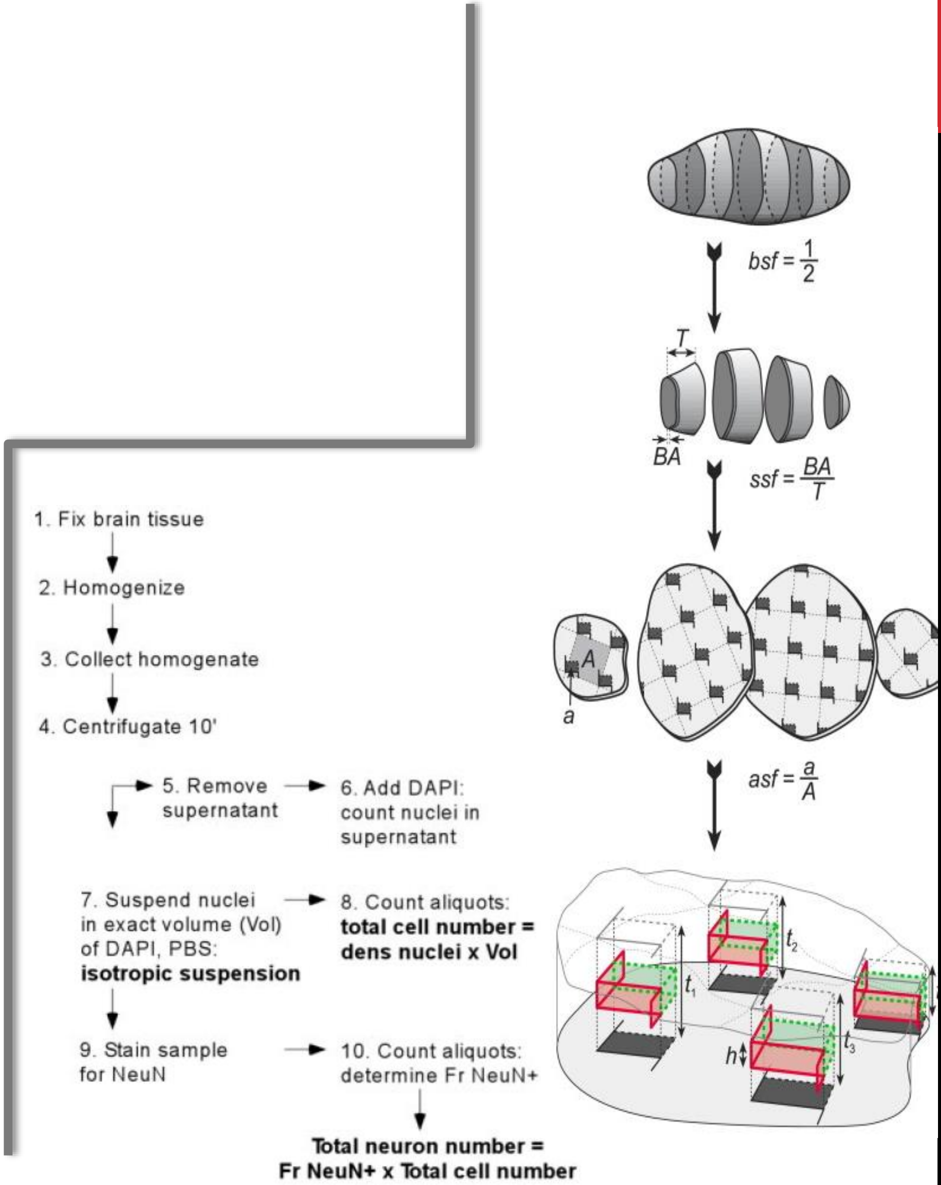
“It is commonly assumed that glia outnumber neurons in the brain and specifically in humans by a factor of 10 or 50 despite the lack of data for these assumptions {Kandel, 2000} .

Azevedo, Herculano-Houzel, Lent et al. (2009). Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. *The Journal of comparative neurology*, *513*(5), 532-41.

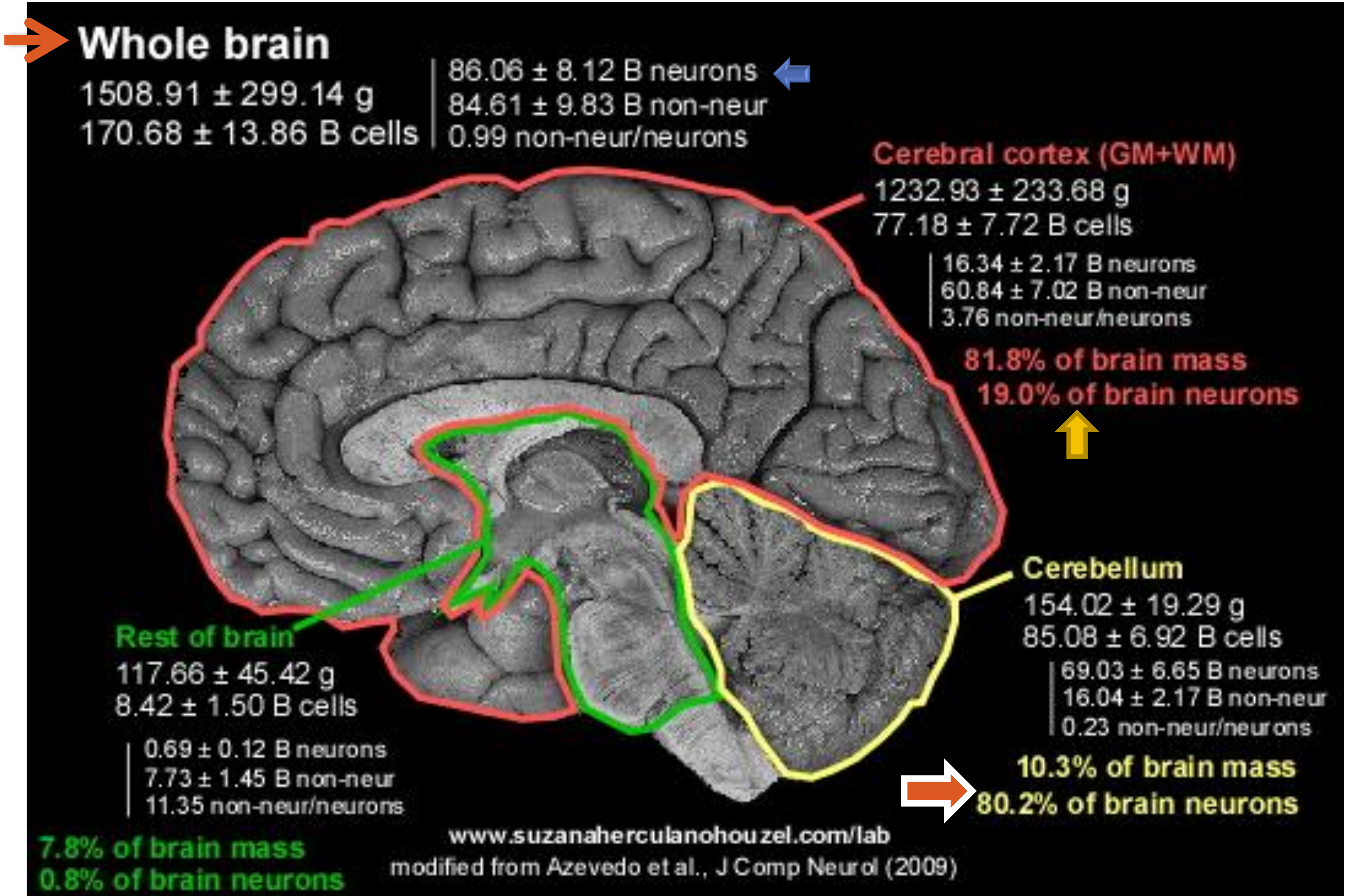
THE ISOTROPIC FRACTIONATOR

Method:

1. Make soup of brain.
2. Highlight neurons.
3. Count density in a "cup of soup".
4. Density * "cup size" = # Neurons.



FINDINGS: - HUMANS:



FINDINGS: - HUMANS:

86 Billion neurons and 84 billion "Glia".

More Neurons than Glia!

- Cerebral Cortex: Just 19% of neurons d size and mass (*82*%)!
- Cerebellum: Just 10% of brain mass, But ~69 billion neurons - 80%!
- ***Cortex & Cerebellum Size = Same relative size as other apes***

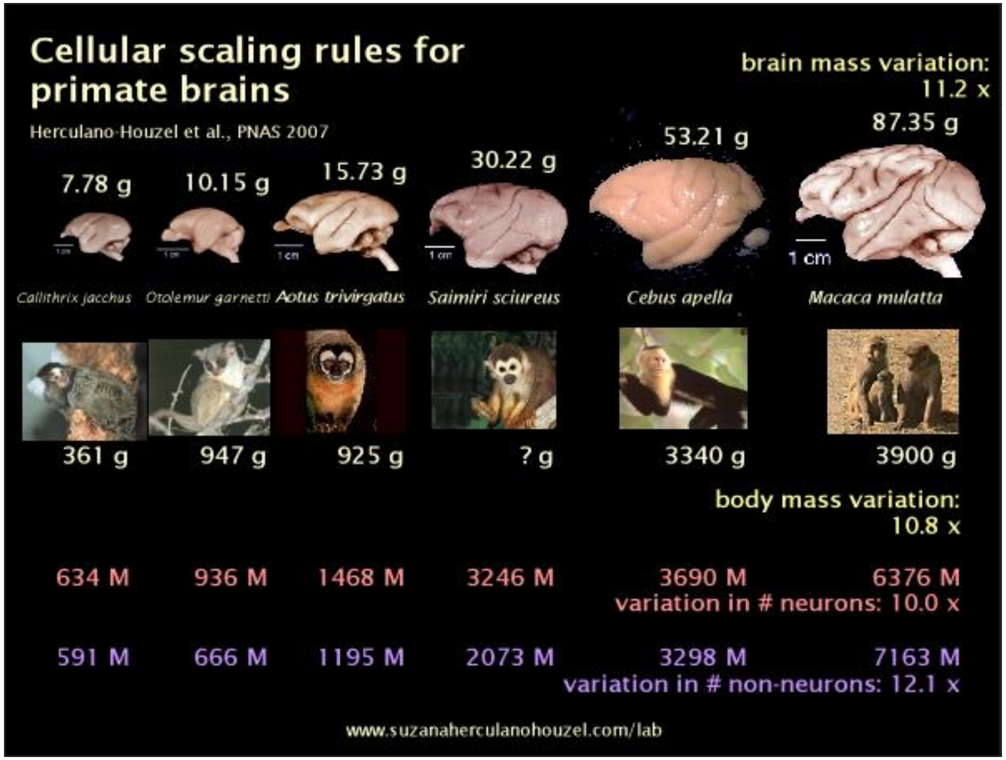
Equal Numbers of Neuronal and Nonneuronal Cells Make the Human Brain an Isometrically Scaled-Up Primate Brain; HERCULANO-HOUZEL et al., J. of Comparative Neurology, 2009

WHAT MAKES US *SPECIAL*?

Absolute Number of Neurons.

Why?:

We Have the Largest PRIMATE Brain!



WHAT MAKES US *SPECIAL*: BIGGEST PRIMATE BRAIN

(Efficient) Primate Brain Scaling

Rodents – ***Hypermetric*** Increase.

Different Specie Orders' Brains SCALE Differently!

X10 neurons in **Primates** → X11 larger brain.

X10 neurons in rodents →**X35** larger brain.

Linear, economical **cellular scaling rules** apply to primate brains. Herculano-Houzel et al, Natl Acad Sci USA (2007).;
Equal Numbers of Neuronal and Nonneuronal Cells Make the Human Brain an Isometrically Scaled-Up Primate Brain. Herculano-Houzel et al. Journal of Comparative Neurology 513:532–541 (2009)

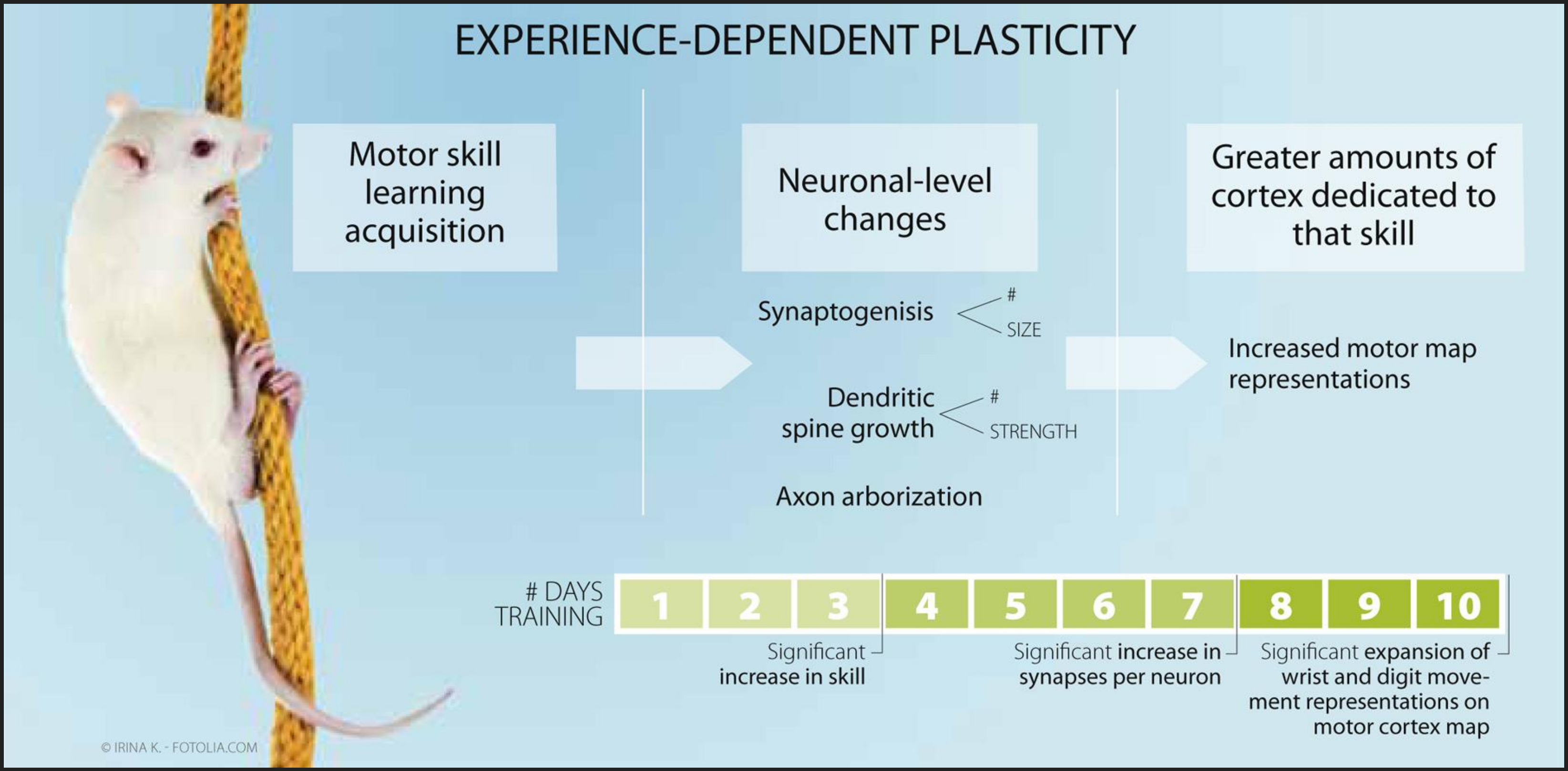
POTENTIAL SOURCES OF HUMAN "SPECIALNESS":

- **Specific Neuroanatomical regions** (Area 10 Prefrontal, lateral cerebellum..) ?
- **Connectivity** (eg: Bees)
- **Lengthy infant Development.**
- **Genes.** (Fox2 – Language..)
- **Absolute # Neurons**
- **…**

NEUROPLASTICITY: THE FLEXIBLE BRAIN

DAN OFER

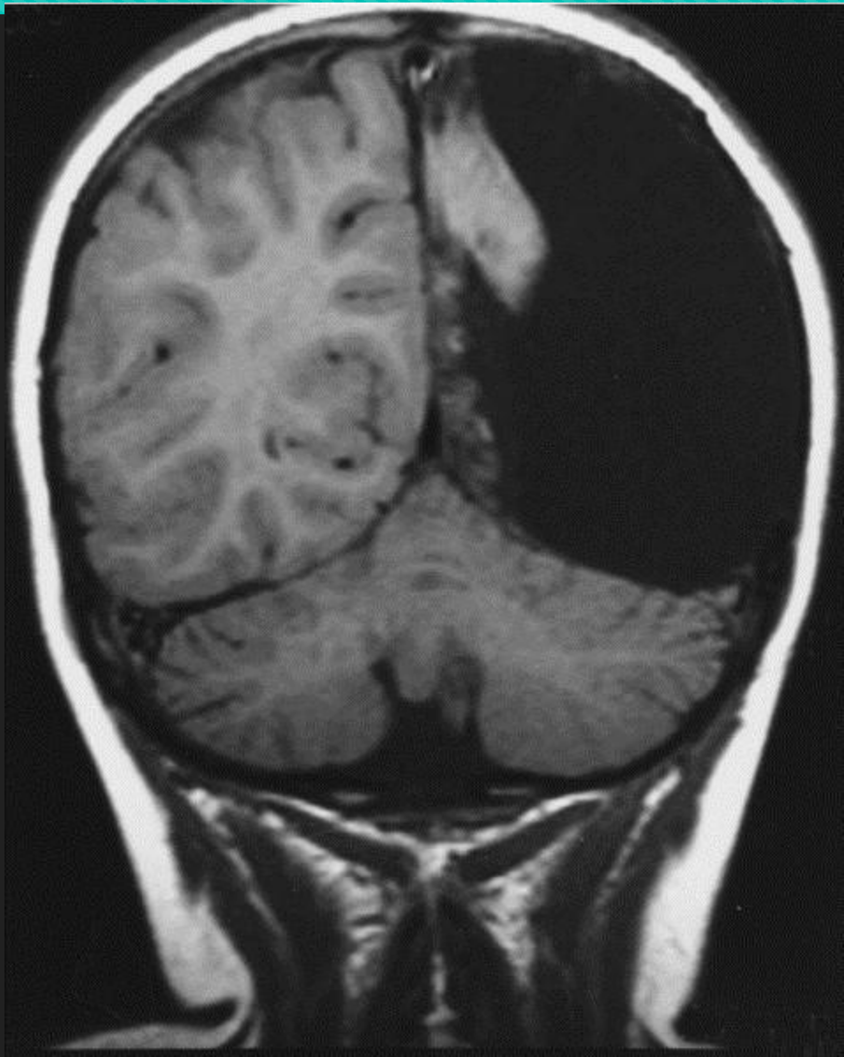
The Brain is PLASTIC! : Learning New skills



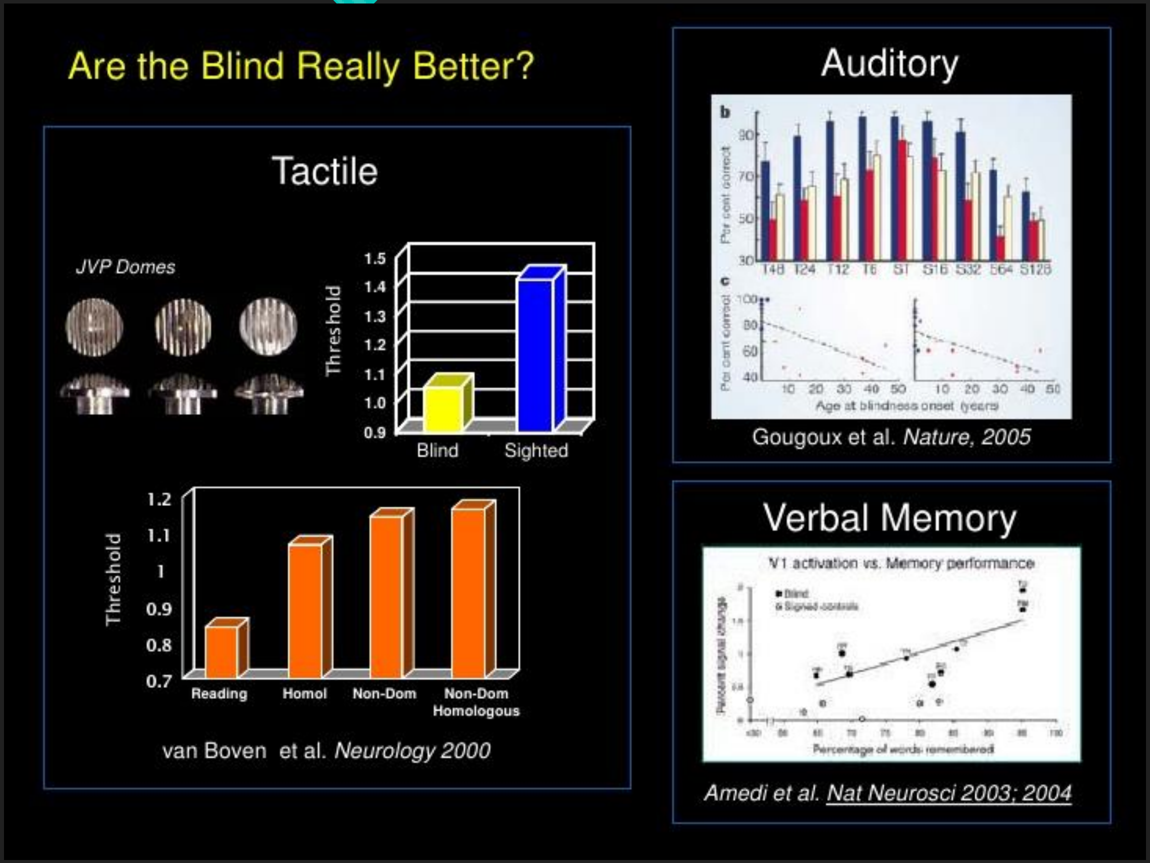
The Brain is PLASTIC! : Adapting to tissue damage (Hemispherectomy)

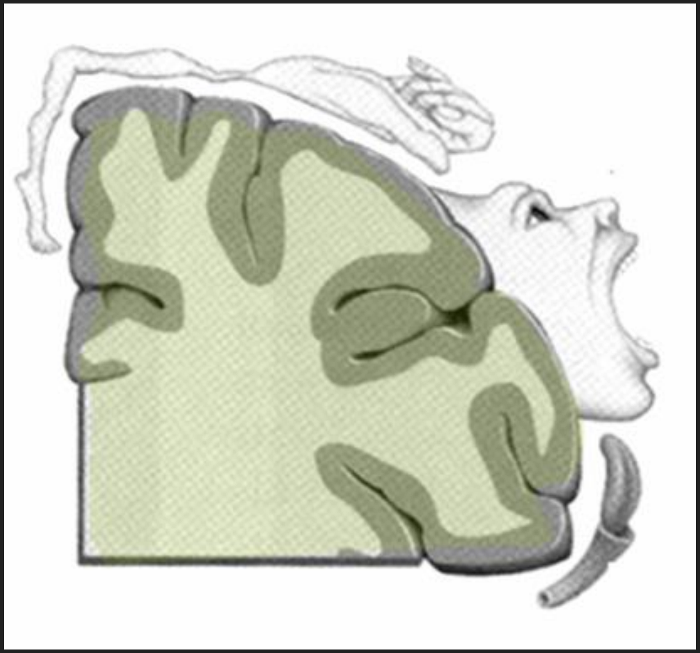
- Treatment for severe epilepsy, hydrocephalus, etc'.
- Normally done in children <6 Y.
- In most cases: FULL Recovery!

"no significant long-term effects on memory, personality, or humor, and minimal changes in cognitive function overall"



The Brain is PLASTIC! :
Adapting to Sensory loss





Voss, P., Collignon, O., Lassonde, M. and Lepore, F. (2010), Adaptation to sensory loss. WIREs Cogn Sci

Periods in NeuroPlasticity: pedals or brakes?

Dan Ofer

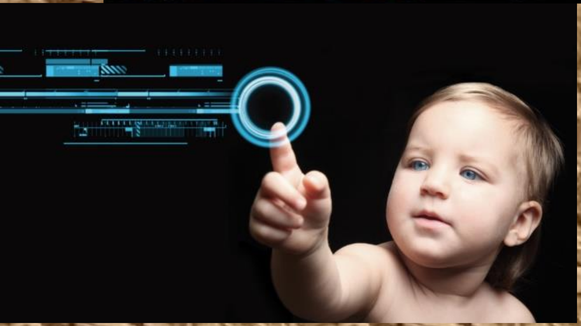
Neuroplasticity & Development

- Brains over time
- Experience dependence
- “Periods”

Stability & Plasticity

- Pedals or Brakes?
- How Stability is Maintained
- Experiments & Findings
- The Answer is…

The Early brain:



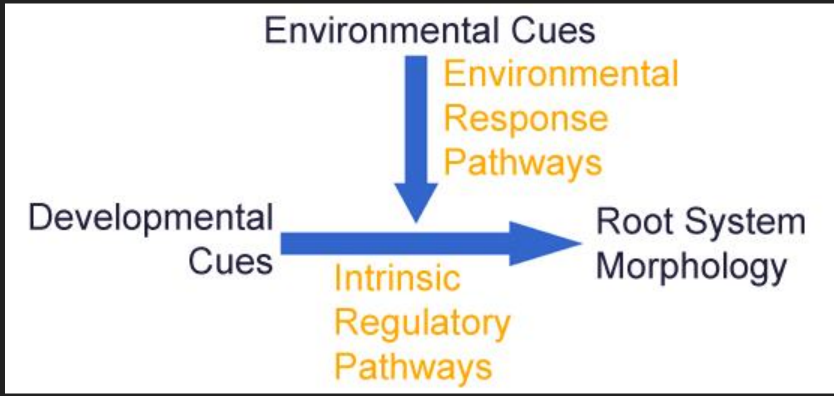
Young	Old
Learning is Easy	Learning is HARD!
Totally new abilities acquired (walking, talking..)	No new "tricks".
Most neural activity is Excitatory*	Most neural cell-cell messages are **Inhibitory**

*** Bavelier, & Hensch et al.. (2010). Removing brakes on adult brain plasticity: From molecular to behavioral interventions. Journal of Neuroscience,**

Experience and Neurodevelopment

- **Experience Dependent** Plasticity ~ Environmental input modulates.
  - Doesn't apply for all cortical circuits!
  - Different types, circuits, **periods**.
  - Depends on organism, even for the same senses ..

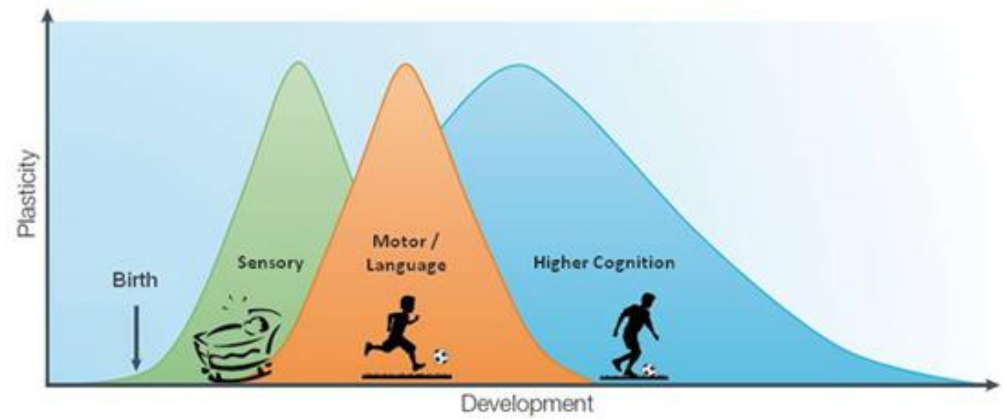
-> LET'S TALK *TIME*!



Sensitive periods

- Periods of increased sensitivity during development.
- Effects of experience are enhanced.
- **Quantitative Difference**

Fig 1: Windows of plasticity in brain development



Adapted from Hensch, T. K. (2005). Critical period plasticity in local cortical circuits. *Nature Reviews Neuroscience*, *6*(11), 877–888.

Sensitive periods (II)

Languages

0 – 6 + Years

Social Norms & behavior

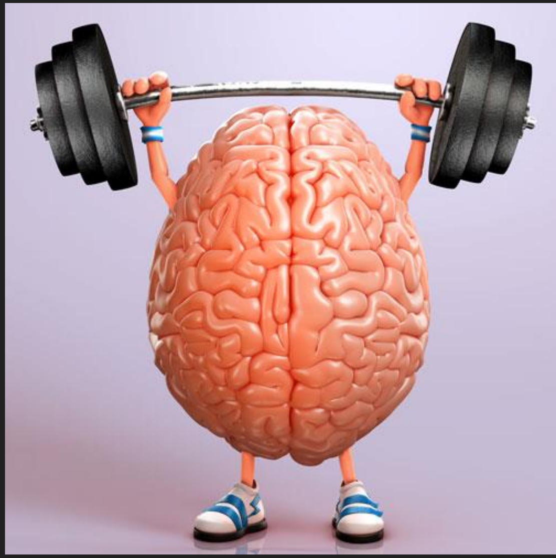
2.5 Years +

LeBlanc JJ, Fagiolini M. Autism: a "critical period" disorder? Neural Plast. 2011
Montessori, Maria (1949). *The Absorbent Mind*

Critical periods

A strict time window during which environmental experience provides information essential for a function's development and "fixates" it, permanently.

<u>*Qualitative*</u> Difference



CRITICAL PERIOD PLASTICITY IN LOCAL CORTICAL CIRCUITS. Hensch. NATURE REVIEWS NEUROSCIENCE. (2005)

Critical period for ......

…imprinting in the chick
…brain sexual differentiation
…extraocular muscle development
…visual plasticity
…monocular deprivation
…addiction vulnerability
…wing pattern induction in the polyphenic tropical butterfly
…GABAergic receptor blockade for induction of a cAMP-mediated long-term depression at CA3-CA1 synapses
…methamphetamine-induced spatial deficits
…second-language acquisition
…experience-dependent Plasticity in Visual Connections in Xenopus
…lung cancer susceptibility
…cross-modal plasticity in blind humans
…nicotine exposure effects
…disruption of primary auditory cortex by synchronous auditory inputs
…functional vestibular development in zebrafish
…right hemisphere recruitment in American Sign Language processing
…barrel cortex critical period plasticity
…feminization in tilapia
…developmental climbing fibre plasticity
…sensory map plasticity
…sensitivity to juvenile hormone
…language acquisition
…LTP at thalamocortical synapses
…caste determination in Bombus terrestris and its juvenile hormone correlates

…nicotine-induced disruption of synaptic development in rat auditory cortex
…activity-dependent synapse elimination in developing cerebellum
…conversion of ectodermal cells to a neural crest fate
…psychosis
…verbal language development
…reduced brain vulnerability to injury.
…chorda tympani nerve terminal field development
…the sensitivity of basal forebrain cholinergic neurones to NGF deprivation
…light-induced phase advances of the circadian locomotor activity rhythm in golden hamsters
…the influence of peripheral targets on the central projections of developing sensory neurons
…the specification of motor pools in the chick lumbosacral spinal cord
…axon regrowth through a lesion in the developing mammalian retina
…long-term potentiation in primary sensory cortex
…song learning in the zebra finch
…restoration of normal stereoacuity in acute-onset comitant esotropia
…transcription for induction of a late phase of LTP.
…regeneration capability of adult rat retinal ganglion cells after axotomy
..synaptogenesis
..experience-dependent synaptic plasticity in rat barrel cortex
..peripheral specification of dorsal root ganglion neurons

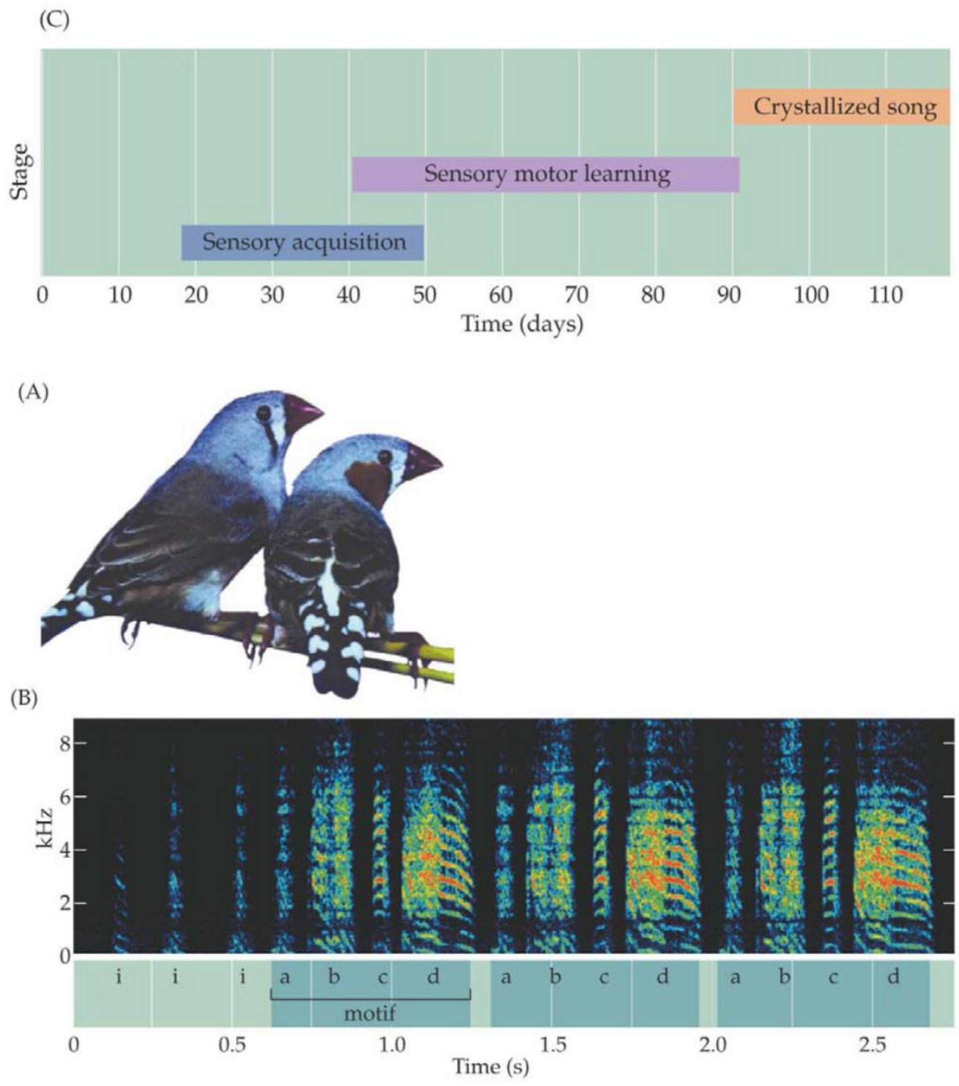
Critical period: Parental Imprinting

Critical Period for Song Acquisition

Selectivity for songs of own species.

In the lack of own species' song ….adaptation.

Critical period ends at puberty

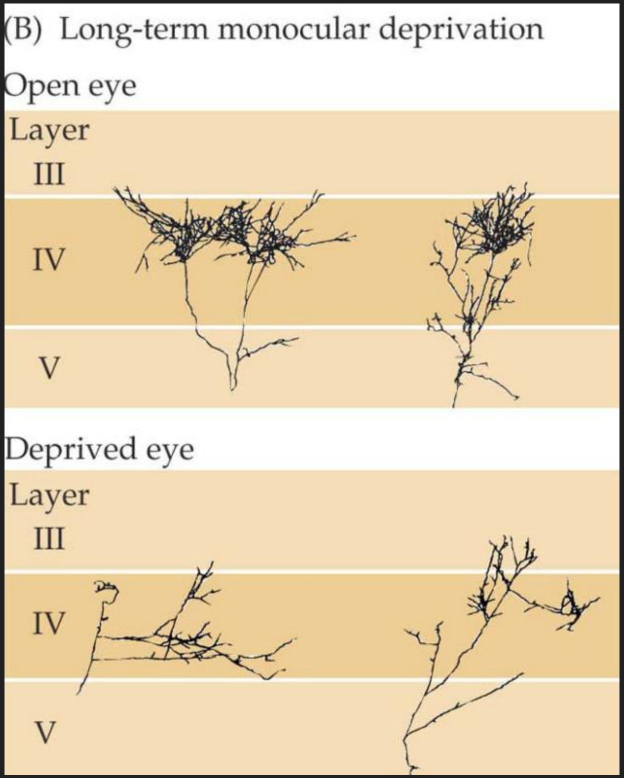


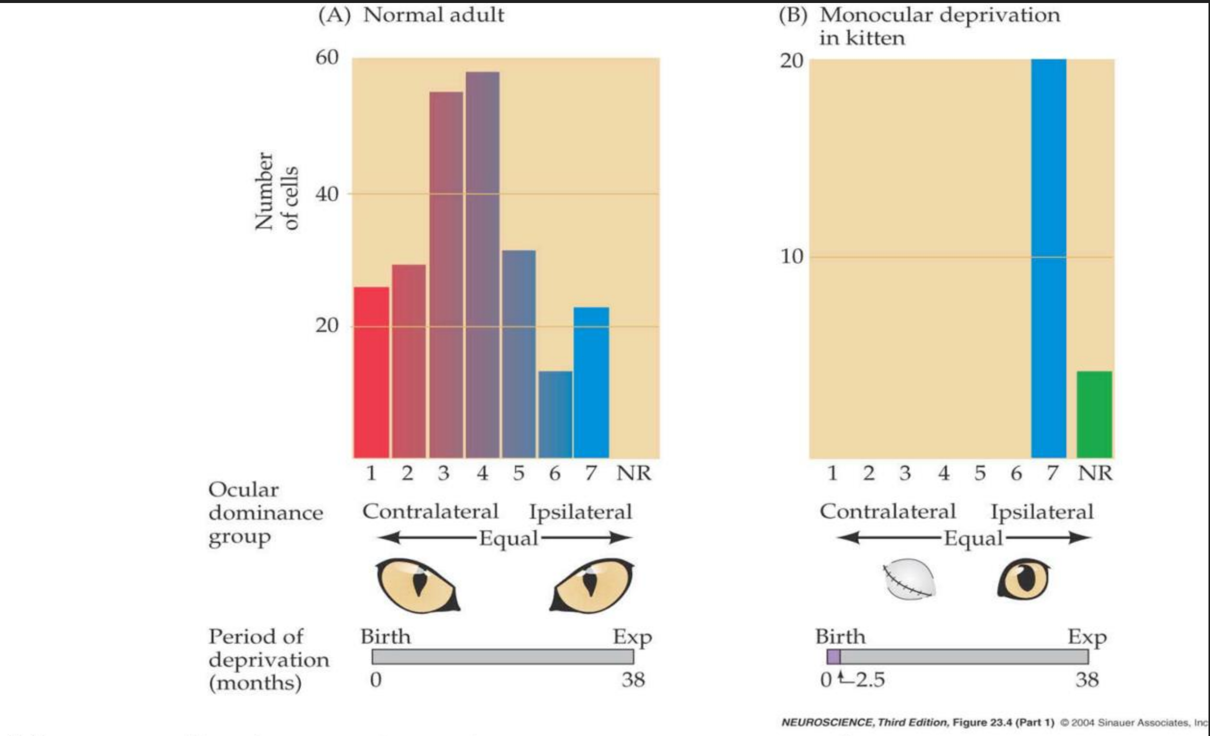
Critical period: ocular dominance monocular deprivation

- Hubel & Wiesel.
- Showed that ocular deprivation during CP causes monocular dominance, *Ambylopia*.
- Only during *critical period*.
- Common experimental system for critical period in visual system.

Wiesel, Hubel (1963). "Effects of visual deprivation on morphology and physiology of cell in the cat's lateral geniculate body". Journal of Neurophysiology

Critical period: ocular dominance



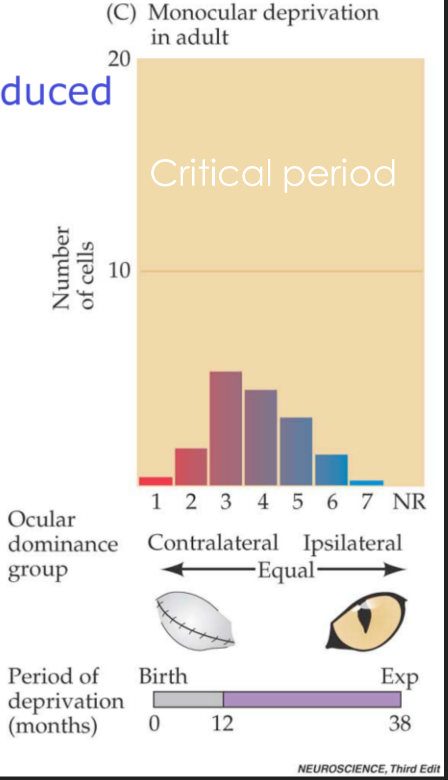


More cells in cortex become monocular

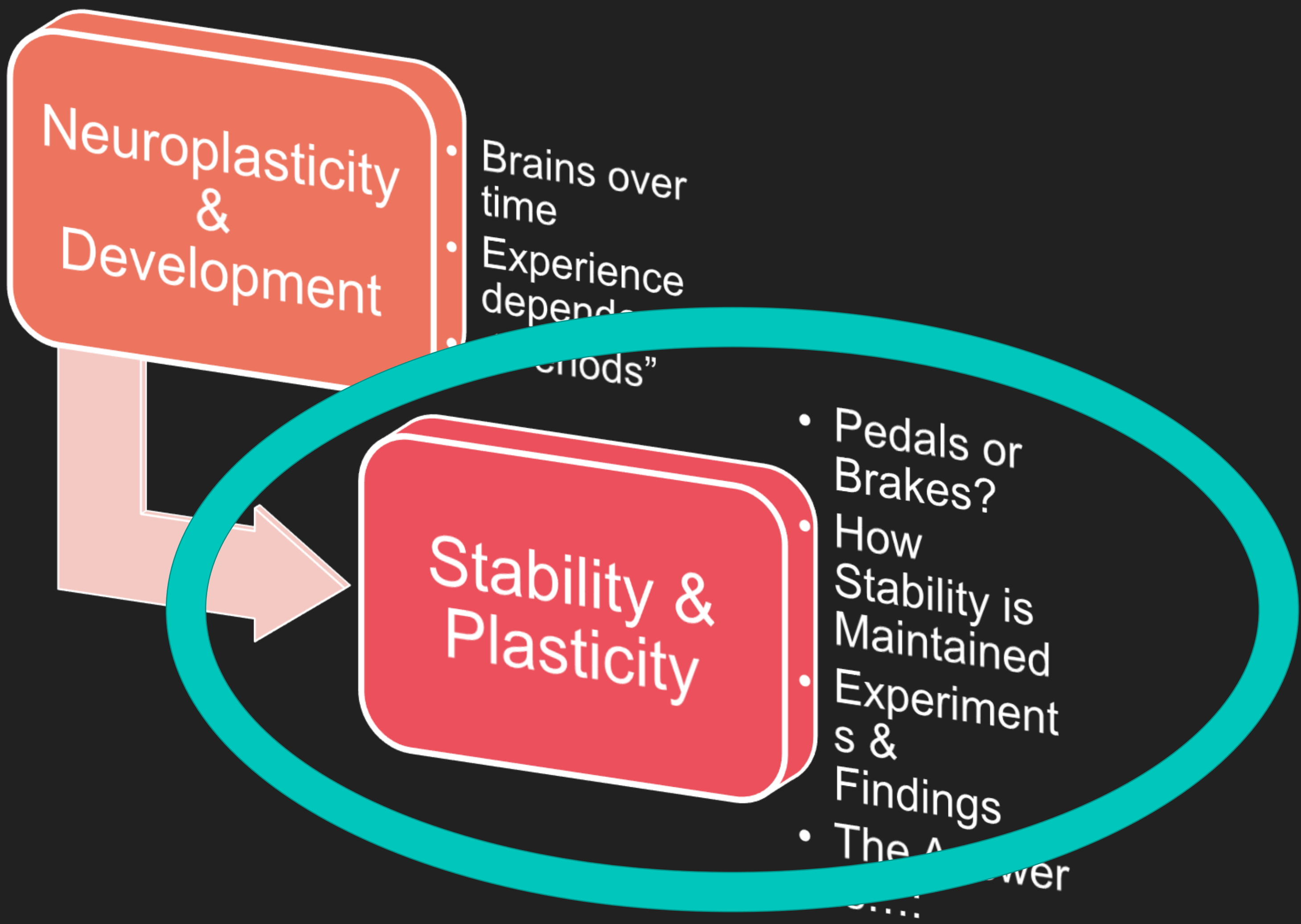
Critical period: ocular dominance

Can this be just an outcome of reduced activity from one eye?

No. Monocular deprivation in the adult does not change the physiology or the anatomy.



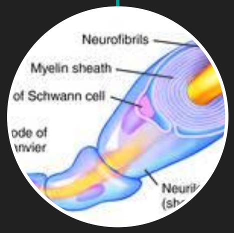
- Only during *critical period*.
- Common experimental system (for critical period).


Neuroplasticity & Development
Brains over time
Experience
Stability & Plasticity
Pedals or Brakes?
How Stability is Maintained
Experiments & Findings

Questions:

- What is the "default" state of plasticity in the brain?
  - Plastic or stable?
- What are the factors that control or regulate cortical plasticity?
  - State "maintenance".
  - Switching between states.
- Could we make adult brains pliable & plastic?

(I) Structural Stabilization:



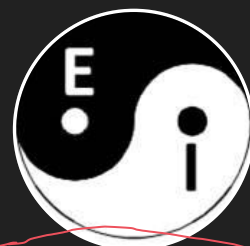
Myelinization

Glia, Astrocytes

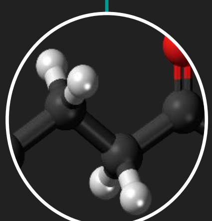
Perineuronal nets. Parvalbumin Intern eurons

Experience-driven plasticity of visual cortex limited by myelin and Nogo receptor. Science. (2005).
Bavelier, Hensch, et'. Removing Brakes on Adult Brain Plasticity: From Molecular to Behavioral Interventions. J. Neuroscience (2010).
Bardin, J. Neurodevelopment: unlocking the brain. *Nature* **487**, 24–6 (2012).
Hensch. Critical period plasticity in local cortical circuits. *Nat. Rev. Neurosci.* (2005).

(II) Functional Stabilization:



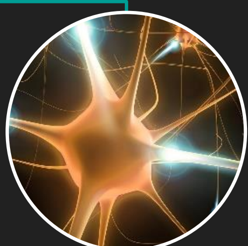
$$\frac{\text{Excitation}}{\text{Inhibiton}}$$



GABA

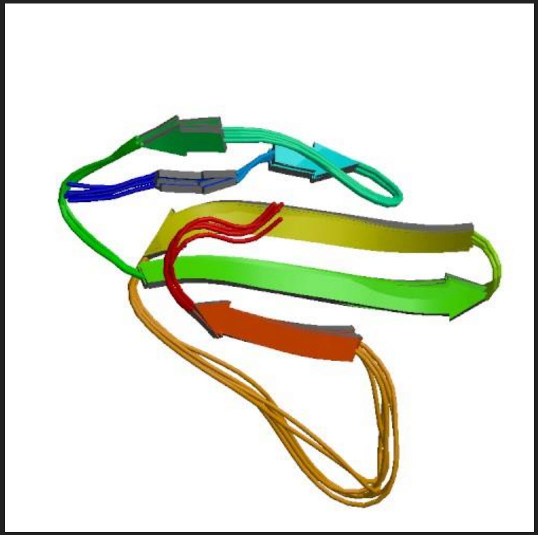
Inhibitory. **Required for Crit. P!**

LYNX 1



More: HDAC. .

Lynx1 *brakes* Plasticity in the Adult Cortex



Acetylcholine Antagonist.

- Binds to Ach receptors.
- ToLIP (Toxin Like Protein)

Morishita, Hensch, et al'. "Lynx1, a cholinergic brake, limits plasticity in adult visual cortex". *Science* (2010).
"Lynx for braking plasticity". *Science* (2010).

Lynx1 brakes Plasticity in the Adult Cortex

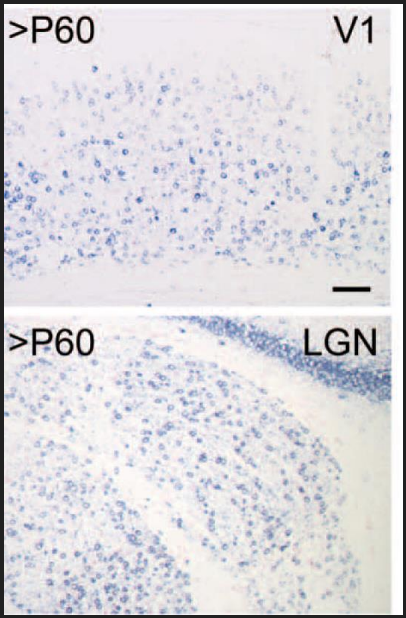
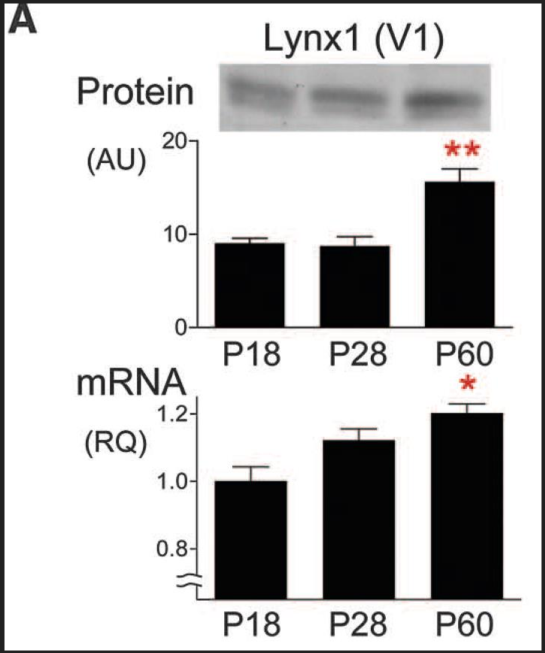
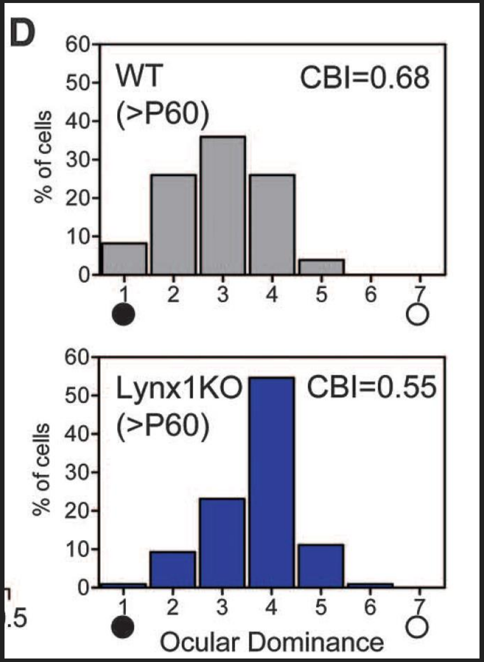


Fig. 1. Lynx1 expression increases in adulthood to limit visual plasticity. (**A**) Expression of Lynx1 protein (top) and mRNA (bottom) across the critical period (CP) (pre-CP: P18; CP: P28; post-CP: P60). $^{**}P < 0.01$, $^{*}P < 0.05$, one-way analysis of variance.



Morishita, Hensch, et al'. "Lynx1, a cholinergic brake, limits plasticity in adult visual cortex". *Science* (2010).

Lynx1 brakes Plasticity in the Adult Cortex



(D) Short-Term Monocular Deprivation shifts the ocular dominance distribution of Lynx1 knock-out (KO) mice [bottom], but not in wild-type (WT) mice.

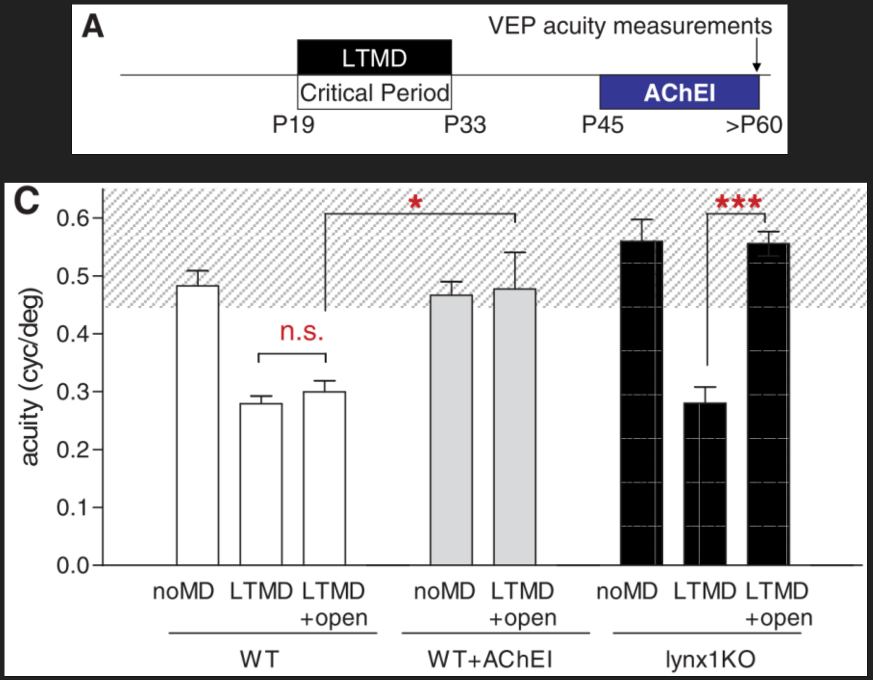
Lynx1 KO reopens Critical Period Plasticity in the Adult visual Cortex

Fig. 3. Recovery from amblyopia in Lynx1 KO mice.

(A) After long-term MD (LTMD) spanning the critical period, the deprived eye was reopened & VEP (visual evoked potential) acuity was measured in V1.

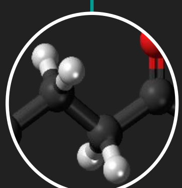
(C)Visual acuity in WT mice (white) without deprivation [no MD] decreases after LTMD spanning CP and endures. Reopening the deprived eye together with Ach inhibitor (AChEI) restores vision.

Lynx1 KO mice (black bars) spontaneously recover from LTMD simply by reopening the deprived eye to reach normal levels.



Functional Stabilization:

$$\frac{\text{Excitation}}{\text{Inhibiton}}$$



GABA

LYNX1

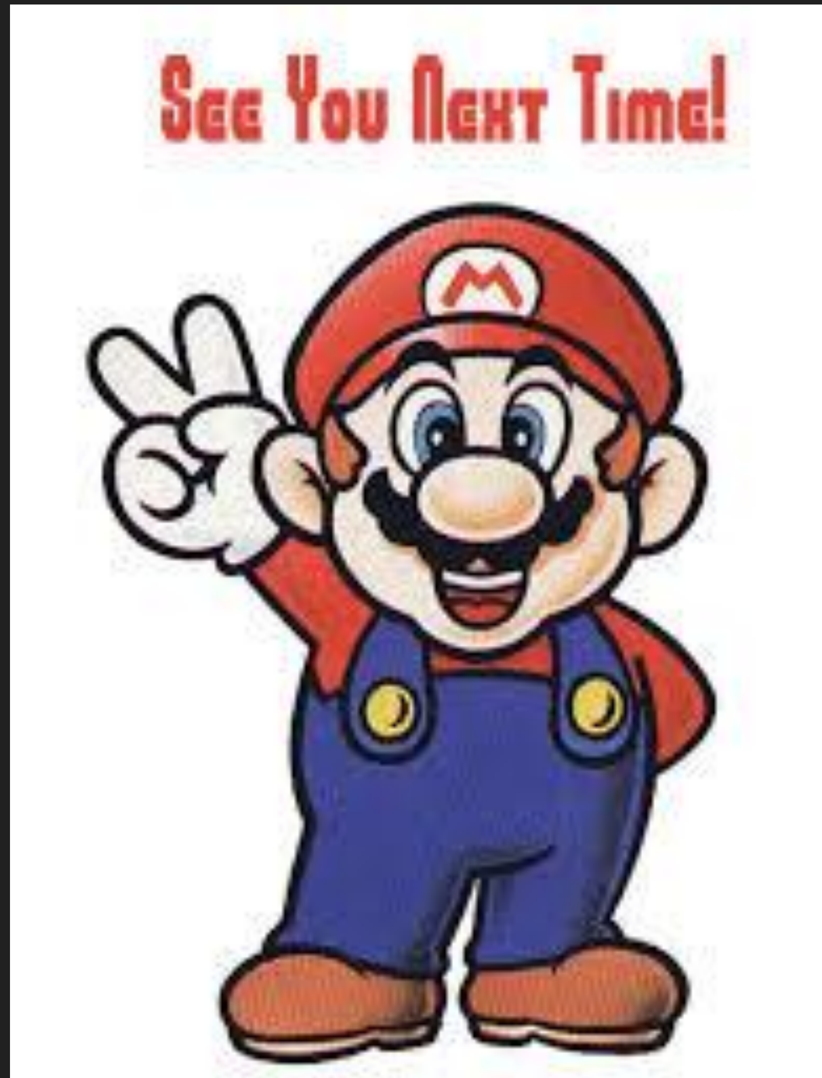
More Factors:

(**HDAC** – Histone-Deacetylase..)

Conclusions:

- ***Default state is <u>plastic</u>, not stable.***
- **Stable state is maintained by molecular brakes. (Lynx1, others).**
- **E/I ratio important to critical period "timer" activation.**
- **Don't confuse Critical and Sensitive periods!**

- **Many more factors to discover?**
- **MASSIVE clinical potential.**


See You Next Time!