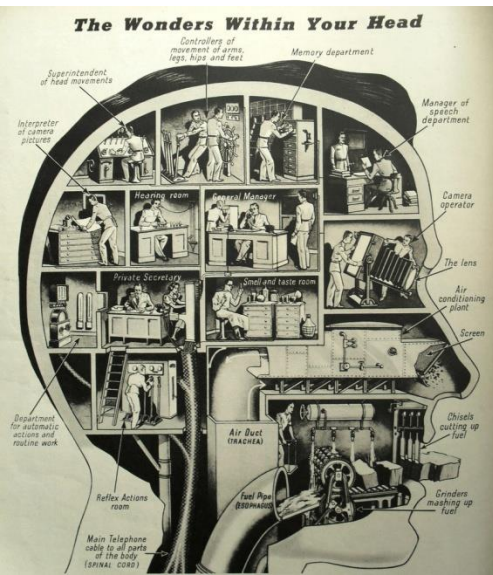
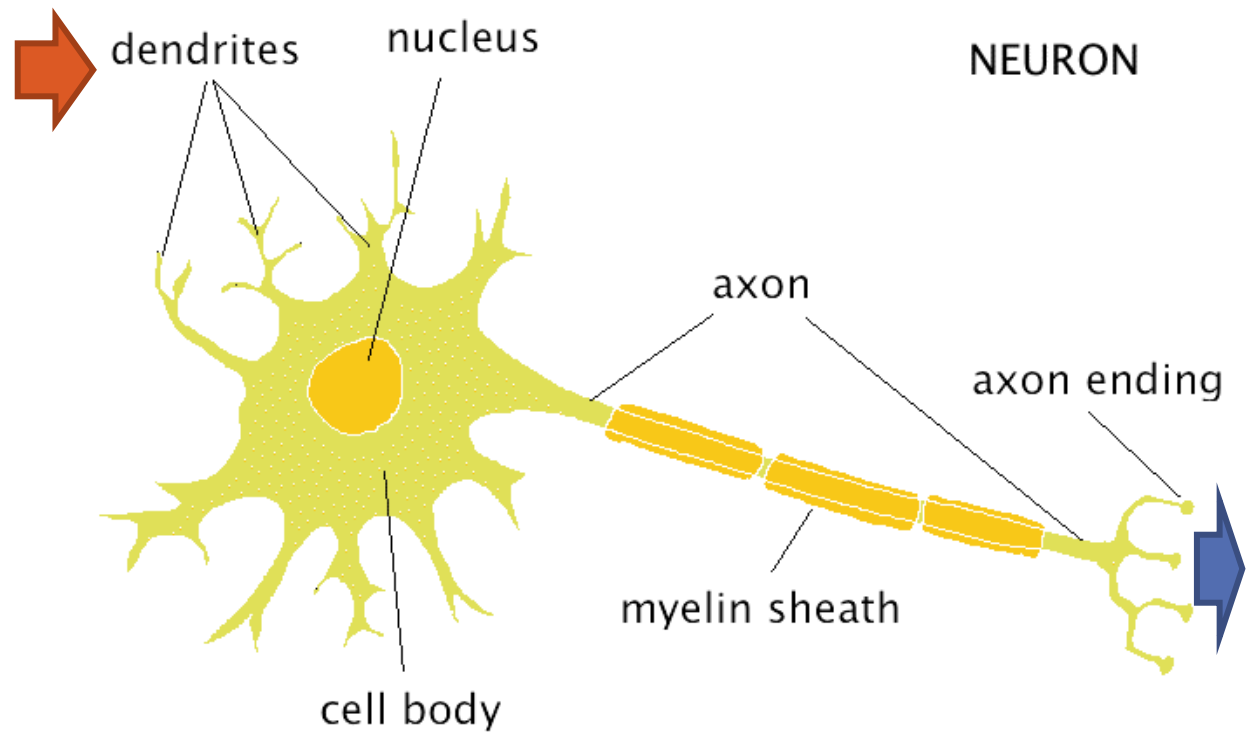


NEURON:

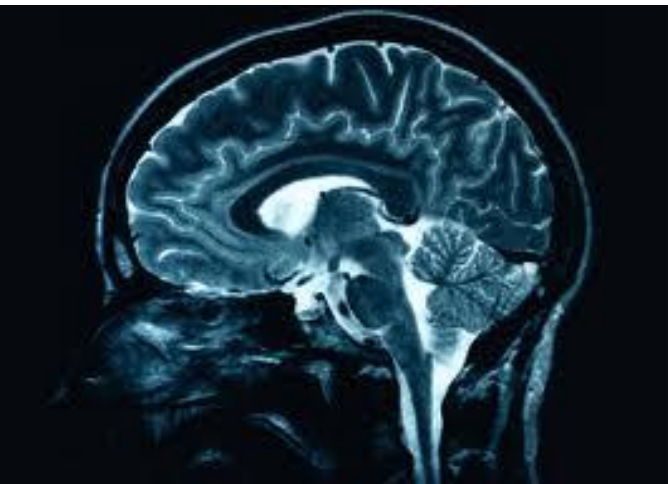



Glial cells are nerve cells that don't carry nerve impulses.
Include: Immune system, support, nutrients..

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

NO! Evidence


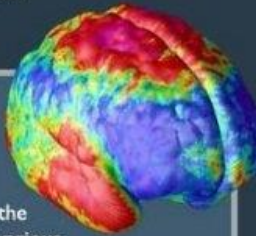
1. : fMRI. PET scans.
2. Effects of Damage.
3. Evolution.(Wasted space)





You use only 10% of your Brain

Over the years, the myth that you only use about 10% of your brain has been widely spread with the source of this myth often falsely attributed to Albert Einstein. Amazing amounts of research have gone into mapping the brain, in terms of figuring out the function of various parts of the brain, and, to date, no area of the brain has been found that doesn't have some function, even though that function may not be yet wholly understood. Brain scans, courtesy of Positron Emission Tomography (PET) and Functional Magnetic Resonance Imaging (fMRI) technologies, show us that, even while we are sleeping, every part of the brain shows at least a small amount of activity and most areas of the brain are active at any given moment, assuming the person being scanned hasn't ever suffered some form of brain damage. If 90% of the brain wasn't used for anything, then damage to that 90% of the brain shouldn't affect a person at all. In reality though, damage to just about any part of the brain, even tiny amounts of damage, tend to have profound effects on the person who suffers that damage, proving that we use all of the brain and not just 10%



5 BRAIN MYTHS:

MYTH #2: BIGGER = BETTER BRAIN

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

MYTH #3: HUMAN BRAINS ARE THE RELATIVELY LARGEST

1. Brain/body mass ratio
2. Encephalization quotient

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

MYTH #4: BIGGER BRAIN = MORE NEURONS THAN A SMALLER BRAIN

neuronal density = # neurons relative to mass of brain

MYTH #5: 100 BILLION NEURONS

Neurons are the fundamental building blocks of any nervous system. These cells, tree-like branches which reach out with their neighbors, forming vast electrical and chemical network that is our brain. It's our neurons that allow our brains to do all of these things more rapidly and efficiently than any machine.

DEAR (FUTURE) SCIENTISTS, WHO CAN TELL ME:



- How Many Cells in the brain?
 - % Neurons? 10%? 25%?
 - % Glia? 90%? 1%?

I. Comparative Brains: Isotropic Fractionation + Findings

II. Is the Human Brain *Neuroanatomically* Unique?

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

“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

1. Method

I. Theoretical basis.

II. How it works.

2. Benefits

3. Findings:

- a. Rats & Glia
- b. Humans.

1. Fix brain tissue
2. Homogenize
3. Collect homogenate
4. Centrifuge 10'

5. Remove supernatant
6. Add DAPI: count nuclei in supernatant

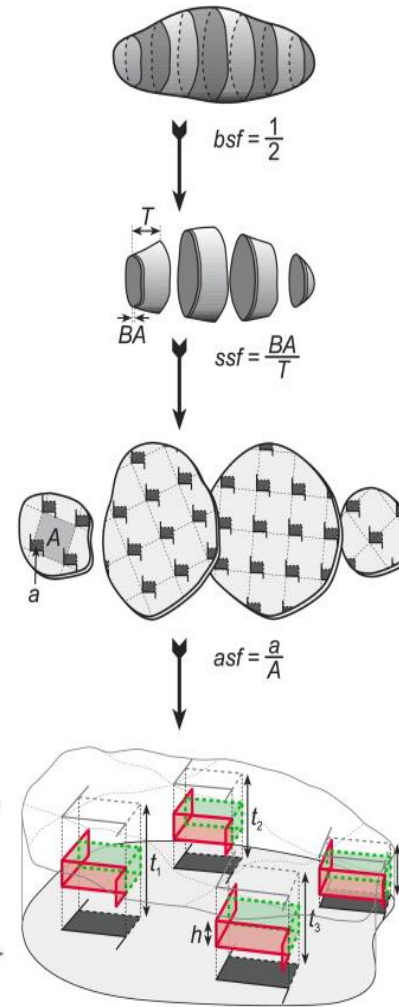
7. Suspend nuclei in exact volume (Vol) of DAPI, PBS: isotropic suspension

9. Stain sample for NeuN

8. Count aliquots: **total cell number = dens nuclei x Vol**

10. Count aliquots: determine Fr NeuN+

Total neuron number = Fr NeuN+ x Total cell number

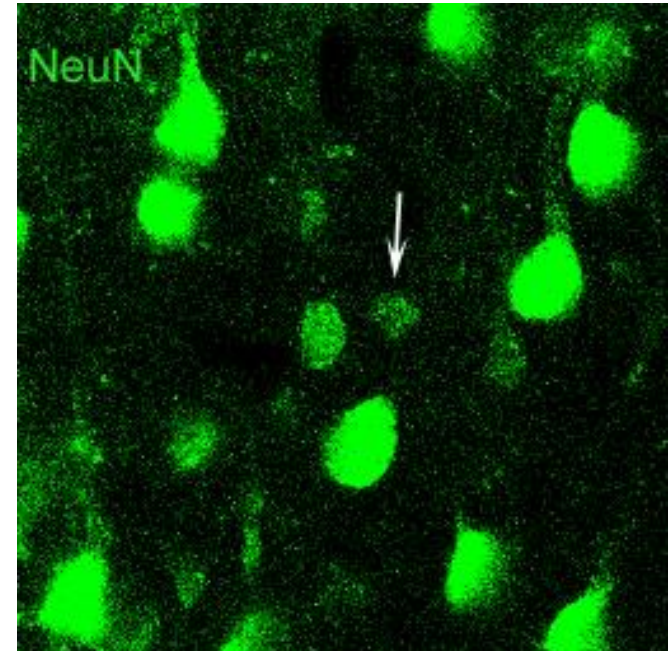


ISOTROPIC FRACTIONATION

THEORETICAL BASIS: 2 AXIOMS

1. 1 Cell = 1 Nucleus

2. **NeuN** - neuronal nuclei
specific protein



Iso = Equal

Mullen, et al. (1992). "NeuN, a neuronal specific nuclear protein in vertebrates". *Development* **116**;

ISOTROPIC FRACTIONATION

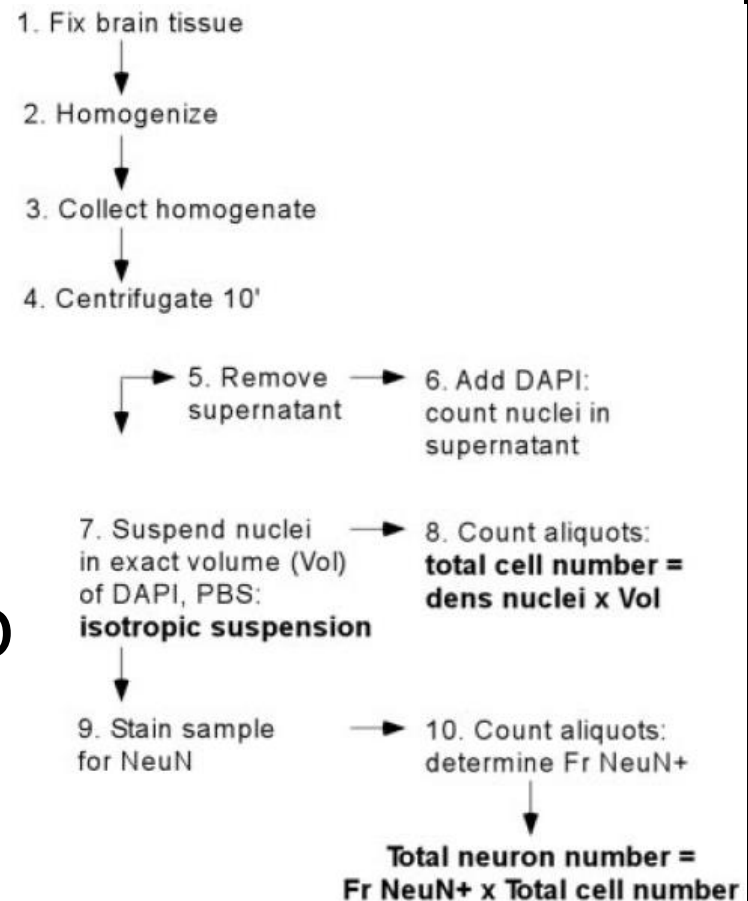
HOW IT WORKS (I):

A. "Slice" Preserved Brain
(Or structures)

B. "Stir" (Homogenize +
Centrifugate)

C. **DAPI** (DNA dye) Stain.

D. "Pour"
homogenate+DAPI into
Vat(s) in a **isotropic**
suspension



ISOTROPIC FRACTIONATION

HOW IT WORKS (II):

E. Extract (8+) aliquots
(דגימות)

F. Count with hemocytometer →
(= microscope counting).

$$\text{Total Cell \#} = \text{Nuclei Density} \times \text{Volume}$$

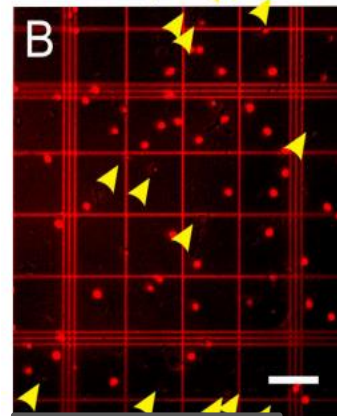
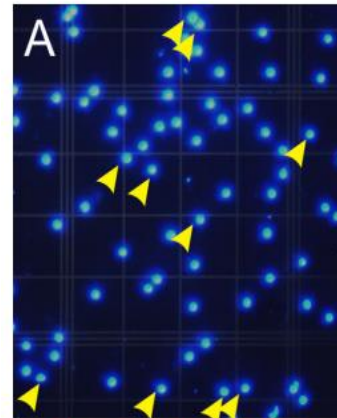
G. Add NeuN specific Antigen
(Mark Neurons).

H. Count "Neurons" (NeuN⁺)

$$\text{Glia Cell\#} = \text{Total Cell\#} - \text{\#NeuN+}$$

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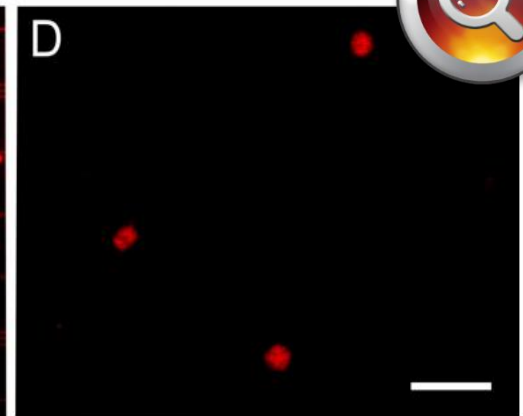
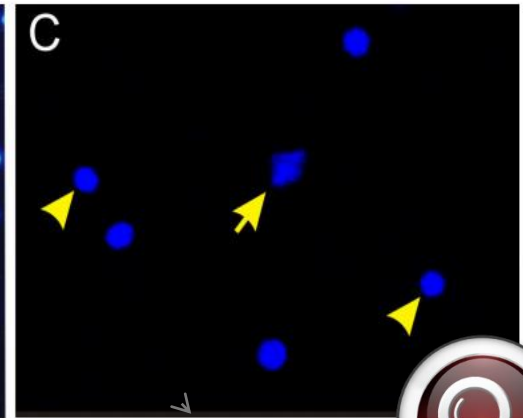
A: DAPI



B: NeuN

Arrowheads = NeuN
negative (=Glia)

F.A.C. AZEVEDO ET AL.



Aspect of the nuclei in the hemocytometer. A,B: Typical low-magnification fluorescent micrographs of the same field of cerebellar cell nuclei in suspension stained with DAPI (A) and for NeuN immunoreactivity (B). The arrowheads indicate nuclei that are NeuN negative and therefore identified as nonneuronal nuclei. All other nuclei are NeuN positive and therefore identified as neuronal. Note that nuclei are intact and well scattered. C,D: High-magnification confocal image of NeuN-negative (arrowheads; arrow, nonneuronal nucleus undergoing cell division) and

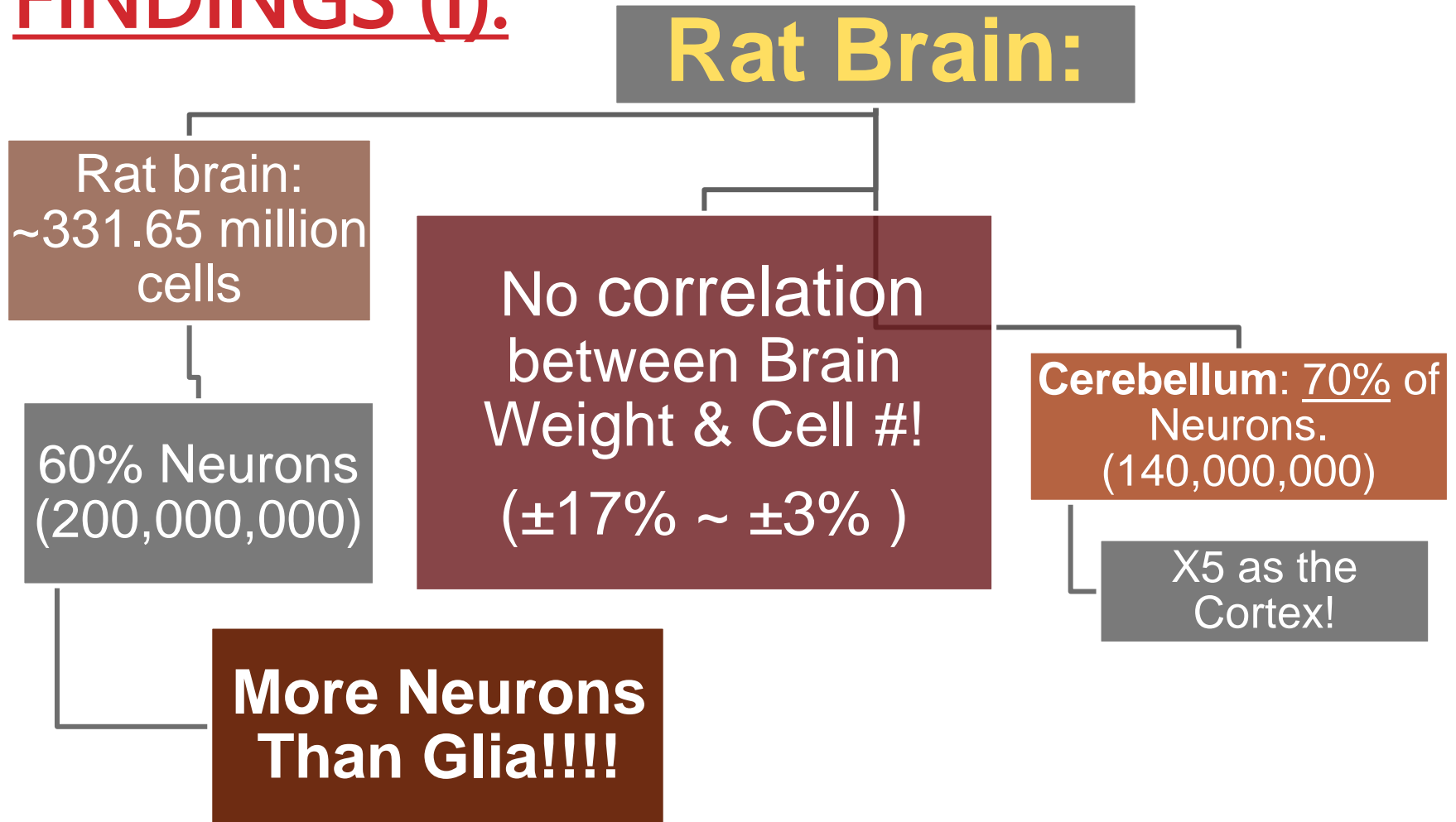
ISOTROPIC FRACTIONATION

BENEFITS:

**Absolute,
accurate
quantitative
count** of
Neurons, Glia

Less room for human error.
Can Analyze whole brain, not just
slices or regions.
Yields absolute Cell Count
independent of Brain Volume/Mass.

ISOTROPIC FRACTIONATION FINDINGS (I):



Herculano-Houzel and Lent; Isotropic Fractionator: A Simple, Rapid Method for the Quantification of Total Cell and Neuron Numbers in the Brain; *Journal of Neuroscience*, 2005

FINDINGS (II): - HUMANS:

→ Whole brain

1508.91 ± 299.14 g

170.68 ± 13.86 B cells

86.06 ± 8.12 B neurons

84.61 ± 9.83 B non-neur

0.99 non-neur/neurons

Cerebral cortex (GM+WM)

1232.93 ± 233.68 g

77.18 ± 7.72 B cells

16.34 ± 2.17 B neurons

60.84 ± 7.02 B non-neur

3.76 non-neur/neurons

81.8% of brain mass

19.0% of brain neurons

Cerebellum

154.02 ± 19.29 g

85.08 ± 6.92 B cells

69.03 ± 6.65 B neurons

16.04 ± 2.17 B non-neur

0.23 non-neur/neurons

10.3% of brain mass

80.2% of brain neurons

Rest of brain

117.66 ± 45.42 g

8.42 ± 1.50 B cells

0.69 ± 0.12 B neurons

7.73 ± 1.45 B non-neur

11.35 non-neur/neurons

7.8% of brain mass

0.8% of brain neurons

www.suzanaherculanohouzel.com/lab

modified from Azevedo et al., J Comp Neurol (2009)

FINDINGS (III): - HUMANS:

Our brain has 86 ± 8 billion NeuN+
("neurons") and ~84.6 billion "Glia".

NOT 100 Billion!

- *More* Neurons than Glia!
Nonneuronal/Neuronal ratio = 0.99 for whole human brain.
- Cerebral Cortex: contains just 19% of neurons despite size and mass (~~82%~~)!
- Cerebellum: Just 10% of brain mass, But ~69 billion neurons - 80%!

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

IS THE HUMAN BRAIN 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”

CORTEX SIZE

“Oversized Neo-cortex” - **82%**
of the Brain's mass.

The cortex contains only **19%**
of neurons!



*Cerebellar cortex & Cerebellum
Size = Same relative size as Apes*

BUT! Mass =!> Neuron

**“No Correlation of Variance between
Brain Weight & # neurons!”**

(Semendeferi, 2001)

CLAIMS OF HUMAN UNIQUENESS: **CORTICAL FOLDING?**

No!

The *folding ratio* increases along with overall brain volume

Humans: 2.86;

Dolphins and whales- 4.0 - 8.55..

Von Bonin (1941); (Macphail, 247)



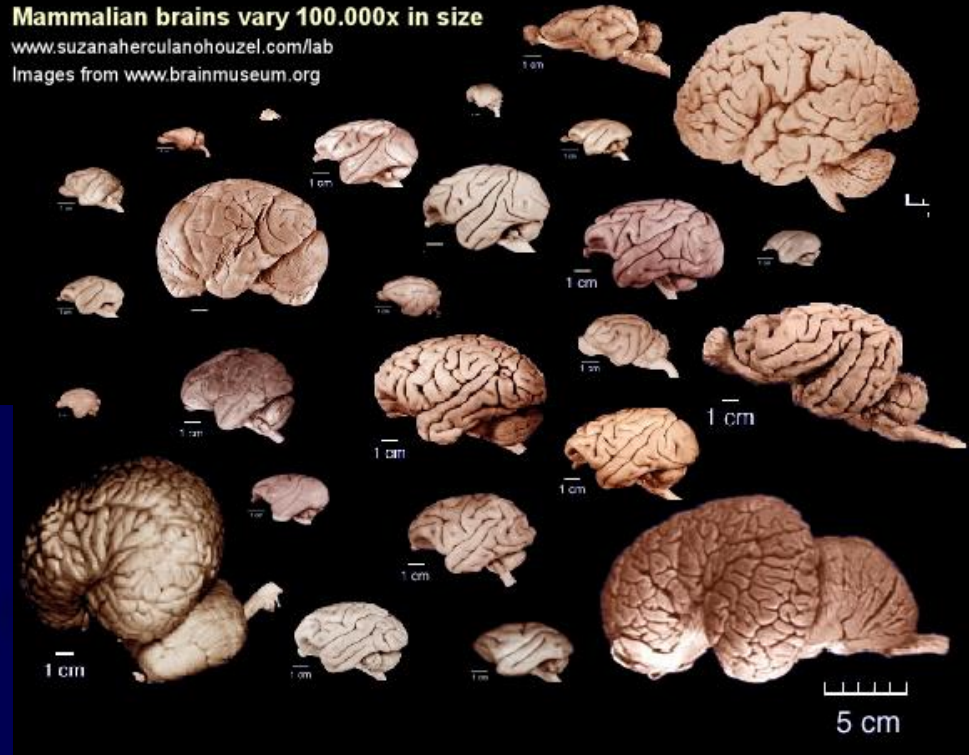
CLAIMS OF HUMAN UNIQUENESS: BRAIN SIZE

Absolute Size?

Mammalian brains vary 100,000x in size

www.suzanaherculanohouzel.com/lab

Images from www.brainmuseum.org



Human

Elephant

Dolphin

Gorilla

Dog

Cat

Macaque

Mouse

5cm



CLAIMS OF HUMAN UNIQUENESS: **BRAIN/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

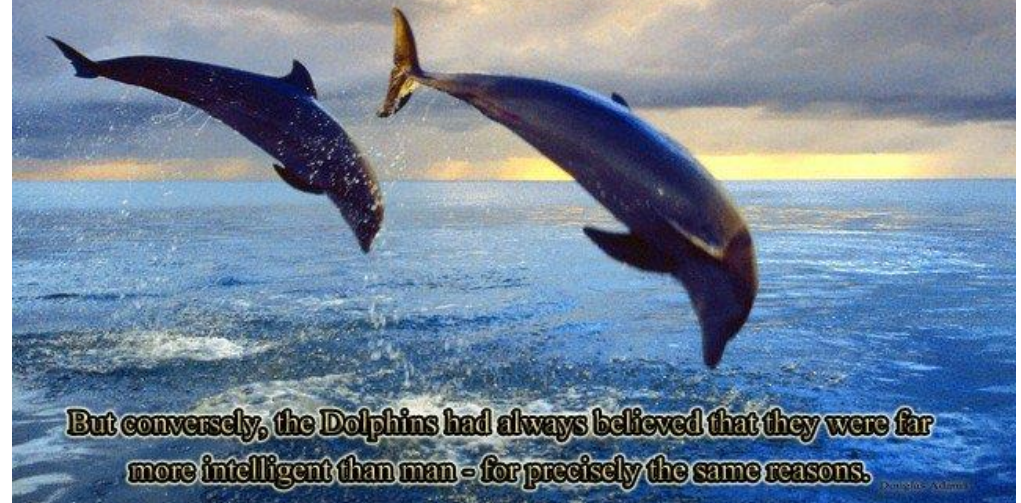
Elephants: 1/560

Horses: 1/600

Sharks: 1/2500



On the planet earth, man had always assumed that he was more intelligent than Dolphins because he had achieved so much - the wheel, New York, wars & so on - whilst all the Dolphins had ever done was muck about in the water having a good time.



But conversely, the Dolphins had always believed that they were far more intelligent than man - for precisely the same reasons.

Kuhlenbeck (1973)

CLAIMS OF HUMAN UNIQUENESS: **ENCEPHALIZATION**

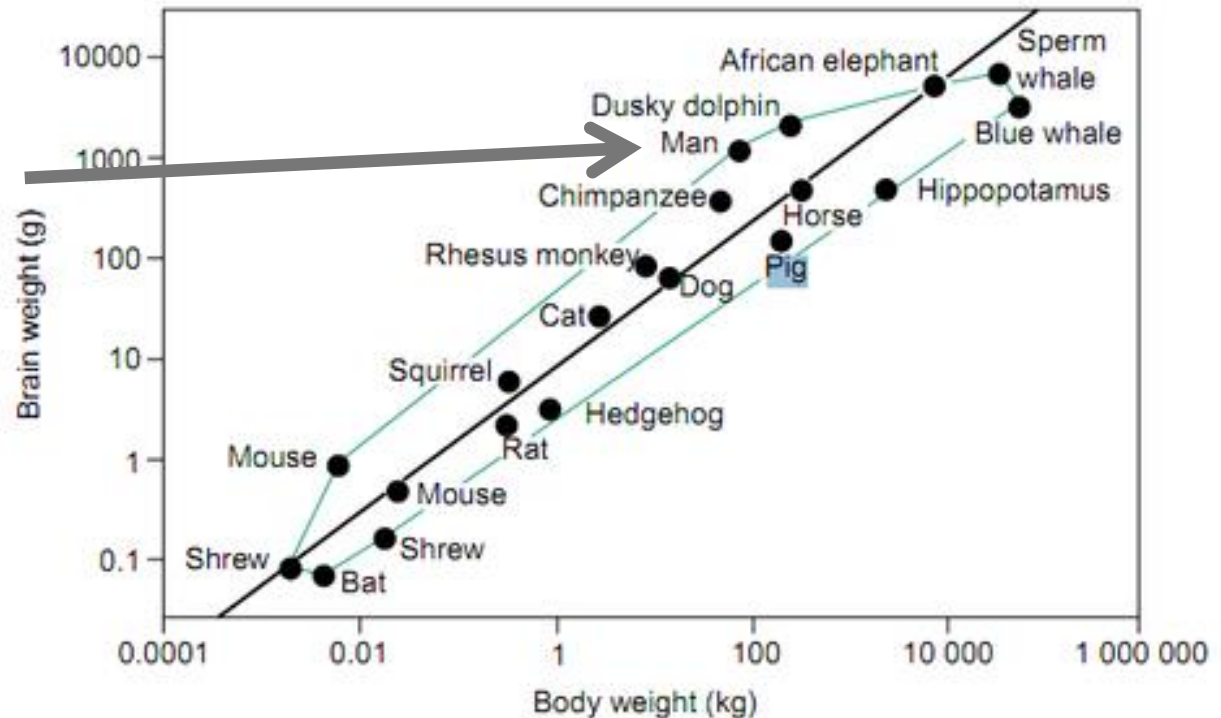
Encephalization Quotient : האם המוח
גדול מהמצופה עבור חיה עם גודל גוף כזה?

$E.Q > 1$: bigger brain than expected.

Human E.Q ~ 7



Jerison (1973)



CLAIMS OF HUMAN UNIQUENESS: 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**

No!

- The expected body–brain ratio depends on the Species compared!
- Compared to **Primates: E.Q of 3**
- Compared to small **monkeys: E.Q 1.1!**

“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)

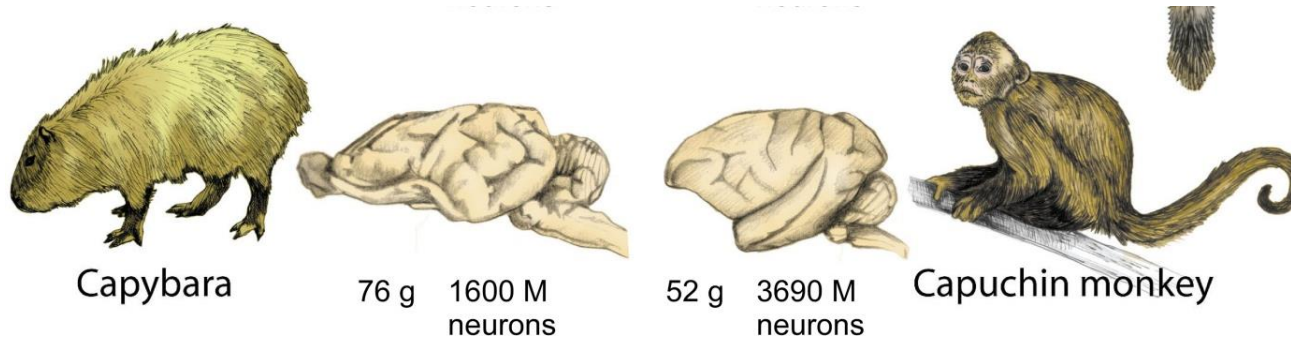
(Barton, 2006; Herculano-Houzel et al., 2007).

The human brain in numbers: a linearly scaled-up primate brain; Herculano-Houzel, 2009

WHAT MATTERS: *RELATIVE OR ABSOLUTE BRAIN SIZE ?*

Absolute?

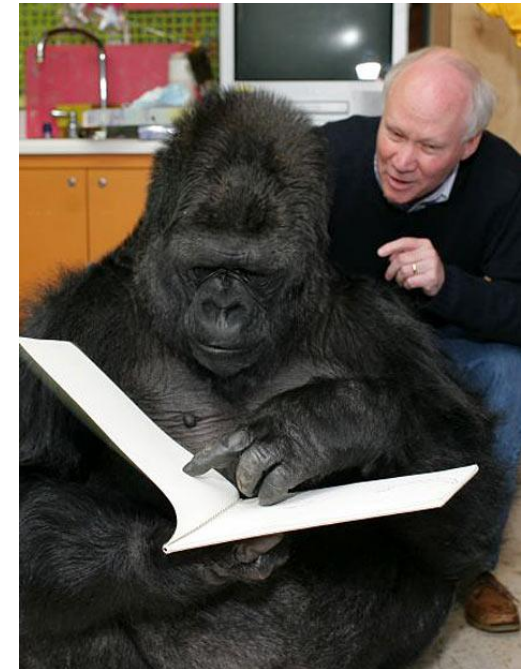
Capybara vs Capuchin Monkey:



Relative?

Gorilla Vs Capuchin

(Roth and Dicke, 2005)



WHAT MAKES US *SPECIAL*?

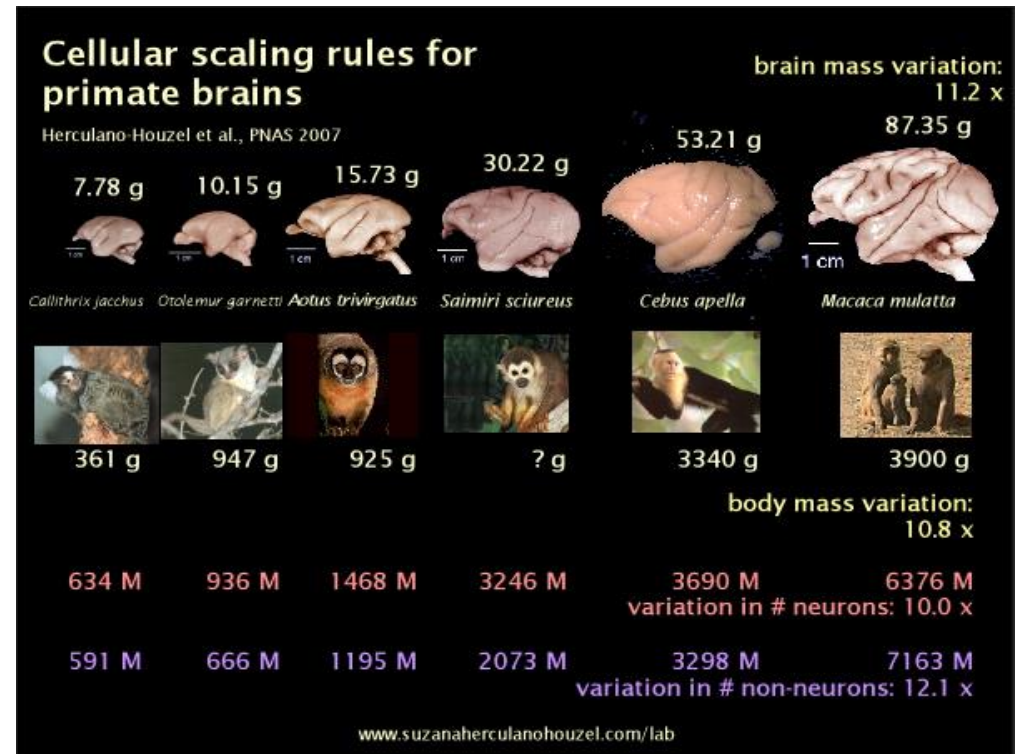
1. Absolute Number of Neurons.

Why?

2. We Have the Largest **PRIMATE** Brain!

Different Species Orders'
Brains SCALE
Differently!

*Primates Vs Rodentia Vs
Insectivores...



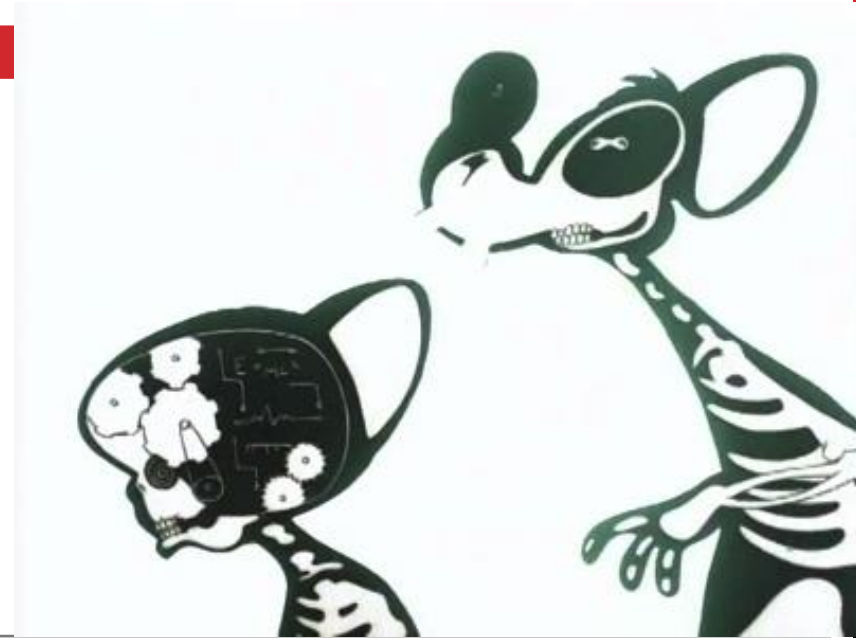
WHAT MAKES US *SPECIAL*: BIGGEST PRIMATE BRAIN

3. (Efficient) Isometric Primate Brain Scaling.

"**Primate** brain size increases isometrically as a function of **neuron** number".

Rodents – Hypermetric
Increase.

- "average neuronal size increases together with neuronal number, but not in primates"



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:

- **Neuroanatomical regions (Area 10 Prefrontal, specific layers of cortex..)**
- **Lengthy infant Development (Increased Learning Plasticity/development).**
- **Connectivity (Dendritic connection density..)**
- **Genes.**
- **Special Cellular traits**
- **Absolute # Neurons**
- ...