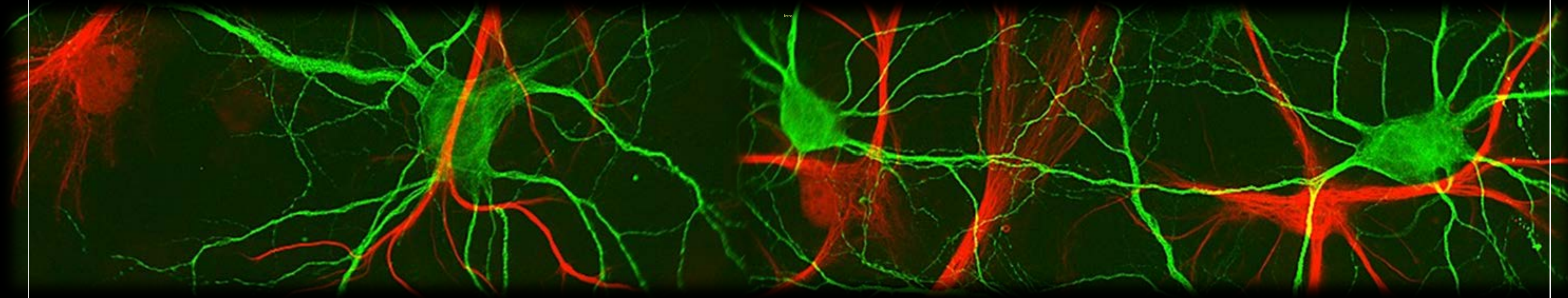
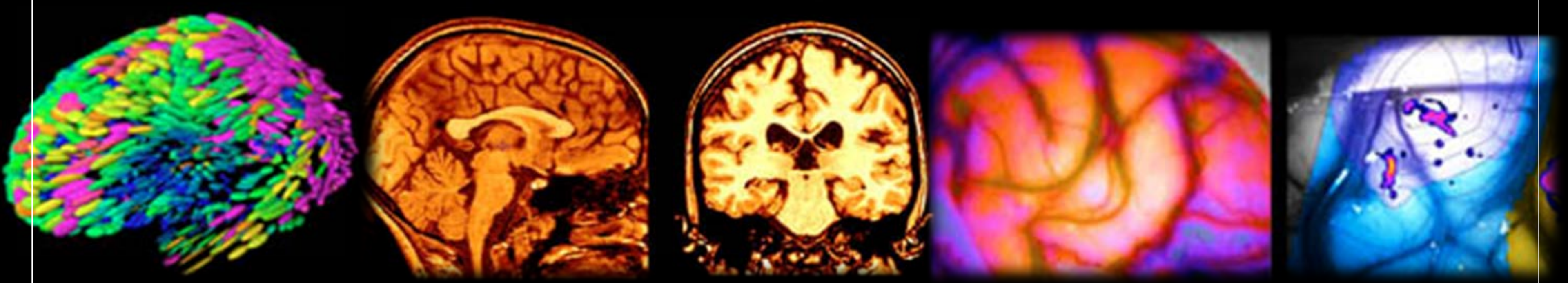
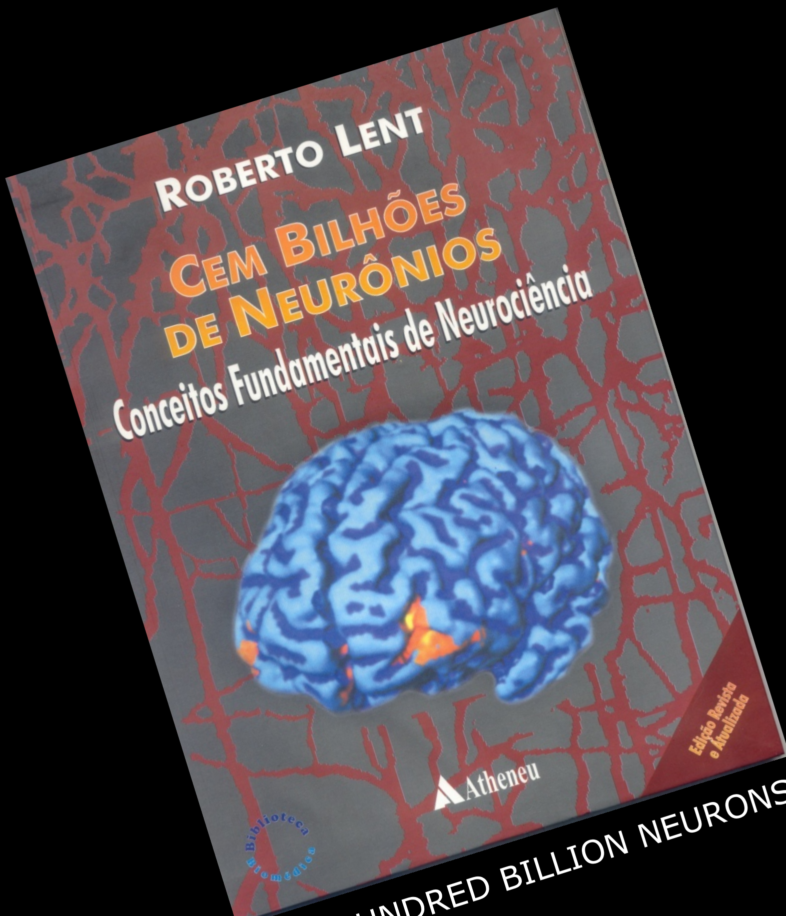


CHALLENGING SOME DOGMAS OF QUANTITATIVE NEUROSCIENCE ON EVOLUTION, DEVELOPMENT AND PATHOLOGY OF THE BRAIN

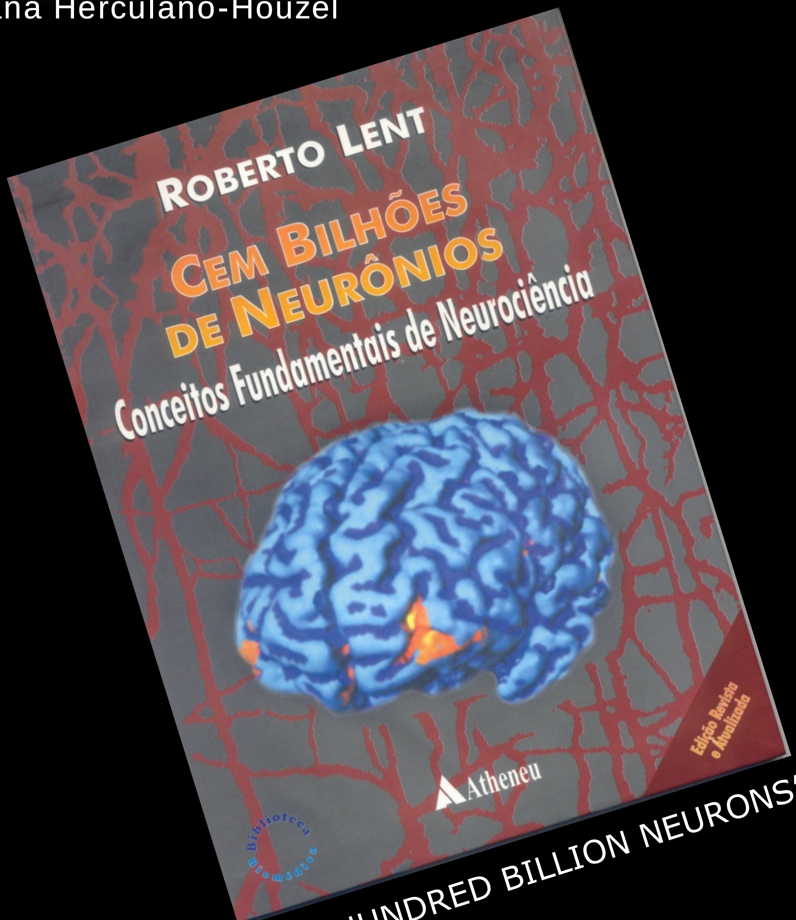


Instituto de Estudos Avançados – USP - 2011



"ONE HUNDRED BILLION NEURONS"

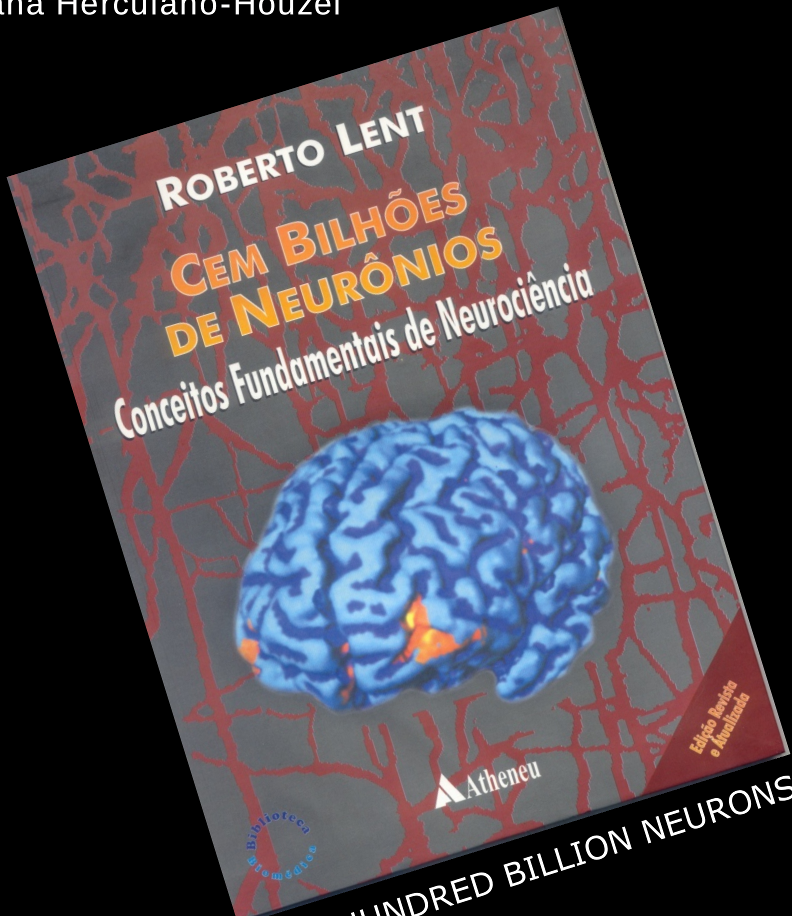
Suzana Herculano-Houzel



"ONE HUNDRED BILLION NEURONS"

Suzana Herculano-Houzel

“IS THERE ANY SOUND EVIDENCE THAT THE ABSOLUTE NUMBER OF NEURONS IN THE HUMAN BRAIN IS REALLY ONE HUNDRED BILLION?”



“ONE HUNDRED BILLION NEURONS”

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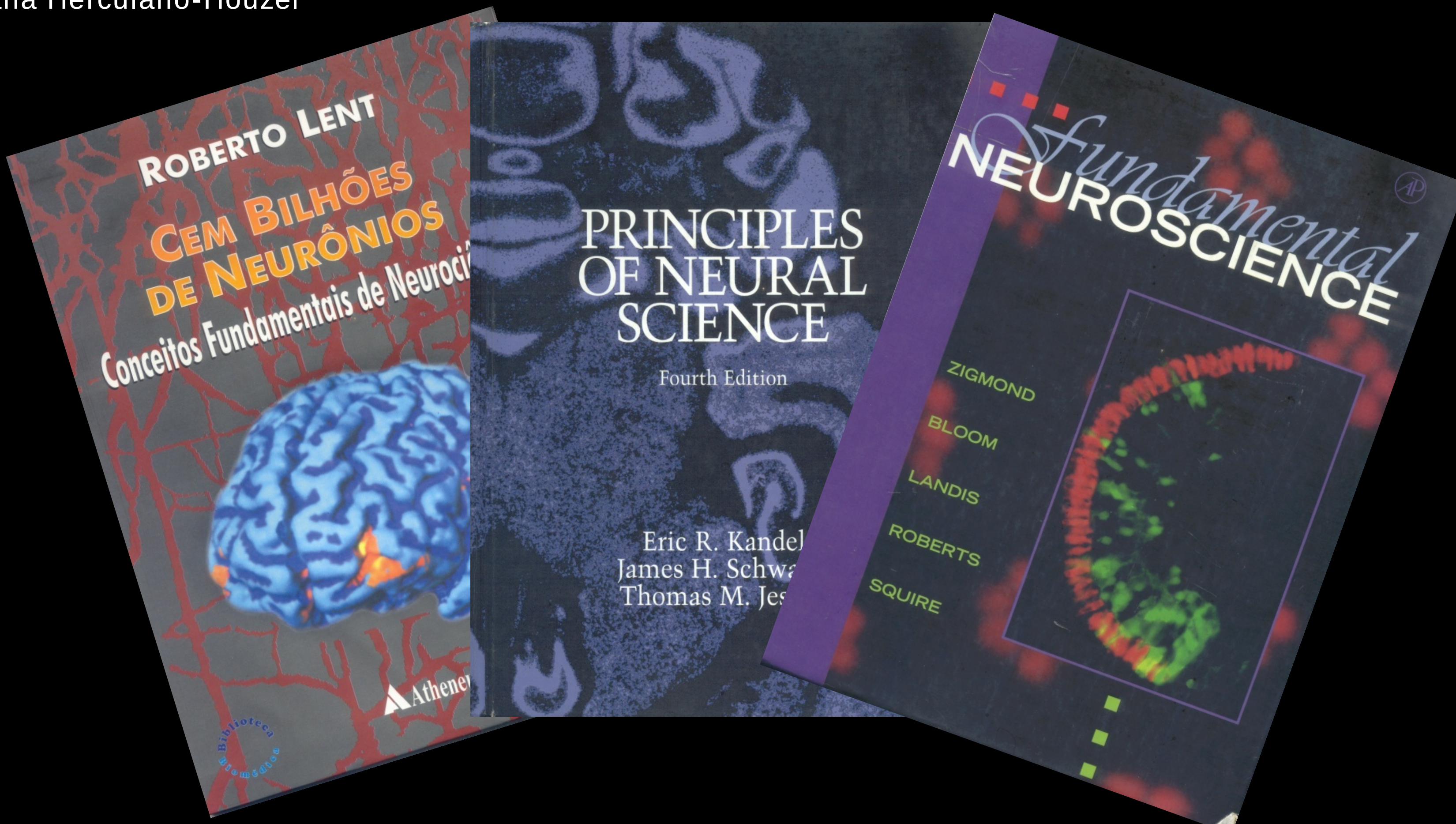


Suzana Herculano-Houzel

"IS THERE ANY SOUND EVIDENCE THAT THE ABSOLUTE NUMBER OF NEURONS IN THE HUMAN BRAIN IS REALLY ONE HUNDRED BILLION?"

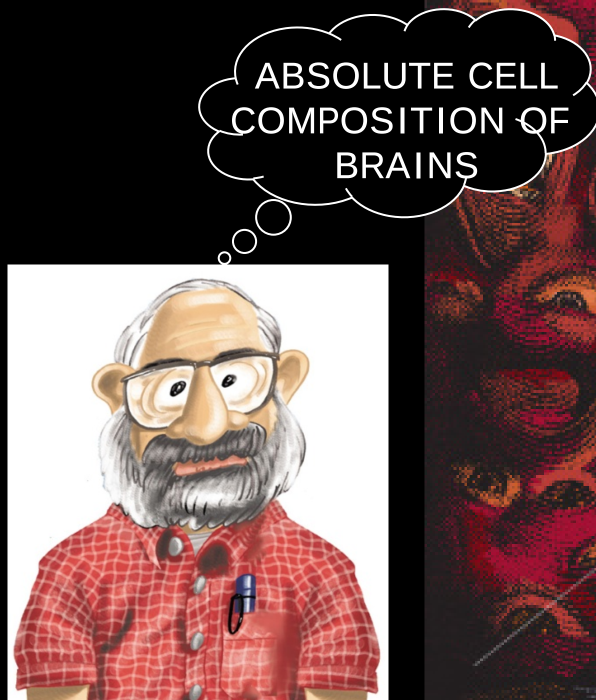
Arch Neurol. 2007;64:639-642

Contribution of Intermediate Progenitor Cells to Cortical Histogenesis

NEUROLOGICAL REVIEW

Stephen C. Noctor, PhD; Verónica Martínez-Cerdeno, PhD; Arnold R. Kriegstein, MD, PhD

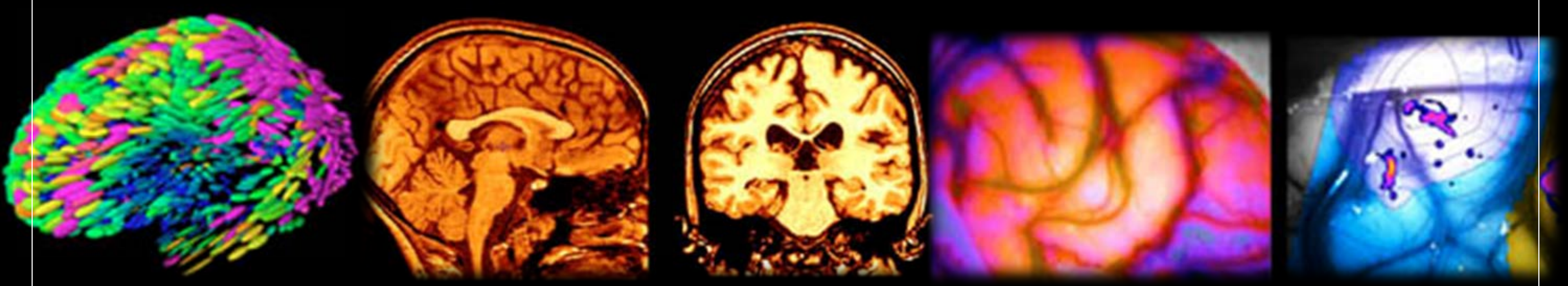
The mature brain is composed of 100 billion to 200 billion neurons and perhaps 10 times as many glial cells. Generation of the 1 trillion diverse, complex cells that regulate every aspect of behavior is accomplished in human beings during a brief span of just 3 to 4 months. This critical period of gestation is sensitive to interference from environmental, pathogenic, and genetic factors, and defects in proliferation at this stage of development can produce severe cortical malformations such as lissencephaly. We review the current state of understanding of cortical progenitor cells in the embryonic cerebral cortex.


ABSOLUTE CELL COMPOSITION OF BRAINS


ROBERTO LENT
CEM BILHÕES DE NEURÔNIOS

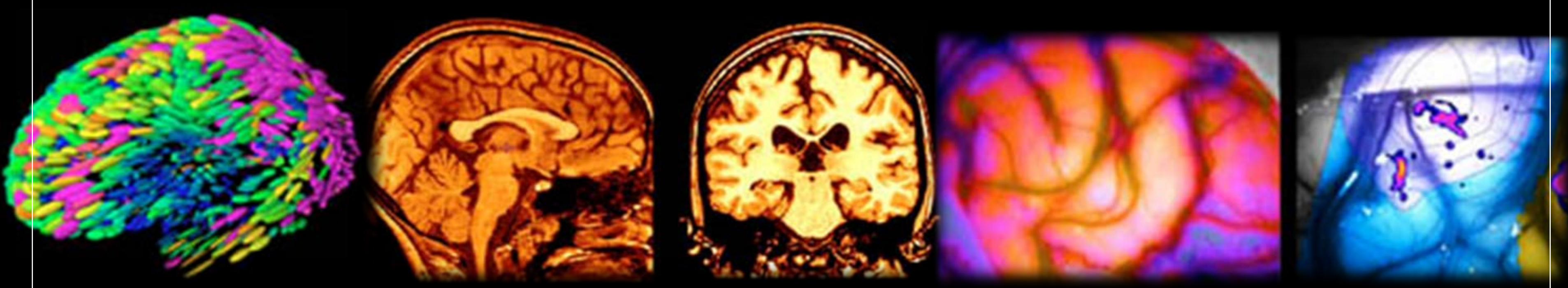
WHY IS THIS QUESTION IMPORTANT?

WHAT MAKES A BRAIN BIGGER OR SMALLER?



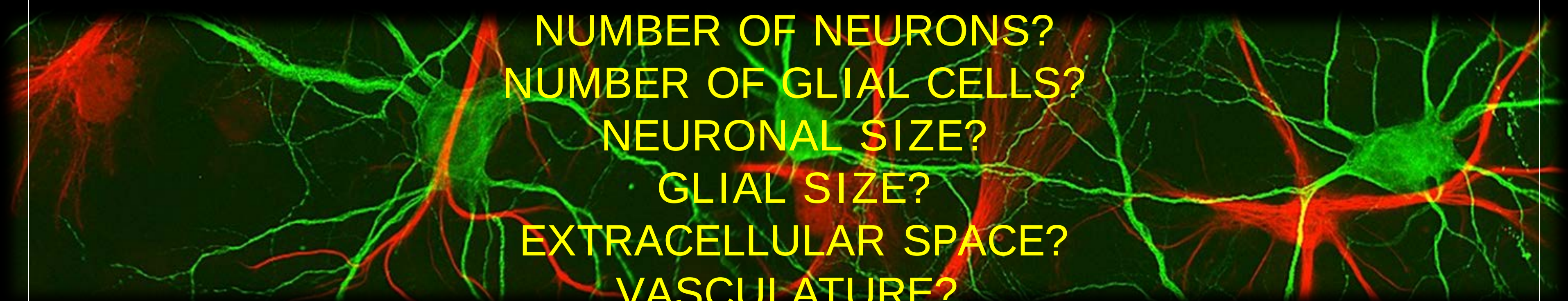
EVOLUTION
DEVELOPMENT
PATHOLOGY

WHAT MAKES A BRAIN BIGGER OR SMALLER?



EVOLUTION
DEVELOPMENT
PATHOLOGY

WHAT MAKES A BRAIN BIGGER OR SMALLER?



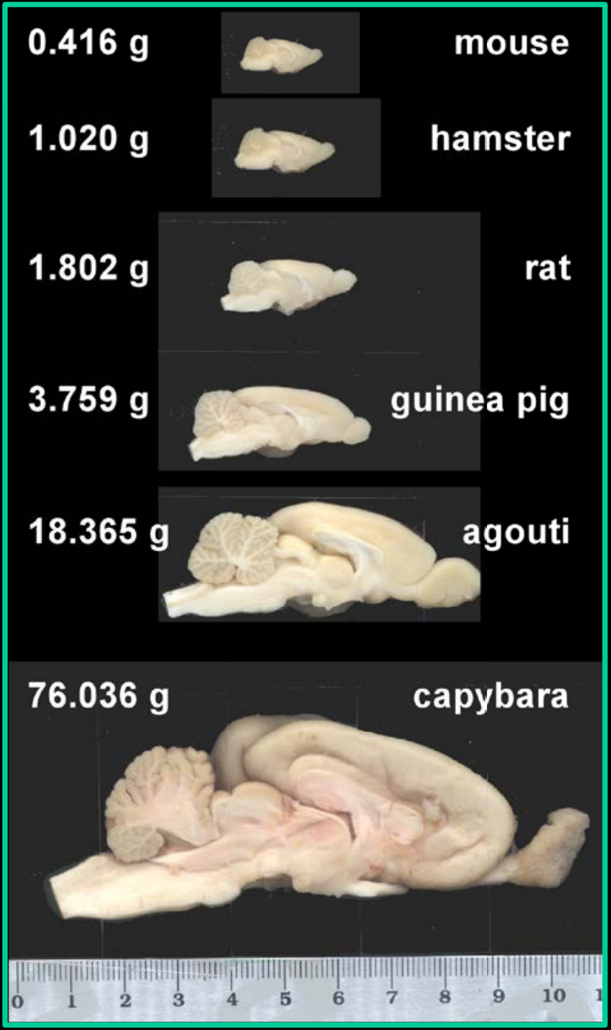
NUMBER OF NEURONS?
NUMBER OF GLIAL CELLS?
NEURONAL SIZE?
GLIAL SIZE?
EXTRACELLULAR SPACE?
VASCULATURE?

TO ANSWER THIS SCALING QUESTION ONE NEEDS:

TO ANSWER THIS SCALING QUESTION ONE NEEDS:

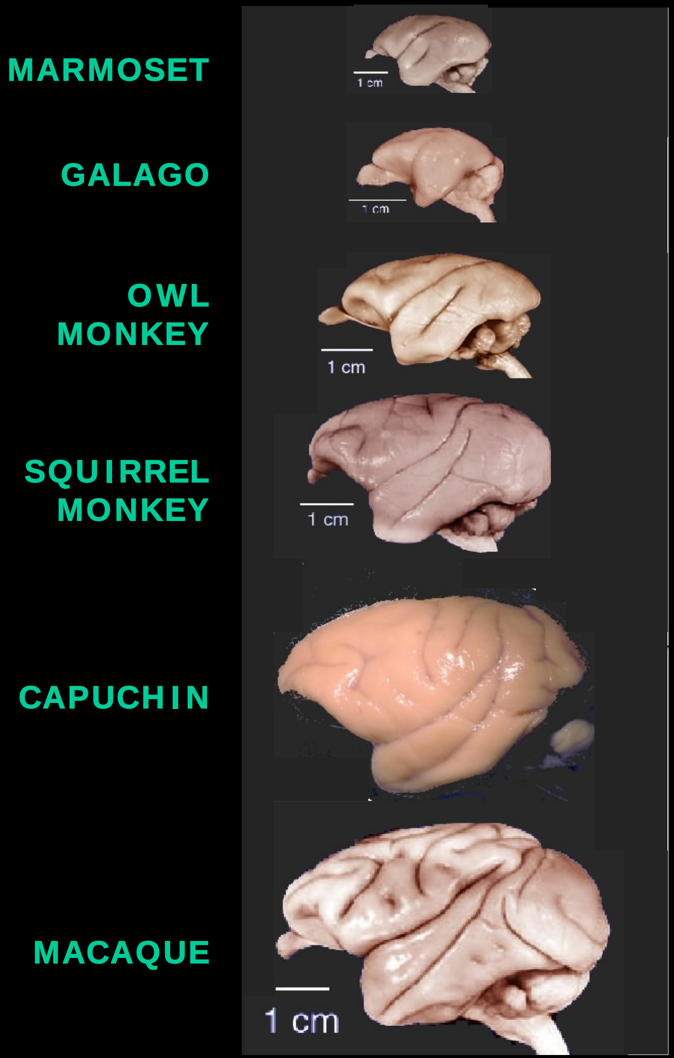
1. A SERIES OF BRAINS OF DIFFERENT SPECIES WITH DIFFERENT SIZES

RODENTIA –
AN ORDER WITH BRAINS VARYING 180X IN SIZE

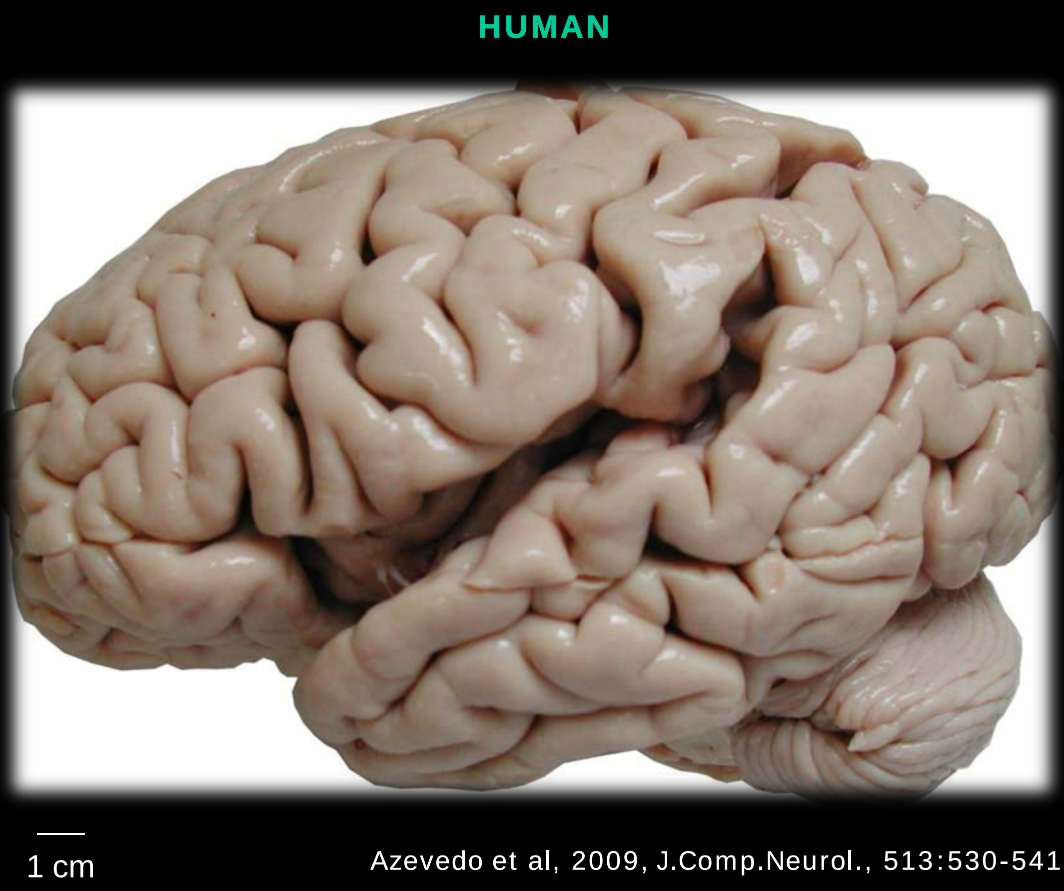


Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

PRIMATES – AN ORDER WITH BRAINS VARYING 500X IN SIZE



Herculano-Houzel et al, 2007, PNAS 104:3562-3567



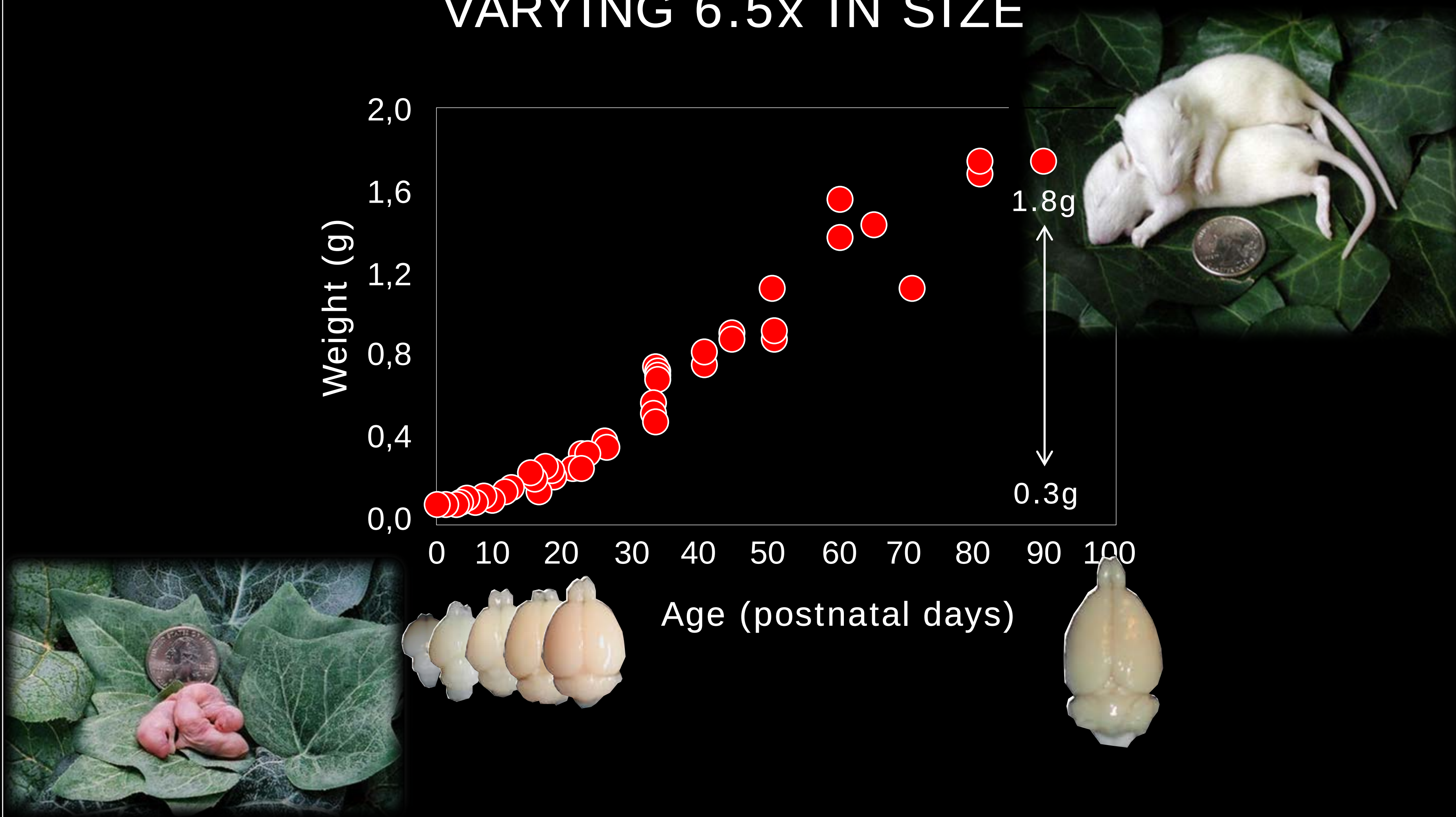
Azevedo et al, 2009, J.Comp.Neurol., 513:530-541

TO ANSWER THIS SCALING QUESTION ONE NEEDS:

1. A SERIES OF BRAINS OF DIFFERENT SPECIES WITH DIFFERENT SIZES

2. A SERIES OF BRAINS WITH DIFFERENT AGES, IN THE SAME SPECIES

RATTUS NORVEGICUS –
A SPECIES WITH POSTNATAL BRAINS VARYING 6.5x IN SIZE



Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

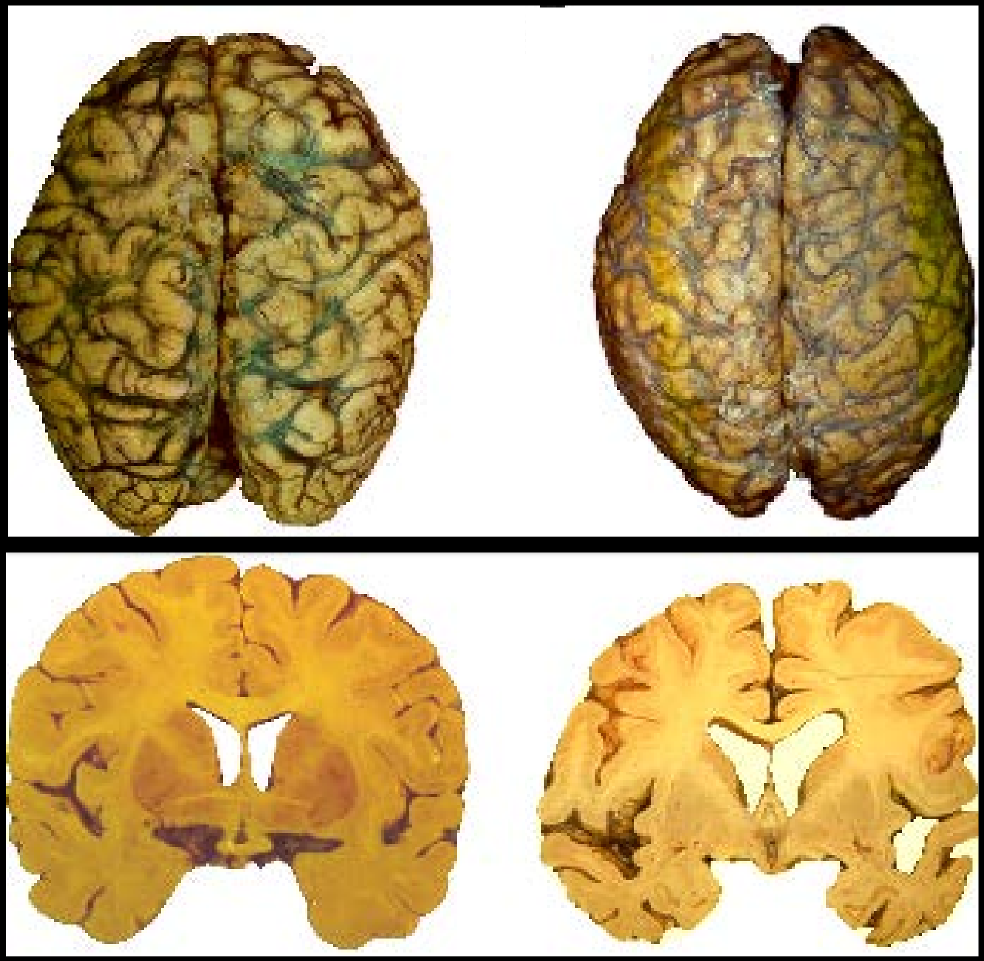
TO ANSWER THIS SCALING QUESTION ONE NEEDS:

1. A SERIES OF BRAINS OF DIFFERENT SPECIES WITH DIFFERENT SIZES

2. A SERIES OF BRAINS WITH DIFFERENT AGES, IN THE SAME SPECIES

3. A SERIES OF BRAINS WITH KNOWN PATHOLOGIES

ALZHEIMER´S DISEASE
BRAINS OBTAINED FROM DECEASED SUBJECTS AT THE SÃO PAULO BRAIN BANK (USP)



TO ANSWER THIS SCALING QUESTION ONE NEEDS:

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2. A SERIES OF BRAINS WITH DIFFERENT AGES, IN THE SAME SPECIES
3. A SERIES OF BRAINS WITH KNOWN PATHOLOGIES
4. A RELIABLE METHOD FOR ESTIMATING CELL NUMBERS AND SIZE

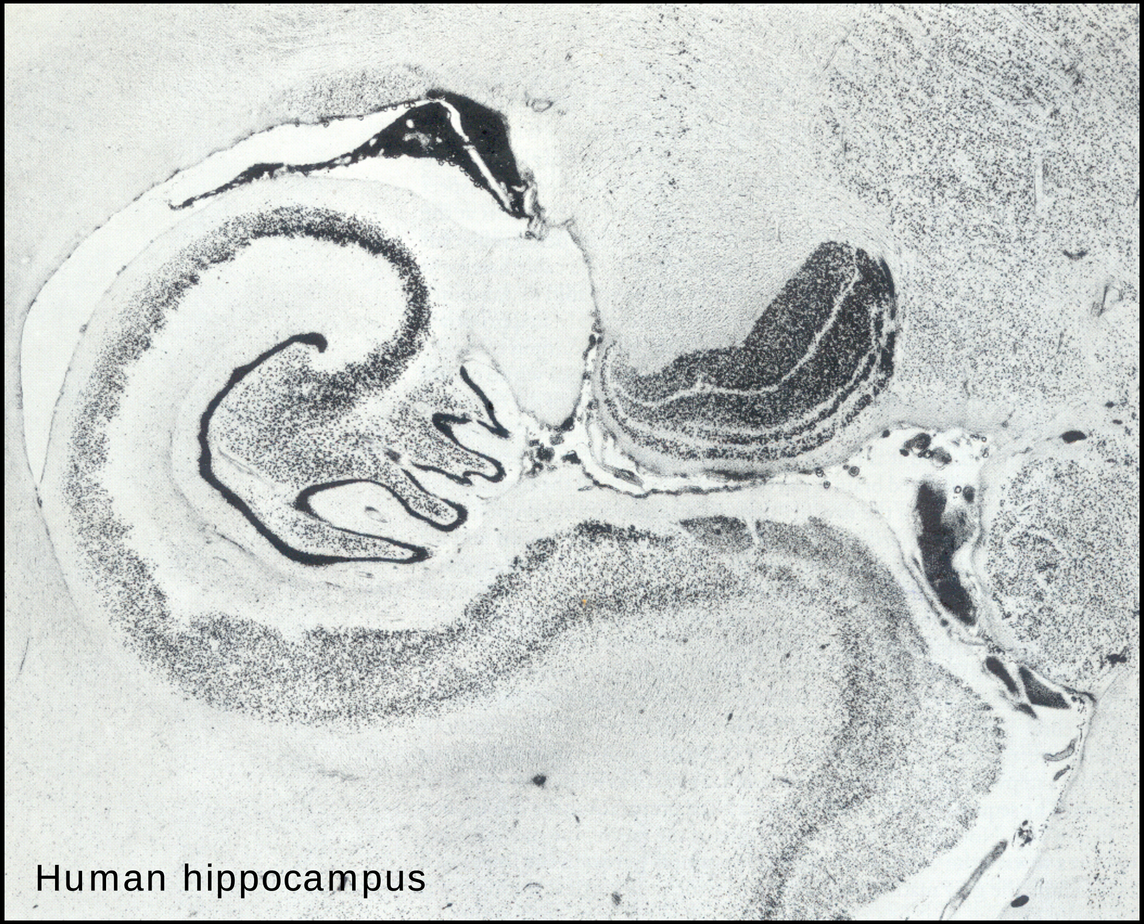
ISOTROPIC FRACTIONATOR

A RELIABLE METHOD FOR ESTIMATING CELL NUMBERS AND SIZE

Herculano-Houzel & Lent, 2005, J. Neurosci. 25:2518-2521

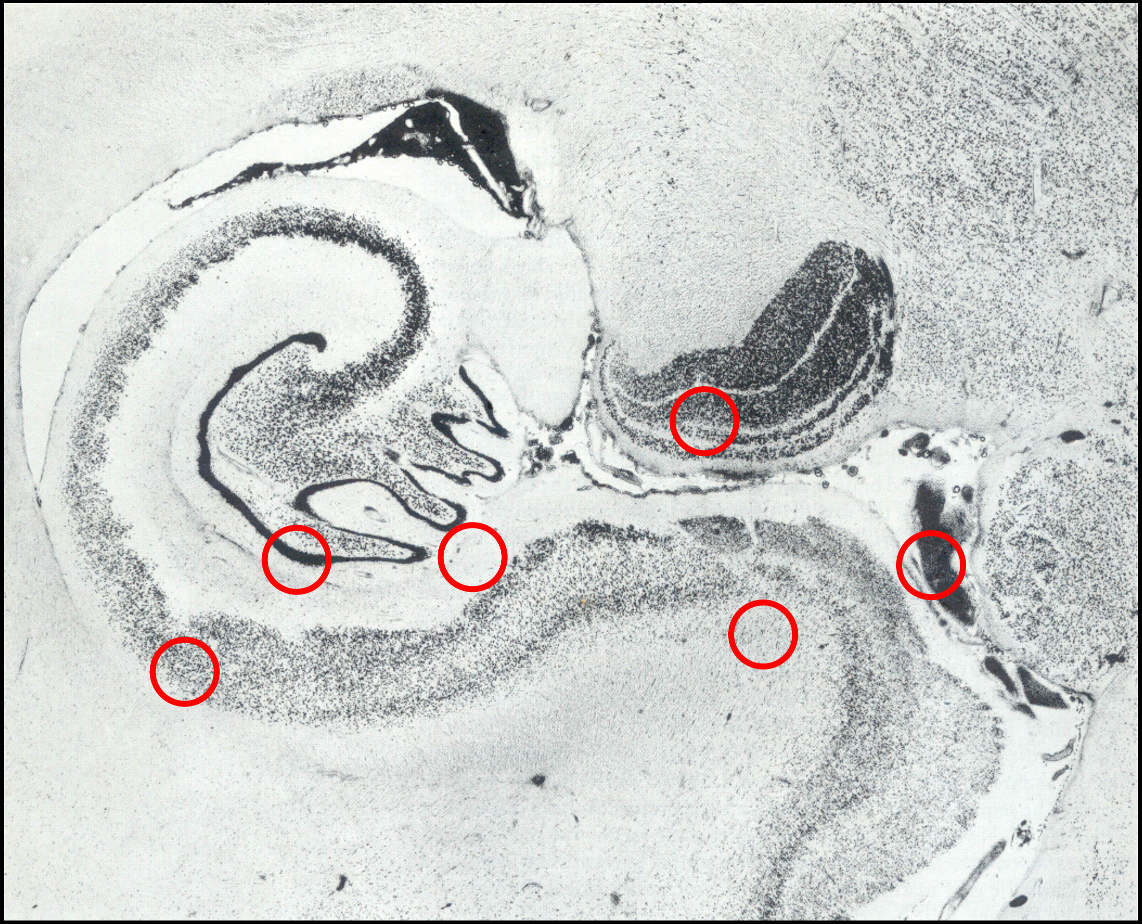
STEREOLOGICAL METHODS
(INNAPROPRIATE FOR THIS PURPOSE)

*THE NERVOUS TISSUE IS HIGHLY ANISOTROPIC

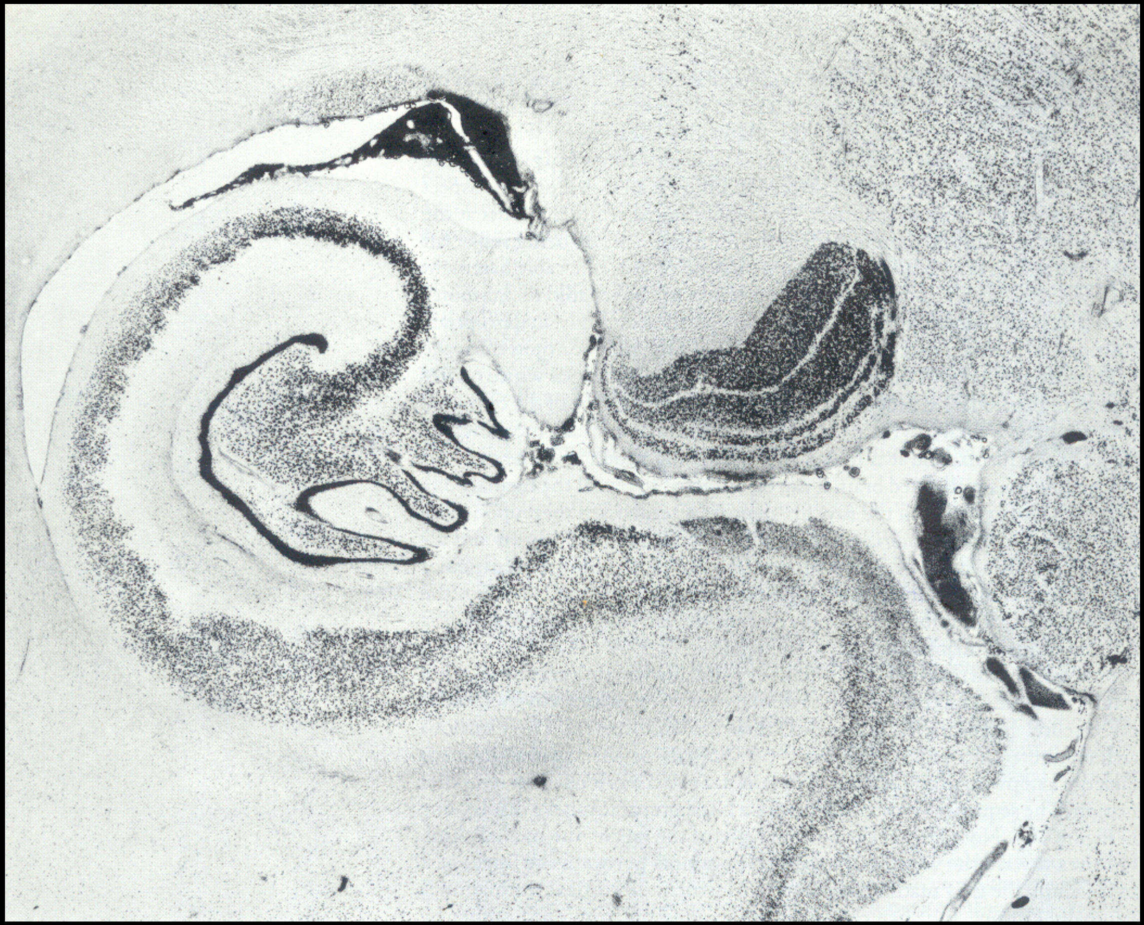


STEREOLOGICAL METHODS
(INNAPROPRIATE FOR THIS PURPOSE)

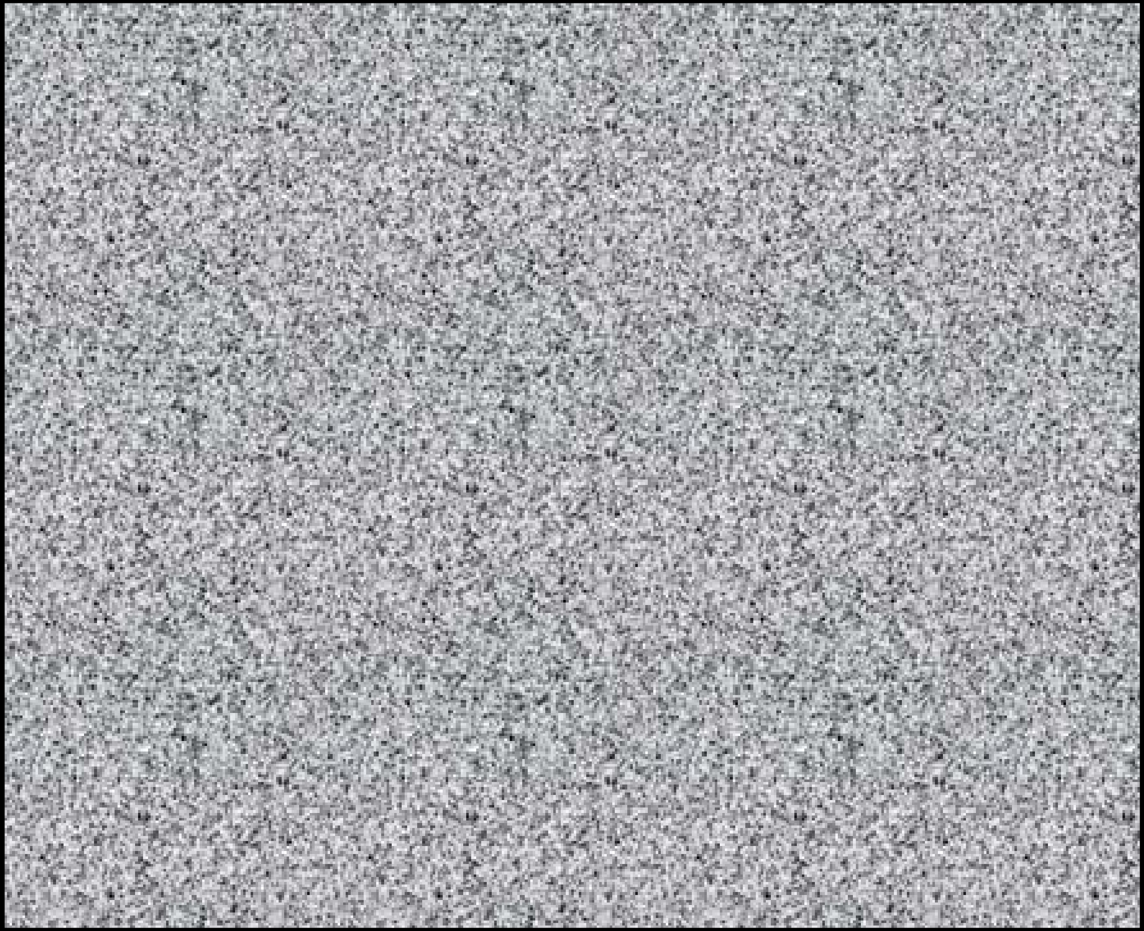
*MEAN DENSITIES HAVE HIGH VARIANCES
*ESTIMATION OF ABSOLUTE NUMBERS OF CELLS DEPENDS ON BRAIN VOLUME



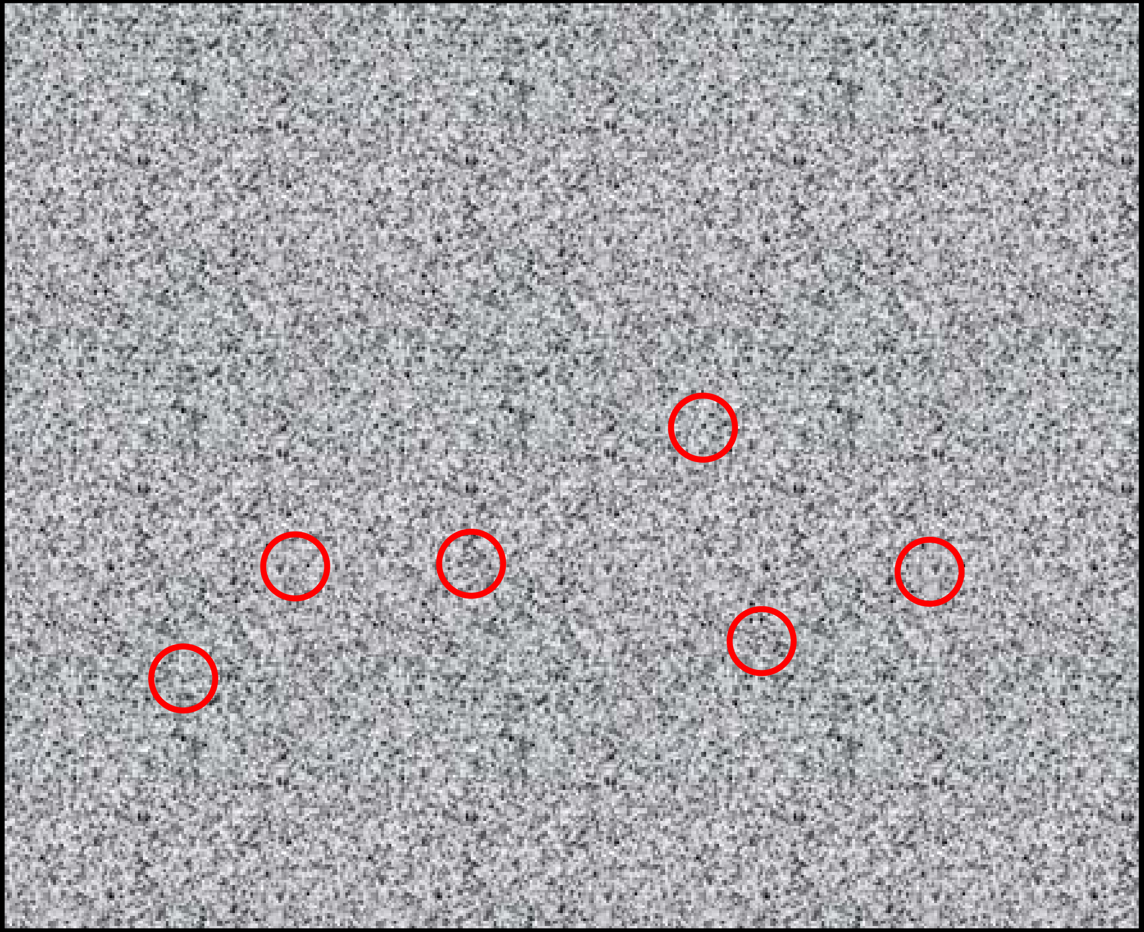
ISOTROPIC FRACTIONATION MEANS TRANSFORMING A ANISOTROPIC TISSUE…



…INTO A ISOTROPIC MEDIUM

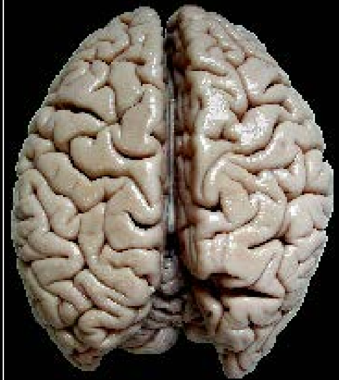


MEASURED DENSITIES BECOME MORE RELIABLE, AND VOLUMES CAN BE CHOSEN AT WILL



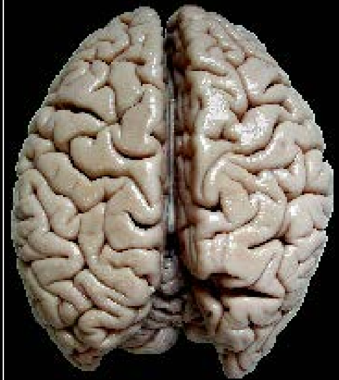
THE METHOD

Herculano-Houzel & Lent, 2005, J.Neurosci. 25:2518-2521



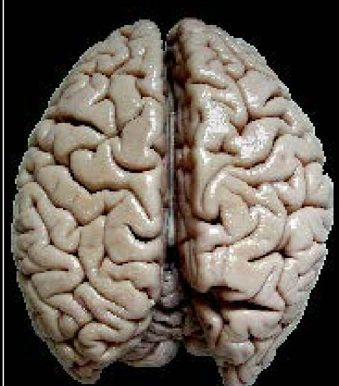
Fixed brain

MENINGES ARE REMOVED



Fixed brain

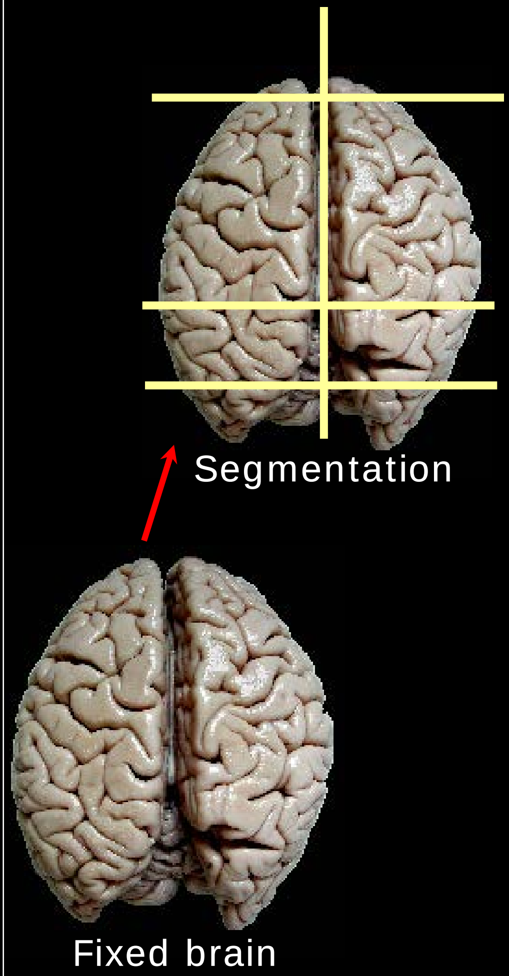
MENINGES ARE REMOVED



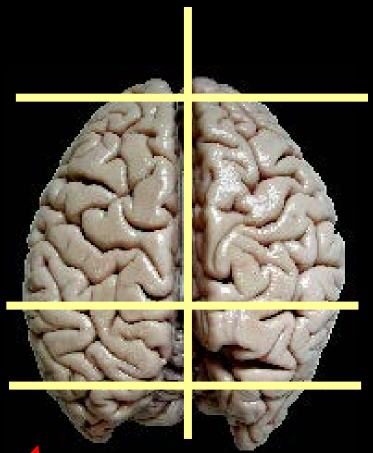
Fixed brain

THE METHOD

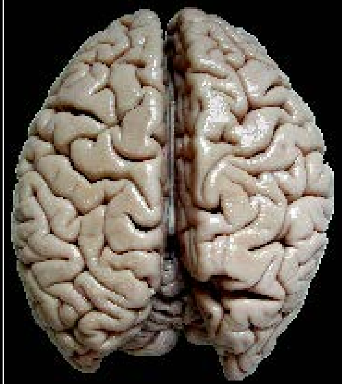
Herculano-Houzel & Lent, 2005, J.Neurosci. 25:2518-2521



BRAIN IS SEGMENTED INTO REGIONS OF INTEREST

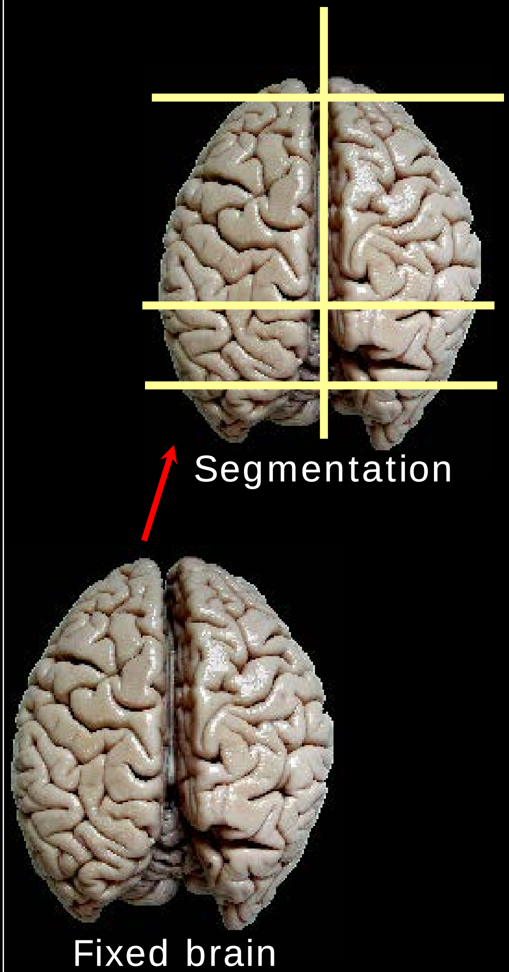


Segmentation

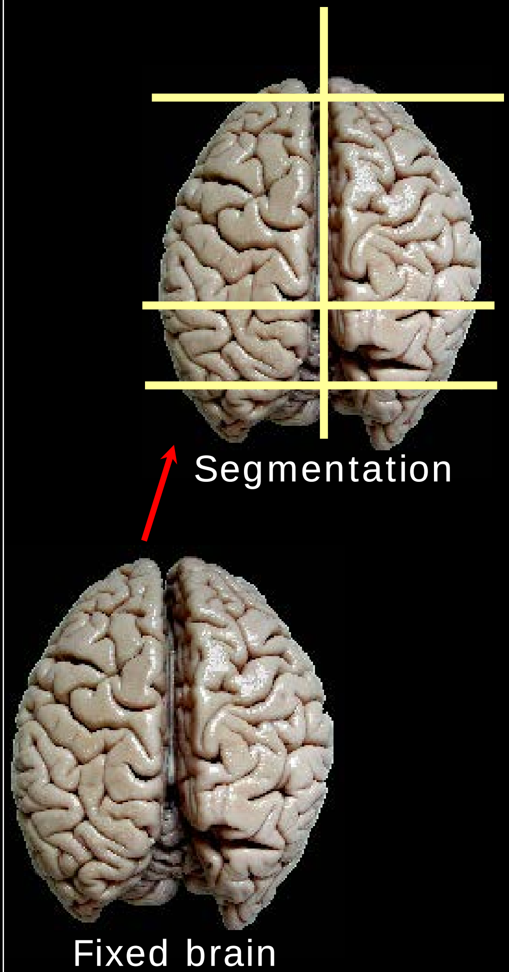


Fixed brain

BRAIN IS SEGMENTED INTO REGIONS OF INTEREST

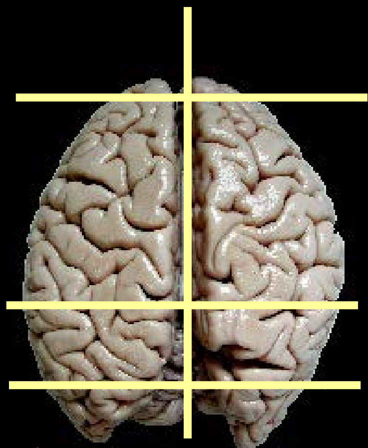


DIFFERENT REGIONS OF INTEREST ARE SEPARATED



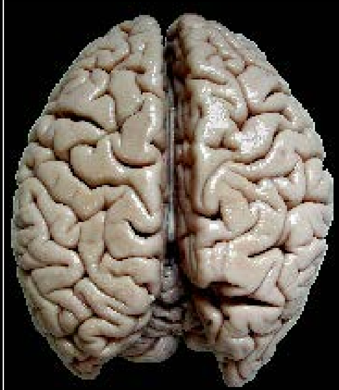
THE METHOD

Herculano-Houzel & Lent, 2005, J.Neurosci. 25:2518-2521



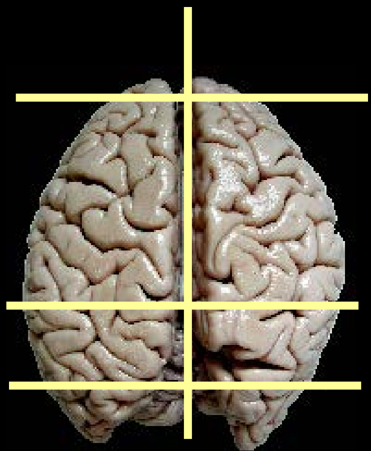
Segmentation

Fractionation
in potters



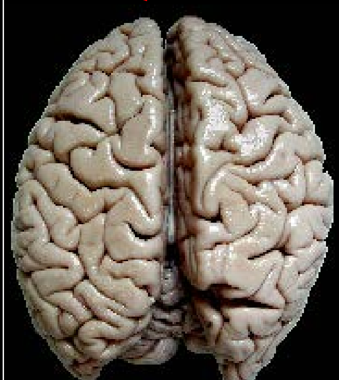
Fixed brain

TISSUE IS FRACTIONED



Segmentation

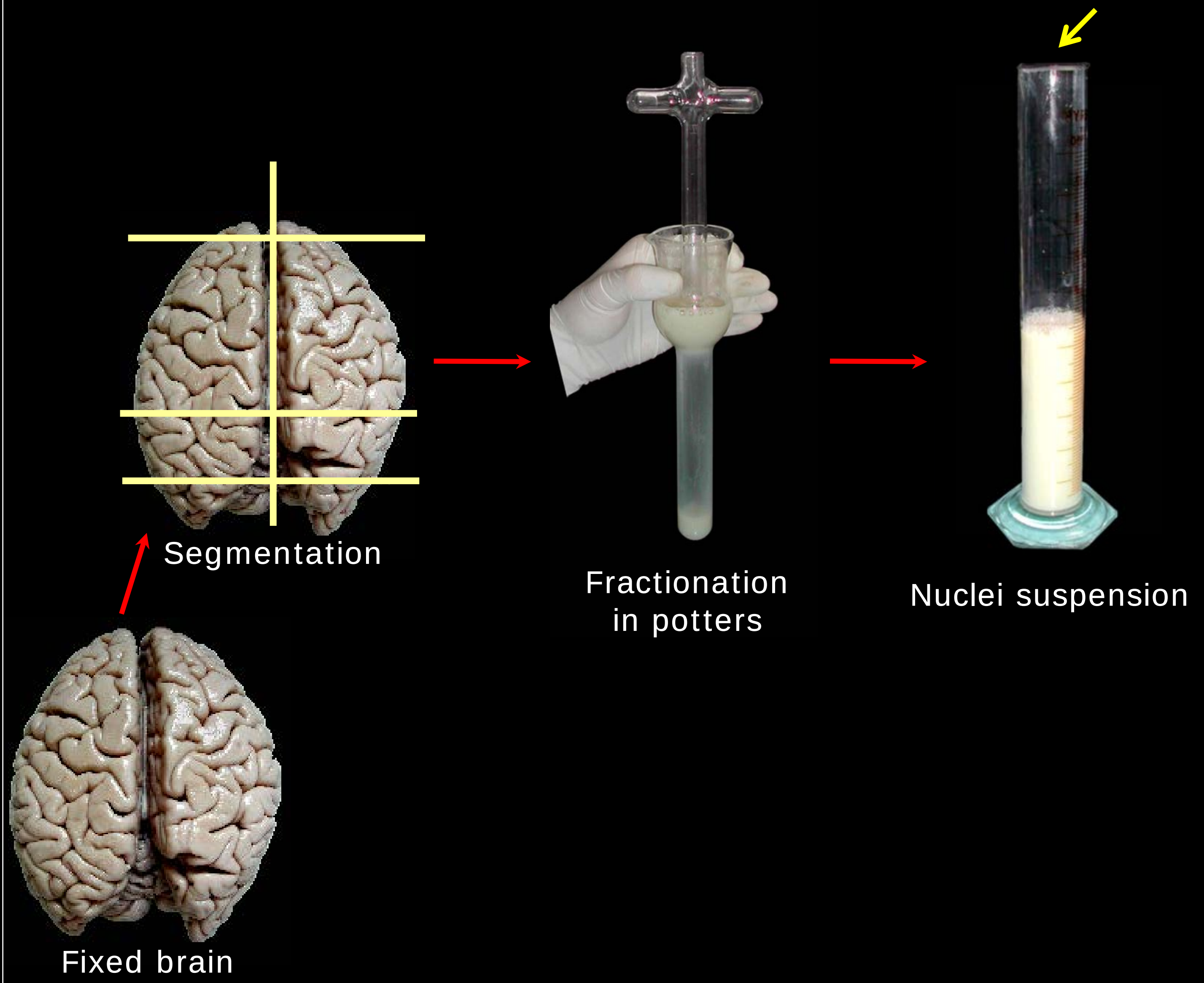
Fractionation in potters



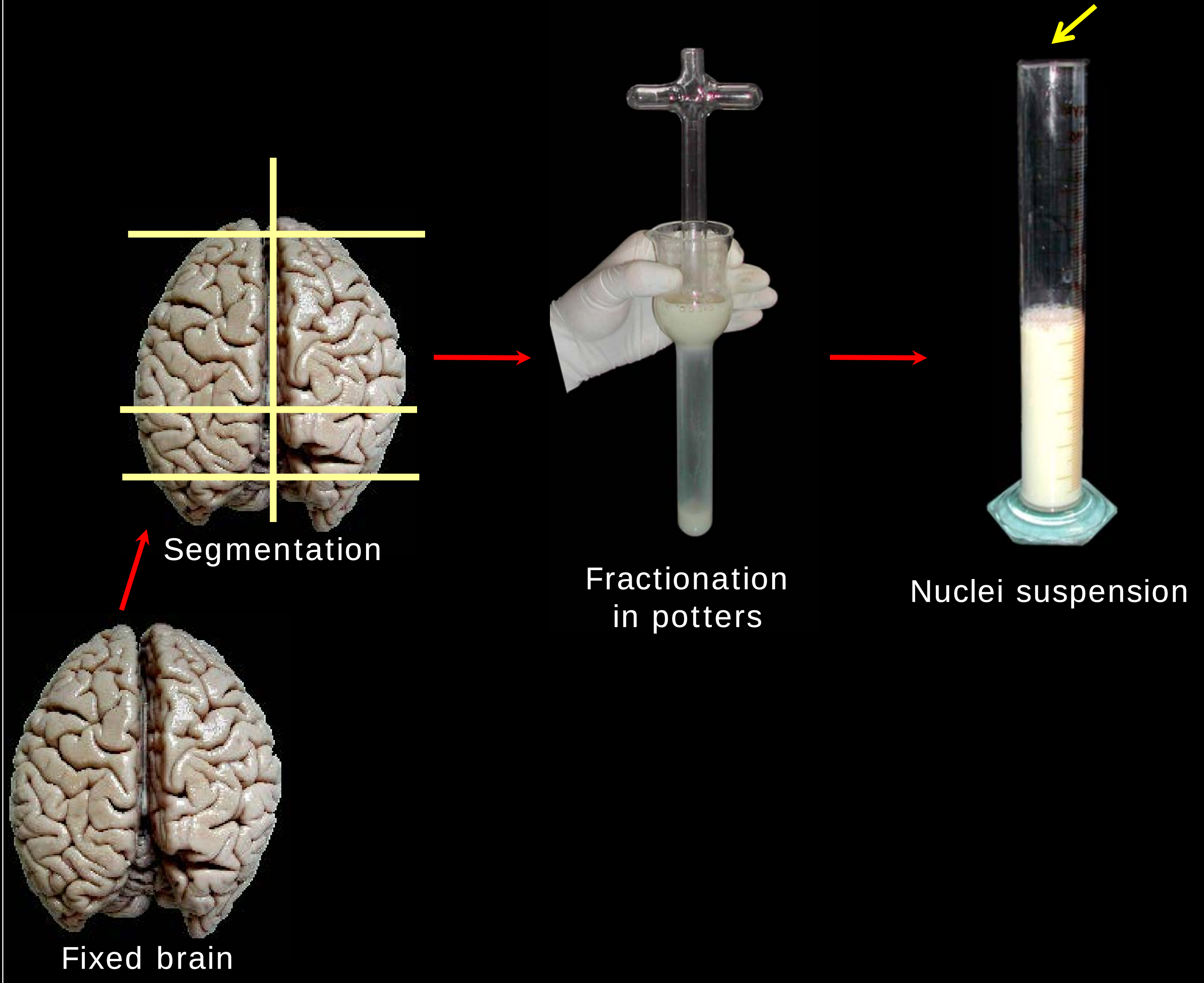
Fixed brain

THE METHOD

Herculano-Houzel & Lent, 2005, J.Neurosci. 25:2518-2521



NUCLEI SUSPENSIONS ARE COLLECTED AND STAINED



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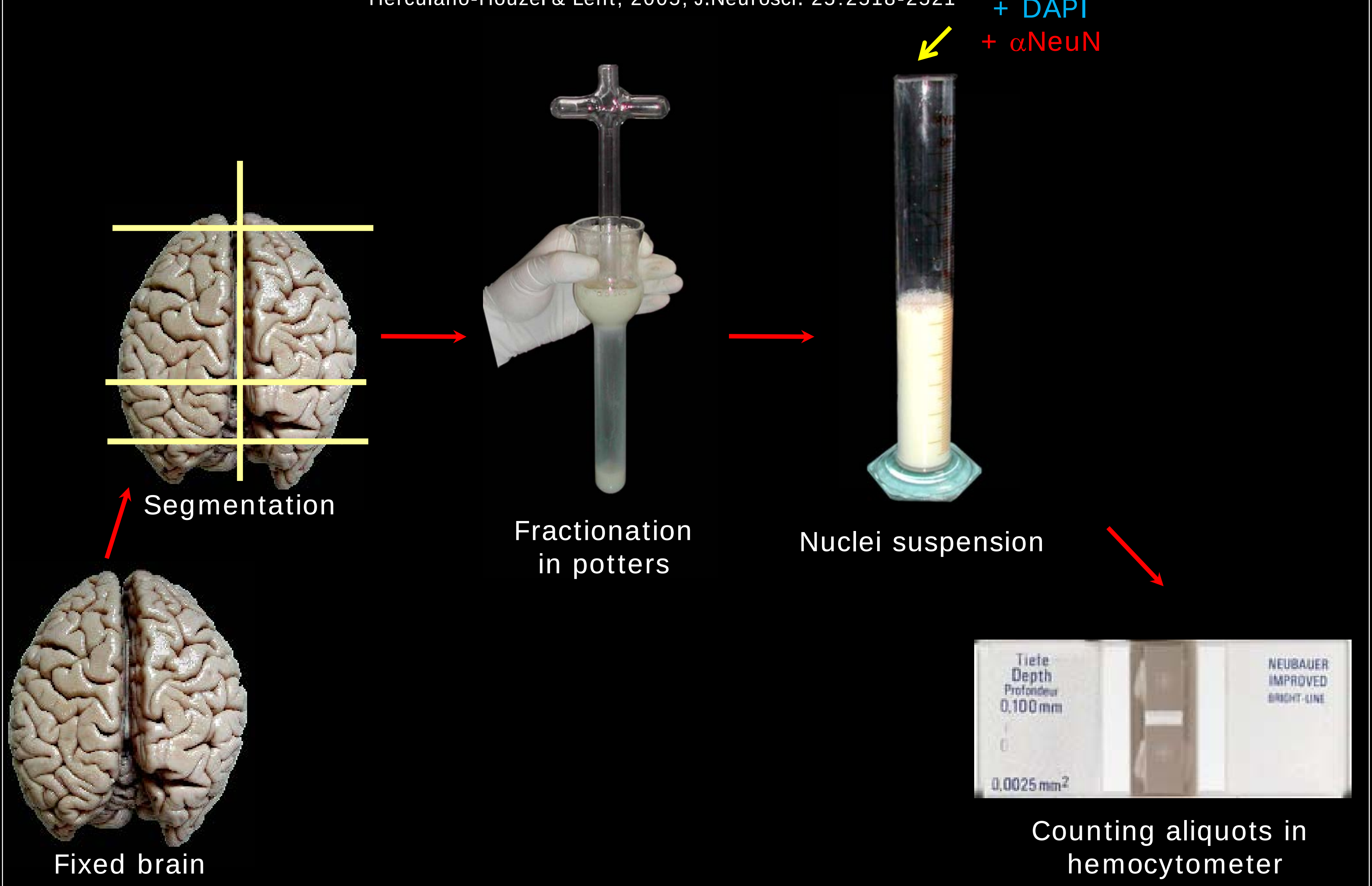
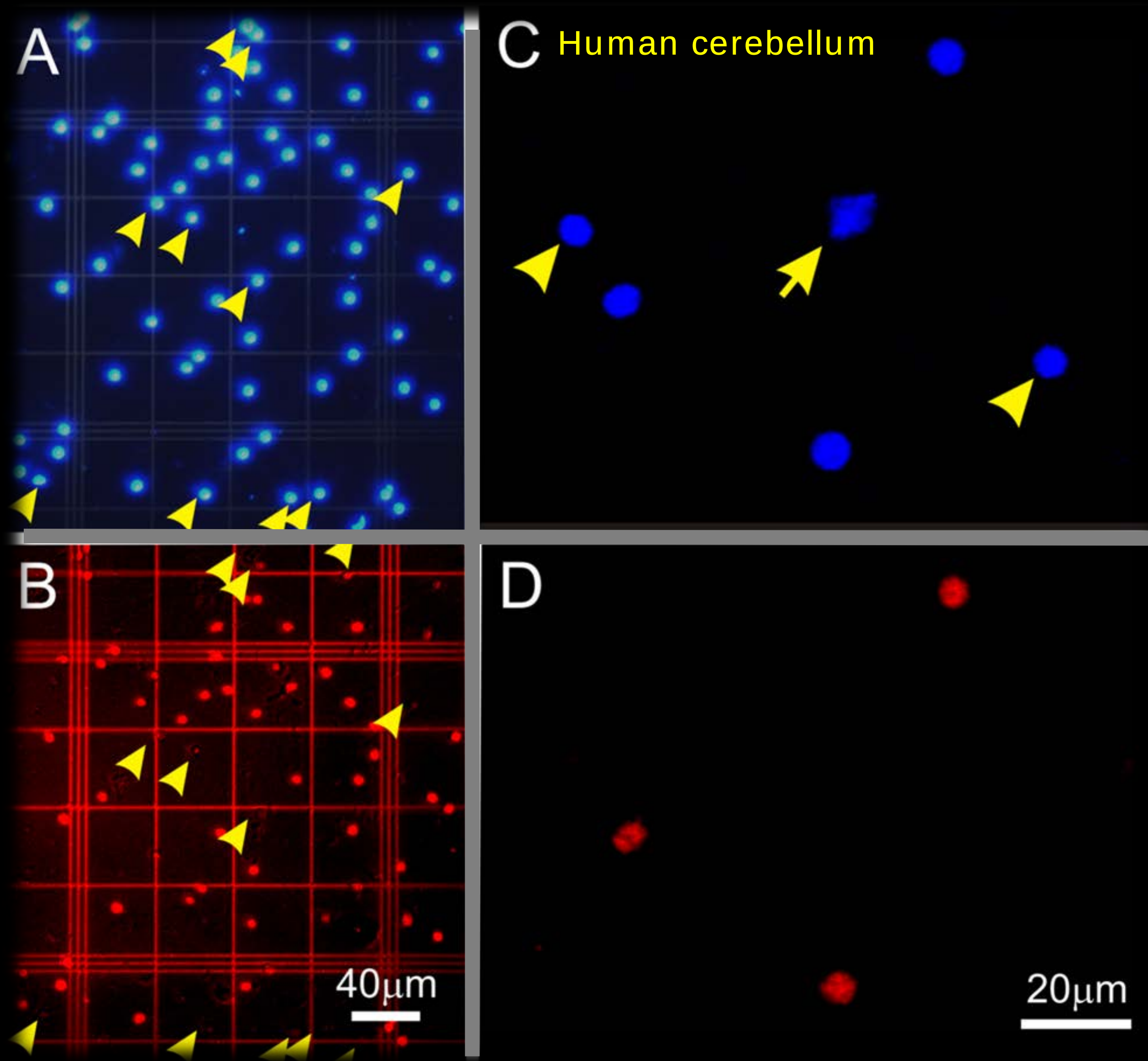


NUCLEI ARE COUNTED AT THE NEUBAUER CHAMBER

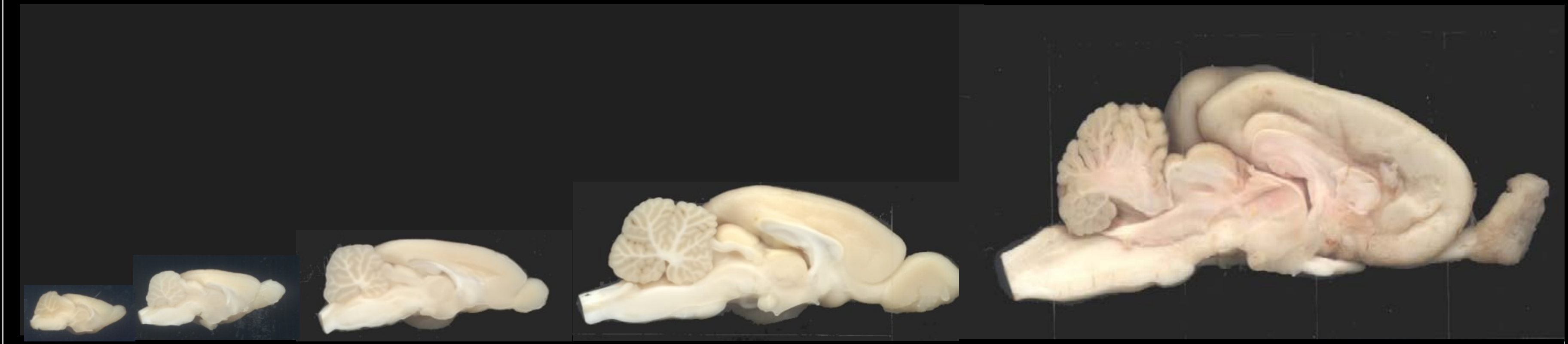


Azevedo et al., 2009, J. Comp. Neurol, 513:530-541

EVOLUTION
DEVELOPMENT
PATHOLOGY

OLD PARADIGMS

THE DOGMAS OF QUANTITATIVE NEUROSCIENCE



Herculano-Houzel, Mota & Lent, 2006, In *Evolution of Nervous Systems*, J. Kaas, ed. (Elsevier)
Lent et al., 2011, Eur. J. Neurosci., in press

EVOLUTION
DEVELOPMENT
PATHOLOGY

FIRST DOGMA:
"THE CEREBRAL CORTEX IS THE PINACLE OF EVOLUTION"
"BRAIN GROWTH IN EVOLUTION MEANS GROWTH OF THE CEREBRAL CORTEX"

Neuroanatomical Correlates of Intelligence

Eileen Luders[1], **Katherine L. Narr**[1], **Paul M. Thompson**[1], and **Arthur W. Toga**[1,*]
[1] Laboratory of Neuro Imaging, Department of Neurology, UCLA School of Medicine, Los Angeles, CA, USA

The cerebral cortex holds two thirds of the brain's neurons and thus appears to be a promising candidate for determining the primary neuroanatomical correlates of intelligence. Measures of cortical thickness range between 1.5 and 4.5 mm, and although linked with other measures of gray matter (Narr et al., 2005), they might be more closely related to intellectual abilities than volumetric or intensity-based gray matter concentration measures (Narr et al., 2007).

Published in final edited form as:
Intelligence. 2009 March 1; 37(2): 156–163. doi:10.1016/j.intell.2008.07.002.

IS IT TRUE?

FIRST DOGMA:
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“BRAIN GROWTH IN EVOLUTION MEANS GROWTH OF THE CEREBRAL CORTEX”

Neuroanatomical Correlates of Intelligence

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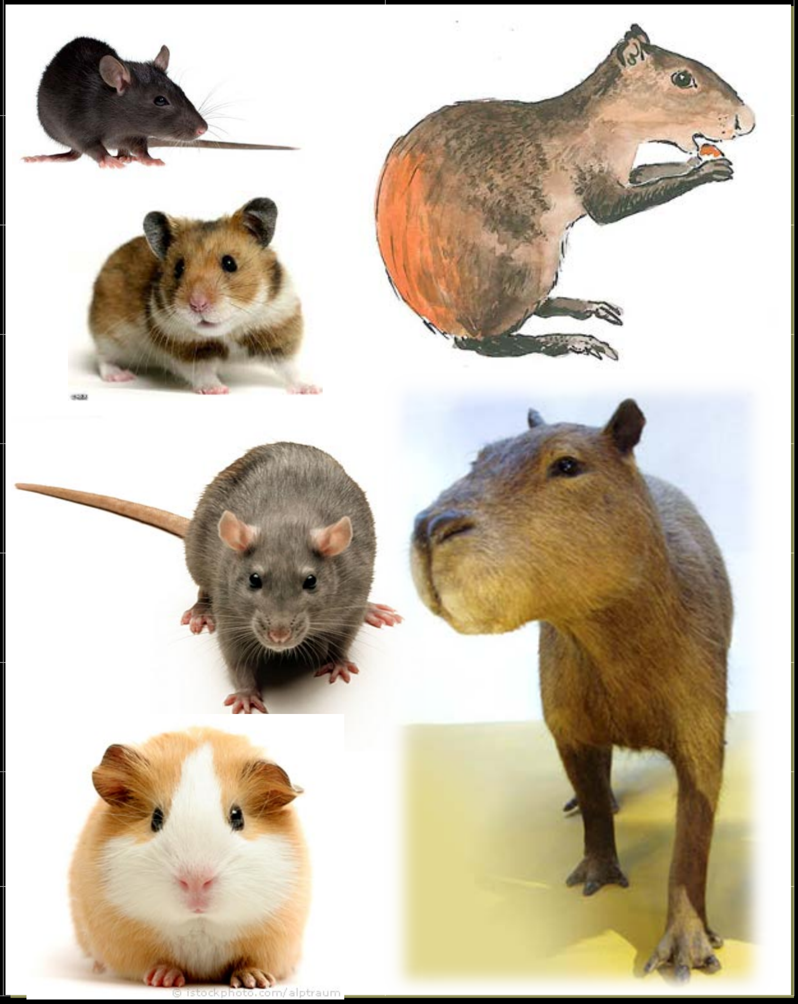
COMPARATIVE CELLULAR COMPOSITION OF THE BRAINS OF SIX RODENT SPECIES

Species	Body mass, g	Brain mass, g
Mouse	40.4 ± 11.6	0.416 ± 0.028
Hamster	168.11 ± 13.6	1.020 ± 0.147
Rat	315.1 ± 102.9	1.802 ± 0.313
Guinea pig	311.0 ± 49.1	3.759 ± 0.499
Agouti	2843.3 ± 195.5	18.365 ± 2.061
Capybara	47500.0 ± 3535.5	76.036 ± 3.787
Variation	**1176x**	**183x**



Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

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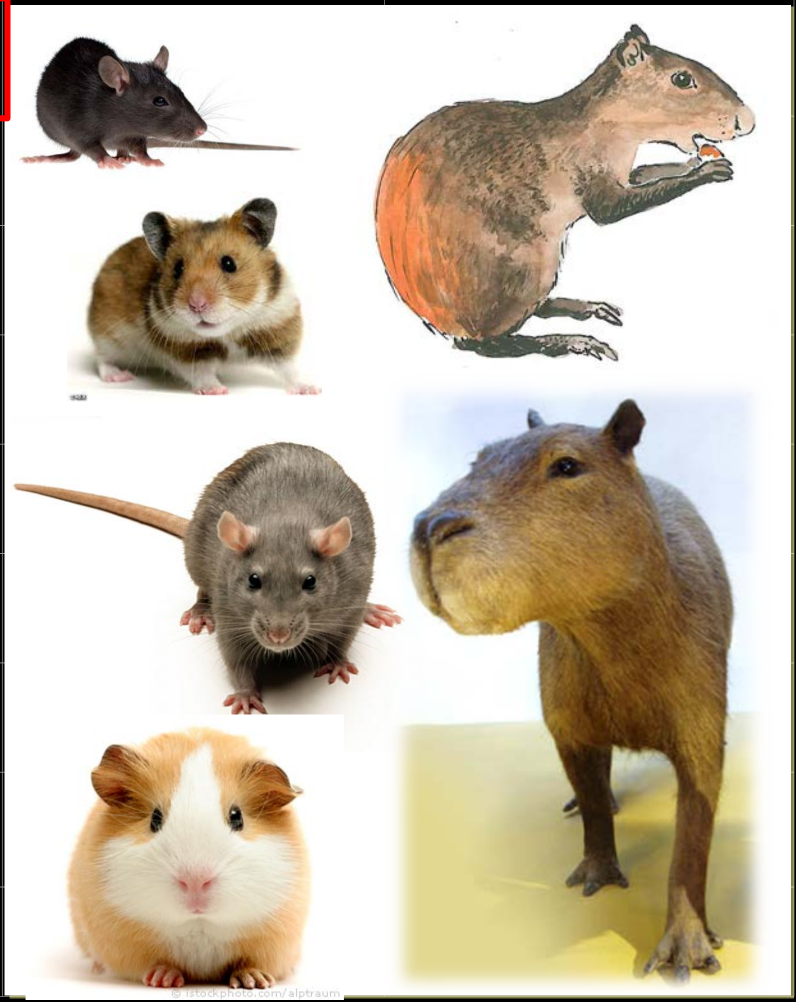

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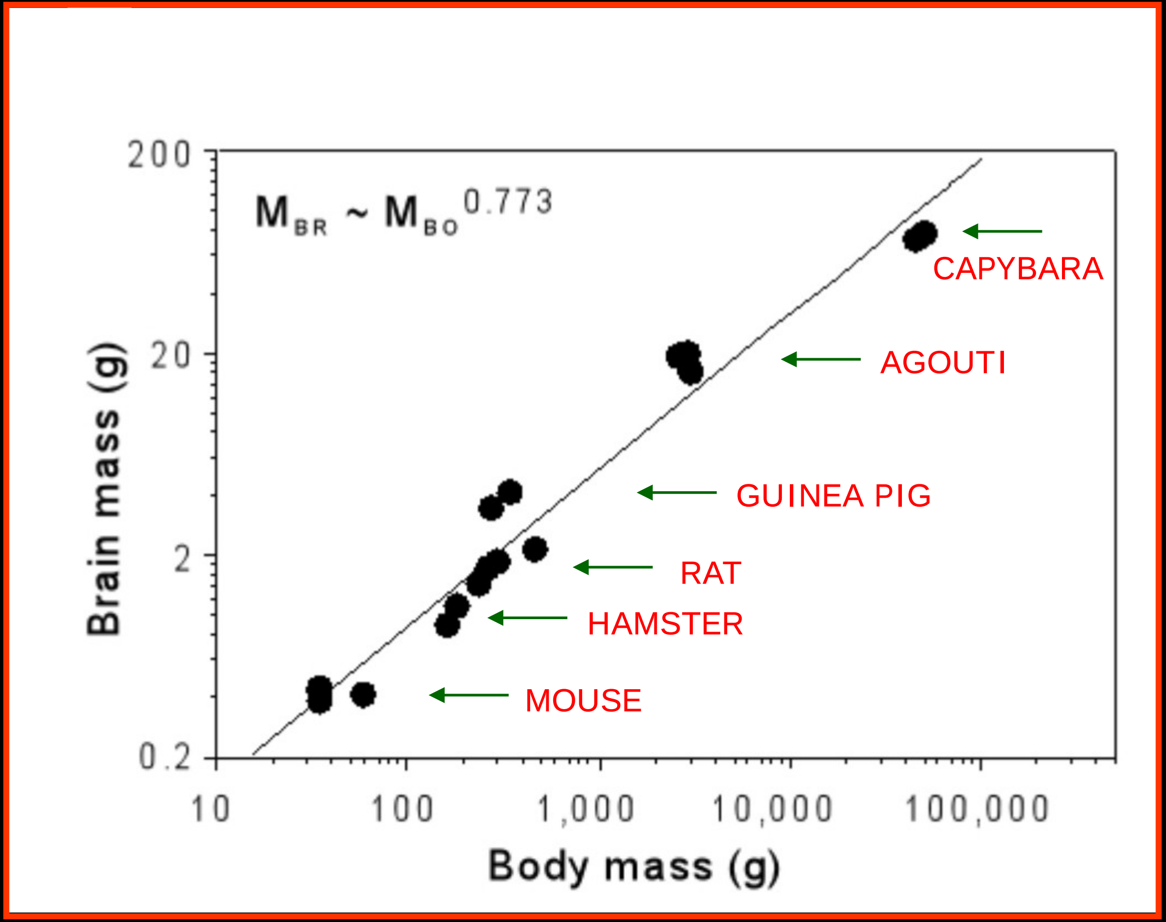
BIGGER BODIES, BIGGER BRAINS
(POWER FUNCTION IN RODENTS)



Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

COMPARATIVE CELLULAR COMPOSITION OF THE BRAIN OF SIX PRIMATE SPECIES

Species	Body mass, g	Brain mass, g
[Tree shrew]	172.5 ± 3.5	2.752 ± 0.011
Marmoset	361.0 ± 1.4	7.780 ± 0.654
Galago	946.7 ± 102.9	10.150 ± 0.060
Owl monkey	925.0 ± 35.4	15.730
Squirrel monkey	n.a.	30.216
Capuchin	3,340.0	52.208
Macaque	3,900.0	87.346
Variation	**10.8x**	**11.2x**

Herculano-Houzel et al, 2007, PNAS 104:3562-3567

COMPARATIVE CELLULAR COMPOSITION OF THE BRAIN OF SIX <u>PRIMATE</u> SPECIES

Species	Body mass, g	Brain mass, g
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Marmoset	361.0 ± 1.4	7.780 ± 0.654
Galago	946.7 ± 102.9	10.150 ± 0.060
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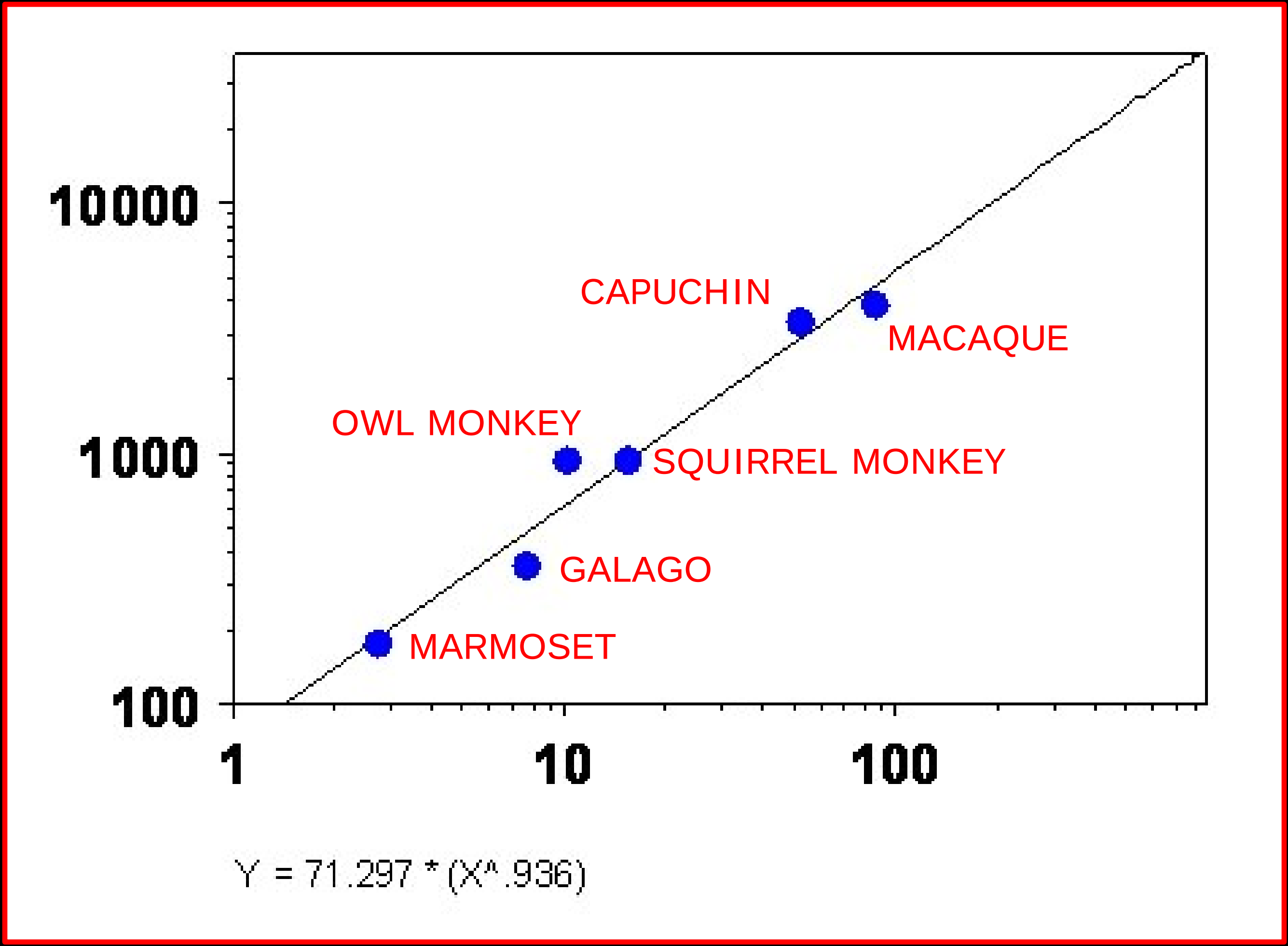
Macaque	3,900.0	87.346
Variation	**10.8x**	**11.2x**

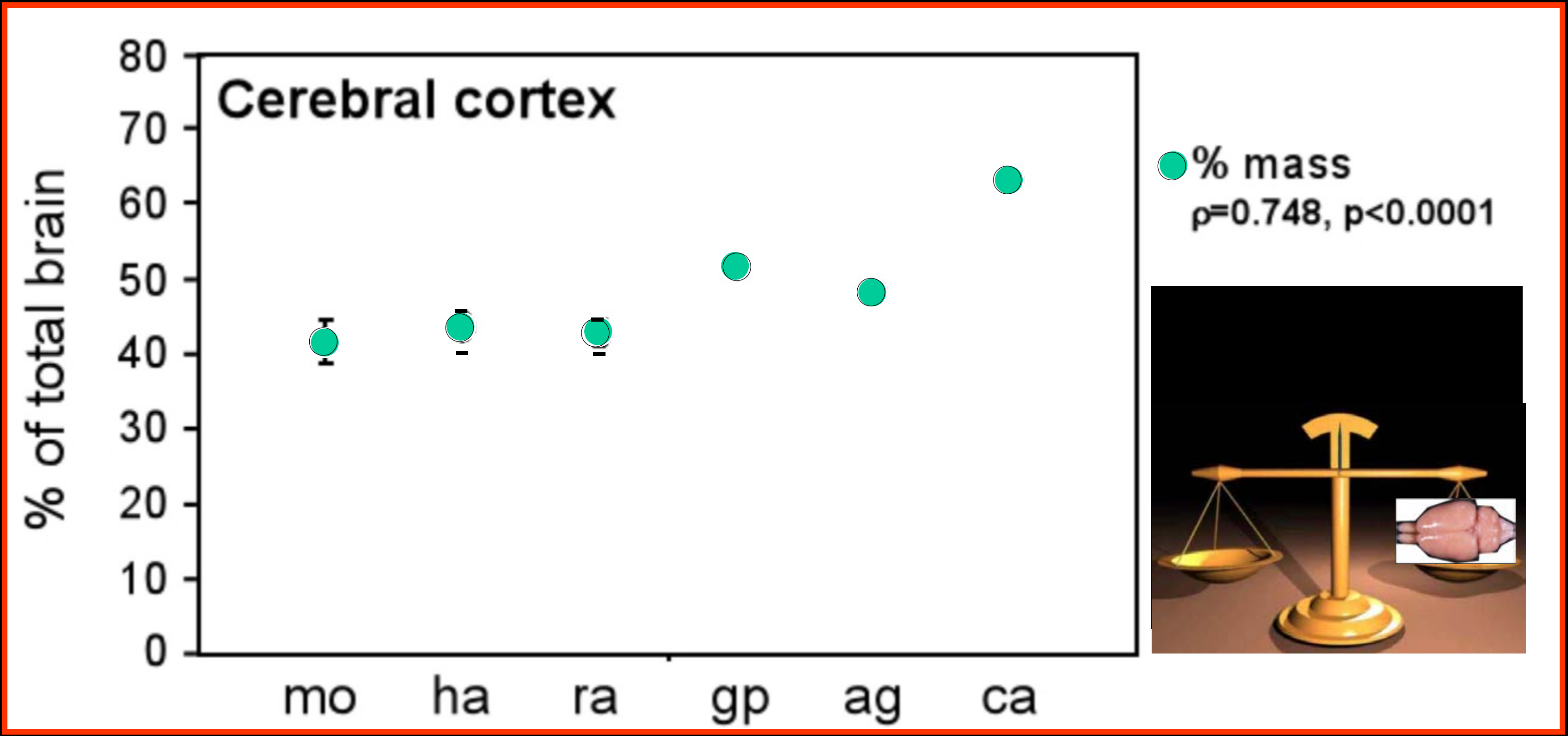
Herculano-Houzel et al, 2007, PNAS 104:3562-3567

BIGGER BODIES, BIGGER BRAINS
(LINEAR FUNCTION IN PRIMATES)



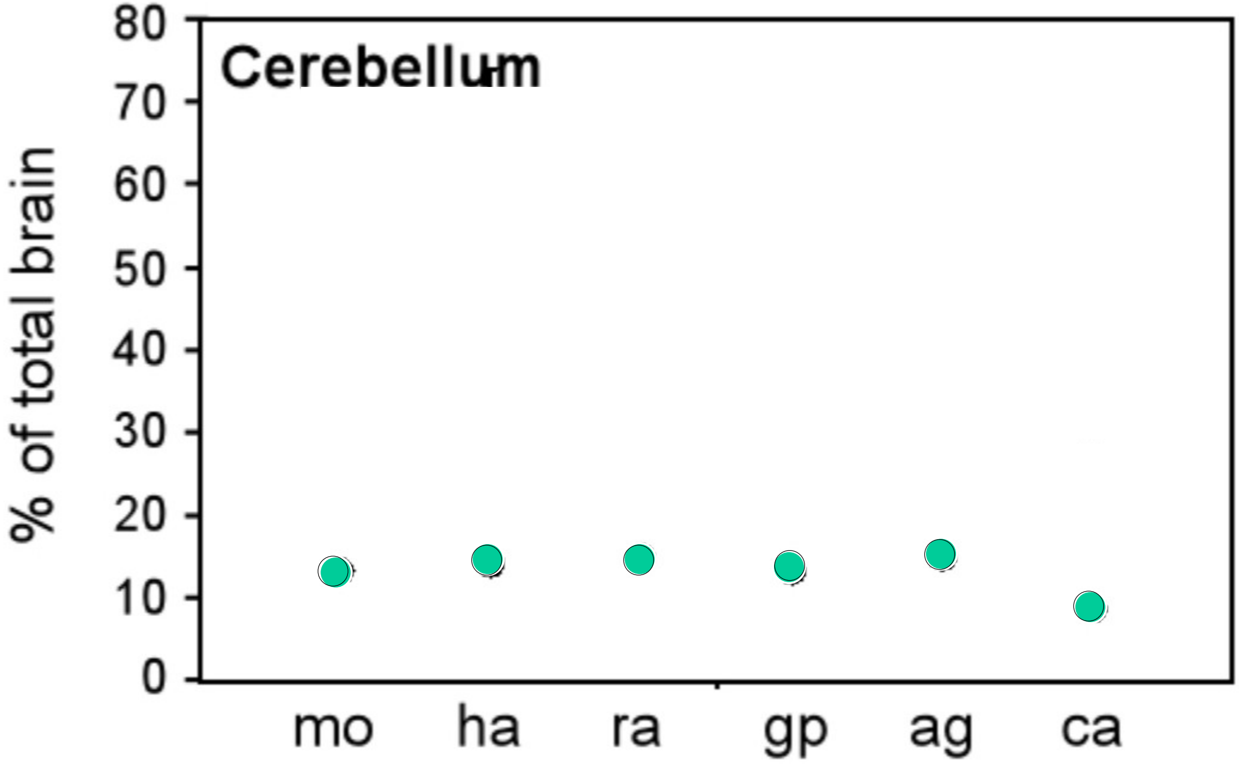
Herculano-Houzel et al, 2007, PNAS 104:3562-3567

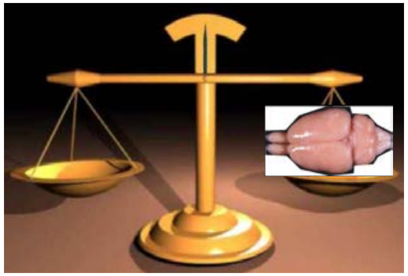
BIGGER BRAINS, BIGGER CORTEX

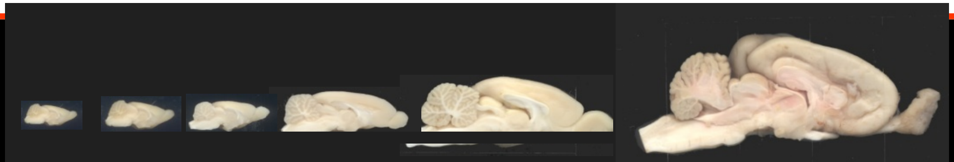


Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

BIGGER BRAINS, BIGGER CORTEX, INVARIANT CEREBELLUM

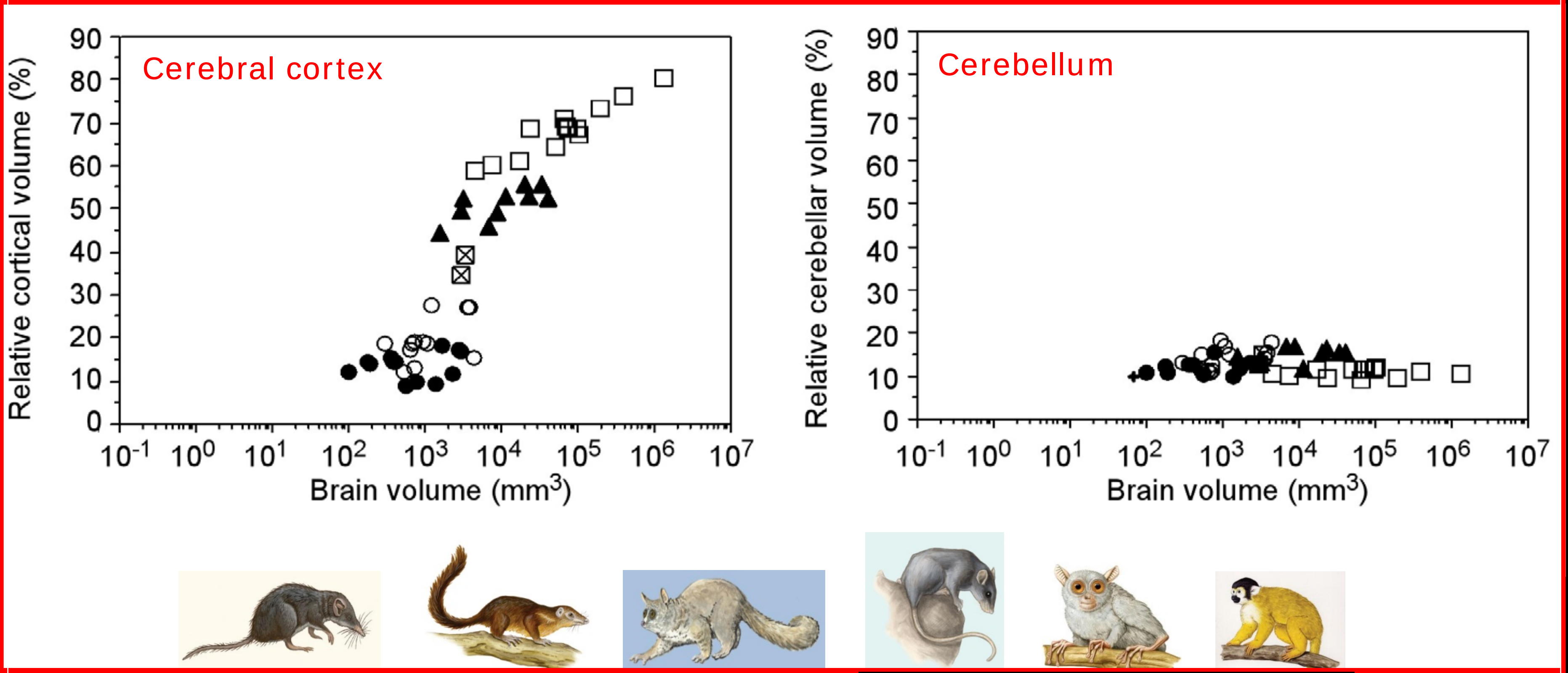






Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

BIGGER BRAINS, BIGGER CORTEX, INVARIANT CEREBELLUM (SAME FOR OTHER SPECIES)



GROWTH OF BRAIN MEANS GROWTH OF CORTEX
OR
ENCEPHALIZATION = CORTICALIZATION

IS IT REALLY TRUE?

COMPARATIVE CELLULAR COMPOSITION OF THE BRAIN OF SIX RODENT SPECIES

Species	**Body mass, g**	**Brain mass, g**	**Total Cells, $x10^6$**	**Total Neurons, $x10^6$**
Mouse	40.4 ± 11.6	0.416 ± 0.028	108.69 ± 16.25	70.89 ± 10.41
Hamster	168.11 ± 13.6	1.020 ± 0.147	166.12 ± 23.77	89.97 ± 9.55
Rat	315.1 ± 102.9	1.802 ± 0.313	331.65 ± 8.84	200.13 ± 12.17
Guinea pig	311.0 ± 49.1	3.759 ± 0.499	477.87 ± 10.57	239.62 ± 2.79
Agouti	2843.3 ± 195.5	18.365 ± 2.061	1941.46 ± 65.81	856.74
Capybara	47500.0 ± 3535.5	76.036 ± 3.787	4866.44 ± 1080.76	1601.12 ± 81.16
Variation	**1176x**	**183x**	**45x**	**22x**

Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

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Hamster	168.11 ± 13.6	1.020 ± 0.147	166.12 ± 23.77	89.97 ± 9.55
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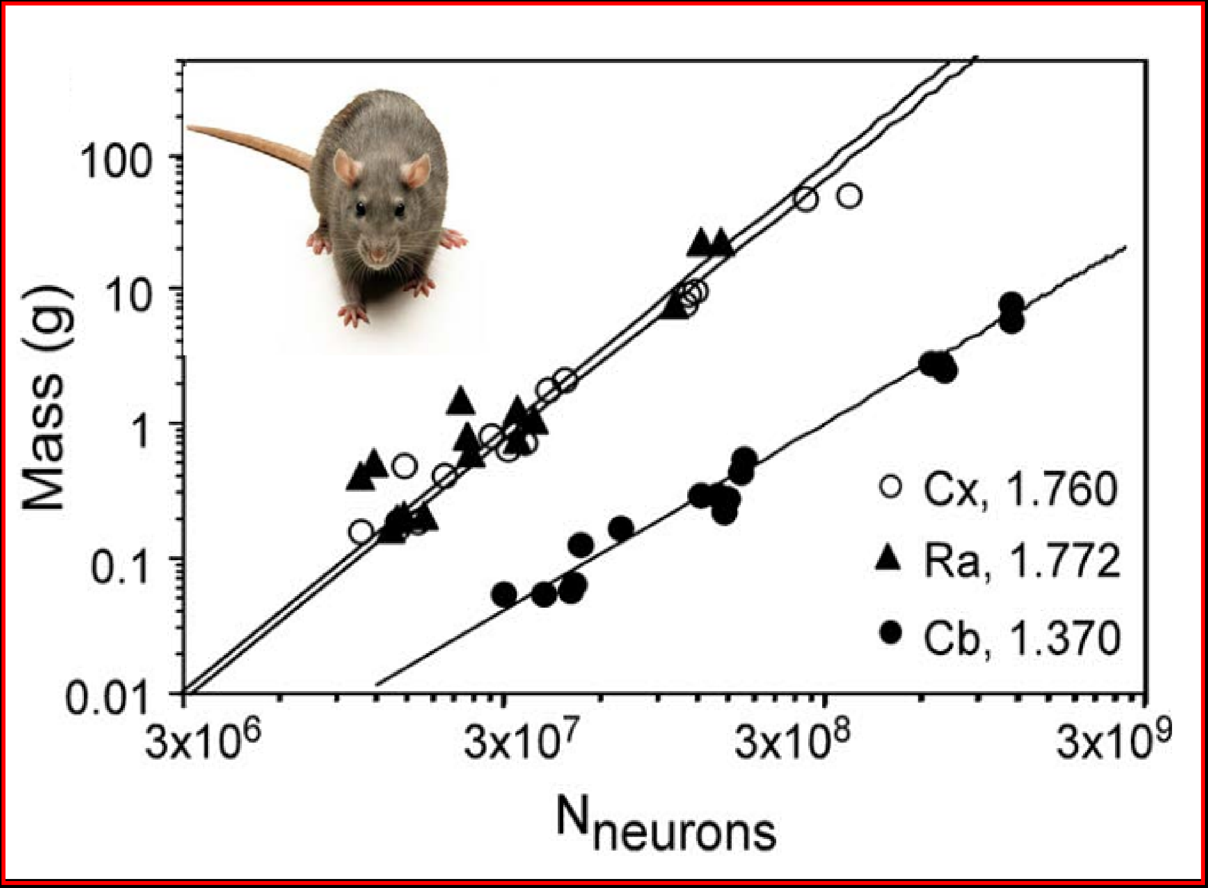
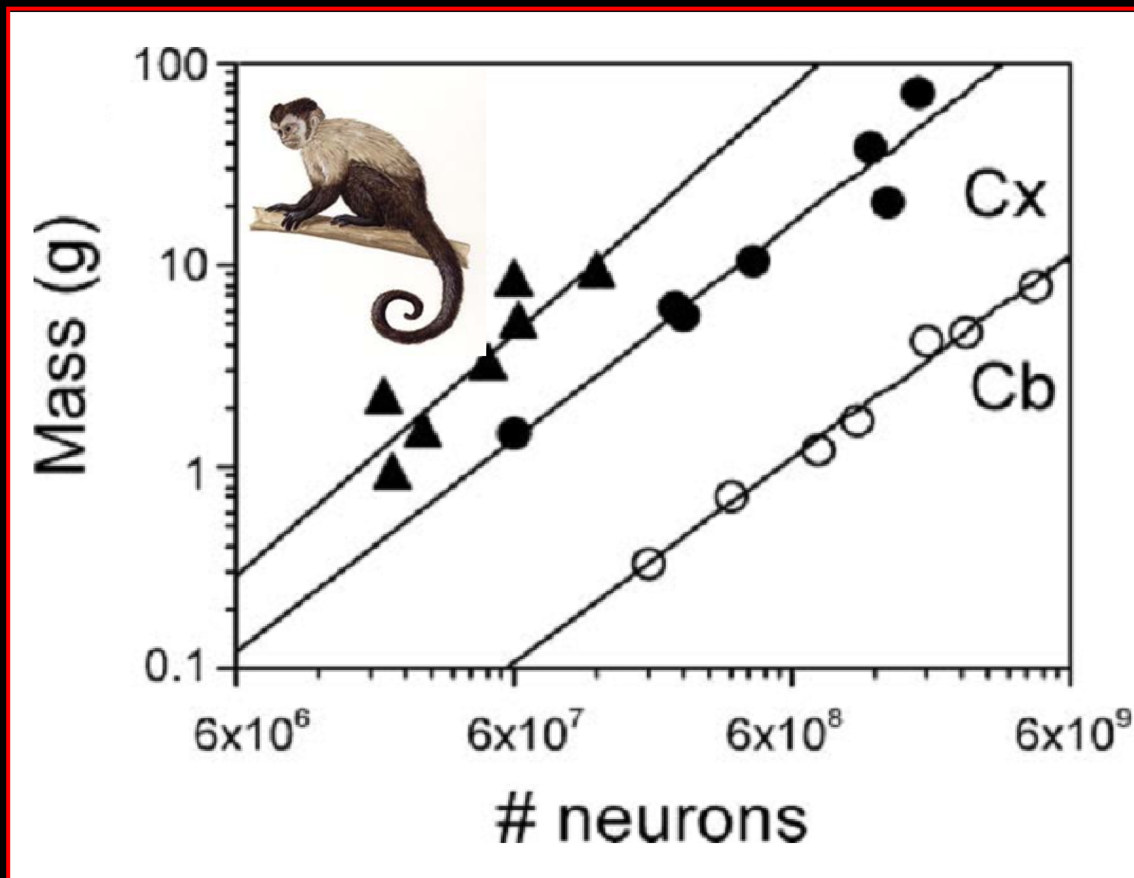
Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

IN RODENTS:
BIGGER BRAINS → MORE NEURONS
(Power scaling function)



Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

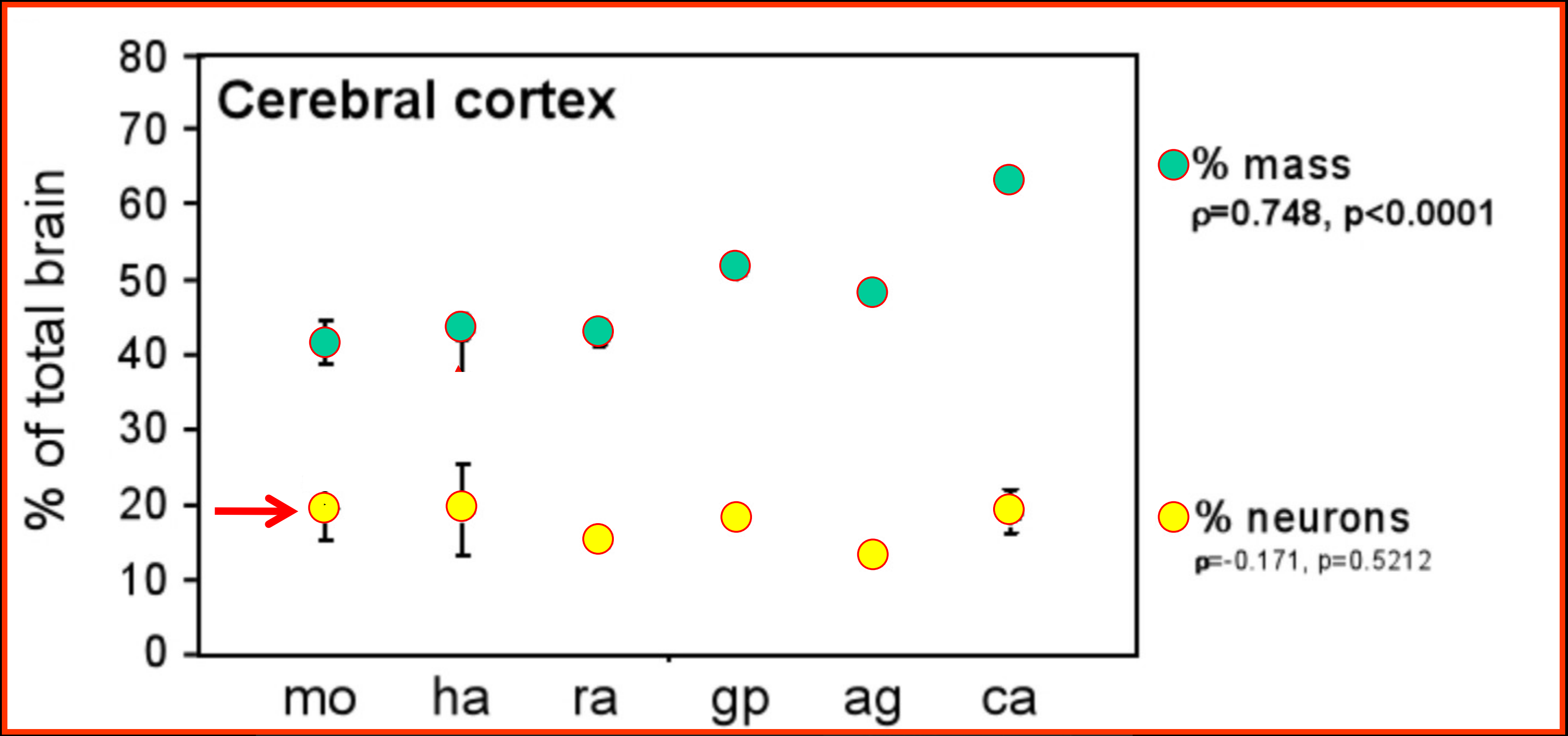
IN PRIMATES:
BIGGER BRAINS → MUCH MORE NEURONS
(Linear scaling function)

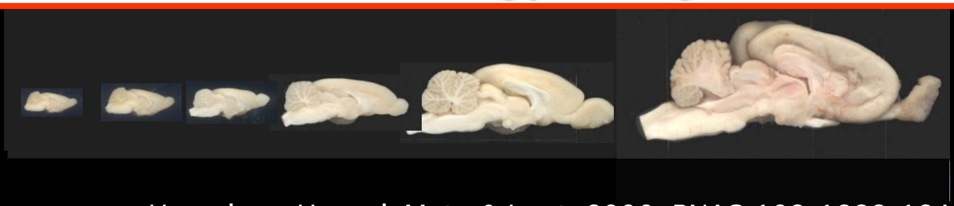


90

Herculano-Houzel et al, 2007, PNAS 104:3562-3567

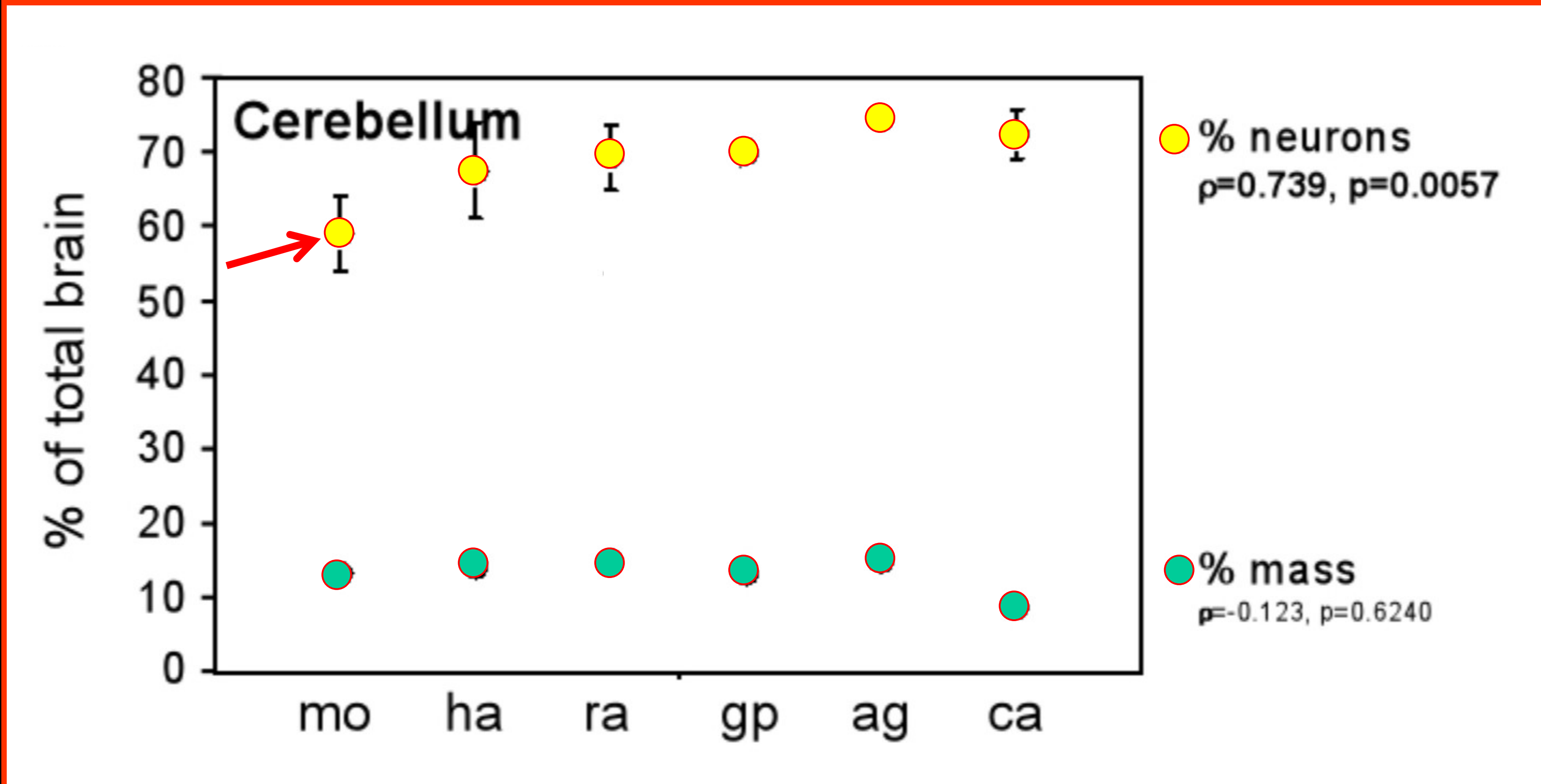
BIGGER BRAINS, INVARIANT PROPORTION OF CORTICAL NEURONS

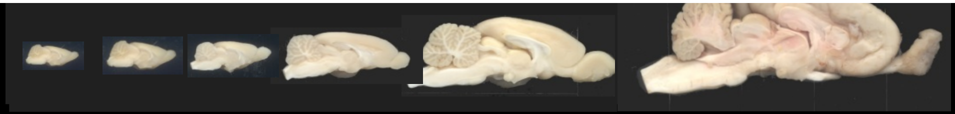




Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

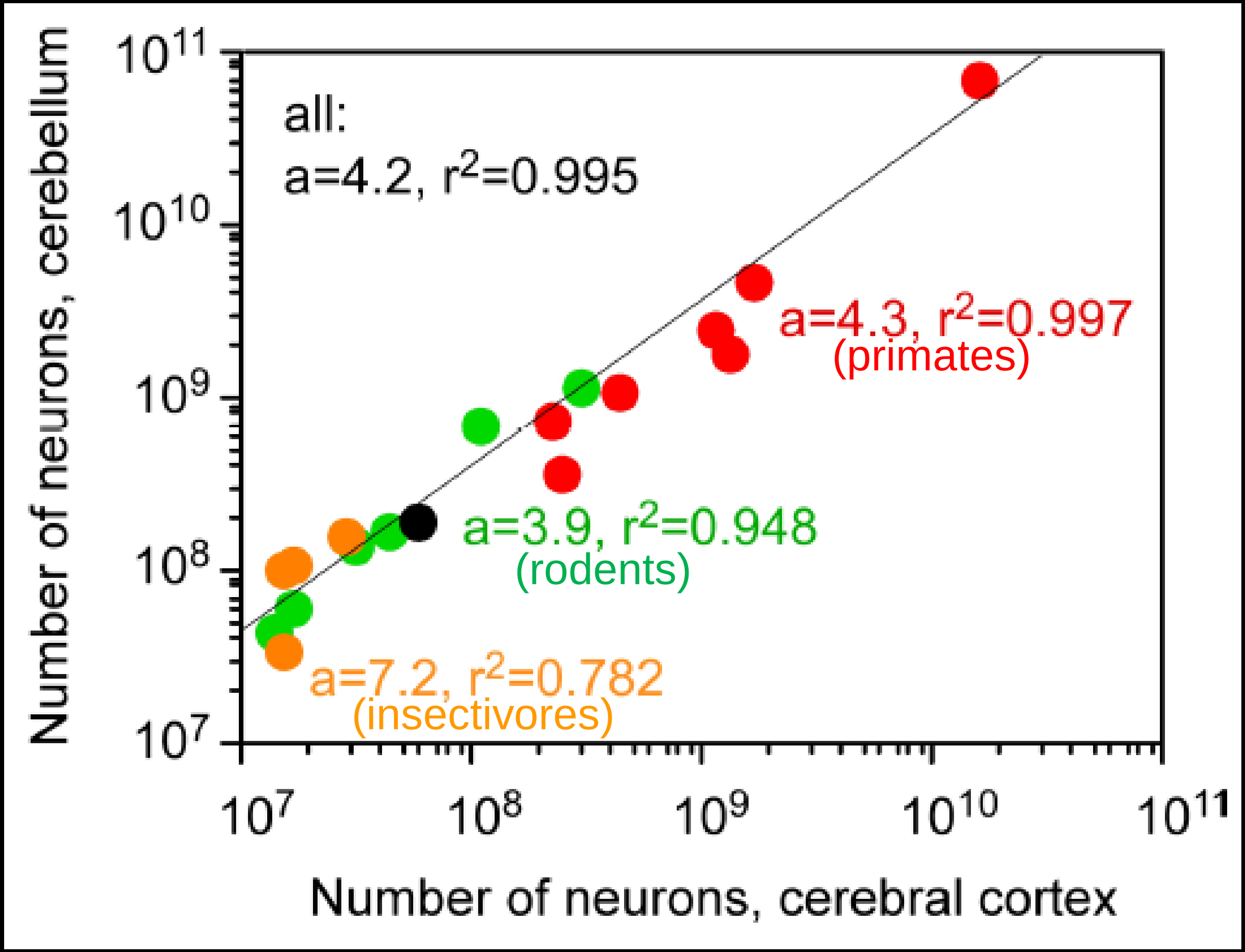
BIGGER BRAINS, LARGER PROPORTION OF CEREBELLAR NEURONS





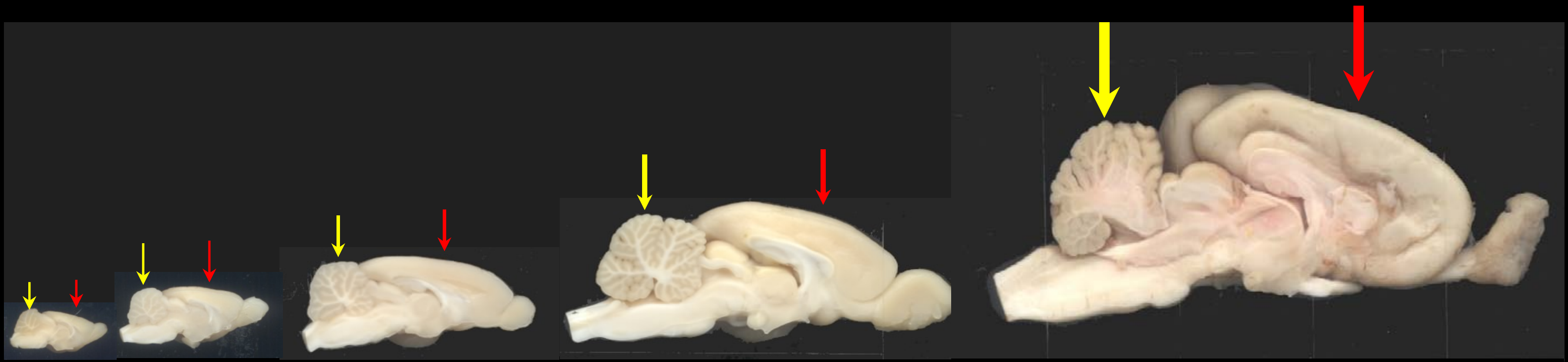
Herculano-Houzel, Mota & Lent, 2006, PNAS 103:1238-1243

COORDINATED SCALING OF CORTICAL AND CEREBELLAR NEURONS



Herculano-Houzel 2010, Front Neuroanat [Epub]

FOR EACH NEURON IN CORTEX THERE ARE 4 NEURONS IN CEREBELLUM (IN ANY SPECIES)

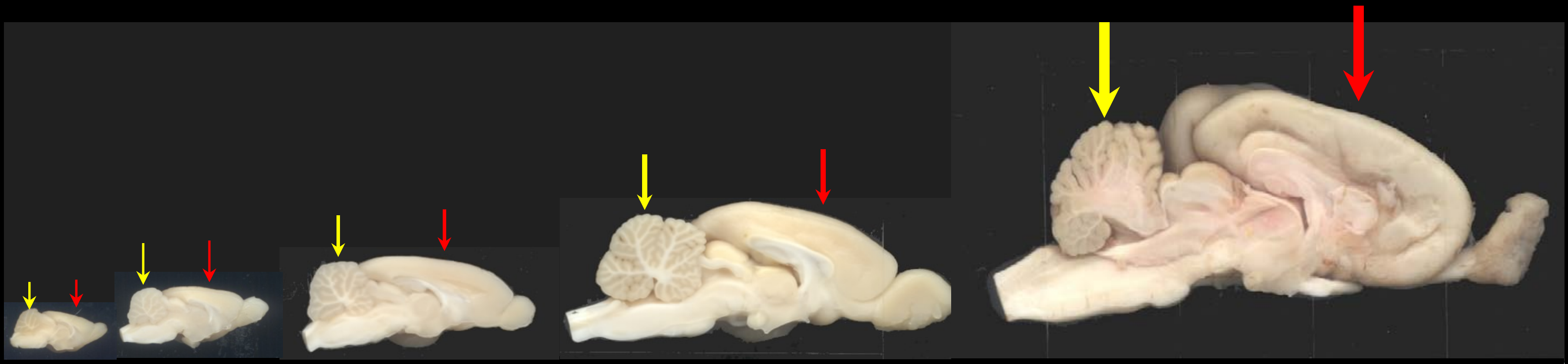


Herculano-Houzel 2010, Front Neuroanat [Epub]

ENCEPHALIZATION ≠ CORTICALIZATION!

OR

GROWTH OF BRAIN MEANS COORDINATED INCREASE IN NUMBER OF CORTICAL AND CEREBELLAR NEURONS

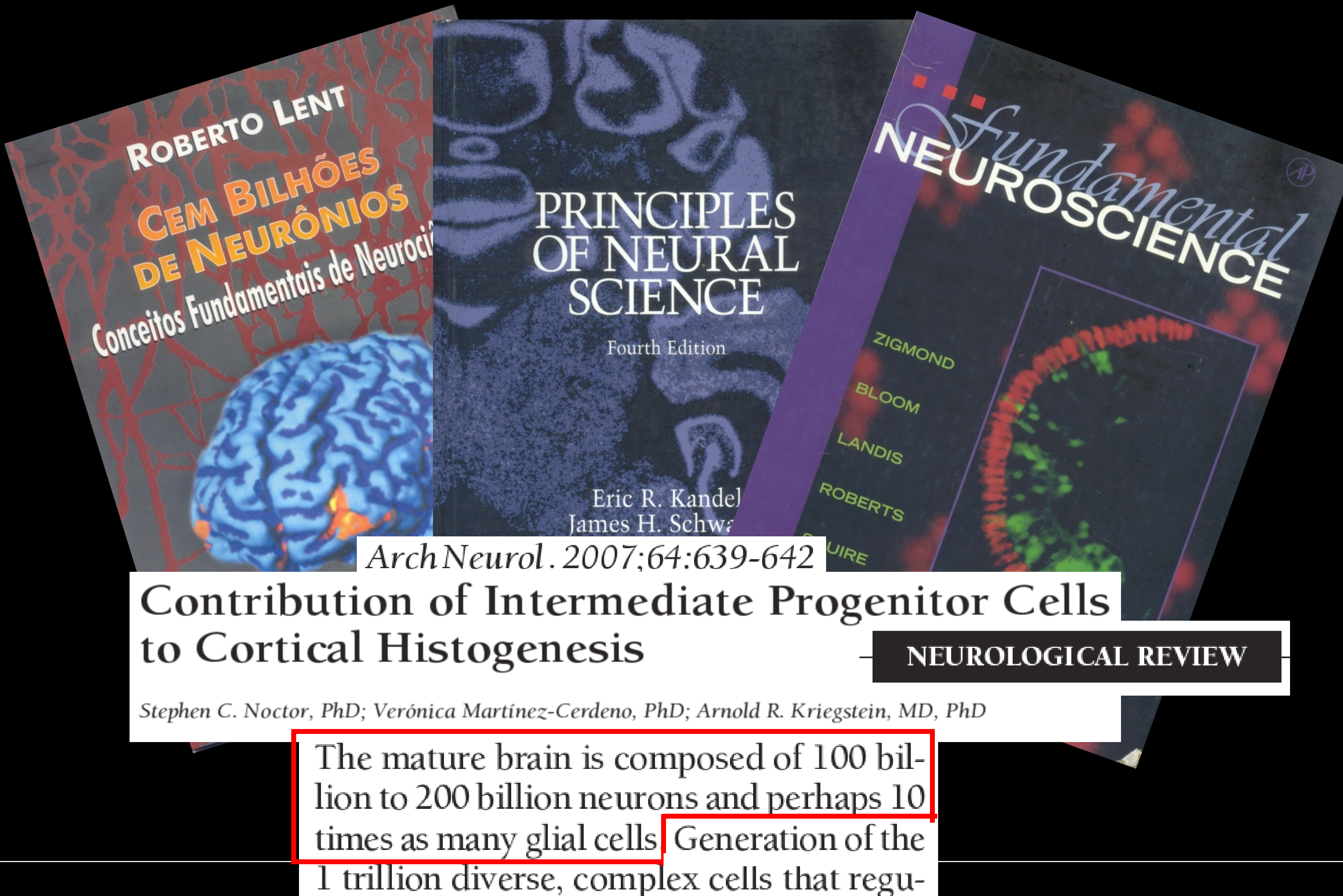


FIRST DOGMA:
“THE CEREBRAL CORTEX IS THE PINACLE OF EVOLUTION”
“BRAIN GROWTH IN EVOLUTION MEANS GROWTH OF THE CEREBRAL CORTEX”

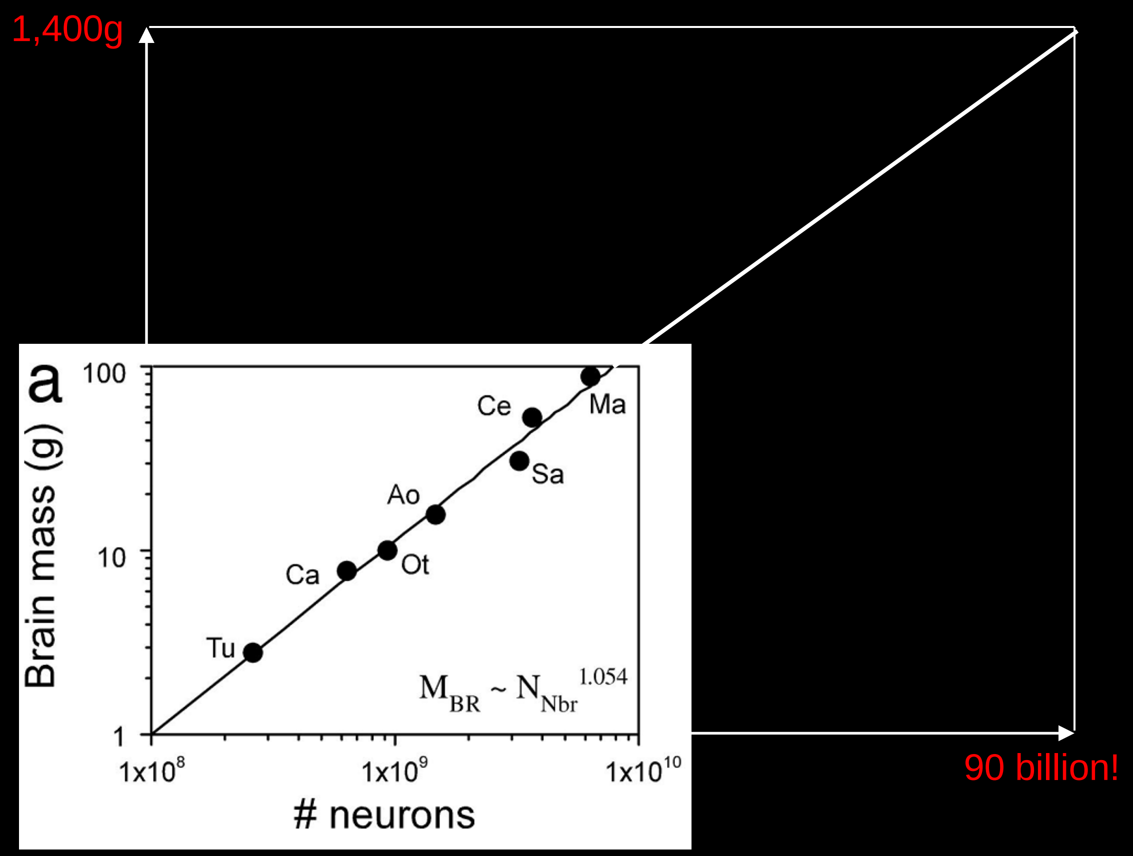
FIRST DOGMA REVISED:
“THE CEREBRAL CORTEX MAY NOT BE THE PINACLE OF EVOLUTION”
“BRAIN GROWTH IN EVOLUTION MEANS THE COORDINATED GROWTH OF CORTEX AND CEREBELLUM”

WHAT ABOUT HUMANS?

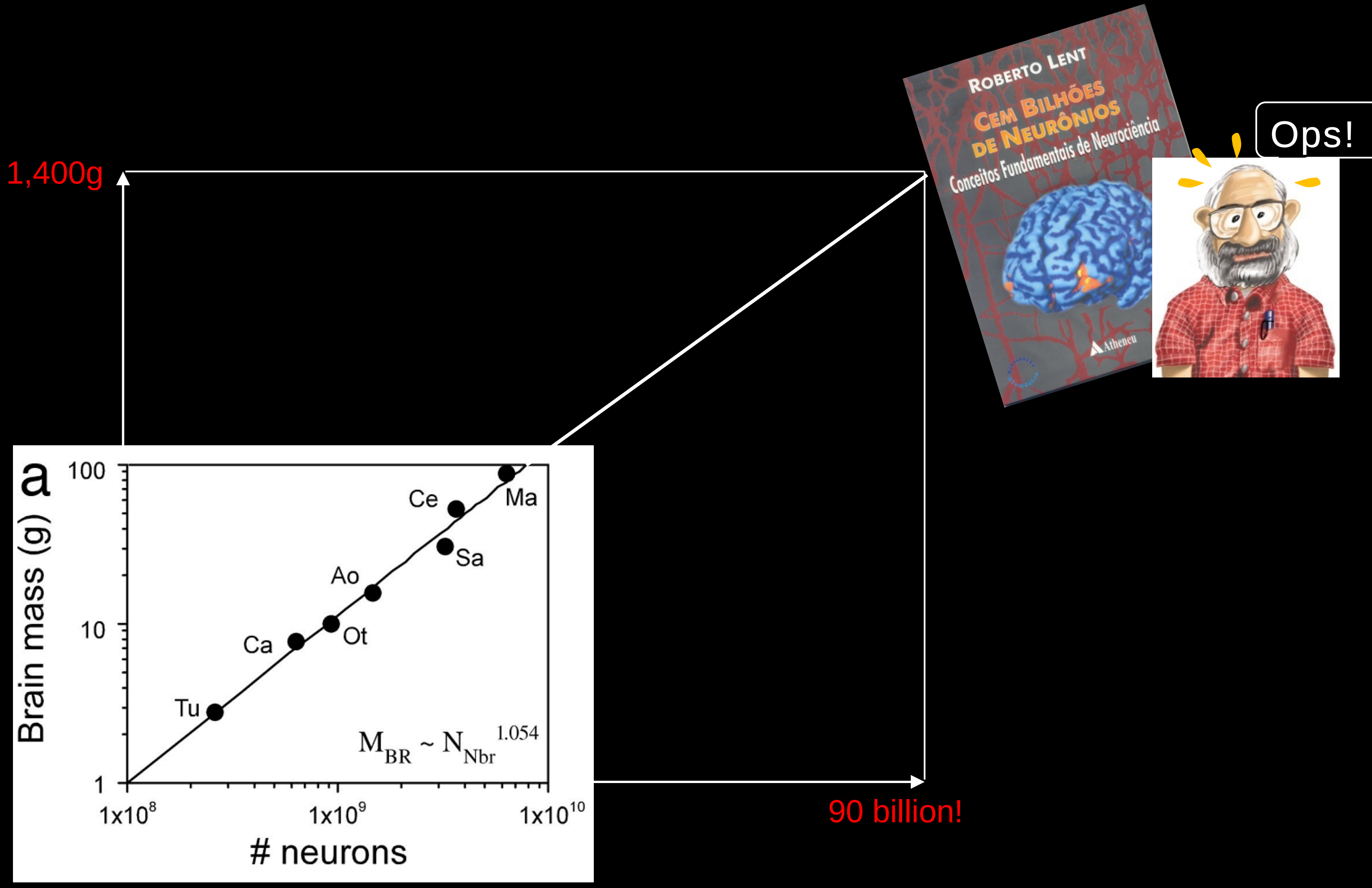
SECOND DOGMA:
"THE HUMAN BRAIN HAS ONE HUNDRED BILLION NEURONS AND 10 TIMES MORE GLIAL CELLS"



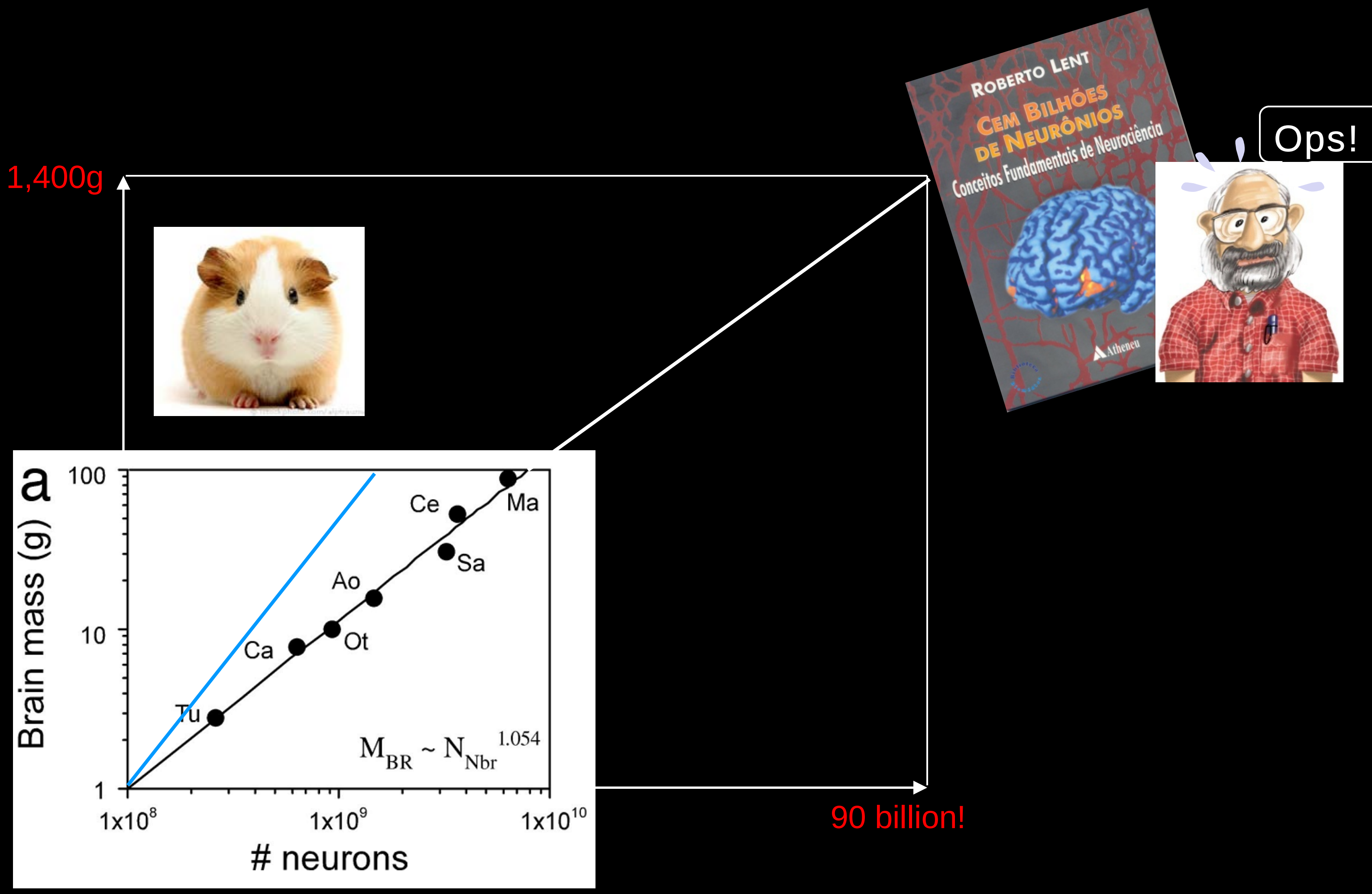
IS IT TRUE?



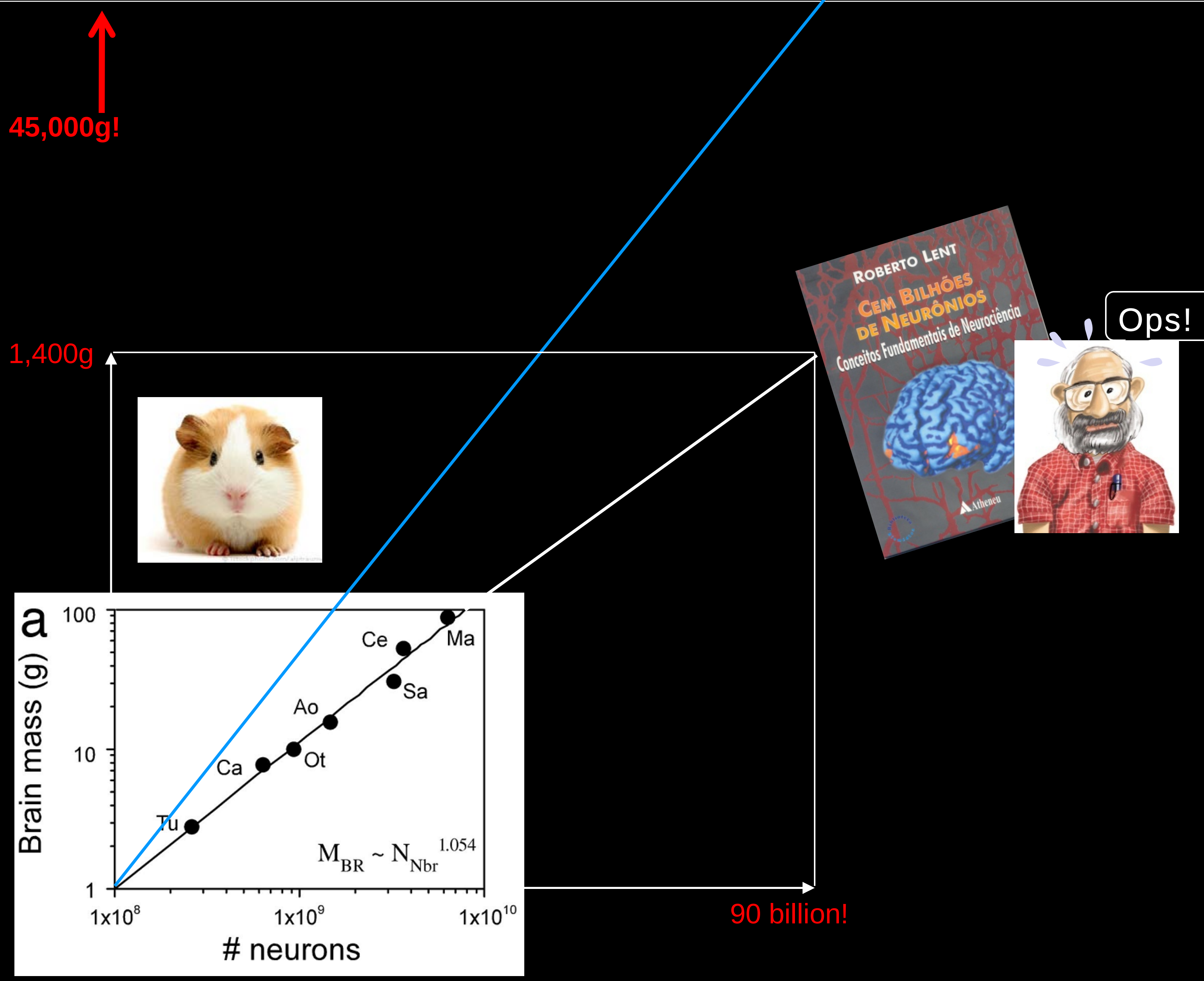
Herculano-Houzel et al, 2007, PNAS 104:3562-3567



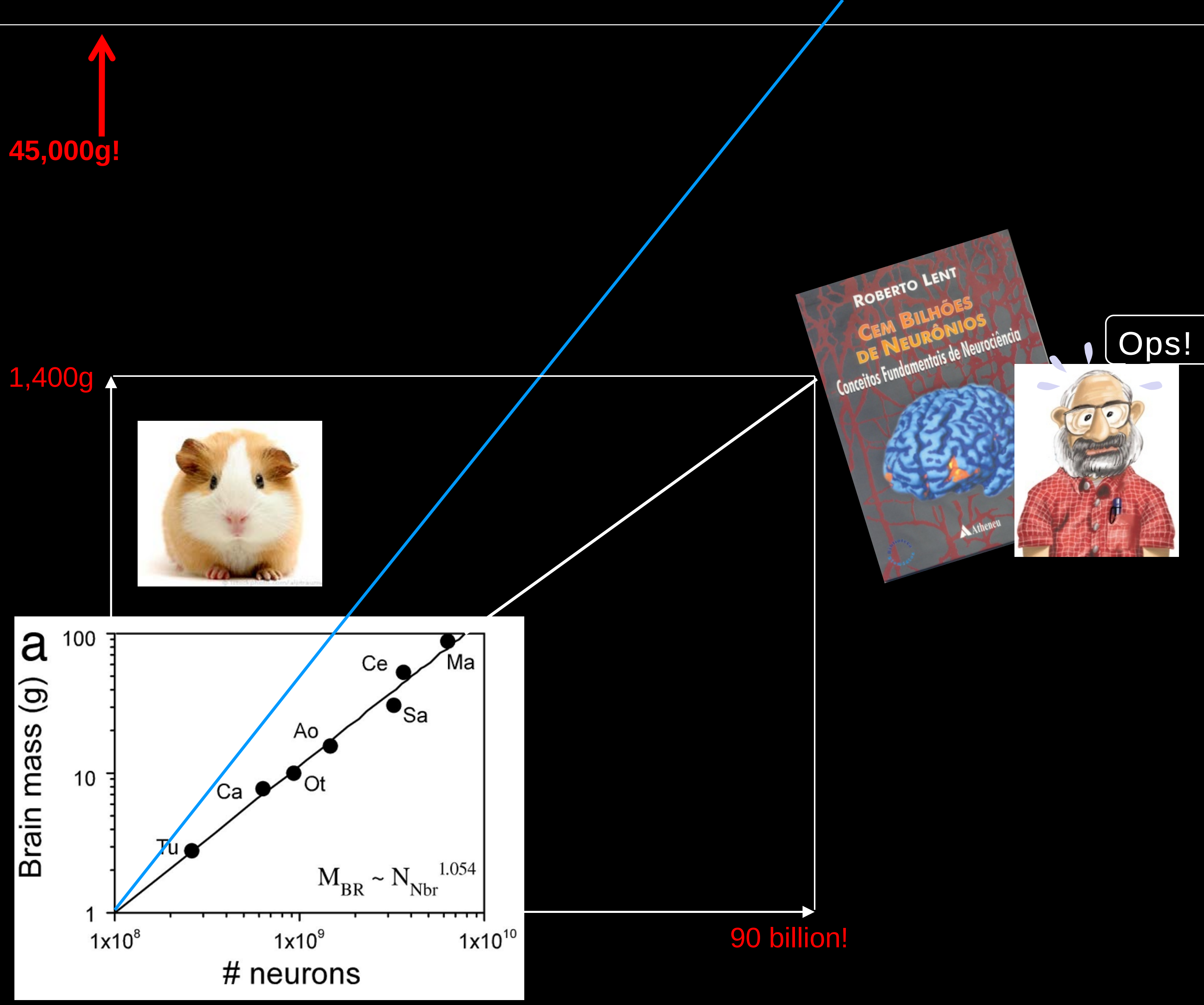
Herculano-Houzel et al, 2007, PNAS 104:3562-3567



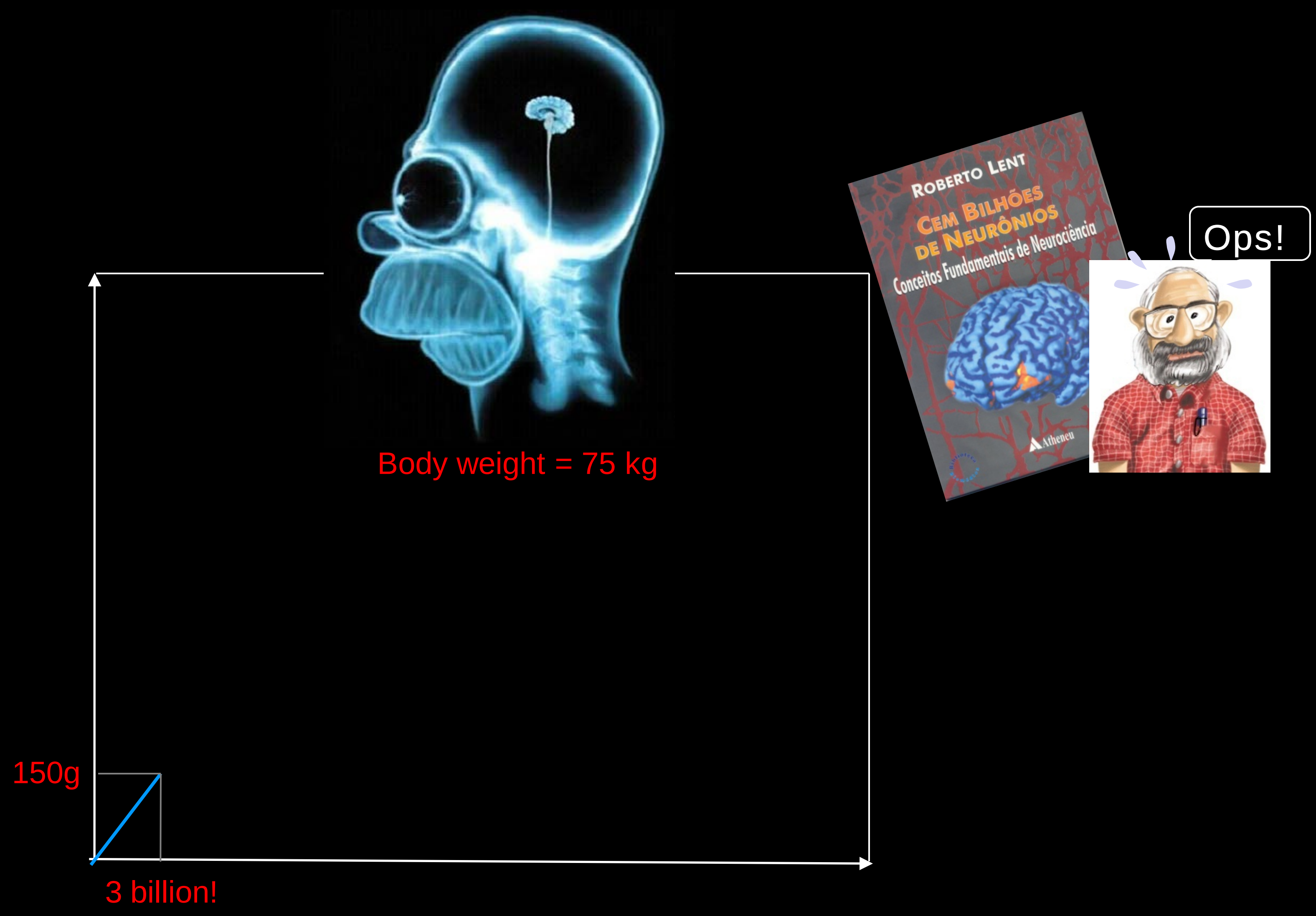
Herculano-Houzel et al, 2007, PNAS 104:3562-3567



Herculano-Houzel et al, 2007, PNAS 104:3562-3567

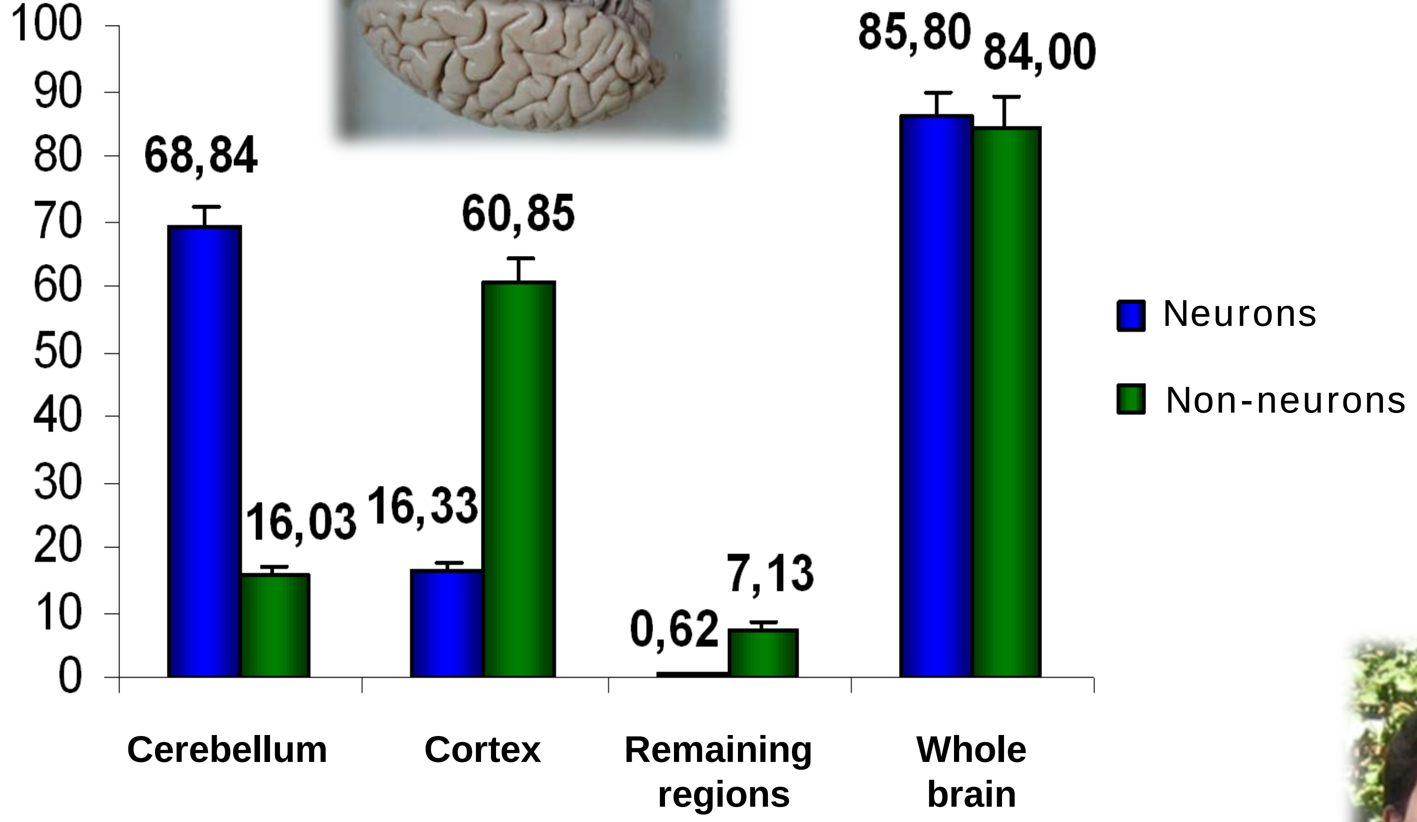


Herculano-Houzel et al, 2007, PNAS 104:3562-3567



Herculano-Houzel et al, 2007, PNAS 104:3562-3567

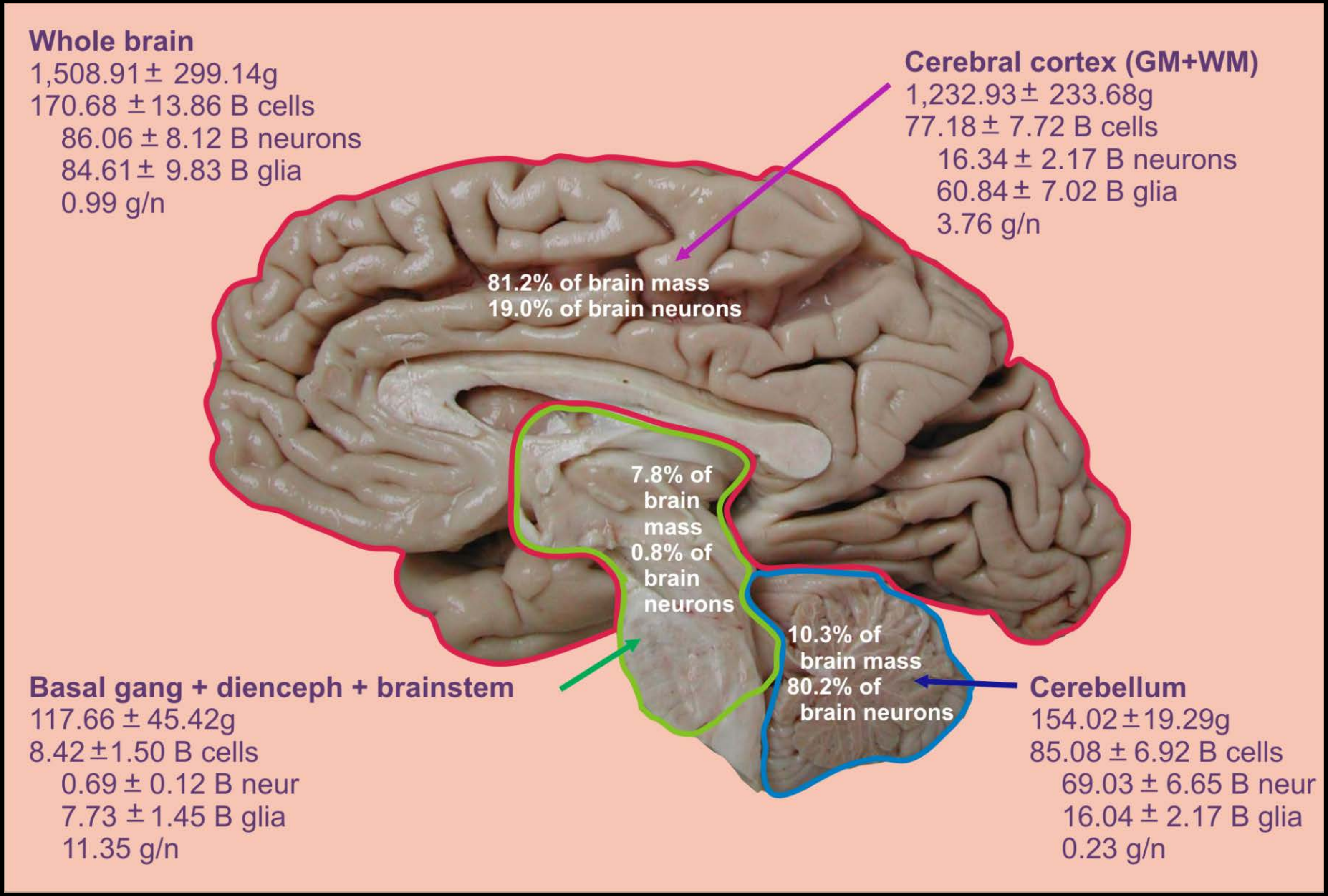
COUNTING NEURONS IN HUMAN BRAIN



Fred Azevedo

Azevedo et al, 2009, J.Comp.Neurol, 513:530-541
in collaboration with the São Paulo Brain Bank, FM-USP

COUNTING NEURONS IN HUMAN BRAIN



Azevedo et al, 2009, J.Comp.Neurol, 513:530-541
in collaboration with the São Paulo Brain Bank, FM-USP

SECOND DOGMA:
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SECOND DOGMA REVISED:
"THE HUMAN BRAIN HAS LESS THAN ONE HUNDRED BILLION NEURONS AND AN EQUAL NUMBER OF GLIAL CELLS"

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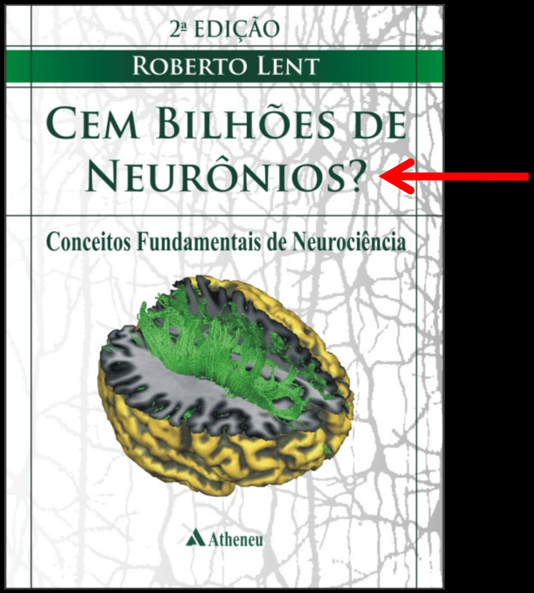
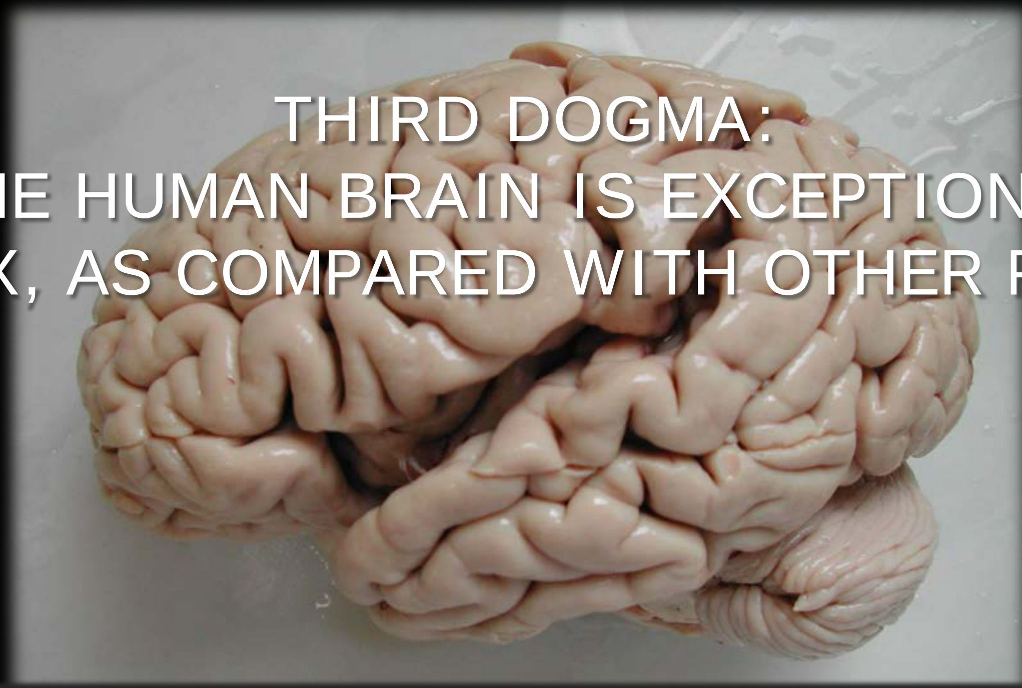


EVOLUTION

DEVELOPMENT

PATHOLOGY



THIRD DOGMA:

"THE HUMAN BRAIN IS EXCEPTIONALLY COMPLEX, AS COMPARED WITH OTHER PRIMATES"

Herculano-Houzel et al, 2007, PNAS 104:3562-3567

EVOLUTION

DEVELOPMENT

PATHOLOGY

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ELSEVIER
Review
TRENDS in Cognitive Sciences Vol.9 No.5 May 2005
Full text provided by www.sciencedirect.com
SCIENCE DIRECT

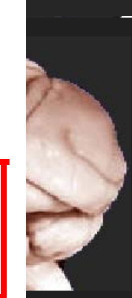
Evolution of the brain and intelligence

Gerhard Roth[1,2] and Ursula Dicke[2]

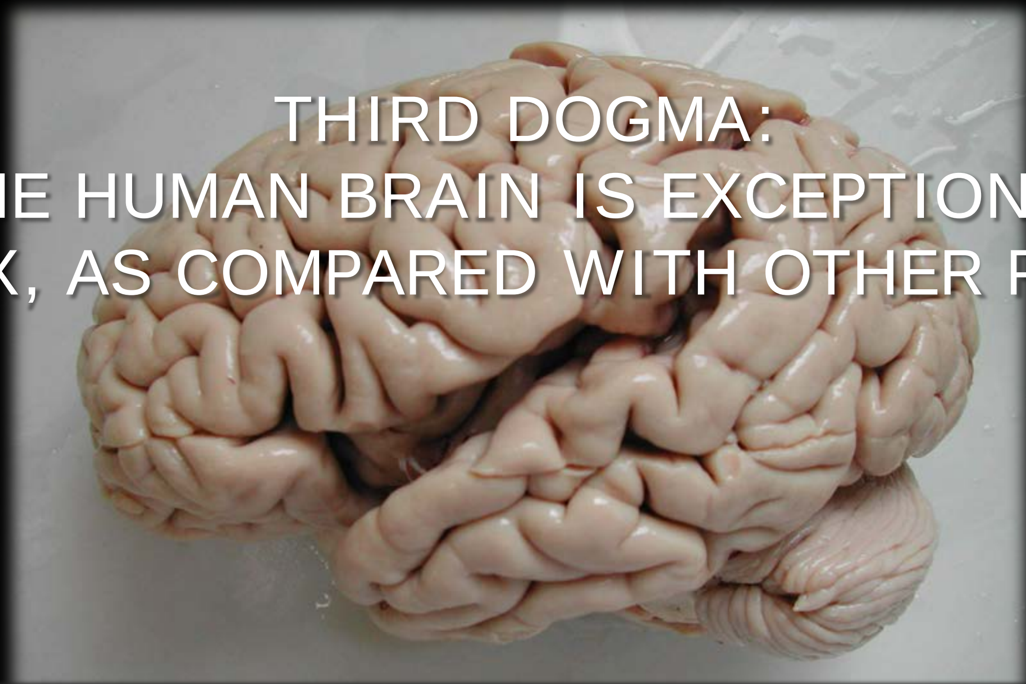
[1]Hanse Institute for Advanced Study, D-27753 Delmenhorst, Germany
[2]Brain Research Institute, University of Bremen, D-28334 Bremen, Germany

Absolute size is the most general of all brain properties (Figure 1; Table 1), and ranges in mammals from brains of small bats and insectivores (weighing less than 0.1 g) to those of large cetaceans (up to 9000 g). It is assumed that animals with larger brains are more intelligent than those with smaller ones [15]. However, monkeys possess brains

Hercular



IS IT TRUE?



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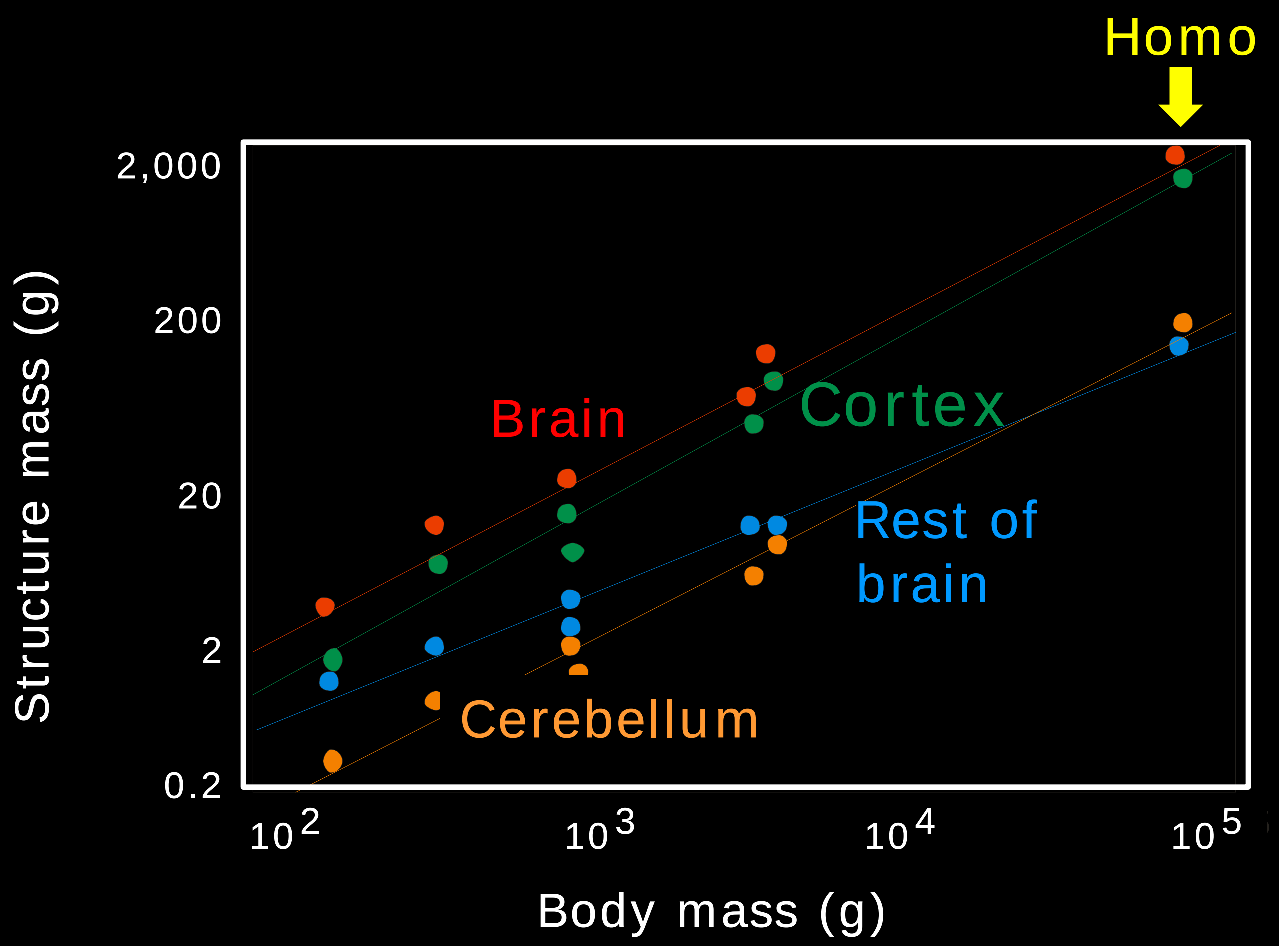
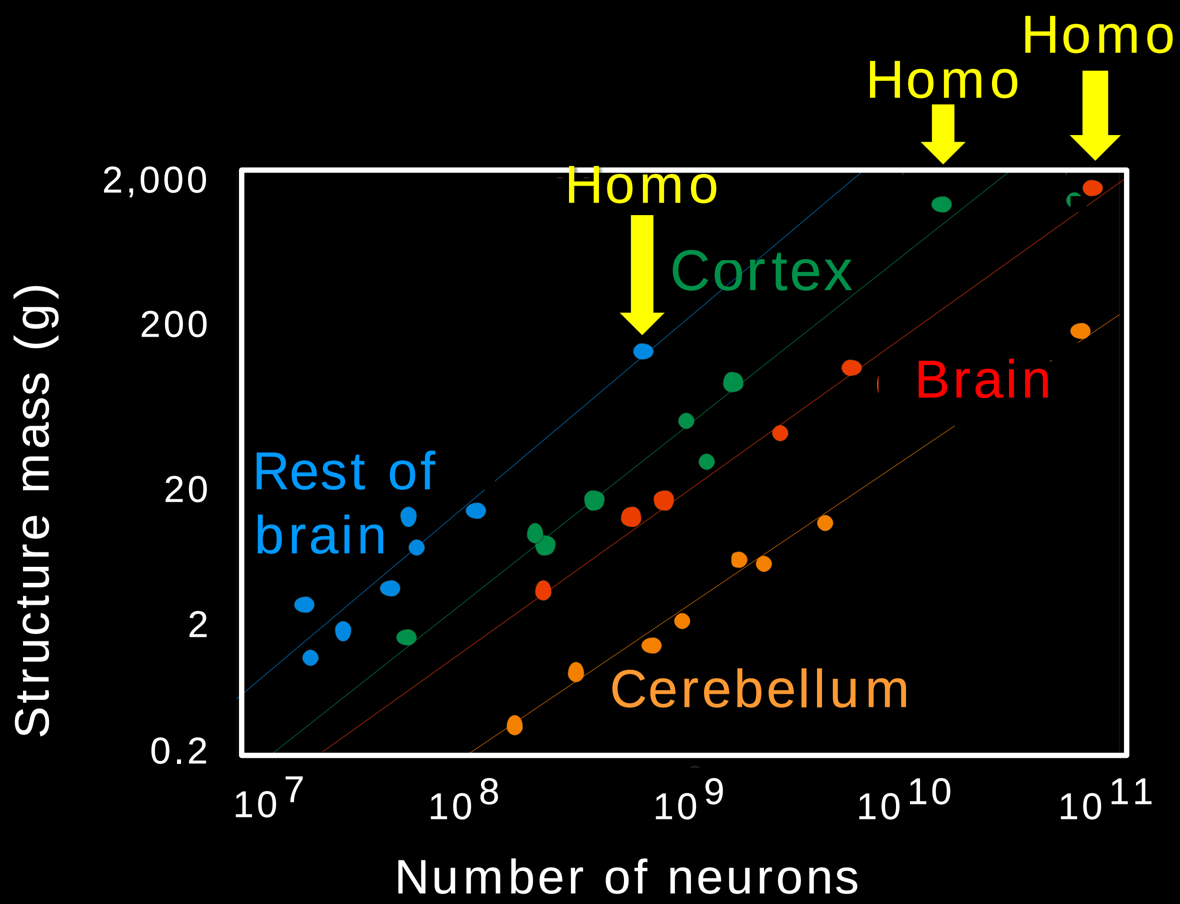
MASS OF BRAIN STRUCTURES FITS WELL IN PRIMATE CURVE



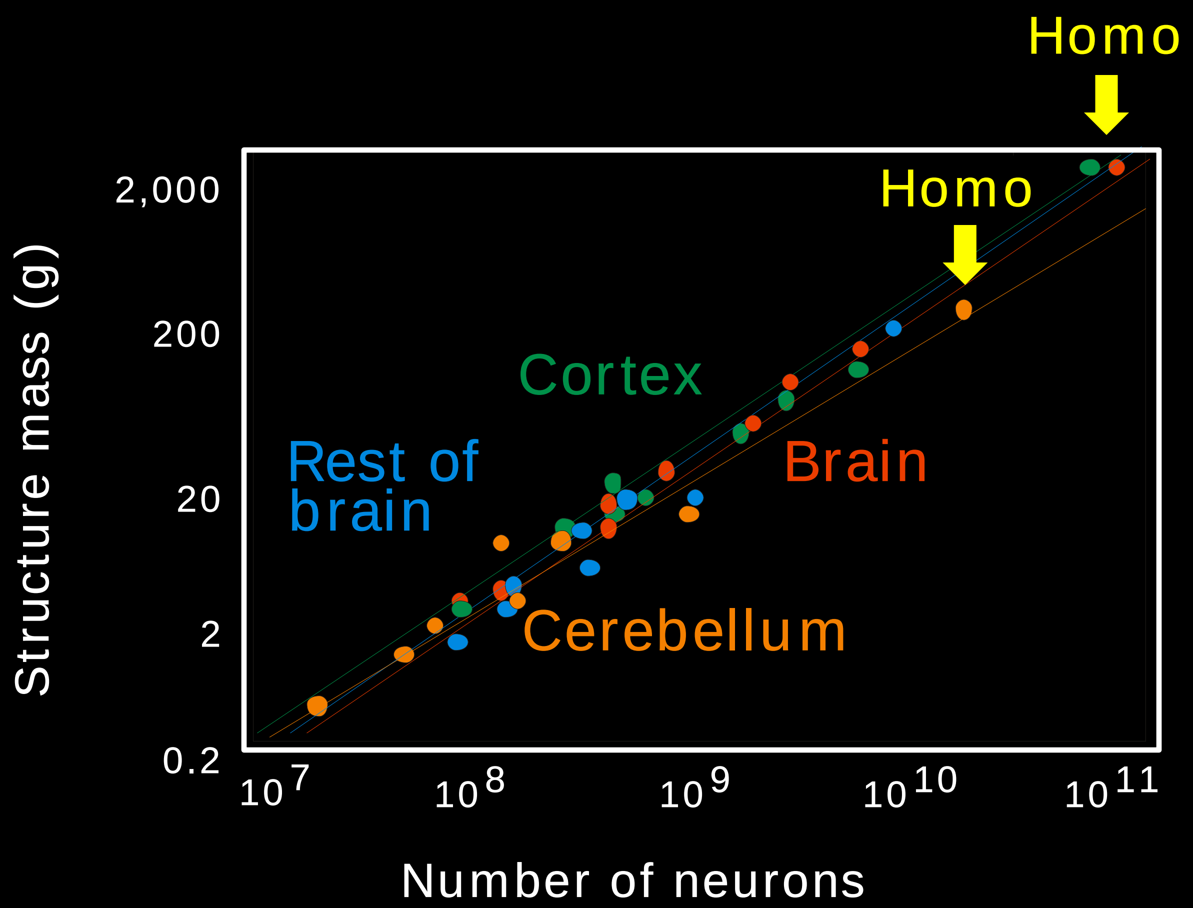
Azevedo et al, 2009, J. Comp. Neurol., 513:530-541

NUMBER OF NEURONS ALSO FIT WELL IN PRIMATE CURVE



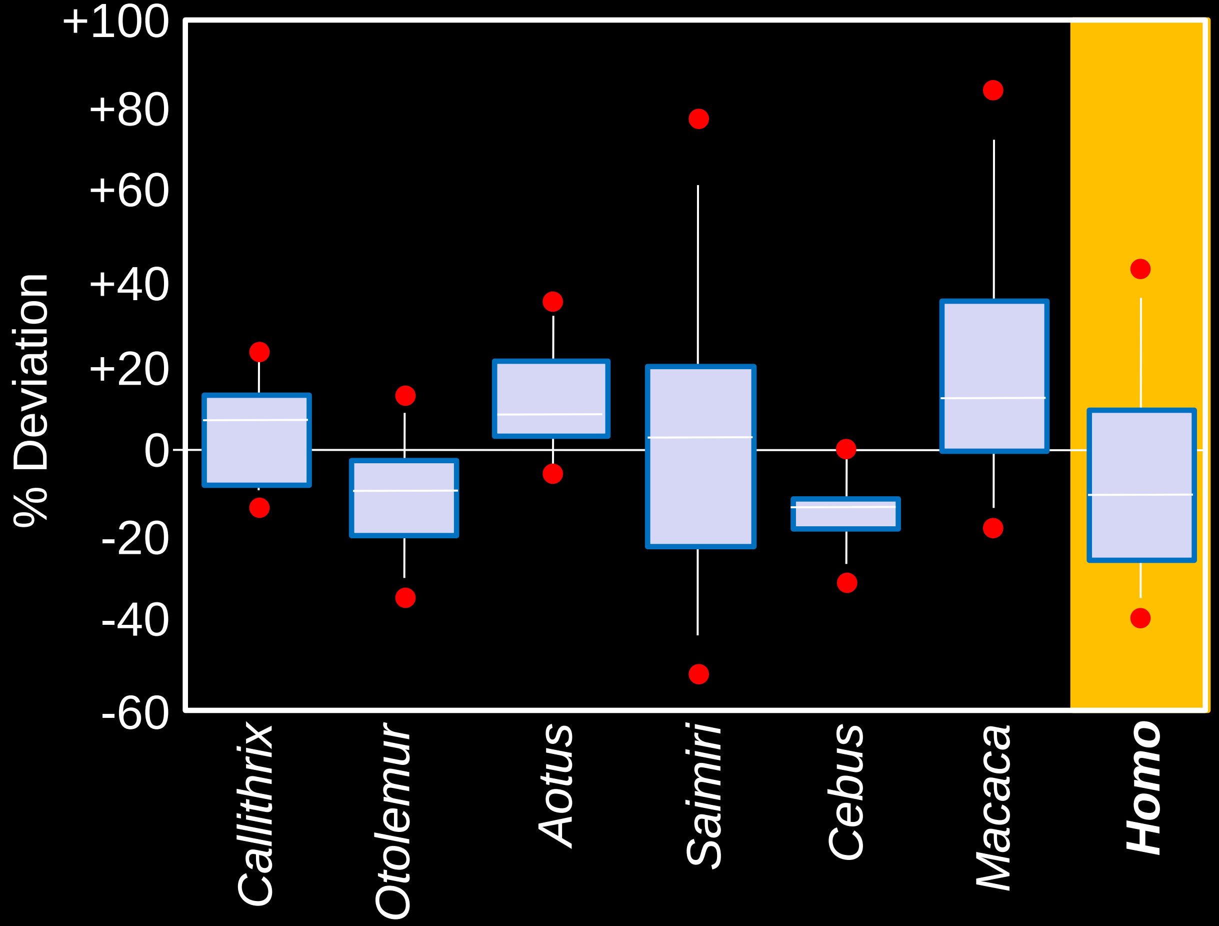
Azevedo et al, 2009, J. Comp. Neurol., 513:530-541

NUMBER OF GLIAL CELLS ALSO FIT WELL IN PRIMATE CURVE



Azevedo et al, 2009, J. Comp. Neurol., 513:530-541

DEVIATION FROM AVERAGE IS SIMILAR FOR ALL PRIMATES



Azevedo et al, 2009, J. Comp. Neurol., 513:530-541

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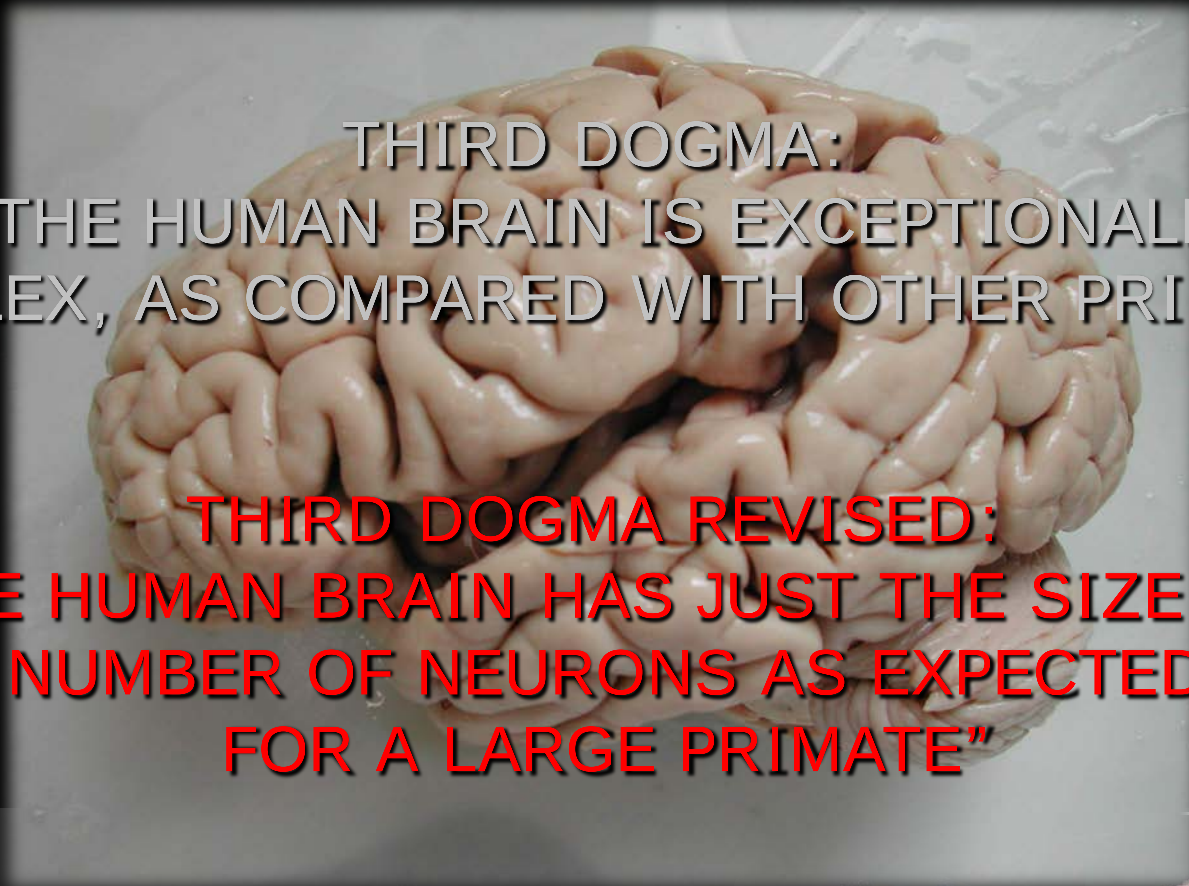
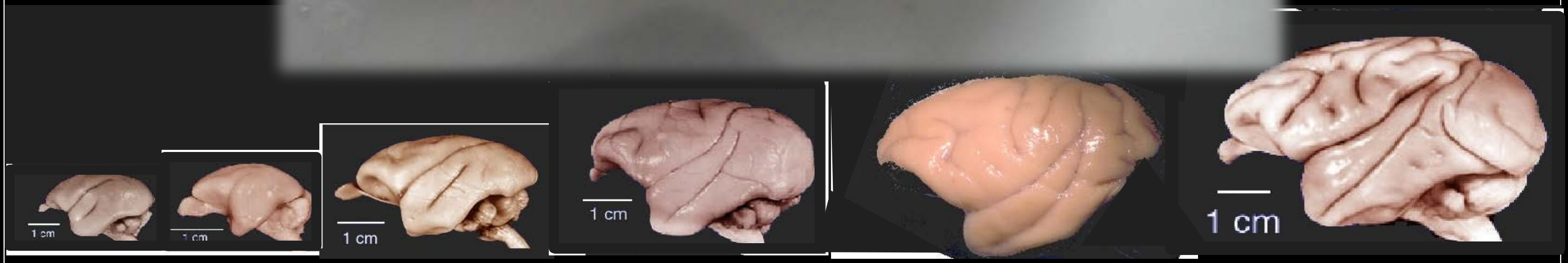
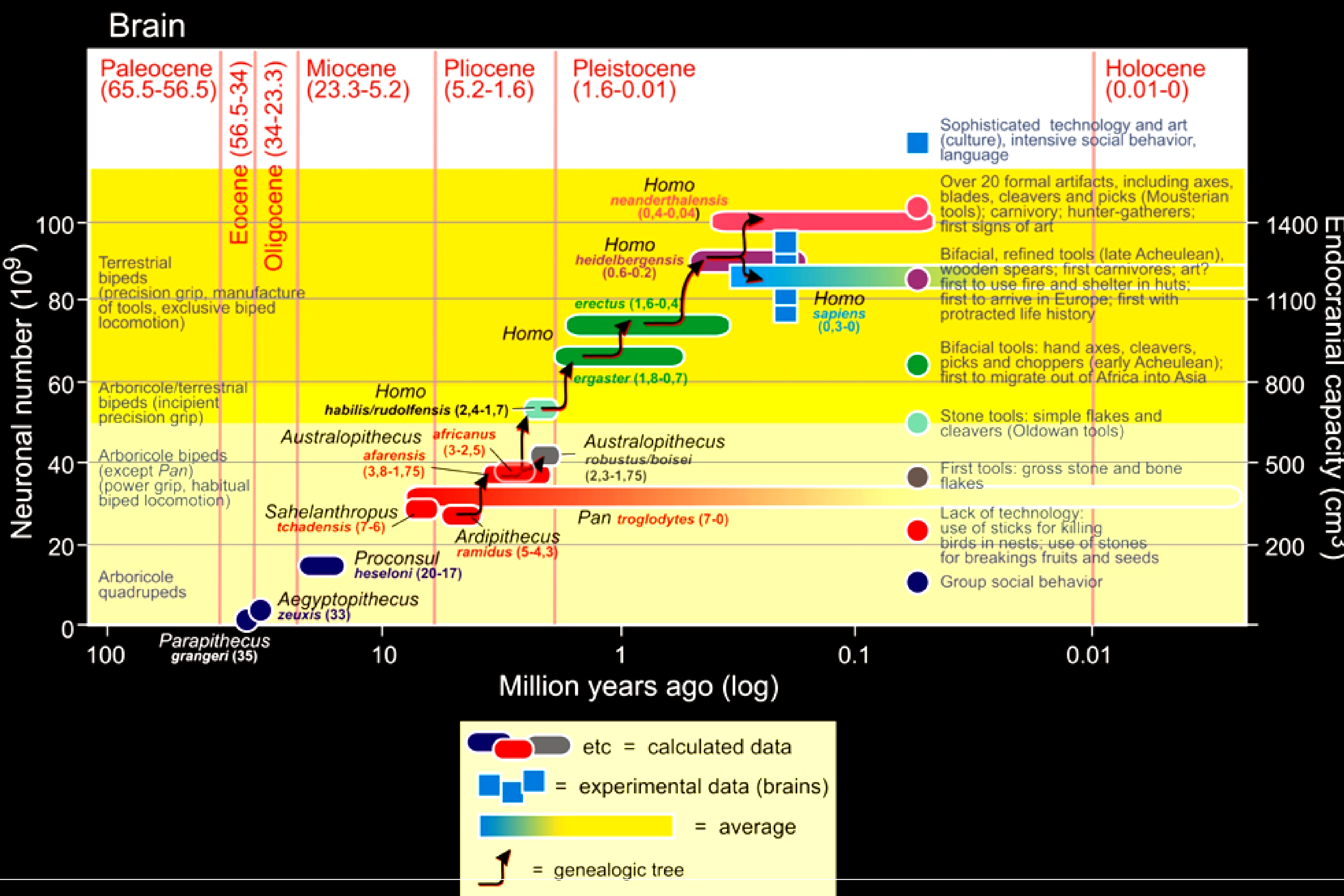


THIRD DOGMA REVISED:
"THE HUMAN BRAIN HAS JUST THE SIZE AND NUMBER OF NEURONS AS EXPECTED FOR A LARGE PRIMATE"



Azevedo et al, 2009, J. Comp. Neurol., 513:530-541

THE BRAIN OF HOMININS INFERRED

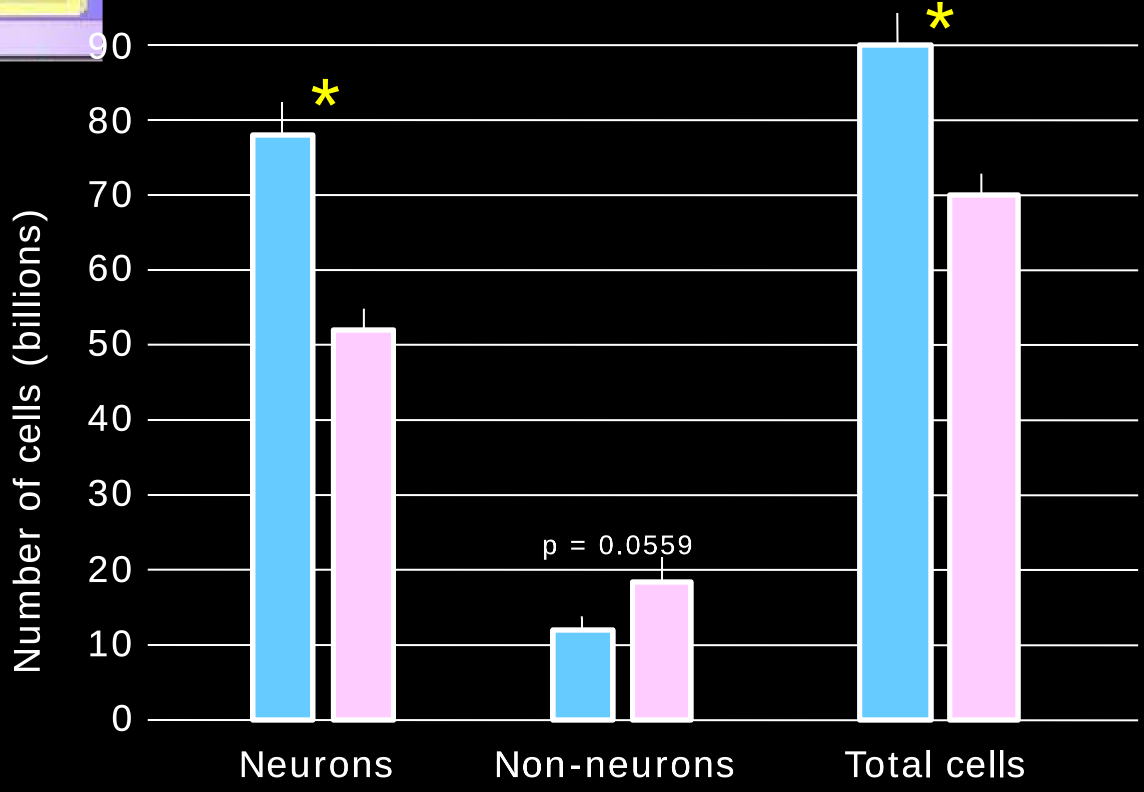


BRAIN CELL COMPOSITION: ♂ vs. ♀

ABSOLUTE NUMBERS

CEREBELLUM

Males (n=5; 71-83yo)
Females (n=6; 60-75yo)



Humberto Moraes

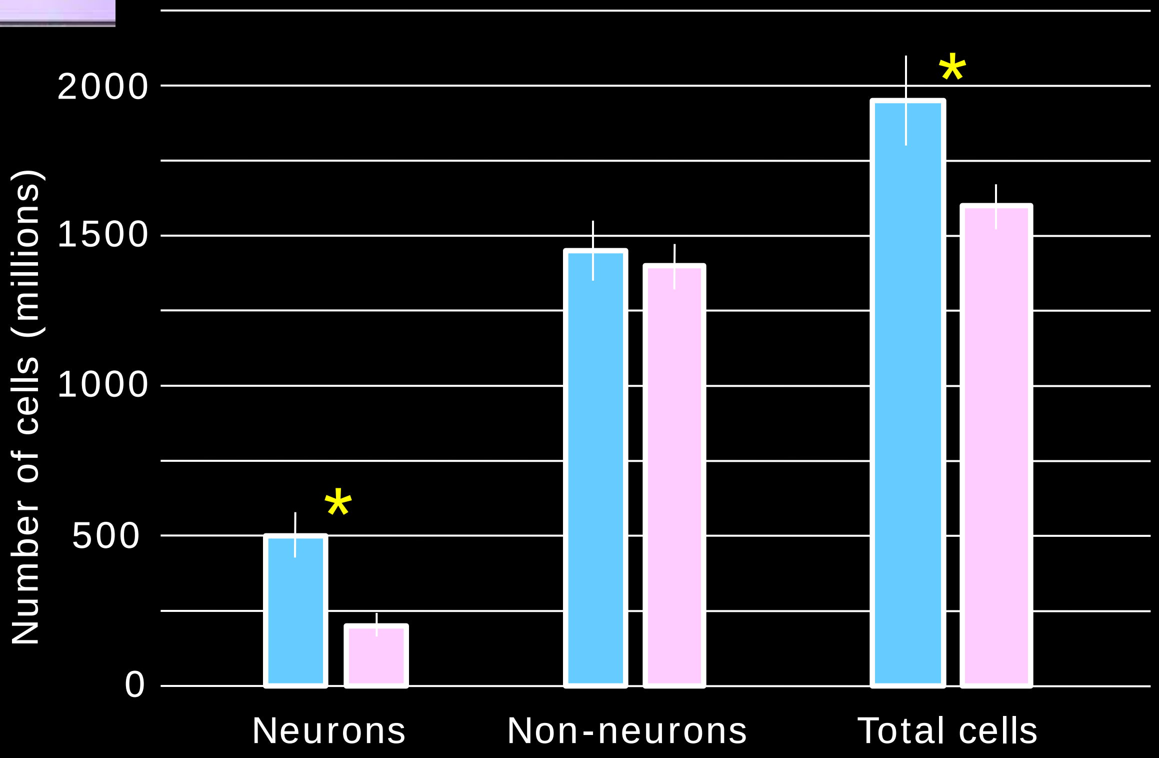
Moraes et al, 2011,
work in progress

BRAIN CELL COMPOSITION: ♂ vs. ♀

ABSOLUTE NUMBERS

HIPPOCAMPAL FORMATION

Males (n=5; 71-83yo)
Females (n=6; 60-75yo)

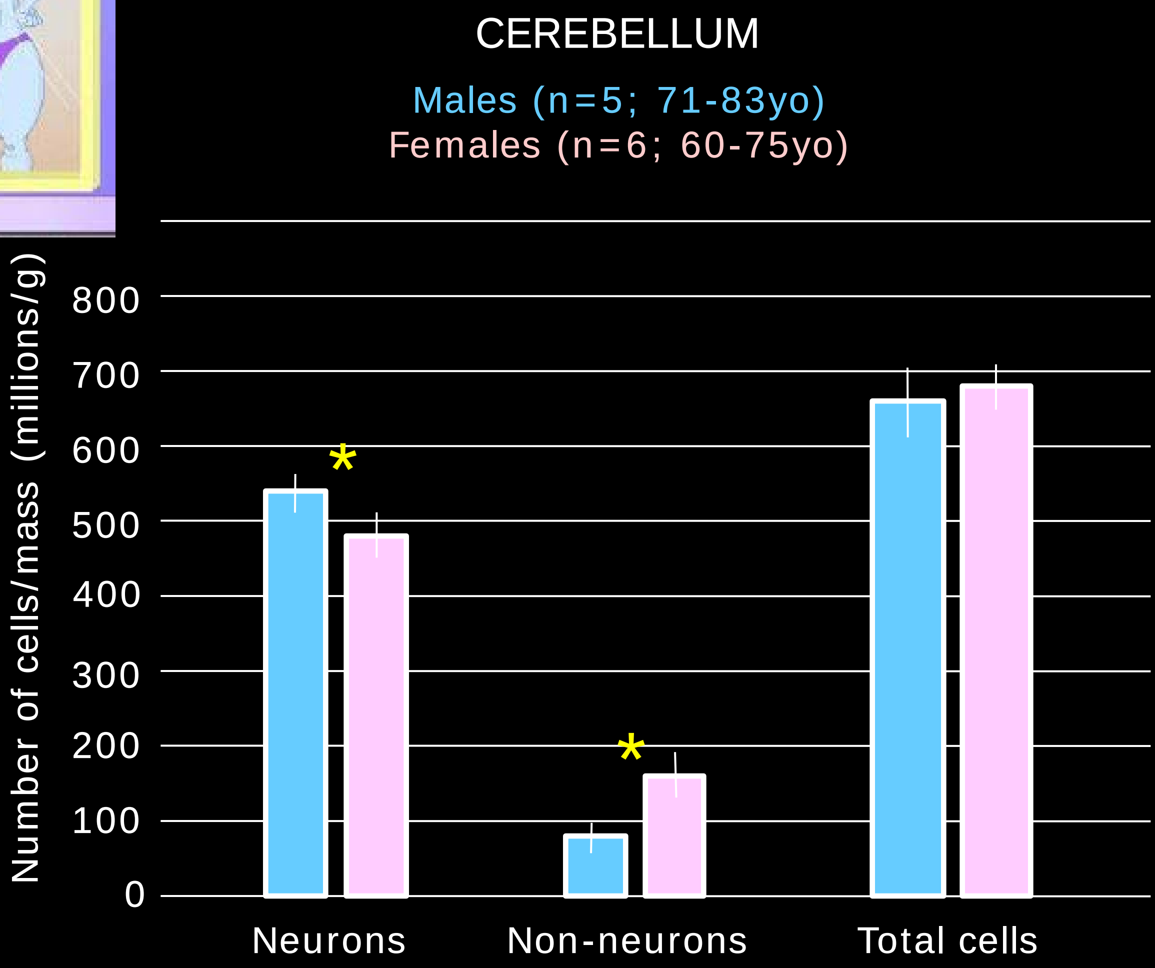


Moraes et al, 2011, work in progress

Humberto Moraes

BRAIN CELL COMPOSITION: ♂ vs. ♀

CELL DENSITY



Moraes et al, 2011,
work in progress

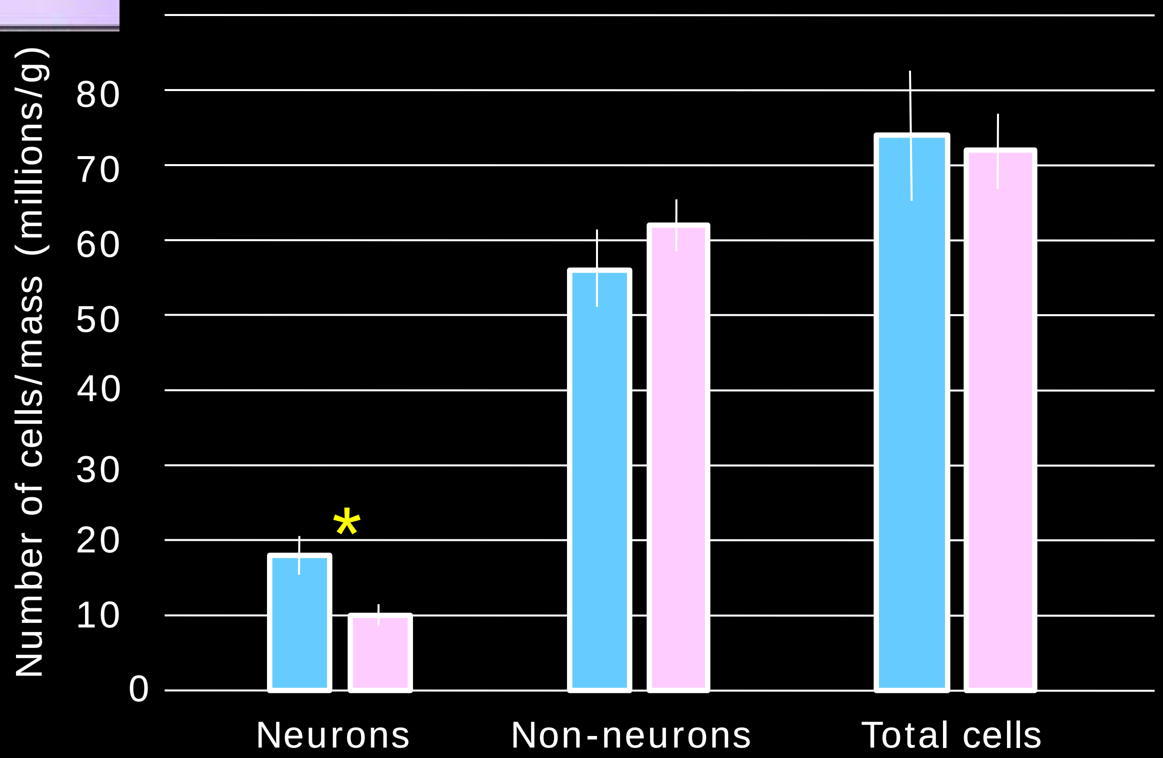
Humberto Moraes

BRAIN CELL COMPOSITION: ♂ vs. ♀

CELL DENSITY

HIPPOCAMPAL FORMATION

Males (n=5; 71-83yo)
Females (n=6; 60-75yo)



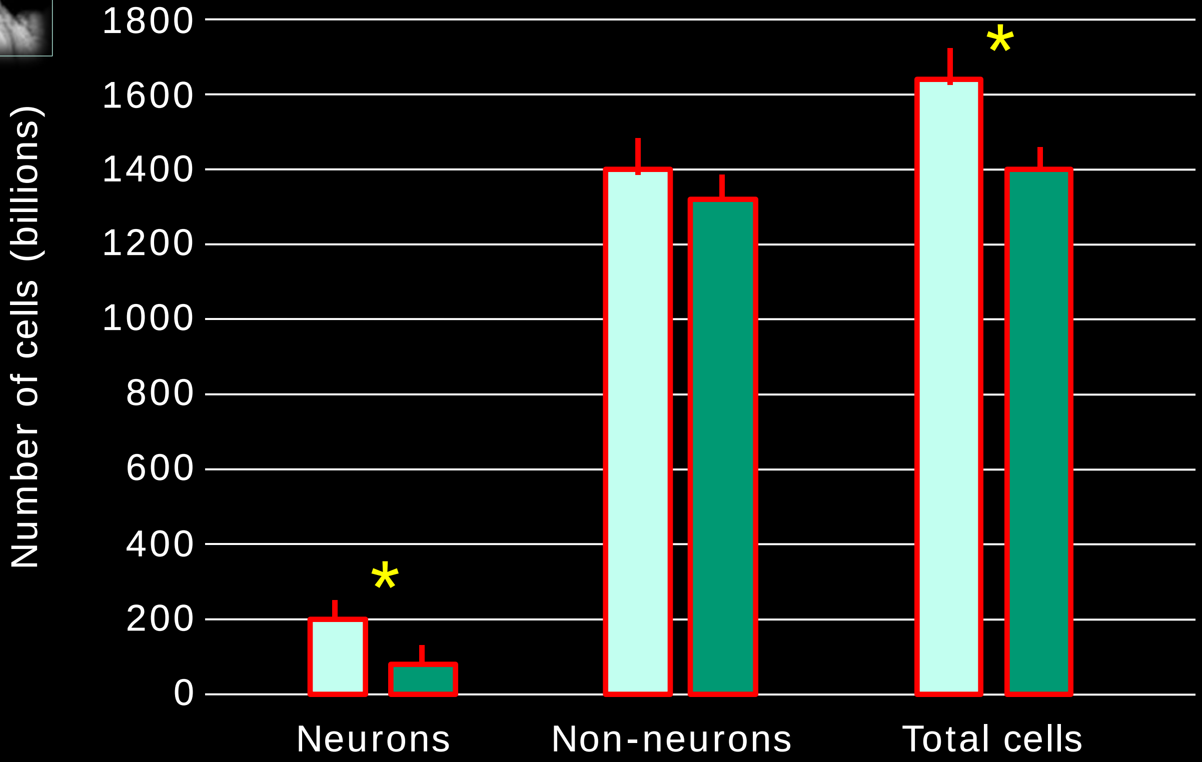
Moraes et al, 2011,
work in progress

Humberto Moraes

BRAIN CELL COMPOSITION:
DEMENTED vs. NON-DEMENTED

HIPPOCAMPAL FORMATION + AMYGDALA

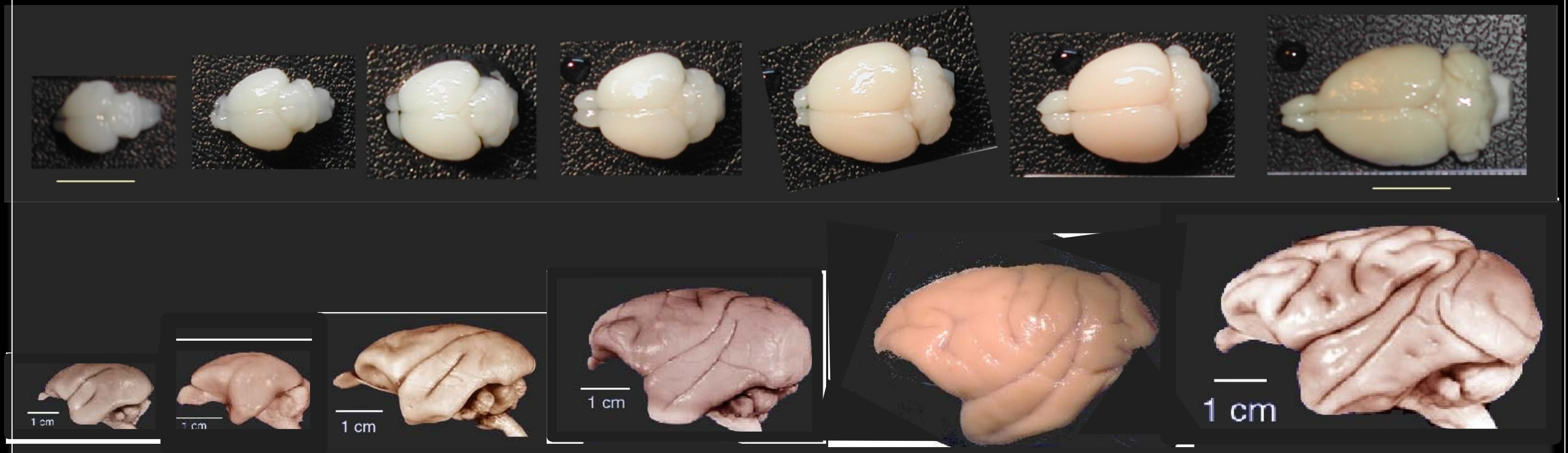
CDR = 0 (n=5, 72-88yo)
CDR = 3 (n=4, 71-86yo)



Humberto Moraes

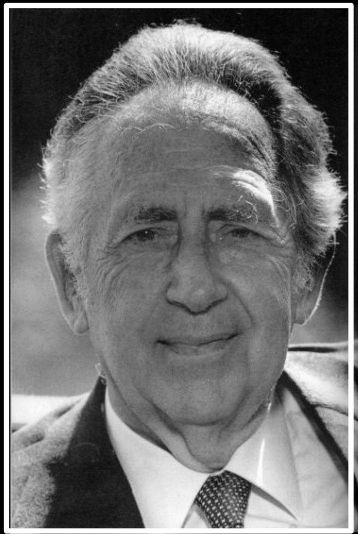
Moraes et al, 2011, work in progress

HOW WOULD EXPANSION OF THE BRAIN TAKE PLACE?

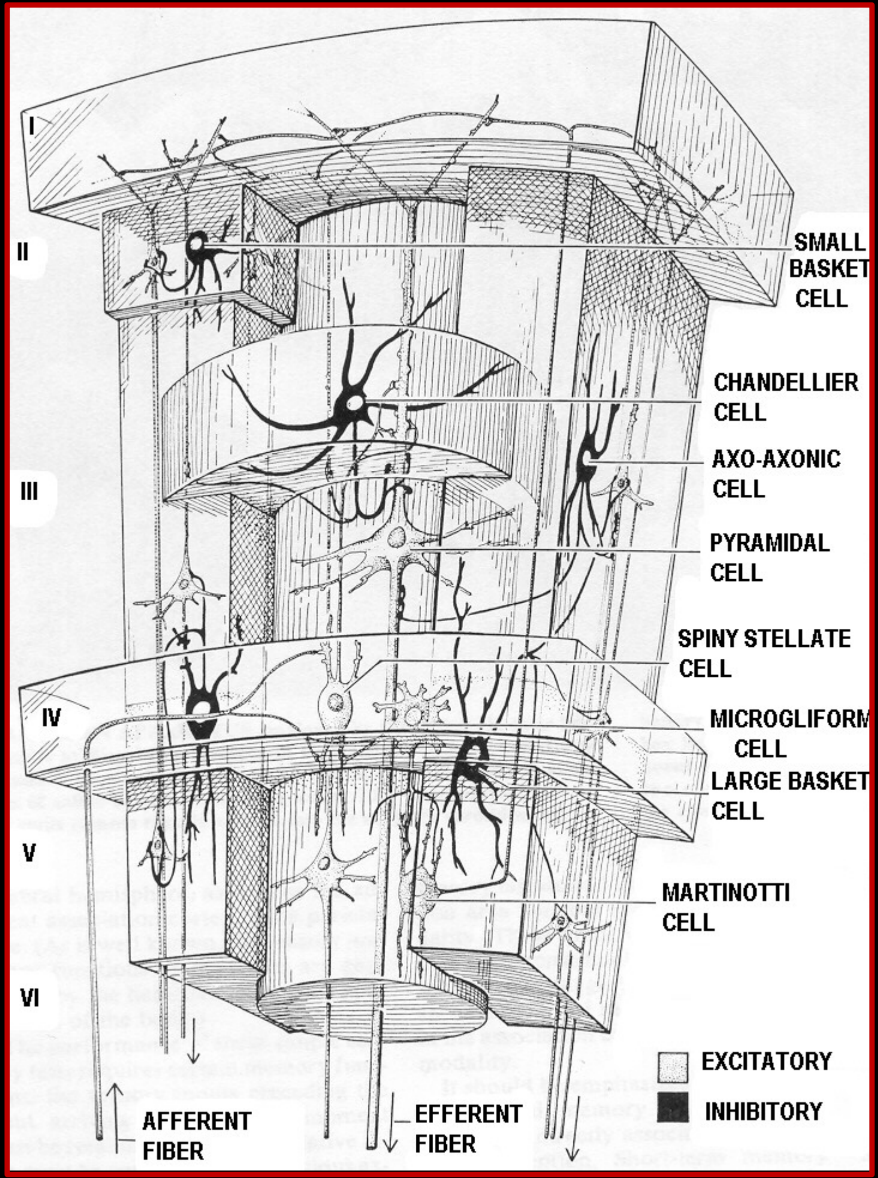


Herculano-Houzel et al, 2007, PNAS 104:3562-3567

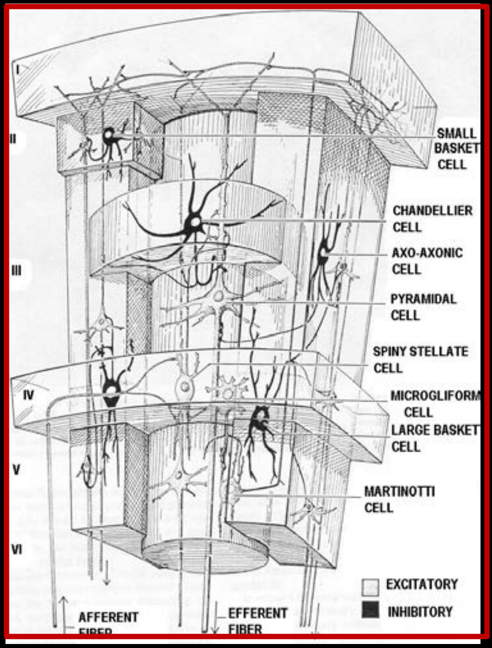
CORTICAL MODULES AND SURFACE BRAIN GROWTH



J. Szentagothai (1912-1994)



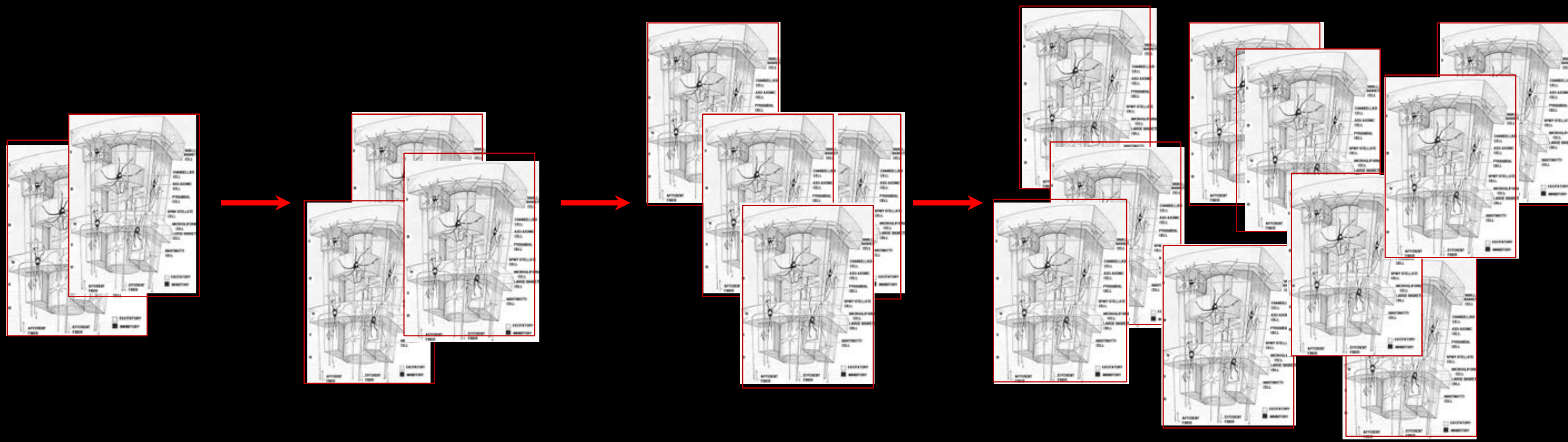
IS THERE A CONSTANT NUMBER OF NEURONS IN EVERY CORTICAL MODULE?

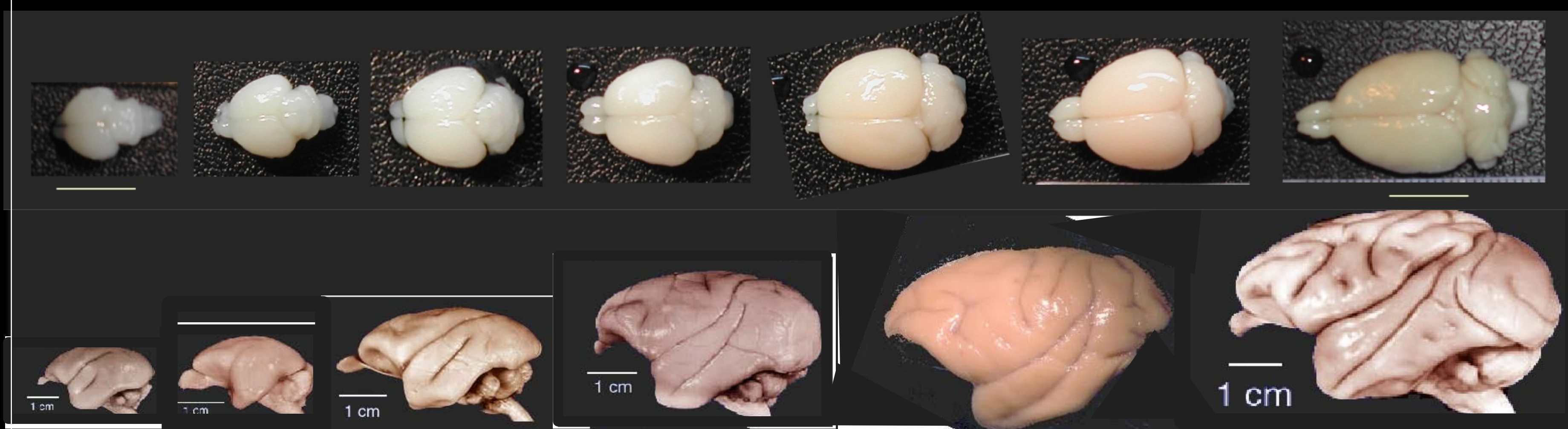


= 150,000 neurons/mm^2

Rockel et al., Brain 103:221-244 (1980)
The Basic Uniformity of Neocortical Structure
(mice, rats, cats, macaques, humans,
2D counts)

FOURTH DOGMA:
"BRAINS GROW IN EVOLUTION AND DEVELOPMENT BY THE ADDITION OF UNIFORM MODULES"





Herculano-Houzel et al, 2007, PNAS 104:3562-3567

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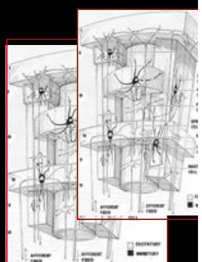


Brain Research Bulletin 75 (2008) 398–404

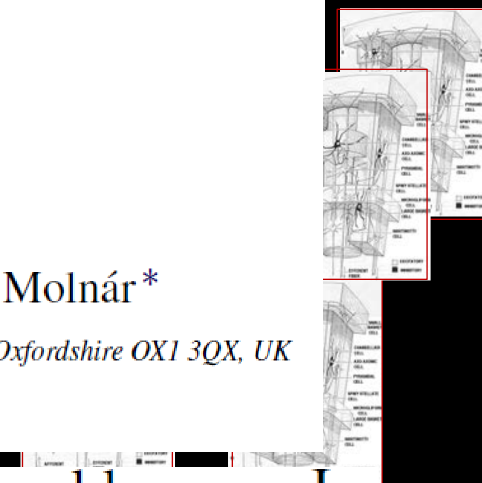
Review

Evolution of cortical neurogenesis

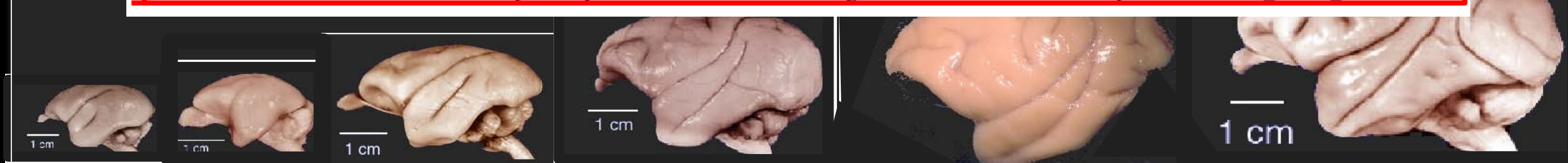
Omar Abdel-Mannan [1], Amanda F.P. Cheung [1], Zoltán Molnár *

Department of Physiology, Anatomy and Genetics, Le Gros Clark Building, University of Oxford, Oxfordshire OX1 3QX, UK

Received 14 September 2007; accepted 17 October 2007
Available online 20 November 2007

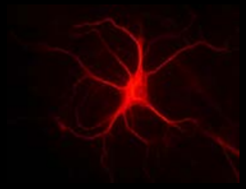


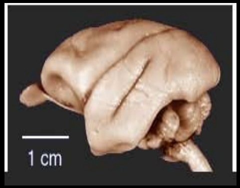
tex or increased numbers in tangential sheet would occur. In fact, one of the puzzling dogmas in comparative studies on the mammalian cerebral cortex is the constant number of neurons in an arbitrary unit column, despite the diversity of cortical thickness and relative proportion of layers across species [43]. The

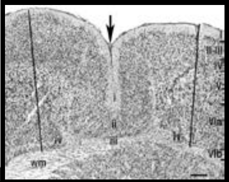


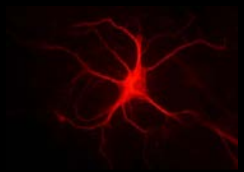
Herculano-Houzel et al, 2007, PNAS 104:3562-3567

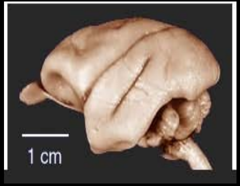
QUANTIFICATION OF CORTICAL MODULES IN PRIMATES







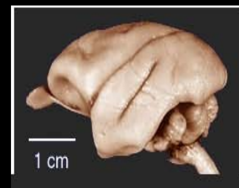


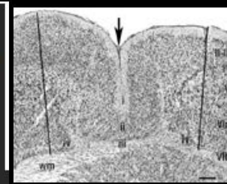


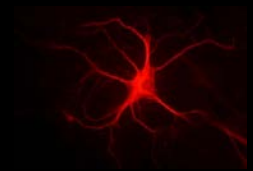
Species	M, g	A, mm^2	T, mm	N, millions	D_{neur}, 1000/mg	N/A, 1000
***Tupaia glis* (n=2)**	0.515 0.063	497 158	1.089 0.021	21.95 1.60	38.16 7.42	**47.09 18.18**
***Callithrix jacchus* (n=3)**	2.042 0.120	1534 273	1.310 0.235	120.33 43.30	54.24 23.34	**78.00 22.70**
***Otolemur garnetti* (n=2)**	2.556 0.129	1745 331	1.462 0.196	88.50 14.75	31.90 7.26	**50.83 1.18**
***Aotus trivirgatus* (n=3)**	3.698 0.663	2214 213	1.499 0.039	200.32 67.34	47.96 15.34	**92.96 39.07**
***Callimico goeldi* (n=1)**	3.872	1953	1.600	178.77	38.55	**91.53**
***Saimiri sciureus* (n=3)**	6.996 0.356	5250 1332	1.465 0.023	645.73 43.74	80.92 9.68	**129.67 39.62**
***Macaca fascicularis* (n=1)**	10.459	9381	1.413	400.74	32.94	**42.71**
***Macaca radiata* (n=1)**	15.493	8441	1.572	829.60	43.81	**98.28**
***Cebus apella* (n=2)**	15.820 4.982	7653 29	1.767 0.147	930.67 507.78	51.08 15.44	**121.73 66.80**
***Papio sp.* (n=2)**	36.334 8.233	16689 3052	2.034 0.028	1420.34 18.07	33.73 7.23	**86.65 16.93**
Variation	70.6 x	29.2 x	1.6 x	60.7 x	2.4 x	**3.0 x**

Herculano-Houzel et al., 2008, PNAS, 105:12593-12598

QUANTIFICATION OF CORTICAL MODULES IN PRIMATES







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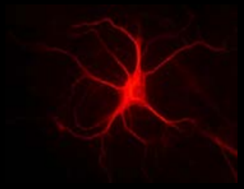

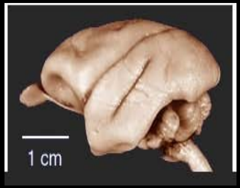

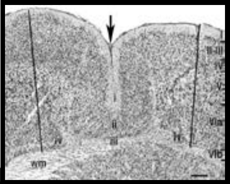

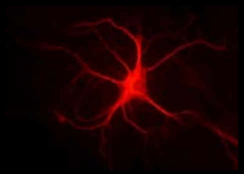

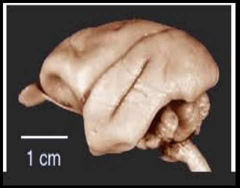

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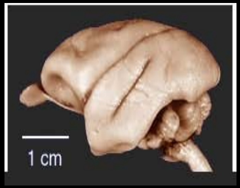

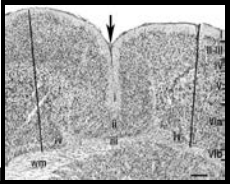

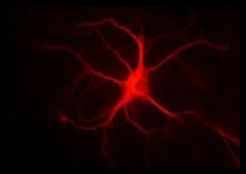

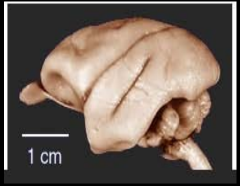

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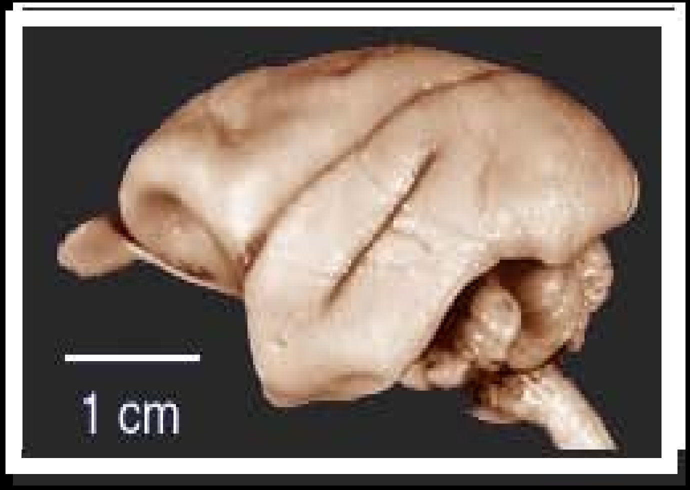
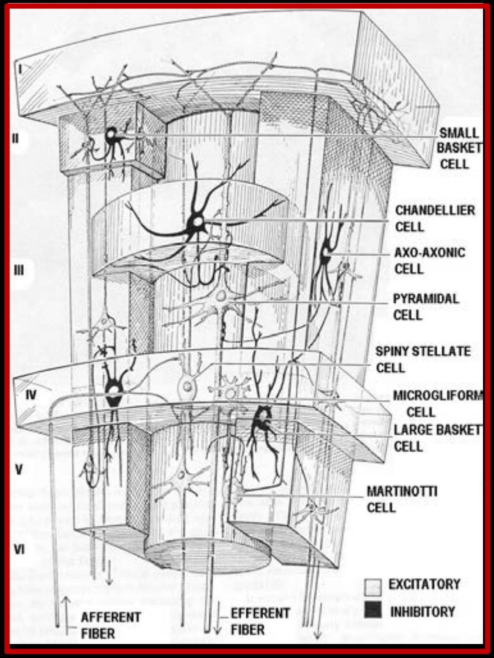
Herculano-Houzel et al., 2008, PNAS, 105:12593-12598

THE DOGMA PREDICTS: SURFACE AREA OF DIFFERENT MAMMALS SHOULD CORRELATE LINEARLY WITH NEURONAL NUMBER



α



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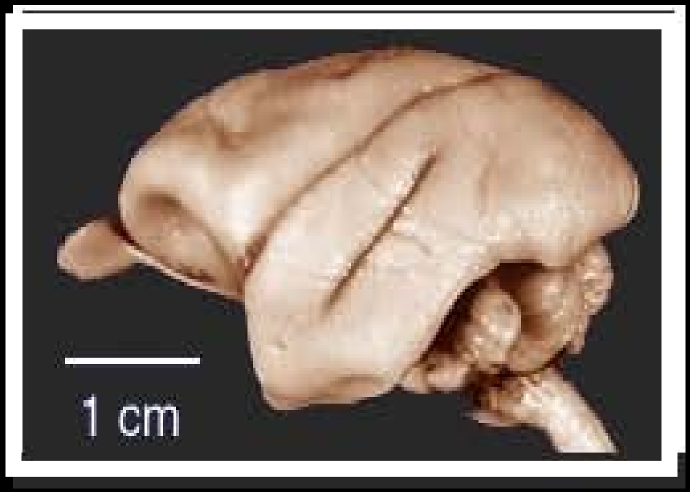

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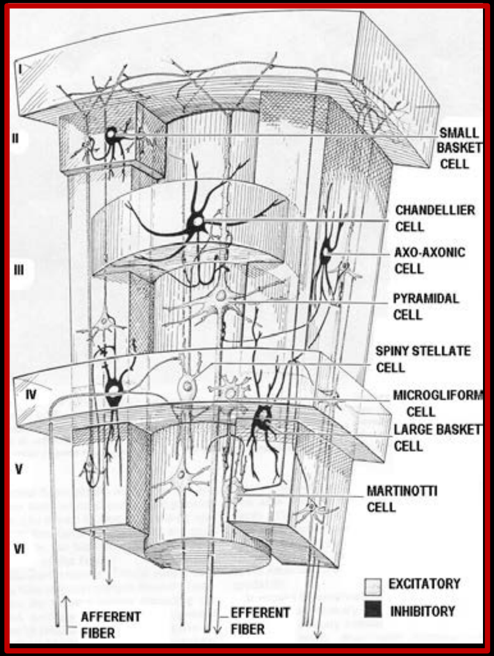
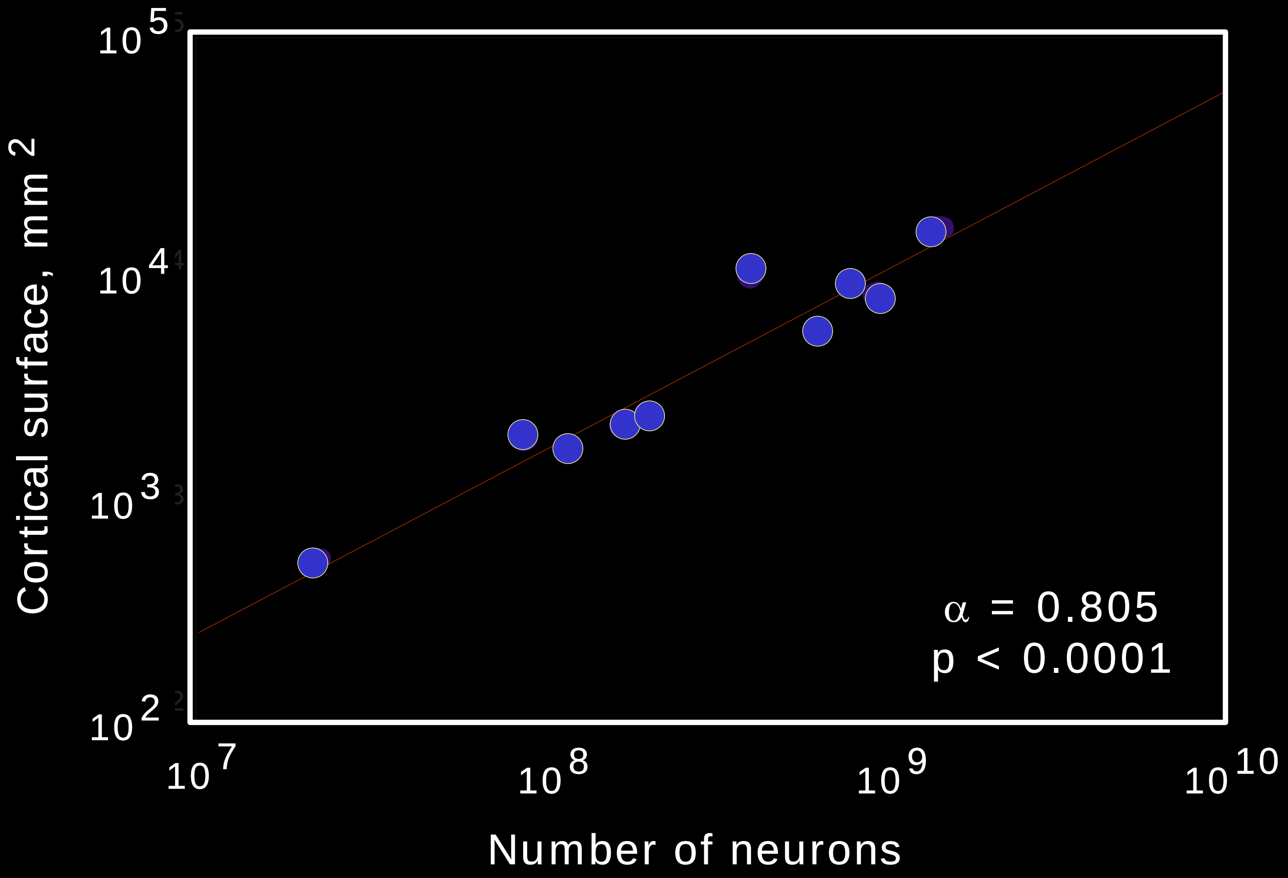


IS IT TRUE?

NO, SURFACE AREA OF DIFFERENT PRIMATES CORRELATES WITH NEURONAL NUMBER AS A POWER FUNCTION

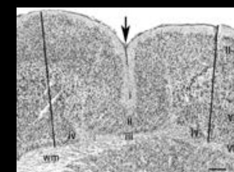


Herculano-Houzel et al., 2008, PNAS 105:12593-12598

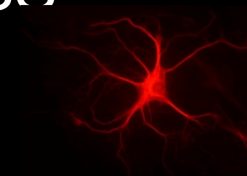
ANOTHER PREDICTION: FOR MODULES TO BE UNIFORM, NEURONAL DENSITY SHOULD CORRELATE INVERSELY WITH CORTICAL THICKNESS

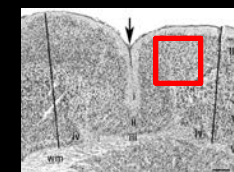
N = A X T X D

X

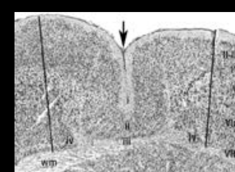


X





N/A = T X D



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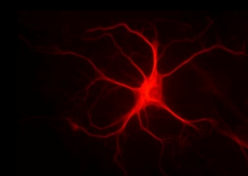

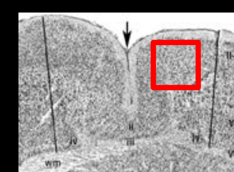

IF N/A IS CONSTANT, WHEN T INCREASES,
D SHOULD DECREASE
(INVERSE CORRELATION)

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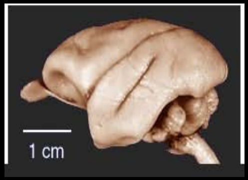

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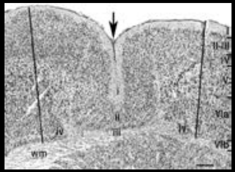

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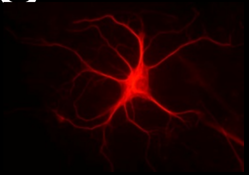

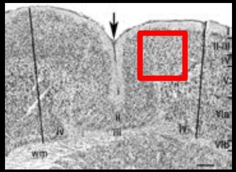

IS IT TRUE?

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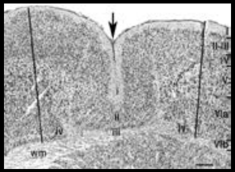

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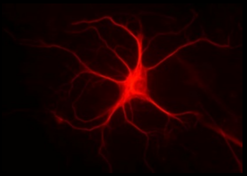

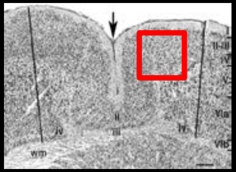

IF N/A IS CONSTANT, WHEN T INCREASES,
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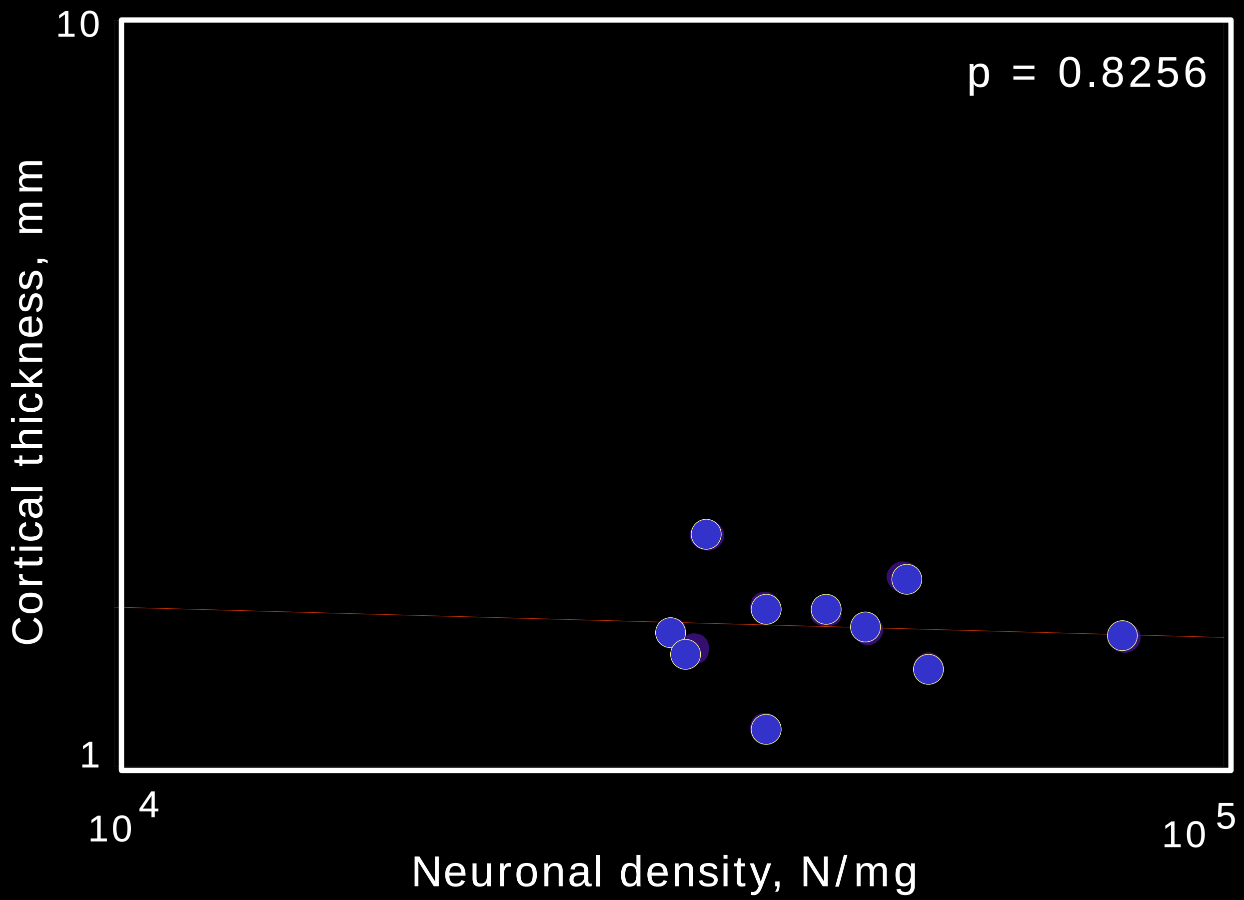
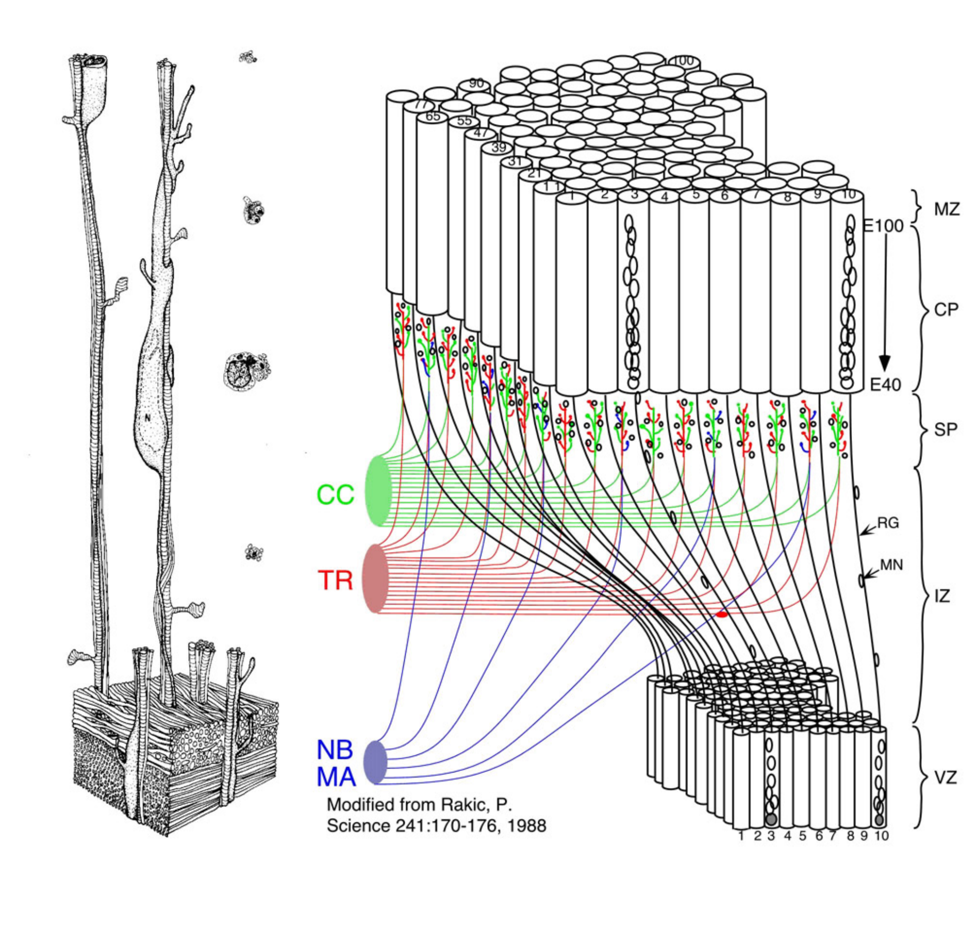
NO,
NEURONAL DENSITY DOES NOT CORRELATE AT ALL WITH CORTICAL THICKNESS

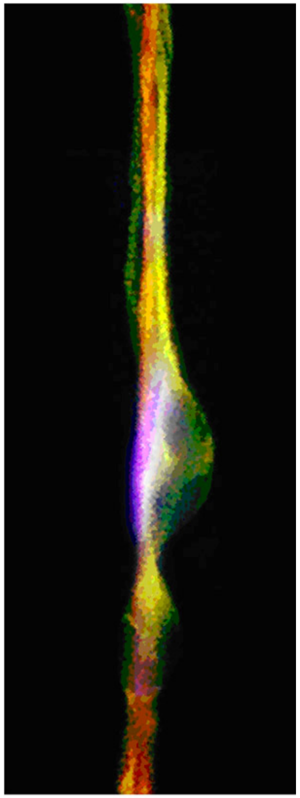


Herculano-Houzel et al., 2008, PNAS 105:12593-12598

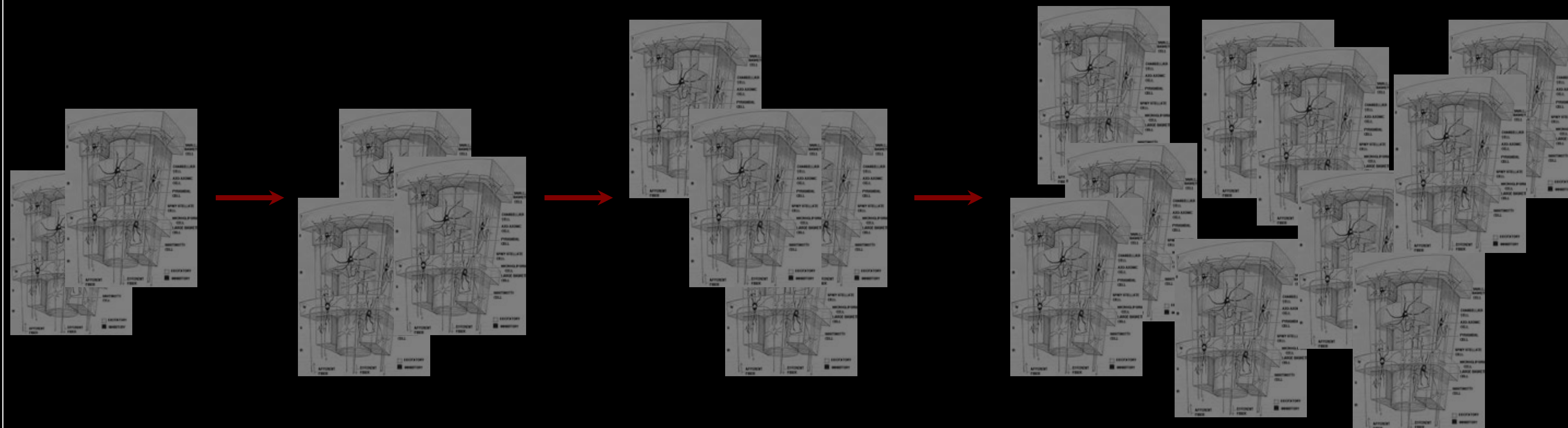
EVOLUTION
DEVELOPMENT

Pasko Rakic, Yale Univ.





FOURTH DOGMA:
“BRAINS GROW IN EVOLUTION AND DEVELOPMENT BY THE ADDITION OF UNIFORM MODULES”



FOURTH DOGMA REVISED:
“BRAINS GROW IN EVOLUTION AND DEVELOPMENT BY THE ADDITION OF <u>NON-UNIFORM</u> MODULES”

Herculano-Houzel et al., 2008, PNAS 105:12593-12598

EVOLUTION

DEVELOPMENT

Fabiana Bandeira

FIFTH DOGMA:
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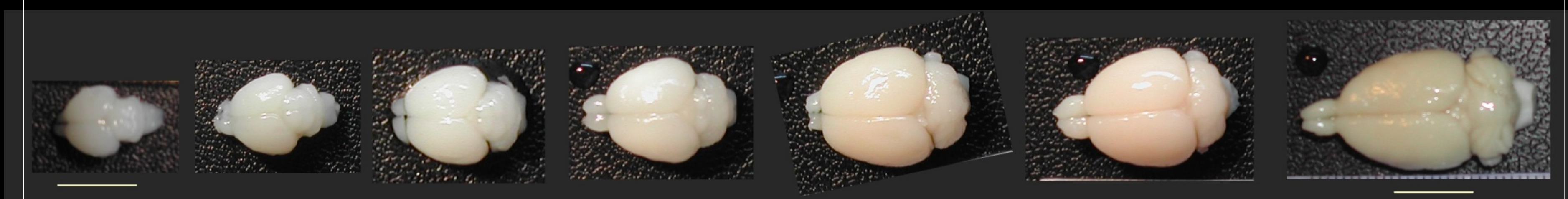

EVOLUTION

DEVELOPMENT

Fabiana Bandeira

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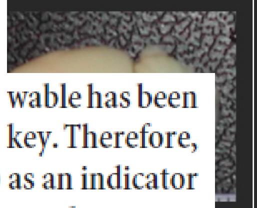
The Journal of Neuroscience, February 1, 2003 • 23(3):937–942 • 937

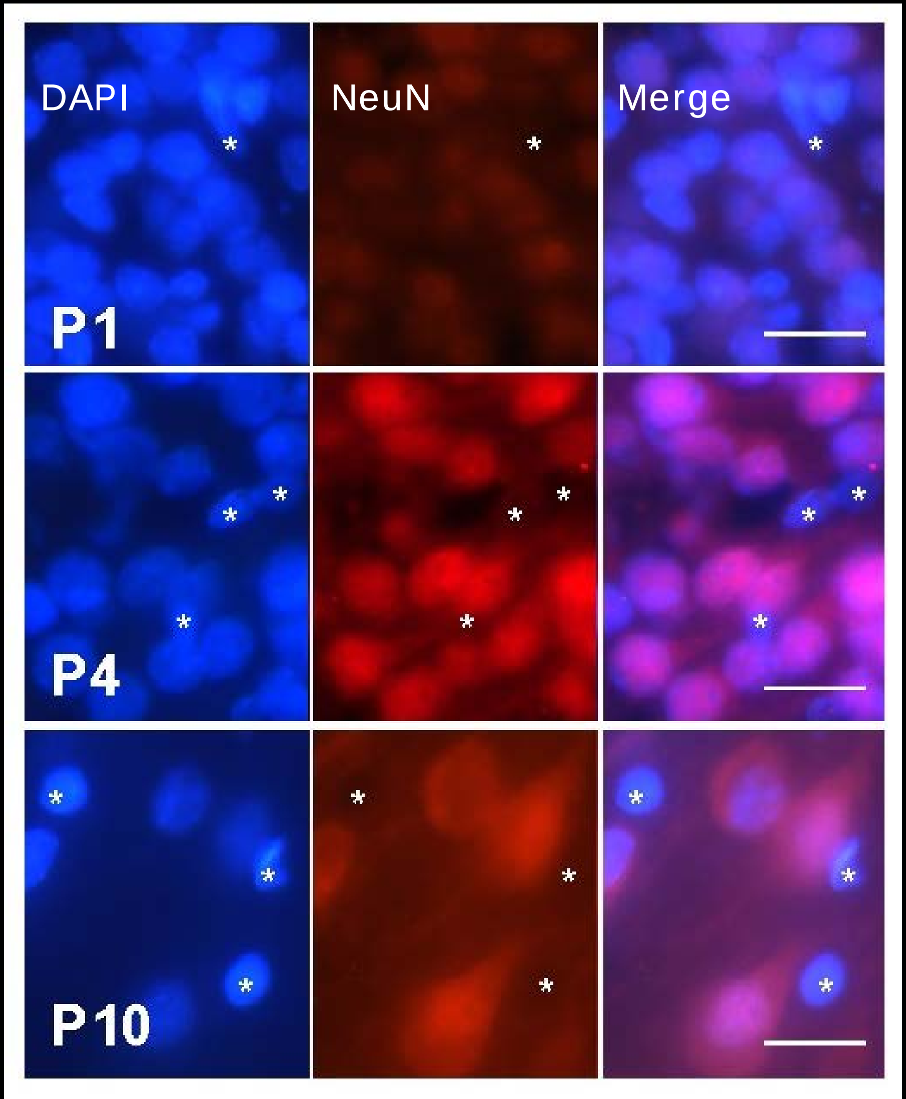
Nonrenewal of Neurons in the Cerebral Neocortex of Adult Macaque Monkeys

Daisuke Koketsu,[1] Akichika Mikami,[2] Yusei Miyamoto,[1] and Tatsuhiro Hisatsune[1]
[1]Department of Integrated Biosciences, University of Tokyo, Kashiwa 277-8562, Japan, and [2]Primate Research Institute, Kyoto University, Inuyama 484-8506, Japan



The concept th … wable has been challenged by … key. Therefore, we have reexamined this issue in two different Macaque species using the thymidine analog bromodeoxyuridine (BrdU) as an indicator of DNA replication during cell division. We found several BrdU+/NeuN+ (neuronal nuclei) double-labeled cells, but cortical neurons, distinguished readily by their size and cytological and immunohistochemical properties, were not BrdU positive. We examined in detail the frontal cortex, where it is claimed that the largest daily addition of neurons has been made, but did not see migratory streams or any sign of addition of new neurons. Thus, we concluded that, in the normal condition, cortical neurons of adult primates, similar to other mammalian species, are neither supplemented nor renewable.

PRECAUTION:
CHECK WHETHER NeuN IS EXPRESSED IN DEVELOPING ANIMALS



Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

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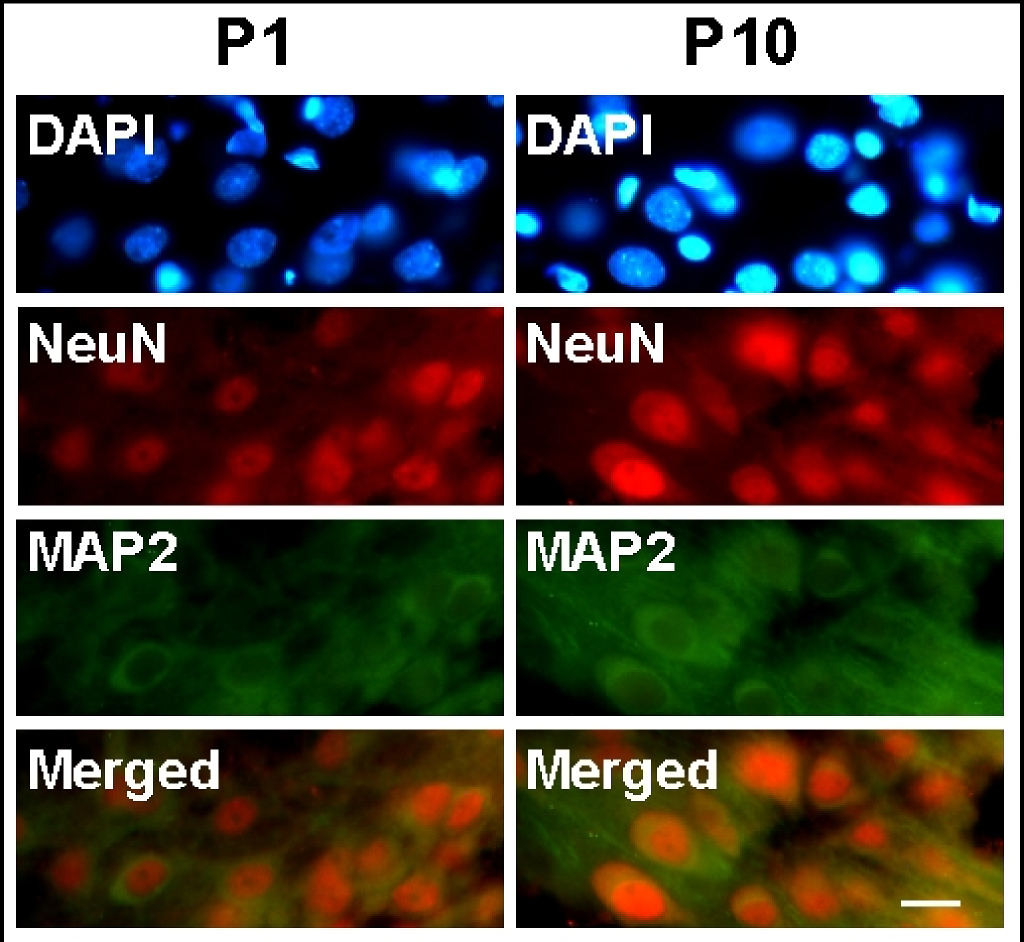
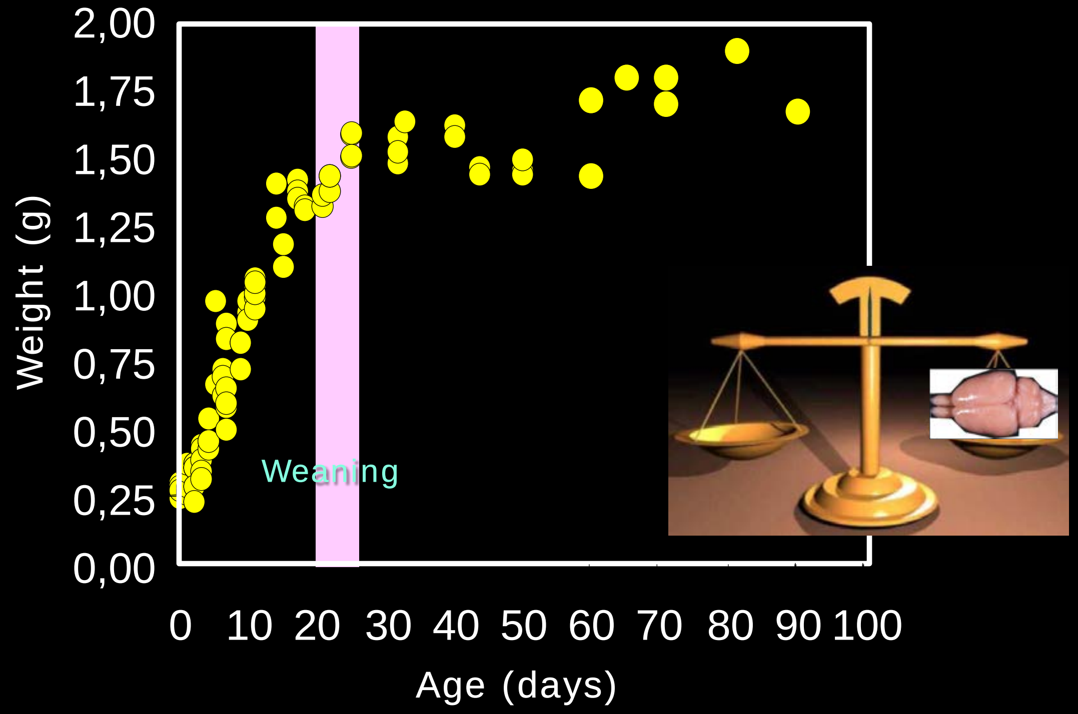
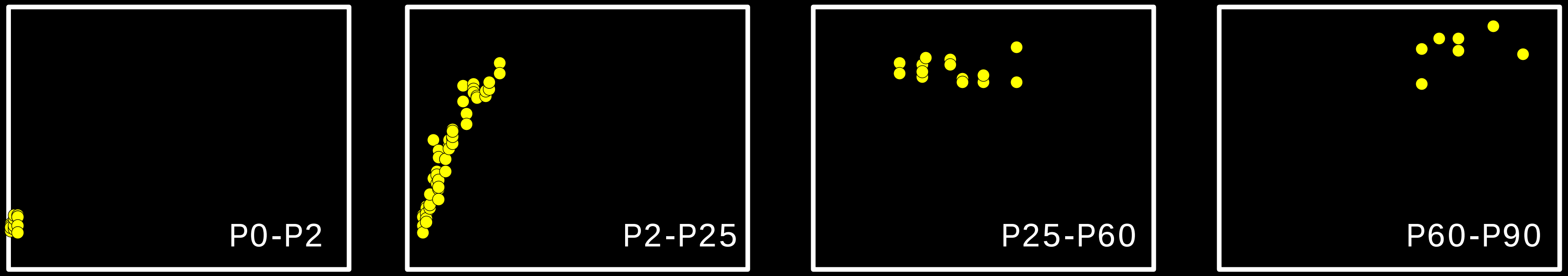


Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

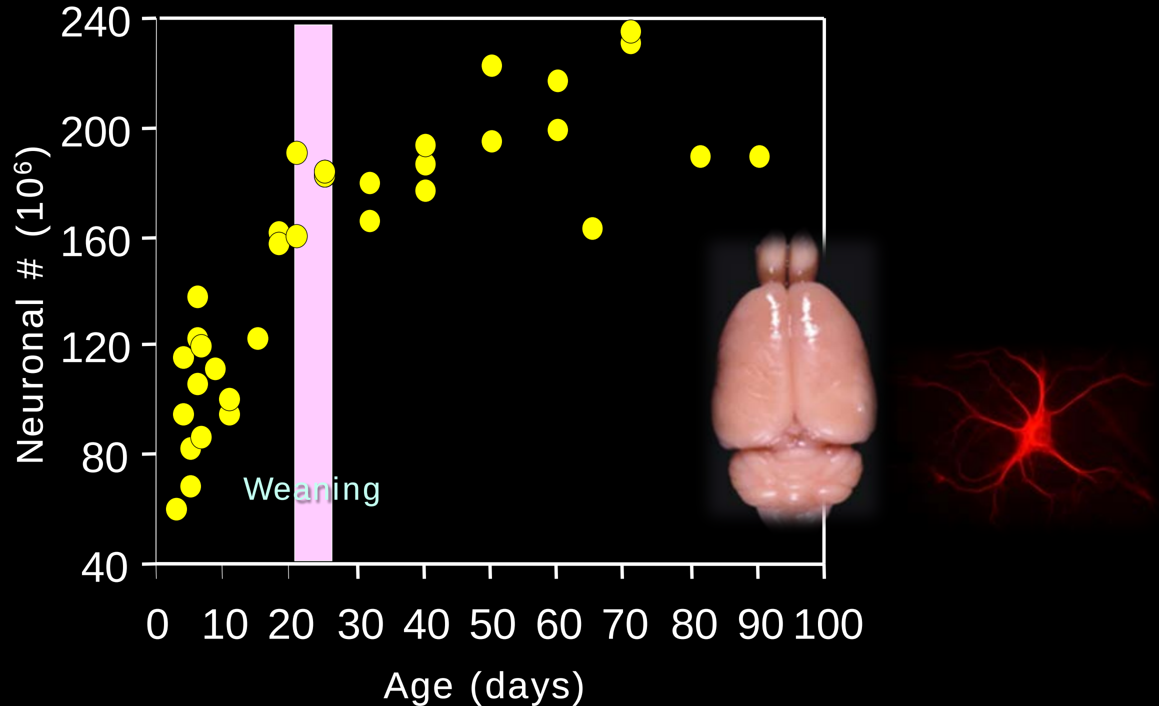
BRAIN WEIGHT ALONG DEVELOPMENT

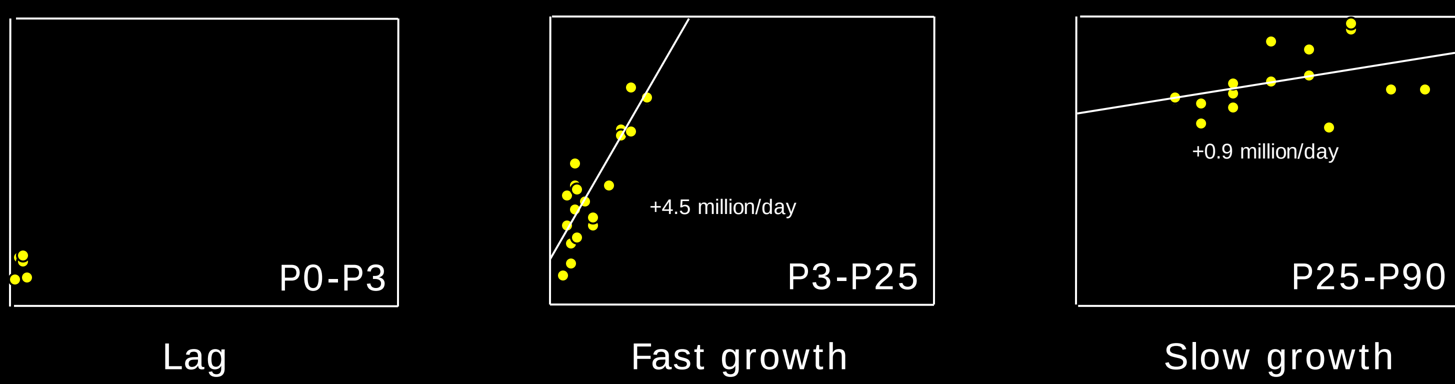




Lag | Fast growth | No growth | Slow growth

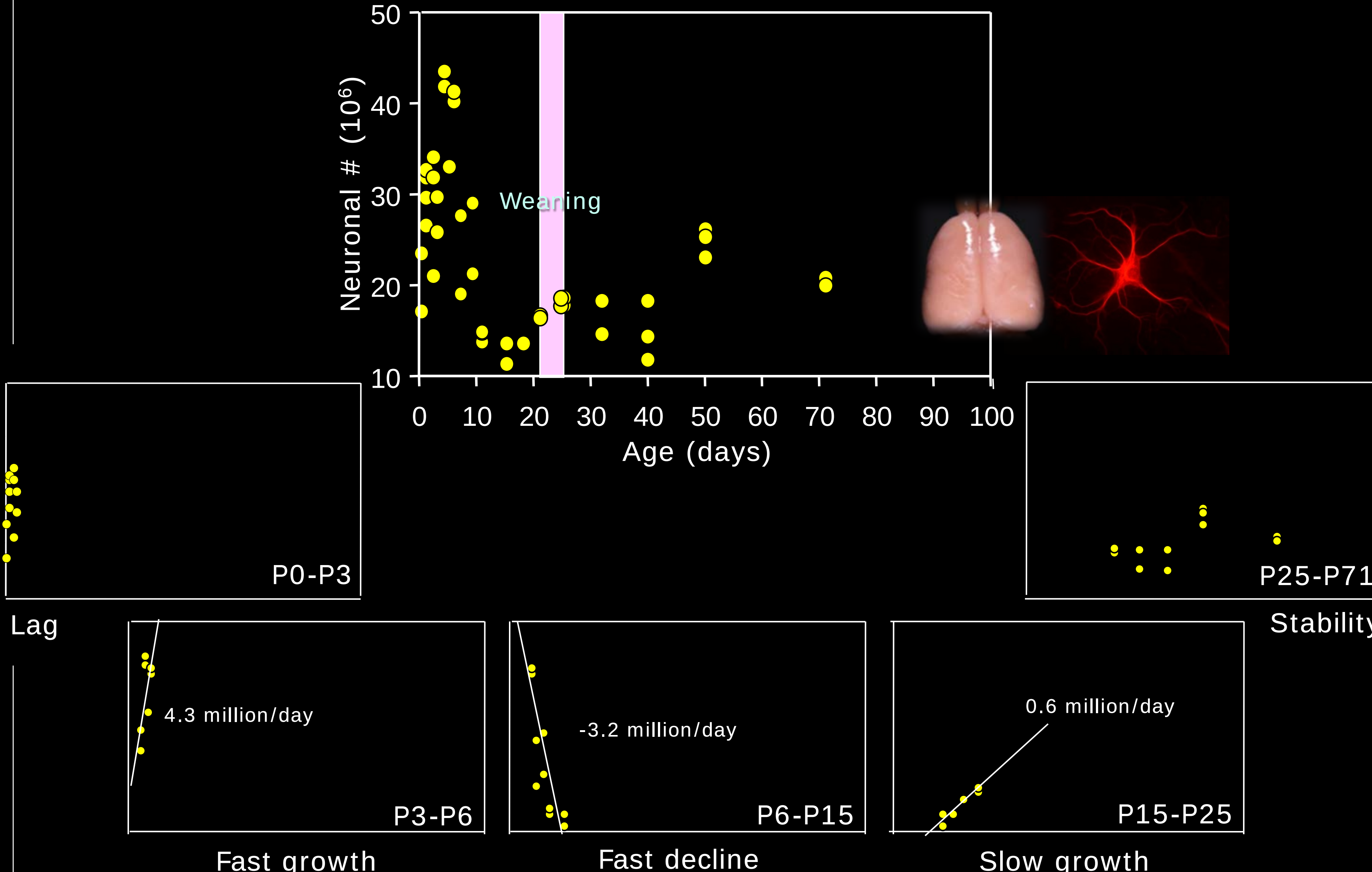
BRAIN NEURONAL NUMBER





Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

NEOCORTEX NEURONAL NUMBER



Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

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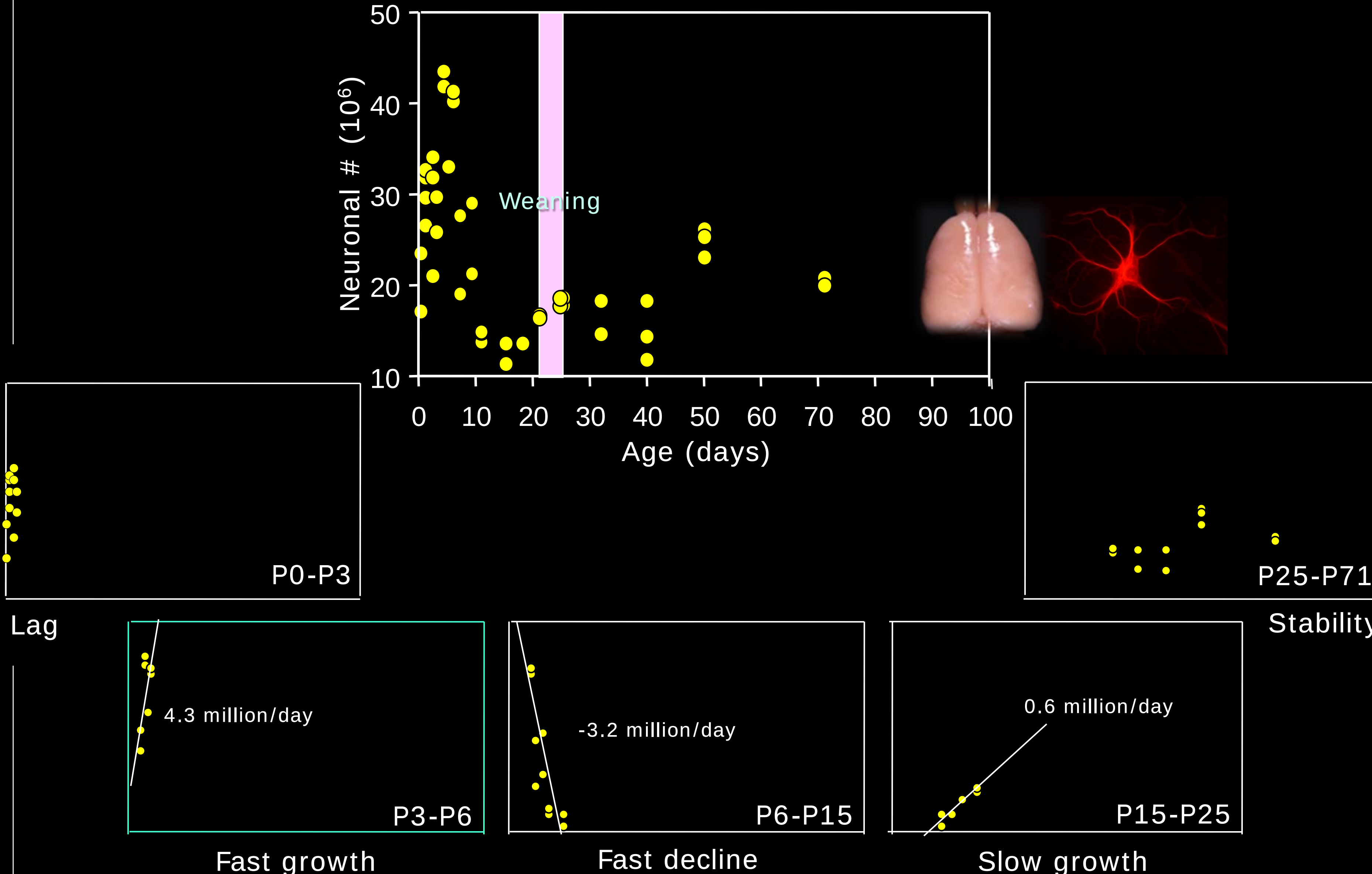

Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

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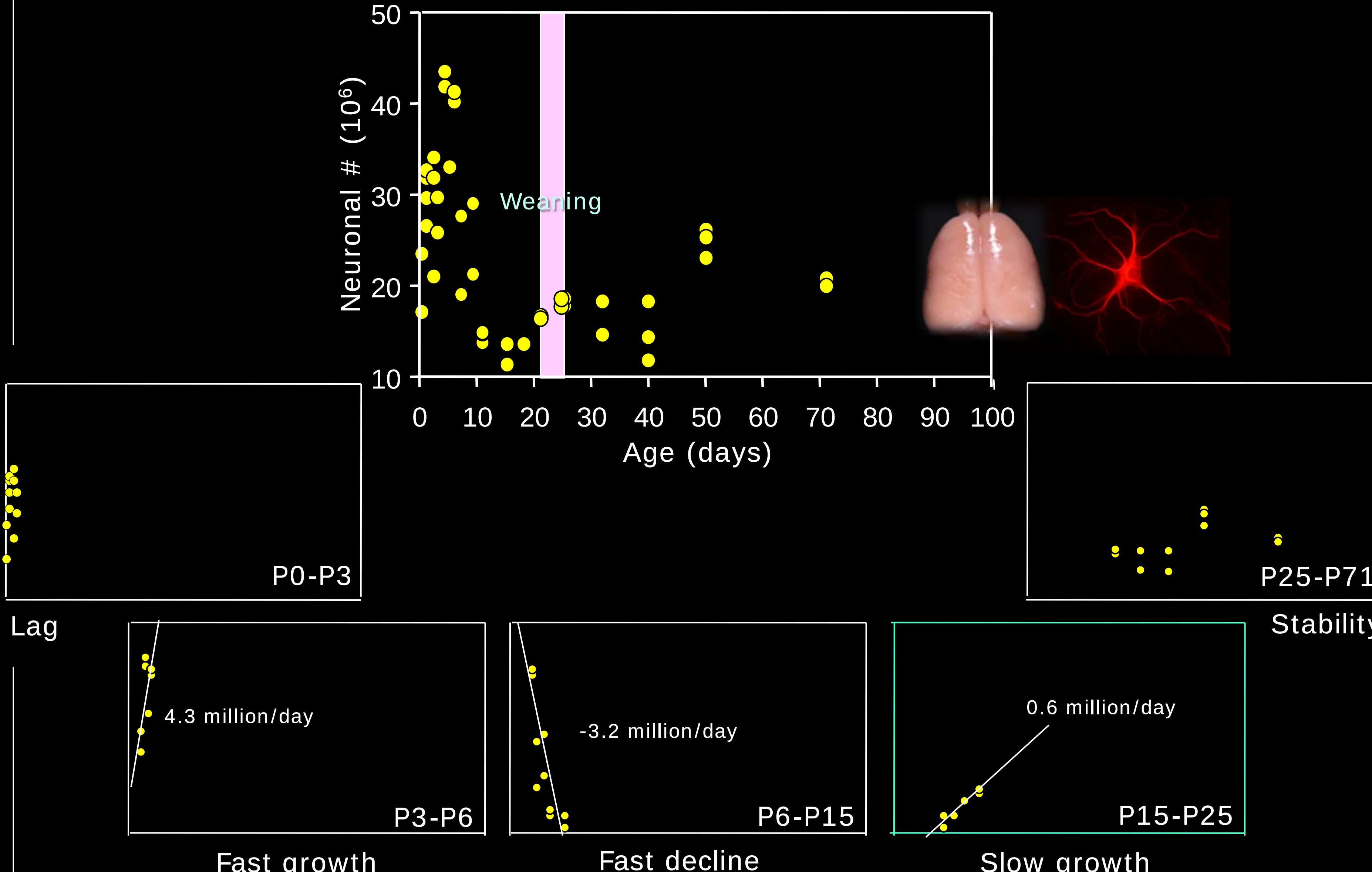
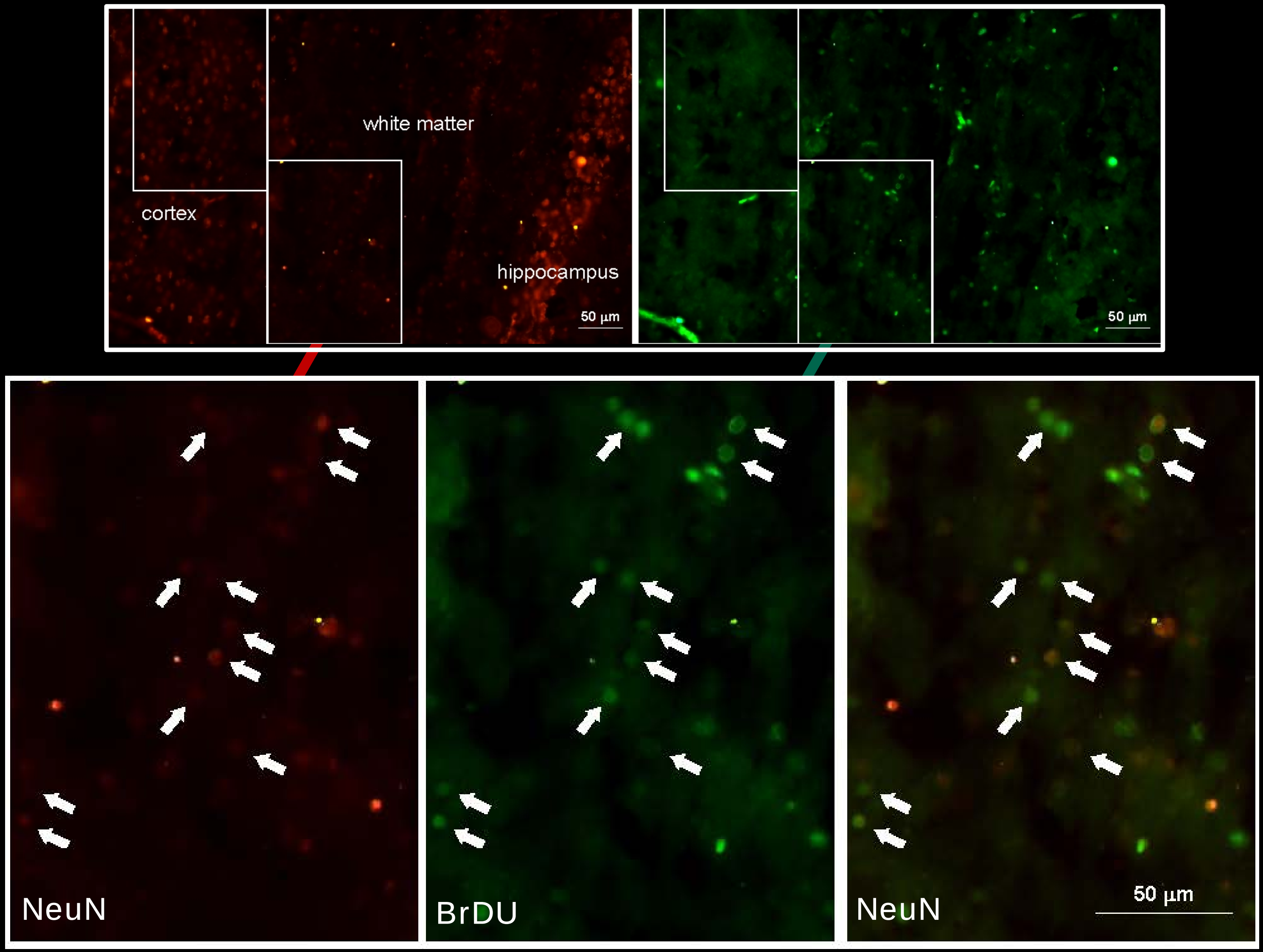


Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

YES, THERE IS NEUROGENESIS IN NEOCORTEX



Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

FIFTH DOGMA:
"BRAINS GROW IN DEVELOPMENT BY PRENATAL NEURONAL PROLIFERATION IN CORTEX"

FIFTH DOGMA REVISED:
"BRAINS GROW IN DEVELOPMENT BY PRENATAL AND POSTNATAL NEURONAL PROLIFERATION IN CORTEX"

Bandeira, Lent & Herculano-Houzel, 2009, PNAS 106:14108-14113

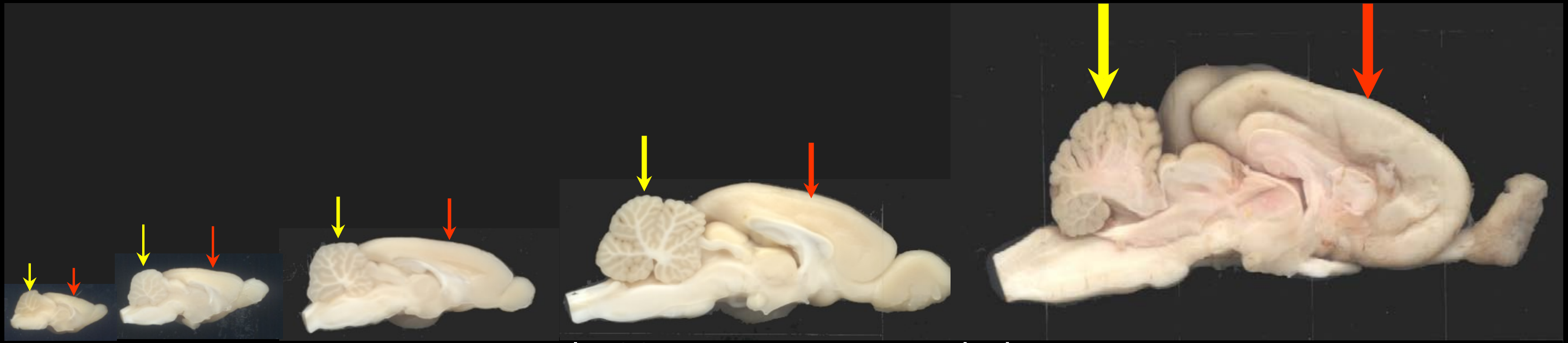
CONCLUSIONS

1. DIFFERENT CELL SCALING RULES APPLY FOR CORTEX, CEREBELLUM AND REMAINING AREAS

2. COORDINATED SCALING OF CORTEX AND CEREBELLUM SEEMS TO BE THE TRUE EVOLUTIONARY RULE FOR BIGGER BRAINS

3. ABSOLUTE NUMBER OF NEURONS IN THE ADULT HUMAN BRAIN IS LOWER THAN 100 BILLION

4. THE RATIO BETWEEN NEURONS AND GLIAL CELLS IN HUMANS IS JUST 1:1



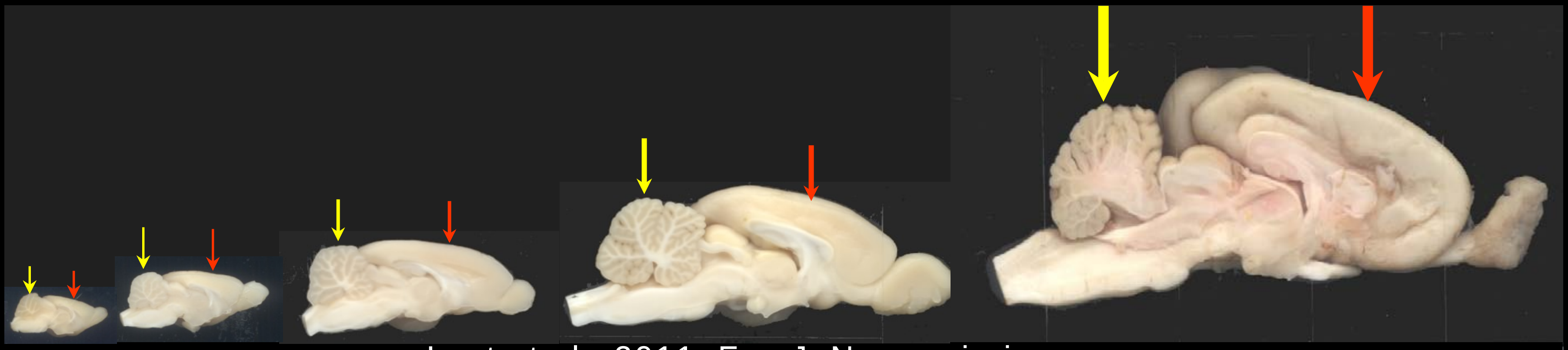
Lent et al., 2011, Eur. J. Neurosci., in press

CONCLUSIONS

5. CONSIDERING THEIR NEURONAL POPULATION, HUMANS ARE ONLY LARGE PRIMATES

6. EVOLUTION DOES NOT OCCUR BY ADDITION OF UNIFORM MODULES

7. THERE ARE TWO WAVES OF NEURONAL ADDITION POSTNATALLY IN THE CEREBRAL CORTEX, SUGGESTING NEUROGENESIS



Lent et al., 2011, Eur. J. Neurosci., in press

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