Speed limits in mammalian brains: scaling constraints from biophysics

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synapse.princeton.edu/~sam/kitp.ppt

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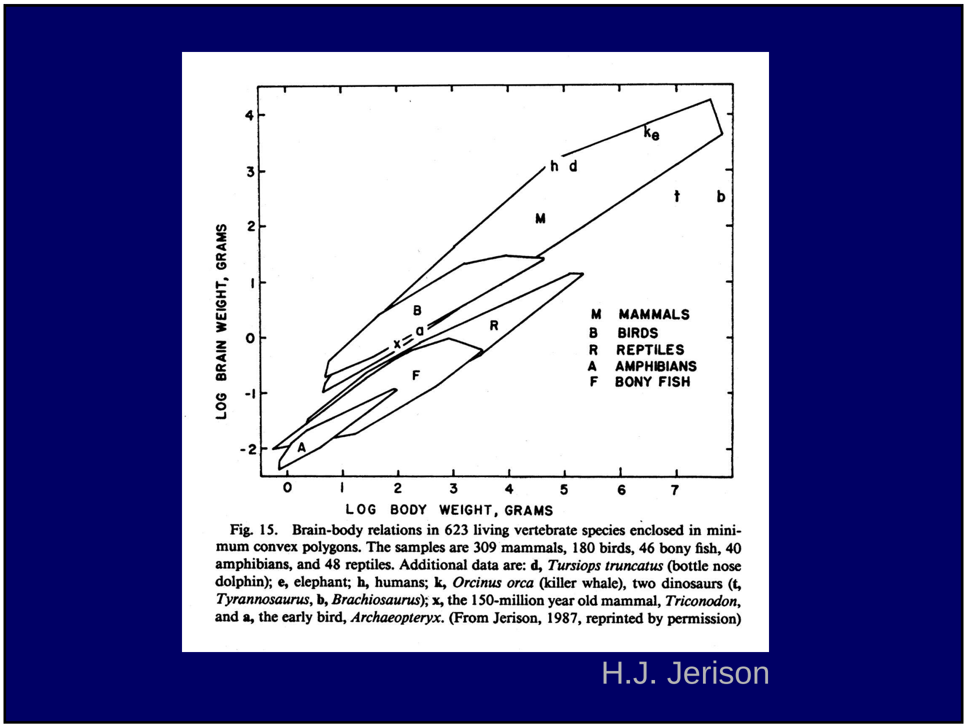
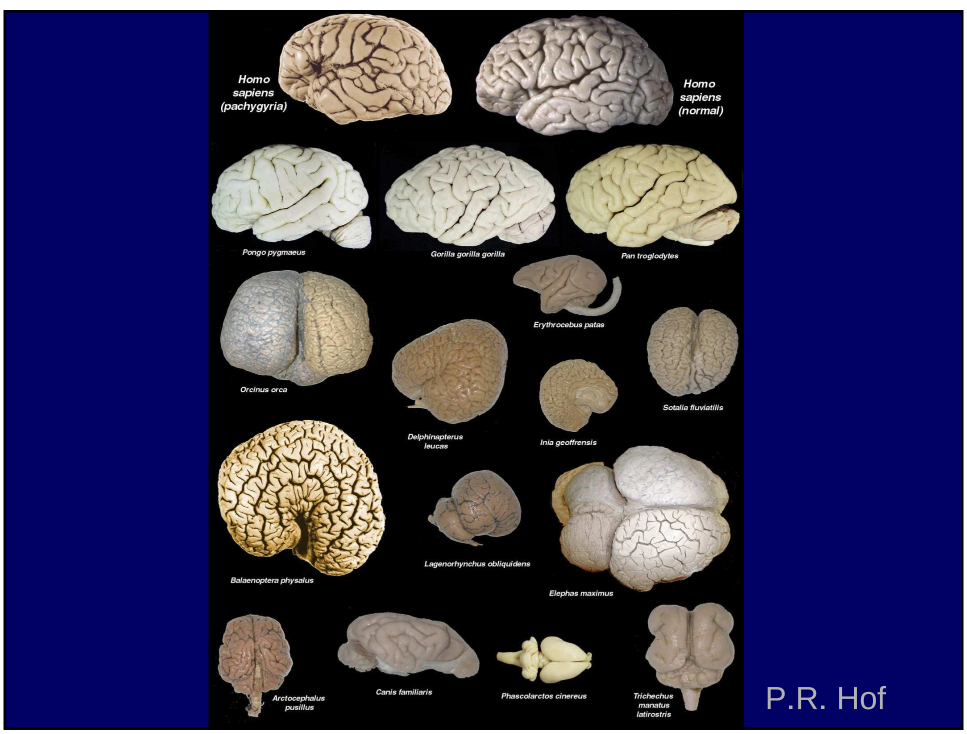
Optical physiology and synaptic learning rules:

Shari Gelber
Daniel O'Connor
Ilker Ozden
Dmitry Sarkisov
Shy Shoham
Megan Sullivan
Gayle Wittenberg

Brain scaling and evolution:

Mark Burish
Damon Clark
Kim Harrison
Hao Yuan Kueh
Jennifer Shultz
Matt Wagers
Krysta Wyatt


LOG BRAIN WEIGHT, GRAMS
LOG BODY WEIGHT, GRAMS
M MAMMALS
B BIRDS
R REPTILES
A AMPHIBIANS
F BONY FISH
Fig. 15. Brain-body relations in 623 living vertebrate species enclosed in minimum convex polygons. The samples are 309 mammals, 180 birds, 46 bony fish, 40 amphibians, and 48 reptiles. Additional data are: d, Tursiops truncatus (bottle nose dolphin); e, elephant; h, humans; k, Orcinus orca (killer whale), two dinosaurs (t, Tyrannosaurus, b, Brachiosaurus); x, the 150-million year old mammal, Triconodon, and a, the early bird, Archaeopteryx. (From Jerison, 1987, reprinted by permission)
H.J. Jerison


Homo sapiens (pachygyria)
Homo sapiens (normal)
Pongo pygmaeus
Gorilla gorilla gorilla
Pan troglodytes
Erythrocebus patas
Orcinus orca
Sotalia fluviatilis
Delphinapterus leucas
Inia geoffrensis
Lagenorhynchus obliquidens
Balaenoptera physalus
Elephas maximus
Arctocephalus pusillus
Canis familiaris
Phascolarctos cinereus
Trichechus manatus latirostris
P.R. Hof

Inferring general functional principles
with comparative anatomy

86 HISTOLOGY OF THE NERVOUS SYSTEM

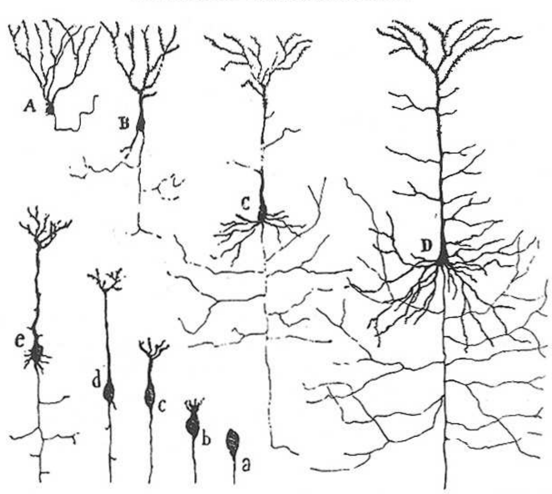


FIG. 23. Diagram of the phylogenetic and ontogenetic development of pyramidal cells.

The upper series of cells shows this type of neuron in various vertebrates: *A*, frog; *B*, wall lizard; *C*, rat; *D*, human. The lower series of drawings indicates the ontogenetic development of psychic or pyramidal cells of the cerebral cortex: *a*, neuroblast without a dendritic trunk; *b*, beginning of the dendritic trunk and terminal tuft; *c*, a more developed trunk; *d*, appearance of axon collaterals; *e*, formation of dendritic processes on the cell body and trunk.

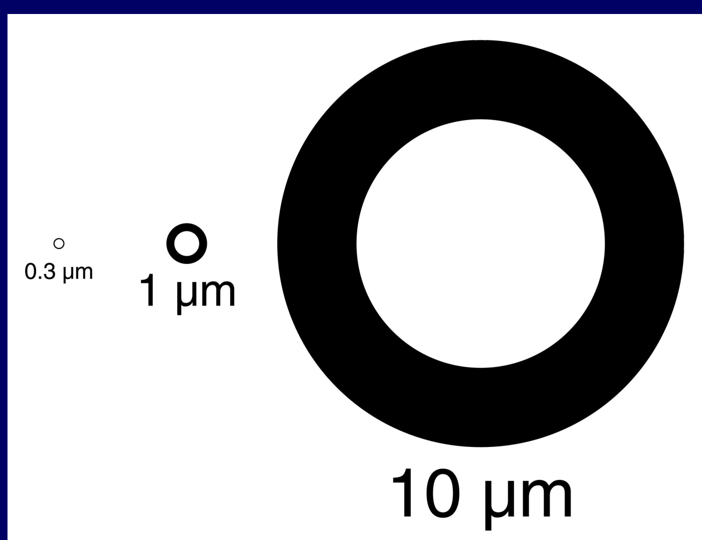
Ramon y Cajal

We would now like to compare neurons not just from similar animals, but from animals throughout the zoological series, and more particularly from vertebrates. In doing so, we shall carefully limit comparisons to homologous cells in corresponding neural centers. The result of this exercise is rather surprising. From the appearance of the very first vertebrates, some individual neurons or groups of neurons have been modified more or less continuously before reaching their current state of refinement. In contrast, some neurons remain unchanged over long periods of time, seemingly impervious to all progress.

Different degrees of improvement in neurons.

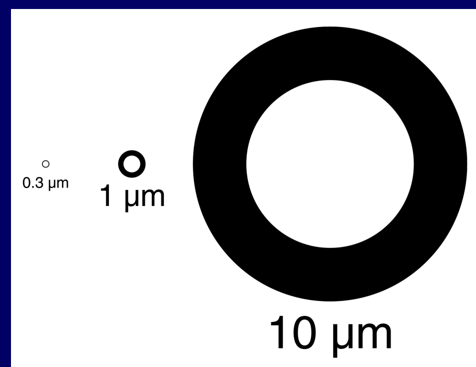
This suggests that the nervous system can be divided into two quite distinct systems by the differential action of evolution on large groups of constituent cells. One group, confined to the sensory nervous system, appears to have reached an endpoint in refinement, at least as far as the differentiation of its constituent neurons is concerned; it appears now to be susceptible only to increases in cell number or size. The other group, found mainly in the central nervous system—and more particularly in the cerebral cortex—has continued to evolve, and during the course of refinement has always matched the progression of the animal series, increasing both in size and refinement.

Axons



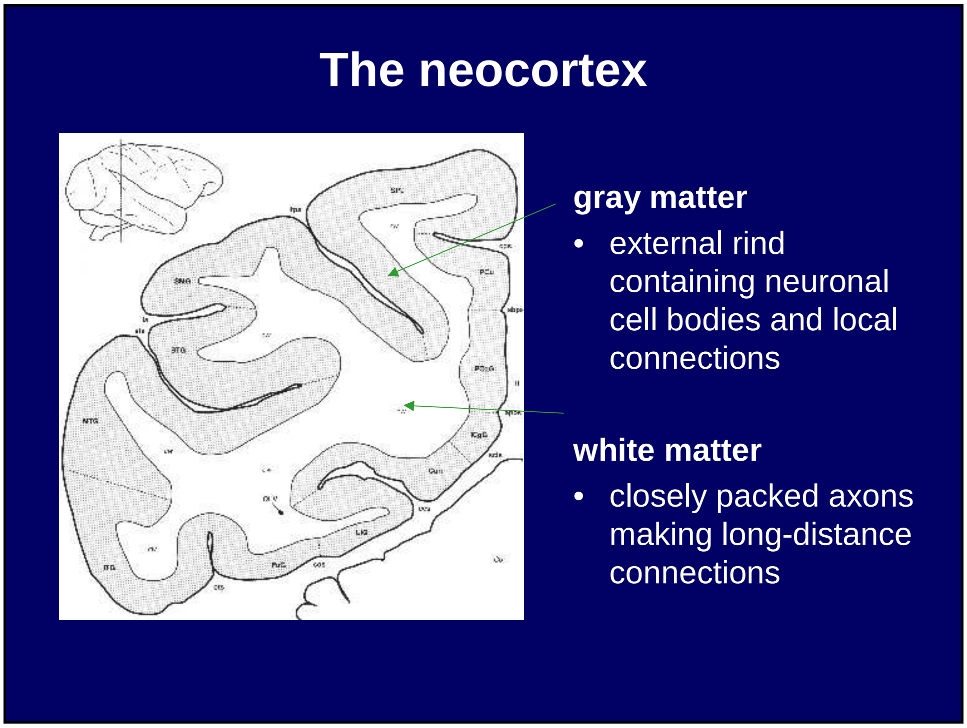
Functional advantages of axon size and type

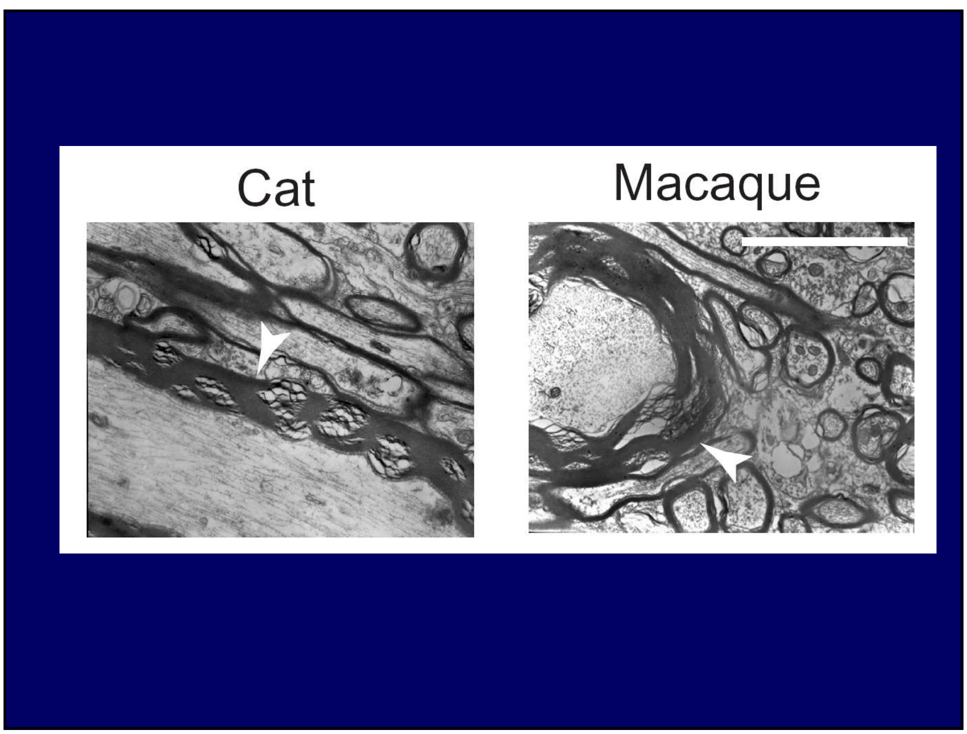
Compactness (35-70% of axons)
Per-spike energy cost (30-65%)
Extreme speed (0-5%)



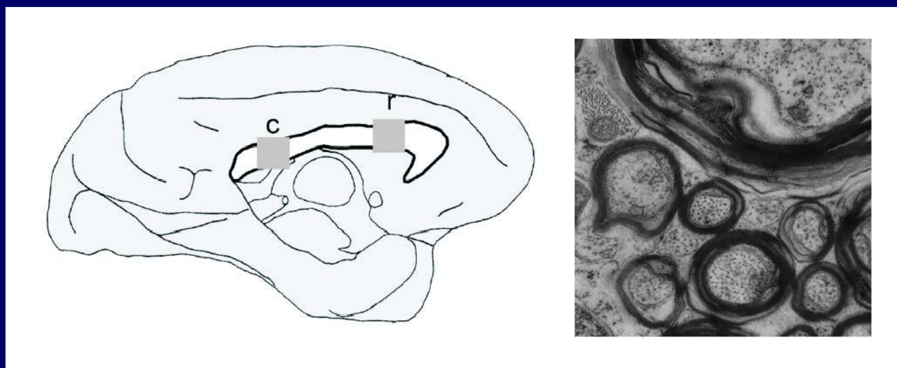
Explaining scaling trends with biophysical principles

- **Are white matter axons under selection pressure for speed?**
  - **Synaptic delays and action potentials: 1 msec**
  - **Synaptic potentials: 10-100 msec**
  - **Cross-brain conduction: <u>10-200 msec</u>**
- **Can ultrastructural trends account for gross scaling trends?**
  - **Geometric "accounting"**


The neocortex
gray matter
• external rind containing neuronal cell bodies and local connections
white matter
• closely packed axons making long-distance connections

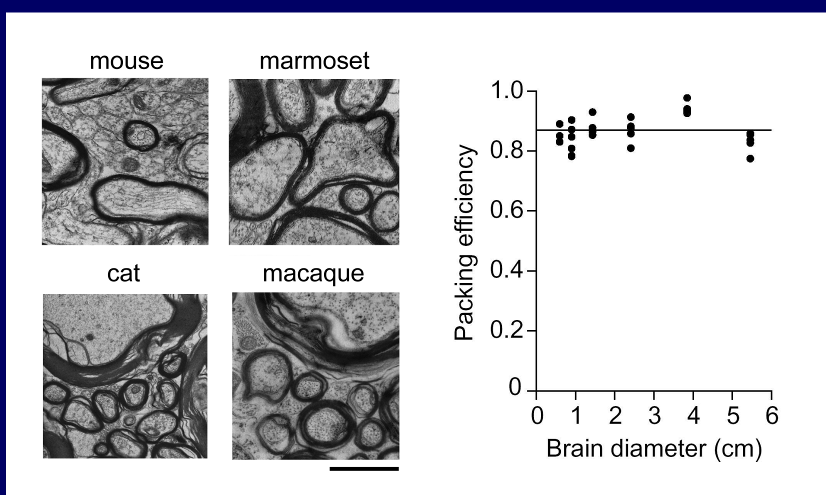

Cat
Macaque

Axons of the corpus callosum

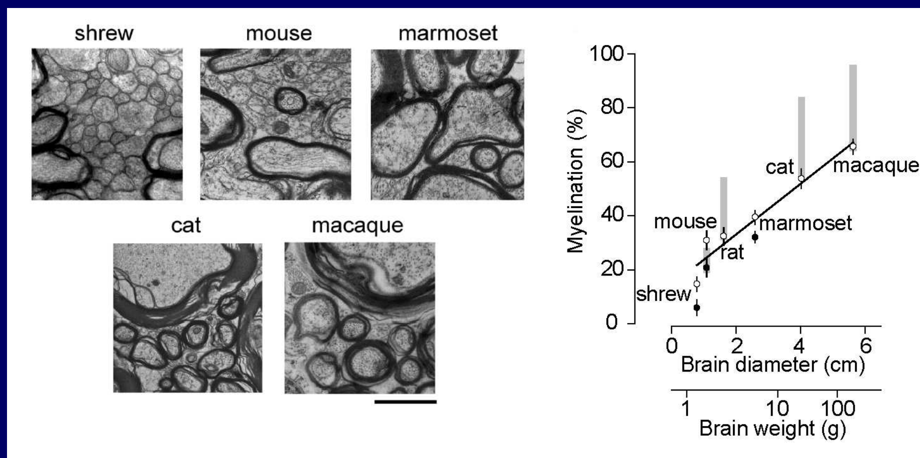


J.R. Shultz, K.H. Harrison, M.W. Wagers, K.D. Wyatt, M.J. Burish

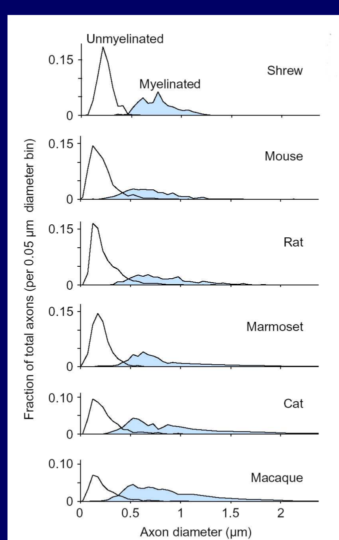
Axons of the corpus callosum are well-packed

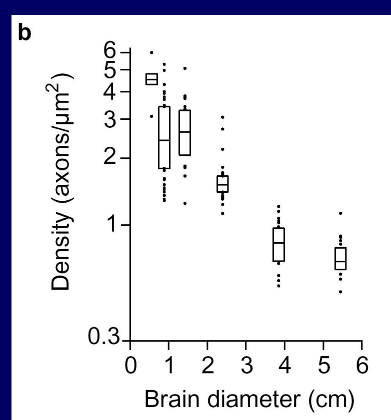


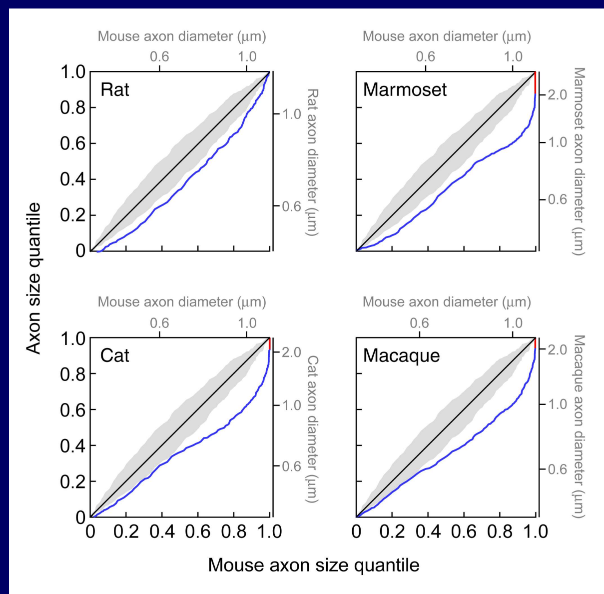
Myelination becomes more prevalent in larger brains



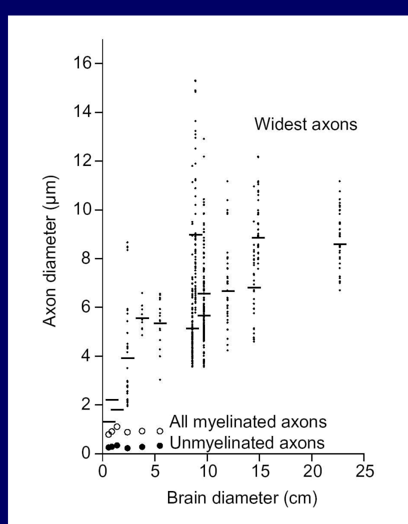
Axon density decreases in larger brains

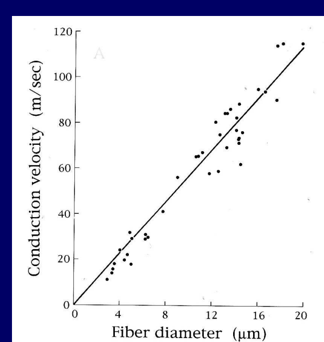






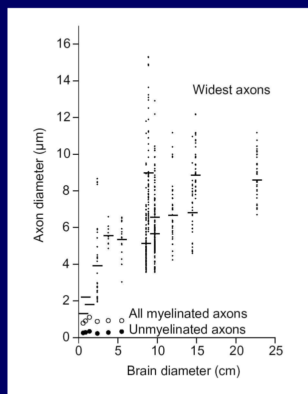
The largest axons increase in size with brain diameter

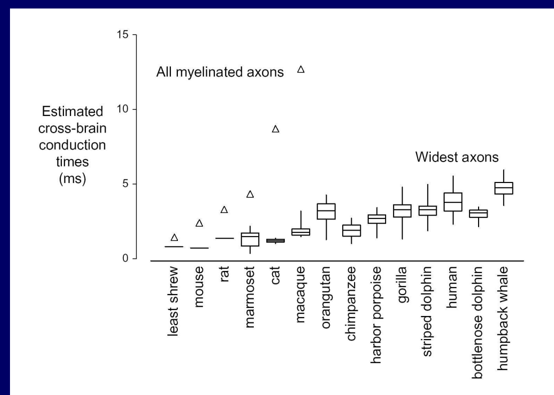




J.M. Ritchie
(Hursh 1939)

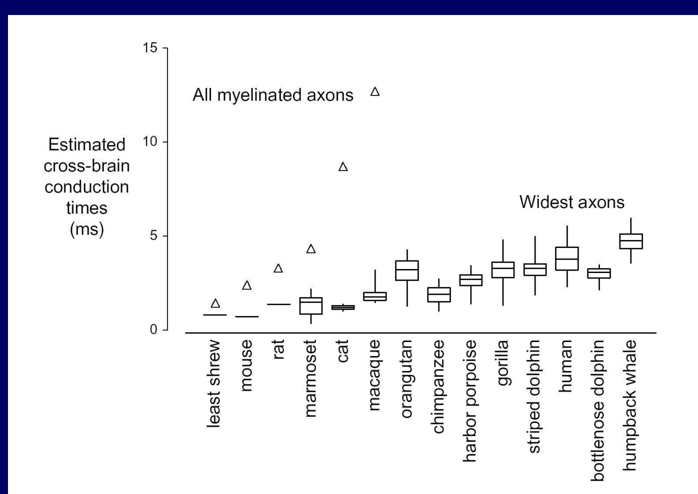
2. Minimal cross-brain conduction time is ~2 milliseconds*





*(but the slowest times can be of order 1 second!)

Preservation of shortest cross-brain conduction times

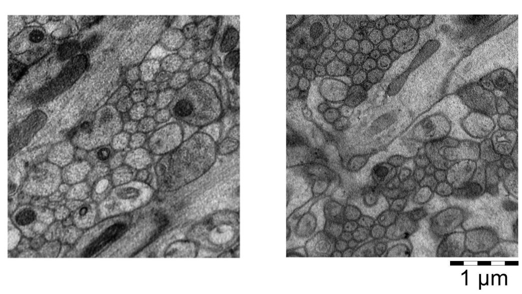


Axon scaling in other pathways

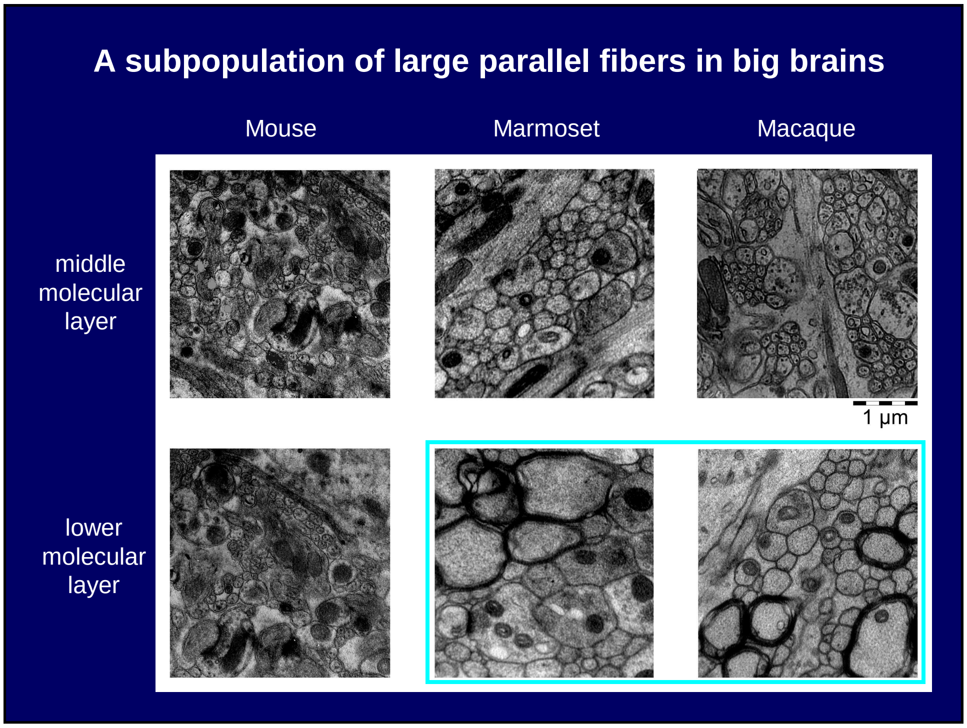
- **Corticospinal axons for fine movement**
- **V1 to MT projecting axons**
- **Optic nerve**
- **Cerebellar parallel fibers**

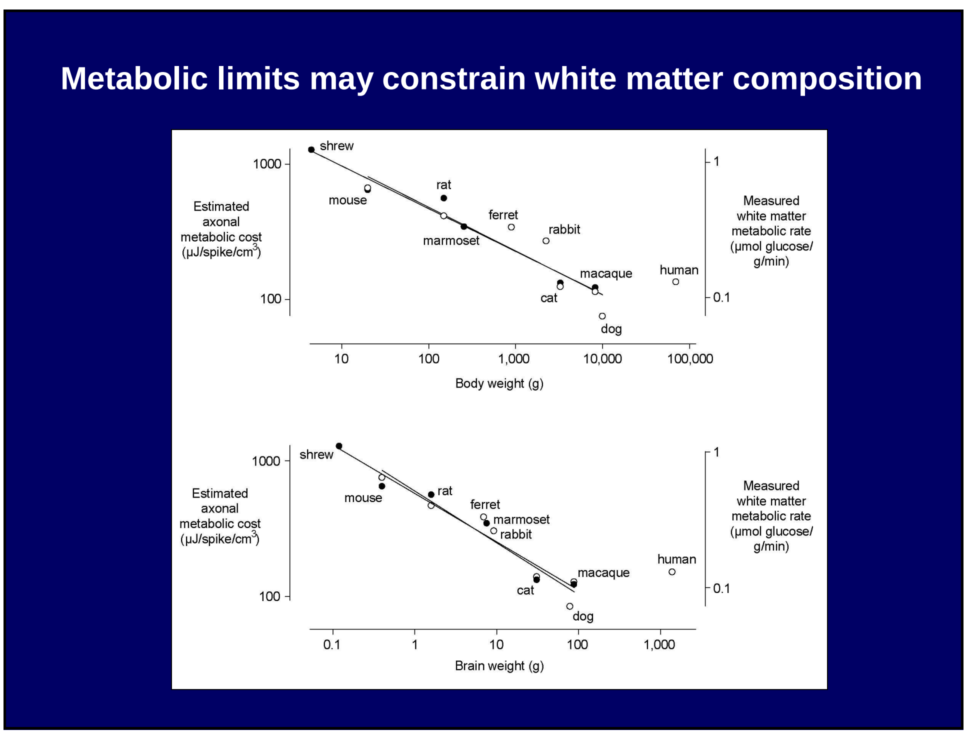
Parallel fibers have small diameters even in large brains

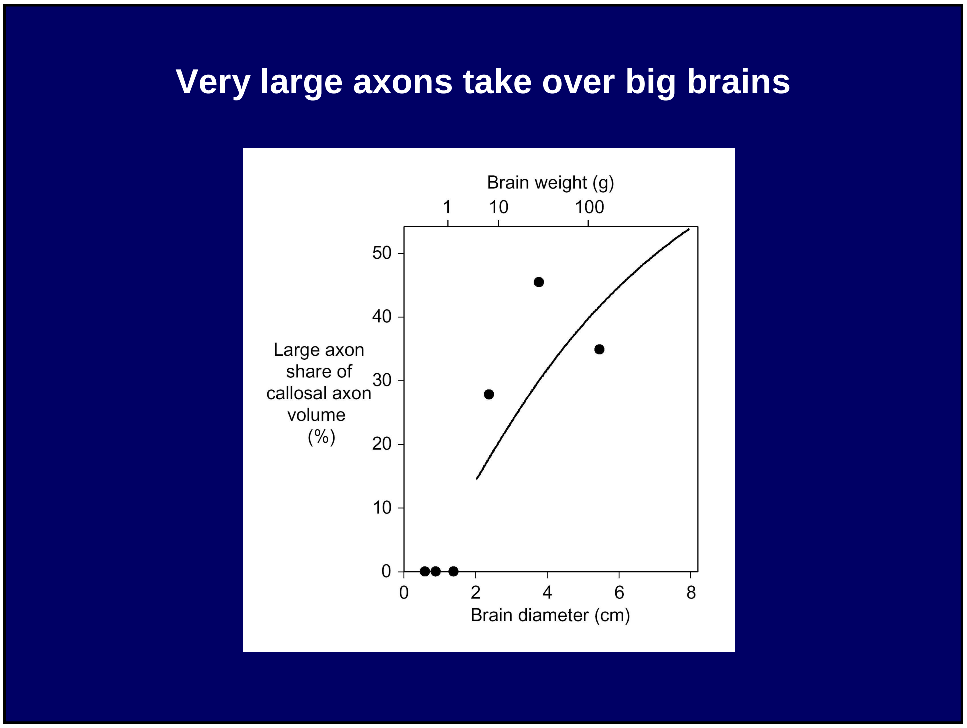
Marmoset **Macaque**

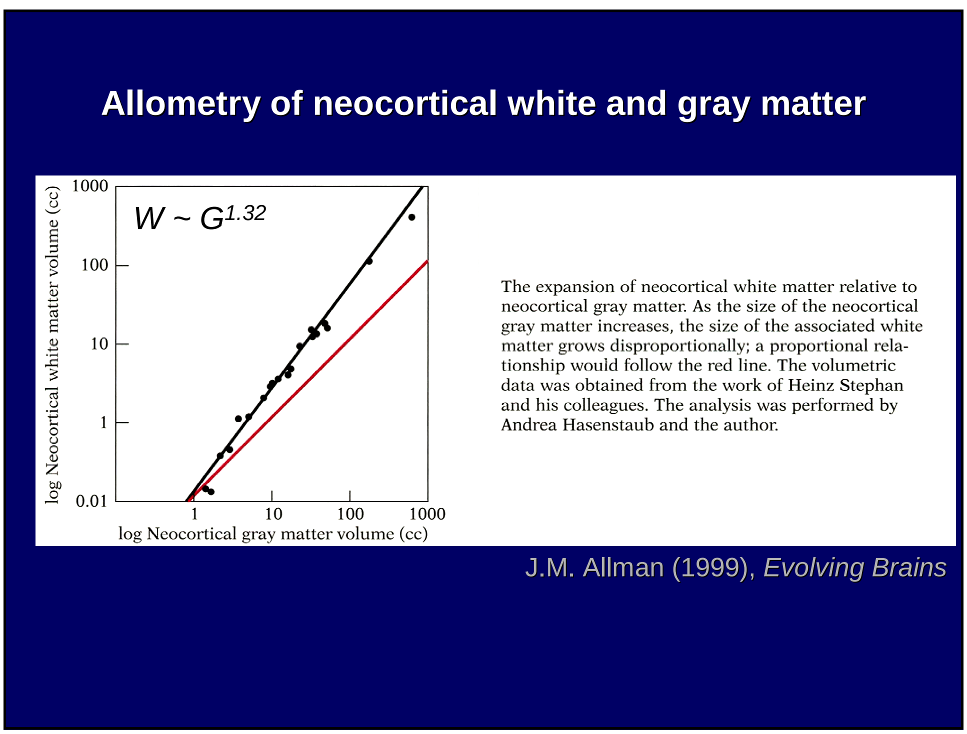


K.D. Wyatt

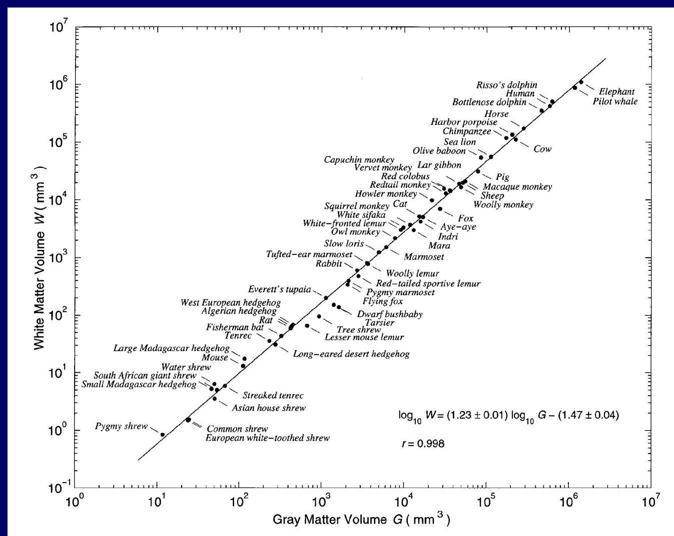

A subpopulation of large parallel fibers in big brains
Mouse
Marmoset
Macaque
middle molecular layer
lower molecular layer
1 µm


Metabolic limits may constrain white matter composition
Estimated axonal metabolic cost (µJ/spike/cm3)
Measured white matter metabolic rate (µmol glucose/ g/min)
shrew
mouse
rat
ferret
rabbit
marmoset
macaque
human
cat
dog
1000
100
1
0.1
10
100
1,000
10,000
100,000
Body weight (g)
0.1
1
10
100
1,000
Brain weight (g)


Very large axons take over big brains
Brain weight (g)
1
10
100
50
40
30
20
10
0
Large axon share of callosal axon volume (%)
0
2
4
6
8
Brain diameter (cm)


Allometry of neocortical white and gray matter
W ~ G1.32
1000
100
10
1
0.01
log Neocortical white matter volume (cc)
1
10
100
1000
log Neocortical gray matter volume (cc)
The expansion of neocortical white matter relative to neocortical gray matter. As the size of the neocortical gray matter increases, the size of the associated white matter grows disproportionally; a proportional relationship would follow the red line. The volumetric data was obtained from the work of Heinz Stephan and his colleagues. The analysis was performed by Andrea Hasenstaub and the author.
J.M. Allman (1999), Evolving Brains

A length minimization argument for white matter volume



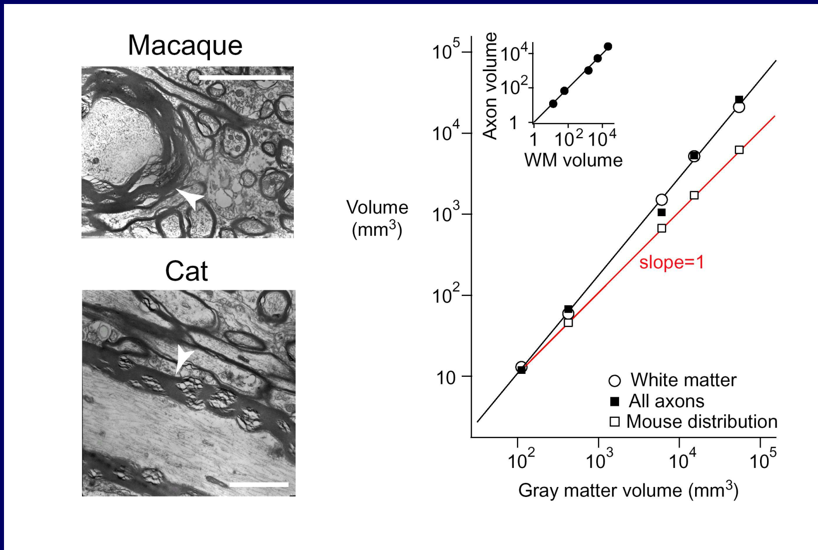
Zhang and Sejnowski (2000) *PNAS* 97:5621

Length minimization alone cannot predict volume

$$W = \sum_{i=1}^{n} aL_i = (na)\left(\frac{1}{n}\sum_{i=1}^{n} L_i\right). \qquad \textbf{[3]}$$

Zhang and Sejnowski (2000) *PNAS* 97:5621-5626

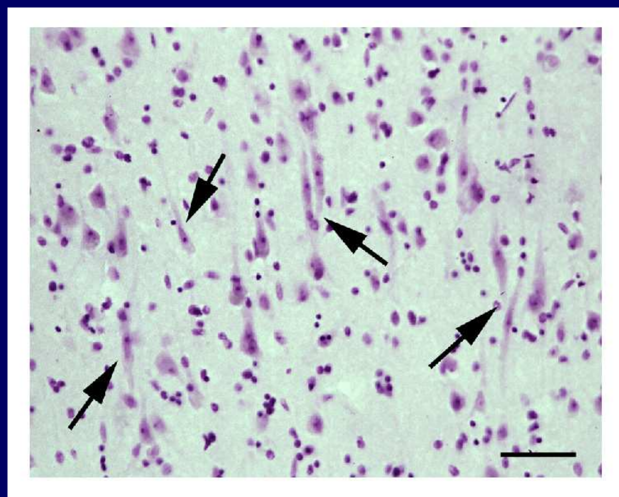
Giant axons drive white matter volume in big brains



Conclusions from looking at neocortical axons

1. **White matter composition varies with brain size**
2. **The fastest cross-brain conduction times are 2-5 msec**
3. **Metabolic limits may constrain white matter composition**
4. **Very large axons take over big brains**

Spindle cells: a source of large axons?



Nimchinsky et al. (1999)
PNAS 96:5268

Neuron density is smaller in large brains

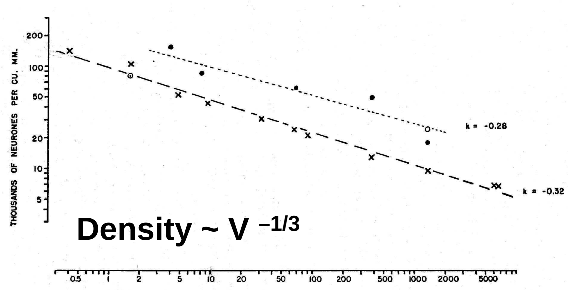


Fig. 1 Neurone density in the cerebral cortex of various adult mammals in relation to average total brain weight (Log Scales). × = Values from Tower and Elliott ('52a) and present study for species with the following average total brain weights (from Count, '47 with the exception of elephant and whale): Mouse 0.4 gm, rat 1.6 gm, guinea pig 4.75 gm, rabbit 9.3 gm, cat 31 gm, dog 65 gm, monkey *(Macacca)* 88.5 gm, beef 375 gm, man 1320 gm, elephant 6075 gm, and fin whale 6785 gm.

● = Values from Shariff ('53) for agranular cortex of primate species with the following average total brain weights (from Count, '47 and Shariff, '53): *Tarsius* 4 gm, *Hapale* 8 gm, *Cercopithecus* 67 gm, chimpanzee 375 gm, and man 1320 gm.

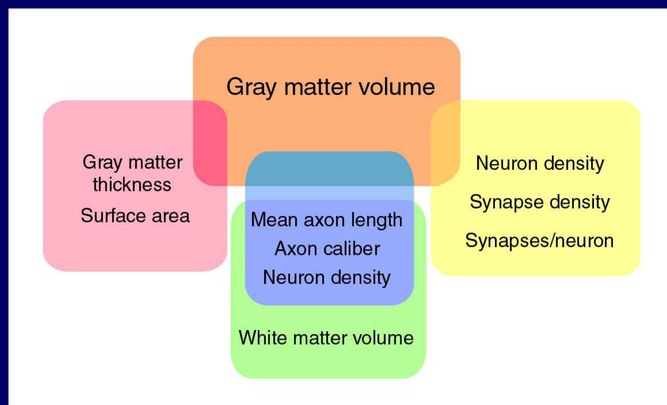
⊙ = Value averaged from data of Sugita ('18a) for rat cortex.

○ = Value calculated from data of von Economo ('26) for human cortex.

The regression coefficients, k, for the equation, $N = K_N W^k$ are shown beside each regression line.

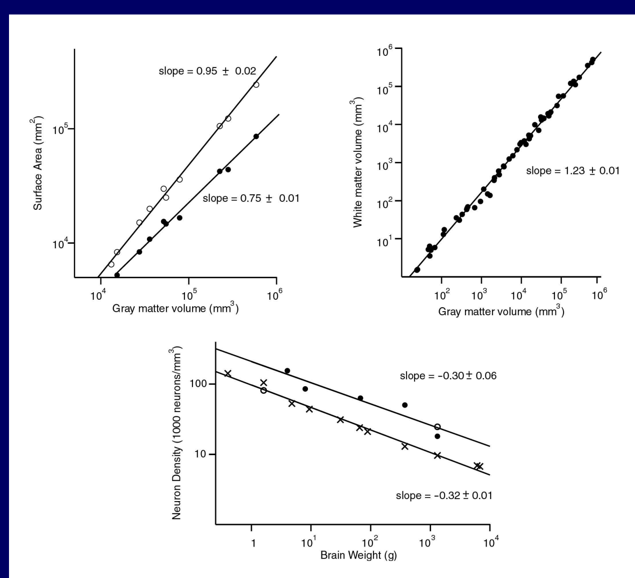
D.B. Tower (1954)
J. Comp. Neurol. 101:9

Links among scaling relationships in the neocortex



K.H. Harrison, P.R. Hof, and S.S.-H. Wang (2002)
Journal of Neurocytology **31**:289-298

Scaling relationships in the mammalian neocortex

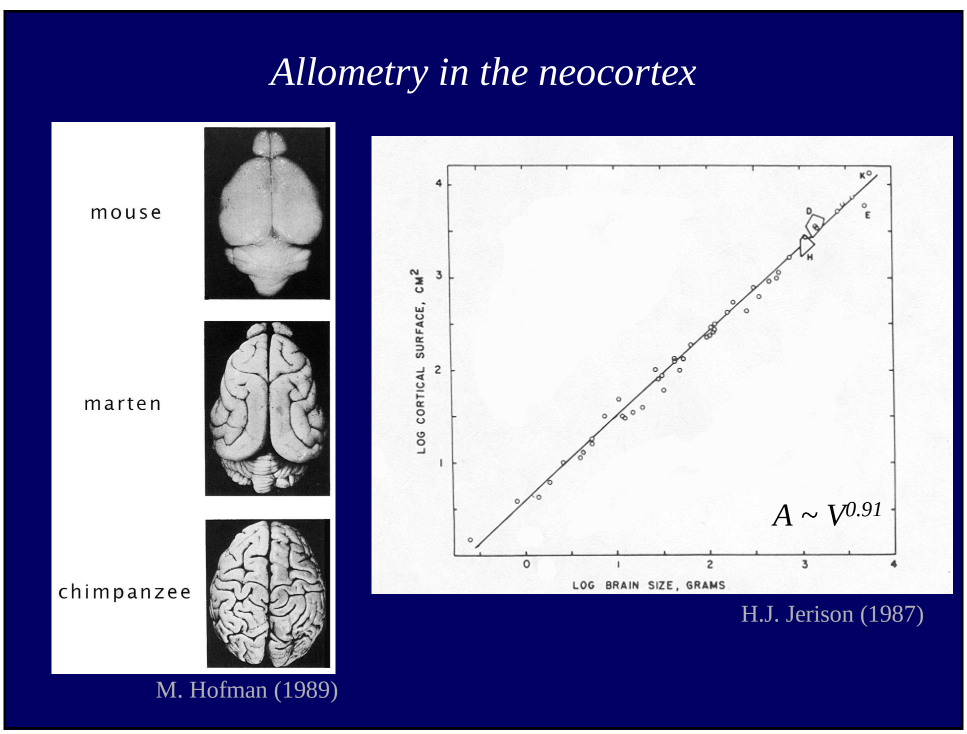


Open Questions

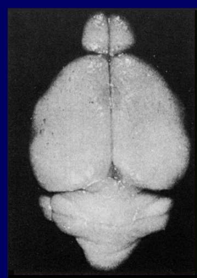
- What functions require cross-brain conduction to be conserved?
- Who are the giant axons and what do they do?
- Why does neuronal density decrease with an orderly power law?
- What underlies other intracortical scaling relationships?
- What are other invariant quantities of neocortex?
- How do these principles apply to other systems?

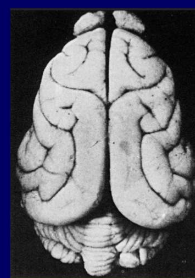
"Sometimes I wonder if there's more to life than unlocking the mysteries of the universe."

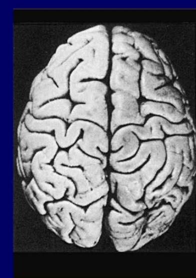

The end


Allometry in the neocortex
mouse
marten
chimpanzee
M. Hofman (1989)
LOG CORTICAL SURFACE, CM²
LOG BRAIN SIZE, GRAMS
A ~ V^0.91
H.J. Jerison (1987)

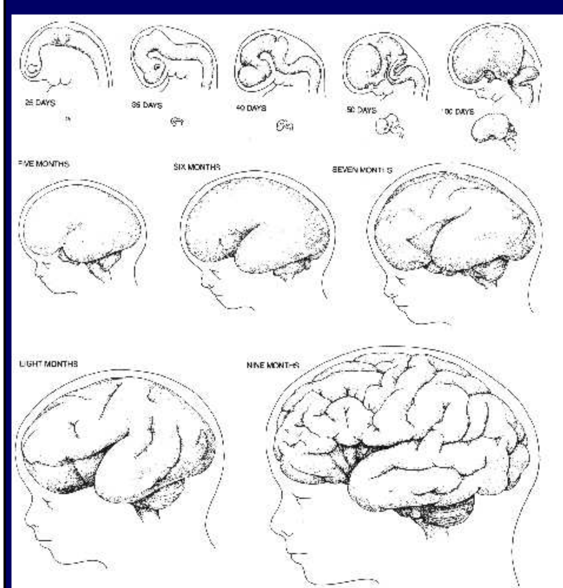
What makes the brain folded?

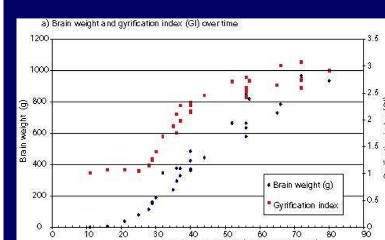




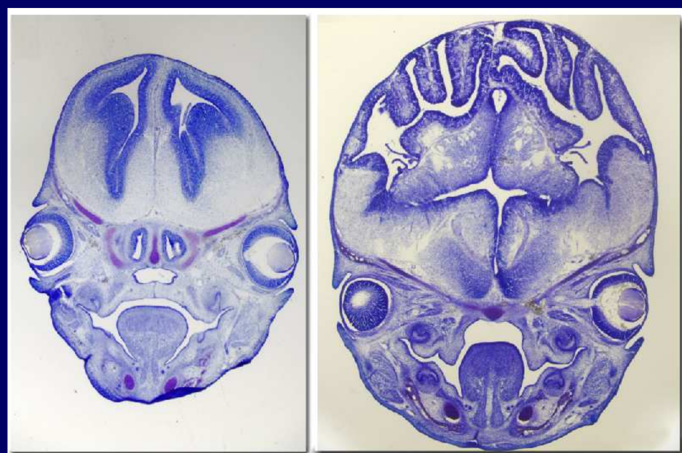


- Development
- Cell biology
- Evolution and optimization



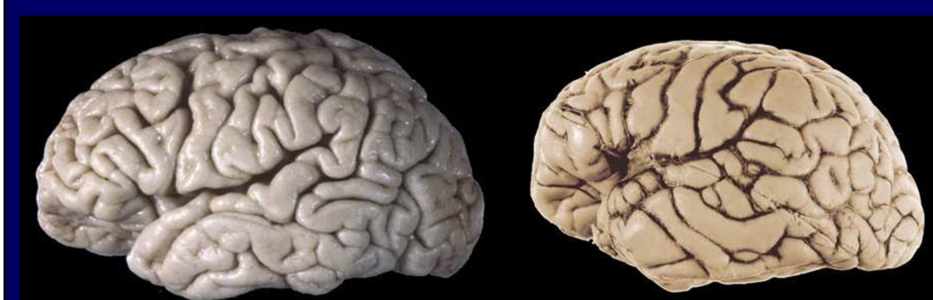


Beta-catenin overexpression induces mouse brains to fold



A. Chenn and C. Walsh (2002) *Science*

Normal brain Pachygyric brain



In some cases, caused by cocaine use during pregnancy. Fewer neurons?