

How to grow brains of different sizes (an analysis of the NIH Paediatric Project data)

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génétique humaine et fonctions cognitives



A Structural MRI Study of Human Brain Development from Birth to 2 Years

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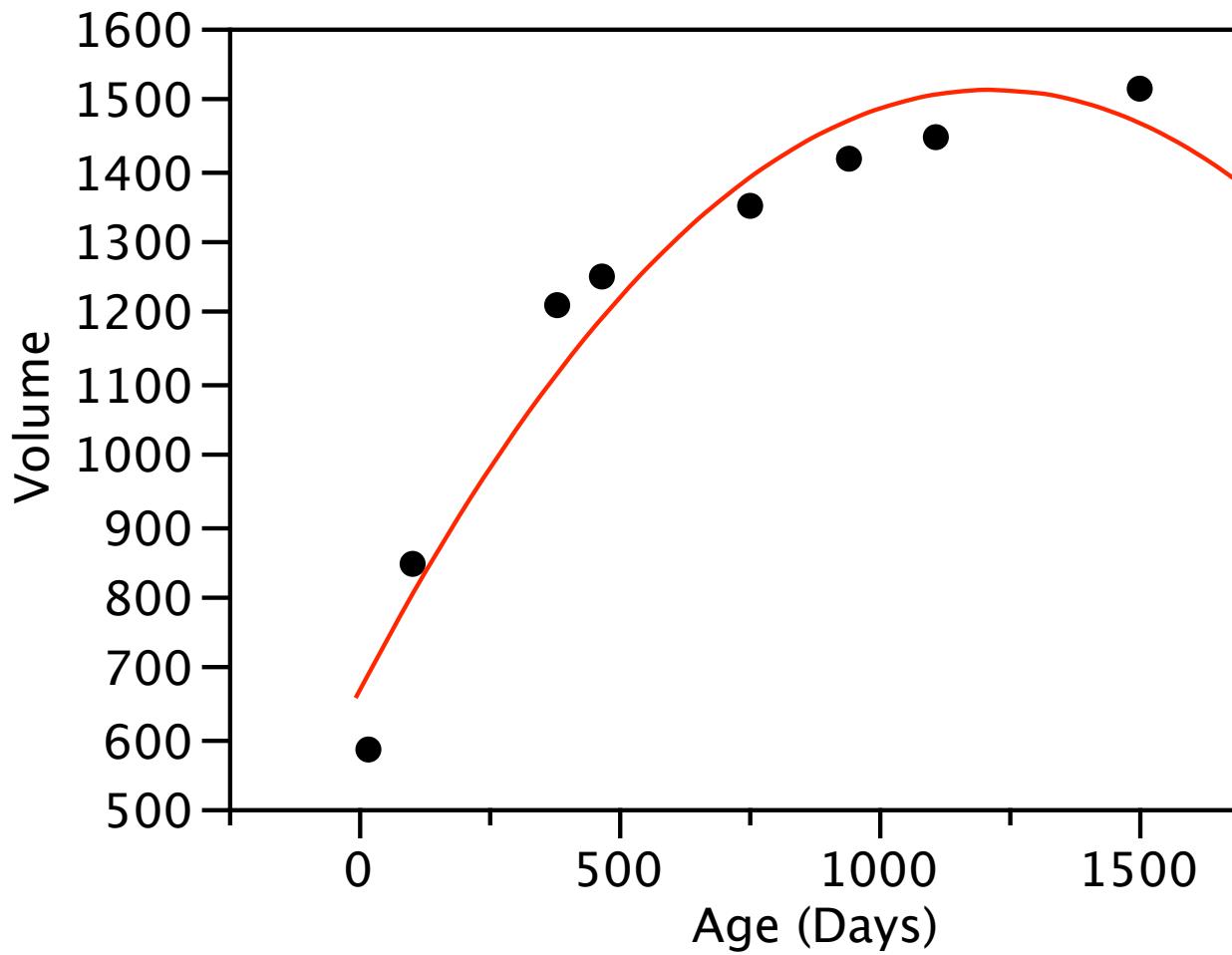
Brain development in the first 2 years after birth is extremely dynamic and likely plays an important role in neurodevelopmental disorders, including autism and schizophrenia. Knowledge regarding this period is currently quite limited. We studied structural brain development in healthy subjects from birth to 2. Ninety-eight children received structural MRI scans on a Siemens head-only 3T scanner with magnetization prepared rapid gradient echo T1-weighted, and turbo spin echo, dual-echo (proton density and T2 weighted) sequences: 84 children at 2–4 weeks, 35 at 1 year and 26 at 2 years of age. Tissue segmentation was accomplished using a novel automated approach. Lateral ventricle, caudate, and hippocampal volumes were also determined. Total brain volume increased 101% in the first year, with a 15% increase in the second. The majority of hemispheric growth was accounted for by gray matter, which increased 149% in the first year; hemispheric white matter volume increased by only 11%. Cerebellum volume increased 240% in the first year. Lateral ventricle volume increased 280% in the first year, with a small decrease in the second. The caudate increased 19% and the hippocampus 13% from age 1 to age 2. There was robust growth of the human brain in the first two years of life, driven mainly by gray matter growth. In contrast, white matter growth was much slower. Cerebellum volume also increased substantially in the first year of life. These results suggest the structural underpinnings of cognitive and motor development in early childhood, as well as the potential pathogenesis of neurodevelopmental disorders.

Main drawbacks

1. Disregard growth
2. Disregard diversity
3. Disregard allometry

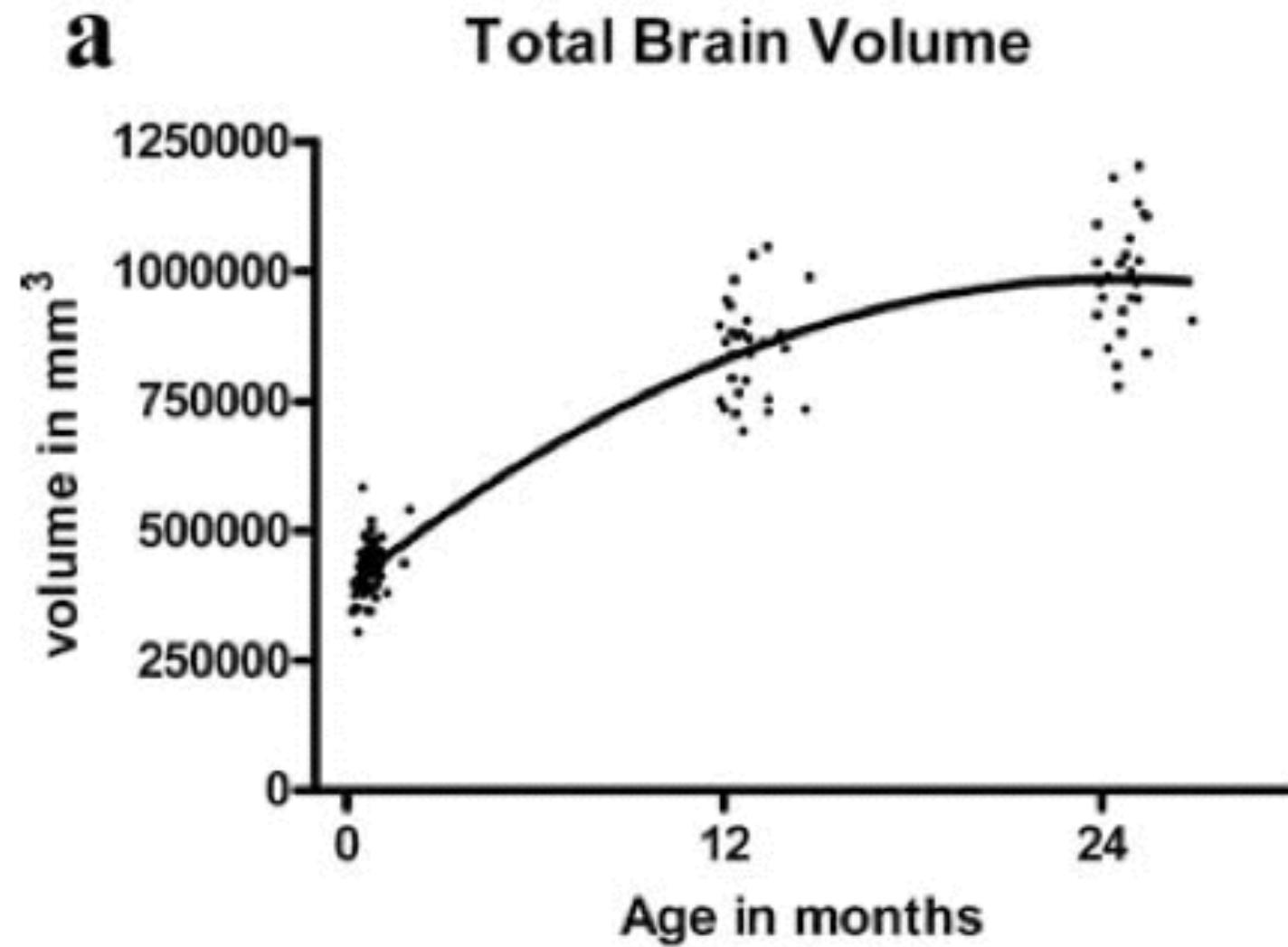
I. Disregarding growth

Parabolic model

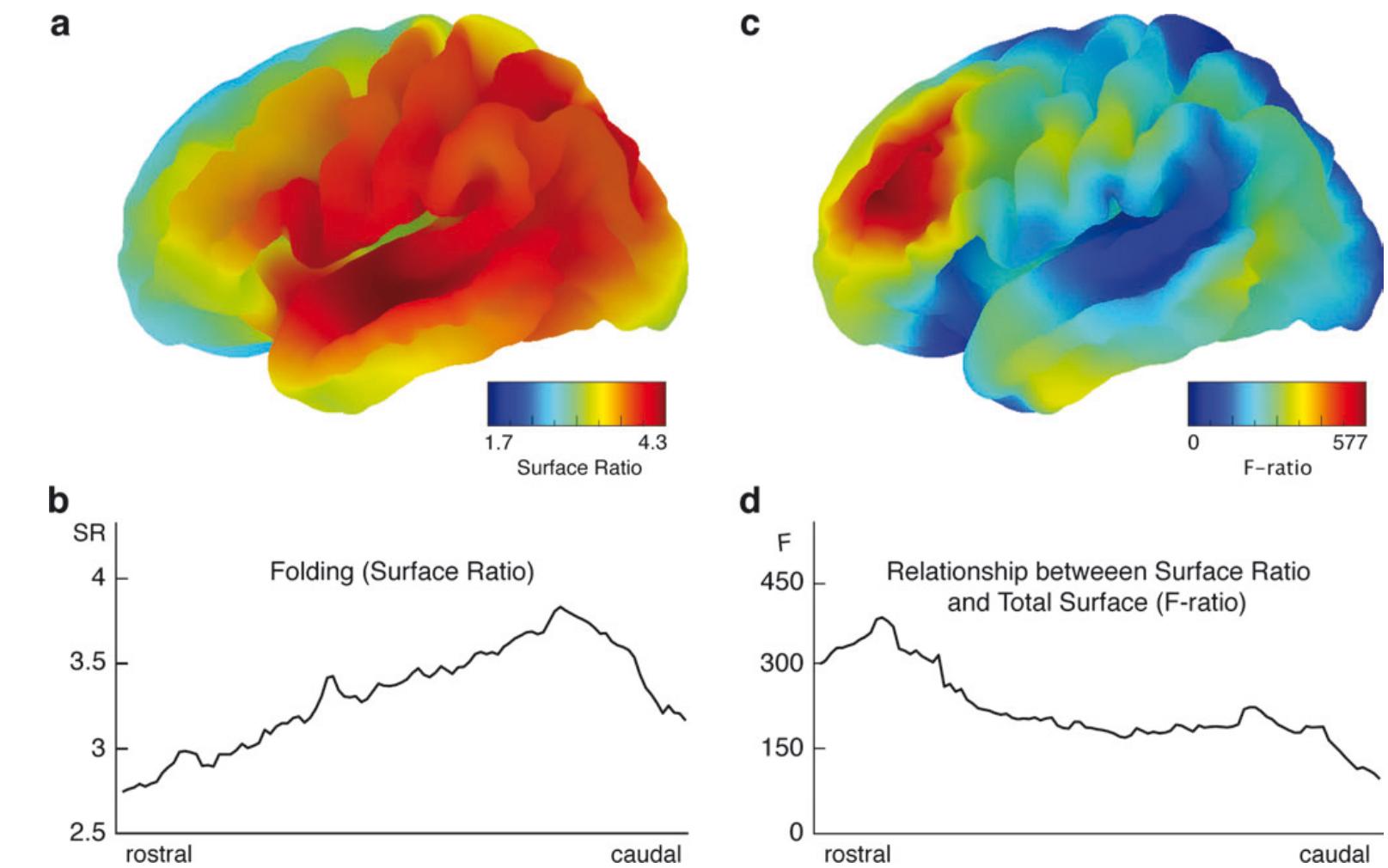
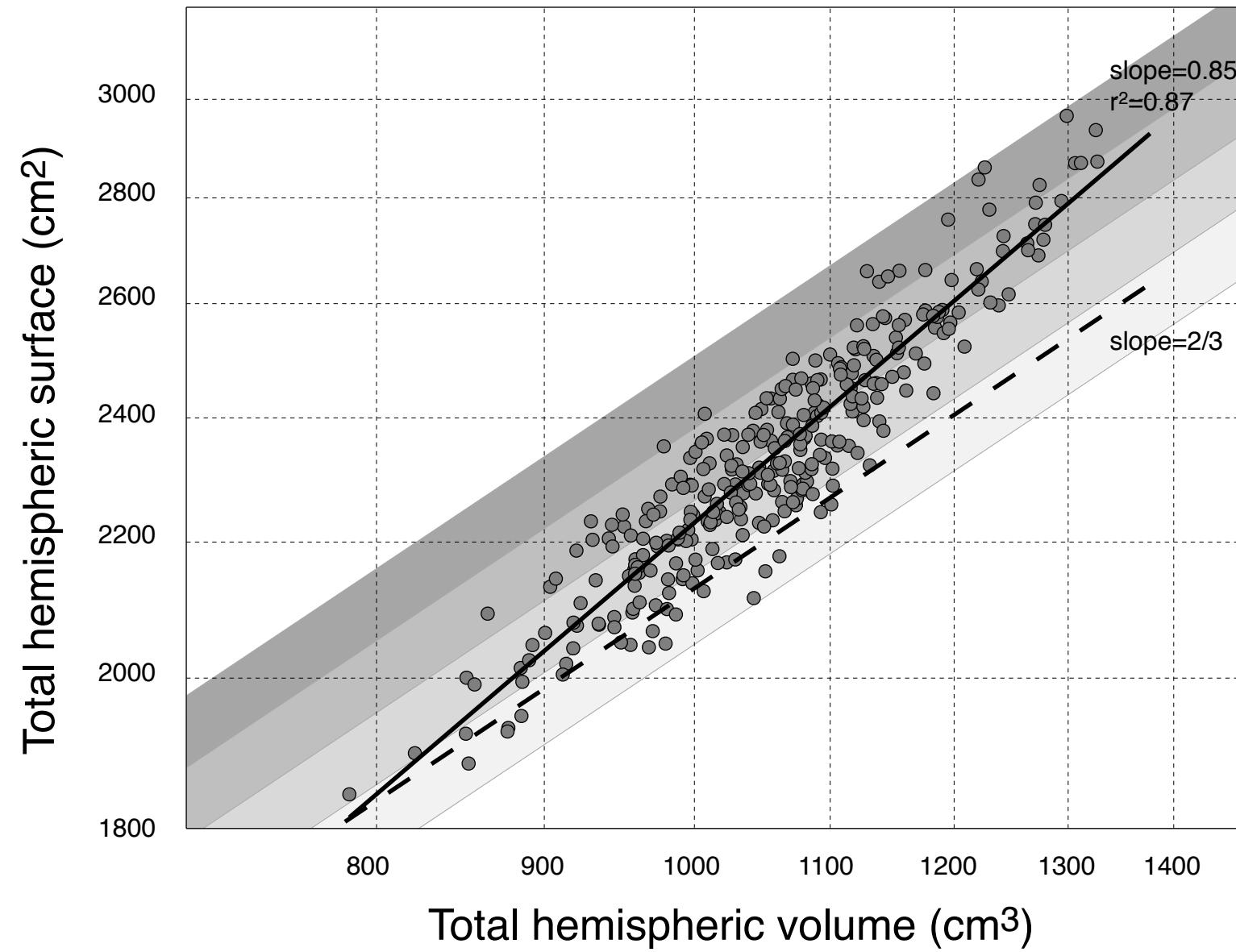


$$\text{Volume} = 910 + 0.64 \text{ Age} - 0.0006 (\text{Age}-661)^2$$

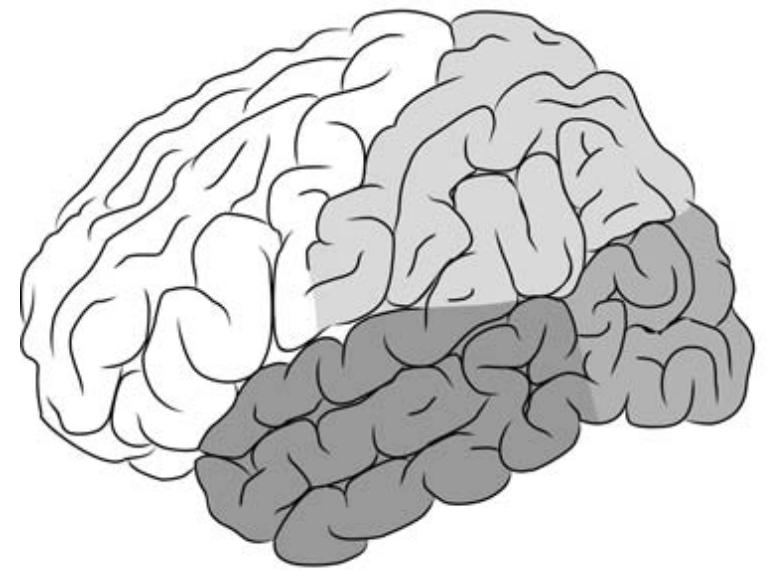
2. Disregarding diversity



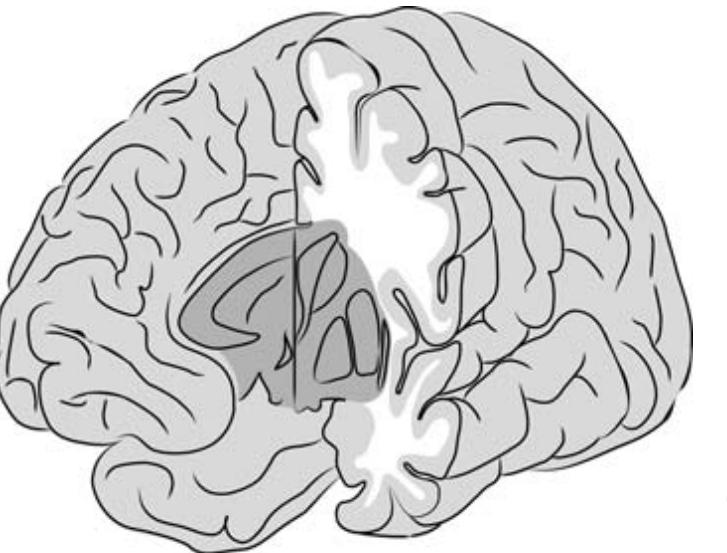
3. Disregarding allometry



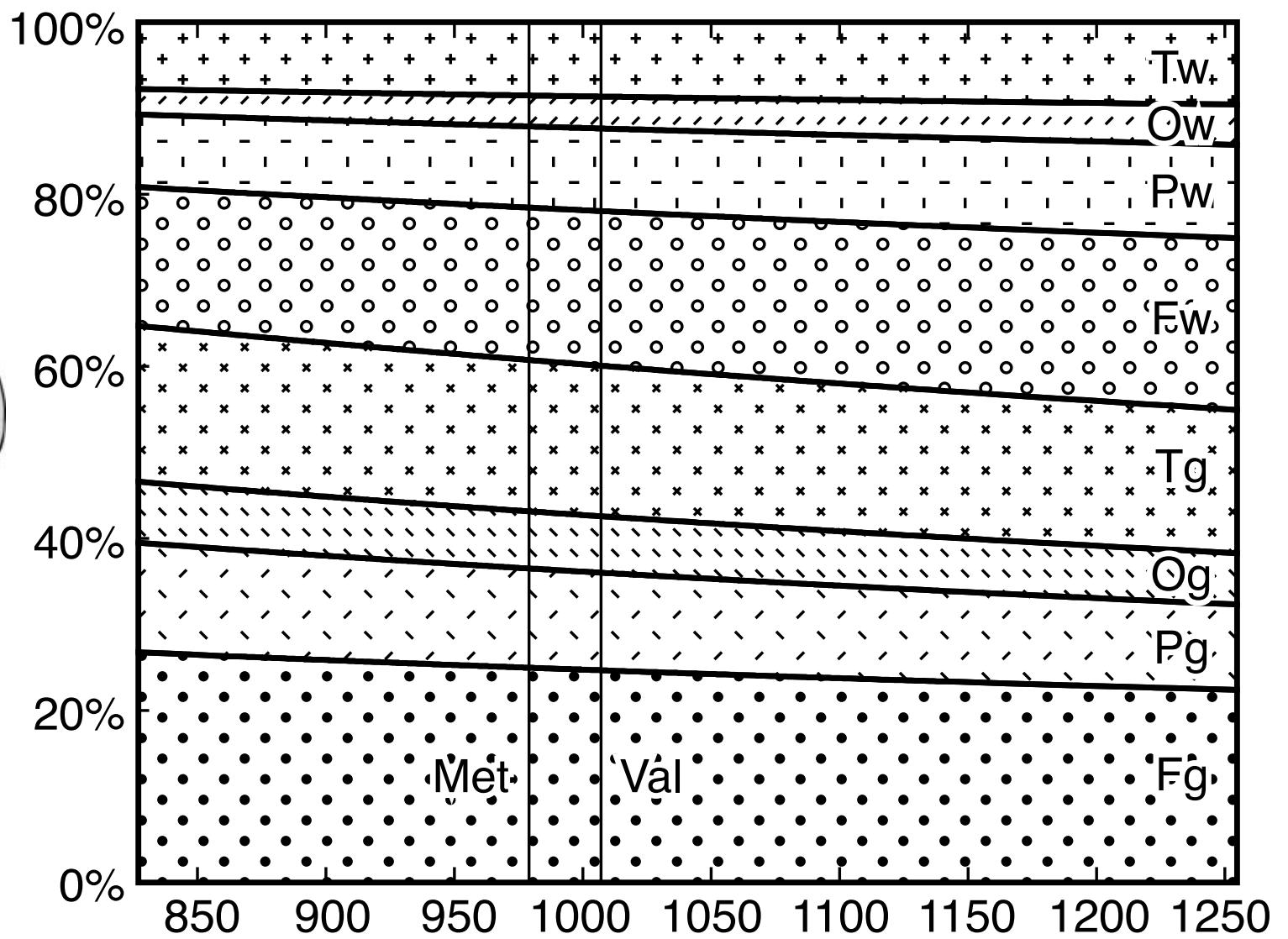
3. Disregarding allometry



Frontal
Parietal
Occipital
Temporal



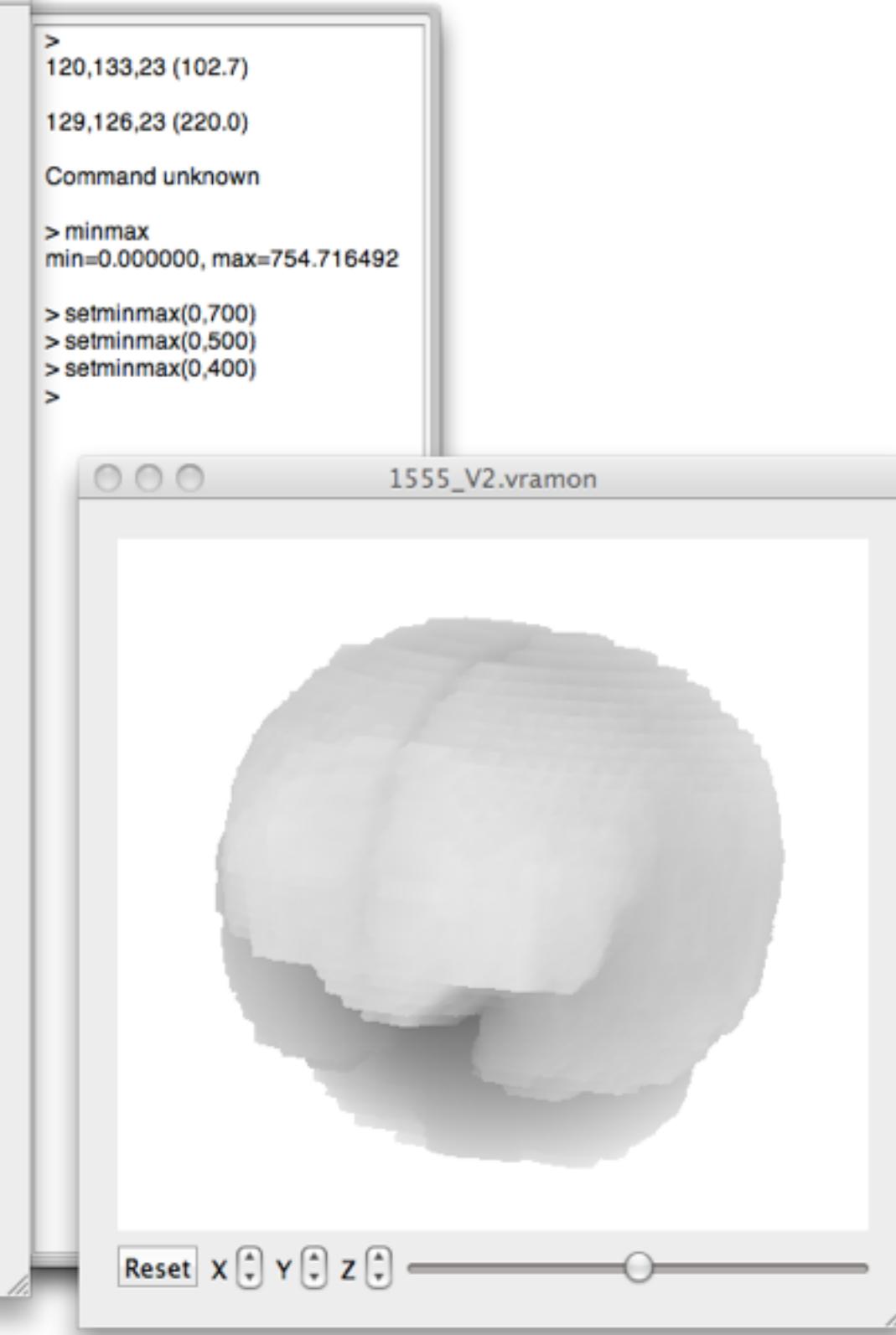
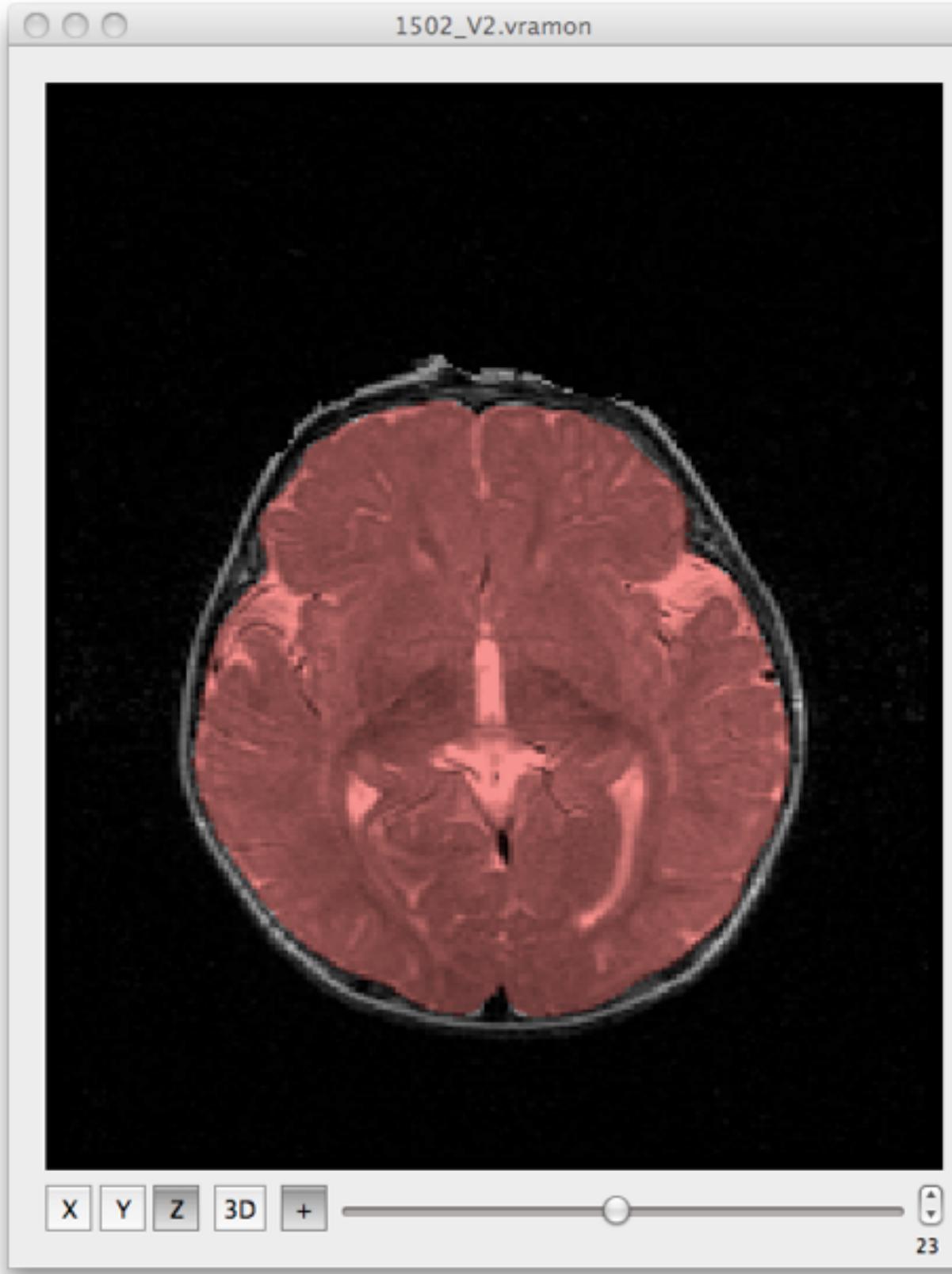
White matter
Grey matter
Subcortical

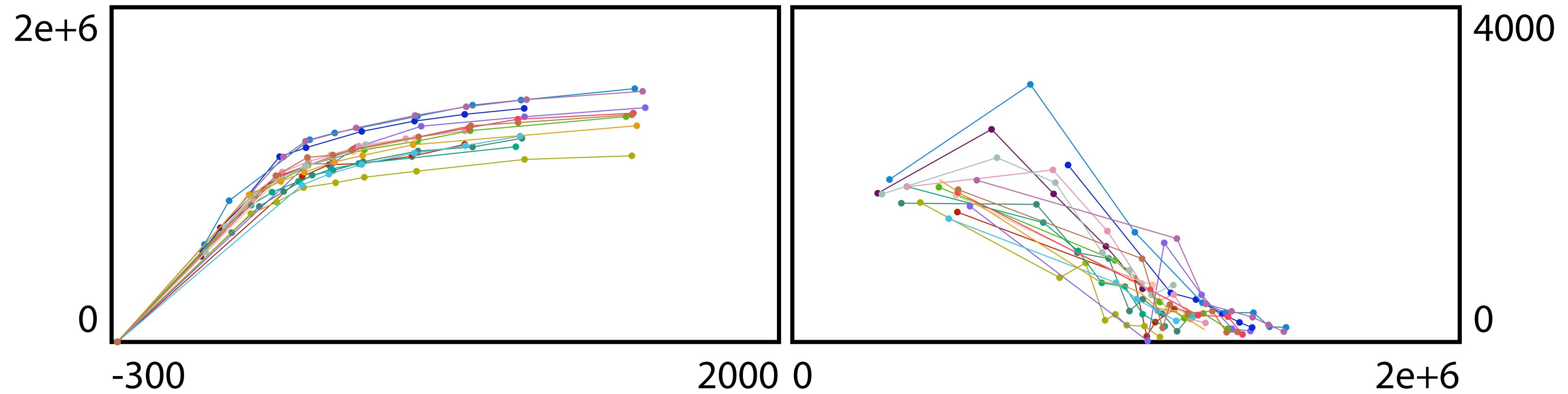


Early brain development

Early brain development

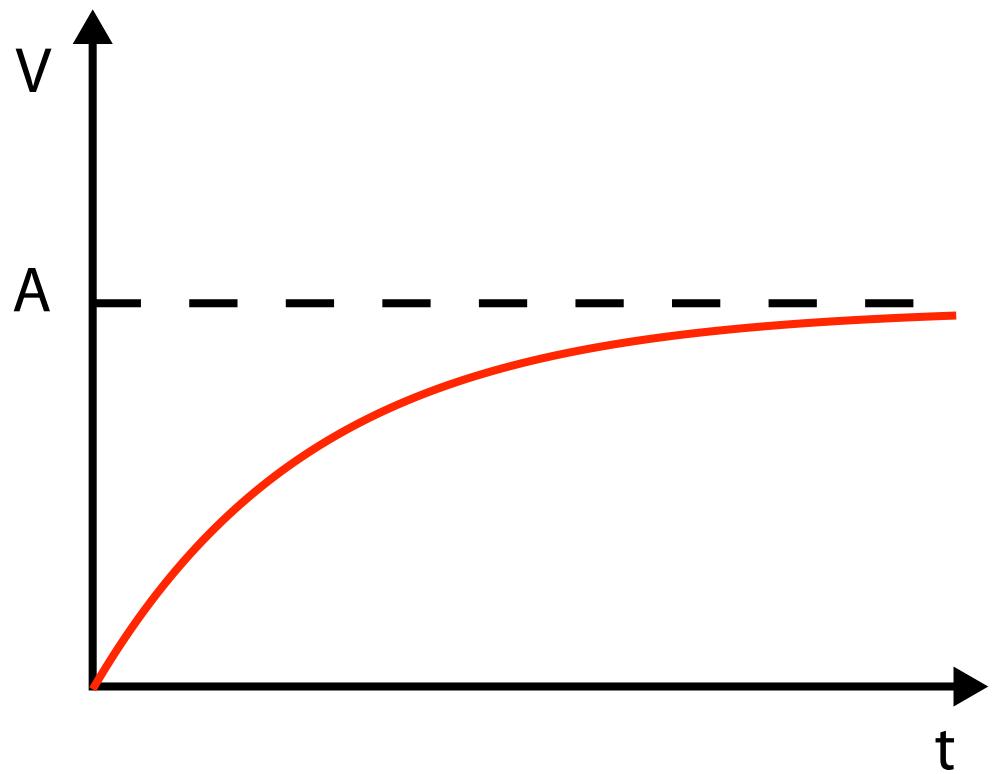
- N=17 (7 females, 8 males)
- Age from 8 days to 4.2 years
- From 5 to 10 visits per subject



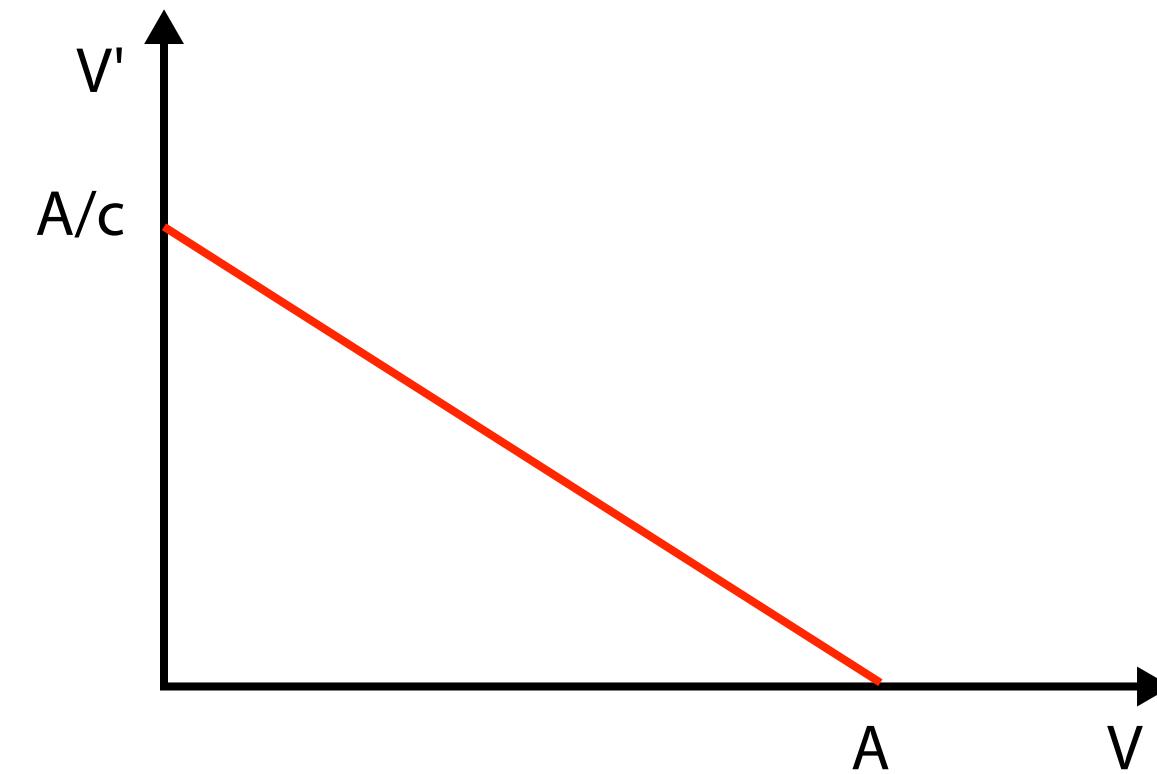


1.35-fold from V_{min} to V_{max}

Von Bertalanffy growth model

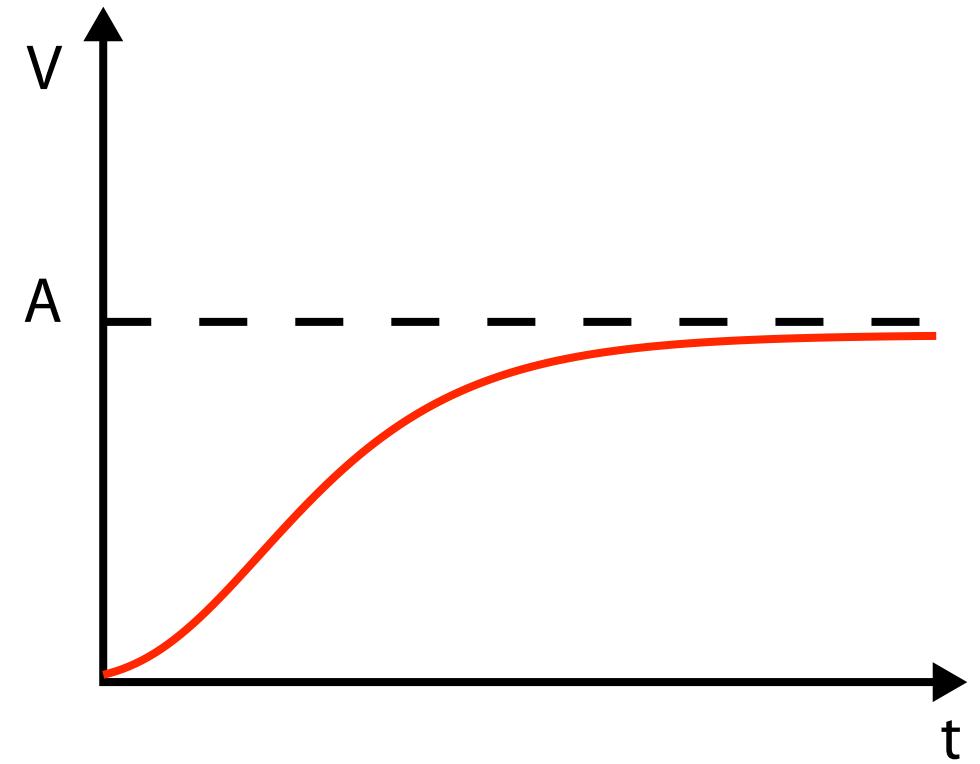


$$V = A \left(1 - e^{-\frac{t}{c}}\right)$$

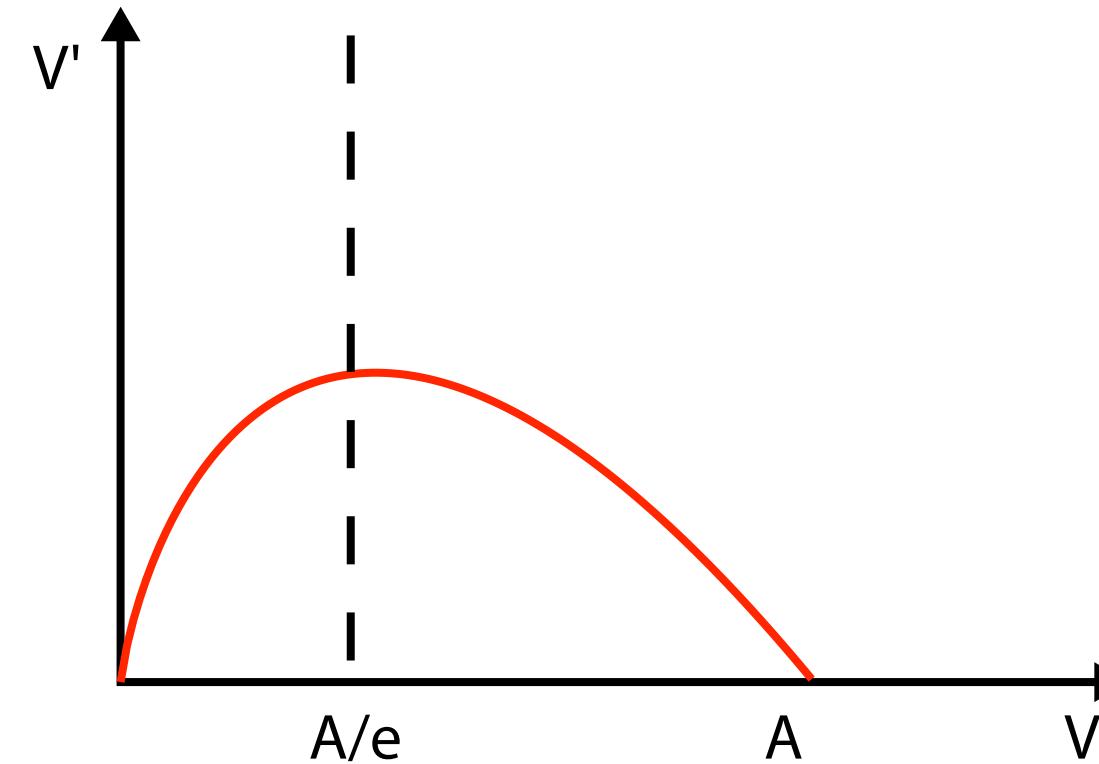


$$V' = \frac{1}{c} (A - V)$$

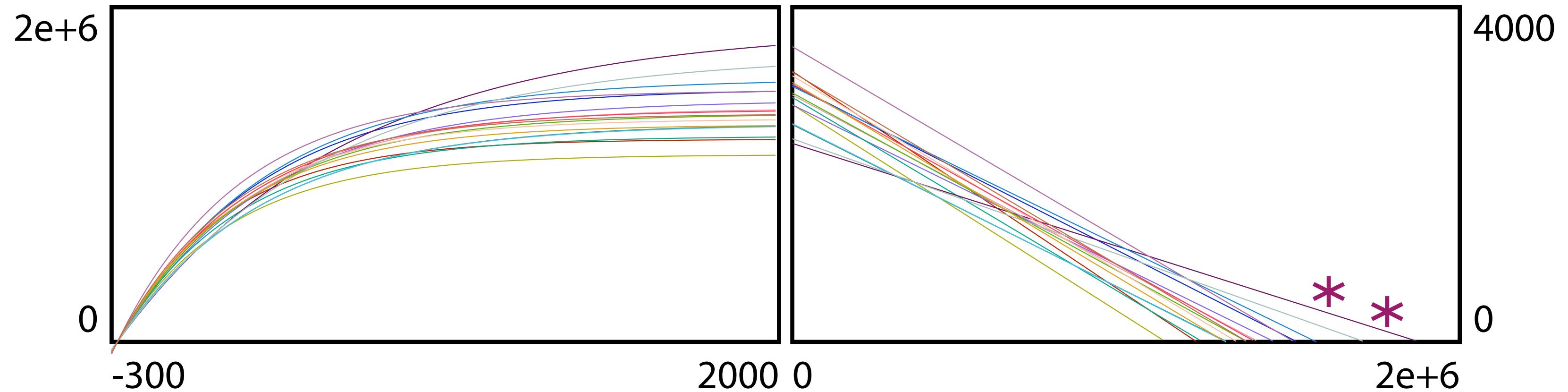
Gompertz growth model

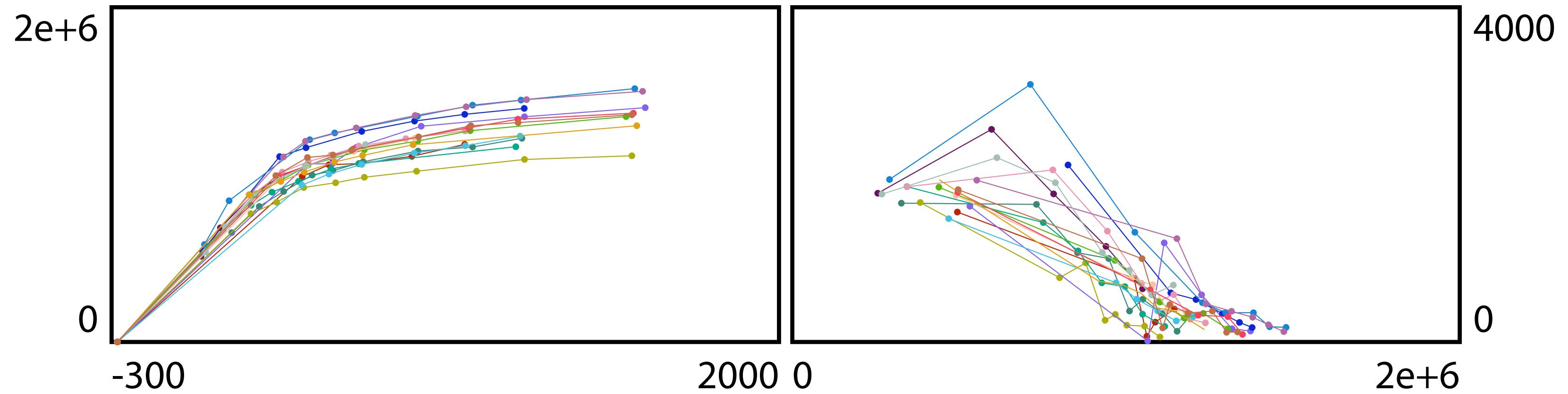


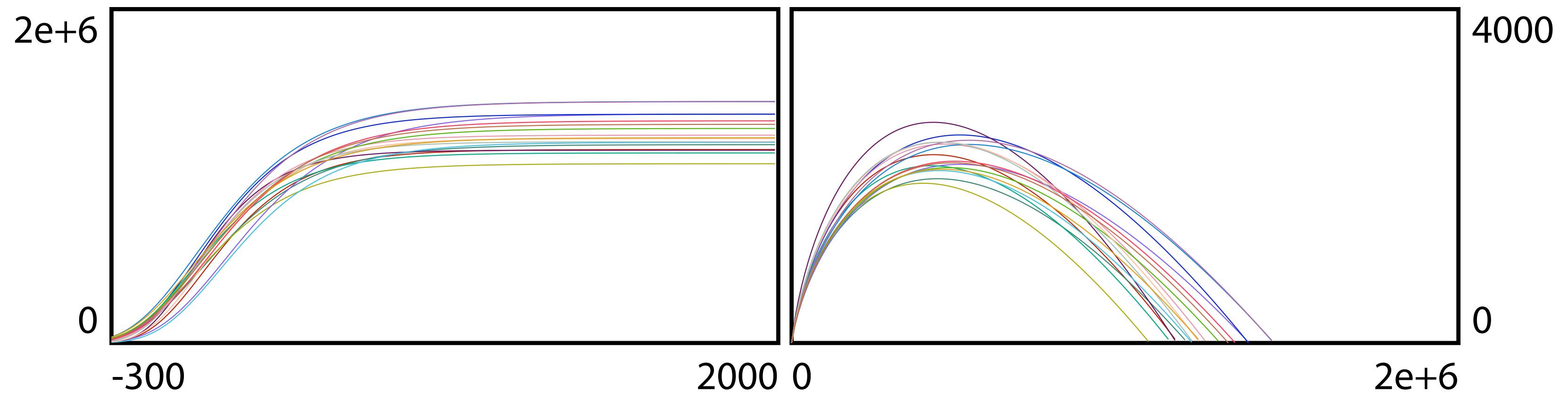
$$V = Ae^{-be^{-\frac{t}{c}}}$$



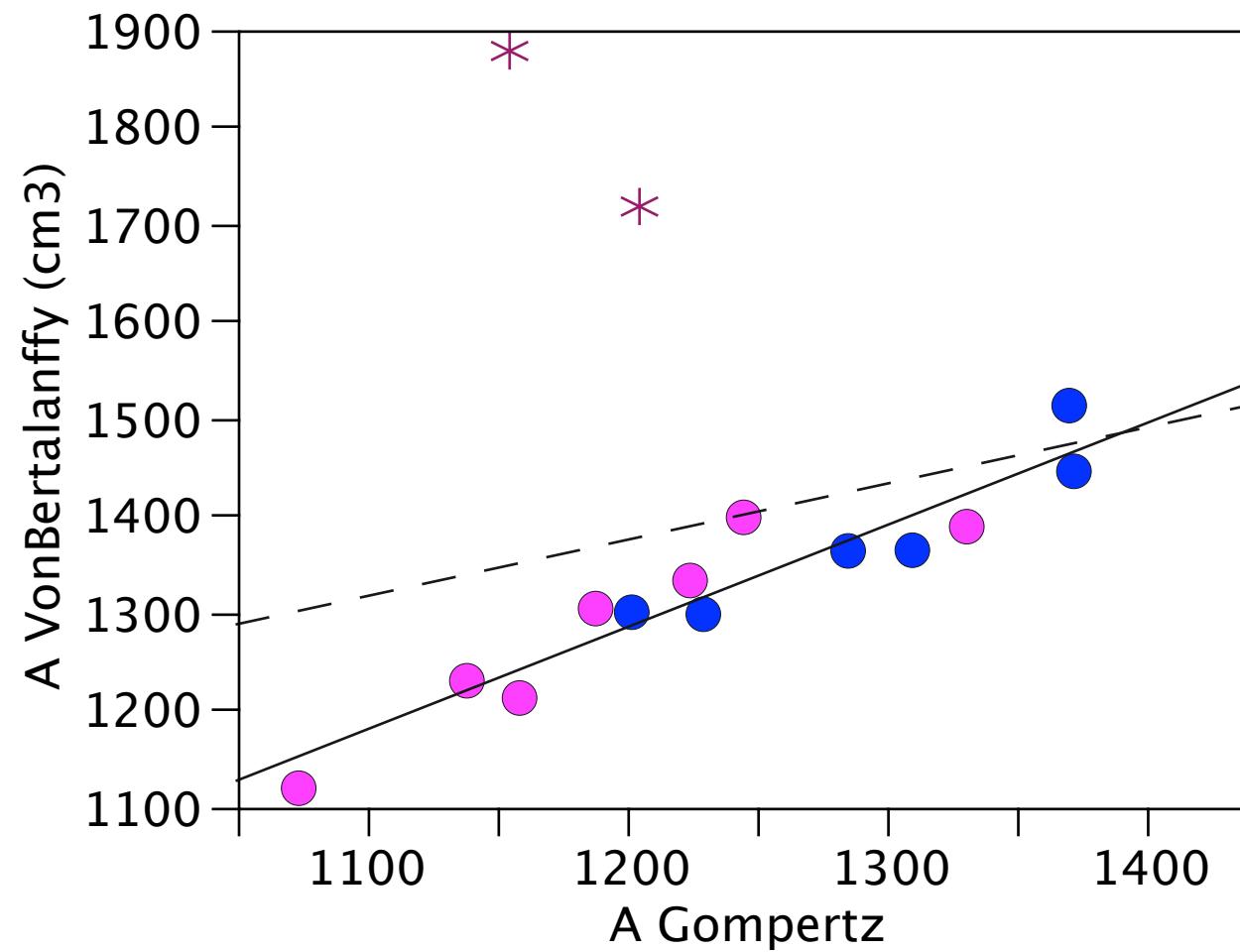
$$V' = \frac{1}{c} \log \left(\frac{A}{V} \right) V$$





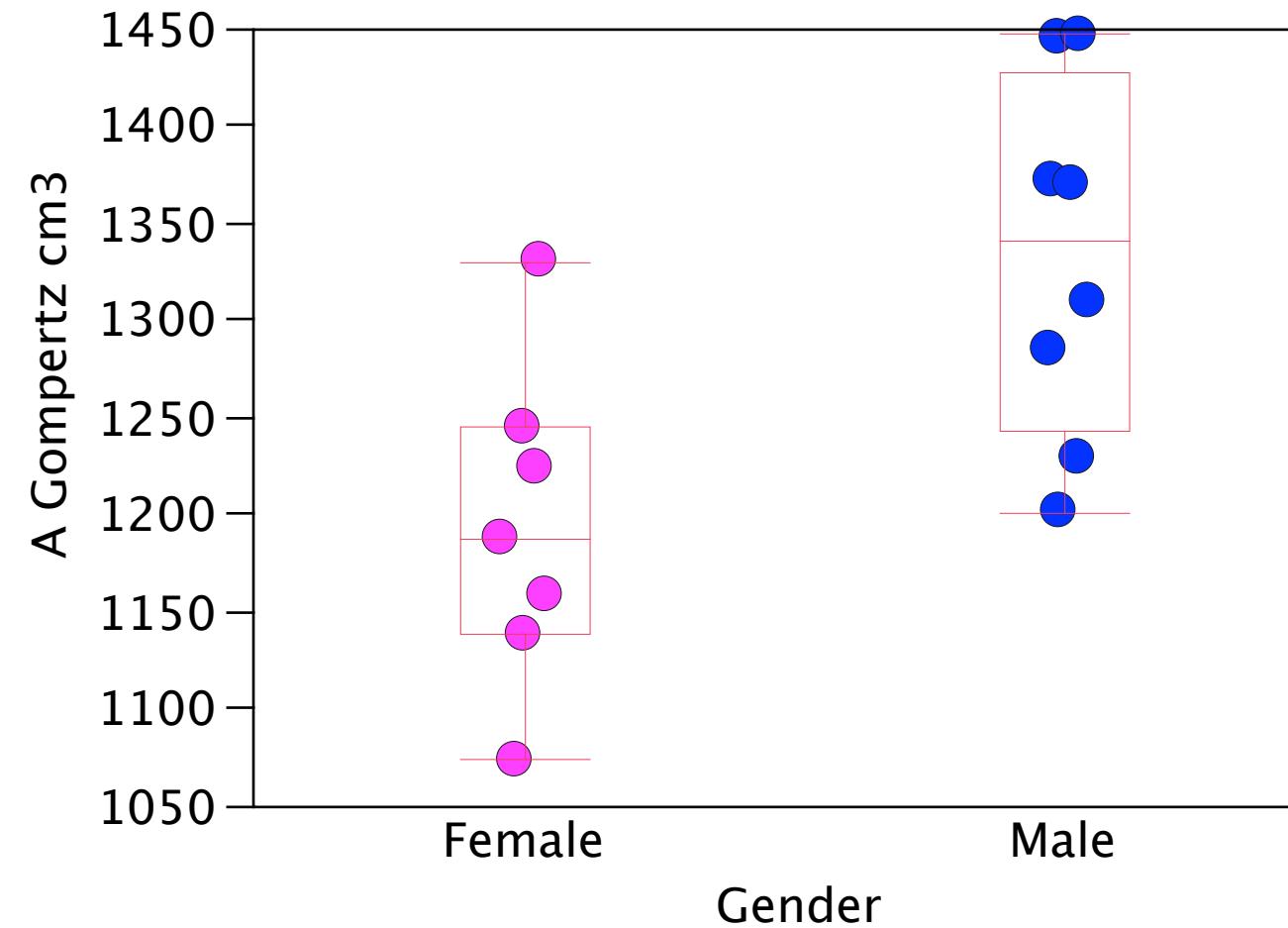


Von Bertalanffy and Gompertz models provide similar estimates for asymptotic brain volume

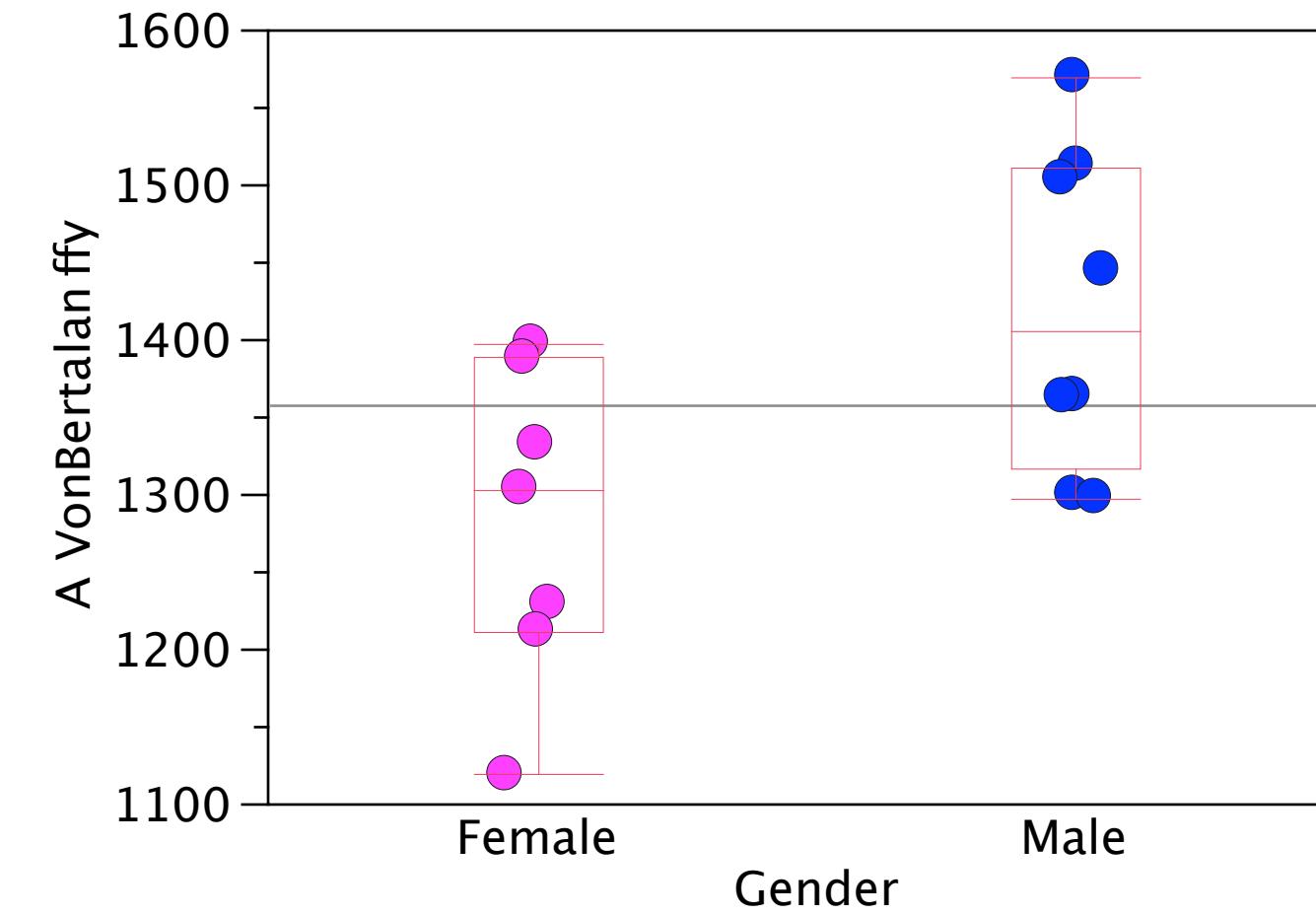


$$A_{VB} = 24354 + 1.05 A_G$$
$$R^2 = 92\%$$
$$F = 154, p < 0.0001$$

The volume of male brains is larger than that of female brains

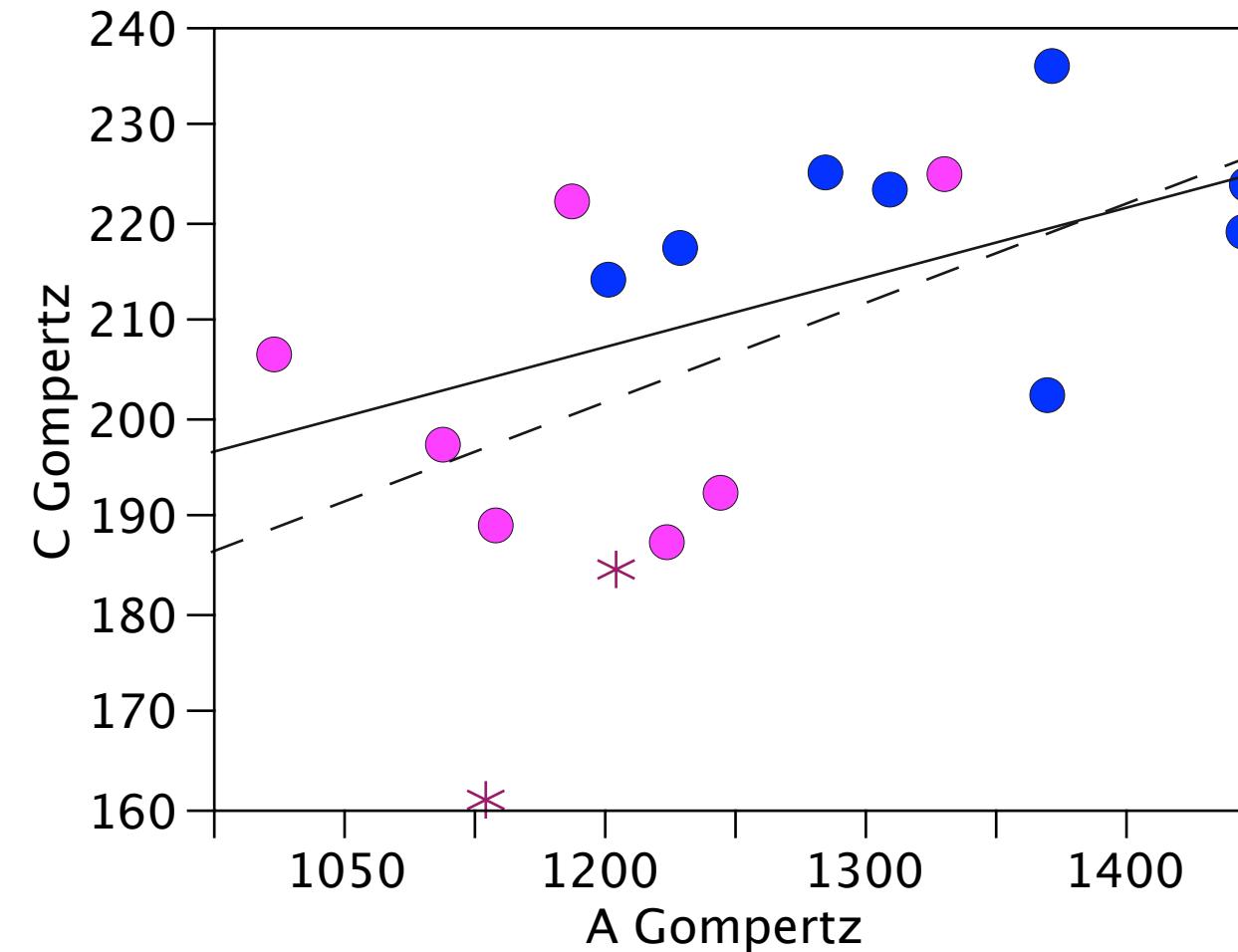


Diff=139 cm³
t=3.069, p 2-tail=0.0090, p 1-tail=0.0045



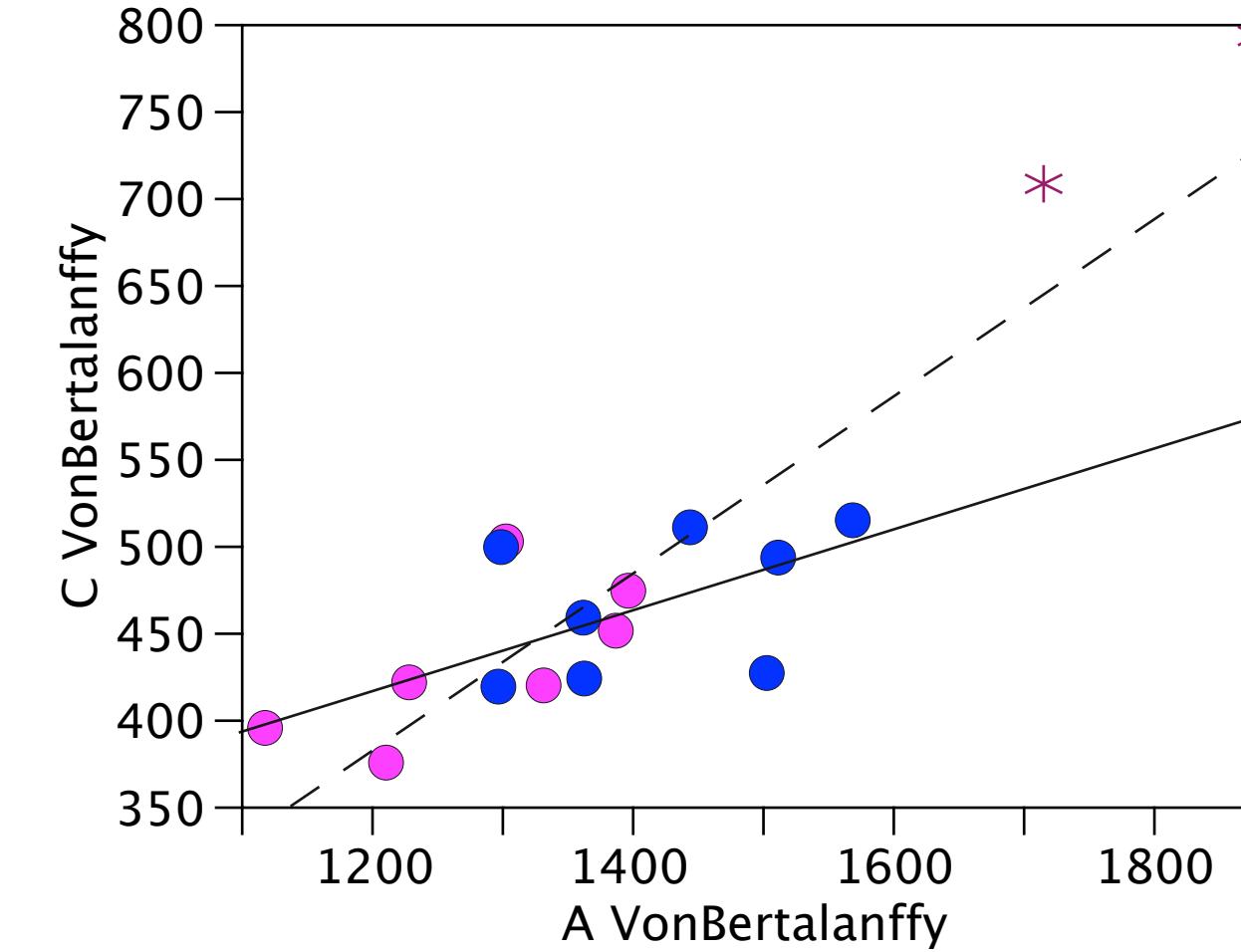
Diff: 136 cm³
t=2.5753, p 2-tail <0.0233, p 1-tail <0.0117

Large brains have slower time constants than small brains



$$C = 122 + A^7/10^5$$

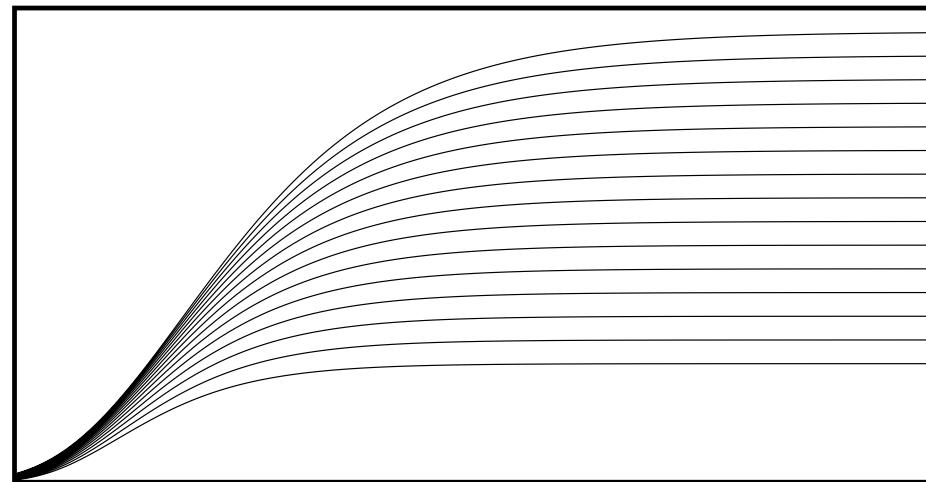
$p = 0.0472$
 $R^2 = 27\%$



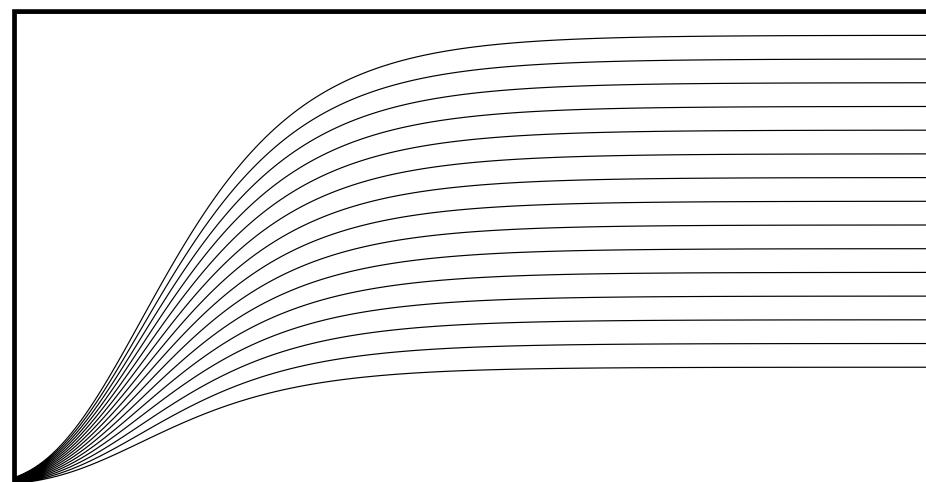
$$C = 136 + A^2/10^4$$

$p = 0.0117$
 $R^2 = 40\%$

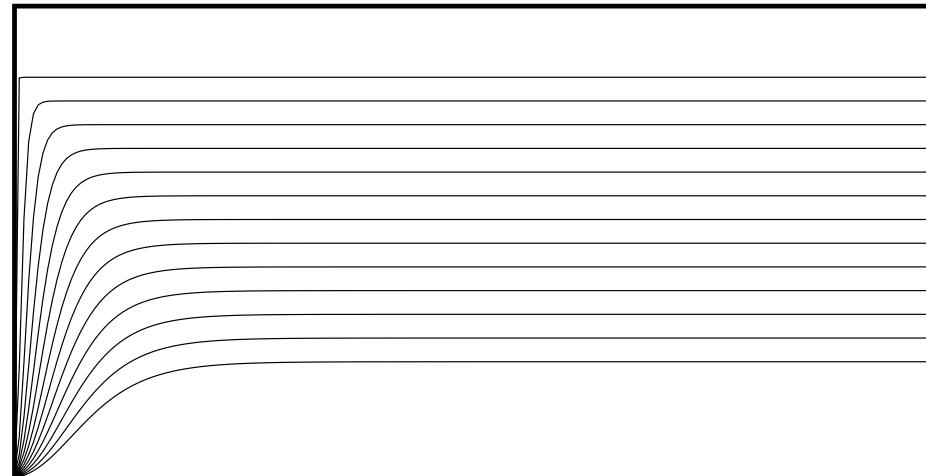
But even then, large brains grow faster than the small ones



$A=500:100:2000$
 $b=4$
 $c=122 + 7.1 \cdot A/10^5$



$A=500:100:2000$
 $b=4$
 $c=193$



$A=500:100:2000$
 $b=4$
 $c=122 - 7.1 \cdot A/10^5$

- How to model the real dynamics of brain growth?
- Which processes are represented by this dynamics?
- What is the spatial organisation of these processes?

Mapping Early Brain Development in Autism

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Although the neurobiology of autism has been studied for more than two decades, the majority of these studies have examined brain structure 10, 20, or more years after the onset of clinical symptoms. The pathological biology that causes autism remains unknown, but its signature is likely to be most evident during the first years of life when clinical symptoms are emerging. This review highlights neurobiological findings during the first years of life and emphasizes early brain overgrowth as a key factor in the pathobiology of autism. We speculate that excess neuron numbers may be one possible cause of early brain overgrowth and produce defects in neural patterning and wiring, with exuberant local and short-distance cortical interactions impeding the function of large-scale, long-distance interactions between brain regions. Because large-scale networks underlie socio-emotional and communication functions, such alterations in brain architecture could relate to the early clinical manifestations of autism. As such, autism may additionally provide unique insight into genetic and developmental processes that shape early neural wiring patterns and make possible higher-order social, emotional, and communication functions.

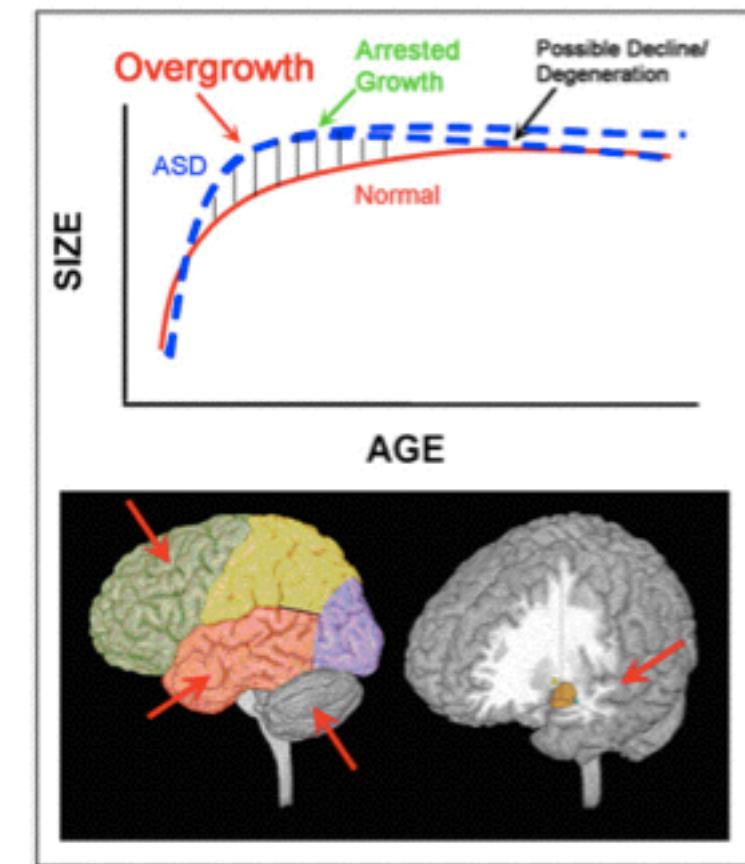


Figure 1. Regional Early Overgrowth in ASD

(A) Model of early brain overgrowth that is followed by arrest of growth. Blue lines represent ASD, while red lines represent age-matched typically developing individuals. In some regions and individuals, the arrest of growth may be followed by degeneration, indicated by the blue dashes that slope slightly downward.

(B) Sites of regional overgrowth in ASD include frontal and temporal cortices, cerebellum, and amygdala.

Childhood and adolescence

Childhood and adolescence

- N=101 (56 females, 45 males)
- Age from 4.5 years to 22.5 years
- 3 visits per subject
- 1.7-fold from V_{min} to V_{max}

