Longitudinal growth analysis of early childhood brain using deformation based morphometry

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Background

- Quantifying brain development for young children is challenging due to the magnitude of neuroanatomical changes and the variation in MRI intensity response over time.

- Deformation based morphometry (DBM) does not require the preliminary tissue classification step or a priori knowledge of the ROI to perform the morphological analysis and is, therefore, minimally influenced by the partial volume effect (PVE).

- In this study, we provide a DBM-based approach for estimating parametric maps of nonlinear volume growth that capture the heterogeneous growth profile of the different brain regions in early childhood.

Subjects & MRI Acquisition Protocols

- A representative healthy sample of subjects in the age range of newborn through 4 years and 6 months of age at enrollment were recruited into the NIH MRI Study of Normal Brain Development (Evans et al., 2006), which is a multi-center study.

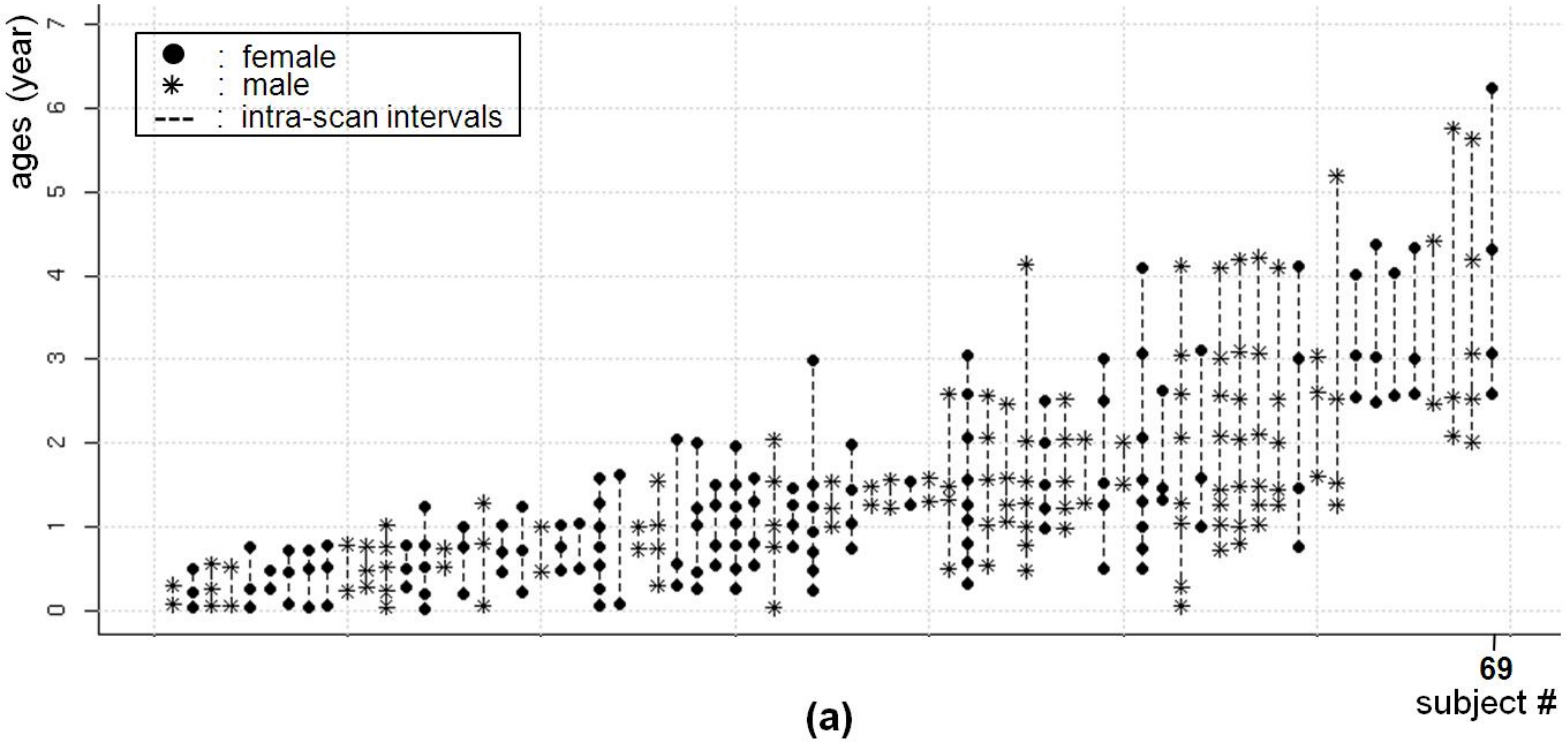
- For the present work, we analyzed 264 MR datasets from 69 subjects
  (F: 140 scans from 36 subjects, M: 124 scans from 33 subjects, all were full term at birth).

- All of subjects had multiple longitudinal scans (45 children completing at least three scans, 22 completing four or more scans). Ages of this dataset range from birth to 6 years.

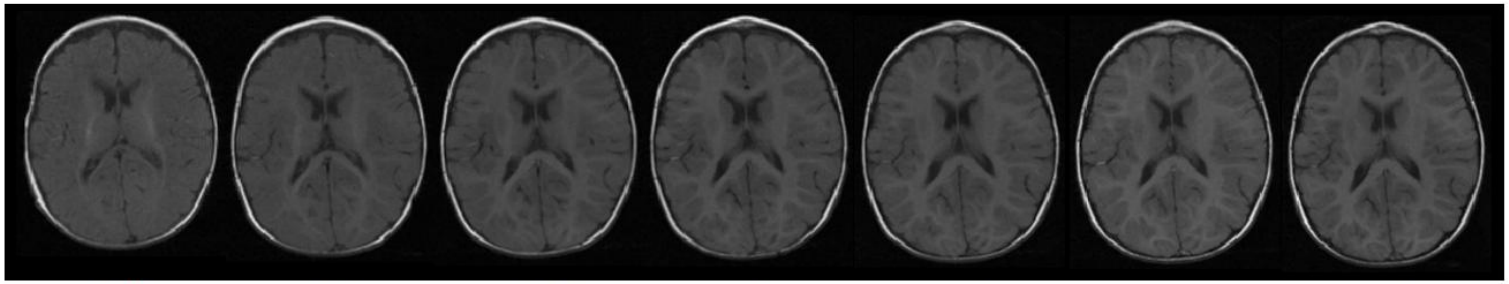
- 2D T1-weighted (T1W) multi-slice spin echo sequence [TR=500ms, TE=12ms] was used. Data were collected parallel to the AC–PC line with a 1 x 1 x 3 mm^3 spatial resolution.

Evans, A.C., Group, B.D.C., 2006. The NIH MRI study of normal brain development. Neuroimage 30, 184–202.

Distribution of MRI scanning across subjects

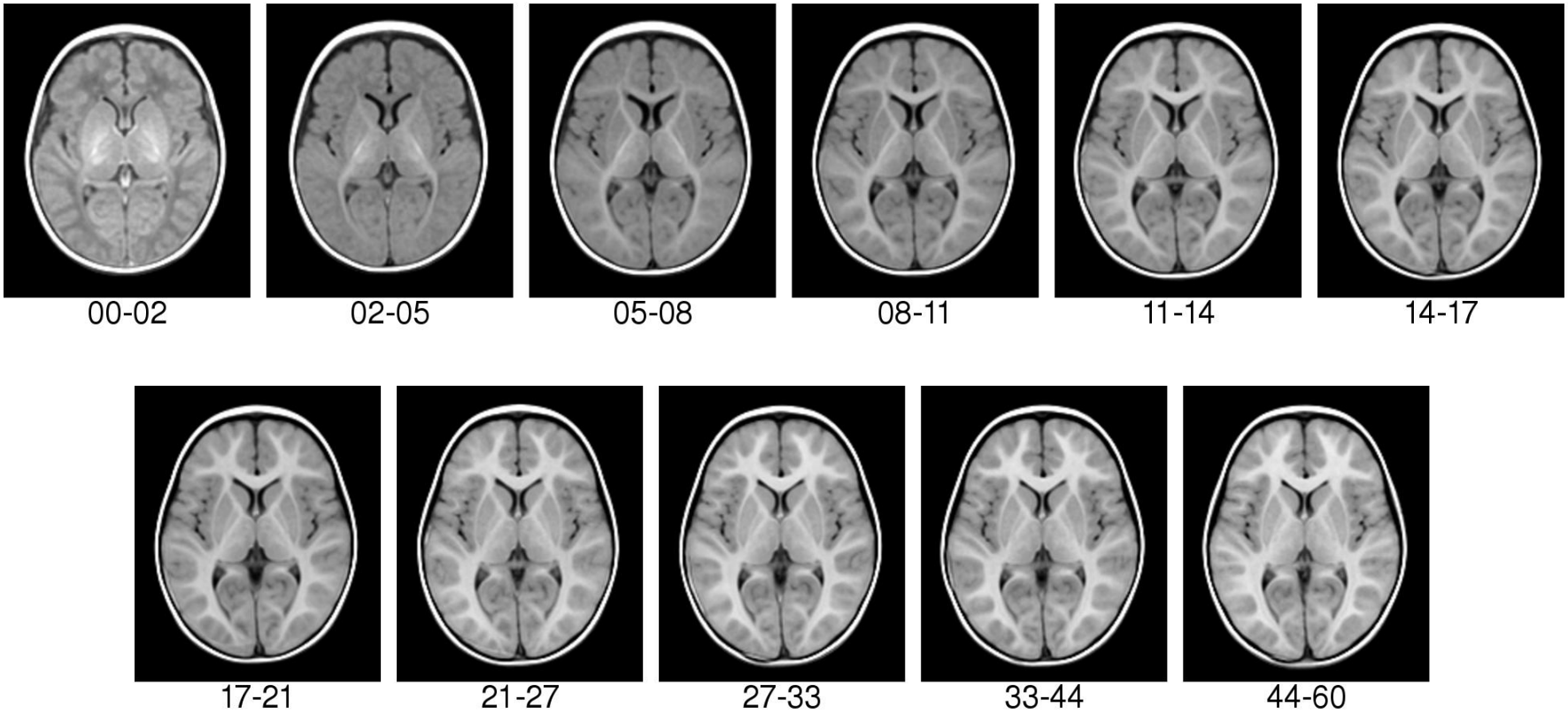


(a)



(b)

Pediatric templates



Vladimir Fonov

Miller, M., A. et al. Statistical methods in computational anatomy. Stat Methods Med Res **6**(3): 267-99 1997.

Guimond, A. et al. Automatic Computation of Average Brain Models. Medical Image Computing and Computer-Assisted Intervention — MICCAI'98**:** 631.

Image preprocessing

(a)Image intensity non-uniformity was corrected using the nonparametric non-uniform intensity normalization method (Sled et al., 1998).

(b) The intensity of each scan was linearly normalized to be in the same range by histogram equalization.

(c) The brain mask was extracted from intensity-corrected MRI data sets (Smith, 2002).

(d) Intensity non-uniformity artifacts were corrected again limited to the brain-masked region.

Image Registration

Two phase image registration

Intra-subject + Inter-subject

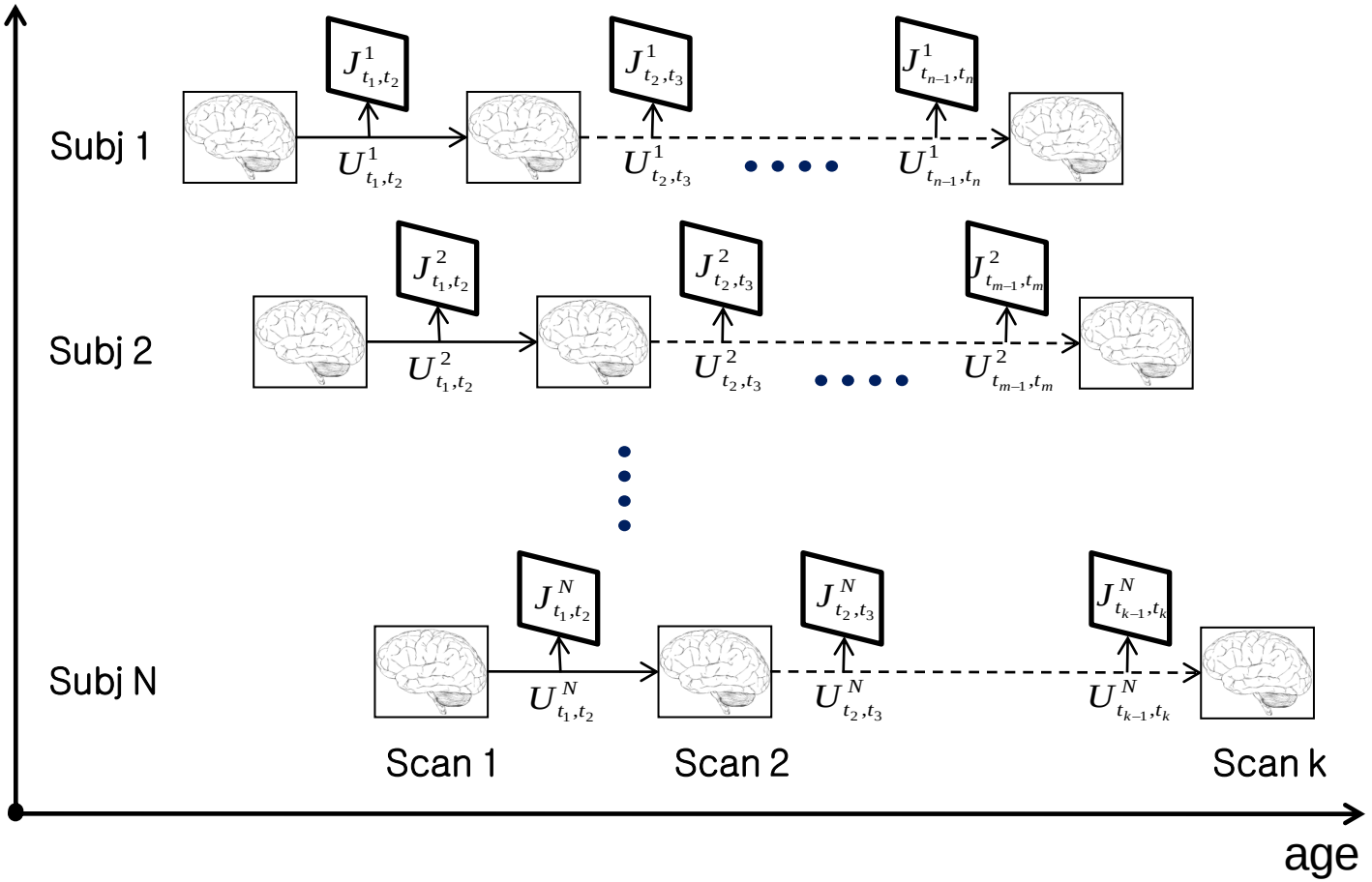


Image Registration

Two phase image registration

Intra-subject + **Inter-subject**

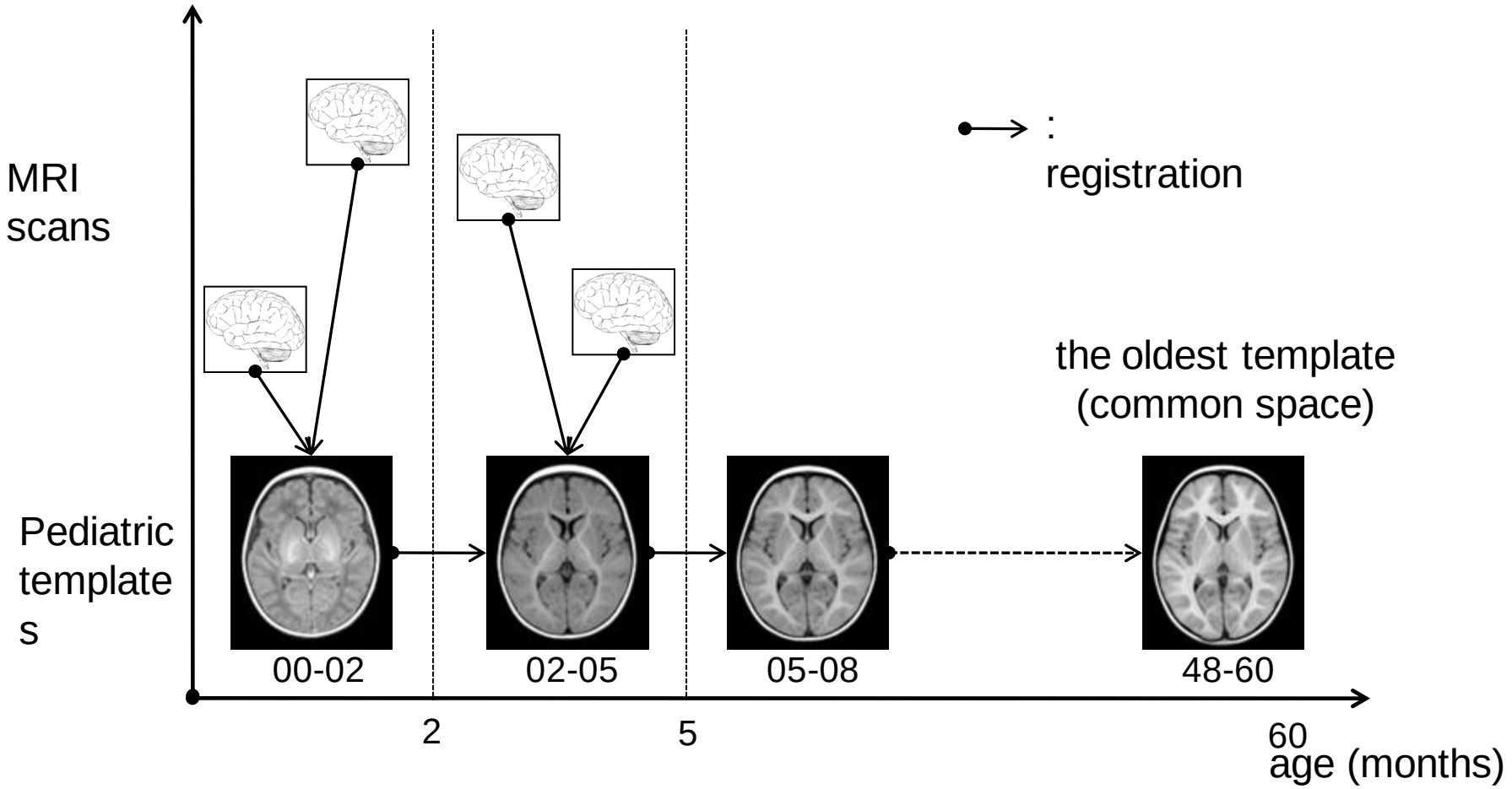


Image Registration

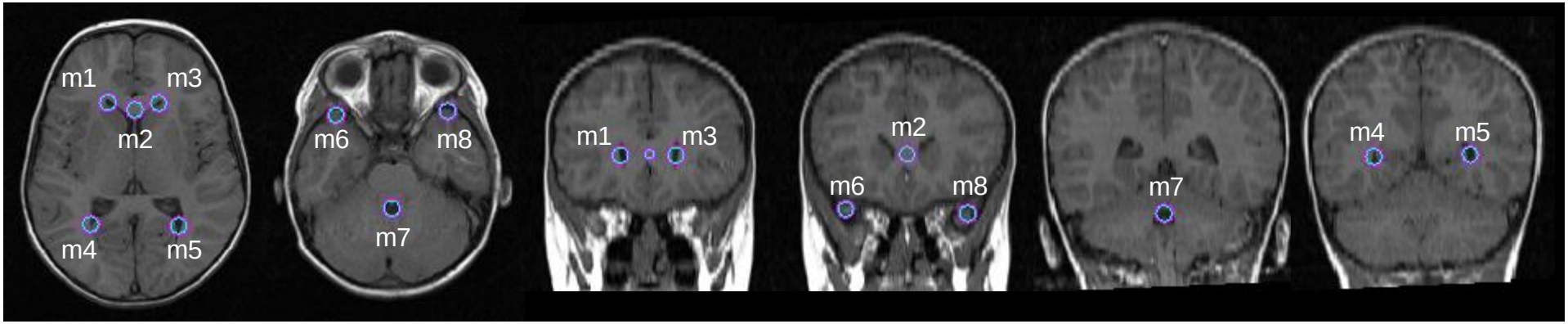
•A global transformation was first estimated using a 9-parameter linear registration to adjust only for overall differences in scale, orientation and position.

• A non-linear registration was then carried out to obtain a precise spatial correspondence of structures between source and target. The similarity metric used in non-linear registration was cross-correlation and the smoothness penalty was the elastic deformation model (Collins et al., 1994; Miller et al., 1997).

• Non-linear registration was carried out in a coarse-to-fine manner with successive control-point spacings of 30mm, 16mm, 12mm, 8mm, 6mm, 4mm and 2mm.

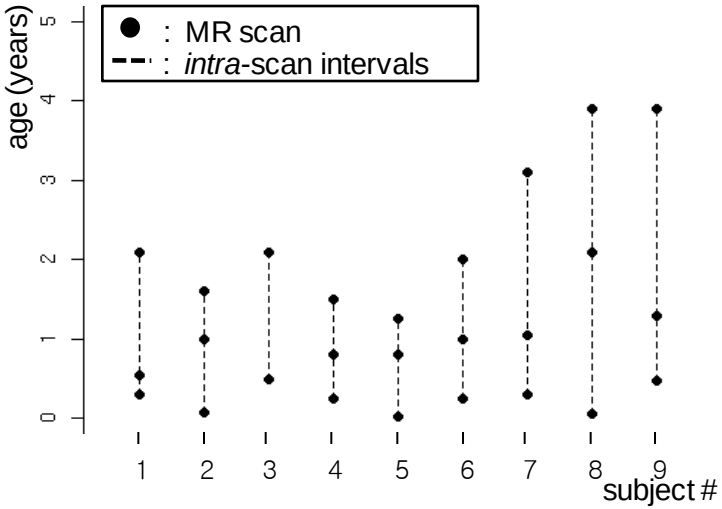
Validation of Registration

- We quantified landmark misalignment in MRI data from nine randomly-selected subjects.
- In each subject, we chose 3 scans that had the biggest time intervals among all of the available scans.
- A physician manually placed 8 landmark points in each individual brain and in the template.
- The point coordinates of these landmarks transformed to the average Template space through the deformation fields obtained by nonlinear registration.

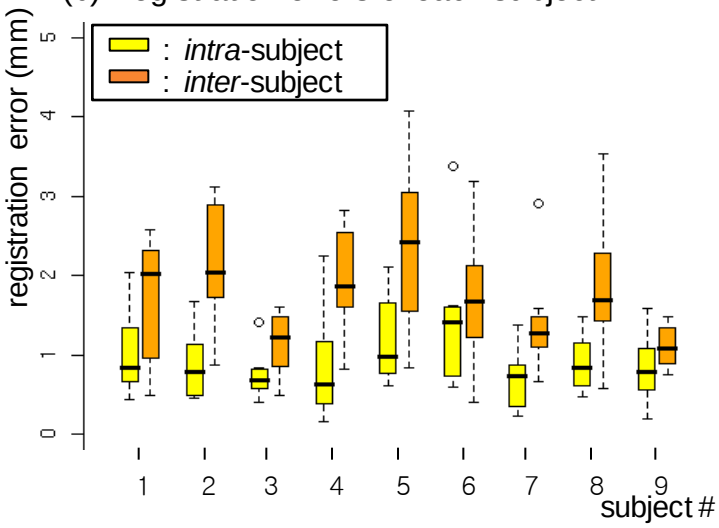


Validation of Registration

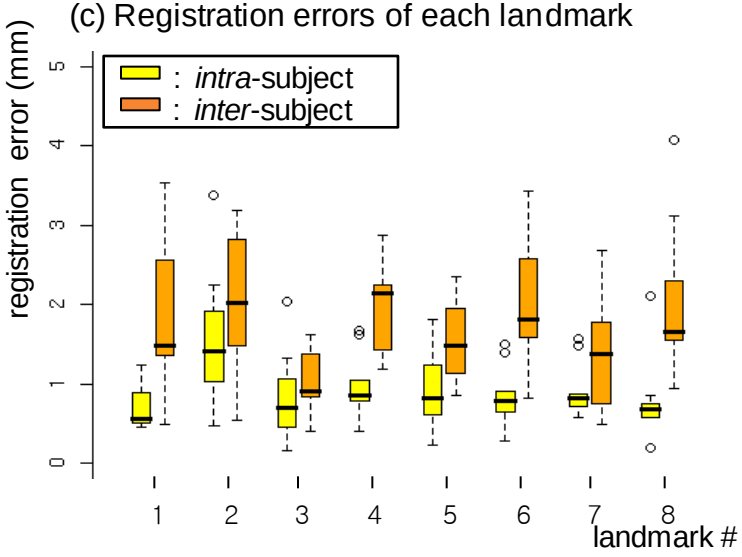
(a) Subjects used for the validation



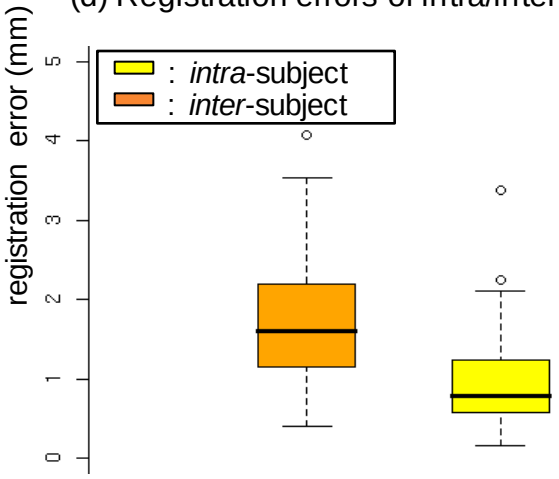
(b) Registration errors of each subject



(c) Registration errors of each landmark



(d) Registration errors of intra/inter subjects



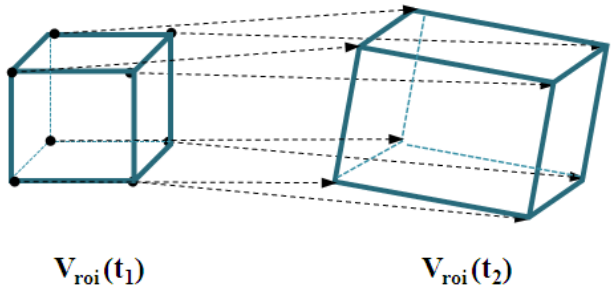
− 1.60

− 0.79

Growth Model

In longitudinal dataset:

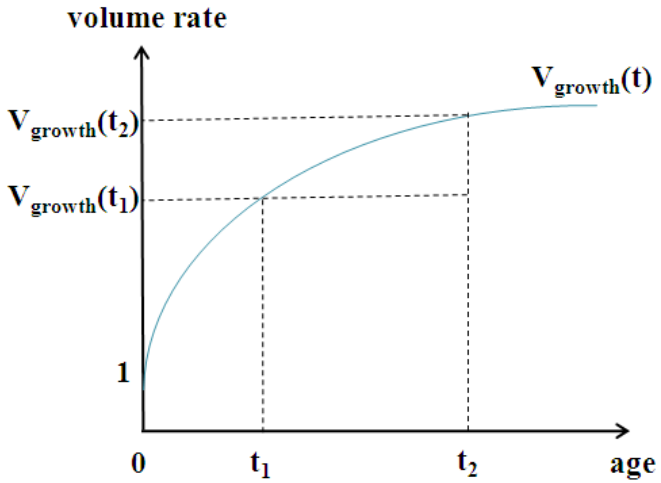
- **Volume of a region-of-interest (ROI)**
  $V_{roi}(t)$: a volume of a ROI at fixed time t,



- **Volume ratio between ROIs**
  $V_{ratio}(t_1,t_2) = V_{roi}(t_2)/V_{roi}(t_1)$

$$J(t_1, t_2) = V_{roi}(t_2) / V_{roi}(t_1)$$

- **Volume ratio between ROIs**
  $V_{growth}(t) = V_{ratio}(0,t) = V_{roi}(t)/V_{roi}(0)$



- **The Jacobian determinant**
  $J(t_1,t_2) = V_{roi}(t_2)/V_{roi}(t_1) = V_{growth}(t_2)/V_{growth}(t_1)$

$$J(t_1, t_2) = V_{growth}(t_2) / V_{growth}(t_1)$$

Growth Model

In order to estimate global volume change, let *ROI(t)* be the 3D region of interest at time t. If the region *ROI(t_1)* deforms to *ROI(t_2)*, the volume of *ROI(t_2)* is given by

$$V_{roi}(t_2) = \int_{ROI(t_2)} dx = \int_{ROI(t_1)} J(x,t)dx$$

In brain imaging, a voxel can be considered as having the same volume size across whole voxels. Therefore, dividing Eq. (2) by the volume *ROI(t_1)* is given by

$$V_{roi}(t_2)/V_{roi}(t_1) = \sum_{ROI(t_1)} \frac{J(x,t)}{m}$$

where m is the number of voxels in *ROI(t_1).* This implies that the mean value of DJ across the ROI can be applied to our growth model to estimate the global volume change of the ROI.

Growth Model

Growth model selection

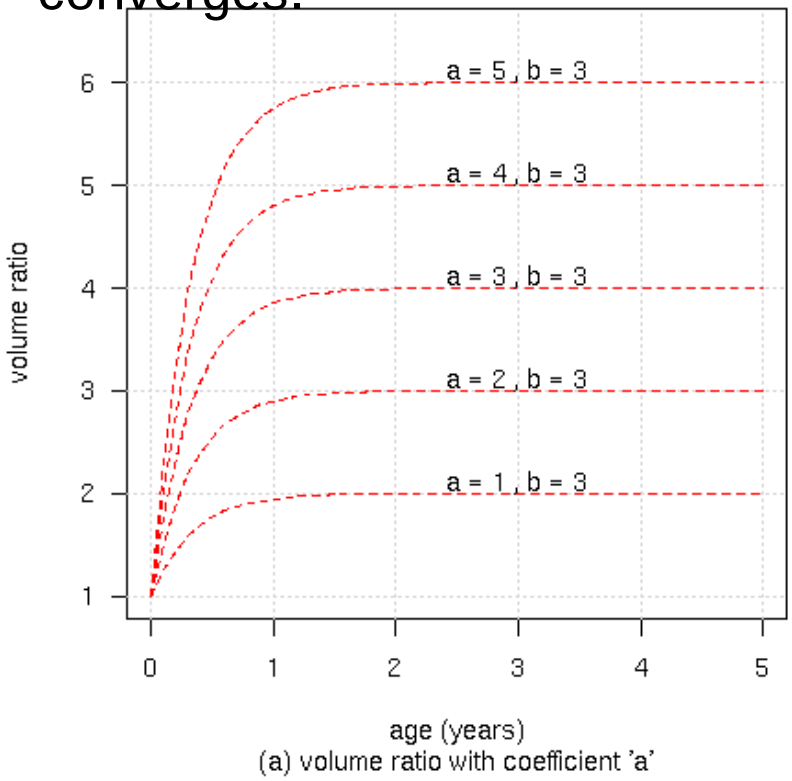
Model	Equation	# of params	RSS	AIC
exponential	$V_{growth}(t) = a \times (1 - e^{-bt}) + 1$	2	0.07514	-879.886
linear	$V_{growth}(t) = a \times t + 1$	1	4.021	-169.478
quadratic	$V_{growth}(t) = a \times t^2 + b \times t + 1$	2	1.151	-391.389
cubic	$V_{growth}(t) = a \times t^3 + b \times t^2 + c \times t + 1$	3	0.2669	-651

We measured RSS and the Akaike information criterion (AIC) (Akaike, 1974) from total brain volume to compare growth models

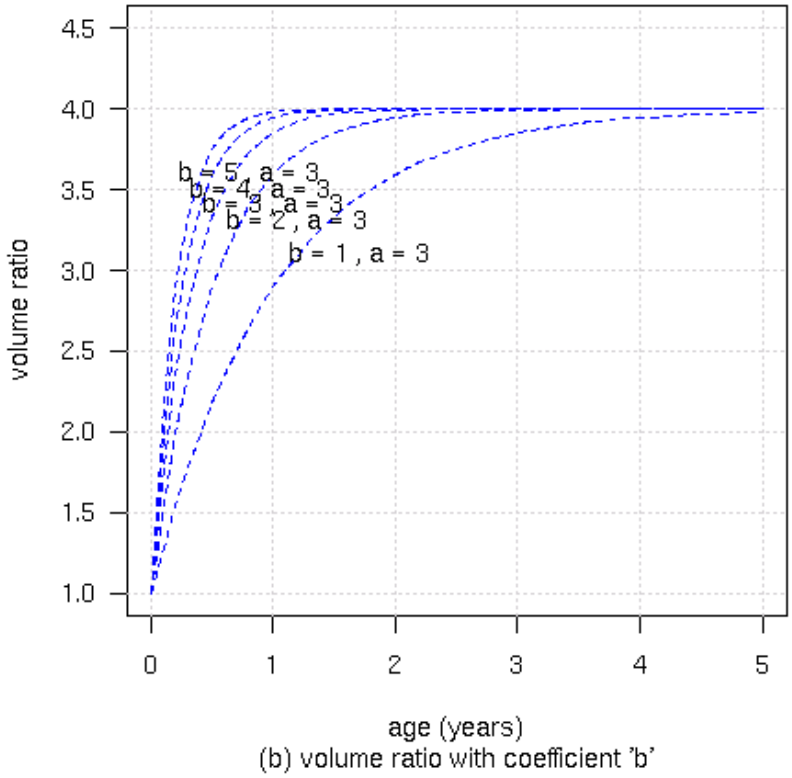
$$AIC = 2k + n \times (\ln(2\pi \cdot RSS / n) + 1),$$

Growth Model

The model coefficient ‘a’ is the amplitude of the growth curve (i.e., V_{growth}) converges to the value of a+1. The model coefficient ‘b’ is a time constant, which indicates how fast the growth curve converges.



(a) volume ratio with coefficient ’a’



(b) volume ratio with coefficient ’b’

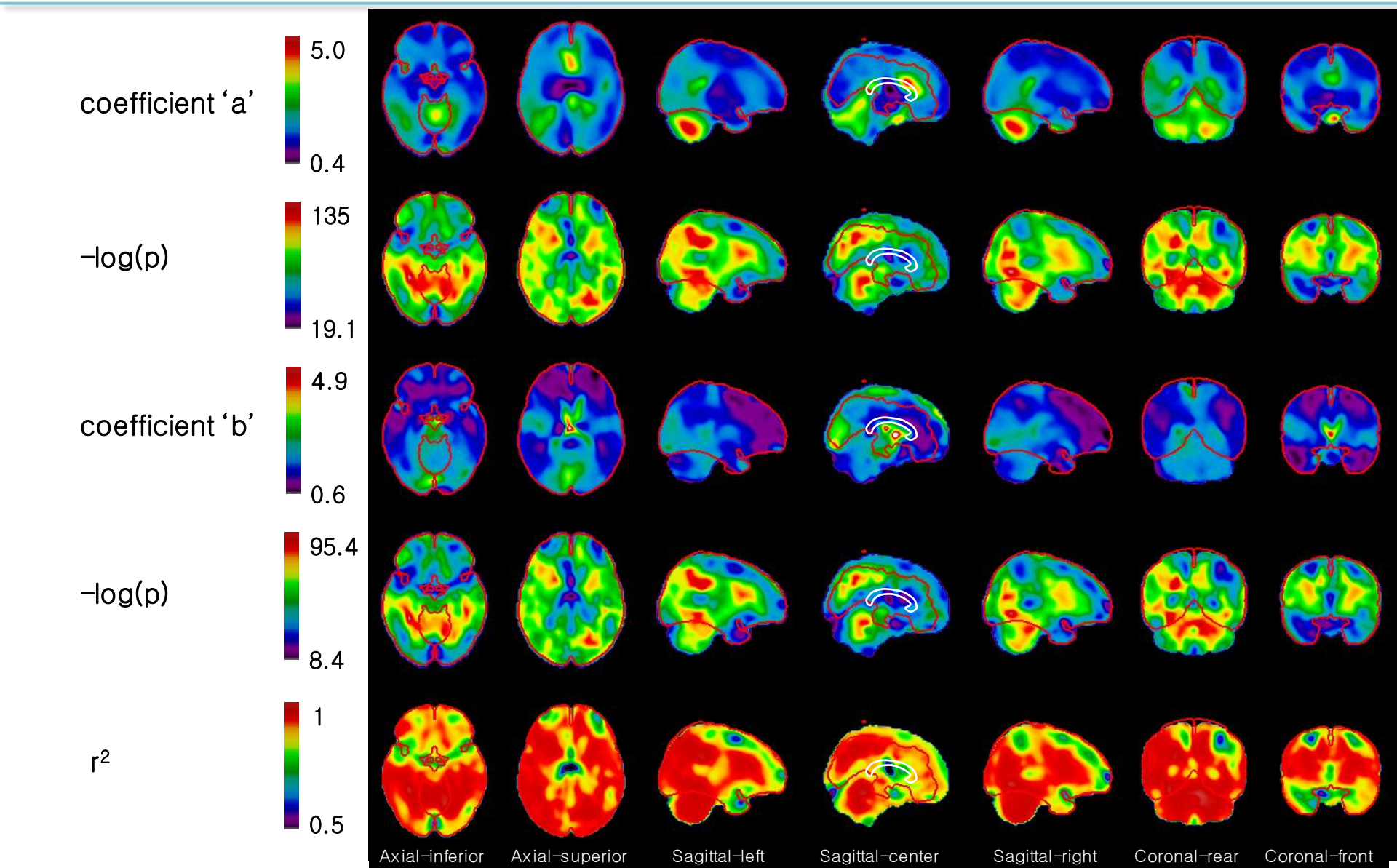
Global growth estimates

Growth estimates from a regional lobe parcellation

Region	coefficient		t-value		r^2	volume/volume-at-birth (%)			volume/maximum-volume (%)			
	a	b	a	b		1year	2year	3year	birth	1year	2year	3year
total brain	1.65	1.39	88.2	51.0	0.983	224	255	263	37.7	84.5	96.1	99.0
left cerebellum	3.03	1.45	75.9	43.6	0.983	332	386	399	24.8	82.4	95.9	99.0
right cerebellum	3.01	1.49	72.4	41.4	0.982	333	386	398	24.9	83.0	96.1	99.1
left frontal lobe	1.52	1.26	62.8	37.0	0.966	209	240	249	39.6	82.9	95.2	98.6
right frontal lobe	1.48	1.25	60.1	35.4	0.963	205	236	244	40.3	82.8	95.1	98.6
left occipital lobe	1.85	1.72	71.9	40.4	0.977	252	279	284	35.1	88.4	97.9	99.6
right occipital lobe	1.85	1.58	74.1	42.1	0.978	247	277	283	35.1	86.6	97.3	99.4
left parietal lobe	1.73	1.43	92.6	53.3	0.985	231	263	270	36.7	84.8	96.4	99.1
right parietal lobe	1.56	1.42	66.6	38.4	0.970	219	247	254	39.0	85.2	96.4	99.1
left temporal lobe	1.91	1.37	79.7	46.3	0.982	243	279	288	34.3	83.3	95.8	98.9
right temporal lobe	1.67	1.39	78.2	45.2	0.979	225	257	264	37.5	84.5	96.1	99.0

Hazlett, H.C., Poe, M., Gerig, G., Smith, R.G., Provenzale, J., Ross, A., Gilmore, J., Piven, J., 2005. Magnetic resonance imaging and head circumference study of brain size in autism: birth through age 2 years. Arch Gen Psychiatry 62, 1366-1376.

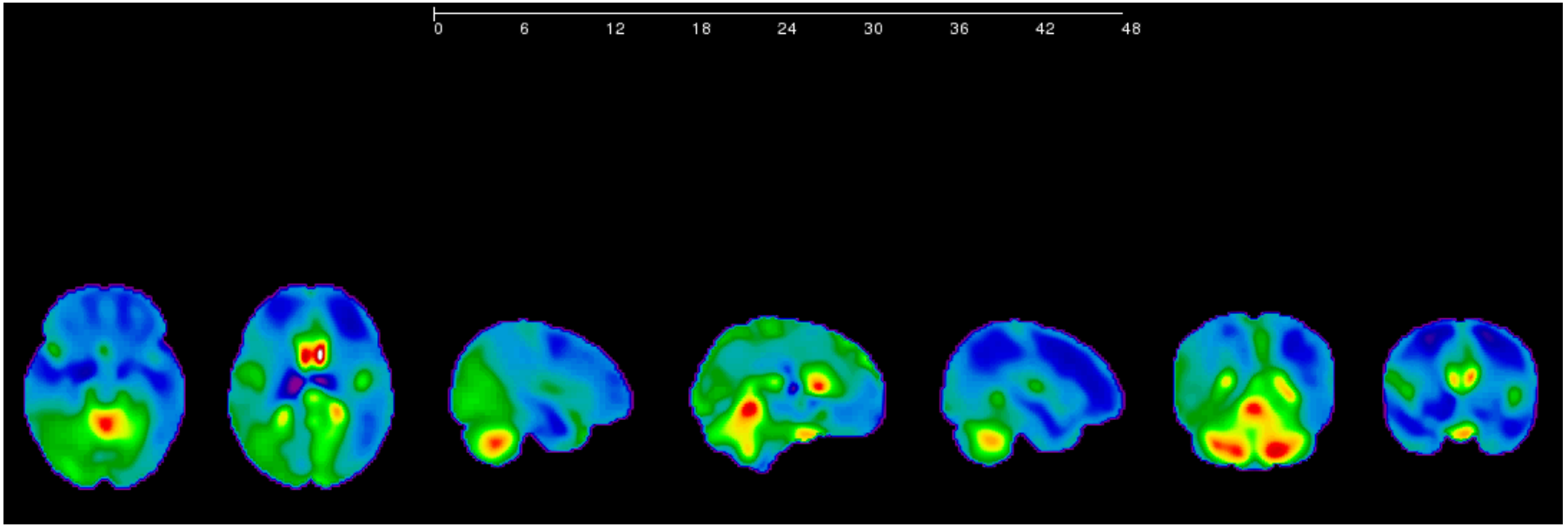
Local growth estimates



Local growth estimates

(a) $V_{growth}(t) = a \times (1 - e^{-bt}) + 1$

(b) $\Delta V_{growth}(t)/\Delta t$



Biological findings

•The cerebellum grows more than any other part of the brain and most parts of the cerebellum reach a volume that is around 4 times that of their equivalent in the newborn (left-cerebellum: a=3.03 and right-cerebellum: a=3.01).
•Left/right occipital lobes (a=1.85), left parietal lobe (a=1.73) and left temporal lobe (a=1.91) grow more than the other regions on cerebral hemispheres.
•The model coefficient 'b' was higher in occipital lobe than in frontal lobe (i.e. left-occipital-lobe: b=1.72, right-occipital-lobe: b=1.58, left-frontal-lobe: b=1.26, and right-frontal-lobe: b=1.25), which indicates that the growth in the posterior brain approaches its maximal volume earlier than that in the anterior brain.
•The corpus callosum also showed a growth pattern in which the posterior portion (i.e., splenium) approaches its maximum volume sooner, and did not grow in volume as much as the anterior portion (i.e., genu).
•We also found that the growth in the sensory-motor area (pre- and post-central cortices) ends earlier than the more anterior parts of the frontal and temporal lobes .
•The left temporal lobe structures were shown to grow more than the right temporal lobe structures (left-temporal-lobe: a=1.91 and right-temporal-lobe: a=1.67). Moreover, the left parietal lobe structures were shown to grow more than the right parietal lobe structures (left-parietal-lobe: a=1.73 and right-parietal-lobe: a=1.56).
•Midbrain structures appear to have high coefficient 'b' values while their coefficient 'a' values are rather low, suggesting that maturity is reached at or soon after birth with little growth later in childhood.

Conclusions

We have generated 3D voxelwise maps of the growth pattern in the entire brain of early childhood.

We made a nonlinear growth model which applied to the Jacobian determinant.

In order to minimize registration error, we used a registration design that combined longitudinal and cross-sectional registration.

Acknowledgements

Special thanks to:

Fonov V,
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Collins DL,
Evans AC,
and
The Brain Development Cooperative Group

Thank you!

Any Question?

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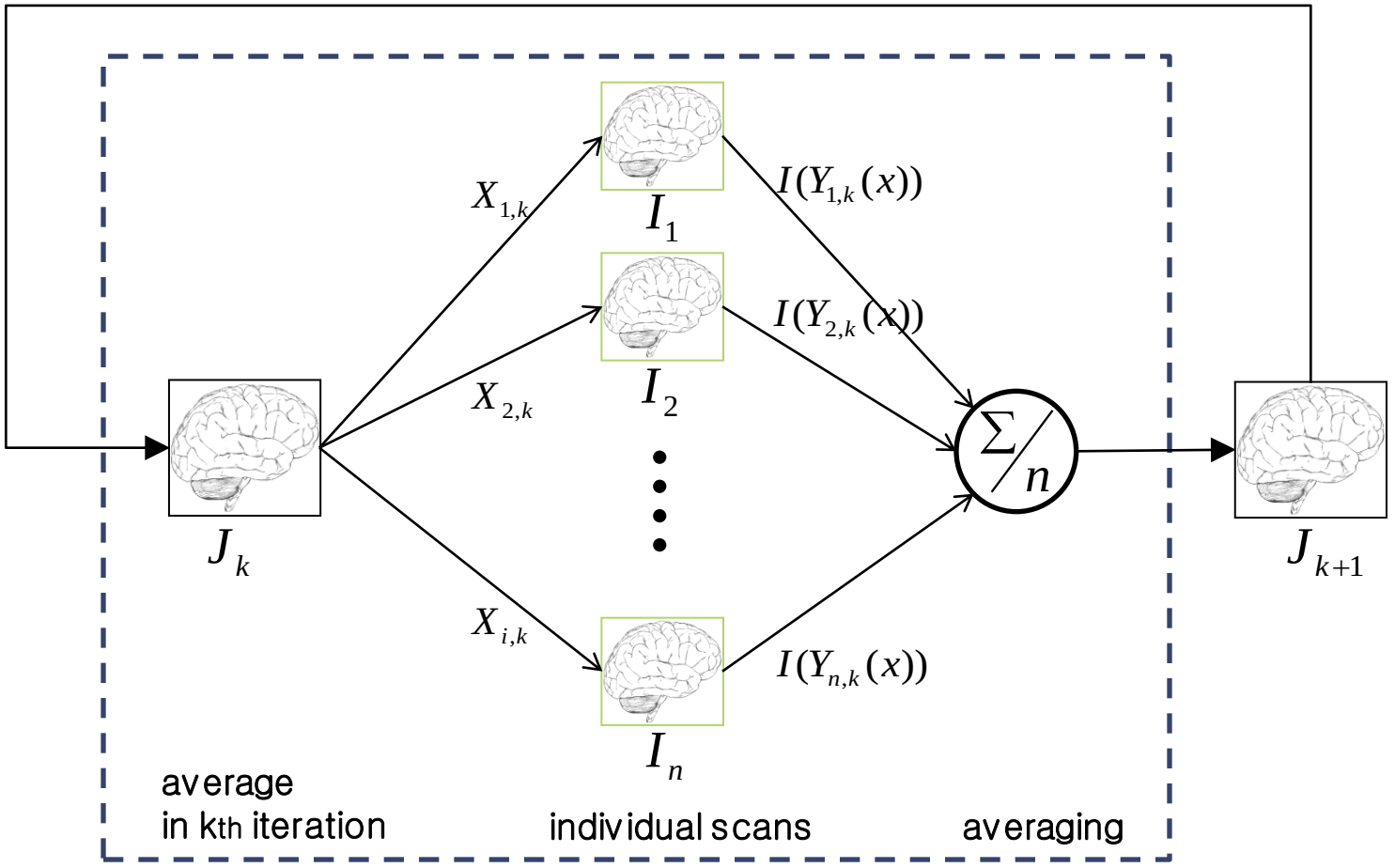
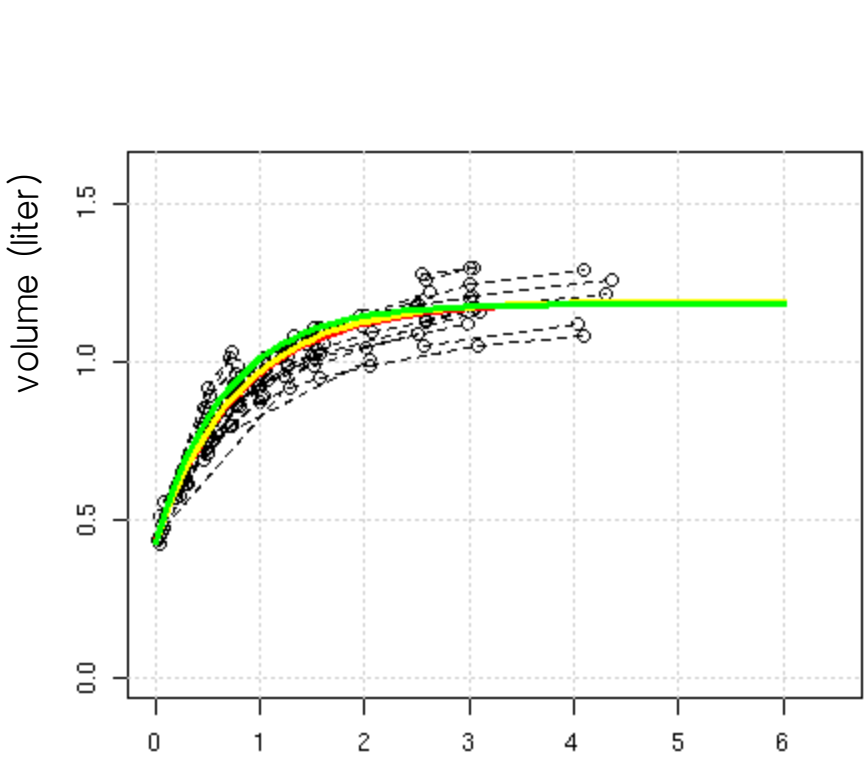
Pediatric templates

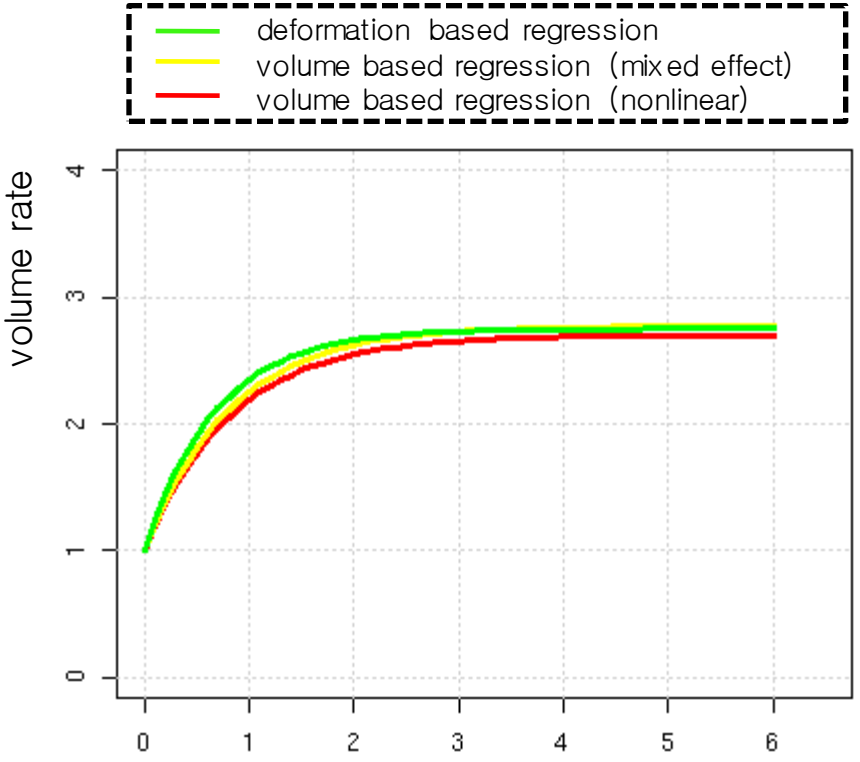


Regressions of total brain volume & volume rate

This graph shows the regression results of total brain volume and the mean Jocobian determinant on total brain



(a) regressions of total brain volume



(b) regressions of volume rate