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Automatic analysis of cerebellar growth trajectories in normal child development

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Background

- The human cerebellum is a fascinating brain structure:
  - small-sized structure, ~ 10% of brain volume
  - complex architecture of tightly folded cortical grey matter, comprising ~50% of all neurons
- highest growth rate of all brain structures during the late fetal and early postnatal life:
  - at birth only 15% of its final volume
  - at age of 2 adult number of neurons are reached
- progressive myelination (until 2nd decade), synaptic / axonal pruning have influence on volume
- it plays an integrating role in various neuronal networks, e.g. motor control and cognitive processing
- it shows pathological volume changes in various neuro-psychiatric disorders (e.g. multiple sclerosis, autism, ADHD, schizophrenia etc.)

Gray's anatomy, 20th edition

Methods

- Automatic segmentation technique
  - accuracy similar to manual segmentation
  - applicable to large subject numbers in a reasonable time frame
- Development and validation of an automatic segmentation pipeline

RASCAL :

- **R**apid **A**utomatic **S**egmentation of the human **C**erebellum **A**nd its **L**obules
- Leave-one-out experiments: generalized kappa overlap = 0.82
- In press: available online 28 Apr 2014 Human Brain Mapping

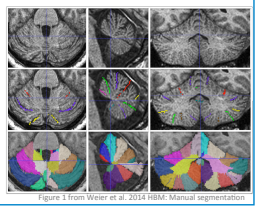
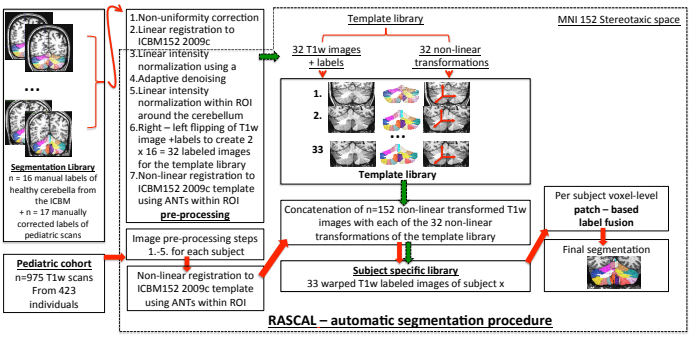
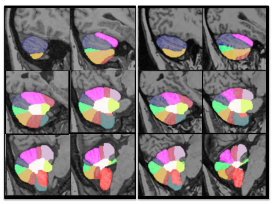


Figure 1 from Weier et al. 2014 HBM: Manual segmentation

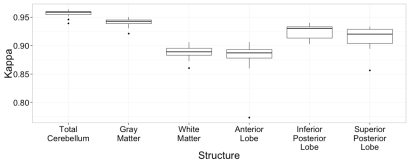


Amendment of RASCAL for pediatric population

- to make the template library most suitable also for pediatric anatomy
- existing template library was increased in number with 17 automatic segmented and manual corrected subjects of NIHPD cohort
- Leave-one-out experiment shows generalized kappa overlap = 0.93



30 years old adult 10 years old child



Leave-one out cross-validation

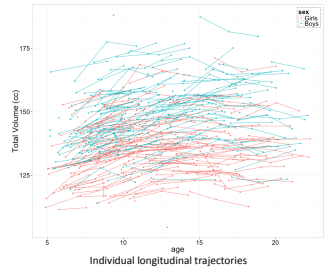
Materials

NIH-funded MRI study of normal brain development
(Evans AC 2006 "The NIH MRI study of normal brain development")

- 433 subjects; age range 4.5-18.5y
- 6 data acquisition sites: 3 Siemens + 3 GE
- MRI protocol:
  3D T1w RF-spoiled gradient echo sequence
  1-mm thick sagittal partitions,
  TR = 22-25 ms, TE = 10-11 ms, flip angle = 30˚,
  FOV = 160-180 mm, 1.0-1.5 slice thickness

	Girls	Boys	Total
Total number of subjects	217	206	423
Total number of datasets	513	460	973
Subjects passed visual QC	199	182	381
Datasets passed visual QC	461	398	859, 12% failure rate
Follow-up time, years mean (min - max)	3.37 (1.54 - 4.72)	3.34 (0.92 - 5.41)	3.35 (0.92 - 5.41)
Age at first scan, years min: max	4.68 - 18.25	4.60 - 19.76	4.60 - 19.76

Methods continued



Individual longitudinal trajectories

Fitting mixed effect model:

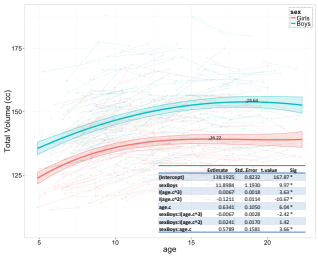
$V=b_0*sex+b_1*Age*sex+b_2*Age^2*sex+b_3*Age^3*sex+e$

- b0, b1, b2, b3 - regression coefficients which are identical for all subjects of the same sex
- e - error term with zero mean

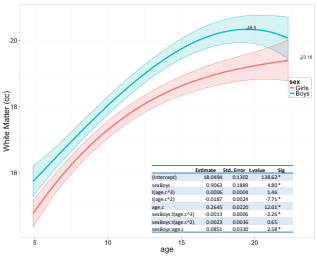
Functional-anatomical distinction in anterior-posterior direction:

- **anterior lobe**: (lobule I-V) mainly involved in sensory-motor tasks
- **superior posterior lobe**: (lobule VI and Crus I) involved in verbal working memory and sensory-motor tasks
- **inferior posterior lobe**: (Crus II – X) involved in speech and visual-spatial processing, limb coordination

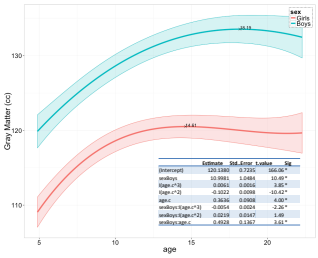
Results



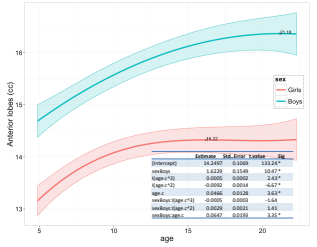
	Estimate	Std. Error	t value	Sig
(Intercept)	138.1925	0.8232	167.87 *	
sexBoys	11.8584	1.1930	9.97 *	
I(age.c^0)	0.0067	0.0018	3.63 *	
I(age.c^2)	-0.1211	0.0114	-10.67 *	
age.c	0.6341	0.1050	6.04 *	
sexBoys:I(age.c^3)	-0.0567	0.0028	-2.42 *	
sexBoys:I(age.c^2)	0.0241	0.0170	1.42	
sexBoys:age.c	0.5789	0.1581	3.66 *	



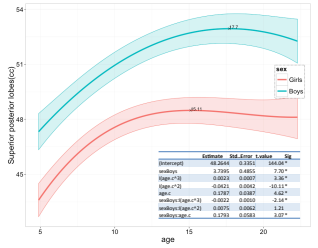
	Estimate	Std. Error	t value	Sig
(Intercept)	18.0494	0.1302	138.62 *	
sexBoys	0.9063	0.1889	4.80 *	
I(age.c^0)	0.0006	0.0004	1.46	
I(age.c^2)	-0.0187	0.0024	-7.71 *	
age.c	0.2645	0.0220	12.01 *	
sexBoys:I(age.c^3)	-0.0013	0.0006	-2.26 *	
sexBoys:I(age.c^2)	0.0023	0.0036	0.65	
sexBoys:age.c	0.0851	0.0330	2.58 *	



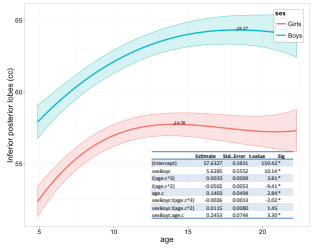
	Estimate	Std. Error	t value	Sig
(Intercept)	120.1380	0.7235	166.06 *	
sexBoys	10.9981	1.0484	10.49 *	
I(age.c^0)	0.0061	0.0016	3.85 *	
I(age.c^2)	-0.1022	0.0098	-10.42 *	
age.c	0.3636	0.0908	4.00 *	
sexBoys:I(age.c^3)	-0.0014	0.0024	-2.26 *	
sexBoys:I(age.c^2)	0.0219	0.0147	1.49	
sexBoys:age.c	0.4928	0.1367	3.61 *	



	Estimate	Std. Error	t value	Sig
(Intercept)	14.2497	0.1069	133.24 *	
sexBoys	1.6229	0.1549	10.47 *	
I(age.c^0)	0.0005	0.0002	2.43 *	
I(age.c^2)	-0.0092	0.0014	-6.67 *	
age.c	0.0466	0.0128	3.63 *	
sexBoys:I(age.c^3)	-0.0005	0.0003	-1.64	
sexBoys:I(age.c^2)	0.0020	0.0021	1.41	
sexBoys:age.c	0.0647	0.0193	3.35 *	



	Estimate	Std. Error	t value	Sig
(Intercept)	48.2644	0.3351	144.06 *	
sexBoys	3.7395	0.4855	7.70 *	
I(age.c^0)	0.0023	0.0007	3.36 *	
I(age.c^2)	-0.0421	0.0042	-10.11 *	
age.c	0.1797	0.0387	4.62 *	
sexBoys:I(age.c^3)	-0.0022	0.0010	-2.14 *	
sexBoys:I(age.c^2)	0.0076	0.0062	1.21	
sexBoys:age.c	0.1793	0.0583	3.07 *	



	Estimate	Std. Error	t value	Sig
(Intercept)	57.6327	0.3835	150.42 *	
sexBoys	5.6285	0.5552	10.14 *	
I(age.c^0)	0.0010	0.0009	1.83 *	
I(age.c^2)	-0.0502	0.0053	-9.41 *	
age.c	0.1400	0.0494	2.84 *	
sexBoys:I(age.c^3)	-0.0036	0.0013	-2.02 *	
sexBoys:I(age.c^2)	0.0115	0.0080	1.45	
sexBoys:age.c	0.2453	0.0744	3.30 *	

Conclusions

- data confirms sexual dimorphism in growth (boys having larger cerebellar volumes than girls)
- girls growth curves peak earlier than boys
- While GM growth is reaching its maximum in adolescence, WM growth is still ongoing until 2nd decade
- peak ages were different between lobes (posterior > anterior)
- results are in line with Tiemeier et al. 2010 (only one longitudinal study available)
  - however different cohort size, different segmentation technique might explain differences in peak ages

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