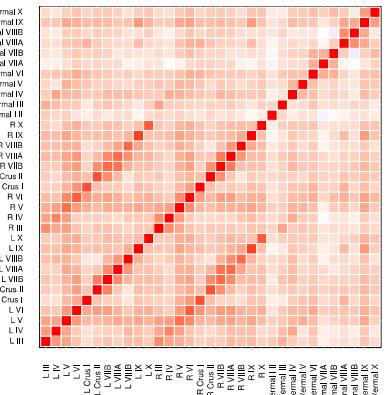


A quantification of normative grey-matter structural variability, covariance, and heritability in the human cerebellum



Christopher J. Steele

christopher.steele@mail.mcgill.ca



Sejal Patel
Gabriel A. Devenyi
Joanne Knight
Bratislav Mišić
Mallar Chakravarty

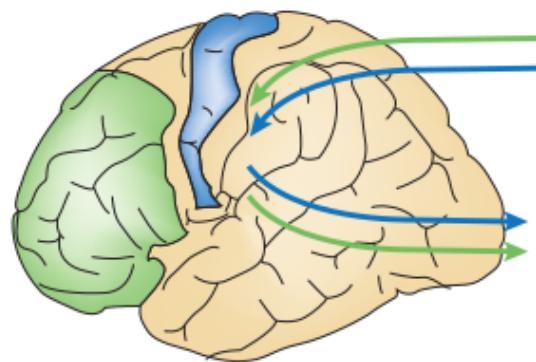
Mallar Chakravarty

Department of Psychiatry

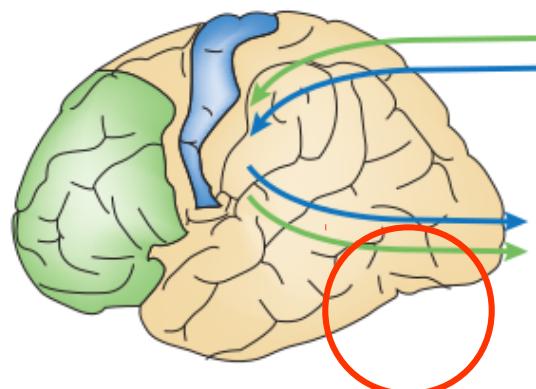
Computational Brain
Anatomy Lab
Douglas Institute CIC
McGill University



The cerebellum: Why do we care?

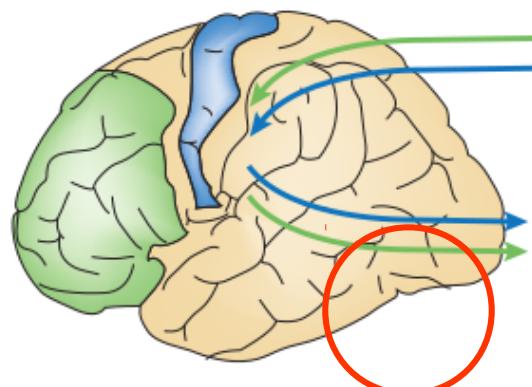


The cerebellum: Why do we care?



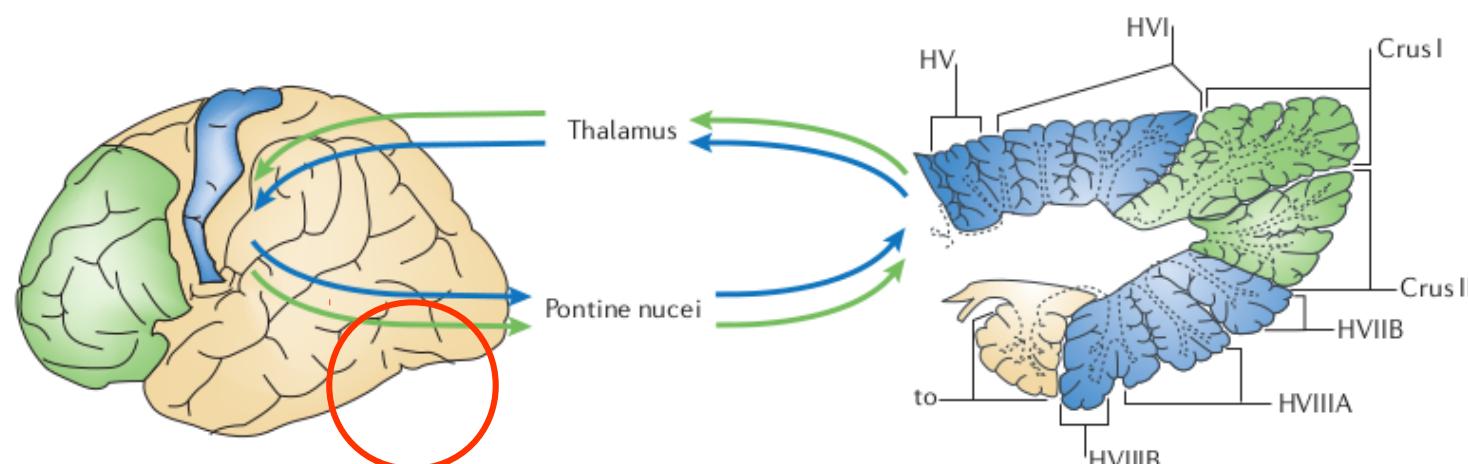
The cerebellum: Why do we care?

- Accounts for over 50% of the neurons in the brain
 - Evolutionary expansion in great apes (Balsters, 2010; Barton & Venditti, 2014)
 - Supports behaviour through reciprocal connections to the cortex



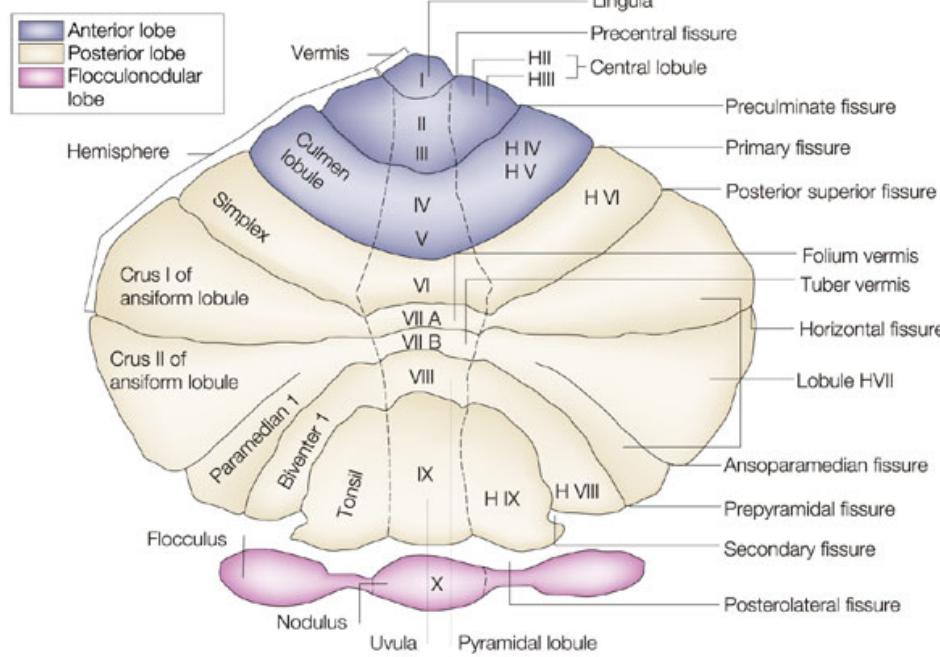
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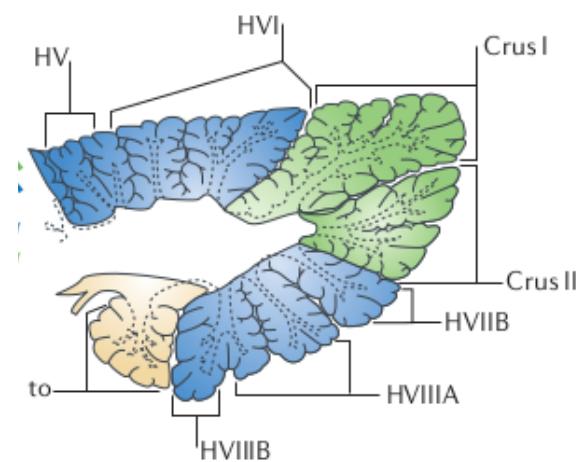
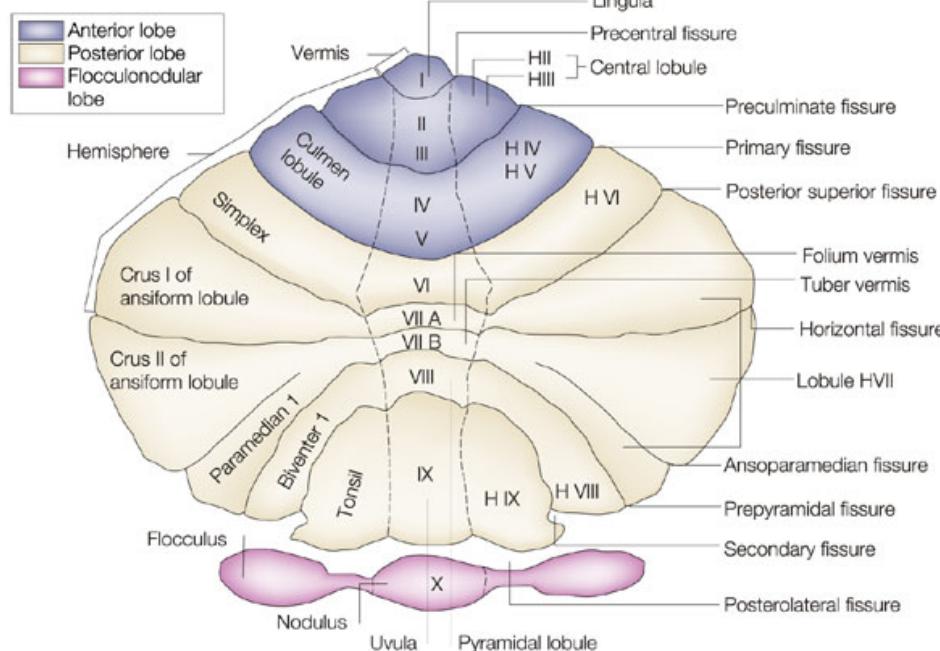


Anatomically-defined lobules exhibit differential structural connectivity, functional connectivity, and task Involvement



The cerebellum: Why do we care?

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Why are you doing this?

- What is “normal” for cerebellar structure?
 - Has been relatively difficult to characterise



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What is the normative structure of the cerebellum?



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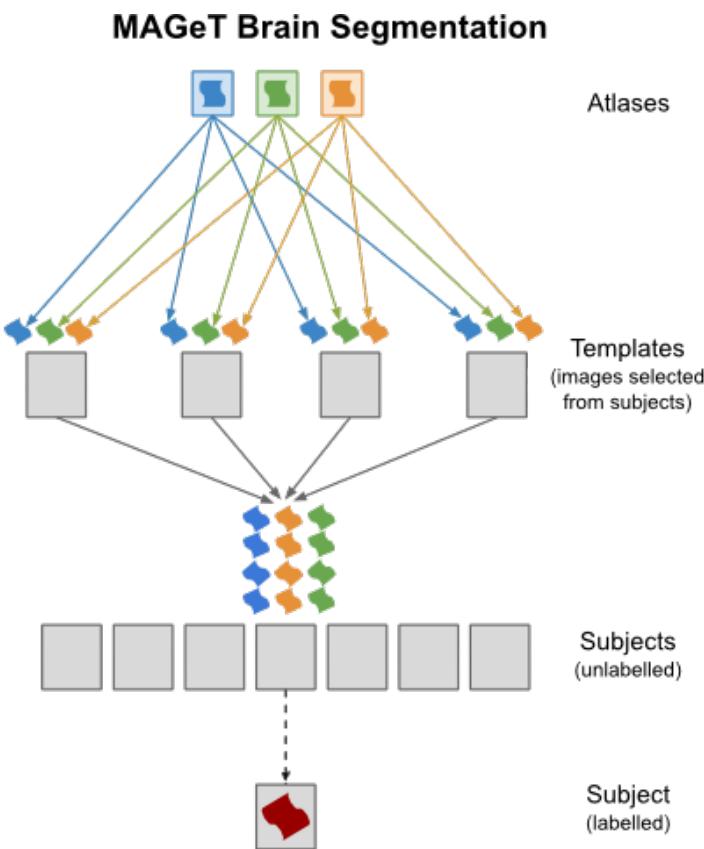
What is the normative structure of the cerebellum?

What is the heritability of cerebellar structure?



Method

- HCP S900 release (327 unrelated, 464 related)



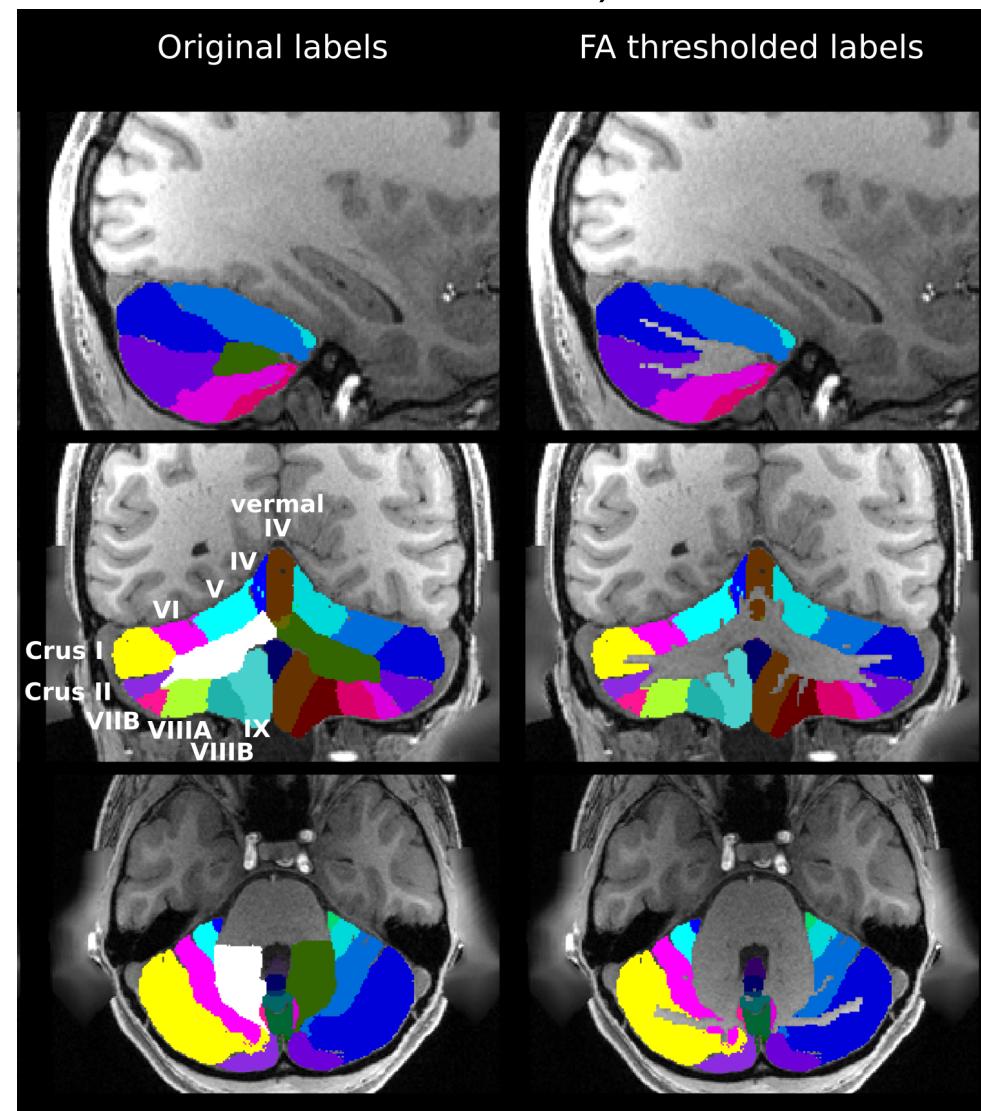
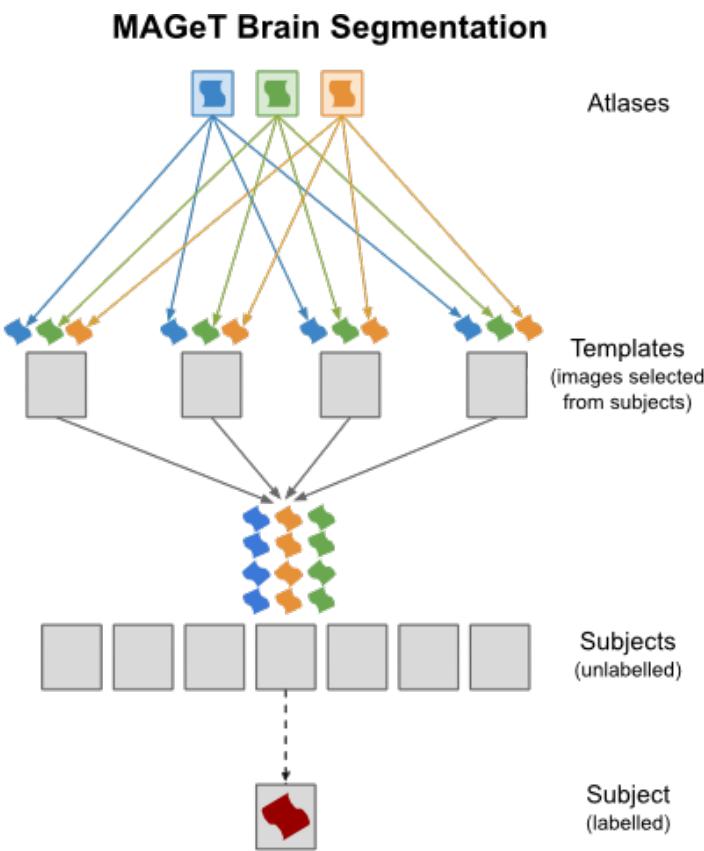
Chakravarty et al., 2013

Park et al., 2014



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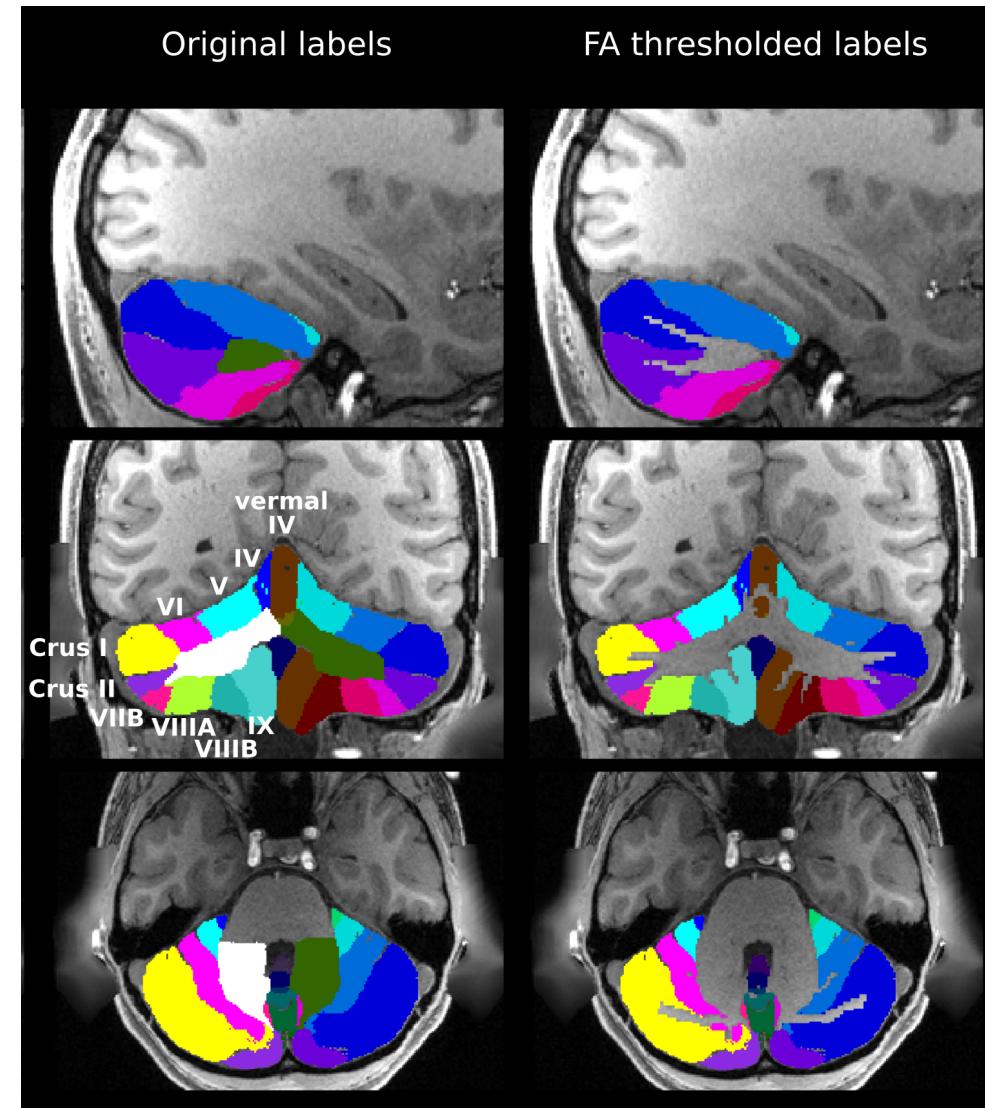


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- Lobular volume
 - Variability
 - Covariance
 - Heritability

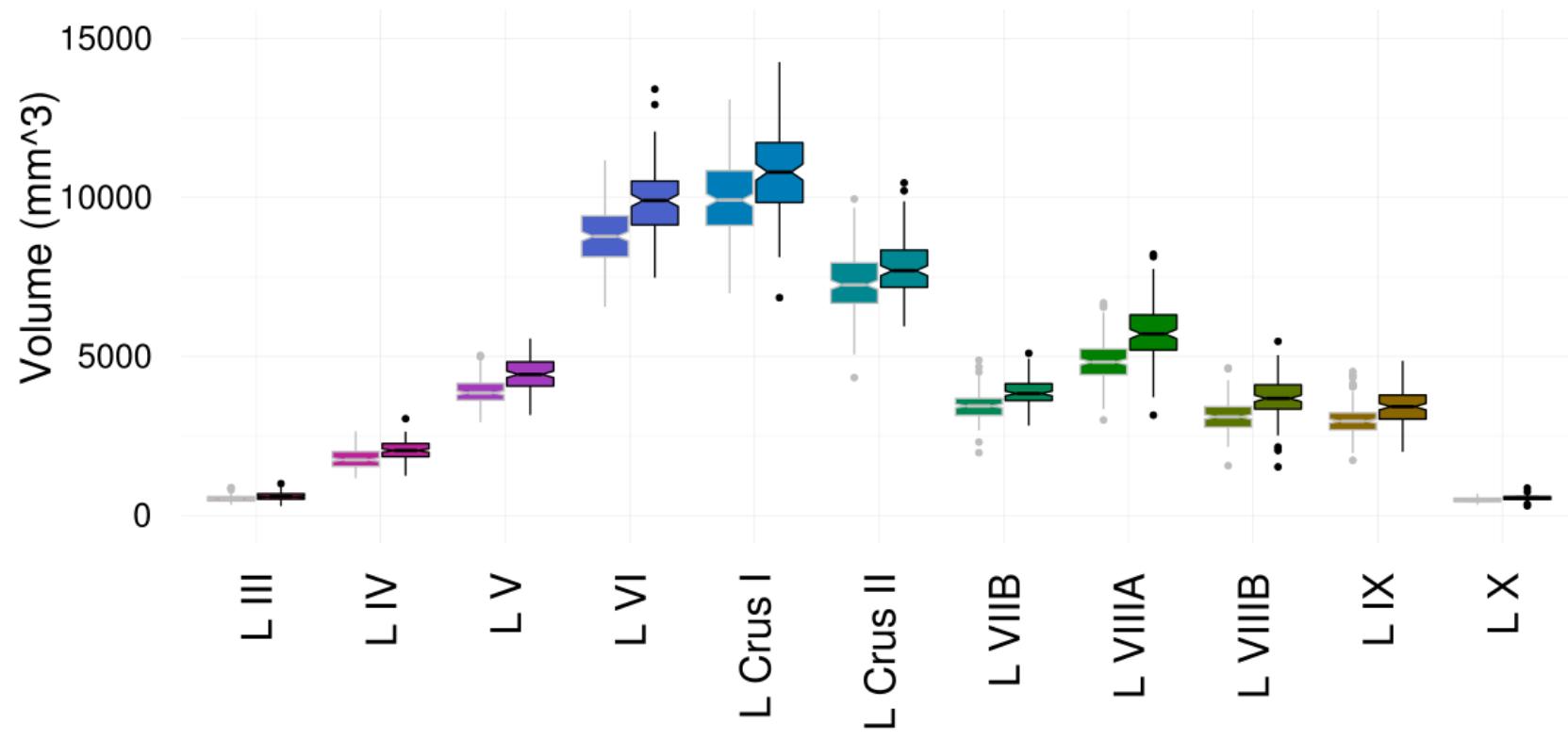
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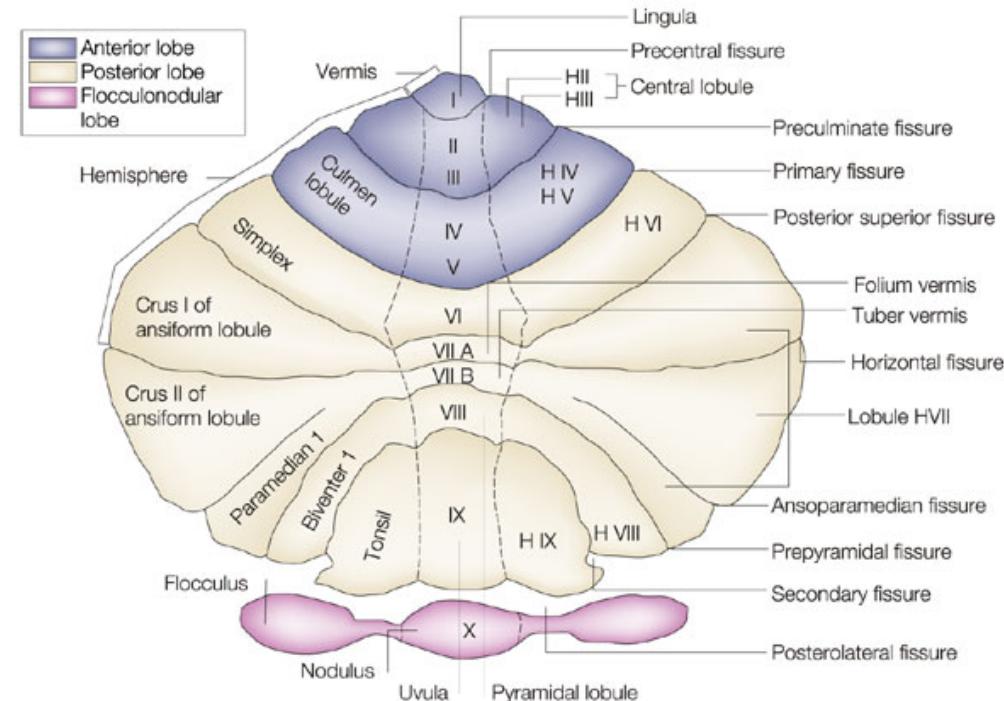
Cerebellar Variability



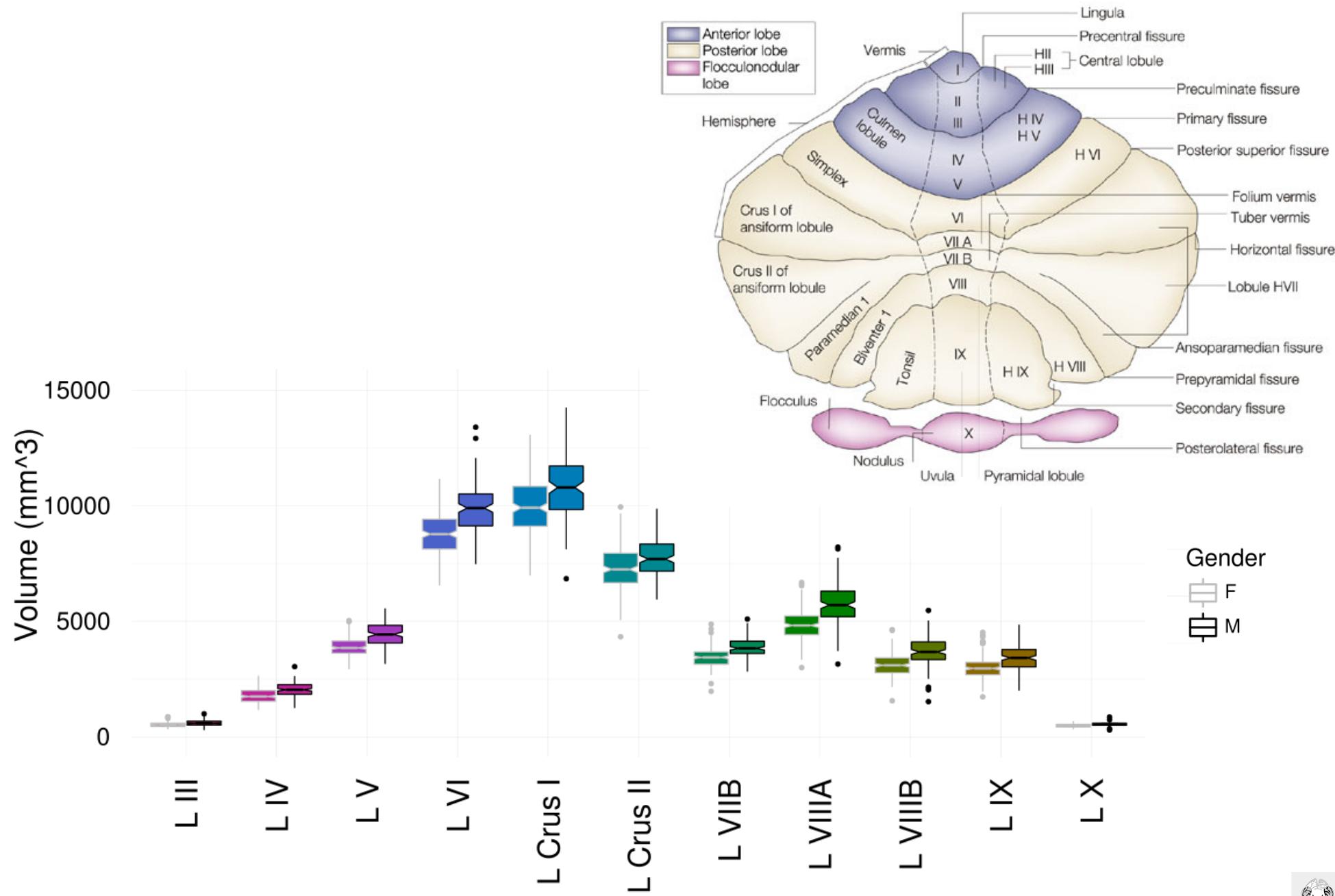
Population Variability: L Hemisphere



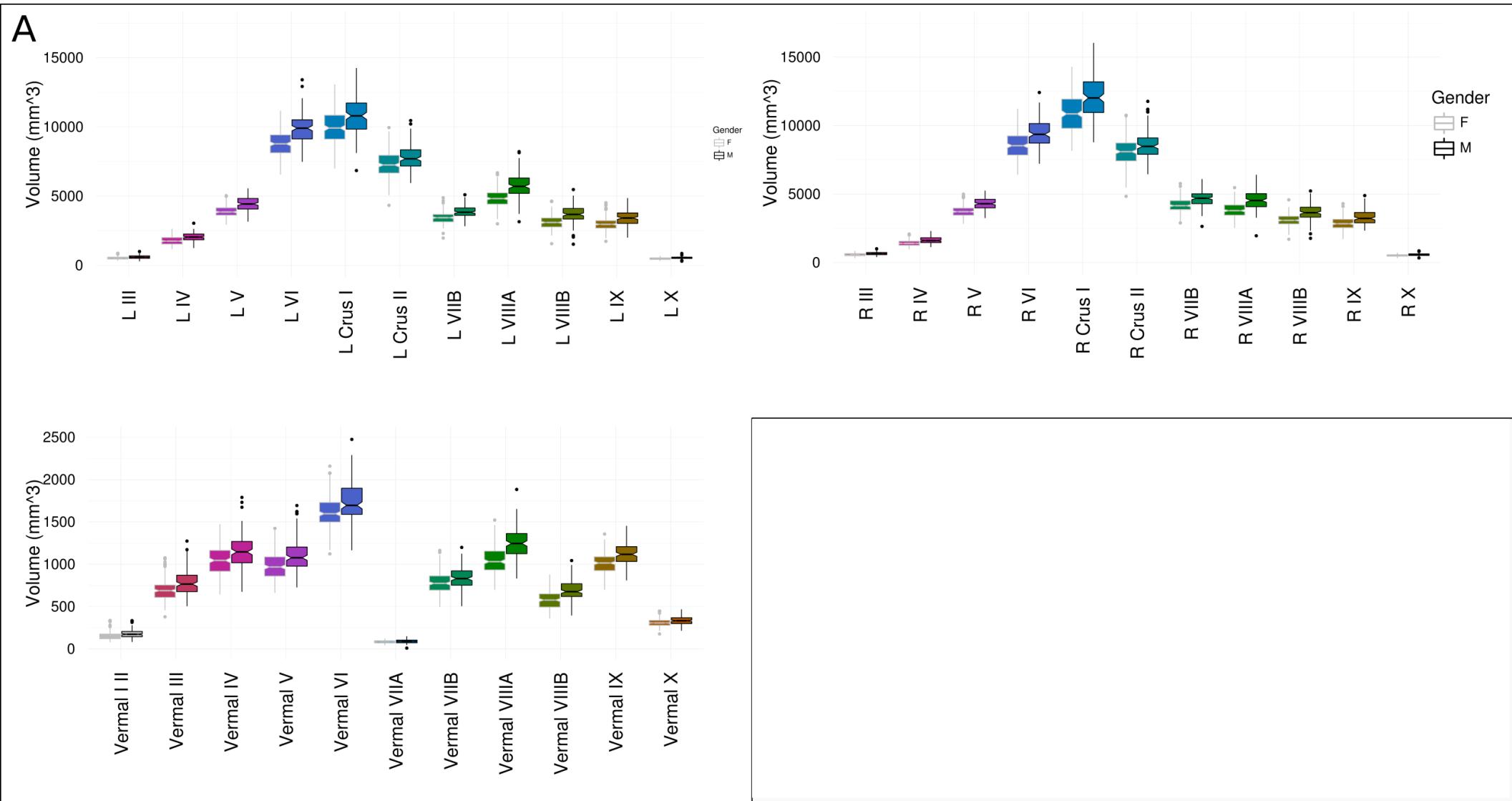
Population Variability: L Hemisphere



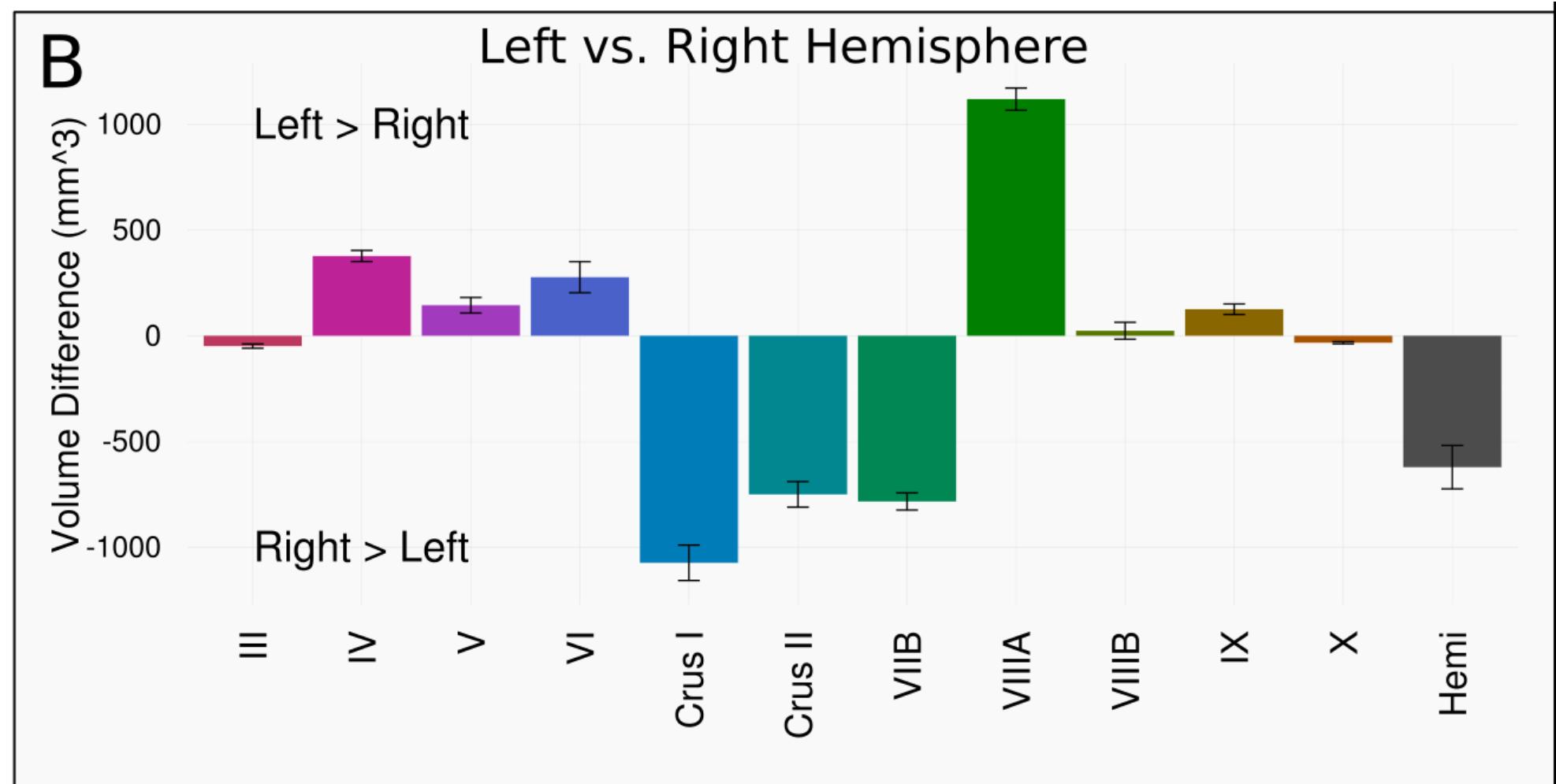
Population Variability: L Hemisphere



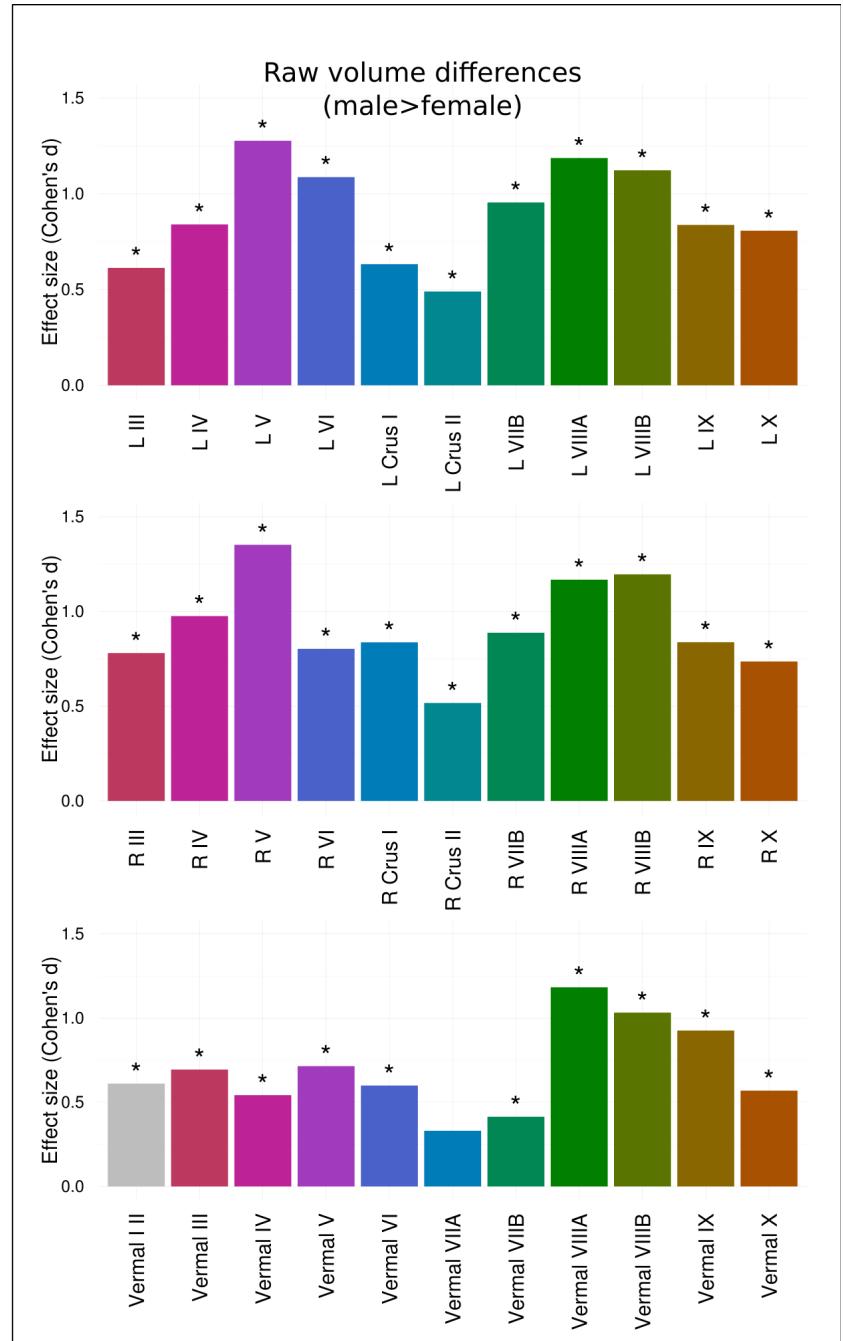
Population Variability: Lobules



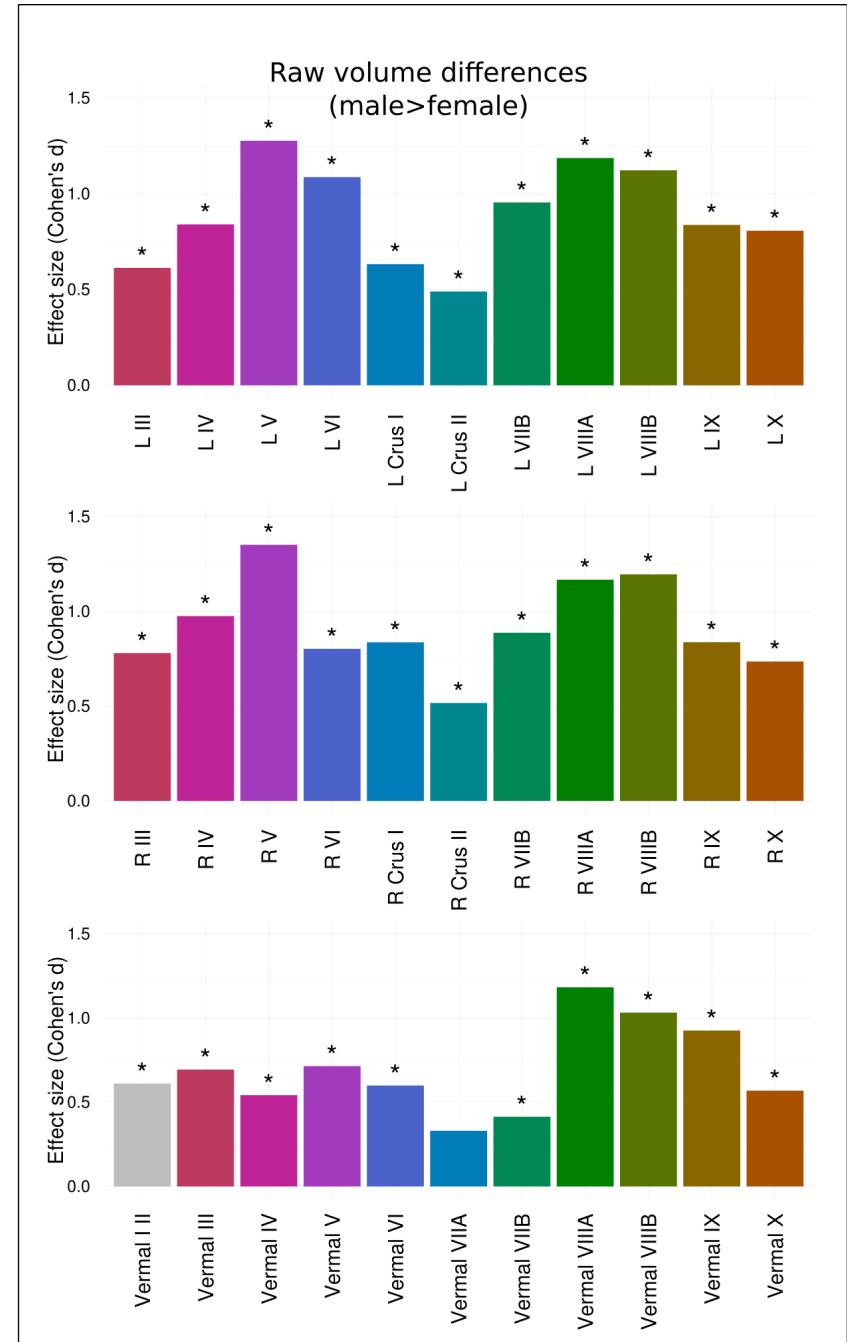
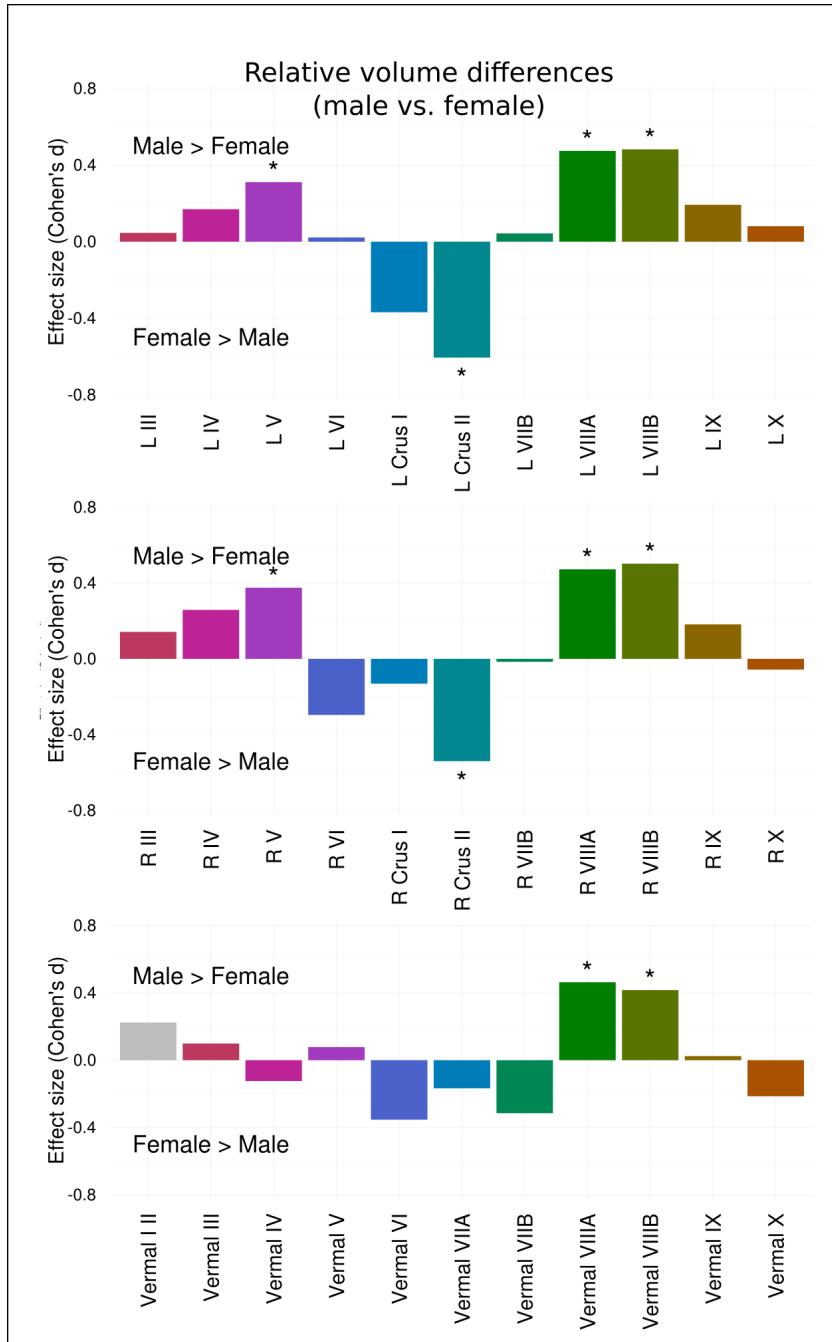
Population Variability: Lobules



Volumetric sex differences



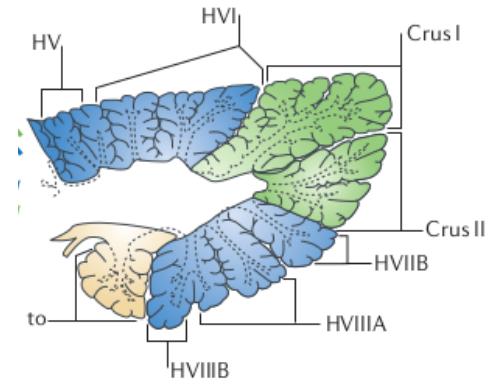
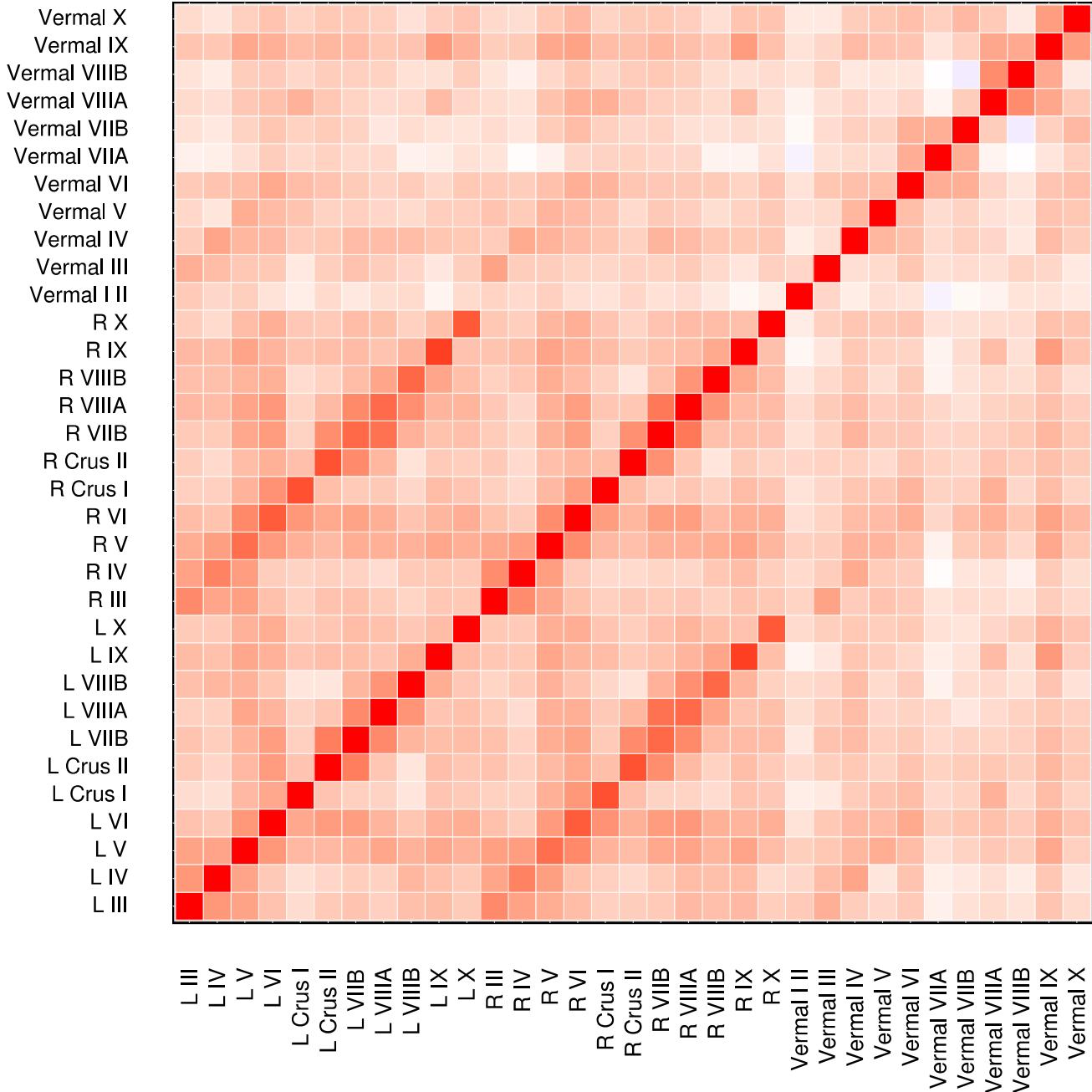
Volumetric sex differences



Cerebellar Covariance



Intra-cerebellar Covariance

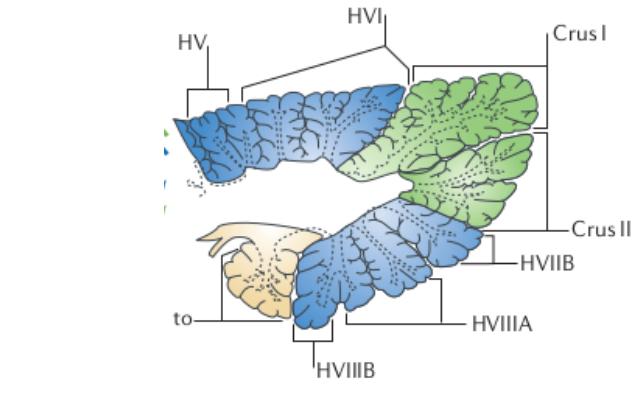
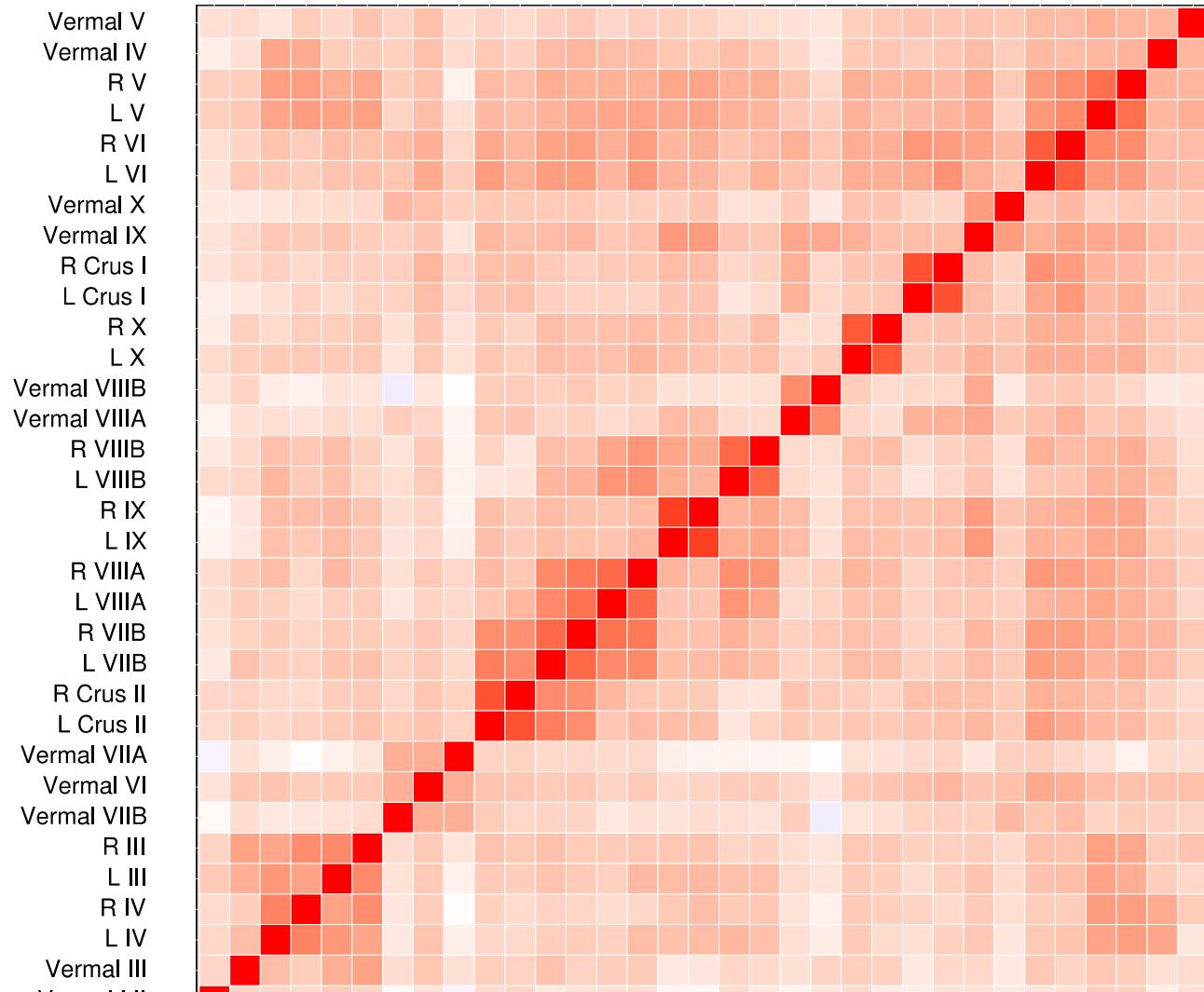


Pearson
Correlation

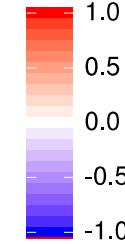
1.0
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Intra-cerebellar Covariance



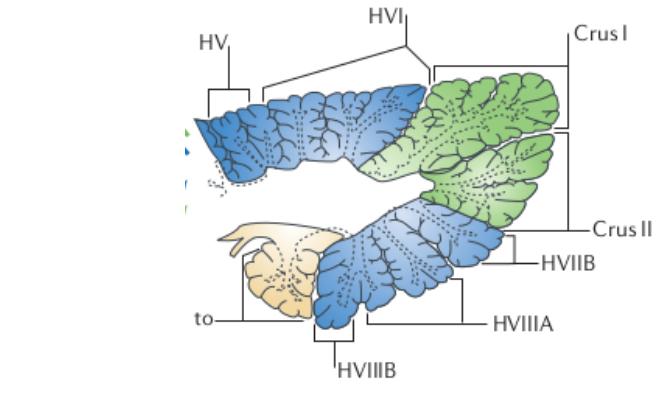
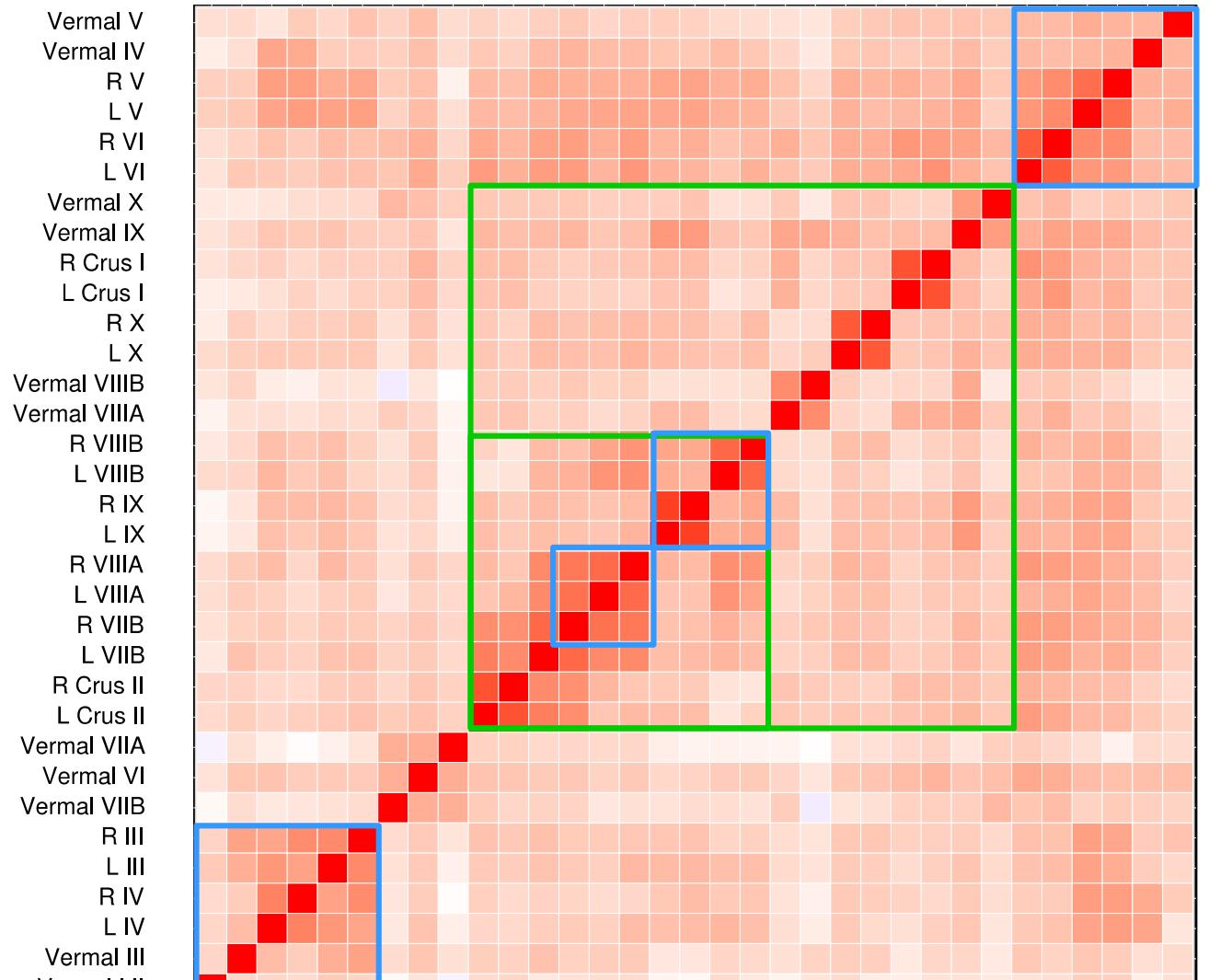
Pearson
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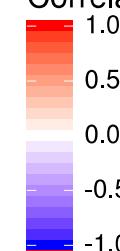
Vermal II
Vermal III
L IV
R IV
L III
R III
Vermal VIIB
Vermal VI
Vermal VIIA
L Crus II
R Crus II
L VIIIB
R VIIIB
L VIIIA
R VIIIA
L IX
R IX
L VIIIB
R VIIIB
Vermal VIII
Vermal VIIIB
L X
R X
L Crus I
R Crus I
Vermal IX
Vermal X
L VI
R VI
L V
R V
Vermal IV
Vermal V



Intra-cerebellar Covariance



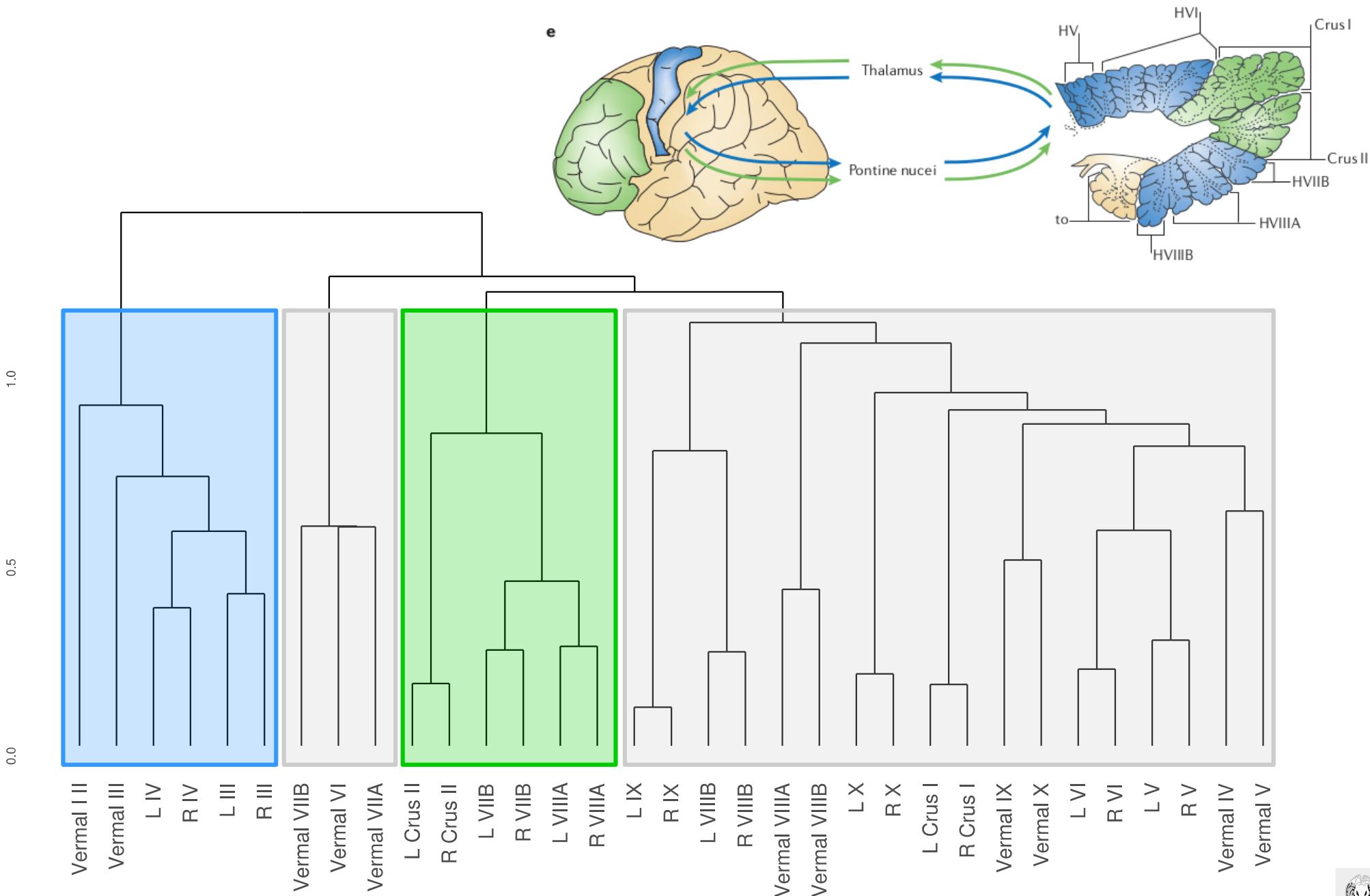
Pearson Correlation



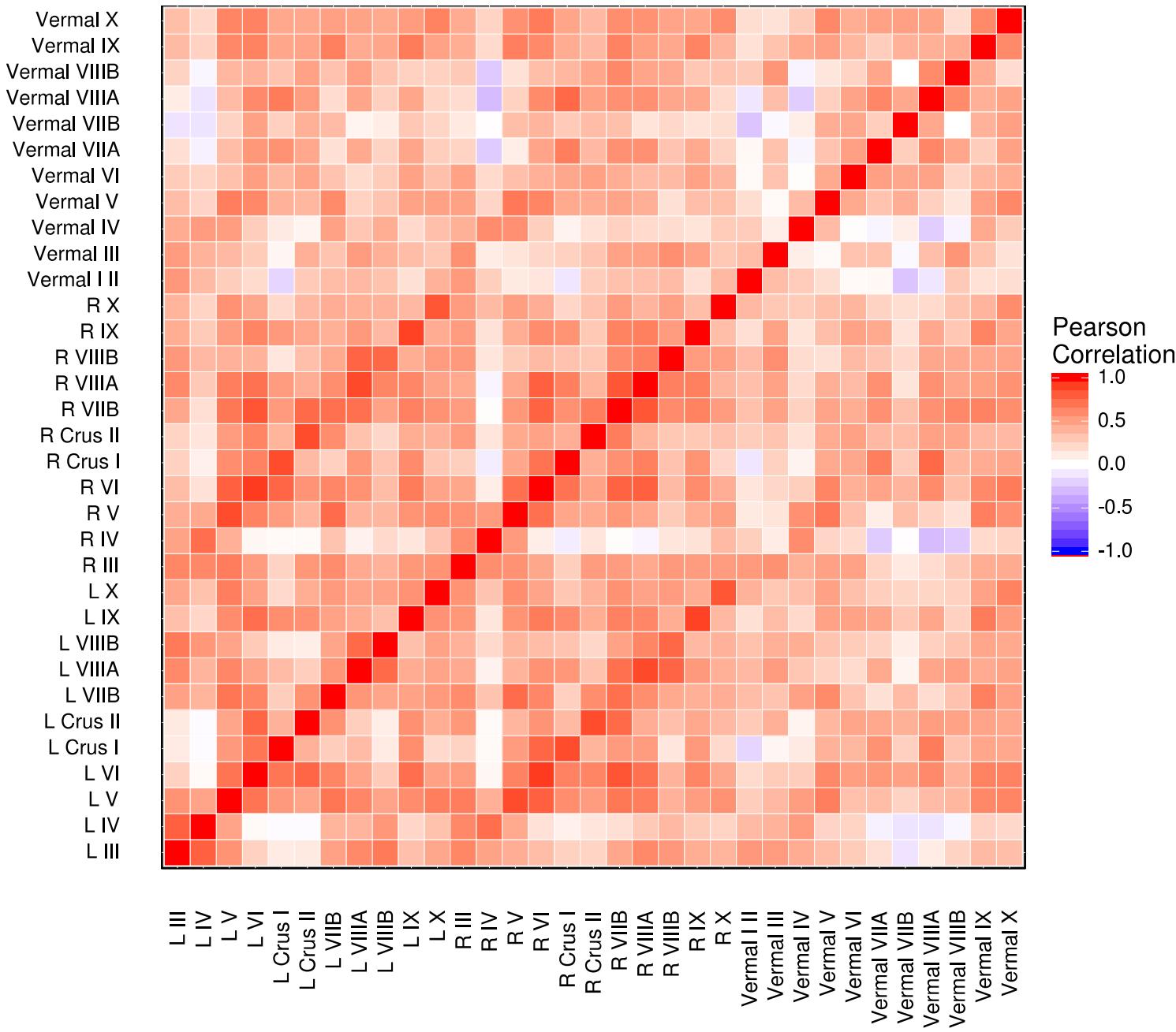
Vermal I
Vermal II
Vermal III
L IV
R IV
L III
R III
Vermal VI
Vermal VIIA
L Crus II
R Crus II
L VIIIB
R VIIIB
L VIIIIA
R VIIIIA
L IX
R IX
Vermal VIIA
Vermal VIIIB
L X
R X
L Crus I
R Crus I
Vermal IX
Vermal X
L VI
R VI
L V
R V
Vermal IV
Vermal V



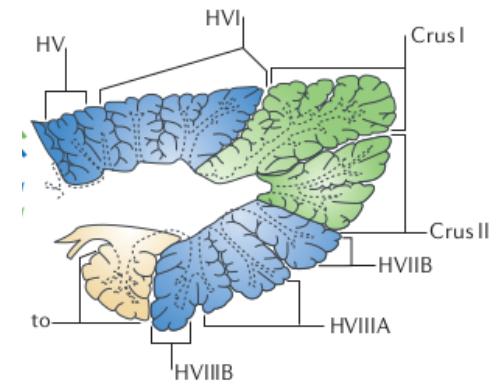
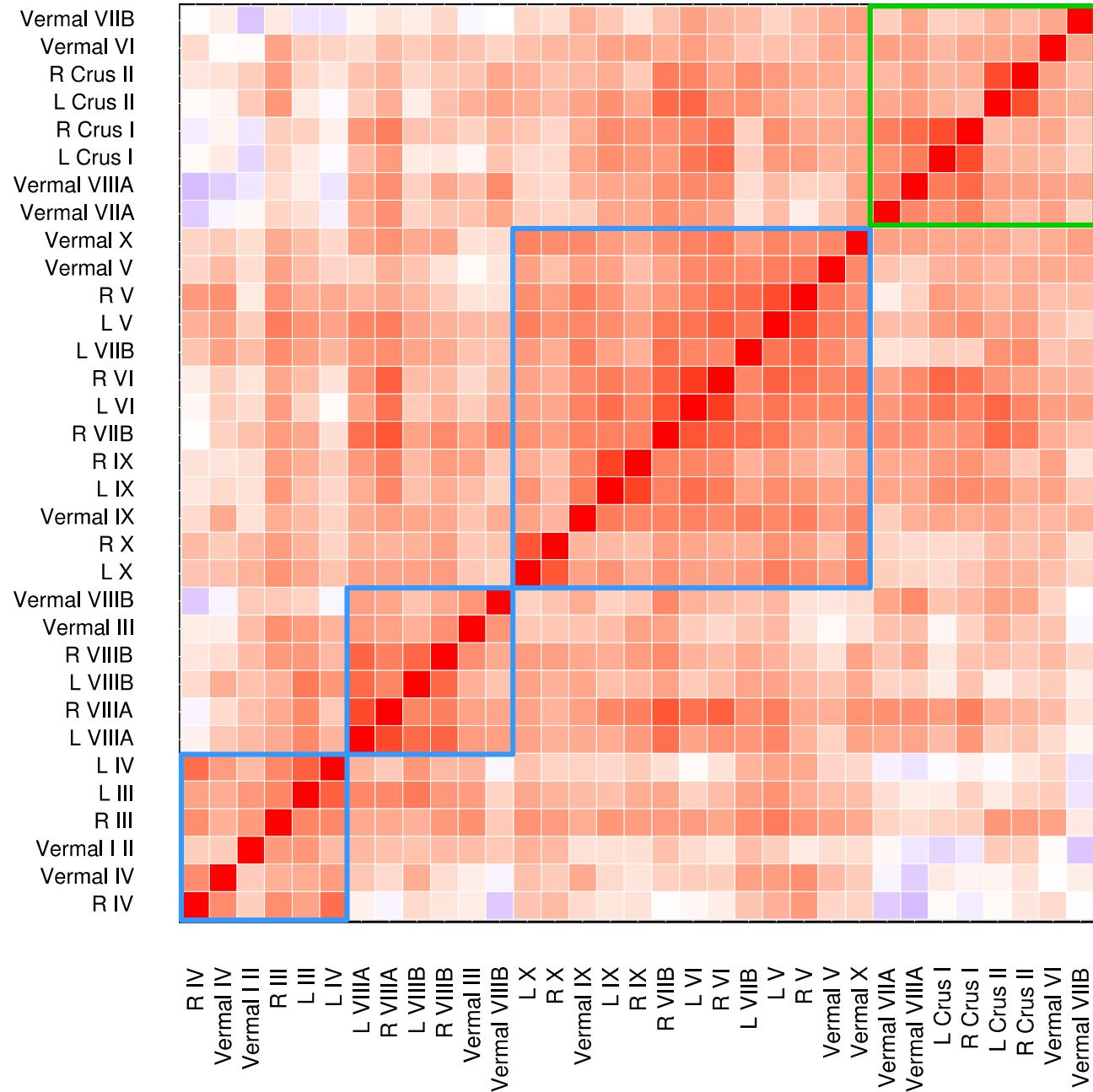
Intra-cerebellar Covariance



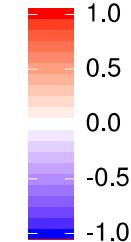
CB-Ctx – CB-Ctx Covariance



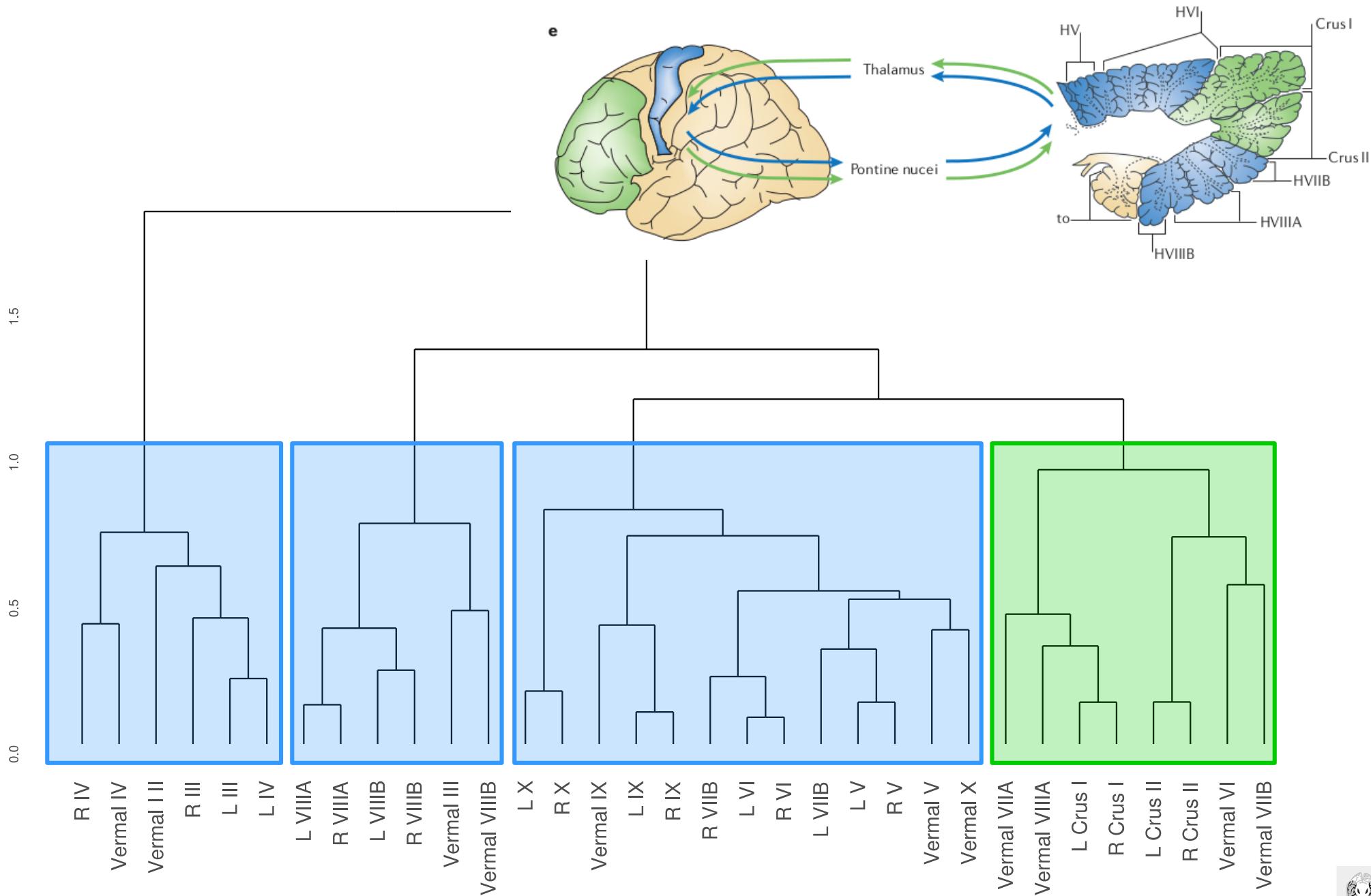
CB-Ctx – CB-Ctx Covariance



Pearson
Correlation



CB-Ctx – CB-Ctx Covariance



Cerebellar Heritability



Lobular Volume: Heritability

- Model
 - genetic (A) variance
 - shared (C) and unique (E) environmental variance
 - Compare ACE to CE
- Estimate the proportion of variance in lobular volume that is explained by genetics
 - controlling for
 - age, gender, and total CB GM volume



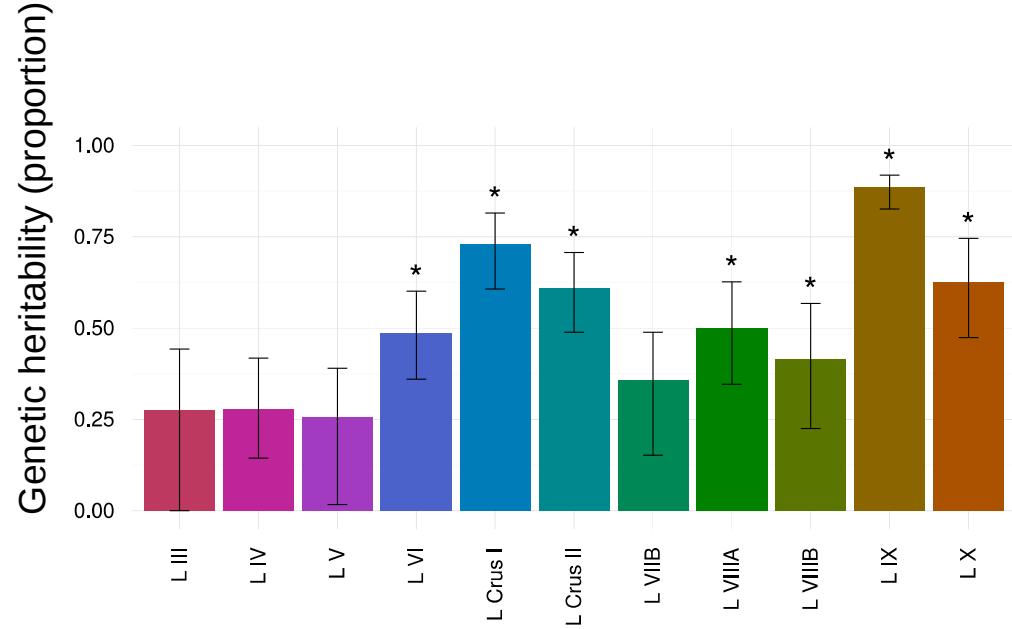
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	N	Females	Males	Mean	Age	Age Range
MZ	166	118	48		29.78	22-36
DZ	152	84	68		28.74	22-35
Non-twin Siblings	146	75	70		29.03	22-36
Total	464	277	186		29.20	22-36

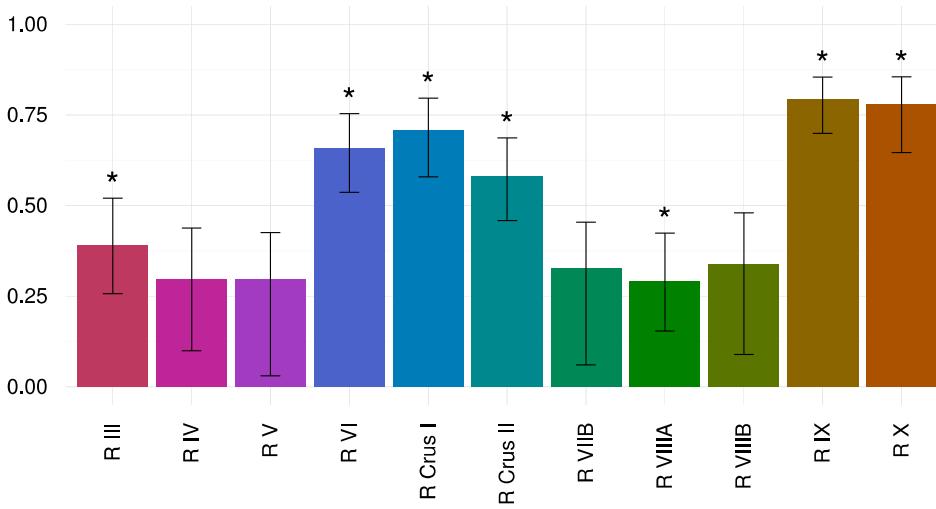
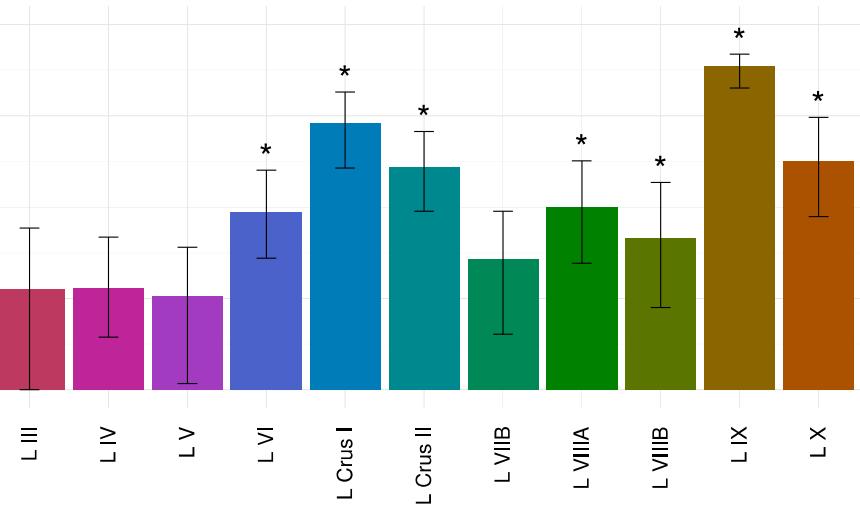


Lobular Volume: Heritability



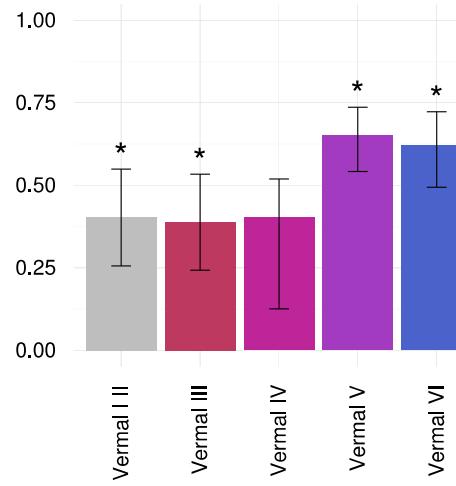
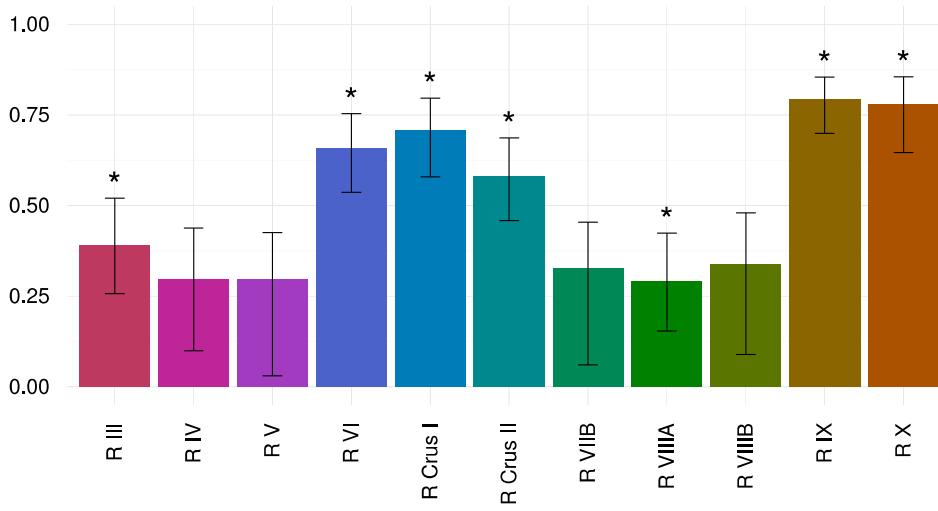
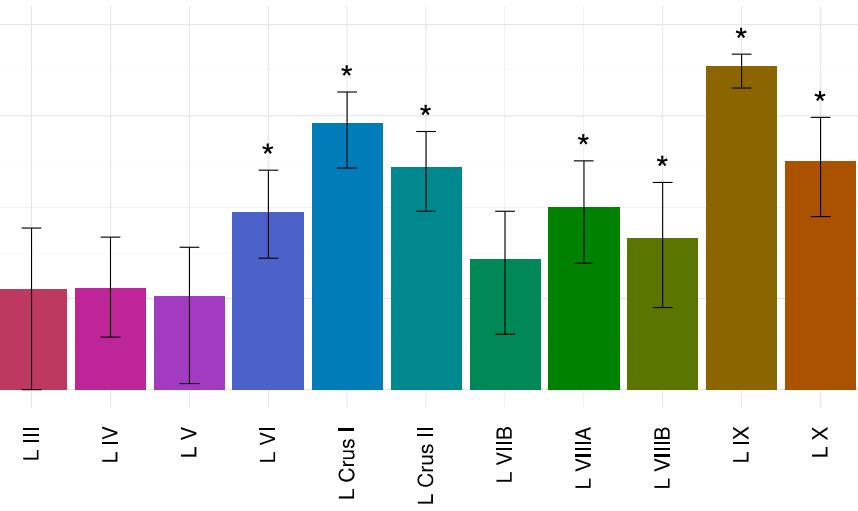
Lobular Volume: Heritability

Genetic heritability (proportion)



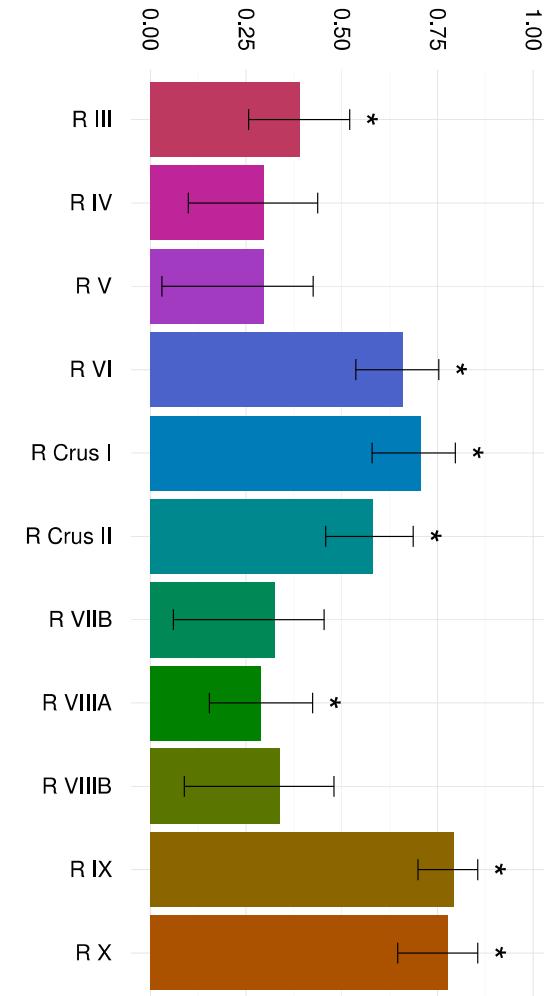
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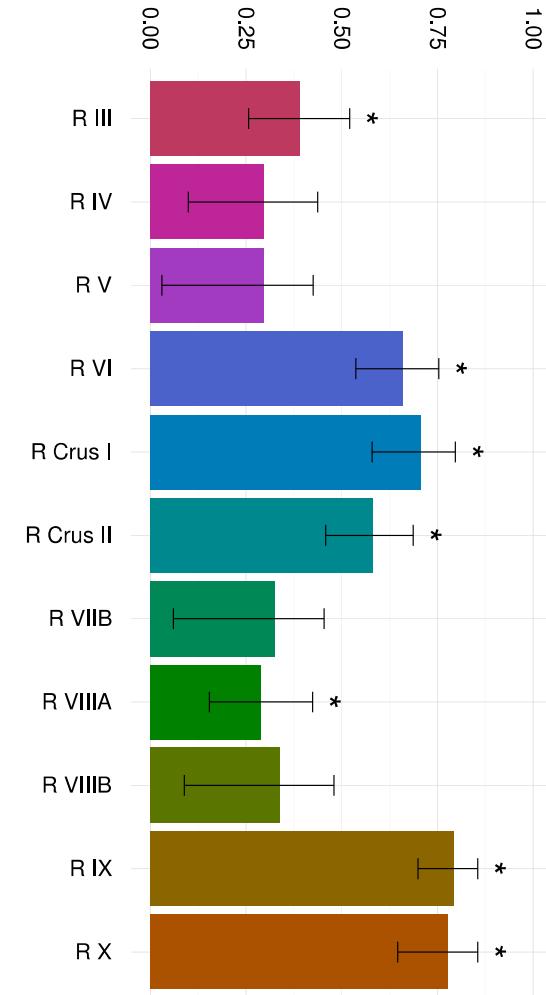
Lobular Volume: Heritability

Heritability

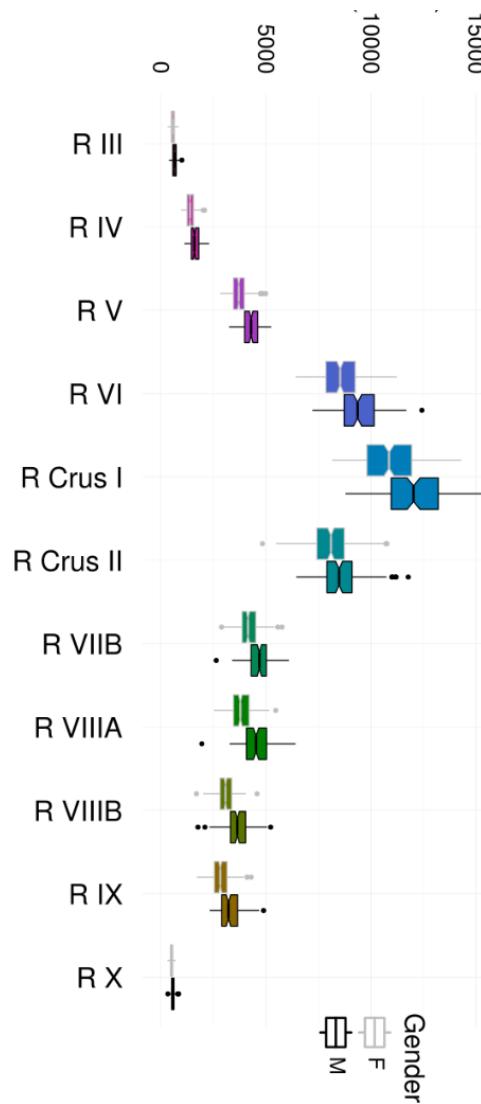


Lobular Volume: Heritability

Heritability

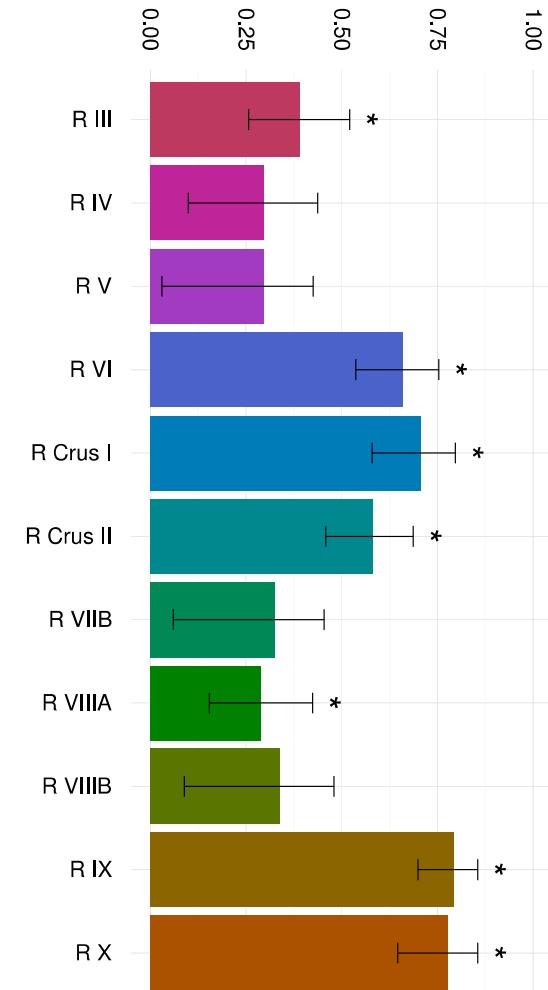


Volume

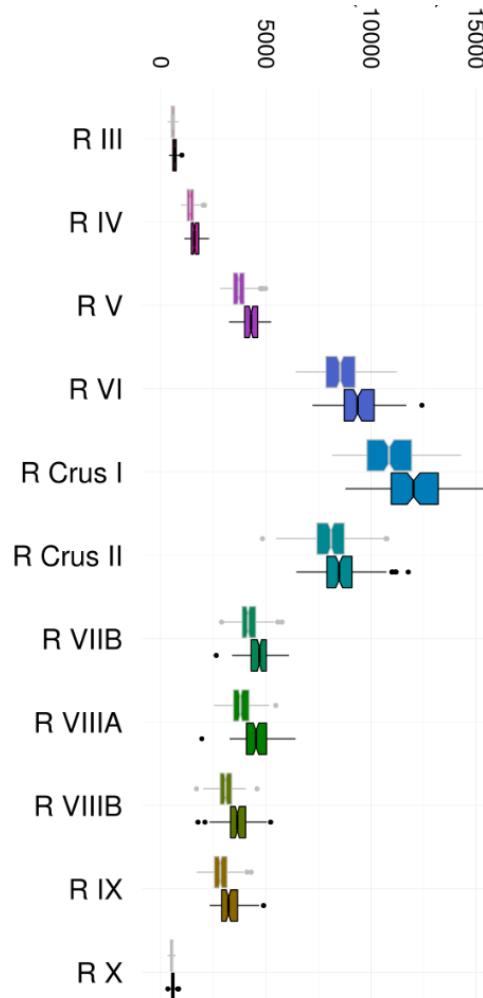


Lobular Volume: Heritability

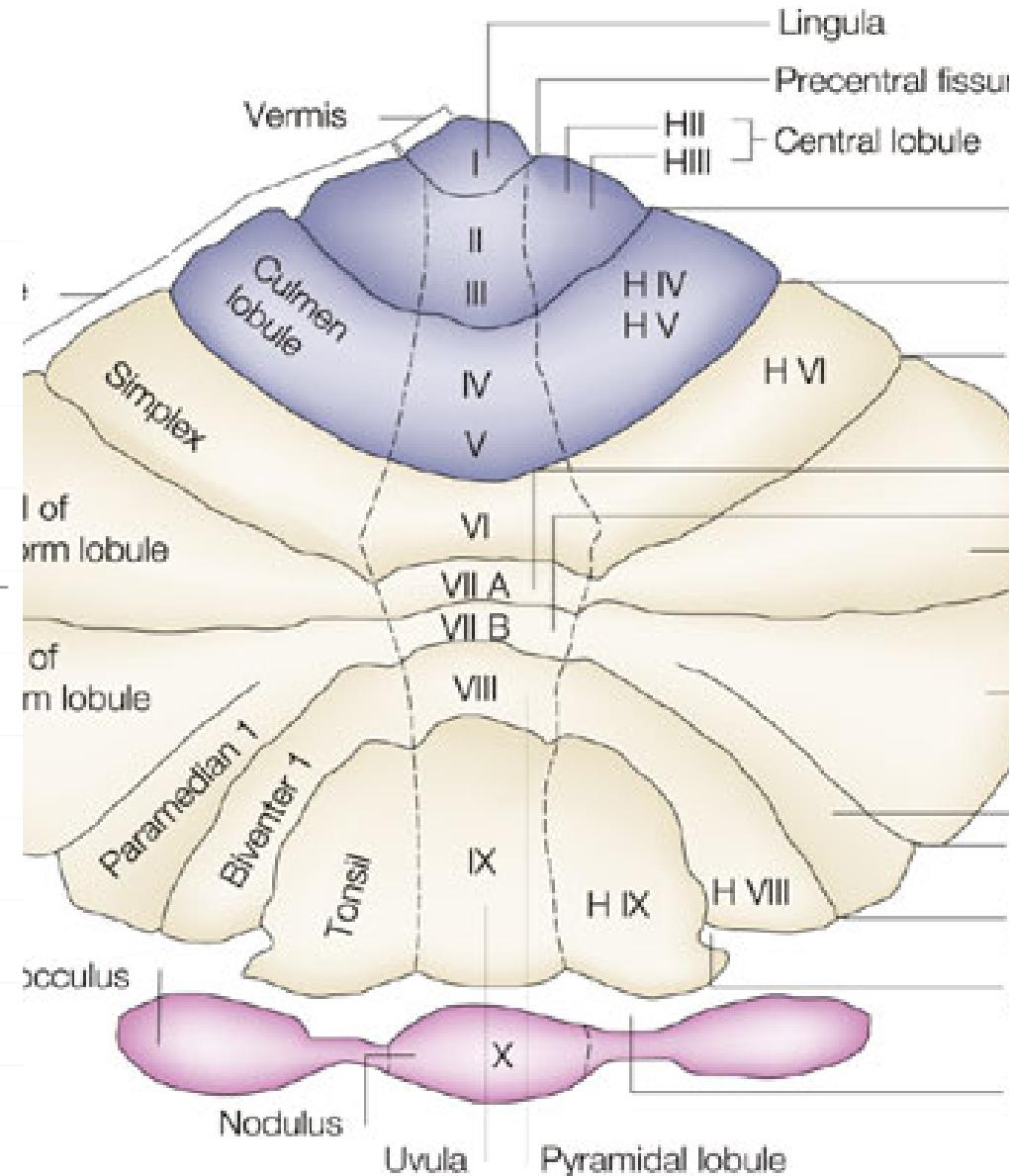
Heritability



Volume

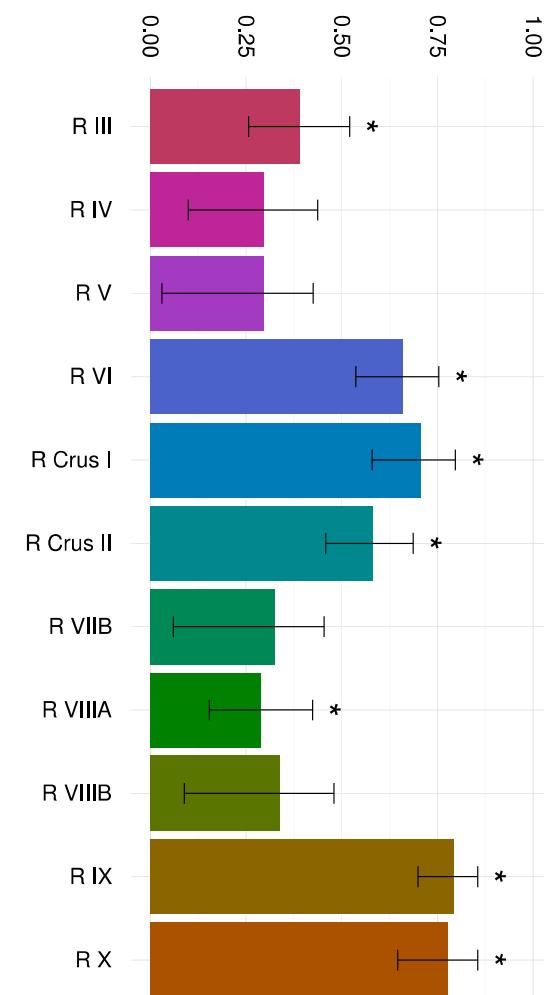


M F
Gender

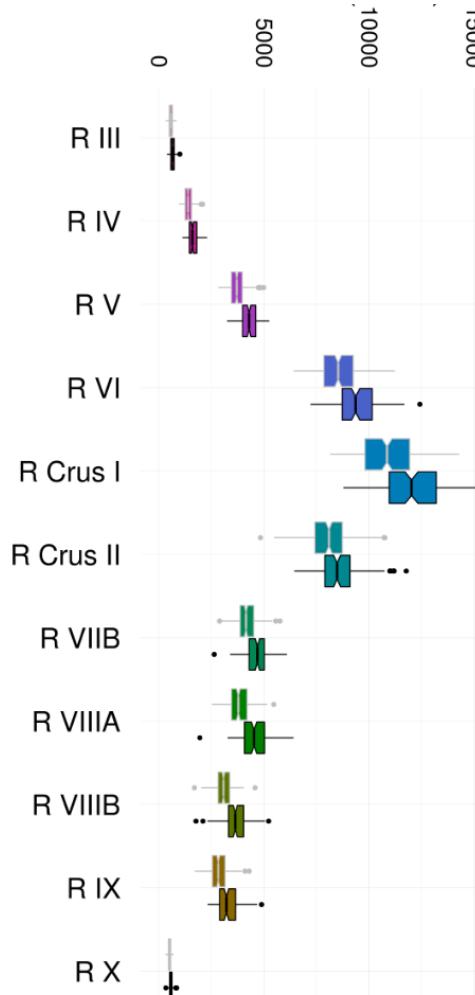


Lobular Volume: Heritability

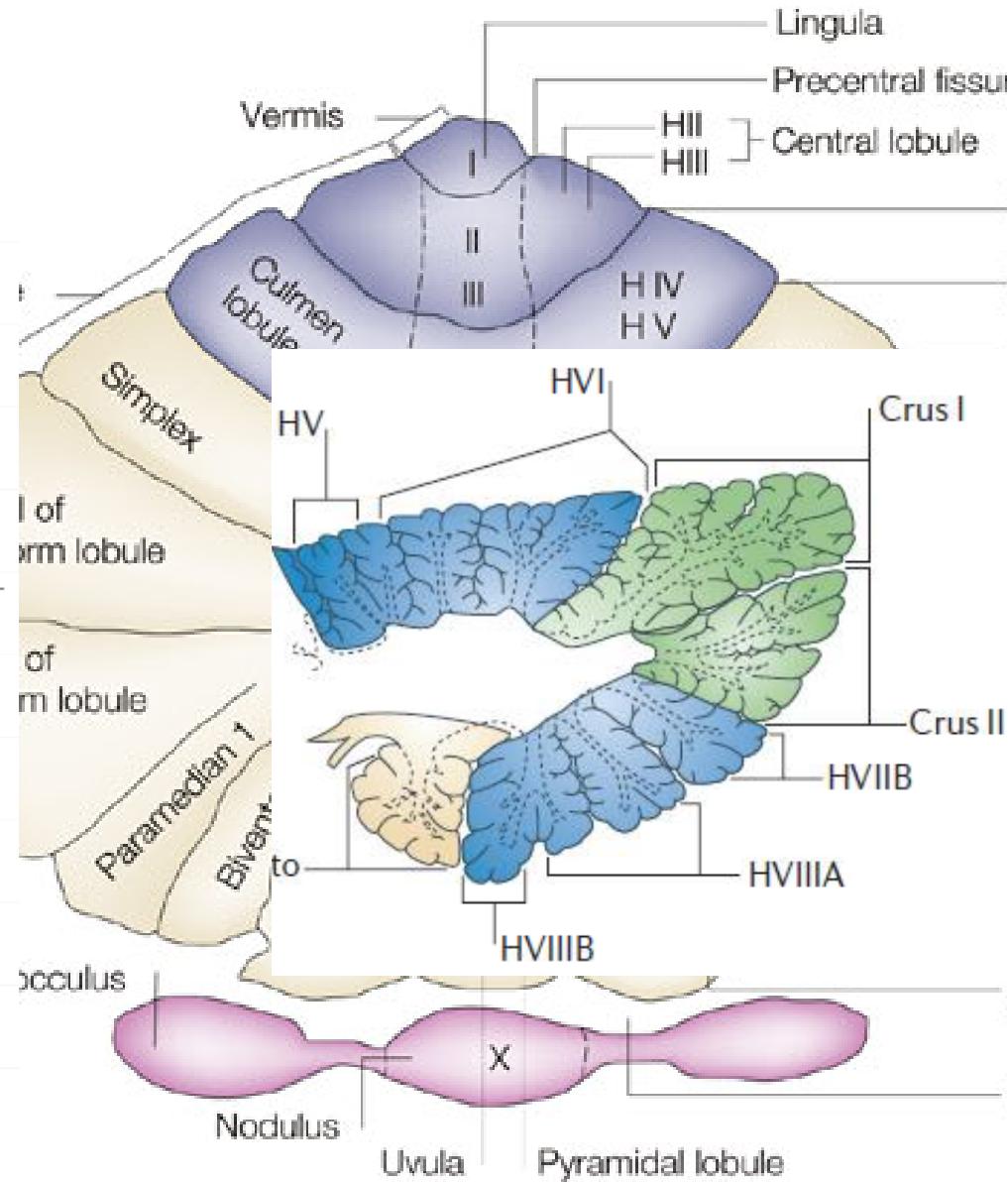
Heritability



Volume

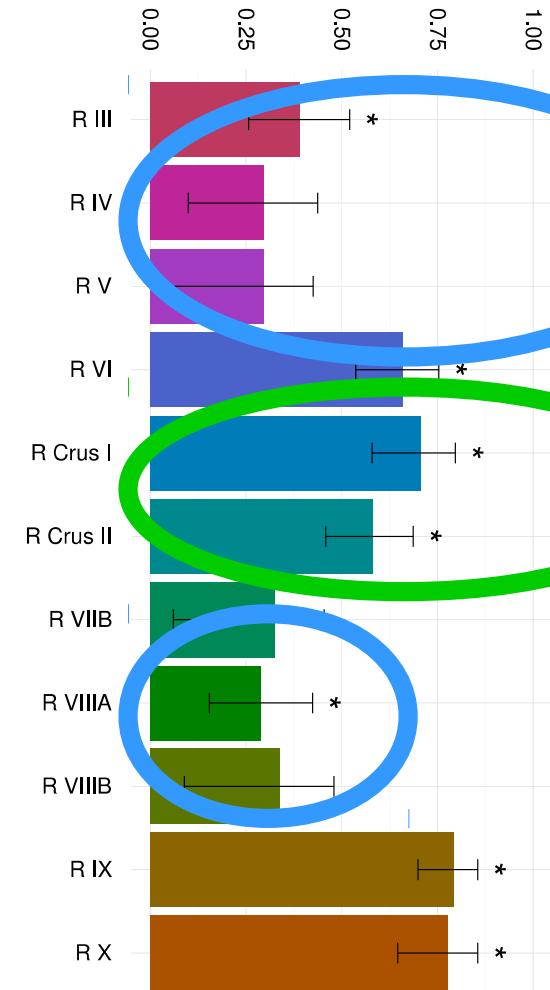


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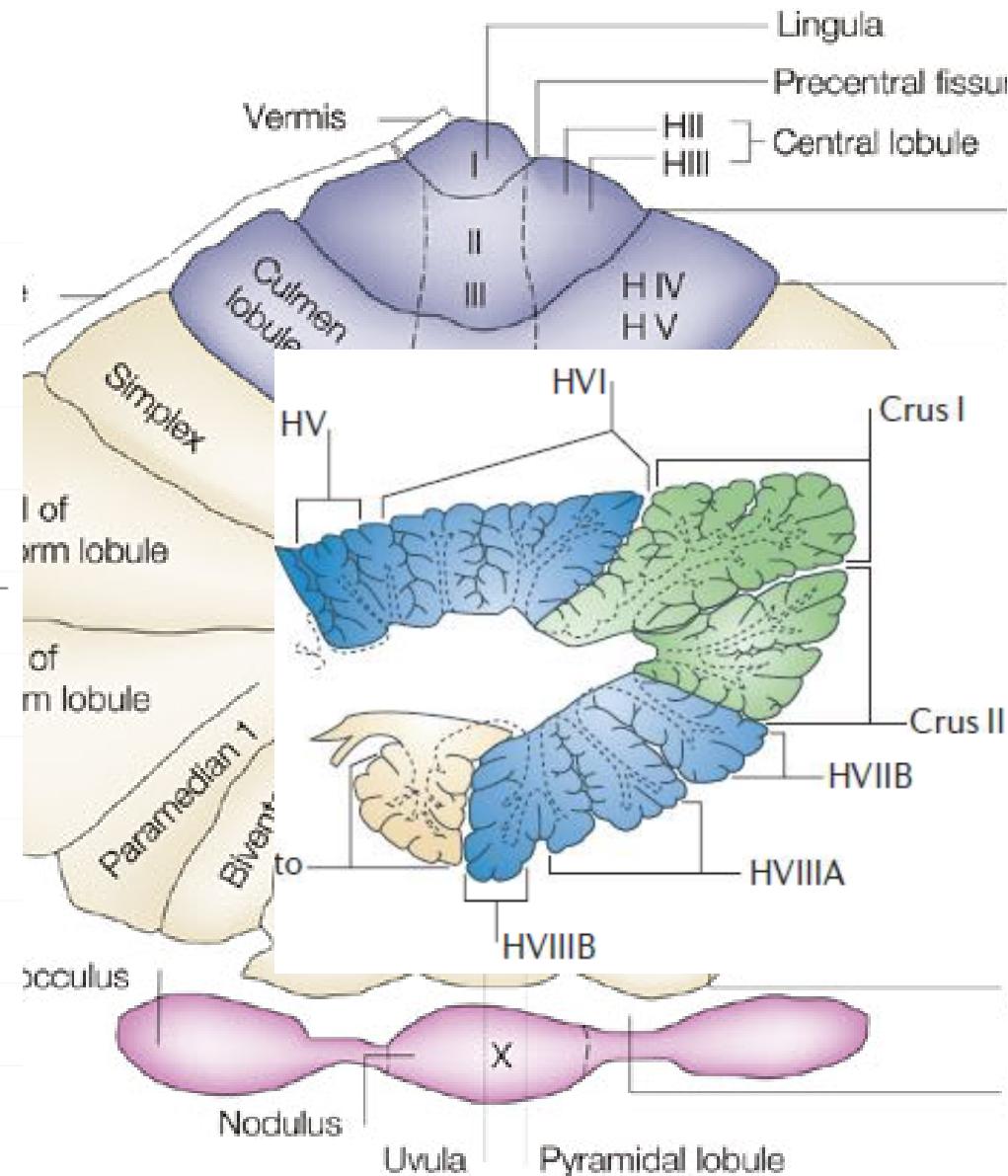
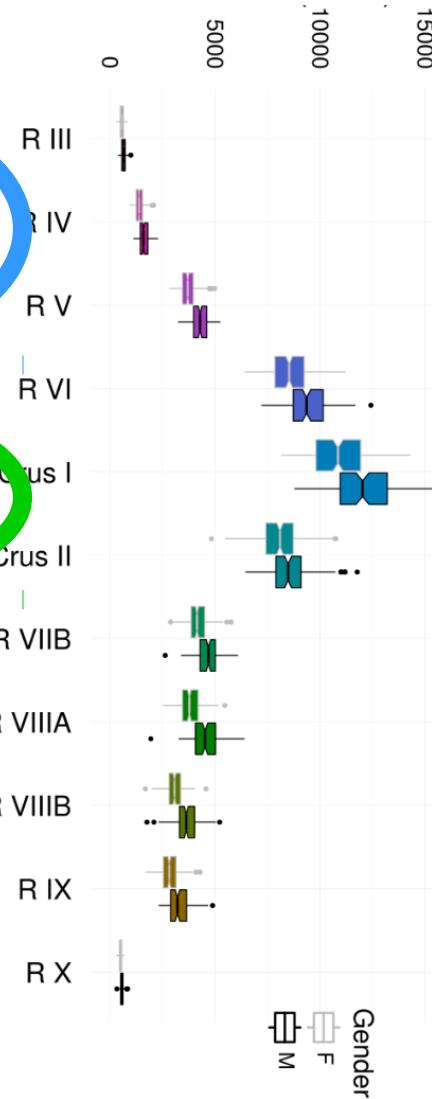


Lobular Volume: Heritability

Heritability

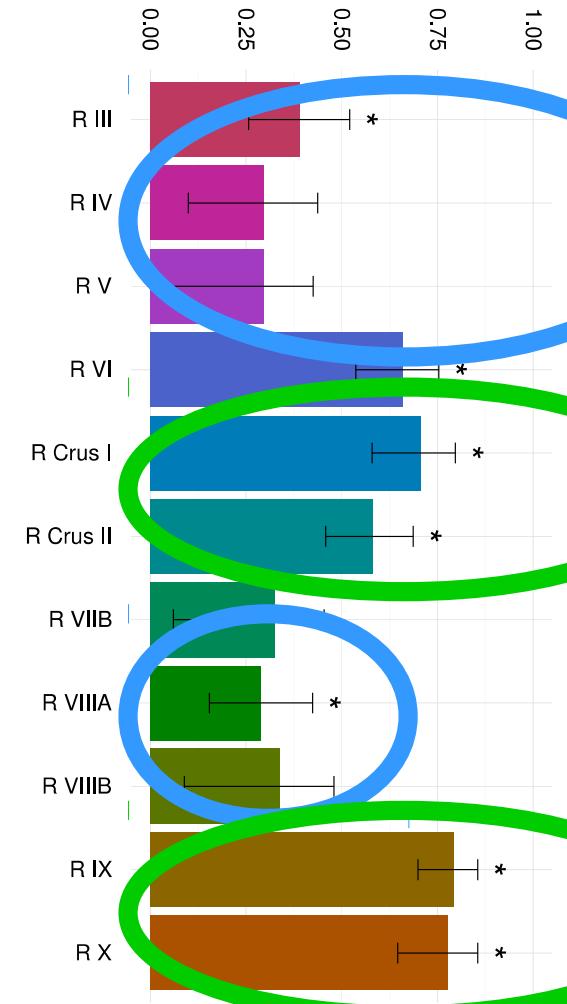


Volume

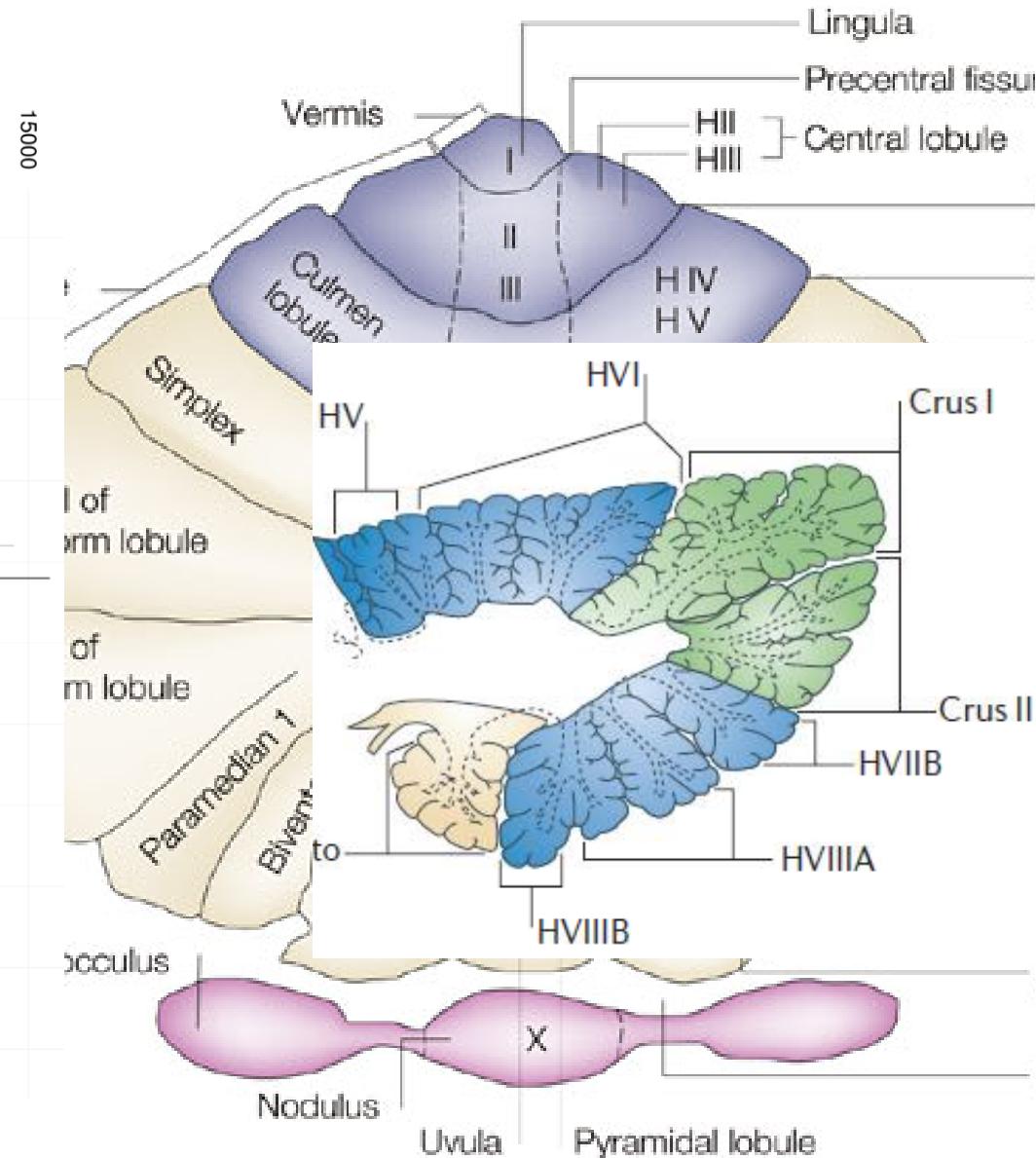
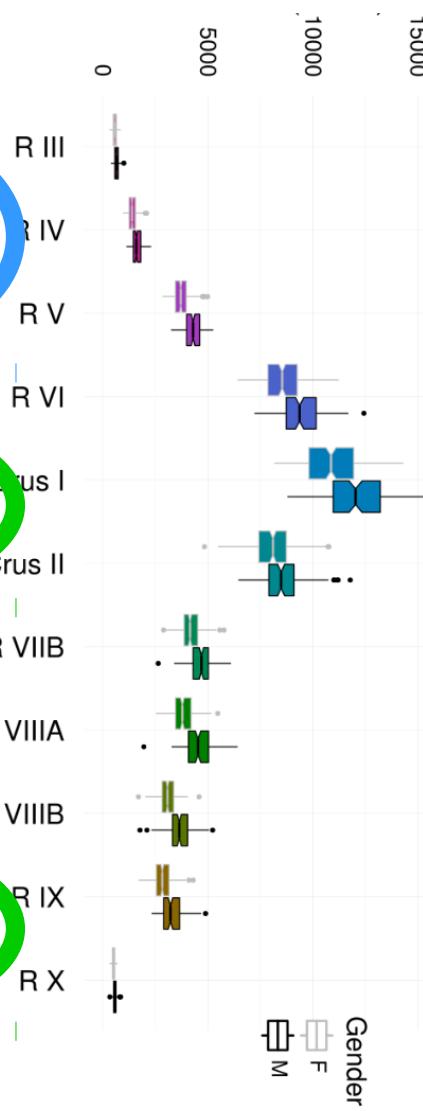


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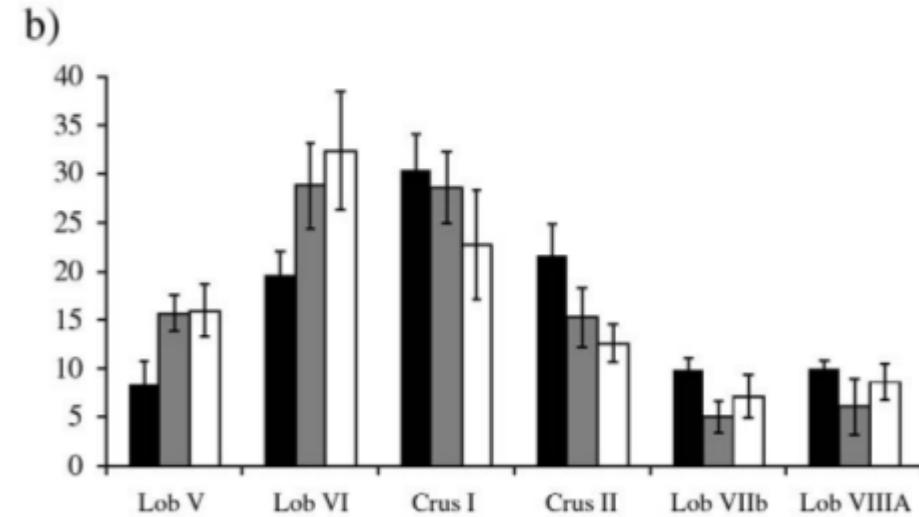
Heritability



Volume



Related to selective evolutionary expansion?

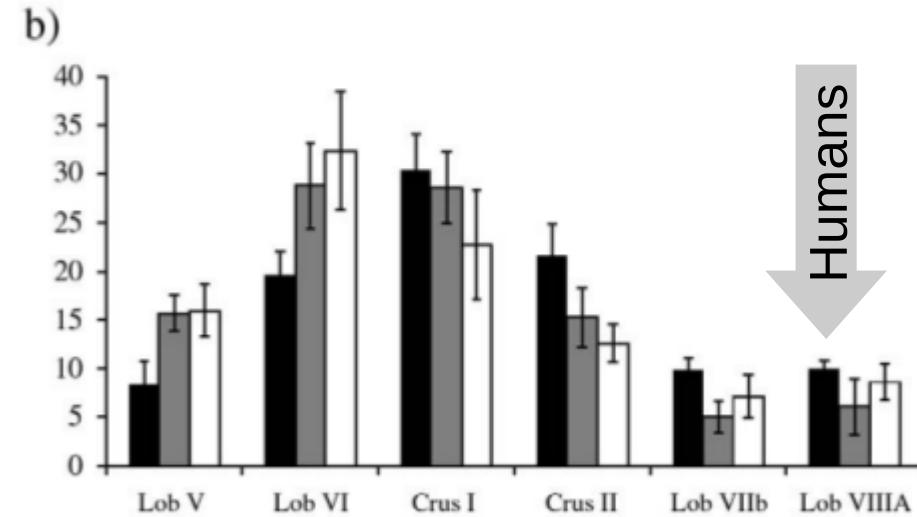


Averaged proportion of masked area occupied by a specific lobule across each primate species.

	Human		Chimp		Capuchin	
	Average (%)	SD	Average (%)	SD	Average (%)	SD
Lobule V	8.53	2.28	15.77	2.49	1.90	2.70
Lobule VI	19.56	2.49	28.86	4.41	32.49	6.04
Crus I	30.38	3.84	28.69	3.66	22.83	5.63
Crus II	21.65	3.23	15.36	3.05	12.72	1.94
Lobule VIIb	9.85	1.34	5.15	1.60	7.22	2.25
Lobule VIIIa	10.02	0.92	6.17	2.89	8.72	1.83



Related to selective evolutionary expansion?

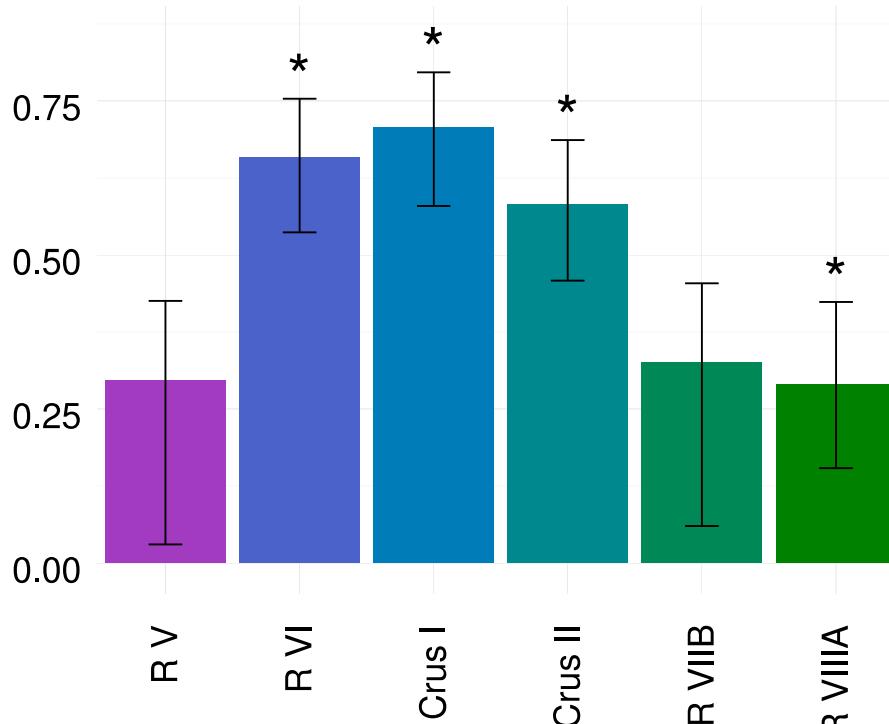


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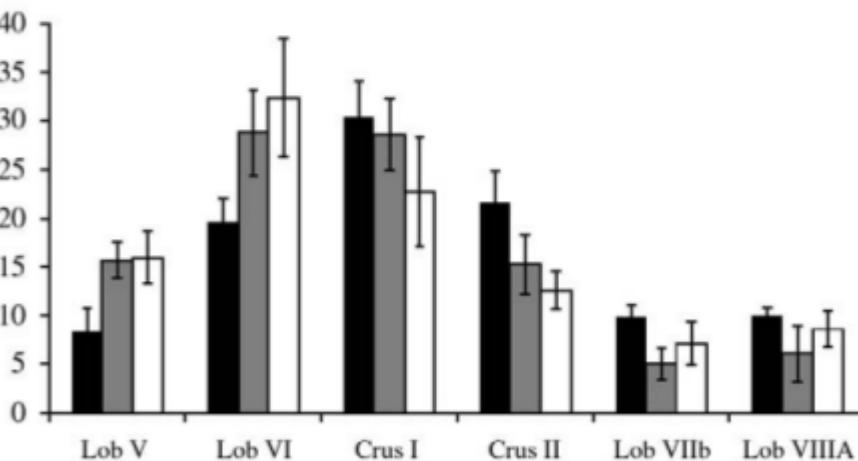
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Related to selective evolutionary expansion?



b)

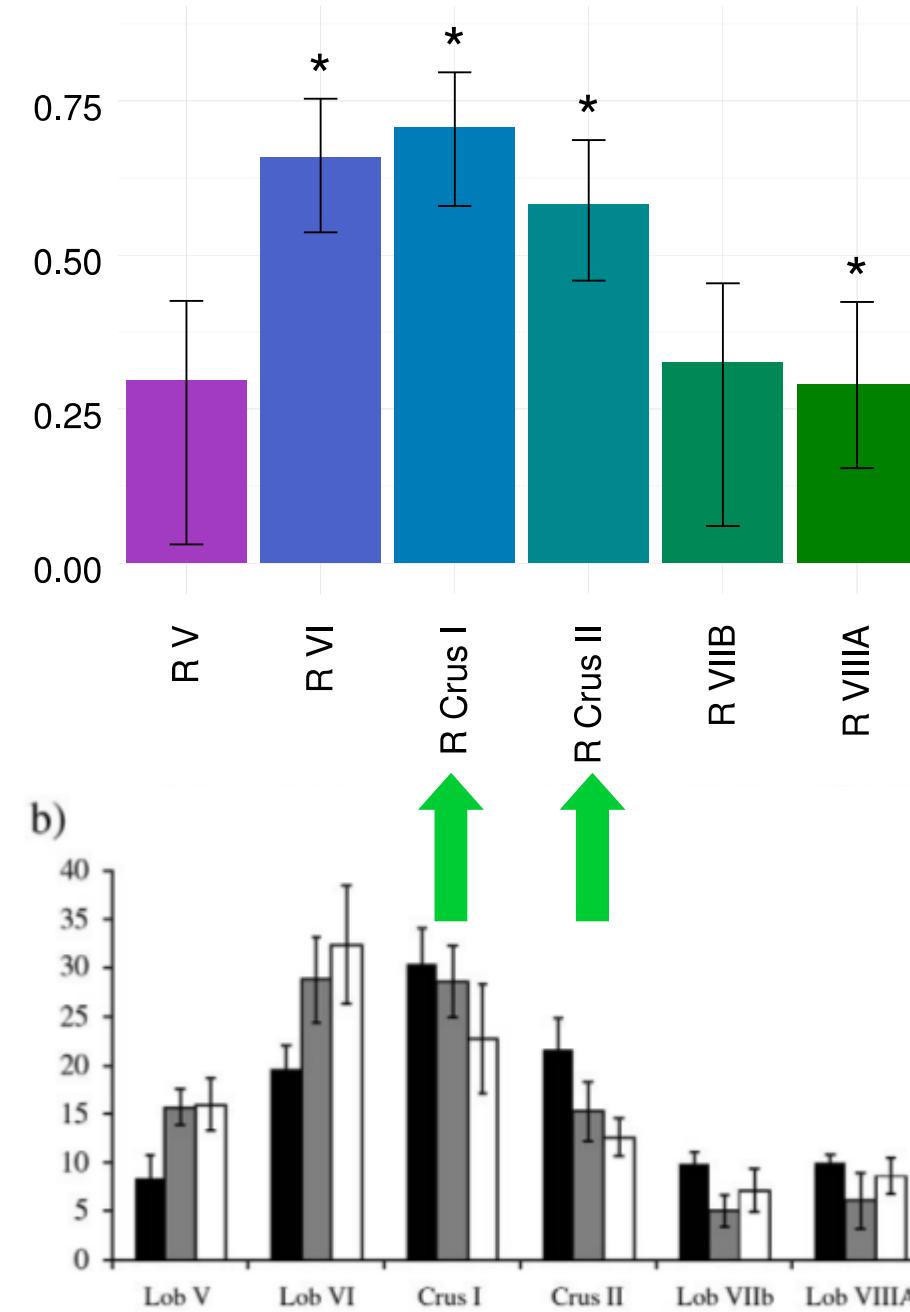


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Related to selective evolutionary expansion?

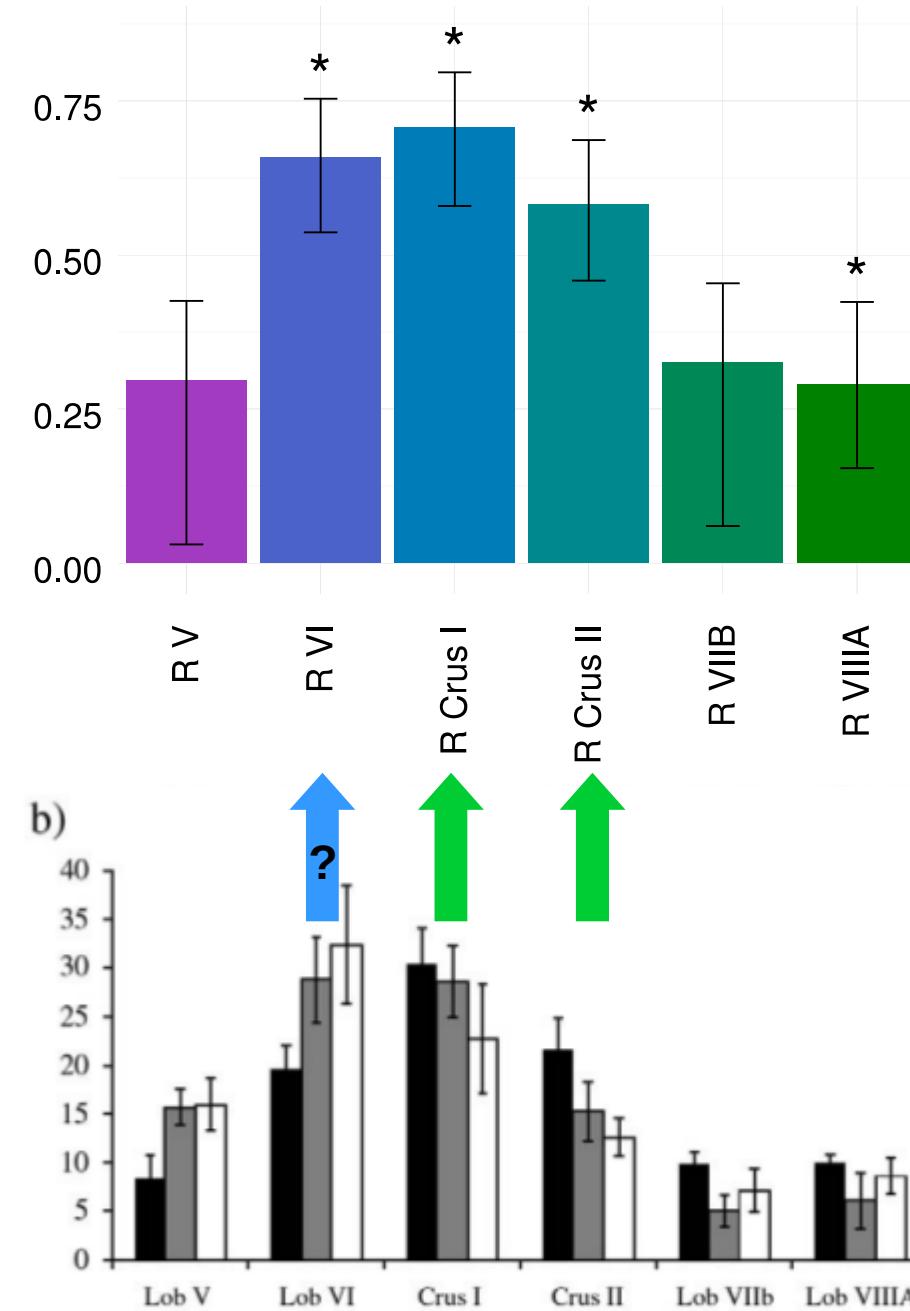


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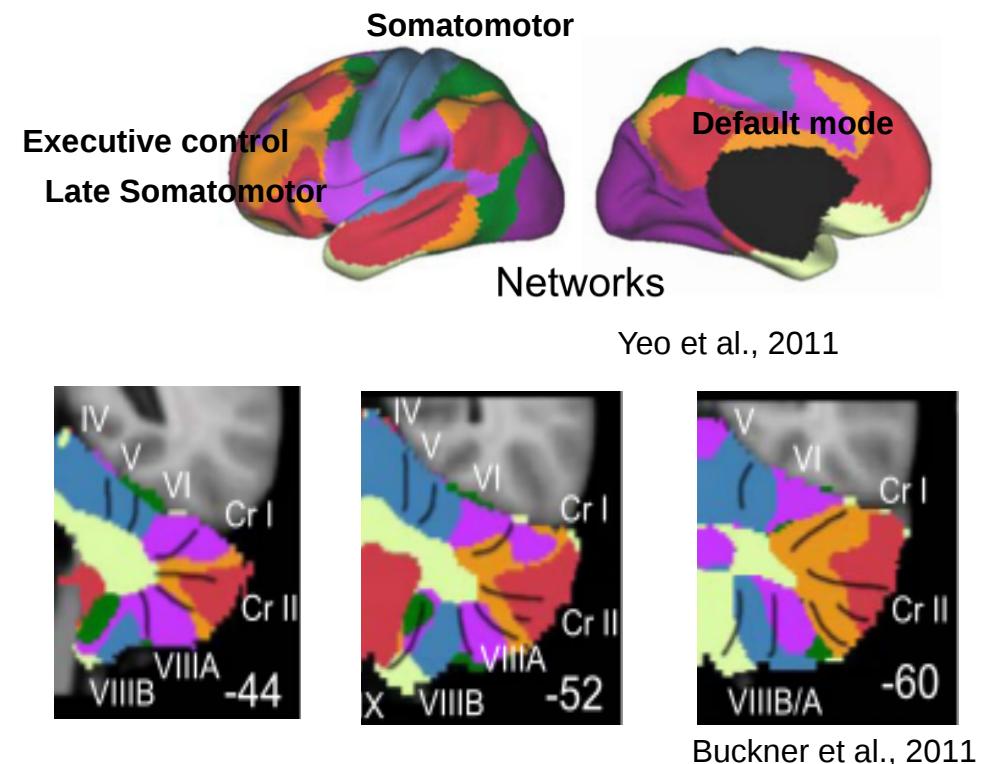
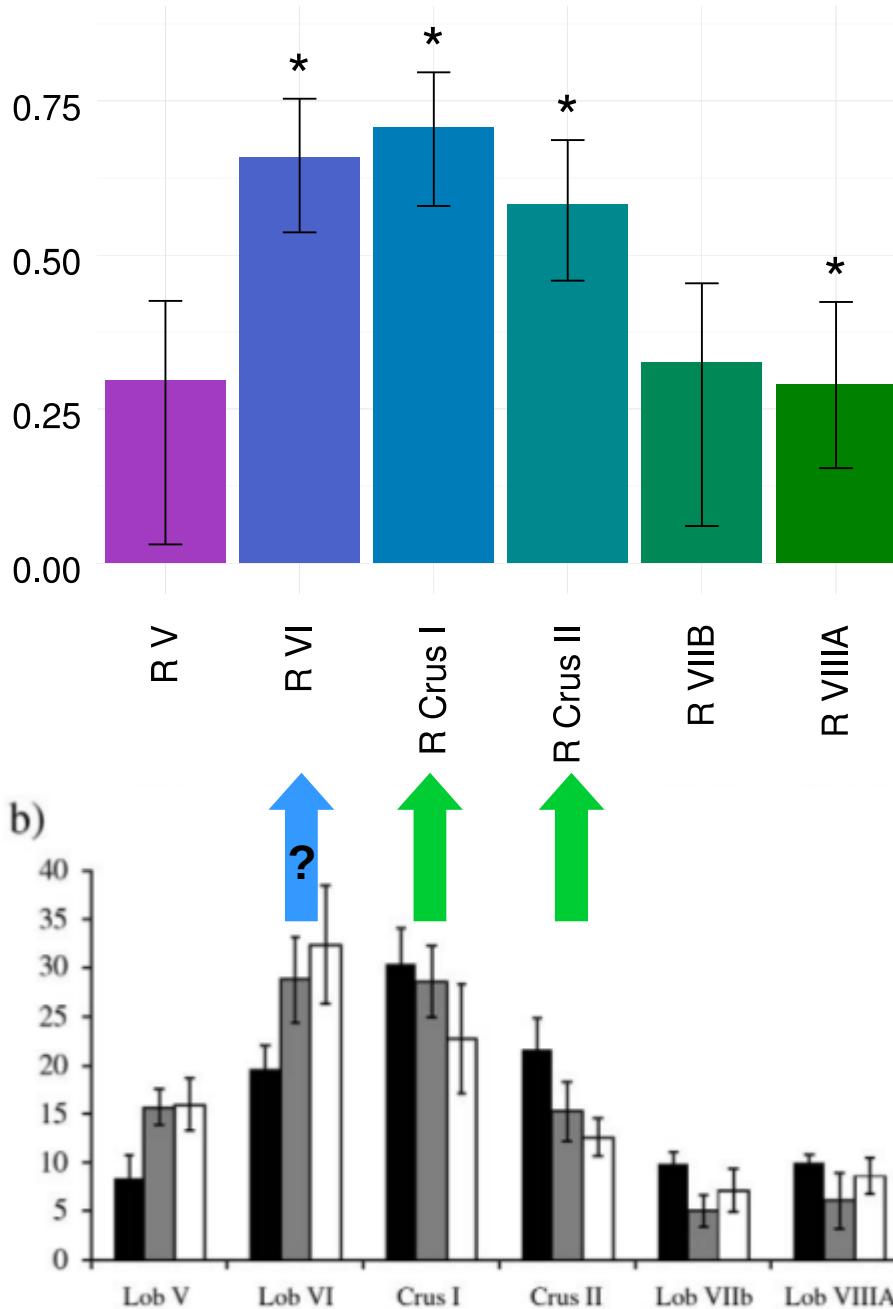


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Lobule VIIb	9.85	1.34	5.15	1.60	7.22	2.25
Lobule VIIIa	10.02	0.92	6.17	2.89	8.72	1.83



Related to selective evolutionary expansion?

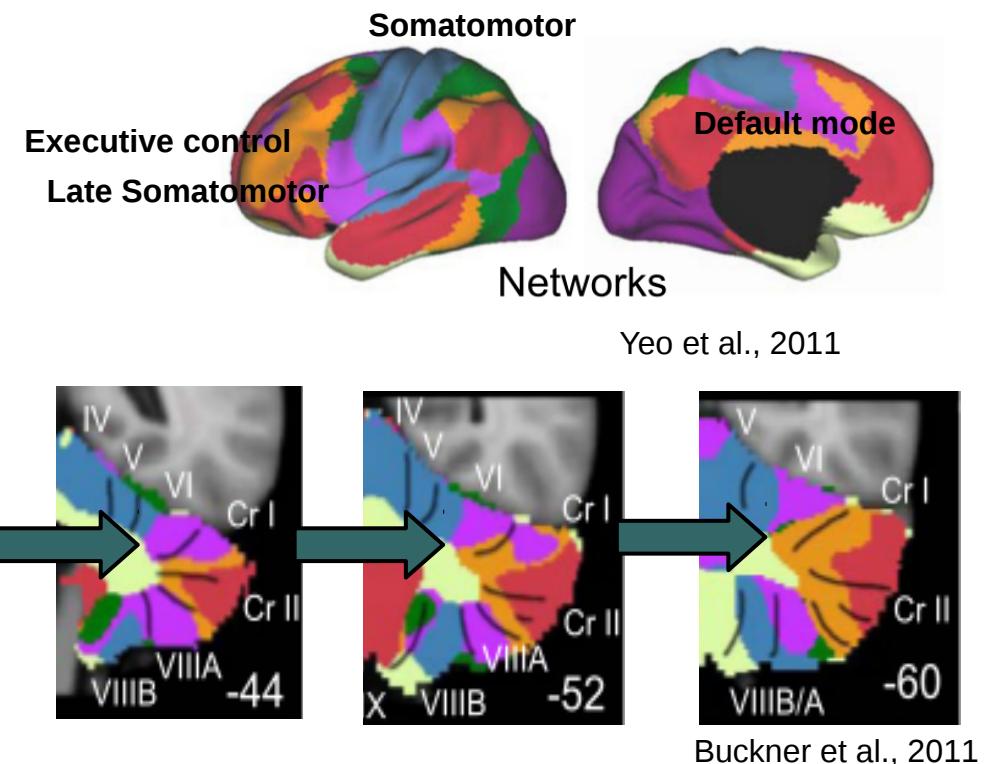
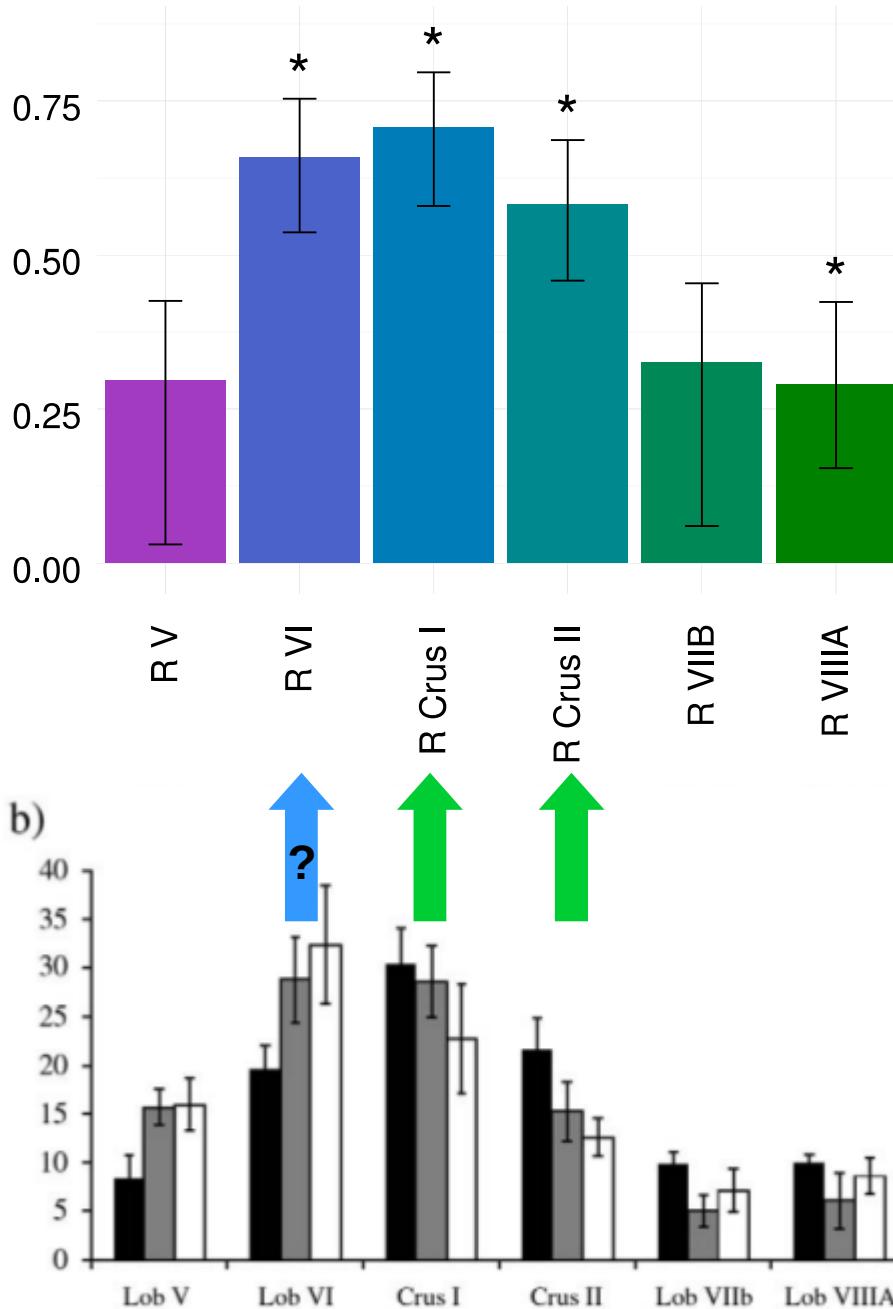


Averaged proportion of masked area occupied by a specific lobule across each primate species.

	Human		Chimp		Capuchin	
	Average (%)	SD	Average (%)	SD	Average (%)	SD
Lobule V	8.53	2.28	15.77	2.28	16.01	2.70
Lobule VI	19.56	2.49	28.86	4.41	32.49	6.04
Crus I	30.38	3.84	28.69	3.66	22.83	5.63
Crus II	21.65	3.23	15.36	3.05	12.72	1.94
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Wrap-up

- Population description of CB lobular structure
 - R vs L differences
 - Differential effect of gender
 - Covariance with cortex
- Lobule-specific differences in heritability
 - Controlled for total CB GM volume
 - Potential links with evolution
 - Vermal and X
 - Phylogenetically oldest and greatest heritability...



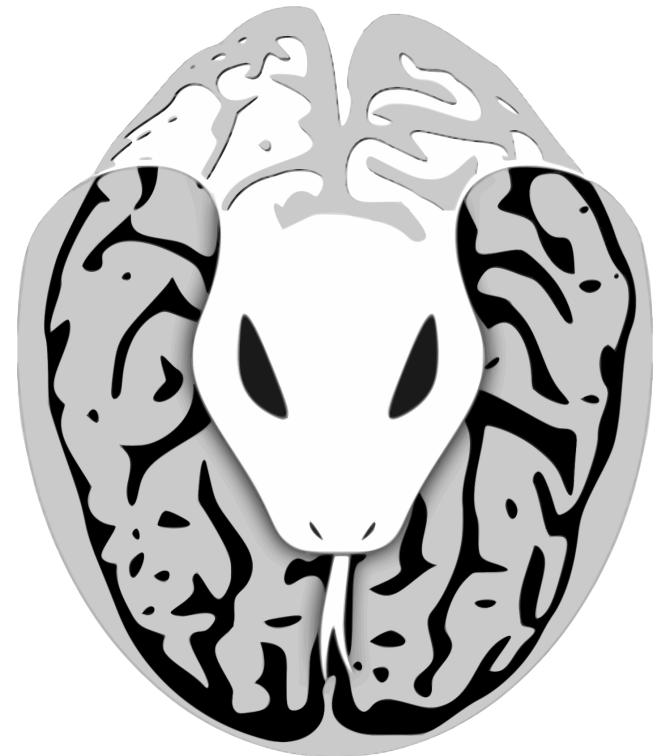
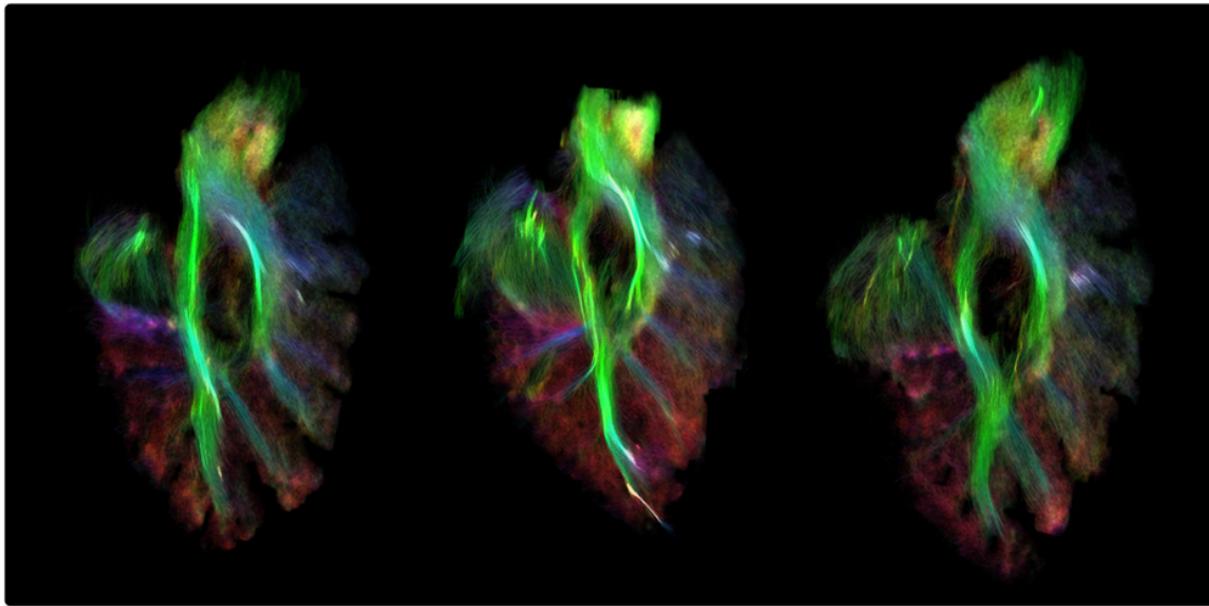
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... the cerebellum as a single unit?



Acknowledgements

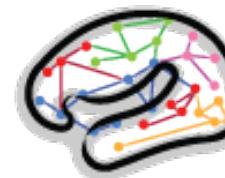


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