Structural brain development during adolescence and its relation to psychiatric disorders

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2016/17 Mozilla Fellow for Science

NSPN
NeuroScience in Psychiatry Network

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wellcome trust
Strategic Award
www.nspn.org.uk

2500+ participants at three time points

700 had in unit assessments for cognitive testing
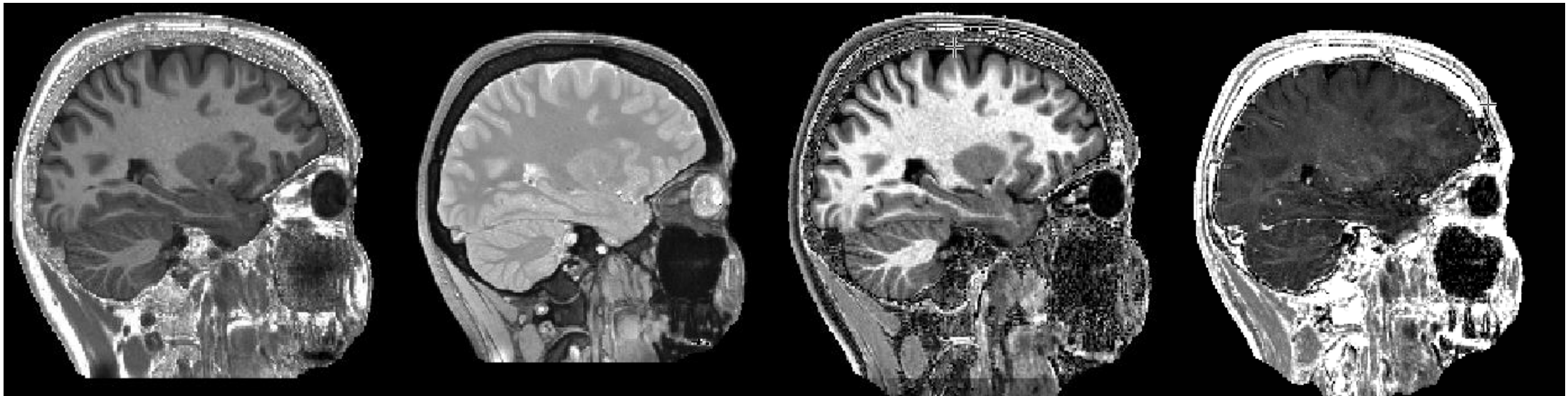
322 questionnaire measures

300 had MRI scans

Quantitative multi-parameter mapping of R1, PD*, MT, and R2* at 3T: a multi-center validation

Nikolaus Weiskopf[1*], John Suckling[2,3,4], Guy Williams[3,5], Marta M. Correia[6], Becky Inkster[2], Roger Tait[3], Cinly Ooi[2,3], Edward T. Bullmore[2,3,4,7] and Antoine Lutti[1,8]
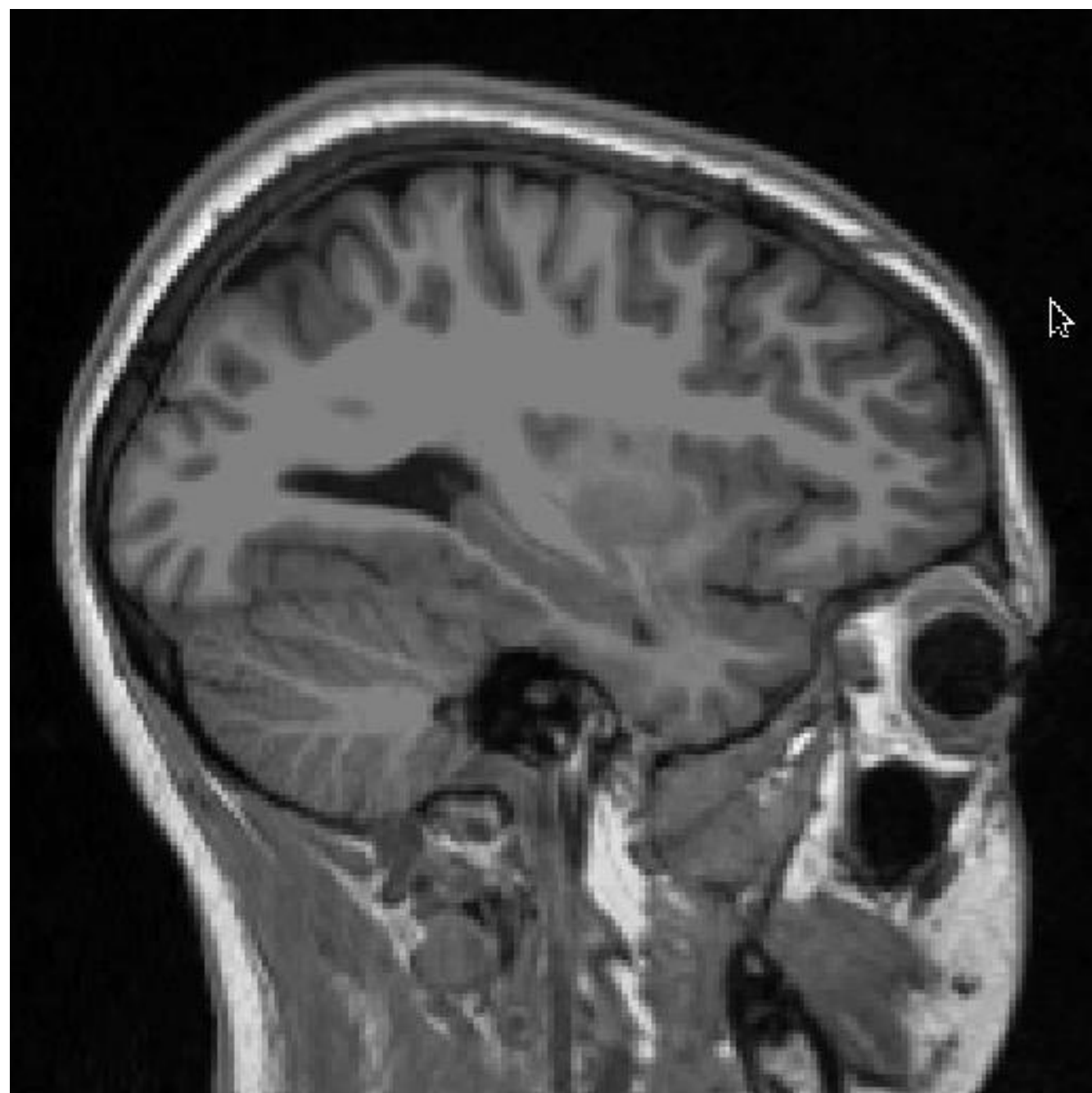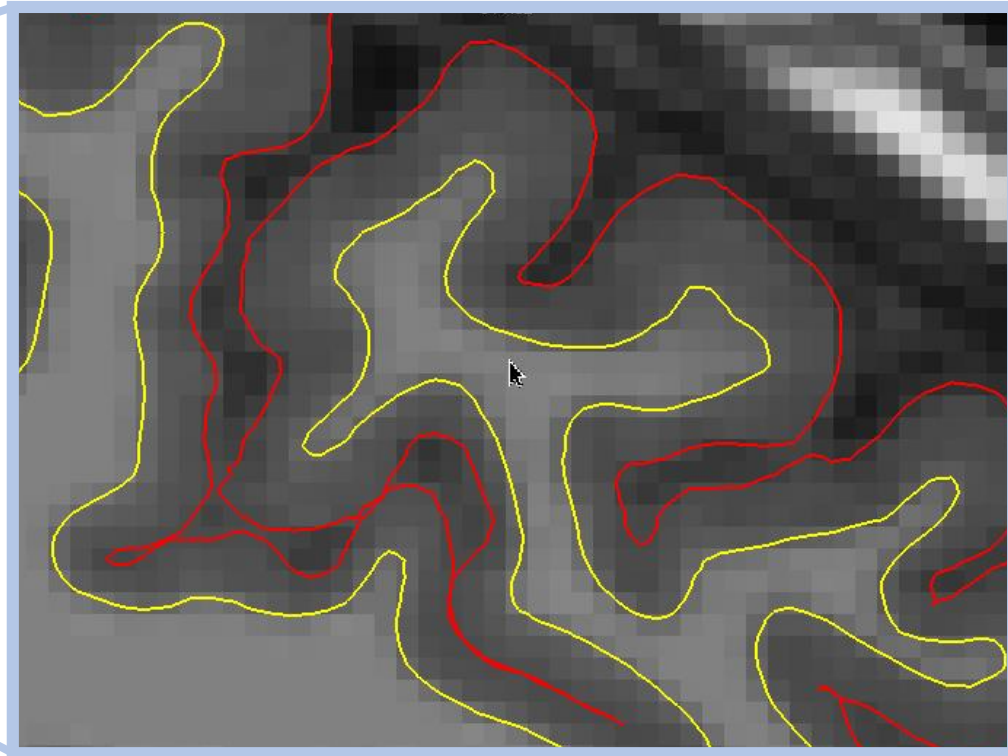
R1 (1/T1)
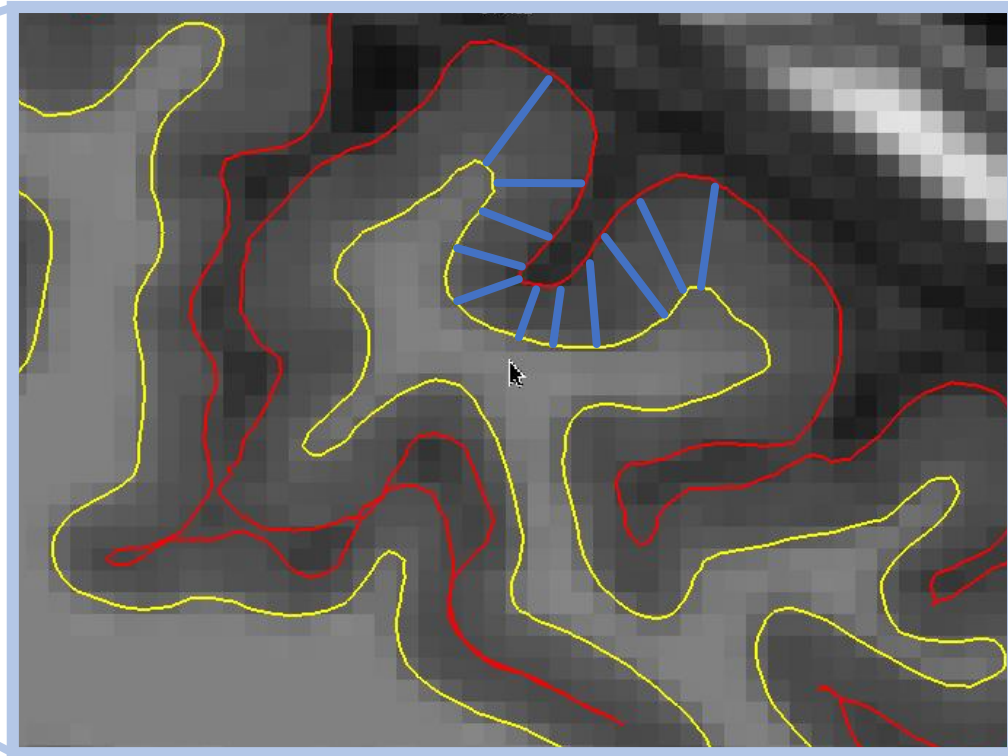Longitudinal relaxation time

Proton Density
(A)

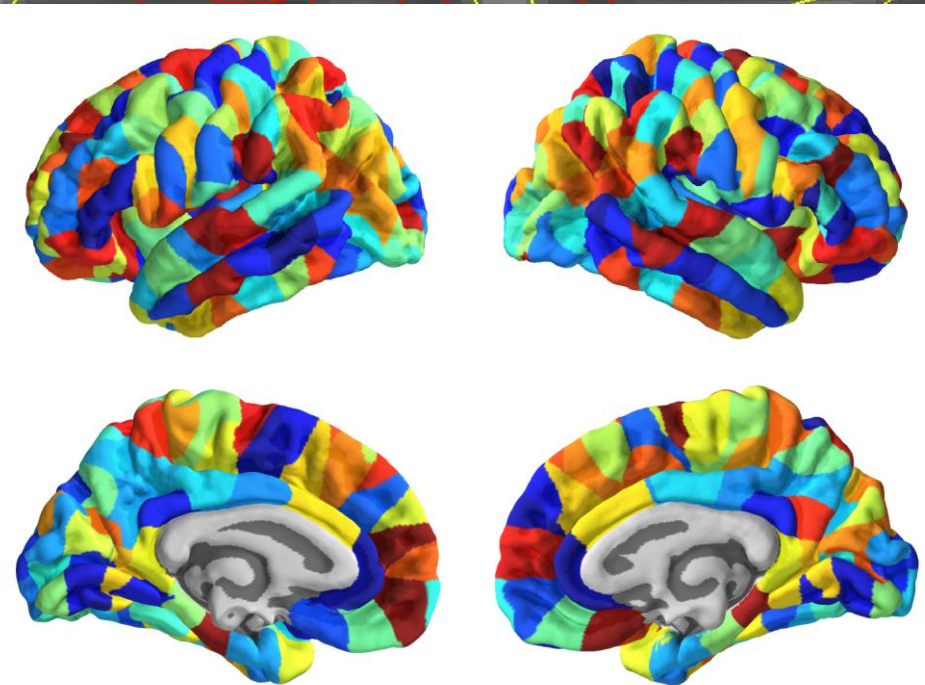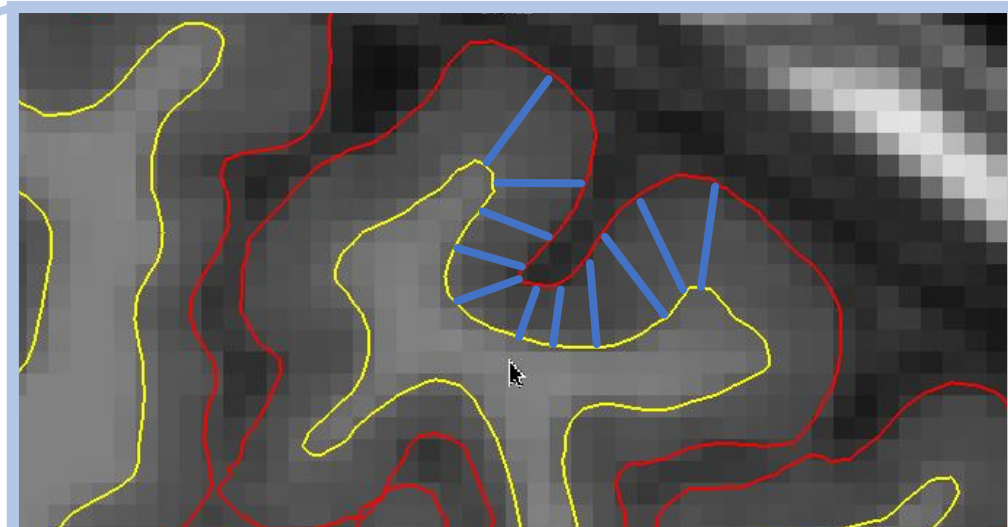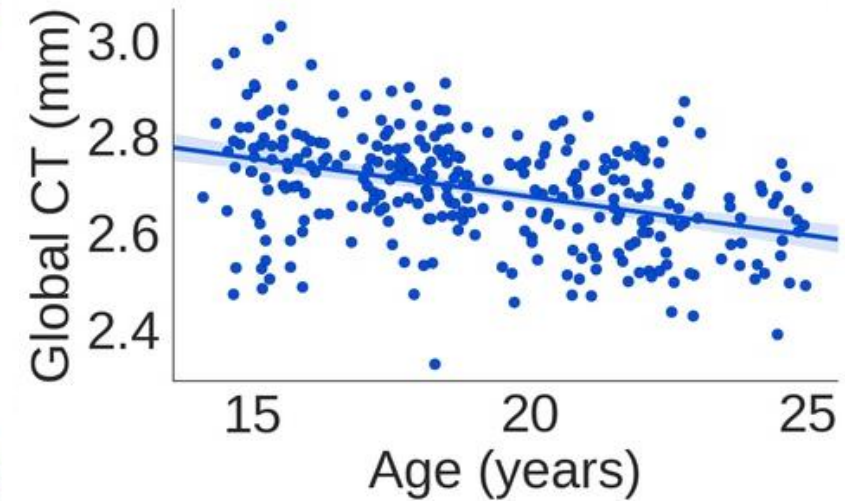Magnetisation Transfer
(MT)

R2* (1/T2*)
Transverse relaxation time

Weiskopf et al, NeuroImage, 2011; Callaghan et al, Neurobiology of Aging, 2014; Lutti et al, NeuroImage, 2014
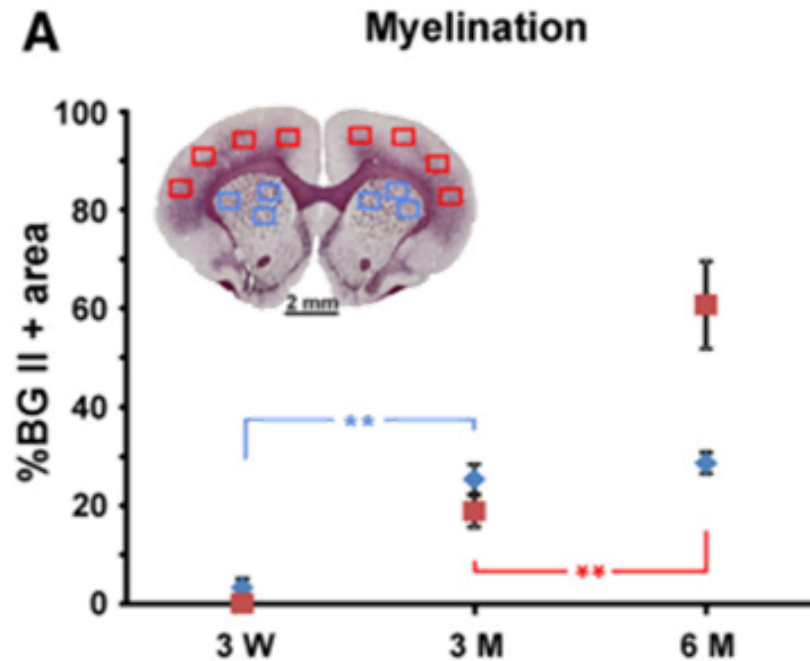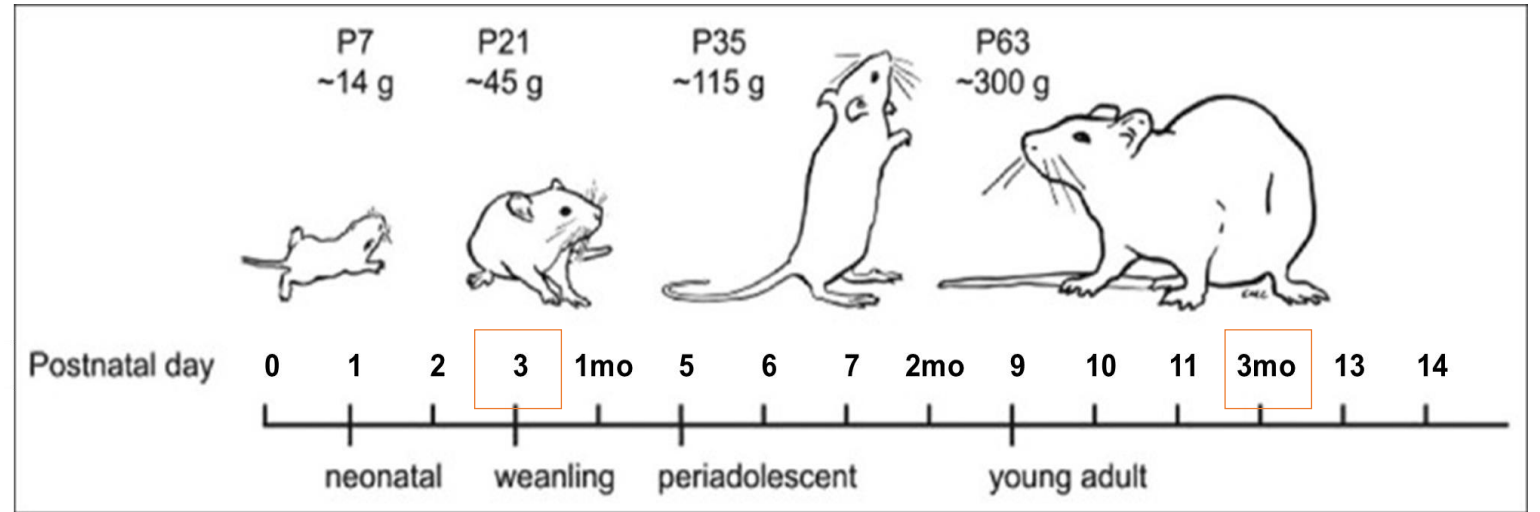
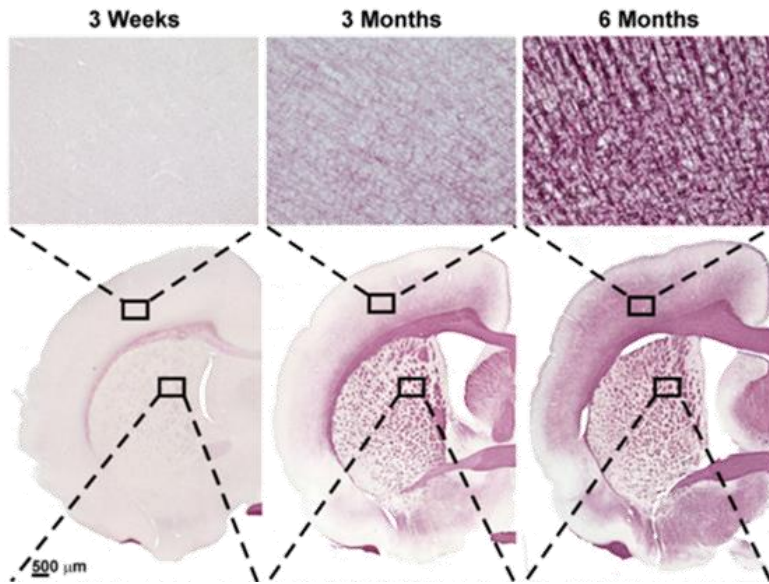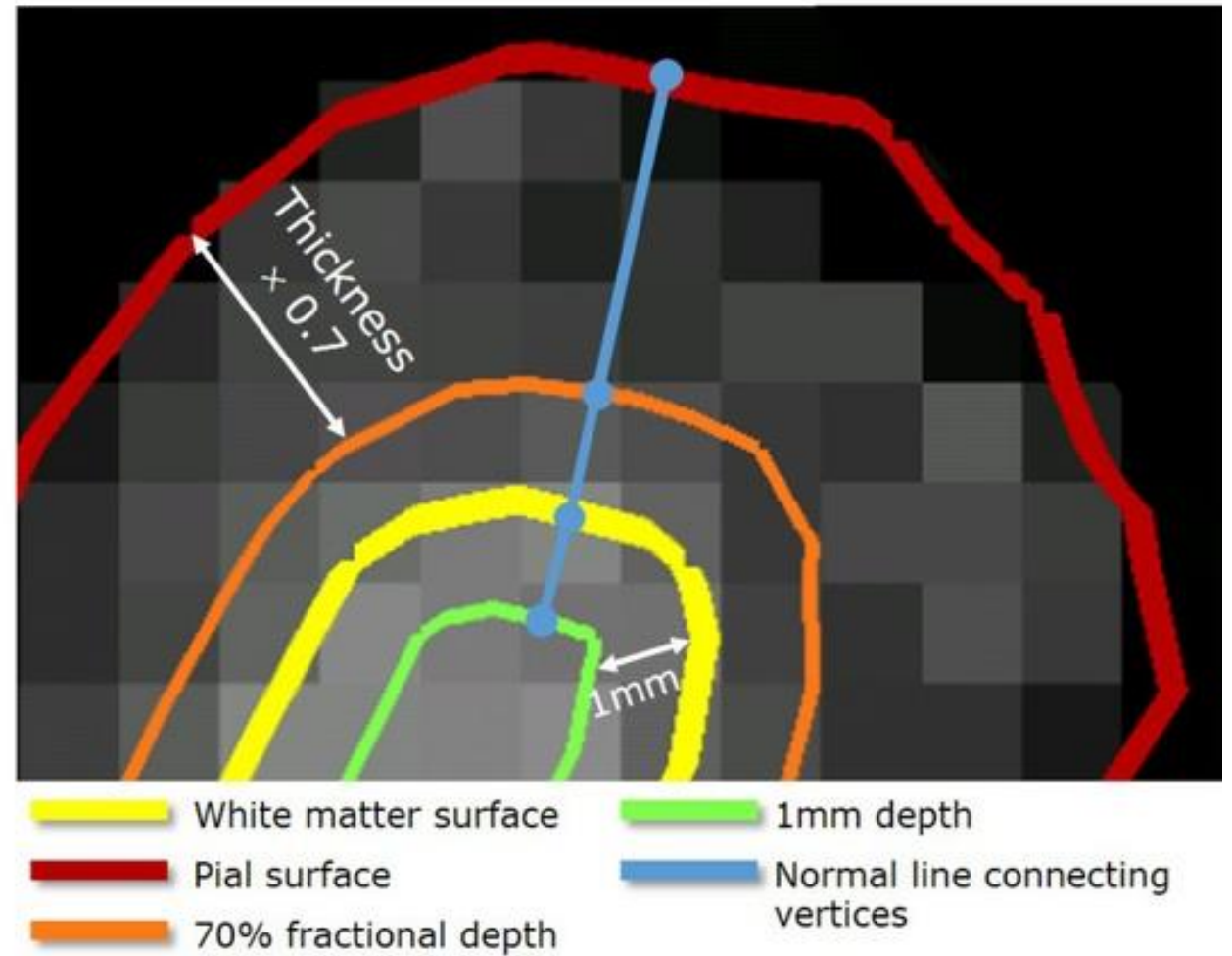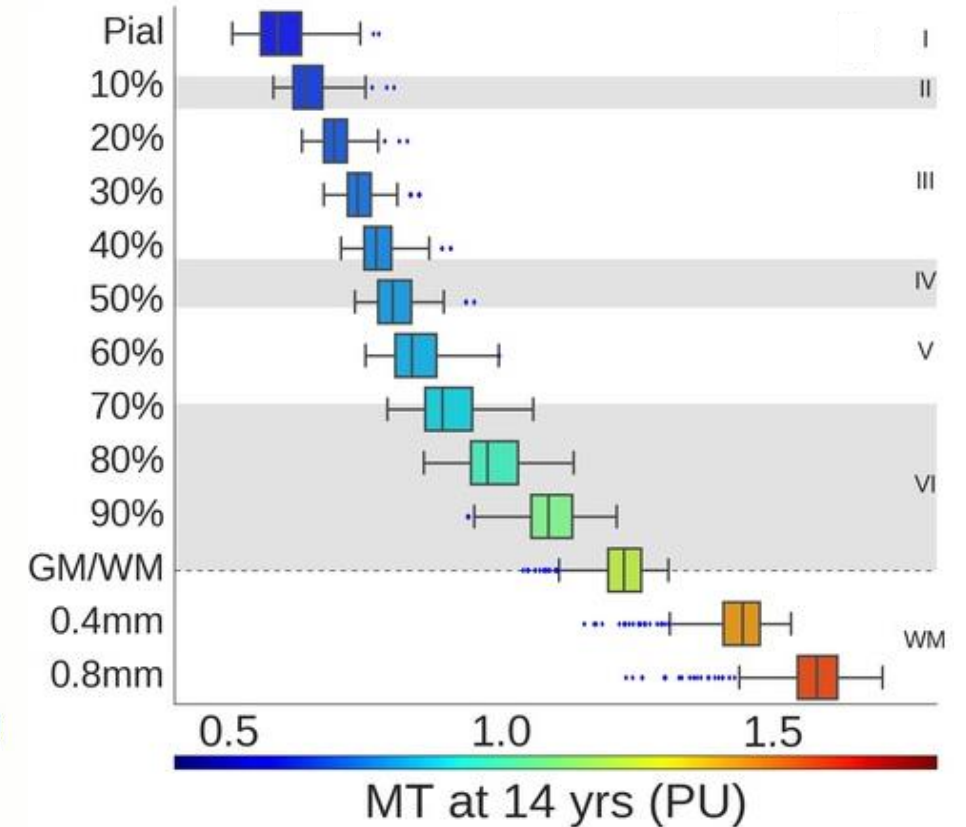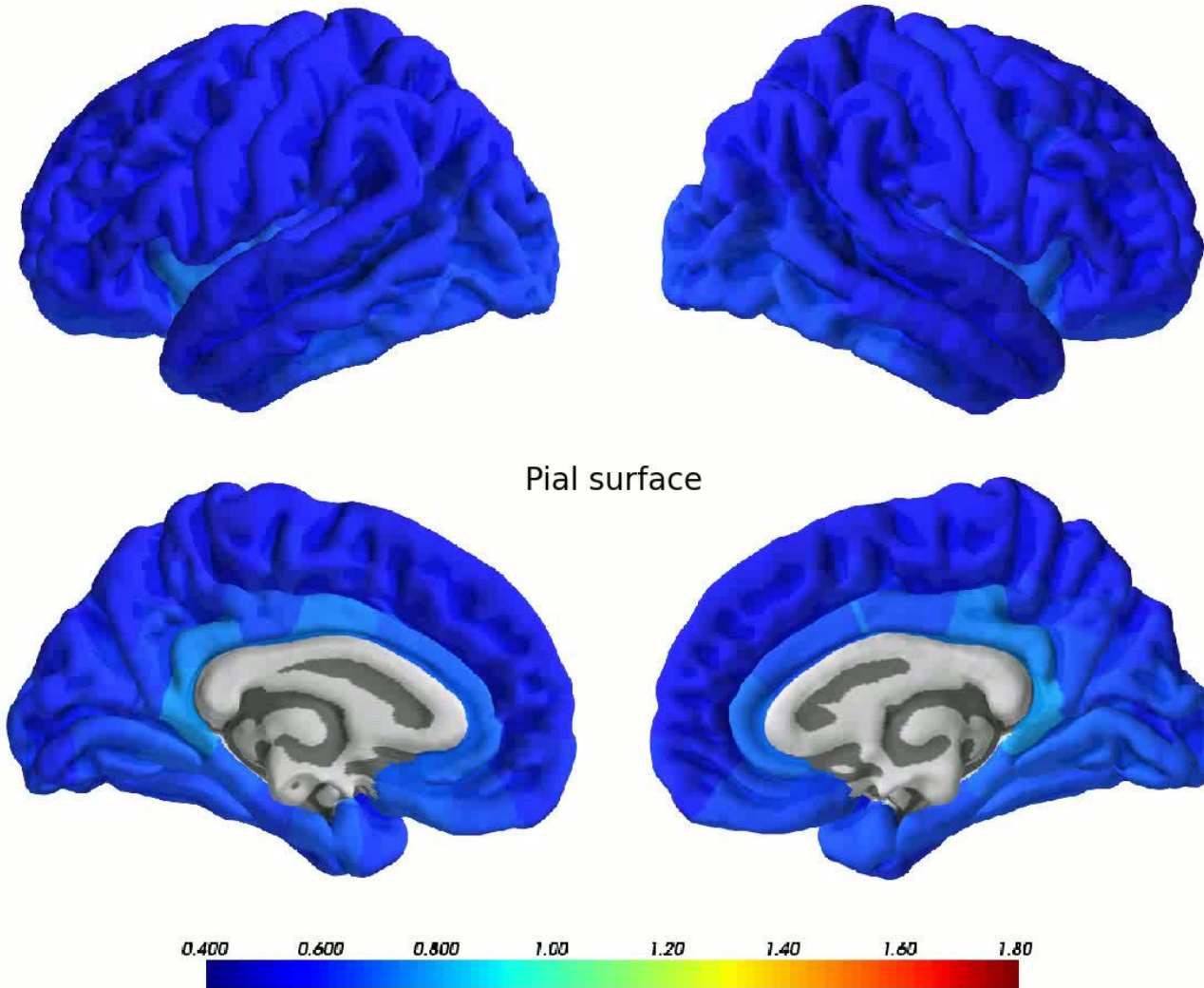# Cortical thickness is regionally patterned, and decreases through adolescence

Whitaker*, Vertes* et al, PNAS, 2016

A Myelination

B Cell Density

Mengler et al, NeuroImage, 2014

White matter surface   1mm depth
Pial surface   Normal line connecting vertices
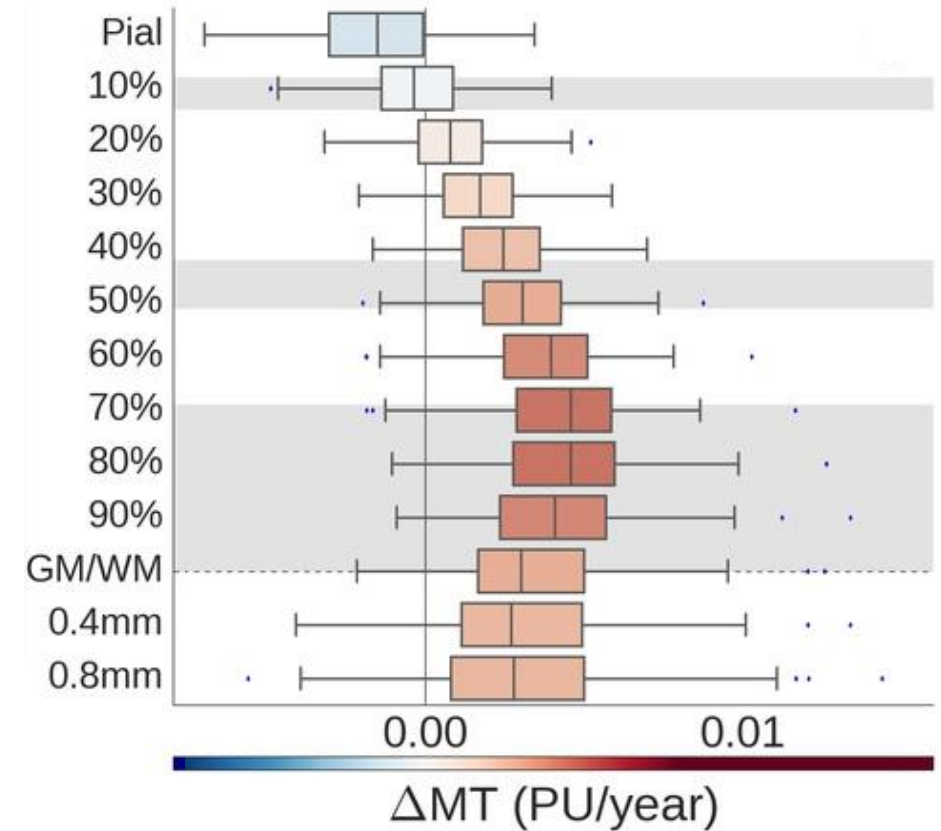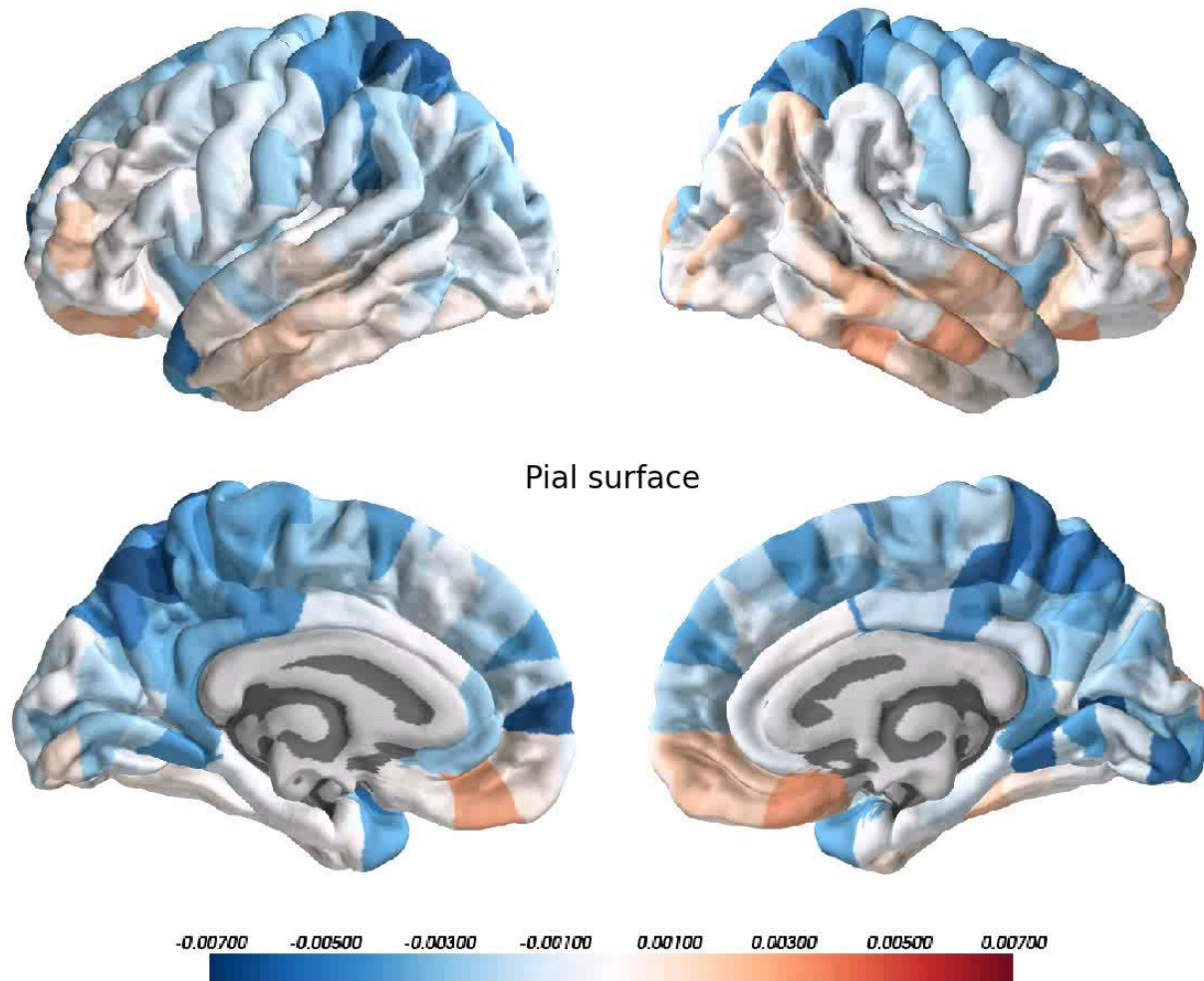70% fractional depth

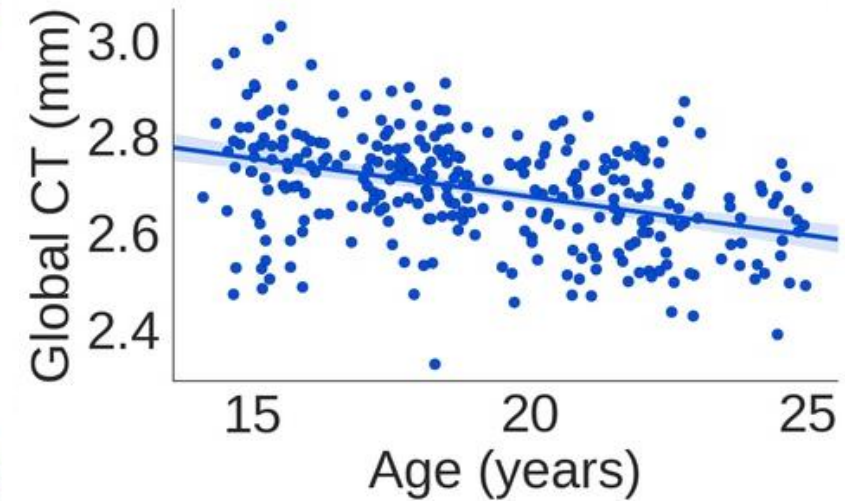Whitaker*, Vertes* et al, PNAS, 2016
Rosas et al, Neurology, 2002

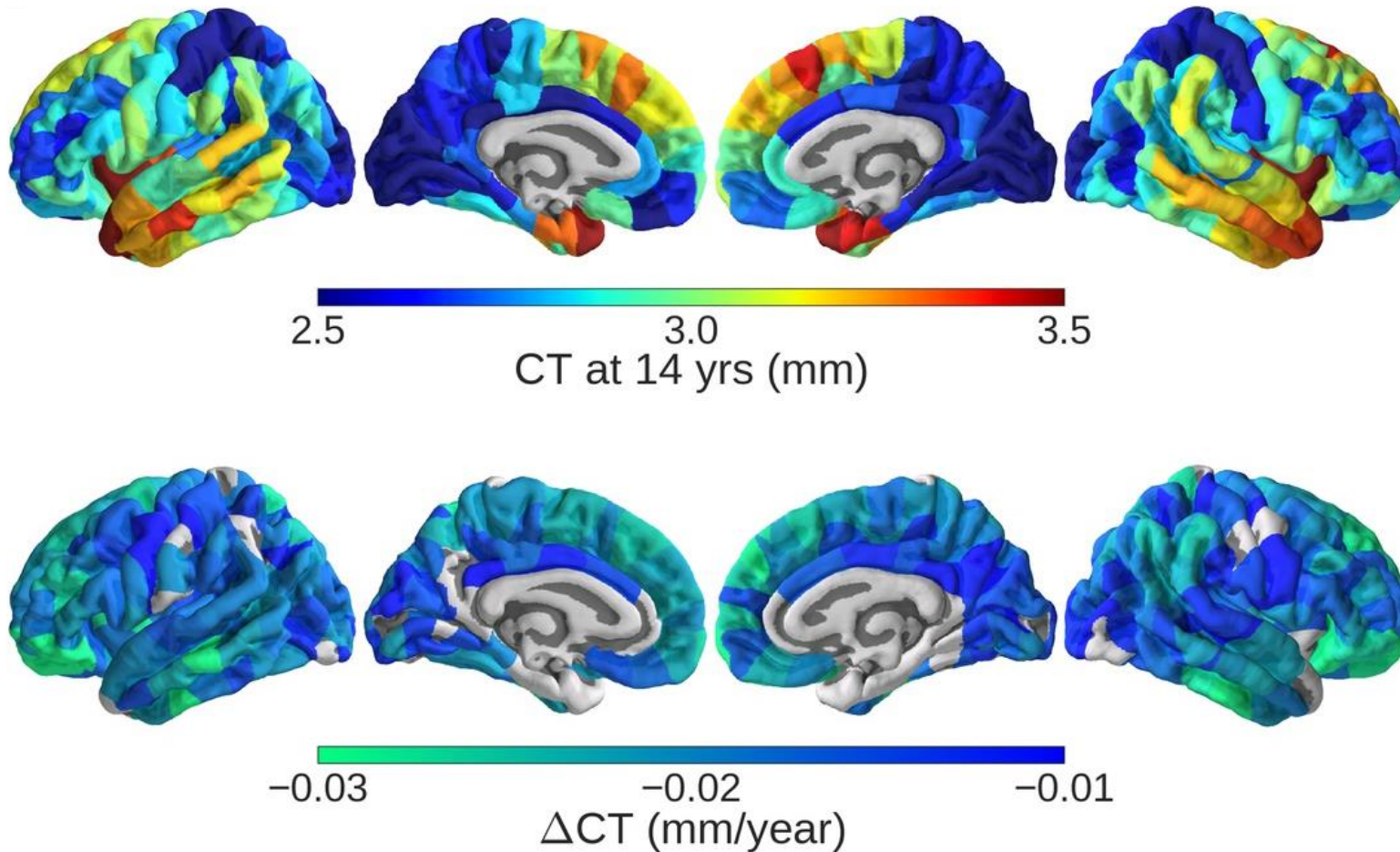# Magnetisation transfer increases from the pial surface into white matter

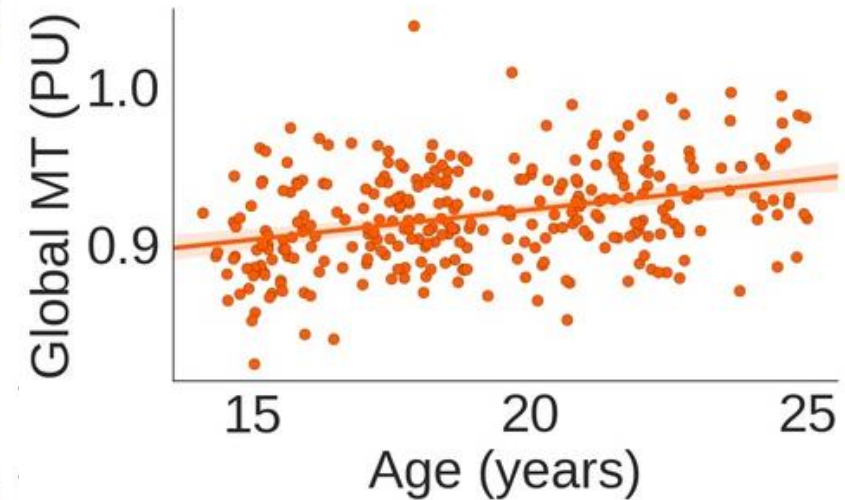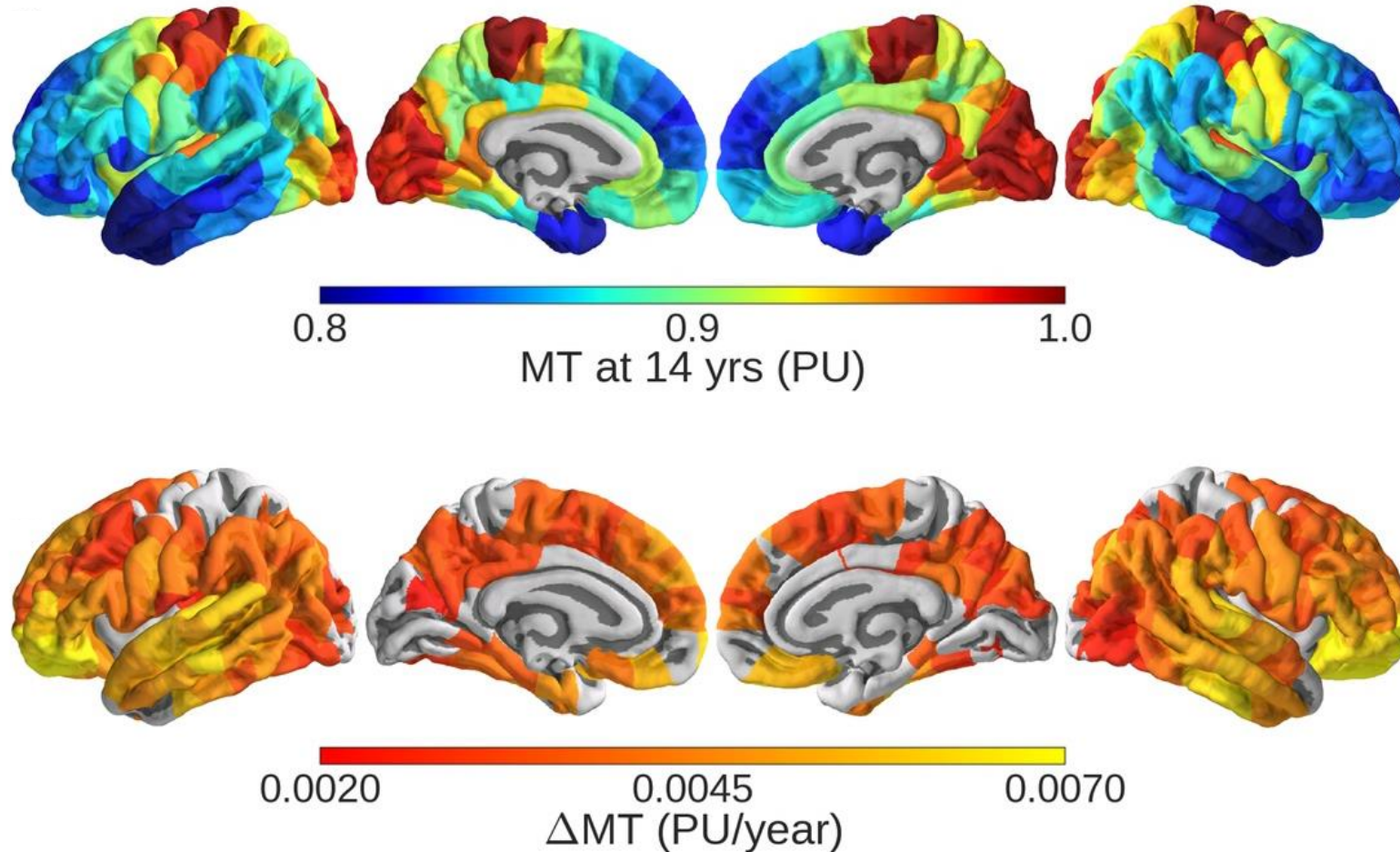

Pial surface

Whitaker*, Vertes* et al, PNAS, 2016

Greatest magnetisation transfer increases during adolescence are within cortex

Pial surface

Whitaker*, Vertes* et al, PNAS, 2016

Cortical thickness is regionally patterned, and decreases through adolescence

CT at 14 yrs (mm)

$\triangle$CT (mm/year)

Intra-cortical magnetisation transfer increases through adolescence

MT at 14 yrs (PU)
0.8   0.9   1.0

ΔMT (PU/year)
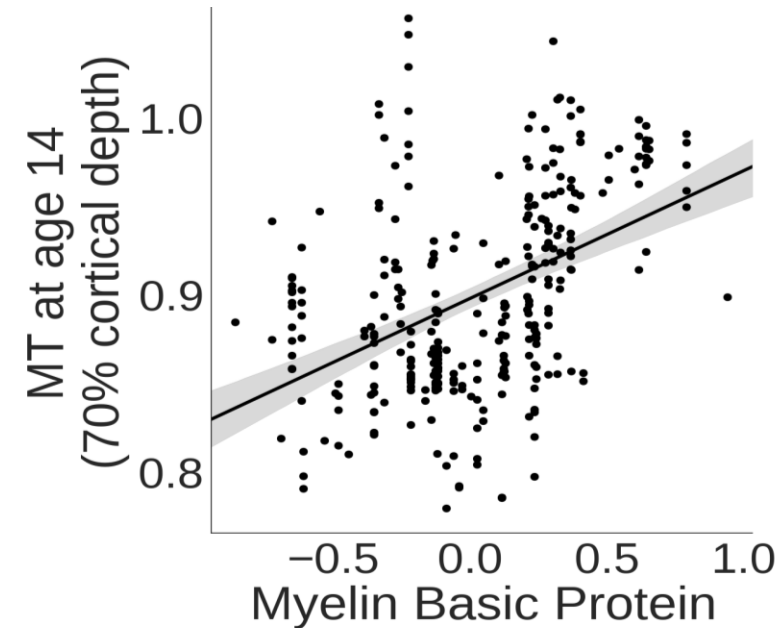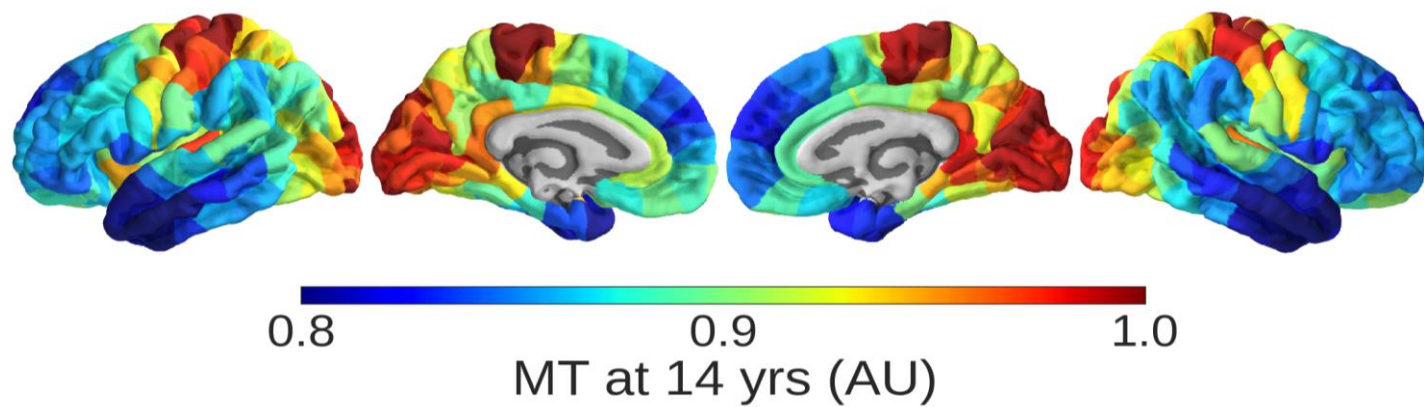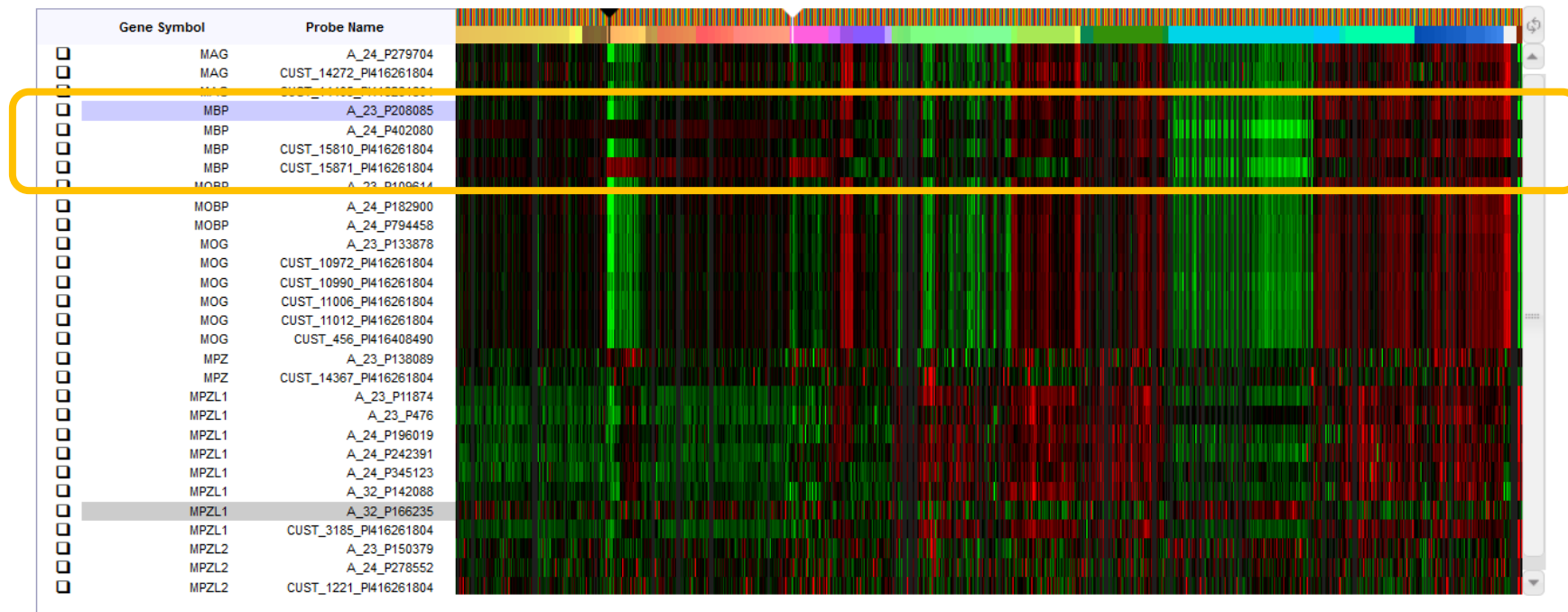0.0020   0.0045   0.0070

Whitaker*, Vertes* et al, PNAS, 2016

Take home:

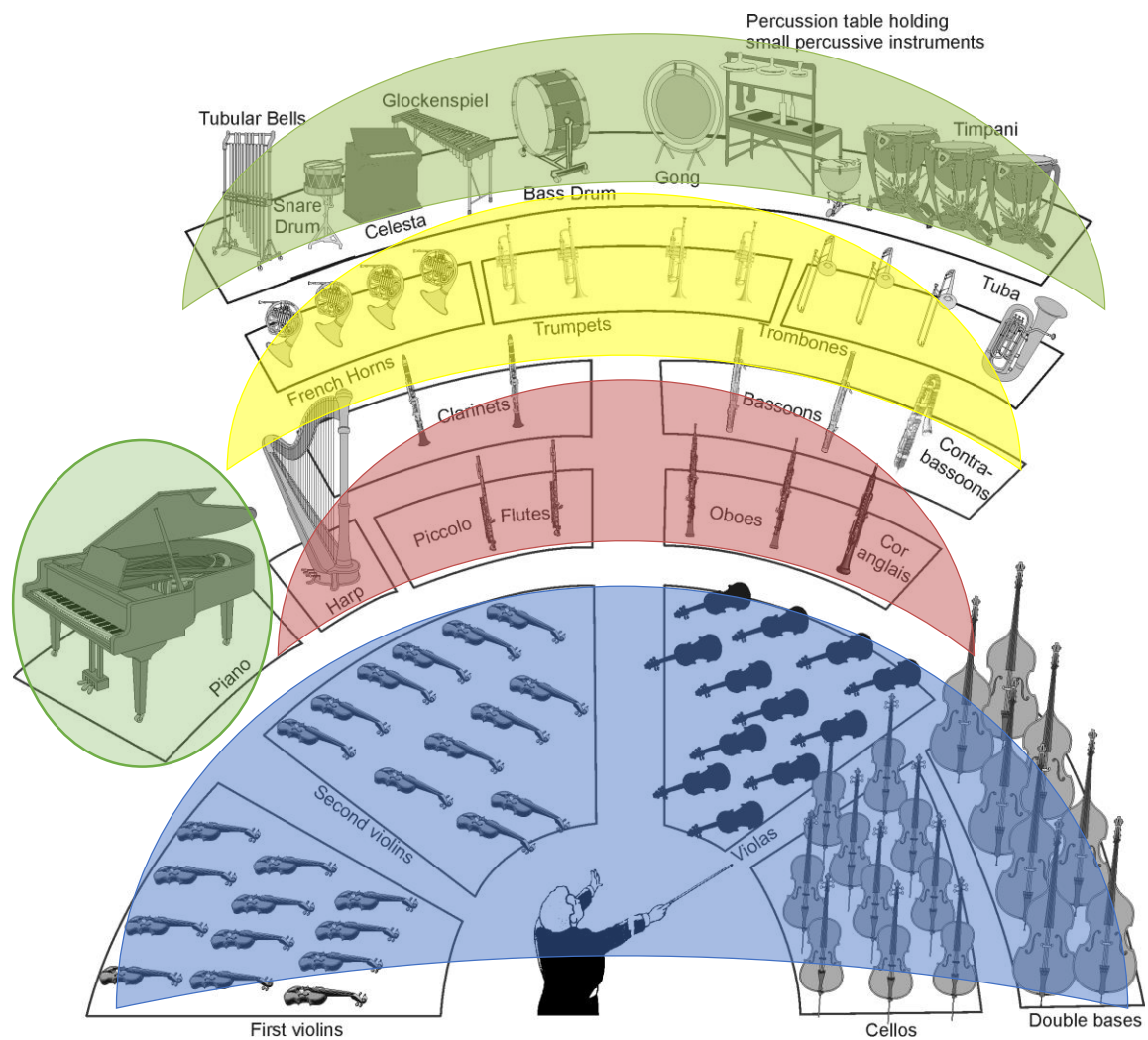adolescent age-related changes in myelin are located within cortex

Dr Petra Vértes
MRC Bioinformatics Fellow

Shen et al, Trends in Neurosciences, 2012

ALLEN BRAIN ATLAS
DATA PORTAL

HOME   GET STARTED   HELP   HUMAN BRAIN ⌄

MICROARRAY   ISH DATA   MRI   DOWNLOAD   BRAIN EXPLORER   DOCUMENTATION   HELP

Gene Symbol	Probe Name
MAG	A_24_P279704
MAG	CUST_14272_PI416261804
MAG	CUST_14405_PI416261804
MBP	A_23_P208085
MBP	A_24_P402080
MBP	CUST_15810_PI416261804
MBP	CUST_15871_PI416261804
MOBP	A_23_P109614
MOBP	A_24_P182900
MOBP	A_24_P794458
MOG	A_23_P133878
MOG	CUST_10972_PI416261804
MOG	CUST_10990_PI416261804
MOG	CUST_11006_PI416261804
MOG	CUST_11012_PI416261804
MOG	CUST_456_PI416408490
MPZ	A_23_P138089
MPZ	CUST_14367_PI416261804
MPZL1	A_23_P11874
MPZL1	A_23_P476
MPZL1	A_24_P196019
MPZL1	A_24_P242391
MPZL1	A_24_P345123
MPZL1	A_32_P142088
MPZL1	A_32_P166235
MPZL1	CUST_3185_PI416261804
MPZL2	A_23_P150379
MPZL2	A_24_P278552
MPZL2	CUST_1221_PI416261804

https://www.alleninstitute.org
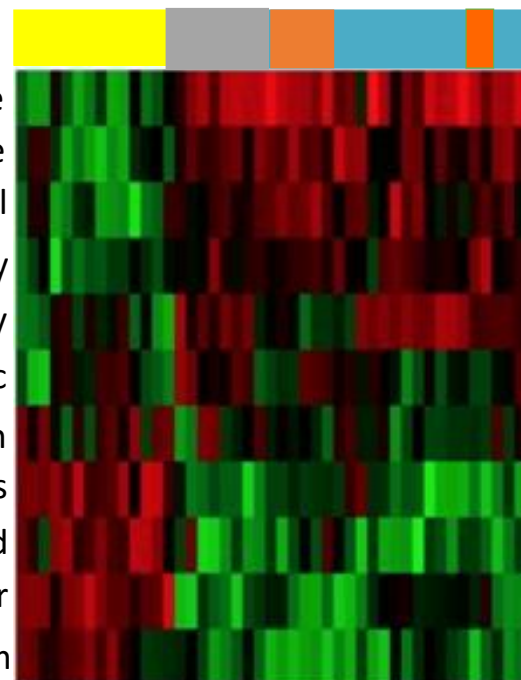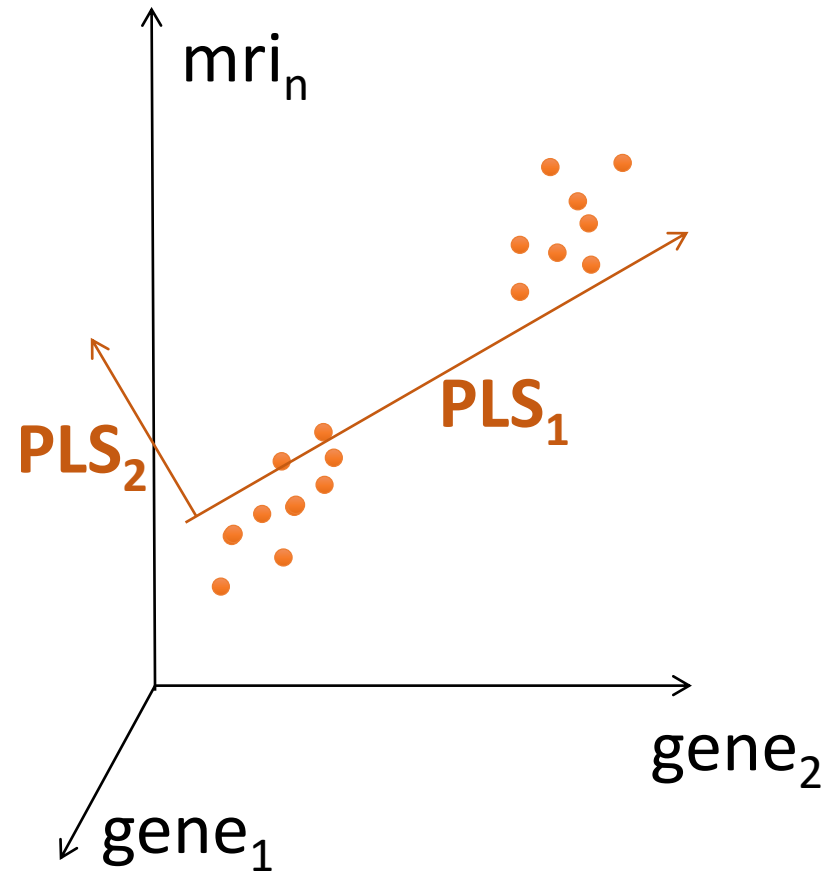
MT at 14 yrs (AU)

Whitaker*, Vertes* et al, PNAS, 2016

Sections of Orchestra
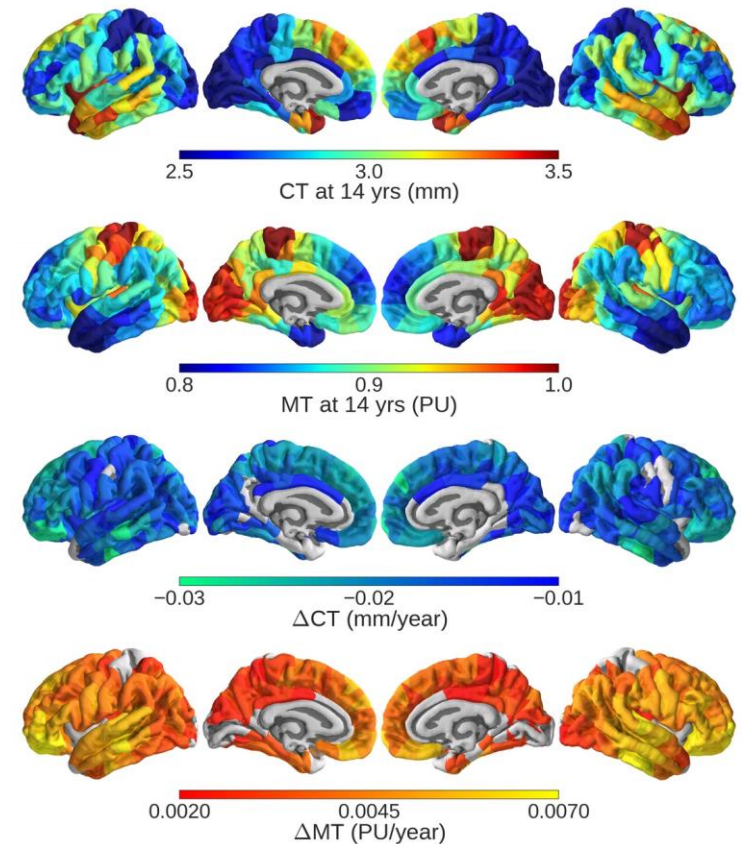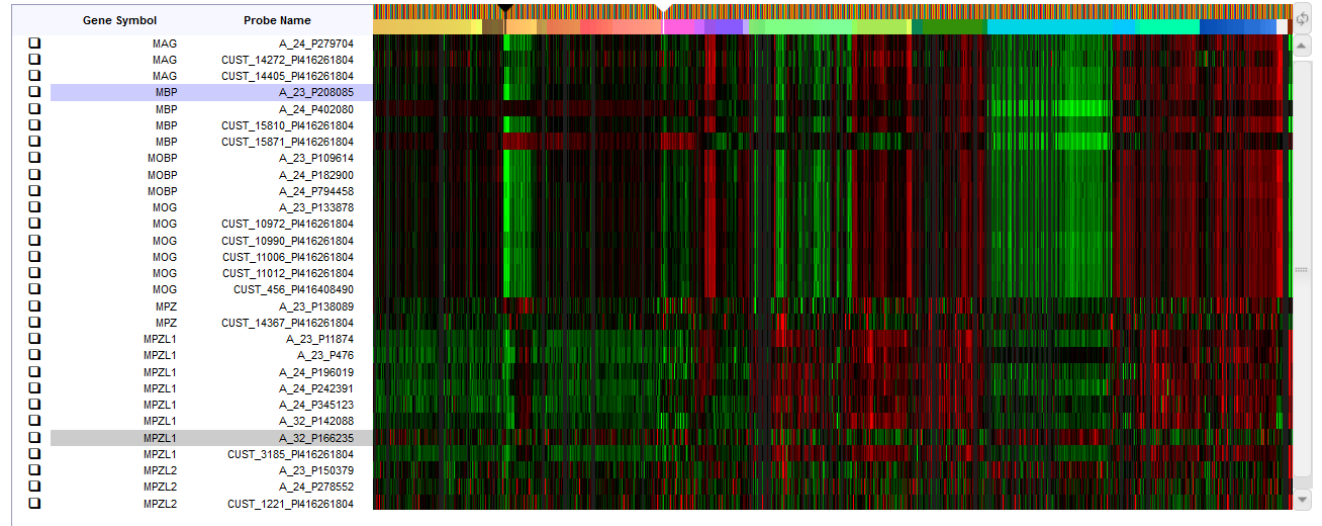
Wood: maple
Wood: spruce
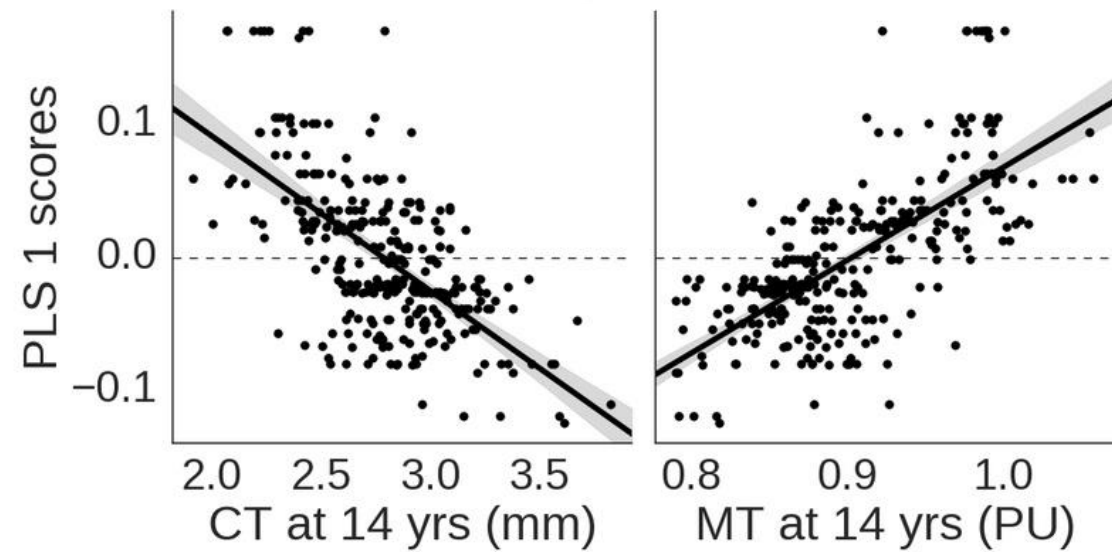steel
ivory
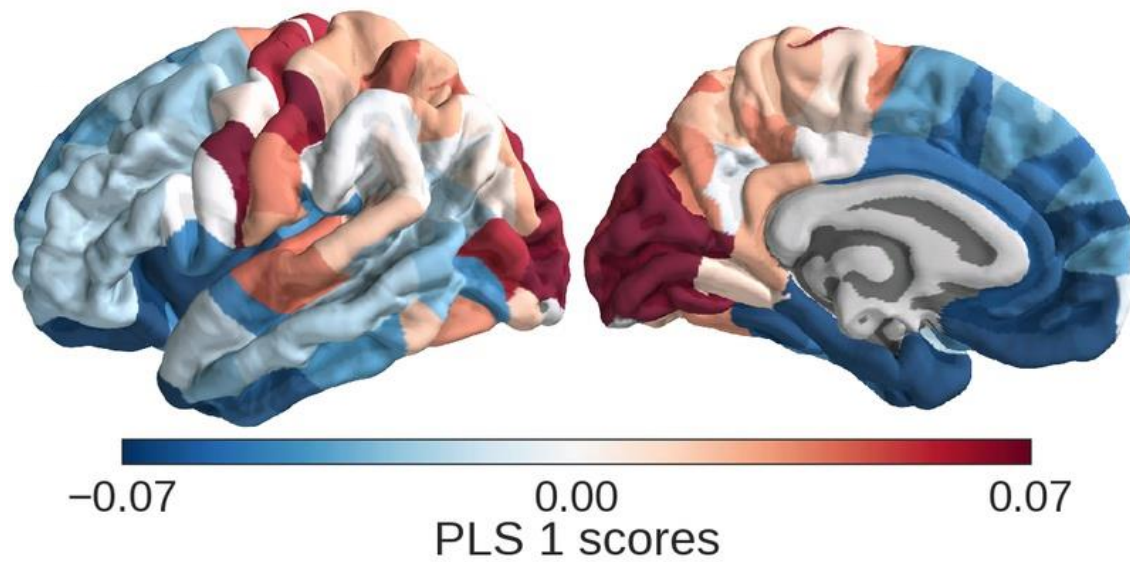ebony
plastic
resin
brass
gold
silver
aluminum

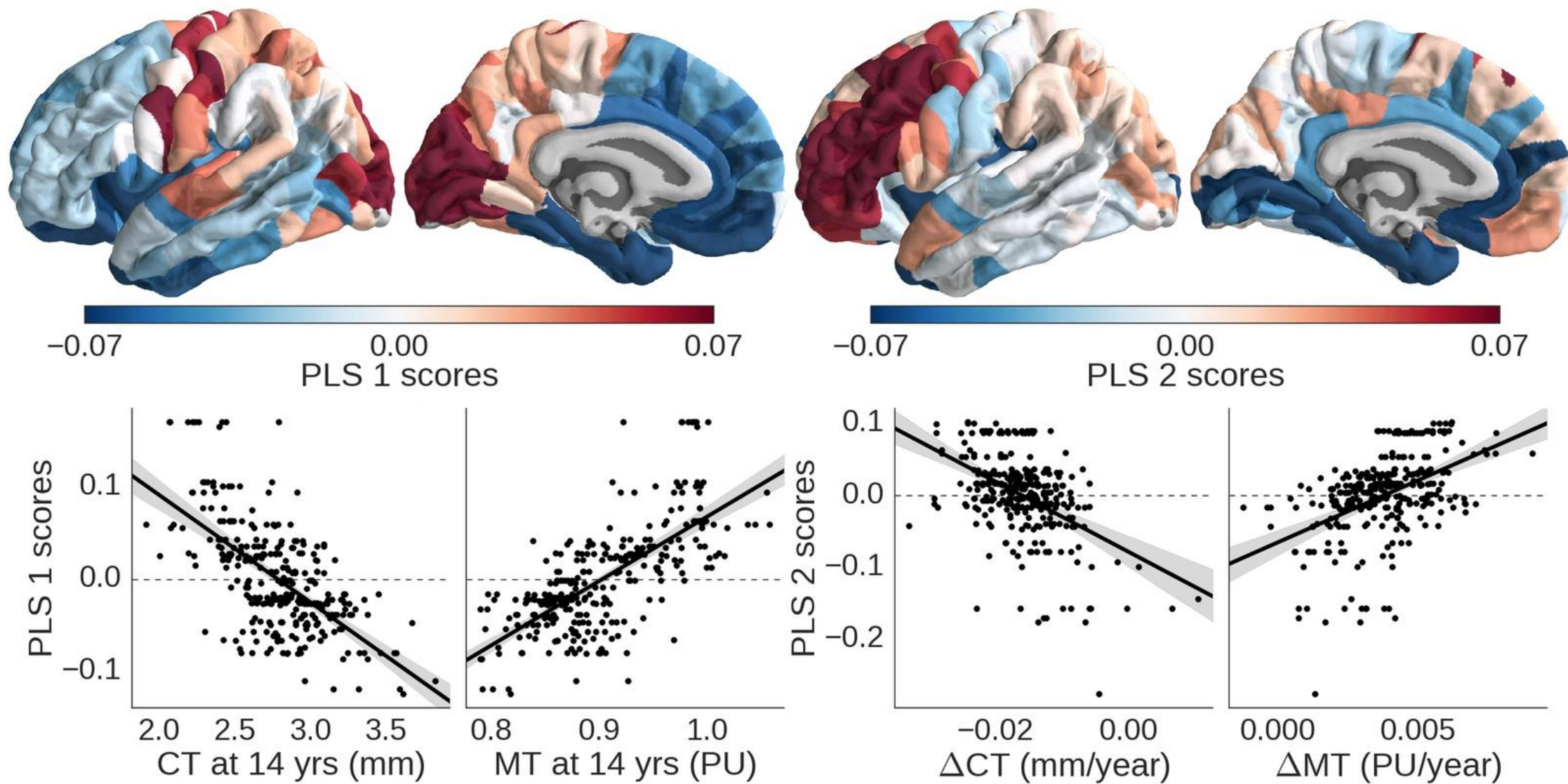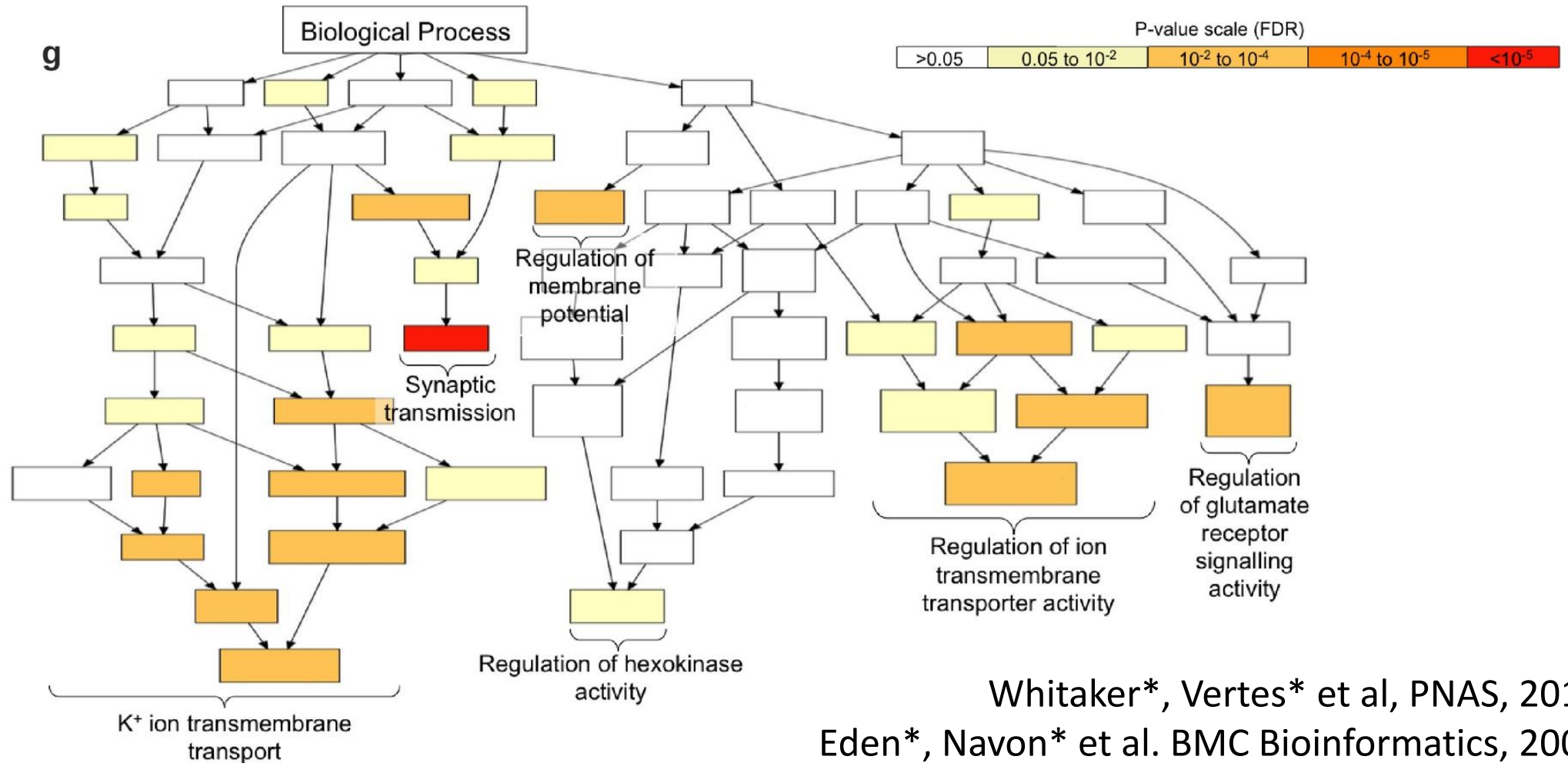**Dr Petra Vértes**
MRC
Bioinformatics
Fellow

$$PLS_1 = w_1 \, gene_1 + w_2 \, gene_2 + \dots + w_n \, gene_n$$

PLS 1 scores

Whitaker*, Vertes* et al, PNAS, 2016

Whitaker*, Vertes* et al, PNAS, 2016

Genes relating to regulation of synapses are expressed in regions changing during adolescence

Whitaker*, Vertes* et al, PNAS, 2016
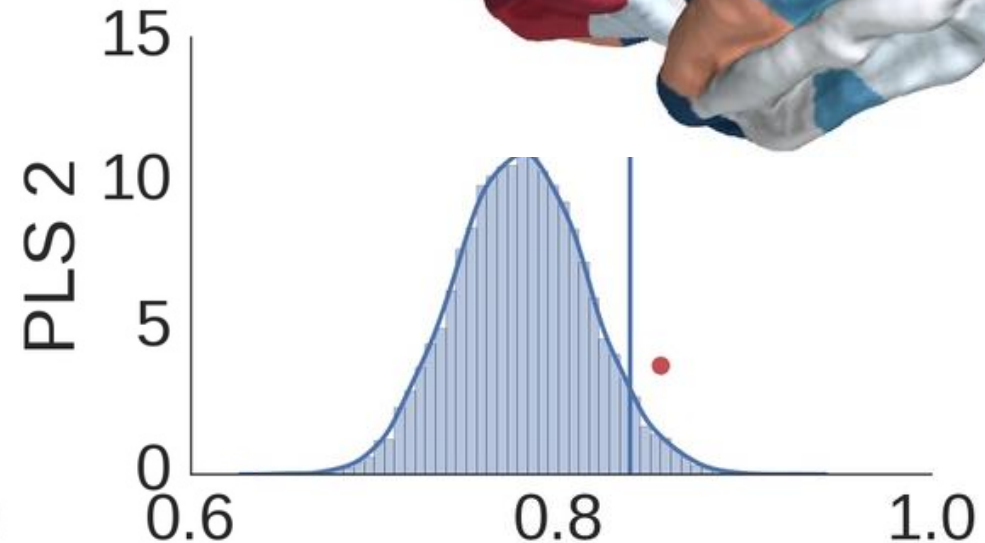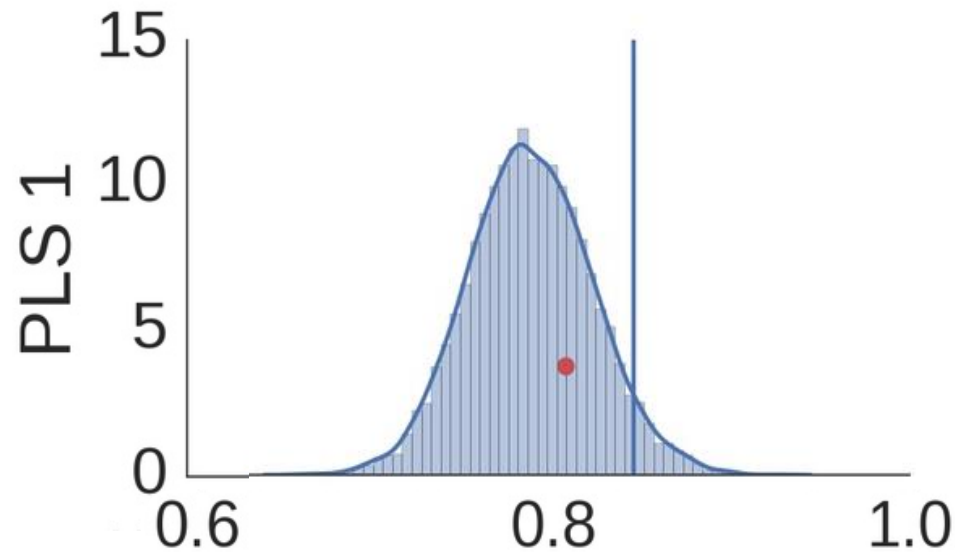Eden*, Navon* et al. BMC Bioinformatics, 2009
http://cbl-gorilla.cs.technion.ac.il

Genes relating to risk of schizophrenia are expressed in regions changing during adolescence

Whitaker*, Vertes* et al, PNAS, 2016
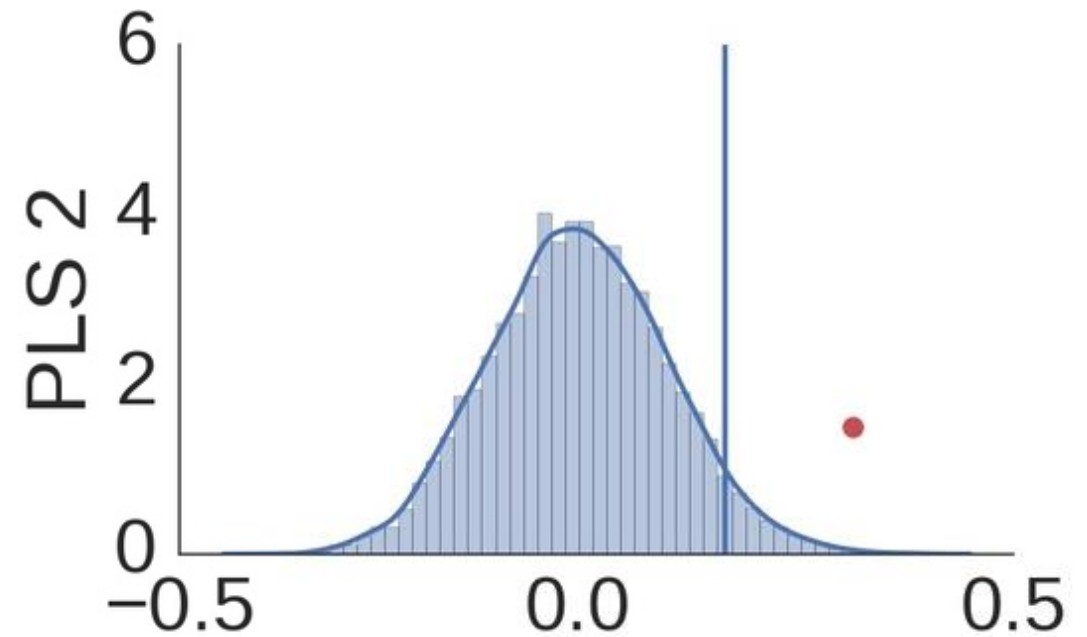
Ripke et al, Nature, 2014

A Transcriptome Database for Astrocytes, Neurons, and Oligodendrocytes: A New Resource for Understanding Brain Development and Function

John D. Cahoy,[1,2]* Ben Emery,[1]* Amit Kaushal,[3,4]* Lynette C. Foo,[1] Jennifer L. Zamanian,[1] Karen S. Christopherson,[1] Yi Xing,[5] Jane L. Lubischer,[6] Paul A. Krieg,[7] Sergey A. Krupenko,[8] Wesley J. Thompson,[9] and Ben A. Barres[1,2]
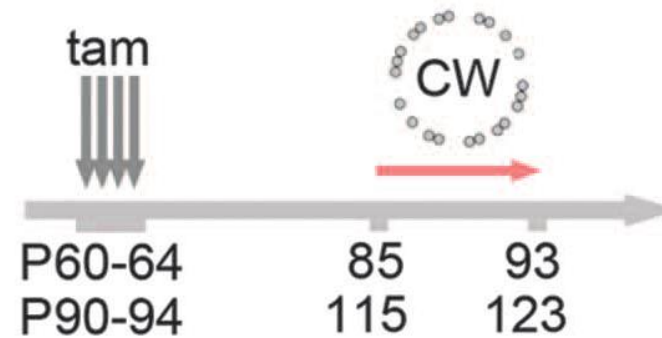
Whitaker*, Vertes* et al, PNAS, 2016
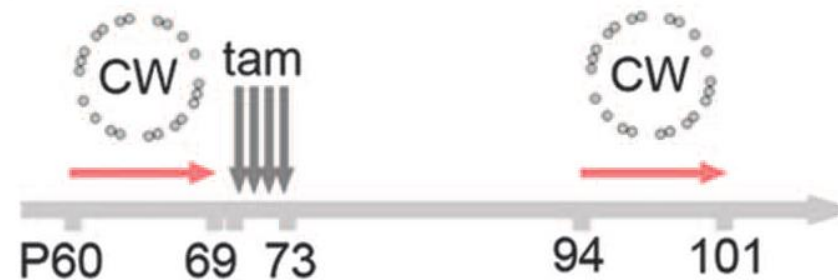Cahoy et al, J Neurosci, 2008

Motor skill learning requires active central myelination

Ian A. McKenzie,[1]* David Ohayon,[1]* Huiliang Li,[1] Joana Paes de Faria,[1]† Ben Emery,[2] Koujiro Tohyama,[3] William D. Richardson[1]‡
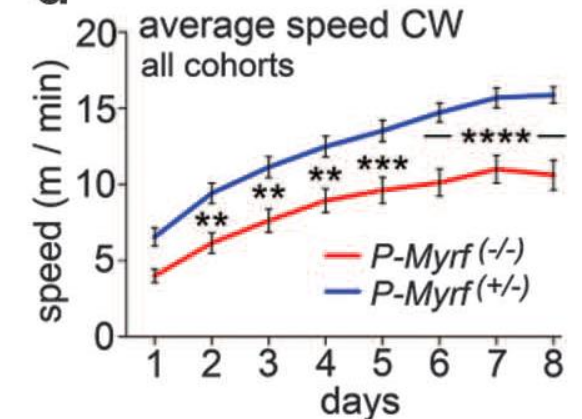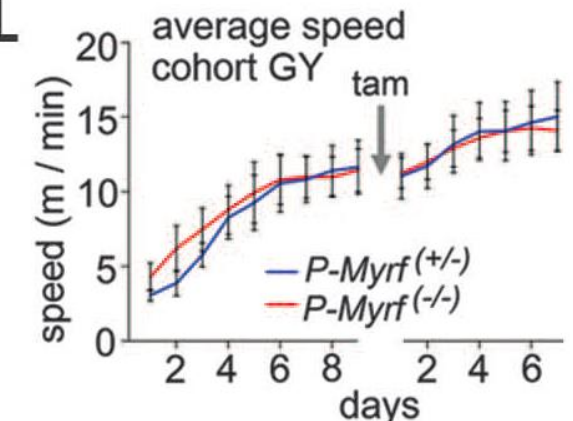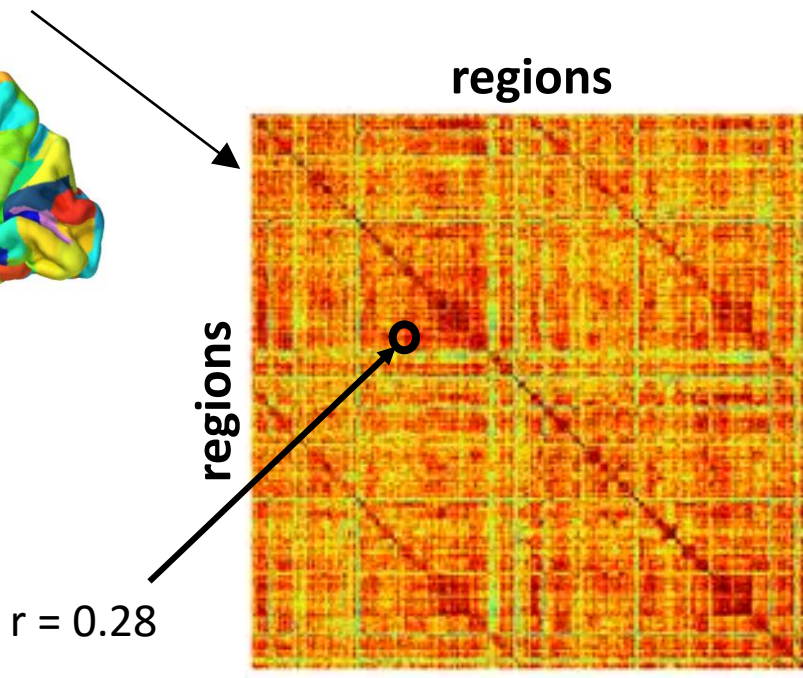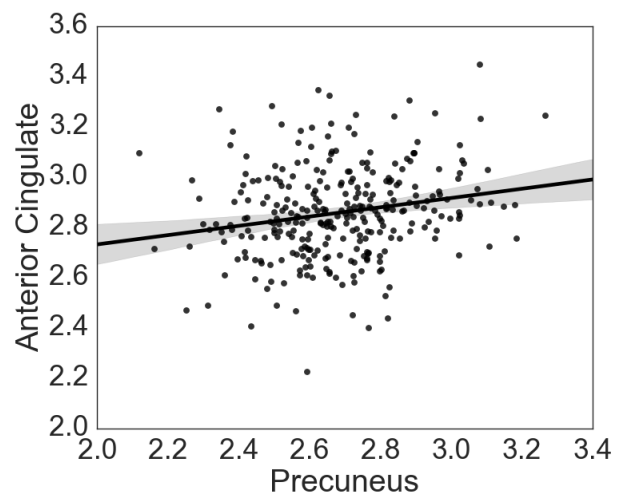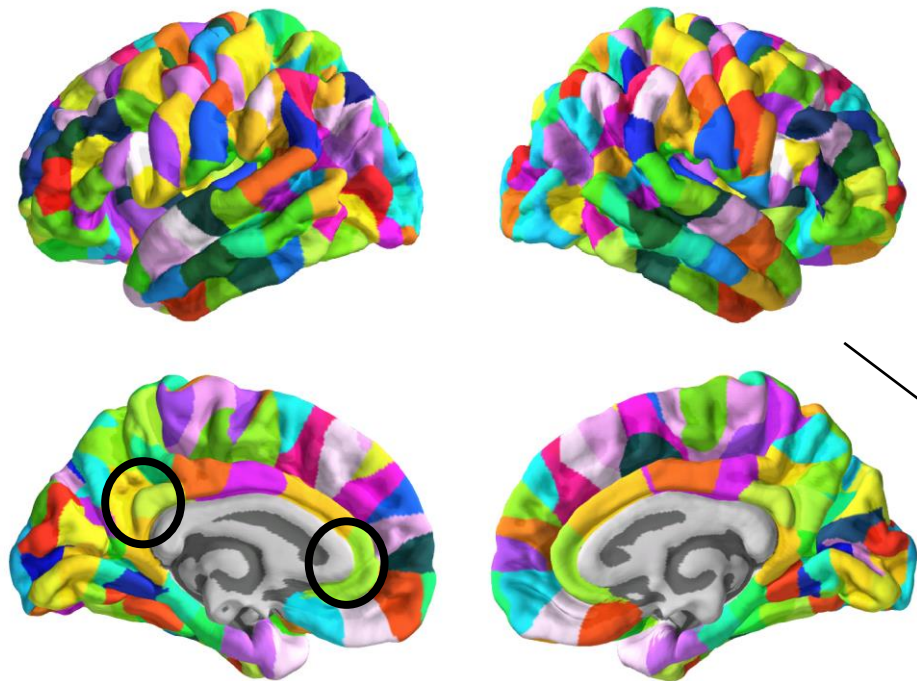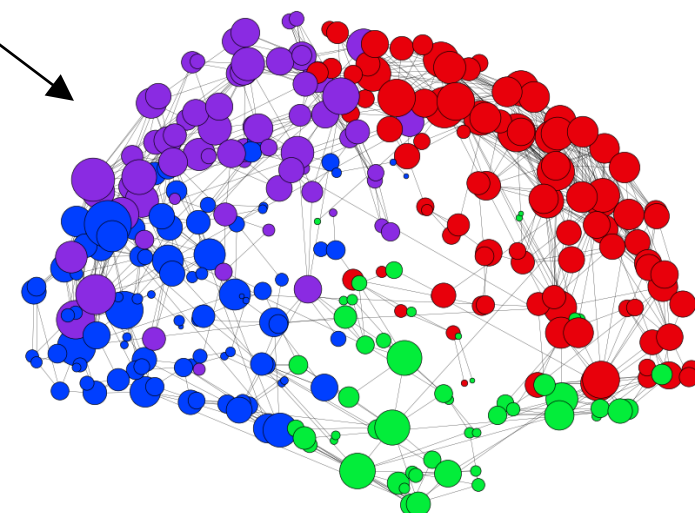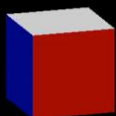
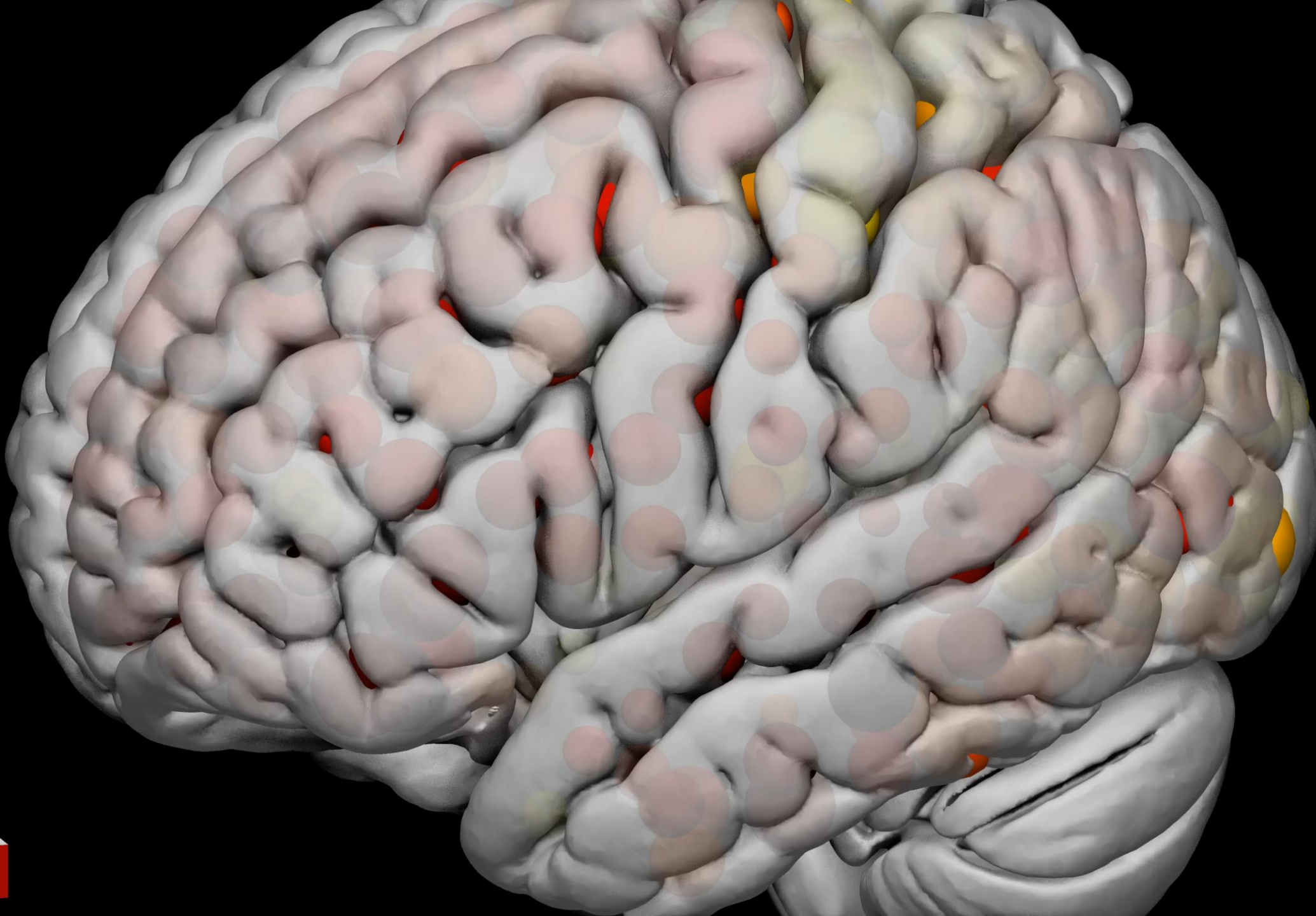McKenzie et al, Science, 2014

Take home:

genes related to changes at the synapse, oligodendrocytes and risk of schizophrenia are located in regions showing most prolonged developmental change
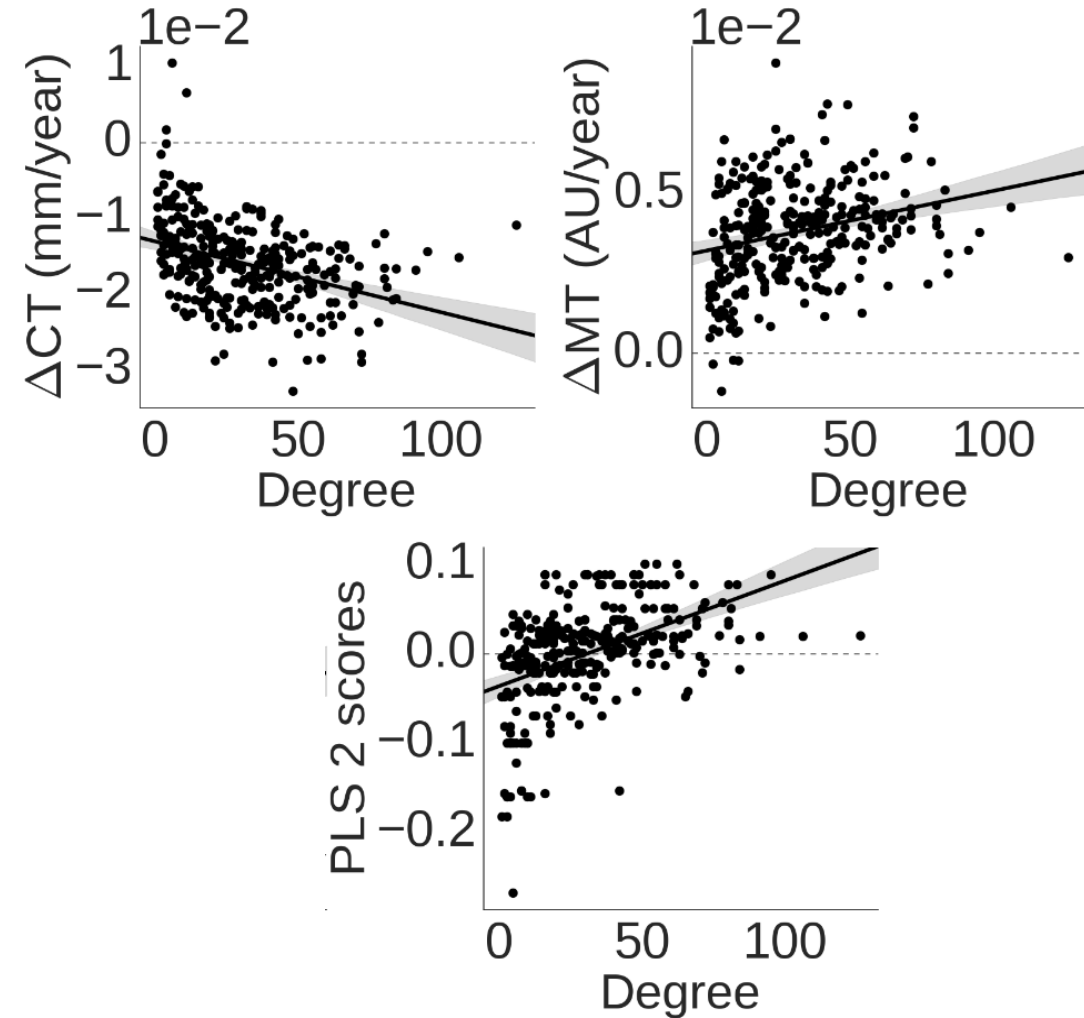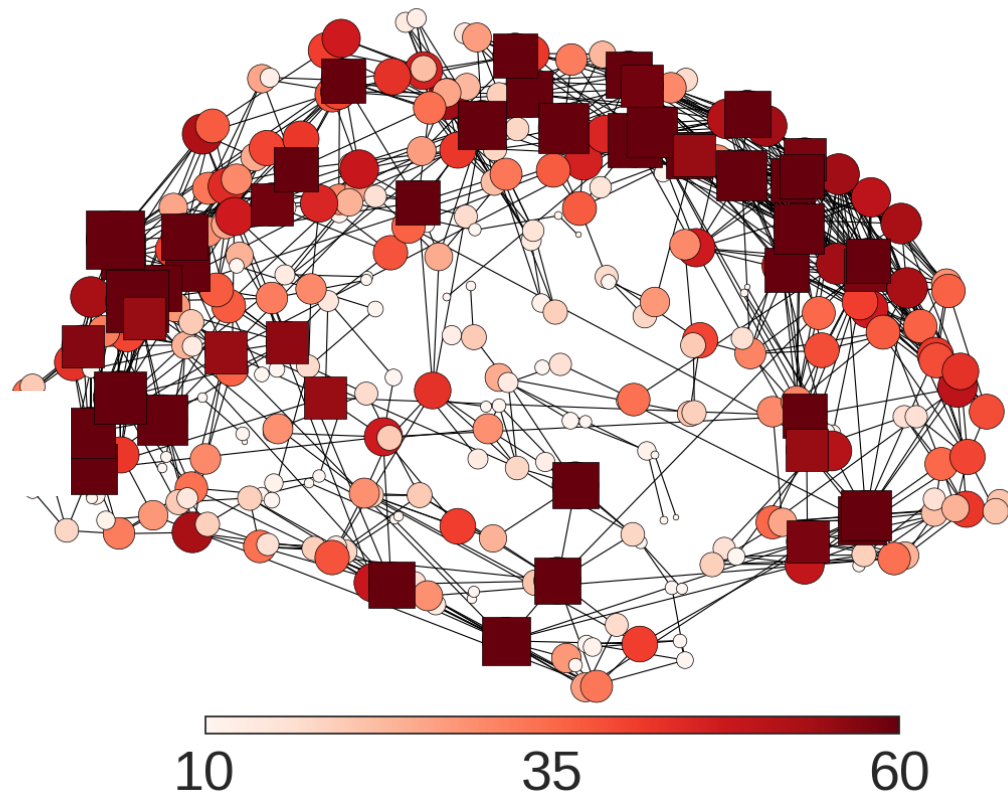
regions

regions

r = 0.28

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Hubs of the structural covariance network change the most during adolescence

Take home:

the hubs of the structural covariance network change the most during adolescence

And now for something slightly different...

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https://science.mozilla.org

KirstieJane / NSPN_WhitakerVertes_PNAS2016

Unwatch ▾ 1   ★ Star 5   ⑂ Fork 2

<> Code   ⓘ Issues 0   ⑂ Pull requests 1   📖 Wiki   ⋀ Pulse   📊 Graphs   ⚙ Settings

Data and analysis code to reproduce the NSPN Manuscript "Adolescence is associated with genomically patterned consolidation of the hubs of the human brain connectome". http://kirstiejane.github.io/NSPN_WhitakerVertes_PNAS2016 — Edit

⊙ 14 commits	⑂ 5 branches	◊ 1 release	👥 1 contributor	⚖ MIT

Branch: master ▾   New pull request   Create new file   Upload files   Find file   Clone or download ▾

KirstieJane committed on GitHub Update README.md   Latest commit b810696 on 28 Jul

📁 CT_MT_ANALYSES	added RESULTS directory	3 months ago
📁 DATA	added DATA directory	3 months ago
📁 FS_SUBJECTS/fsaverageSubP	added FS_SUBJECTS directory	3 months ago
📁 SCRIPTS	added scripts directory	3 months ago
📁 SUPPLEMENTAL_FILES	Added supplementary files	3 months ago
📄 LICENSE	Initial commit	3 months ago

https://github.com/KirstieJane/NSPN_WhitakerVertes_PNAS2016

Reproducible and replicated findings

Discovery (N=100)

Validation (N=197)

Whitaker*, Vertes* et al, PNAS, 2016

Reproducible and replicated findings

Take home:

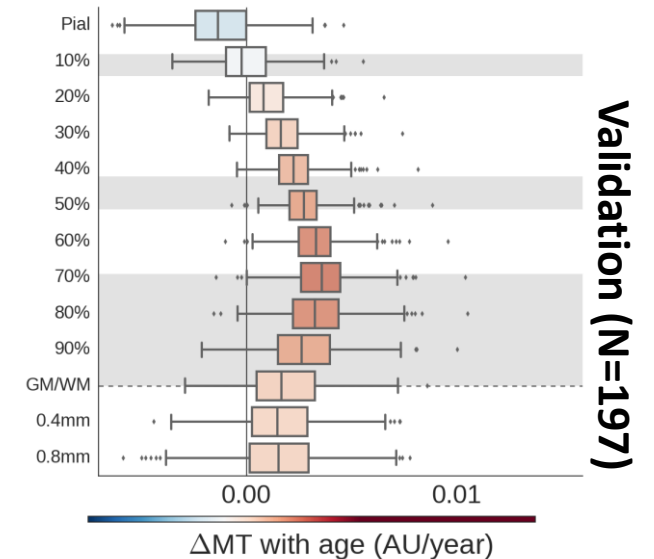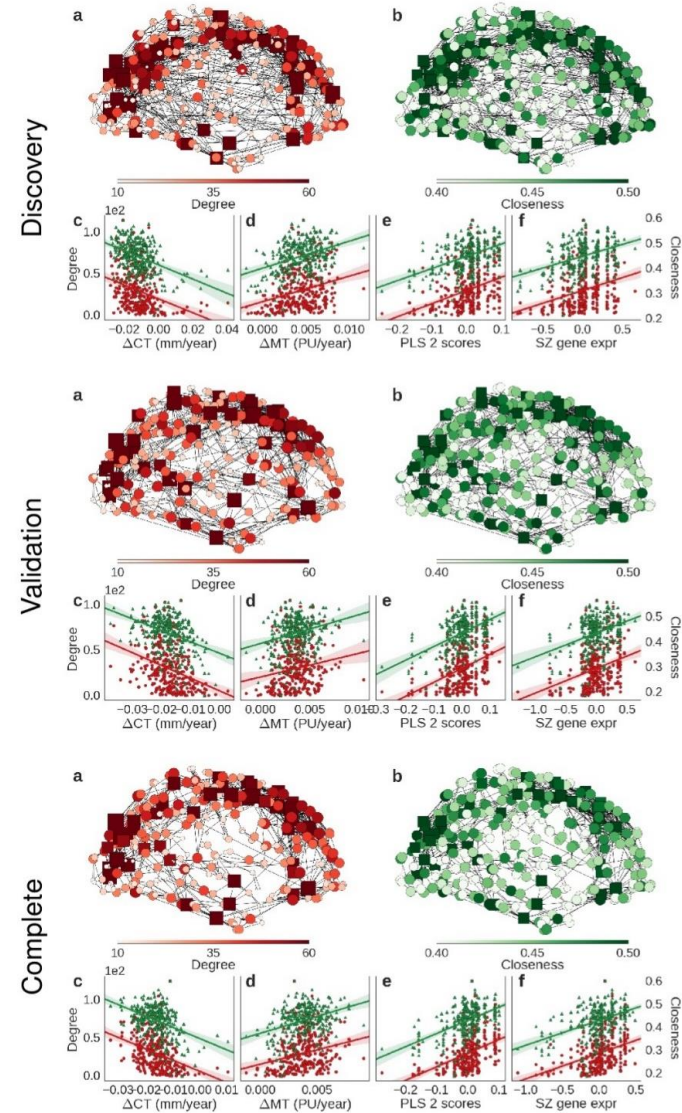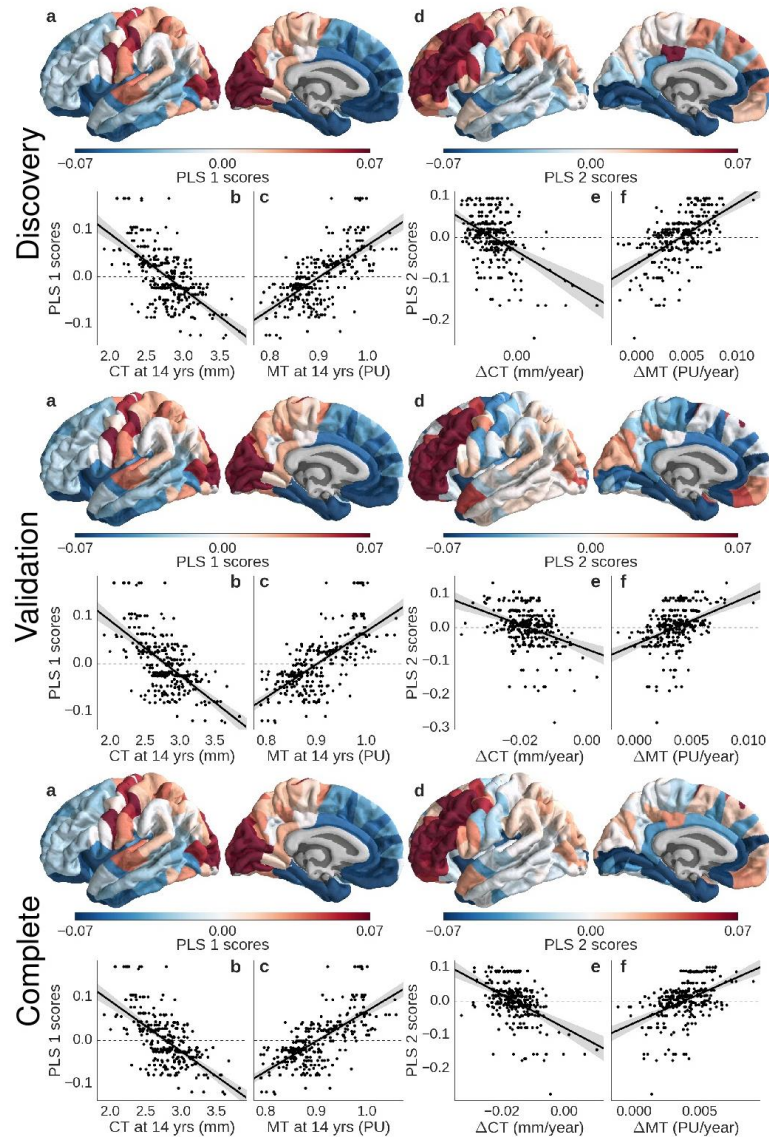all findings replicate in two independent cohorts and all data and code to reproduce these analyses are available on github

Summary

- Adolescent age-related changes in myelin are located within cortex

- Genes related to changes at the synapse, oligodendrocytes and risk of schizophrenia are located in regions showing most prolonged developmental change

- Hubs of the structural covariance network change the most during adolescence

- All findings replicate in two independent cohorts and all data and code to reproduce these analyses are available on github

Thank you!

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Strategic Award

www.nspn.org.uk

- NSPN Leadership team:
  - Prof Ian Goodyer
  - Prof Ed Bullmore
  - Prof Peter Jones
  - Prof Ray Dolan
  - Prof Peter Fonagy
- NSPN Postdocs, PhD students and RAs
- Brain Mapping Unit