

TOWARDS AN OPEN RESEARCH ON THE DEVELOPMENT AND EVOLUTION OF THE BRAIN

INCEPTION ANNUAL MEETING • 8 November 2018

Roberto Toro • Groupe de Neuroanatomie Appliquée et Théorique

Unité de Génétique Humaine et Fonctions Cognitives • Département de Neurosciences • Institut Pasteur

CRI (Centre de Recherches Interdisciplinaires) • Université Paris Descartes

1

The challenge of neurodevelopmental disorders

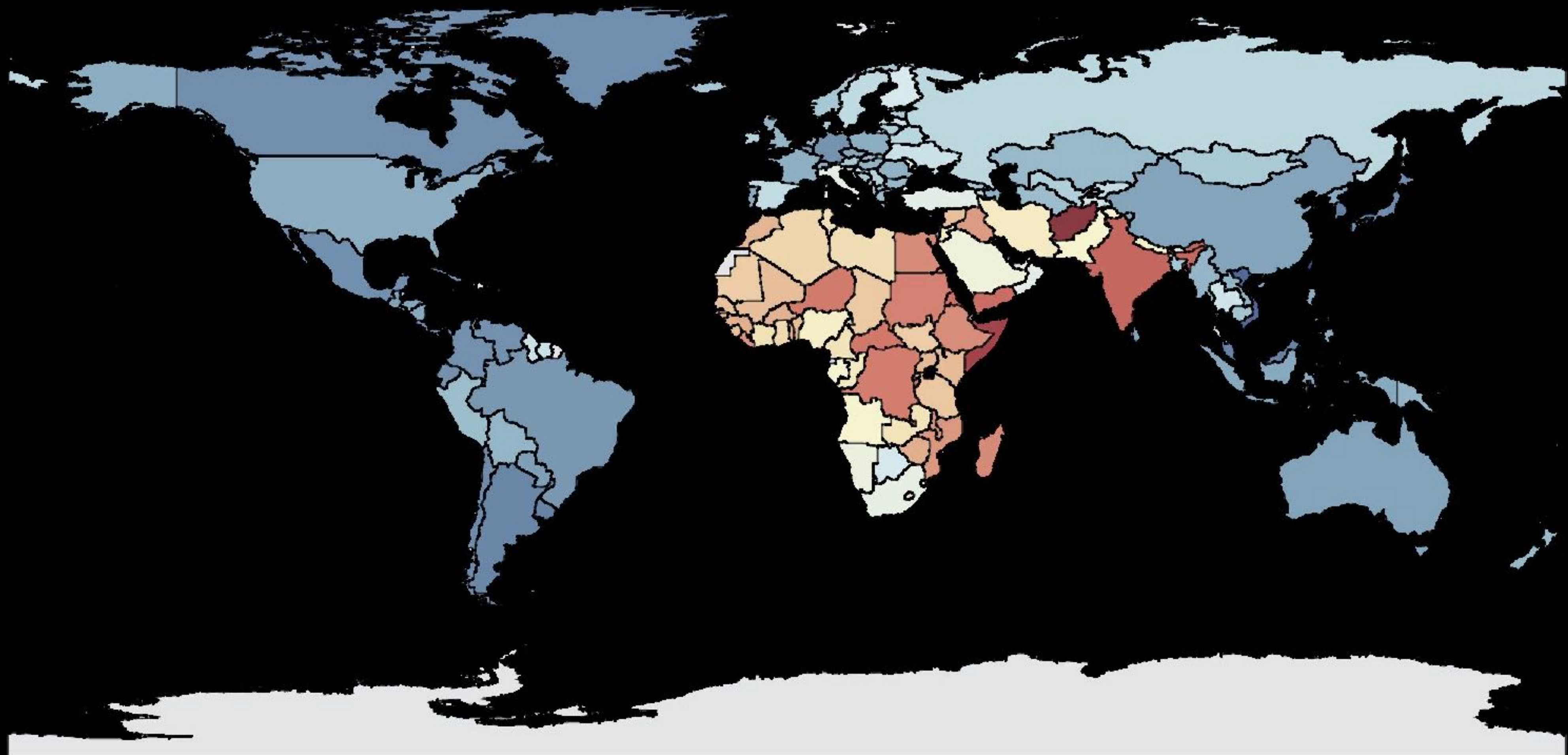


Neurodevelopmental disorders, such as attention deficit and hyperactivity disorder, autism, schizophrenia, or intellectual disability, **affect 15% of the population.**

Across 195 countries, from 1990 to 2016, neurodevelopmental disorders were the **largest contributor to Years Lived with Disability (YLD) among children < 5 years old** (Global Research on Developmental Disabilities 2018, Bill&Melinda Gates Foundation)

The Sustainable Development Goals of the United Nations mandate **systematic monitoring** of the health and wellbeing of all children to **achieve optimal early childhood development.**

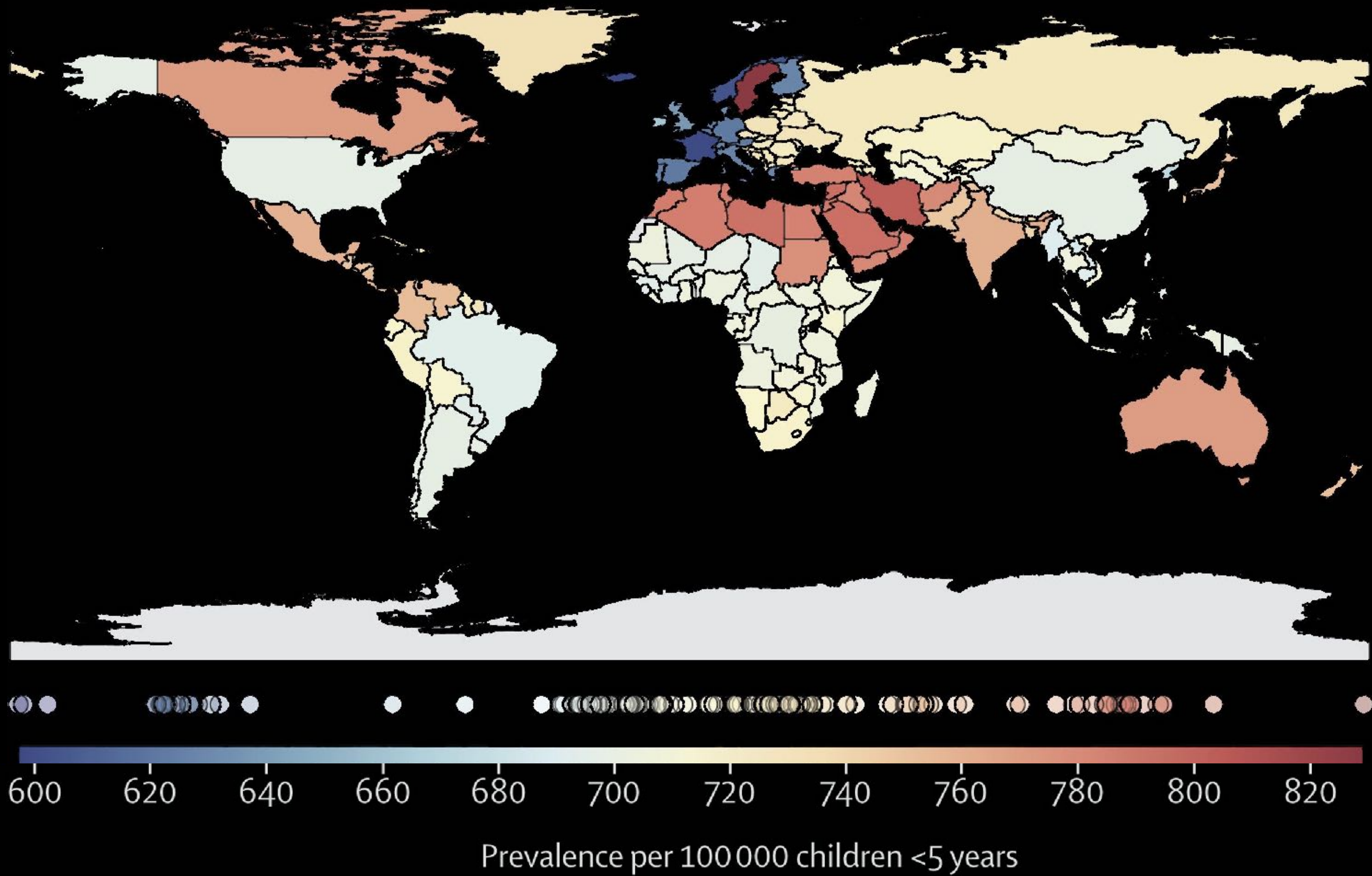
B Developmental intellectual disability



600 800 1000 1200 1400 1600 1800 2000 2200 2400 2600

Prevalence per 100 000 children <5 years

E Autism spectrum disorder



The societal challenge of brain disorders

“In the past 30 years, major advances have been made in the treatment of several serious diseases, such as Leukaemia, heart disease, stroke or AIDS, with reductions in mortality rates of up to 95%.

Unfortunately, this is not the case for mental illness. Mental illnesses affect up to 1 in 5 people, and the WHO indicates that up to 1 in 3 people report sufficient criteria for mental illness at some point of their life.

The main problem is that **we know dangerously little about the functioning and development of the brain.**

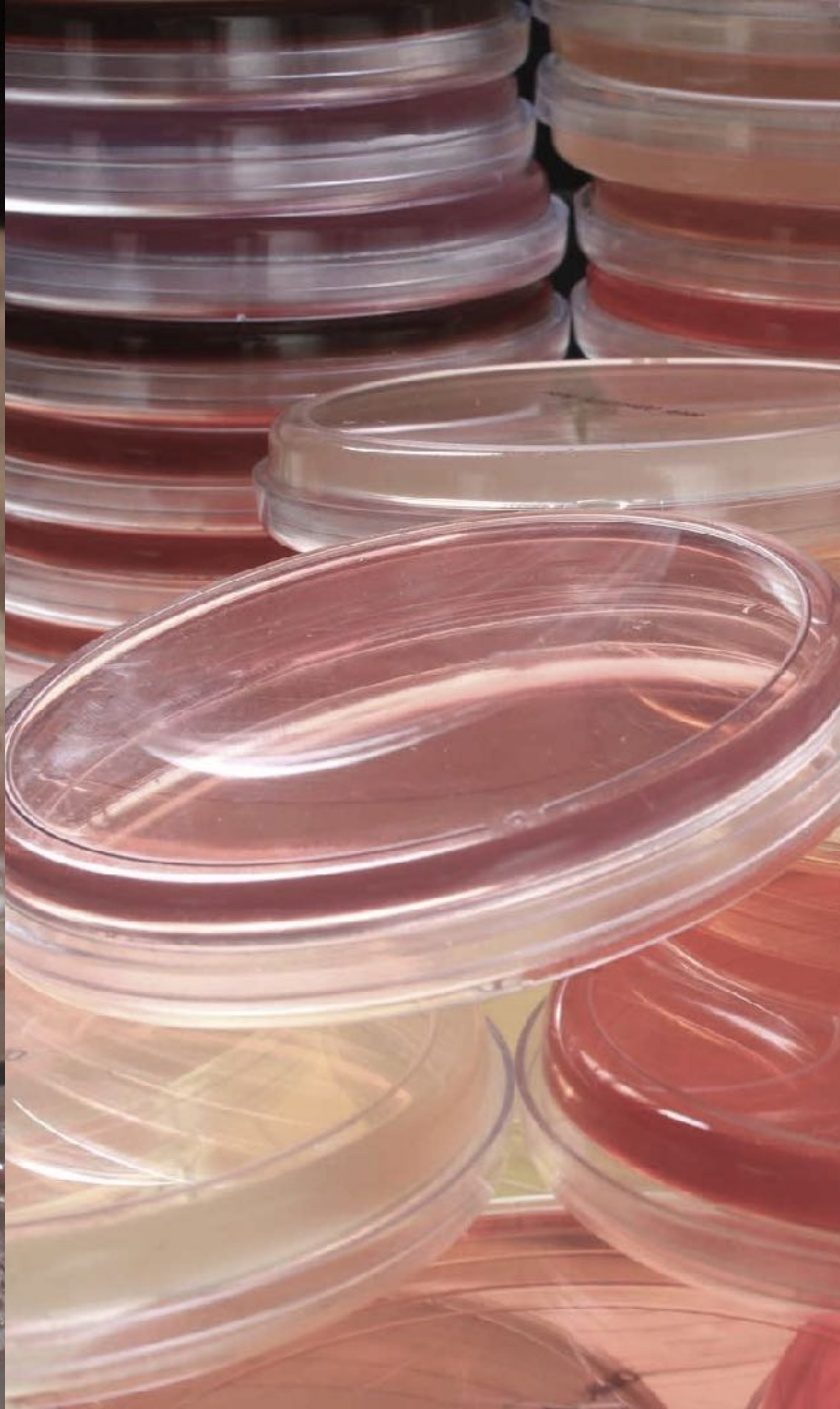
The **traditional framework of neuroscience research seems insufficient** to tackle the surreal complexity of the brain.”

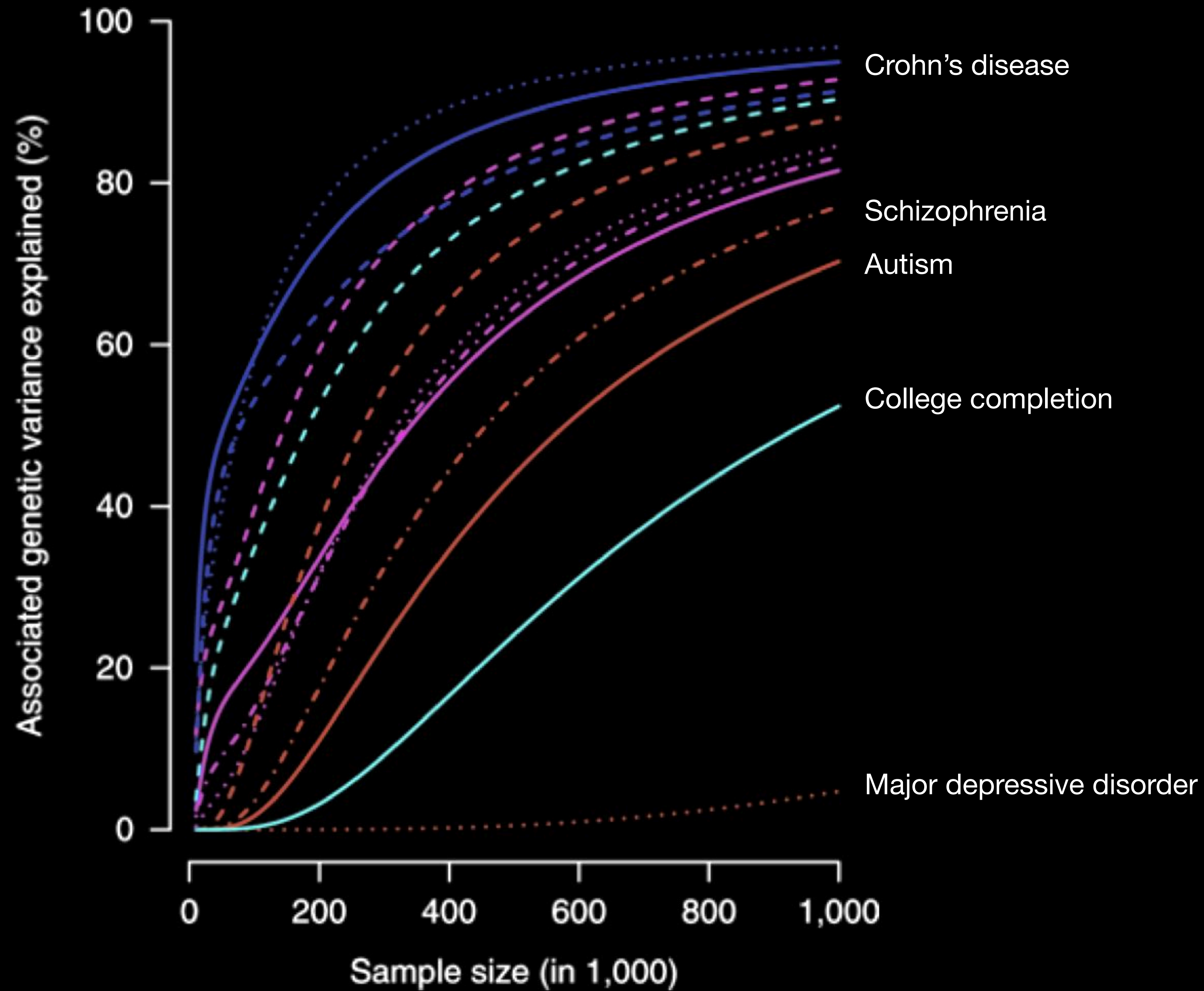
Thomas Insel, NIMH Director 2002-2015

2

Polygenic architectures







ORIGINAL ARTICLE

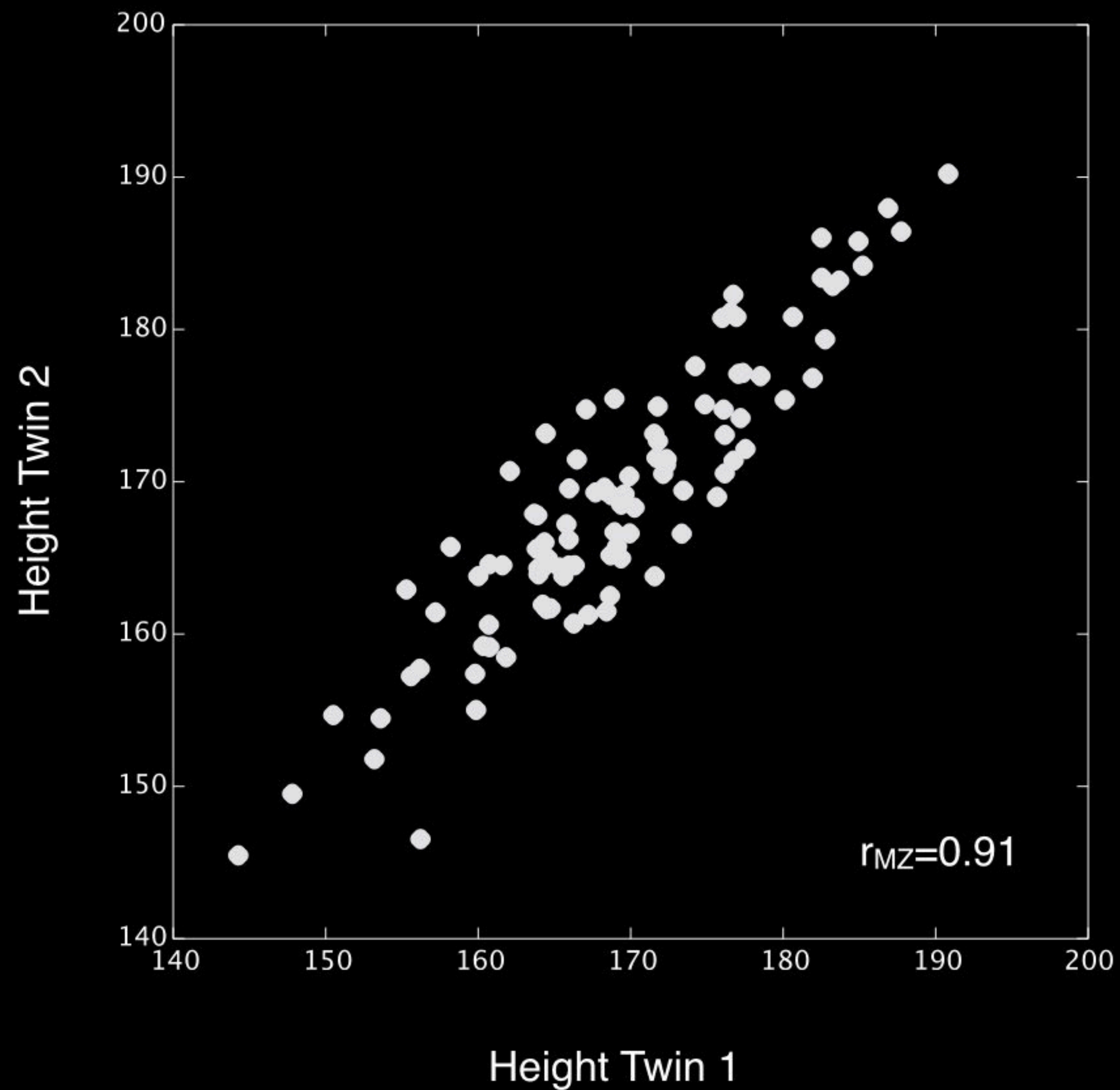
Genomic architecture of human neuroanatomical diversity

R Toro^{1,2,3}, J-B Poline^{4,5}, G Huguet^{1,2,3}, E Loth^{6,7}, V Frouin⁴, T Banaschewski⁸, GJ Barker⁶, A Bokde⁹, C Büchel¹⁰, FM Carvalho^{6,7}, P Conrod^{6,11}, M Fauth-Bühler¹², H Flor¹³, J Gallinat¹⁴, H Garavan^{9,15}, P Gowland¹⁵, A Heinz¹⁴, B Ittermann¹⁶, C Lawrence¹⁷, H Lemaître^{18,19}, K Mann¹², F Nees¹³, T Paus^{17,20,21}, Z Pausova²², M Rietschel²³, T Robbins²⁴, MN Smolka^{25,26}, A Ströhle¹⁴, G Schumann^{6,7,27}, T Bourgeron^{1,2,3,27,28} and the IMAGEN consortium (www.imagen-europe.com)

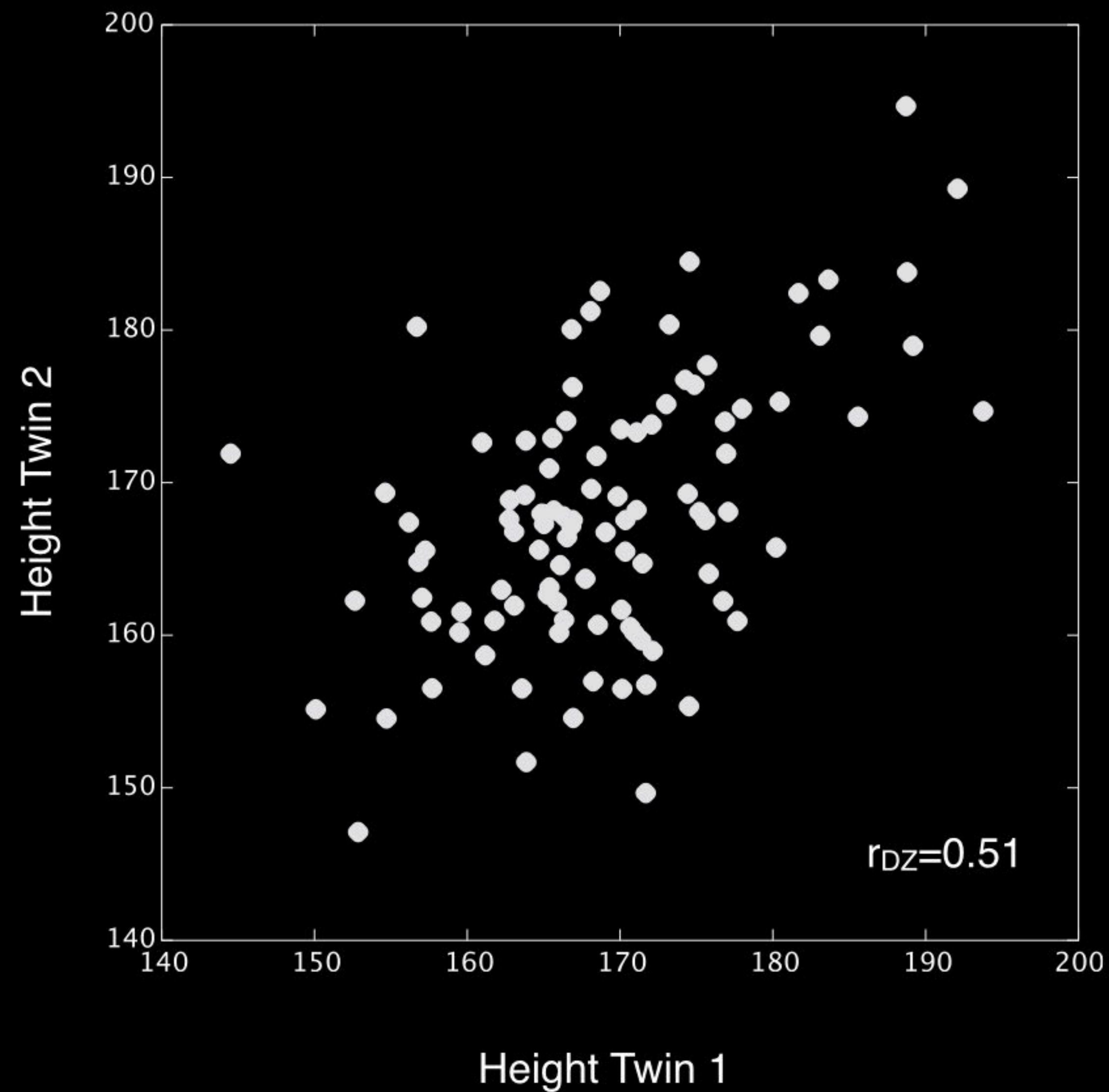
Human brain anatomy is strikingly diverse and highly inheritable: genetic factors may explain up to 80% of its variability. Prior studies have tried to detect genetic variants with a large effect on neuroanatomical diversity, but those currently identified account for < 5% of the variance. Here, based on our analyses of neuroimaging and whole-genome genotyping data from 1765 subjects, we show that up to 54% of this heritability is captured by large numbers of single-nucleotide polymorphisms of small-effect spread throughout the genome, especially within genes and close regulatory regions. The genetic bases of neuroanatomical diversity appear to be relatively independent of those of body size (height), but shared with those of verbal intelligence scores. The study of this genomic architecture should help us better understand brain evolution and disease.

Molecular Psychiatry advance online publication, 16 September 2014; doi:10.1038/mp.2014.99

Monozygotic



Dizygotic



$r =$ **Inheritable factors + Shared environment**

$$r_{MZ} = A + C$$

$$r_{DZ} = \frac{1}{2}A + C$$

$$A = h^2 = 2(r_{MZ} - r_{DZ})$$

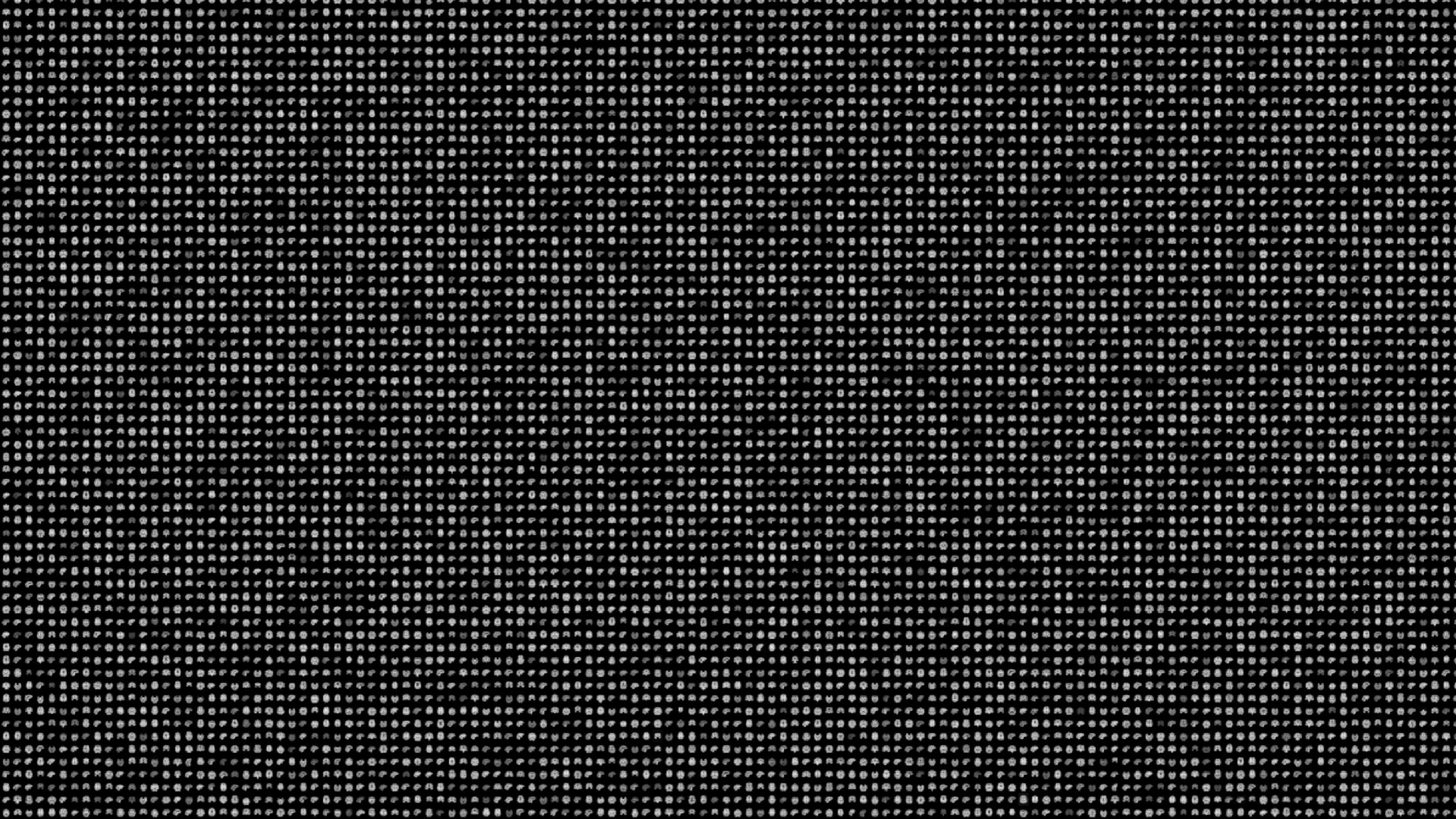
$$C = r_{MZ} - A$$

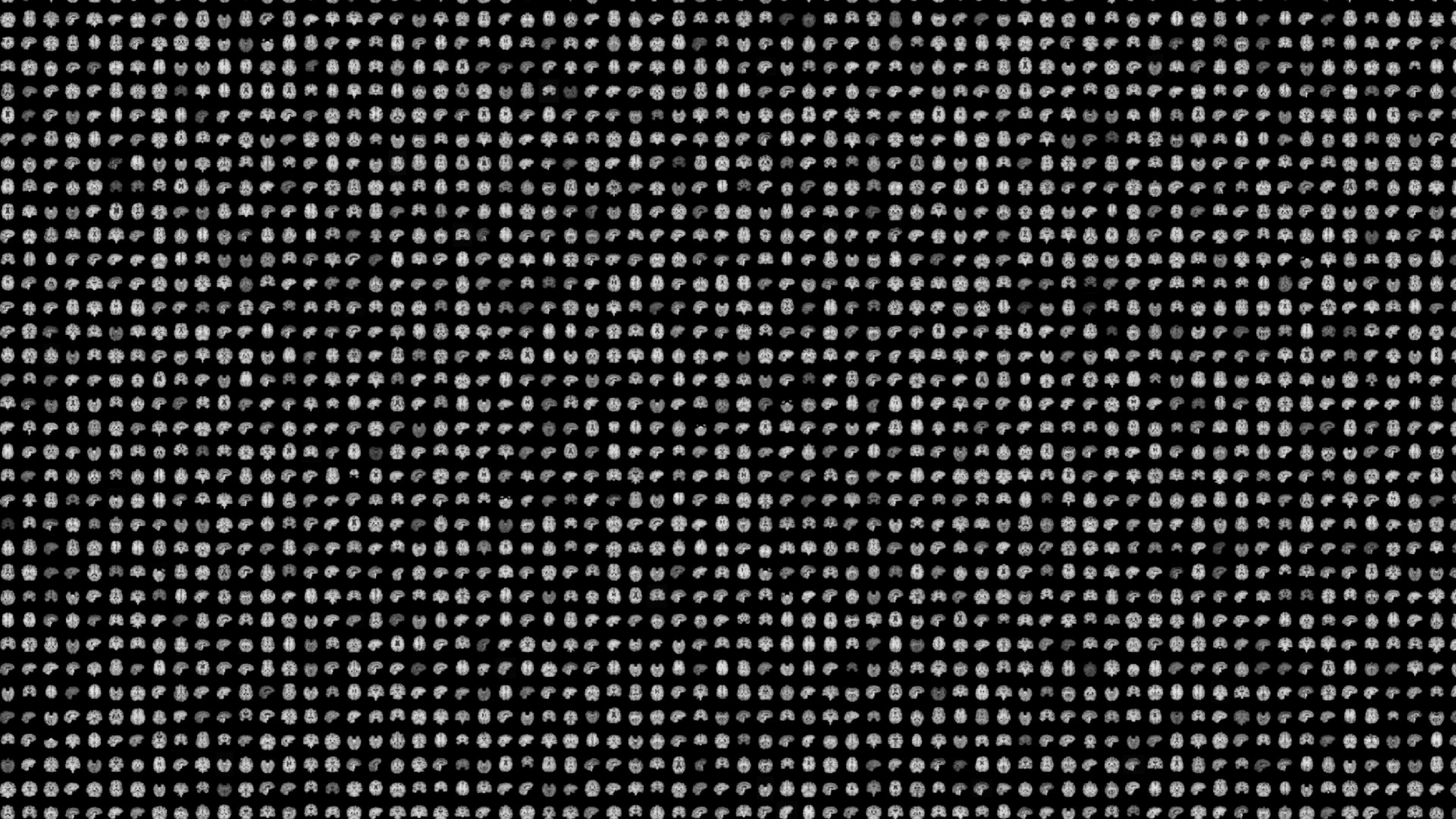
$$E = 1 - A - C$$

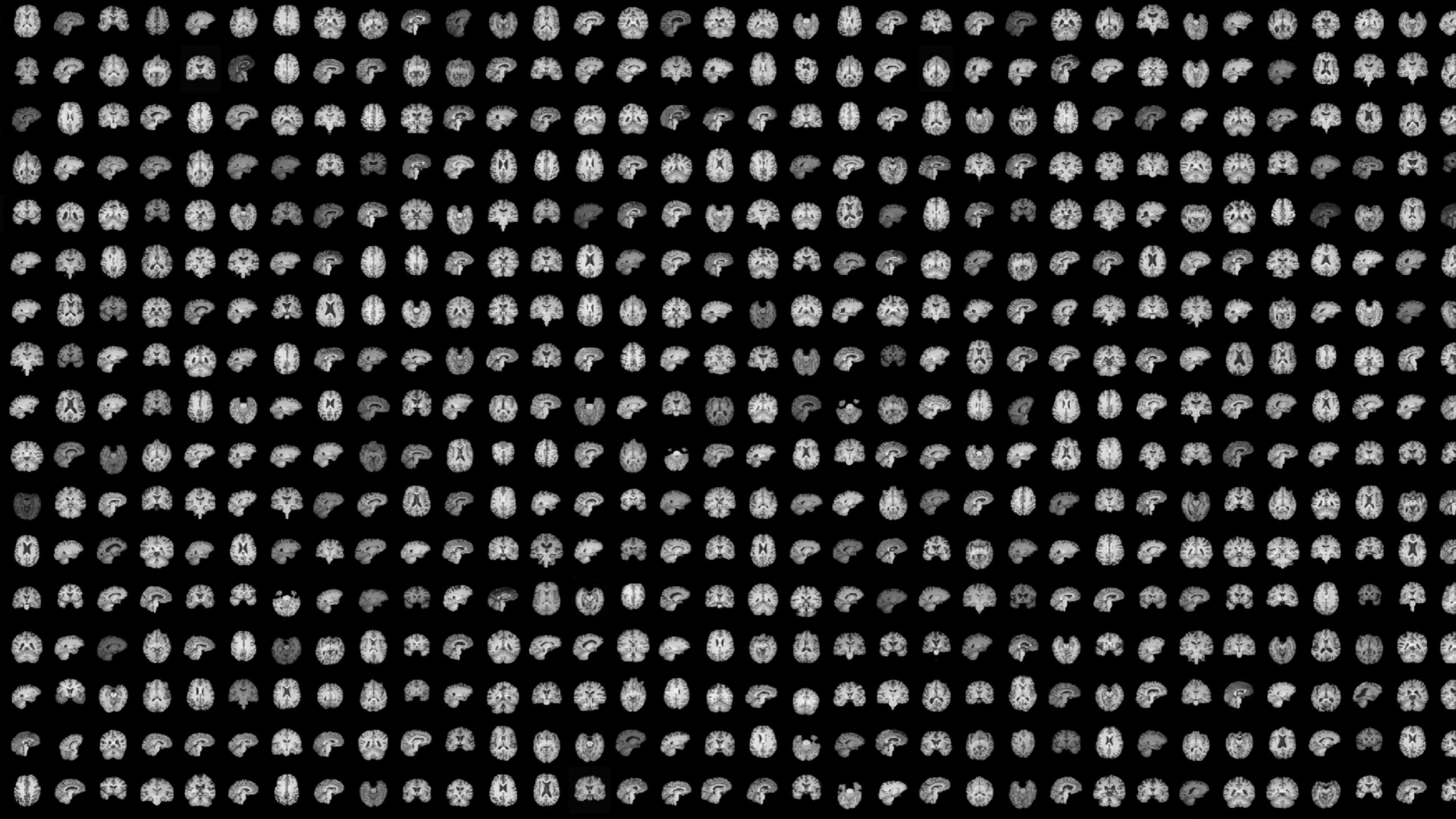
$$r_{MZ} = (1)A + C$$
$$r_{DZ} = (1/2)A + C$$

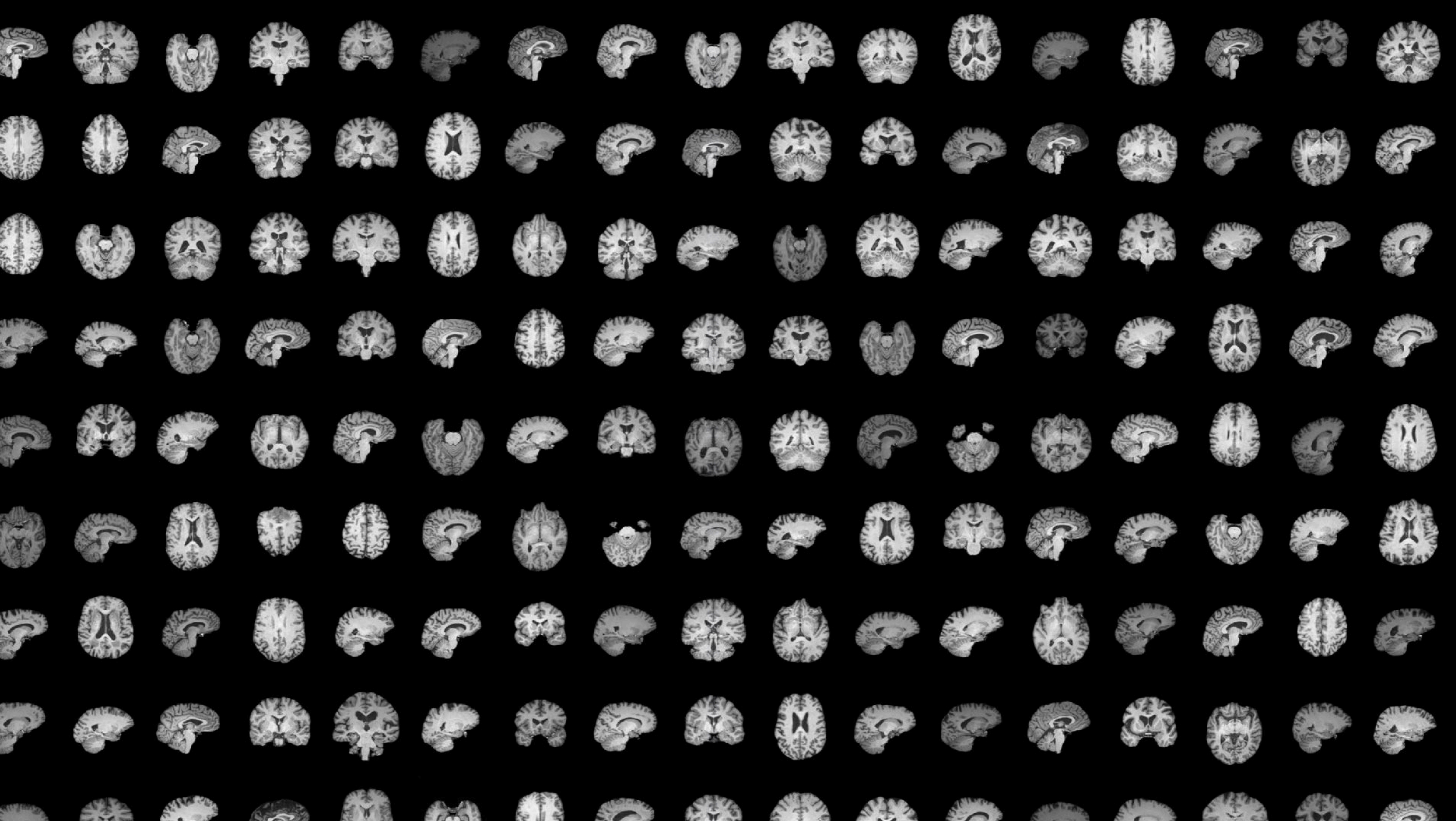


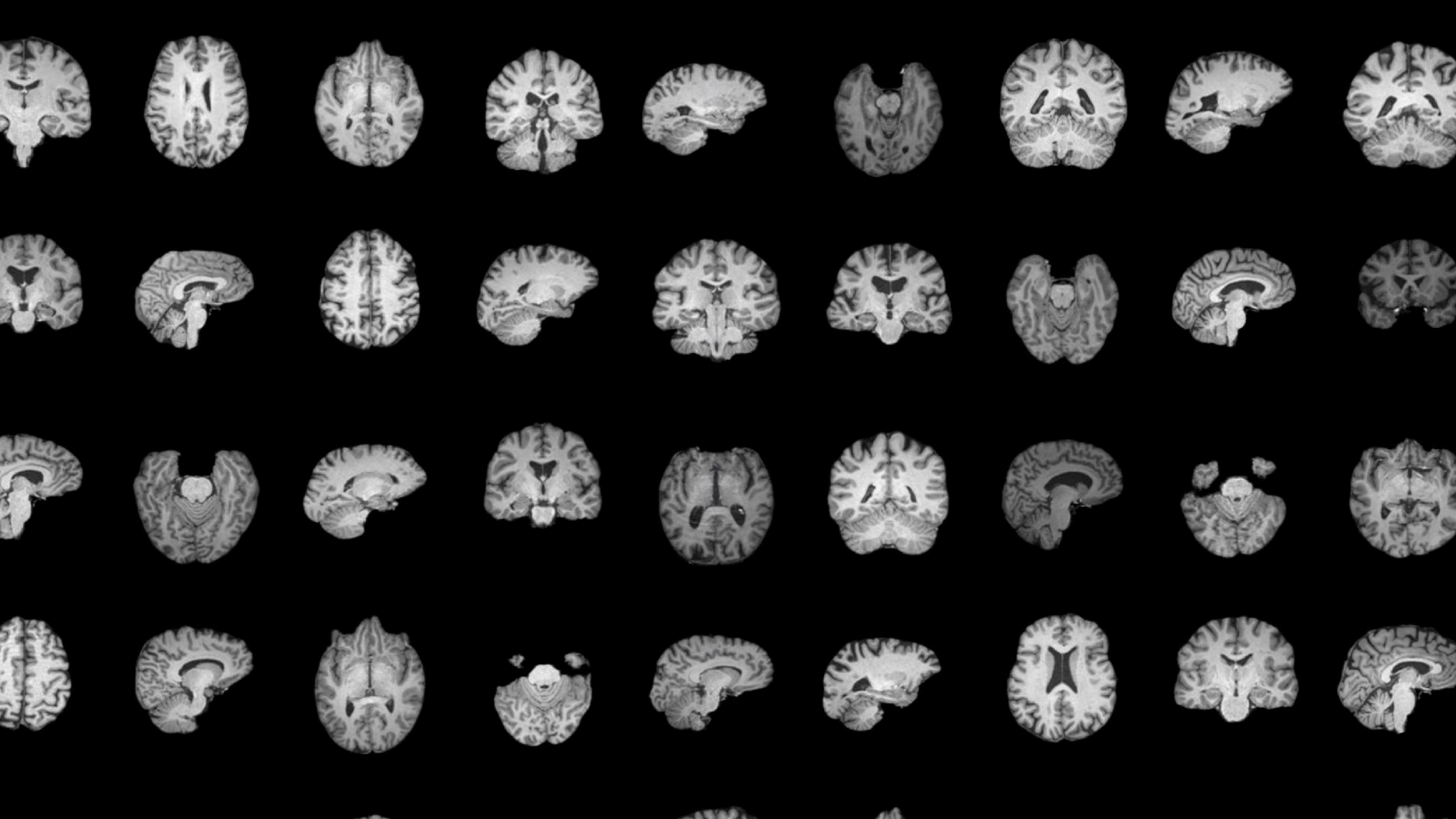
$$r_{ij} = \alpha A + C$$

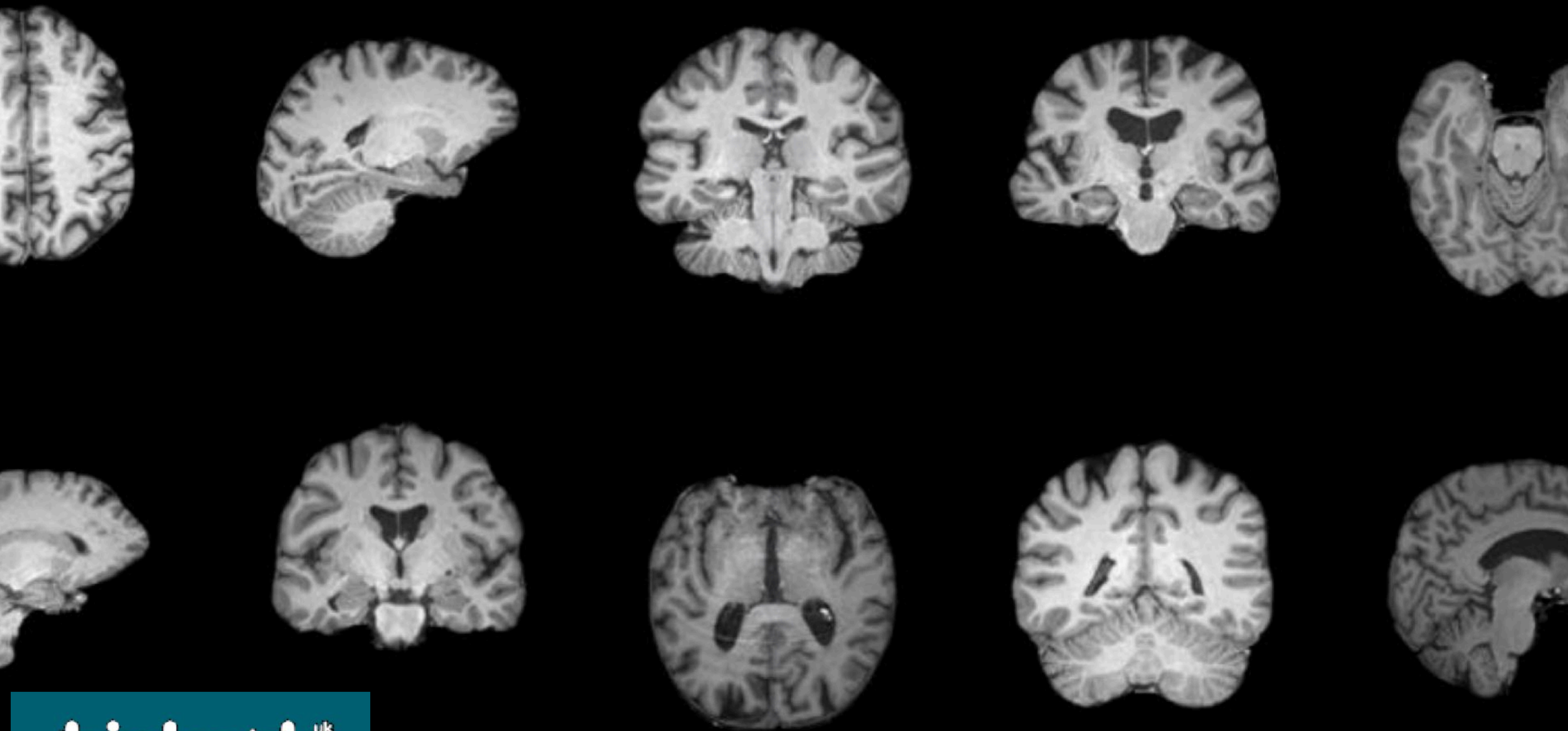




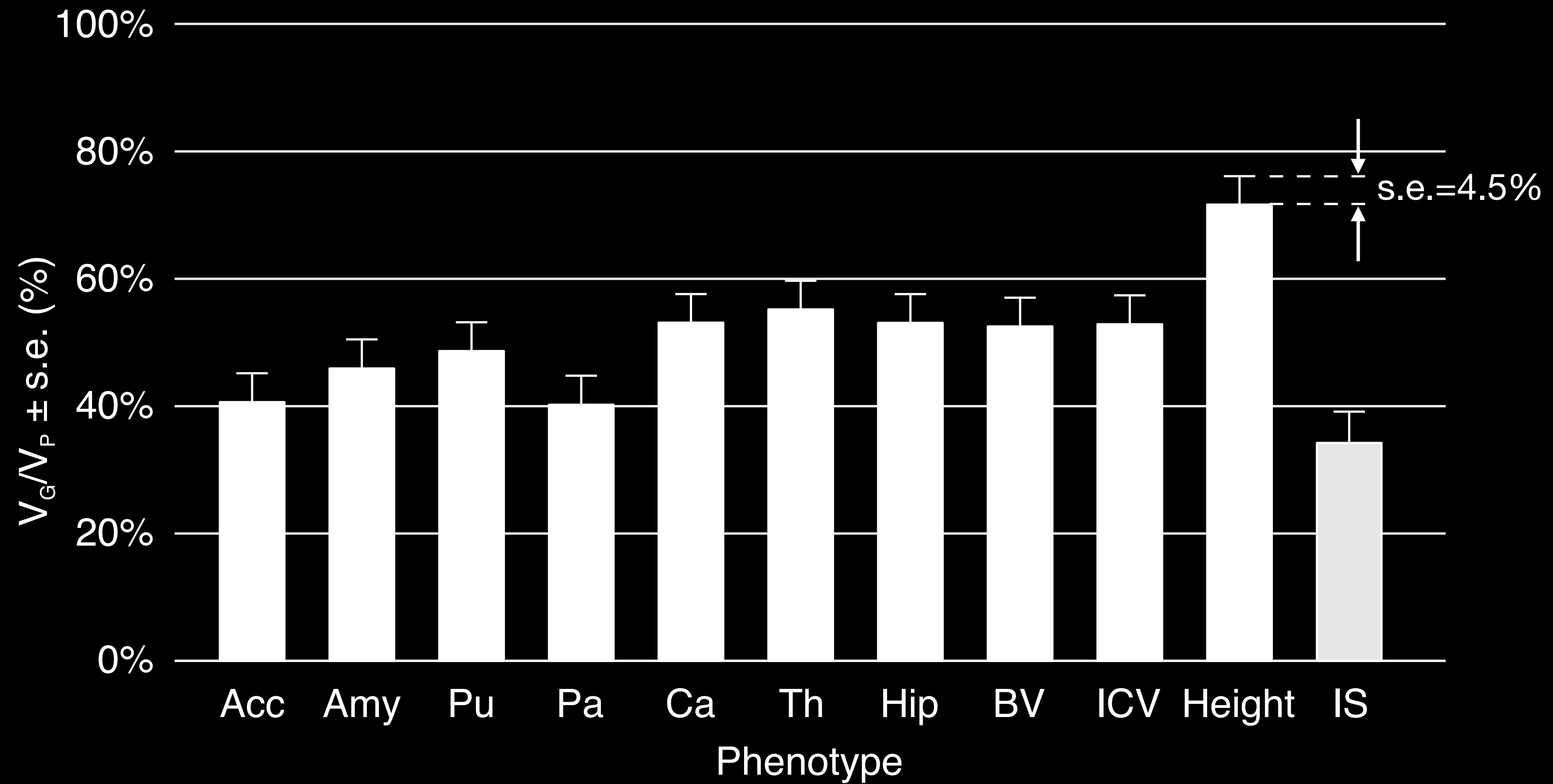




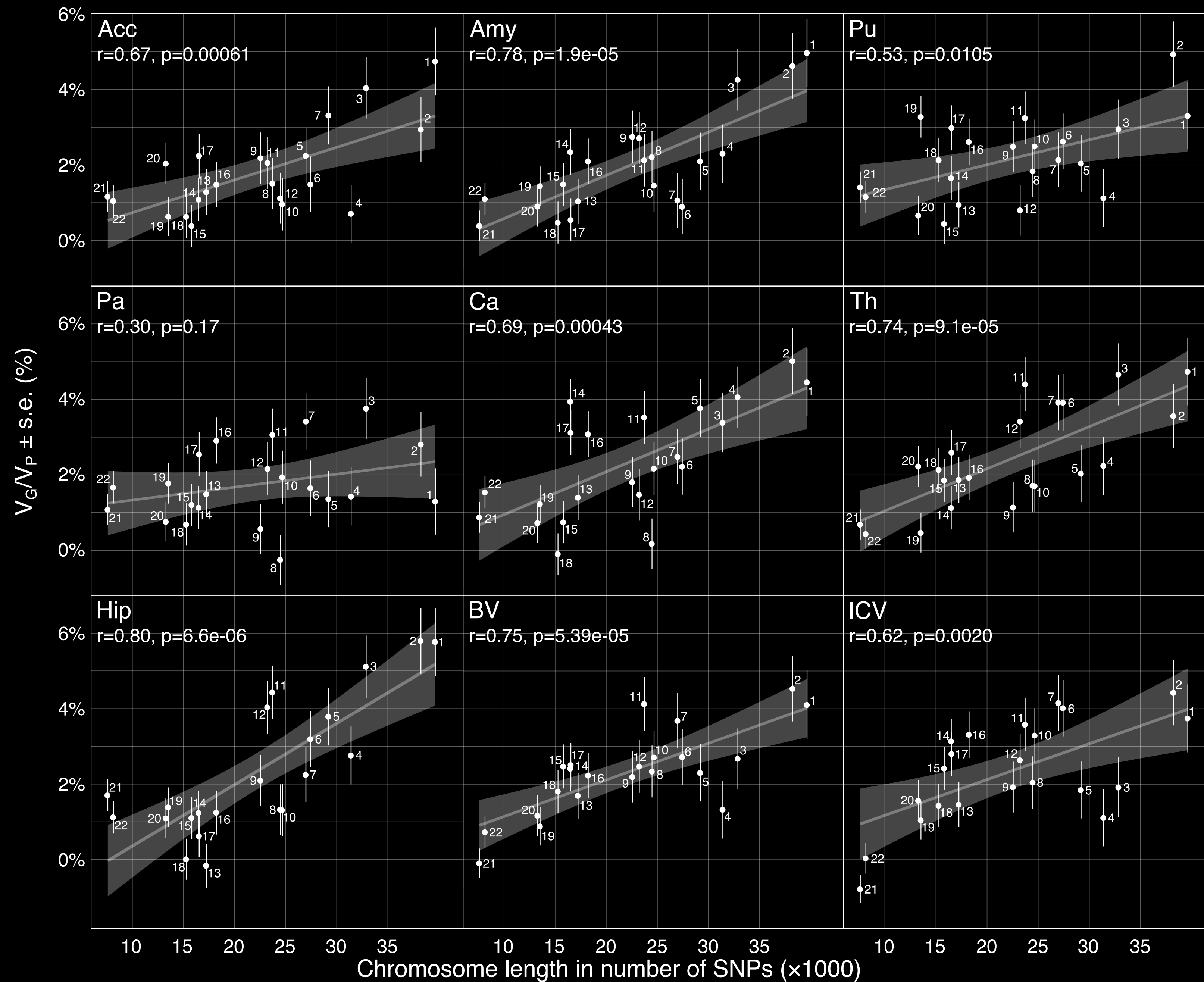




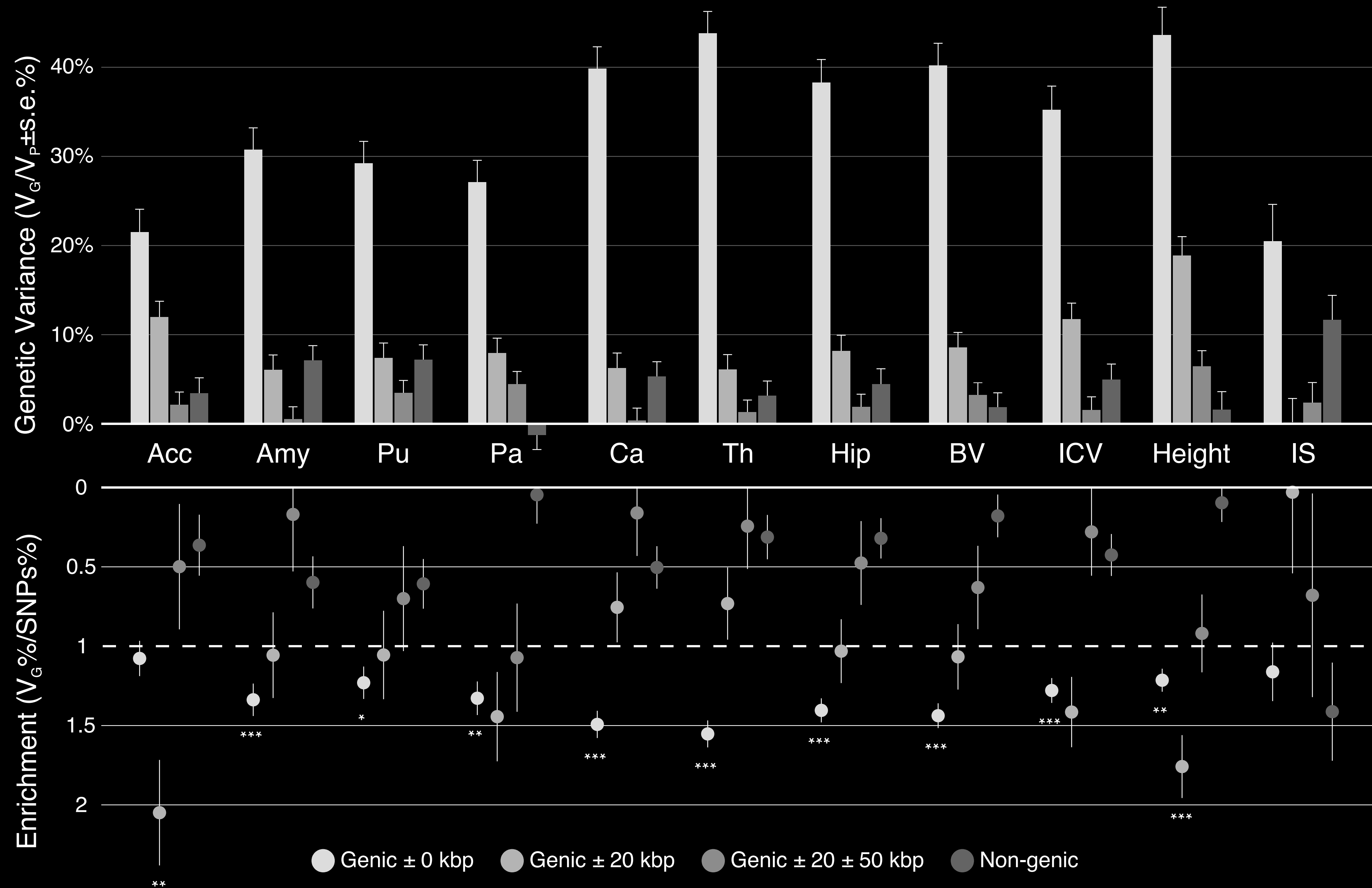
Common genetic variation captures a substantial proportion of neuroanatomical diversity
(MRI and whole-genome genotyping on 20,140 subjects)



Causal variants are widespread across the genome

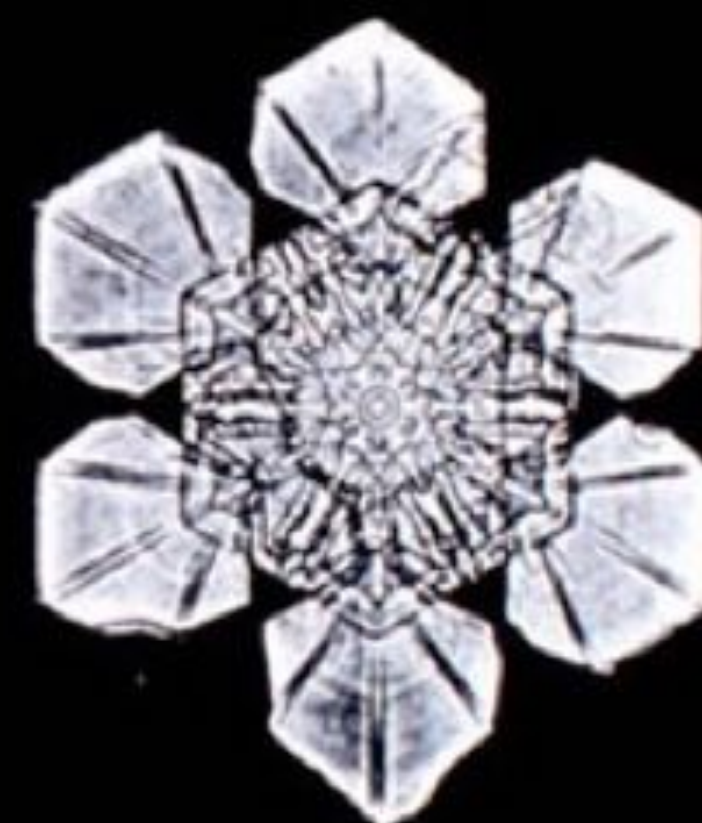


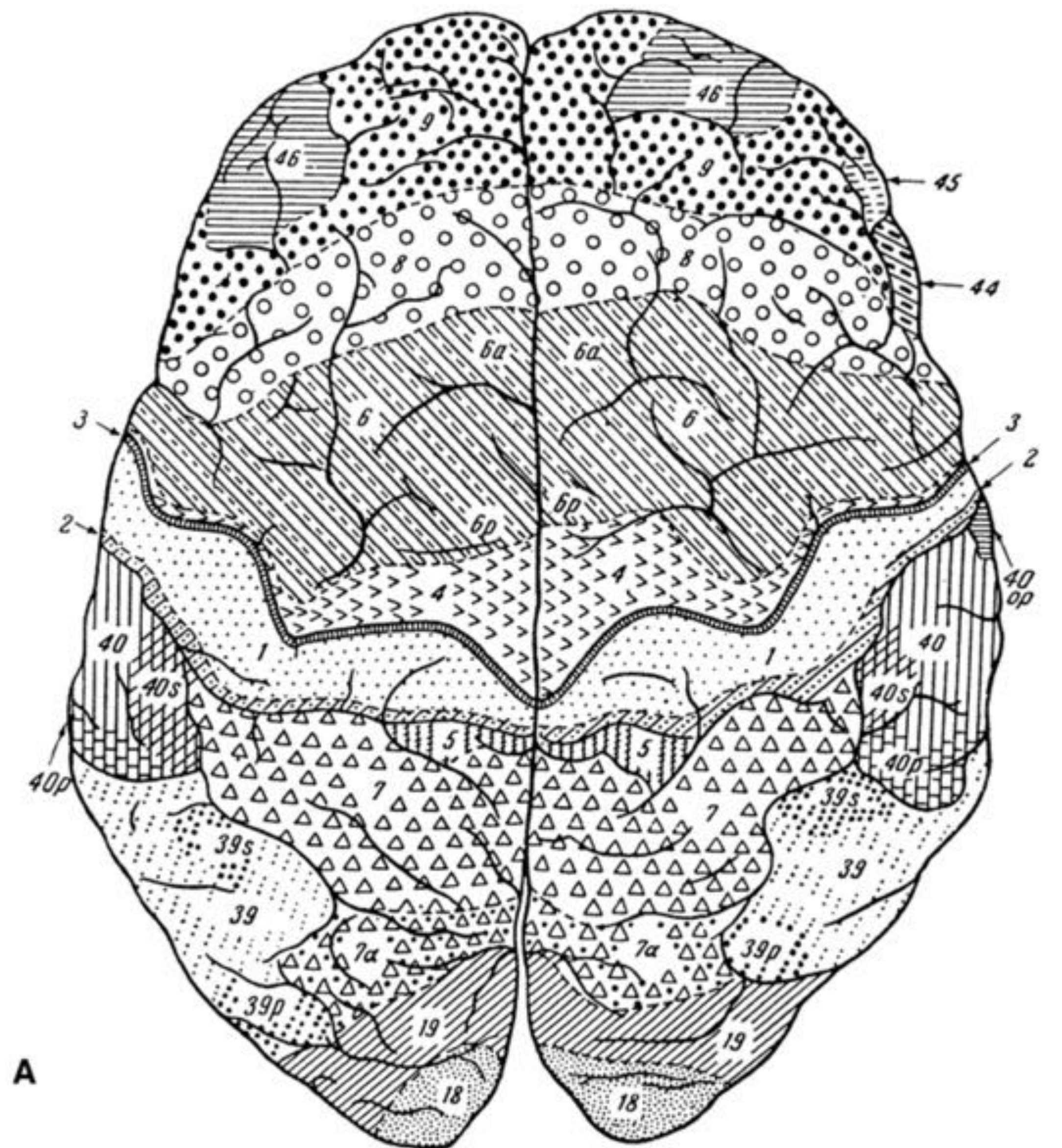
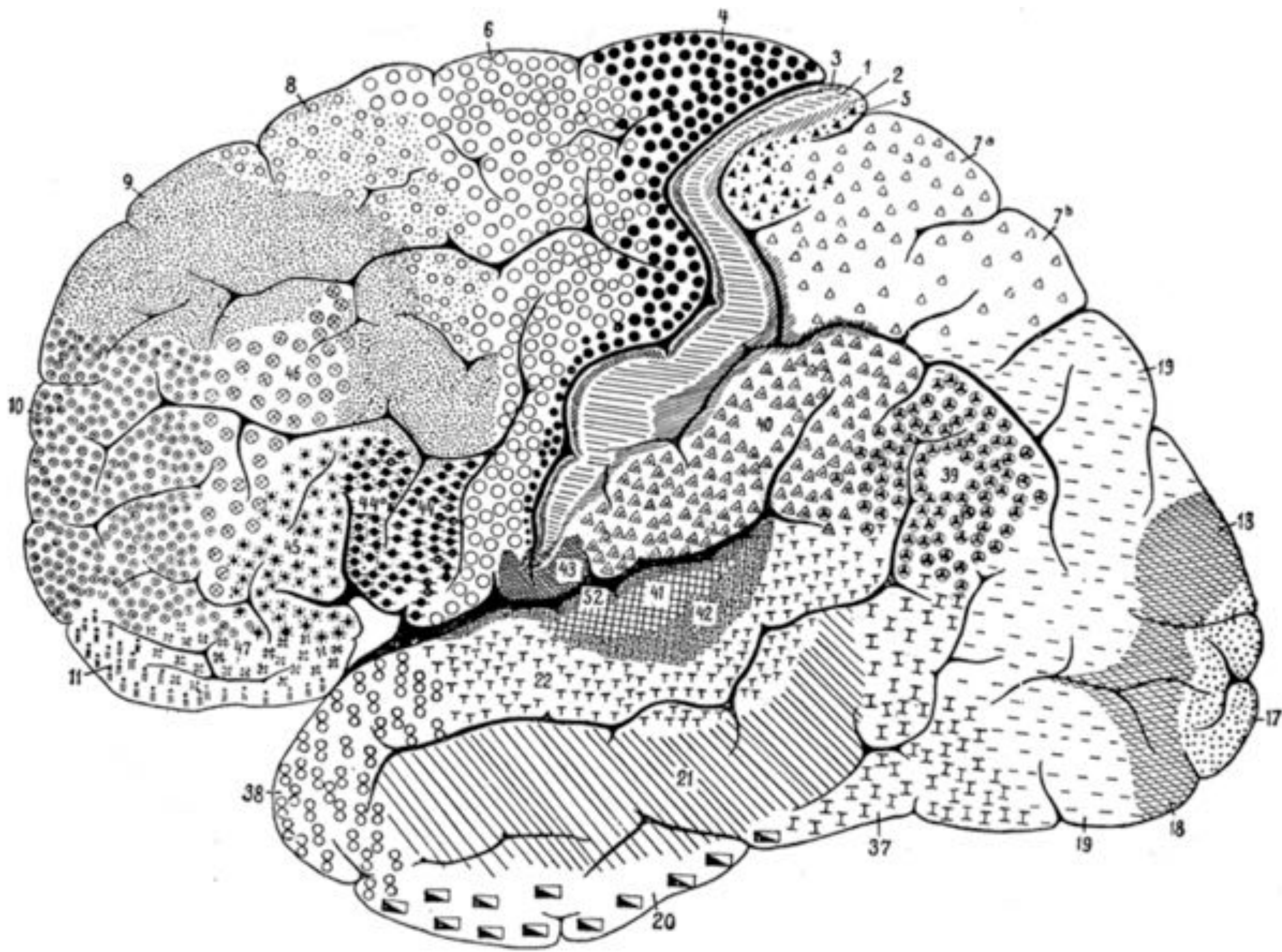
Causal variants are mostly located within genes and in immediately neighbouring regions



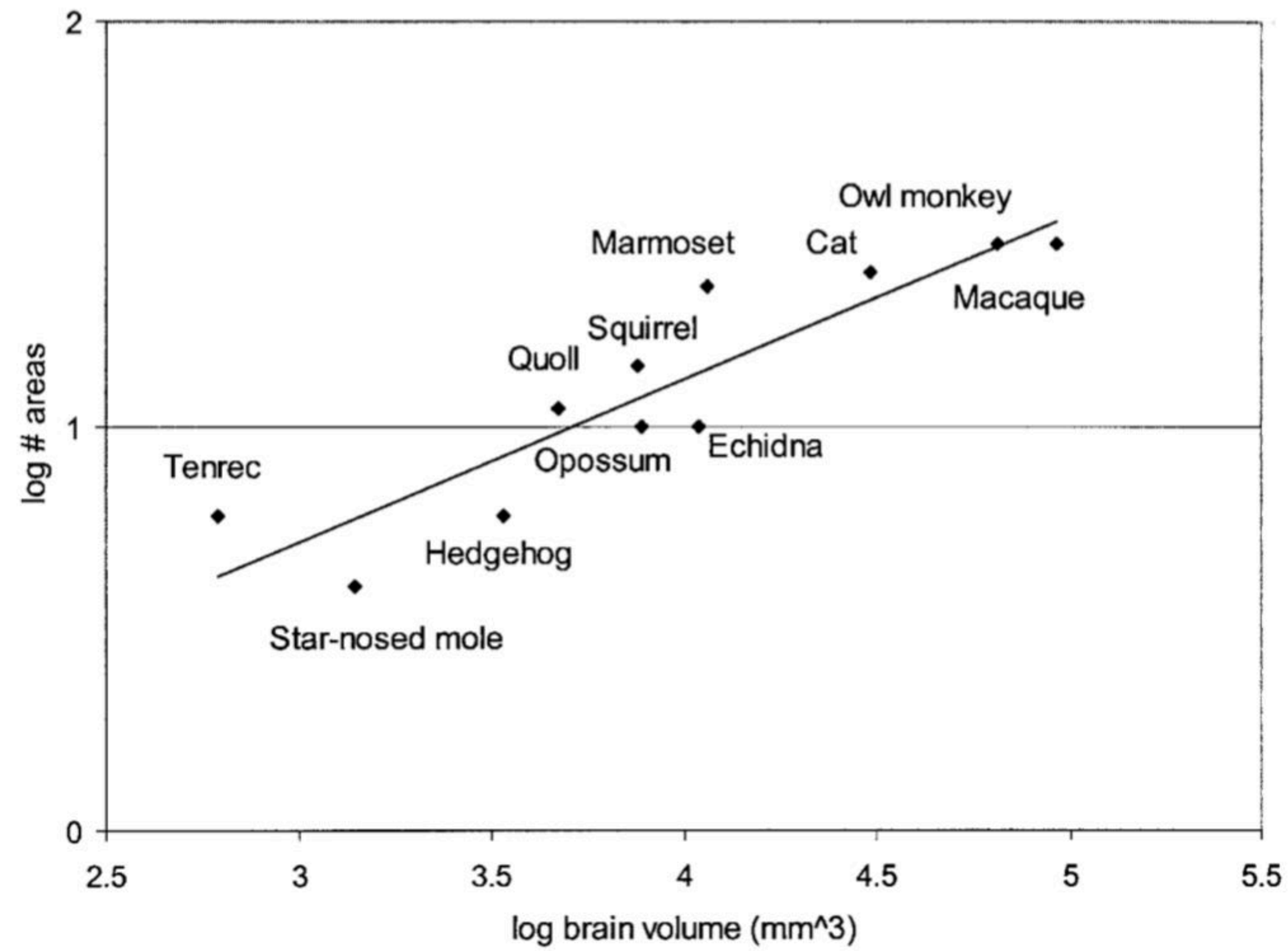
3

Mechanical morphogenesis

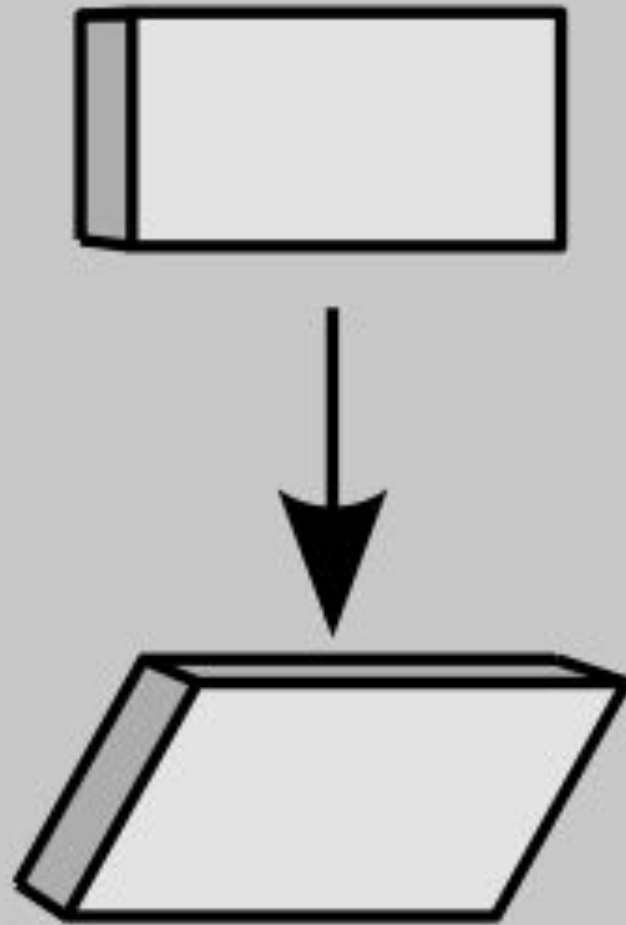




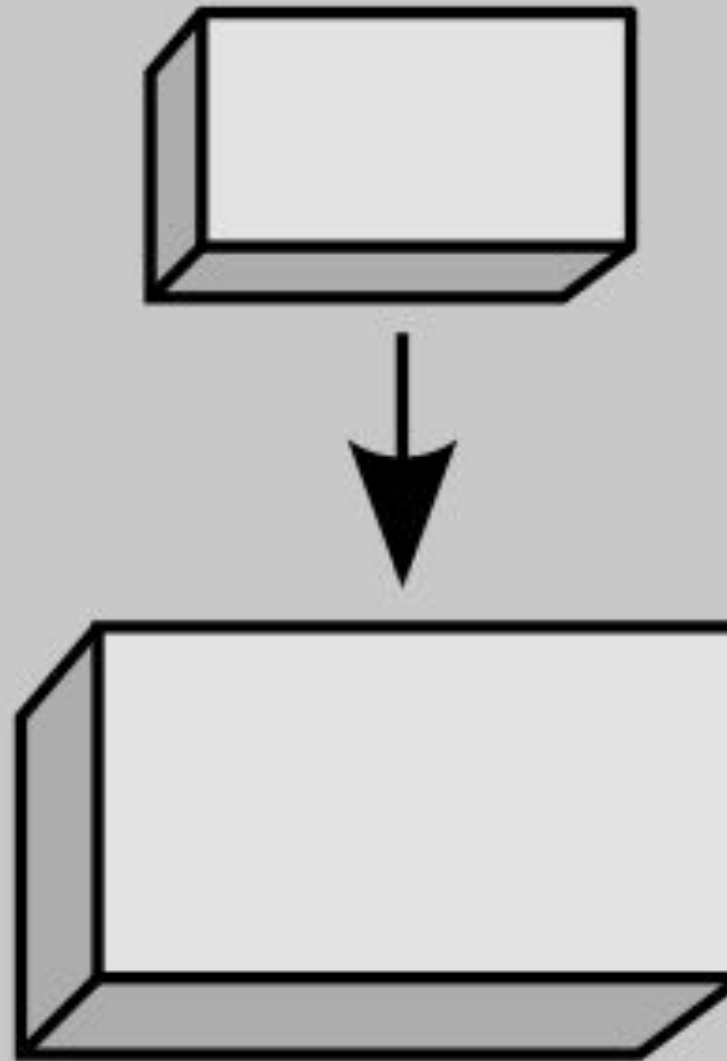
A



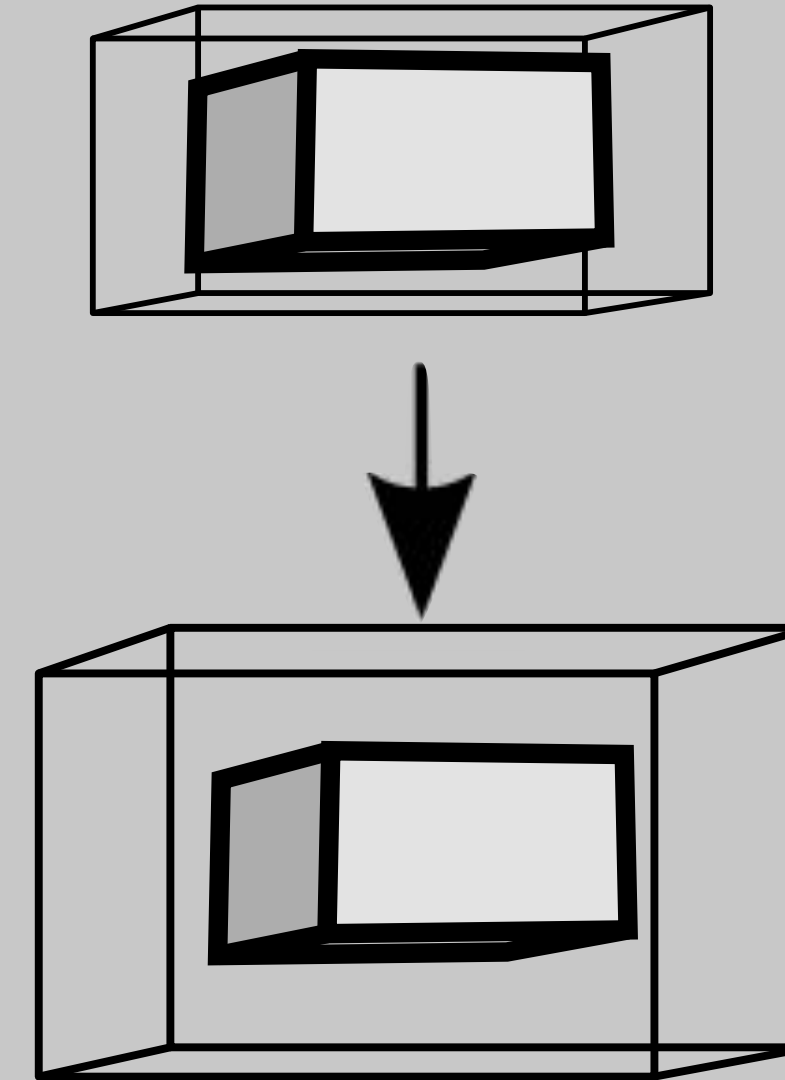
Modelling: Elasticity & Growth



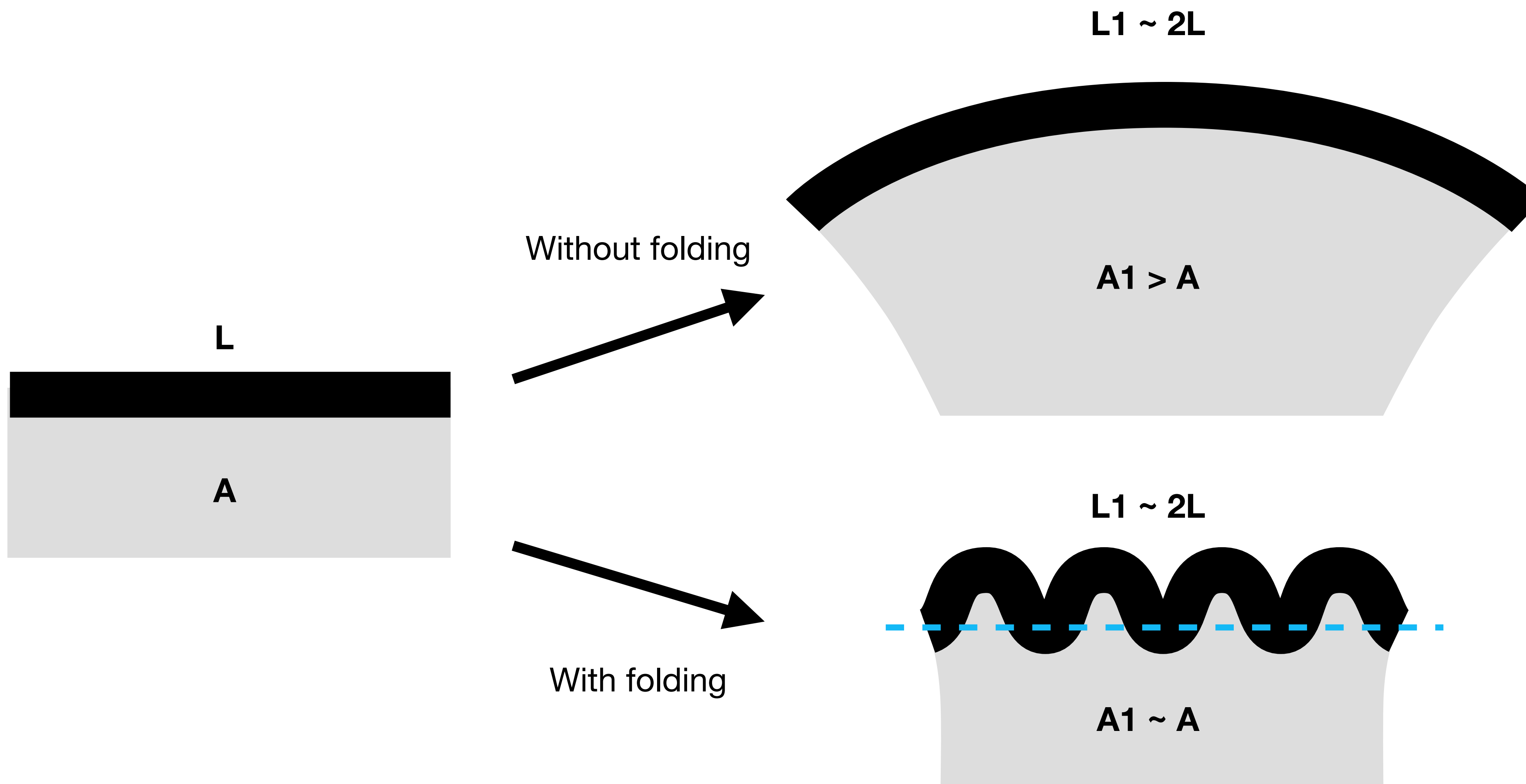
changes in **shape**

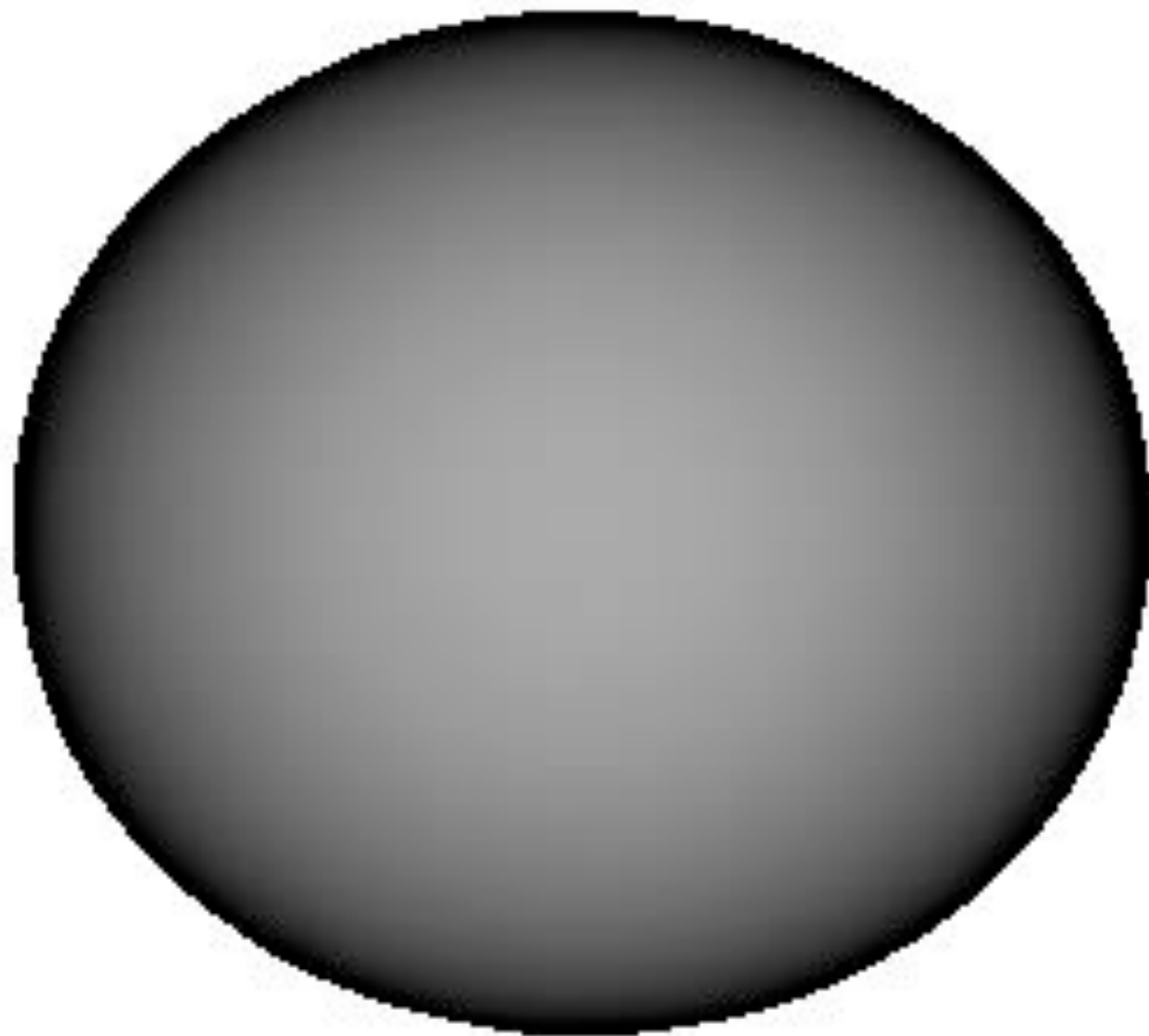


changes in **size**

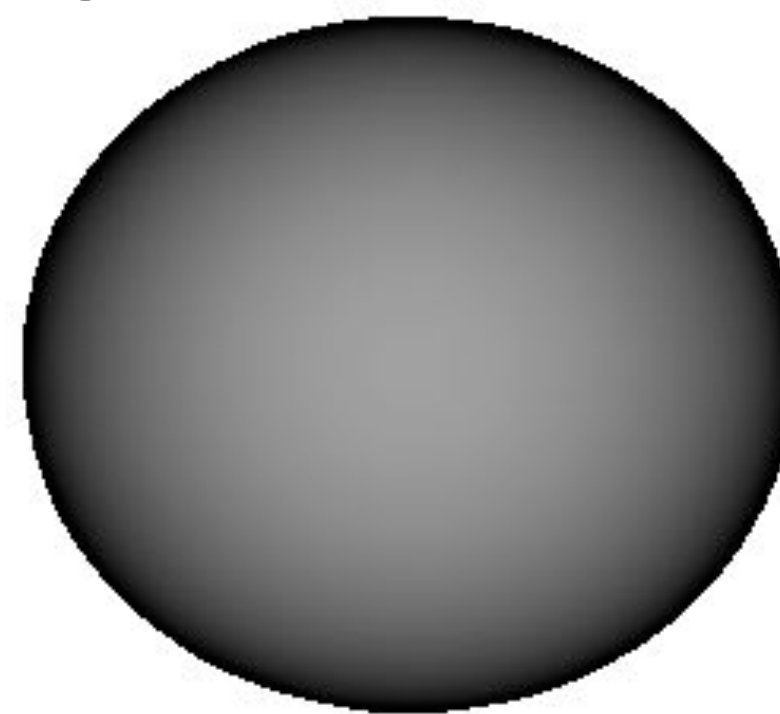


changes in **size at rest**

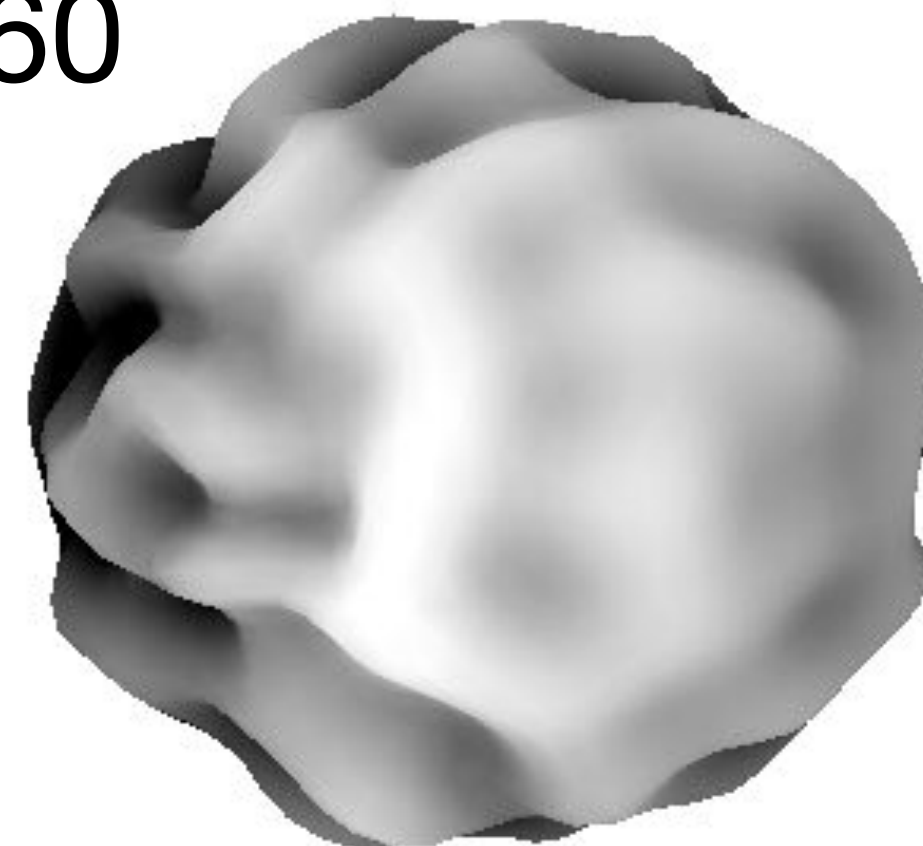




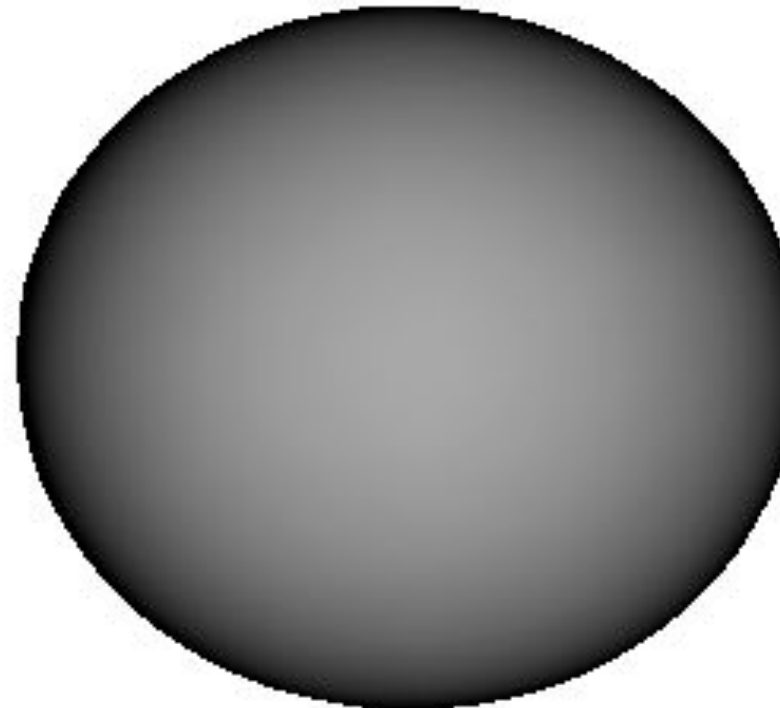
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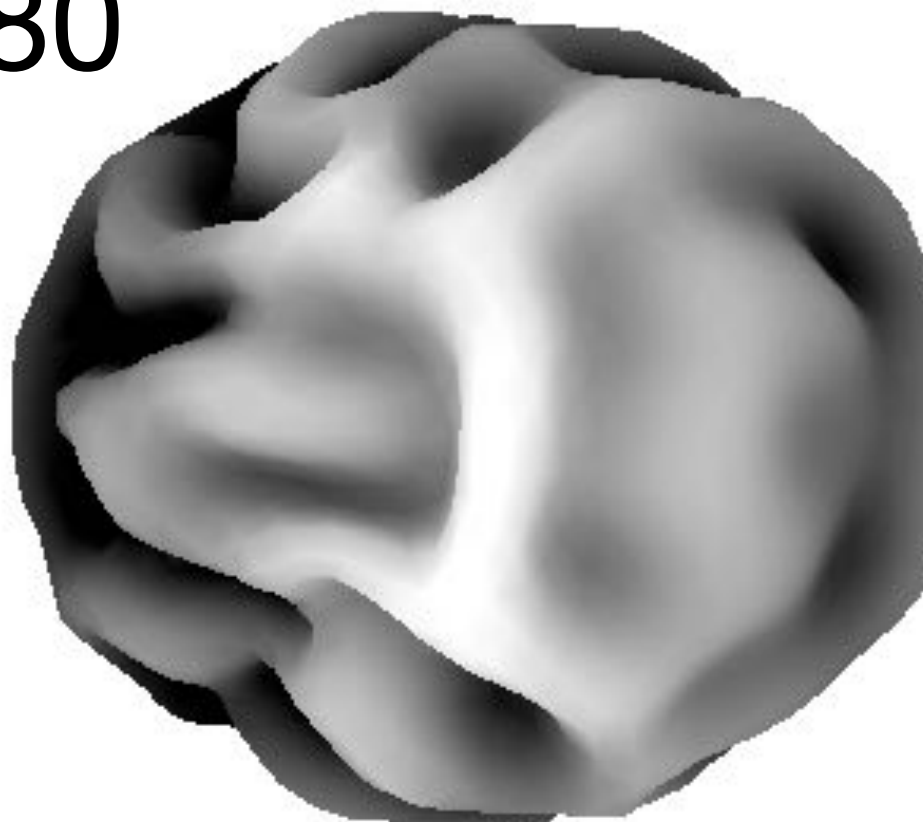
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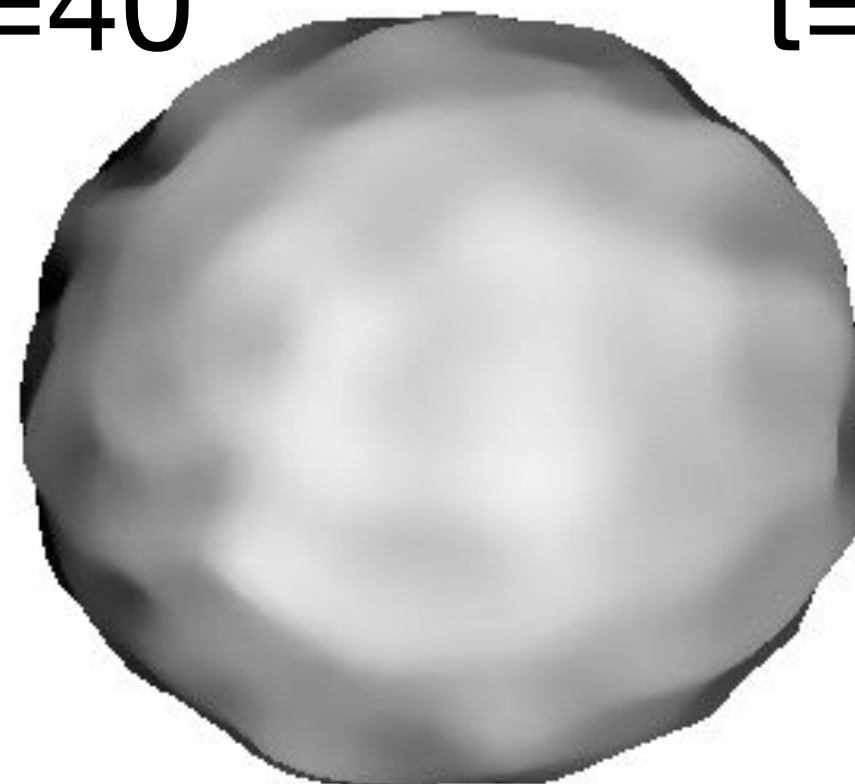
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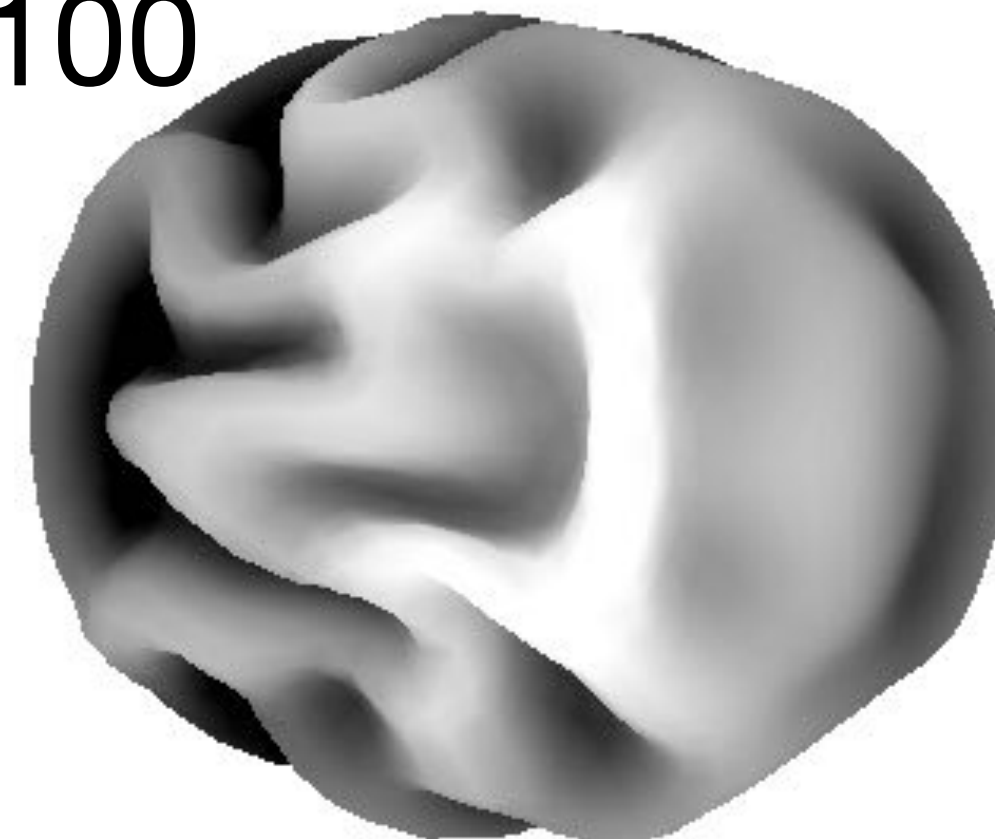
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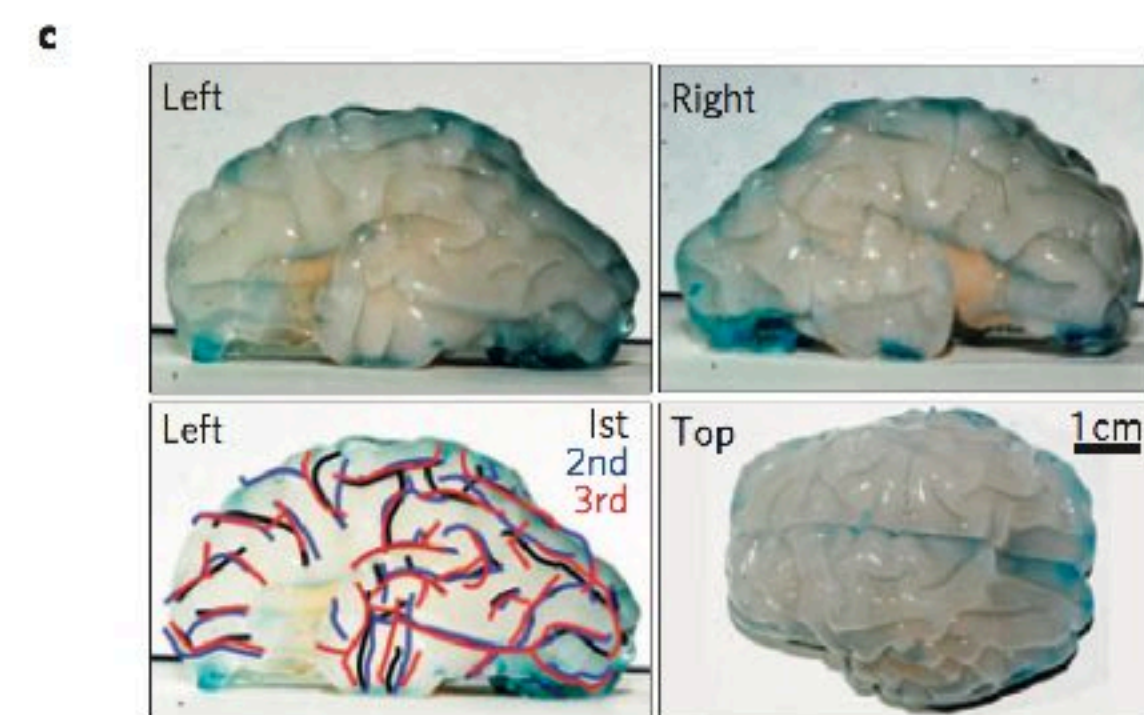
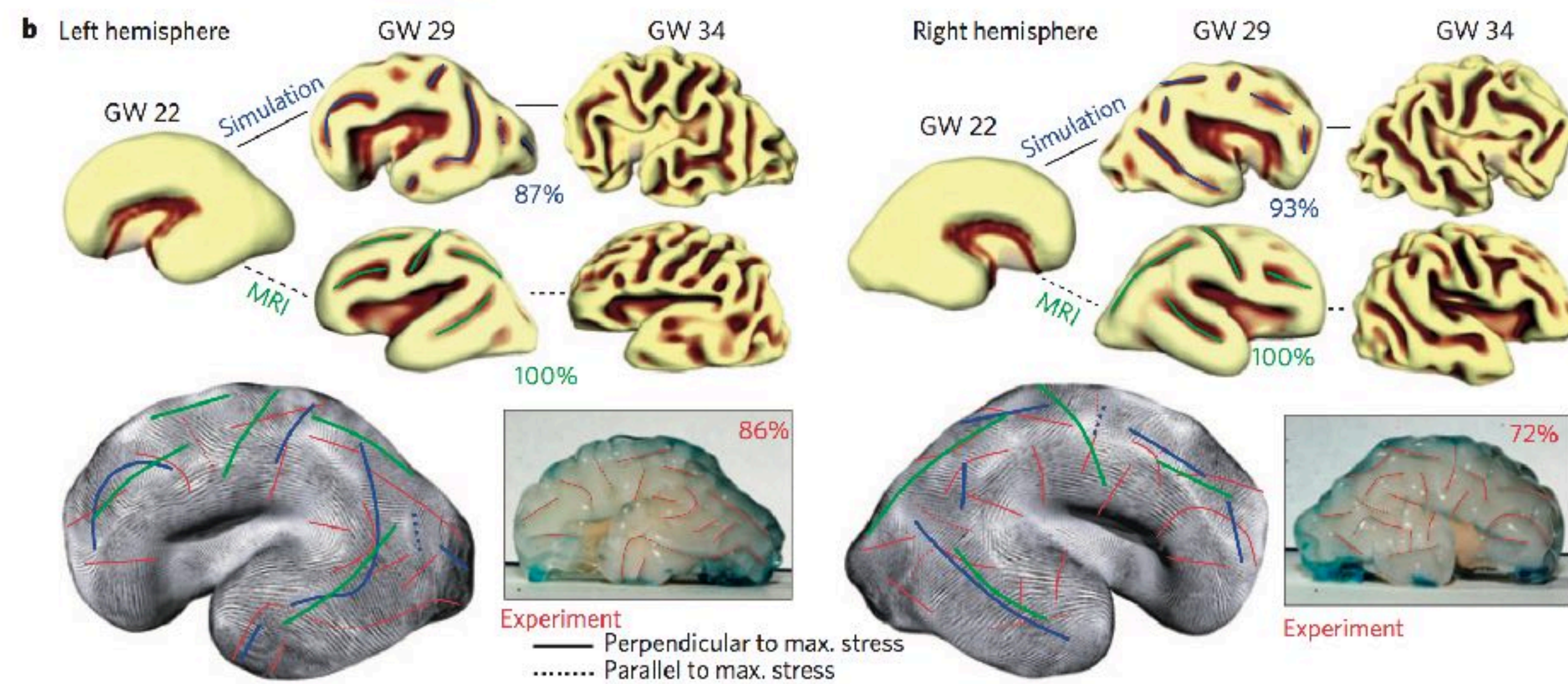
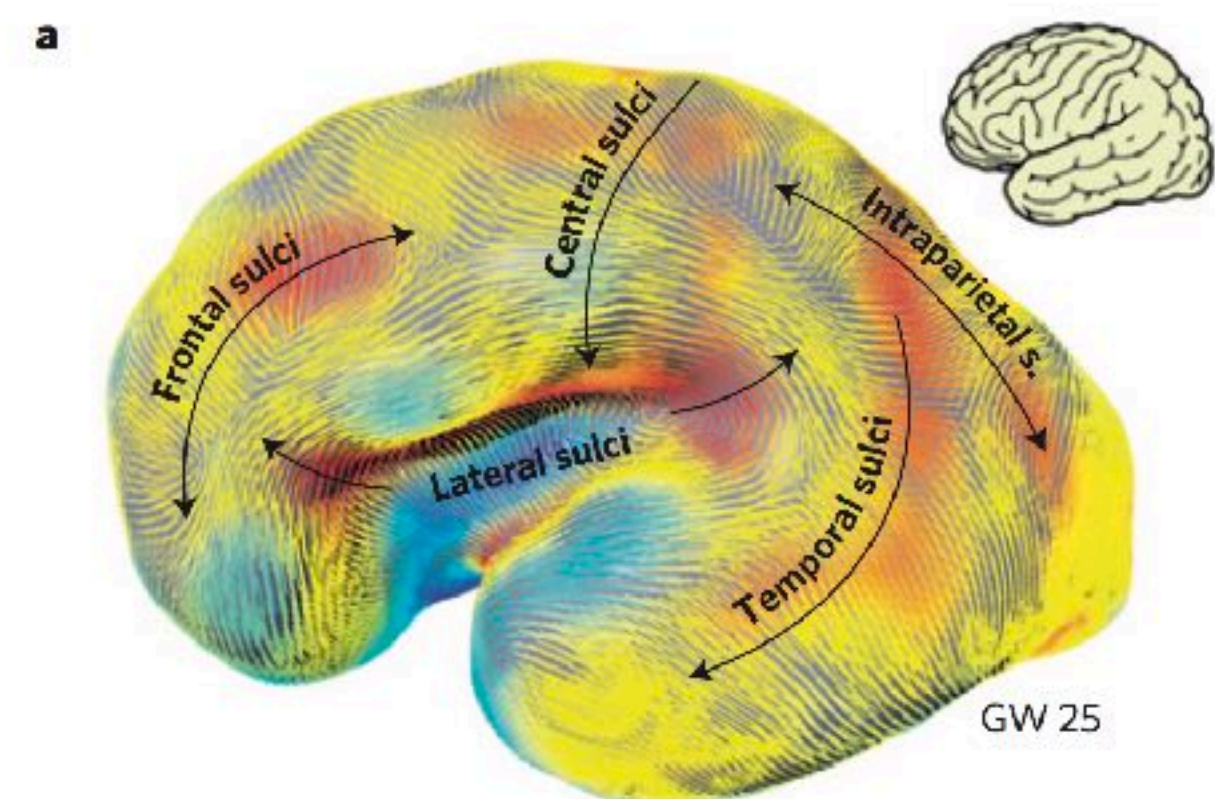
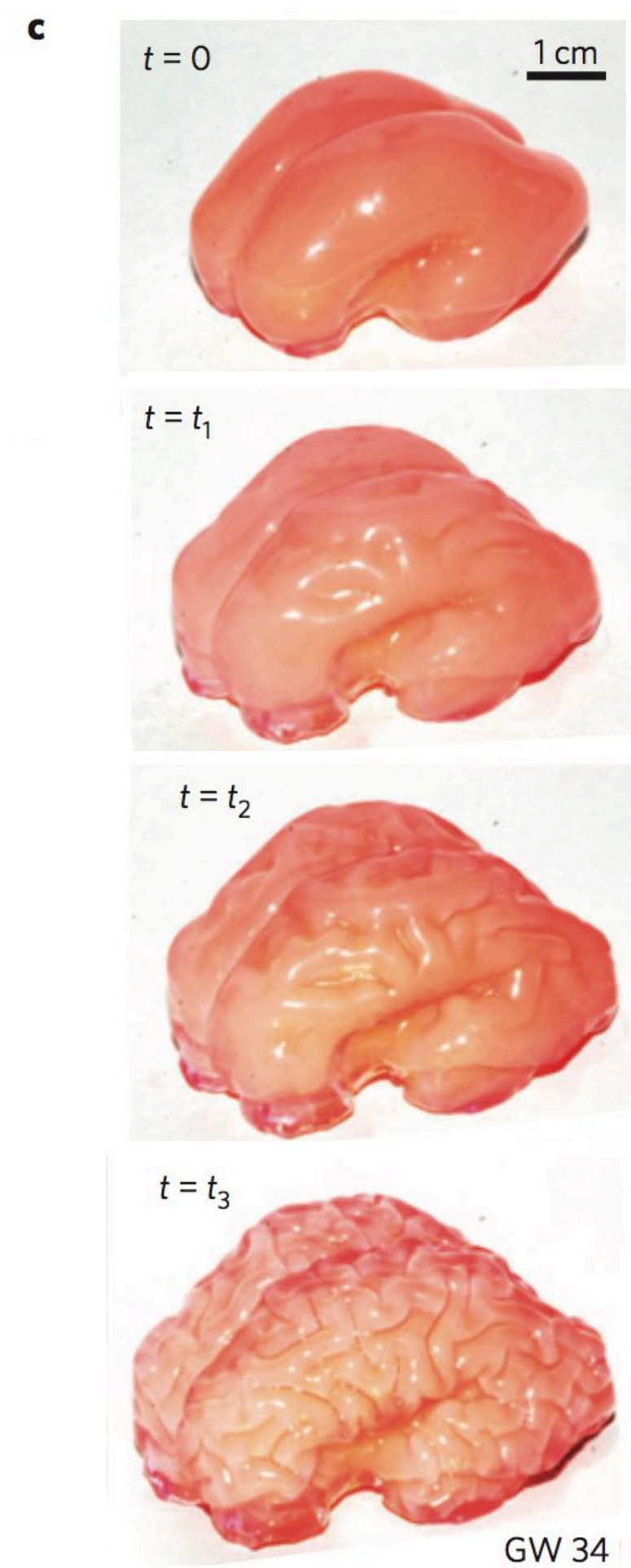
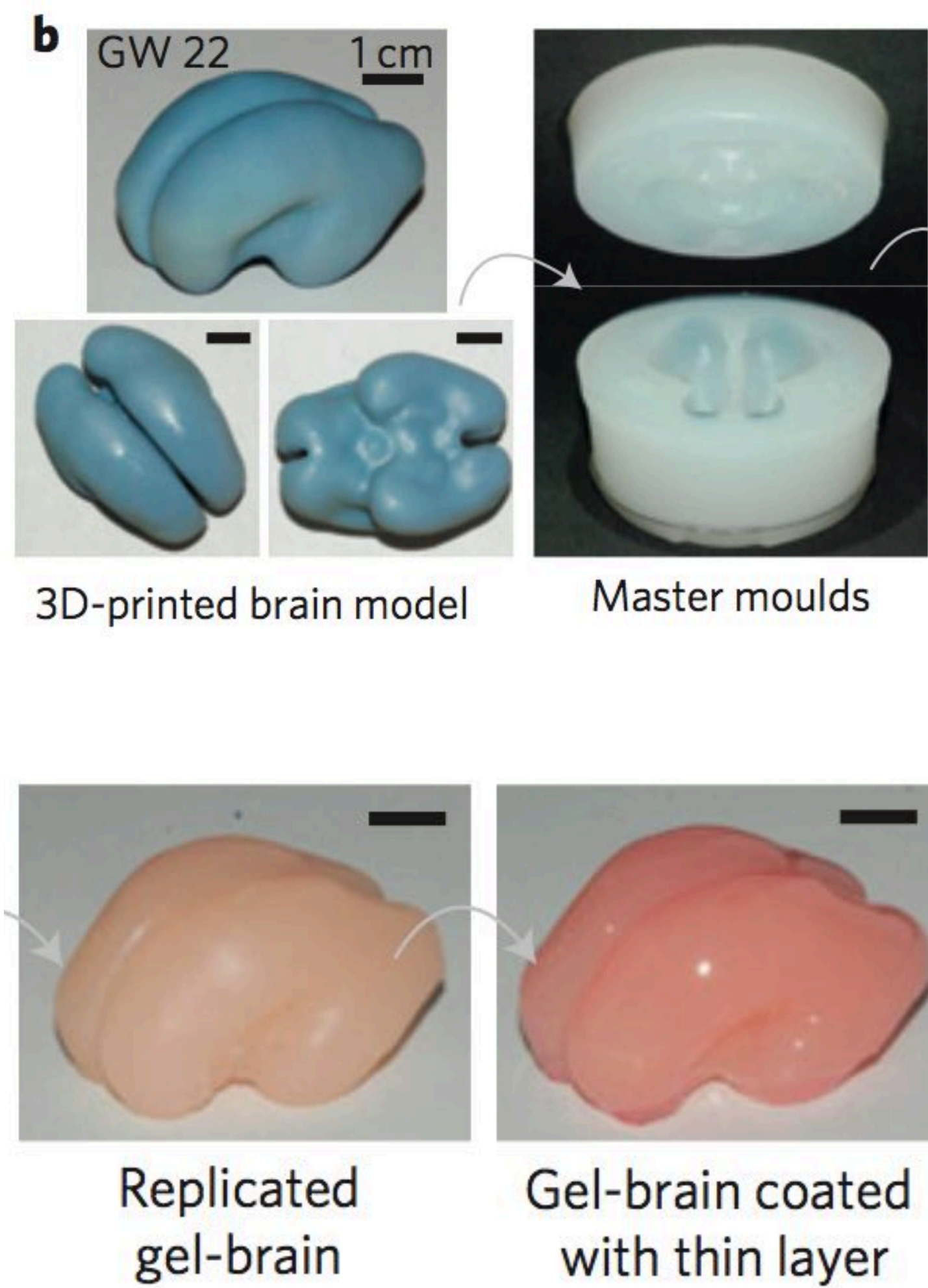


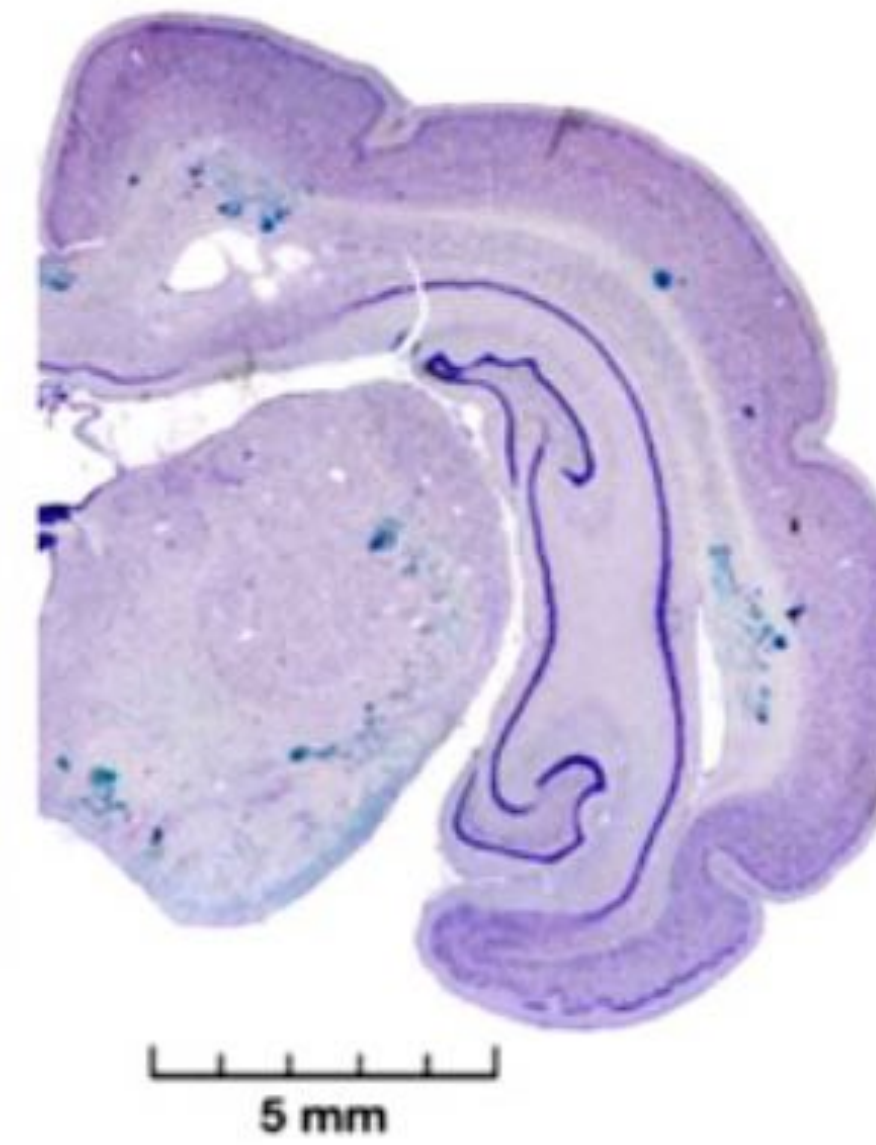
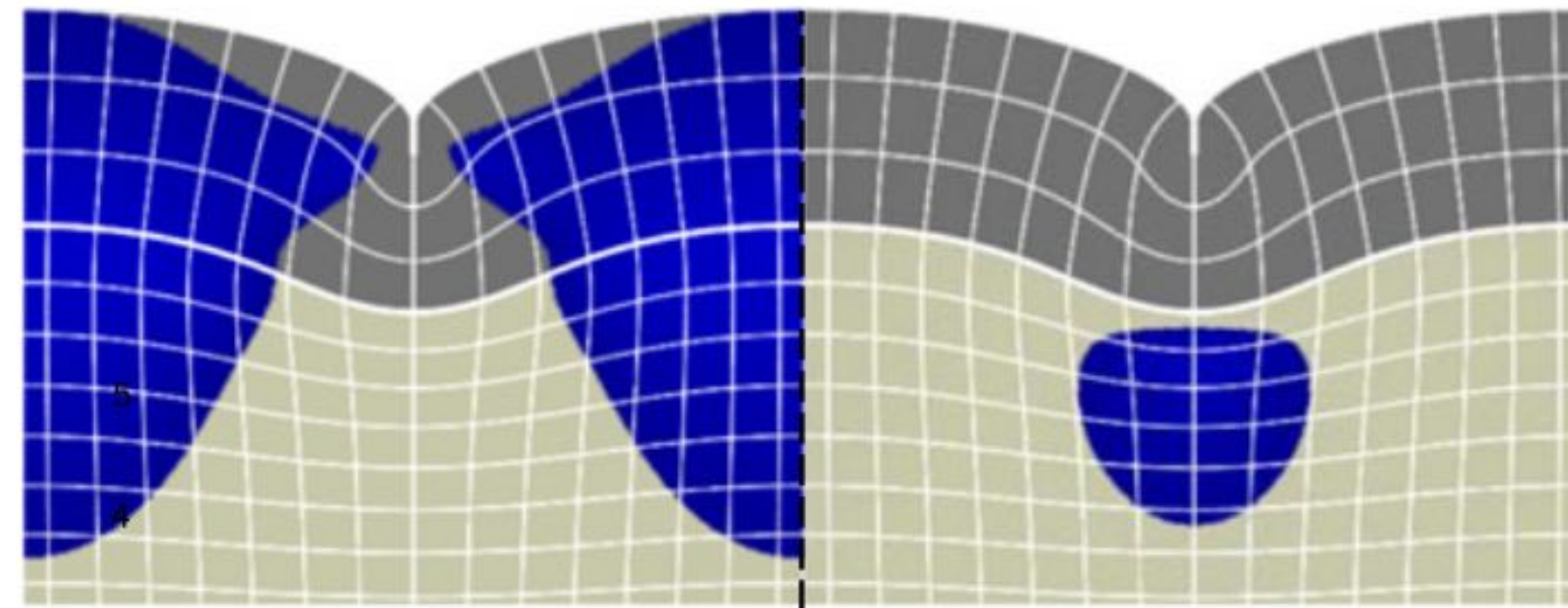
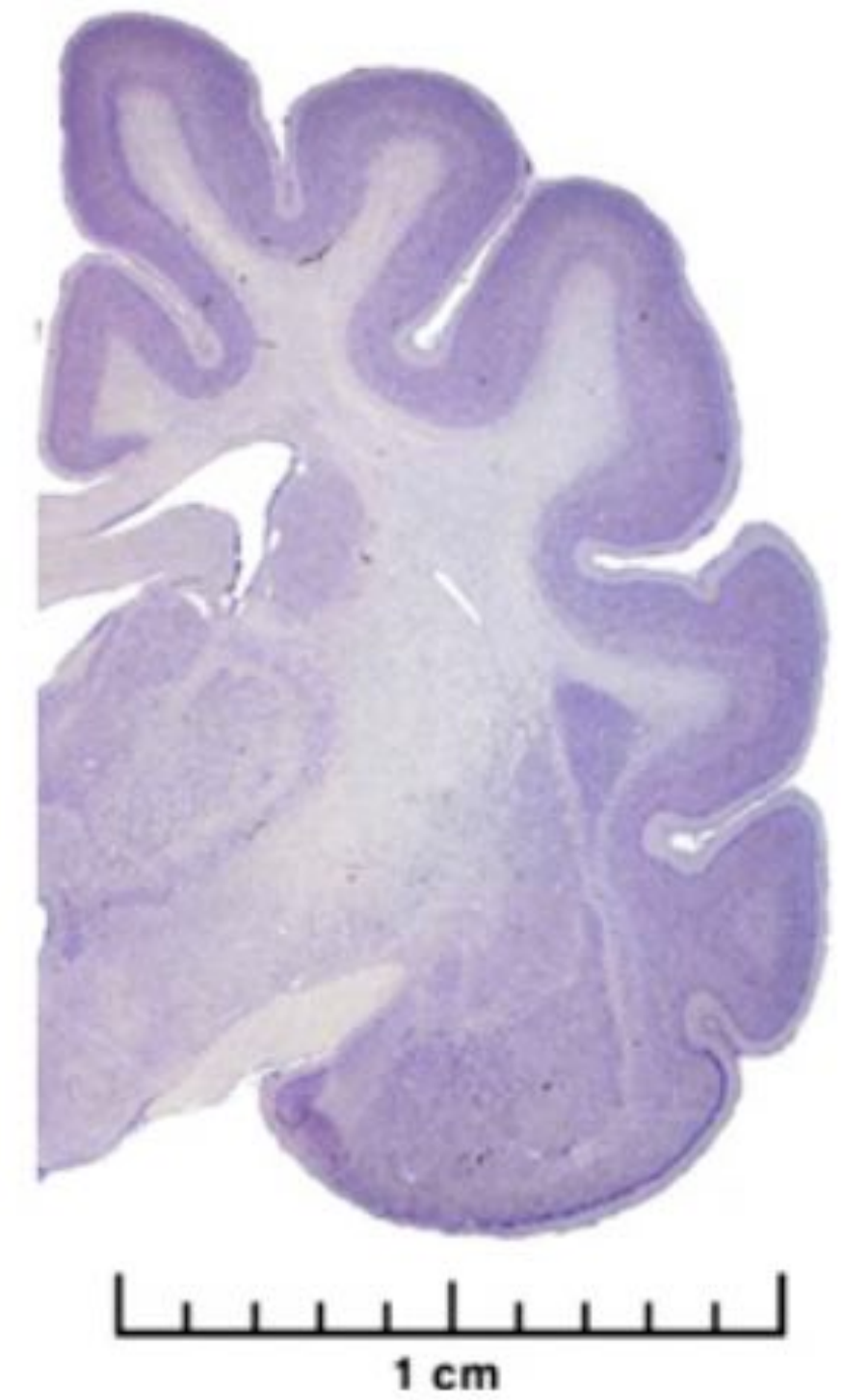
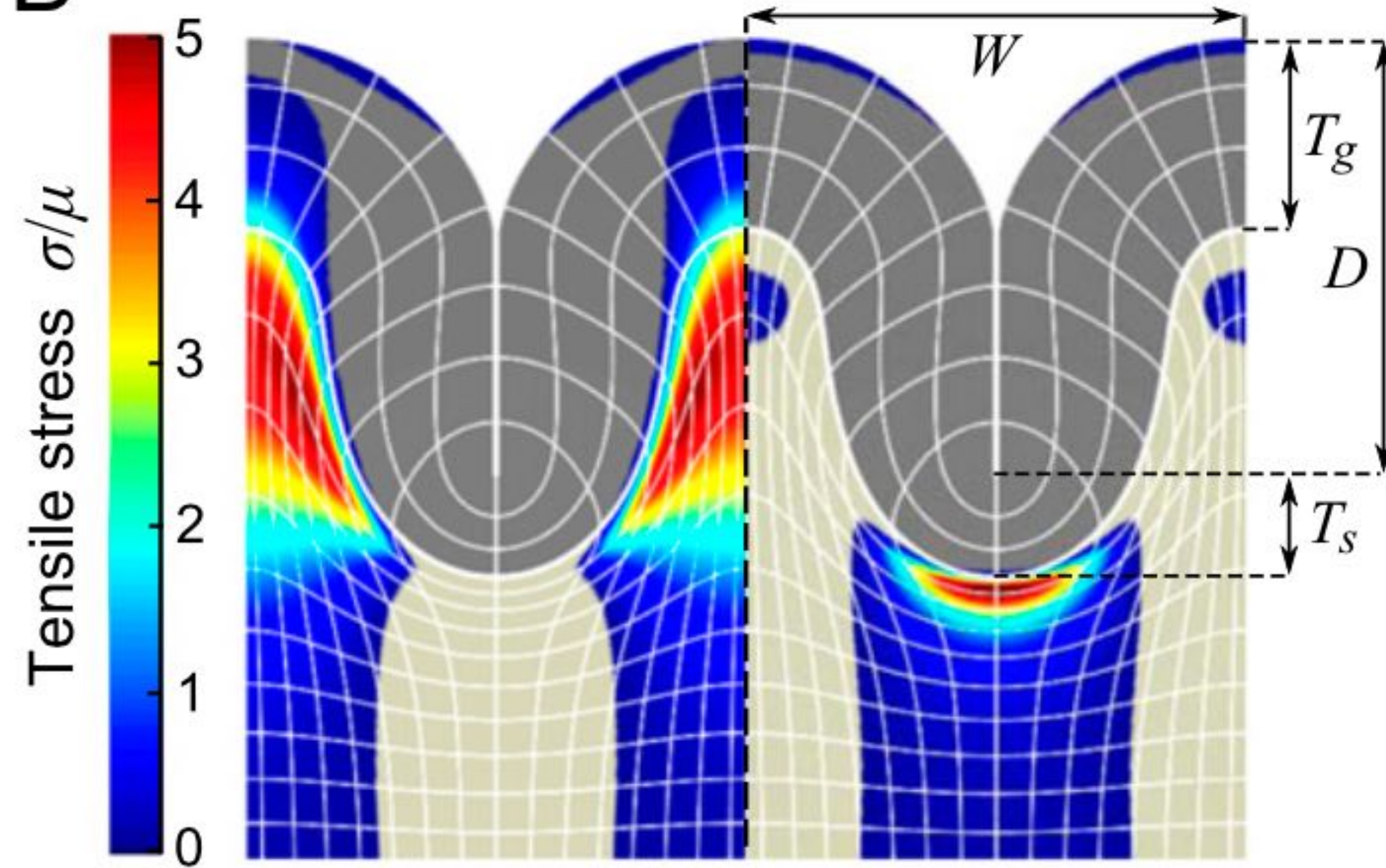
t=40



t=100





A**B**



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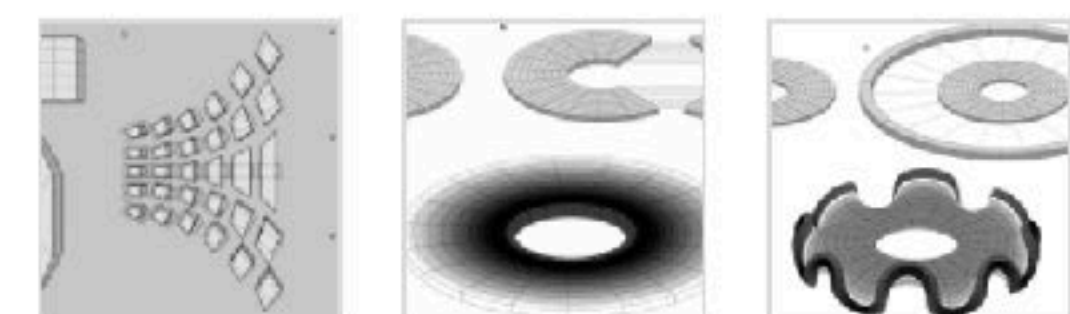
Outline

[Abstract](#)[Keywords](#)

1. Introduction
2. Development of neocortical arealisation
3. The physics of mechanical morphogenesis
4. Effect of mechanical forces on neocortical develop...
5. Conclusion

[Author contributions statement](#)[Additional information](#)[Acknowledgments](#)[References](#)[Show full outline](#) ▾

Figures (3)



Cortex

Available online 20 March 2018

In Press, Uncorrected Proof ?



Special issue: Research report

Mechanical morphogenesis and the development of neocortical organisation

Ophélie Foubet ^{a, b, c}, Miguel Trejo ^d, Roberto Toro ^{a, b, c} [Show more](#)<https://doi.org/10.1016/j.cortex.2018.03.005>[Get rights and content](#)

Abstract

The development of complex neocortical organisations is thought to result from the interaction of genetic and activity-dependent processes. We propose that a third type of process – mechanical morphogenesis – may also play an important role. We review theoretical and experimental results in physics showing how even homogeneous growth can produce a variety of forms, in particular neocortical folding. The mechanical instabilities that produce these forms induce heterogeneous patterns of stress at the scale of the organ. We review the evidence showing how these stresses can influence cell proliferation, migration and apoptosis, cell differentiation and shape, migration and axonal guidance, and could thus be able to influence regional neocortical identity and connectivity.

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Effects of mechanics on developing tissue

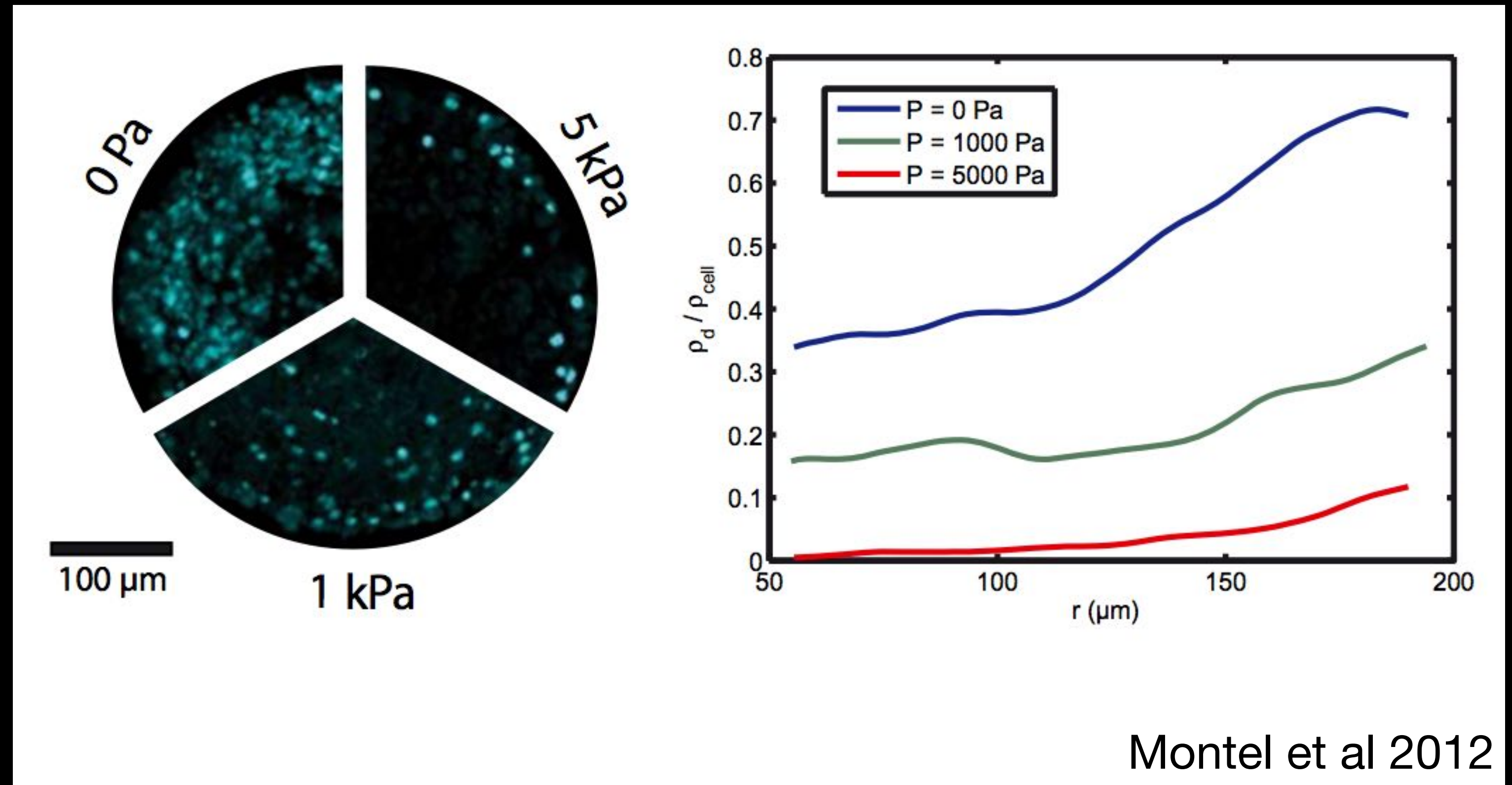
Cell proliferation

Cell fate

Cell shape

Axonal guidance

Neural stem cells (culture): division peak at 1-4 kPa.
In gels softer than ~10 Pa, spreading, self-renewal and differentiation is completely inhibited (Fung, 1993; Rodriguez et al., 1994; Cheng et al., 2009; Montel et al., 2012, Saha et al., 2008)



Effects of mechanics on developing tissue

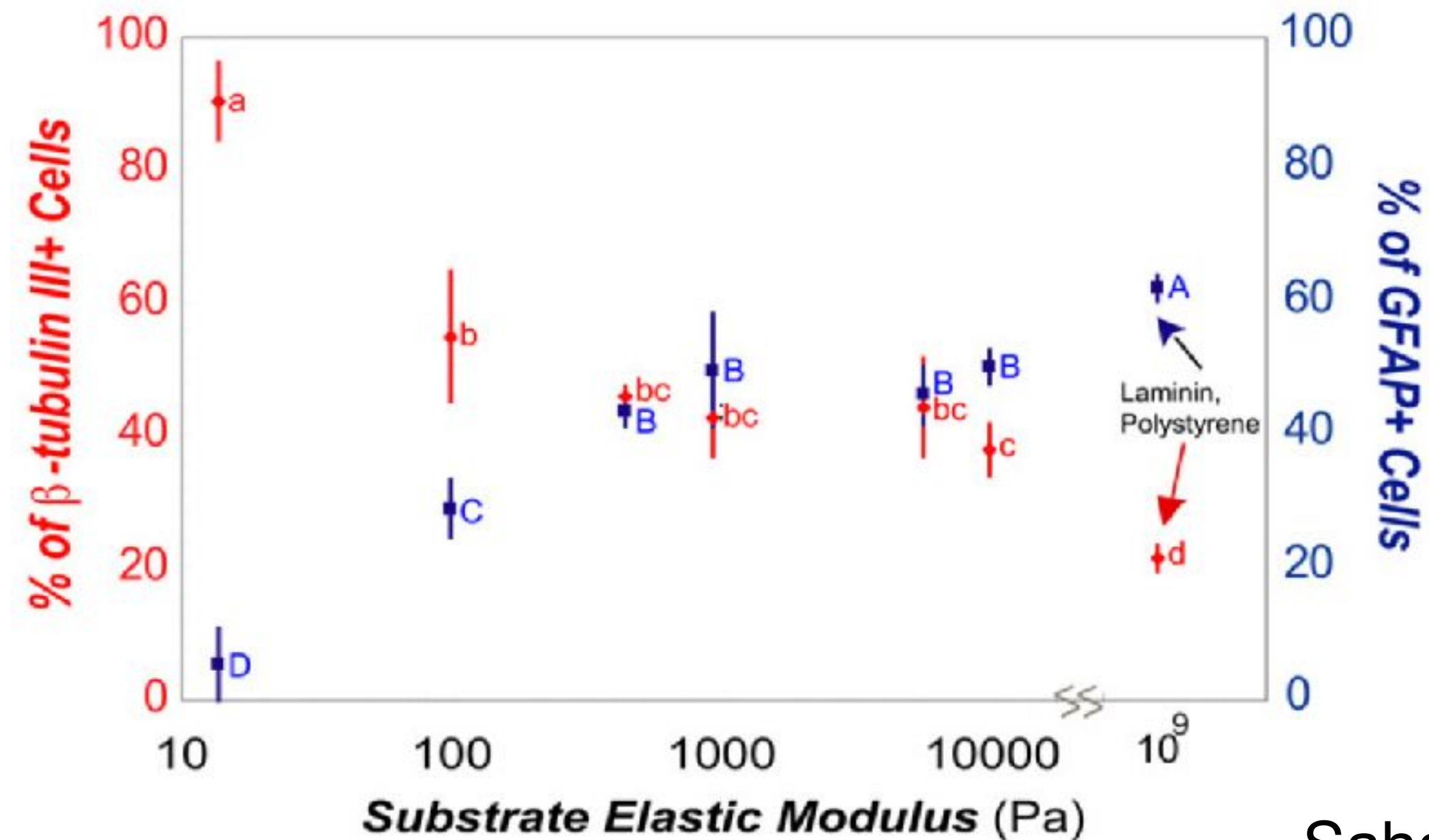
Cell proliferation

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Naive mesenchymal stem cells cultured on a substrate mimicking the elasticity of brain, muscle or bone, differentiated respectively into branched cells similar to neurons, myoblasts or polygonal cells similar to osteoblasts. Soft gels produce mostly neurones, whereas increasingly harder gels (up to 1-10 kPa) produced progressively more glial cells.



Saha et al 2008

Effects of mechanics on developing tissue

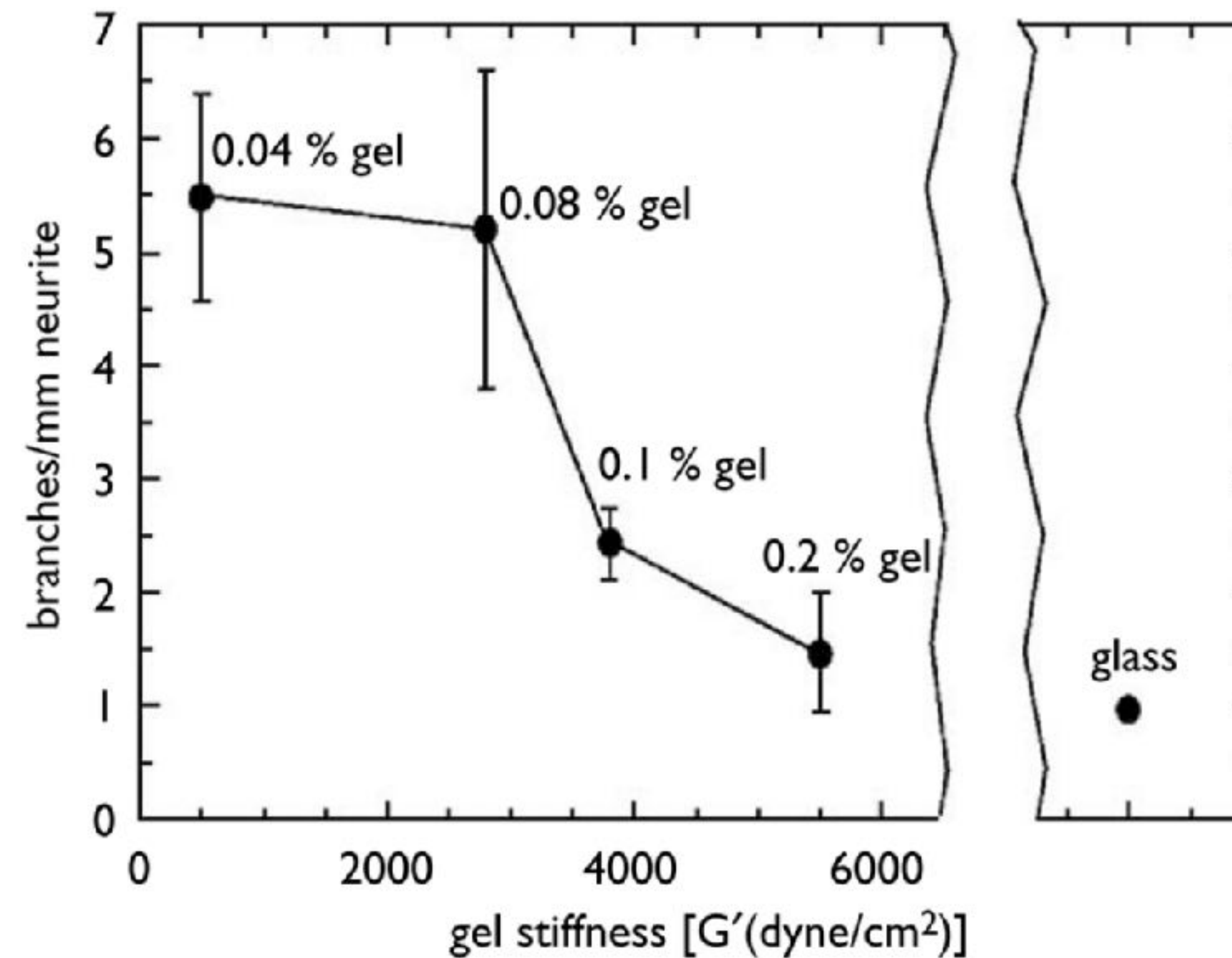
Cell proliferation

Cell fate

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Axonal guidance

Neurons cultured on soft substrates (50-300 Pa) develop up to 3 times more branching than those cultured on stiffer gels (300-550 Pa, Flanagan et al (2002)).



Flanagan et al 2002

Effects of mechanics on developing tissue

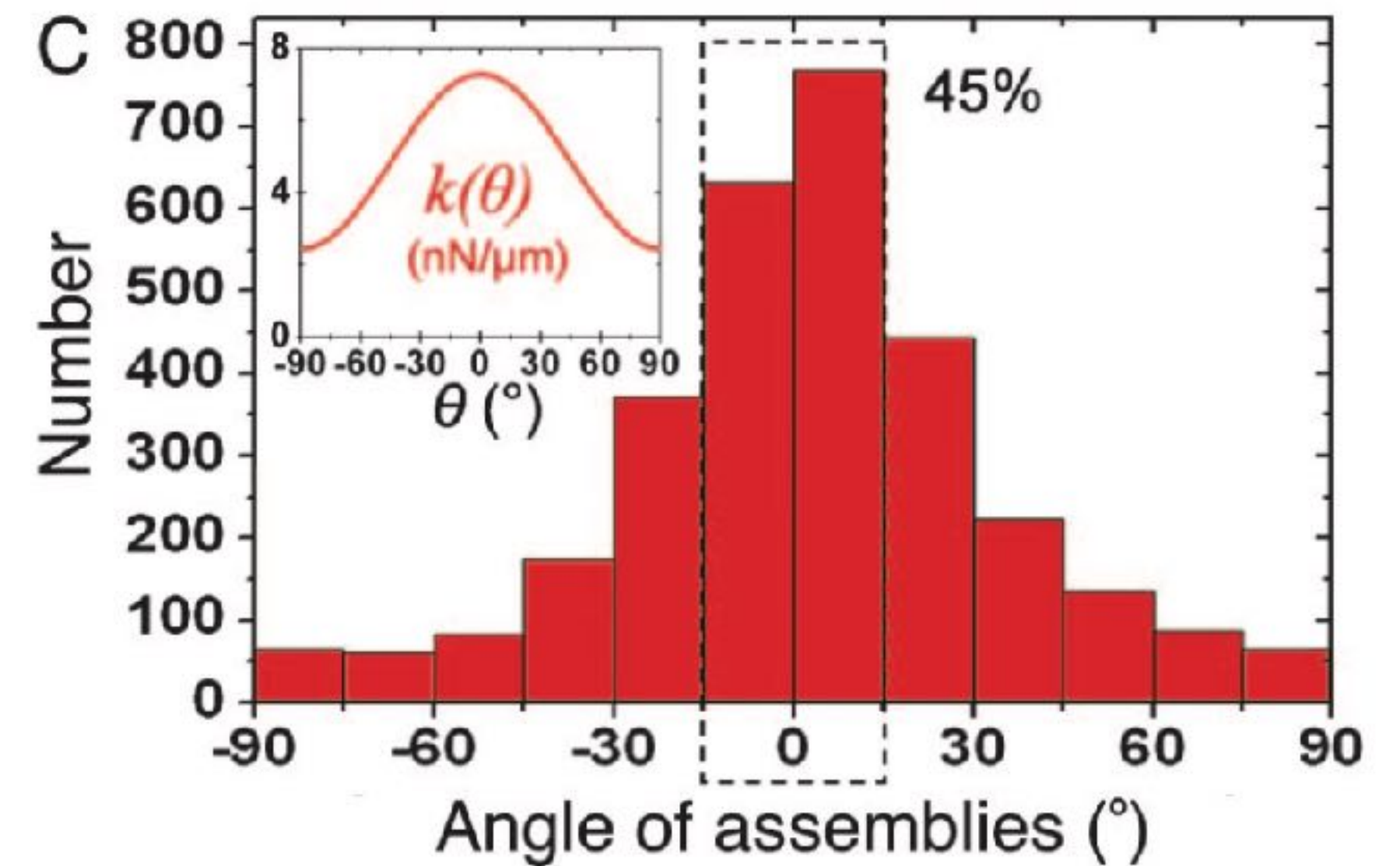
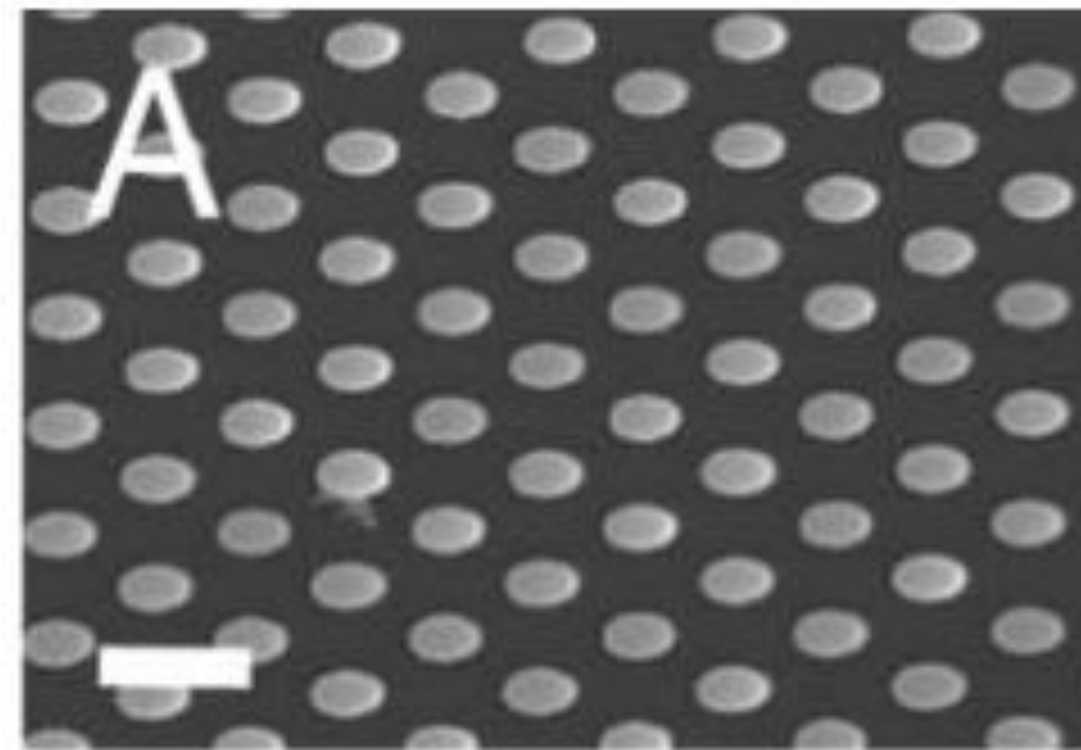
Cell proliferation

Cell fate

Cell shape

Axonal guidance

Cell migration and axonal pathfinding respond to mechanical clues (Saez et al., 2007).



Saez et al 2007



FIIND

Ferret Interactive
Integrated Neuro
Development Atlas



Groupe de neuroanatomie appliquée et théorique, Institut Pasteur, France

Roberto Toro (P.I.) is leader of the group of applied and theoretical neuroanatomy at the unit of human genetics and cognitive function, department of neuroscience of the Institut Pasteur. After a degree in engineering, he obtained a Master and a PhD in Neuroscience at the University of Paris 6, France. He is interested on the development and evolution of the brain, which he studies through mathematical modelling, magnetic resonance imaging and genomics.



Radboud University Nijmegen, The Netherlands

Paul Tiesinga is professor of Neuroinformatics and chair of the department of Neuroinformatics. He has a master in Theoretical Physics and a PhD in physics from Utrecht University. He was a postdoc in the physics department at Northeastern University and a Sloan postdoctoral fellow at the Salk Institute. He was associate professor in the Physics & Astronomy department at the University of North Carolina in Chapel Hill. Paul Tiesinga moved to the Radboud University Nijmegen in 2009 to establish the Neuroinformatics department. He has served as director of the Donders Centre for Neuroscience and is member of the Governing Board of the International Neuroinformatics Facility (INCF).



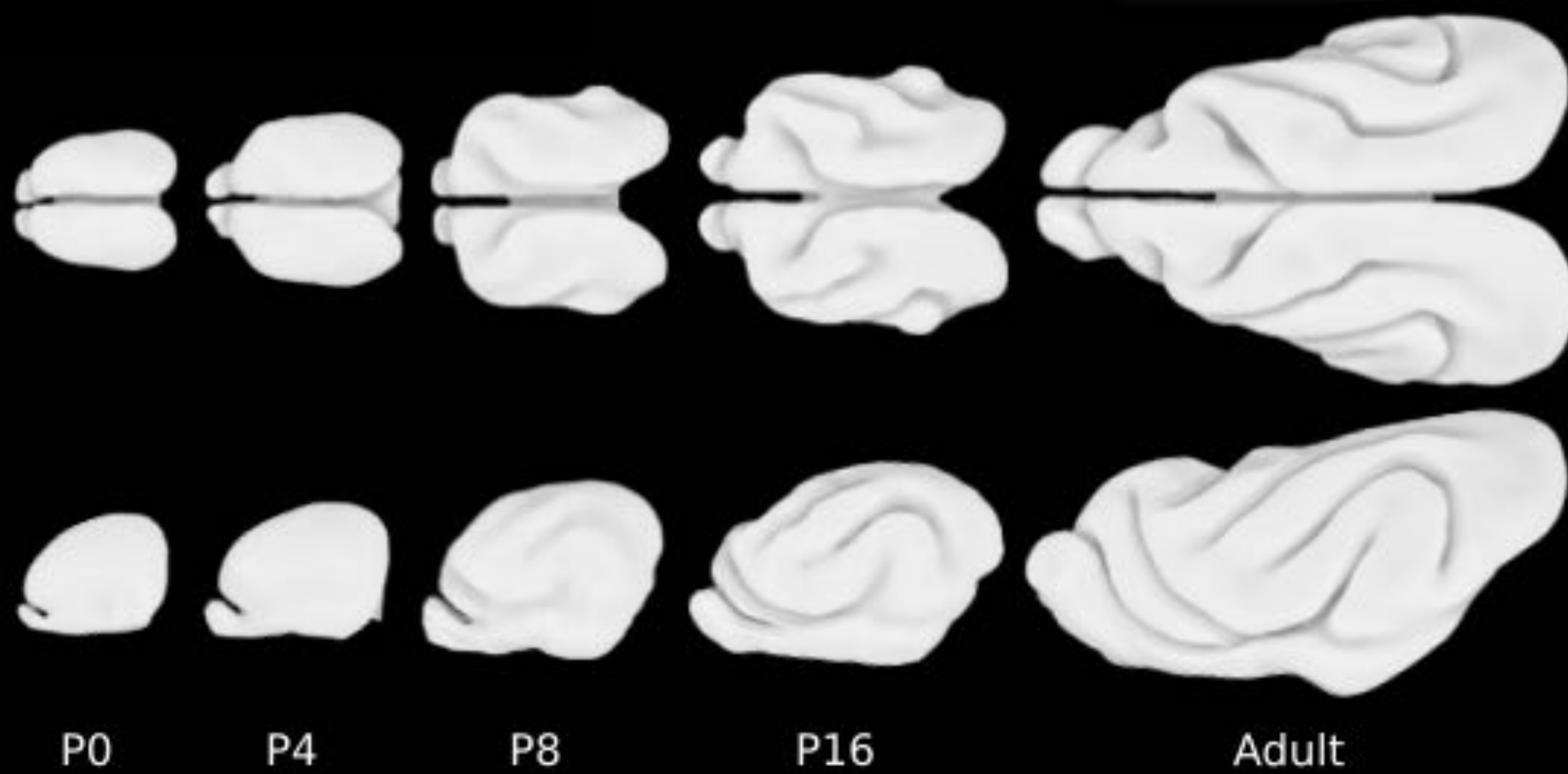
MIRCen, Commissariat aux Énergies Alternatives, France

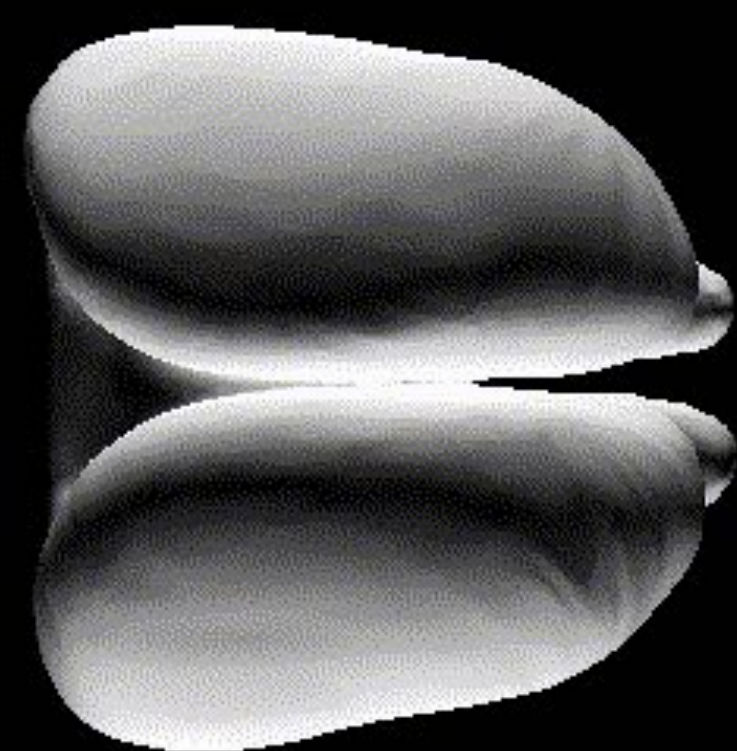
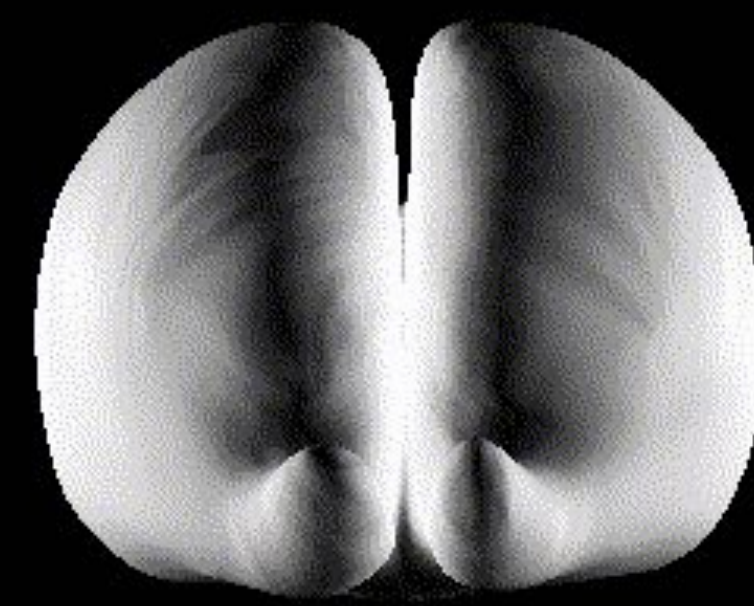
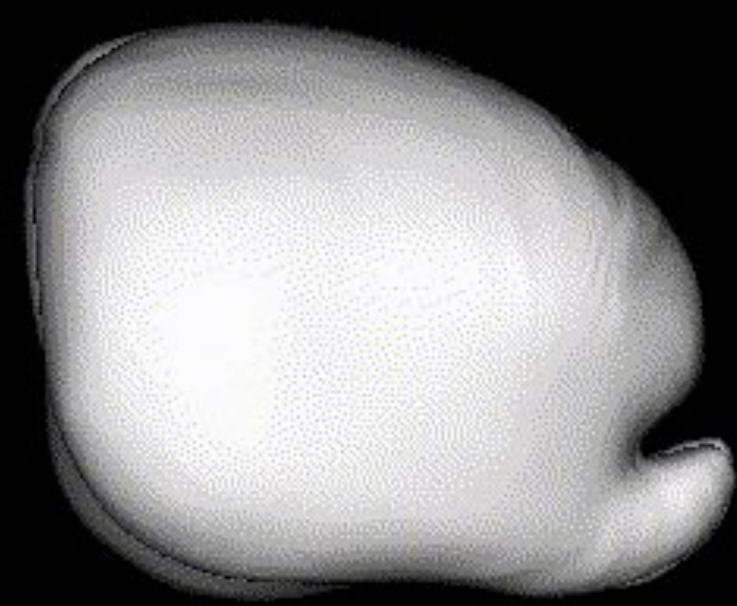
Thierry Delzescaux has a PhD in image processing, and is researcher at the CEA. He specialises in preclinical research (experimental models), image processing in neurodegenerative diseases (Alzheimer's, Parkinson's, Huntington's), multimodal co-registration of in vivo (PET, MRI, CT) and post mortem (histology, autoradiography, immunohistochemistry) brain images, 3D reconstruction and image analysis of post mortem / ex vivo data, anatomo-functional studies in rodents and primates. Thierry Delzescaux is coordinator of the BrainRAT project (Brain Reconstruction and Analysis Toolbox) developed by the image processing team of the MIRCen and integrated into [BrainVISA](#) software.

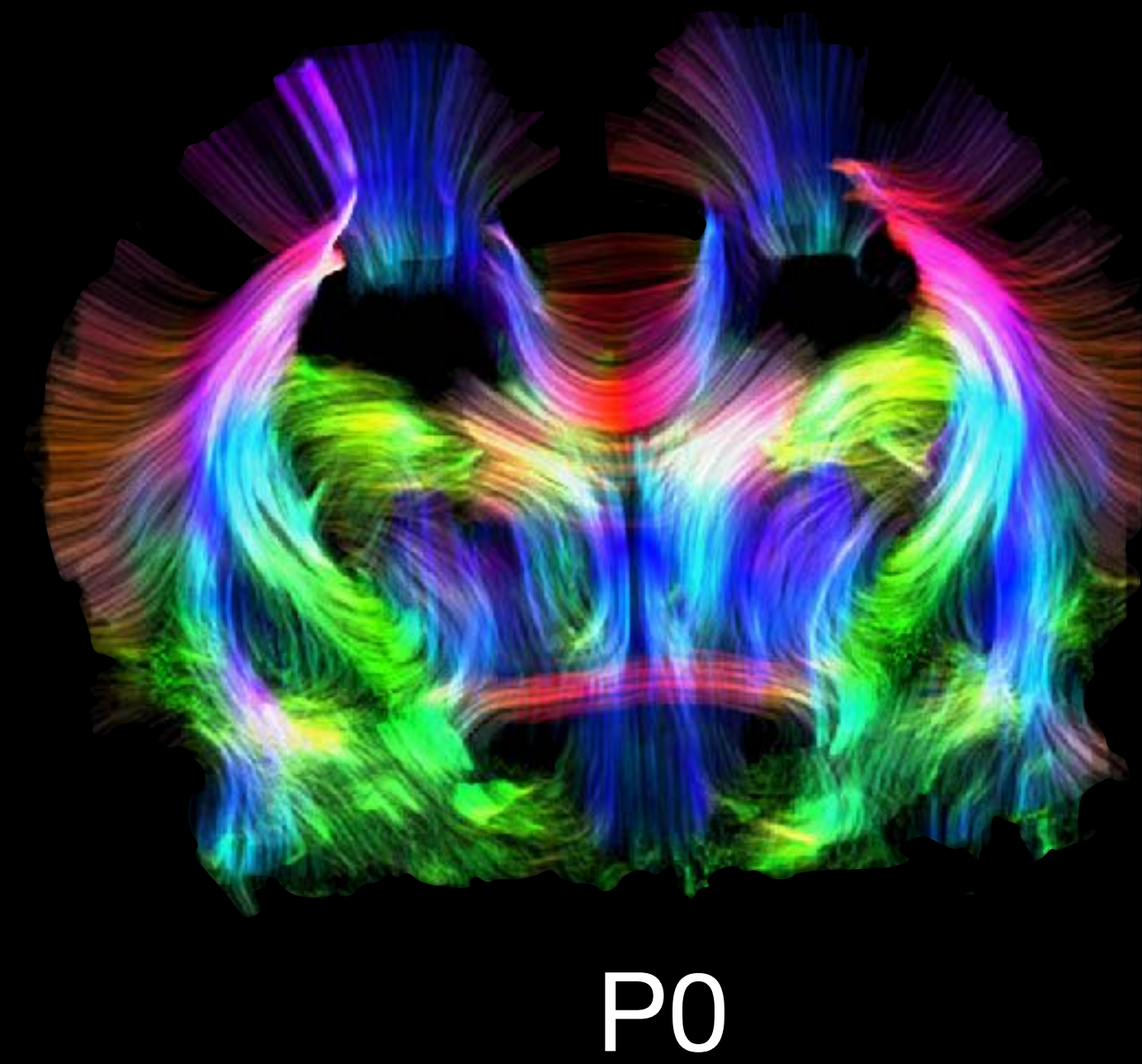
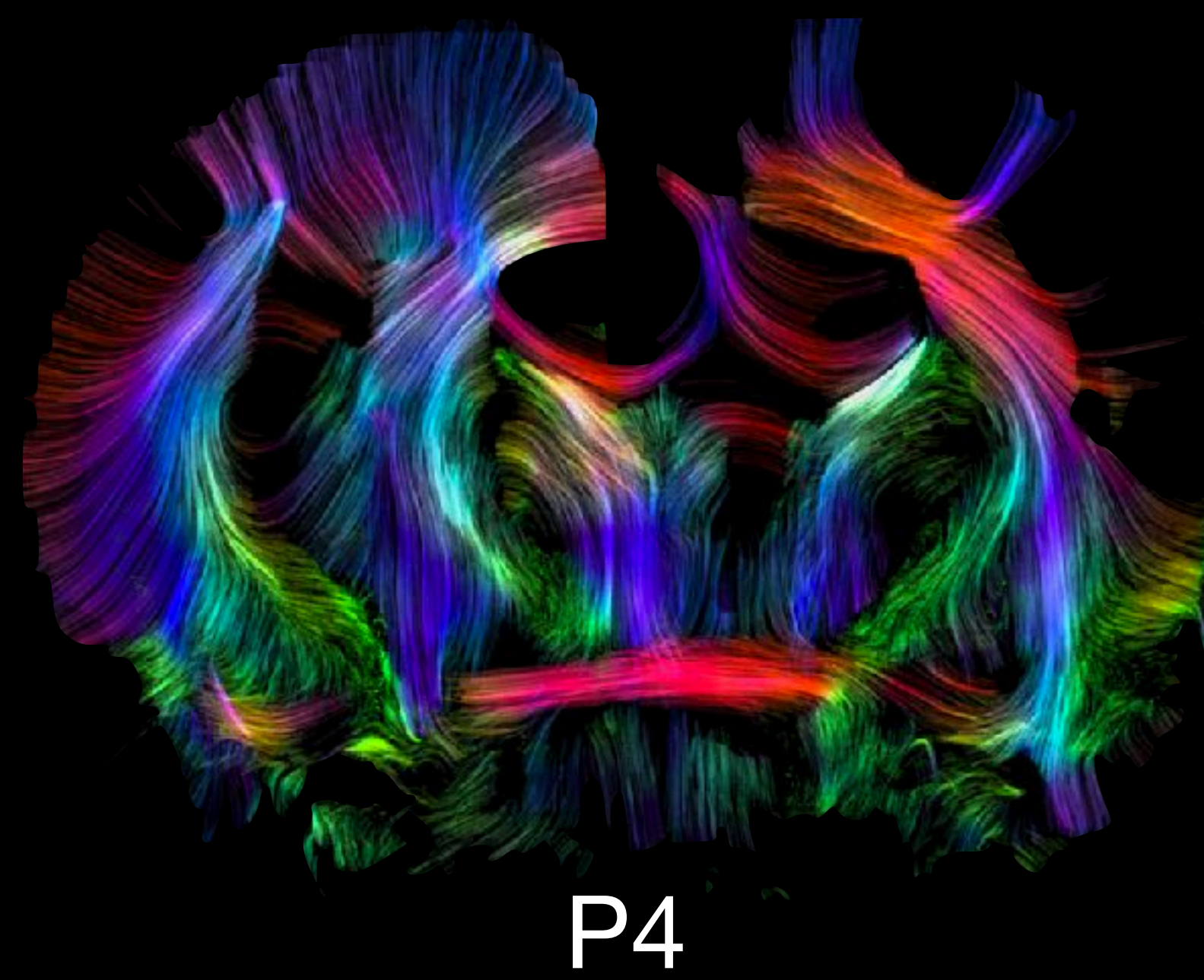
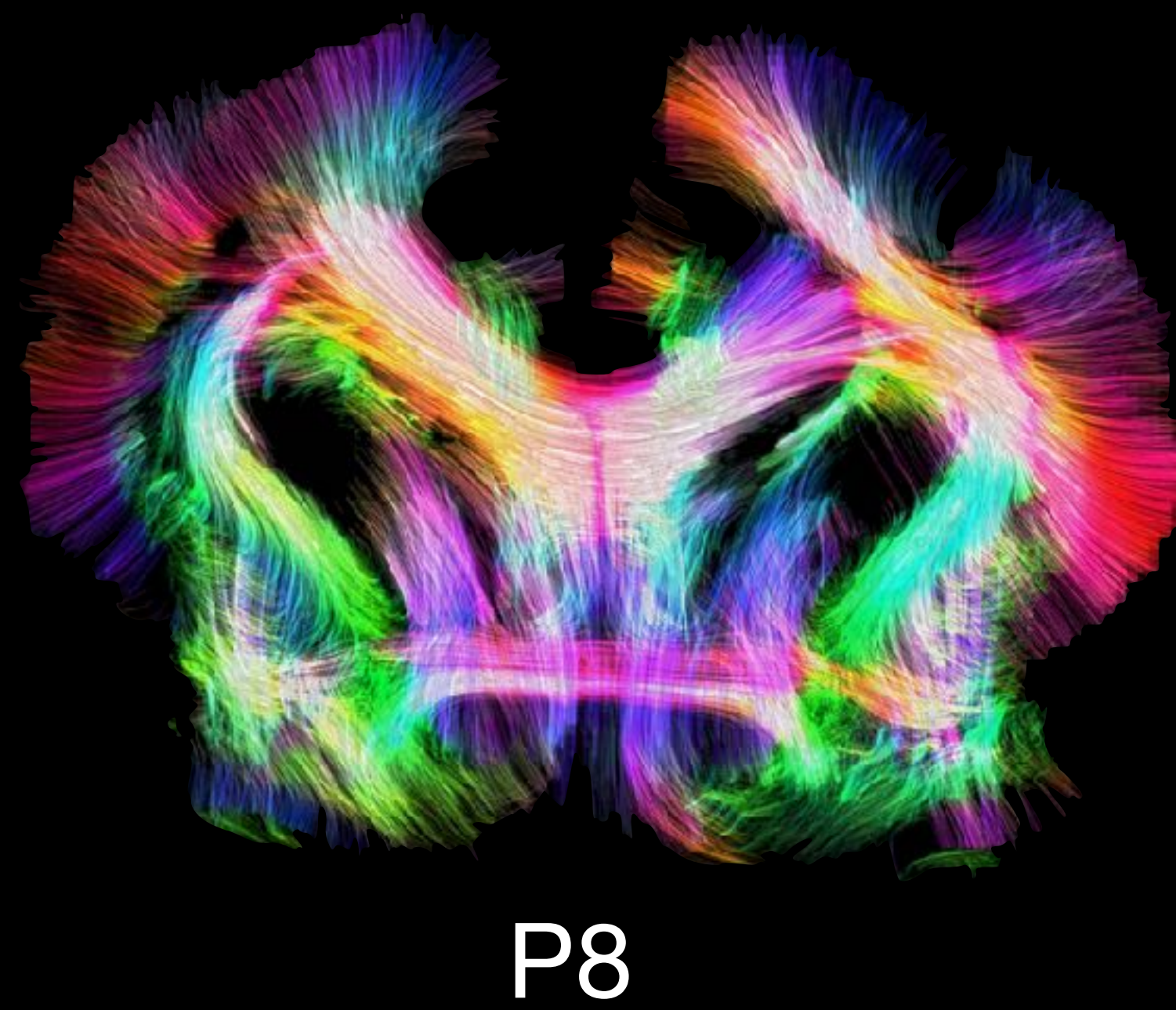
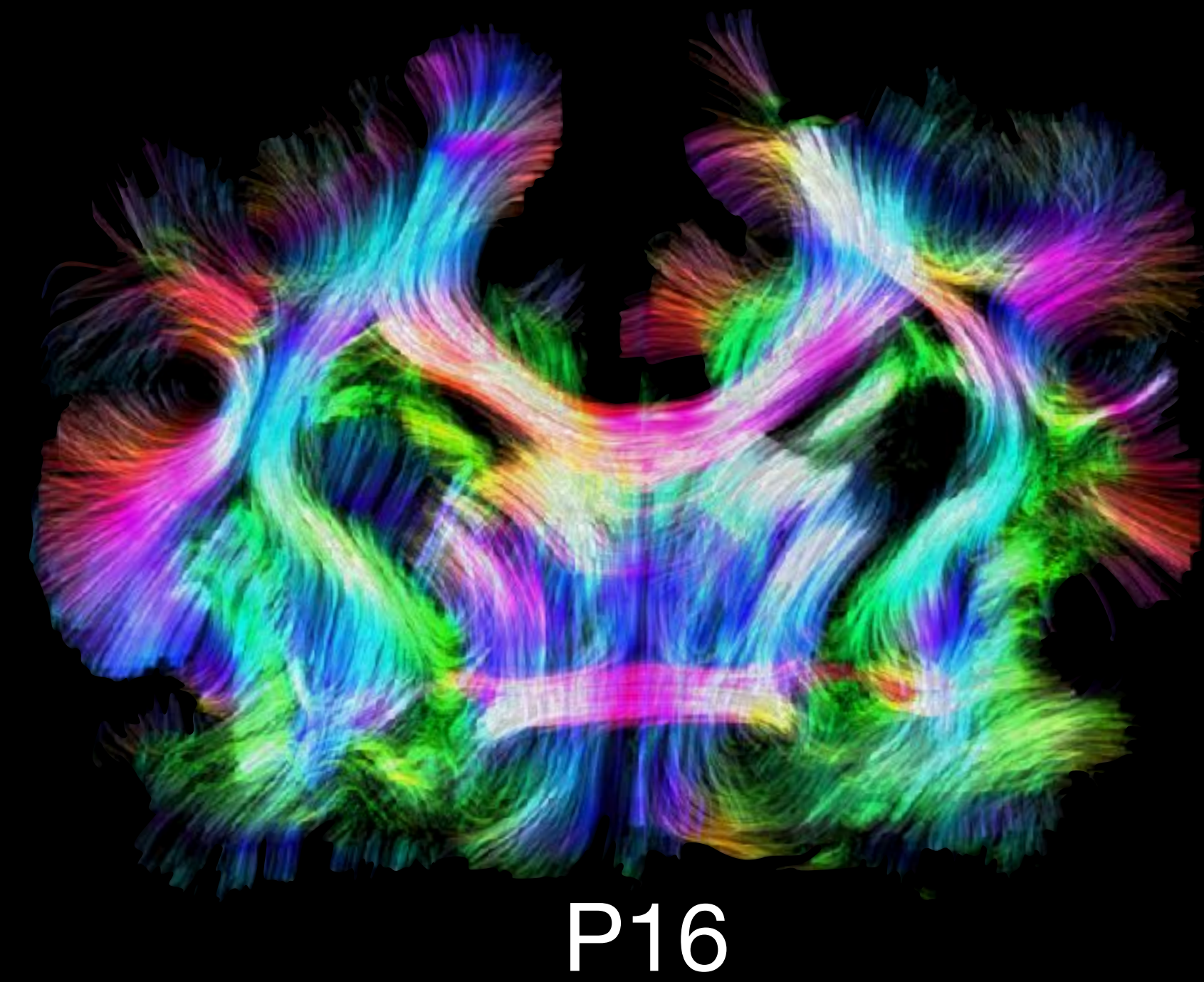
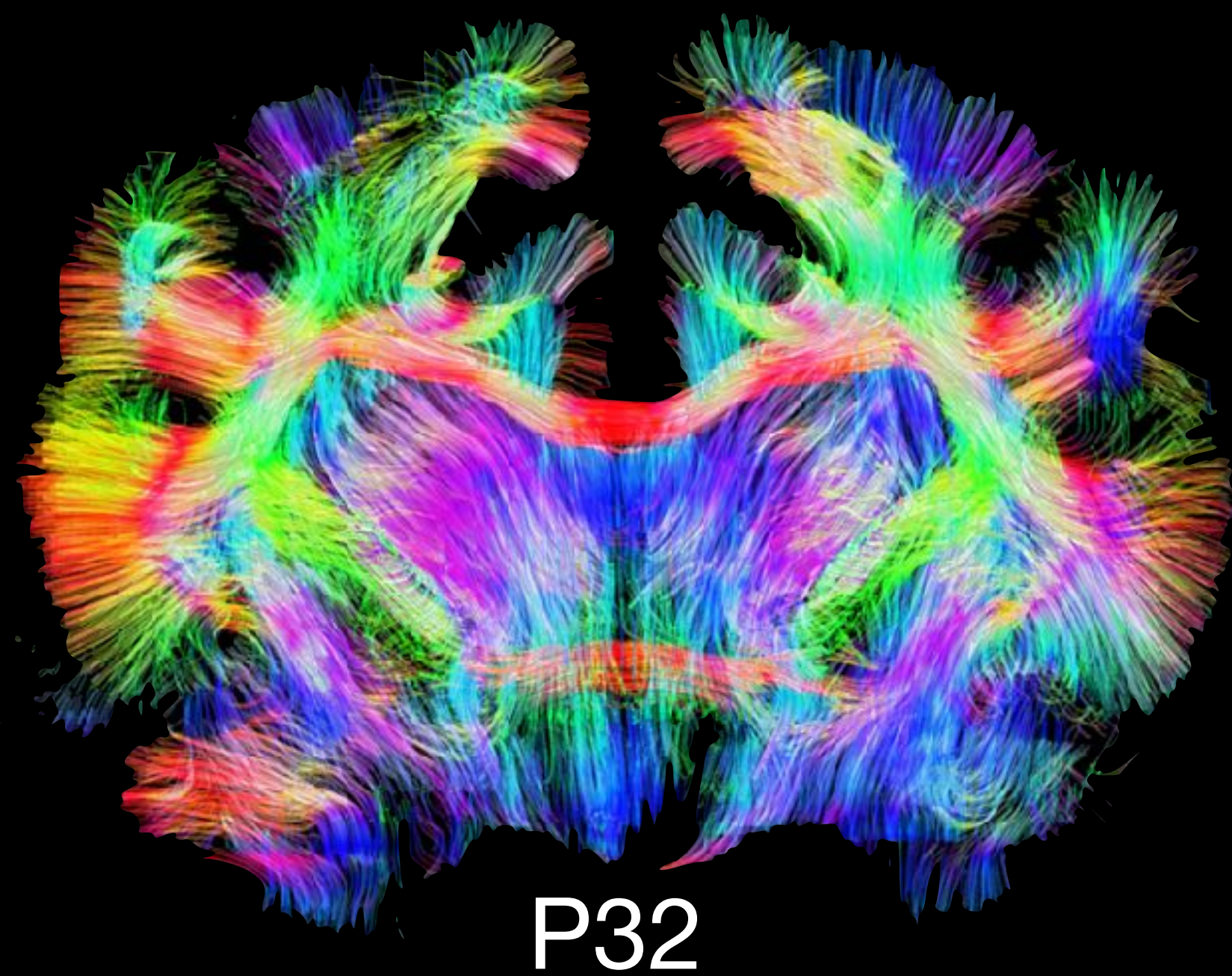


McGill Centre for Integrative Neuroscience, Quebec, Canada

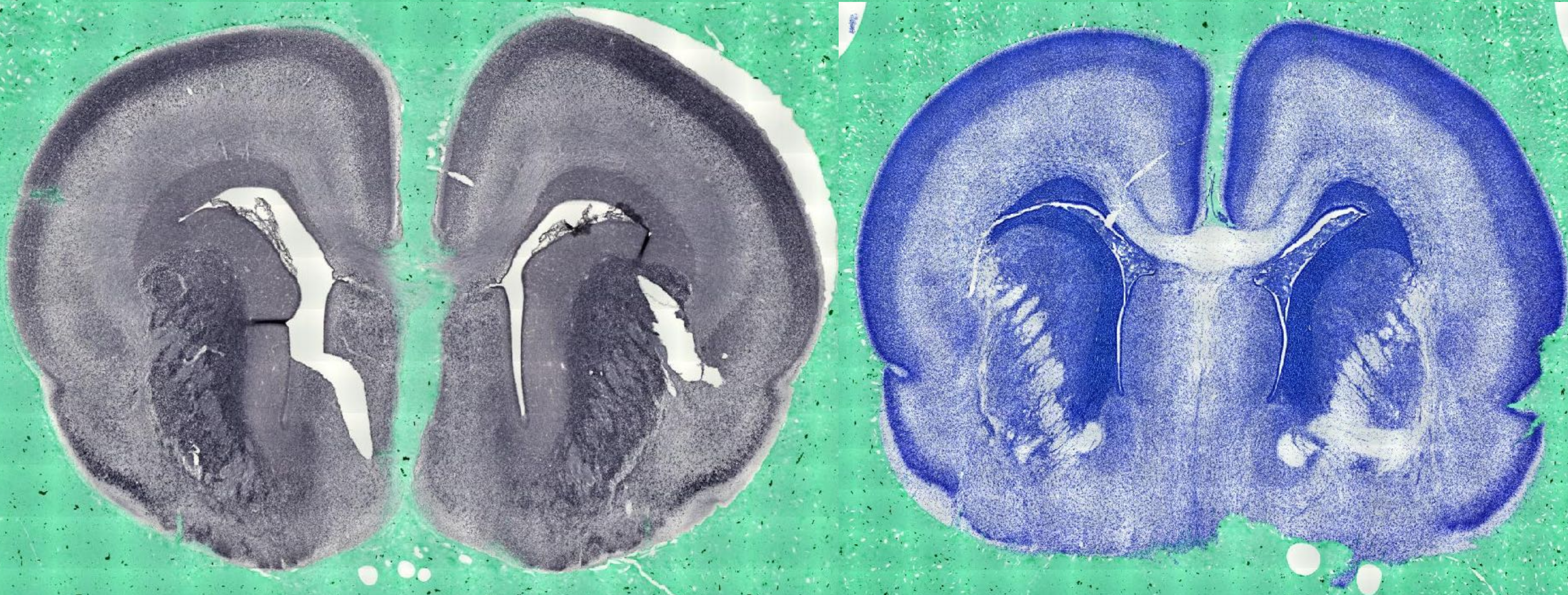
Alan Evans was originally trained in physics at Liverpool University in the U.K. After completing his PhD in biophysics he then spent 5-year at Atomic Energy of Canada Ltd. in Ottawa, working on the physics and biochemical analysis of positron emission tomography (PET) data. In 1984, he moved to the Montreal Neurological Institute (MNI) at McGill University in Montreal to continue his PET research. His research interests include multi-modal brain imaging with PET and MRI, image processing and large-scale brain database analysis. During his 25 years at the MNI, he has held numerous leadership roles, most notably as director of the McConnell Brain Imaging Centre. Alan Evans is a founding member of the International Consortium for Brain Mapping and one of the founders of the Organization for Human Brain Mapping, serving in numerous positions since 1995. In 2003 he received a prestigious Senior Scientist Award from the Canadian Institutes of Health Research.







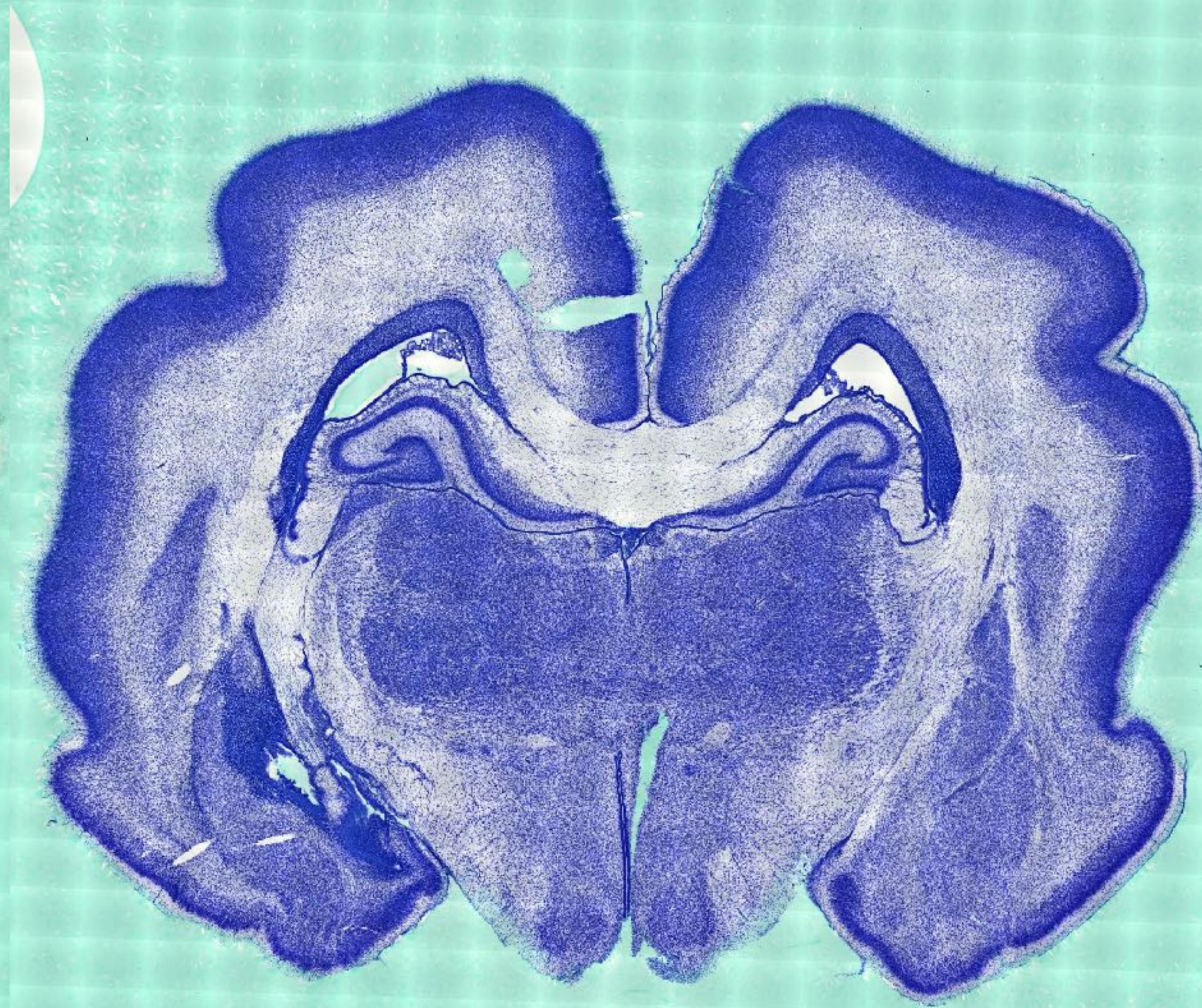
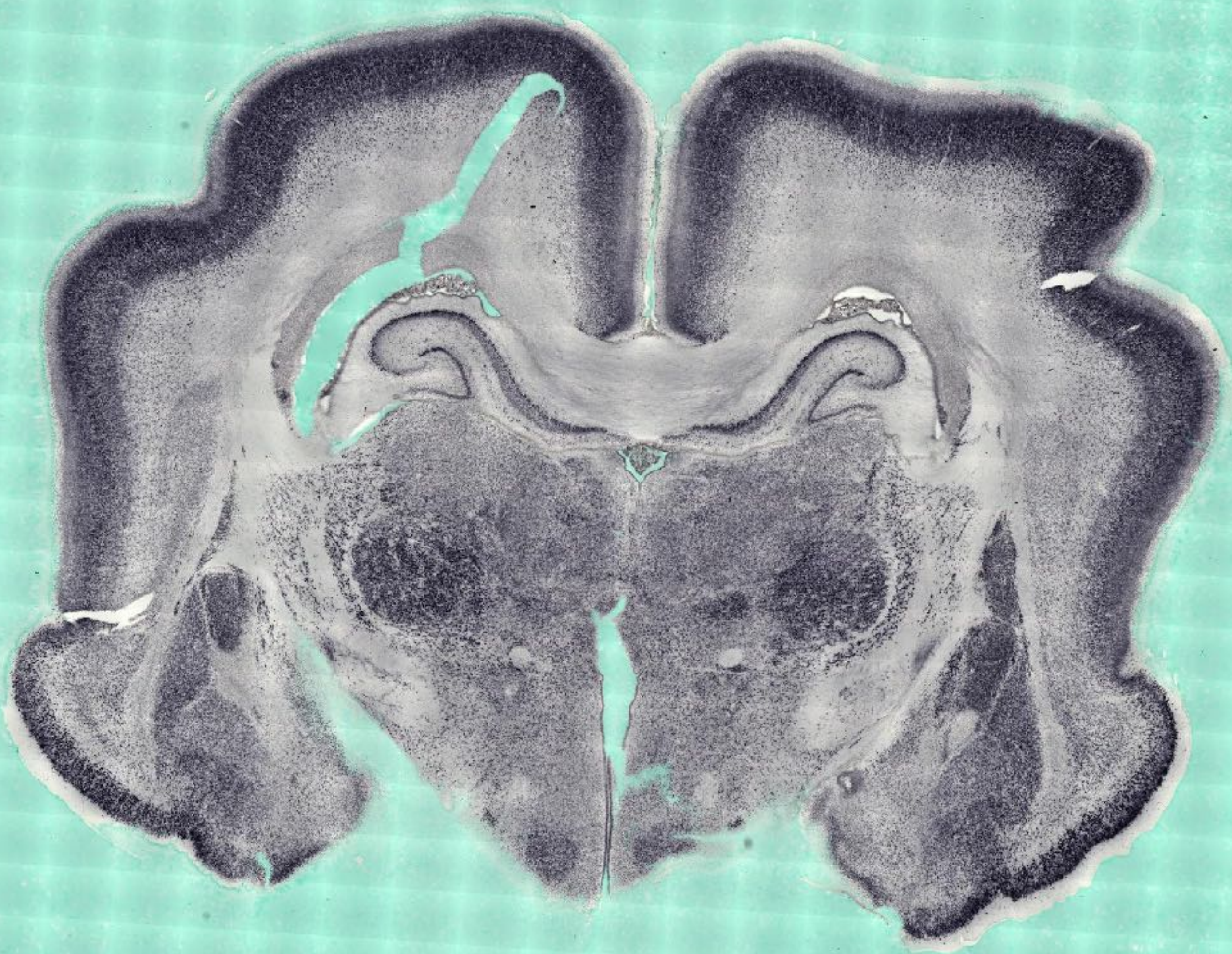
P4



100μm



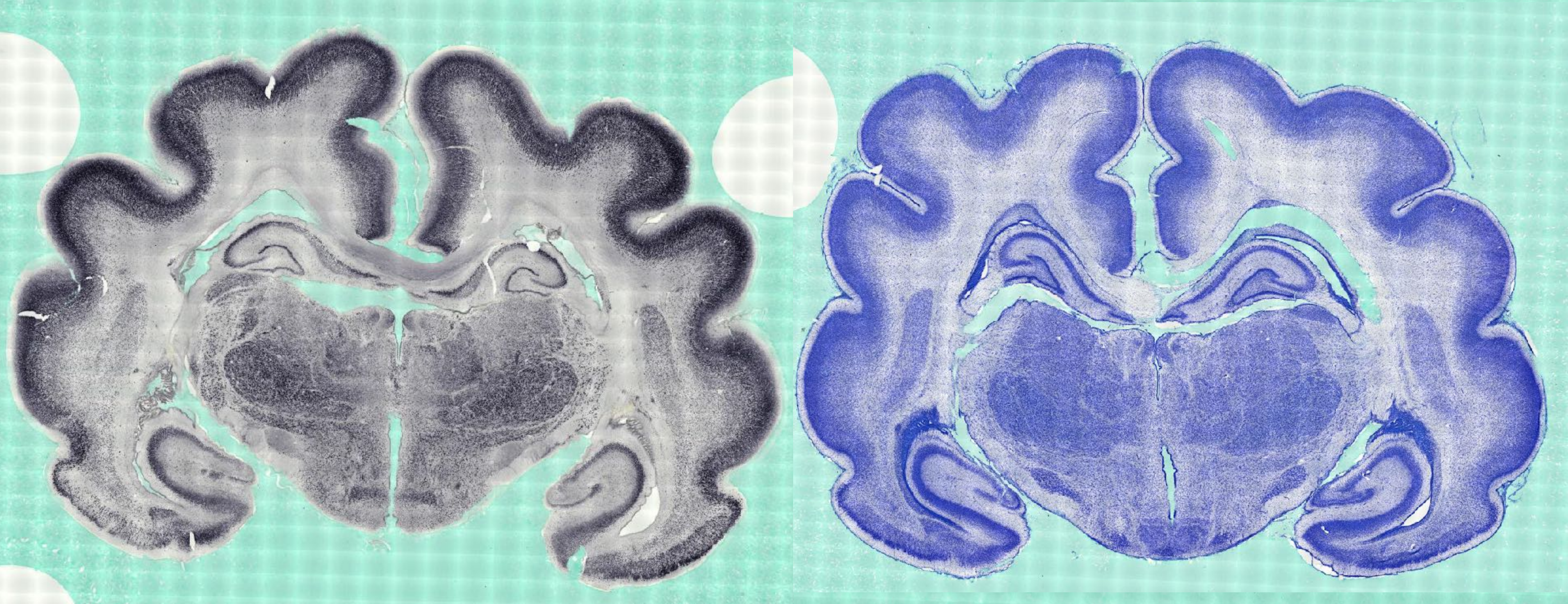
P8



100μm



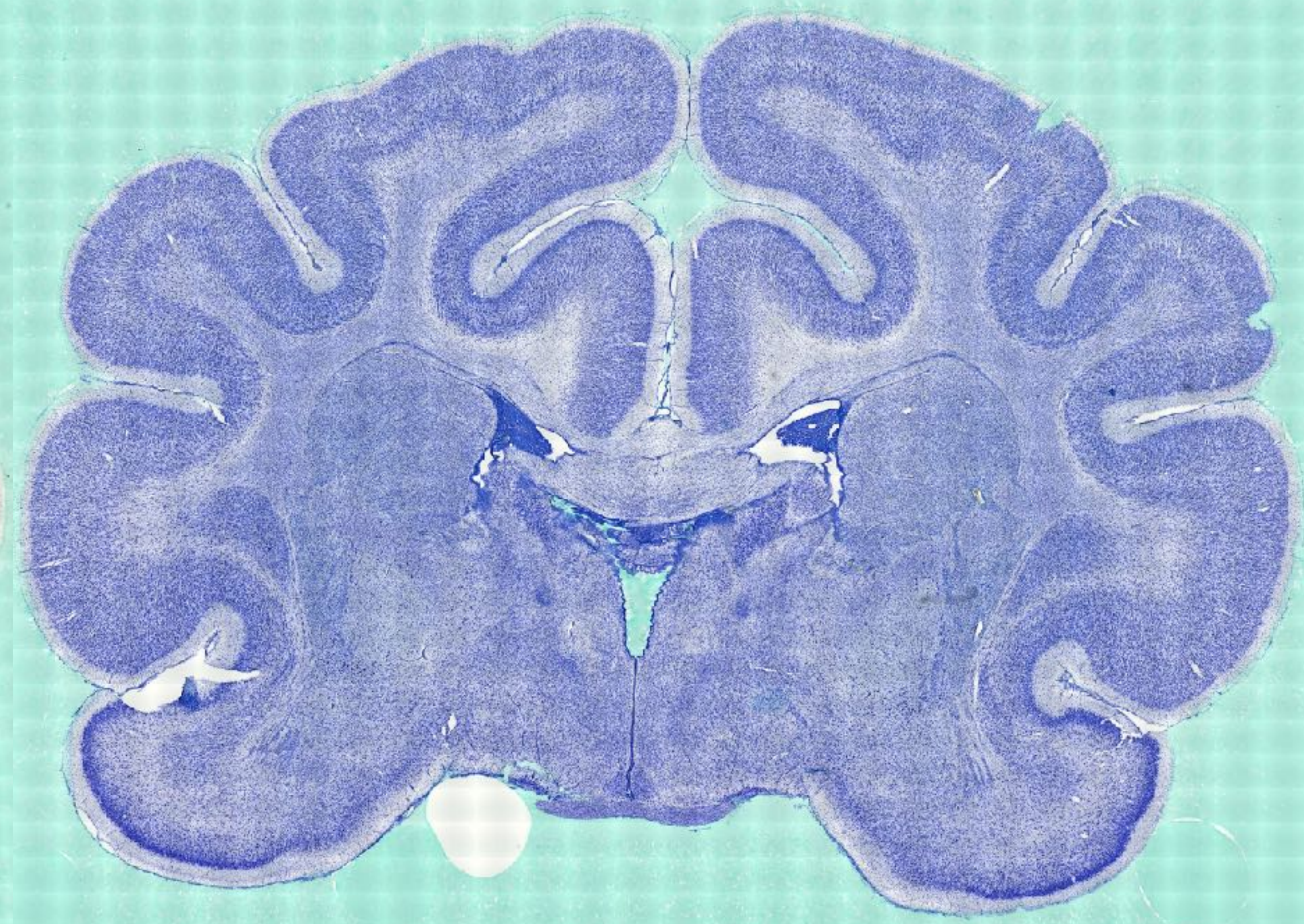
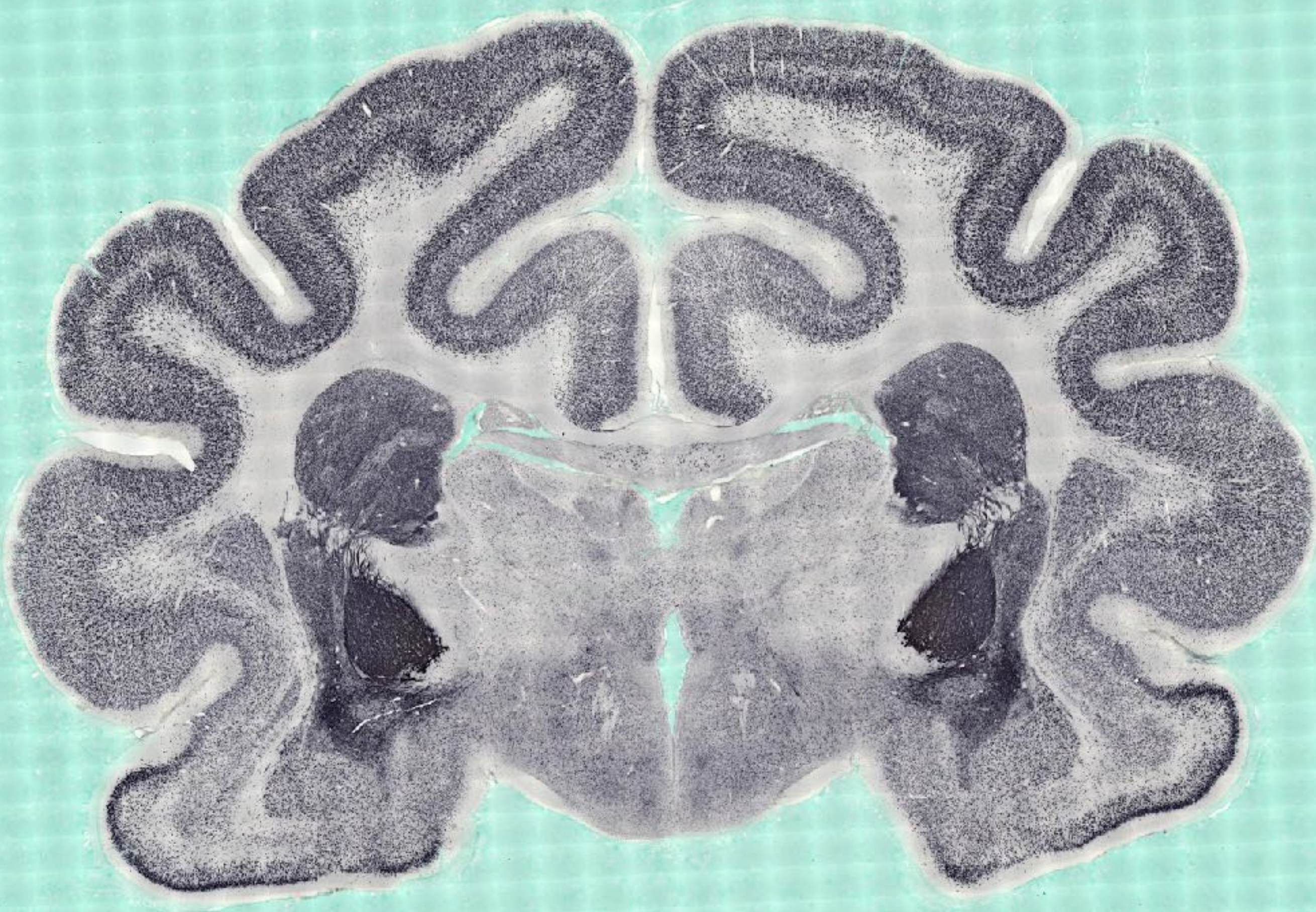
P16



200μm



P32




200μm



BrainBox

br... 27

r03ert0 (Log Out)



BrainBox


Real-time collaboration in neuroimaging

Enter the URL of an MRI (.nii.gz)
Go

Baboon

br... 848 27

r03ert0 (Log Out)



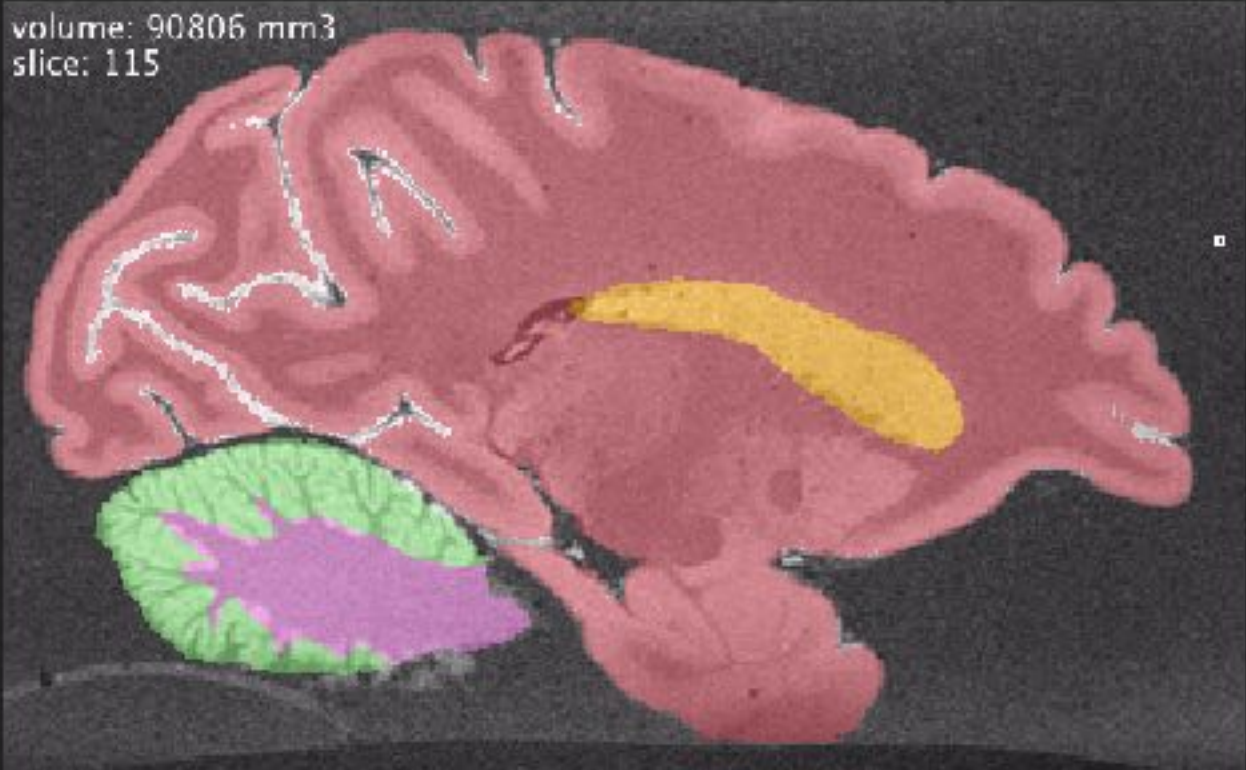
BrainBox

Name	Baboon
Data source	http://braincatalogue.org/data/Baboon/MRI.nii.gz
Inclusion date	9/20/2016

Volume Annotations				
Name	Value	Project	Modified	Access
Cerebrum	10 regions	braincatalogue	Invalid Date	👁️🔍🔗
Hippocampus	Foreground	braincatalogue	Invalid Date	👁️🔍🔗
Striatum	Foreground	braincatalogue	Invalid Date	👁️🔍🔗

Text Annotations				
Name	Value	Project	Modified	Access
MRI quality	Good	braincatalogue	11/16/2016	👁️🔍🔗
Specimen quality	Good	braincatalogue	11/16/2016	👁️🔍🔗
Comments	Right temporal lobe slightly damaged	braincatalogue	11/16/2016	👁️🔍🔗

volume: 90806 mm3
slice: 115



[-] [Sag] [Cor] [Axi] [5] [10] [15] [+]


Chat (206 connected)

u211 entered
me: me
u211 left
u213 entered

braincatalogue

br... 27

r03ert0 (Log Out)



braincatalogue

http://braincatalogue.org

by r03ert0

Our aim is to celebrate the diversity of the vertebrate brain by making high quality data, open and freely available to everyone.

2 Collaborators
6 Annotations
35 MRI Files

Access

Nickname	Name	Collaborators	Annotations	MRI Files
anyone	Any BrainBox User	👁️🔍 + -	👁️🔍 + -	👁️🔍 + -
katjaq	katja heuer	👁️🔍🔗 + -	👁️🔍🔗 + -	👁️🔍🔗 + -

Annotations

Name	Type	Value	Display
Cerebrum	volume	Foreground	👁️
Hippocampus	volume	Foreground	👁️
Striatum	volume	Foreground	👁️
MRI quality	text	GoodMediumBad	👁️
Specimen quality	text	GoodDamaged	👁️
Comments	text	freeform	👁️

MRI Files

URL	Name
http://braincatalogue.org/data/Babo Baboon on/MRI.nii.gz	Babo Baboon on/MRI.nii.gz
http://braincatalogue.org/data/BlackBlack rhinoceros _rhinoceros/MRI-n4.nii.gz	BlackBlack rhinoceros _rhinoceros/MRI-n4.nii.gz
http://braincatalogue.org/data/BlackBlackbuck buck/MRI-n4.nii.gz	BlackBlackbuck buck/MRI-n4.nii.gz
http://braincatalogue.org/data/Bottl Bottlenose dolphin enose_dolphin/MRI-n4.nii.gz	Bottl Bottlenose dolphin enose_dolphin/MRI-n4.nii.gz
http://braincatalogue.org/data/Cat/ Cat MRI-n4.nii.gz	Cat/ Cat MRI-n4.nii.gz
http://braincatalogue.org/data/Chee Cheetah tah/MRI.nii.gz	Chee Cheetah tah/MRI.nii.gz
http://braincatalogue.org/data/Chim Chimpanzee panzee/MRI-n4.nii.gz	Chim Chimpanzee panzee/MRI-n4.nii.gz
http://braincatalogue.org/data/Crab Crab-eating macaque -eating_macaque/MRI.nii.gz	Crab Crab-eating macaque -eating_macaque/MRI.nii.gz
http://braincatalogue.org/data/Ferre Ferret t/MRI-n4.nii.gz	Ferre Ferret t/MRI-n4.nii.gz
http://braincatalogue.org/data/GiantGiant panda _panda/MRI.nii.gz	GiantGiant panda _panda/MRI.nii.gz



BrainBox

BrainBox allows you to visualise, segment and annotate collaboratively any brain MRI dataset available online. Segmentations and annotations are automatically saved. Point BrainBox to your own nii.gz or mgz data online, or participate in the projects created by the community.

Enter the URL of an MRI (.nii.gz or .mgz) and click Go

▼ A list of brains to try

Go



[Home](#)

Blog

Collaborative Annotation

MicroDraw is a web application by [NAAT](#) to visualise and annotate collaboratively high resolution histology data. Annotations are vectorial, and you can use boolean operations to combine, subtract and split regions. Point MicroDraw to your own DeepZoom data, or try the sample data below!

Enter a DeepZoom image URL

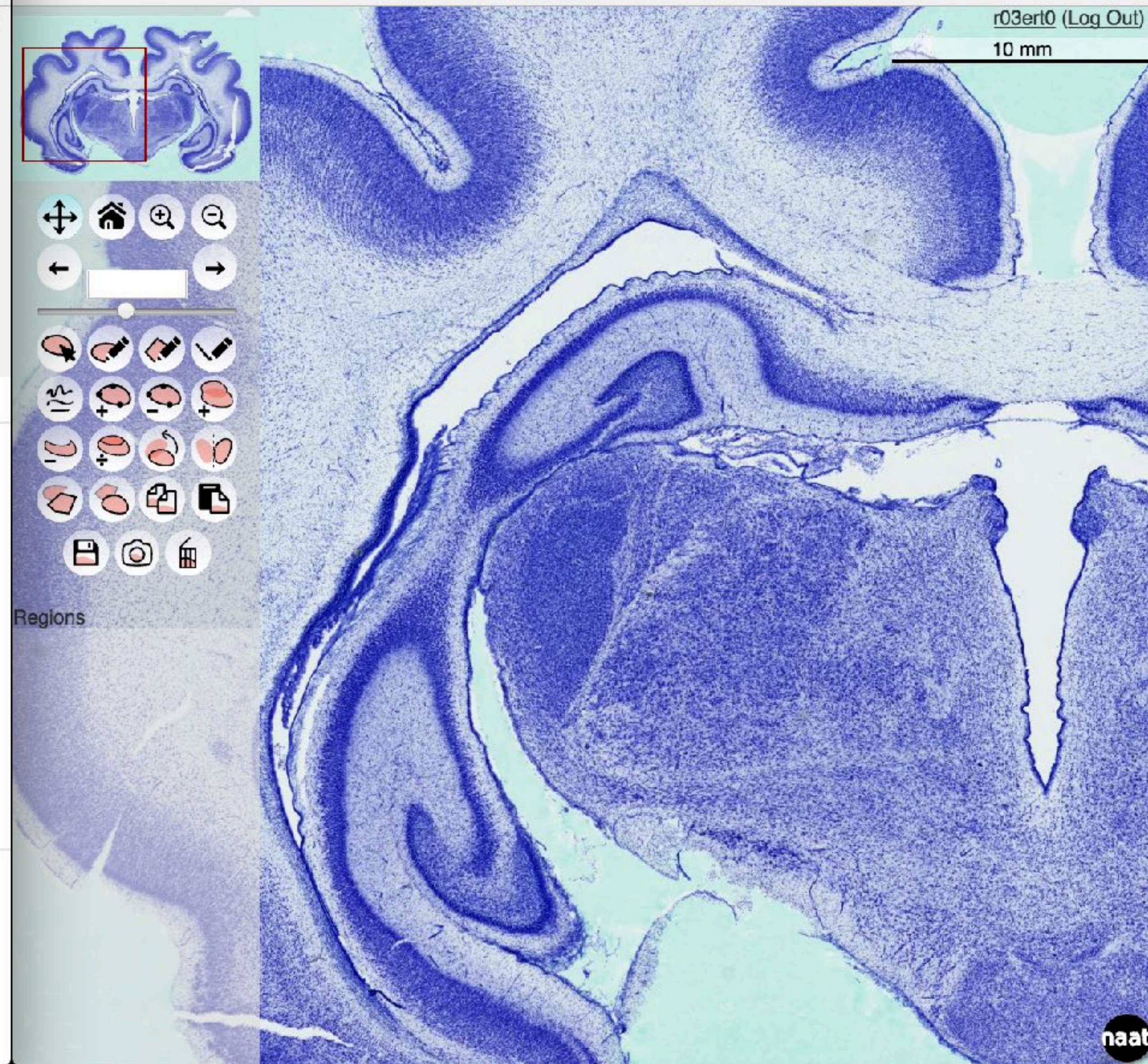
Go

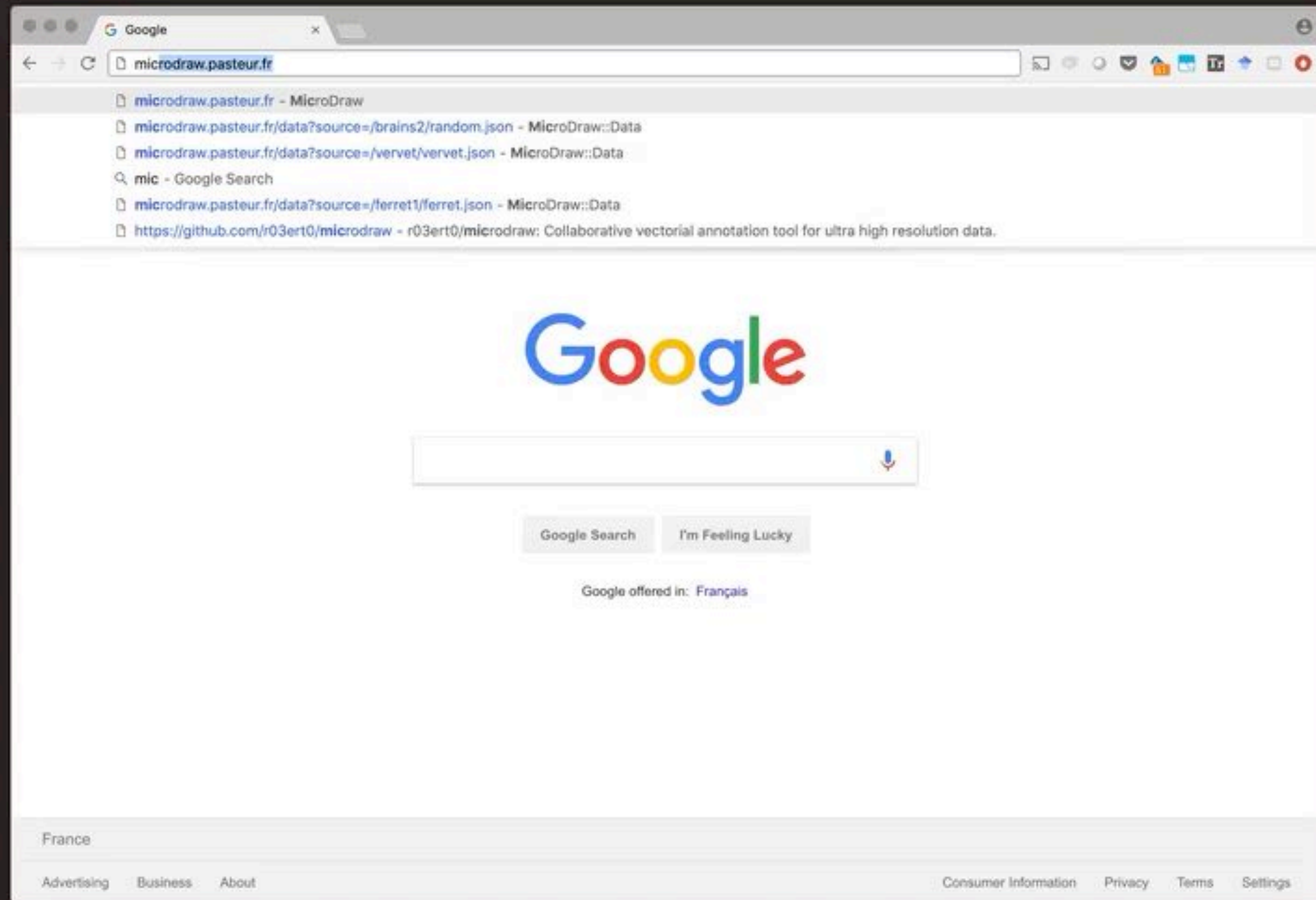
Datasets

MicroDraw can use ontologies such as [Neurolex](#) to create community curated atlases, but also to annotate staining artefacts. We are currently hosting DeepZoom versions of several macaque brains from the Allen Institute for Brain Research, a 1 micron

Application

MicroDraw is based on open source frameworks to ensure its maintainability and extensibility. The interactive multi-resolution visualisation is based on [OpenSeadragon](#). The vectorial annotation is based on [Paper](#). The concurrent versioning is based on Git





Project UNFOLD

Mechanical
morphogenesis of
neocortical organisation



Groupe de neuroanatomie appliquée et théorique, Institut Pasteur, France

Roberto Toro (P.I.) (PhD) is leader of the group of applied and theoretical neuroanatomy at the unit of human genetics and cognitive function, department of neuroscience of the Institut Pasteur. After a degree in engineering, he obtained a Master and a PhD in Neuroscience at the University of Paris 6, France. He is interested in the development and evolution of the brain, which he studies through mathematical modelling, magnetic resonance imaging and genomics.



Wave physics for medicine

Charlie Demené (associate professor, implication 3.6 p-m), expert in ultrasensitive Doppler tomography of small animals and acoustic radiation force. His laboratory is a sub-unit of Institut Langevin (Inserm/CNRS/ESPCI Paris). The research team Inserm U979 is led by Prof. Mickaël Tanter and consists of physicists developing biomedical imaging and therapeutic techniques, mostly based on ultrasound, for preclinical and clinical research. The team is internationally renowned for having introduced novel imaging modalities based on ultrafast ultrasound imaging, such as shear wave elastography, ultrasensitive Doppler or functional ultrasound imaging



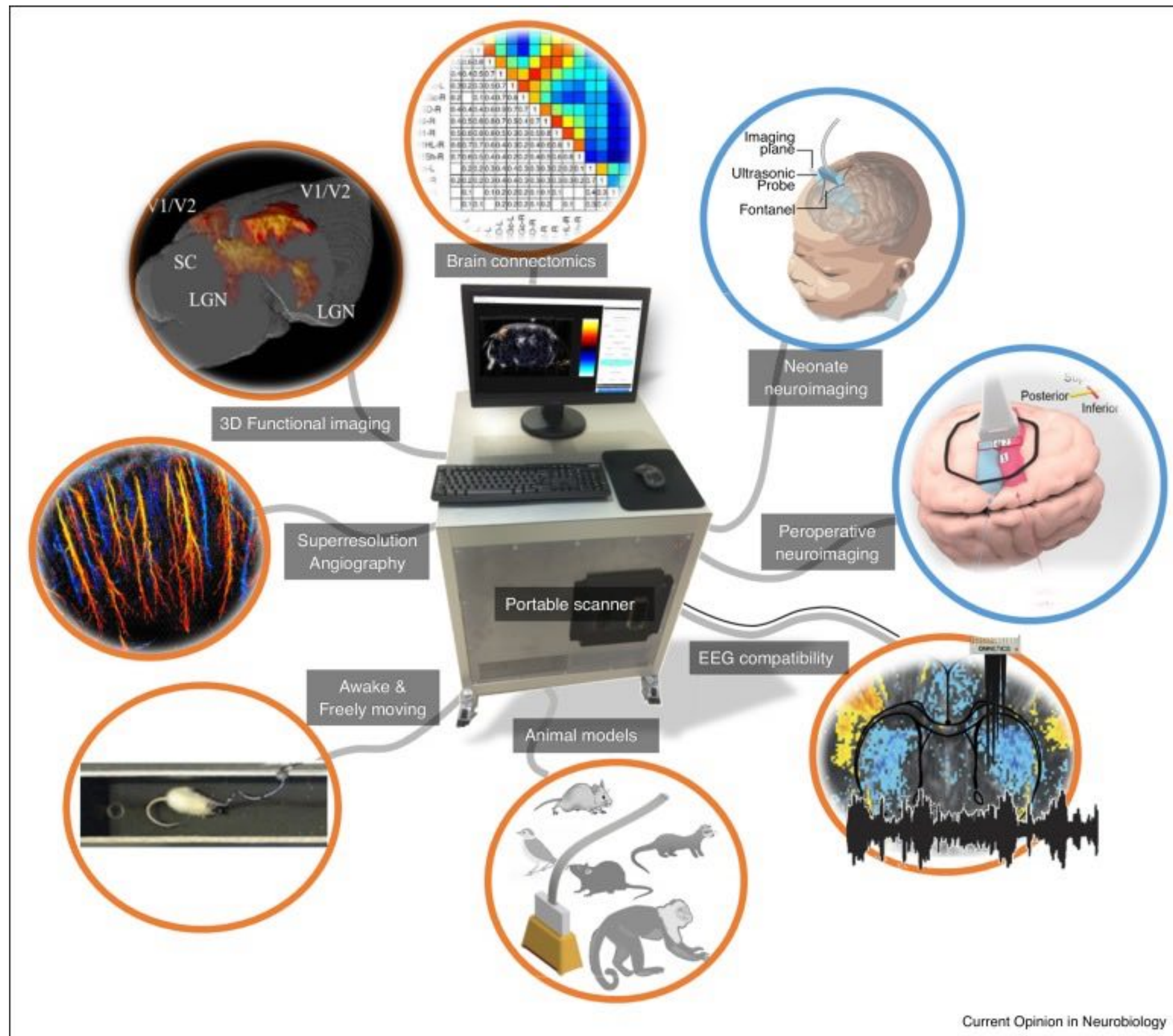
Groupe de neuroanatomie appliquée et théorique, Institut Pasteur, France

Yves Boubenec (PhD) is part of the laboratory set up at ENS Paris by Pr. Shihab Shamma, a world-wide expert on electrophysiology in behaving ferrets and in audition. He leads the ferret facility at ENS Paris since its creation in 2012, and is an expert in animal training and behavior, electrophysiology and imaging in the behaving ferret, as well as advanced data analysis. There is an ongoing collaboration between Dr. Boubenec with Charlie Demené and Mickaël Tanter, member of the ESPCI team, to investigate auditory perception and cognitive processes in the behaving ferret using functional ultrasound (fUS) imaging. An ultrasound scanner is available in the LSP, and the platform hosts a complete ferret facility in-house, as well as the necessary experimental space and equipment for performing the planned experiments.

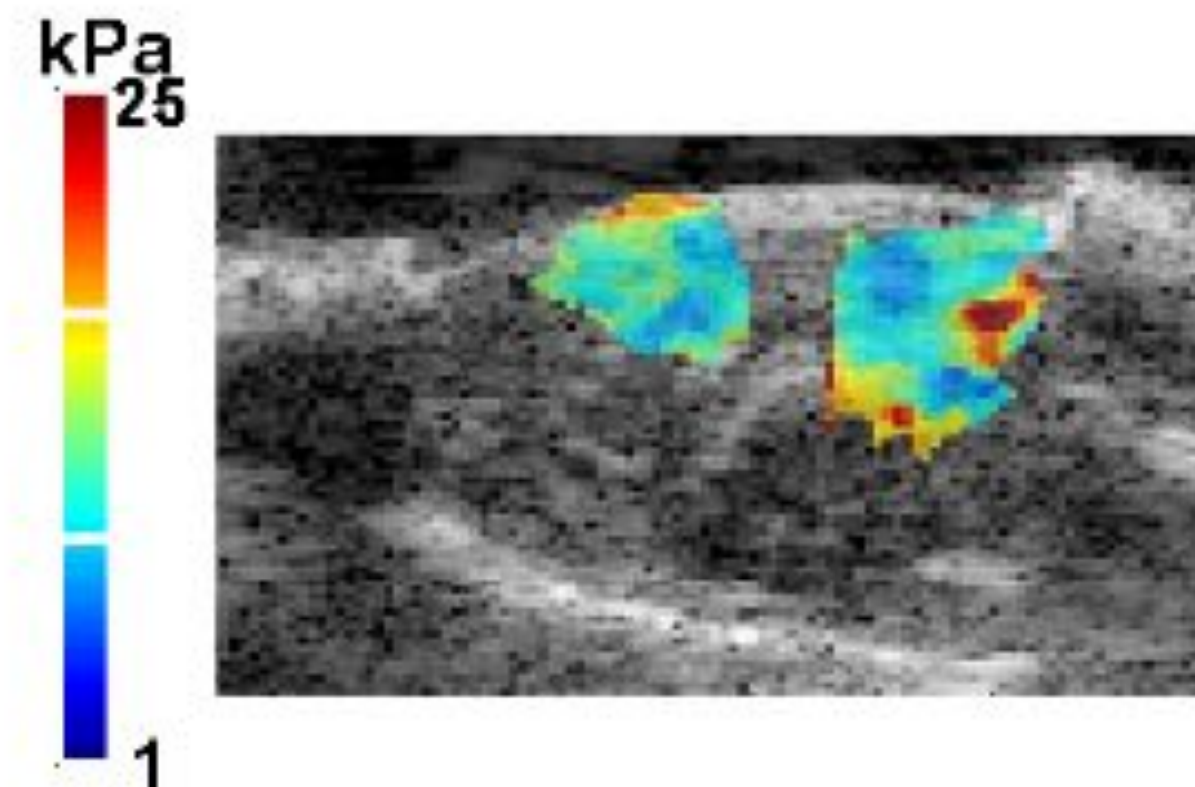
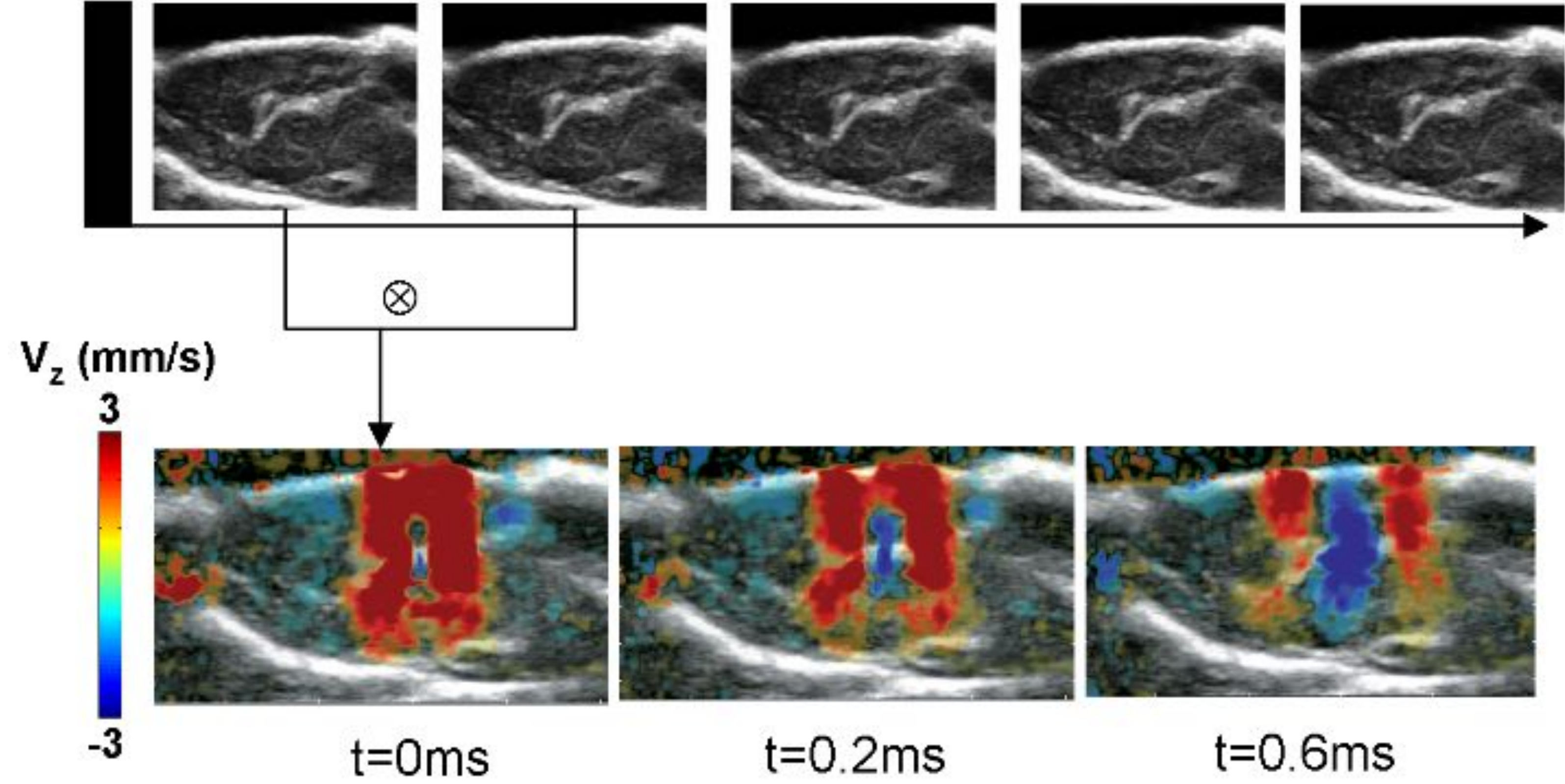
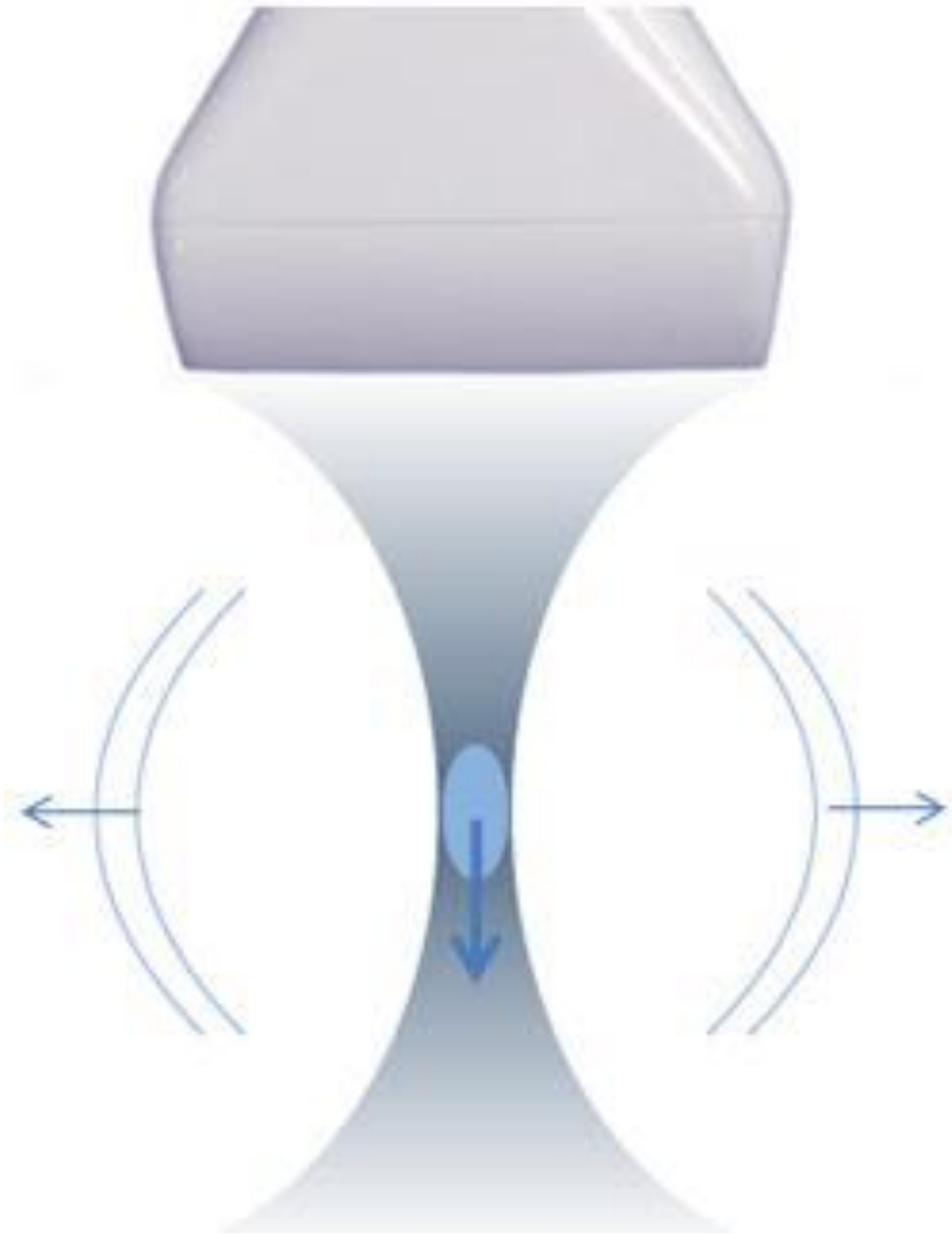


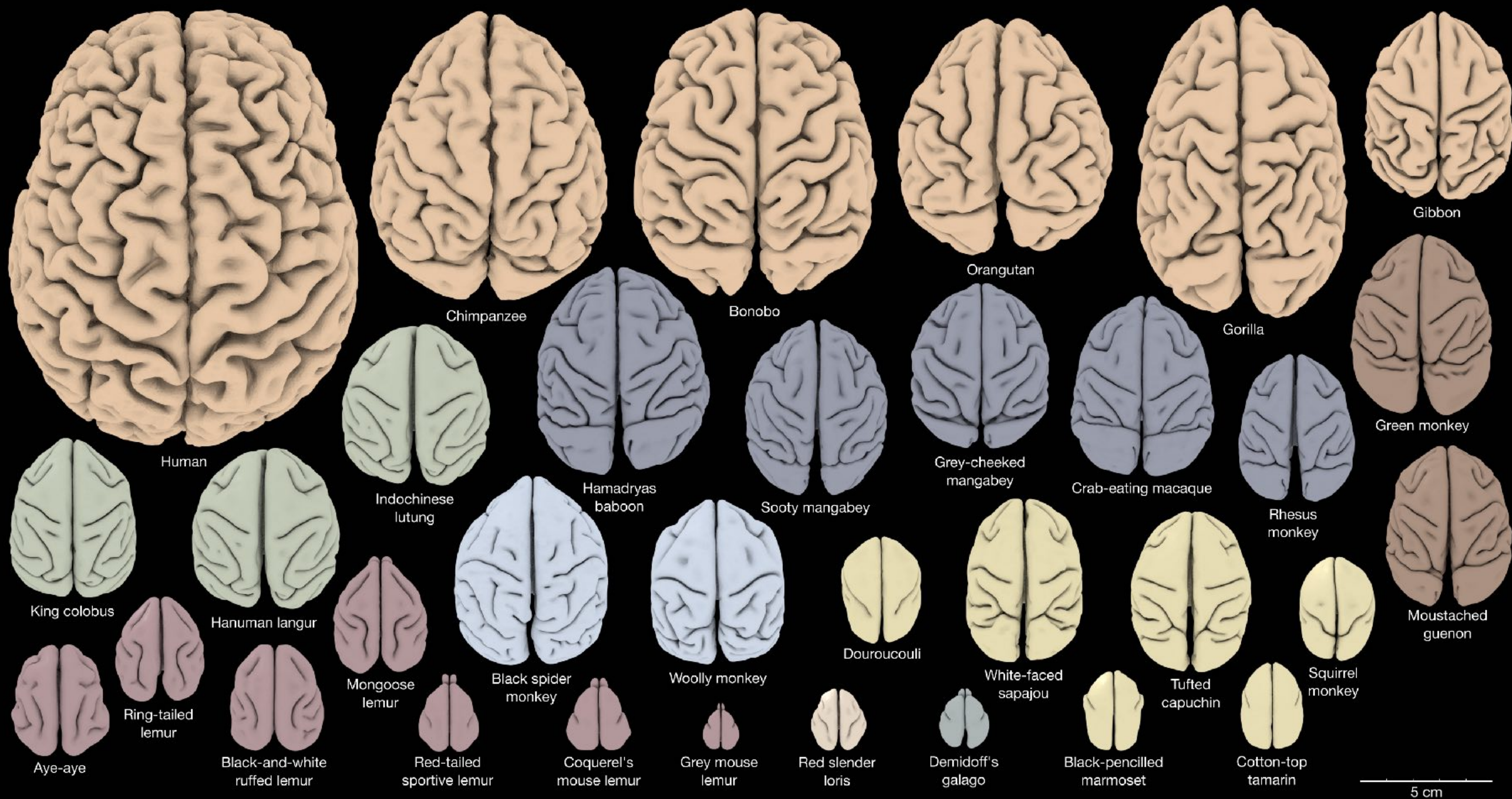
Groupe de neuroanatomie appliquée et théorique, Institut Pasteur, France

L. Mahadevan (Prof, PhD, FRS, Lola England de Valpine Professor of applied mathematics, organismic and evolutionary biology and physics) is a renowned expert in the field, with a long track record of highly influential contributions to the modelling of biological phenomena, in particular brain folding. Partners SEAS and IP are currently collaborating in the mechanical modelling of ferret brain folding, a collaboration that will be the basis of the modelling task in project UNFOLD.



90 μ s burst
70 ultrasonic images at 10 000 Hz





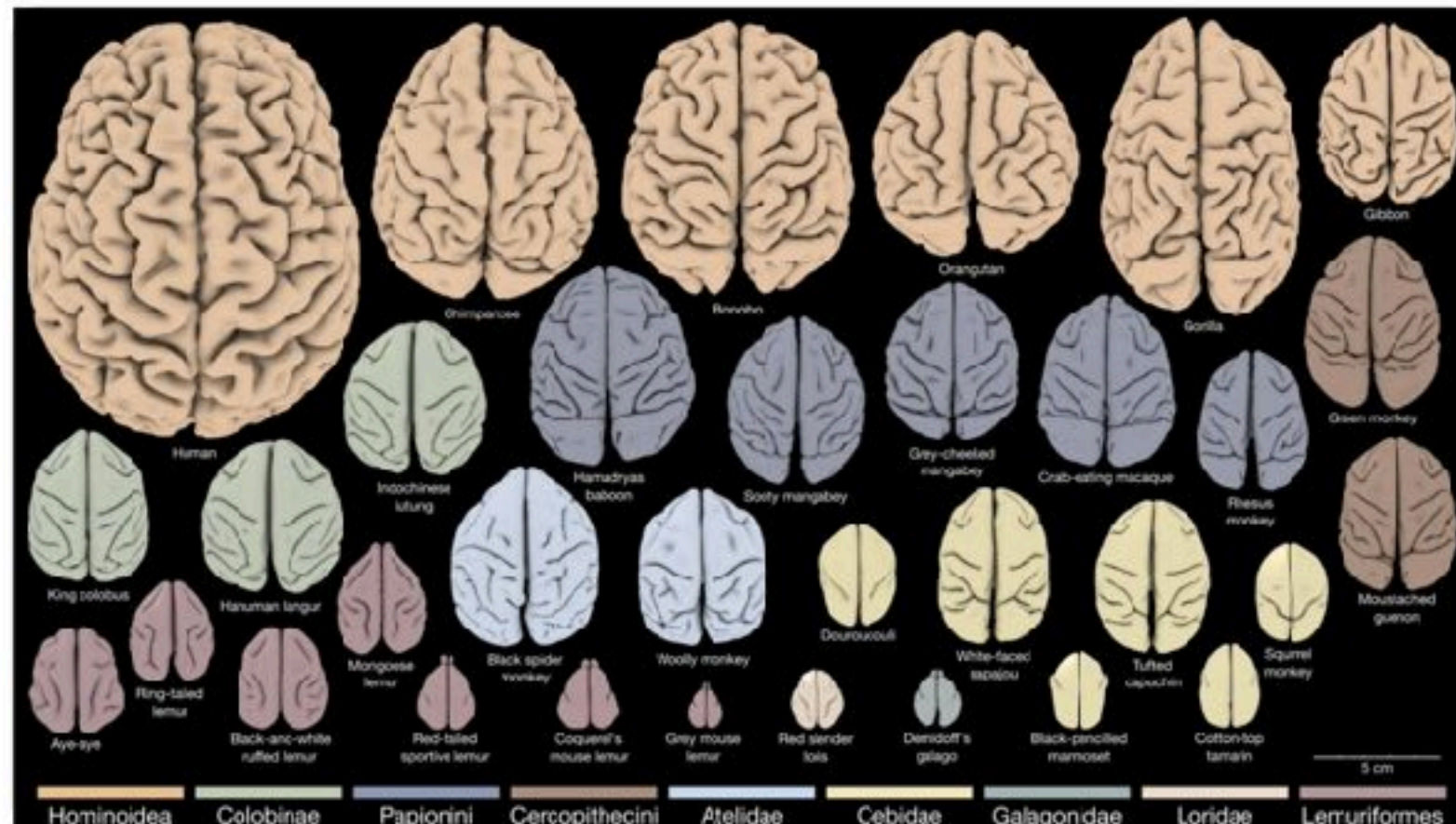


katja heuer
@katjaQheuer

Following

we are preparing our paper for
[@biorxivpreprint](#): Evolution of neocortical
folding: A phylogenetic comparative analysis
of MRI from 33 primate species

with [@R3RT0](#) [@ofgulban](#) Pierre-Louis Bazin,
Anastasia Osoianu, Romain Valabregue,
Mathieu Santin, Marc Herbin



5:45 AM - 13 Jul 2018

72 Retweets 197 Likes



7 72 197



Tweet your reply



vin @neoosho · 13 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 2 others

Very beautiful illustrations of the cortical landscape 🍷🍷🍷

3



HCP News @HumanConnectome · 13 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 2 others

Check it out [@ChadFromStL](#)

4



OHBM Trainees @OHBM_Trainees · 13 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 2 others

Beautiful work 🍷🍷🍷

1



Nico Schuck @nico_schuck · 13 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 3 others

beautiful figure! would it be OK by you if we printed it and hang it up on the wall
in our lab?

5



katja heuer @katjaQheuer · 13 Jul 2018

Totally! <3 :D how nice!

If you dm me your email address, I will send you the high res :)

2 1



Erika R @erikaraven · 13 Jul 2018

It's glorious! Can I have high res too? 🍷🍷🍷

2 2



katja heuer @katjaQheuer · 13 Jul 2018

yes, with pleasure! :)

The high res version is quite big though. Maybe the best is to put it on
[@ZENODO_ORG](#) and paste the link here :)

2 10



Erika R @erikaraven · 13 Jul 2018

Oh yes, good idea 🍷🍷🍷

2



Armin Raznahan @bogglerapture · 13 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 2 others

Super excited for this paper! You know it's going to be a banger ...



1 3

1 more reply



Amy O, PhD @neuroamyo · 15 Jul 2018

Replying to [@katjaQheuer](#) [@R3RT0](#) and 2 others

Awesome! And beautiful figure! 🍷 I wonder if there's been a mixup with the
crab-eating macaque and rhesus labels? I work with both species and they look
flipped from what I expect.

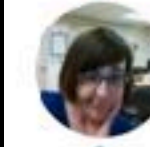
3 2



Roberto Toro @R3RT0 · 15 Jul 2018

Could happen! we only see the MRIs, never the real animals... what we have as
crab-eating macaque brain is slightly larger than rhesus, and then, have a
slightly more folded. Is that correct? 🍷 (Crab-eating) > 🍷 (Rhesus) ?

1 1

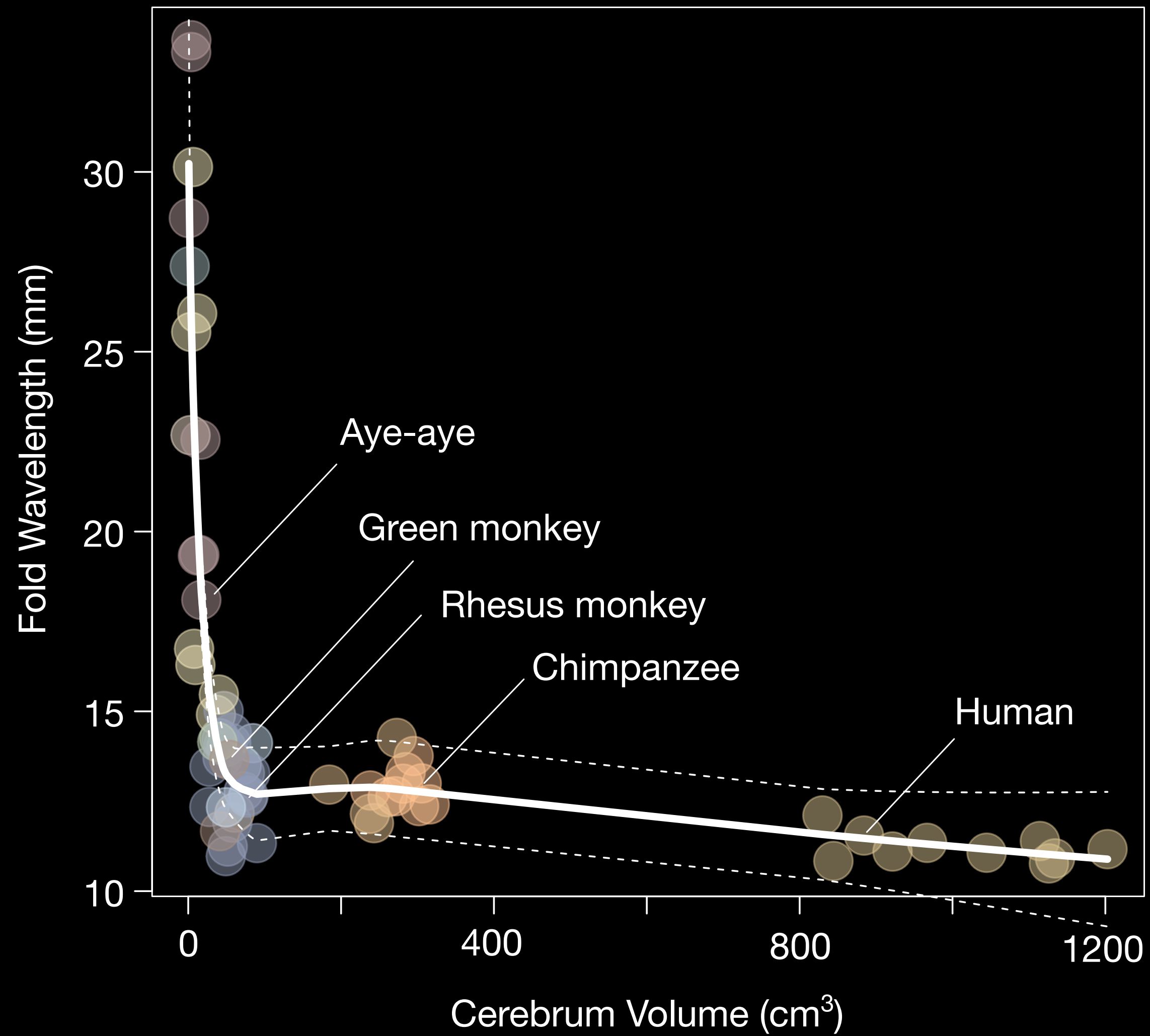


Amy O, PhD @neuroamyo · 15 Jul 2018

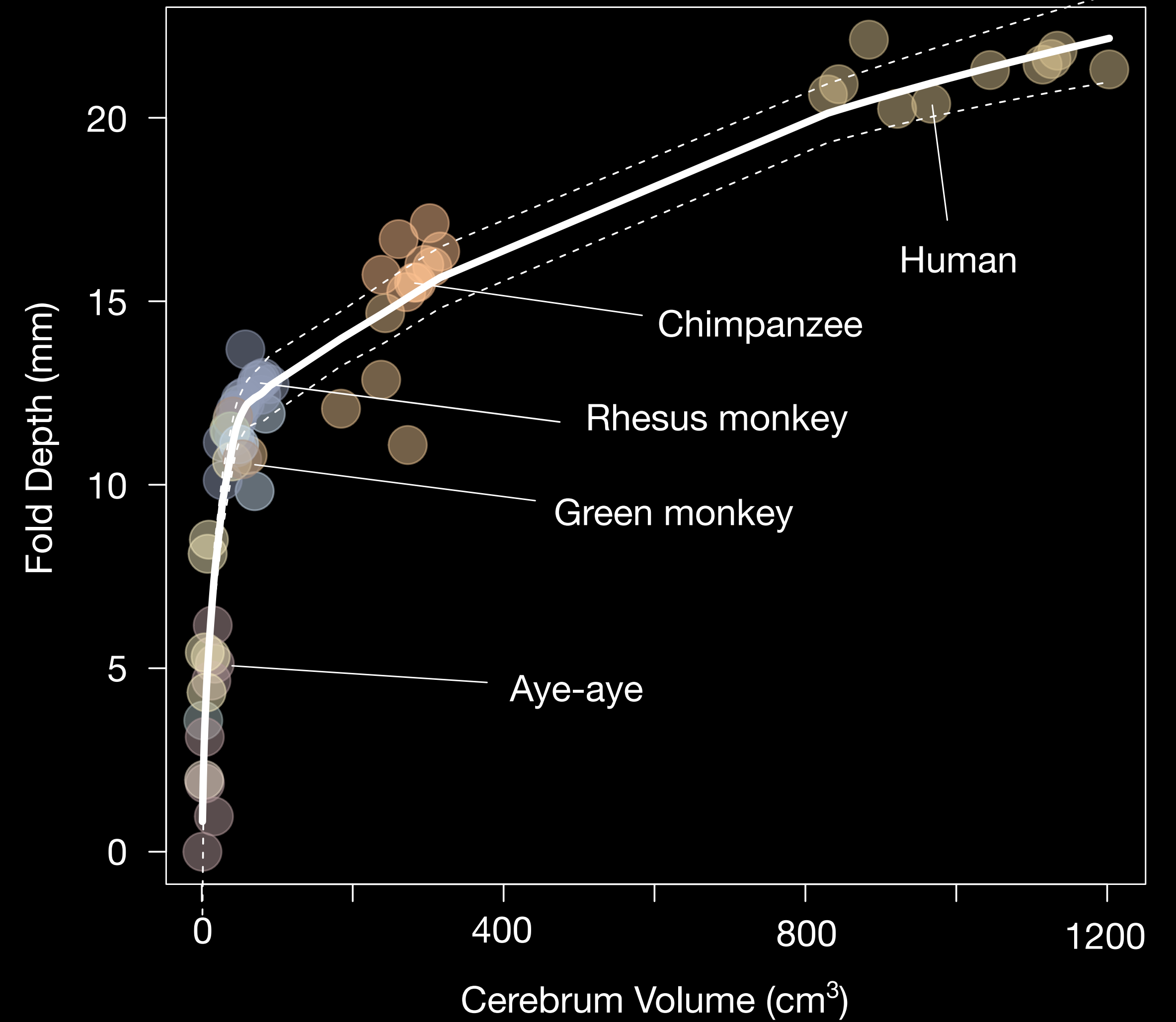
Pretty sure it's the opposite. Crab eating macaque brains are smaller than
rhesus. That's why I'm confused and think they're flipped. We do MRIs on our

The width of brain folds is strongly conserved across primates

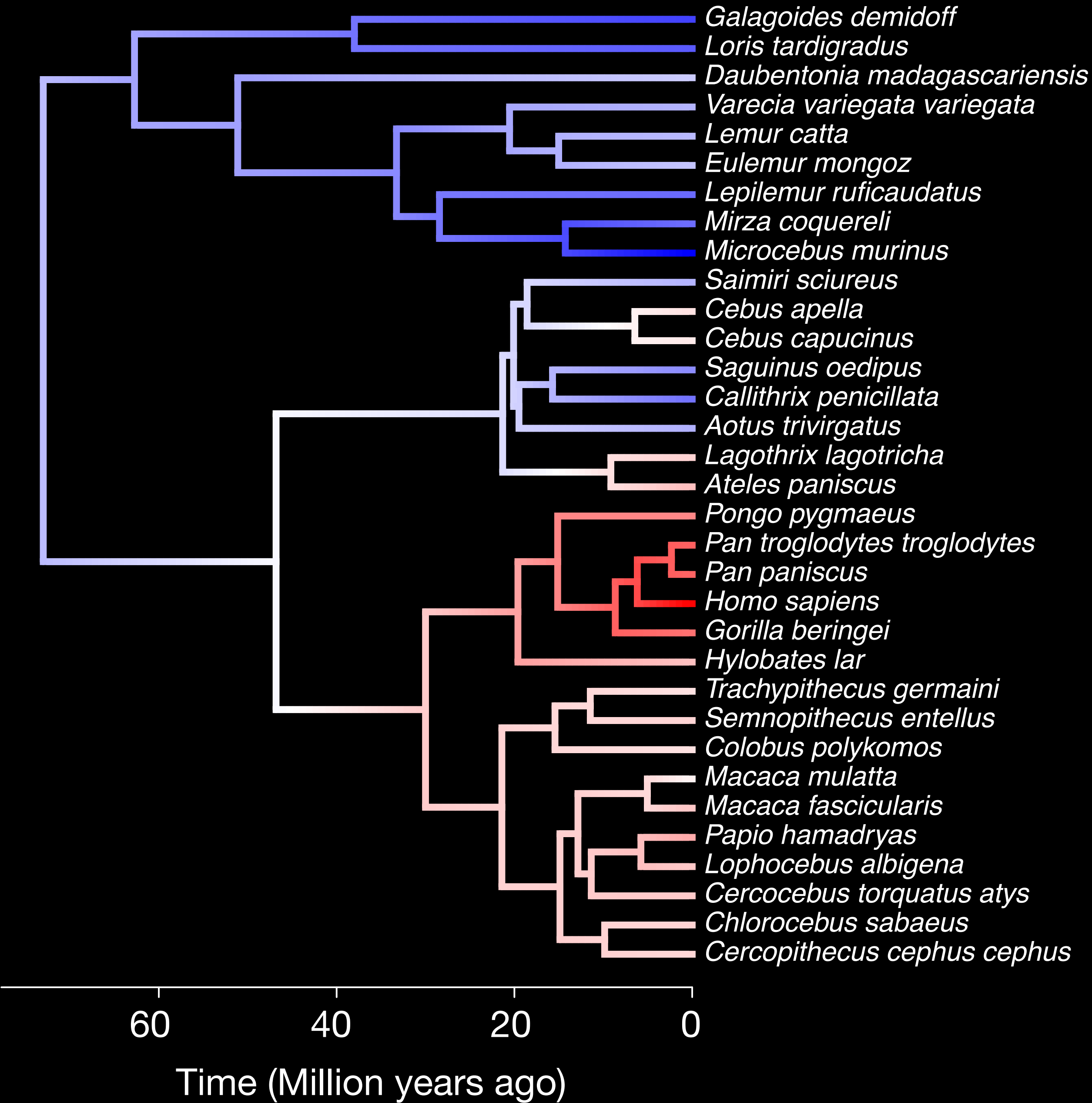
a. Fold Wavelength vs. Volume



b. Fold Depth vs. Volume



Neocortical expansion has occurred several times during primate evolution



4

Data analysis





IMPAC

IMaging-PsychiAtry Challenge: predicting autism

A data challenge on Autism Spectrum Disorder detection

Deadline: July 1, 2018 - 8 pm (UTC)

-129

Days

20

Hours

11

Minutes

35

Seconds

DISCOVER

What is this challenge?

Autism spectrum disorder (ASD) is a severe psychiatric disorder that affects 1 in 166 children.

There is evidence that ASD is reflected in individuals brain networks and anatomy. Yet, it remains unclear how systematic these effects are, and how large is their predictive remain unclear. The large cohort assembled here can bring some answers. Predicting autism from brain imaging will provide biomarkers and shed some light on the mechanisms of the pathology.

Joining the competition

The goal of the competition is to predict the diagnostic status from brain imaging data in the hidden test set. The data of the test set are on a server, hidden from participants. Prediction is done by submitting Python code that will be first trained by the server on training images, and then applied to predict on the hidden test set.

Prizes

The best performers will be awarded prizes at the end of the competitive period, based on the metrics used during the challenge: 1st - 3000 €, 2nd - 2000 €, 3rd - 1000 €, from 4th to 10th - 500 €.

The timeline

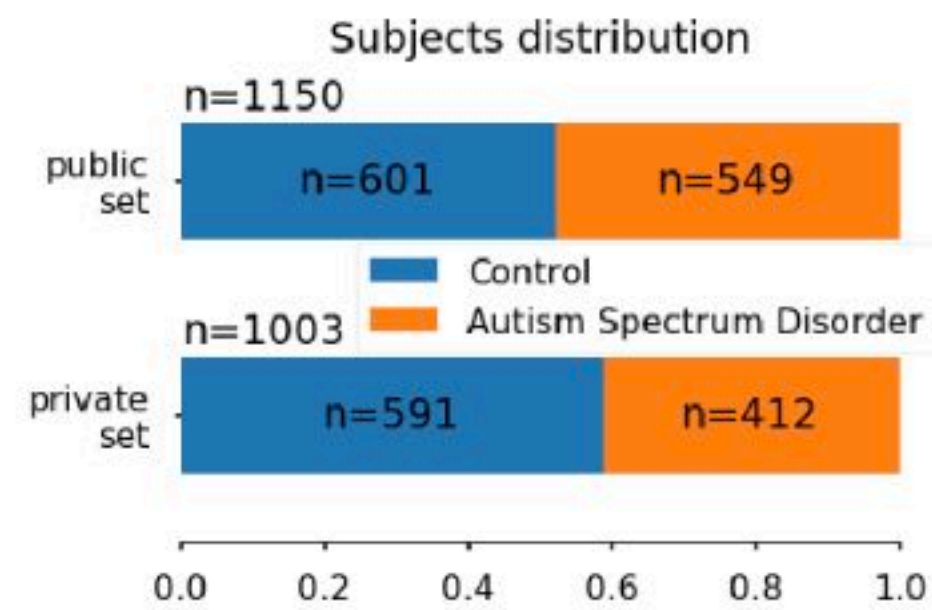
This challenge is made of 2 phases:

1. a **competitive phase** up to July 1 in which participants can submit their solutions to the [RAMP](#) platform. A Q&A session regarding the challenge and technical platform is organized May 14;
2. a **collaborative phase** from July 1 to July 7. This last day will coincide with the awards ceremony.

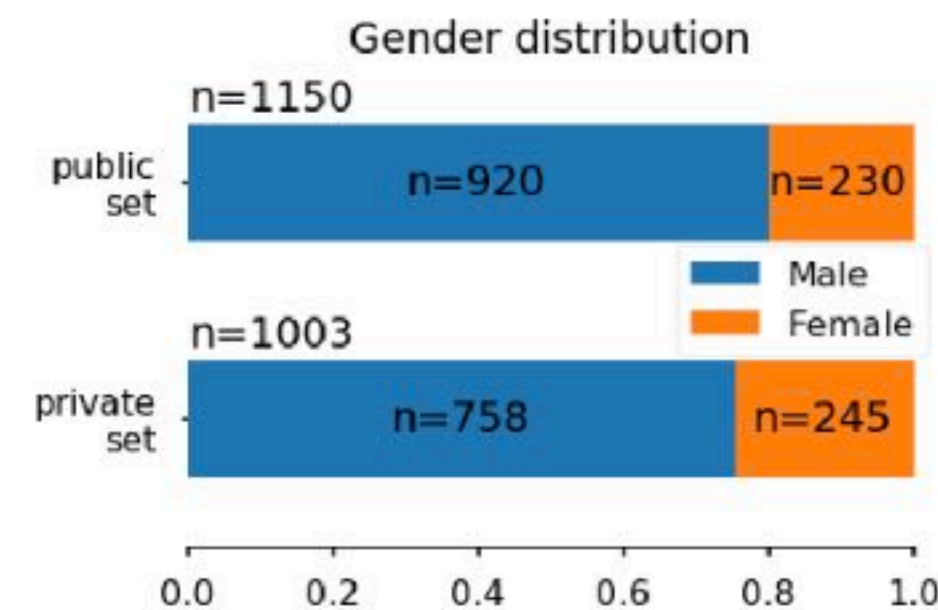
A big data challenge

 Brain images from more than 2000 individuals

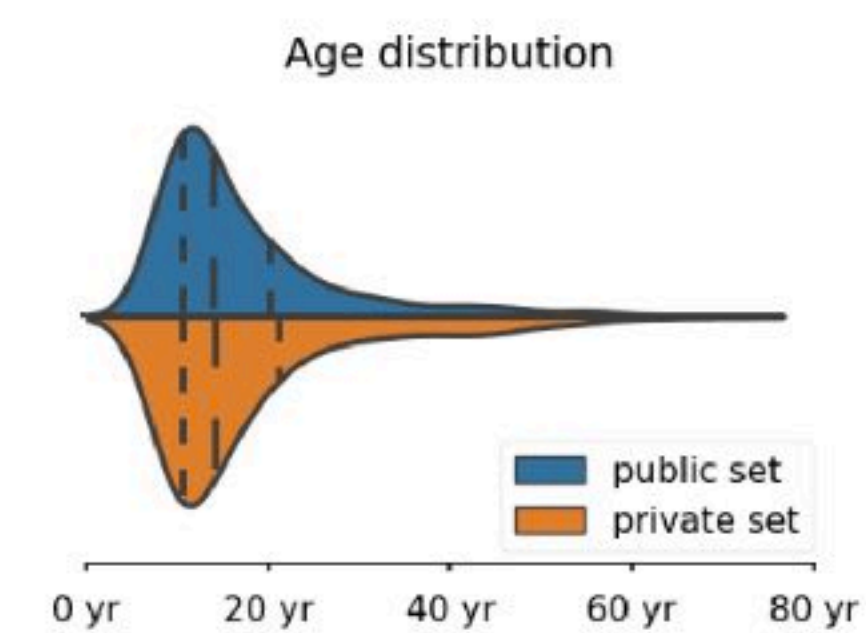
Patient vs Control distribution



Gender distribution



Age distribution



 Multimodal imaging data

Structural MRI

- Preprocessed with FreeSurfer and FSL
- Gray matter volume, area, and thickness
- Average for each Desikan cortical parcel.

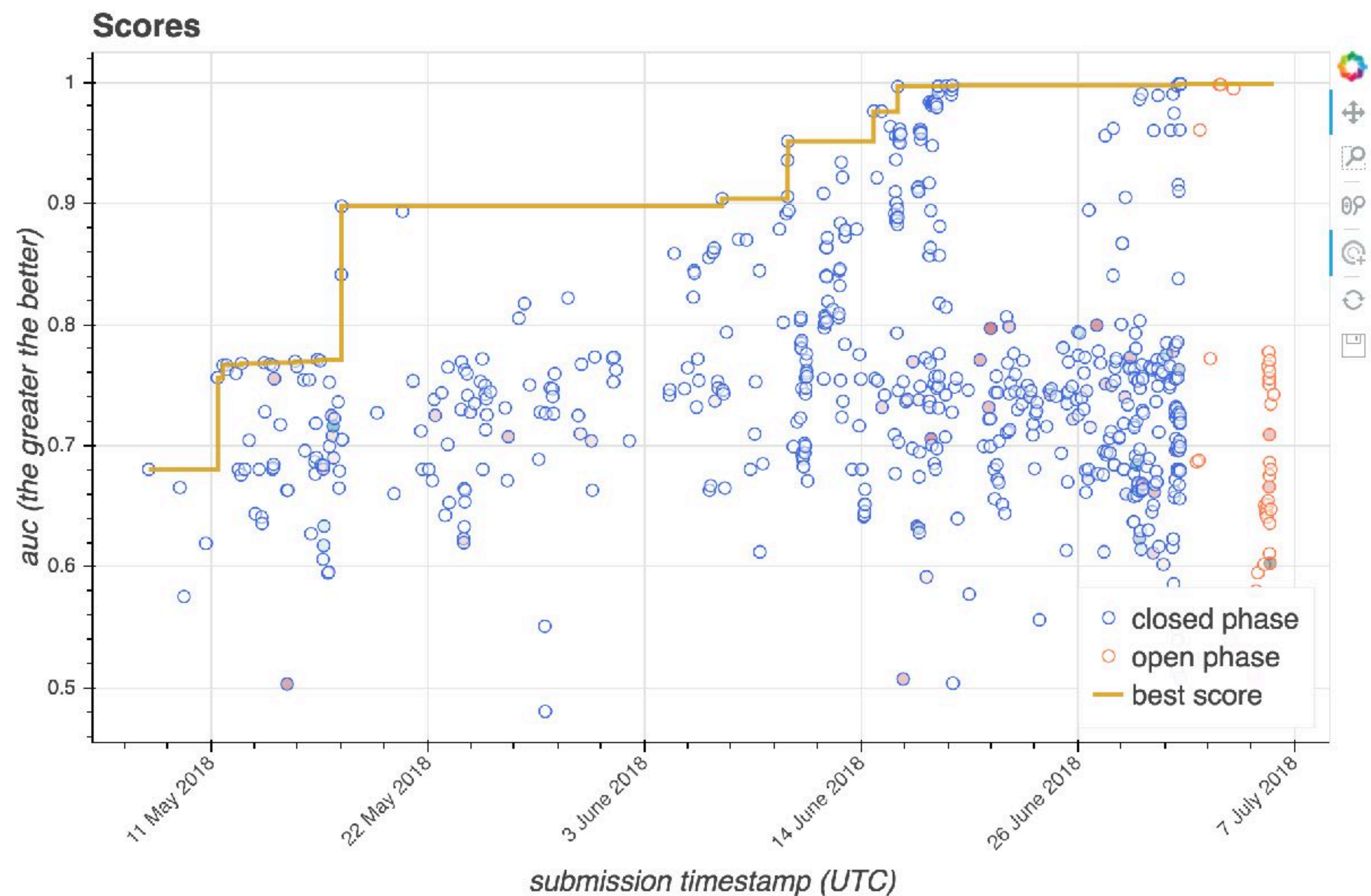
Functional MRI

- Resting state fMRI
- Time series extracted on different atlases

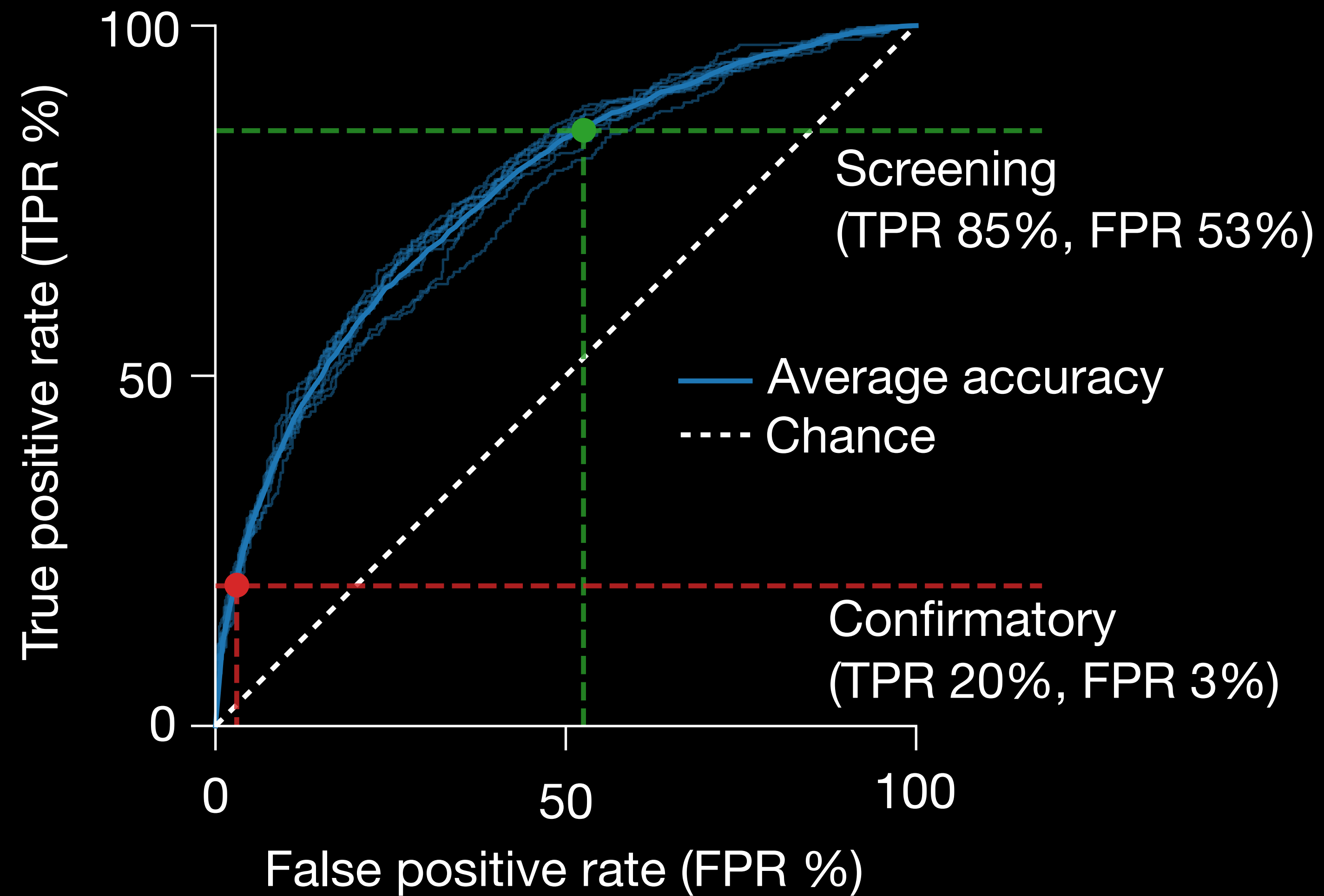
 Coding framework, for competition and collaboration

The challenge will be carried out on the **RAMP platform**. It enables competition and collaboration on data-science problems, using the Python language. To start "hacking", a starting kit is available. It provides a simple working example which can be expanded to more advanced solutions.

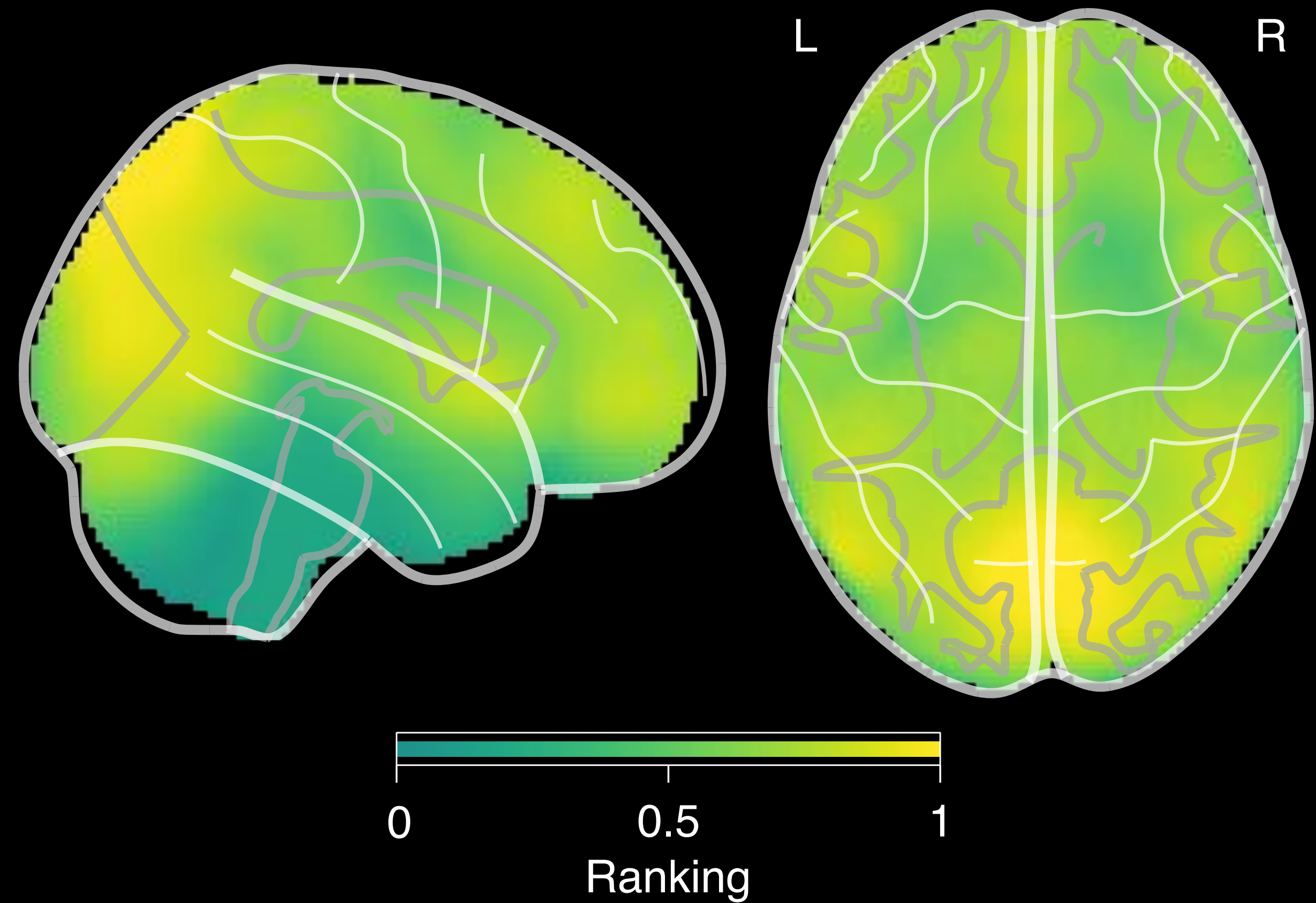
Autism Spectrum Disorder classification, 2018 data challenge



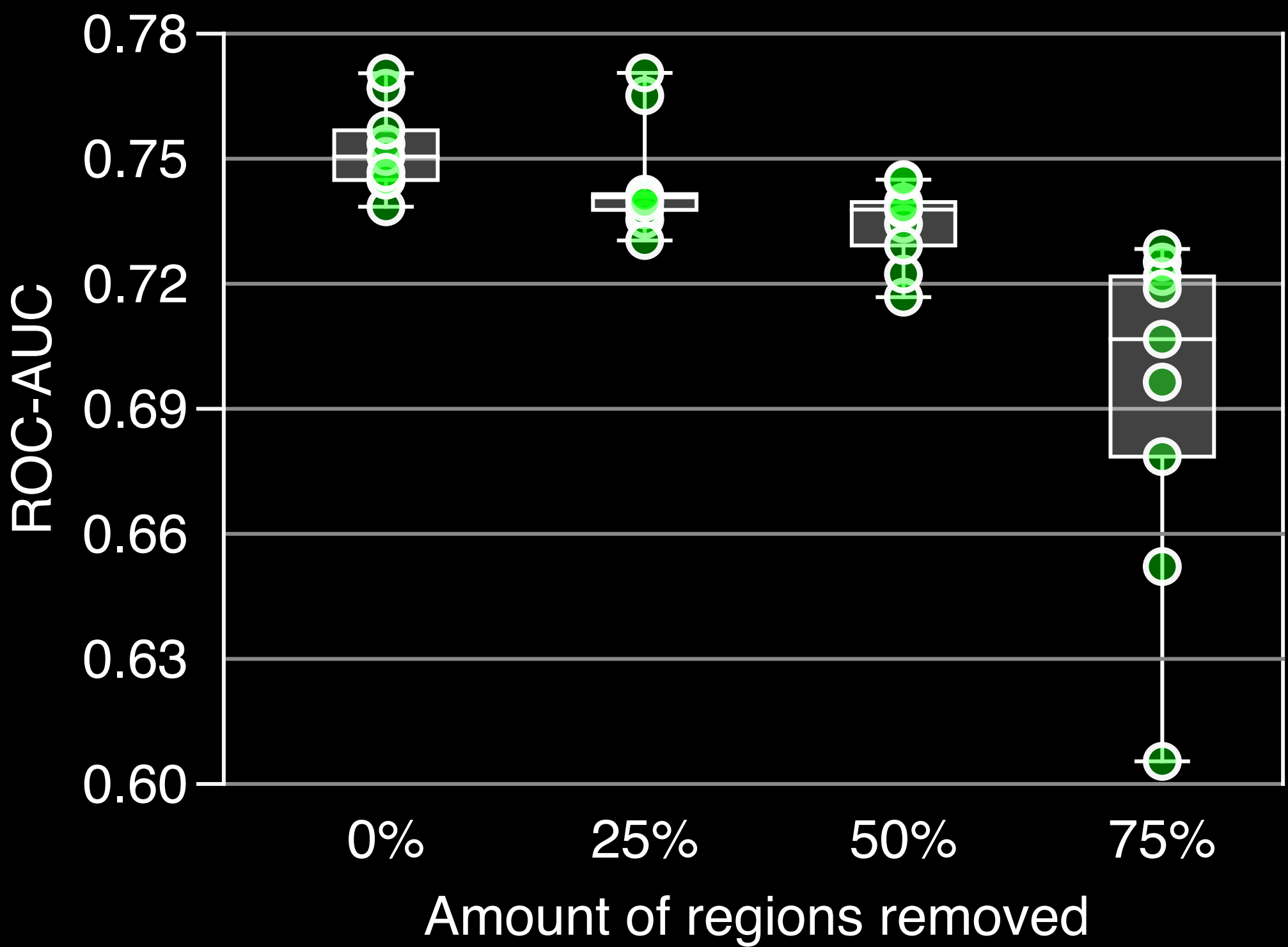
c. Prediction accuracy ($AUC=0.76\pm0.01$)



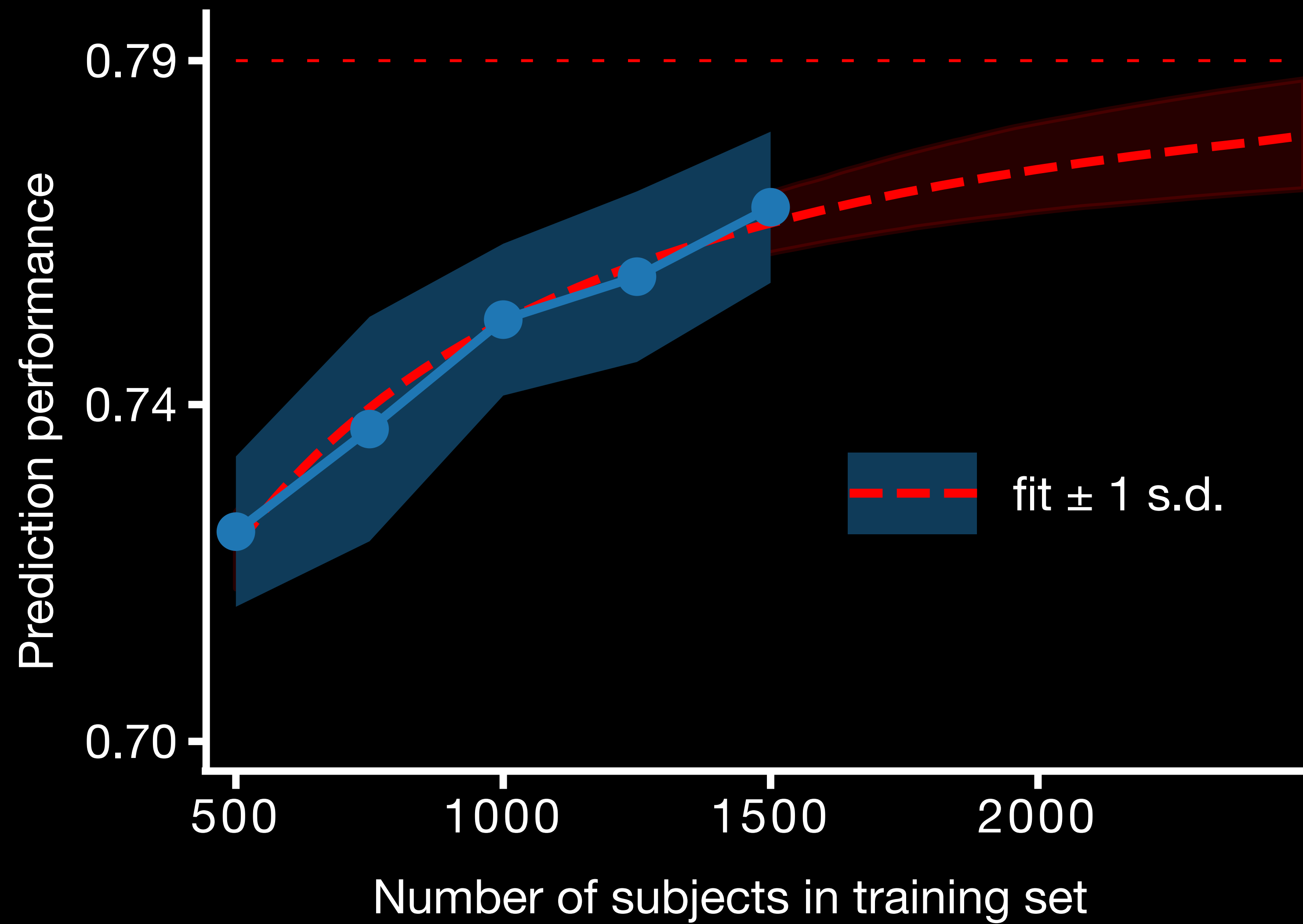
a. Importance of regions for functional MRI



b. Change in accuracy after region removal



d. Prediction for various sample sizes



Conclusion

Progress in the study of neurodevelopmental disorders will require **extremely large sample sizes** (~1M), and the development of a **different kind of data analysis approaches**.

In absence of major genes, **brain imaging phenotypes can provide an alternative rich source of biological information**: they are strongly polygenic, and their variability is affected by some of the same genomic regions that determine the risk to neurodevelopmental disorders.

Data sharing and open science approaches may provide important strategies to tackle this challenge.

Nicolas Traut	Institut Pasteur, Paris
Anne Biton	
Thomas Bourgeron	
Ophélie Foubet	
Céline Delettre	Pasteur, Paris; UKE, Hamburg
Katja Heuer	Pasteur, Paris; Max Planck, Leipzig
Victor Borrell	Instituto de Neurociencia, Alicante
Cristina Llinares	
Isabel Reillo	
Gael Varoqaux	Inria
Guillaume Lemaitre	
Benoit Larrat	Neurospin, Saclay
Sébastien Mériaux	
Rembrandt Bakker	Donders Institute, Nijmegen
Paul Tiesinga	
Thierry Delzescaux	MIRCen, Ile-de-France
Anne-Sophie Hérard	
Alan Evans	MNI, Montréal
Tristan Glatard	
Thomas Deffieux	ESPCI, Paris
Mickael Tanter	

