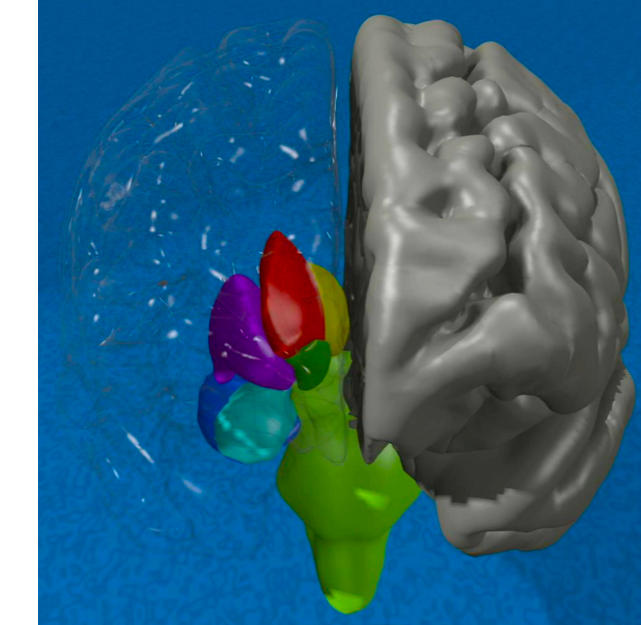
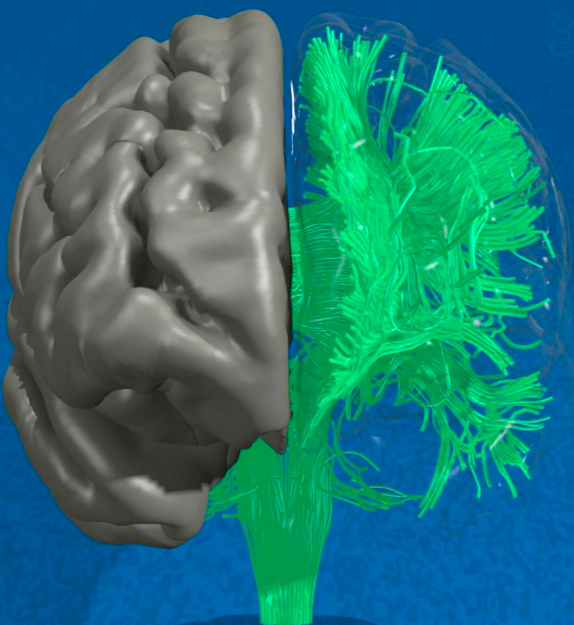


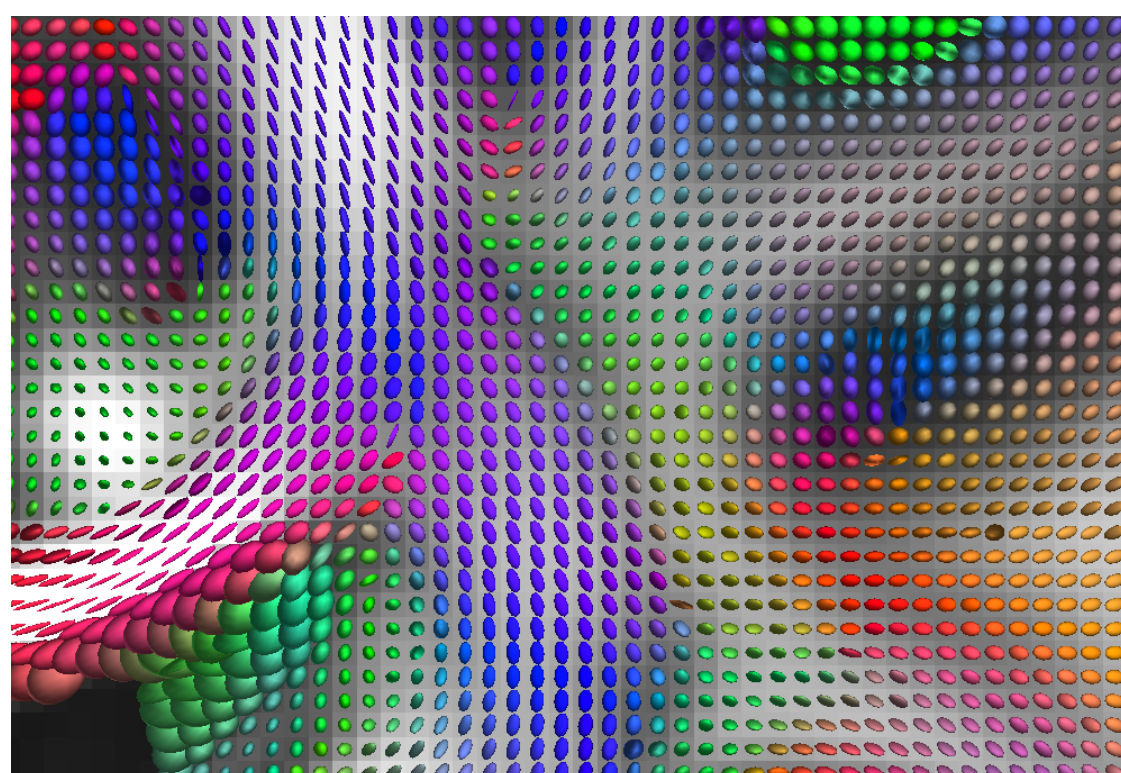
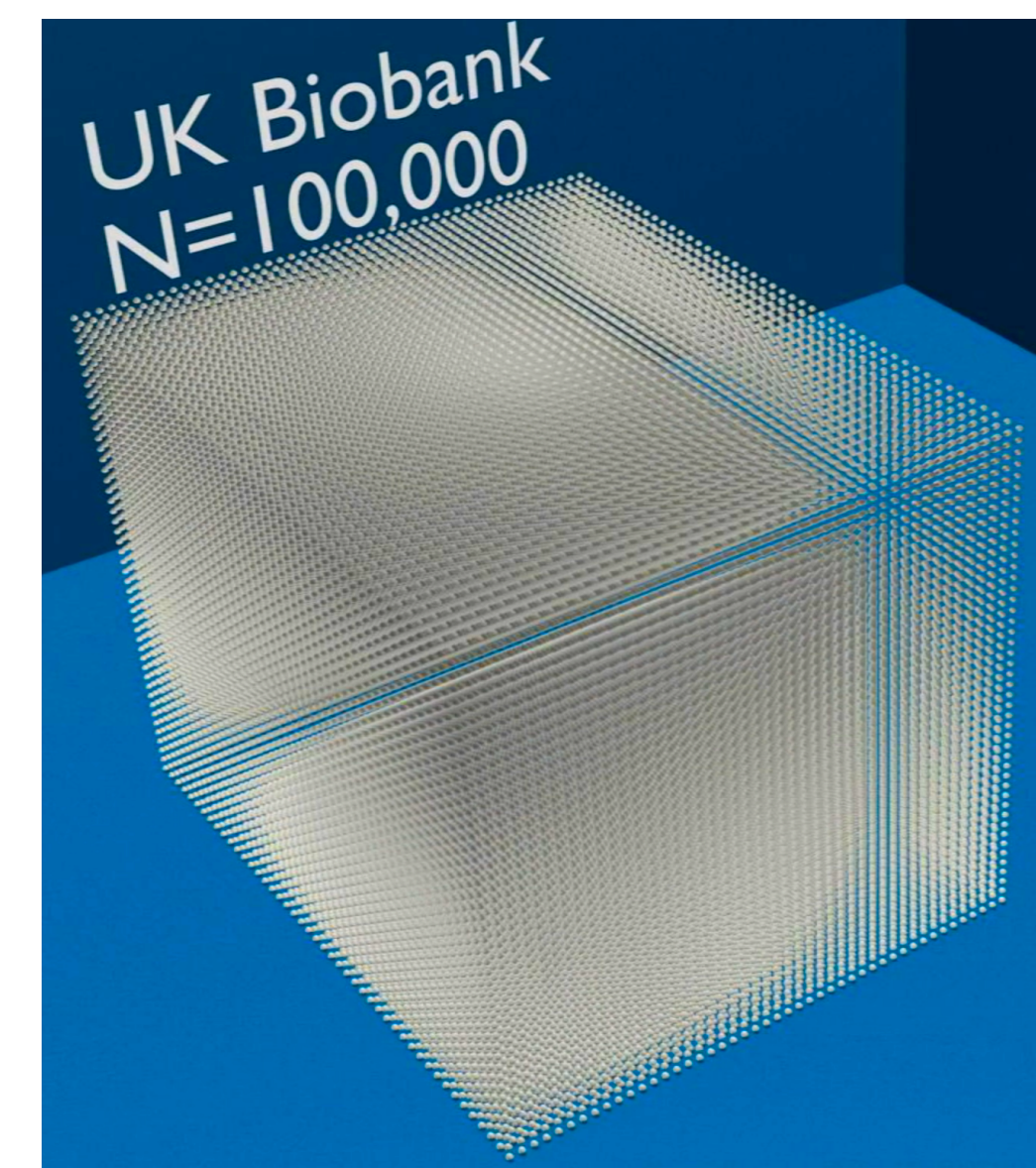
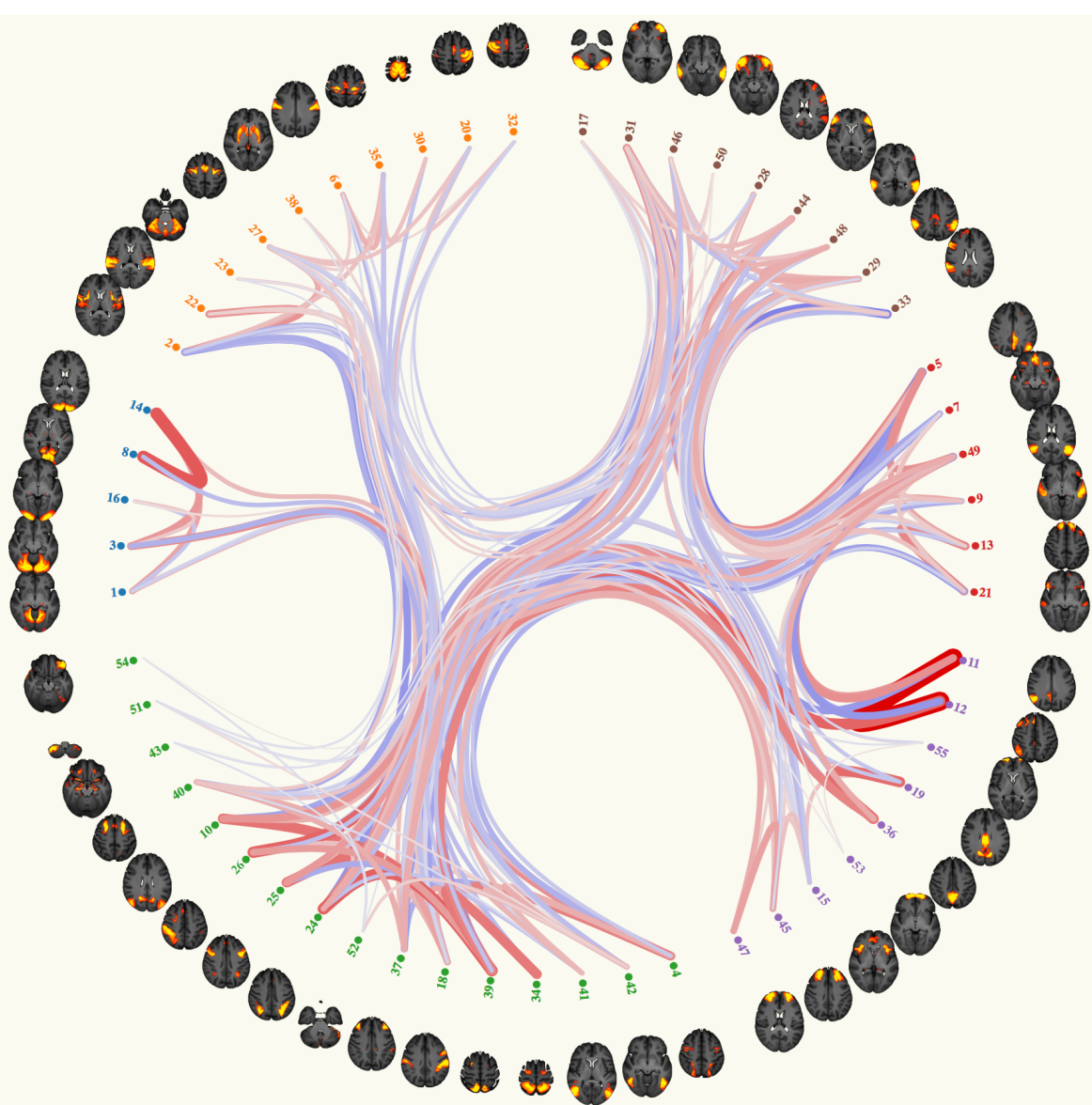


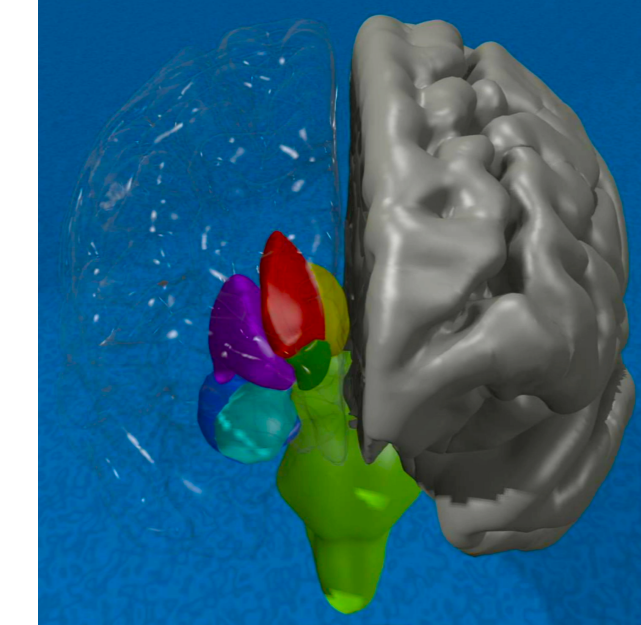
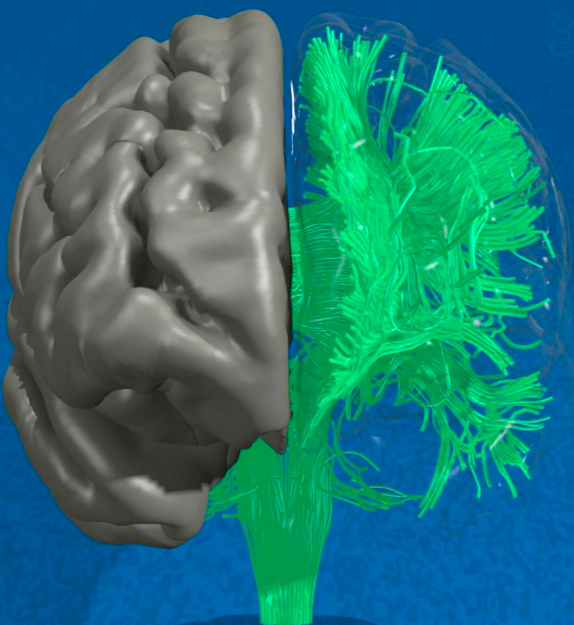
Brain Imaging in UK Biobank

Fidel Alfaro Almagro
WIN, University of Oxford
(a.k.a FMRIB)

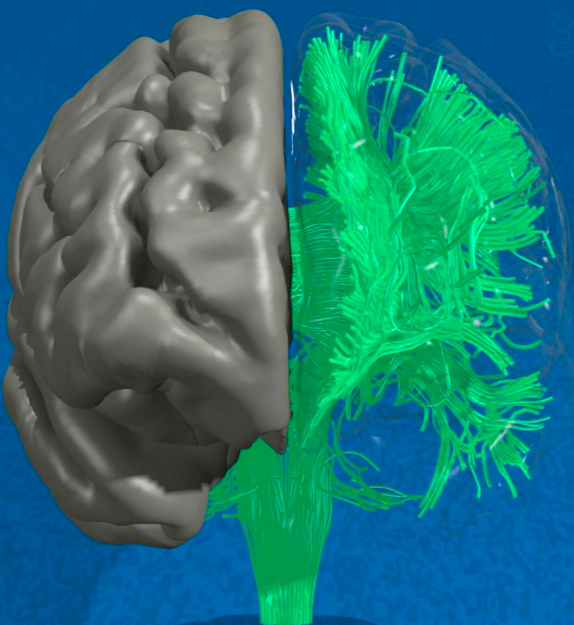
 [@NeuroFidelity](https://twitter.com/NeuroFidelity)

 @NeuroFidelity@nbigtech.es

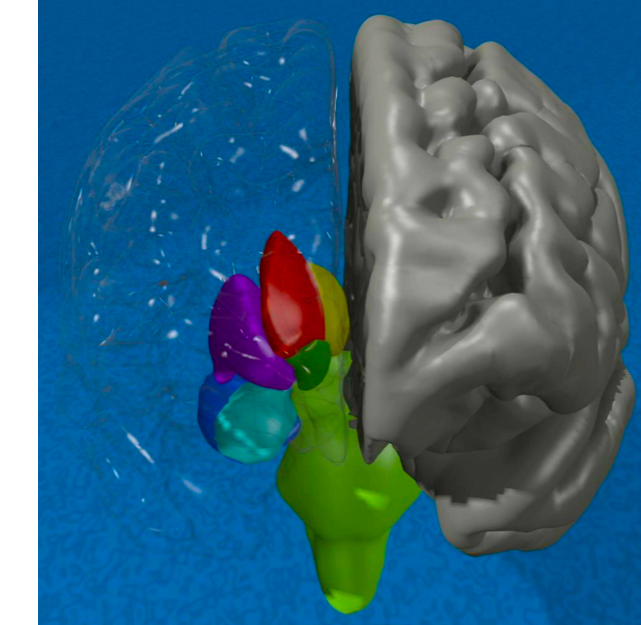




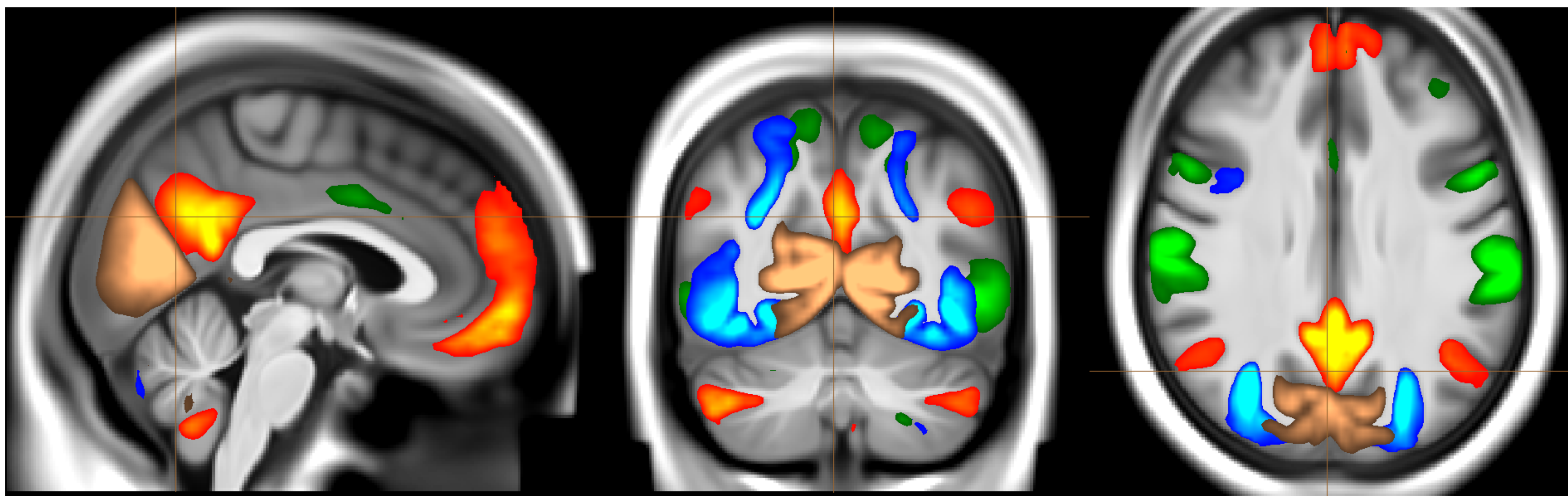
1. **Background**
2. Brain Imaging Project
3. Brain Imaging: What can we do?

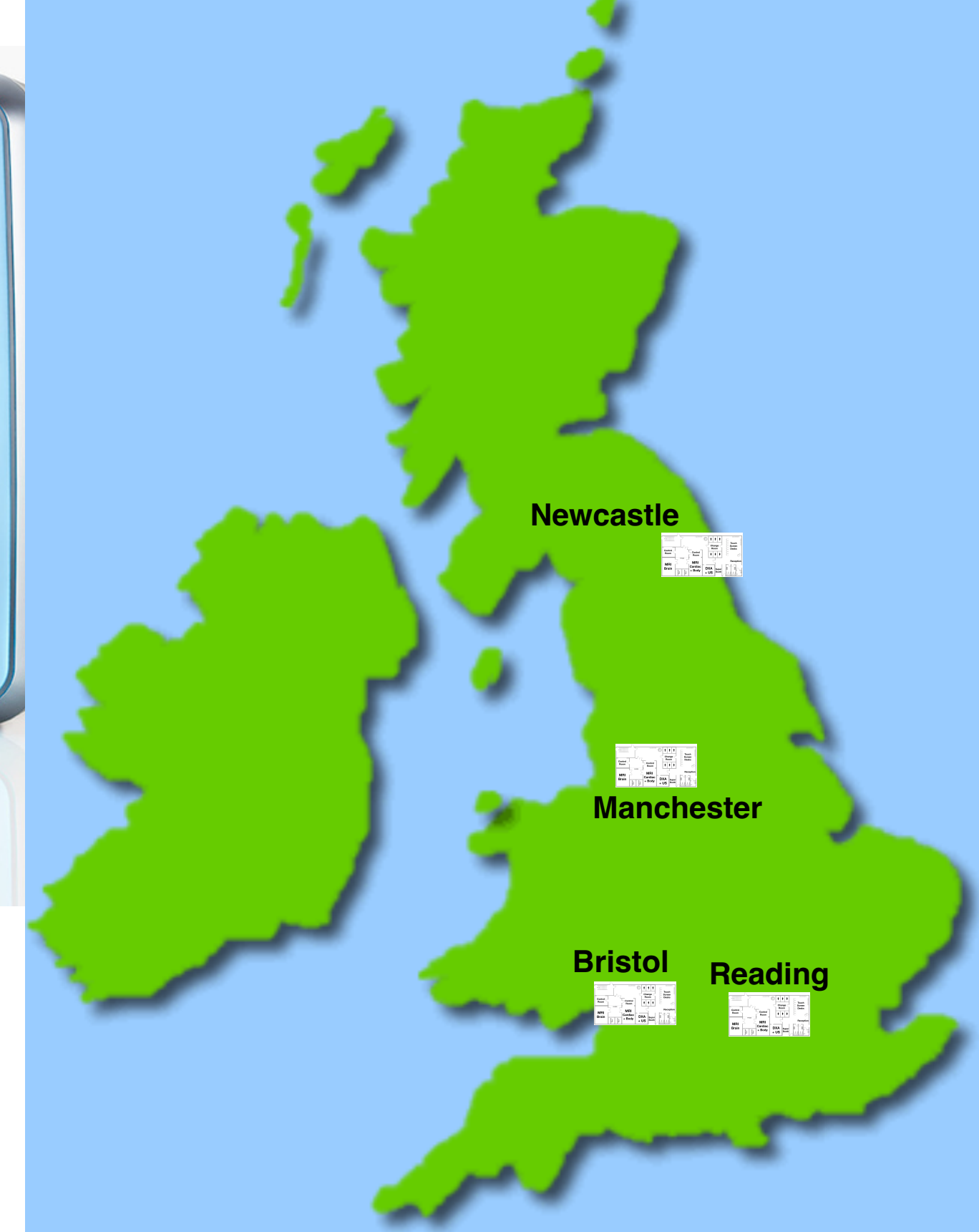
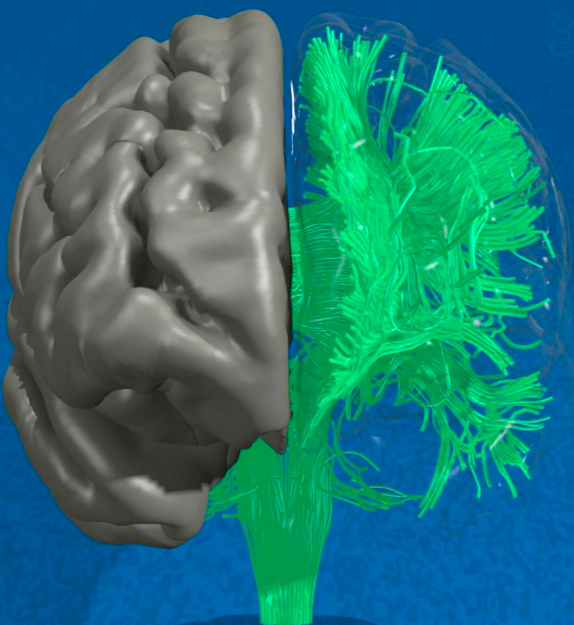


- Brain imaging scientific direction:
Stephen Smith, Karla Miller (Oxford), Paul Matthews (Imperial)
- Brain imaging analysis pipeline:
Fidel Alfaro Almagro, Stephen Smith (Oxford) and many others



- Prospective epidemiological study: 500,000, 45-75y, UK residents
- Genetic data + biological samples + lifestyle information + health records.
- Discover early markers & risk factors of disease





Imaging extension

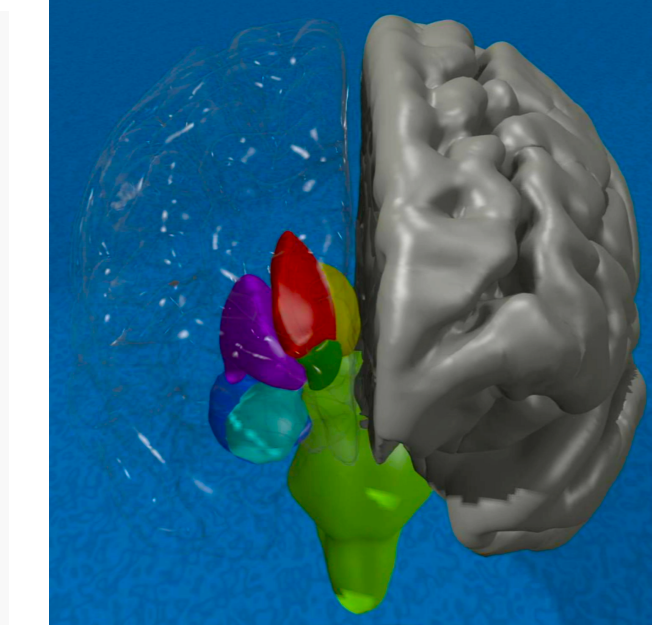
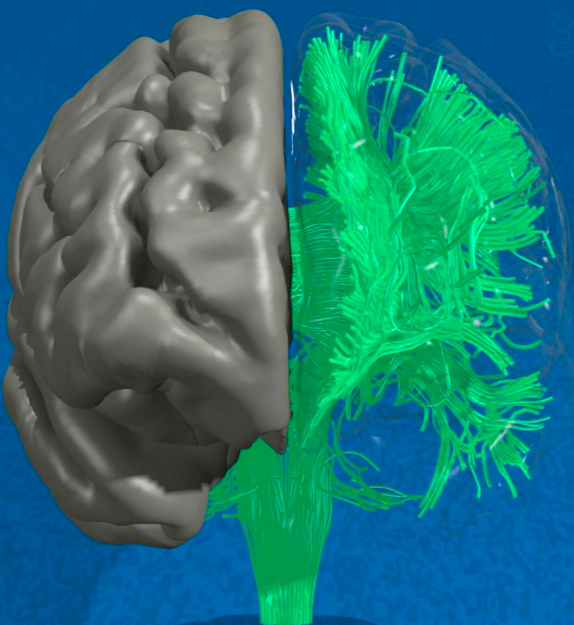
100,000 participants
+ 60,000 2nd timepoint

How do you scan 160,000 subjects?

4 dedicated centres, 72 subjects/day, 7 days/week

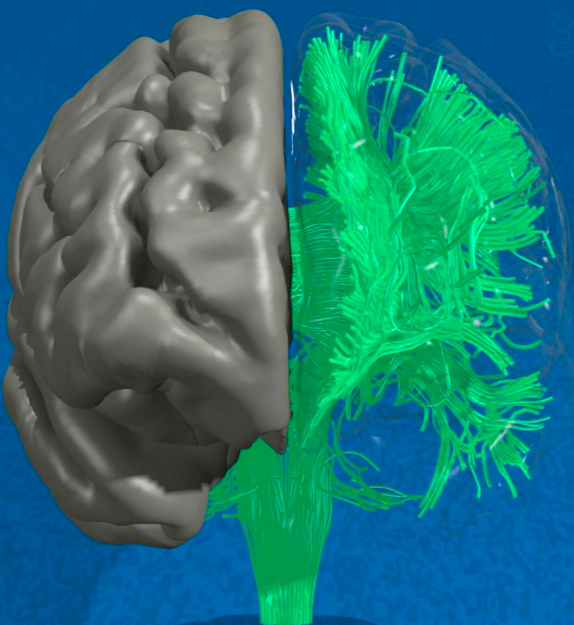
What imaging data can
feasibly be acquired
in a 4-hour visit?

- Brain MRI (3T)
- Cardiac & body MRI (1.5 T)
- DXA bone density
- Carotid UltraSound

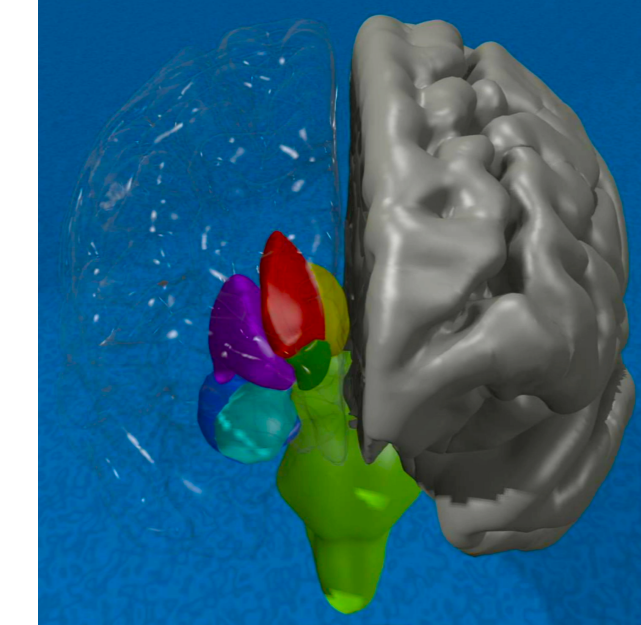


Data Access <http://www.ukbiobank.ac.uk/register-apply>

- Open for use by researchers worldwide
- Application process (protection of sensitive subject data, etc)
- Modest data access fee to fund indefinite maintenance of resource
- No preferential access to scientists helping run UK Biobank !



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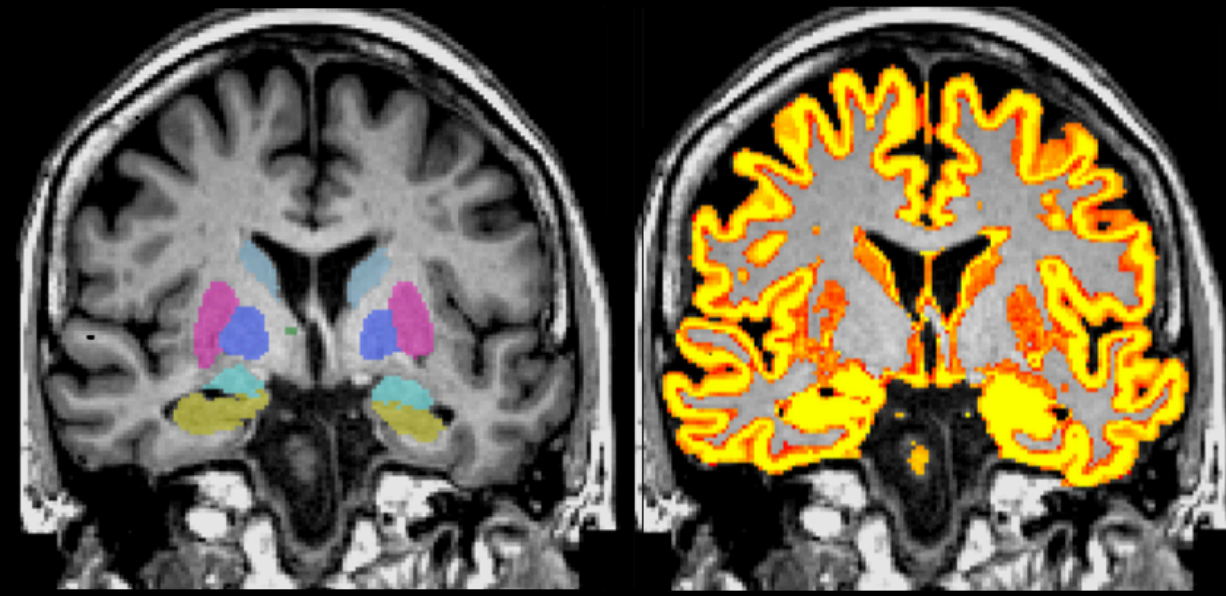


1. Background
2. **Brain Imaging Project**
3. Brain Imaging: What can we do?

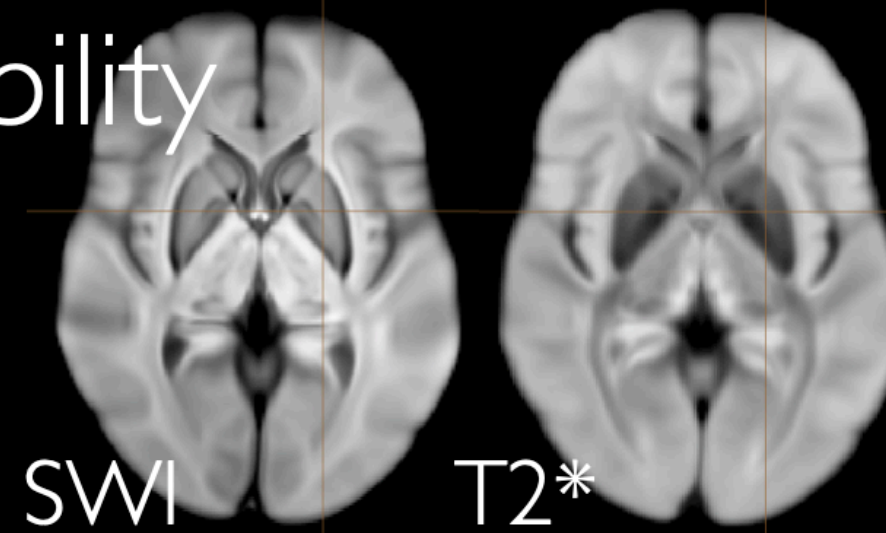
35 mins per subject

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Imaging study

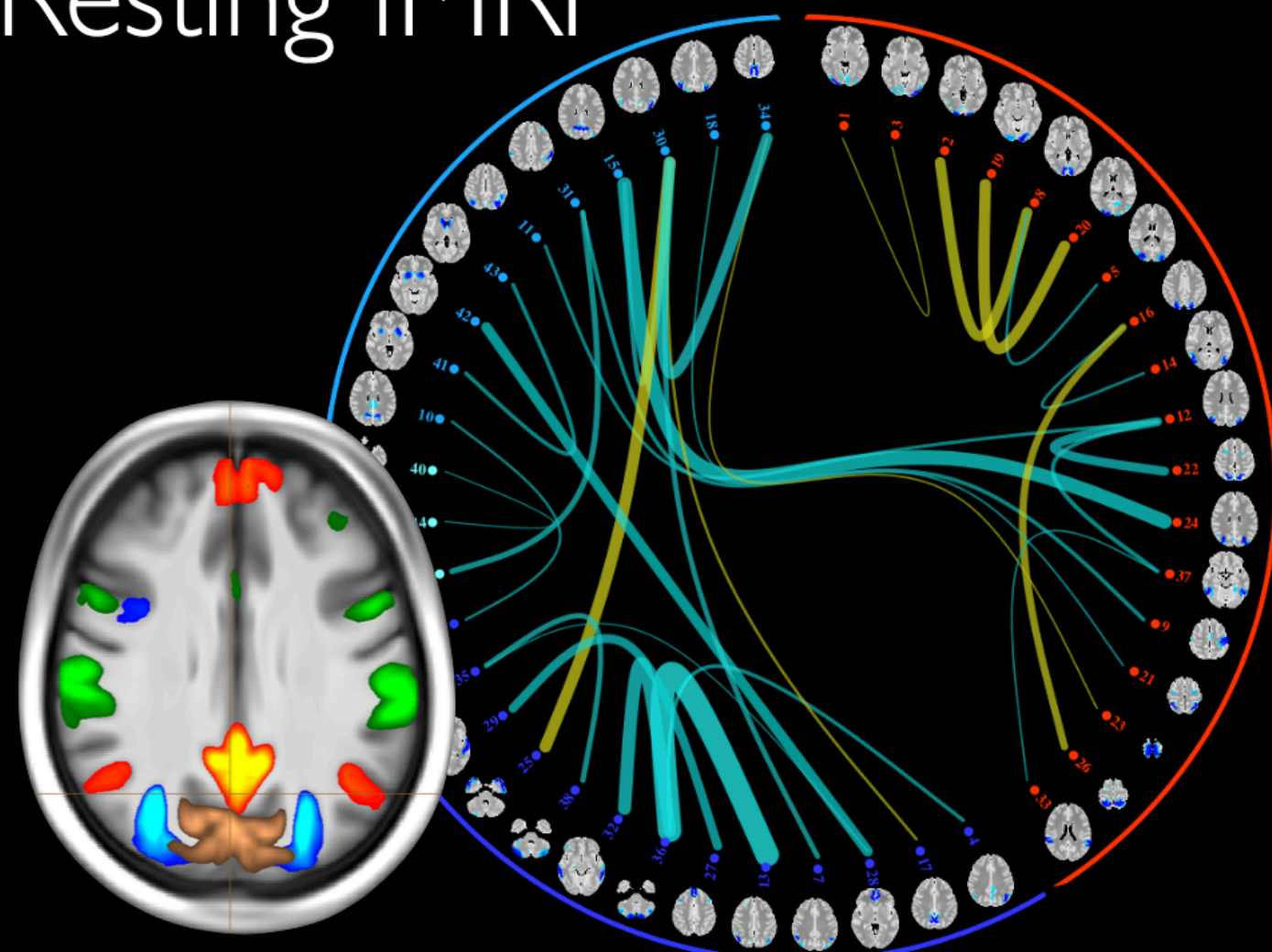
T1-weighted



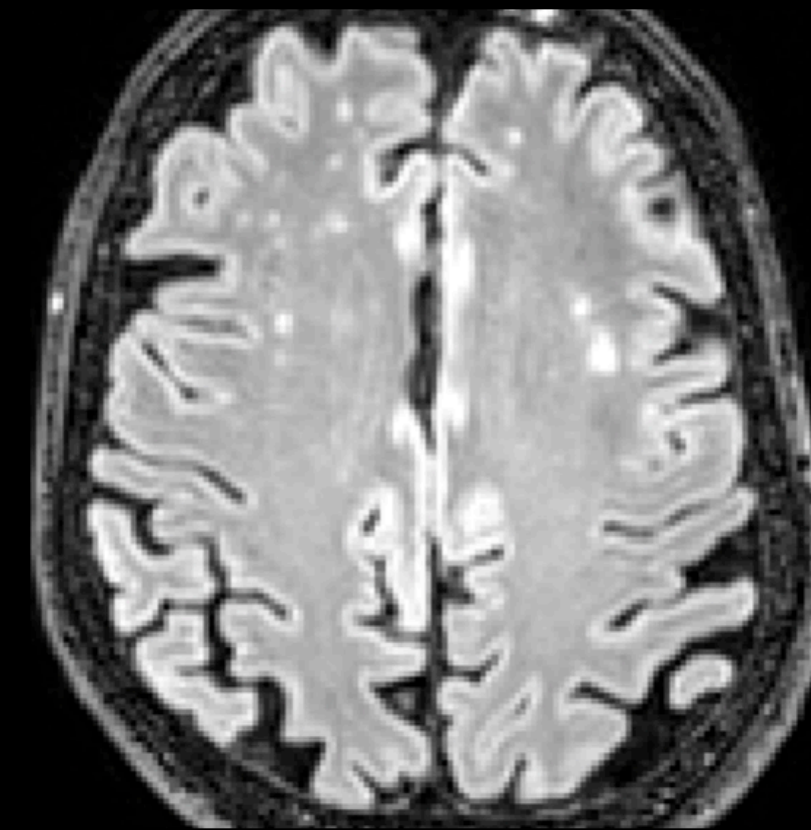
Susceptibility
contrast



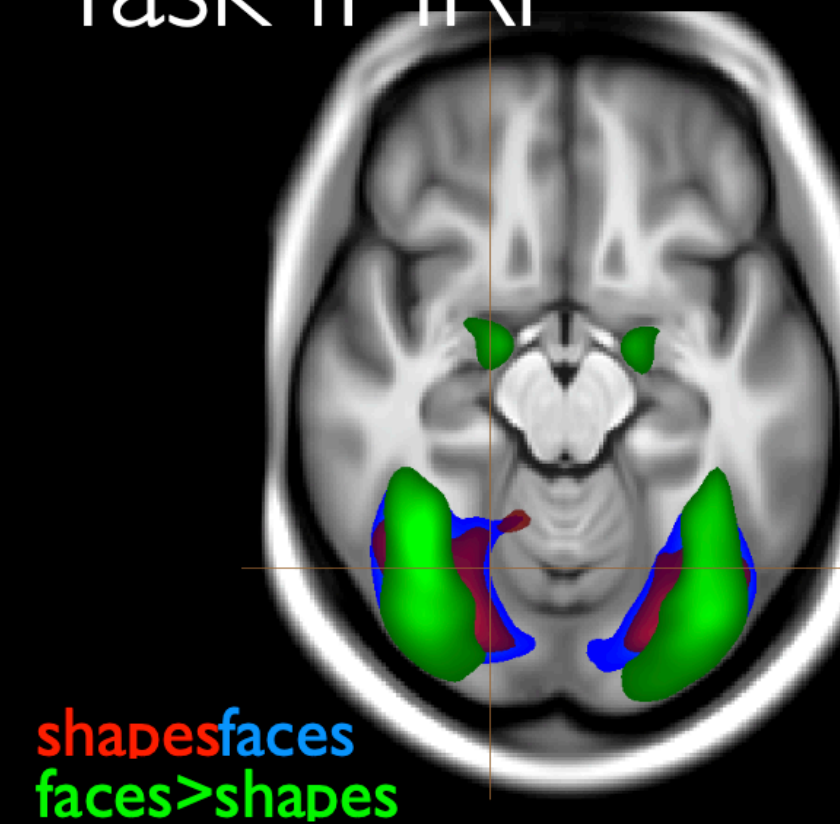
Resting fMRI



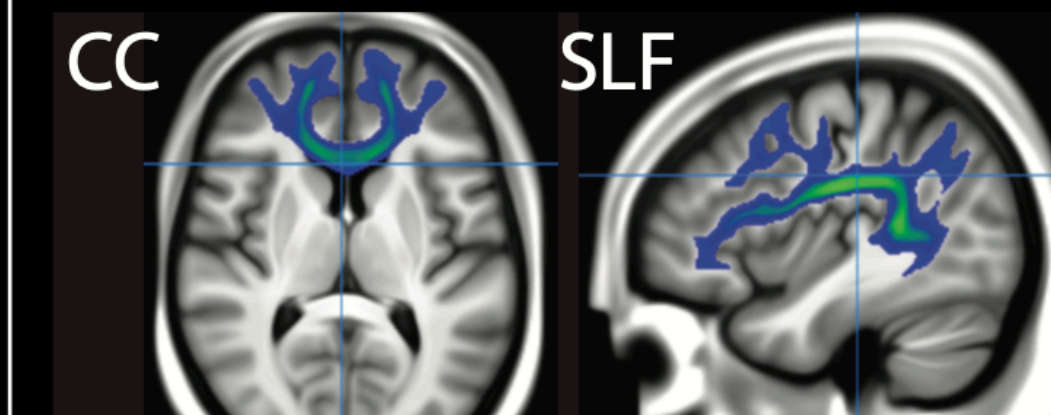
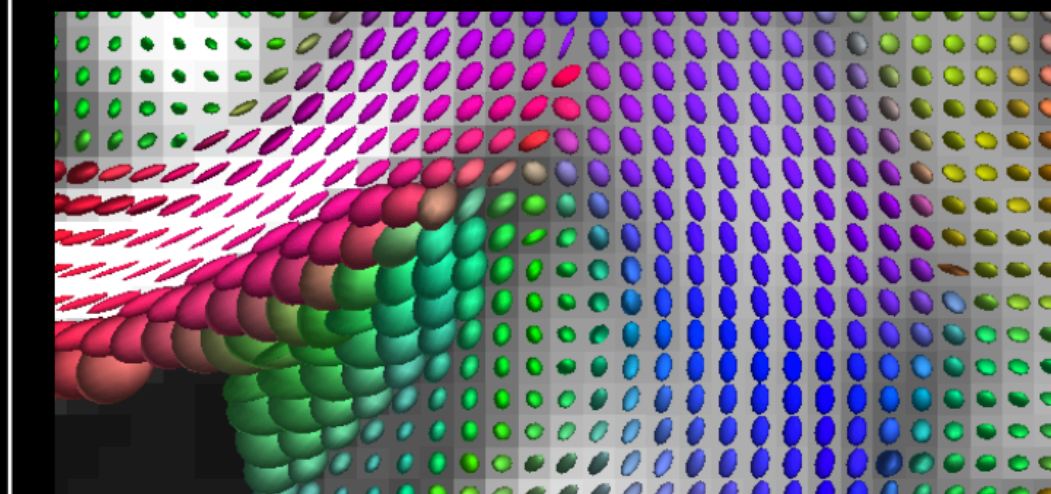
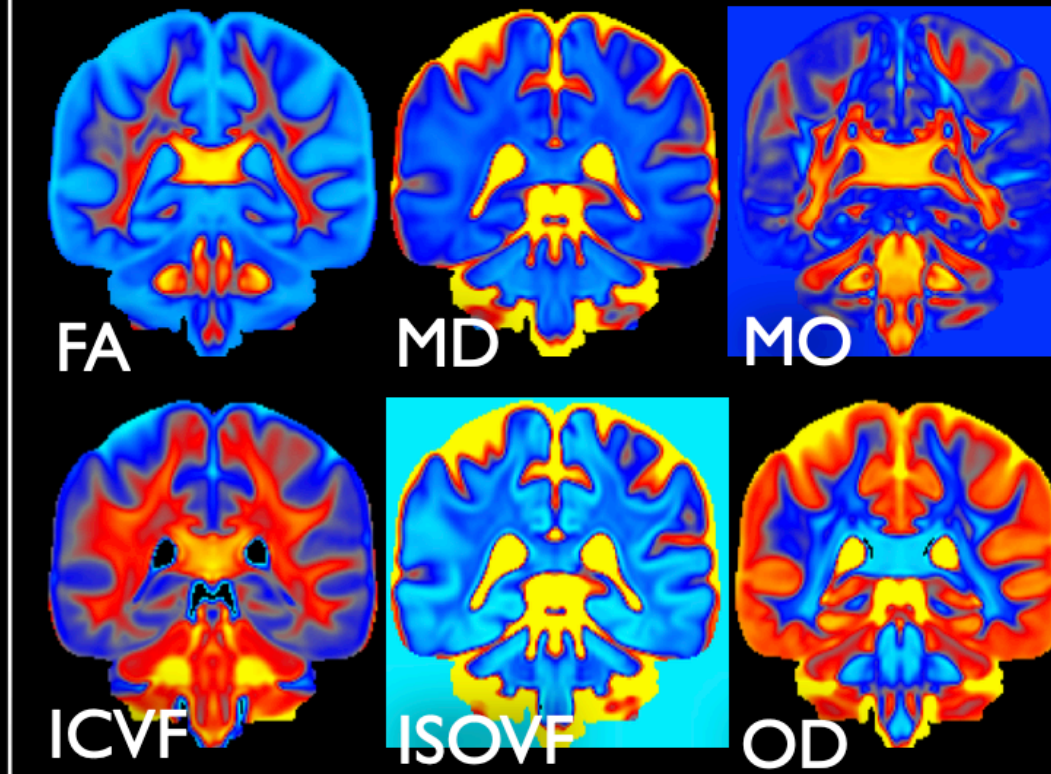
T2 FLAIR



Task fMRI

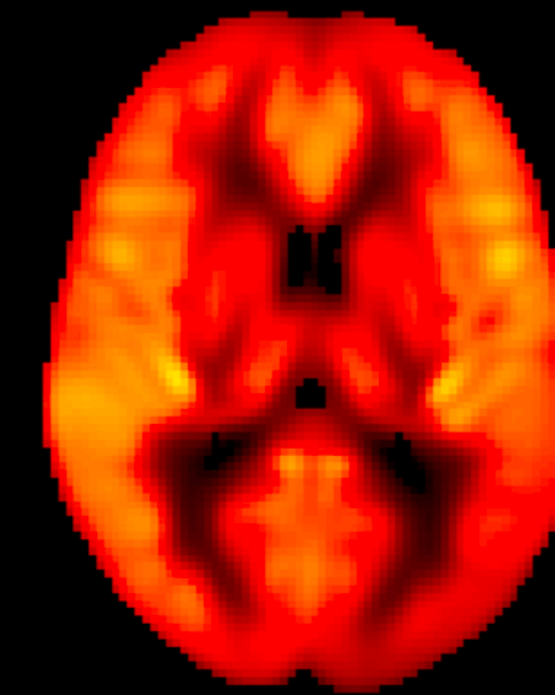


Diffusion MRI



ASL

(repeat
scans
only)

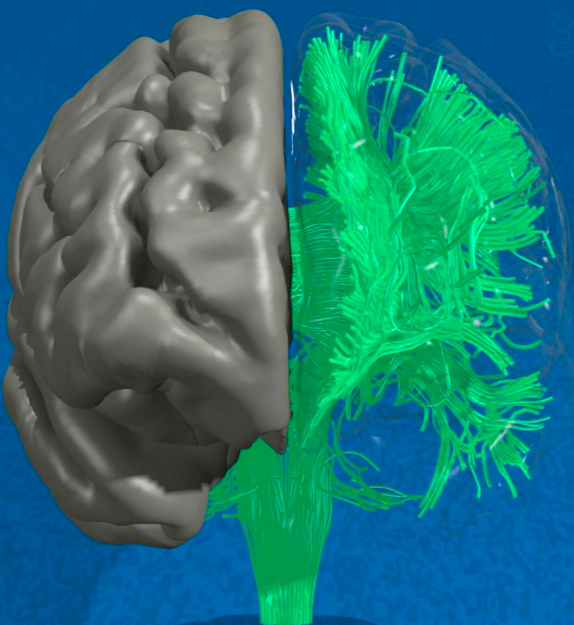


Biobank Neuro Protocol

T1	5min	1 mm iso	3D MPRAGE, sagittal, R=2, TI/TR=880/2000ms
rfMRI	6min	2.4 mm iso	EPI MB=x8 TR=0.735 s , TE=39ms, R=1, flip angle=52°, fat sat
tfMRI	4min	as rfMRI	as rfMRI, Hariri faces/shapes “emotion” task
T2 FLAIR	6min	1.05 x 1 x 1 mm	FLAIR, 3D SPACE, sagittal, R=2, PF 7/8, fat sat, TI/TR=1800/5000ms, elliptical
dMRI	7min	2 mm iso	EPI MB=x3, 50x b=1000, 50x b=2000 , TE=92ms, fat sat, topup-fieldmap
swMRI	2.5min	0.8 x 0.8 x 3 mm	3D GRE, axial, R=2, PF 7/8, TE1/TE2/TR=9.4/20/27ms

- 3T scanner, 32-channel head-coil
- fMRI & dMRI: accelerated by UMinn CMRR multiband
- phase-encoding-reversed fieldmap from dMRI (FSL-*topup*)
- dMRI: monopolar encoding (better SNR; eddies fixed by FSL-*eddy*)

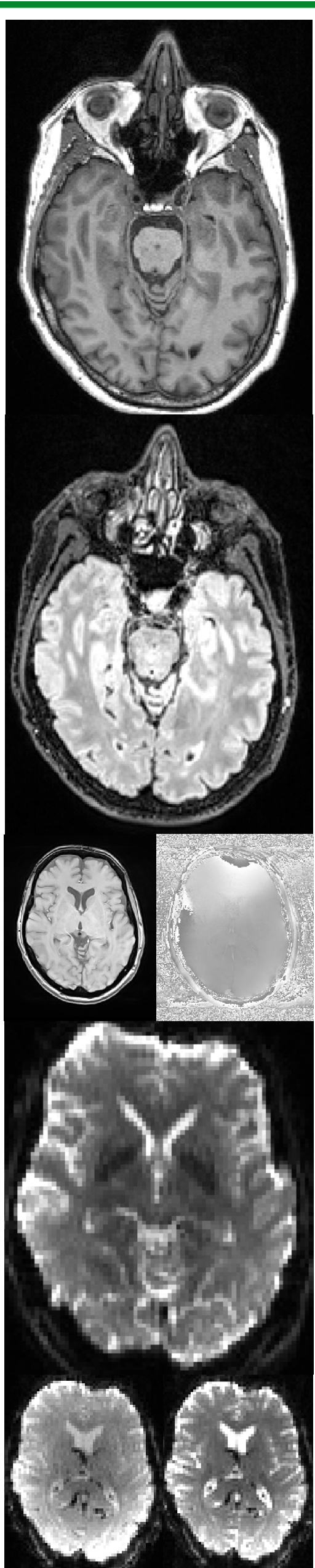
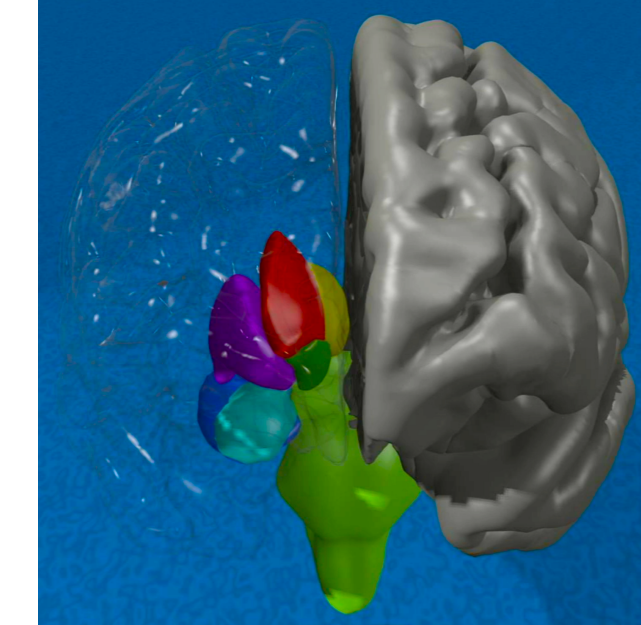
(Miller et al, Nature Neuroscience 2016)



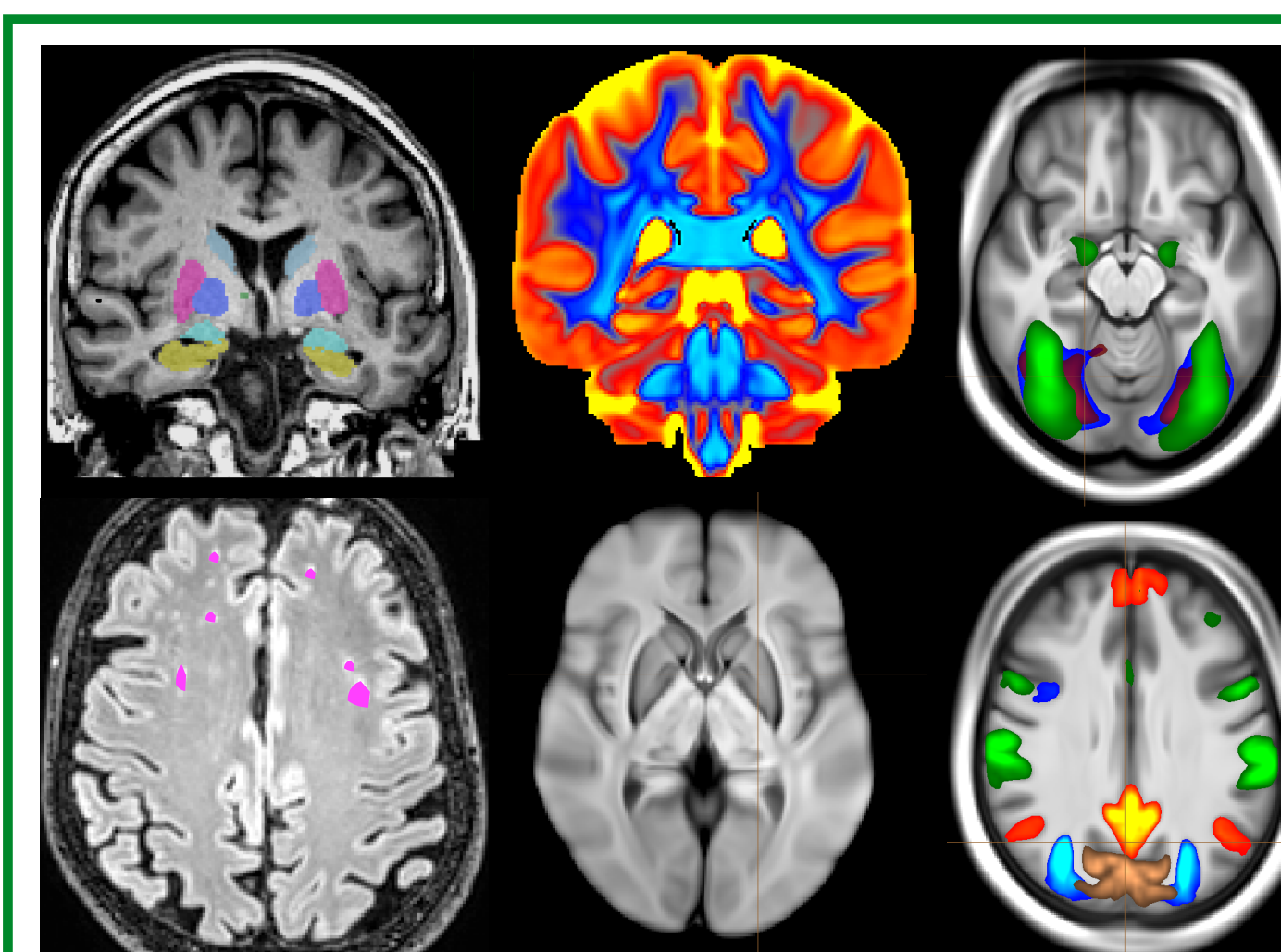
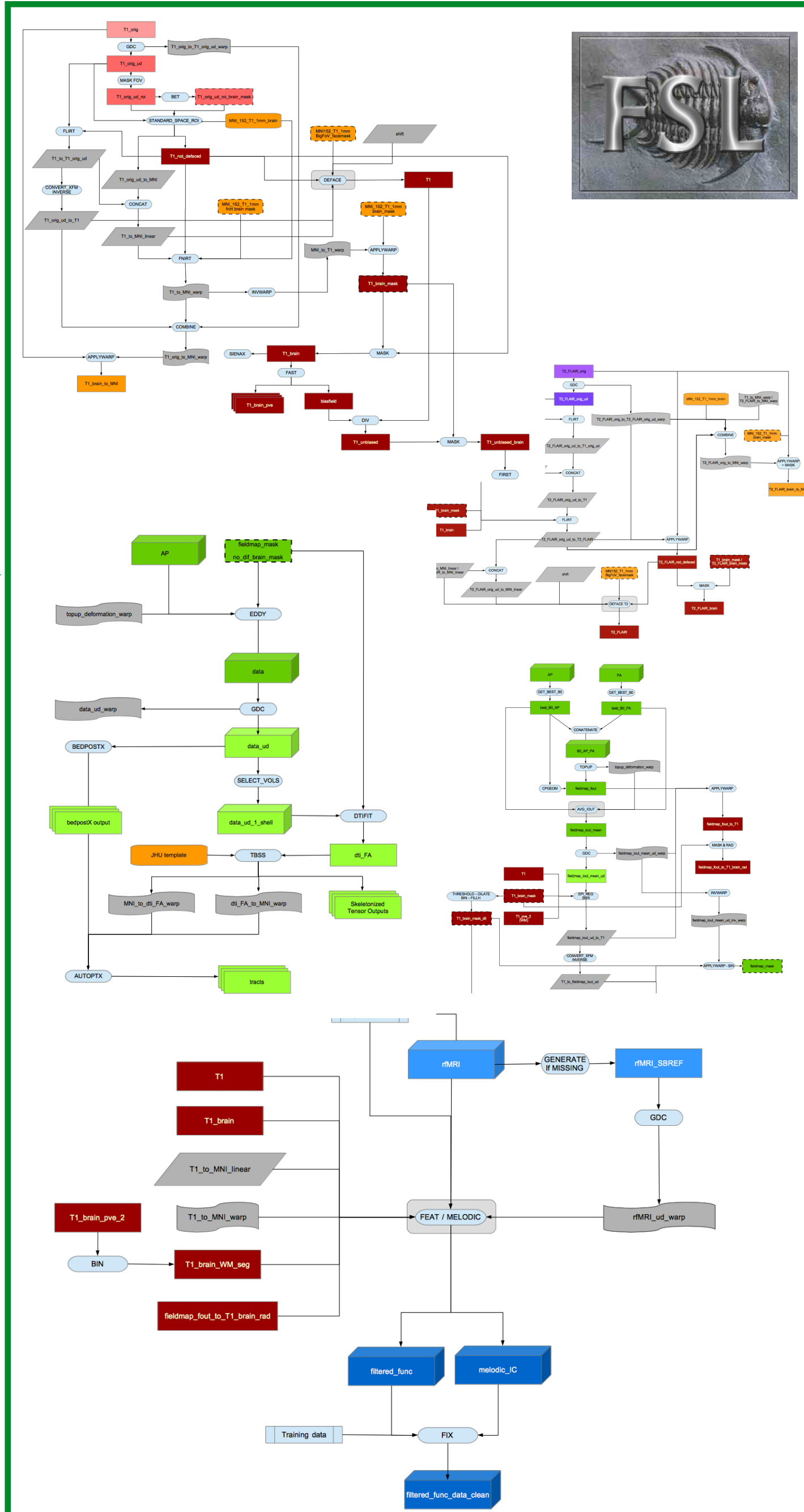
raw data

automated processing

open-access database



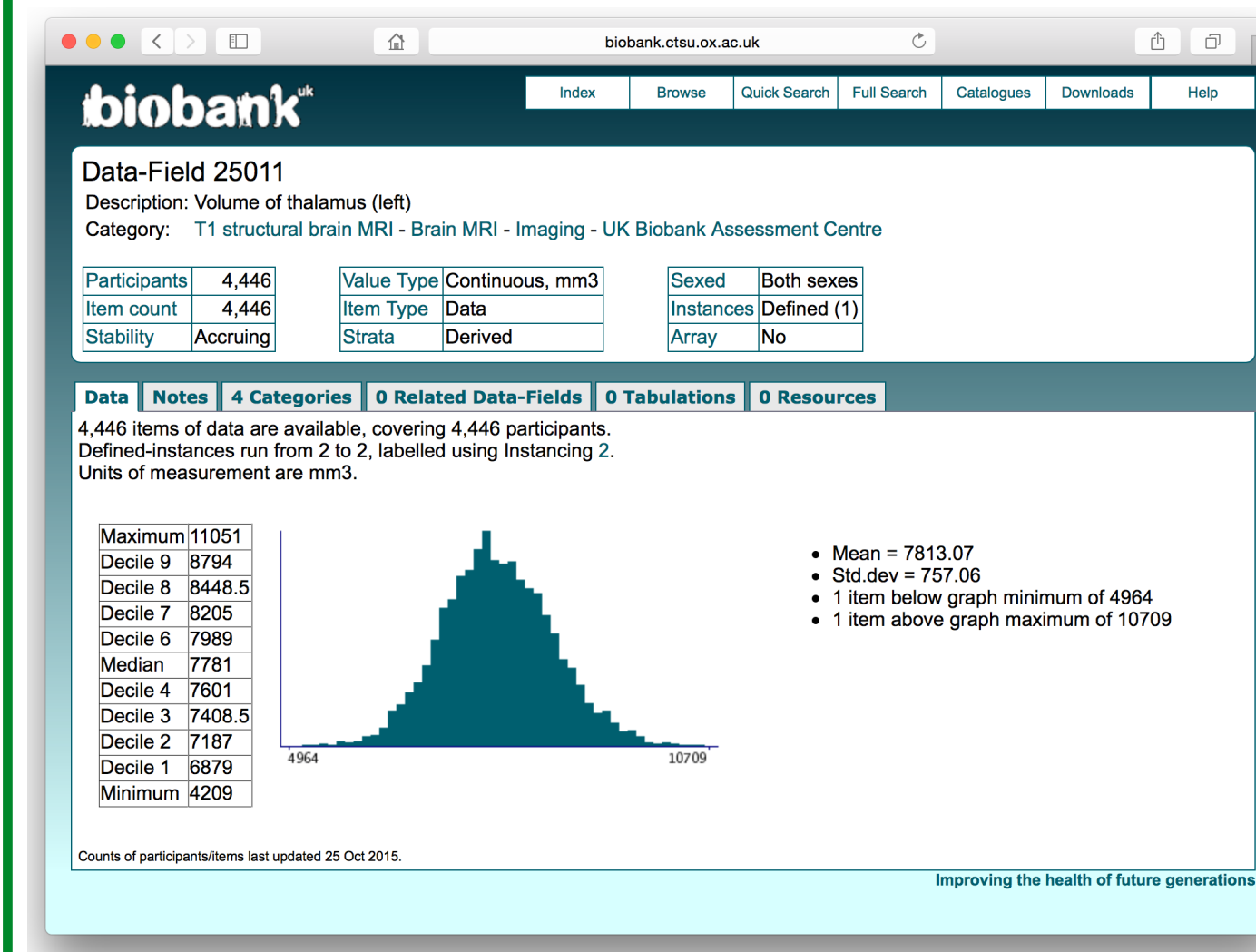
raw DICOMs

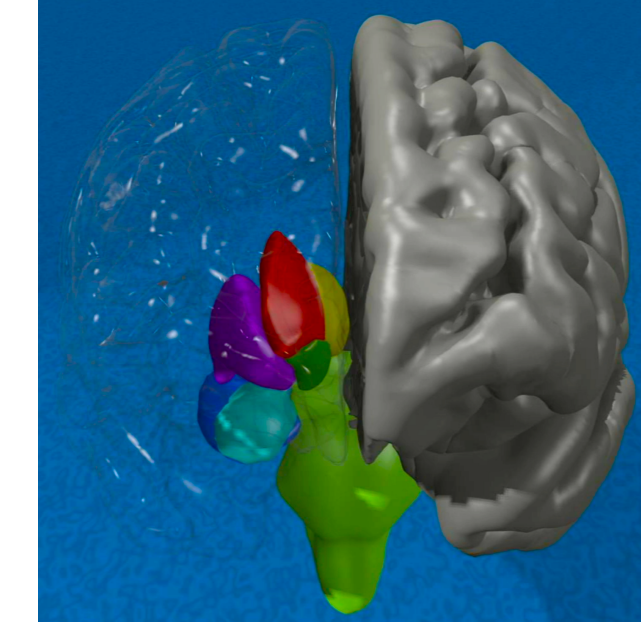


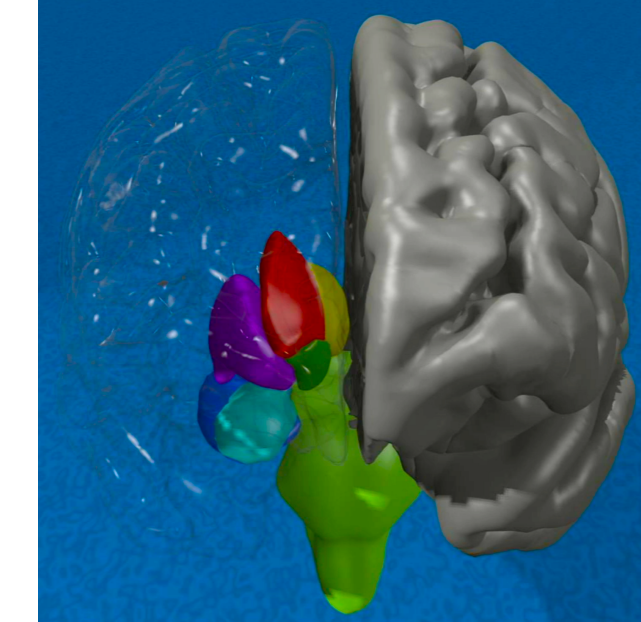
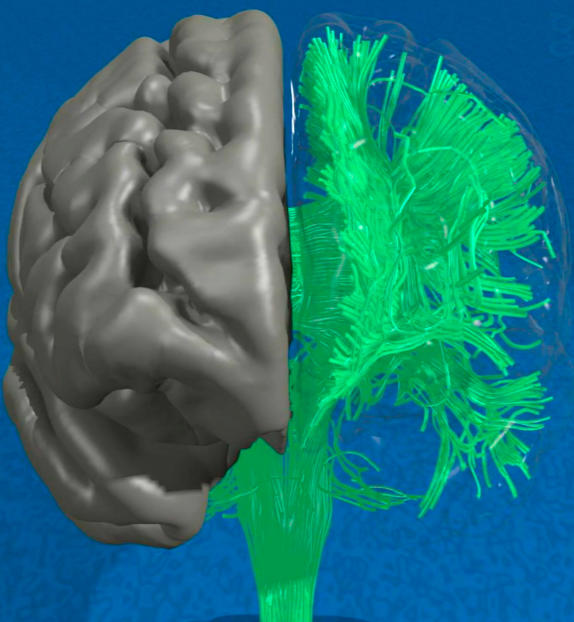
raw and processed NIFTI data

+

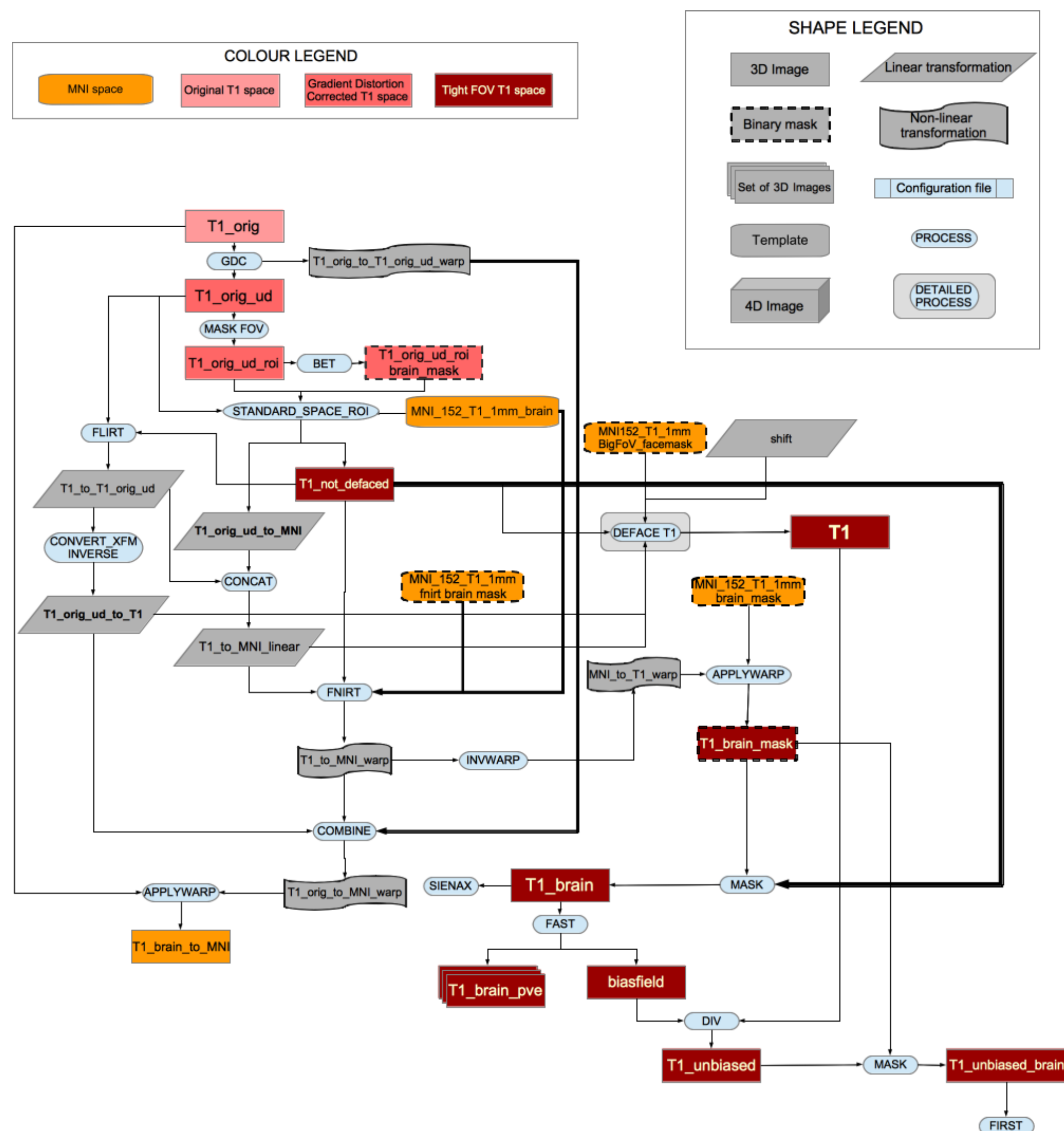
imaging-derived phenotypes
(IDPs - summary measures)



[illegible]

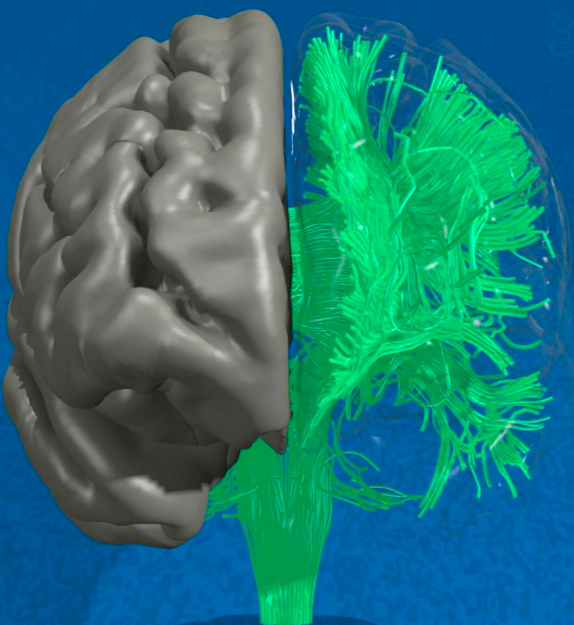


(Alfaro-Almagro et al, NeuroImage, 2018)



- **Processing pipeline:** Fully automated computing structure.
- Basic blocks are neuroimaging tools (e.g. FSL): Process the images and generate a new output image or value that can be used in the next step.
- The pipeline structure is mainly written in **bash** and **python**.
- The basic blocks that are not FSL are tools written in Matlab, R, Java, etc. Some of them belong to software libraries such as FreeSurfer.

* FMRIB Software Library



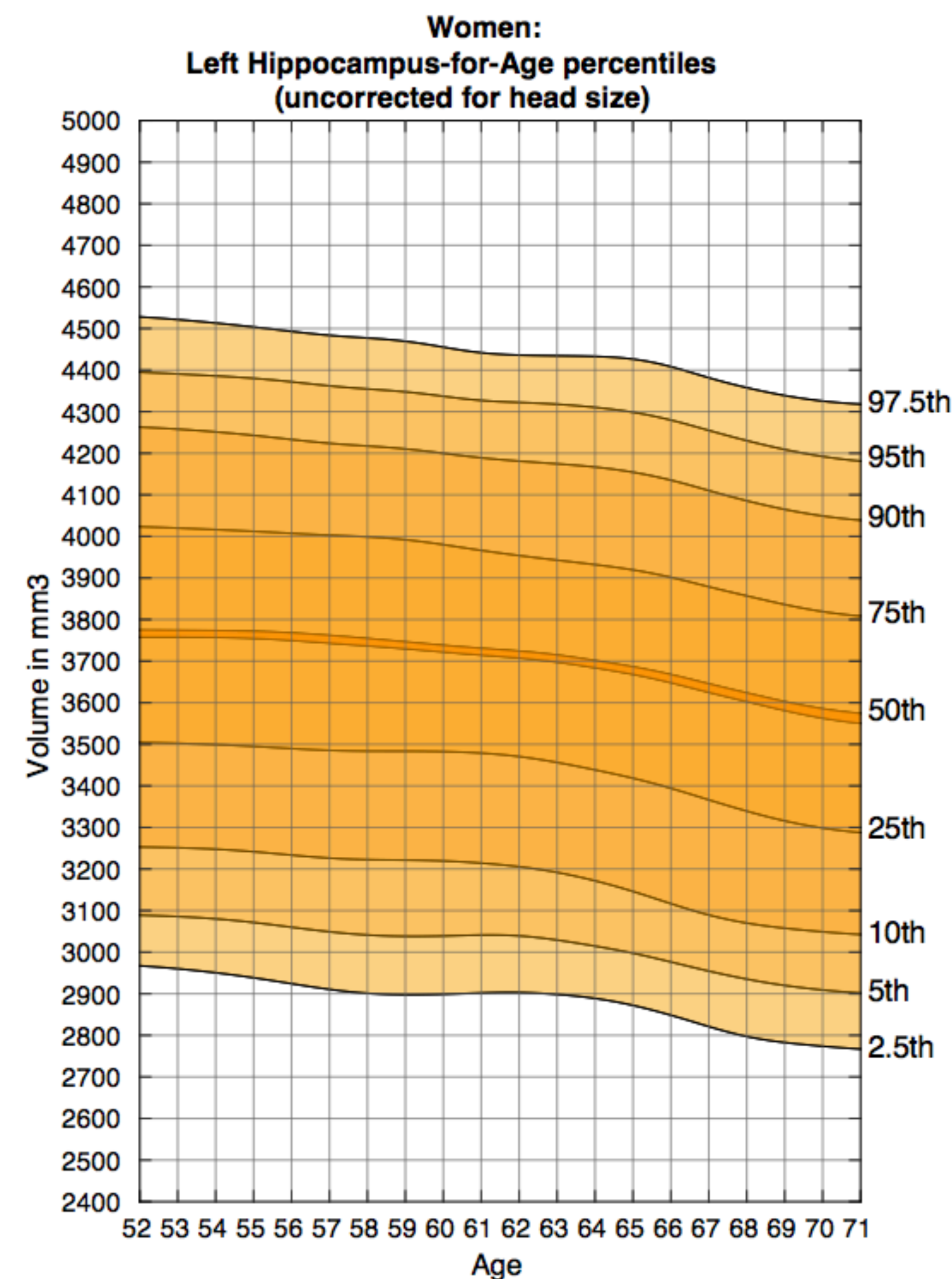
FSL tools in the pipeline

Nomograms with normative percentiles of subcortical volumes derived from over 19,700 people in UK Biobank

FSL Tool	Number of IDPs
FIRST	29
SIENAX	11
FLIRT + FNIRT + FAST + VBM	139
Bianca	3
FEAT	16
dtifit + eddy + TBSS	432
dtifit + eddy + Tractography	243
FIX + Melodic + FSLNets	3472



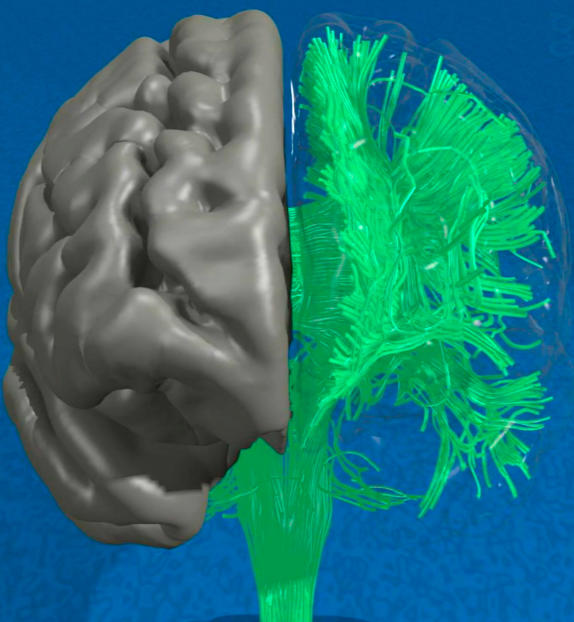
Cool clinical papers!



(Nobis et al, NeuroImage: Clinical, 2019)

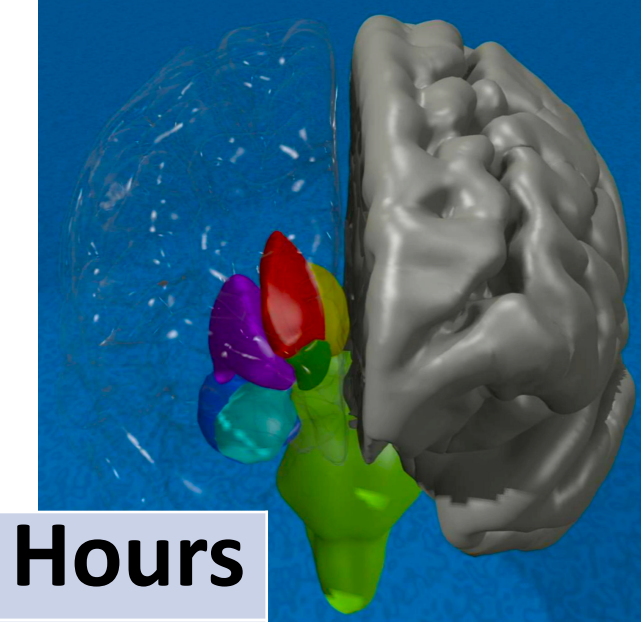


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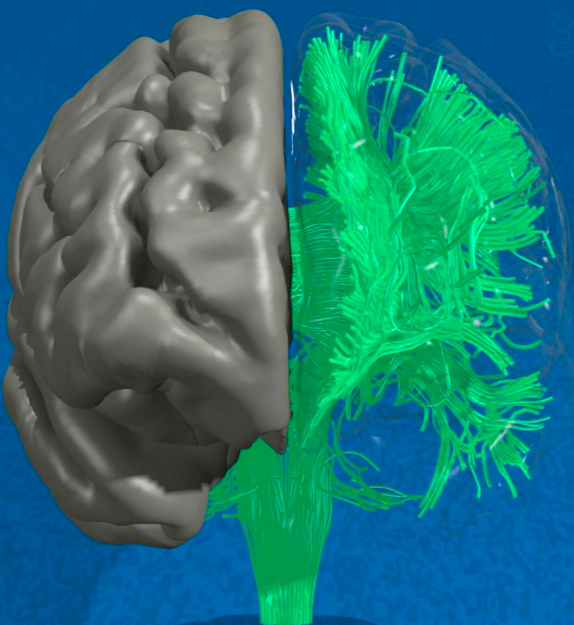
Big Data Needs for the pipeline

- ~6 GB per subject = ~1 PB total data
- ~21 CPU hours and 1 GPU hours per subject. Some of the tasks may run in parallel, reducing it to ~12 CPU hours.
- With no GPUs, ~60 CPU hours per subject
- Imaging researchers may run their own analyses in the cloud
- Easy to run on DNA Nexus - RAP
- Repo: https://git.fmrib.ox.ac.uk/falmagro/uk_biobank_pipeline_v_1.5
- Docker: <https://git.fmrib.ox.ac.uk/paulmc/fbp-dockerfile>
- More resources: <https://www.fmrib.ox.ac.uk/ukbiobank/>
- For any question: fidel.alfaroalmagro@ndcn.ox.ac.uk

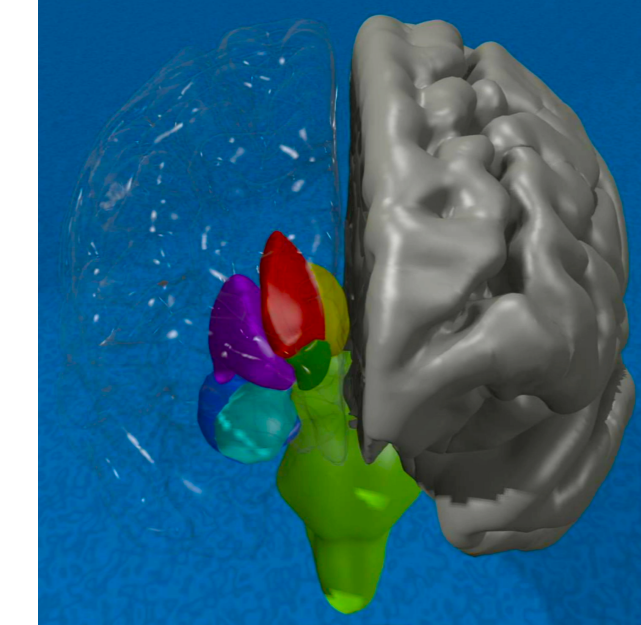


CPU Job	Hours
T1 + T2 FLAIR proc	2.5
swMRI proc	0.2
QSM	0.4
ASL	0.6
Topup	0.3
dMRI proc	0.2
TBSS	0.5
NODDI	0.2
Melodic	2.1
FIX	0.5
Feat	1
FreeSurfer	12
IDP Generation	0.15
Total CPU Hours	20.65

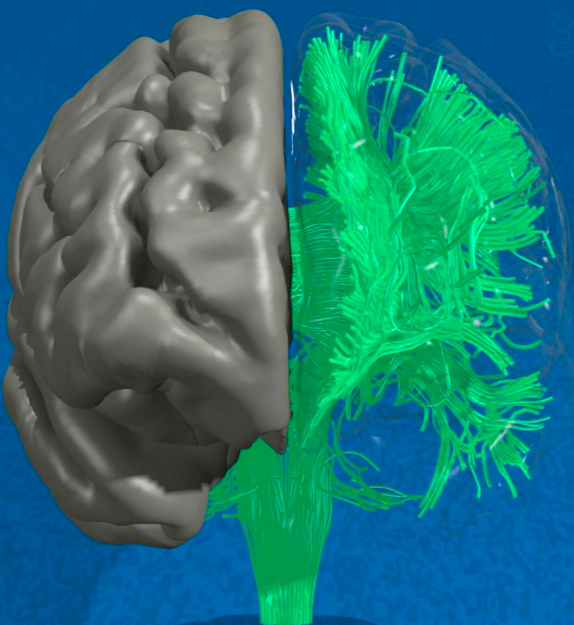
GPU Job	Mins
EDDY	18
bedpostx	9
autoPtx	29
Total GPU Hours	~1



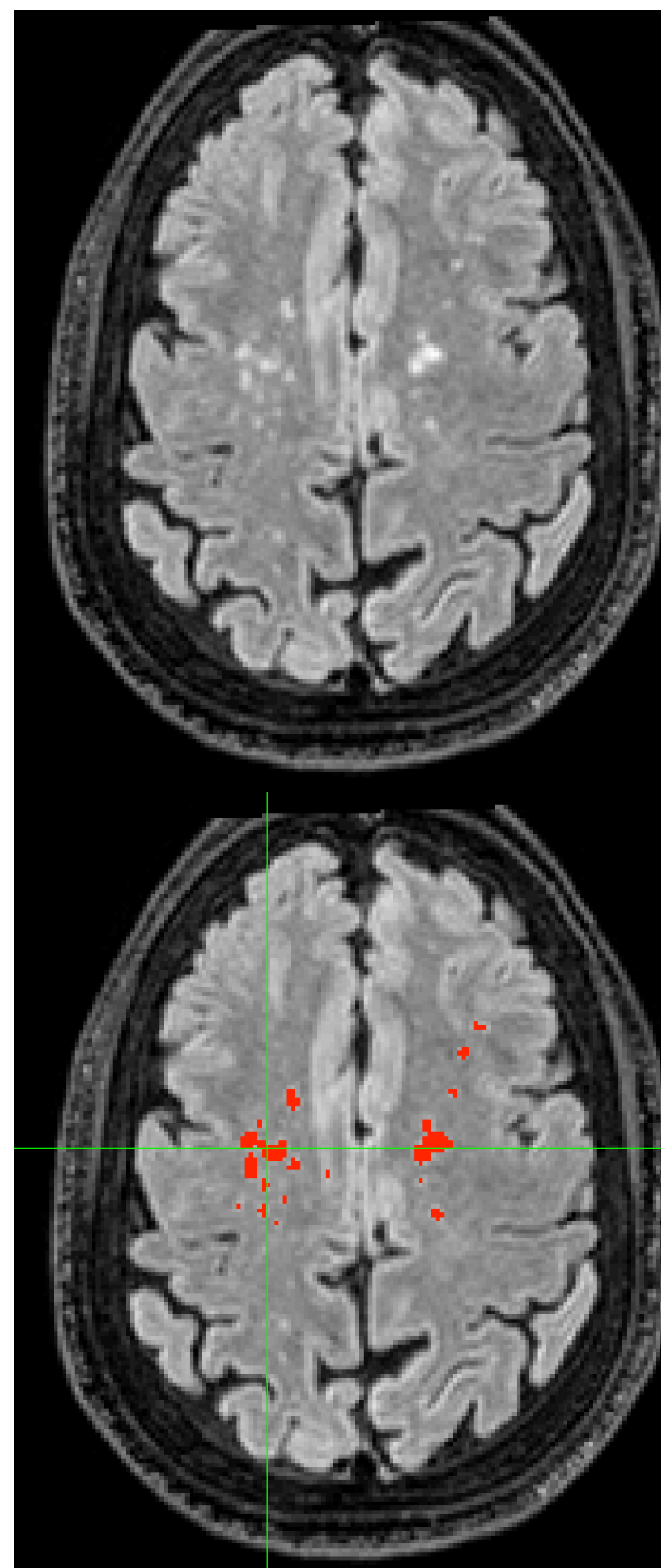
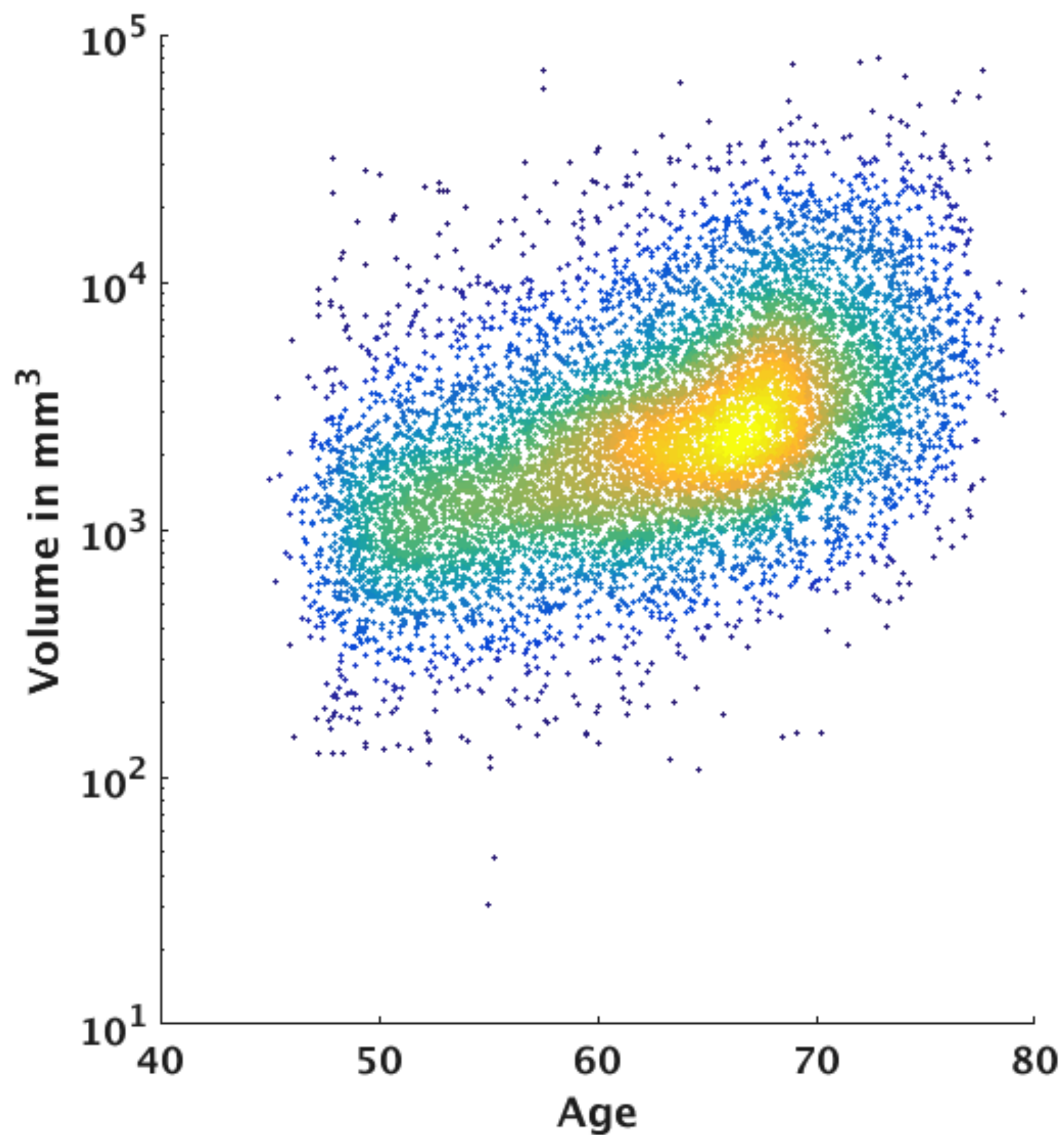
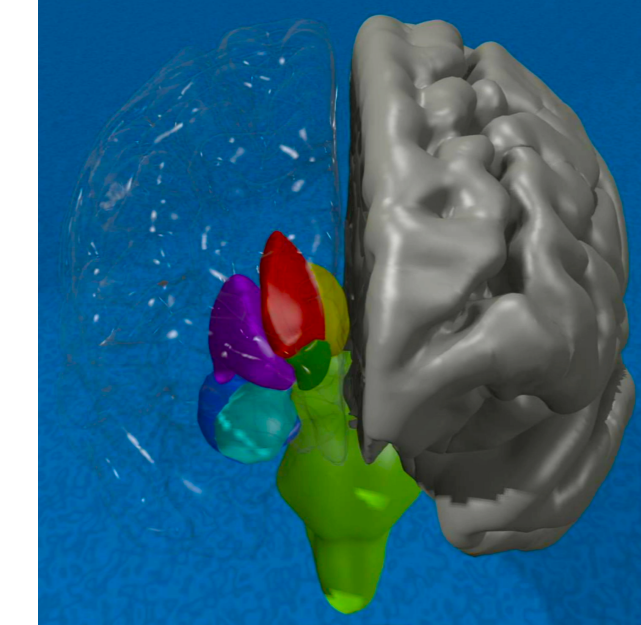
biobank^{uk}



1. Background
2. Brain Imaging Project
3. **Brain Imaging: What can we do?**

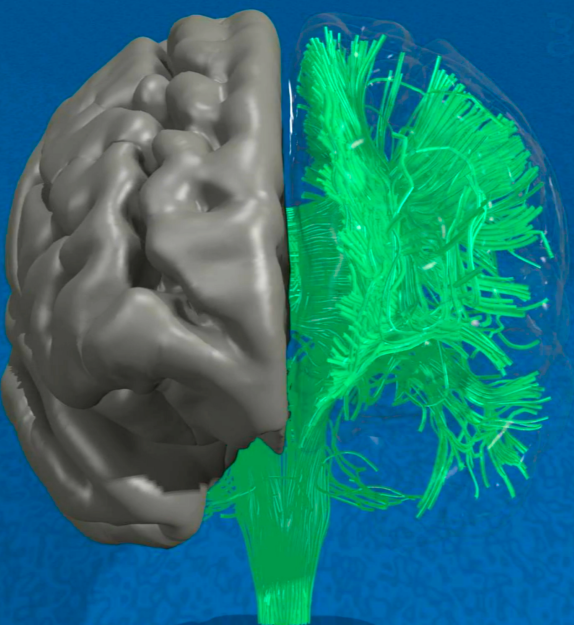


T2 FLAIR lesions: Correlation with age



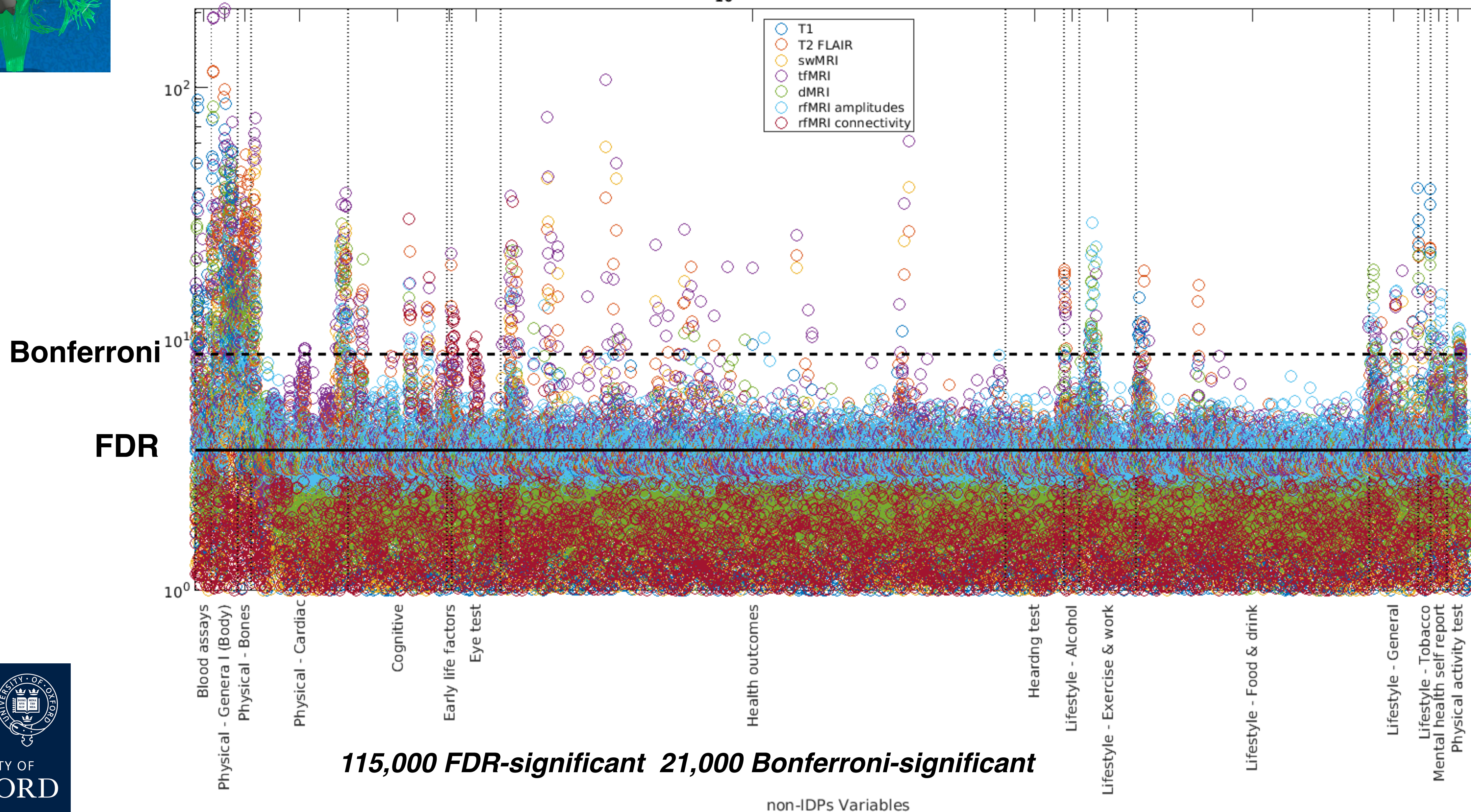
BIANCA

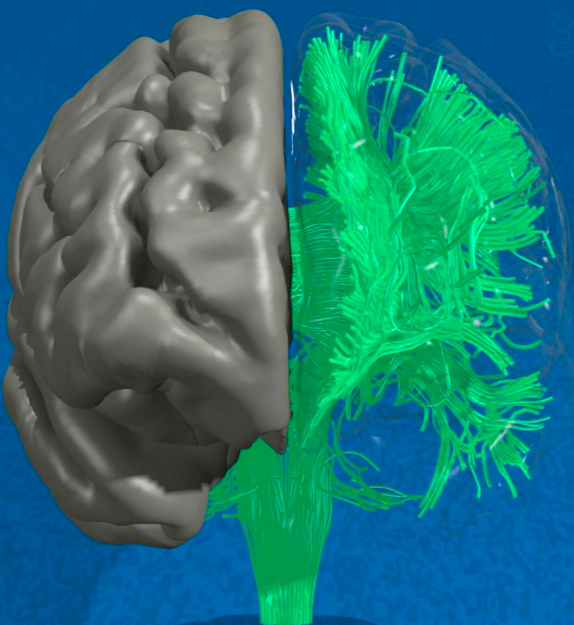
(Griffanti et al, NeuroImage 2018)



23.5 million univariate associations 2,641 IDPs x 8,907 non-IDPs (21,400 subjects)

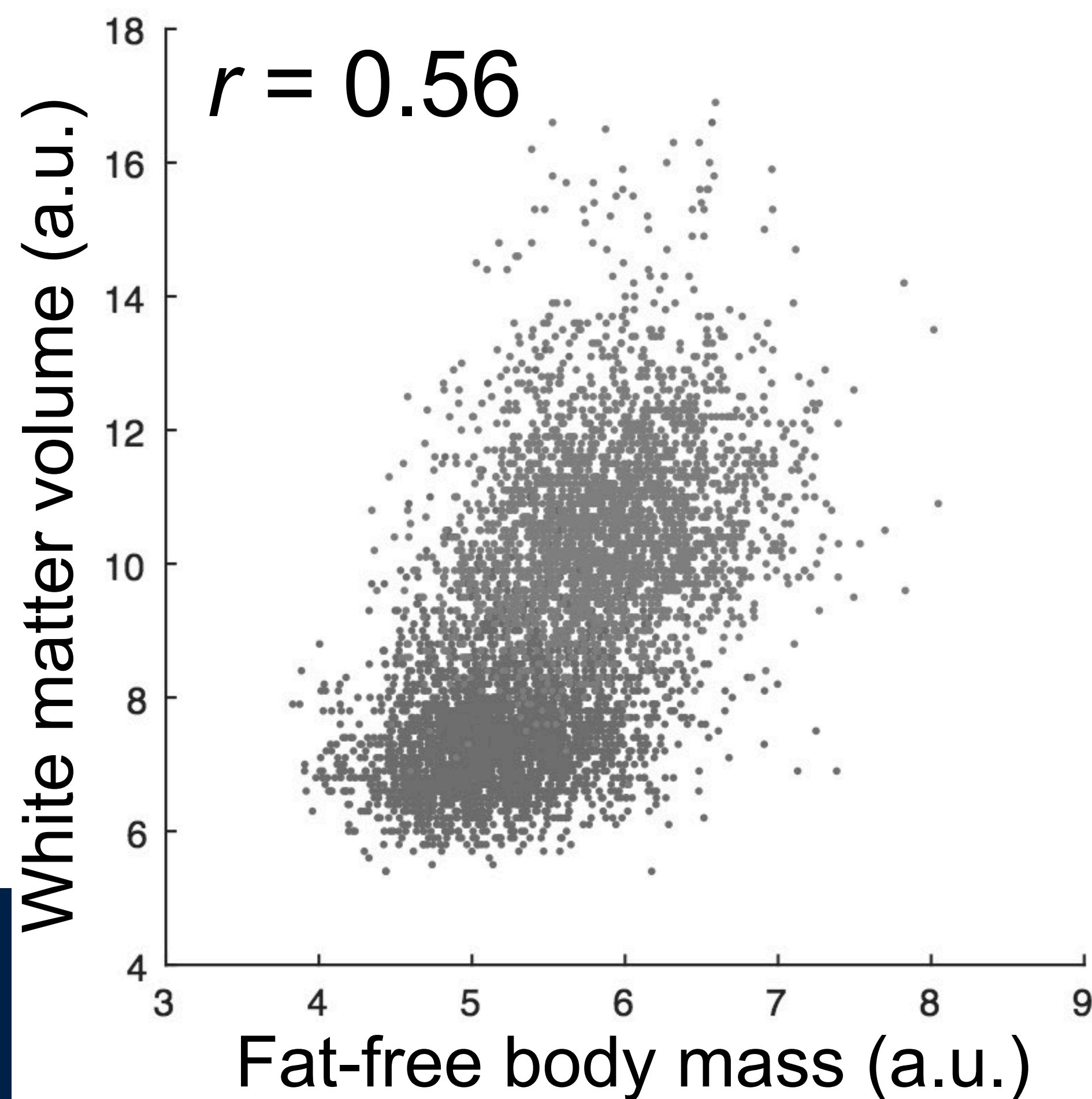
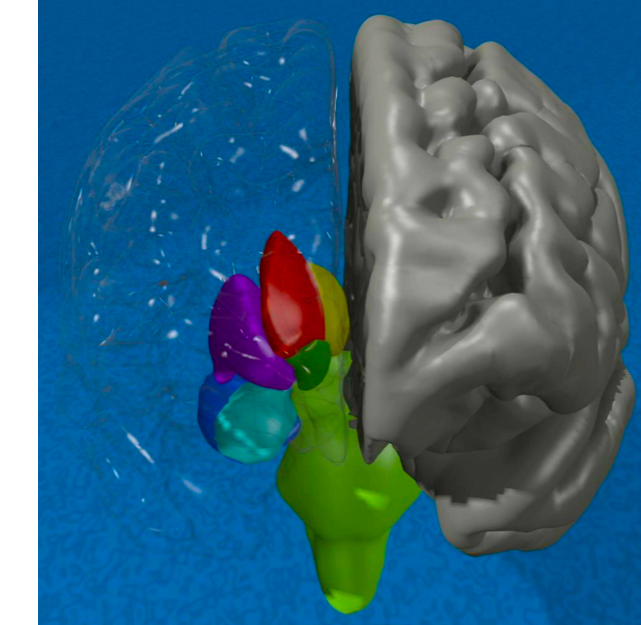
$-\log_{10}(\text{P values})$ full unconfounding

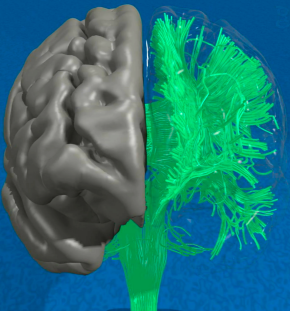




Danger of ignoring confounds

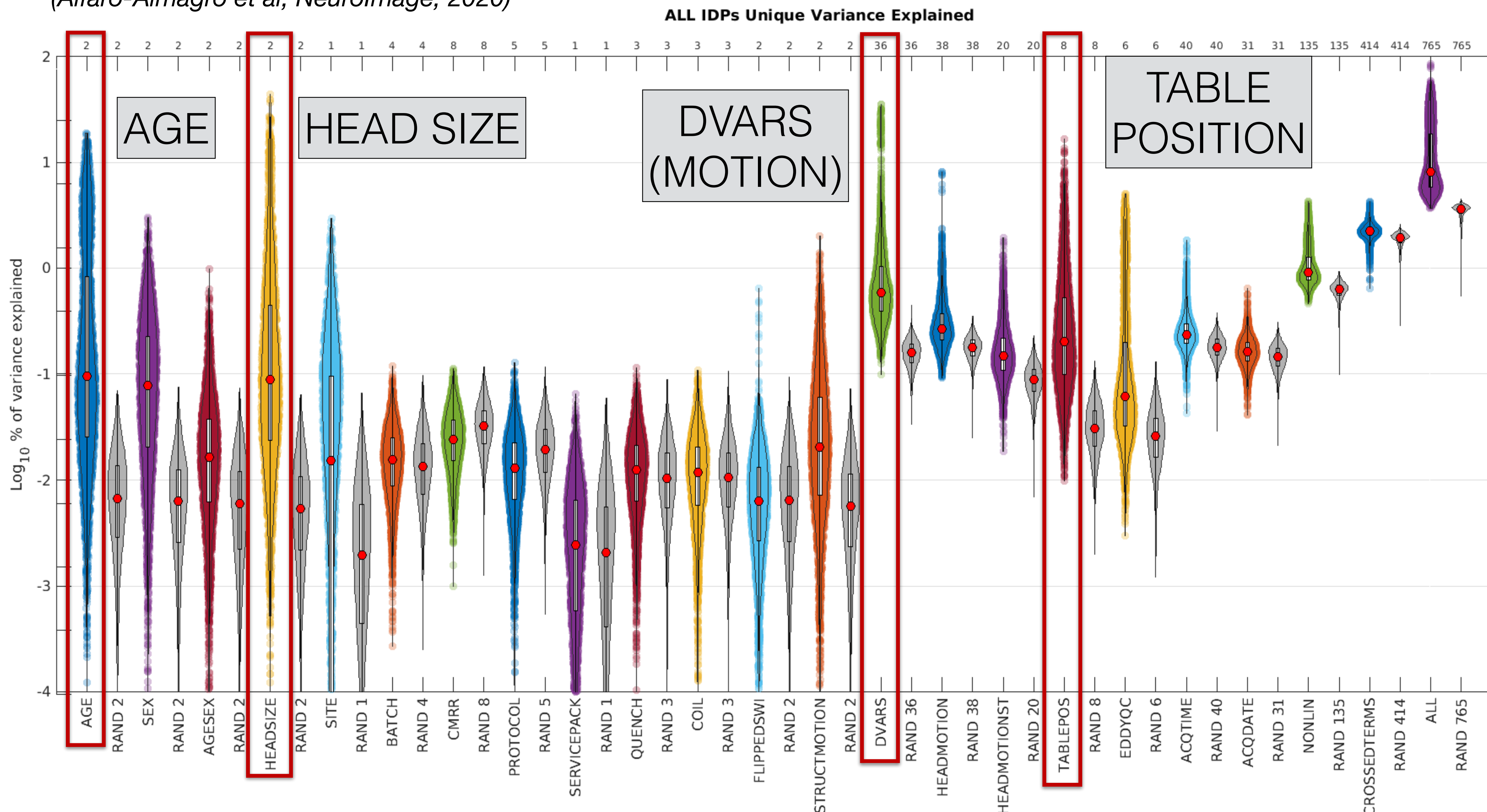
- Simple associations affected dramatically by shared confounds
- Including inappropriate pooling across groups

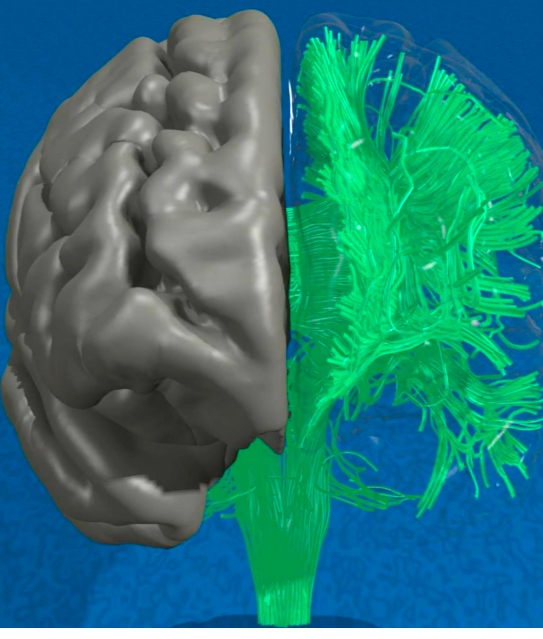




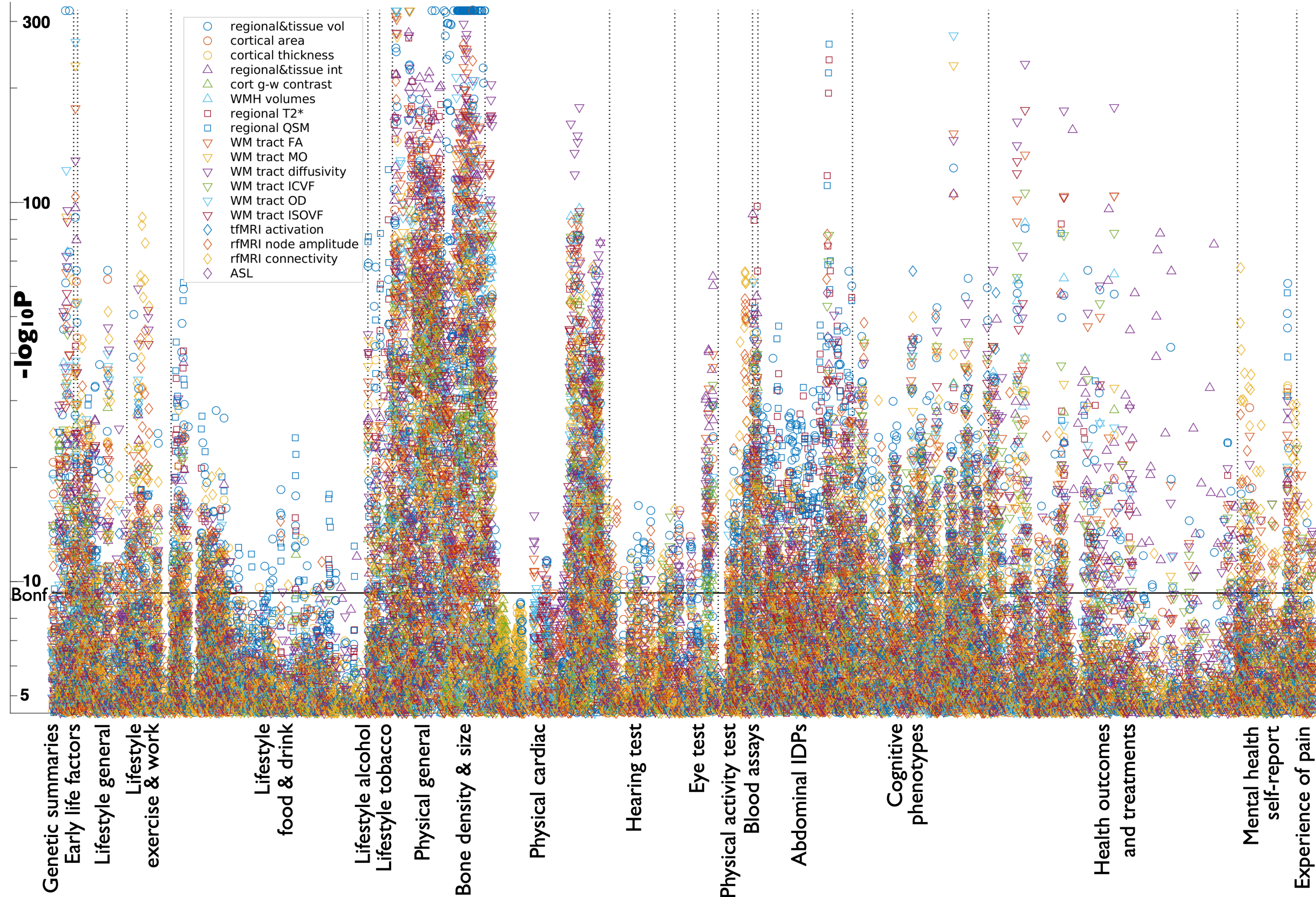
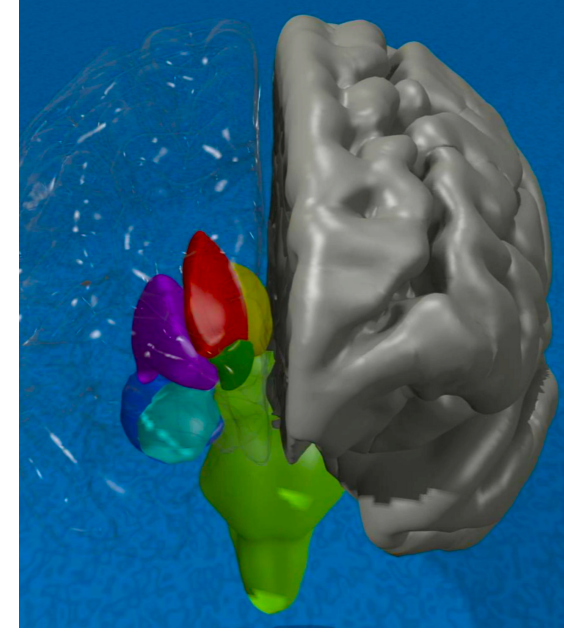
Confounds in imaging

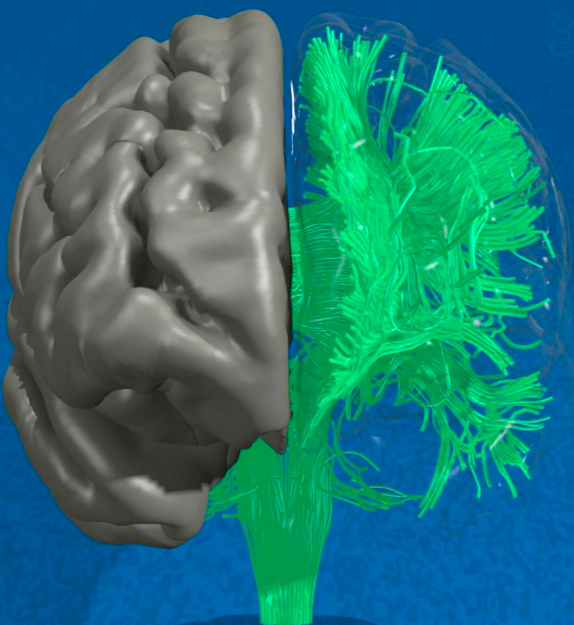
(Alfaro-Almagro et al, NeuroImage, 2020)



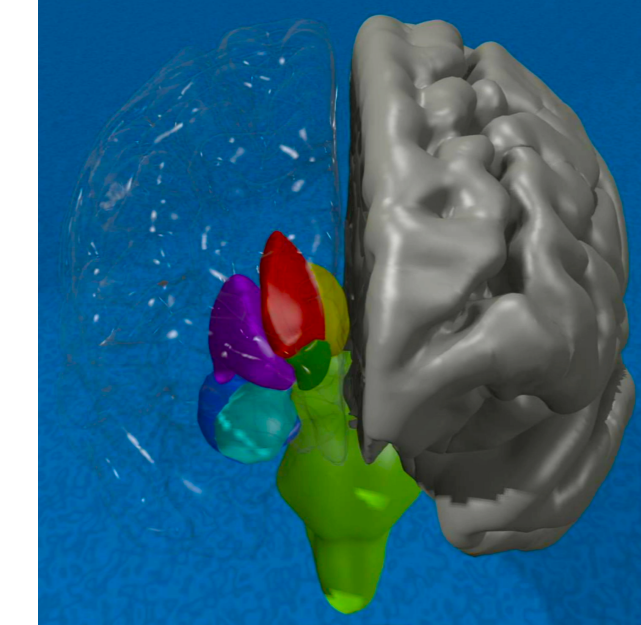


63k UKB subjects: 108m pairwise associations IDPs-vs-nIDPs, 1.2m FDR-significant, 210k Bonferroni-significant



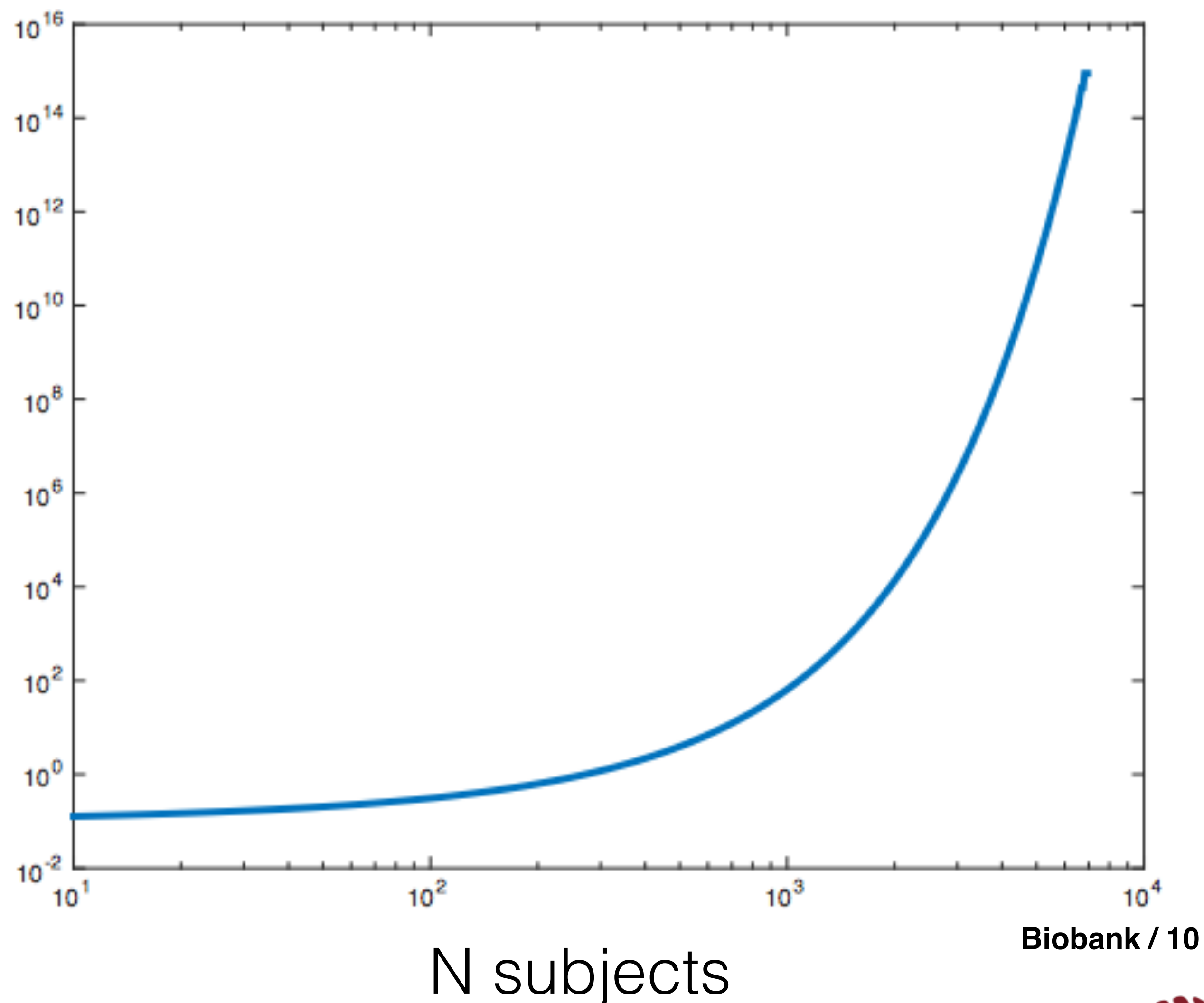


stats of Big Data



Number of different tests
passing Bonferroni
with very low correlation
given $r=0.1$

Probably better if we start
reporting more size effects
and power in correlations?



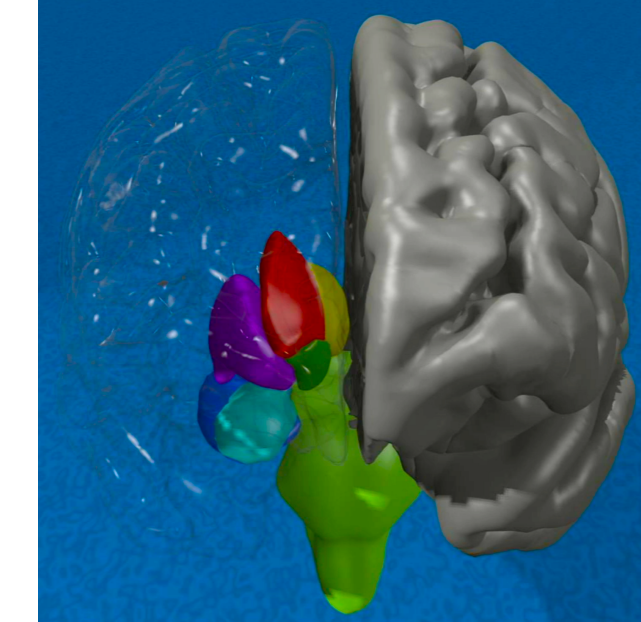
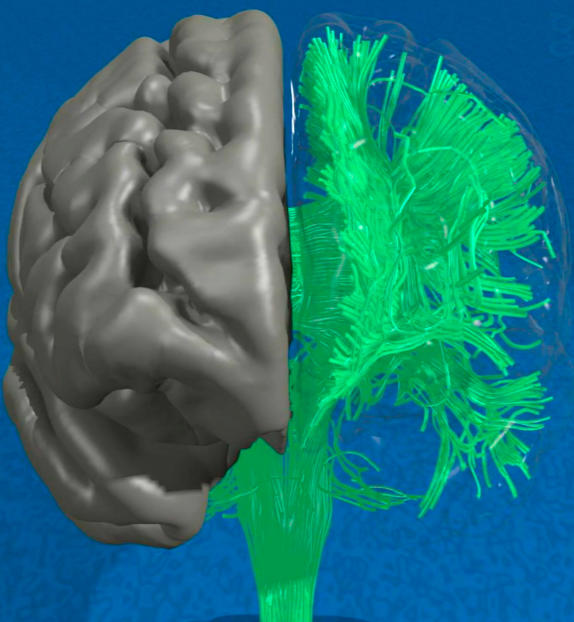
(Steve Smith & Tom Nichols, Neuron, 2018)



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wellcome
centre
integrative
neuroimaging



THANK YOU

Brain Imaging Contributors

Scientific direction Stephen Smith, Karla Miller (FMRIB, Oxford)

Processing pipeline Fidel Alfaro-Almagro (FMRIB, Oxford)

Additional input on acquisitions/protocols/reconstruction/processing Neal Bangerter (Brigham Young), Kamil Ugurbil, Essa Yacoub, Steen Moeller, Eddie Auerbach (CMRR, U Minnesota), Junqian Gordon Xu (Mount Sinai), David Thomas, Daniel Alexander, Gary Zhang, Enrico Kaden (UCL), Alessandro Daducci (EPFL), Tony Stoecker (Rhineland Study/Bonn), Stuart Clare, Heidi Johansen-Berg (FMRIB, Oxford), Deanna Barch, Greg Burgess, Nick Bloom, Dan Nolan, Michael Harms, Matt Glasser (Washington U), Doug Greve, Bruce Fischl, Jonathan Polimeni (MGH), Andreas Bartsch (Heidelberg), Anna Murphy (Manchester), Fred Barkhof (VU Amsterdam/UCL), Christian Beckmann (Donders Nijmegen), Chris Rorden (U South Carolina), Peter Weale, Iulius Dragonu (Siemens UK), Steve Garratt (Project Manager, UK Biobank Imaging)

Additional input on image processing pipeline Mark Jenkinson, Jesper Andersson, Stamatios Sotiropoulos, Saad Jbabdi, Ludovica Griffanti, Gwenaëlle Douaud, Eugene Duff, Moises Hernandez Fernandez, Emmanuel Vallee, Gholamreza Salimi-Khorshidi (FMRIB, Oxford)

IT/informatics Duncan Mortimer, David Flitney, Matthew Webster, Paul McCarthy (FMRIB, Oxford), Alan Young, Jonathan Price, John Miller (CTSUS, Oxford)

UK Biobank Imaging Working Group Chair: Paul Matthews (Imperial), Jimmy Bell (Westminster), Andrew Blamire (Newcastle), Rory Collins (Oxford/UK Biobank), Steve Garratt (UK Biobank), Tony Goldstone (Imperial), Nicholas Harvey (Southampton), Paul Leeson (Oxford), Karla Miller (Oxford), Stefan Neubauer (Oxford), Tim Peakman (UK Biobank), Steffen Petersen (Queen Mary College), Stephen Smith (Oxford), Cathie Sudlow (Edinburgh/UK Biobank)

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