UNIVERSITY OF OXFORD

FMRIB
Oxford Centre for Functional MRI of the Brain

Progress and Challenges in Large-Scale and Translational Neuroimaging Projects

Eugene Duff, FMRIB Analysis Group
University of Oxford

Overview

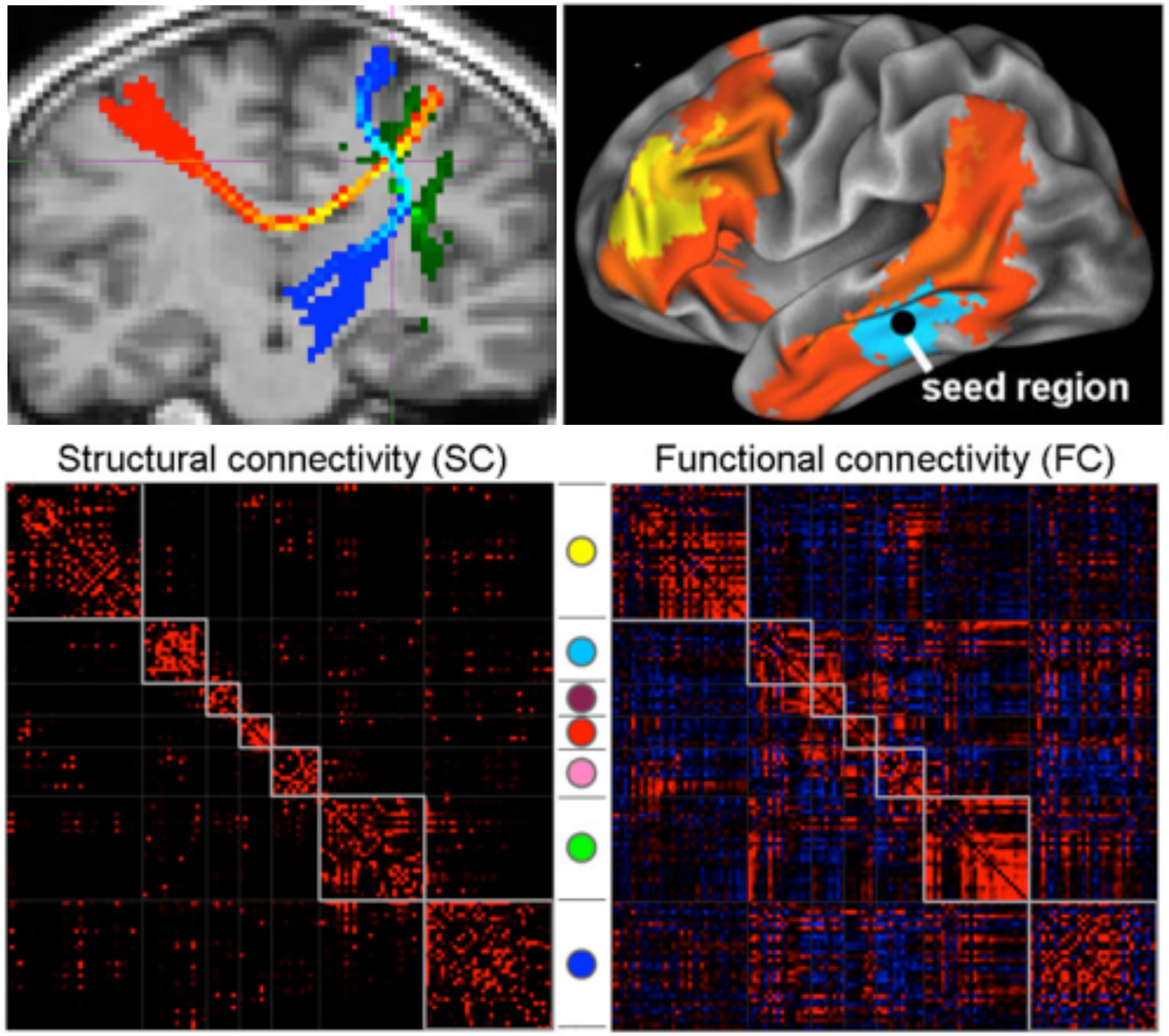
Review of the large-scale studies we are working on at FMRIB

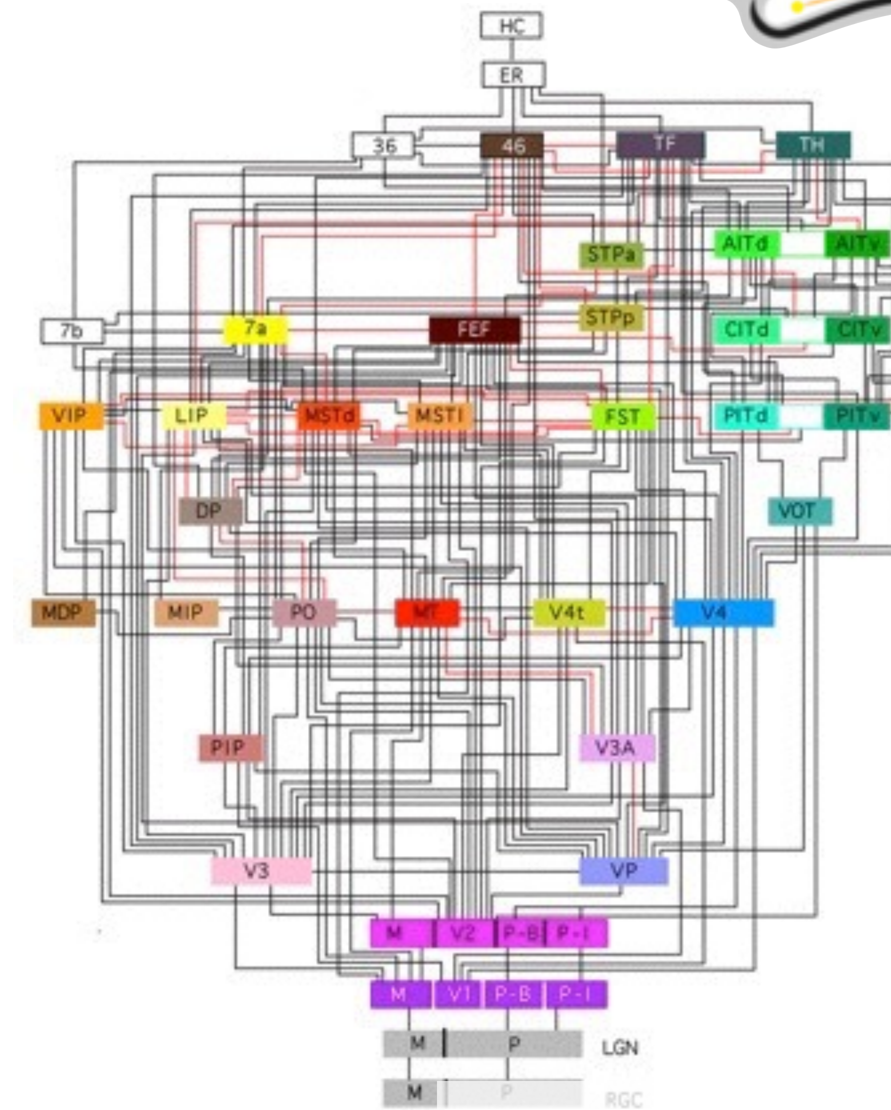
- Human Connectome Project
- Developing Human Connectome Project
- UK Biobank Imaging extension
- Multi-study identification of pharmacological biomarkers

Themes

- Pipeline development and applications
- Multi-modal analysis methods
- Automated QA
- Sparse methods
- Meta-analysis and multi-study inference

Human Connectome Project



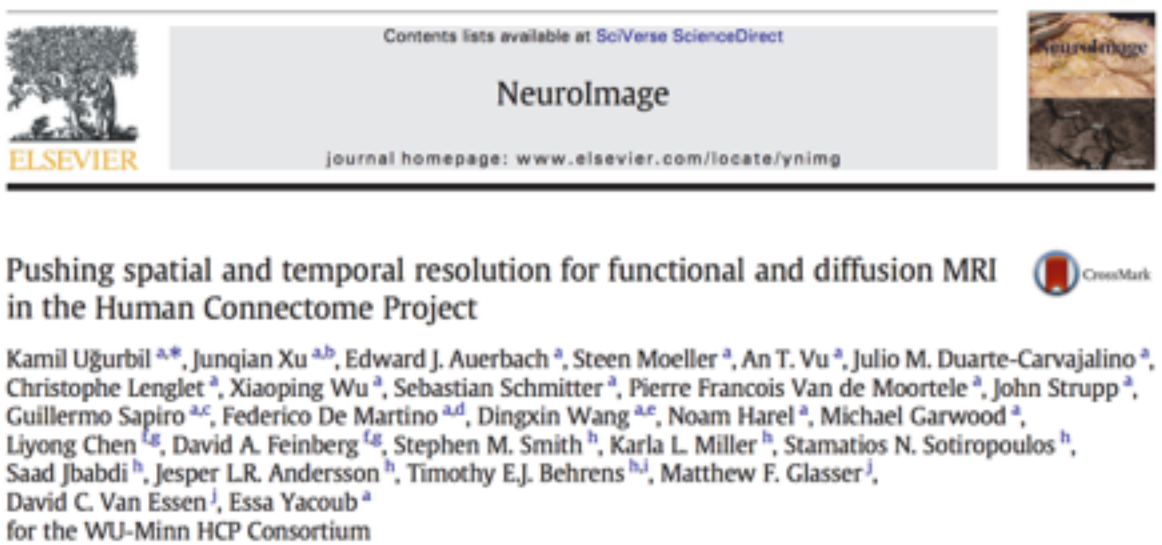


Felleman & Van Essen, 1991

- $30m project: the best *in vivo human macro-connectome mapping*
- Main groups: WashU (Van Essen), UMinn (Ugurbil) & FMRIB
- Diffusion-MRI↔Resting-FMRI↔behavioural measures↔genetics
- 1200 subjects
- Data and network models freely available

Human Connectome Project

Acquisition



Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

ELSEVIER

Pushing spatial and temporal resolution for functional and diffusion MRI in the Human Connectome Project

Kamil Uğurbil [a,*], Junqian Xu [a,b], Edward J. Auerbach [a], Steen Moeller [a], An T. Vu [a], Julio M. Duarte-Carvajalino [a], Christophe Lenglet [a], Xiaoping Wu [a], Sebastian Schmitter [a], Pierre Francois Van de Moortele [a], John Strupp [a], Guillermo Sapiro [a,c], Federico De Martino [a,d], Dingxin Wang [a,e], Noam Harel [a], Michael Garwood [a], Liyong Chen [f,g], David A. Feinberg [f,g], Stephen M. Smith [h], Karla L. Miller [h], Stamatios N. Sotiropoulos [h], Saad Jbabdi [h], Jesper L.R. Andersson [h], Timothy E.J. Behrens [h,i], Matthew F. Glasser [j], David C. Van Essen [j], Essa Yacoub [a]
for the WU-Minn HCP Consortium

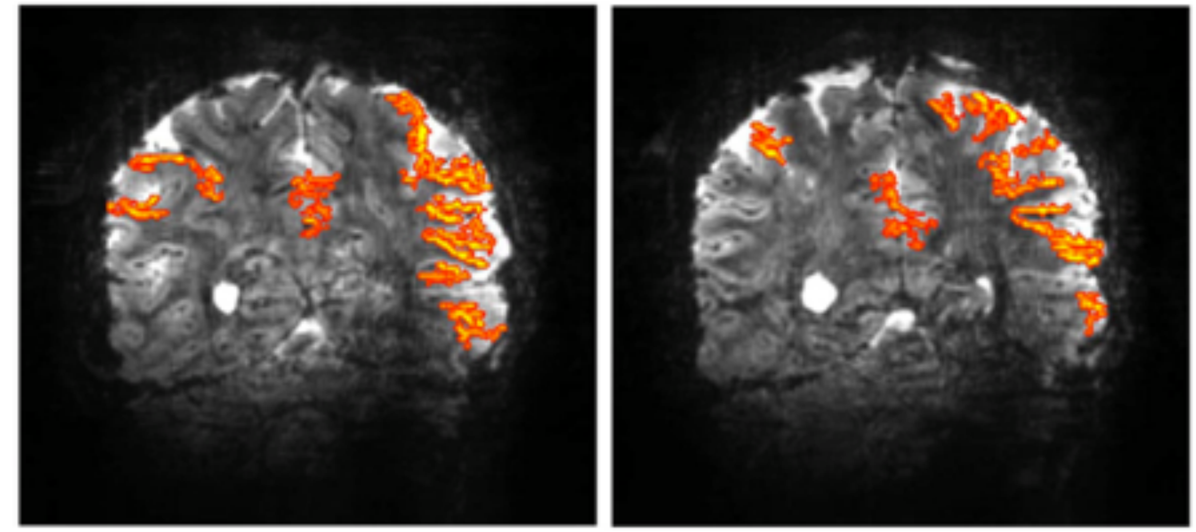
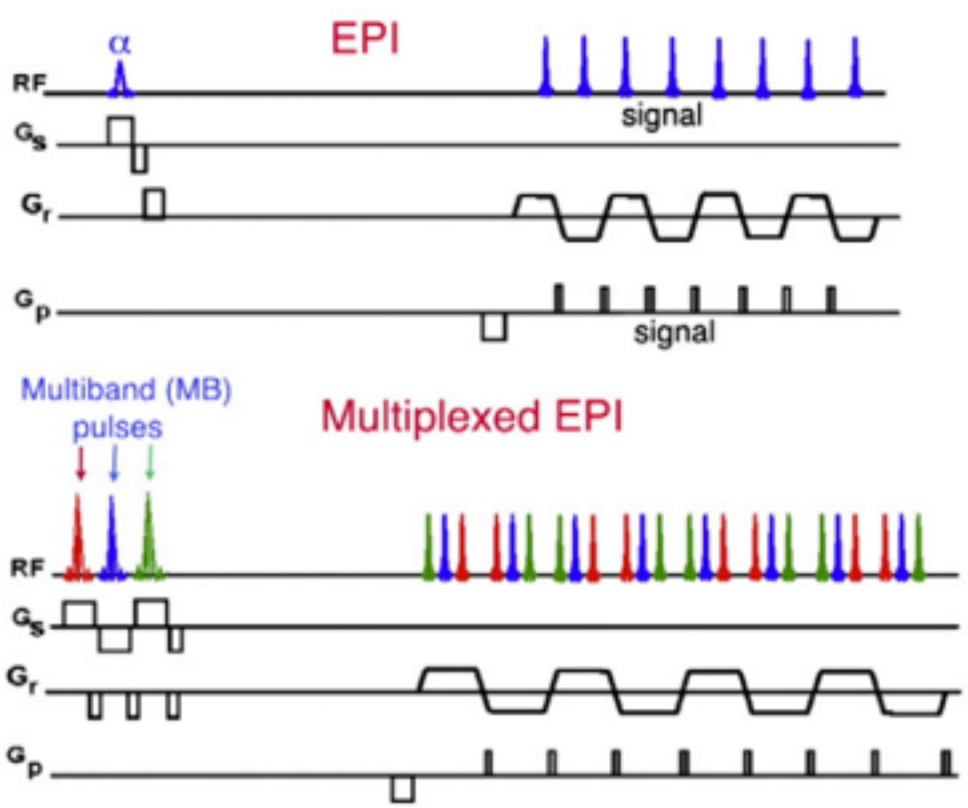
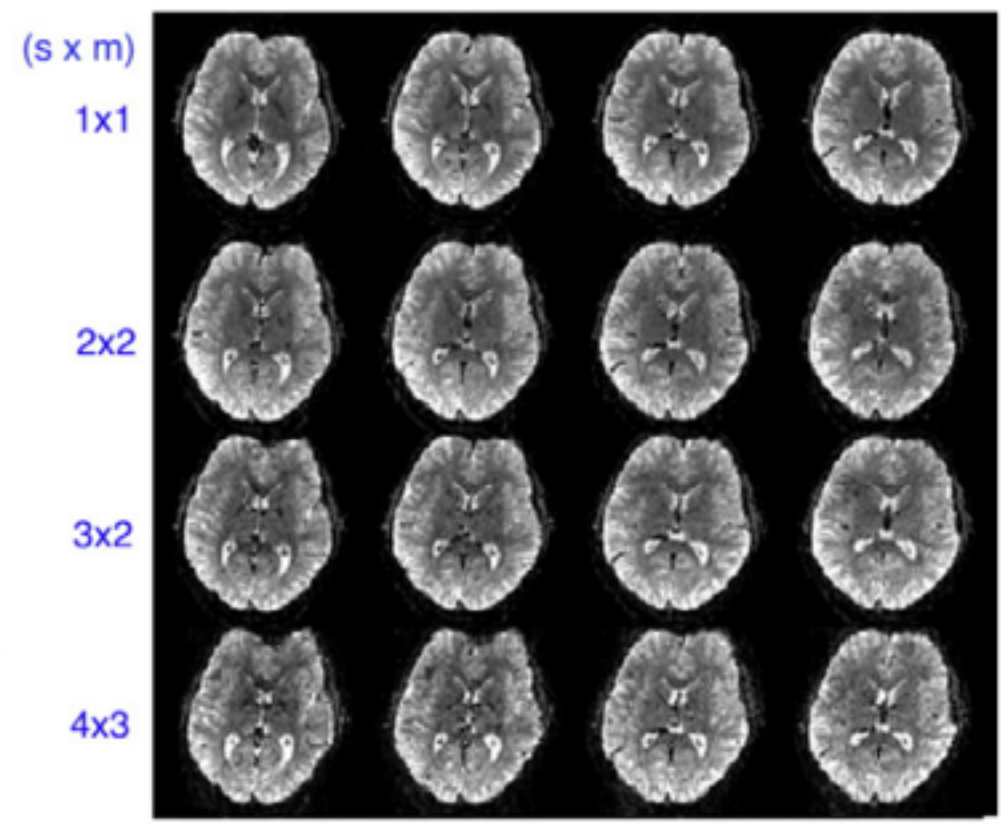


Fig. 3. Functional maps at 7 T obtained with slice and phase-encode acceleration. Two representative coronal slices showing functional activation maps obtained with 16 fold two dimensional acceleration (4 fold slice (i.e. MB = 4) and 4 fold in-plane phase encode accelerations) for a complex visuo-motor dissociation task; 90 slices were acquired in 1.5 s with 1 × 1 mm^2 in plane resolution 2 mm slice thickness. A total of 252 images were obtained with the subjects performing the task during three blocks of on-off periods. Maximal aliasing in these data was 16 fold. Adapted from Moeller et al. (2008, 2010).

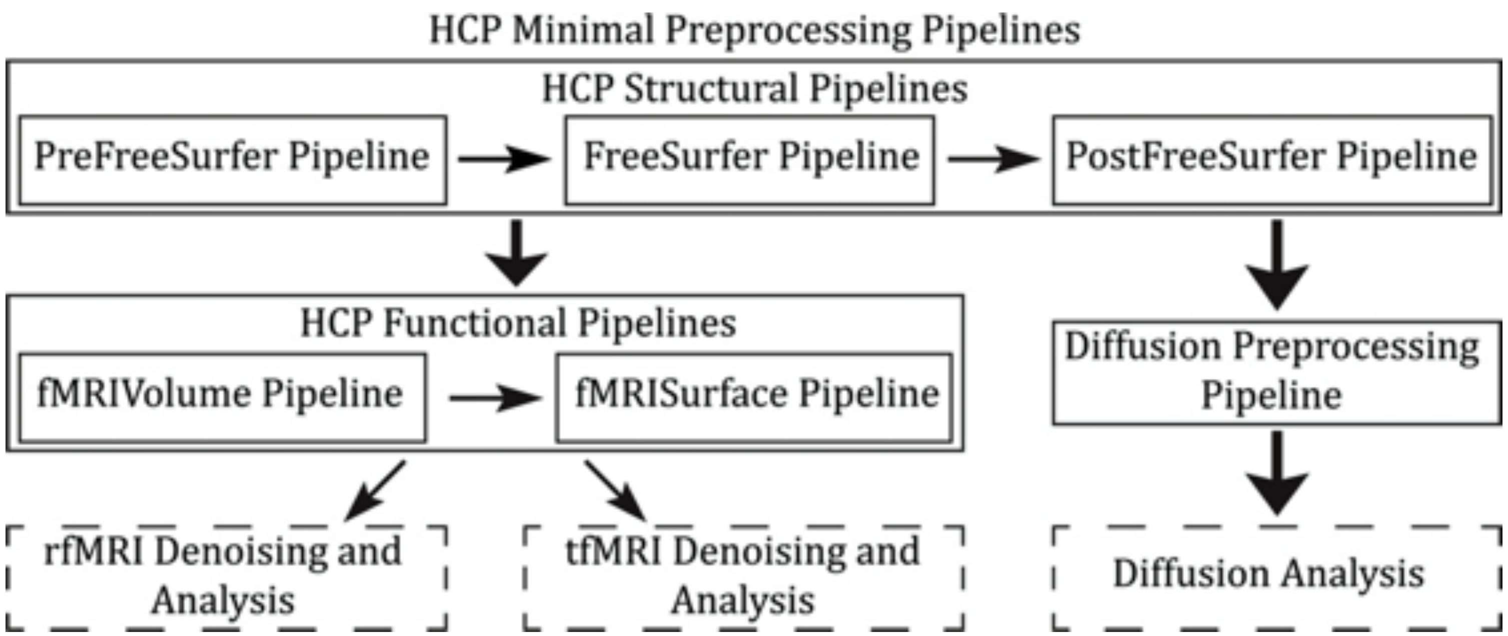


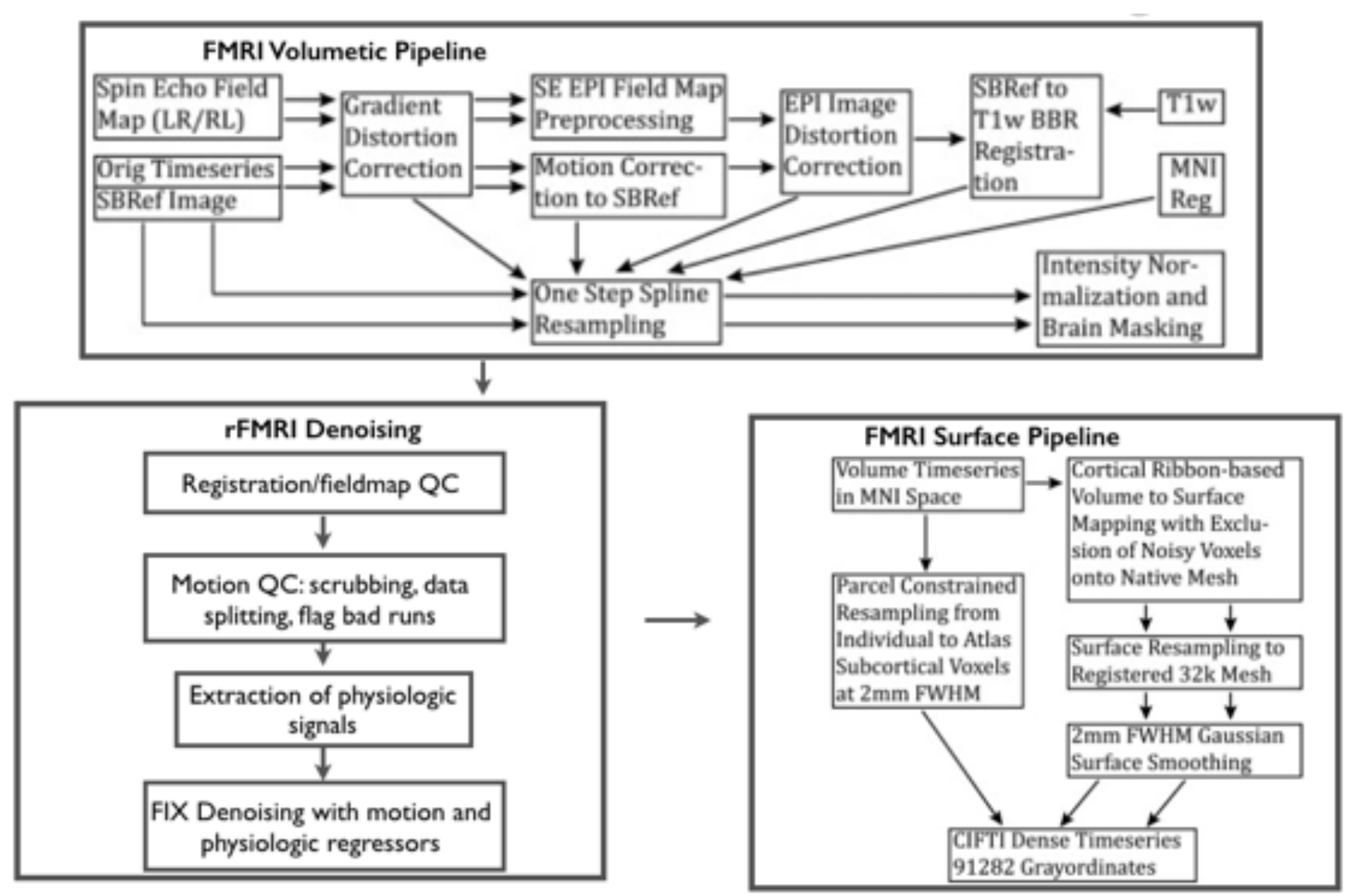


- Parallel Imaging: Multiband Acquisitions

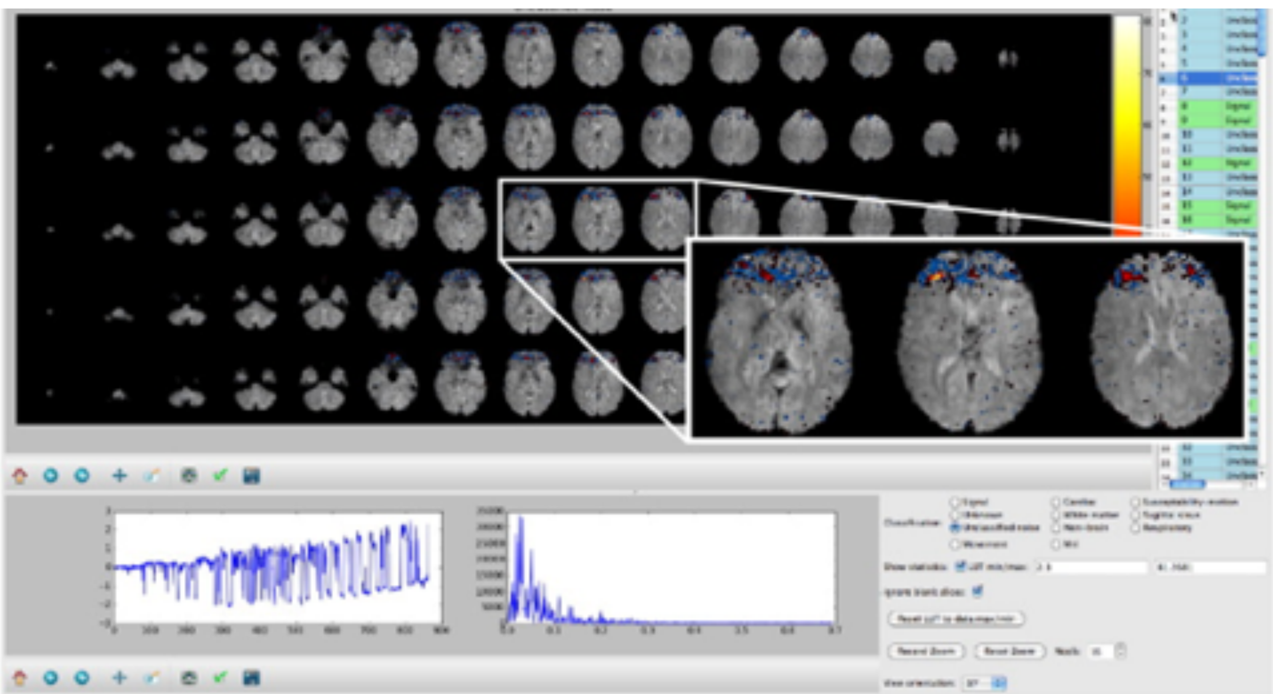
Human Connectome Project

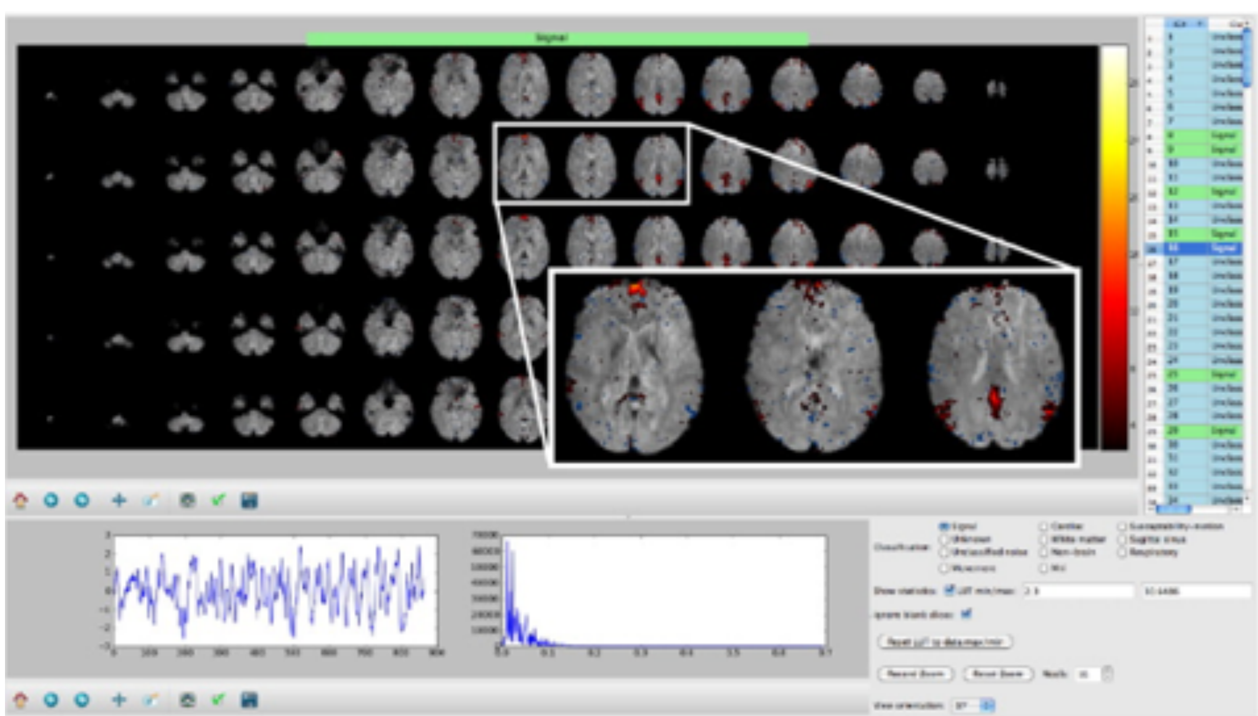
Analysis Pipelines





FSL FIX





Identifies and removes artifactual components from FMRI time series.

– Utilises spatial and temporal signatures identified from large, human generated training dataset (multiband and standard EPI – can train your self)

Workflow:

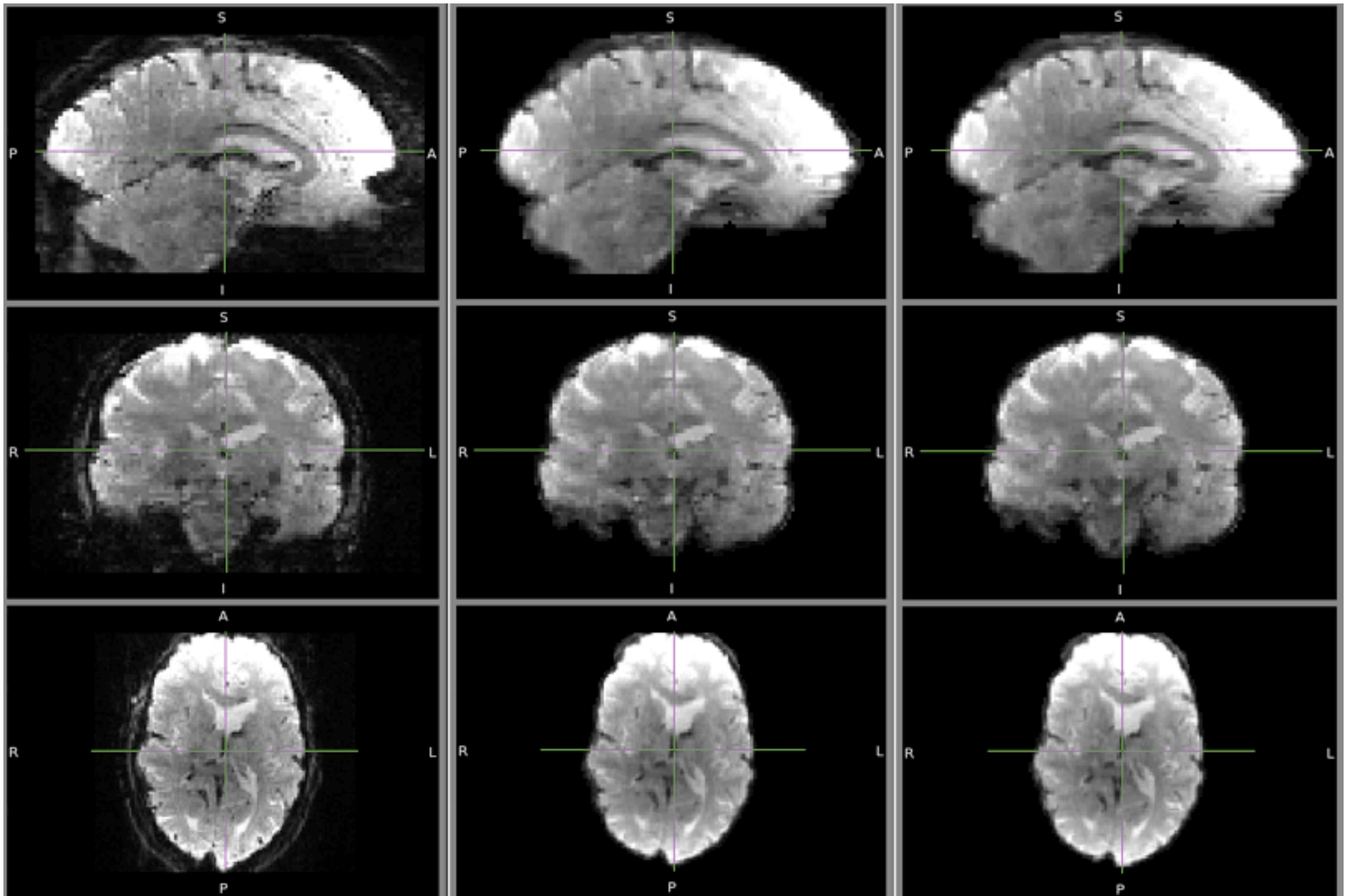
1) preprocess 2) run ICA 3) run FIX 4) run analysis (Feat, Melodic)

– Currently available as download (need MATLAB, R).

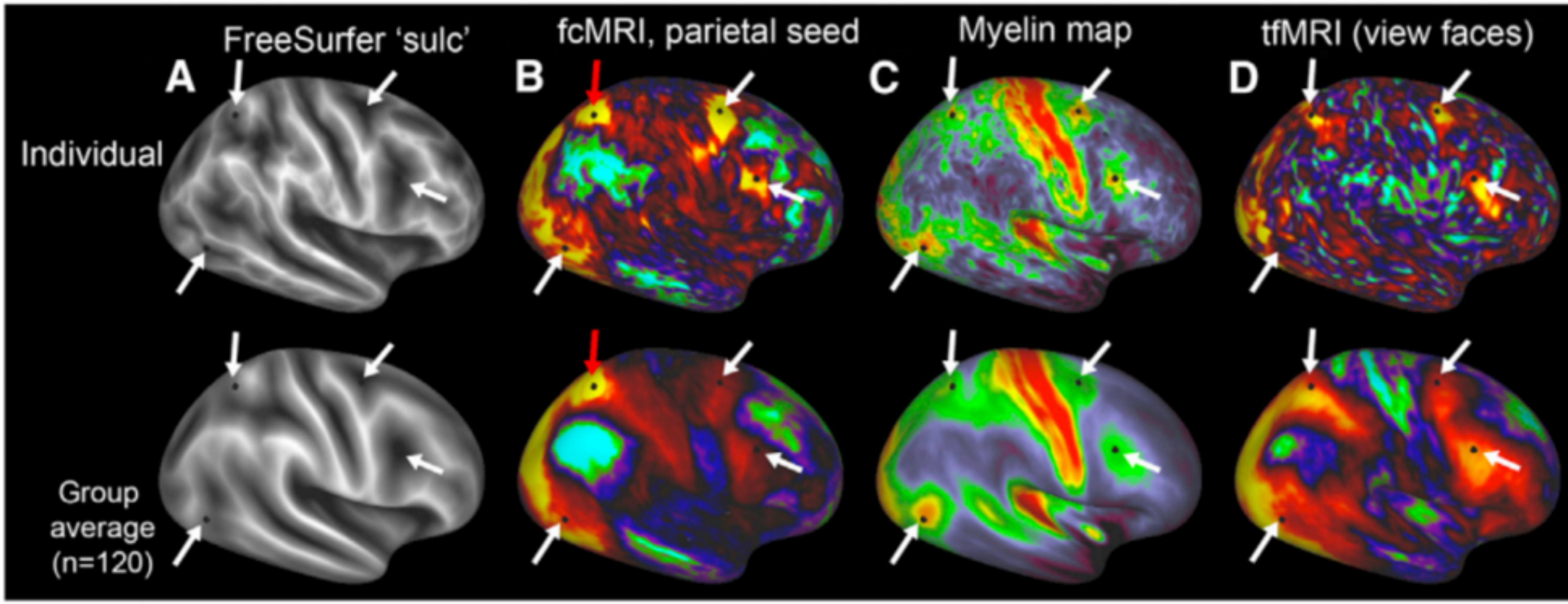
http://fsl.fmrib.ox.ac.uk/fsl/

FSL FIX

raw data (multiband 6) **+ preprocessing** **+ ICA+FIX**



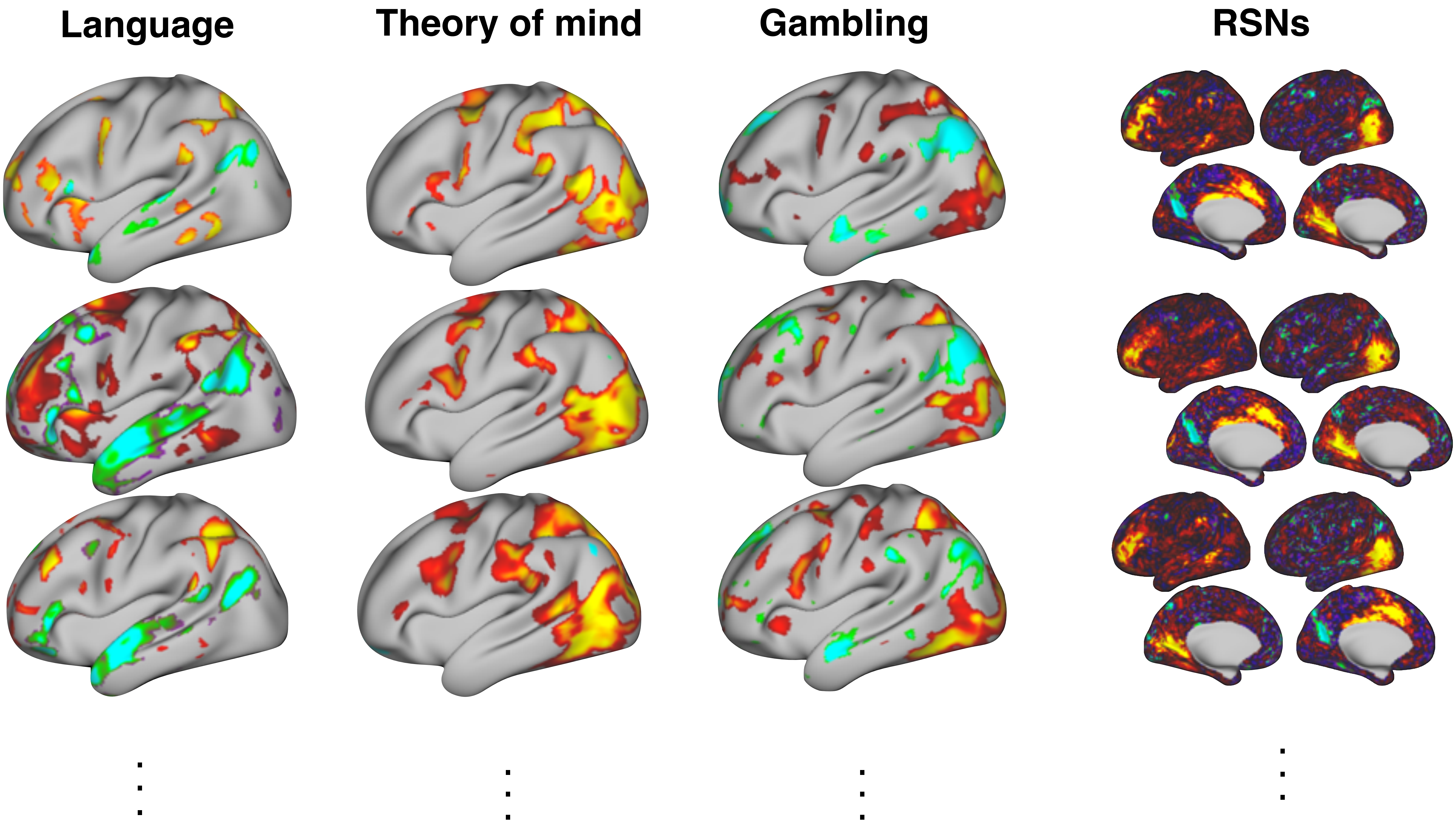
Multimodal parcellation



Glasser, Van Essen et al, under review

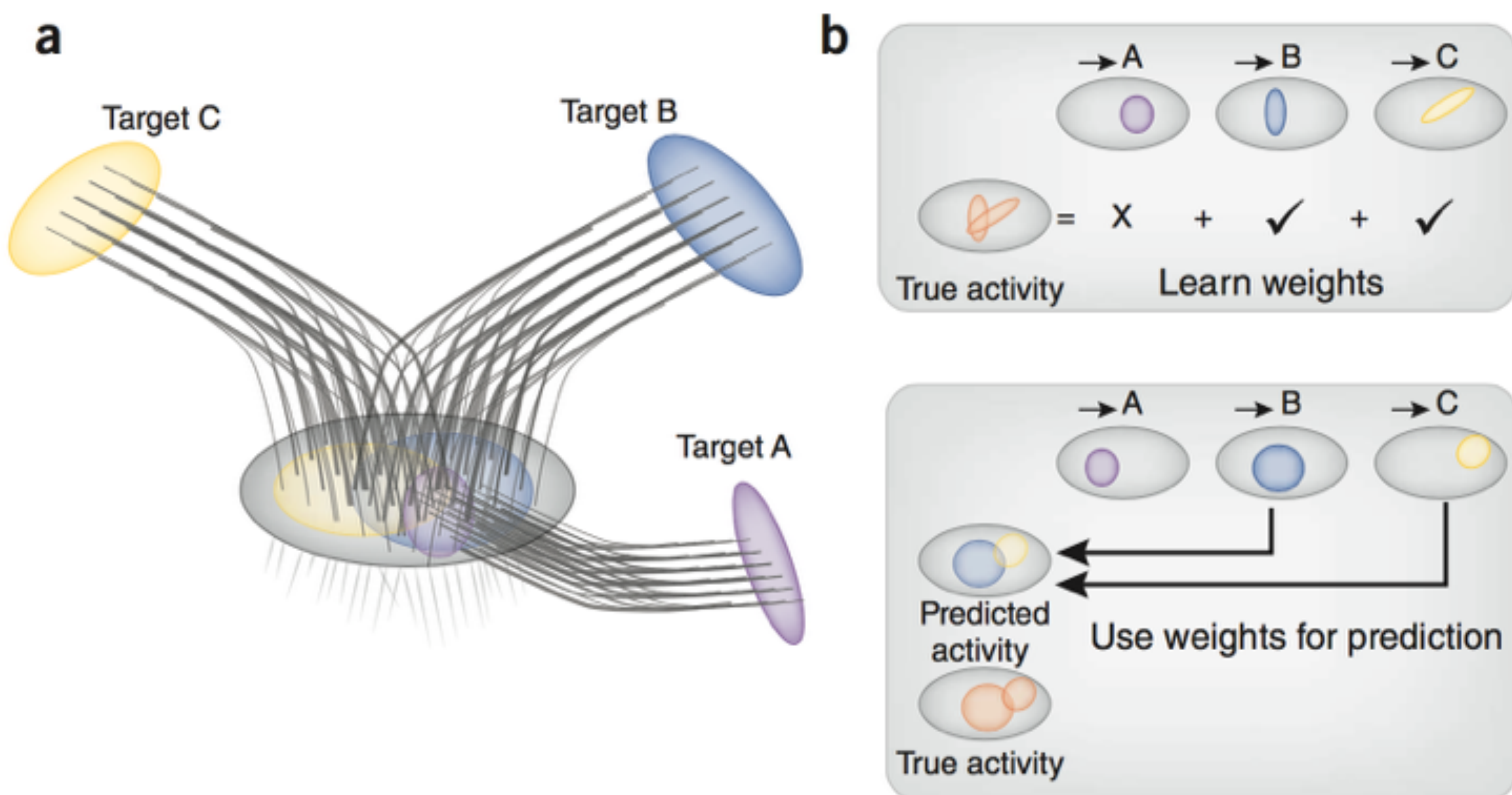
Human Connectome Project

Individual differences



Human Connectome Project

Using connectivity as a signature of functional areas



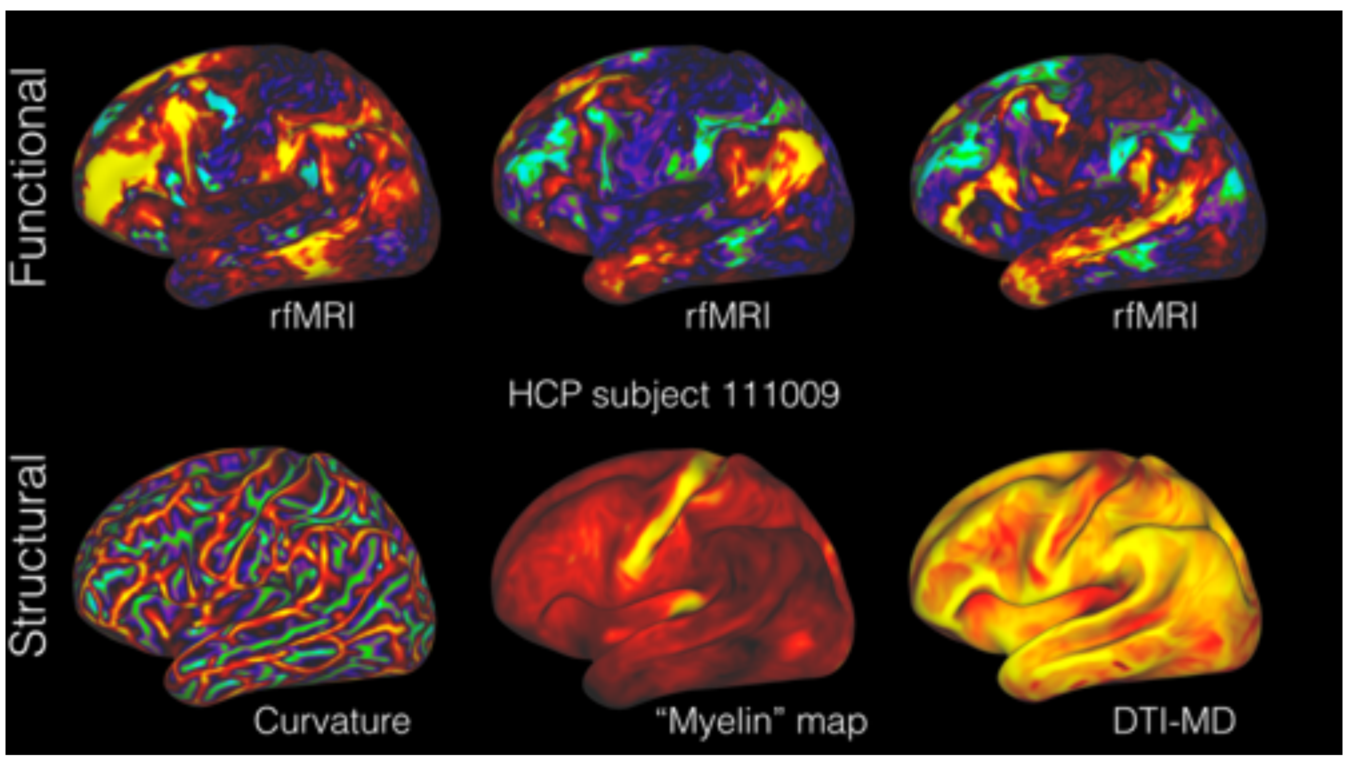
Train

Test

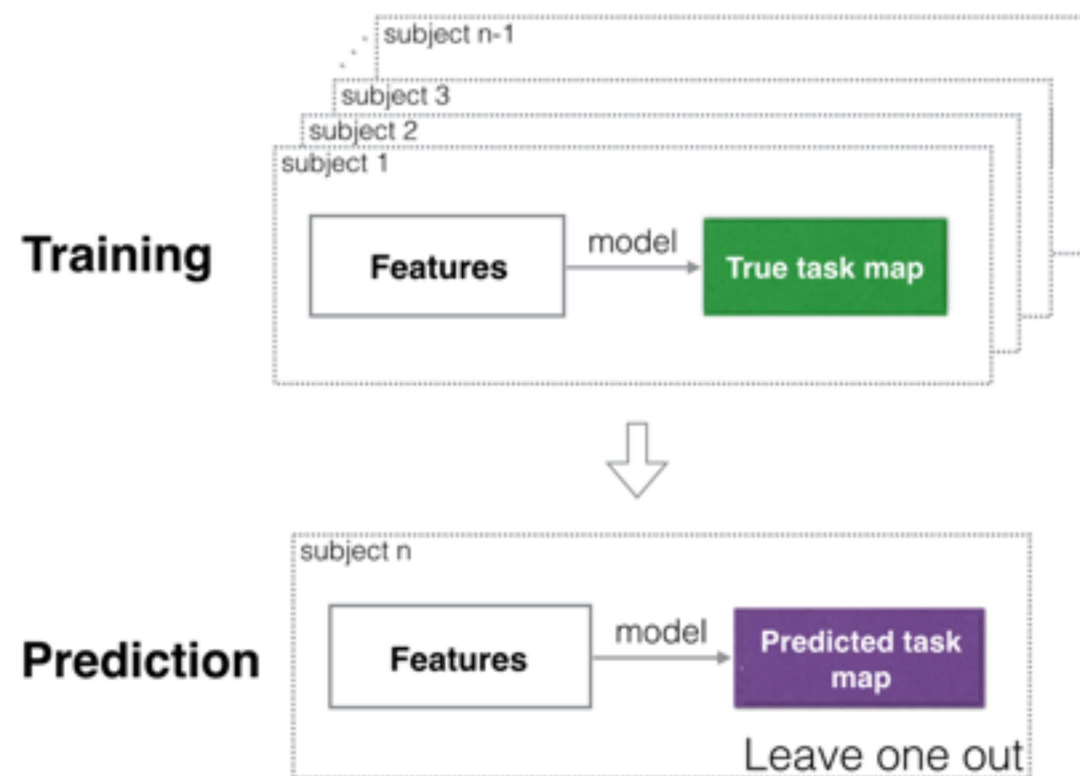
Jbabdi&Behrens Nat Neurosci. (News and views) 2012

Human Connectome Project

Using connectivity as a signature of functional areas

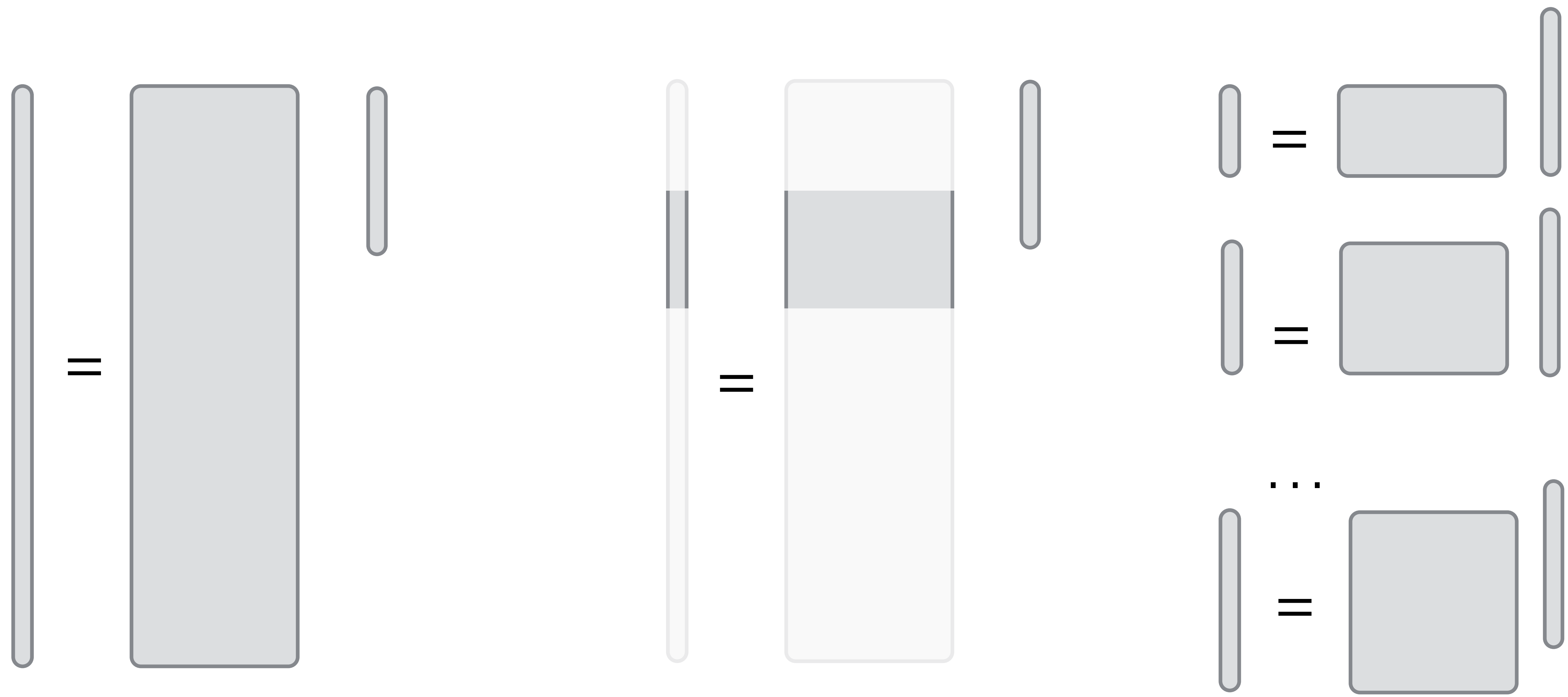


Features



Human Connectome Project

Using connectivity as a signature of functional areas



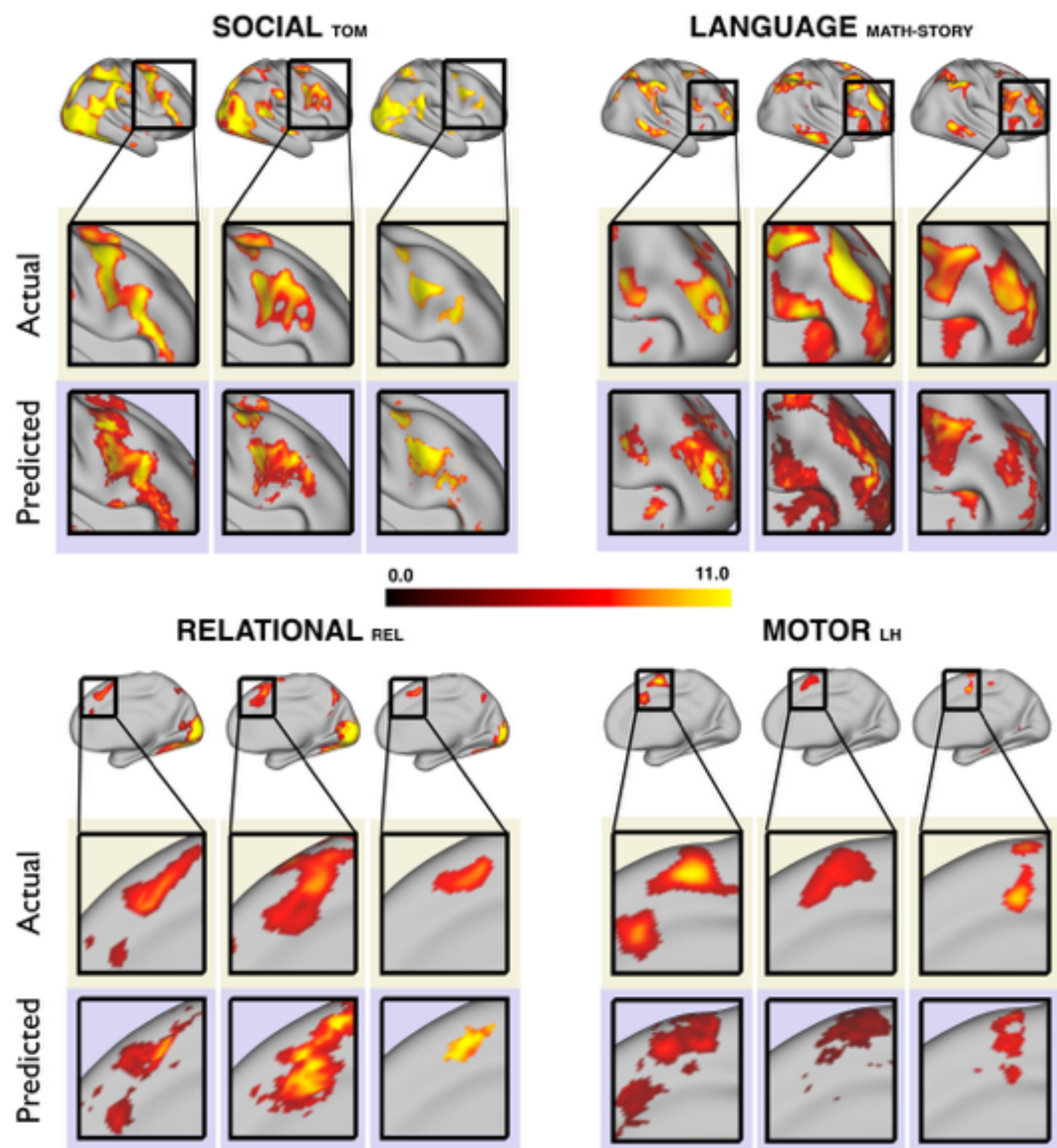
activation Nx1 | features Nx107 | betas 1x107

50 filters -> 50 GLMs per subject
Filters based on group ICA
average betas (Leave-One-Out predictions)

Human Connectome Project

Using connectivity as a signature of functional areas

Results



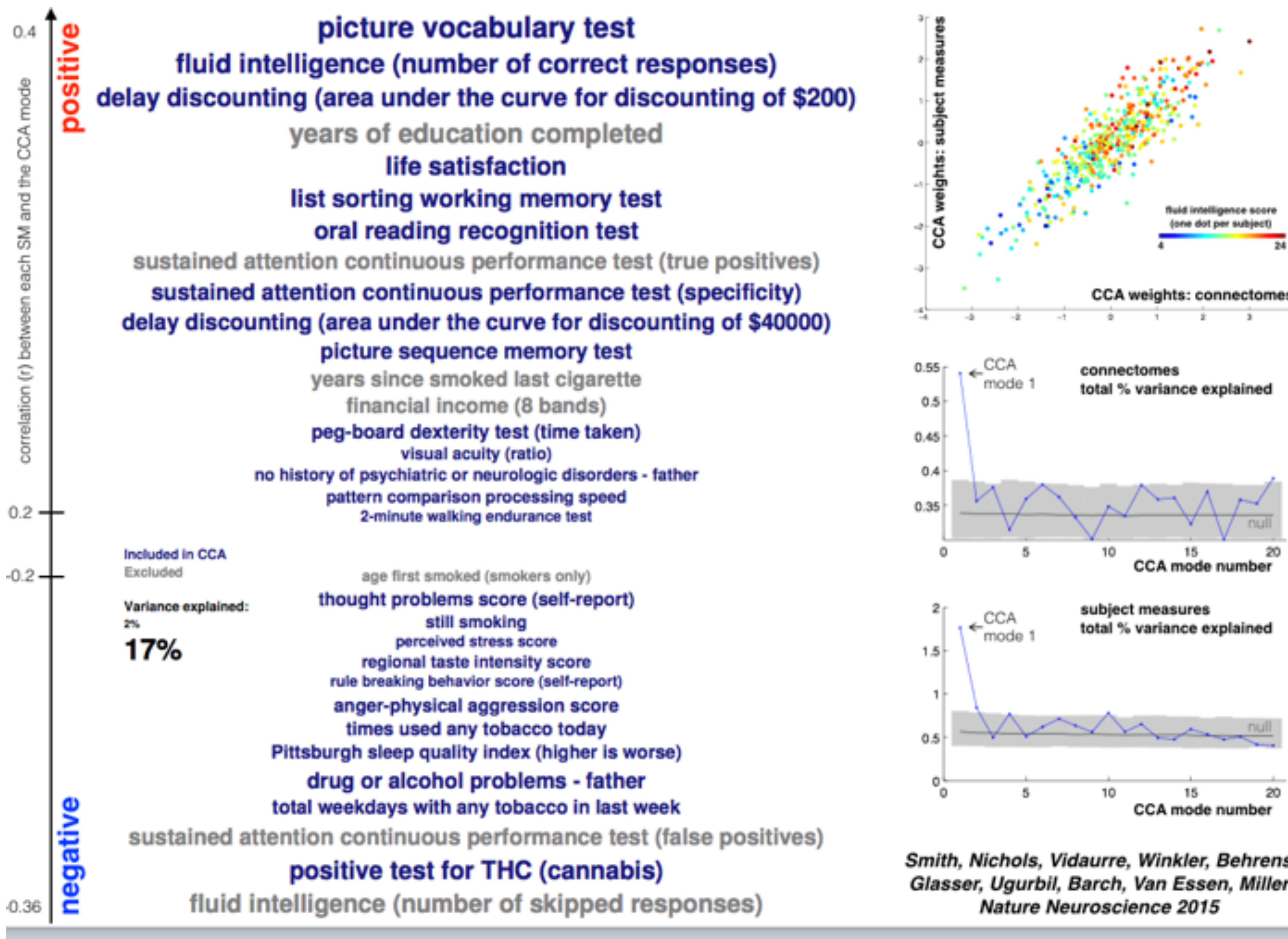
Human Connectome Project

nature neuroscience

A positive-negative mode of population covariation links brain connectivity, demographics and behavior

Stephen M Smith[1], Thomas E Nichols[2], Diego Vidaurre[3], Anderson M Winkler[1], Timothy E J Behrens[1], Matthew F Glasser[4], Kamil Ugurbil[5], Deanna M Barch[4], David C Van Essen[4] & Karla L Miller[1]

We investigated the relationship between individual subjects' functional connectomes and 280 behavioral and demographic measures in a single holistic multivariate analysis relating imaging to non-imaging data from 461 subjects in the Human Connectome Project. We identified one strong mode of population co-variation: subjects were predominantly spread along a single 'positive-negative' axis linking lifestyle, demographic and psychometric measures to each other and to a specific pattern of brain connectivity.



Smith, Nichols, Vidaurre, Winkler, Behrens, Glasser, Ugurbil, Barch, Van Essen, Miller
Nature Neuroscience 2015

Human Connectome Project

nature neuroscience

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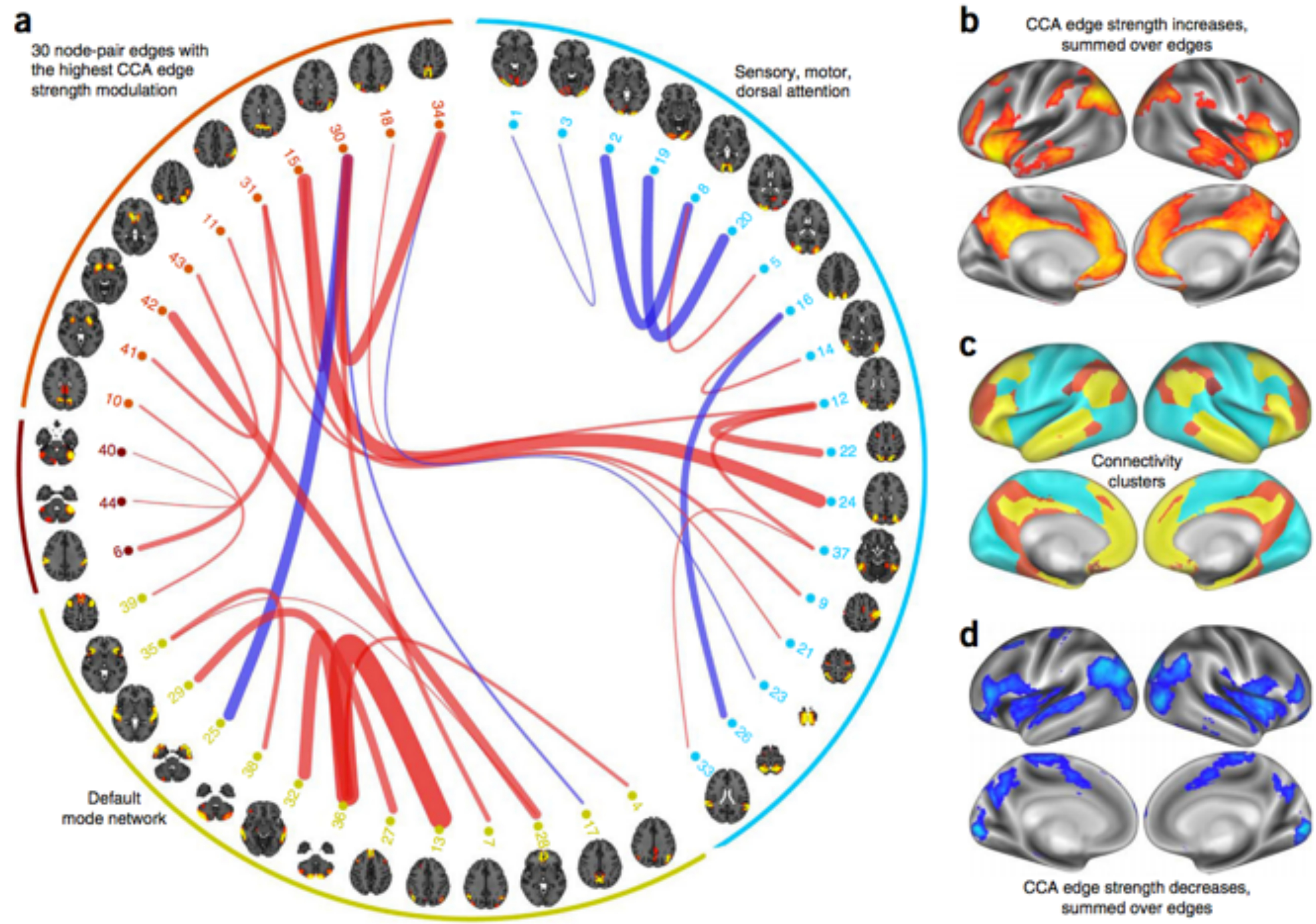


Developing Human Connectome Project

In utero dynamic MRI: Edwards & Hajnal

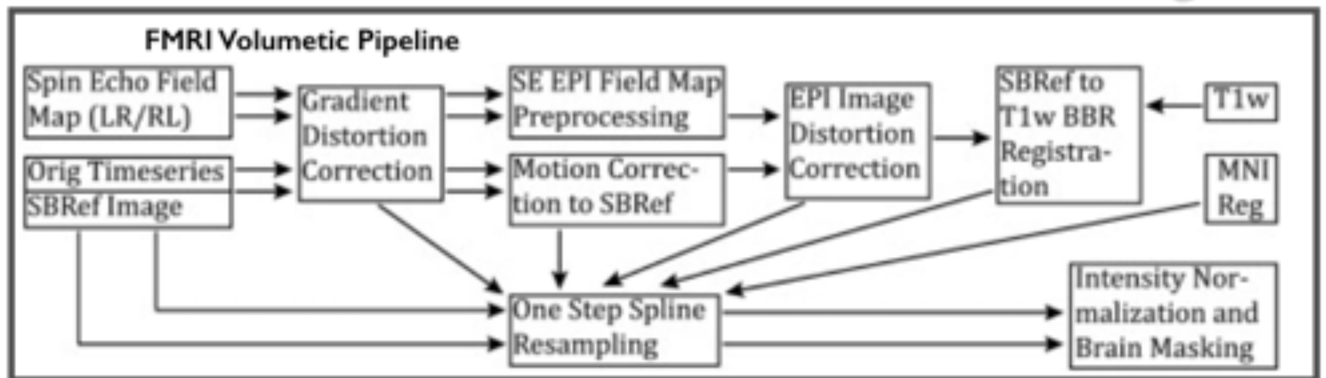
- Now extend brain connectivity mapping to understand brain ***development***...
- ... imaging babies before and after birth (>1000 babies)
- ... and modelling the effects of genes and environment
- *Collaboration between FMRIB Oxford, Kings and Imperial*

Developing Human Connectome Project

Updates to pipelines

Rewritten EPI2Struct

Automated selection of fieldmaps, templates



New age-dependent templates

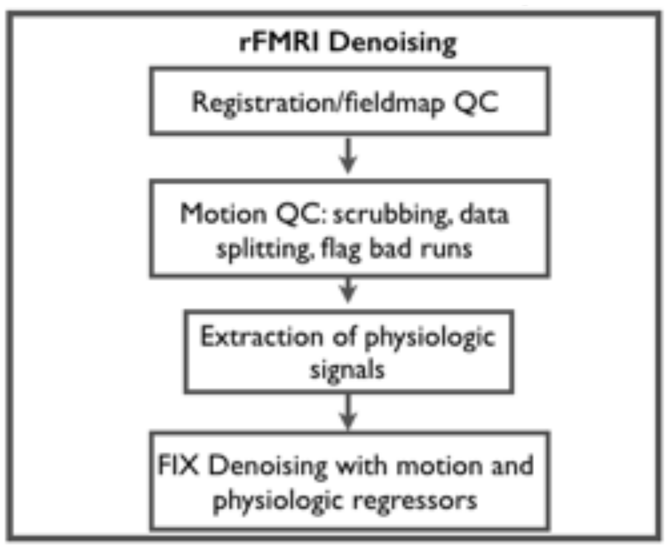
Updated Resampling

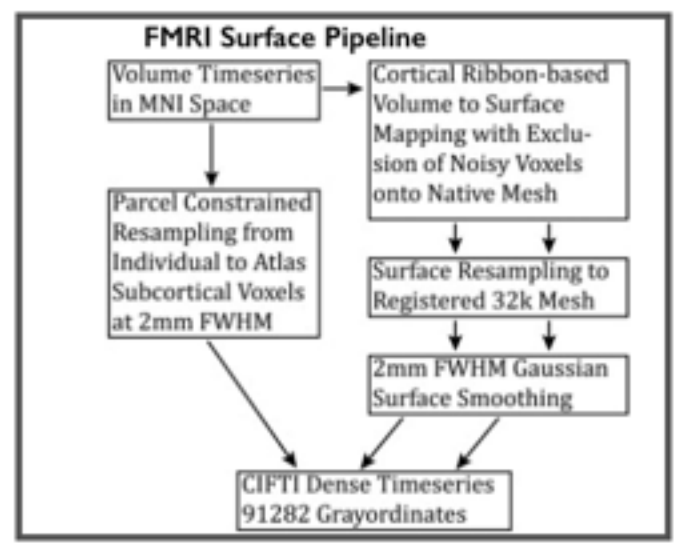
MB pre-MC cleanup

Slice to volume reg

Robustified Motion Corr

Upgraded FIX automatic artefact cleanup





Adjusted surface projection

MSM Surface registration

Developing Human Connectome Project

Initial surface projections and ICA

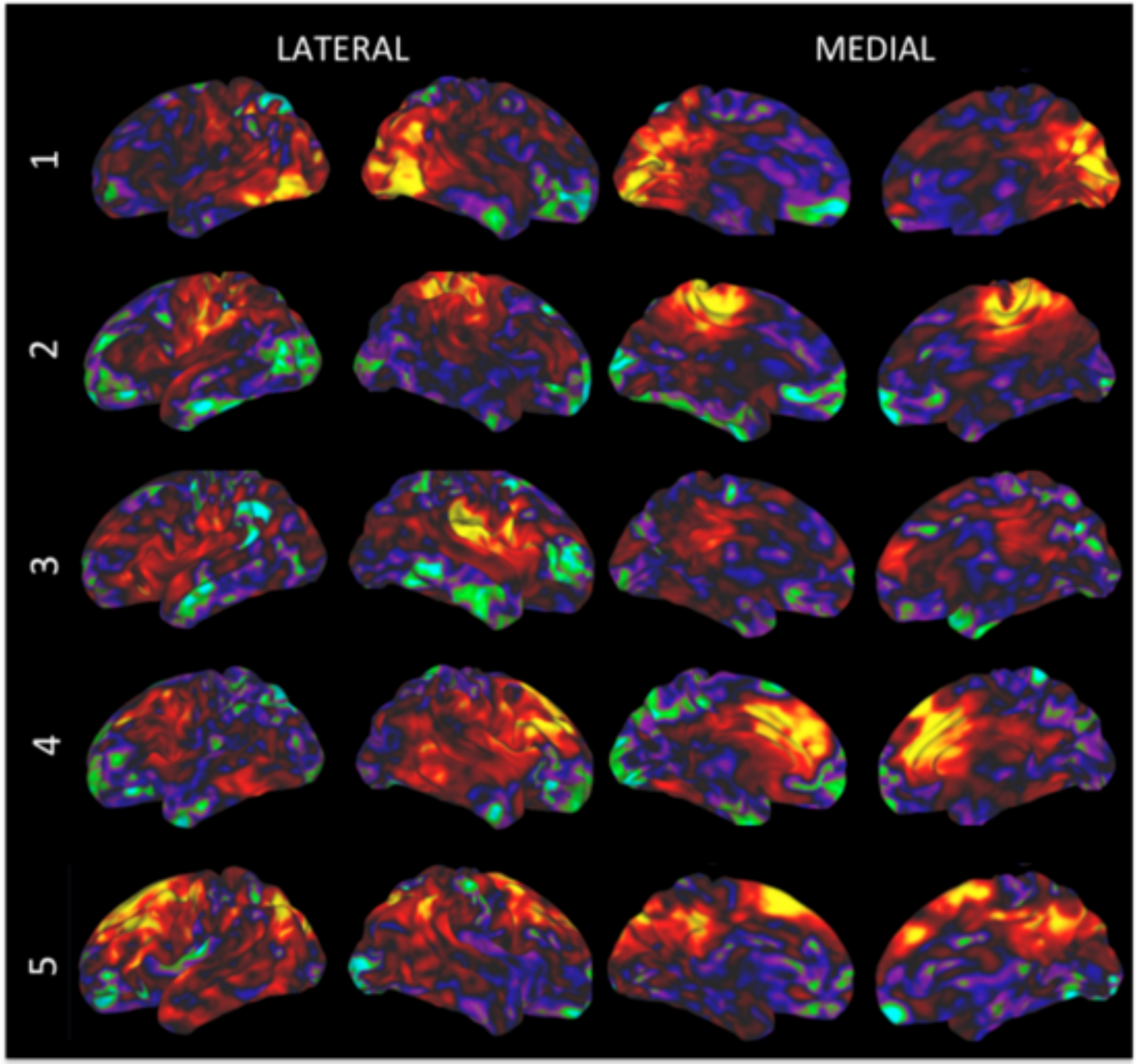
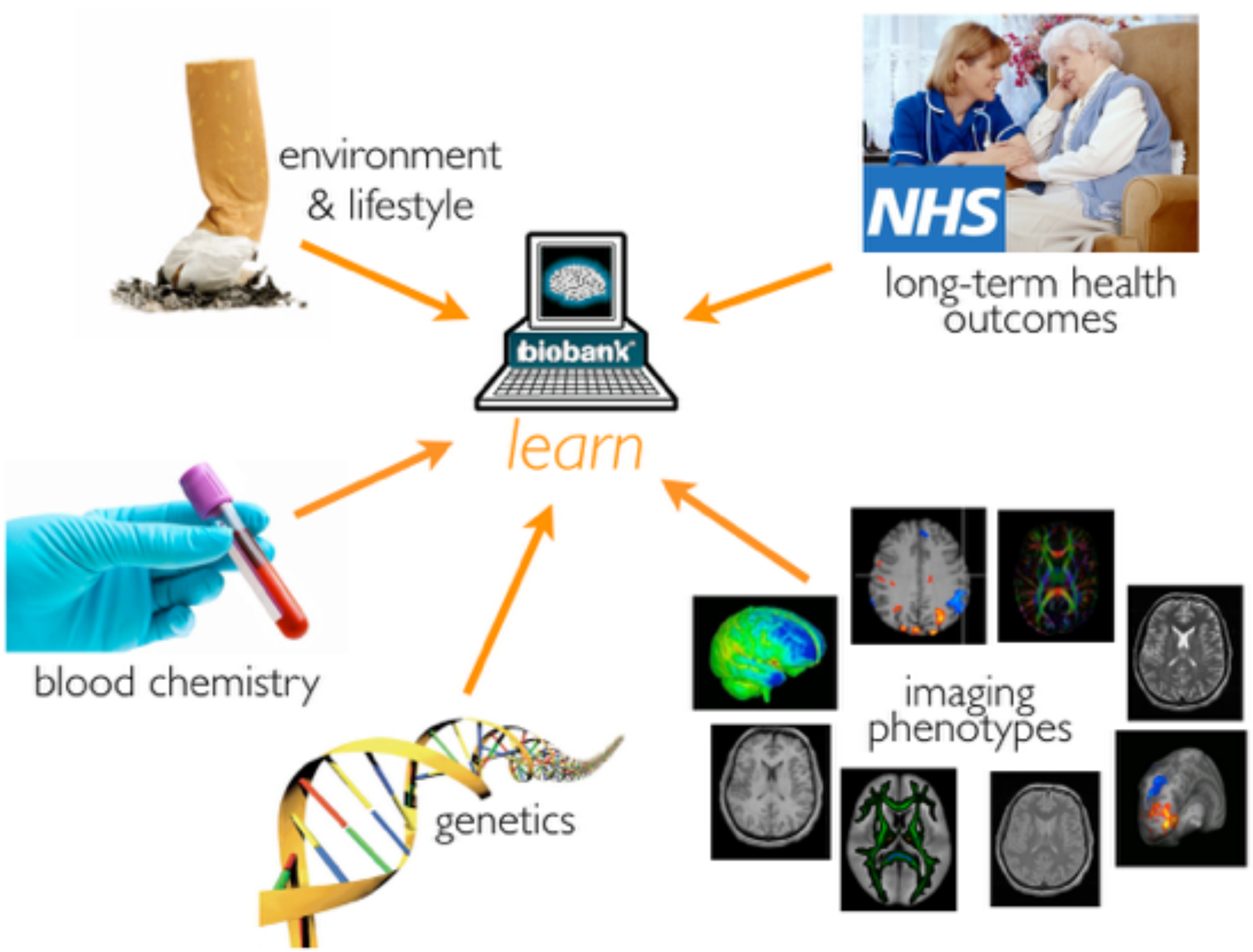


Figure 1. Resting state networks resulting from a group ICA performed on 8 subjects spanning 35-42 weeks PMA. These show some correlation with the following adult networks: 1=Visual; 2=Somatomotor; 3=Auditory; 4=Executive control; 5=Frontal parietal

biobank uk Imaging study

- 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

- Original prospective epidemiological study: 500,000, 45-70y
- Imaging Extension: bring back **100,000** for brain, heart, body imaging
- Discover multi-modal early imaging markers of disease



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- How do you scan 100,000 subjects?
  - 3 dedicated centres, 54 subjects/day, 7 days/week, 5 years!
- What imaging data can you get in 100,000 subjects?
  - 35 mins each: brain MRI, cardiac+body MRI, bone density, carotid US

- **Brain imaging** (3T Siemens Skyra, 32ch, multiband fMRI/dMRI)

  - **T1 anatomical (5 mins)**
  - **T2 FLAIR (6 mins)**
  - **Multi-shell diffusion (7.5 mins)**
  - **Resting FMRI (6 mins)**
  - **Task FMRI (4 mins)**
  - **Susceptibility-weighted (2.5 mins)**

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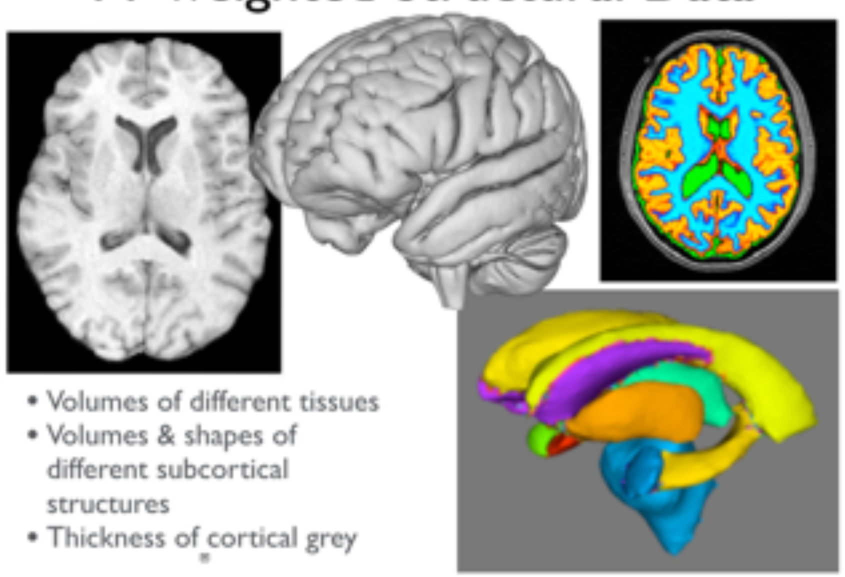
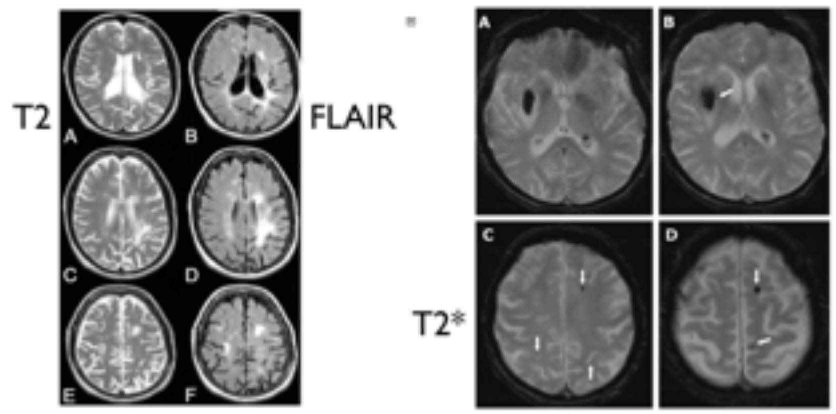
T1-weighted Structural Data



- Volumes of different tissues
- Volumes & shapes of different subcortical structures
- Thickness of cortical grey

T2, PD, FLAIR, T2* Structural

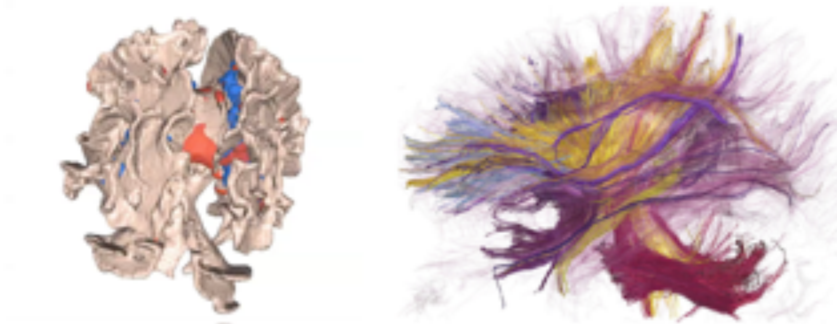


Zivadinov, Frontiers in Bioscience, 2004

Koennecke, Neurology, 2006

- Lesion volumes (& spatial distribution) *Multiple sclerosis...*
- Microbleed volumes *Stroke...*
- CSF volume *Alzheimer's...*

Diffusion Data

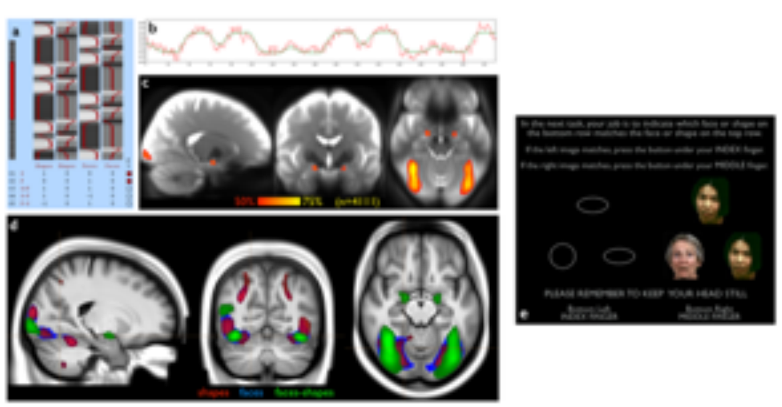


multiple sclerosis: Ceder, NeuroImage, 2007

James Fallon, UCSD

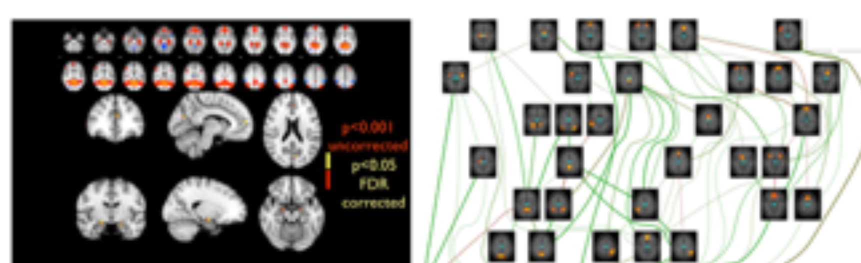
- Structural connectivity (white-matter tracts) *psychiatric diseases...*
- White matter biological properties *white matter pathologies...*

Task FMRI



- Localise brain function & networks *psychiatric diseases...*

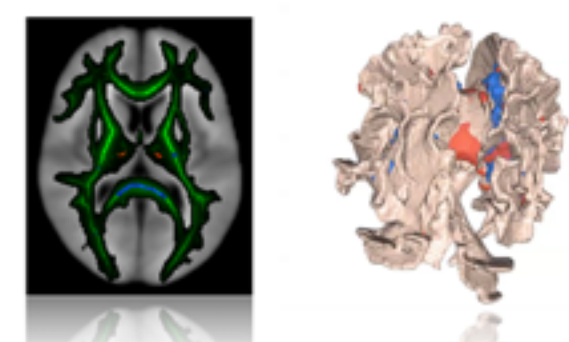
Resting FMRI



Filippini, PNAS, 2009

- Measure *all* functional networks *potentially all pathologies....*

TBSS : Tract-Based Spatial Statisics



- Need: robust "voxelwise" cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)

biobank uk
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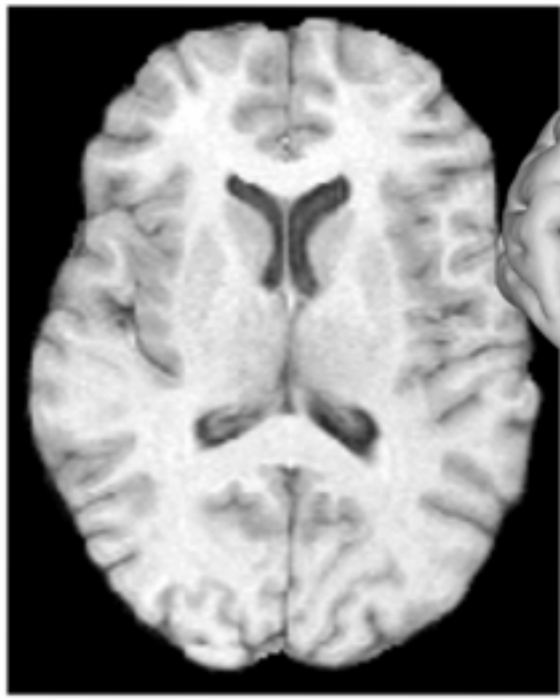
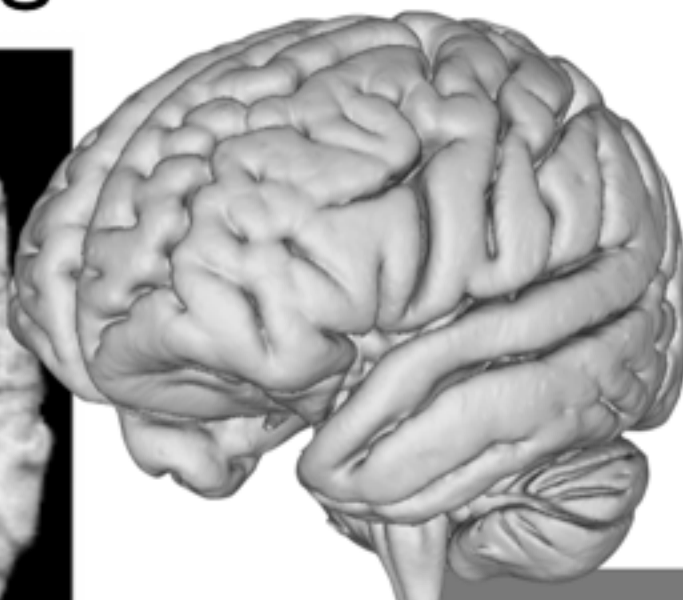
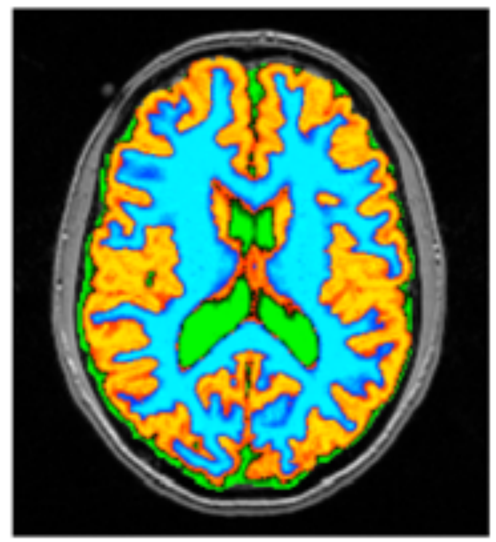
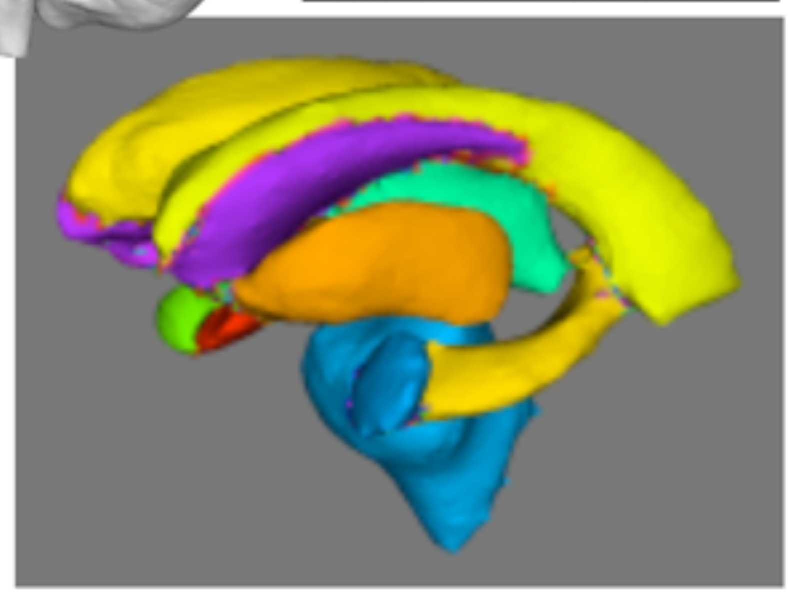
T1-weighted Structural Data









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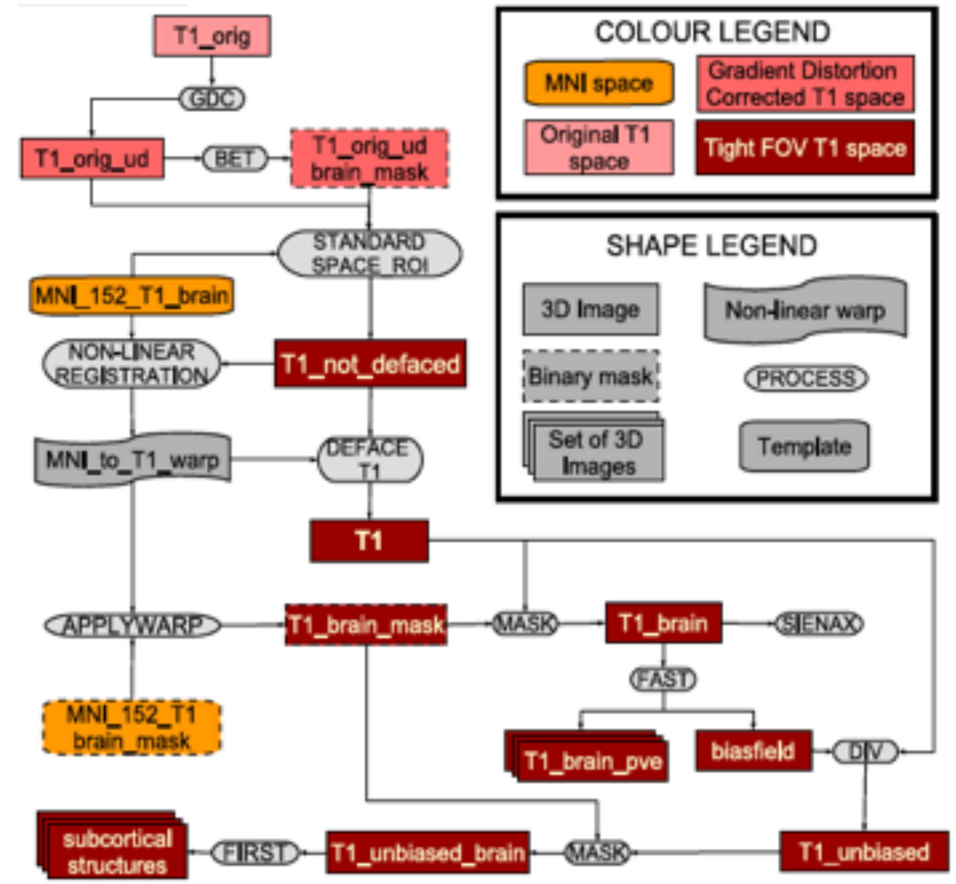

Fig 1: Structural T1 pipeline

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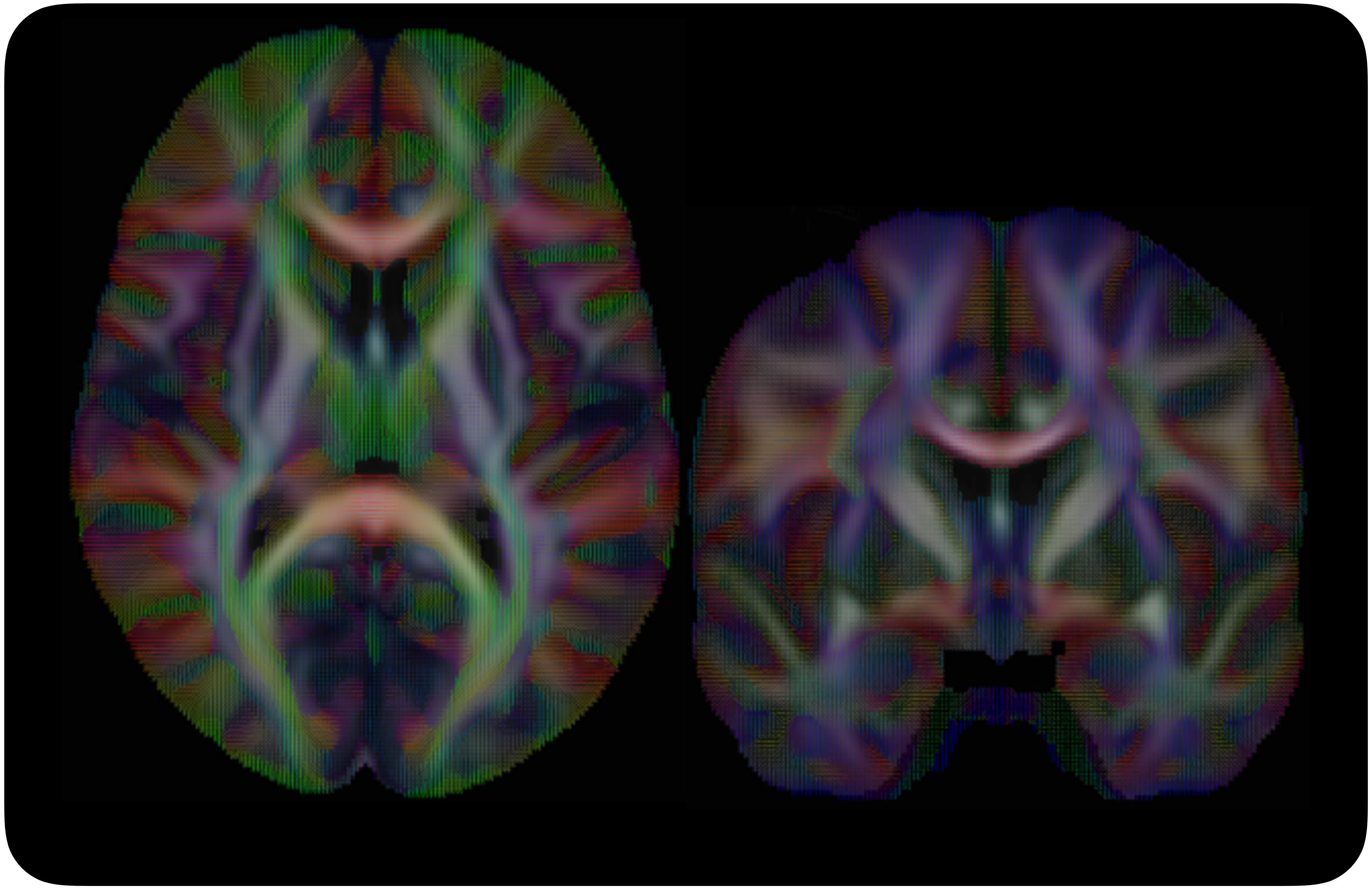

probabilistic dMRI modelling: dominant fibre direction **averaged over 4000 subjects**

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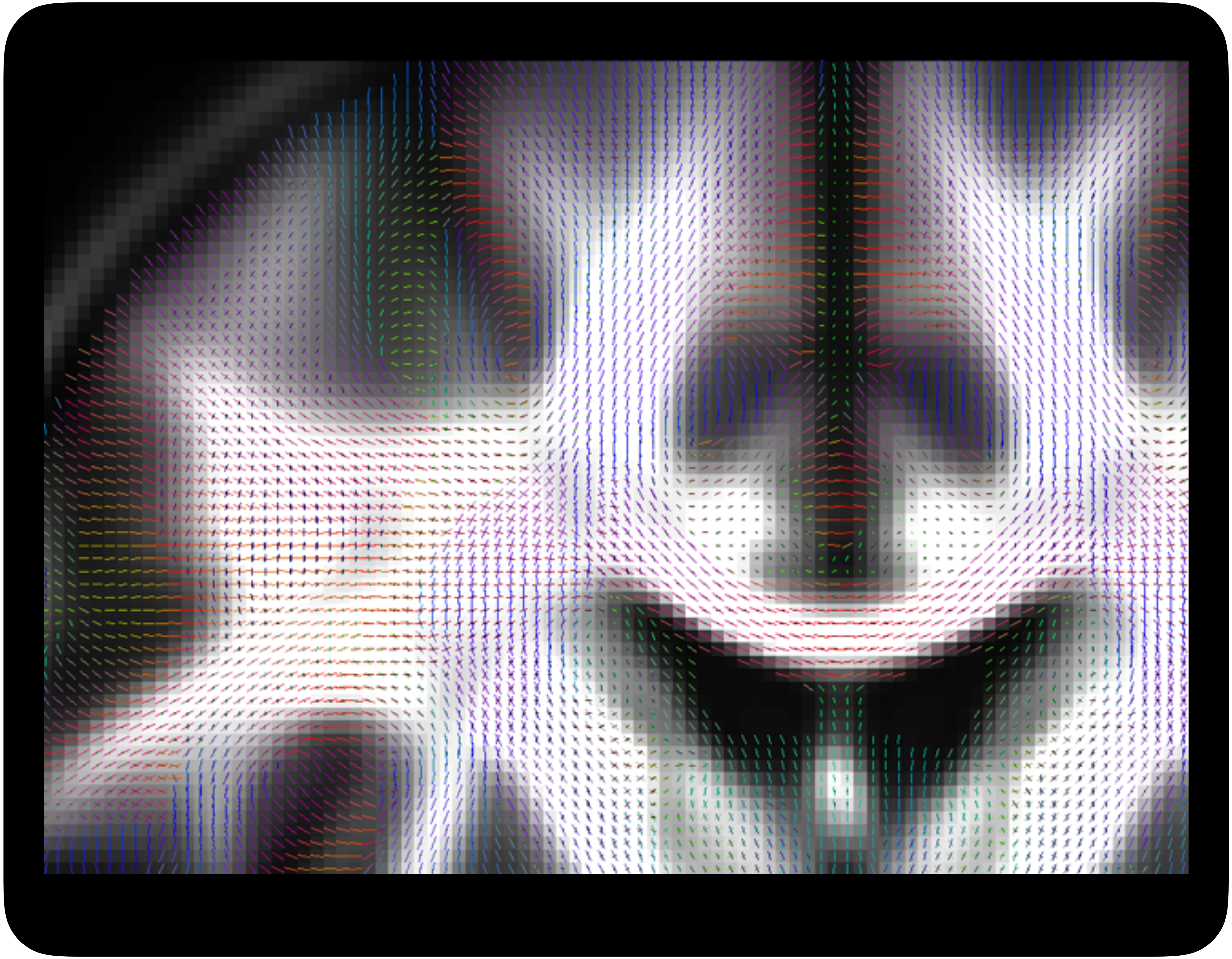

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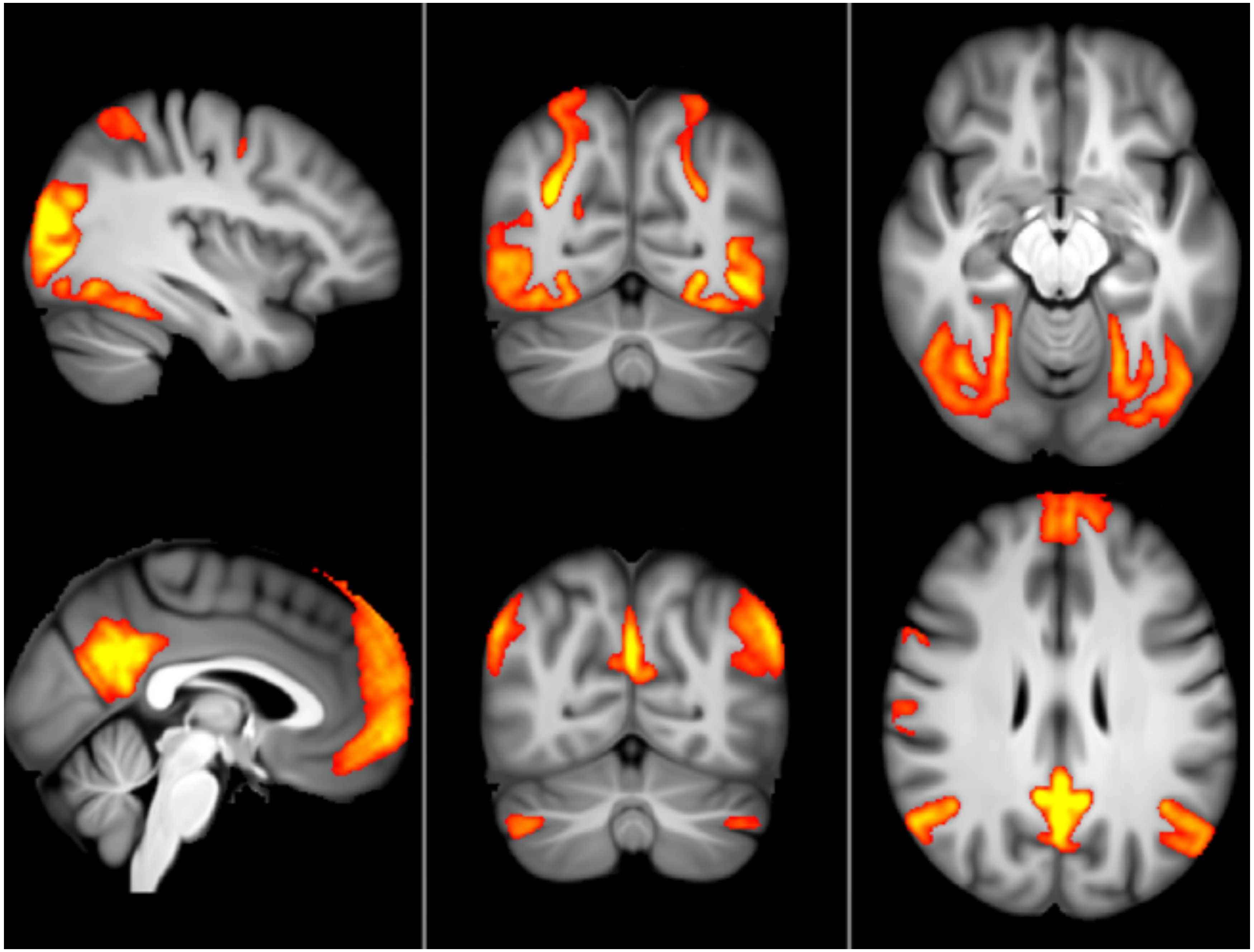
Resting-state networks: 4000-subject group-ICA

Dorsal attention

Default mode



$2.4 \times 2.4 \times 2.4 mm^3$

MB=8, TR=0.73s

tinyurl.com/ukbbrain

biobank uk
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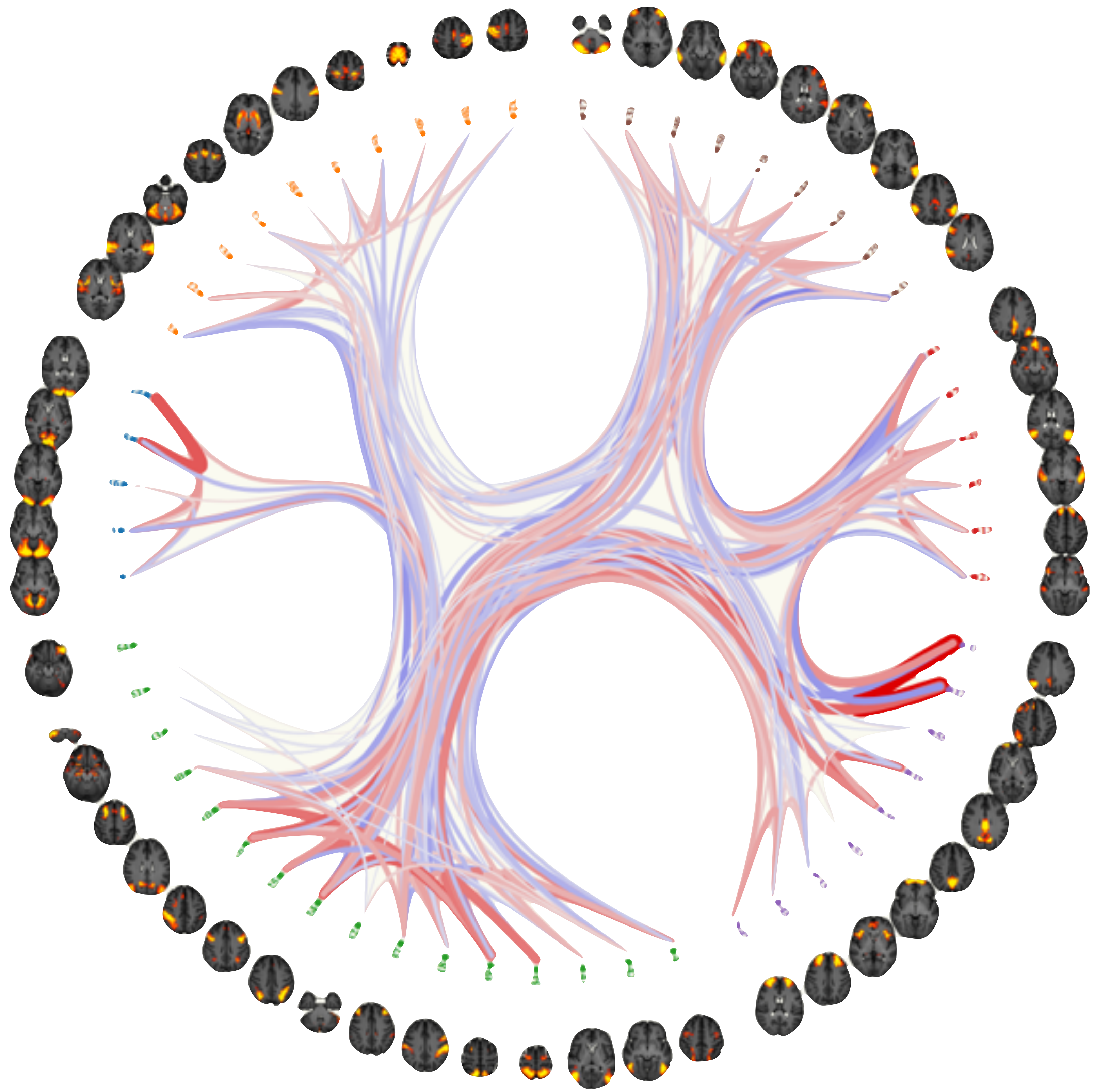
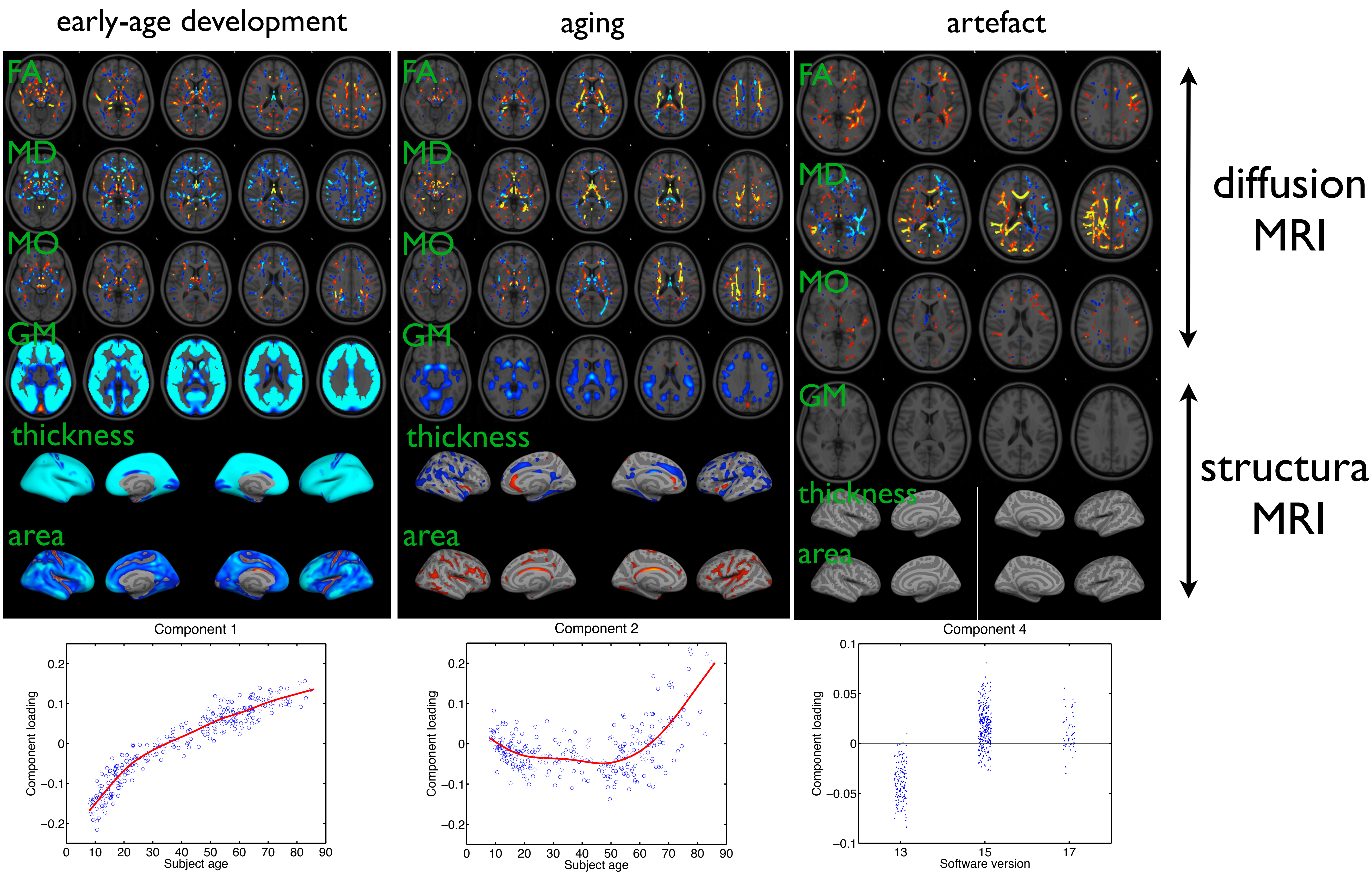


$2.4 \times 2.4 \times 2.4 mm^3$
MB=8, TR=0.73s

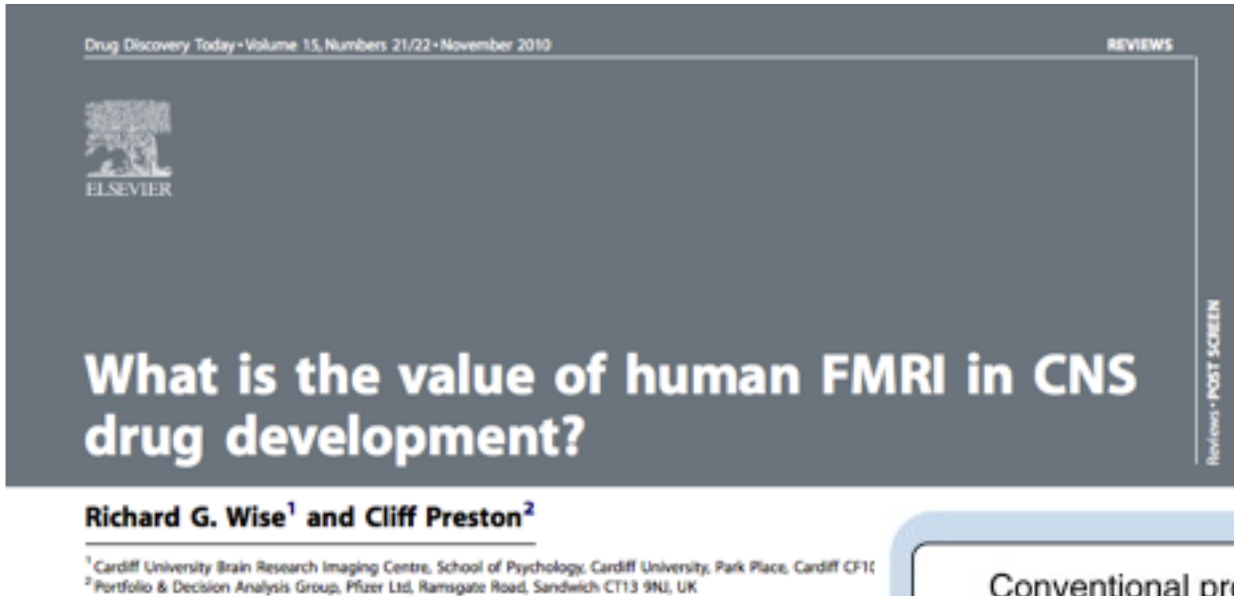
tinyurl.com/ukbbrain

Multivariate population modelling: multimodal Bayesian ICA



484 healthy subjects, ages 8-85y, from collaborators in Oslo (Fjell et al.)

FMRI Biomarker Identification


Drug Discovery Today • Volume 15, Numbers 21/22 • November 2010 REVIEWS

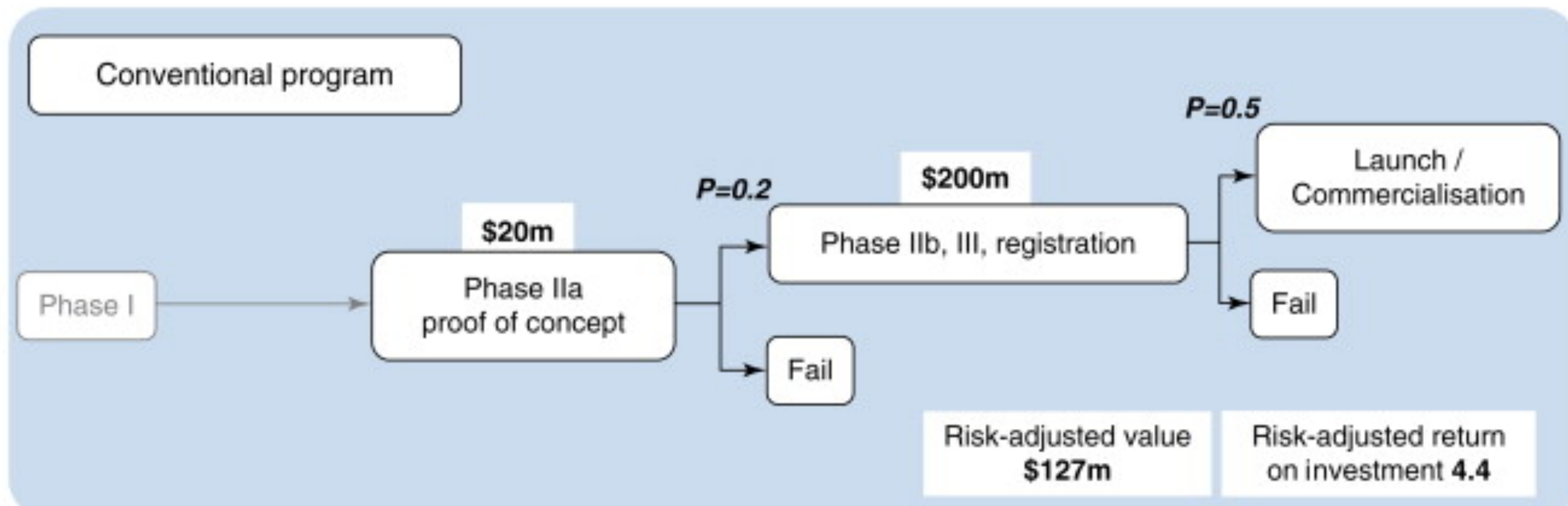
ELSEVIER

Reviews • POST SCREEN

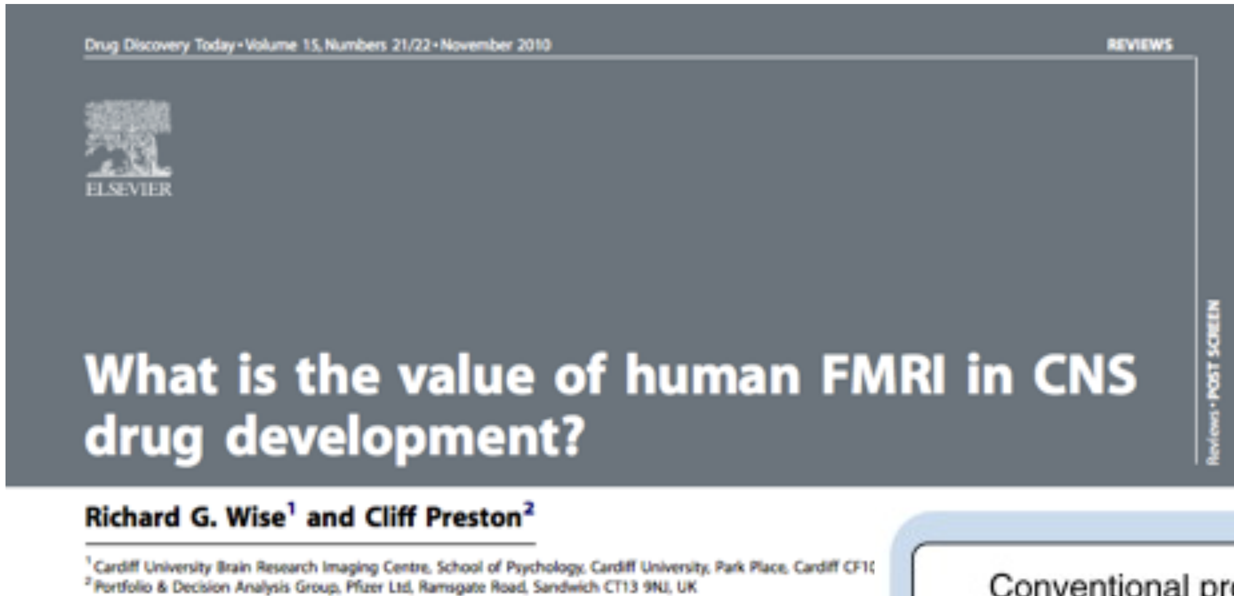
What is the value of human FMRI in CNS drug development?

Richard G. Wise[1] and Cliff Preston[2]

[1] Cardiff University Brain Research Imaging Centre, School of Psychology, Cardiff University, Park Place, Cardiff CF1(
[2] Portfolio & Decision Analysis Group, Pfizer Ltd, Ramsgate Road, Sandwich CT13 9NJ, UK



FMRI Biomarker Identification



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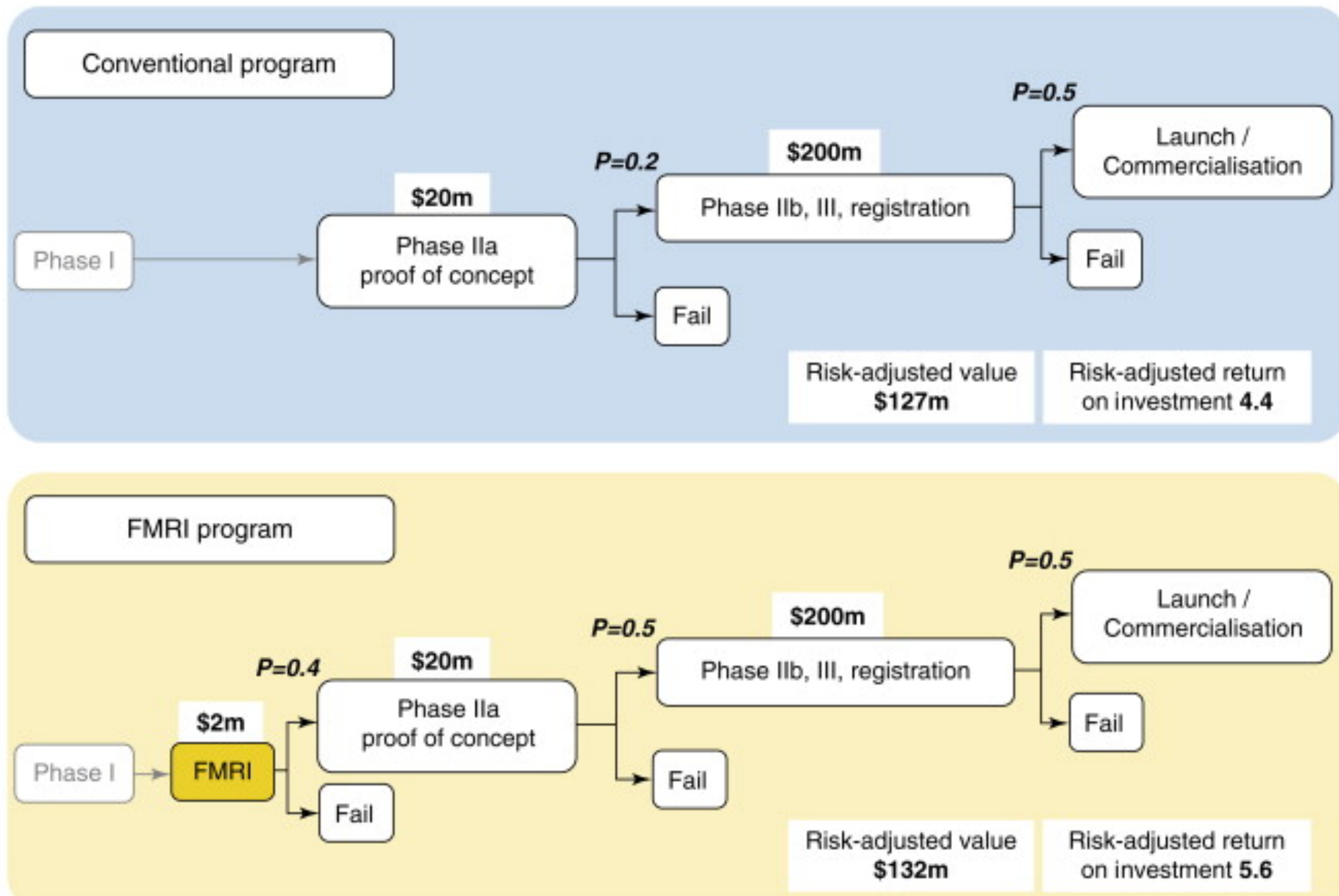
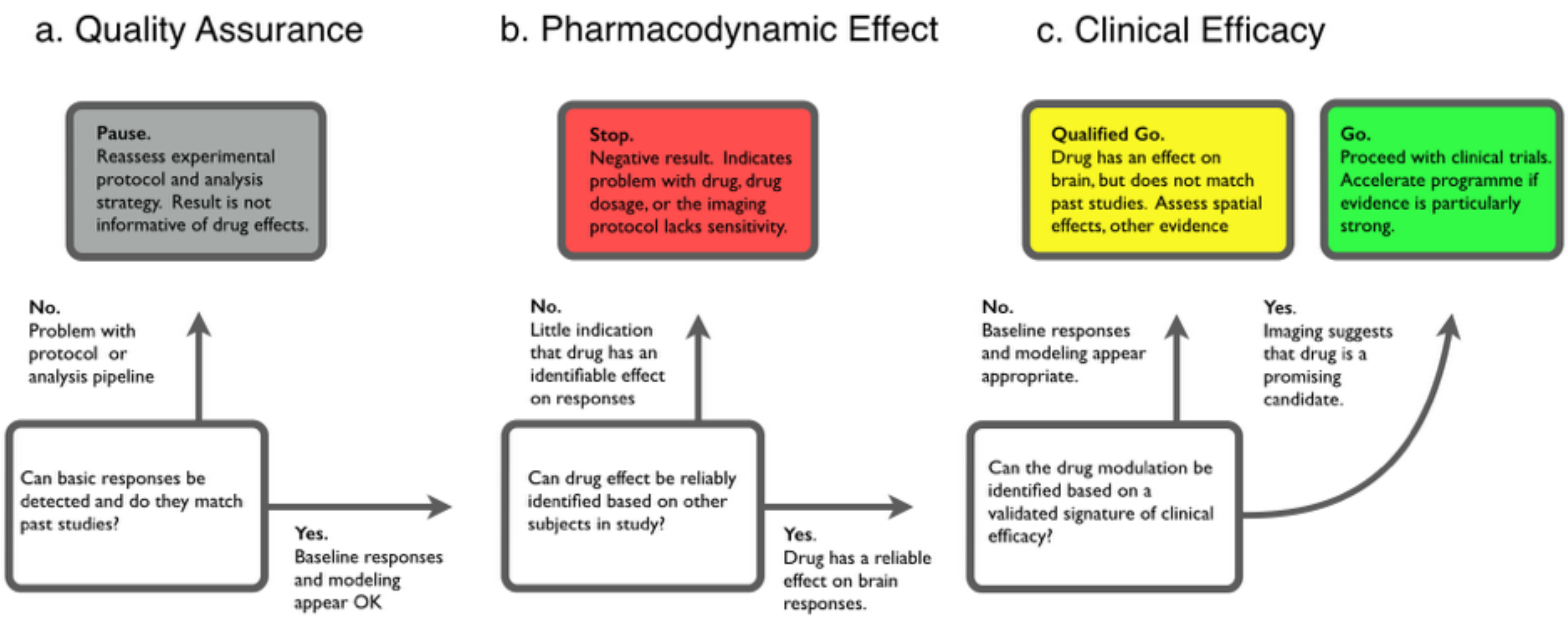
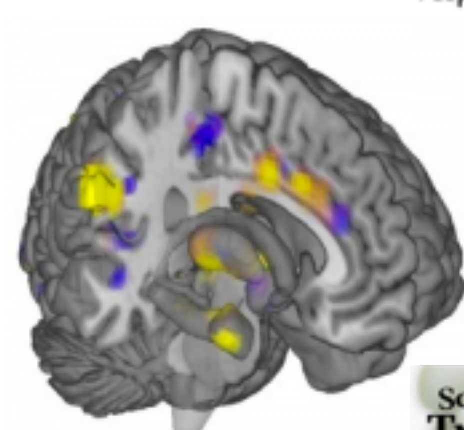
Reviews • POST SCREEN



Drug Discovery Today

FMRI Biomarker Identification





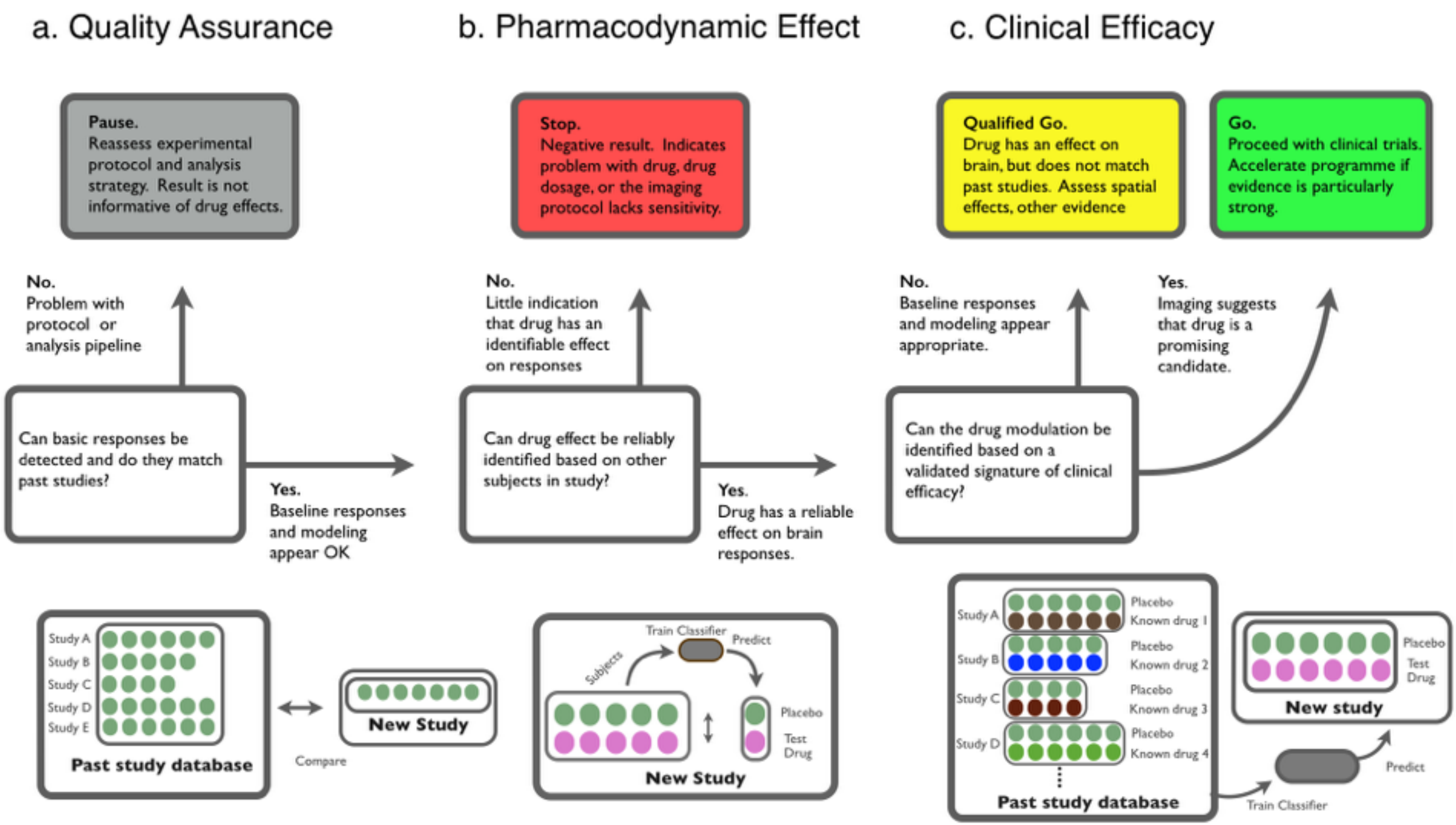
RESEARCH ARTICLE

NEUROIMAGING

Learning to identify CNS drug action and efficacy using multistudy fMRI data

Eugene P. Duff,[1]* William Vennart,[2] Richard G. Wise,[3] Matthew A. Howard,[4] Richard E. Harris,[5] Michael Lee,[1] Karolina Wartolowska,[1] Vishvarani Wanigasekera,[1] Frederick J. Wilson,[2] Mark Whitlock,[2] Irene Tracey,[1] Mark W. Woolrich,[1,6] Stephen M. Smith[1]

FMRI Biomarker Identification



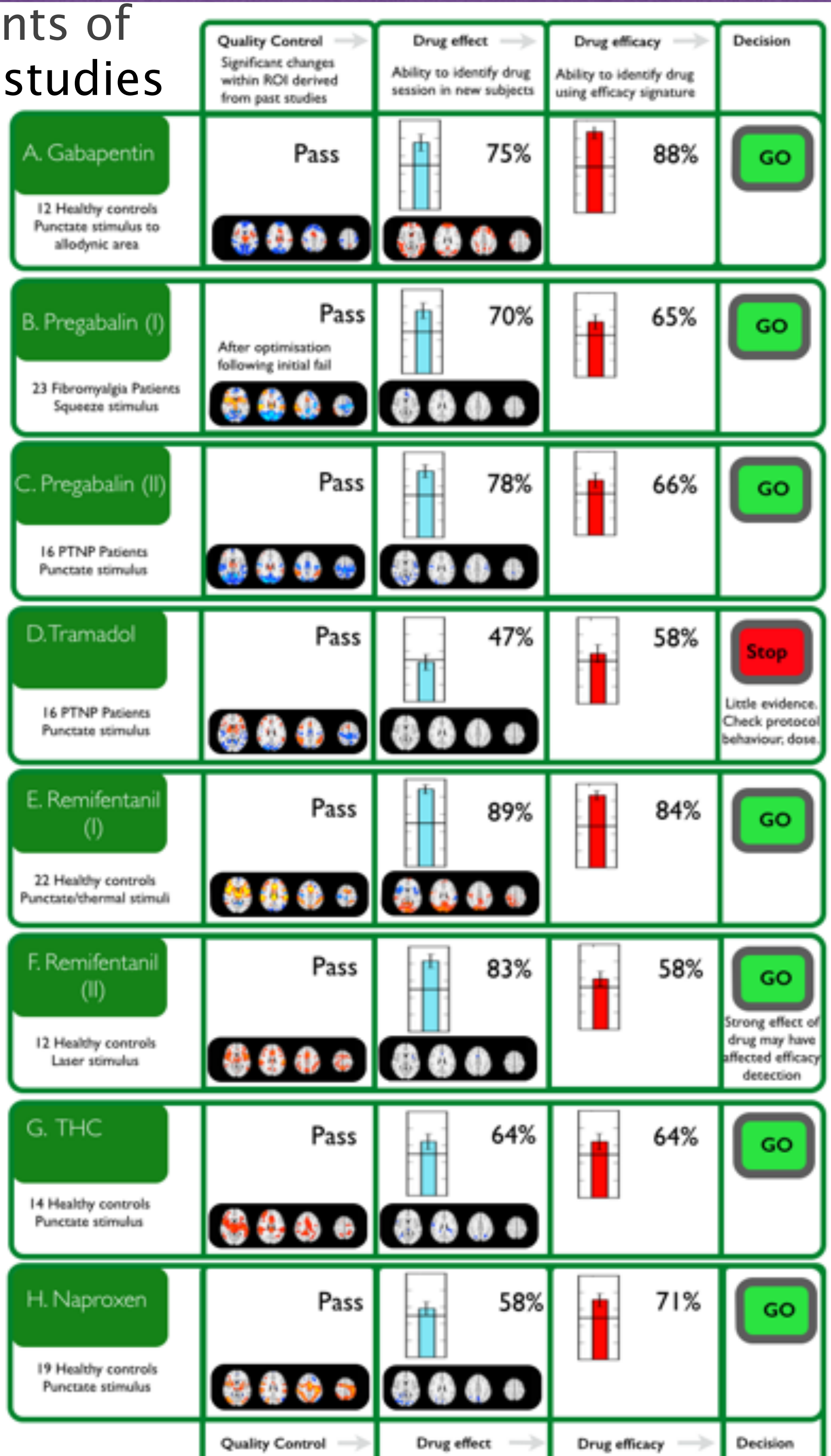
Stimulus validity assessment. Test for differences between responses of test study and responses elicited in validated existing studies.

Cross-validated signature of pharmacodynamic effect. Train MVPA algorithm to discriminate drug from control session maps. Test on held-out subjects (i.e. leave-one-subject-out cross validation).

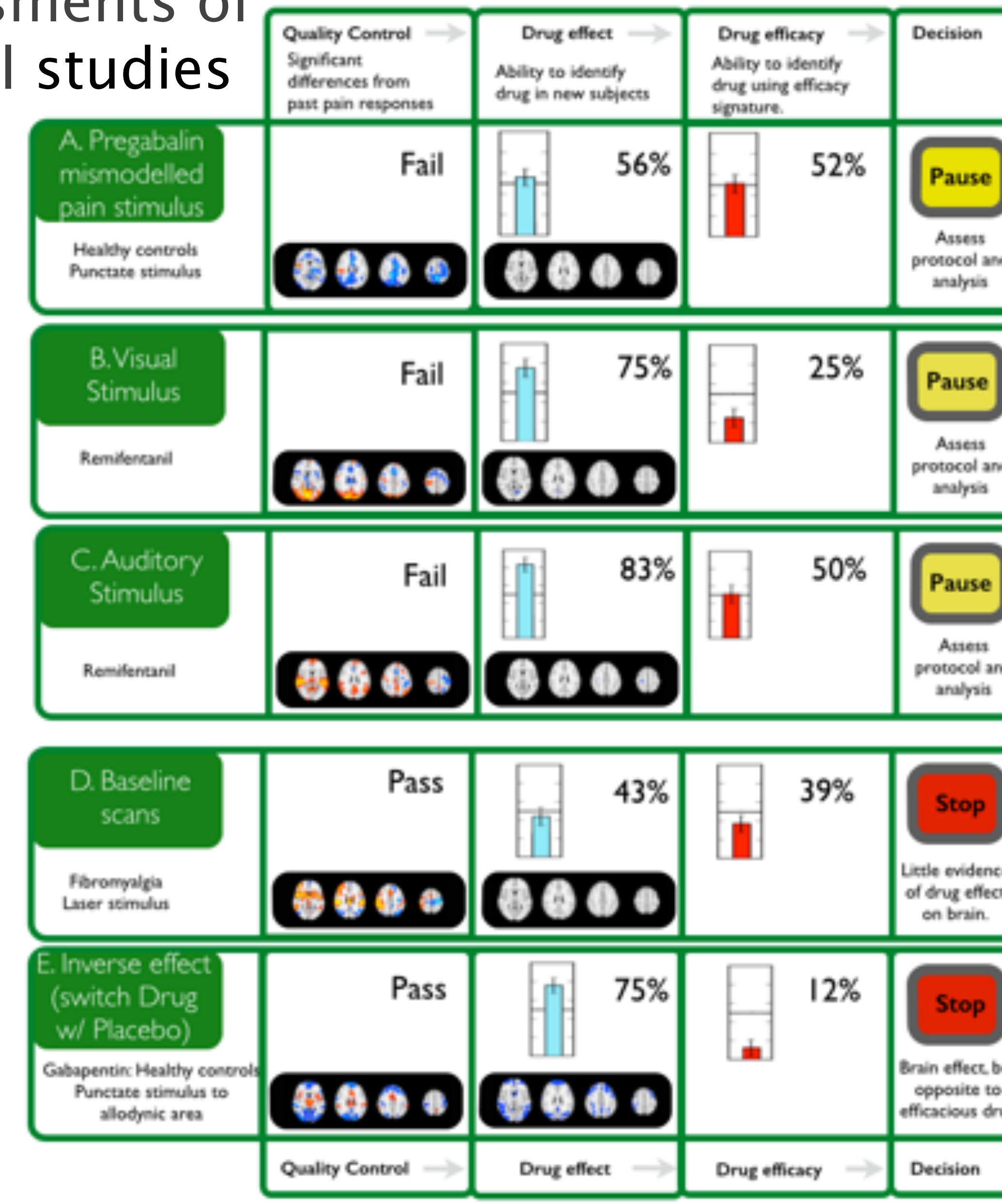
Multi-study signature of efficacy. Train MVPA algorithm to identify brain responses associated with established efficacious drugs, using a set of existing studies studies. Determine whether algorithm successfully identifies the presence of the test compound.

FMRI Biomarker Identification

Assessments of analgesic studies



Assessments of control studies



RESEARCH ARTICLE

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Learning to identify CNS drug action and efficacy using multistudy fMRI data

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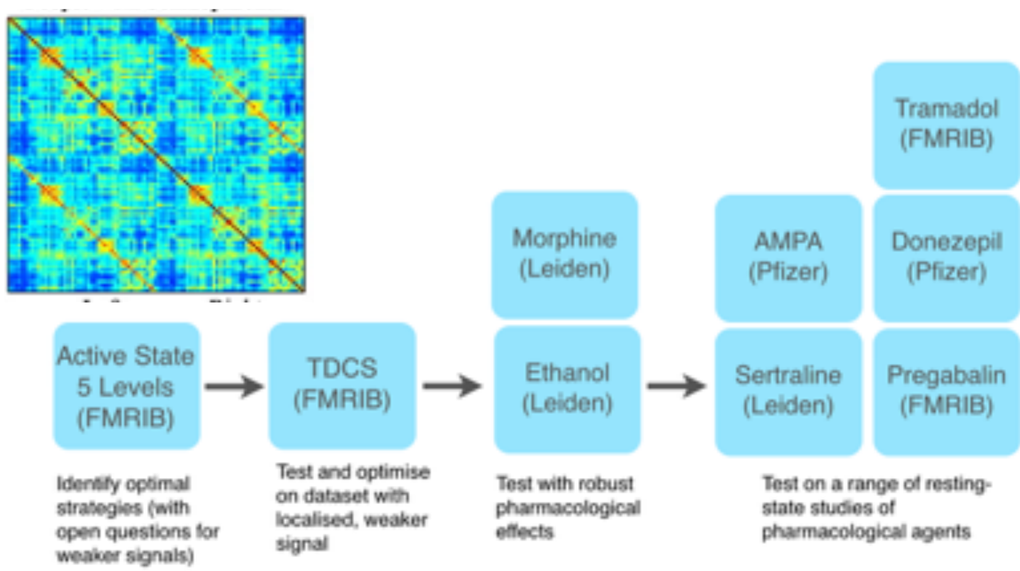
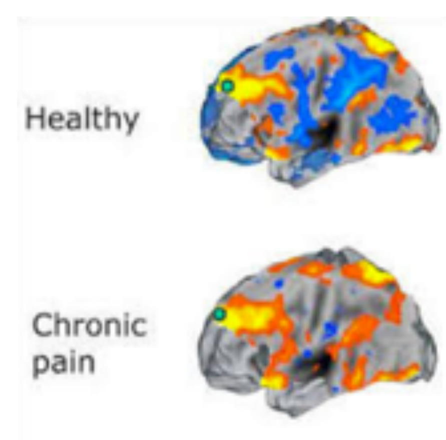
FMRI Biomarker Identification

Resting-state pharmacologic studies

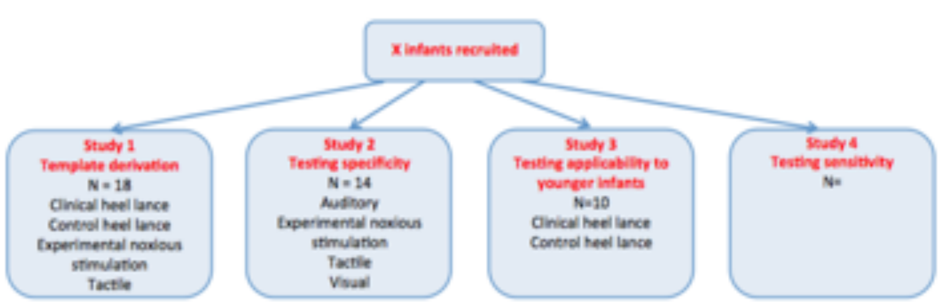


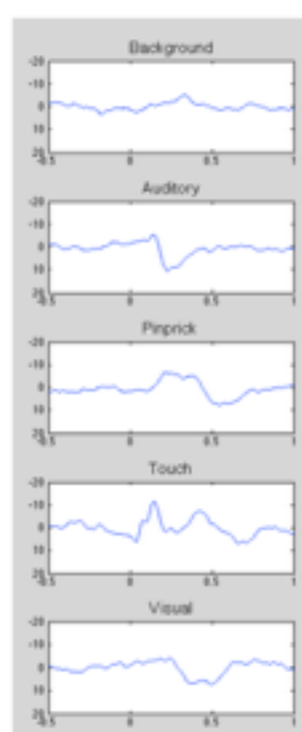
Biomarker for Antidepressant Action

Biomarker for Chronic Pain

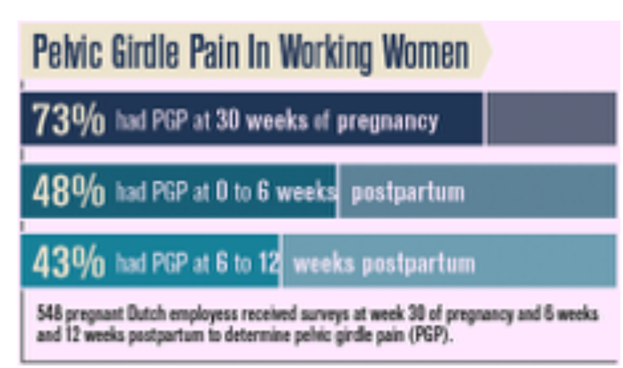


Pain Biomarker for Newborn babies (FMRI & EEG)





Predictors of postpartum pain



Summary

Brain imaging is moving to the realm of big data, multimodal data, and multi-study data.

Work at FMRIB is grappling with the increasing complexity of analysis pipelines, data exploration, and identification of structure.

Challenges of integration of modalities remain.

- We have been cautious about implementing complex biophysical models
- Sparse methods are crucial

Automated QC is under development

There is still a central role for tradional, smaller studies.

- Analyses need to be integrated into large-scale and multi-scale frameworks.

FMRIB Analysis Group

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