

MRI Connectomics

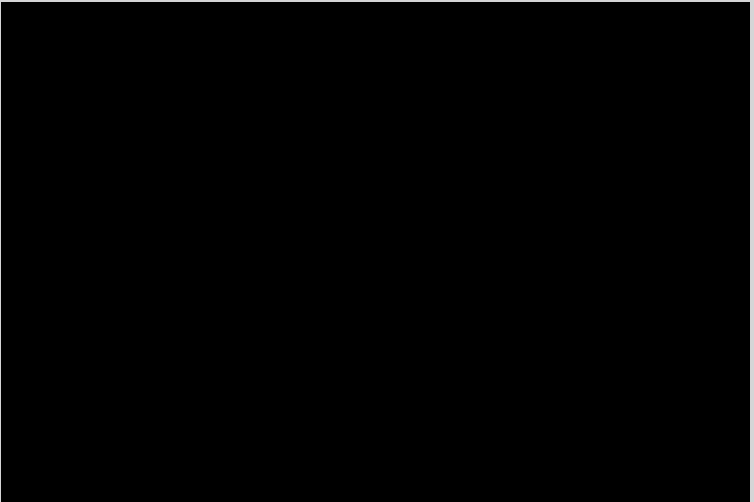
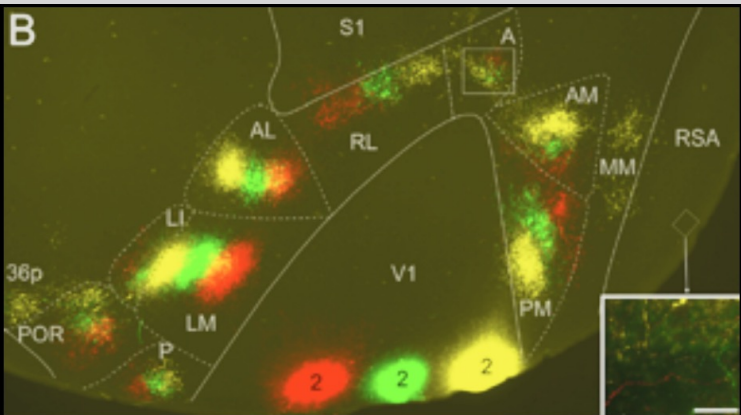
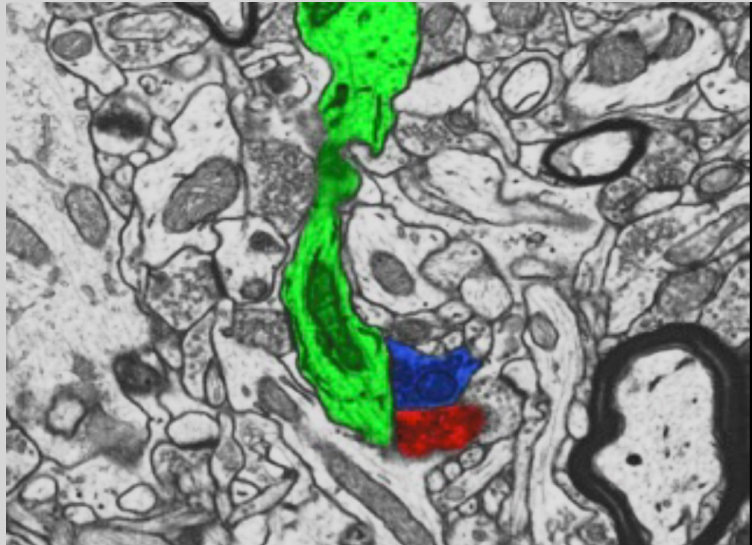
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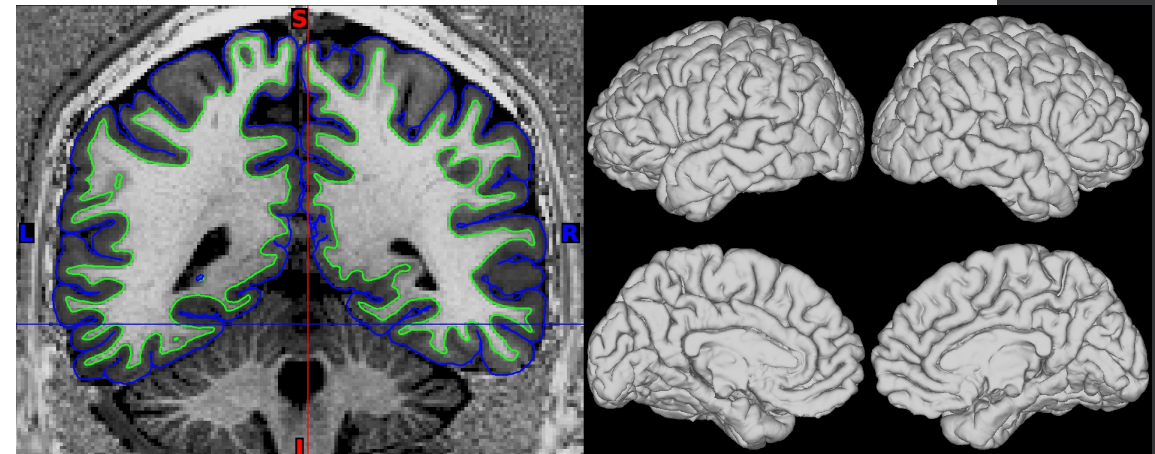
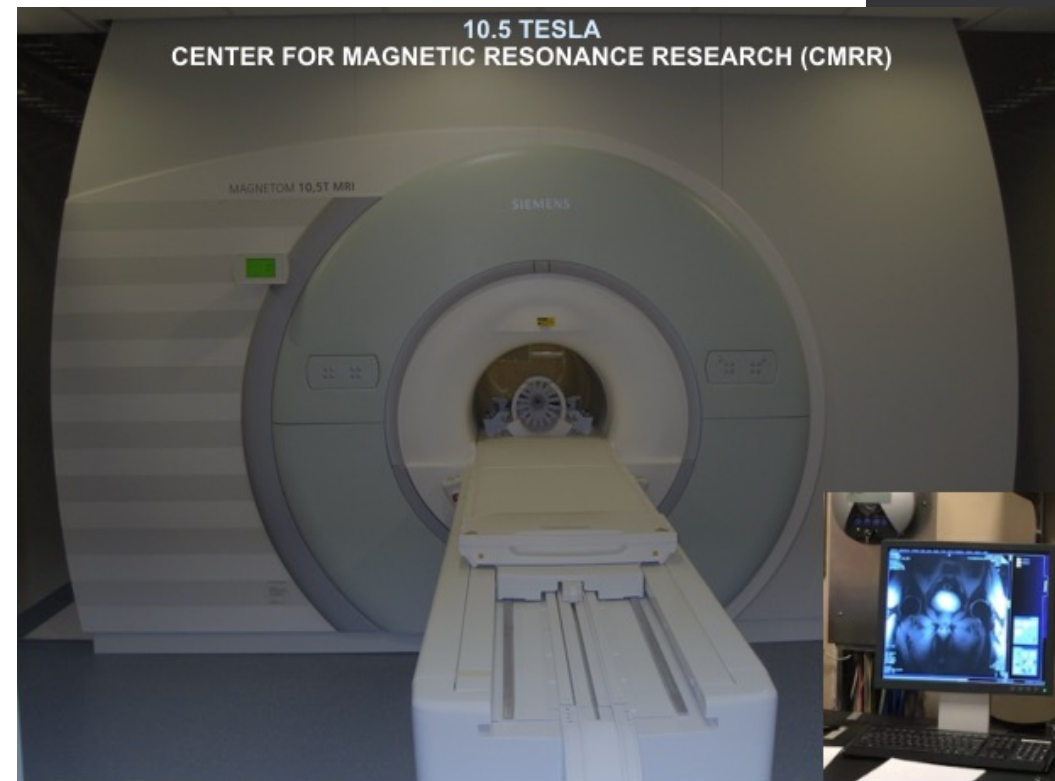
What is a connectome or Crash course on connectome and MRI

Macro-connectome brain level, long distance	Meso-connectome Cellular, long distance	Micro-connectome Synapses
	<p data-bbox="924 672 1661 1076">B S1 A AM AL RL MM RSA LI V1 PM 36p POR P LM 2 2 2</p> <p data-bbox="1014 1100 1592 1200">Mouse area V1 connections (Wang & Burkhalter, 2008)</p> 	

- “Comprehensive” map of neuronal connections

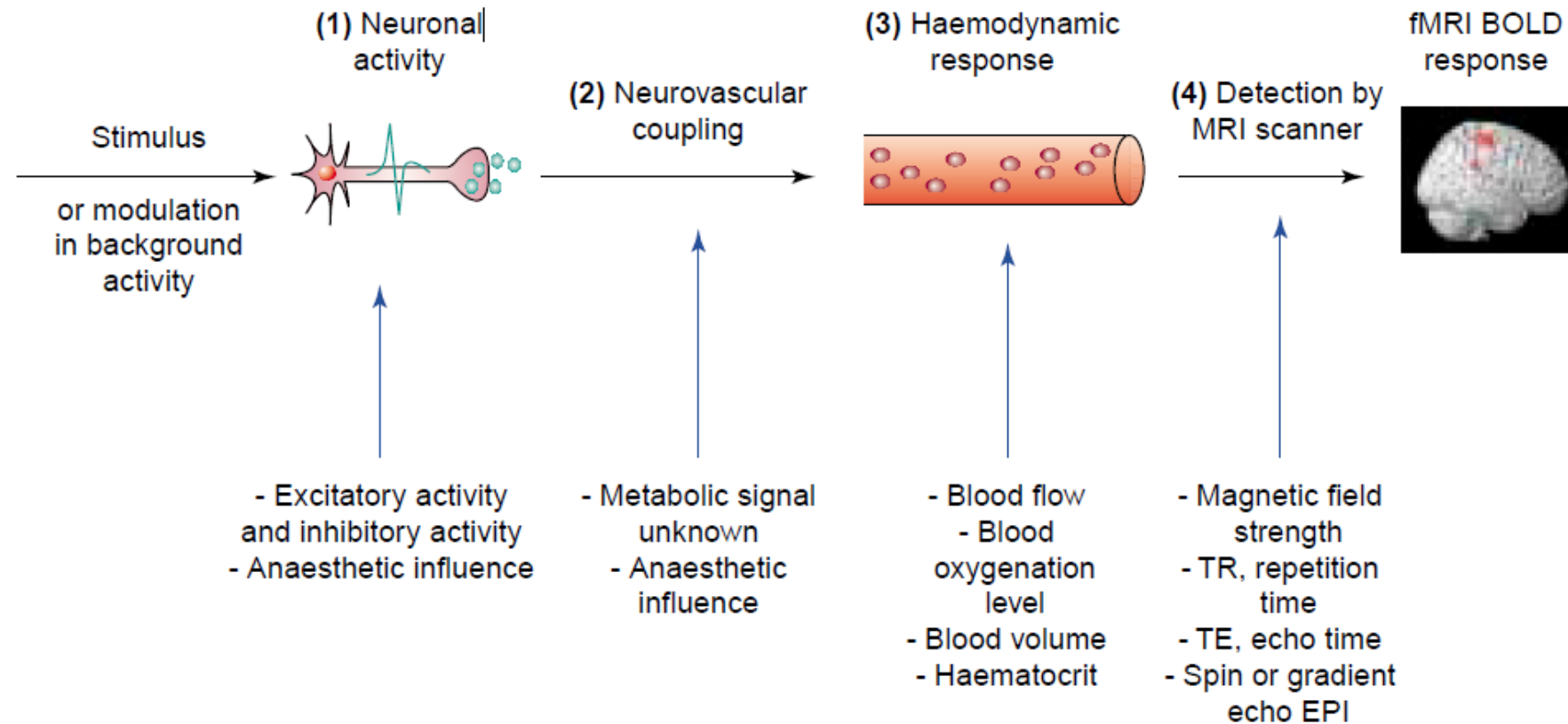
MRI as a method of measurement

- “Functional” connections – full/partial correlations
 - “Functional MRI” – **T2*-weighted BOLD**, SWIFT, ASL
 - But also EEG, MEG and many more
- “Structural connections” – track probabilities
 - **DWI**
- Structural data
 - Cortical thickness, cortical folding, volume/shape of structures...
- Microstructural data – “MRI histology”
 - Relaxation metrics (T1, T2, T1 ρ , T2 ρ , RAFF...) as markers of myelin, iron content
 - SWI
 - Multiple derived metrics as NODDI (water distribution, membrane integrity), T1w/T2w ratio (“myelin maps”)



fMRI BOLD signal

– what do we measure?



Underlying neural activity

Dissociation/decoupling - regionality:

- vascular hypothesis
- local circuitry-based explanations
- regionality of HRF
- **gamma band power** of LFPs (nominally 40–100 Hz) most correlated with the subsequent vasodilation and/or increased oxygenation
- → Activity of interneurons as the primary driver of BOLD?

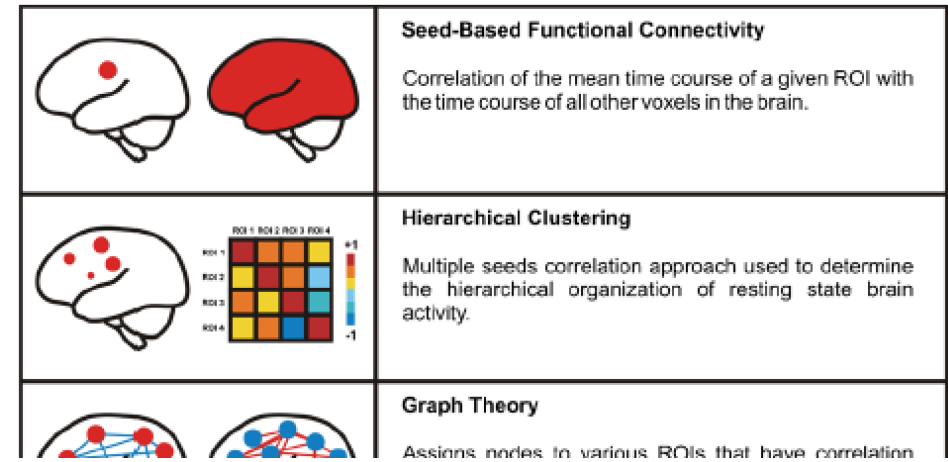
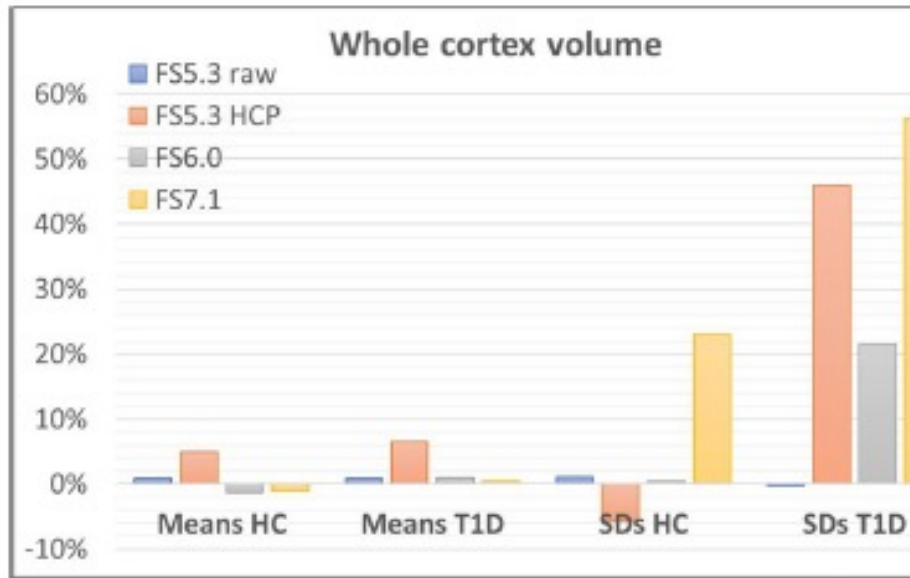
Effect	Metabolic signals and spike rate correlated	Metabolic signal and spike rate dissociated	Metabolic signal and LFP correlated	Metabolic signal and LFPs dissociated
Region				
Visual cortex	Rees et al., 2000; Logothetis et al., 2001; Kim et al., 2004; Shmuel et al., 2006; Goense and Logothetis, 2008;	Kayser et al., 2004; Niessing et al., 2005; Maier et al., 2008; Rauch et al., 2008; Viswanathan, 2008; Sirotin and Das, 2009.	Logothetis et al., 2001; Moosmann et al., 2003; Niessing et al., 2005; Koch et al., 2006; Shmuel et al., 2006; Goense and Logothetis, 2008	Logothetis et al., 2001; Koch et al., 2006; Maier et al., 2008; Sirotin and Das, 2009
Primary auditory cortex	Mukamel et al., 2005; Nir et al., 2007.	Nir et al., 2007.	Mukamel et al., 2005; Nir et al., 2007.	
Neocortex (includes parietal and frontal cortex)	Smith et al., 2002; Hyder, 2004; Kida et al., 2006.	Devor et al., 2007.	Brinker et al., 1999; Goldman et al., 2002; Laufs et al., 2003a; Laufs et al., 2003b; Ureshi et al., 2004; Debener et al., 2005; Hewson-Stoate et al., 2005; Kida et al., 2006; Gsell et al., 2006; Martin et al., 2006; Devor et al., 2007; Masamoto et al., 2008; Huttunen et al., 2008; Scheeringa et al., 2009.	Hewson-Stoate et al., 2005; Masamoto et al., 2008; Meltzer et al., 2008
Hippocampal area	Englot et al., 2008; 2009.	Schridde et al., 2008; Ekstrom et al., 2009. Ojemann et al., 2009.	Canals et al., 2008; Englot et al., 2008; 2009; Ekstrom et al., 2009; Ojemann et al., 2009.	Sanchez-Arroyos et al., 1993; Uecker et al., 1997; Schridde et al., 2008; Angenstein et al., 2009; Ekstrom et al., 2009.
Cerebellum		Mathiessen et al., 1998; 2000. Caesar et al., 2003; Thomsen et al., 2004.	Mathiesen et al., 1998; 2000. Thomsen et al., 2004.	Caesar et al., 2003.

resting state fMRI

- Evoked neural activity and haemodynamic signals – $R > 0.9$
- Spontaneous activity – R in the range of 0.0-0.3
- **i.e. low correlations not caused by methodological issues**
- **mismatch between observed BOLD dynamics and predicted dynamics from structural connectome**
- Vessel-autonomous oscillations (in mice persisting even after pharmacological blockage of glutamatergic transmission)
- Spontaneous movements – need for monitoring...

Data processing

- Multitude of options
 - Inferences?
 - Data dredging?



		Cortex whole	Frontal lobe	Parietal lobe	Temporal lobe	Occipital lobe	Anterior cingulate	Posterior cingulate	Thalami	Hippocampi
FS5.3 with careful manual correction	HC (average [SD])	0.3313 [0.0235]	0.1207 [0.0093]	0.0805 [0.0066]	0.0752 [0.0049]	0.0315 [0.0037]	0.0034 [0.0004]	0.0034 [0.0004]	0.0105 [0.0010]	0.0059 [0.0004]
	T1D (average [SD])	0.3187 [0.0182]	0.1158 [0.0080]	0.0773 [0.0053]	0.0729 [0.0049]	0.0299 [0.0022]	0.0034 [0.0004]	0.0033 [0.0004]	0.0098 [0.0008]	0.0059 [0.0005]
	% inter-group dif. p (uncorrected)	-3.80%	-4.05%	-4.01%	-3.12%	-5.10%	1.08%	-4.64%	-6.87%	-0.17%
FS5.3 raw	HC (average [SD])	0.3341 [0.0238]	0.1173 [0.0094]	0.0756 [0.0064]	0.0761 [0.0053]	0.0329 [0.0040]	0.0034 [0.0004]	0.0035 [0.0004]	0.0102 [0.0010]	0.0058 [0.0004]
	T1D (average [SD])	0.3214 [0.0181]	0.1133 [0.0070]	0.0722 [0.0050]	0.0740 [0.0052]	0.0312 [0.0022]	0.0035 [0.0004]	0.0034 [0.0004]	0.0095 [0.0007]	0.0057 [0.0005]
	% inter-group dif. p (uncorrected)	-3.81%	-3.44%	-4.52%	-2.66%	-5.24%	1.85%	-3.82%	-6.79%	-0.53%
FS5.3 HCP	HC (average [SD])	0.3477 [0.0221]	0.1268 [0.0097]	0.0810 [0.0065]	0.0810 [0.0042]	0.0350 [0.0033]	0.0037 [0.0004]	0.0037 [0.0005]	0.0105 [0.0011]	0.0055 [0.0004]
	T1D (average [SD])	0.3394 [0.0265]	0.1243 [0.0112]	0.0780 [0.0068]	0.0791 [0.0069]	0.0335 [0.0024]	0.0037 [0.0005]	0.0035 [0.0004]	0.0098 [0.0010]	0.0056 [0.0005]
	% inter-group dif. p (uncorrected)	-2.38%	-2.01%	-3.64%	-2.41%	-4.10%	0.62%	-4.66%	-6.82%	2.10%
FS6.0	HC (average [SD])	0.3271 [0.0236]	0.1173 [0.0098]	0.0754 [0.0064]	0.0755 [0.0047]	0.0341 [0.0045]	0.0032 [0.0004]	0.0035 [0.0004]	0.0104 [0.0011]	0.0054 [0.0004]
	T1D (average [SD])	0.3218 [0.0221]	0.1156 [0.0094]	0.0730 [0.0056]	0.0746 [0.0055]	0.0332 [0.0031]	0.0033 [0.0004]	0.0034 [0.0004]	0.0097 [0.0010]	0.0055 [0.0004]
	% inter-group dif. p (uncorrected)	-1.62%	-1.50%	-3.27%	-1.25%	-2.51%	2.45%	-1.43%	-6.96%	1.22%
FS7.1	HC (average [SD])	0.3276 [0.0289]	0.1194 [0.0113]	0.0756 [0.0074]	0.0734 [0.0059]	0.0327 [0.0048]	0.0032 [0.0004]	0.0034 [0.0004]	0.0107 [0.0012]	0.0056 [0.0005]
	T1D (average [SD])	0.3202 [0.0284]	0.1163 [0.0117]	0.0735 [0.0066]	0.0718 [0.0069]	0.0316 [0.0035]	0.0032 [0.0005]	0.0033 [0.0004]	0.0102 [0.0011]	0.0057 [0.0006]
	% inter-group dif. p (uncorrected)	-2.27%	-2.60%	-2.90%	-2.27%	-3.42%	1.86%	-1.32%	-4.61%	1.25%

Aftermath...

Editorial FREE

Dimitri M Kullmann

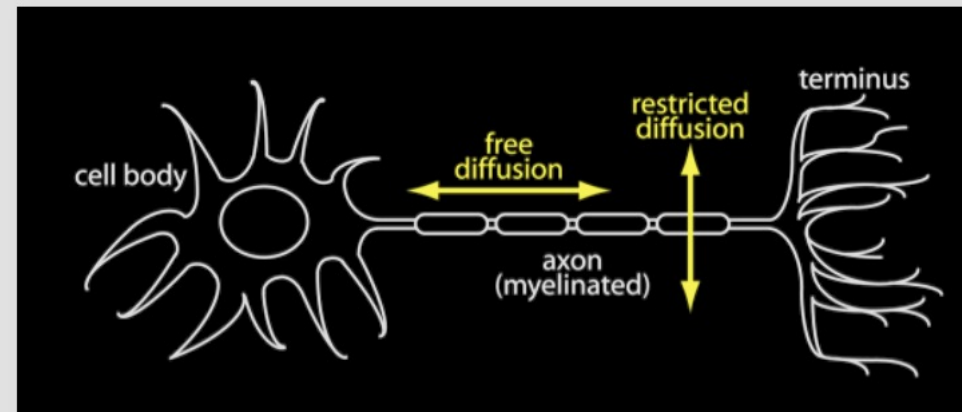
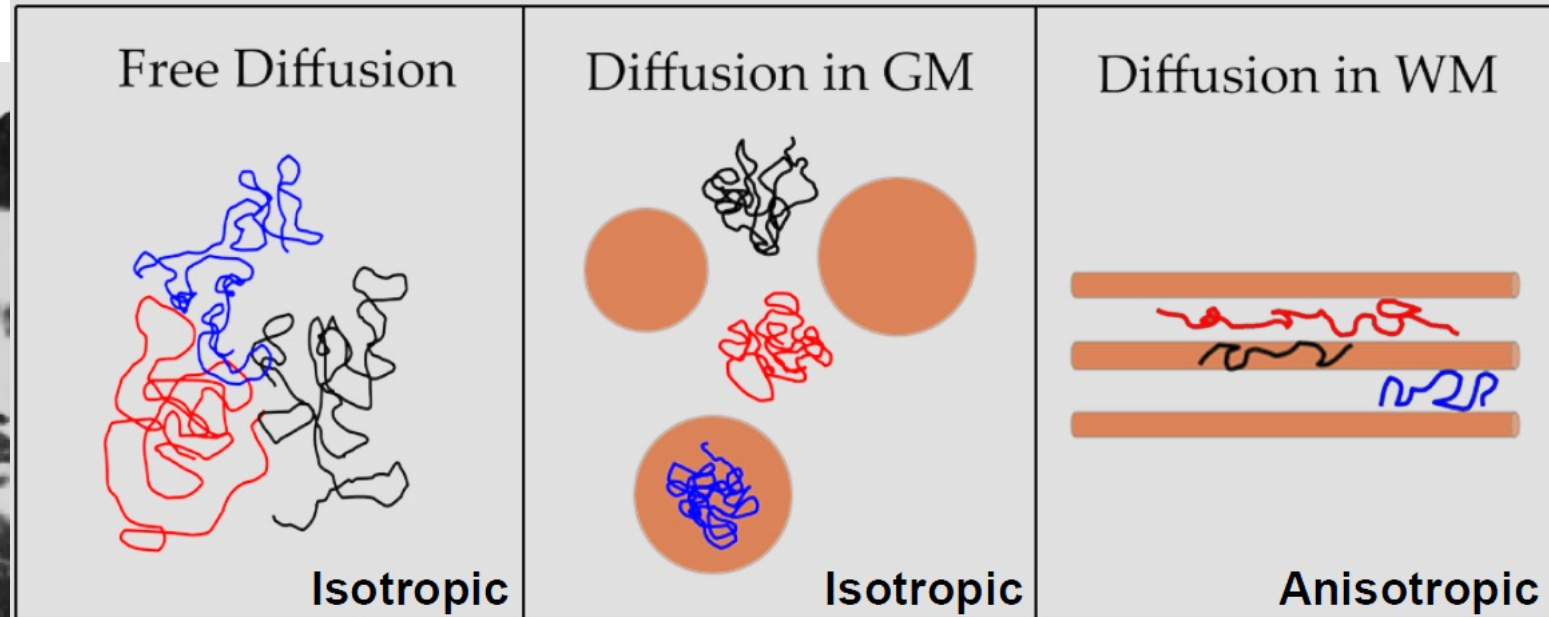
Brain, Volume 143, Issue 4, April 2020, Page 1045,

<https://doi.org/10.1093/brain/awaa082>

Published: 21 April 2020

Brain receives far more manuscript submissions than can reasonably be sent for formal peer review. Although the reasons for editorial rejection are diverse and include such factors as under-powered study design, limited conceptual novelty or remoteness from clinical translation, the motivation behind the authors' work is rarely in doubt. Nevertheless, there remains a small number of submissions where the route to clinical application or to improved understanding of disease mechanisms is very difficult to infer, leaving one asking, 'Why did the authors undertake this work in the first place?' Such manuscripts disproportionately report on functional MRI in groups of patients without a discernible hypothesis. **Showing that activation patterns or functional connectivity motifs differ significantly is, on its own, insufficient justification to occupy space in *Brain*.** Given that functional MRI is ~30 years old and continues to divert many talented young researchers from careers in other fields of translational neuroscience, it is worth reiterating two of the most troubling limitations of the method (and these are not the notorious pitfalls such as failure to correct for multiple comparisons or circular inference). First, the fundamental relationship between the blood oxygenation level-dependent (BOLD) signal and neuronal computations remains a complete mystery. As a direct consequence, it is extremely difficult to conclude that functional connectivity as measured by functional MRI genuinely measures information exchange between brain regions. Second, effect sizes are quasi-impossible to infer, leading to an anomaly in science where statistical significance remains the only metric reported. A

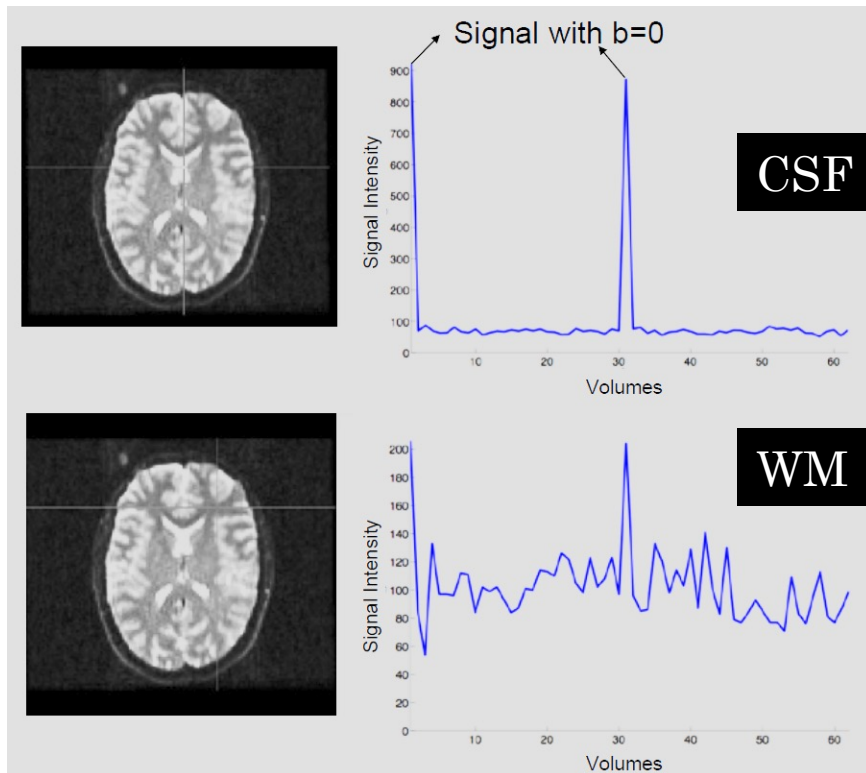
DWI



DWI

- Diffusion weighting is modulated by:
 - Gradient strength
 - Diffusion time
 - Gradient orientation

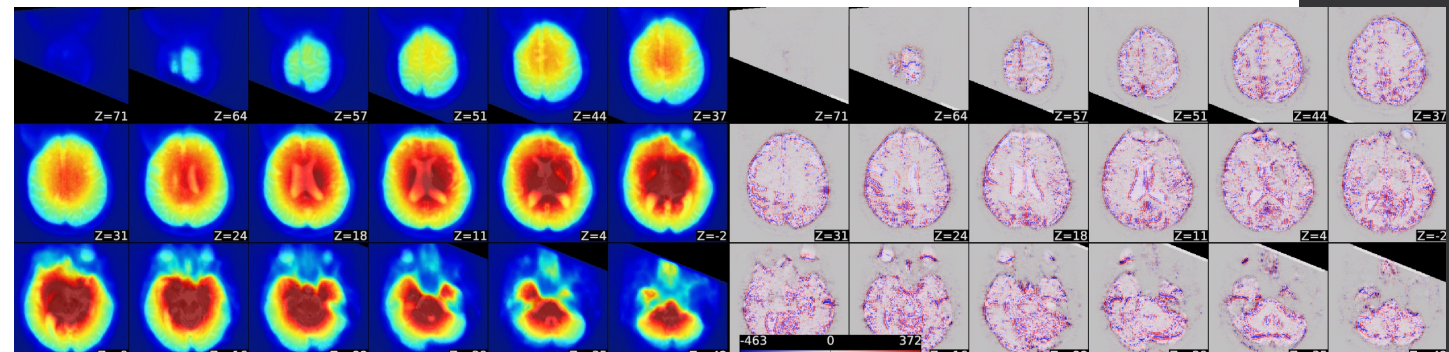
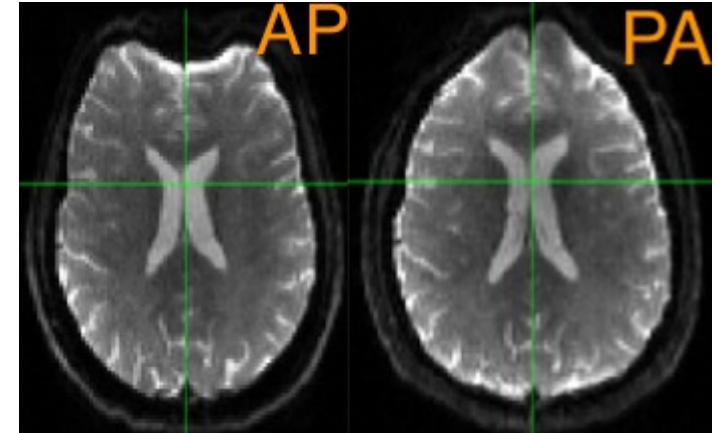
- Images acquired with a gradient along x have contrast sensitive to the diffusion of water molecules along x.



- Utilisation
 - DTI
 - Kurtosis
 - NODDI
 - Fiber orientation distribution / density
 - Tractography
 -

Problems with MRI data

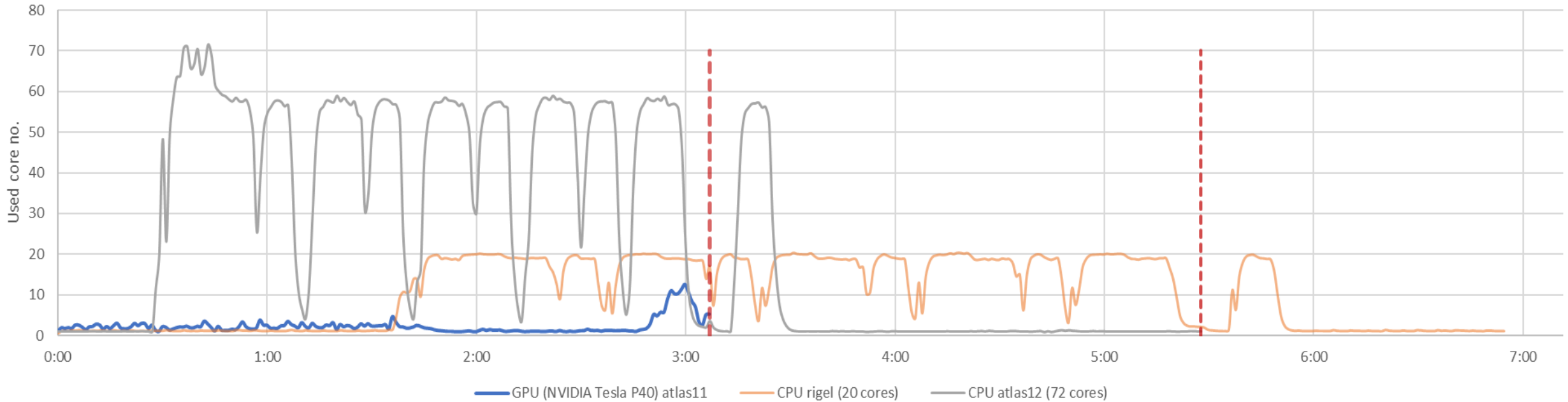
- Noise, artifacts (Gibbs ringing, standing waves, chemical shifts, magic angle...)
- Gradient non-linearities
- Distortions
 - Susceptibility-induced
 - Eddy current-induced
- Subject movement
 - Gross movement
 - Intra-volume movement
 - i.e. movement within the bias field and changes of the susceptibility field
- Intra-volume temporal differences
- Signal dropouts
- Cardiac and respiratory cycle
- Blood and CSF flow



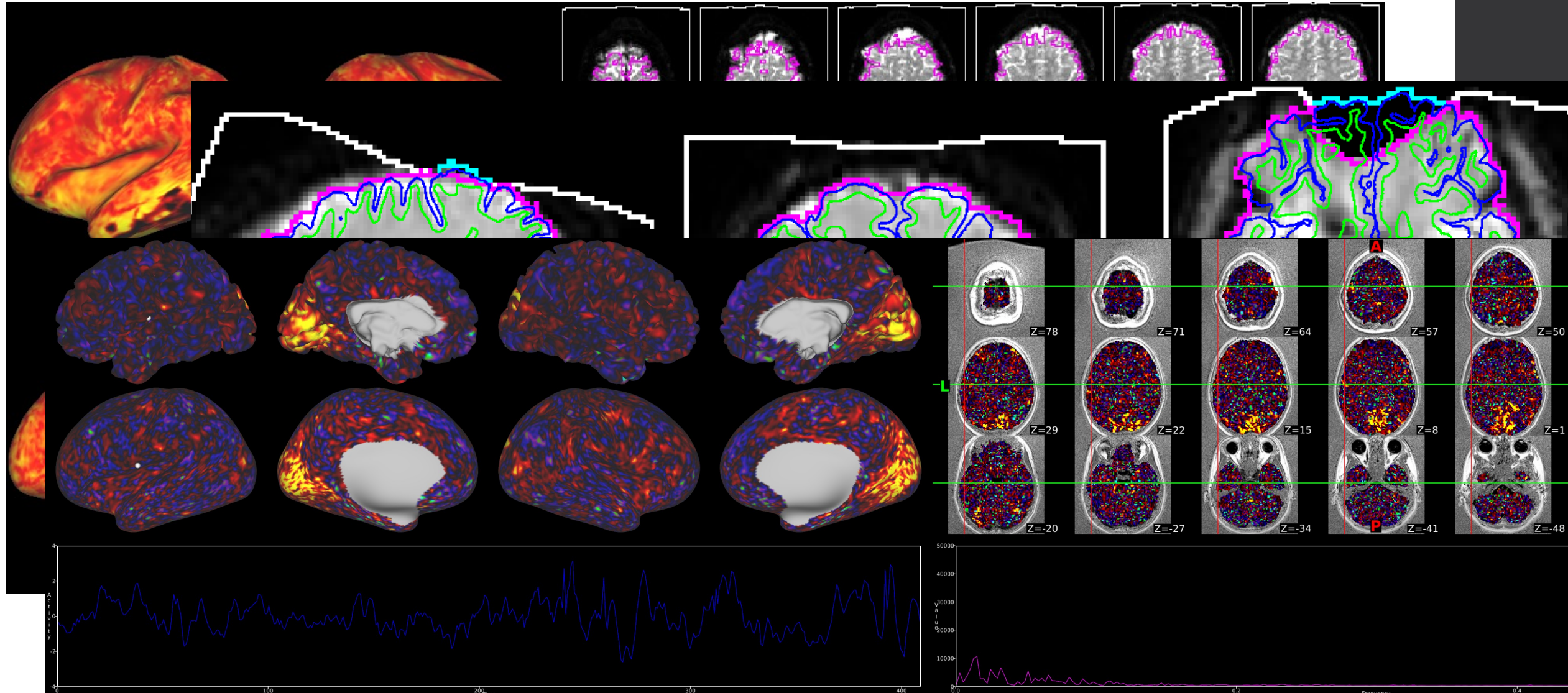
Computing power requirements

CPU load comparison during DWI

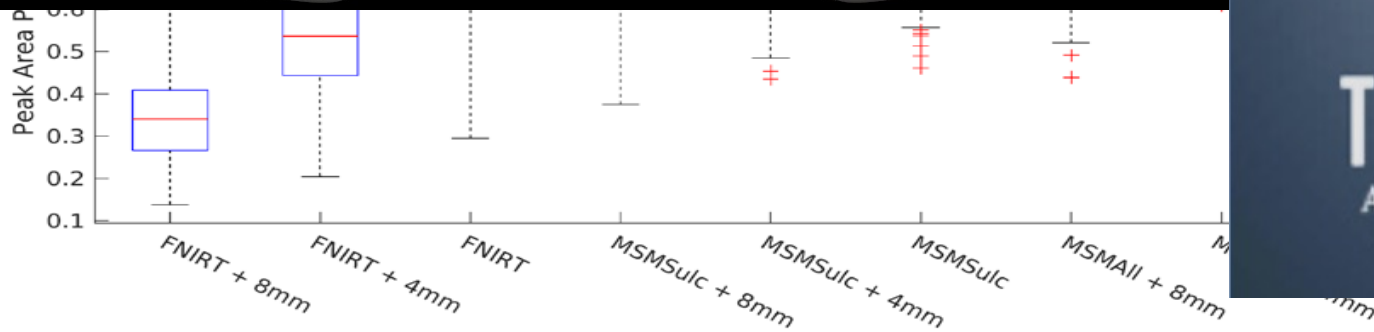
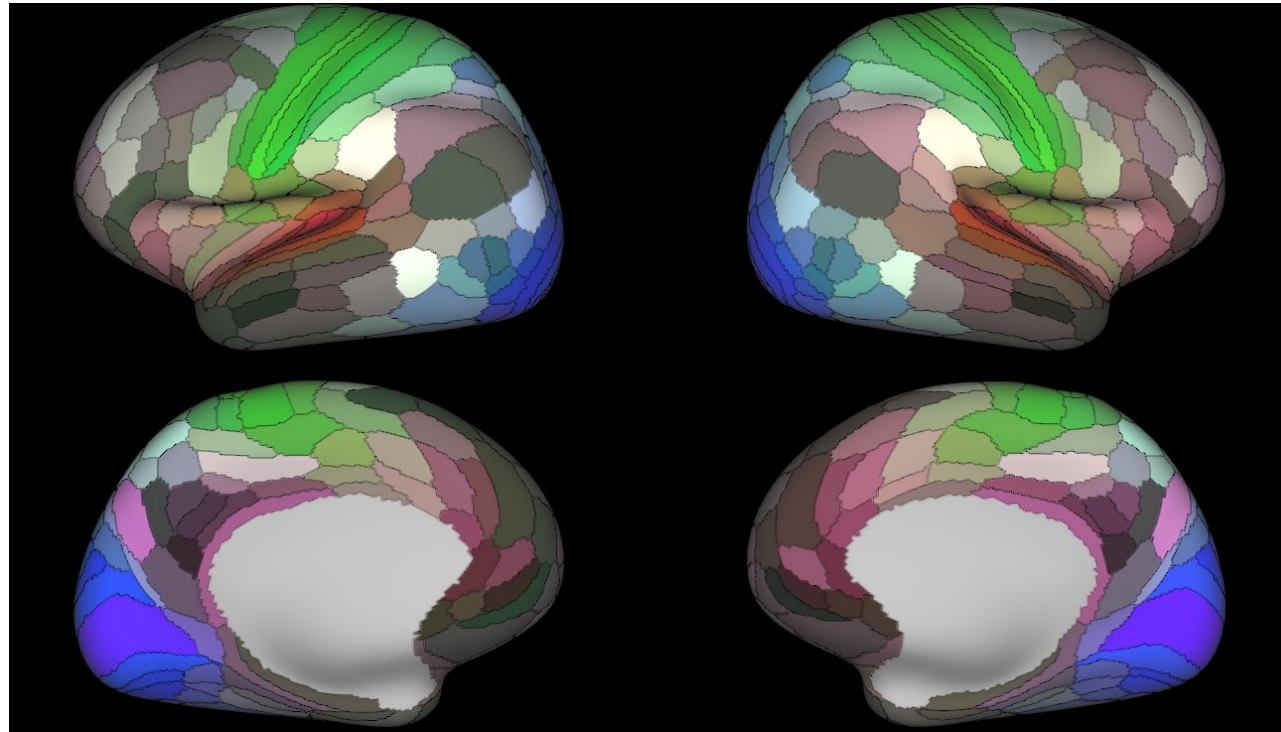
red lines mark the completion of GPU and 72-core CPU processing



Quality control

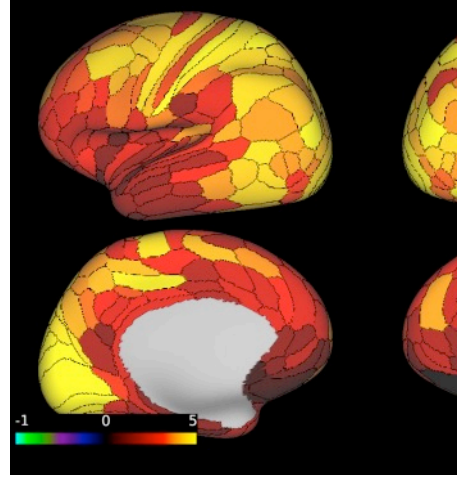


Group analysis and brain parcellation

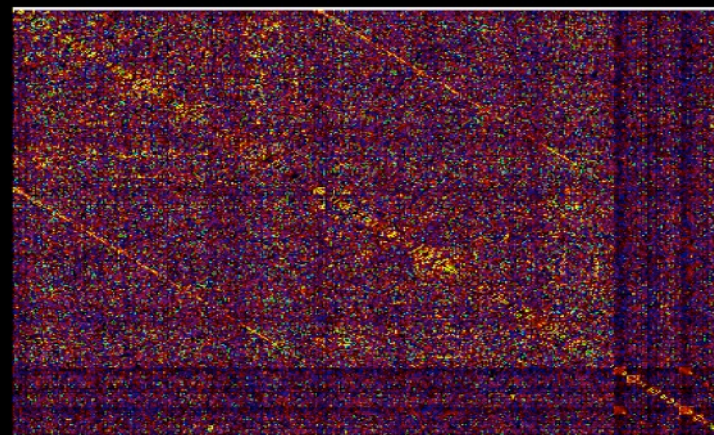
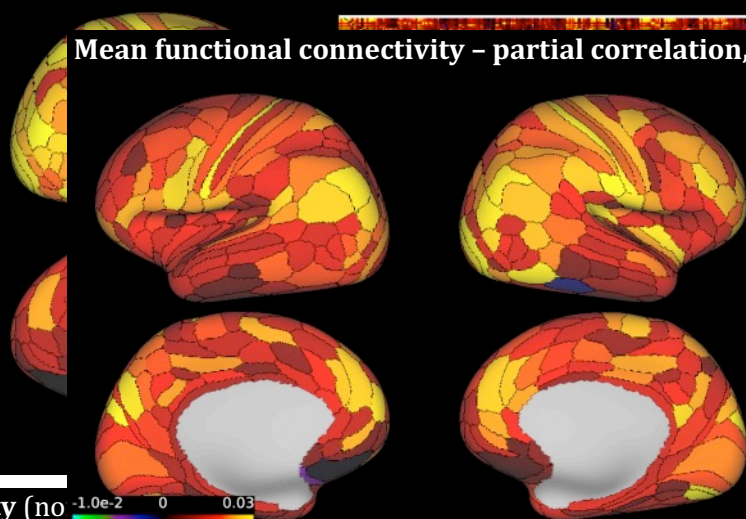


Connectome matrices

Mean functional connectivity (correlation of signal courses)

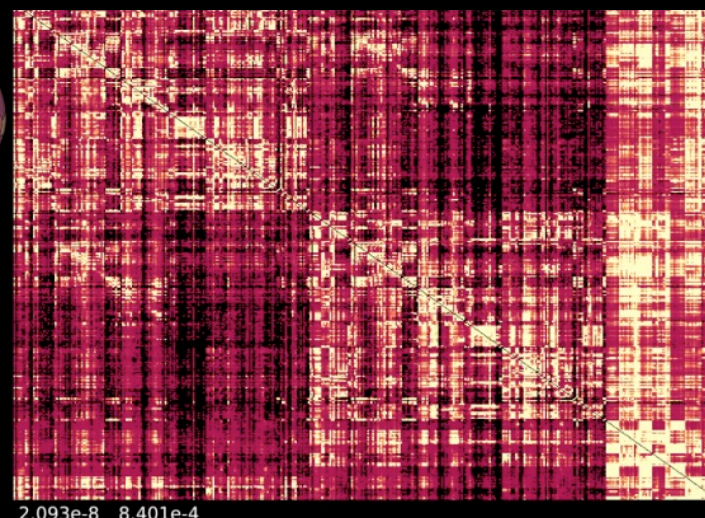
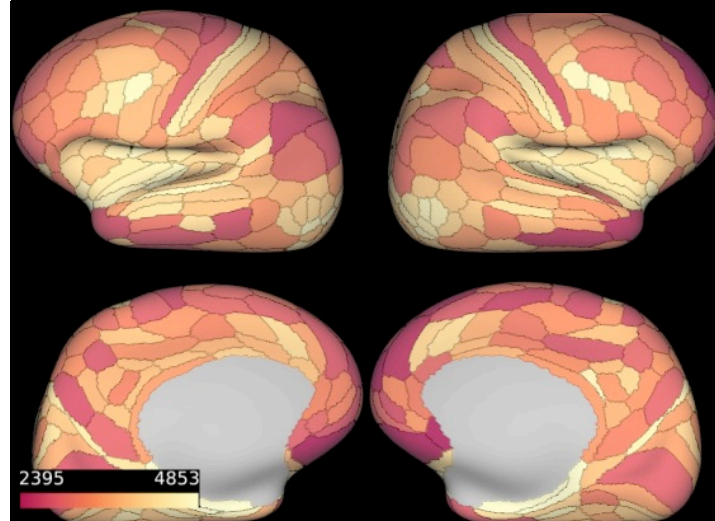


Mean functional connectivity - partial correlation, regularised using ridge regression



Mean structural connectivity (no

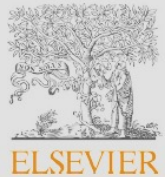
-1.0e-2 0 0.03



Utilisation in real studies

Structural connectome of tremor

Parkinsonism and Related Disorders 95 (2022) 28–34



Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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



Tremor associated with similar structural networks in Parkinson's disease and essential tremor

Pavel Filip^{a,b,*}, Kristína Burdová^a, Zdeněk Valenta^c, Robert Jech^a, Viktória Kokošová^d, Marek Baláz^e, Silvia Mangia^b, Shalom Michaeli^b, Martin Bareš^{e,f}, Lubomír Vojtíšek^g

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ARTICLE INFO

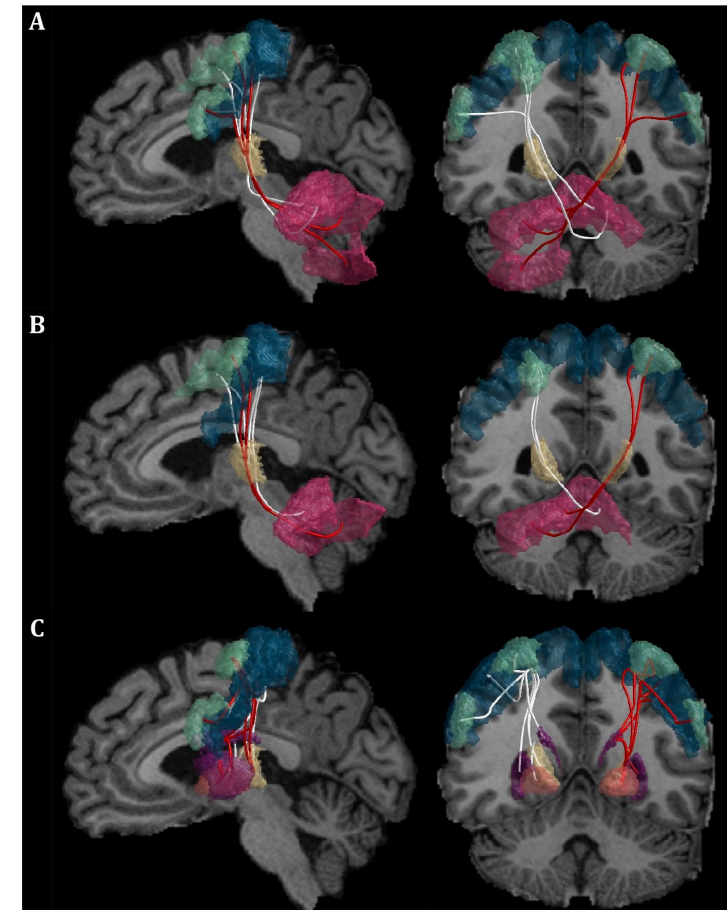
Keywords:

Tremor
Probabilistic tractography
Structural connectome
Parkinson's disease
Essential tremor

ABSTRACT

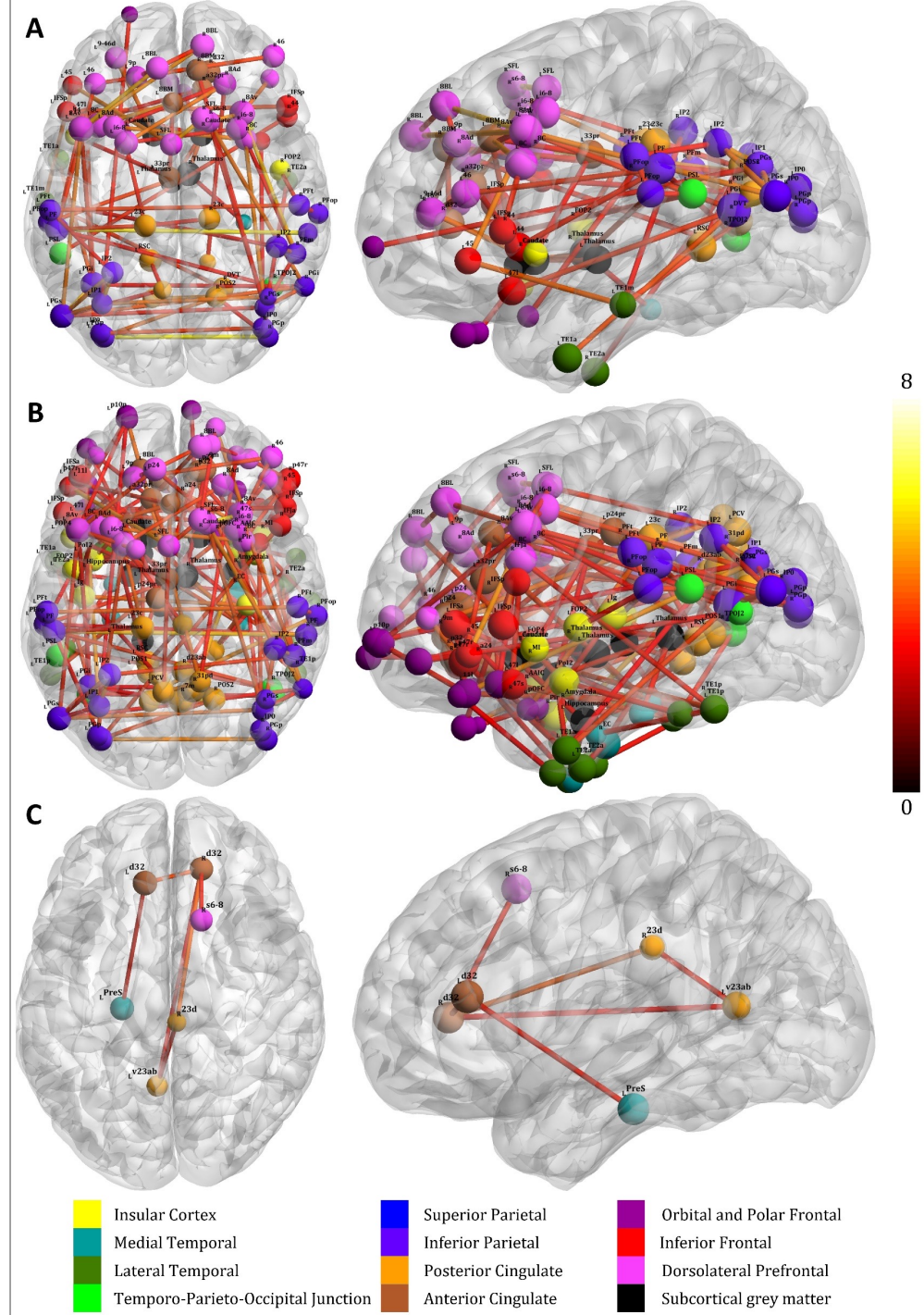
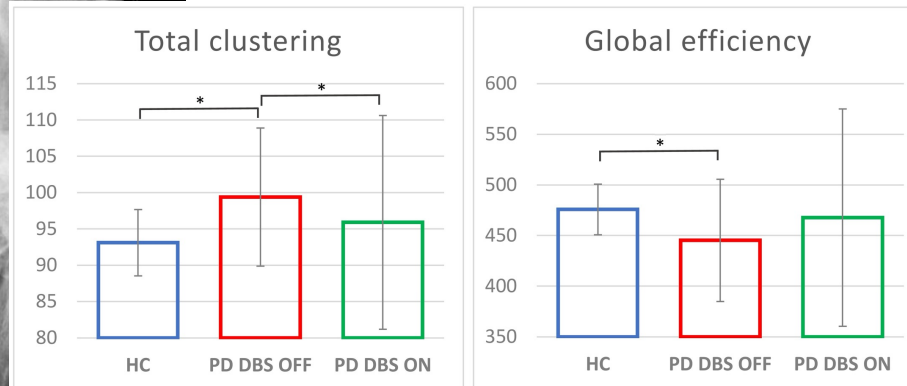
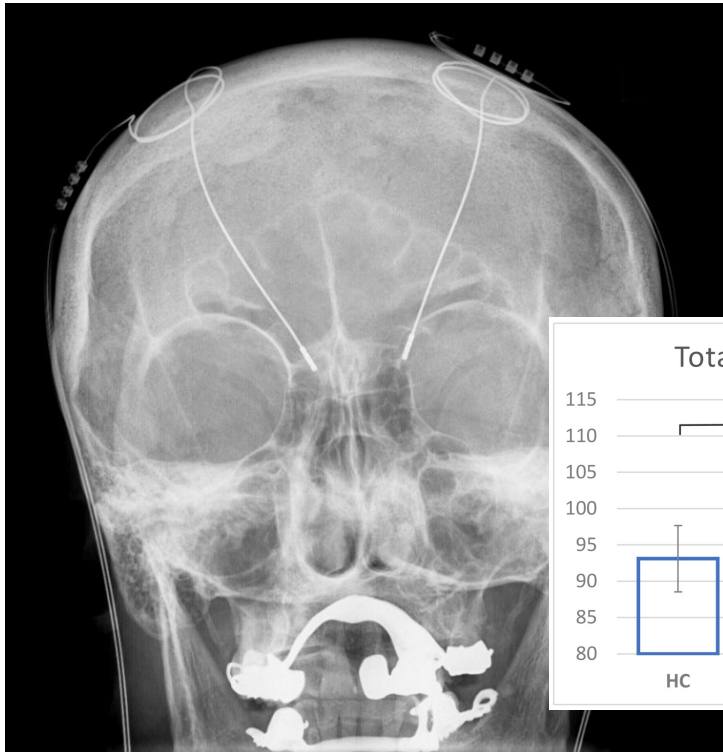
Introduction: Despite substantial clinical and pathophysiological differences, the characteristics of tremor in Parkinson's disease (PD) and essential tremor (ET) patients bear certain similarities. The presented study delineates tremor-related structural networks in these two disorders.

Methods: 42 non-advanced PD patients (18 tremor-dominant, 24 without substantial tremor), 17 ET, and 45 healthy controls underwent high-angular resolution diffusion-weighted imaging acquisition to reconstruct their structural motor connectomes as a proxy of the anatomical interconnections between motor network regions, implementing state-of-the-art globally optimised probabilistic tractography.



Utilisation in real studies

Functional connectome of DBS effect



MRI connectomics



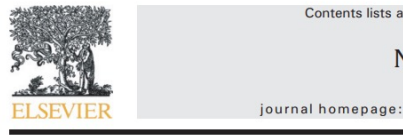
Major brain functions are network-based, not focal

“Soft-science” problem

Still distinguishing between macro / meso / micro-connectome

Further literature...

NeuroImage 80 (2013) 105–124



The minimal preprocessing pipelines

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^a Department of Anatomy and Neurobiology, Washington University Medical School
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^d Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology,
^e Computer Science and AI Lab, Mass. Institute of Technology, Cambridge, MA, US
^f Center for Magnetic Resonance Research, University of Minnesota Medical School
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ARTICLE INFO

Article history:
 Accepted 30 April 2013
 Available online 11 May 2013

Keywords:
 Human Connectome Project
 Image analysis pipeline
 Surface-based analysis
 fMRI
 Grayordinates
 Multi-modal data integration

ABSTRACT

The Human Connectome Project (HCP) provides a rich set of subjects. The MRI scanners and often pipelines for structural level tasks, including surface-based analysis to standardize the HCP. The final grayordinate spatial series while reducing the number of voxels we provide the minimal advice for its use. Finally, we discuss

Introduction and rationale

The Washington University–University of Minnesota Human Connectome Project Consortium (WU–Minn HCP) (D. Van Essen 2012) is charged with bringing data from the major MRI neuroimaging modalities, structural, functional, and diffusion, together into a common framework to enable cross-subject comparisons and multi-analysis of brain architecture, connectivity, and function. Specific imaging modalities include T1-weighted (T1w) and T2-weighted (T2w) structural scans, resting-state and task-based functional scans, and diffusion-weighted MRI scans. Additionally, the HCP is committed to making these complex datasets publicly available and

NeuroImage 80 (2013) 144–168



Resting-state fMRI in the Human Connectome Project

Stephen M. Smith^{a,*}, Christian F. Beckmann^c, Jesper Andersson^b, Gwenaëlle Douaud^a, Eugene Duff^a, David A. Feinberg^d, Ludw. Michael Kelly^a, Timothy Laumann^f, Karla L. Miller^a, Steen N. Gholamreza Salimi-Khorshidi^a, Abraham Z. Snyder^f, An T. V. Essa Yacoub^b, Kamil Ugurbil^b, David C. Van Essen^f, Matthew

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ARTICLE INFO

Article history:
 Accepted 6 May 2013
 Available online 20 May 2013

ABSTRACT

Resting-state functional magnetic resonance brain by acquiring fMRI data while subjects functionally related brain regions spontaneously being acquired for the Human Connectome Project. We provide a detailed in vivo mapping of functional-to make these datasets freely available to the community. The total of 1 h of whole-brain fMRI data at 0.7 s, capitalizing on recent developments of the cohort at higher field strength and decisions taken regarding the fMRI data. Initial results showing data quality and

Introduction

The term “connectome” (Sporns et al., 2005) refers to the mapping of connectivity throughout the brain using such imaging modalities as resting-state functional magnetic resonance imaging (rsfMRI) and diffusion MRI. rsfMRI is used to study connectivity in the brain by acquiring fMRI data from a subject lying “at rest” in the scanner, and utilising the fact that the spontaneous timeseries from functionally related brain regions are correlated (Biswal et al., 1995; De Luca et al., 2005; Fox and Raichle, 2007; Fox et al., 2005; Greicius et al.,

of con allow (and, i dent c al., 2001 estimate level o ever, n indirect

ARTICLE

A multi-modal parcellation of the cerebral cortex

Matthew F. Glasser¹, Timothy S. Coalson^{1,*}, Emma C. Robinson^{2,3,*}, Carl D. Hacker⁴, Kamil Ugurbil⁵, Jesper Andersson², Christian F. Beckmann^{6,7}, Mark Jenkinson^{2,5}

Understanding the amazingly complex human cerebral cortex requires a multi-modal approach. Making an accurate areal map has been a century-old problem. Here, we present a multi-modal parcellation of the cerebral cortex. We delineated 180 areas per hemisphere bounded by function, connectivity, and/or topography in a precisely aligned group of subjects. We used a machine-learning classifier to recognize the multi-modal parcellation. This classifier detected the presence of 96.6% of the cortical areas in new subjects. This will enable substantially improved neuroanatomical precision for studies of the human cerebral cortex and its variation across individuals and in development.

Neuroscientists have long sought to subdivide the human brain into a mosaic of anatomically and functionally distinct, spatially contiguous areas (cortical areas and subcortical nuclei), as a prerequisite for understanding how the brain works. Areas differ from their neighbours in microstructural architecture, functional specialization, connectivity with other areas, and/or orderly intra-area topographic organization (for example, the map of visual space in visual cortical areas)^{1–3}. Accurate parcellation provides a map of where we are in the brain, enabling efficient comparison of results across studies and communication among investigators; as a foundation for illuminating the functional and structural organization of the brain; and as a means to reduce data complexity while improving statistical sensitivity and power for many neuroimaging studies.

The human cerebral cortex has been estimated to contain anywhere from ~50 (ref. 1) to ~200 (refs 3, 4) areas per hemisphere. However, attaining a consensus whole-cortex parcellation has been difficult because of practical and technical challenges that we address here.

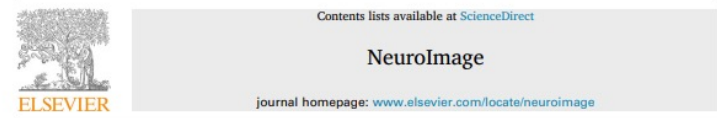
Most previous parcellations were based on only one neurobiological property (such as architecture, function, connectivity or topography), and many cover only part of the cortex. Combining multiple properties provides complementary as well as confirmatory information, as different properties distinguish different sets of areal boundaries, and more confidence can be placed in boundaries that are consistent

derived from T1 images^{5,6,10}. Cortical areas (cortical areas and subcortical nuclei), as a prerequisite for understanding how the brain works. Areas differ from their neighbours in microstructural architecture, functional specialization, connectivity with other areas, and/or orderly intra-area topographic organization (for example, the map of visual space in visual cortical areas)^{1–3}. Accurate parcellation provides a map of where we are in the brain, enabling efficient comparison of results across studies and communication among investigators; as a foundation for illuminating the functional and structural organization of the brain; and as a means to reduce data complexity while improving statistical sensitivity and power for many neuroimaging studies.

The human cerebral cortex has been estimated to contain anywhere from ~50 (ref. 1) to ~200 (refs 3, 4) areas per hemisphere. However, attaining a consensus whole-cortex parcellation has been difficult because of practical and technical challenges that we address here.

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NeuroImage 183 (2018) 972–984



Extending the Human Connectome Project across ages: Imaging protocols for the Lifespan Development and Aging projects

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ARTICLE INFO

ABSTRACT