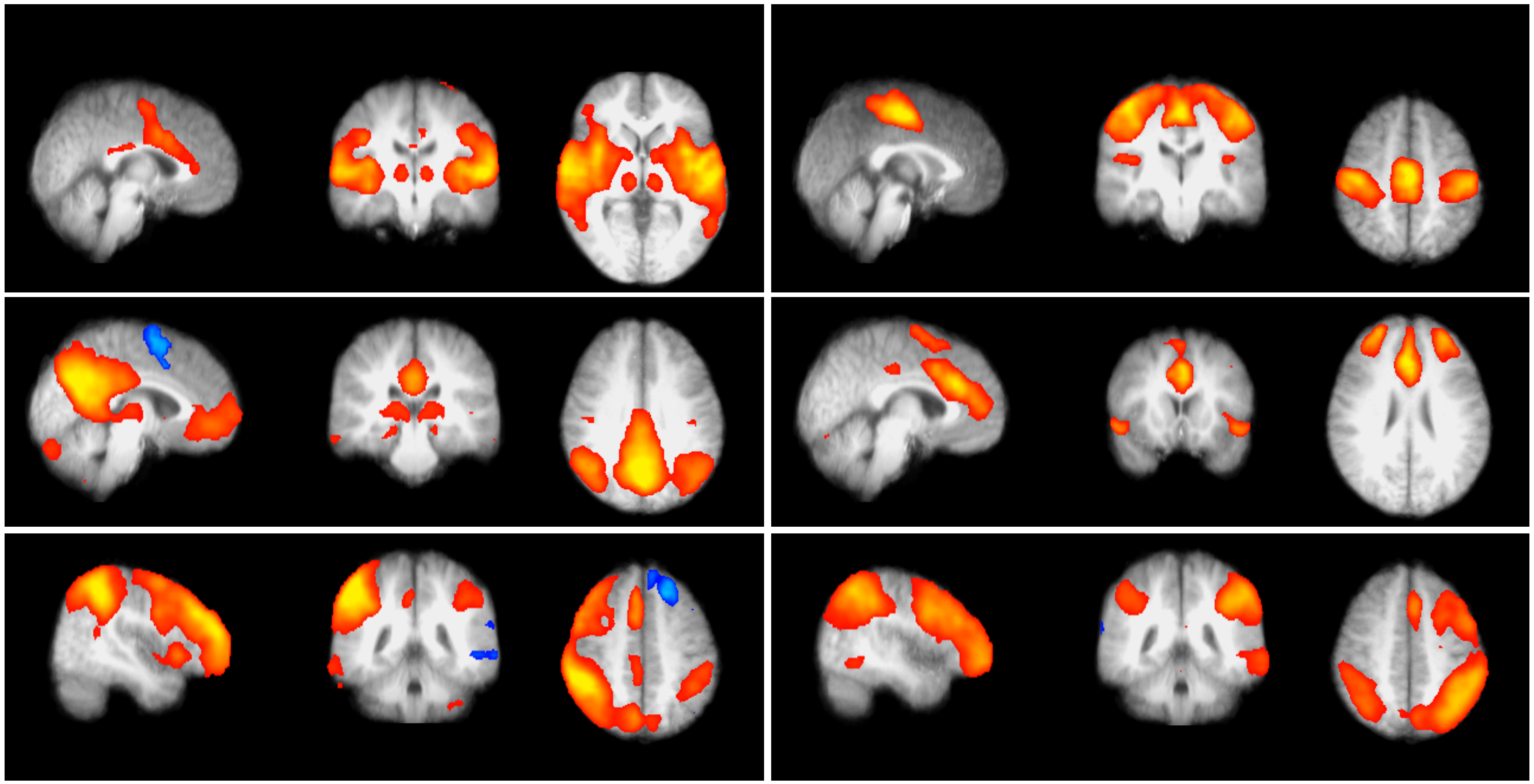
HCP Course 2015

rFMRI background, preprocessing, denoising

Stephen Smith, FMRIB Oxford

Resting-State Networks

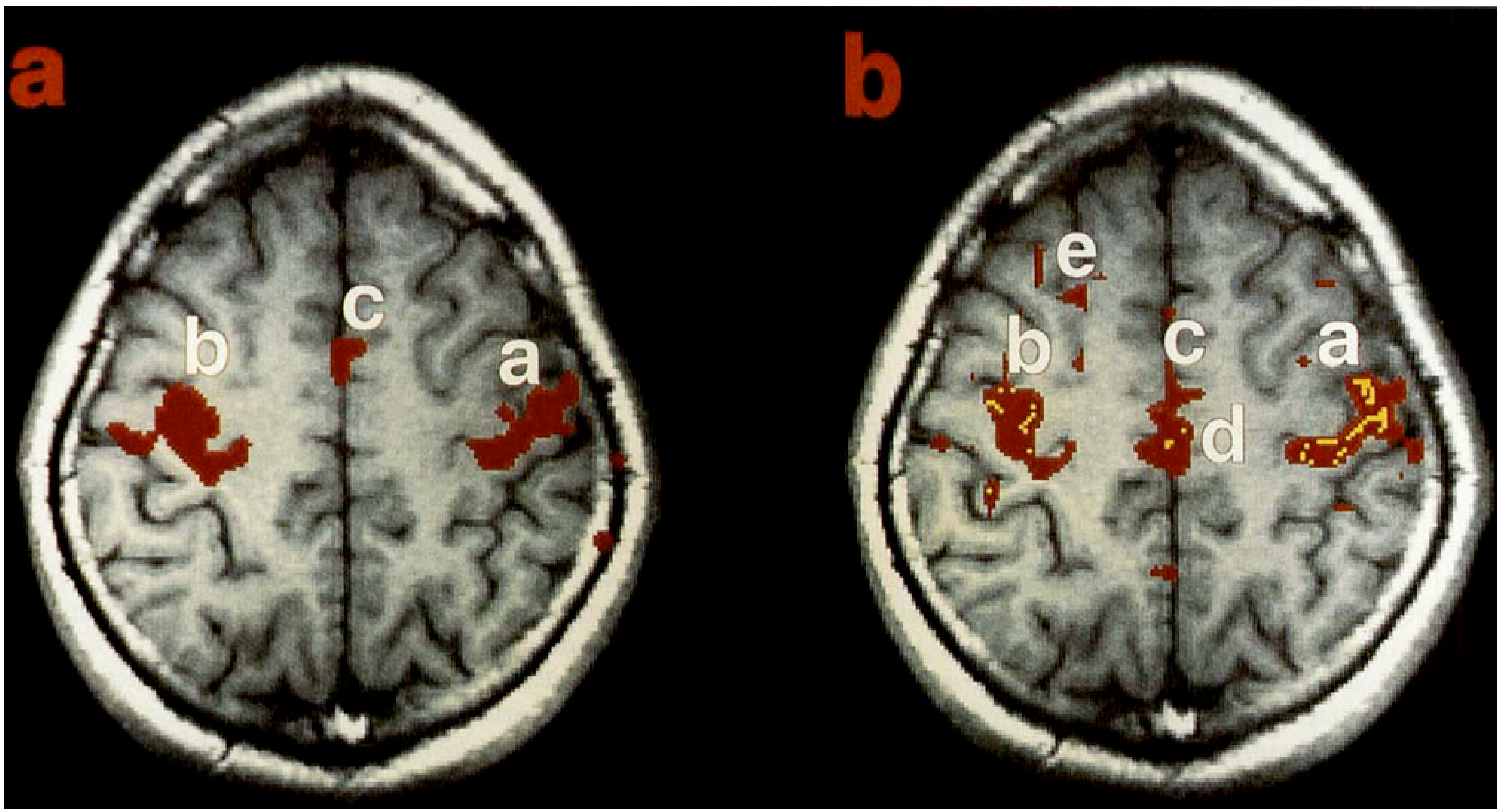


- *Spatial patterns* of correlated temporal dynamics, resembling activation maps
- can be found in FMRI data (BOLD & ASL) obtained under stimulation *and* in resting data
- often described as having low frequency power spectra

Correlations in spontaneous temporal fluctuations

Activation maps from a finger tapping experiment

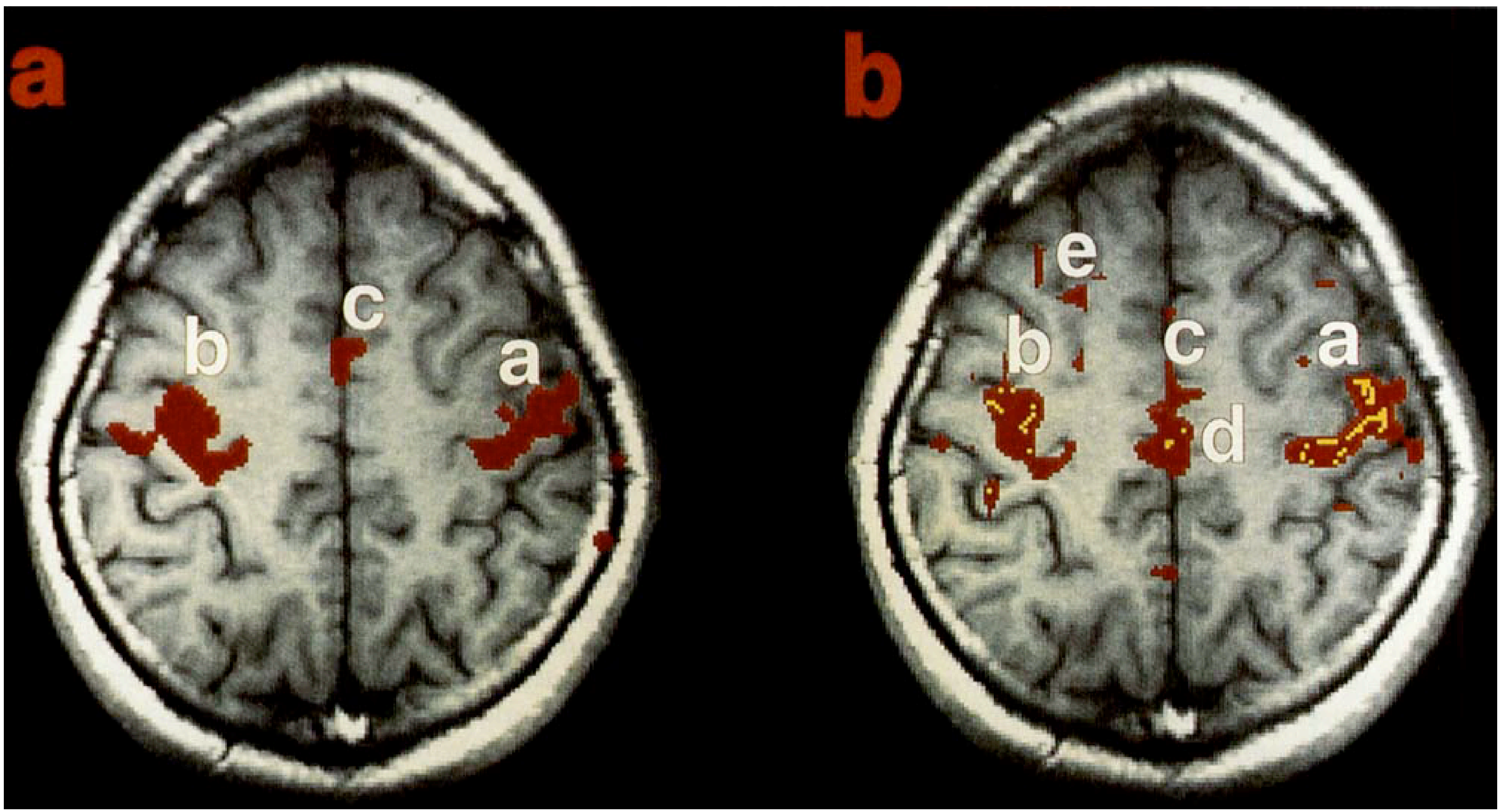
Correlation maps from a resting state experiment



• *Biswal MRM 1995*

Spontaneous correlations = functional connectivity?

- Two areas correlate because they are functionally linked
- Not surprising that this is seen in “resting” data



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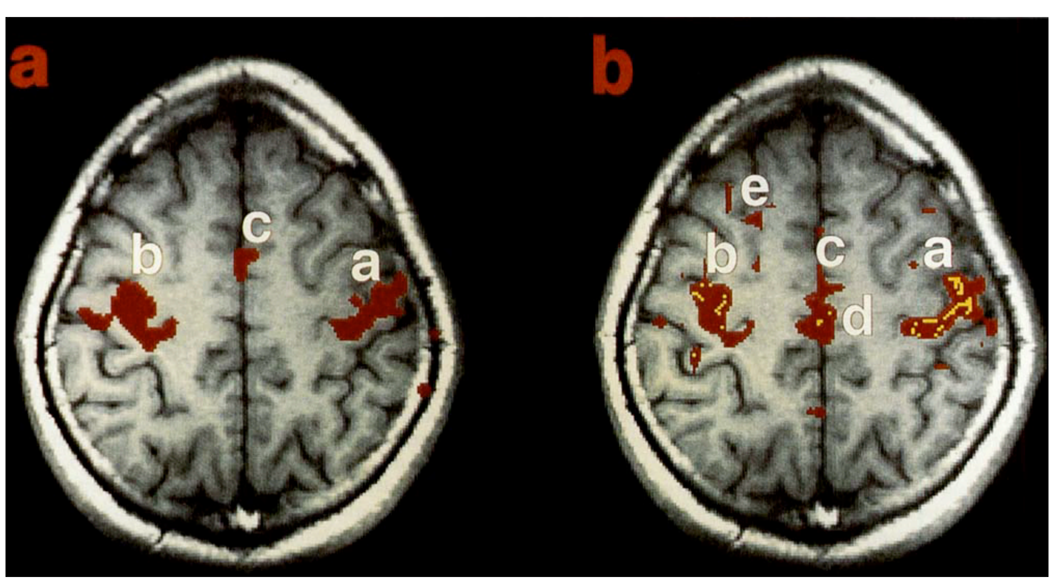
- “functional connectivity” = correlation
  = direct **or** indirect connection

- “effective connectivity” = direct/causal connection



- *Friston HBM 1994*

Spontaneous correlations = functional connectivity?

- Two areas correlate because they are functionally linked
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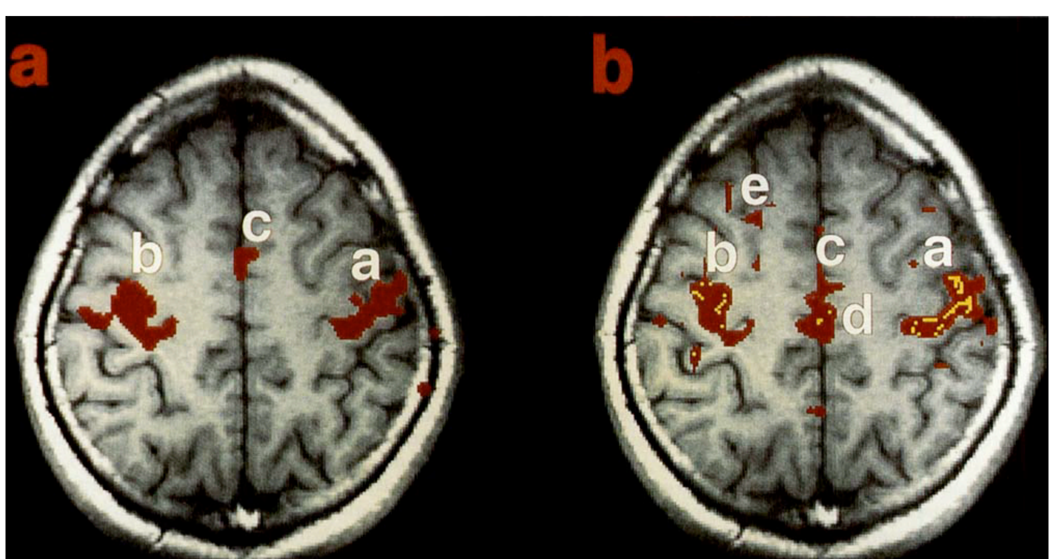
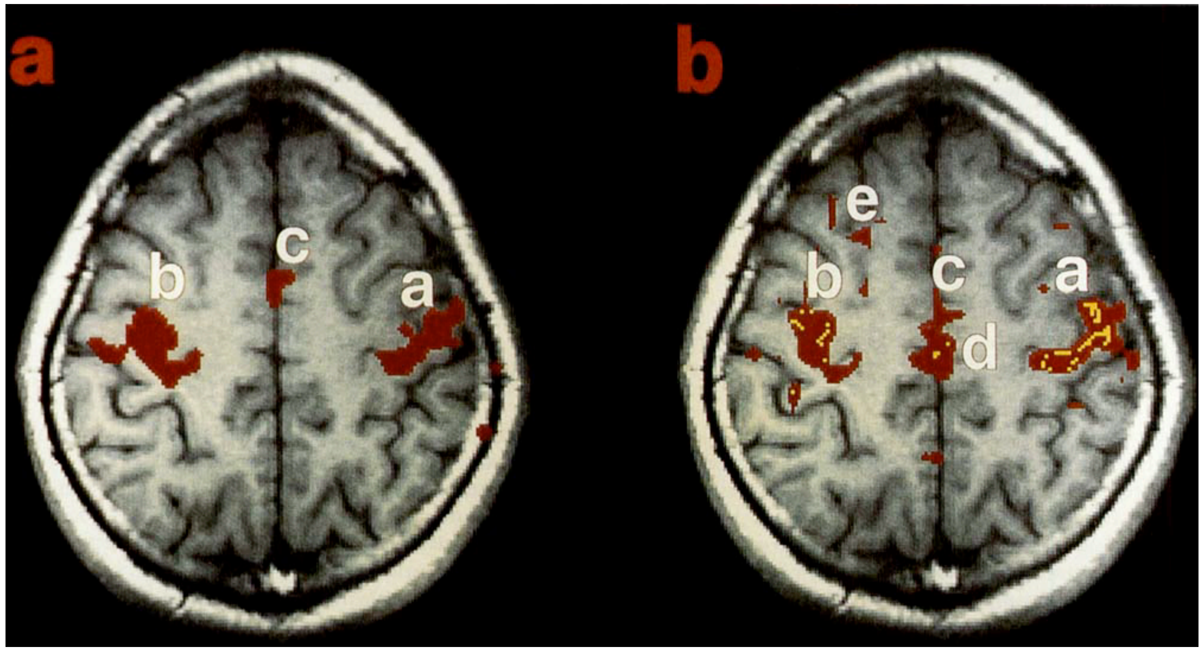
- “functional connectivity” = correlation
  = direct or indirect connection
  - easy to estimate, less meaningful

- “effective connectivity” = direct/causal connection
  - more meaningful, harder to estimate

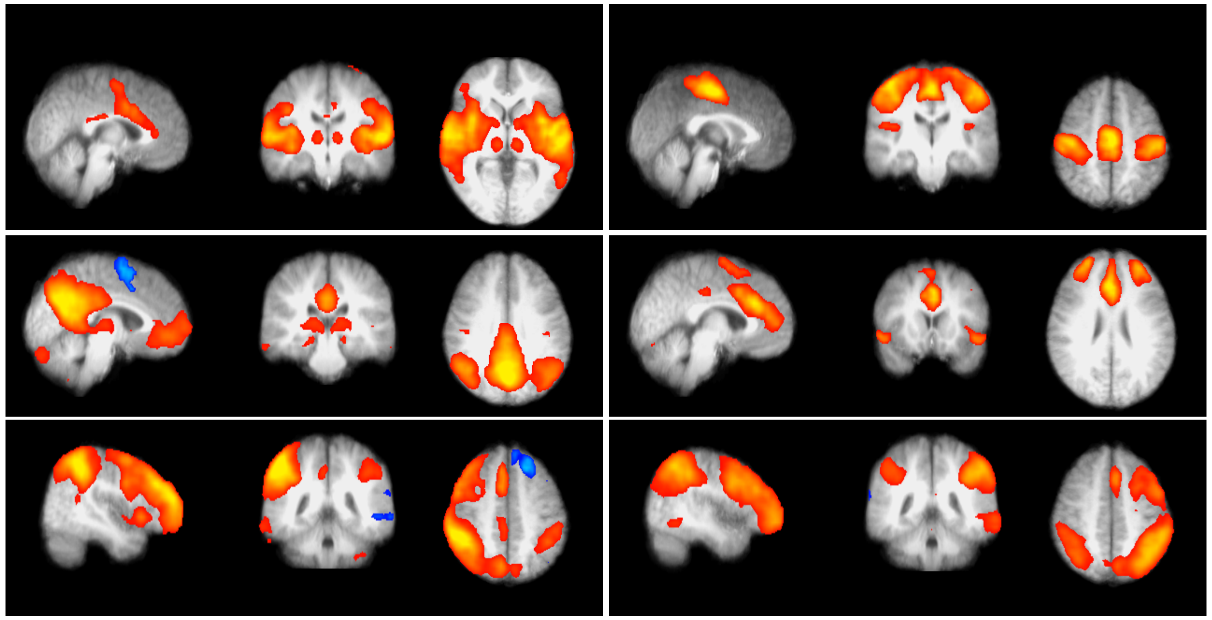


Popular methods for analysing resting FMRI data

- Seed-based correlation

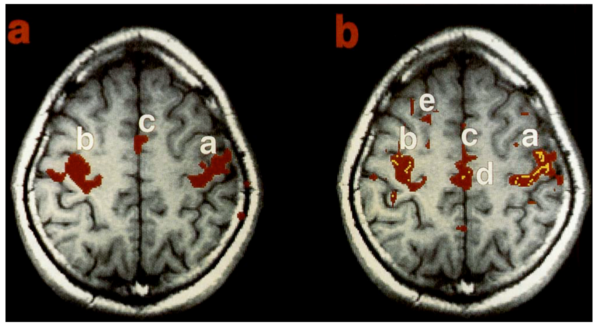


- ICA(independent component analysis)

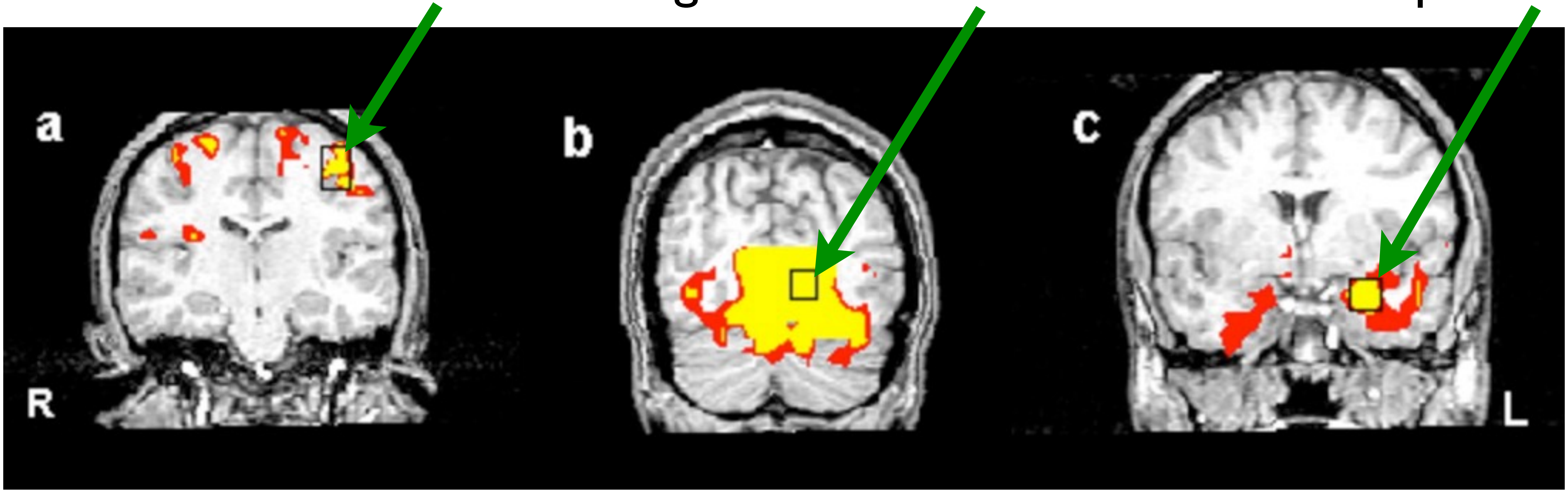


- *review papers*
  - *Calhoun NeuroImage 2008*
  - *Cole Frontiers Sys Neur 2010*

- Seed-based correlation

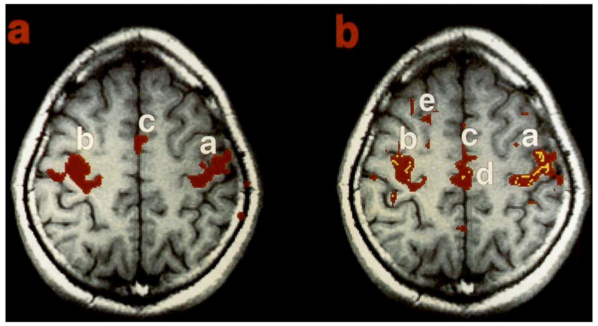


- Different seed locations generate different correlation maps



- *Lowe NeuroImage 1998*

- Seed-based correlation



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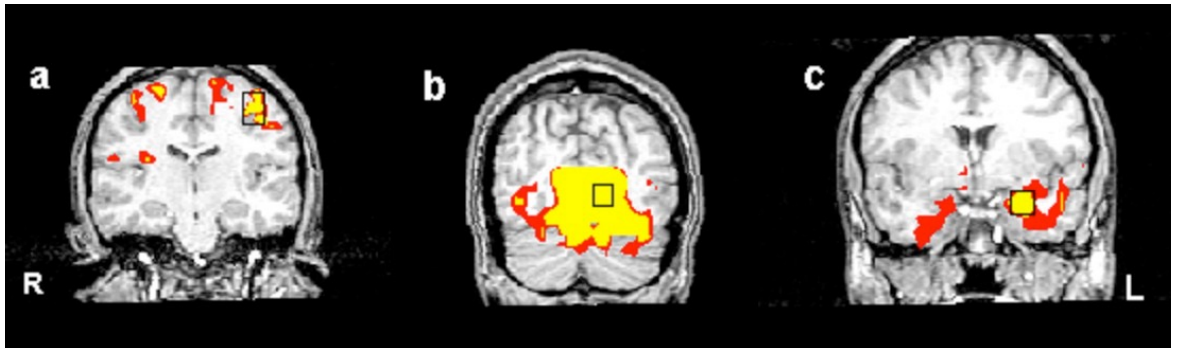
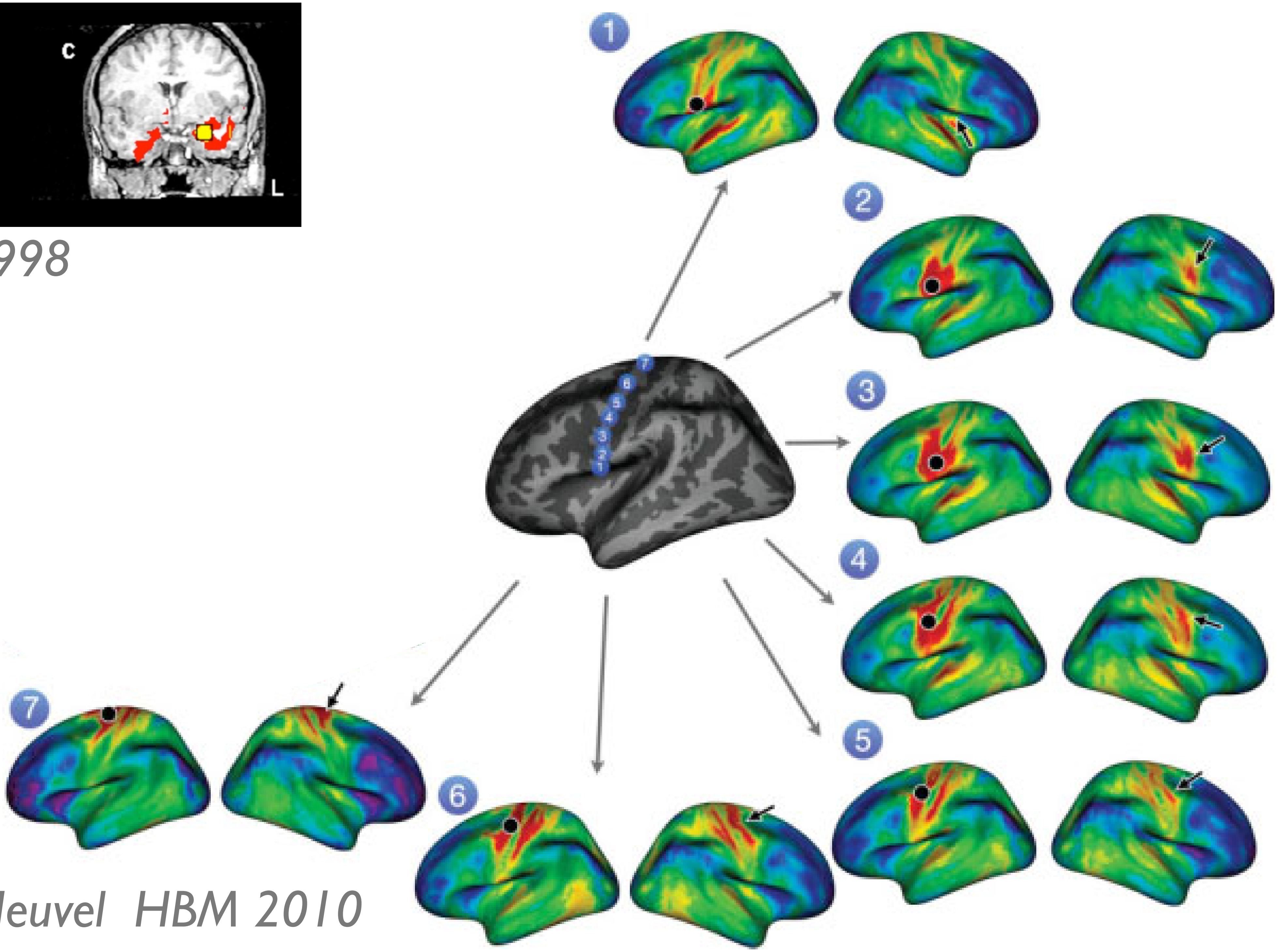


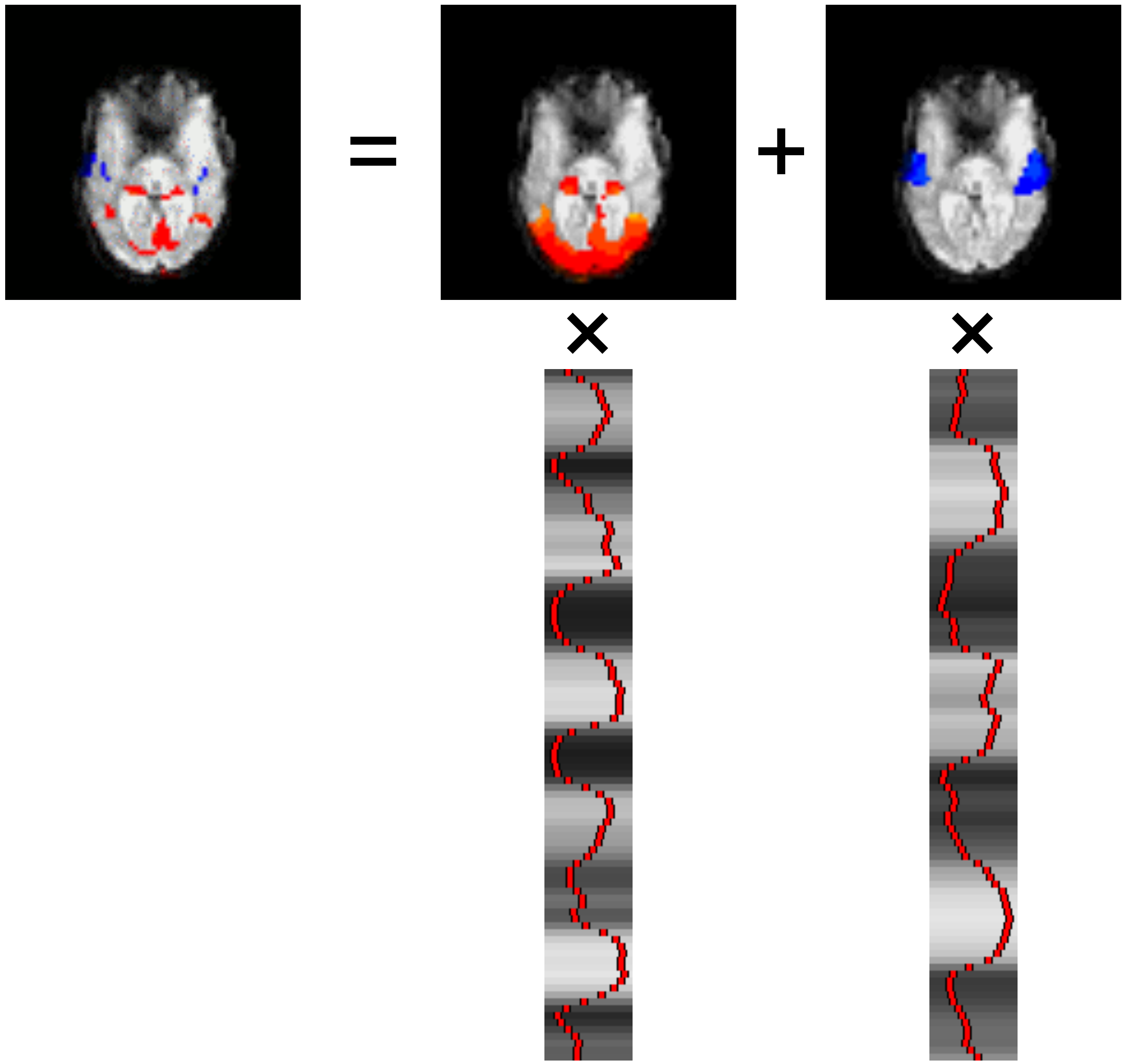
- *Lowe NeuroImage 1998*



- *van den Heuvel HBM 2010*

ICA

ICA decomposes data into a set of distinct spatial maps, each with its own distinct timecourse



- *ICA*
  - *Comon Signal Processing 1994*
  - *Bell Neural Computation 1995*
- *ICA for FMRI*
  - *McKeown Human Brain Mapping 1998*
- *ICA for resting FMRI networks*
  - *Kiviniemi NeuroImage 2003*

- *ICA for FMRI - software*
  - *MELODIC in FSL (Beckmann)*
  - *GIFT (Calhoun)*
  - *BrainVoyager (Formisano)*

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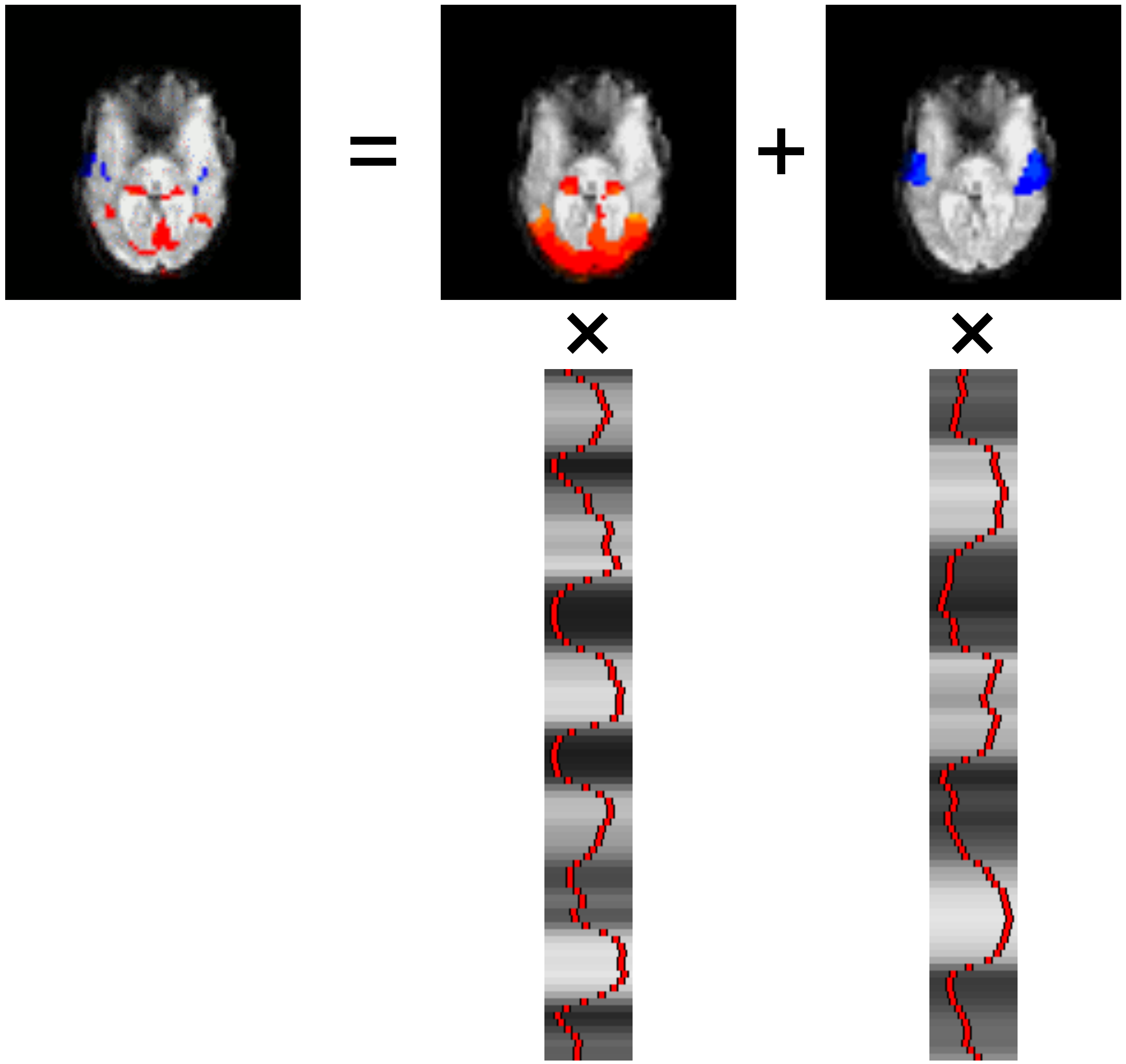

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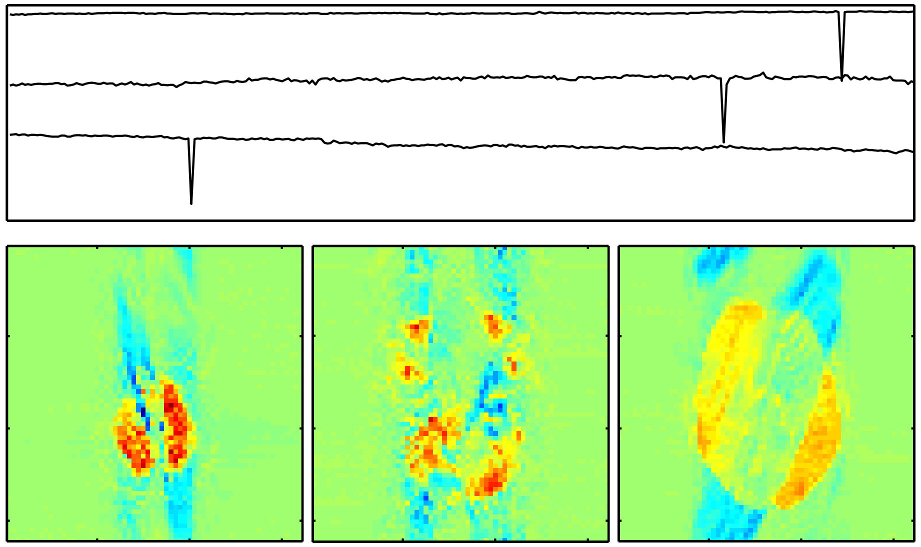

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Good for finding:

- Scanner and physiological artefacts
- Activation
- Resting networks

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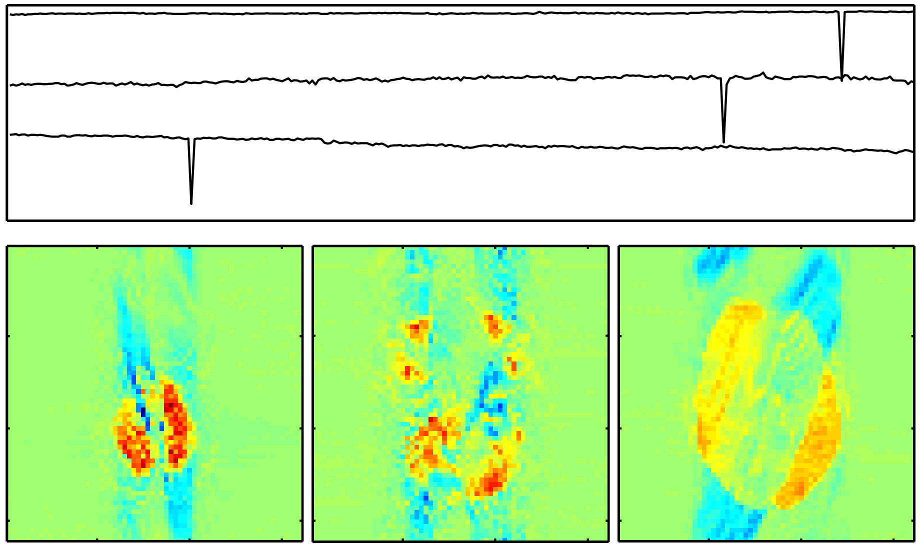

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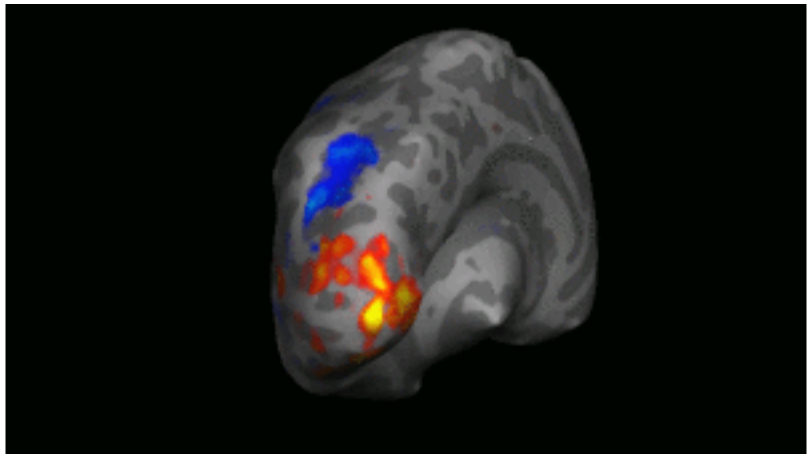

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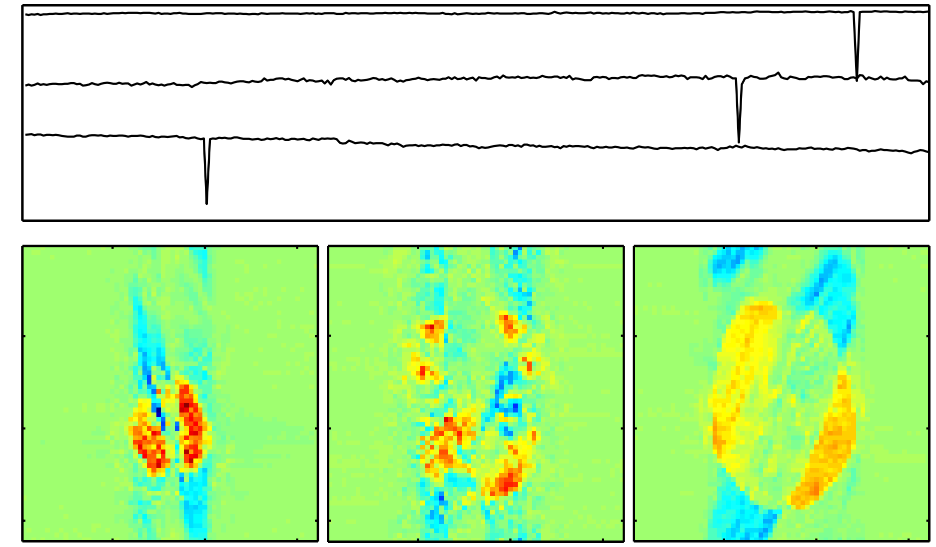

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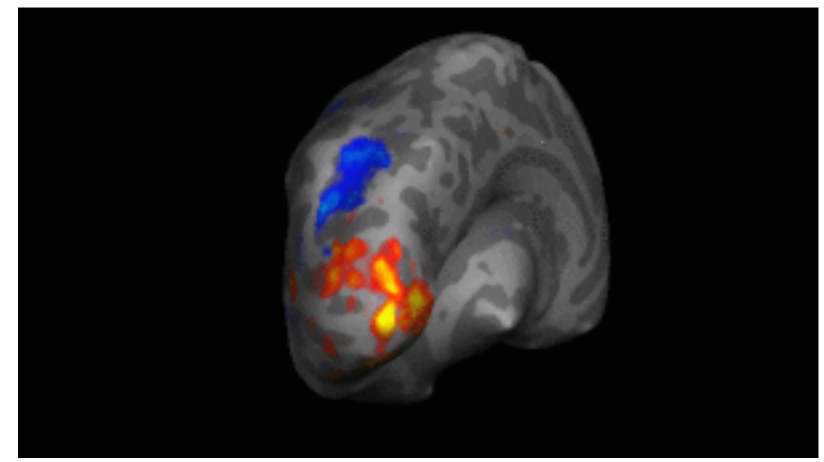

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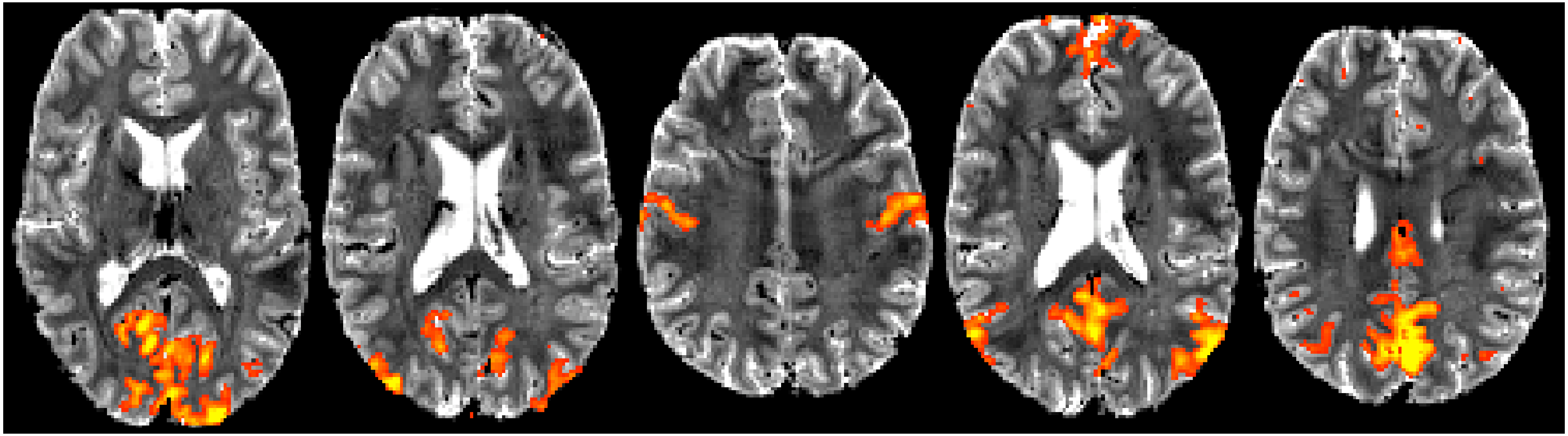
Seed-based correlation vs. ICA

- Seed-based
  - Good: allows you to ask a straightforward question and get an easily interpretable answer
  - Bad: only tells you about the seeds you ask about (though see Cohen's gradient-based parcellation)
- ICA
  - Bad: some components can be hard to interpret, and you may not get a component that clearly relates to the brain-bit you cared about
  - Bad: run-run variability in decomposition (but see ICASSO)
  - Good: the entire dataset is decomposed into "all" the different networks present

Spatial characteristics

- RSNs - multiple grey-matter networks



- Human Connectome Project pilot data (7T, 1.5mm, 6mins) (U Minnesota, E Yacoub & K Ugurbil)

Spatial characteristics

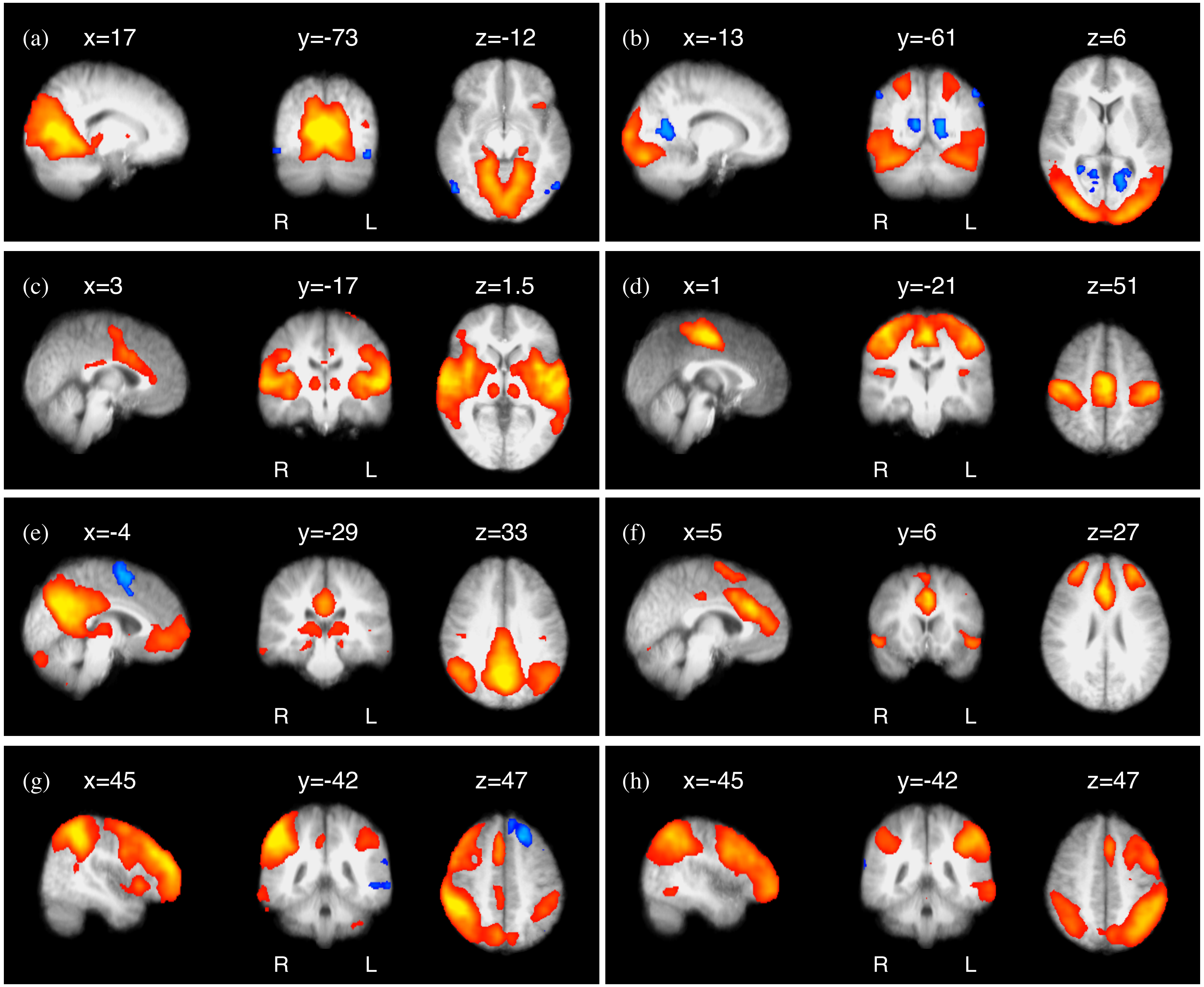
Low-dimensional (~20) ICA gives distinct "resting state networks"

medial visual

auditory

default mode

right fronto-parietal



lateral visual

sensori-motor

executive

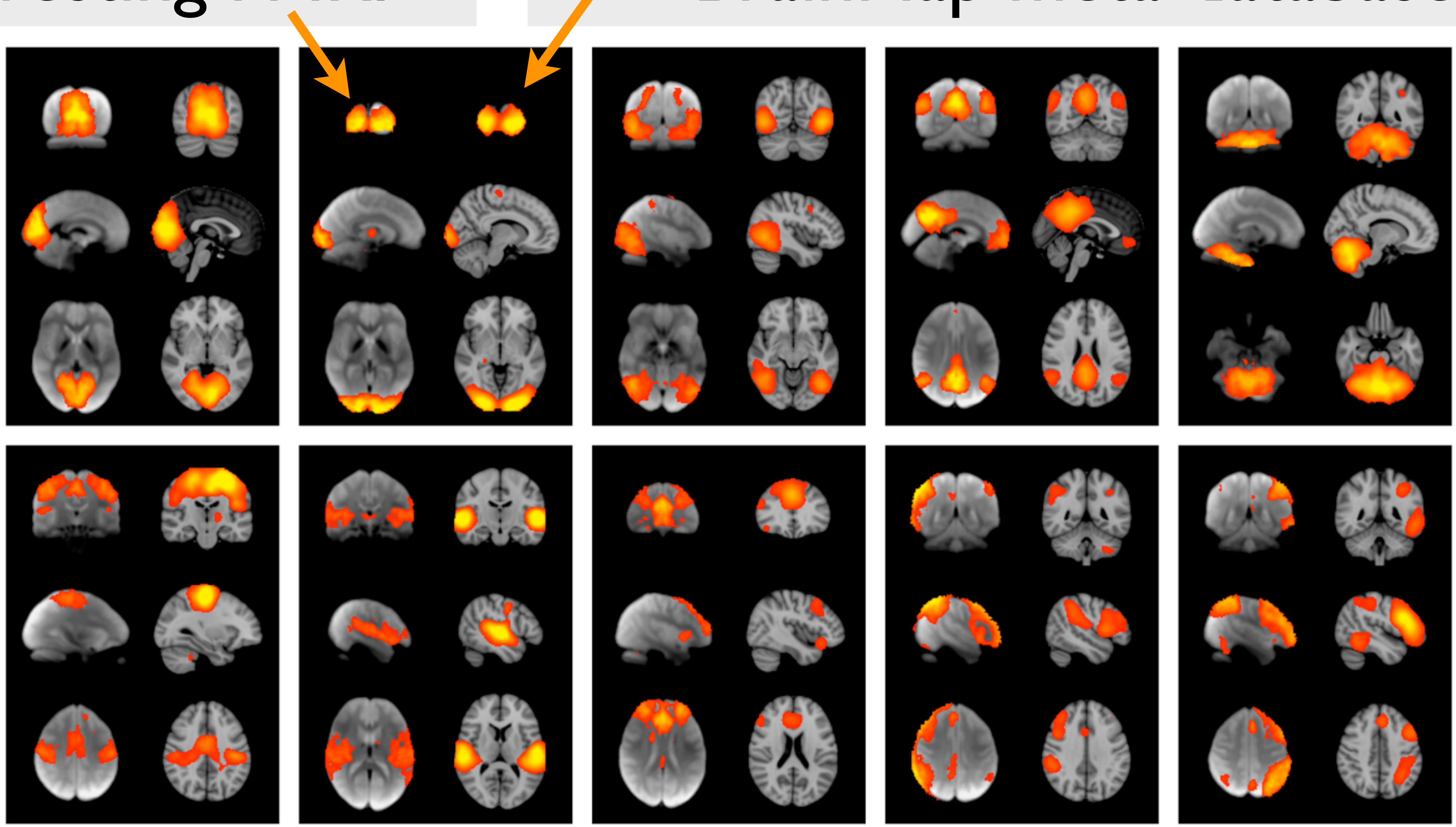
left fronto-parietal

- *Beckmann Phil Trans Roy Soc B 2005*

Correspondence between resting FMRI and task-activation studies

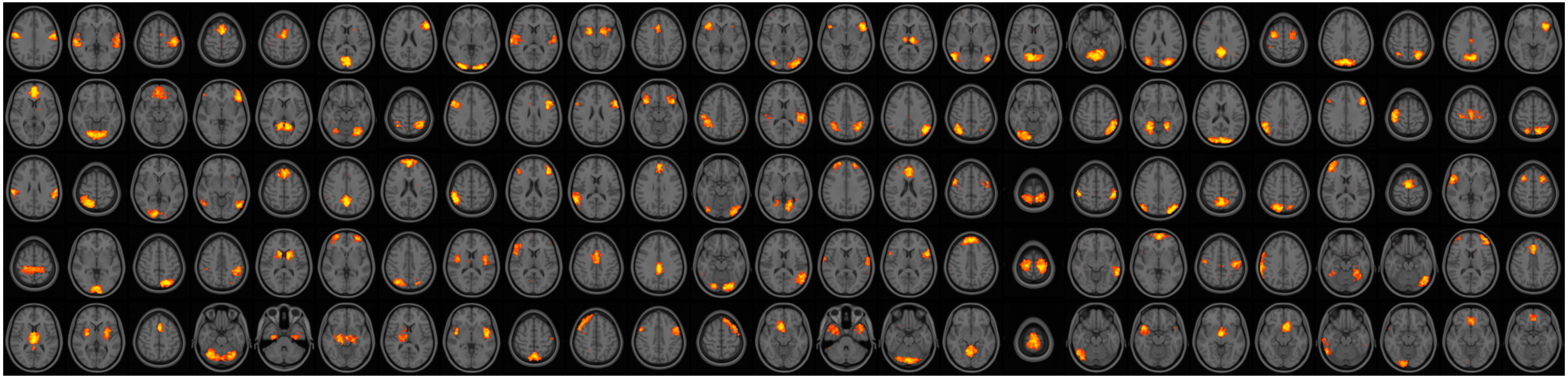
one component from group-ICA on 36-subject resting FMRI

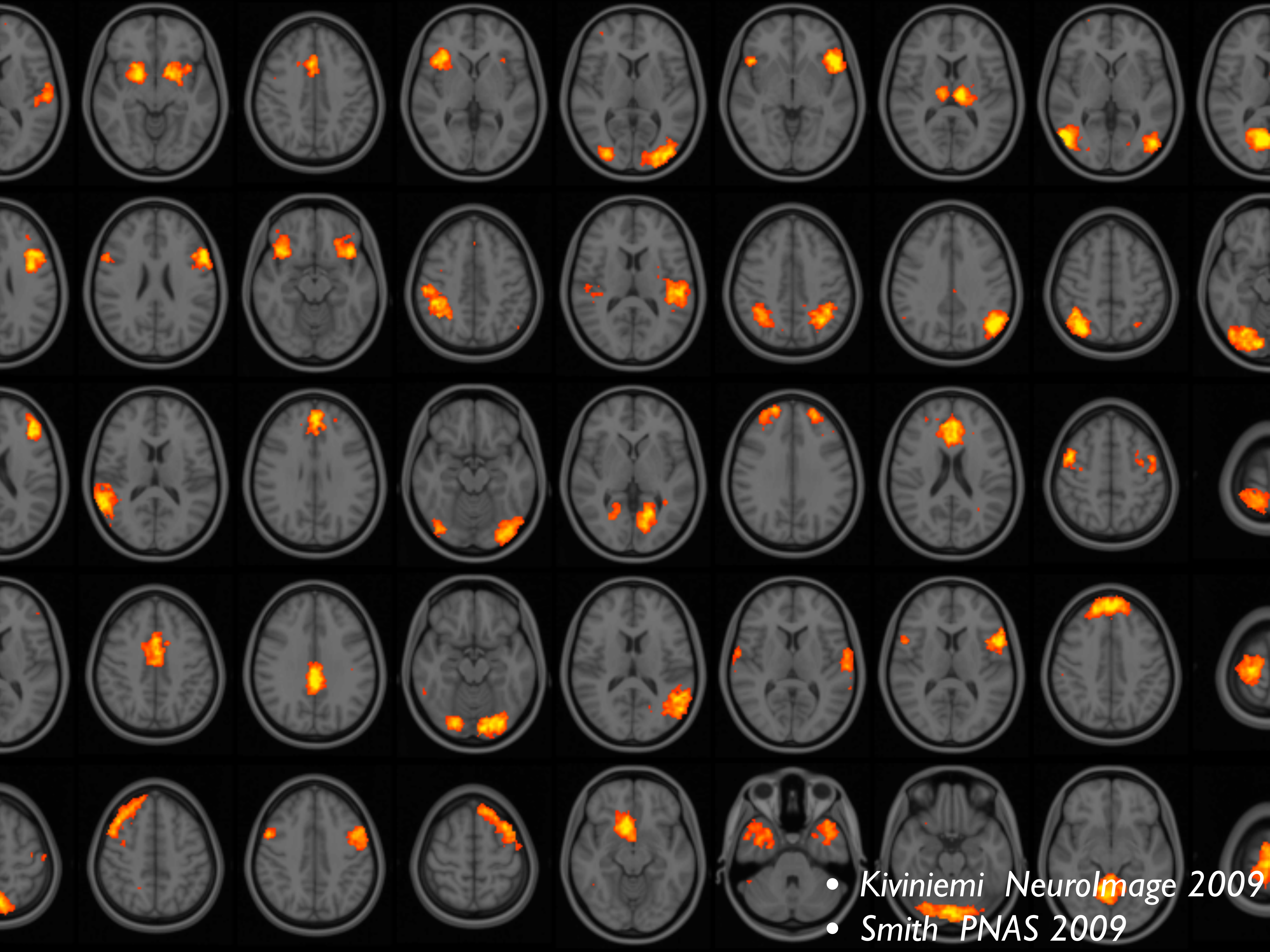
one component from ICA on activation images from 1687 task studies in the San Antonio BrainMap meta-database



• *Smith PNAS 2009*

High-dimensional (~200) ICA gives a “parcellation”

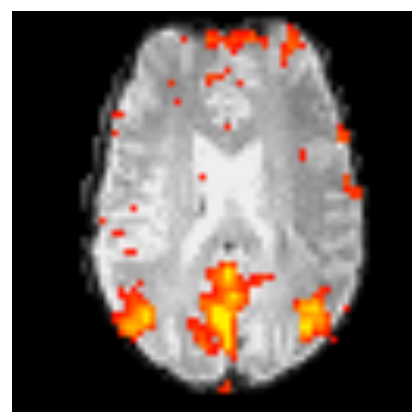


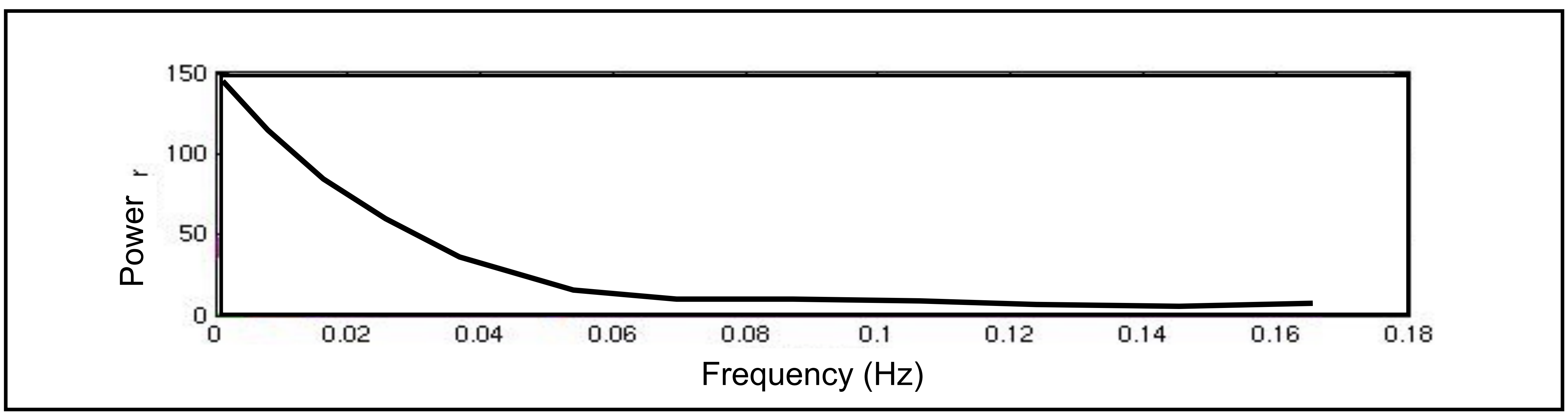


- *Kiviniemi NeuroImage 2009*
- *Smith PNAS 2009*

Temporal characteristics

- Generally described as "low frequency" or "1/f"



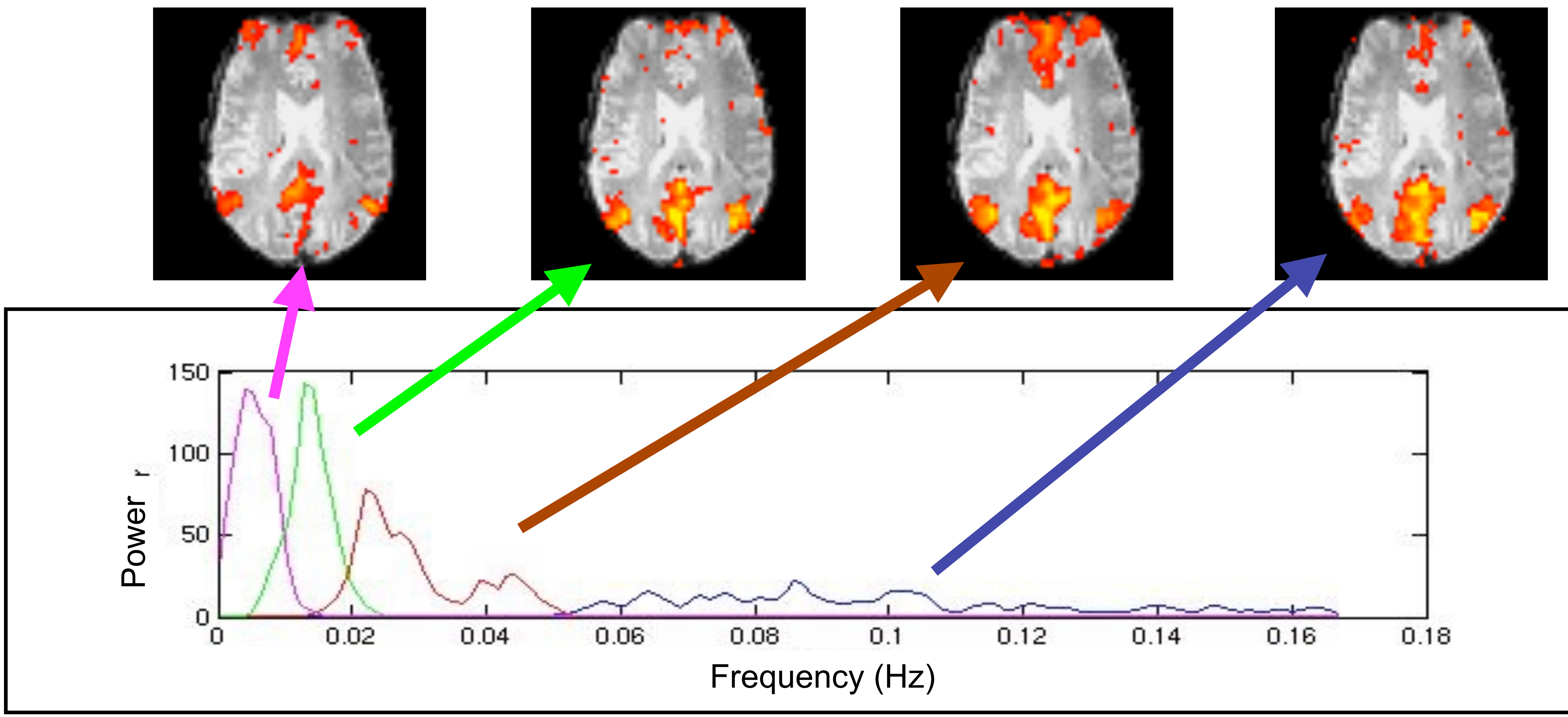


- *Niazy Prog Brain Research 2011*

Temporal characteristics

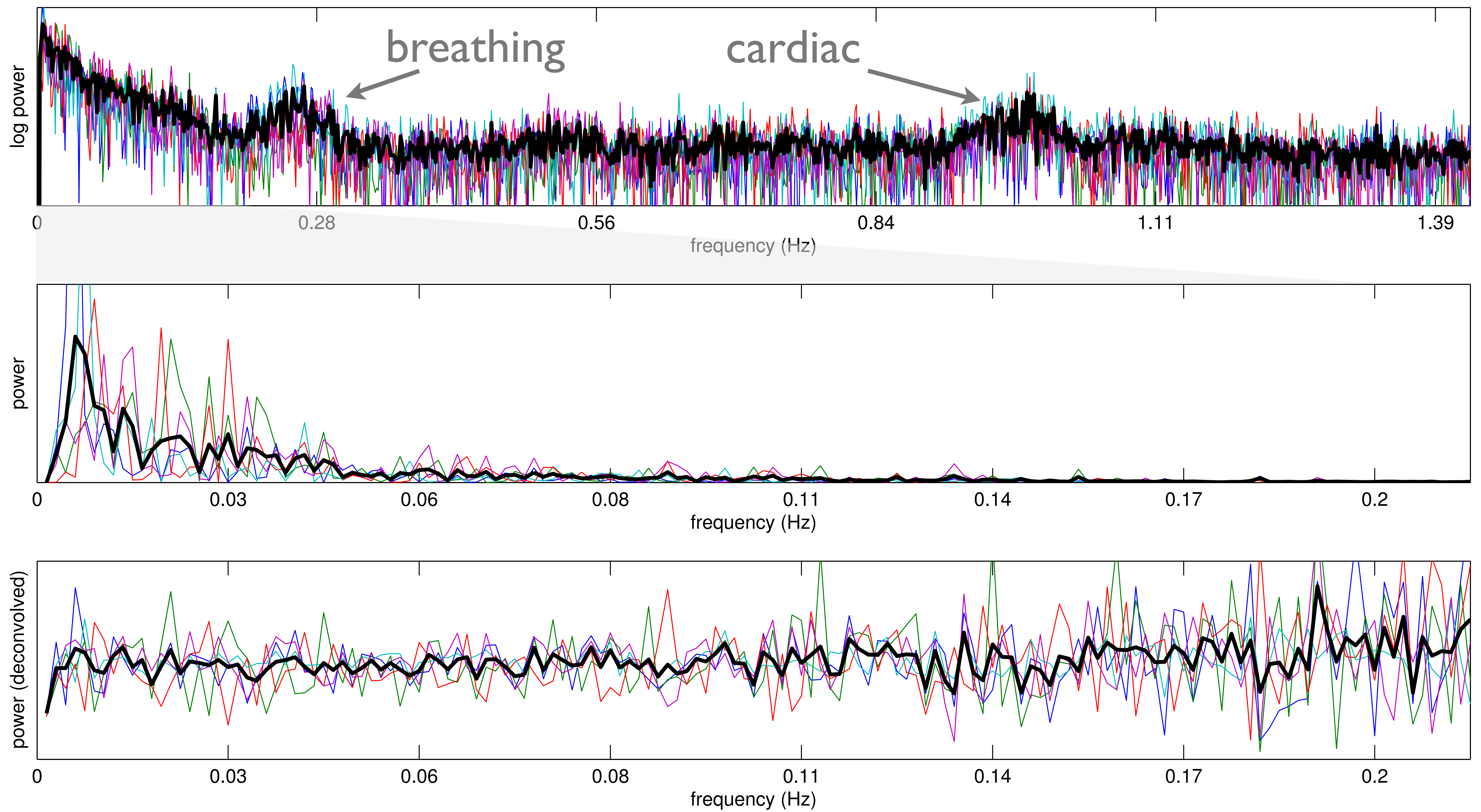
- Generally described as "low frequency" or "1/f"

- Split frequency spectrum into four bands and run ICA on each
- Suggests RSNs are broadband processes temporally



- *Niazy Prog Brain Research 2011*

- Top: Power spectra from 5 RSNS (TR=0.35s).
- Middle: Spectra suggest RSNs in BOLD are "low frequency" (or "1/f")
- Bottom: Deconvolve HRF in original data - now flat up to 0.2Hz



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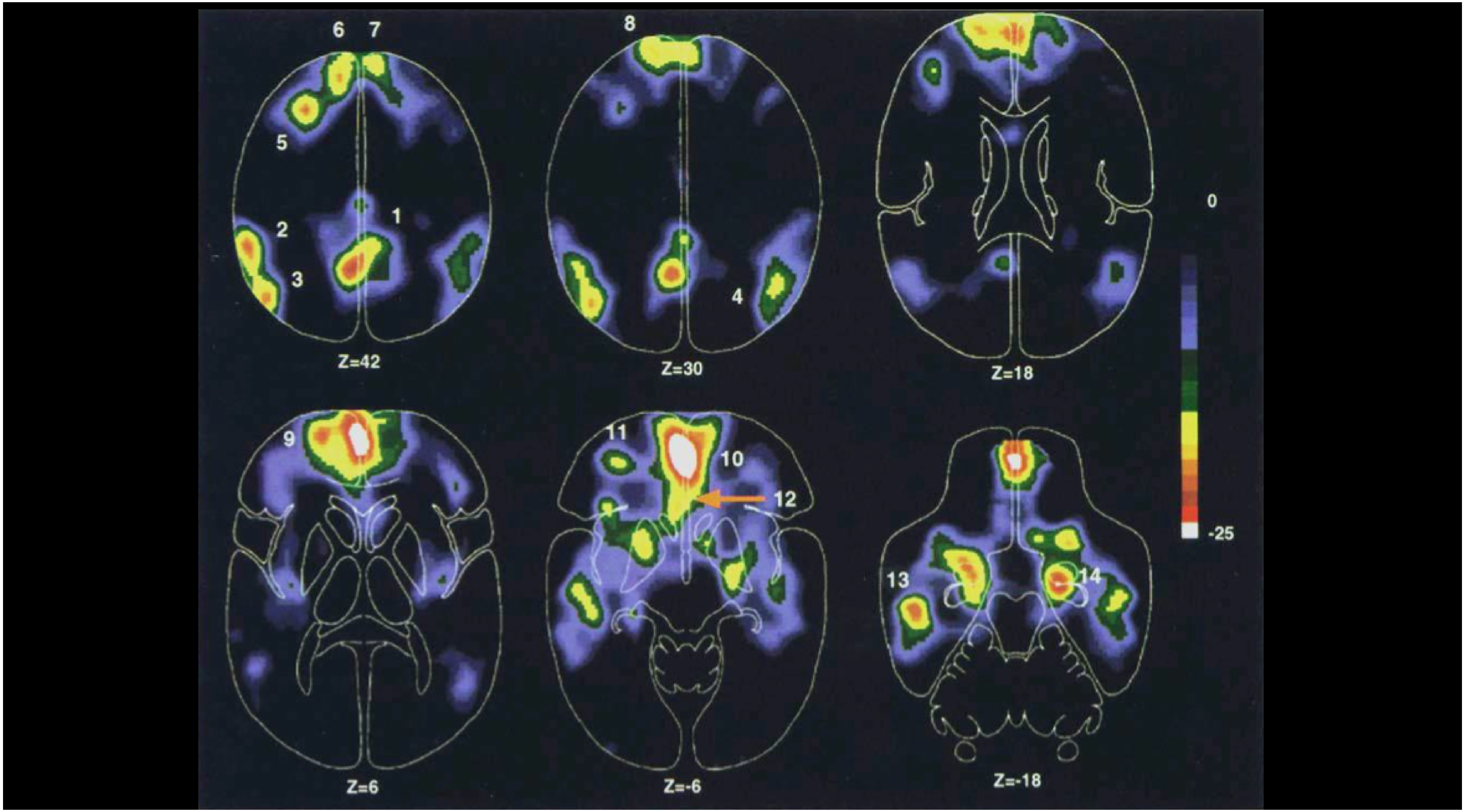
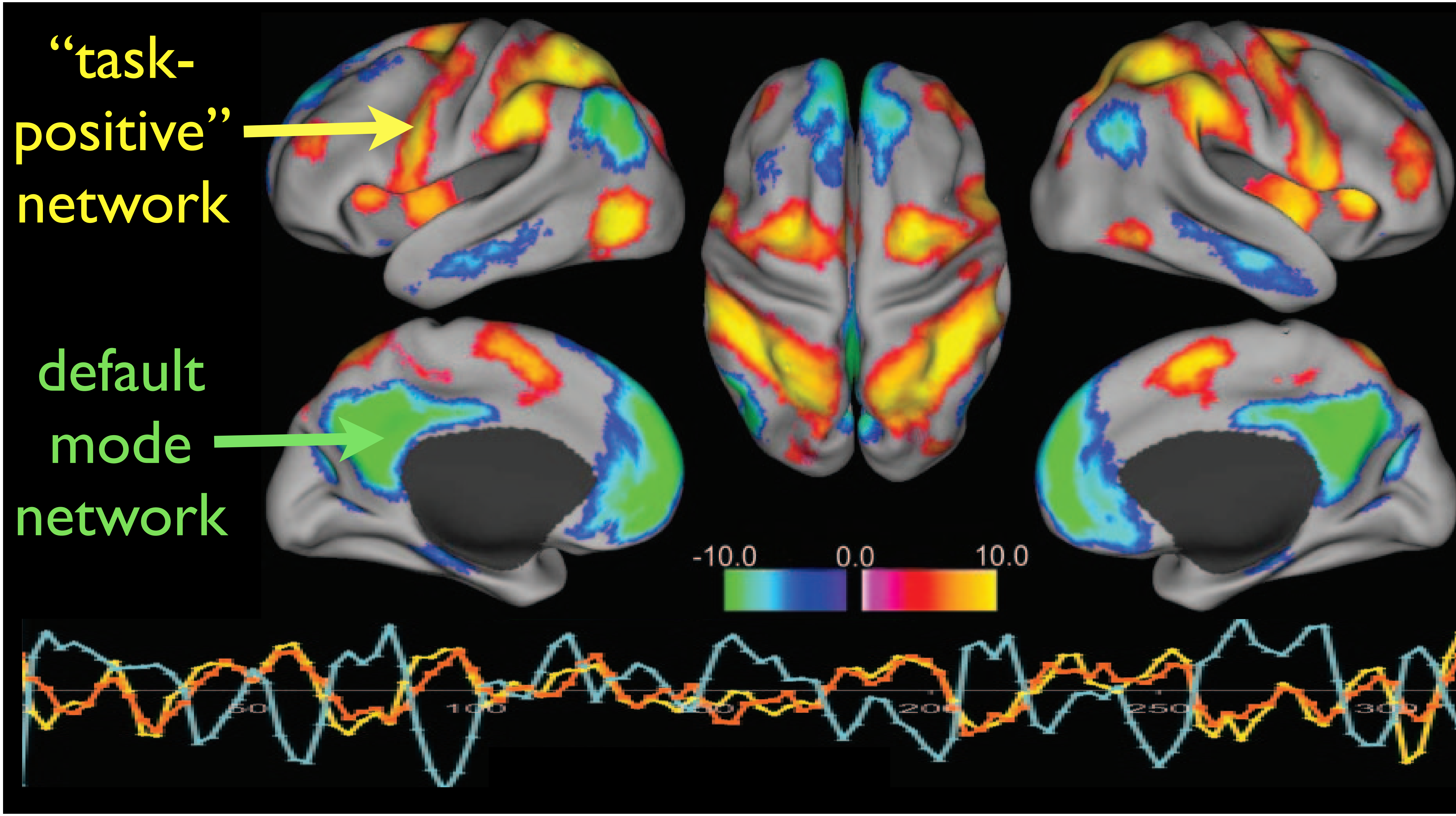
Anti-correlated networks



"Default mode network" - a network that deactivates during many activation studies

- *Shulman JCN 1997*
- *Raichle PNAS 2001*

Anti-correlated networks



"Default mode network" and "task-positive network" are anticorrelated in resting data

- *Fox PNAS 2005*
- *Fox J Neurophys 2009*

rfMRI artefacts & cleanup

- Structured artefacts *much* more of a problem for rfMRI than task-fMRI *(because it's based on correlating timeseries with each other rather than an "external" timeseries - that in general will not be correlated with these confounds)*
    - Head motion
    - Cardiac & breathing cycles
    - Scanner artefacts

rfMRI artefacts & cleanup

- Estimate "confound" timeseries; regress these out of the data:
  - External physiology measurements (RETROICOR)
  - rfMRI-data-derived measurements
    - head motion parameters
    - white-matter / CSF / whole-brain mean timeseries
    - ICA artefact component timeseries
- Highpass / lowpass temporal filters
- "Scrubbing" (delete bad timepoints)

temporal filtering

- Highpass temporal filtering
  - E.g., remove frequences < 0.001 Hz
  - Reasonable to remove slowest data drifts
- Lowpass temporal filtering
  - E.g., common to remove frequencies > 0.1Hz
  - May remove useful signal
  - Not guaranteed to remove much artefact
  - Maybe a "last resort" if other options not available

To demean or Not to demean?

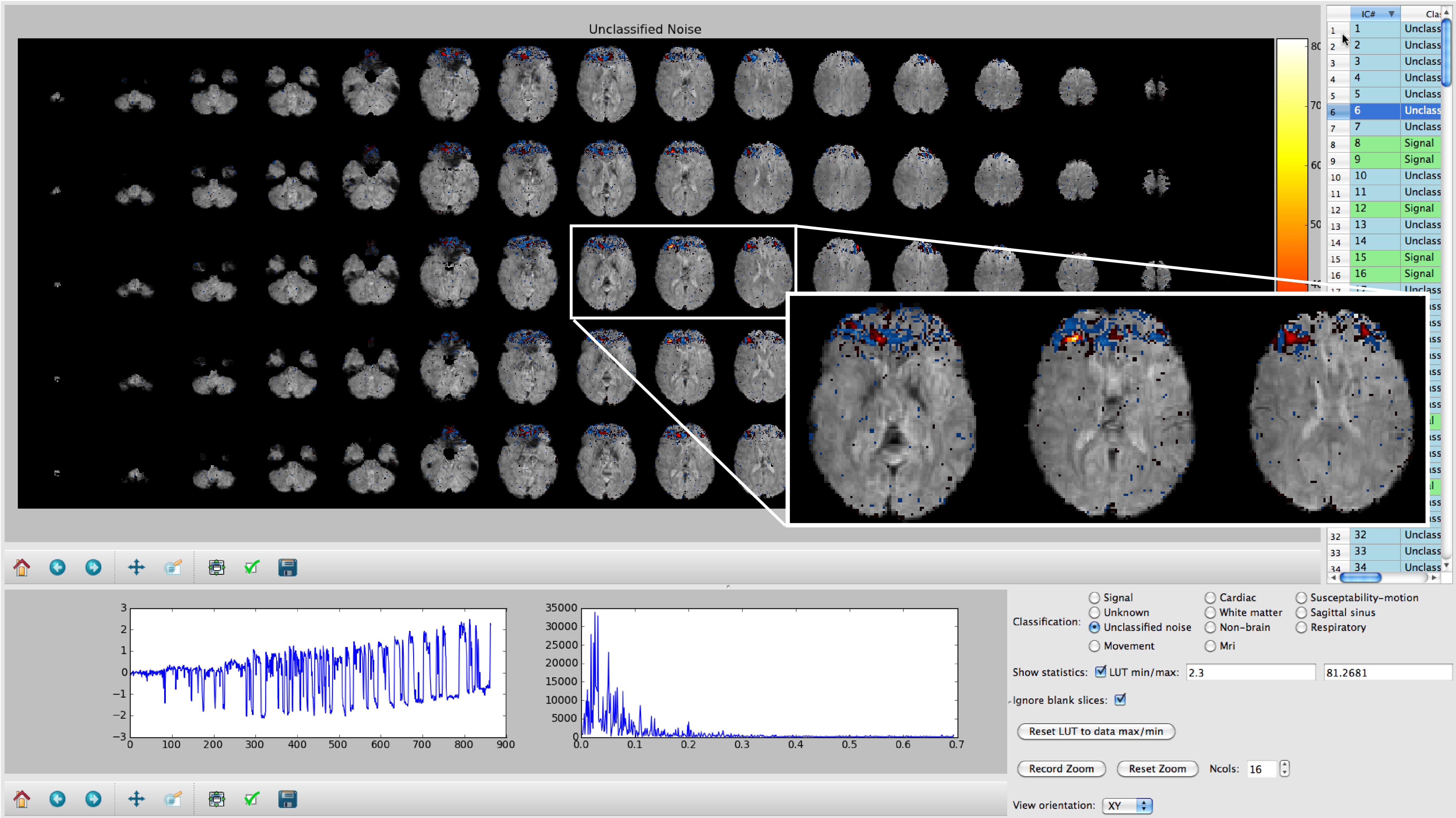
- What about "global signal removal" (mean timecourse over whole brain)?
  - Another source of noise that's good to remove ... ?
  - But what if it contains some "neural" signals of interest?
  - Makes it hard to interpret whether different networks are positively / negatively correlated
  - Fox (J Neurophysiol, 2009), Murphy (NeuroImage 2009), etc.

FIX (FMRIB's ICA-based X-noiseifier)

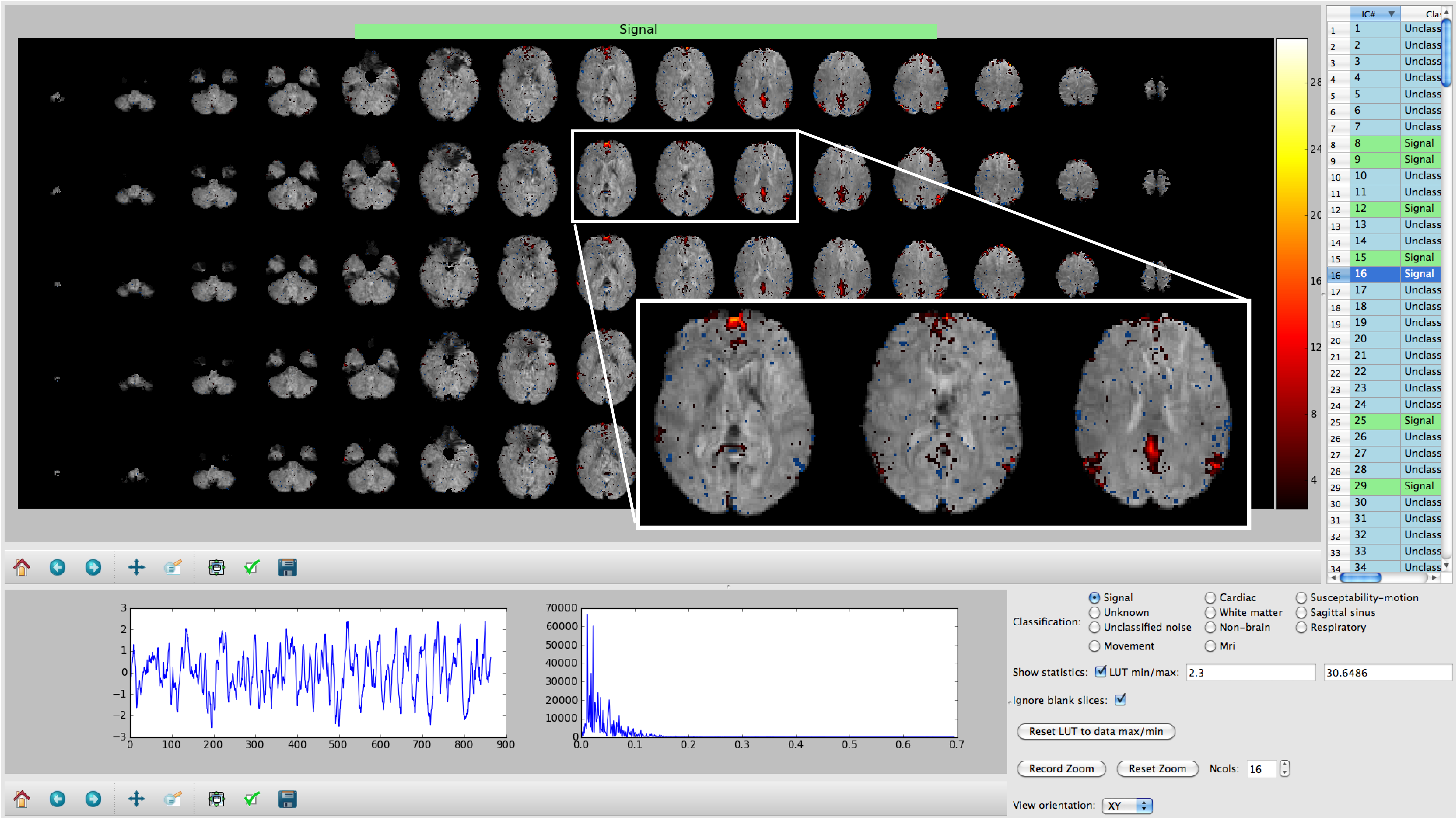
Salimi-Khorshidi NeuroImage 2014
Griffanti NeuroImage 2014

- Preprocessing: head motion correction and drift removal
- FSL's ICA with automatic dimensionality estimation
- FIX
  - classify each ICA component (good v bad)
  - Regress bad ICA timecourses & 24 motion parameters out of data
- FIX component classification accuracy:
  - On good multiband data (eg HCP): 99.5%
  - On "standard" EPI: > 95% TPR, 85% TNR

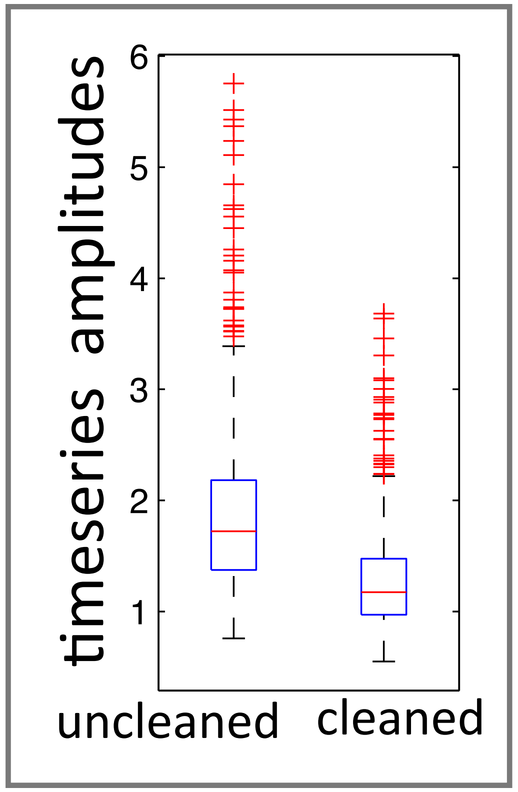
FIX: example artefact component



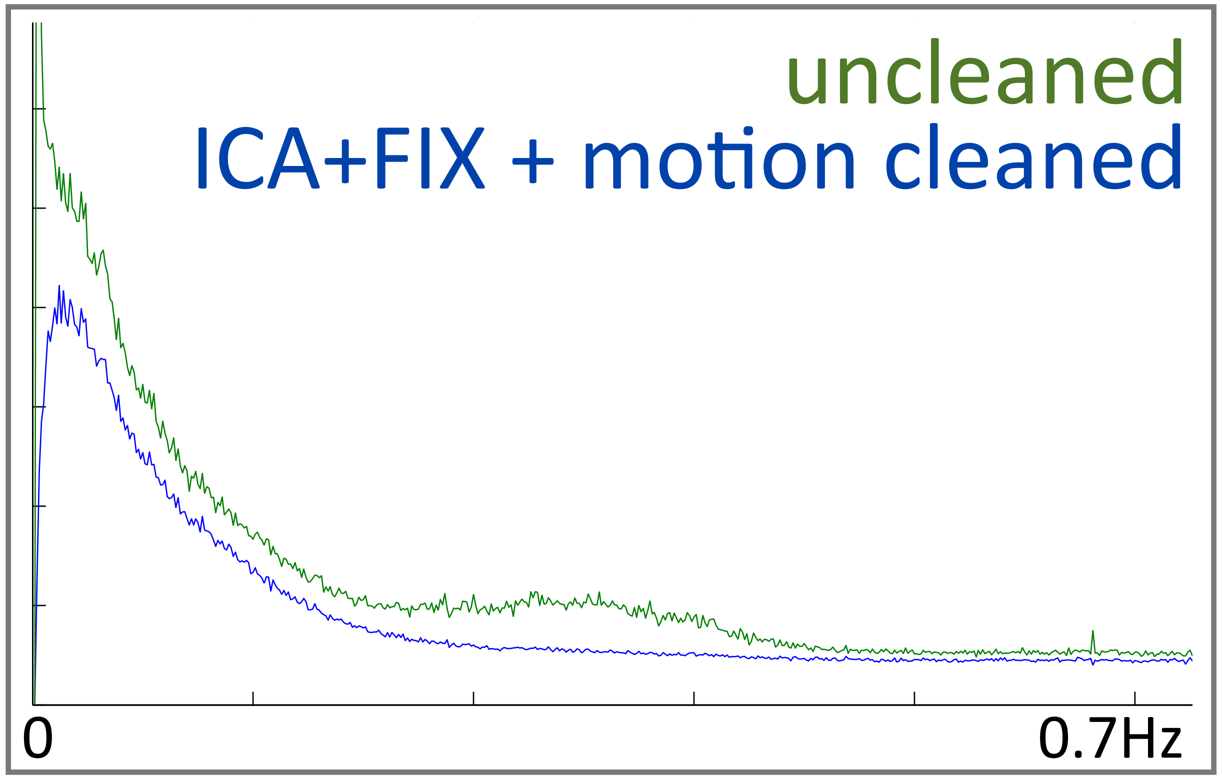
FIX: example good component

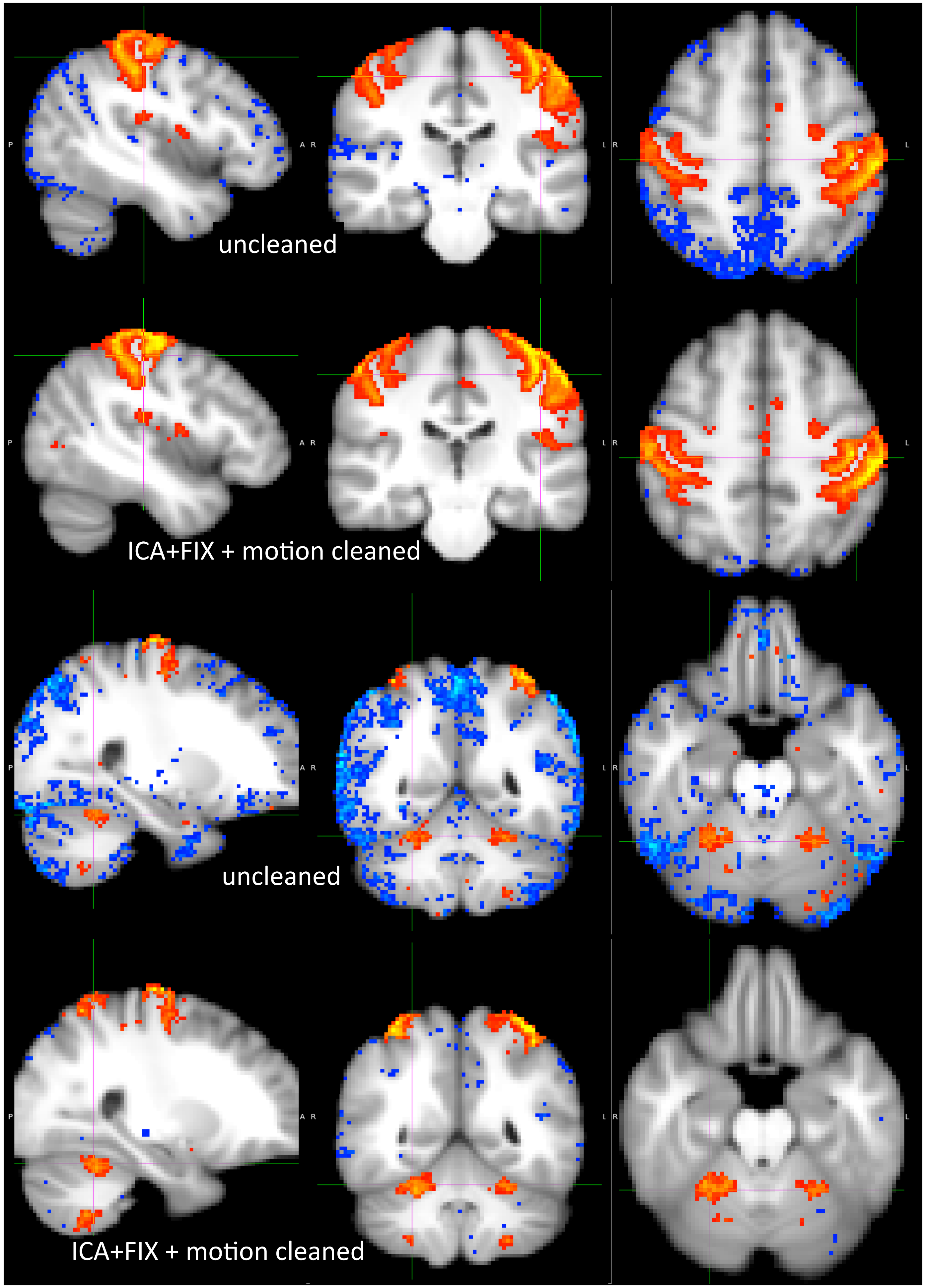


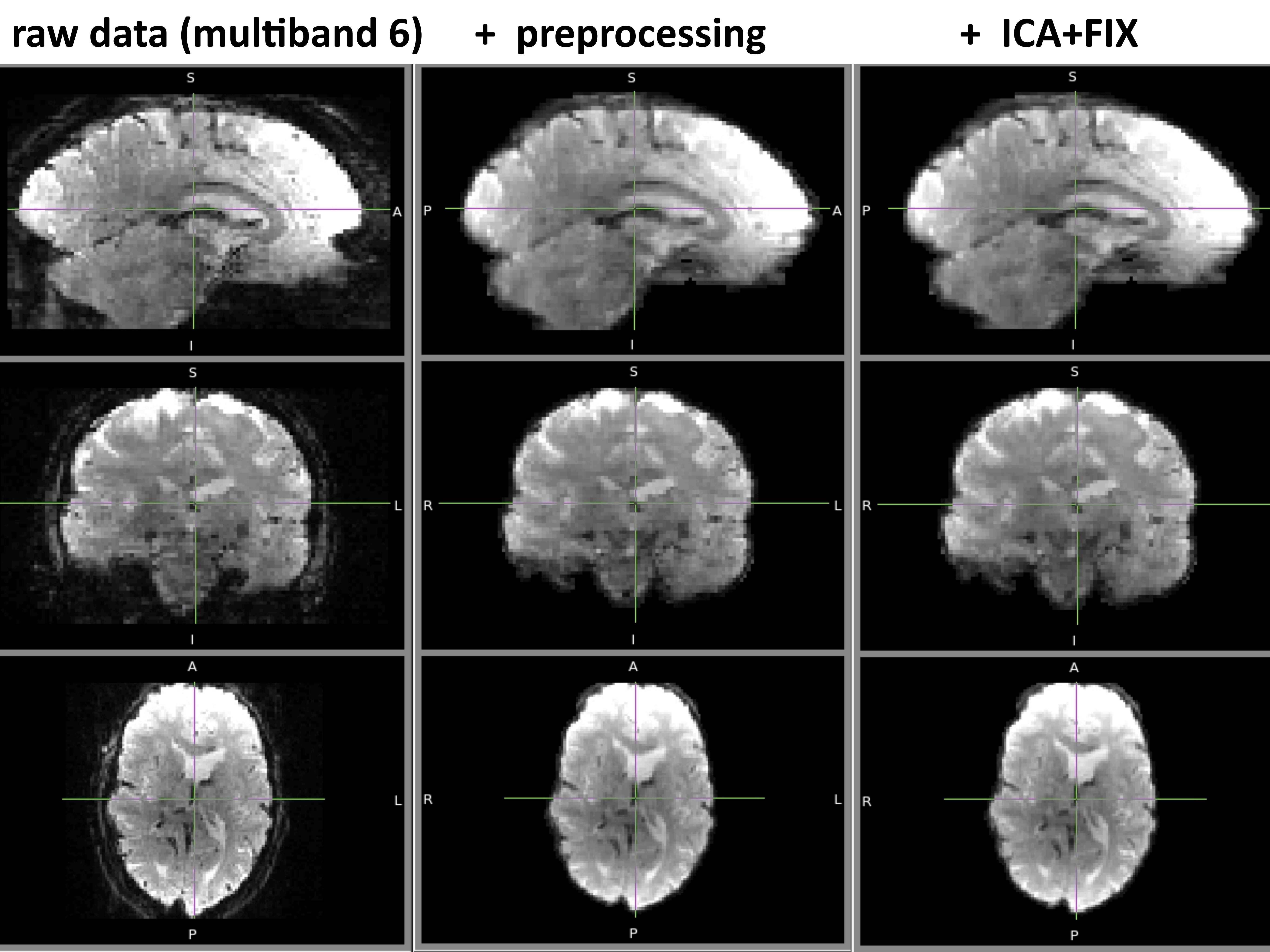
Effect of ICA+FIX cleaning



temporal power spectra






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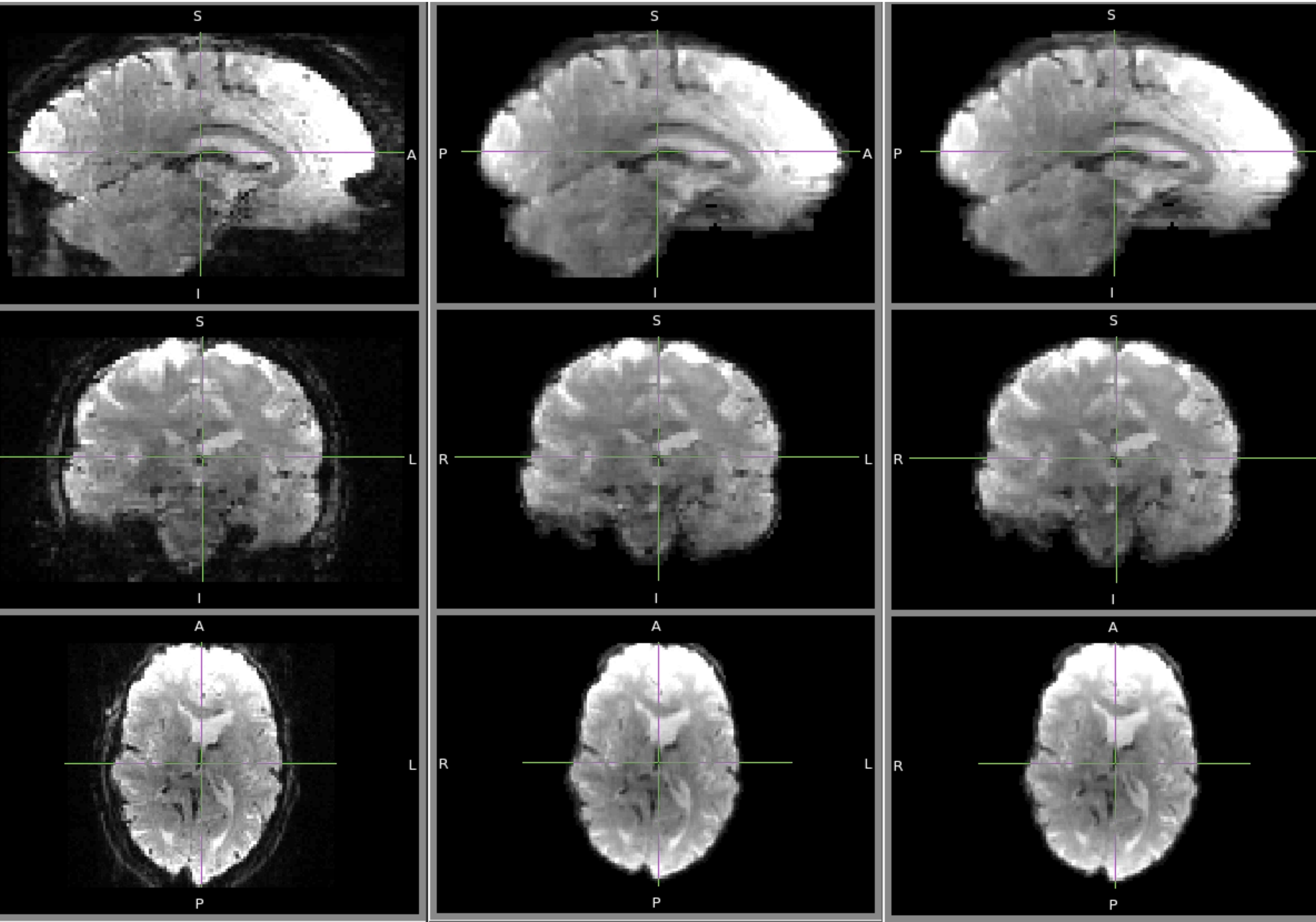

Group-level rfMRI analysis

Group Analysis - Seed-Based

- One seed map per subject
- Simple random-effects cross-subject / cross-group analyses using parametric maps from individual subject seedings. Just like task-FMRI GLM cross-subject modelling
- Easy to interpret, and no problems of "correspondence" (do the maps "mean" the same thing in all subjects?) as long as no registration confounds

Group Analysis - ICA

- For any RSN of interest, take each subject's map corresponding to that RSN, somehow

- Simple random-effects cross-subject / cross-group analyses using RSN maps from individual subject seedings.
  Just like with seed-based

ICA-based methodology for multi-subject RSN analysis

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- Why not just run ICA on each subject separately?
  - Correspondence problem (of RSNs across subjects)
  - Different splittings *sometimes* caused by small changes in the data (naughty ICA!)

ICA-based methodology for multi-subject RSN analysis

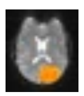
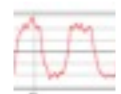
- Why not just run ICA on each subject separately?
  - Correspondence problem (of RSNs across subjects)
  - Different splittings *sometimes* caused by small changes in the data (naughty ICA!)

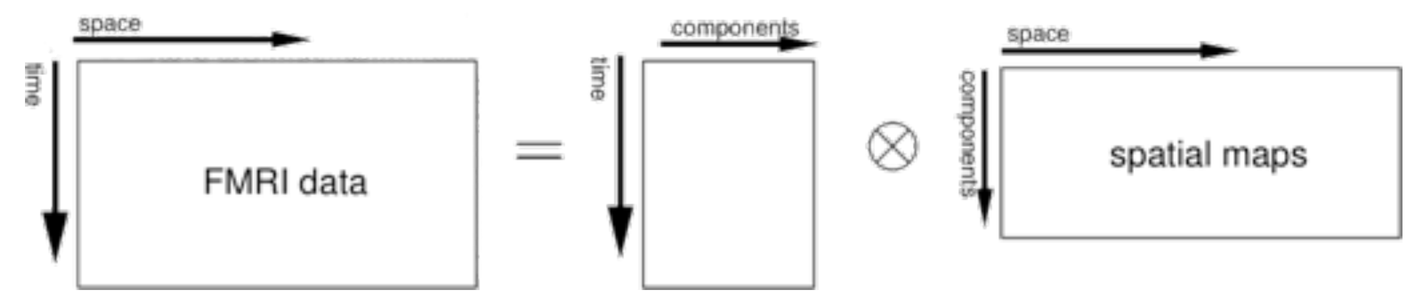
- Instead - start with a "group-average" ICA
  - But then need to relate group maps back to the individual subjects
  - (*Although* - this approach is less good than single-subject ICA at removing/ignoring session-specific noise)

ICA models for RSN analysis

Single-Session ICA

each ICA component comprises:

 spatial map & timecourse 



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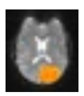
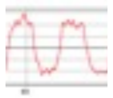
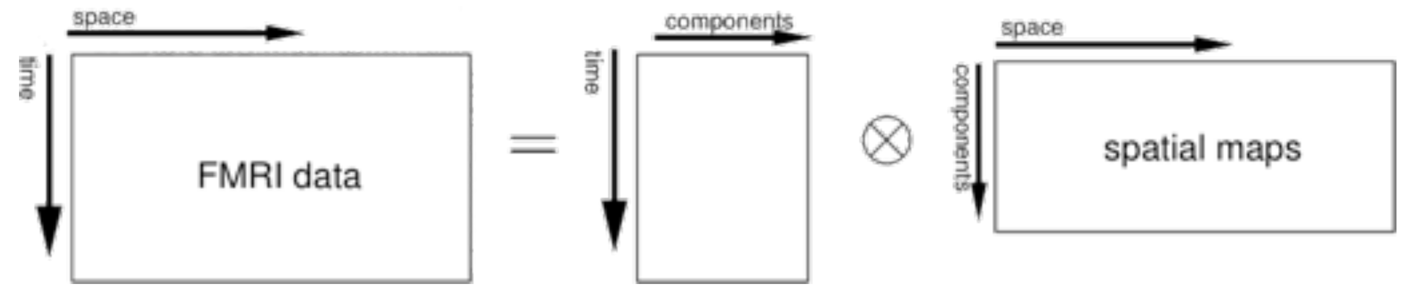
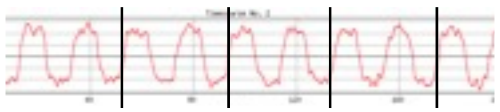
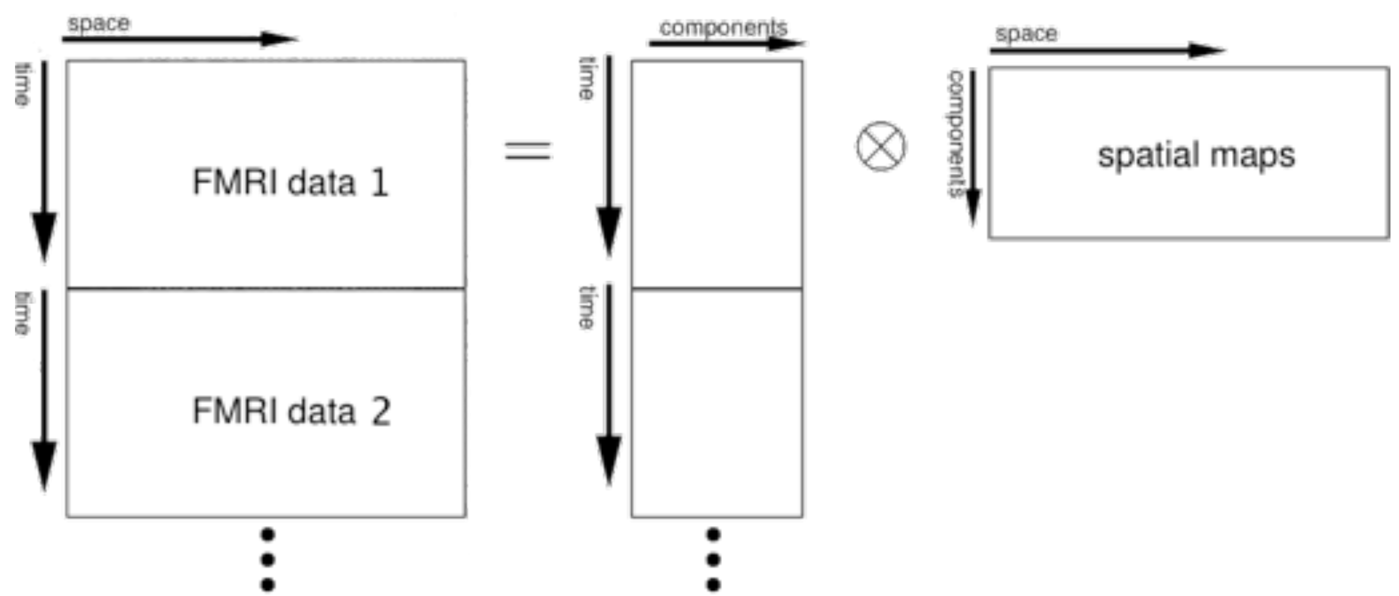
 spatial map & timecourse 



Multi-Session or Multi-Subject ICA:
Concatenation approach

each ICA component comprises:

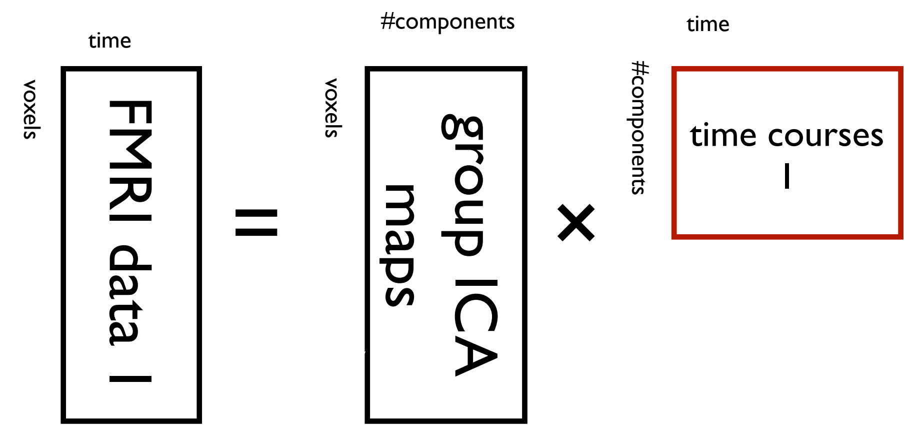
 spatial map & timecourse
(that can be split up into subject-specific chunks) 



dual regression

dual regression

- **dr_stage1_subject[#SUB].txt -** the *timeseries* outputs of stage 1 of the dual-regression.



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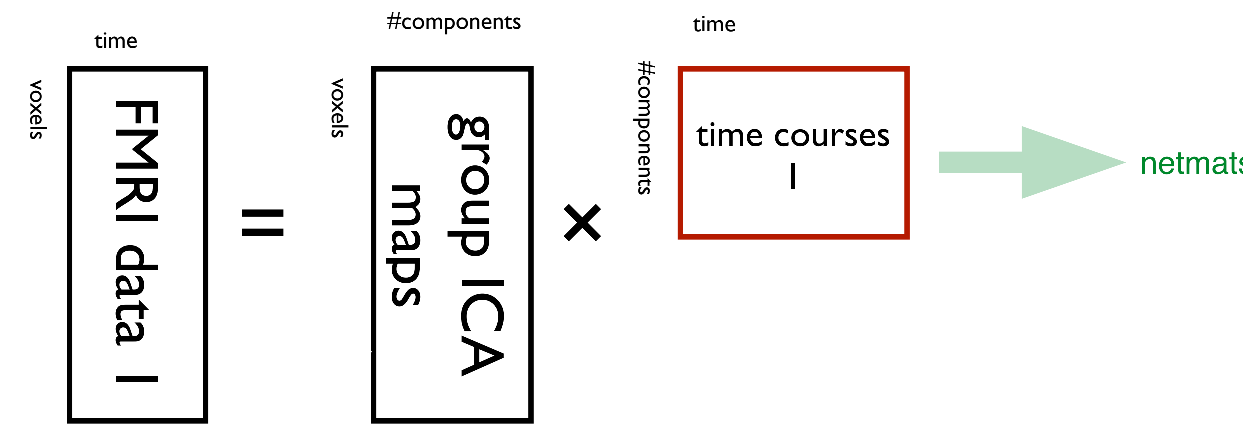
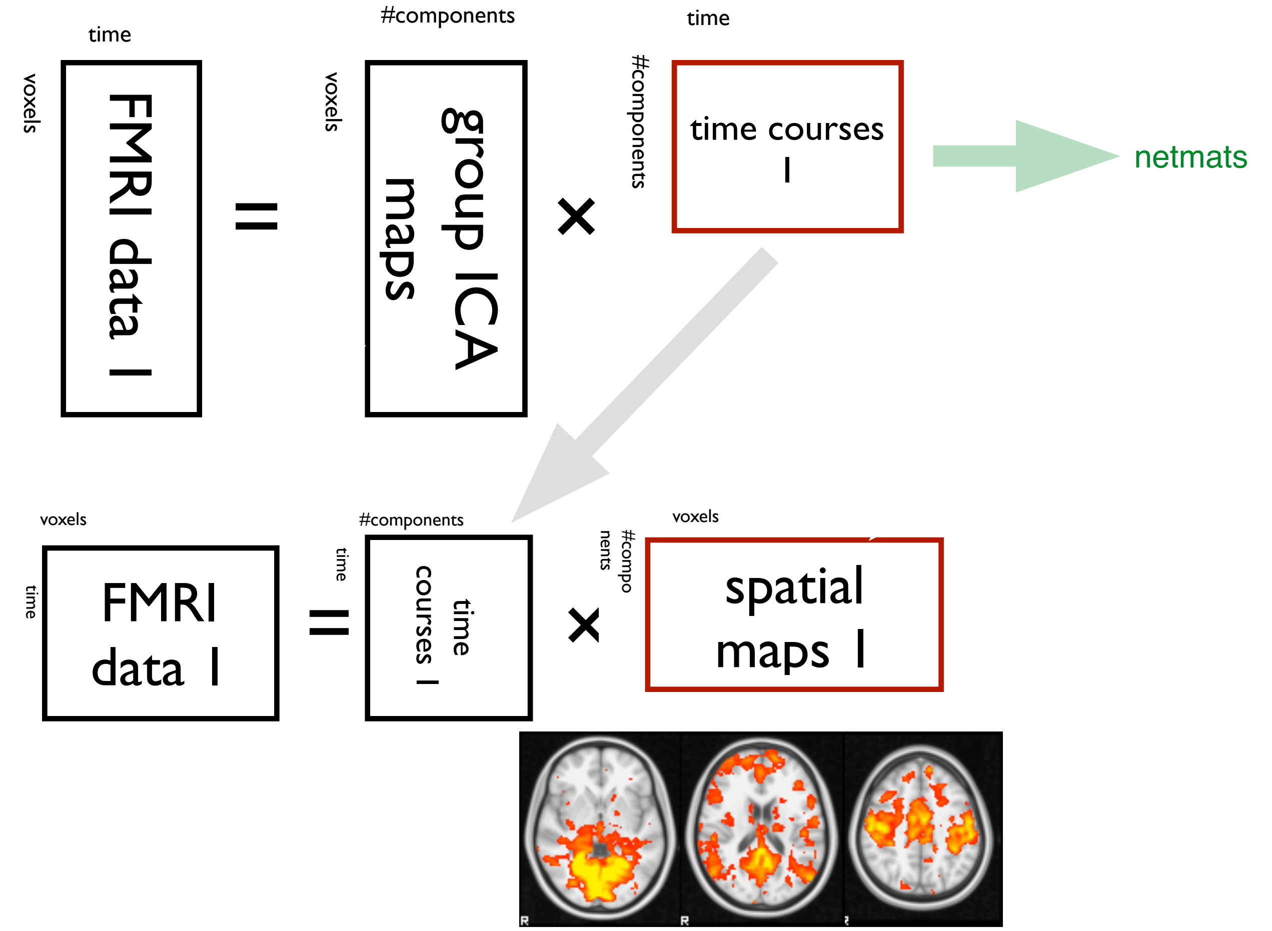


dual regression

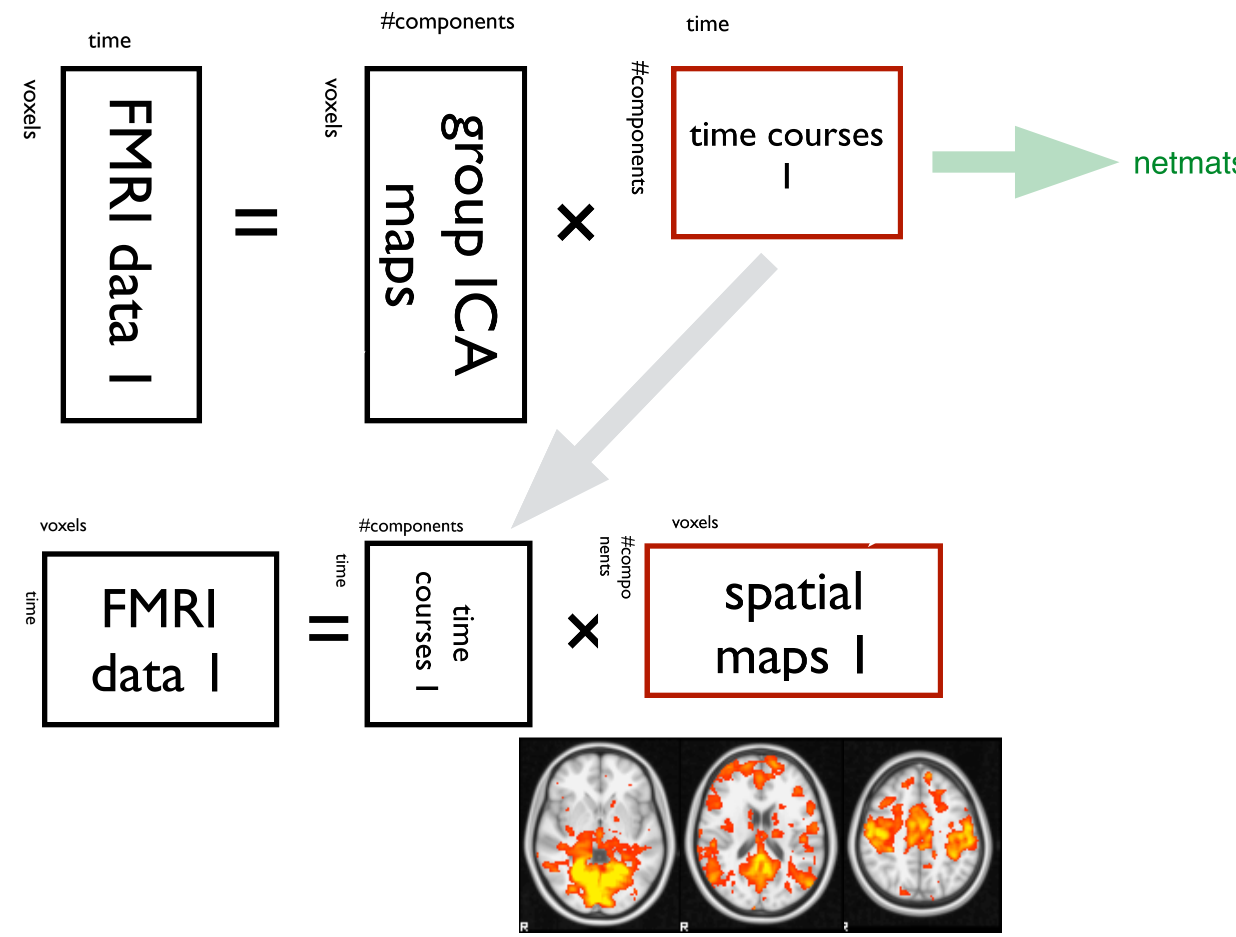
- **dr_stage1_subject[#SUB].txt** - the *timeseries* outputs of stage 1 of the dual-regression.

- **dr_stage2_subject[#SUB].nii.gz** - the *spatial maps* outputs of stage 2 of the dual-regression.



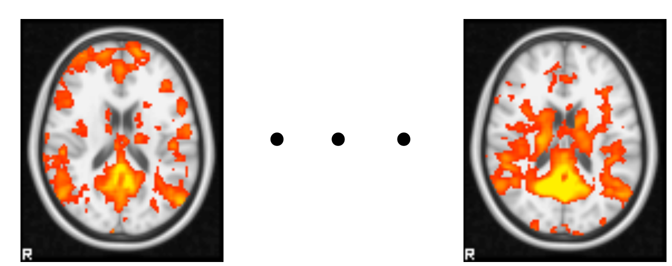
dual regression

- **dr_stage1_subject[#SUB].txt** - the *timeseries* outputs of stage 1 of the dual-regression.



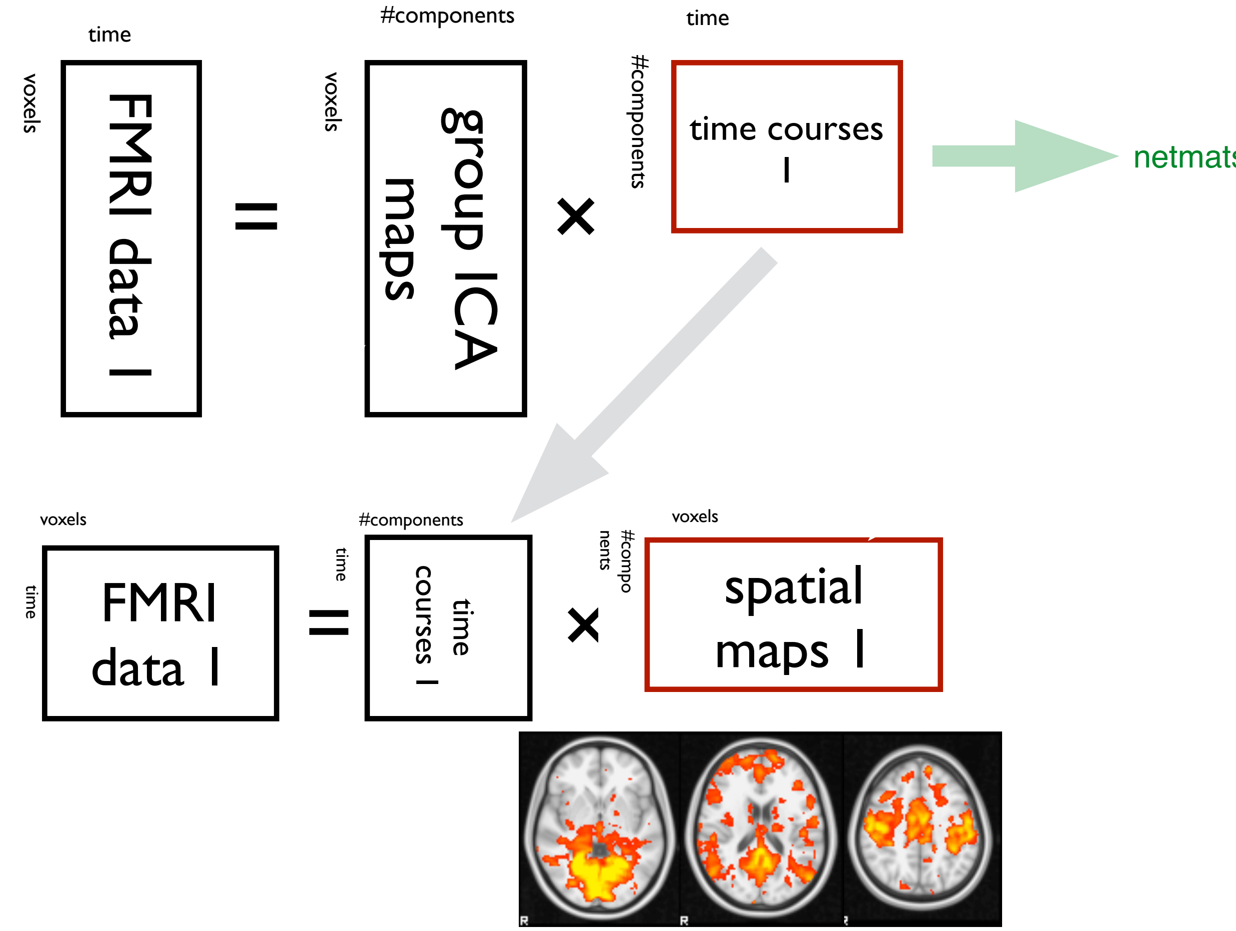
- **dr_stage2_subject[#SUB].nii.gz** - the *spatial maps* outputs of stage 2 of the dual-regression.

- **dr_stage2_ic[#ICA].nii.gz** - the re-organised parameter estimate images



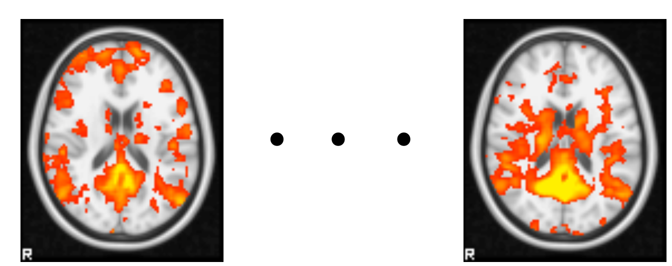
dual regression

- **dr_stage1_subject[#SUB].txt** - the *timeseries* outputs of stage 1 of the dual-regression.



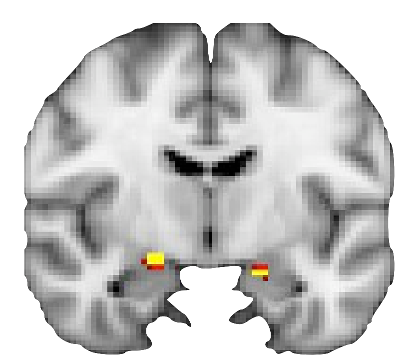
- **dr_stage2_subject[#SUB].nii.gz** - the *spatial maps* outputs of stage 2 of the dual-regression.

- **dr_stage2_ic[#ICA].nii.gz** - the re-organised parameter estimate images

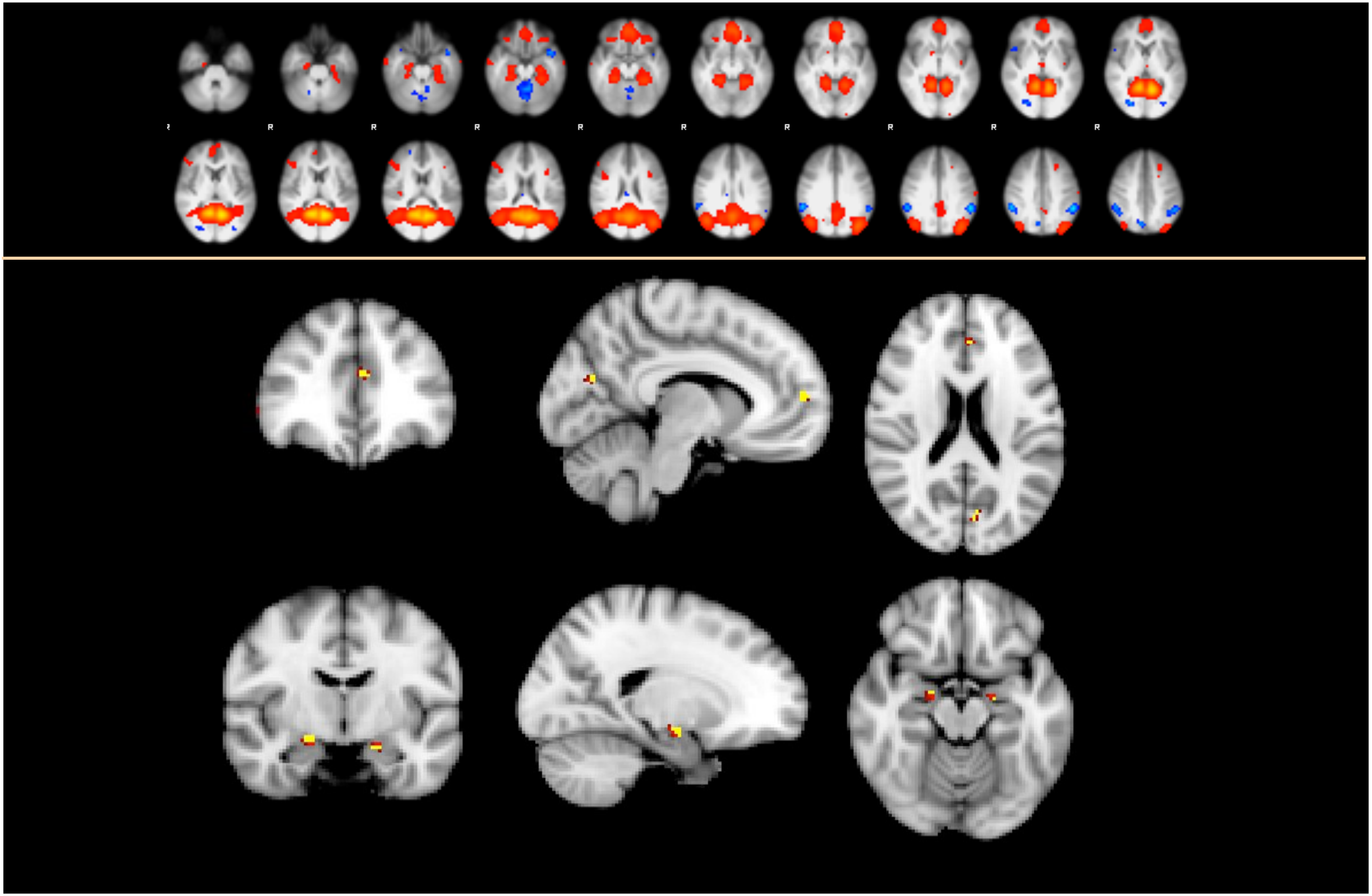


- **dr_stage3_ic[#ICA]_tstat[#CON].nii.gz** - the output from randomise

  (corrected for mc across voxels but not across #components!!)



Altered functional connectivity in young, healthy carriers of APOE-ε4

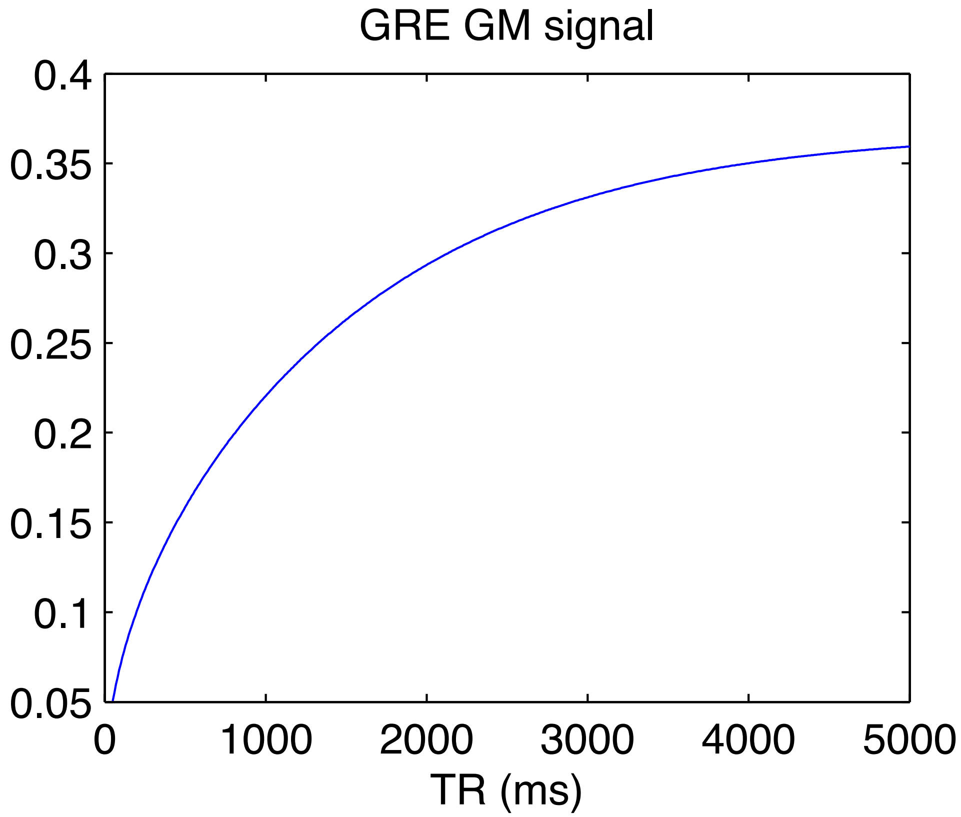


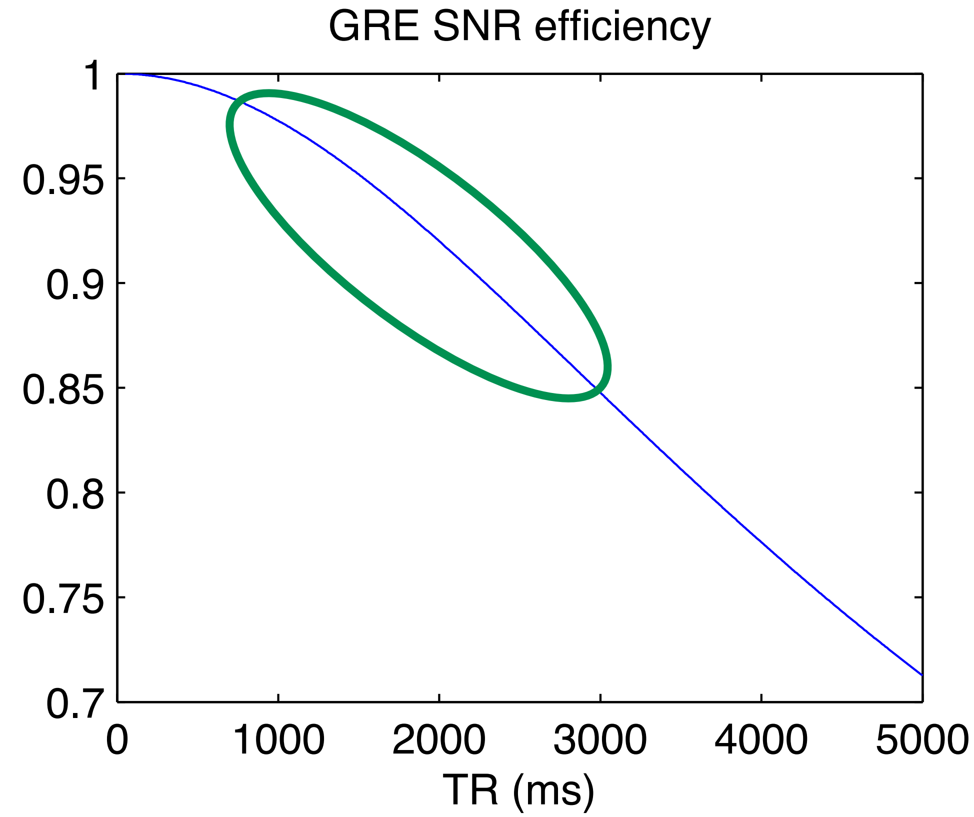
• *Filippini PNAS 2009*

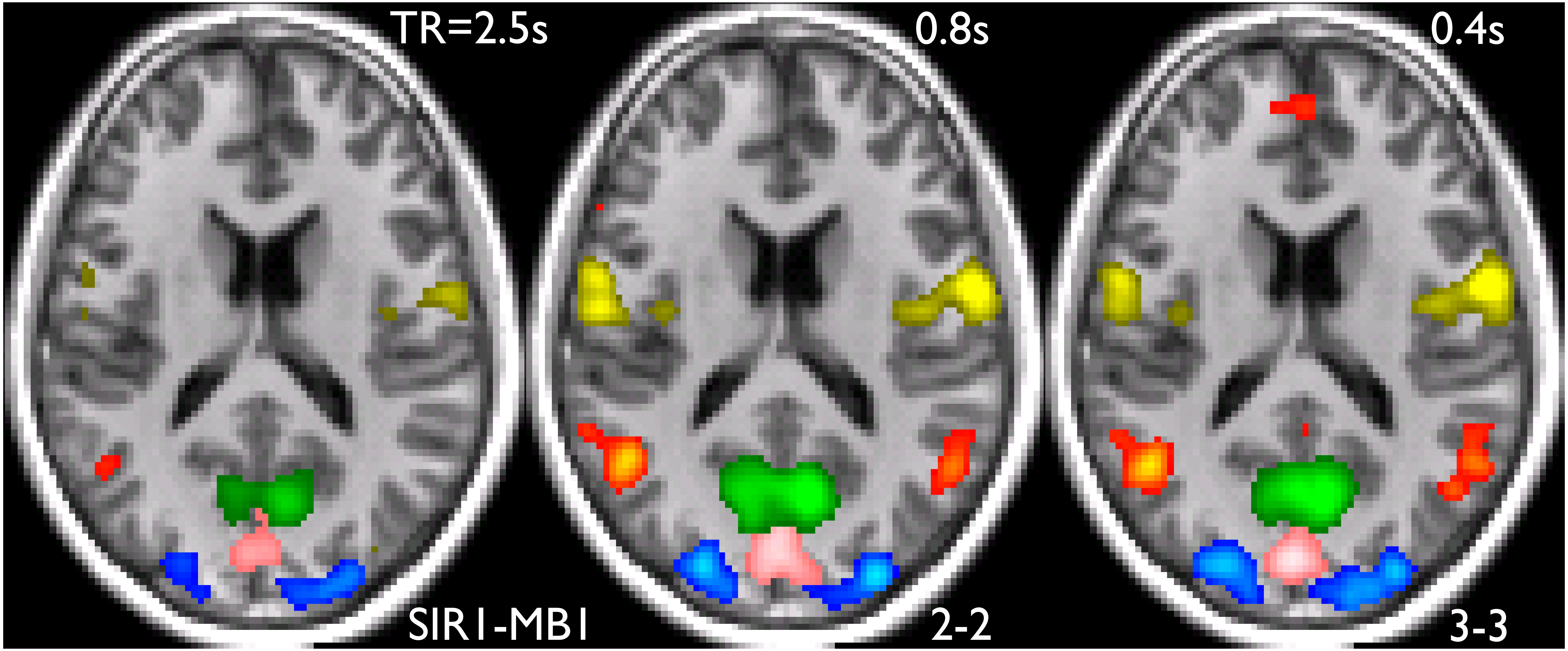
HCP

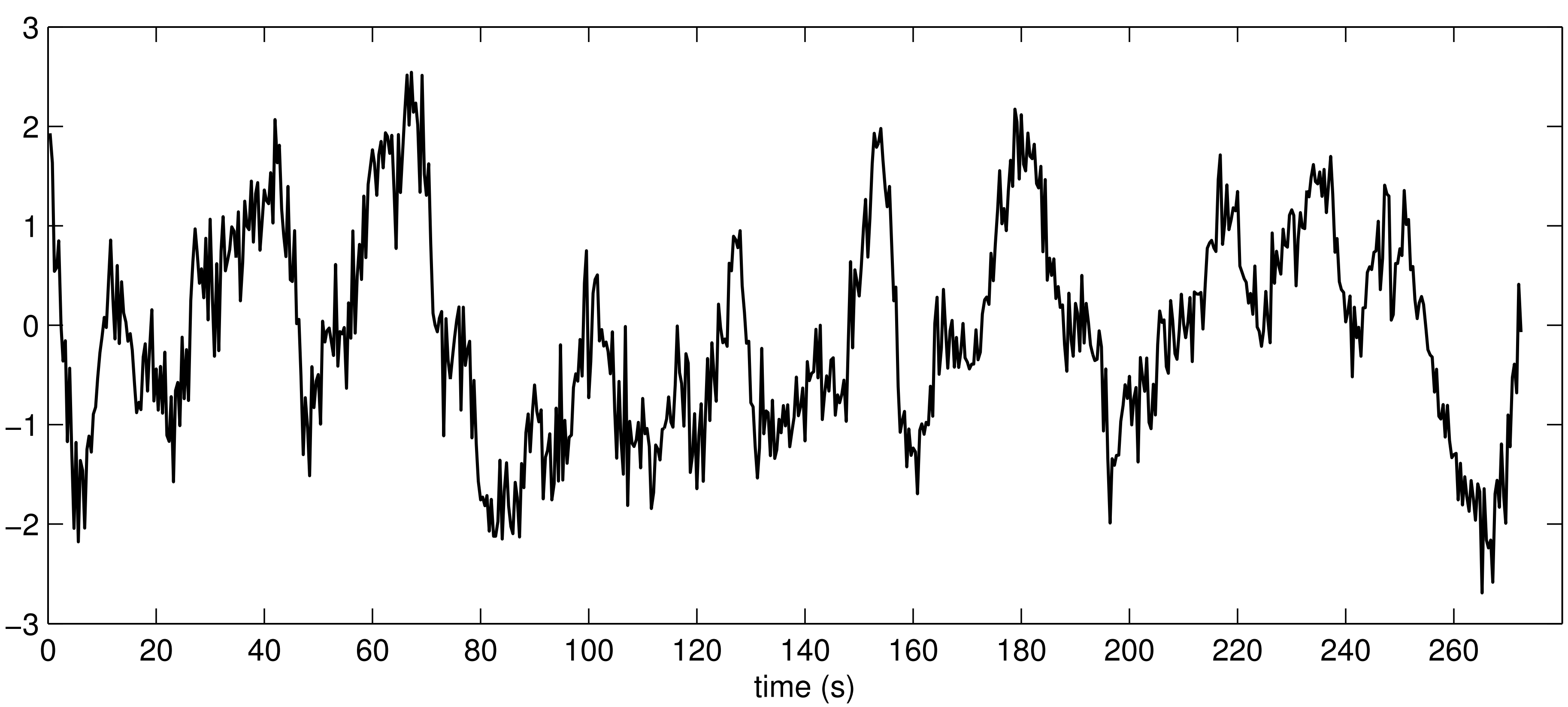
Signal & Noise Considerations

- Main SNR effect (when reducing TR) is *signal loss* due to reduced T_1-relaxation period
- This loss almost balanced by the sqrt(N) increase in effective SNR









- Increased DoF and temporal sampling
- Non-Gaussianity
- Non-stationarity
- Interesting temporal dynamics

HCP rfMRI pre-processing summary

- 4D rfMRI data from *spatial ("minimal") pre-processing*, in both volumetric and grayordinate forms

- Weak highpass temporal filtering (>2000s FWHM) applied to both, giving slow drift removal

- MELODIC ICA is applied to volumetric data; artefact components are identified using FIX

- Artefact and motion-related timecourses are regressed out of both volumetric and grayordinate data

- Ongoing investigations into also possibly applying:
    - further motion cleanup / scrubbing
    - further removal of physiological confounds based on physiological monitoring data
    - removal of globally-related signals.

HCP rfMRI data
processing flowchart
and data release info

HCP rfMRI data
processing flowchart
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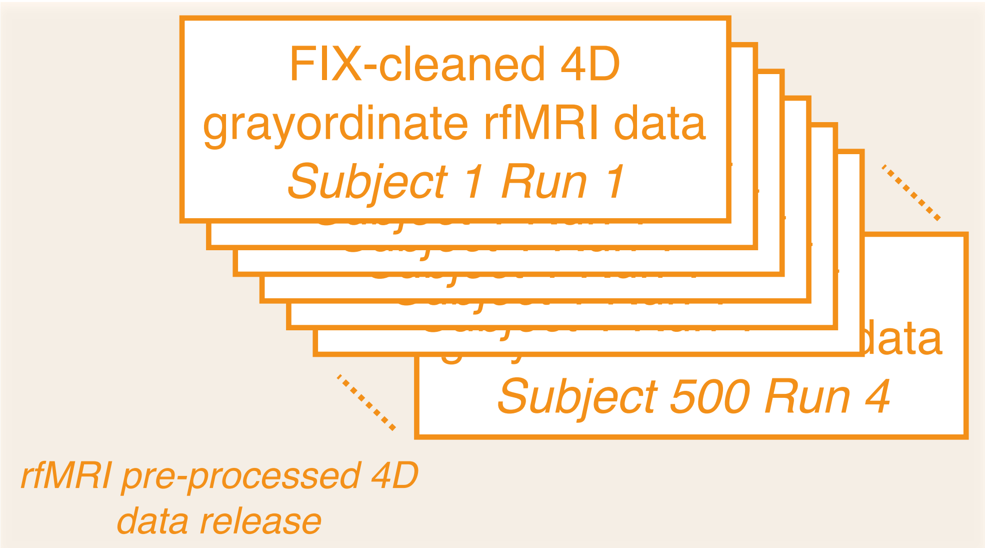
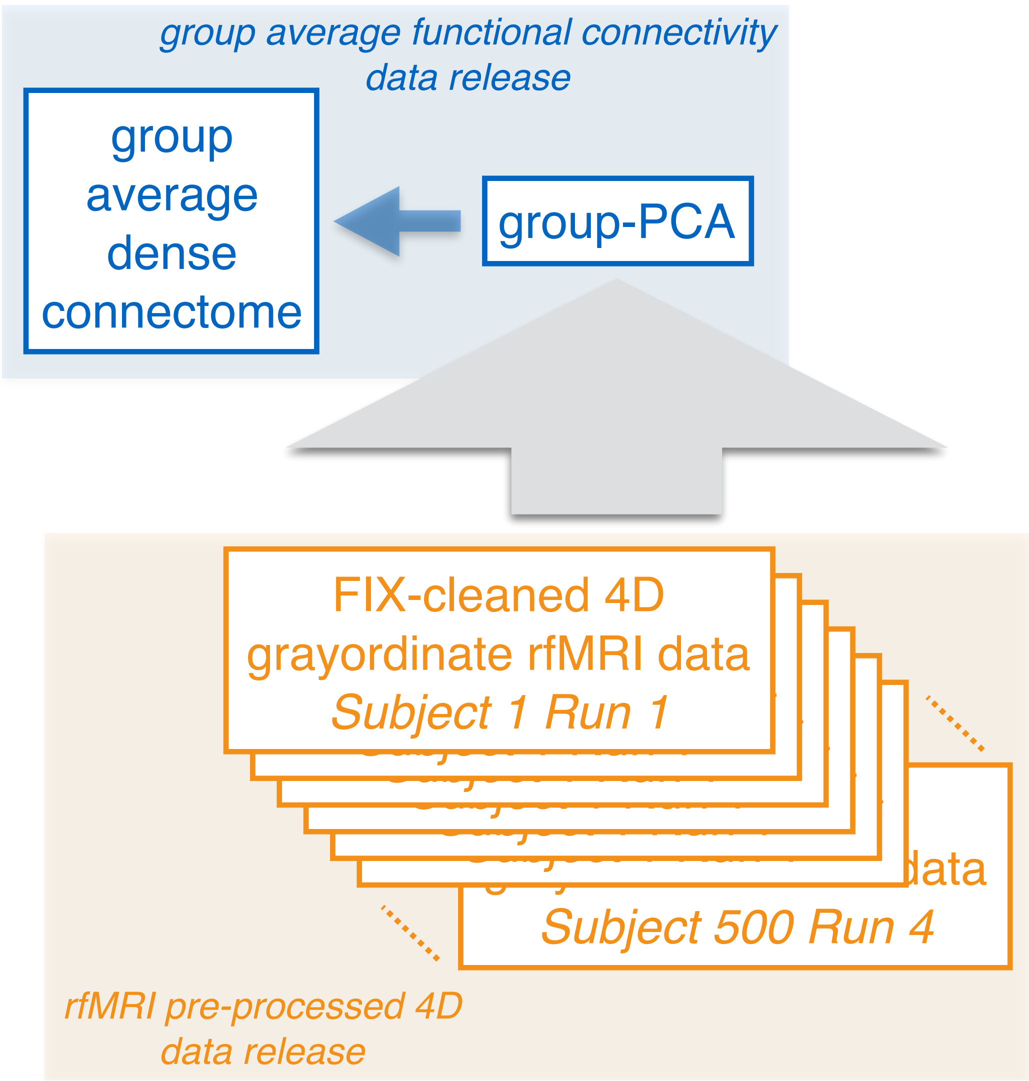
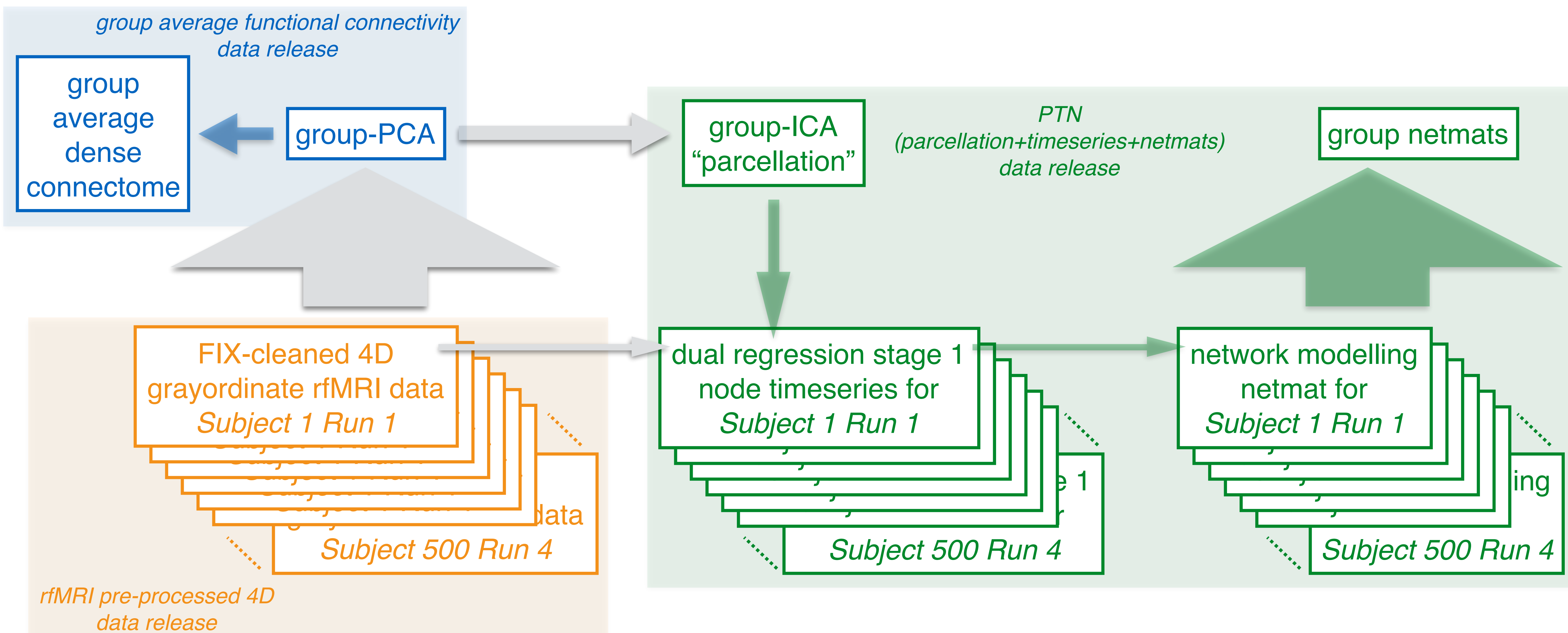


HCP rfMRI data
processing flowchart and data release info



HCP rfMRI data
processing flowchart
and data release info



HCP rfMRI data
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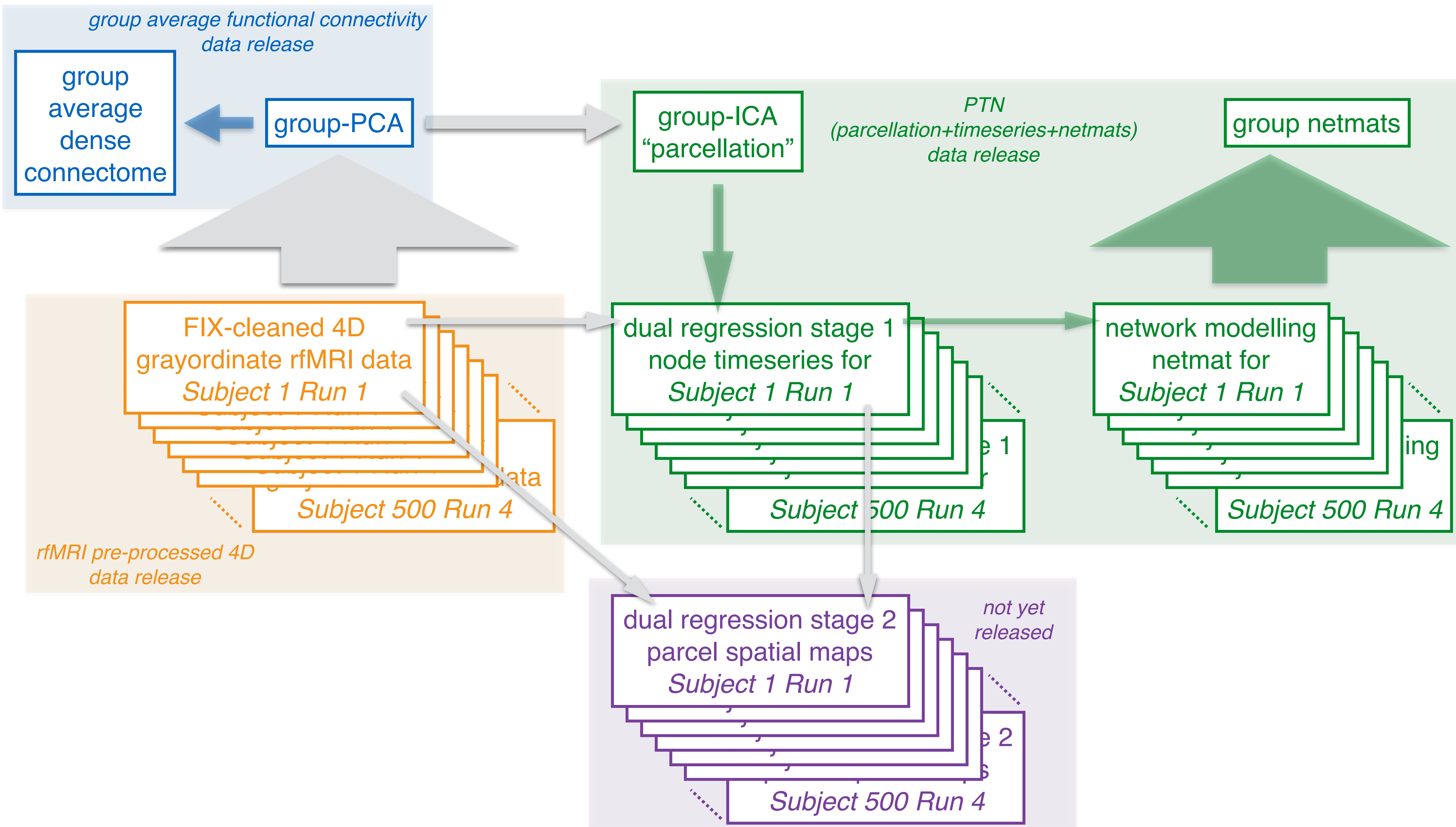

HCP rfMRI data processing flowchart and data release info