

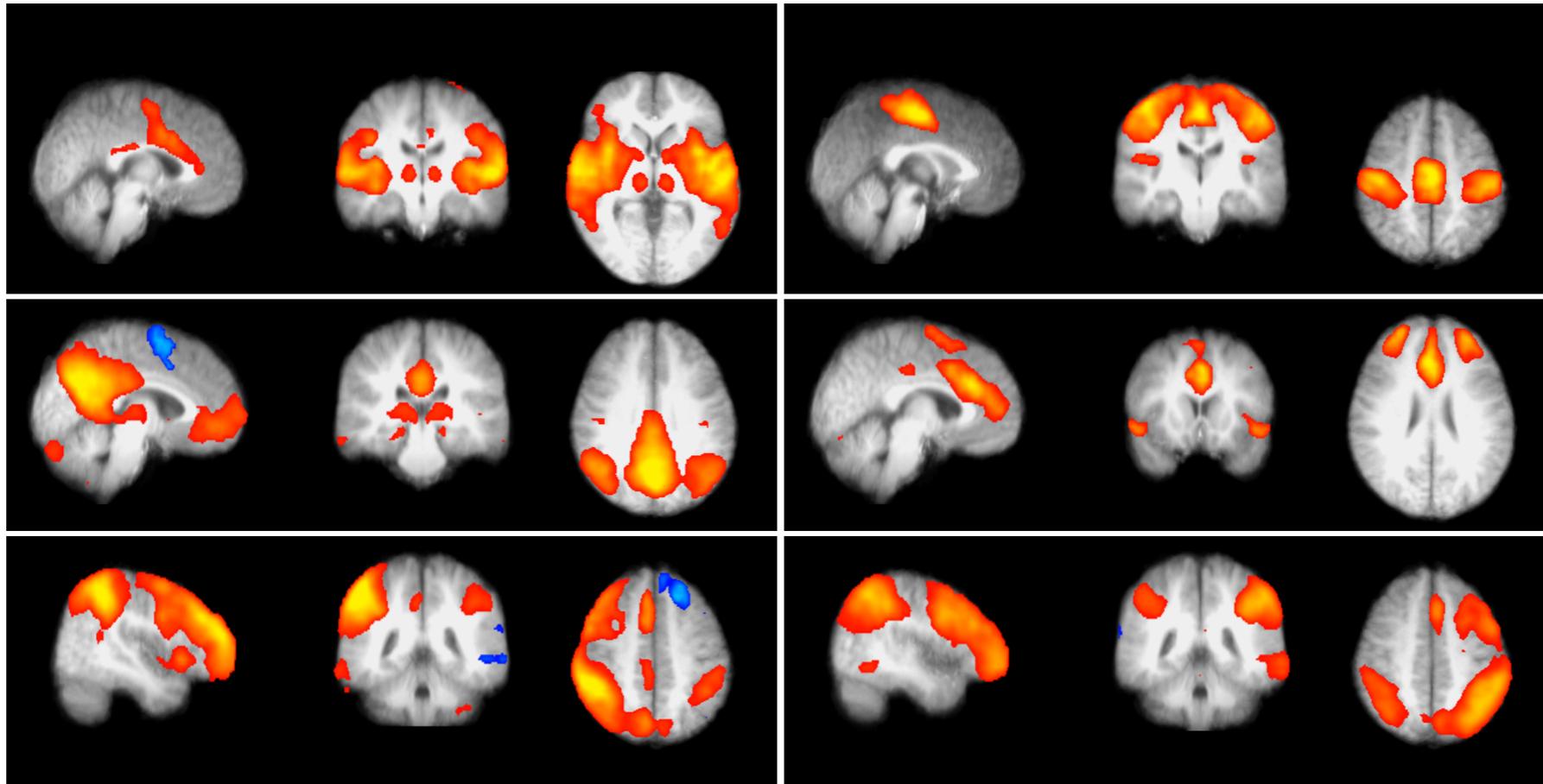
HCP Course 2015

rFMRI network analysis strategies

Stephen Smith, FMRIB Oxford

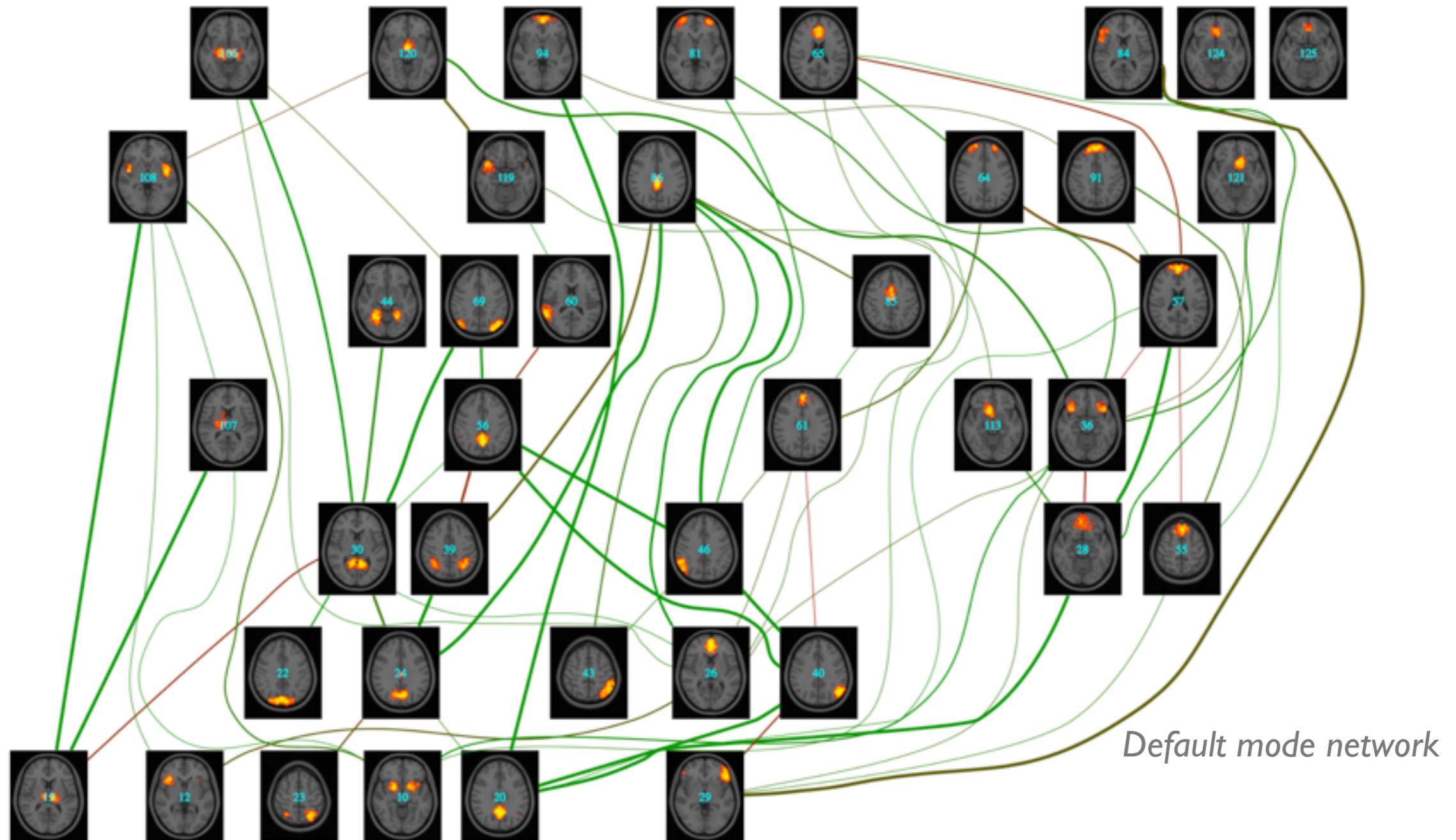
Network Modelling

- Seed-correlation maps, or low-dim ICA, give “networks”



- But these are gross patterns
 - Each map summarised by single timecourse
 - Too simple a model to do more detailed network analysis
- Instead, get detailed parcellation....

Detailed Network Analyses



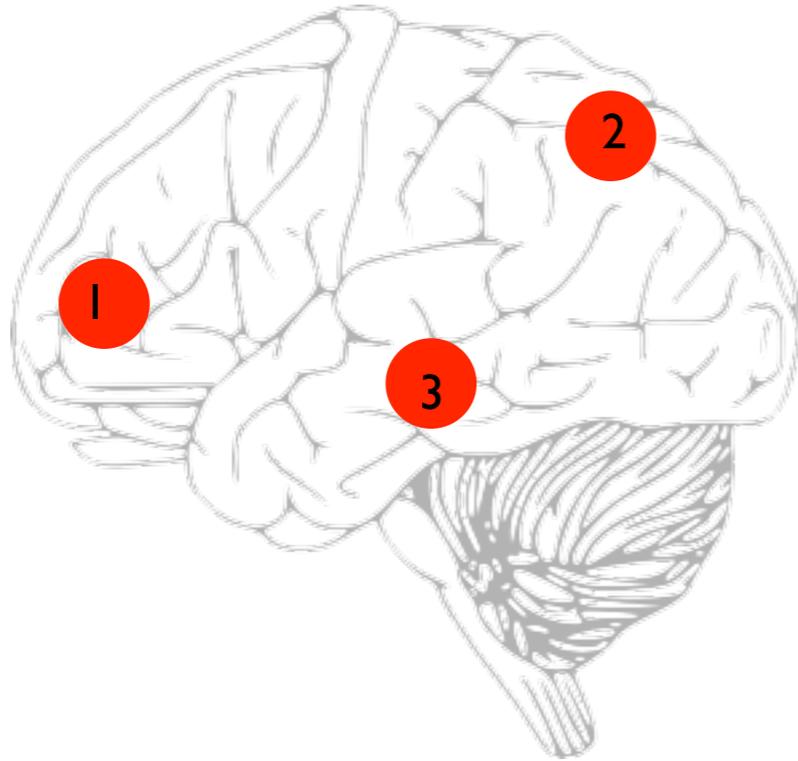
A network model comprises:

- “Nodes” distinct functional voxels/regions
- “Edges” connections between nodes

How to do network estimation from rfMRI?

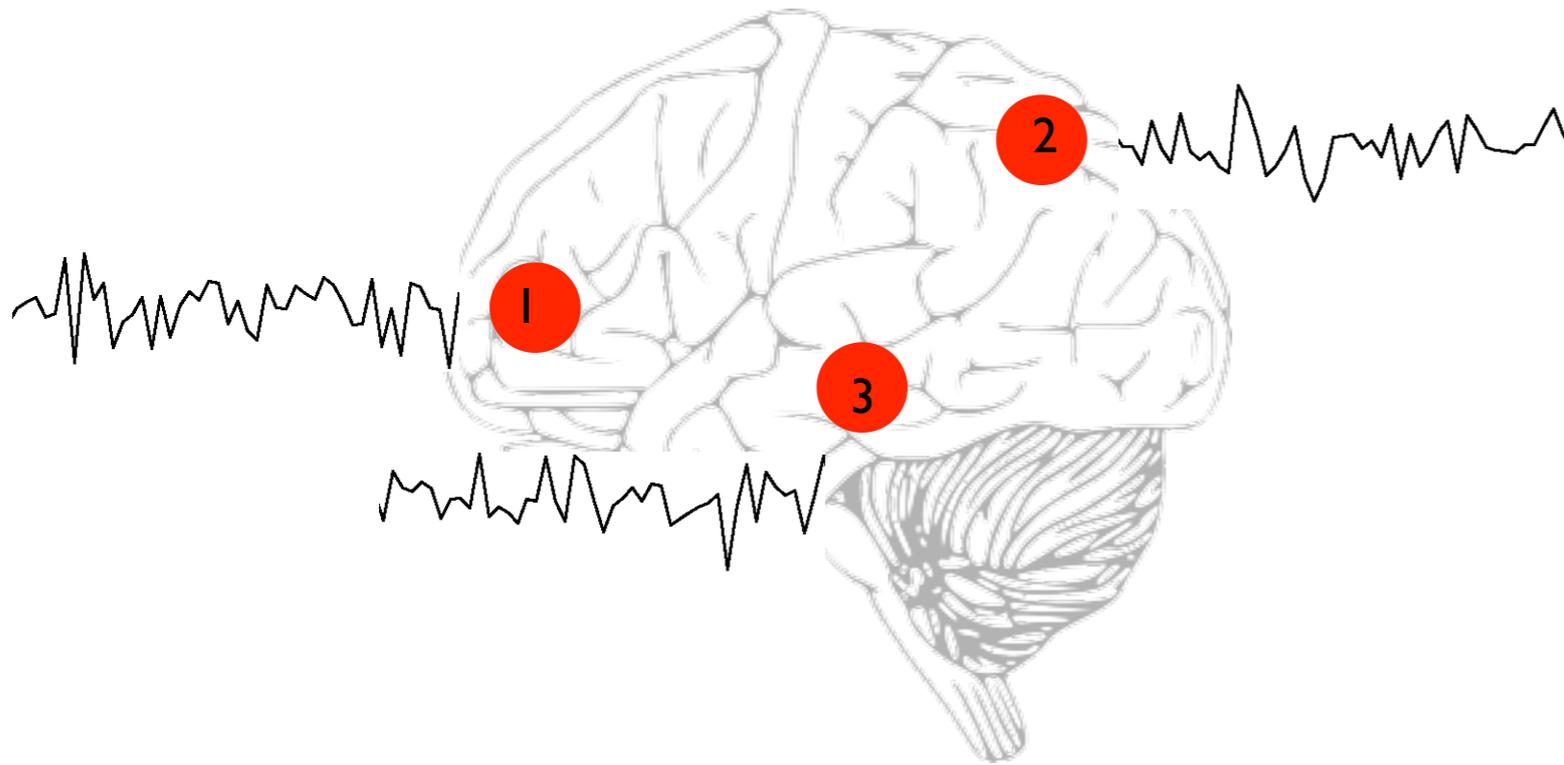


How to do network estimation from rfMRI?



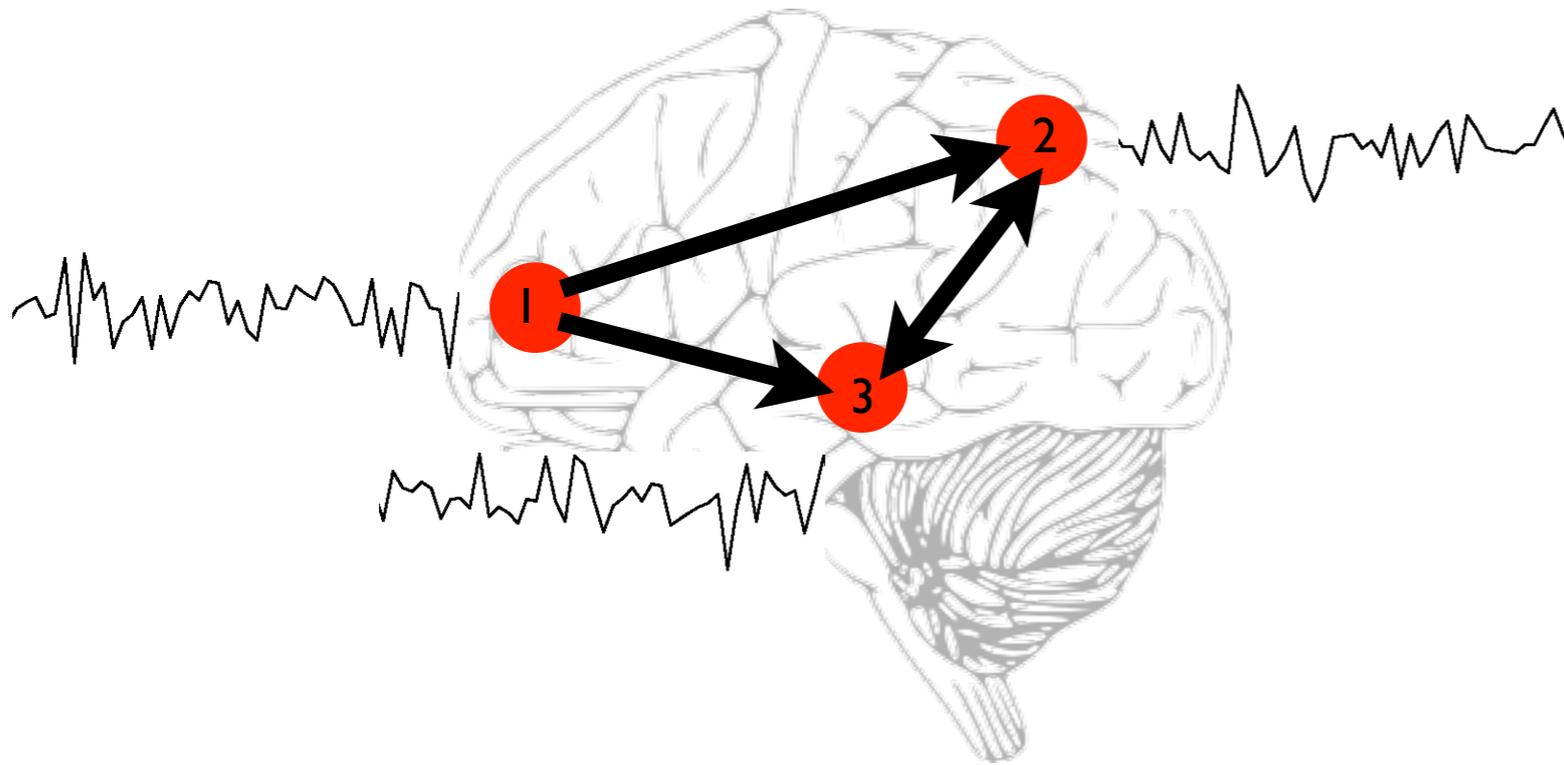
- Define network “nodes” (spatial ROIs or coordinates)

How to do network estimation from rfMRI?



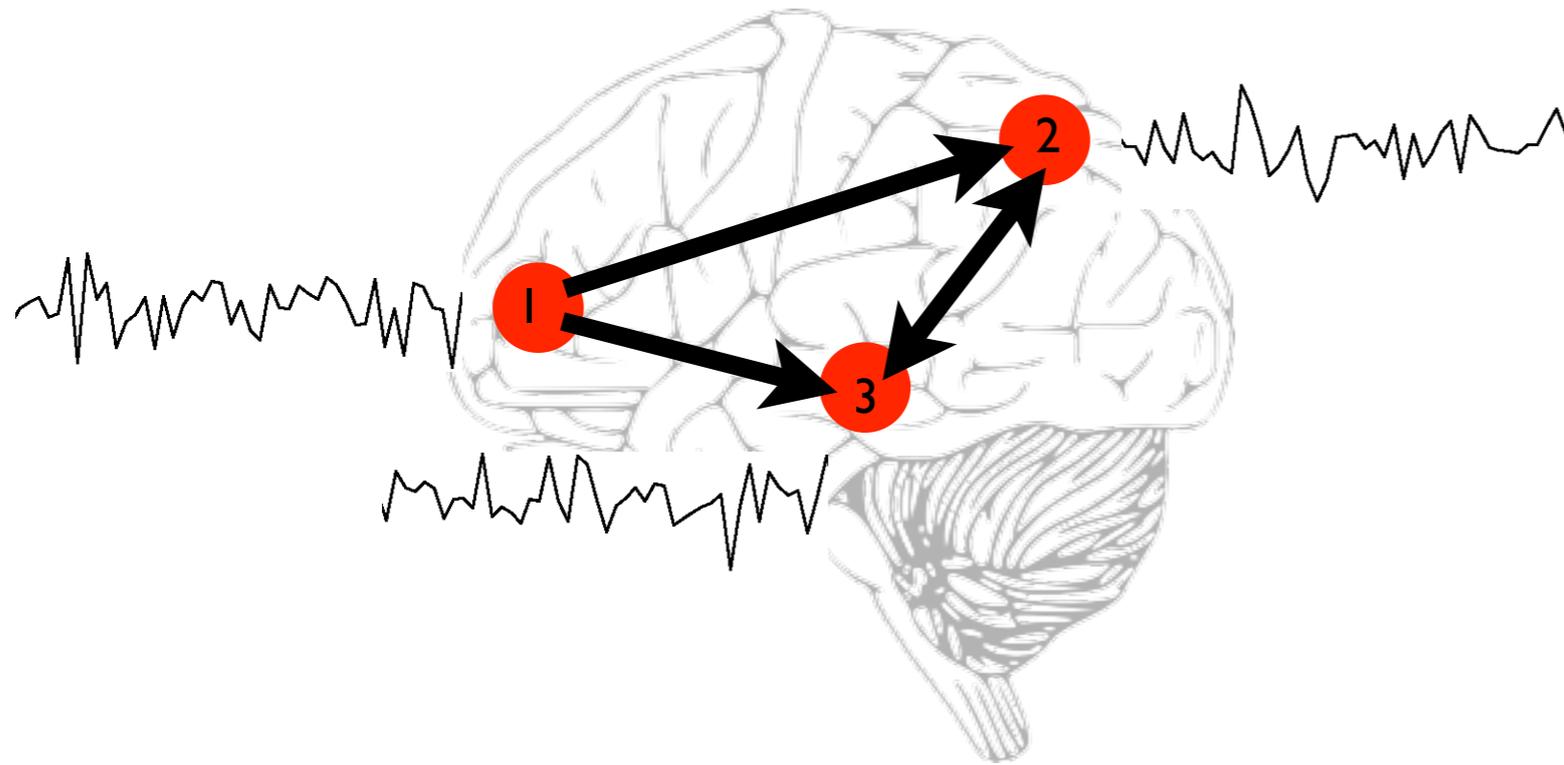
- Define network “nodes” (spatial ROIs or coordinates)
- Identify a timeseries associated with each node

How to do network estimation from rfMRI?



- Define network “nodes” (spatial ROIs or coordinates)
- Identify a timeseries associated with each node
- Estimate the connections between the nodes
 - For example, correlate any pair of timeseries together

How to do network estimation from rfMRI?

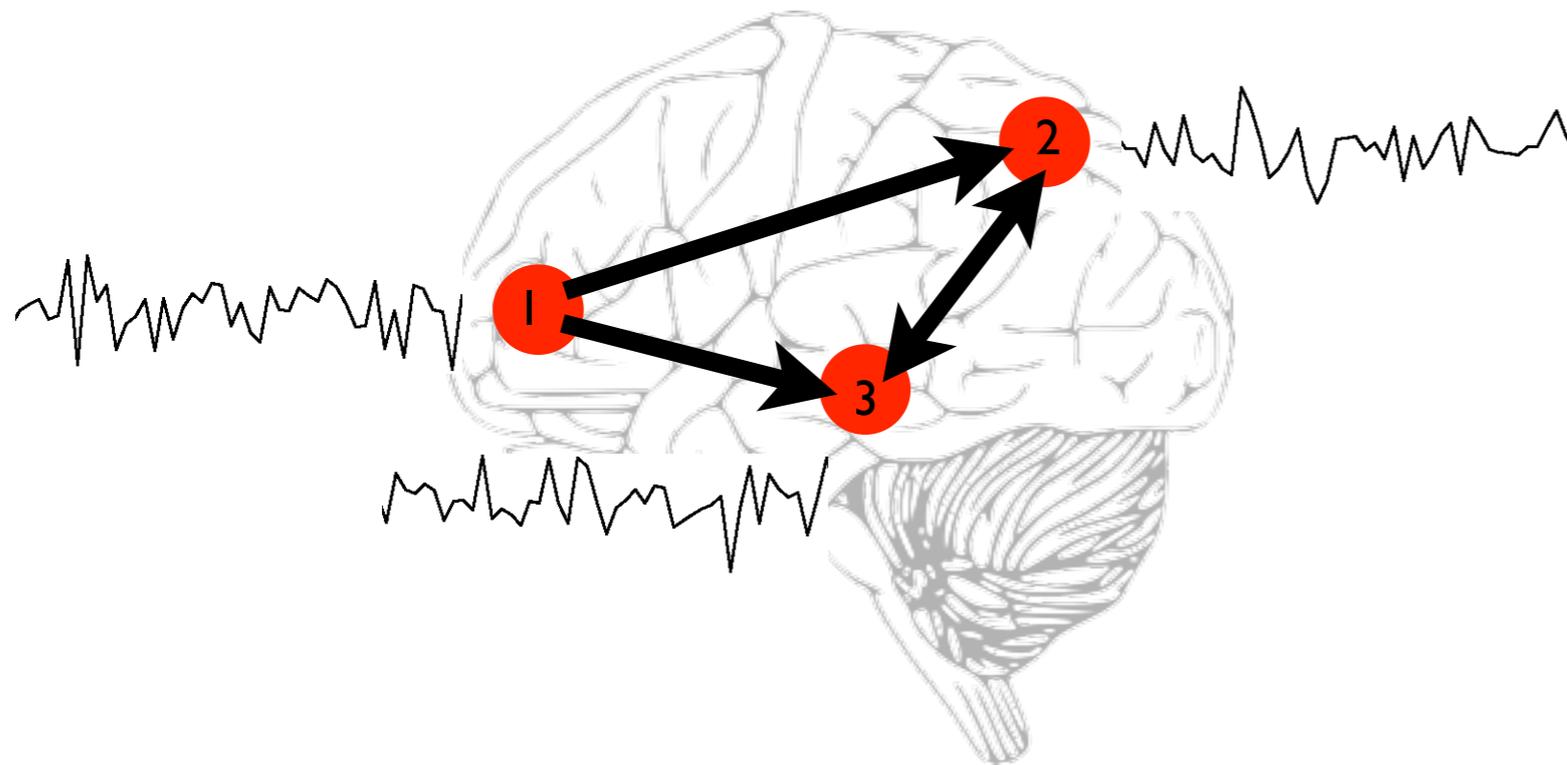


		to		
		1	2	3
from	1	0	0.8	0.7
	2	0	0	0.6
	3	0	0.5	0

network matrix

- Define network “nodes” (spatial ROIs or coordinates)
- Identify a timeseries associated with each node
- Estimate the connections between the nodes
 - For example, correlate any pair of timeseries together

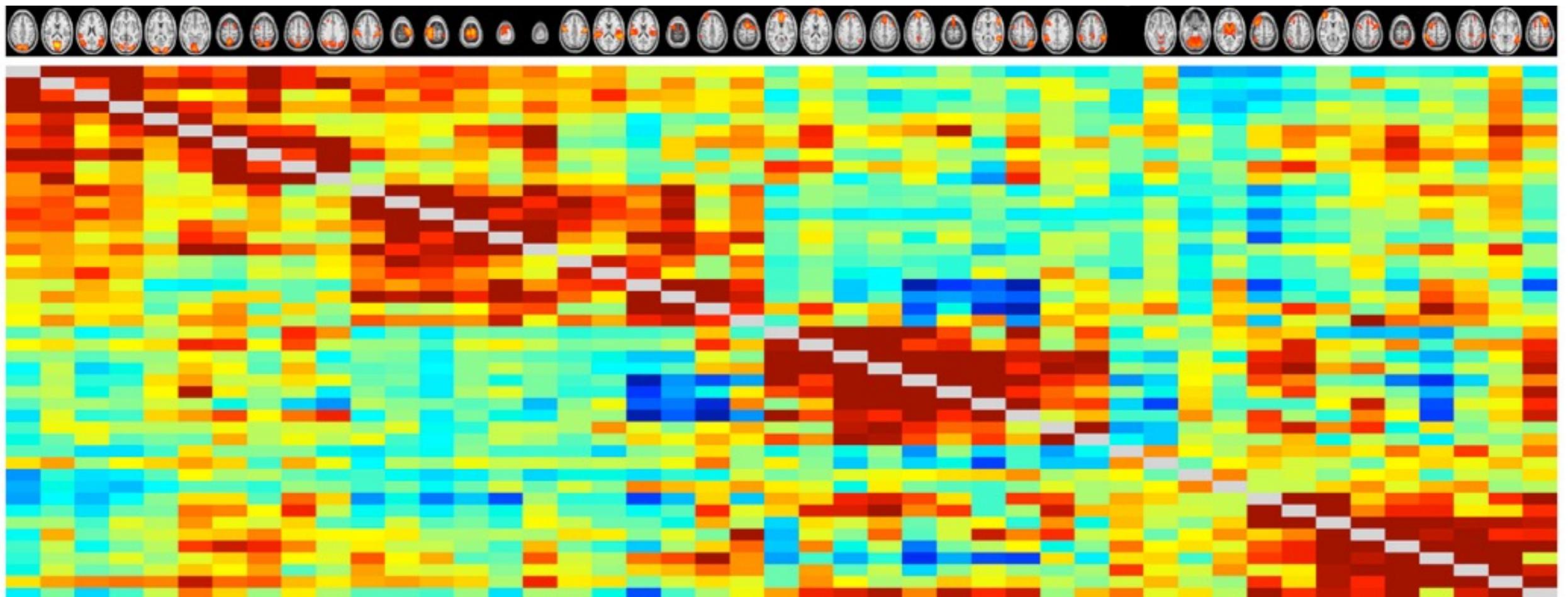
How to do network estimation from rfMRI?



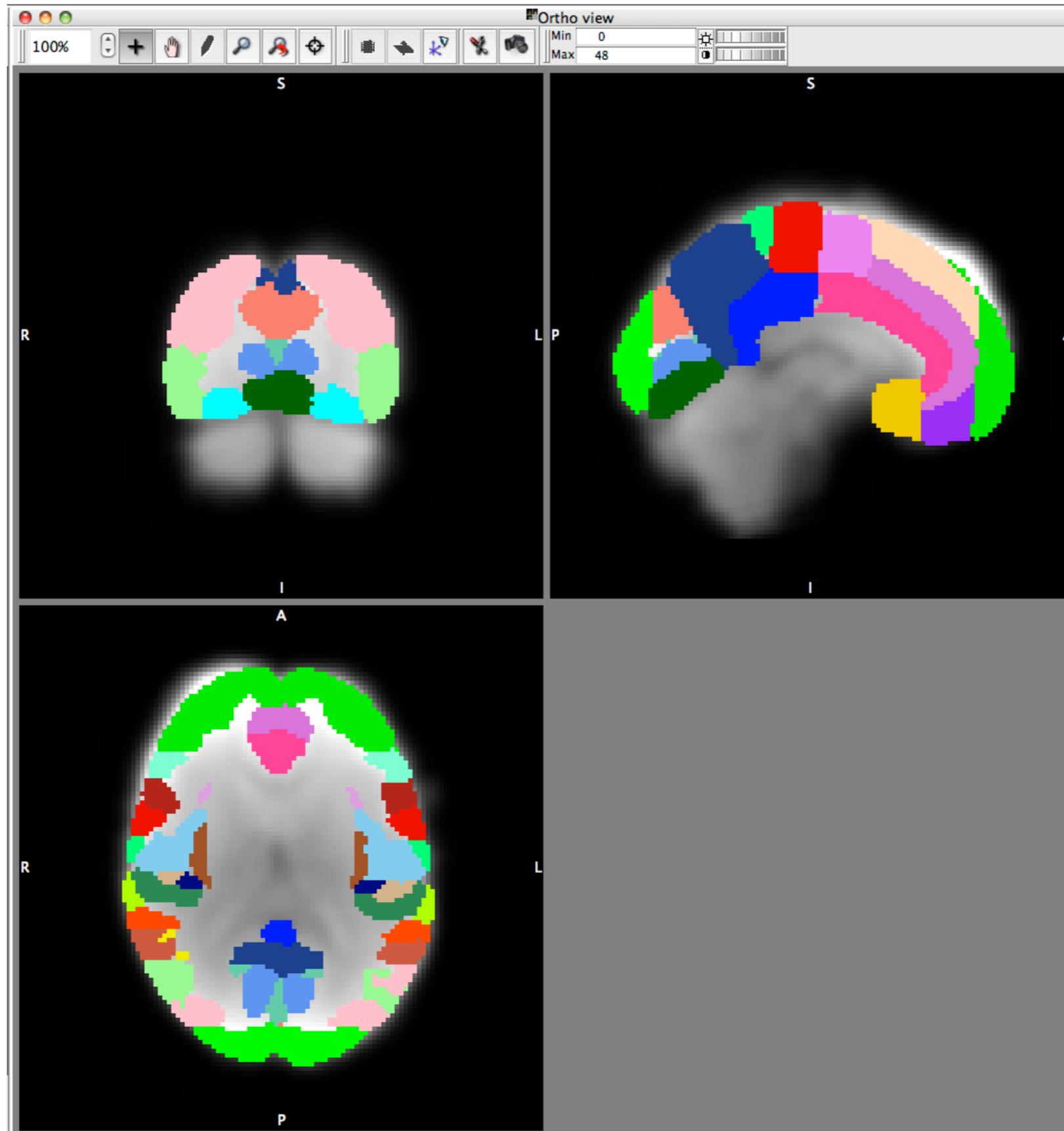
from

	to 1	to 2	to 3
1	0	0.8	0.7
2	0	0	0.6
3	0	0.5	0

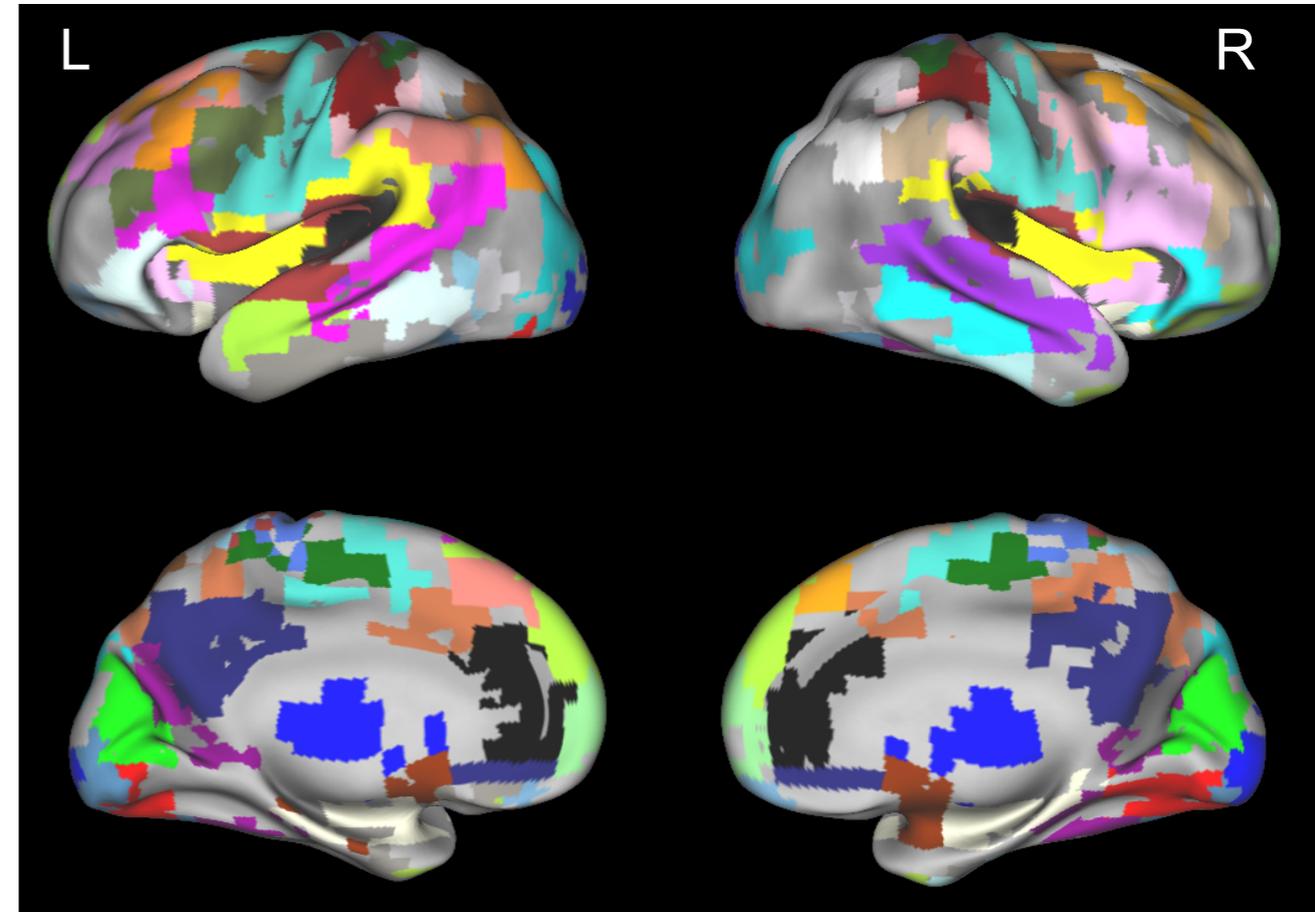
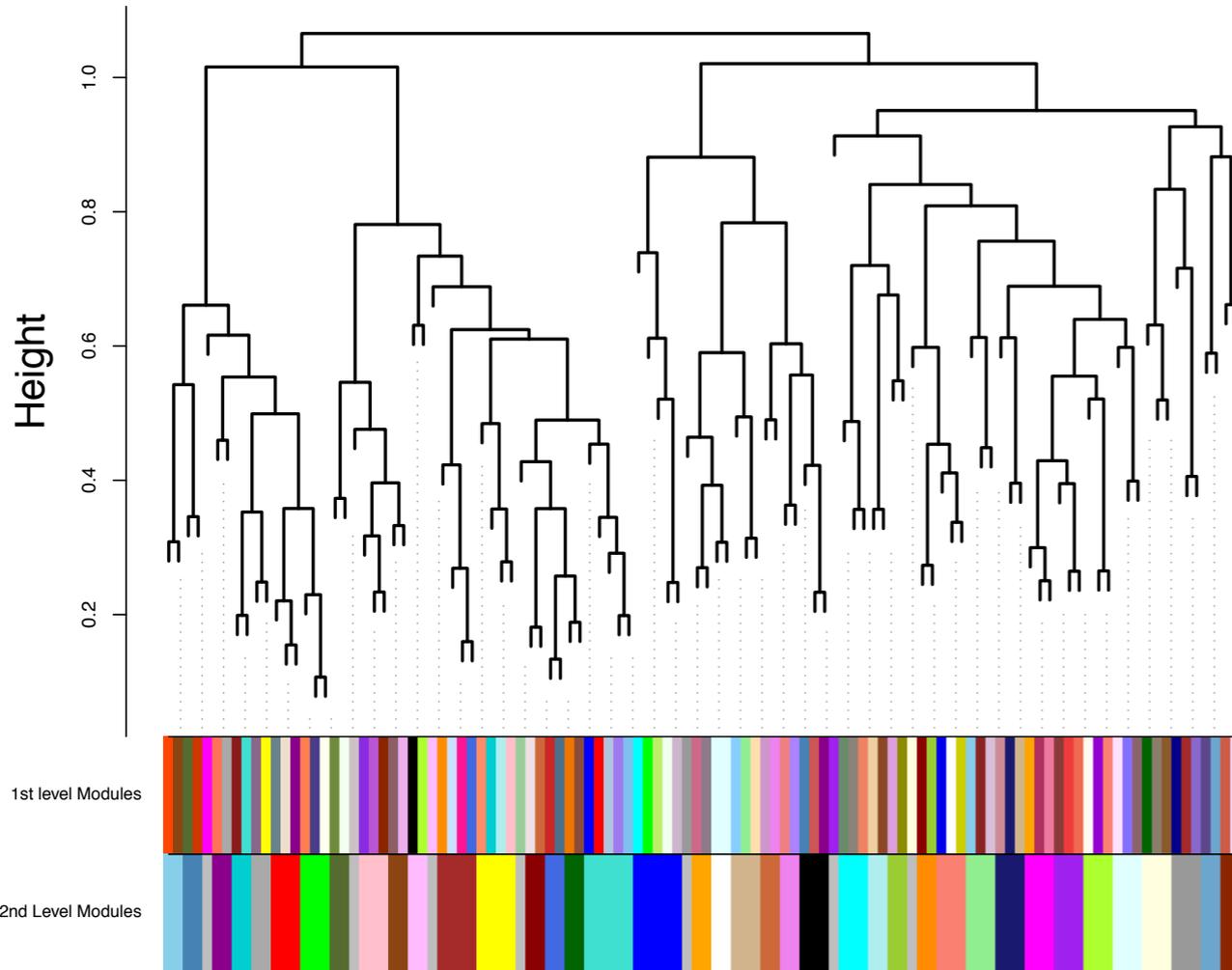
network matrix



Nodes 1: Take ROIs from an atlas



Nodes 2: Clustering of voxels with similar timecourses



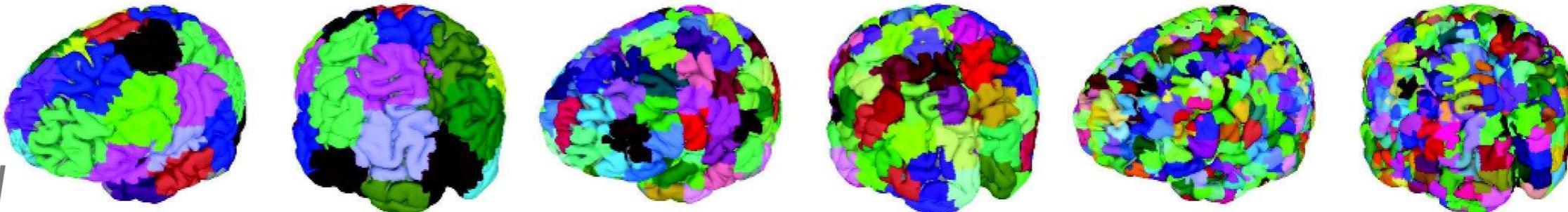
• *Mumford NeuroImage 2010*

50 ROIs

200 ROIs

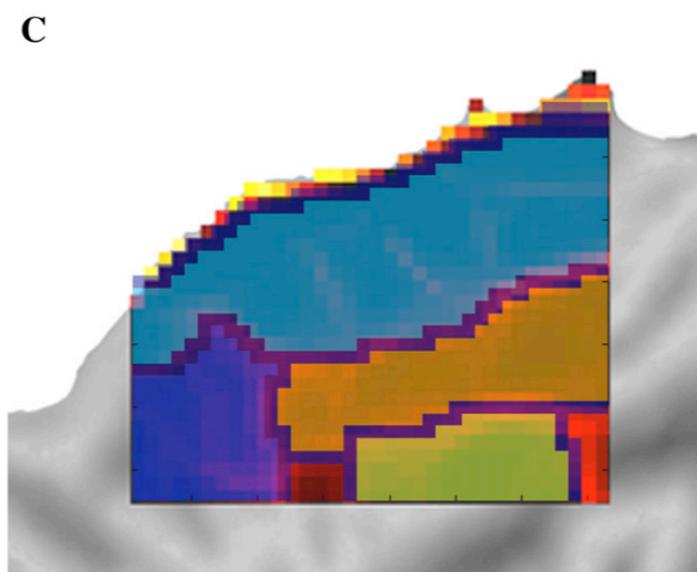
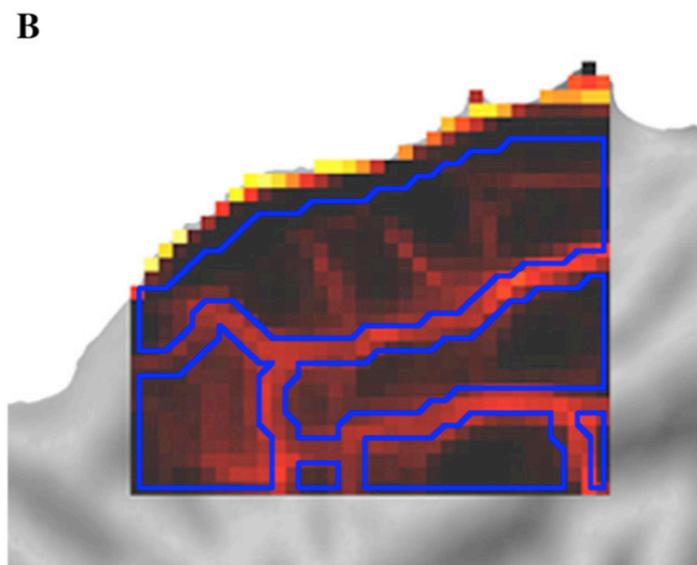
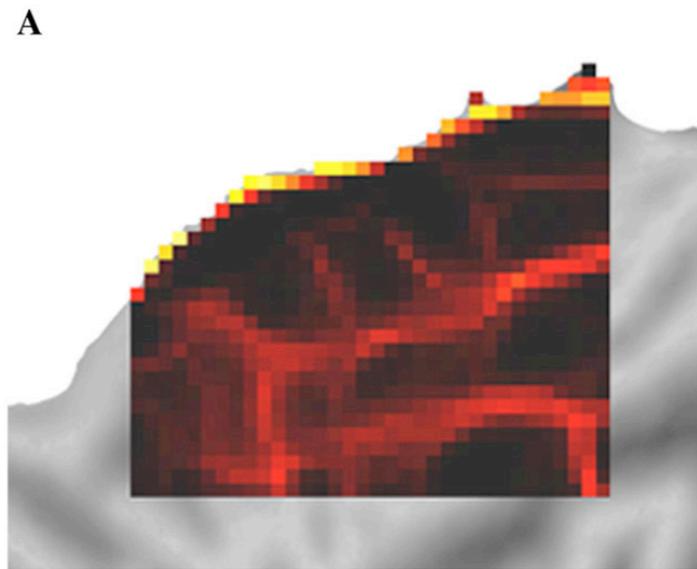
1000 ROIs

• *Craddock HBM 2011*

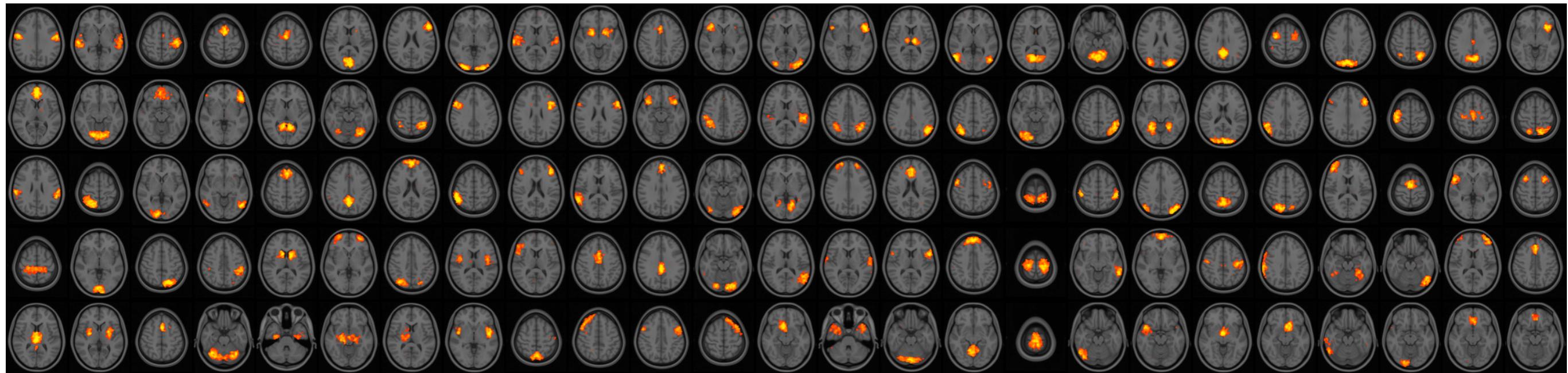


Nodes 3: Gradients in seed-based correlation maps

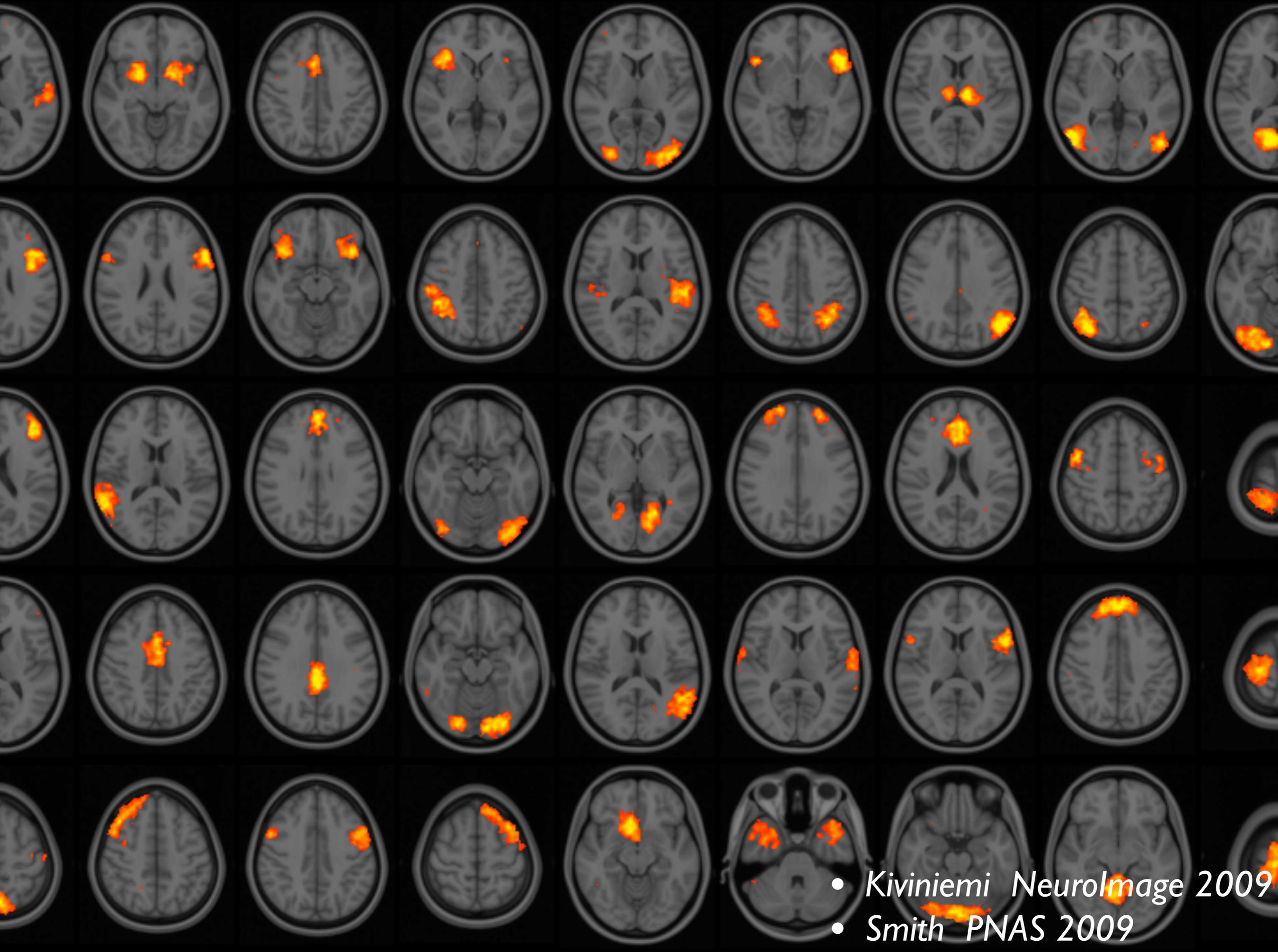
- Get correlation maps, seeding from *all* voxels
- Find boundaries between regions that have different correlation maps



Nodes 4: High-dimensional ICA

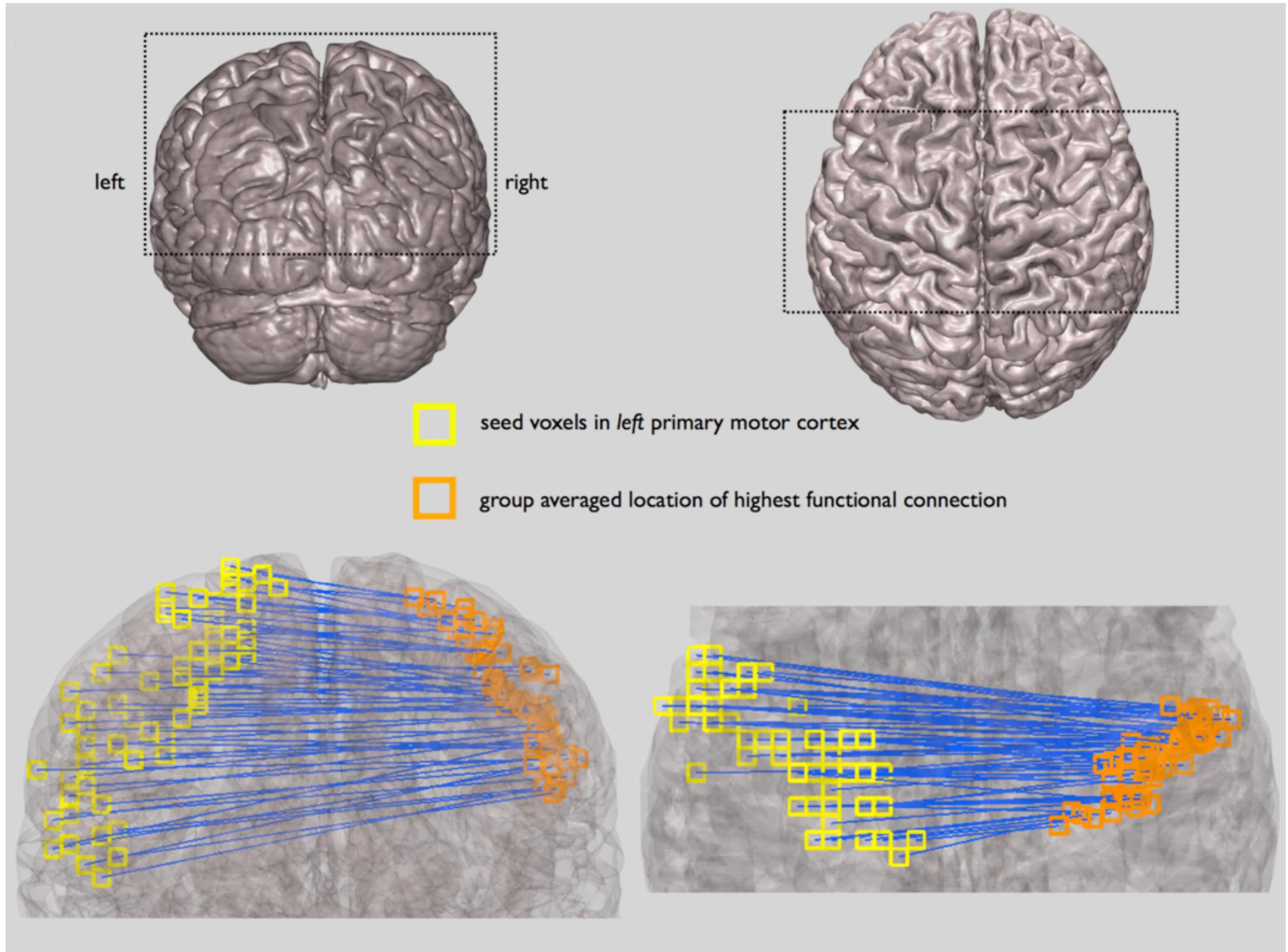


- *Kiviniemi NeuroImage 2009*
- *Smith PNAS 2009*



- *Kiviniemi Neurolmage 2009*
- *Smith PNAS 2009*

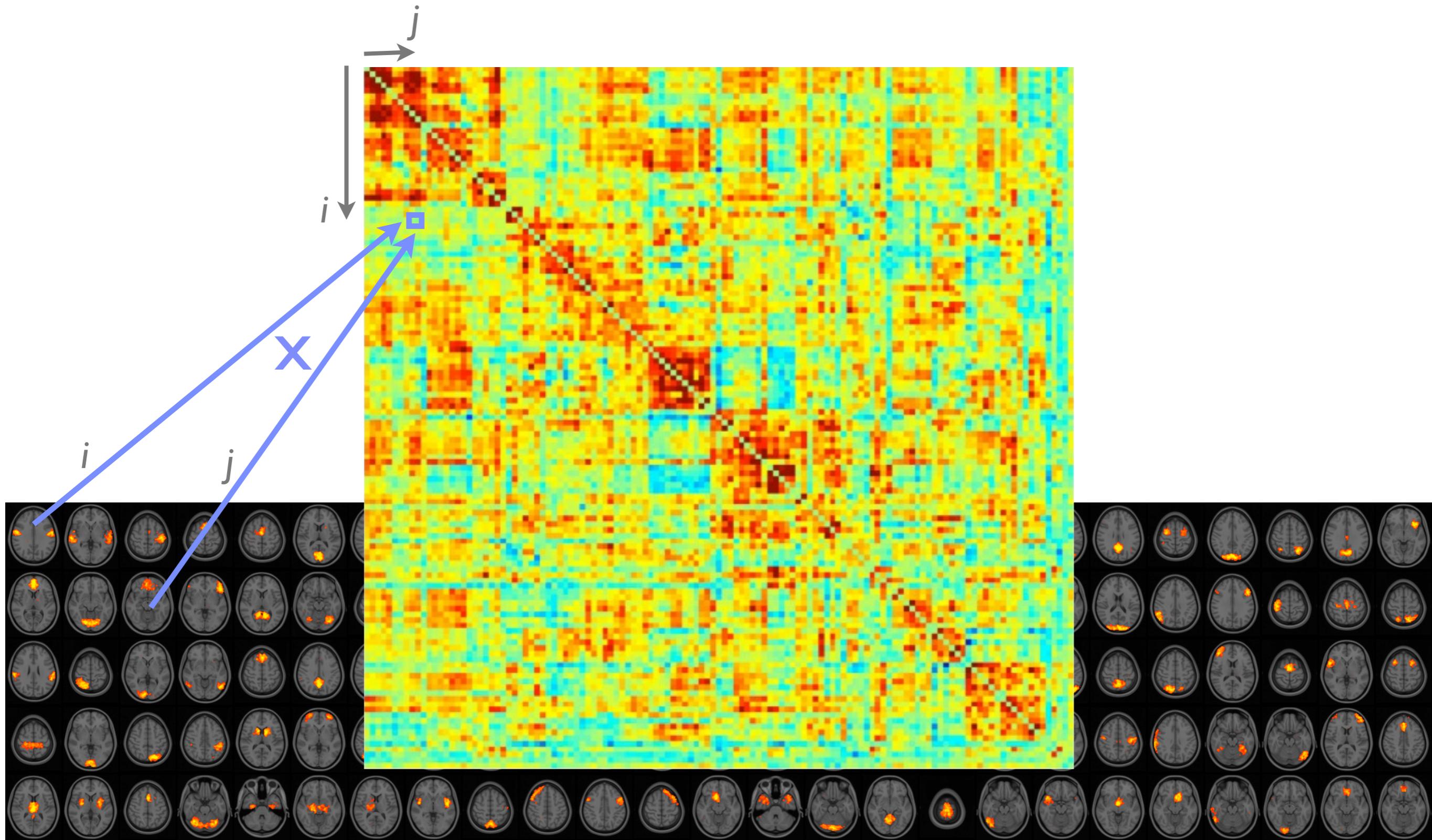
But is “function” uniform within a parcel?



mapping group “parcellation” onto individual subjects

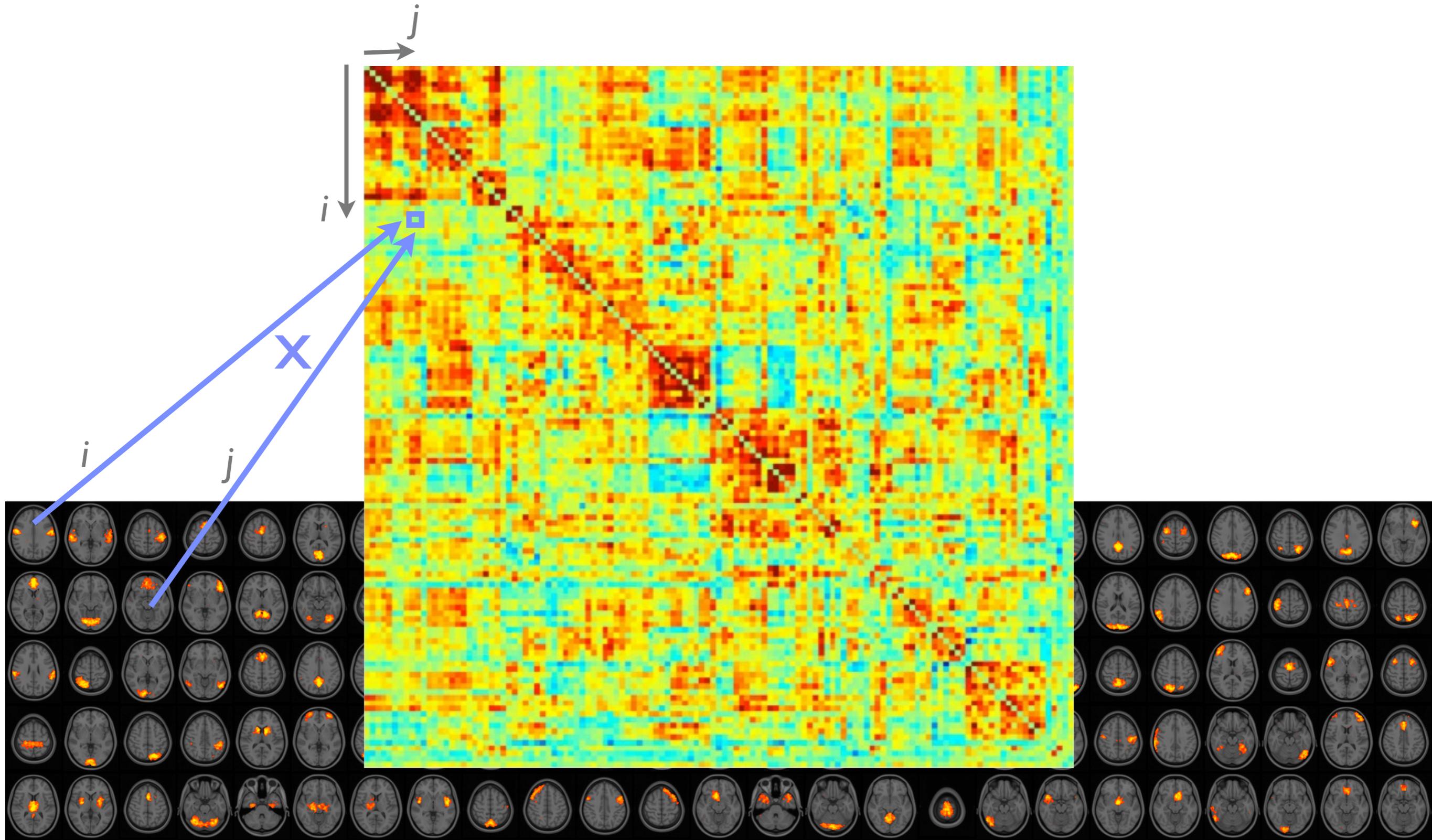
- With a “hard” non-overlapping parcellation you could just mask-average subject-4D-data with each mask to get node timeseries
- With a soft, potentially overlapping, “parcellation” (e.g.) group-ICA, it may be more robust to treat this as a multiple-spatial-regression (dualreg stage I)
- In both cases, alignment between group and subject critical!
- More critical the smaller the parcel size
- “Weighted regression” could help (use reliable voxels only)
- Beware “rank deficient” parcellation (parcels with too similar timecourses)

Edges: estimate connectivity between all pairs of nodes

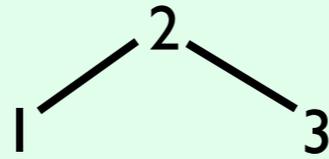


Edges: estimate connectivity between all pairs of nodes

But: what is the right method for estimating connectivity, based on FMRI timeseries?



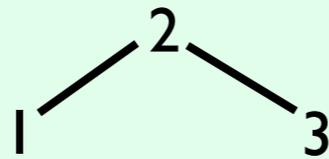
What do we want to estimate?



		to		
		1	2	3
from	1	0	1	0
	2	1	0	1
	3	0	1	0

- What are the network edges?

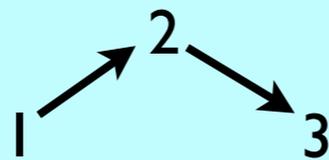
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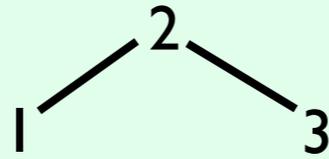
- What are the network edges?

- What is the dominant directionality of the edges?



		to		
		1	2	3
from	1	0	1	0
	2	0	0	1
	3	0	0	0

What do we want to estimate?

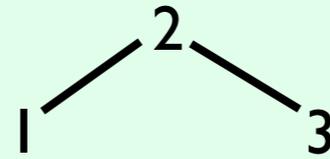


		to		
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from	1	0	1	0
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- What are the network edges?

Direct vs. Indirect Connections

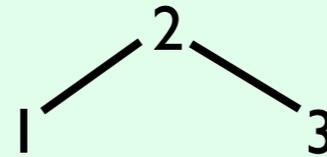
suppose the truth is:



		to	1	2	3
from	1	0	1	0	
2	1	0	1	0	
3	0	1	0	0	

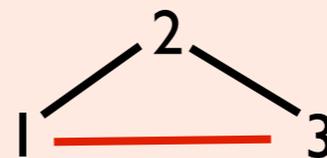
Direct vs. Indirect Connections

suppose the truth is:



		to	1	2	3
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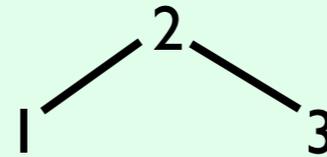
but 1 will correlate with 3, so if we estimate edges using (full) correlation, we will (wrongly) estimate:



		to	1	2	3
from	1	0	1	1	
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	3	1	1	0	

Direct vs. Indirect Connections

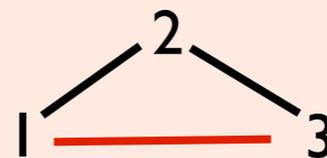
suppose the truth is:



		to	1	2	3
from	1	0	1	0	
	2	1	0	1	
	3	0	1	0	

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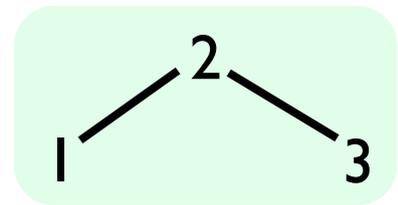
1-3 is referred to as an “indirect connection”



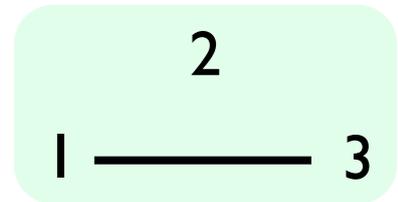
		to	1	2	3
from	1	0	1	1	
	2	1	0	1	
	3	1	1	0	

Disambiguating direct vs. indirect connections

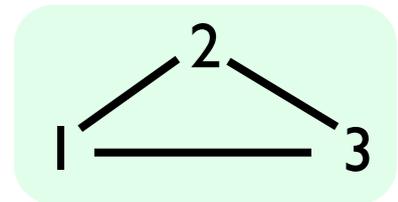
- Need to take into account multiple nodes' timecourses in order to estimate *direct* edges
- E.g., DCM, SEM, Bayes Nets, LiNGAM
- In some cases (e.g. large numbers of nodes, no input timings known), “principled models” such as SEM, DCM are not estimable
- One useful approximation to SEM is “partial correlation”
 - *Marrelec NeuroImage 2006*
 - *Fransson NeuroImage 2008*
 - *Varoquaux NIPS 2010*



vs.

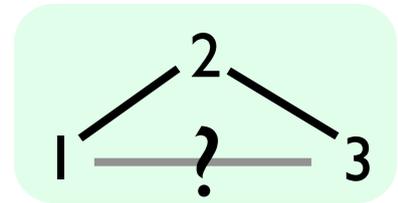


vs.



Disambiguating direct vs. indirect connections using partial correlation

- Before correlating 1 and 3, first regress 2 out of both (“orthogonalise wrt 2”)
- If 1 and 3 are *still* correlated, a direct connection exists
- More generally, first regress *all other nodes’ timecourses* out of the pair in question
- Equivalent to the *inverse covariance* matrix
- Urgh! If you have 200 nodes and 100 timepoints, this is impossible!
- A problem of DoF - need large #timepoints - #nodes



Degrees of freedom and estimability when using partial correlation

- When inverting a “rank-deficient” matrix it is common to aid this with some mathematical conditioning, e.g. force it to be sparse (force low values that are poorly estimated to zero)
- E.g. “ICOV” (regularised inverse covariance)
 - *Friedman Biostat 2008*
- Can improve further when analysing multiple subjects
 - *Varoquaux NIPS 2010*
- But still important to maximise temporal DoF

What do we want to estimate?

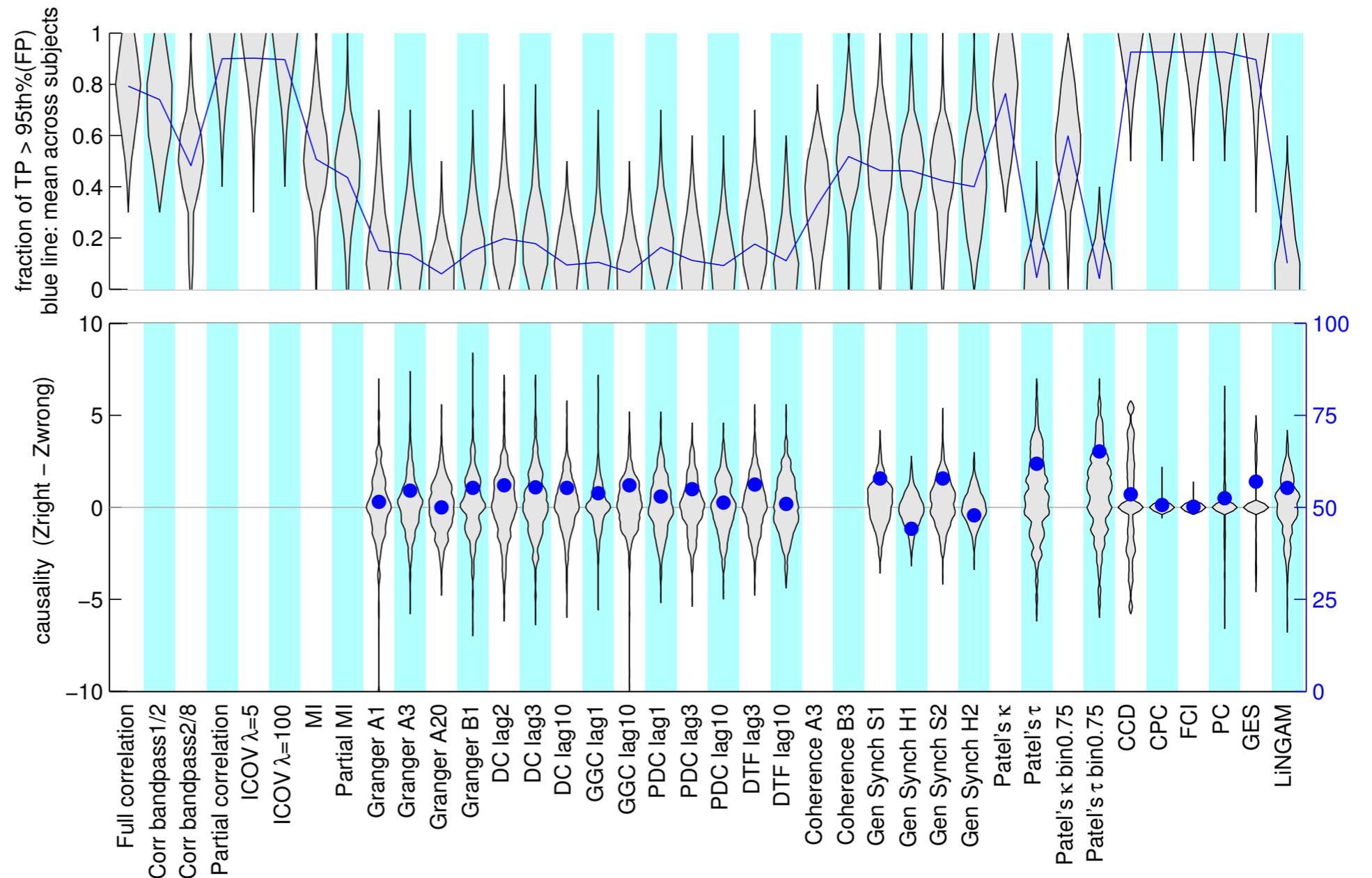
- What is the dominant directionality of the edges?



		to		
		1	2	3
from	1	0	1	0
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- Assumed: dominant directionality is biologically interesting
- Maybe oversimplistic view of neural connectivity (particularly in resting-state)?
- In any case, very hard to estimate well - and *no* mature robust tools yet available..... **don't use Granger !**

Network Modelling Methods for fMRI



Results:

- Correlation good at edge detection: partial better than full
- Directionality *hard* to estimate
- Lag-based methods (Granger) bad
- Atlas-based parcellation bad

Gotcha #1

Inappropriate ROIs yield a bad network

Inappropriate node definition will blur node timeseries together

This yields a bad network matrix for all network modelling methods

E.g. use of structural atlases with large ROIs, such as AAL and Harvard-Oxford...

...or even a data-driven group-level parcellation applied to individual subjects, if subject variability is high

Gotcha #2

Functional Connectivity is not “quantitative”

Full / partial correlation often referred to as “Functional connectivity”

These are **not quantitative measures**:

In addition to telling us about

- changes in network connection strength

it is **also sensitive to**

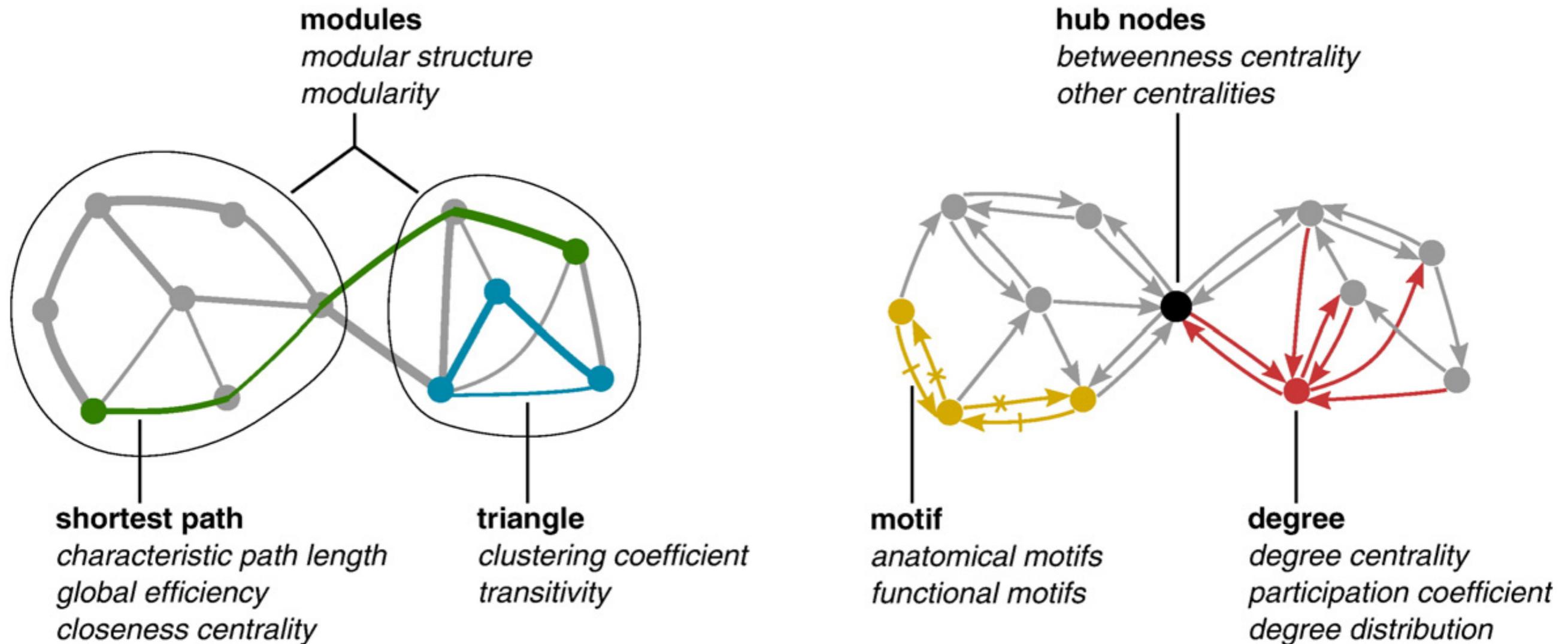
- changes in noise level
- changes in input signal level
- signals passing round other parts of the network

• *Friston BC 2011*

But - BOLD FMRI isn't quantitative anyway....so maybe not get **too** hung up on this? But be careful when interpreting group differences, etc.....

Gotcha #3

Graph theory won't save a bad network matrix!



• Rubinov *NeuroImage* 2010

Danger ! Unless the network matrix is “correct” these measures are meaningless
... in fact - IMHO they are almost always meaningless ...

Gotcha #4

Things change over time

- The “connection” between two brain areas may change over time - so the average correlation might not be meaningful
- What if different networks *are* better modelled as *MAPSxTIMECOURSES* (e.g. low-dim ICA, TFM, PFM)?
- In that case “netmat” correlations aren’t so meaningful.....but still we’re all using them ;-)

graph theory

clusters / hierarchies, network hubs,
network summary statistics (e.g. small-worldness, efficiency)

network modelling from fMRI data

functional connectivity
simpler, less meaningful,
network “discovery”,
better conditioned,
can handle more nodes

full correlation

partial correlation

regularised partial correlation

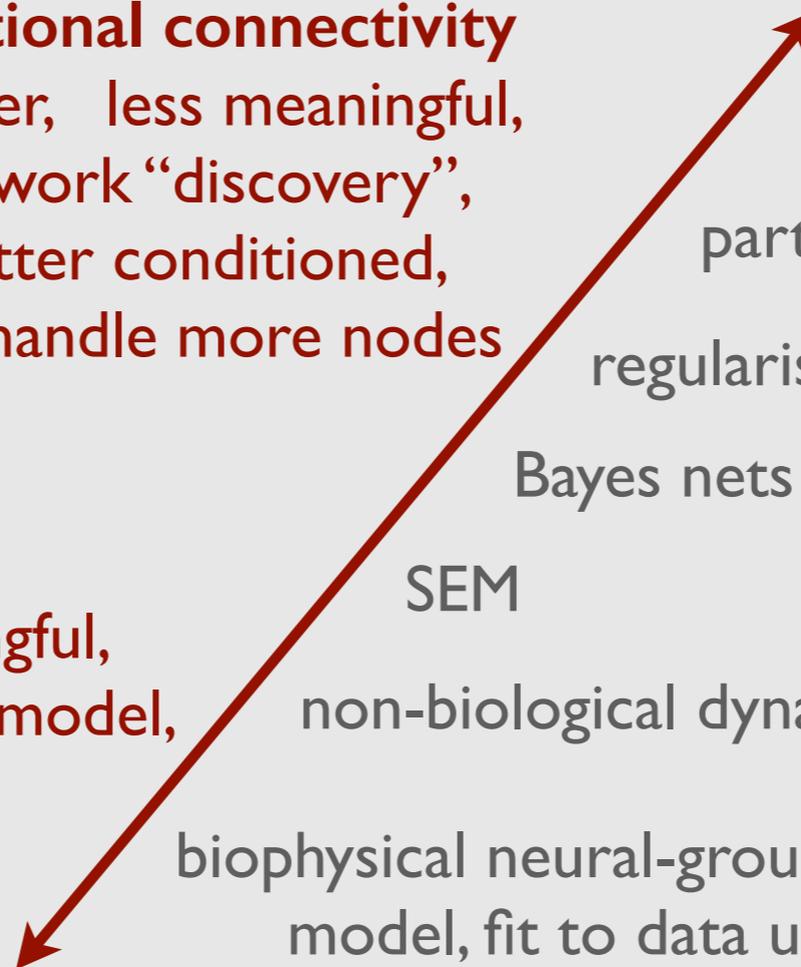
Bayes nets

SEM

non-biological dynamic Bayes nets

effective connectivity
more complex, more meaningful,
pre-specify (constrain) network model,
harder to estimate,
can handle fewer nodes

biophysical neural-groups to fMRI-signal forward
model, fit to data using Bayes (e.g. DCM)



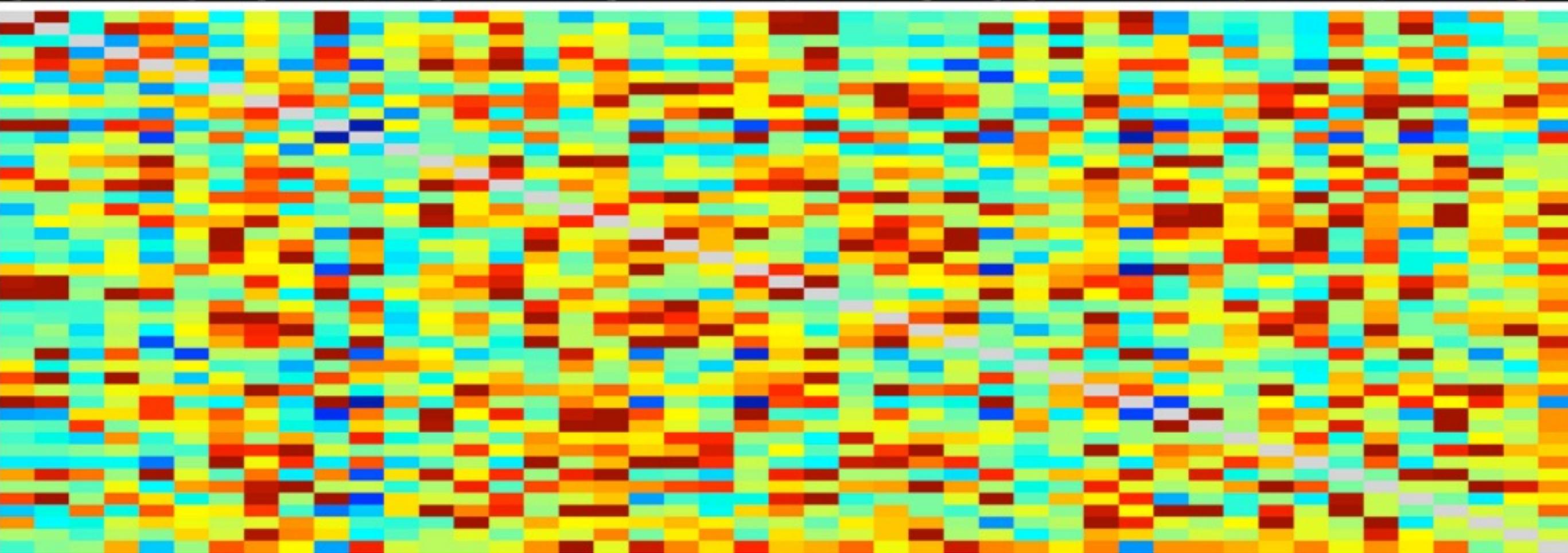
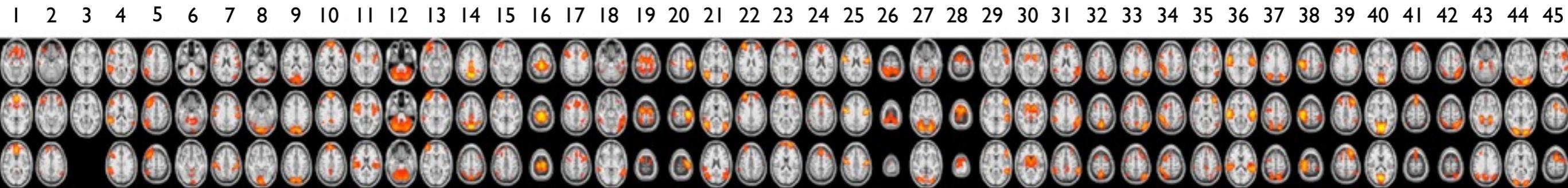
bottom-up neural network simulations

network of individual
neurons simulated

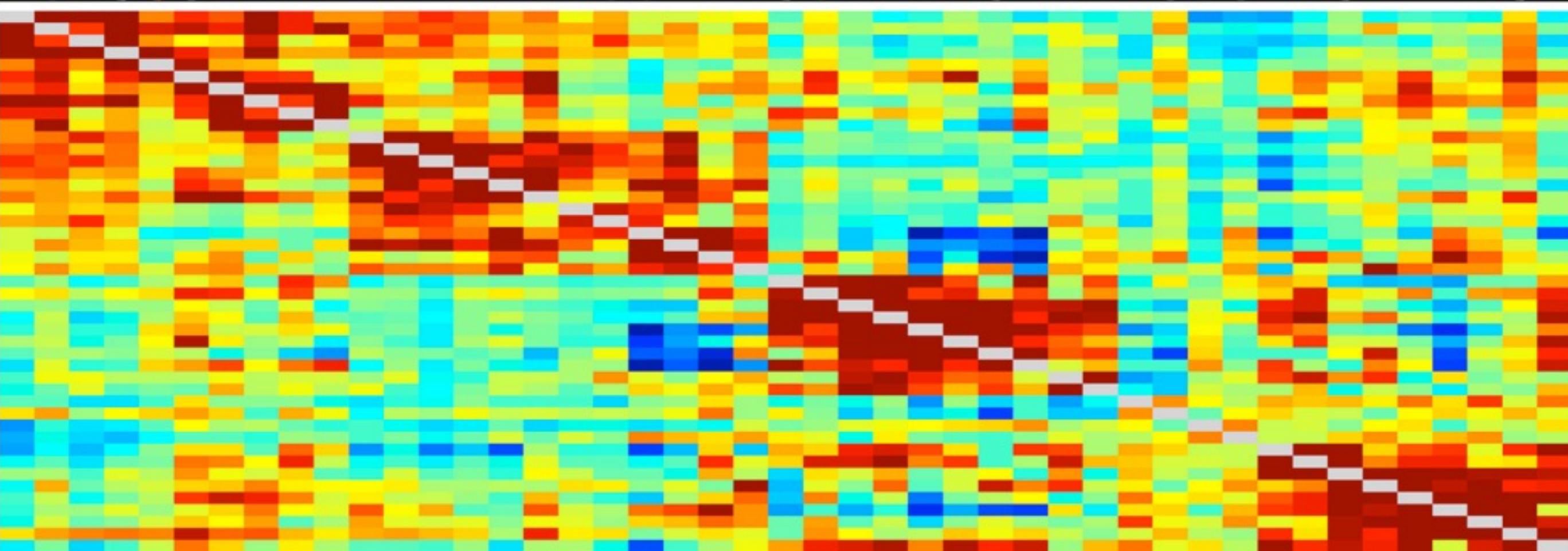
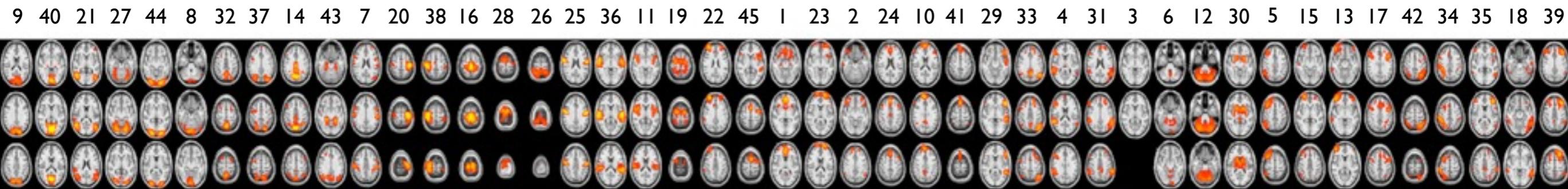
network of groups of
neurons simulated
(e.g. neural mass model)

closeness to (interaction with) real fMRI data

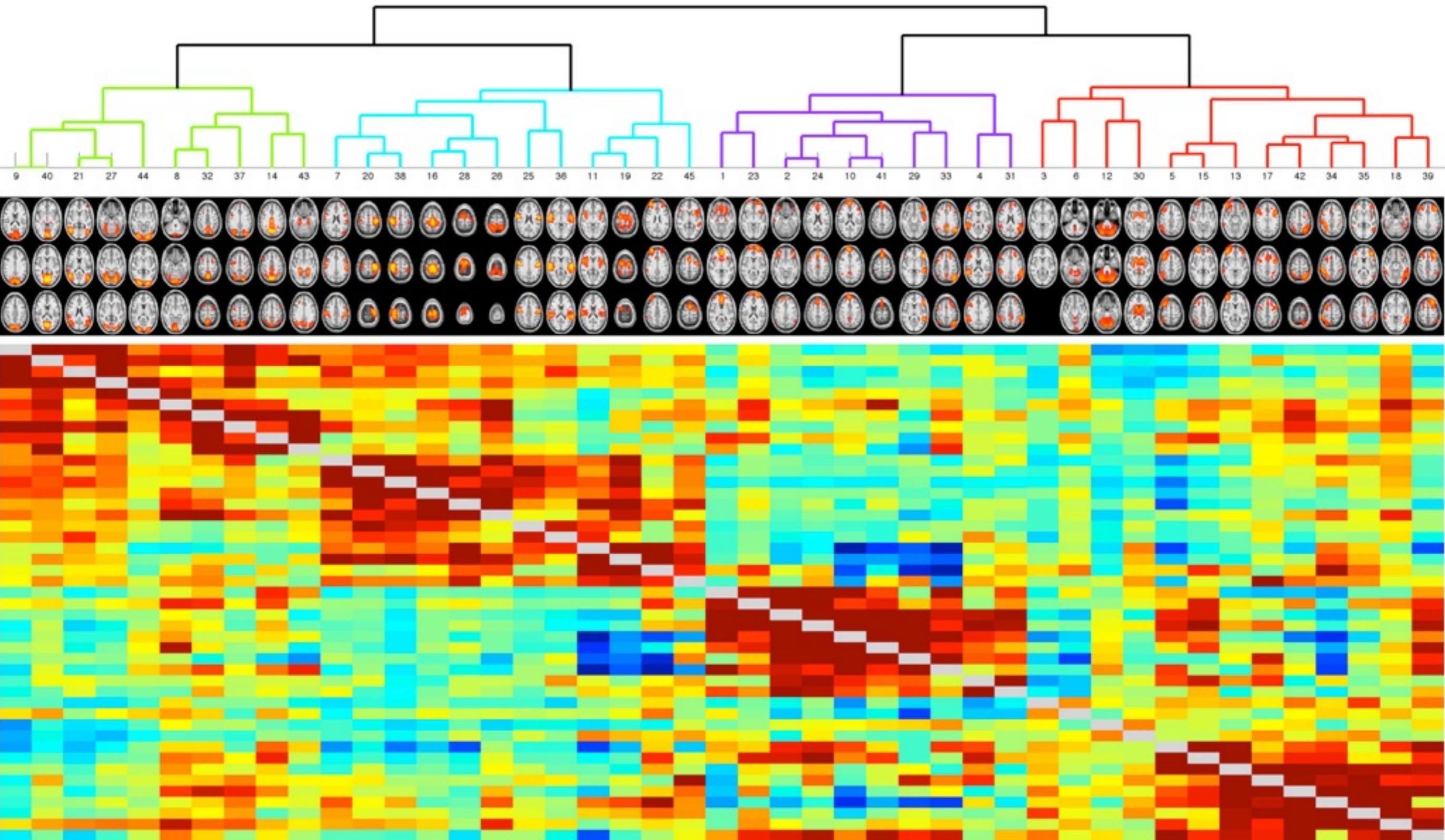
so we get a *Nodes x Nodes* network matrix



reorder node ordering to find clusters

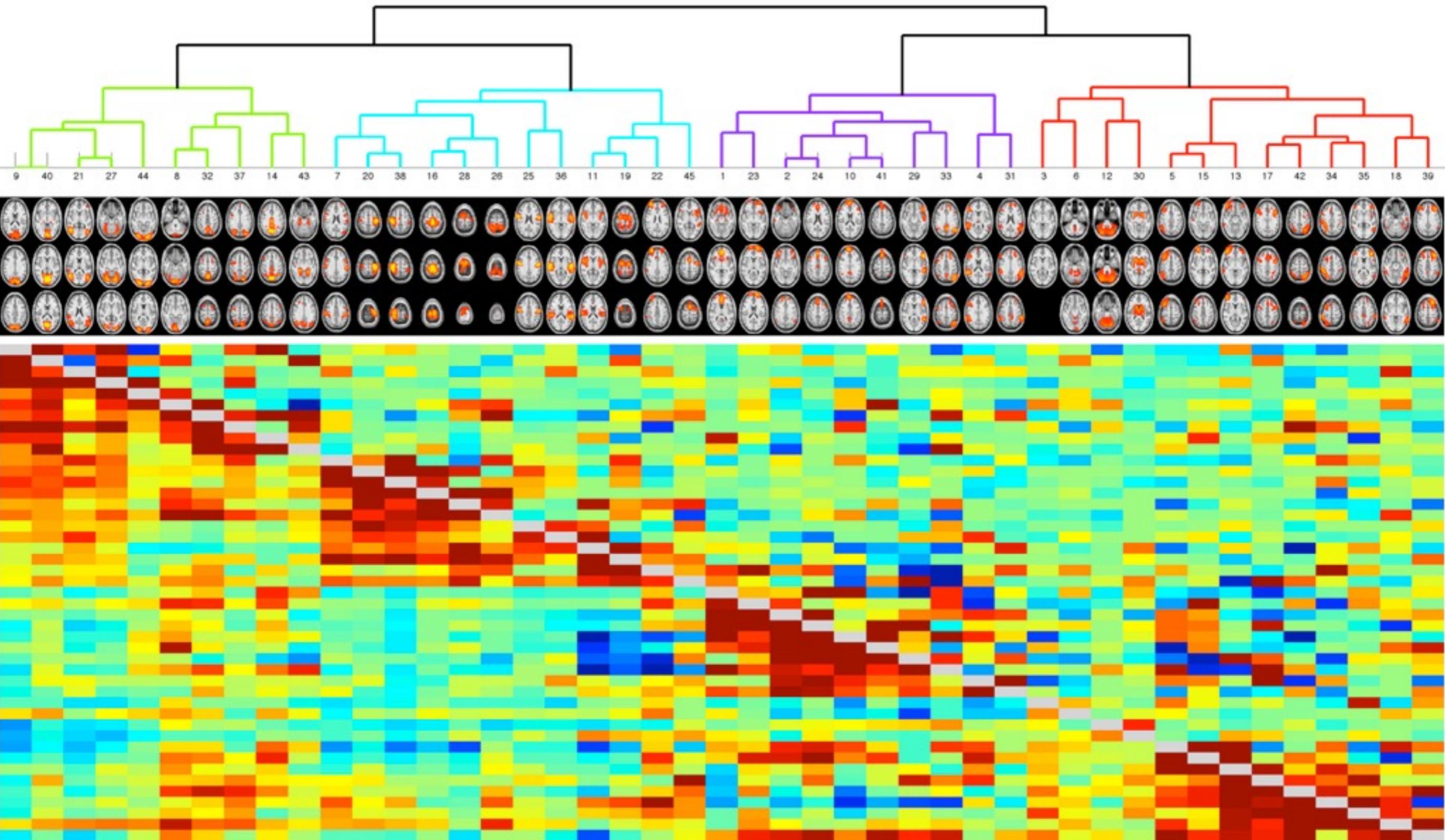


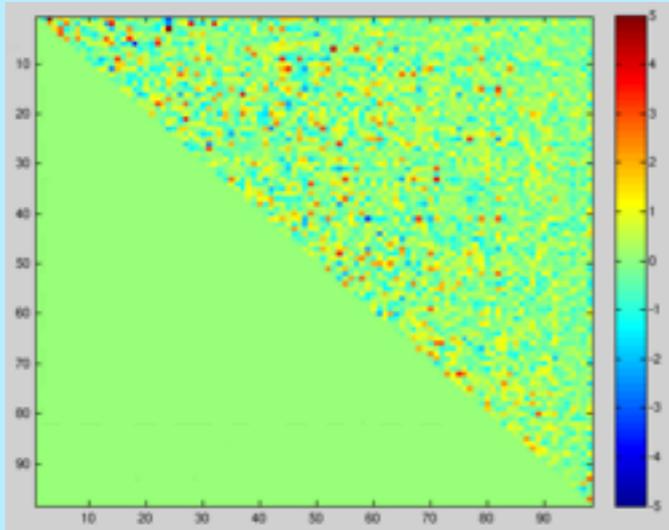
can view hierarchy of clusters



- Cordes *MRI 2002*
- Salvador *Cerebral Cortex 2005*

partial correlation matrix sparser than full



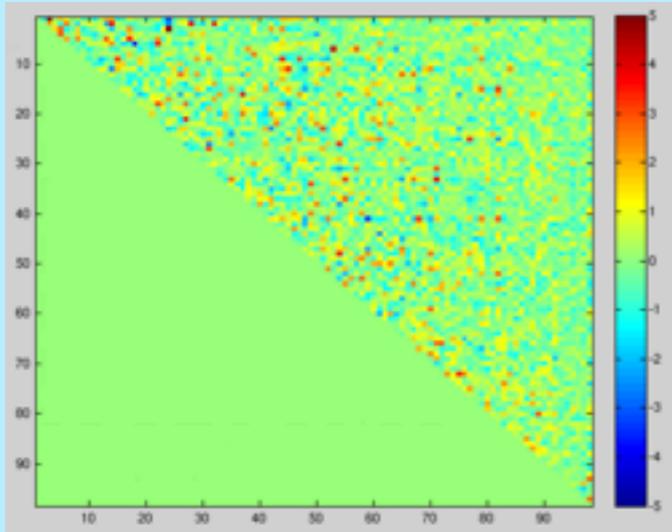


- One subject's network matrix: a 98x98 partial correlation matrix.
- Each element tells us the strength of the edge between two nodes (rows and columns index the nodes)
- As it is symmetric, we only need keep values above the diagonal.
- We “unwrap” all rows to give a single vector of $98 \times 97 / 2 = 4753$ correlation values (edge strengths):



one subject's netmat

cross-subject modelling of netmats

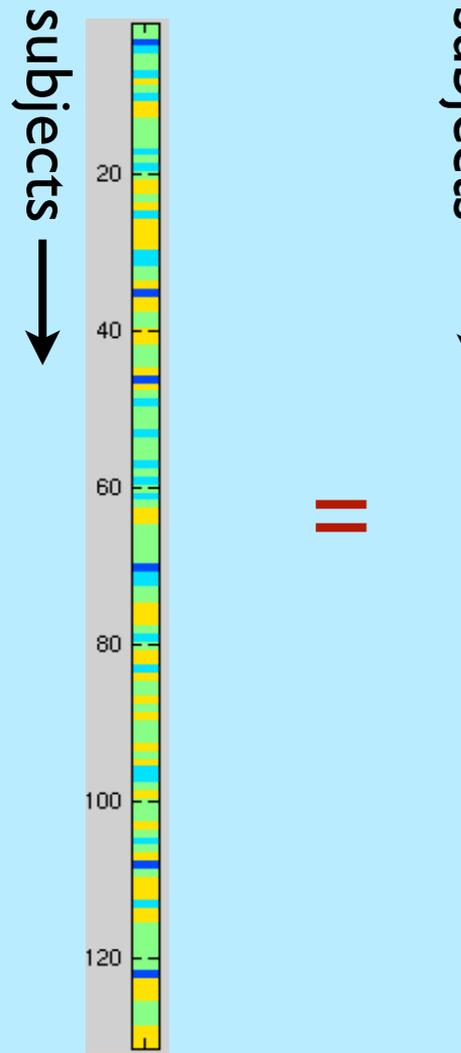


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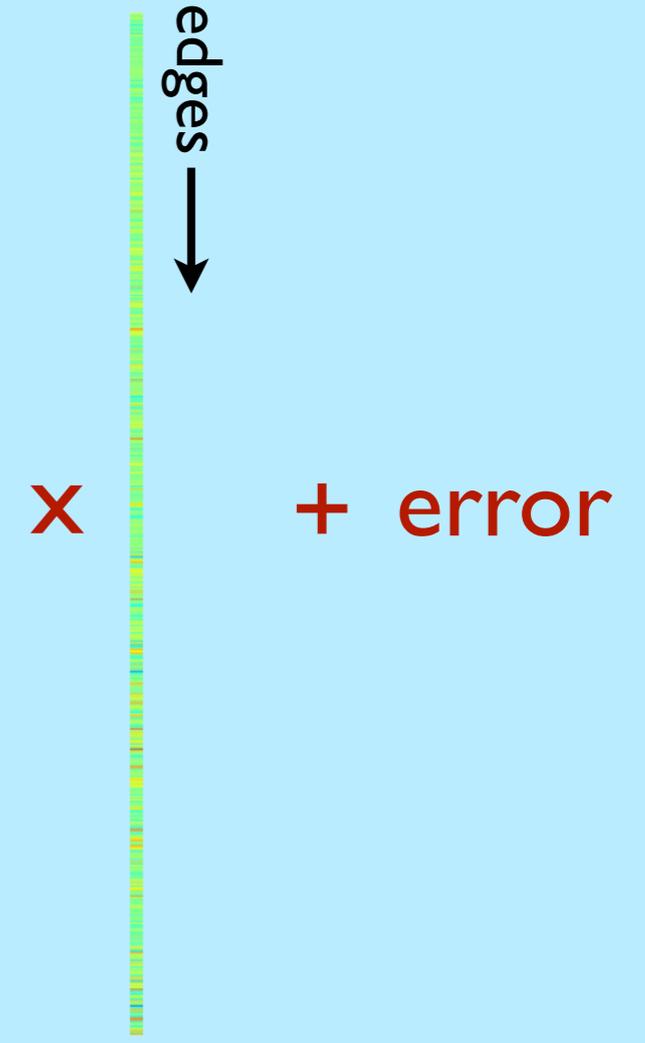
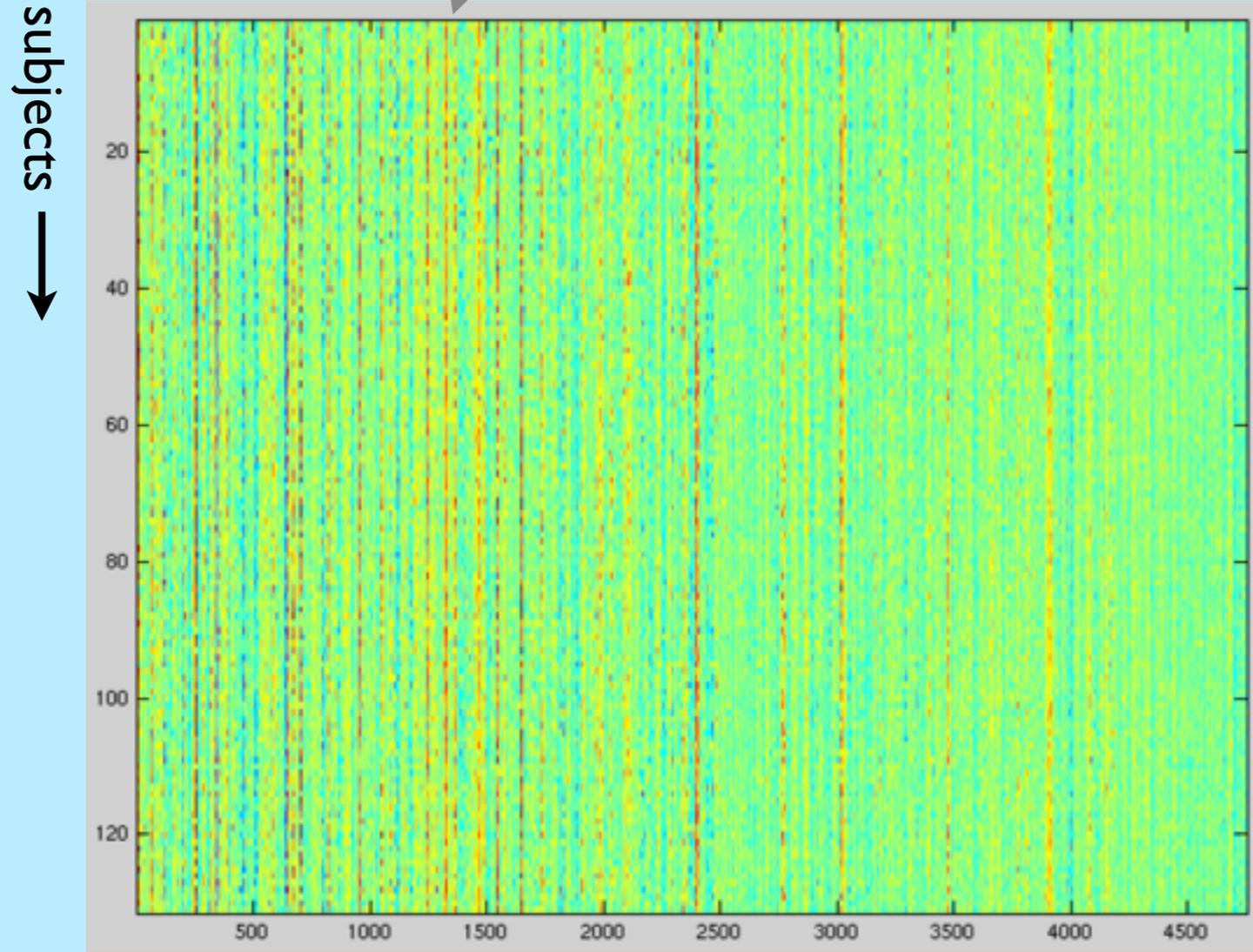


one subject's netmat

modelling of all subjects' netmats



=



behavioural measure
(one value per subject)

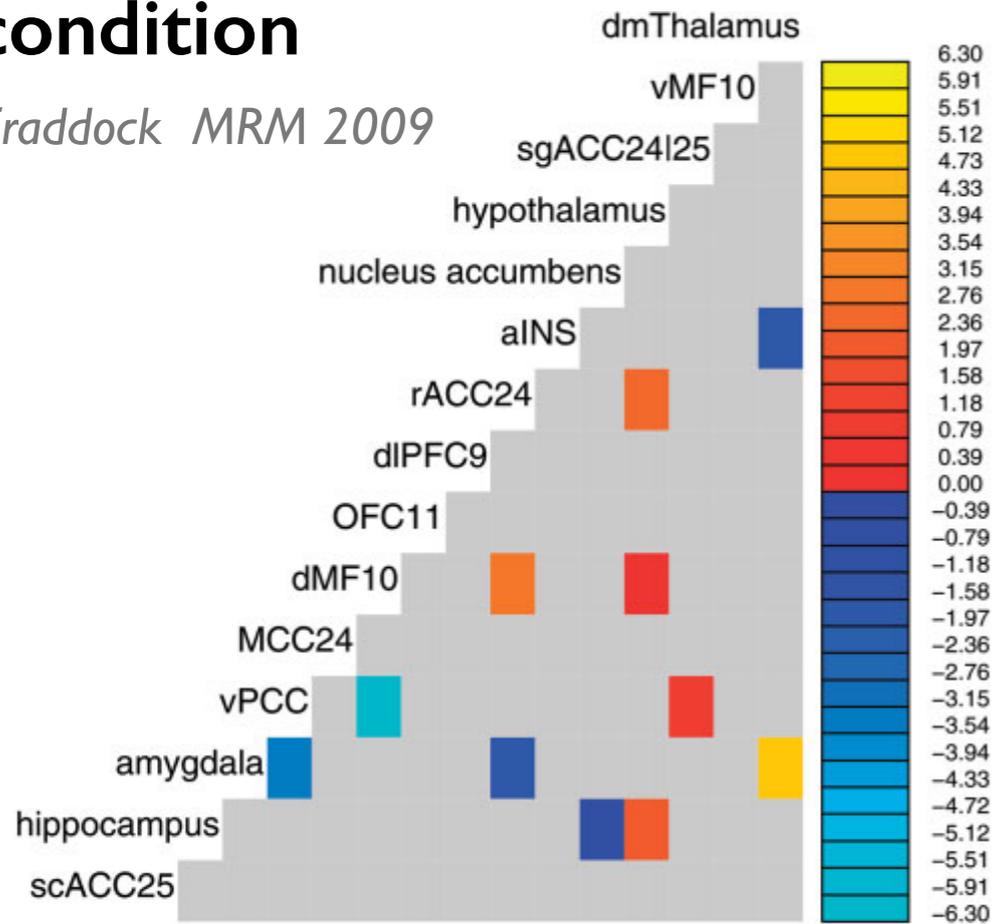
all subjects' network matrices

edge weights
(regression coefficients)

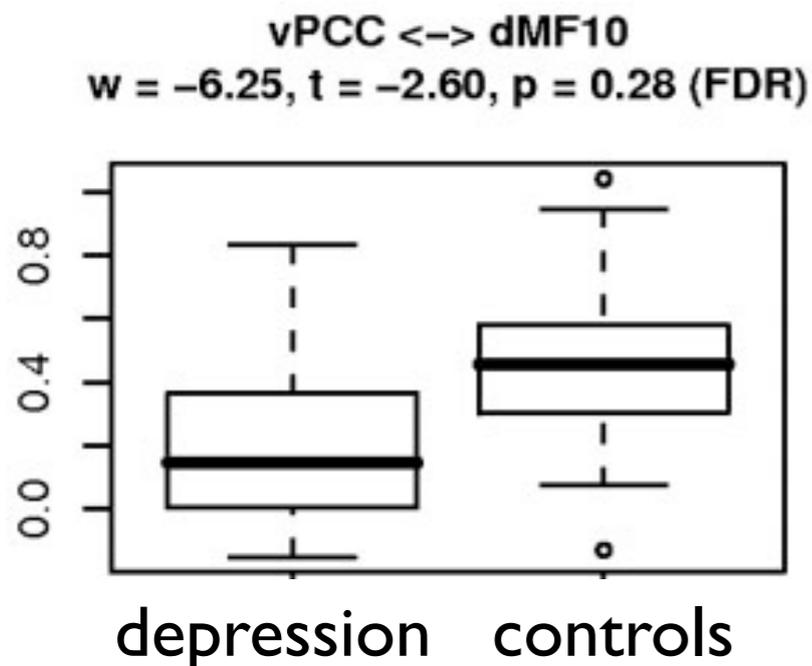
Applications of network matrix

Psychiatric condition

Craddock MRM 2009



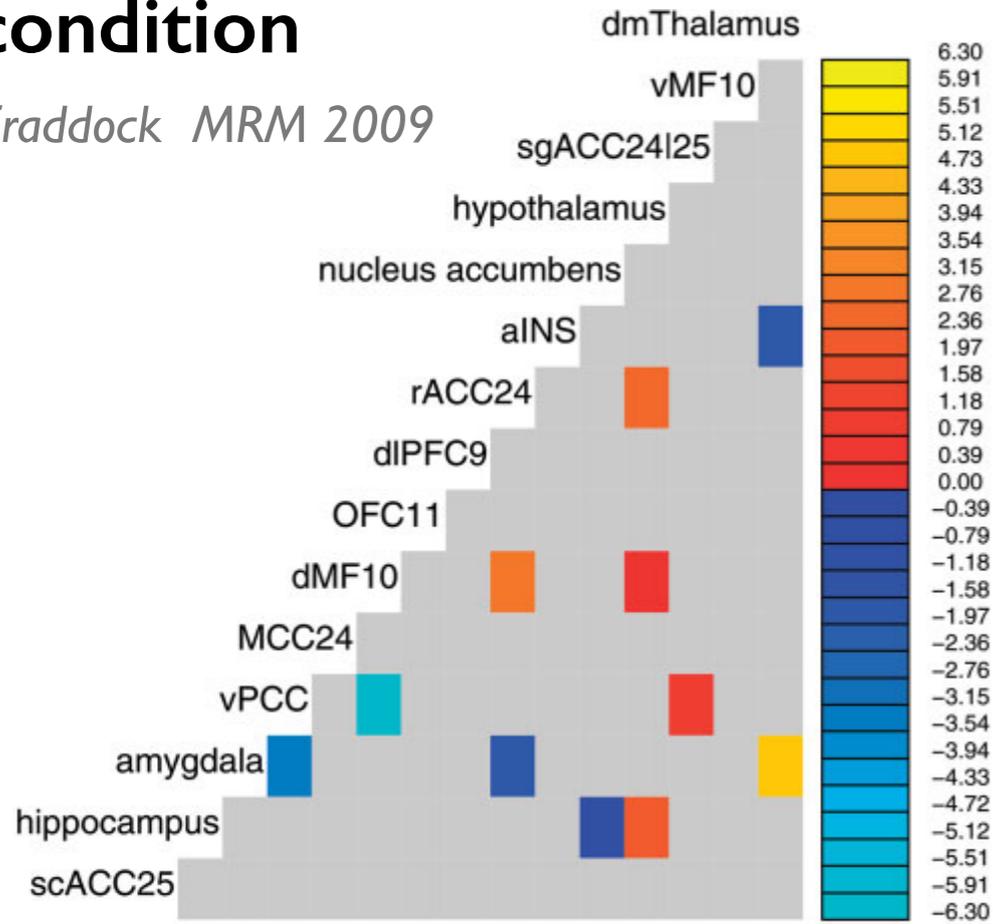
- Machine learning based on “features”
- Edge strengths (features) \Rightarrow SVM
- Training data: learn a combination of edges that predicts disease classification
- Apply to new subjects



Applications of network matrix

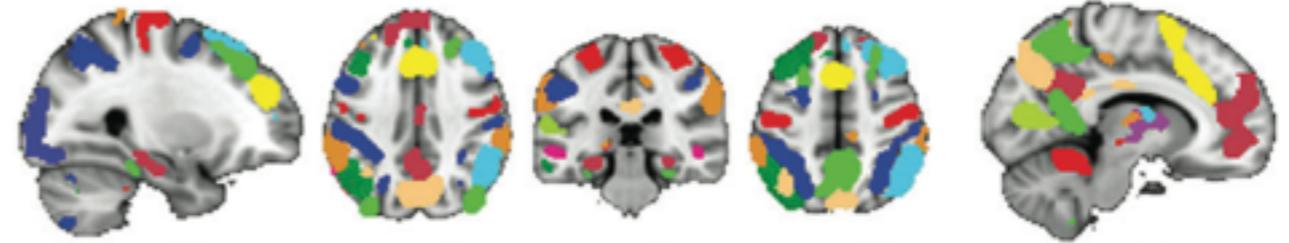
Psychiatric condition

Craddock MRM 2009

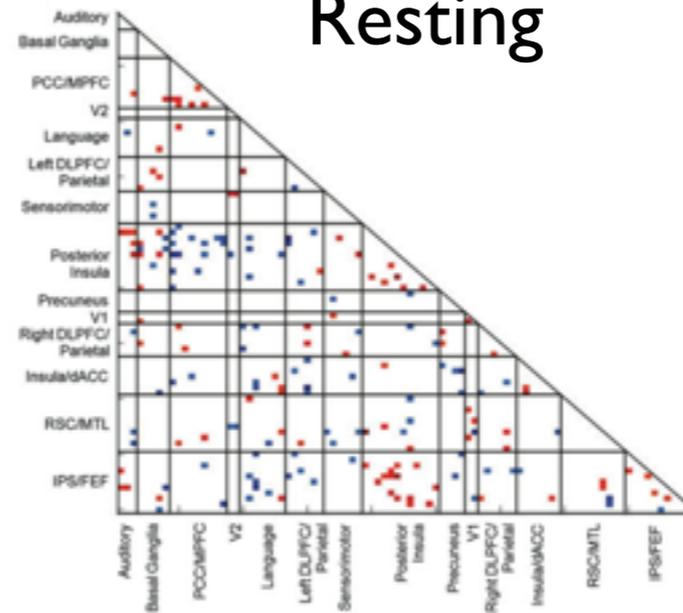


Cognitive state

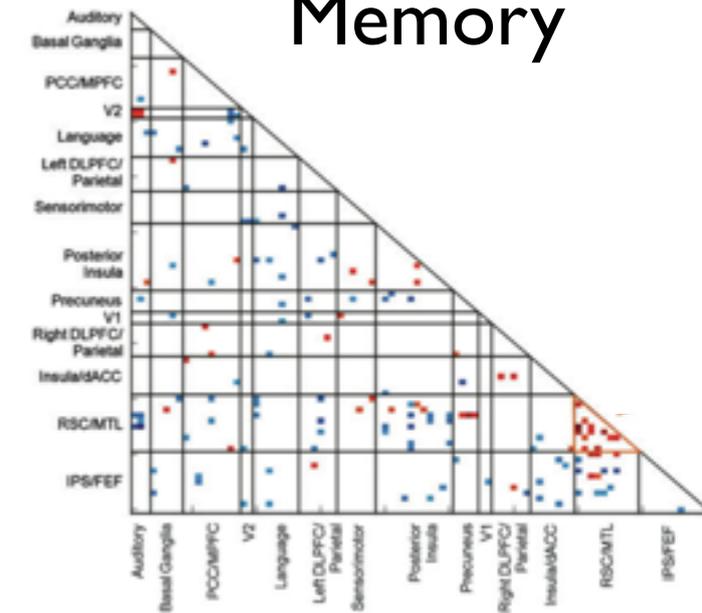
Shirer Cerebral Cortex 2011



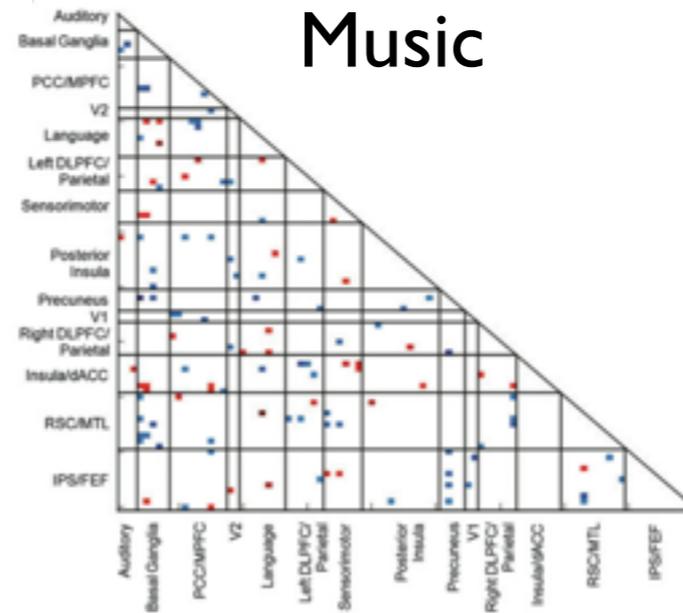
Resting



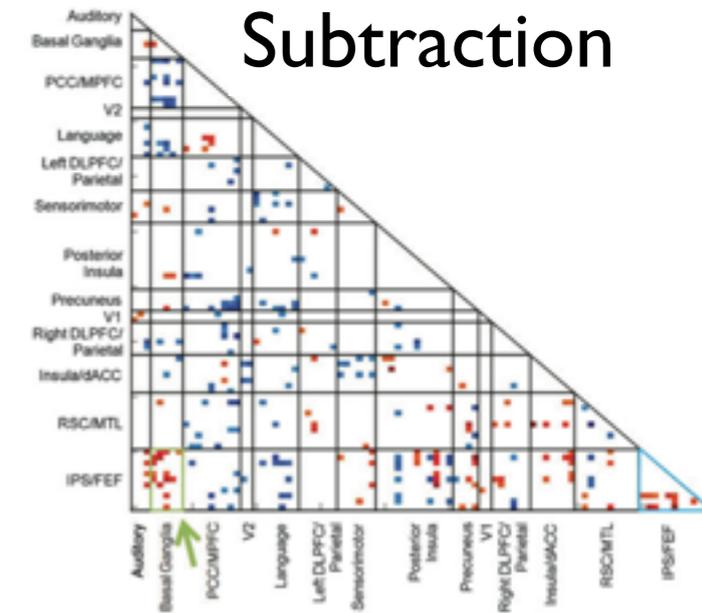
Memory



Music

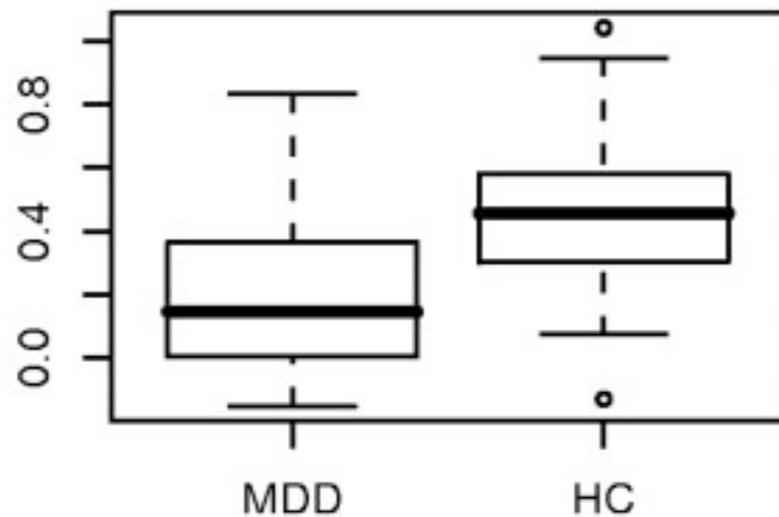


Subtraction



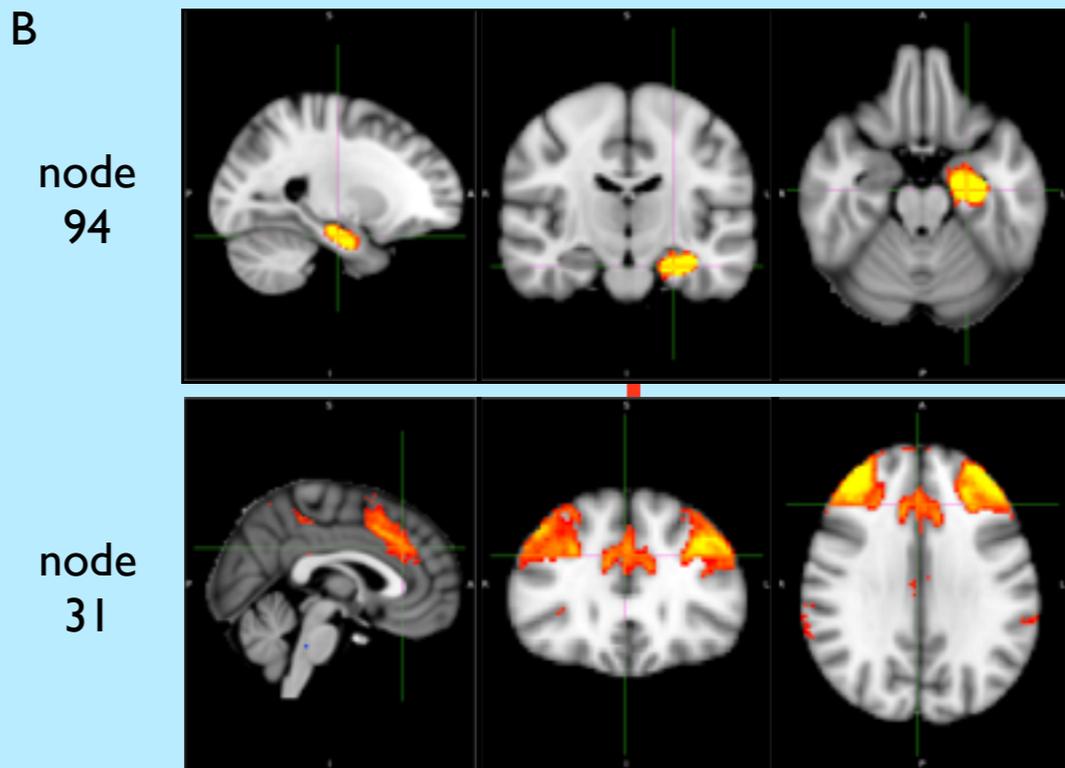
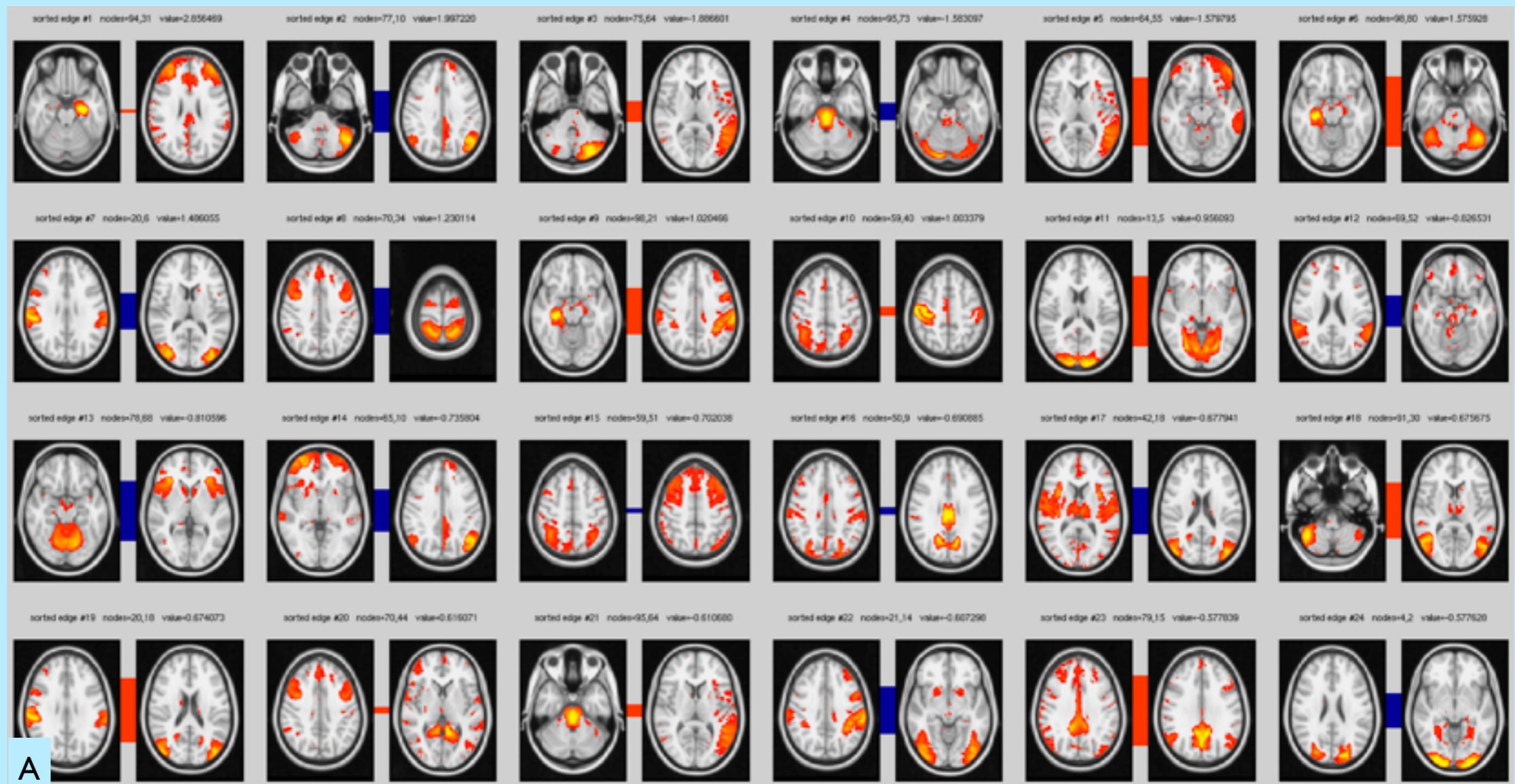
vPCC <-> dMF10

w = -6.25, t = -2.60, p = 0.28 (FDR)

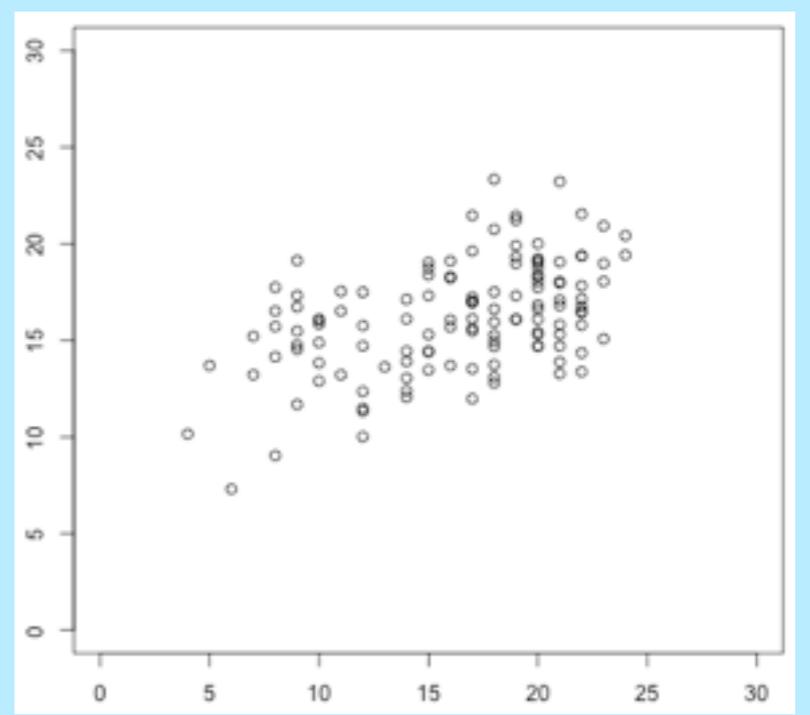


Predicting IQ from HCP

functional netmats



predicted fluid intelligence

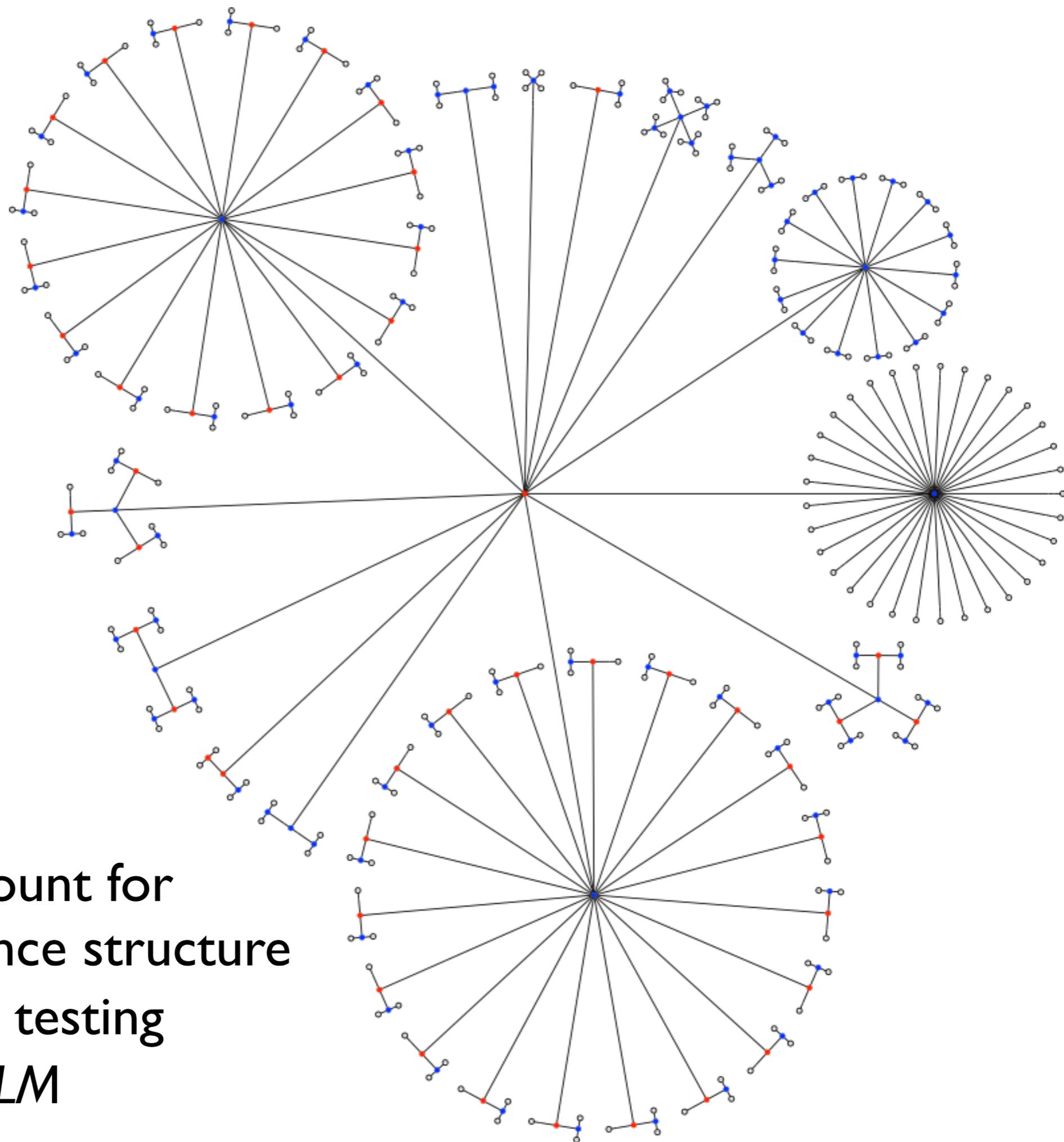


measured fluid intelligence

HCP

family structure

*Anderson Winkler,
Smith, Nichols*



- May need to account for complex covariance structure
- E.g. permutation testing
- *Beta-software: PALM*

nodes & edges vs. “spatial” maps

connectivity testing

- Nodes & edges only one way of finding networks / connectivity
- Not sensitive to *shape* changes in connectivity patterns
- Smaller multiple comparison correction problem

- E.g., seed-based correlation additionally tests for *spatial* (voxelwise-shape) changes in connectivity patterns

- Likewise, group-concat-ICA finds a set of RSN spatial maps that can be regressed into individual subjects to get subject-specific maps for each RSN (“dual-regression”)
- These can be then tested for *shape and amplitude* changes

"HCP500-PTN" 2014 data release

(group **p**arcellations + node **t**imeseries + **n**etwork matrices)

- **Group-average “parcellations”**

Group-ICA (MIGP+MELODIC), dimensionalities $D = 25, 50, 100, 200, 300$

- **Subject-specific sets of “node timeseries”**

For each subject, a representative timeseries per ICA component (“parcel” or “node”) - i.e., $T \times D$ matrices.

Two methods: $ts2=dual-reg$ $ts3=eigentimeseries$

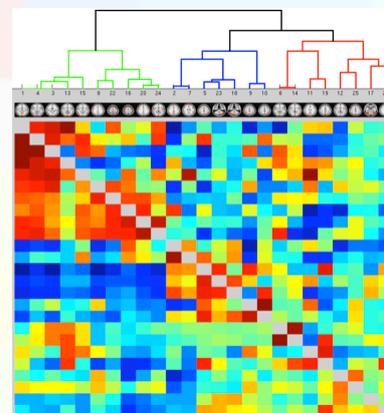
- **Subject-specific netmats (“parcellated connectomes”)**

For each subject, a nodes x nodes matrix – the $D \times D$ functional connectivity between node timeseries, using FSLNets.

Two methods: full correlation & partial correlation (tiny regularisation).

r -to- Z with autocorrelation correction.

Also group-averaged netmats.



HCP “MegaTrawl”

- 5 parcellation levels (25-300)
- interactive connectome browser
- netmat heritability
- netmats predict (or correlate with) subject measures (IQ, smoking, age, sex, etc.) ?

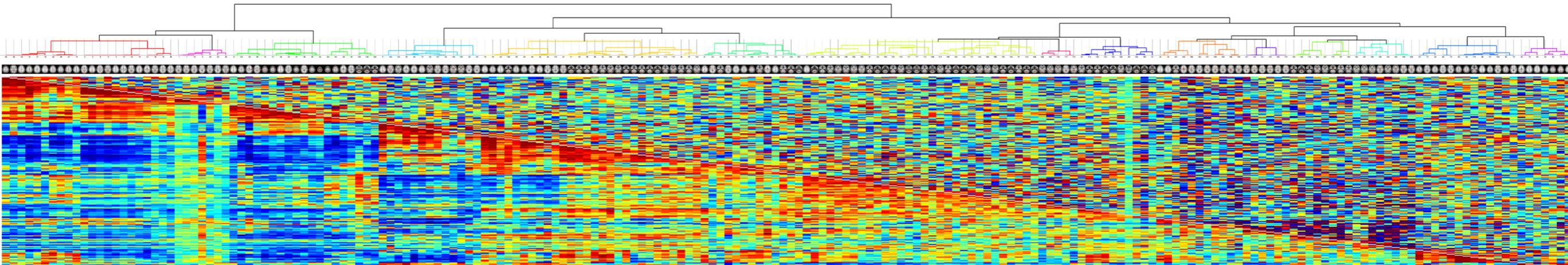
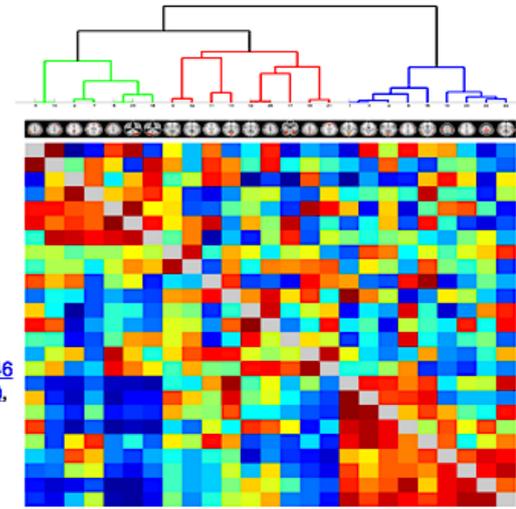
HCP Netmat Analysis

Parcellation=[3T_Q1-Q6related468_MSMSulc_d25](#) NodeTimeseries=ts2 NetmatMethod=3

Group-average network matrix representations: [matrix hierarchy](#) - [nodes+edges 1](#) - [nodes+edges 2](#)

Netmat [heritability calculations](#)

Correlation/prediction results for subject measures: 2 (quarter/release), 3 (sex), 4 (age), 5 (handedness), 7 (rfMRI_motion), 8 (SSAGA_Employ), 9 (SSAGA_Income), 10 (SSAGA_Educ), 11 (SSAGA_InSchool), 12 (SSAGA_Rlshp), 13 (SSAGA_MOBom), 14 (Height), 15 (Weight), 16 (BMI), 17 (SSAGA_BMICat), 18 (SSAGA_BMICatHeaviest), 19 (Blood_Drawn), 20 (Hematocrit_1), 21 (Hematocrit_2), 22 (BPSystolic), 23 (BPDiastolic), 24 (ThyroidHormone), 25 (HbA1C), 26 (Hypothyroidism), 27 (Hypothyroidism_Onset), 28 (Hyperthyroidism), 29 (Hyperthyroidism_Onset), 30 (OtherEndocrn_Prob), 31 (OtherEndocrine_ProbOnset), 32 (Menstrual_RegCycles), 33 (Menstrual_AgeBegan), 34 (Menstrual_CycleLength), 35 (Menstrual_DaysSinceLast), 36 (Menstrual_AgeIrreg), 37 (Menstrual_AgeStop), 38 (Menstrual_MonthsSinceStop), 39 (Menstrual_UsingBirthControl), 40 (Menstrual_BirthControlCode), 41 (FamHist_Moth_Scz), 42 (FamHist_Fath_Scz), 43 (FamHist_Moth_Dep), 44 (FamHist_Fath_Dep), 45 (FamHist_Moth_BP), 46 (FamHist_Fath_BP), 47 (FamHist_Moth_Anxiety), 48 (FamHist_Fath_Anxiety), 49 (FamHist_Moth_DrgAlc), 50 (FamHist_Fath_DrgAlc), 51 (FamHist_Moth_Alz), 52 (FamHist_Fath_Alz), 53 (FamHist_Moth_PD), 54 (FamHist_Fath_PD), 55 (FamHist_Moth_TS), 56 (FamHist_Fath_TS), 57 (FamHist_Moth_None), 58 (FamHist_Fath_None), 59 (ASR_Anxd_Raw), 60 (ASR_Anxd_Pct), 61 (ASR_Witd_Raw), 62 (ASR_Witd_Pct), 63 (ASR_Soma_Raw), 64 (ASR_Soma_Pct), 65 (ASR_Thot_Raw), 66 (ASR_Thot_Pct), 67 (ASR_Attn_Raw), 68 (ASR_Attn_Pct), 69 (ASR_Aggr_Raw), 70 (ASR_Aggr_Pct), 71 (ASR_Rule_Raw), 72 (ASR_Rule_Pct), 73 (ASR_Intr_Raw), 74 (ASR_Intr_Pct), 75 (ASR_Oth_Raw), 76 (ASR_Crit_Raw), 77 (ASR_Intr_Raw), 78 (ASR_Intr_T), 79 (ASR_Extn_Raw), 80 (ASR_Extn_T), 81 (ASR_TAO_Sum), 82 (ASR_Totp_Raw), 83 (ASR_Totp_T), 84 (DSM_Depr_Raw), 85 (DSM_Depr_Pct), 86 (DSM_Anxi_Raw), 87 (DSM_Anxi_Pct), 88 (DSM_Somp_Raw), 89 (DSM_Somp_Pct), 90 (DSM_Avoid_Raw), 91 (DSM_Avoid_Pct), 92 (DSM_Adh_Raw), 93 (DSM_Adh_Pct), 94 (DSM_Inat_Raw), 95 (DSM_Hype_Raw), 96 (DSM_Antis_Raw), 97 (DSM_Antis_Pct), 98 (SSAGA_ChildhoodConduct), 99 (SSAGA_PanicDisorder), 100 (SSAGA_Agoraphobia), 101 (SSAGA_Depressive_Ep), 102 (SSAGA_Depressive_Sx), 103 (Color_Vision), 104 (EVA_Num), 105 (EVA_Denom), 106 (Correction), 107 (Breathalyzer_Over_05), 108 (Breathalyzer_Over_08), 109 (Cocaine), 110 (THC), 111 (Opiates), 112 (Amphetamines), 113 (Methamphetamine), 114 (Oxycontin), 115 (Total_Drinks_7days), 116 (Num_Days_Drank_7days), 117 (Avg_Weekday_Drinks_7days), 118 (Avg_Weekend_Drinks_7days), 119 (Total_Beer_Wine_Cooler_7days), 120 (Avg_Weekday_Beer_Wine_Cooler_7days), 121 (Avg_Weekend_Beer_Wine_Cooler_7days), 122 (Total_Malt_Liquor_7days), 123 (Avg_Weekday_Malt_Liquor_7days), 124 (Avg_Weekend_Malt_Liquor_7days), 125 (Total_Wine_7days), 126 (Avg_Weekday_Wine_7days), 127 (Avg_Weekend_Wine_7days), 128 (Total_Hard_Liquor_7days), 129 (Avg_Weekday_Hard_Liquor_7days), 130 (Avg_Weekend_Hard_Liquor_7days), 131 (Total_Other_Alc_7days), 132 (Avg_Weekday_Other_Alc_7days), 133 (Avg_Weekend_Other_Alc_7days), 134 (SSAGA_Alc_D4_Dp_Sx), 135 (SSAGA_Alc_D4_Ab_Dx), 136 (SSAGA_Alc_D4_Ab_Sx), 137 (SSAGA_Alc_D4_Dp_Dx), 138 (SSAGA_Alc_12_Drinks_Per_Day), 139 (SSAGA_Alc_12_Frq), 140 (SSAGA_Alc_12_Frq_5plus), 141 (SSAGA_Alc_12_Frq_Drk), 142 (SSAGA_Alc_12_Max_Drinks), 143 (SSAGA_Alc_Age_1st_Use), 144 (SSAGA_Alc_Hvy_Drinks_Per_Day), 145 (SSAGA_Alc_Hvy_Frq), 146 (SSAGA_Alc_Hvy_Frq_5plus), 147 (SSAGA_Alc_Hvy_Frq_Drk), 148 (SSAGA_Alc_Hvy_Max_Drinks), 149 (Total_Any_Tobacco_7days), 150 (Times_Used_Any_Tobacco_Today), 151 (Num_Days_Used_Any_Tobacco_7days), 152 (Avg_Weekday_Any_Tobacco_7days), 153 (Avg_Weekend_Any_Tobacco_7days), 154 (Total_Cigarettes_7days), 155 (Avg_Weekday_Cigarettes_7days), 156 (Avg_Weekend_Cigarettes_7days), 157 (Total_Cigars_7days), 158 (Avg_Weekday_Cigars_7days), 159 (Avg_Weekend_Cigars_7days), 160 (Total_Pipes_7days), 161 (Avg_Weekday_Pipes_7days), 162 (Avg_Weekend_Pipes_7days), 163 (Total_Chew_7days), 164 (Avg_Weekday_Chew_7days), 165 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(CardSort_AgeAdj), 201 (Flanker_Unadj), 202 (Flanker_AgeAdj), 203 (PMAT24_A_CR), 204 (PMAT24_A_SI), 205 (PMAT24_A_RTICR), 206 (ReadEng_Unadj), 207 (ReadEng_AgeAdj), 208 (PicVocab_Unadj), 209 (PicVocab_AgeAdj), 210 (ProcSpeed_Unadj), 211 (ProcSpeed_AgeAdj), 212 (DDisc_SV_1mo_200), 213 (DDisc_SV_6mo_200), 214 (DDisc_SV_1yr_200), 215 (DDisc_SV_3yr_200), 216 (DDisc_SV_5yr_200), 217 (DDisc_SV_10yr_200), 218 (DDisc_SV_1mo_40K), 219 (DDisc_SV_6mo_40K), 220 (DDisc_SV_1yr_40K), 221 (DDisc_SV_3yr_40K), 222 (DDisc_SV_5yr_40K), 223 (DDisc_SV_10yr_40K), 224 (DDisc_AUC_200), 225 (DDisc_AUC_40K), 226 (VSPLIT_TC), 227 (VSPLIT_CRTE), 228 (VSPLIT_OFF), 229 (SCPT_TP), 230 (SCPT_TN), 231 (SCPT_FP), 232 (SCPT_FN), 233 (SCPT_TPRT), 234 (SCPT_SEN), 235 (SCPT_SPEC), 236 (SCPT_LNRN), 237 (IWRD_TOT), 238 (IWRD_RTC), 239 (ListSort_Unadj), 240 (ListSort_AgeAdj), 241 (ER40_CR), 242 (ER40_CRT), 243 (ER40ANG), 244 (ER40FEAR), 245 (ER40HAP), 246 (ER40NOE), 247 (ER40SAD), 248 (AngAffect_Unadj), 249 (AngHostil_Unadj), 250 (AngAggr_Unadj), 251 (FearAffect_Unadj), 252 (FearSomat_Unadj), 253 (Sadness_Unadj), 254 (LifeSatisf_Unadj), 255 (MeanPurp_Unadj), 256 (PosAffect_Unadj), 257 (Friendship_Unadj), 258 (Loneliness_Unadj), 259 (PercHostil_Unadj), 260 (PercReject_Unadj), 261 (EmotSupp_Unadj), 262 (InstruSupp_Unadj), 263 (PercStress_Unadj), 264 (SelfEff_Unadj), 265 (FS_InterCranial_Vol), 266 (FS_BrainSeg_Vol), 458 (Endurance_Unadj), 459 (Endurance_AgeAdj), 460 (GaitSpeed_Comp), 461 (Dexterity_Unadj), 462 (Dexterity_AgeAdj), 463 (Strength_Unadj), 464 (Strength_AgeAdj), 465 (NEOFAC_A), 466 (NEOFAC_O), 467 (NEOFAC_C), 468 (NEOFAC_N), 469 (NEOFAC_E), 470 (Noise_Comp), 471 (Odor_Unadj), 472 (Odor_AgeAdj), 473 (PainInterf_Tscore), 474 (Taste_Unadj), 475 (Taste_AgeAdj), 476 (Mars_Log_Score), 477 (Mars_Errs), 478 (Mars_Final),



The screenshot shows a web browser window with the URL `users.fmrib.ox.ac.uk`. The page header features the Human Connectome Project logo and the text "HUMAN Connectome PROJECT" and "Mapping structural and functional connections in the human brain". The main content area is titled "HCP Netmats MegaTrawl" and includes a link to "MegaTrawl documentation". Below this is a table with two columns: "node-timeseries method 2 (dual-regression)" and "node-timeseries method 3 (eigentimeseries)". The table lists five rows corresponding to different ICA dimensions (d=25, 50, 100, 200, 300). Each row contains two blue hyperlinks. At the bottom, there is a link to the "HCP Data Dictionary".

HCP Netmats MegaTrawl

For details of the analyses reported here see the [MegaTrawl documentation](#).

	node-timeseries method 2 (dual-regression)	node-timeseries method 3 (eigentimeseries)
ICA d=25	3T_Q1-Q6related468_MSMSulc_d25_ts2	3T_Q1-Q6related468_MSMSulc_d25_ts3
ICA d=50	3T_Q1-Q6related468_MSMSulc_d50_ts2	3T_Q1-Q6related468_MSMSulc_d50_ts3
ICA d=100	3T_Q1-Q6related468_MSMSulc_d100_ts2	3T_Q1-Q6related468_MSMSulc_d100_ts3
ICA d=200	3T_Q1-Q6related468_MSMSulc_d200_ts2	3T_Q1-Q6related468_MSMSulc_d200_ts3
ICA d=300	3T_Q1-Q6related468_MSMSulc_d300_ts2	3T_Q1-Q6related468_MSMSulc_d300_ts3

For a description of the many different subject measures included with HCP data, see the [HCP Data Dictionary](#).

10 HCP MegaTrawls:

- 5 parcellation levels (25-300)
- 2 node-timeseries estimation methods (dual-regression & eigenregression)

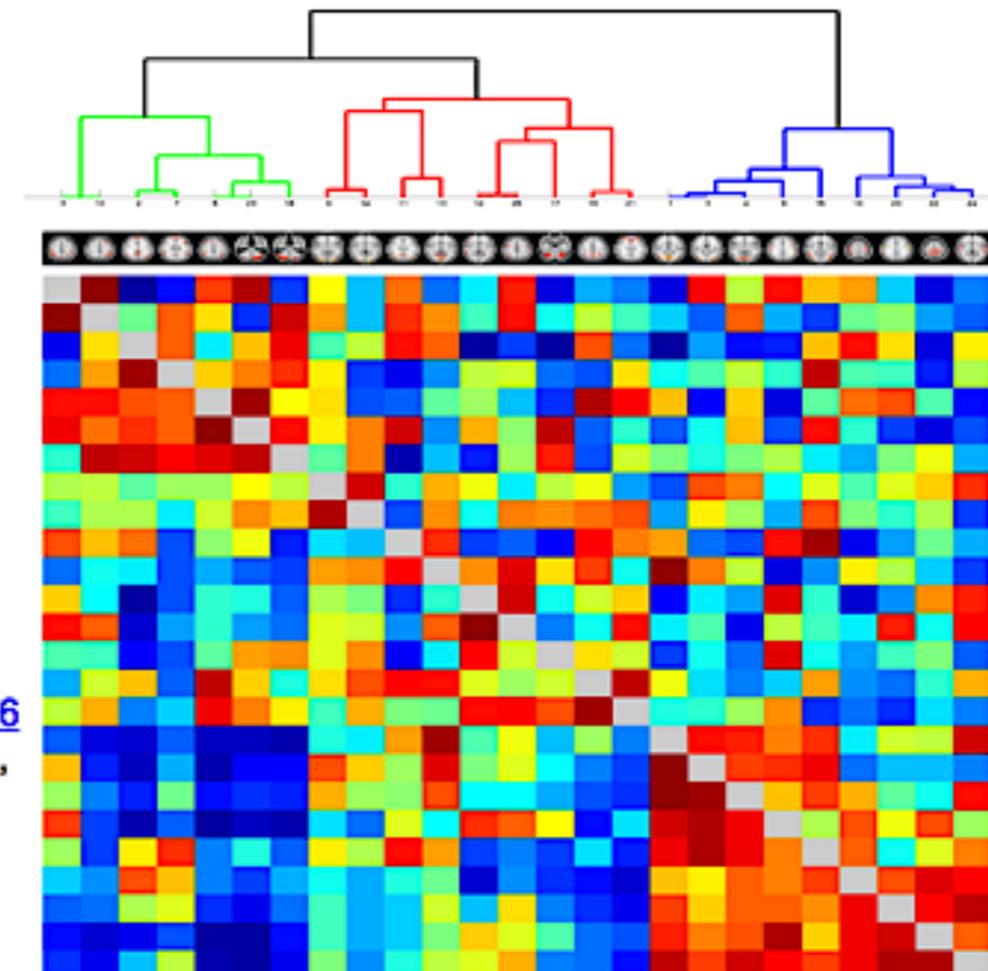
HCP Netmat Analysis

Parcellation=[3T_Q1-Q6related468_MSMSulc_d25](#) NodeTimeseries=ts2 NetmatMethod=3

Group-average network matrix representations: [matrix hierarchy](#) - [nodes+edges 1](#) - [nodes+edges 2](#)

Netmat [heritability calculations](#)

Correlation/prediction results for subject measures: [2 \(quarter/release\)](#), [3 \(sex\)](#), [4 \(age\)](#), [5 \(handedness\)](#), [7 \(rfMRI_motion\)](#), [8 \(SSAGA_Employ\)](#), [9 \(SSAGA_Income\)](#), [10 \(SSAGA_Educ\)](#), [11 \(SSAGA_InSchool\)](#), [12 \(SSAGA_Rlshp\)](#), [13 \(SSAGA_MOBorn\)](#), [14 \(Height\)](#), [15 \(Weight\)](#), [16 \(BMI\)](#), [17 \(SSAGA_BMICat\)](#), [18 \(SSAGA_BMICatHeaviest\)](#), [19 \(Blood_Drawn\)](#), [20 \(Hematocrit_1\)](#), [21 \(Hematocrit_2\)](#), [22 \(BPSystolic\)](#), [23 \(BPDiastolic\)](#), [24 \(ThyroidHormone\)](#), [25 \(HbA1C\)](#), [26 \(Hypothyroidism\)](#), [27 \(Hypothyroidism_Onset\)](#), [28 \(Hyperthyroidism\)](#), [29 \(Hyperthyroidism_Onset\)](#), [30 \(OtherEndocrn_Prob\)](#), [31 \(OtherEndocrine_ProbOnset\)](#), [32 \(Menstrual_RegCycles\)](#), [33 \(Menstrual_AgeBegan\)](#), [34 \(Menstrual_CycleLength\)](#), [35 \(Menstrual_DaysSinceLast\)](#), [36 \(Menstrual_AgeIreg\)](#), [37 \(Menstrual_AgeStop\)](#), 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FSLNets interactive netmat visualisation

Threshold network by

Partial

Threshold percentage



Number of clusters



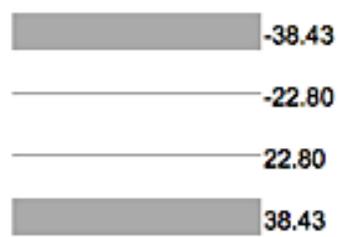
Colour edges by

Partial



Scale edge width by

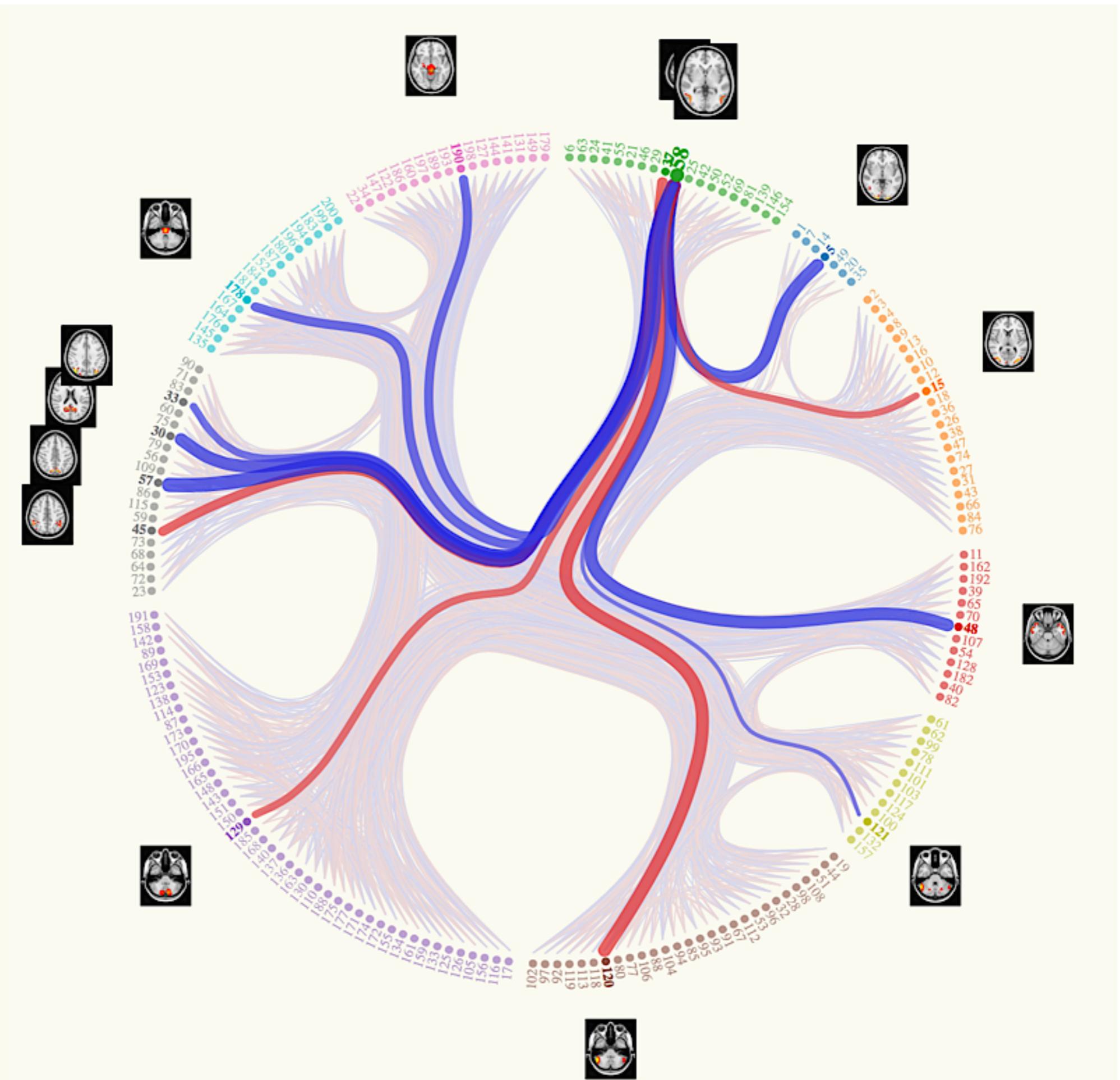
Partial



Colour nodes by

Cluster number

Show subnetwork



Netmat heritability calculations

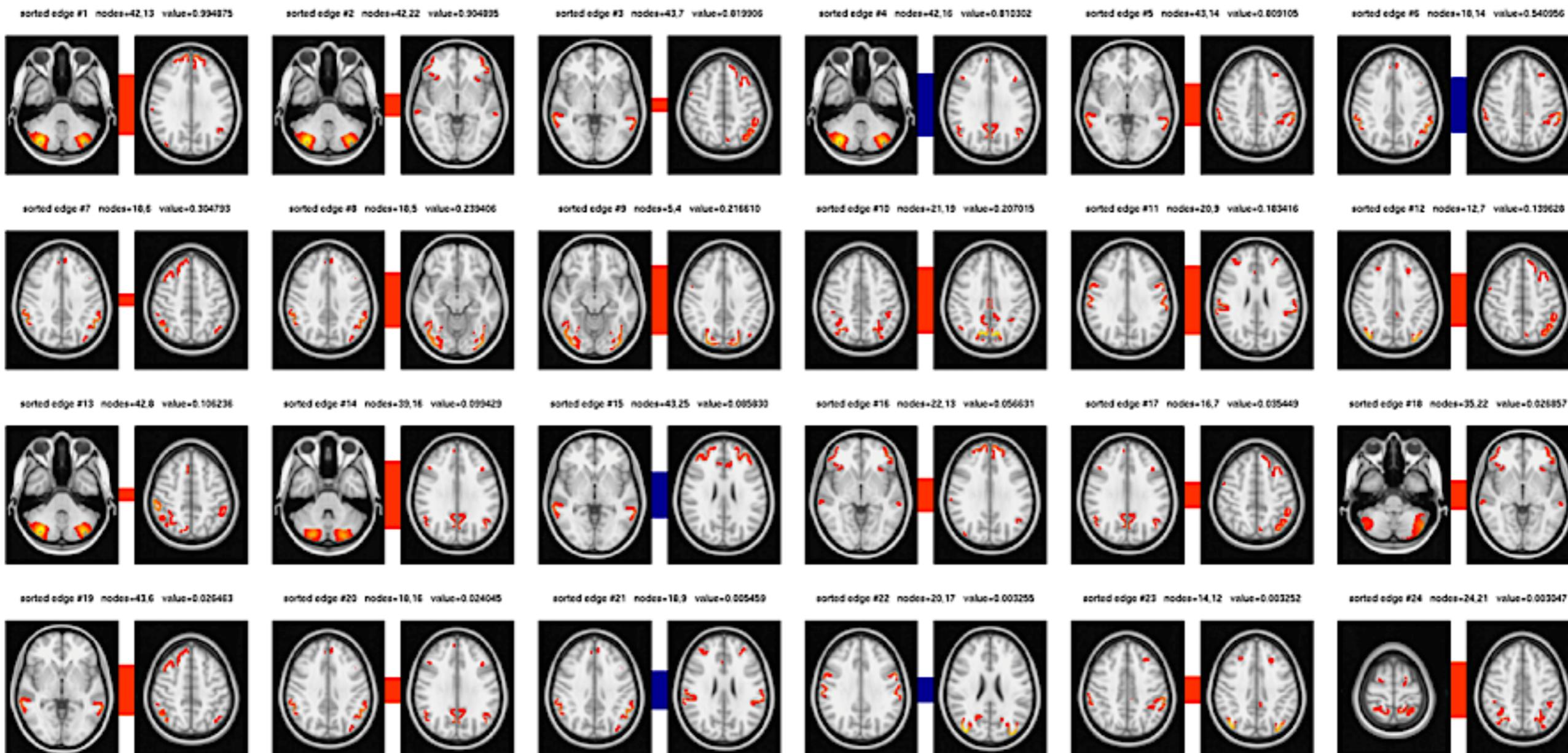
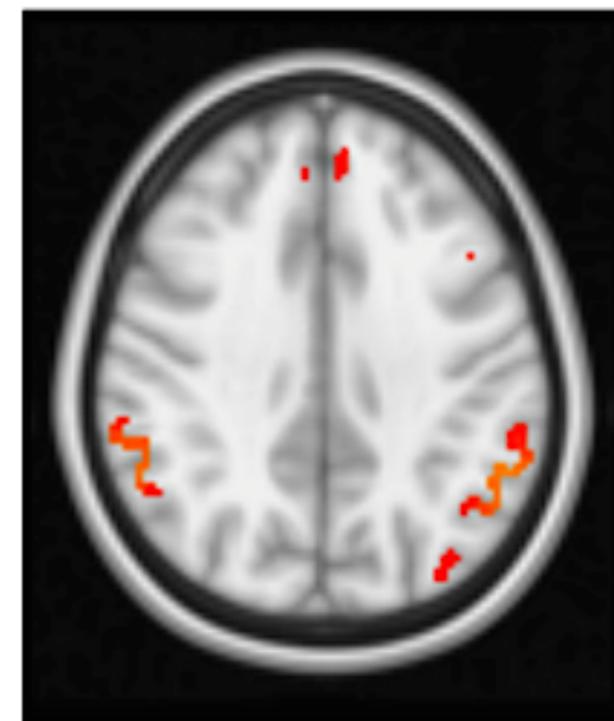
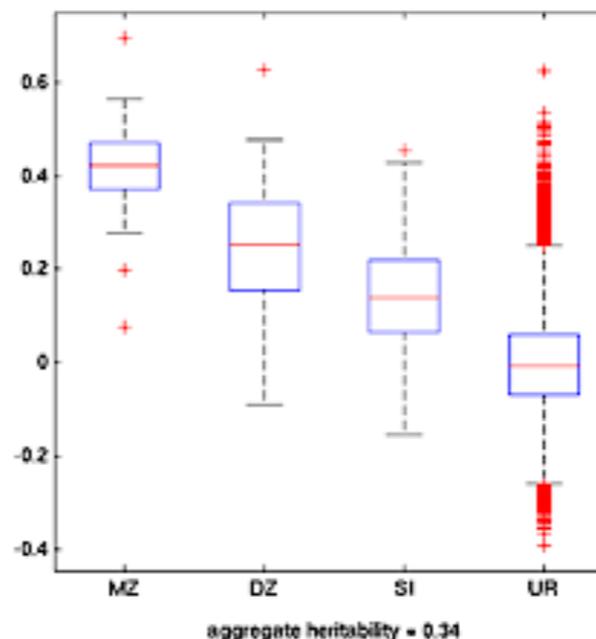
Full-netmat Aggregate Heritability = 0.34

Node with highest netmat-row-wise aggregate heritability:
node=18 heritability = 0.65

Top 24 edges - sorted in decreasing order according to heritability significance
(using APACE).

"value" = $(1 - P_{fwe}) + \text{heritability}/1e4$

Number of significantly heritable edges at $p < 0.05$ (FWE corrected) = 1



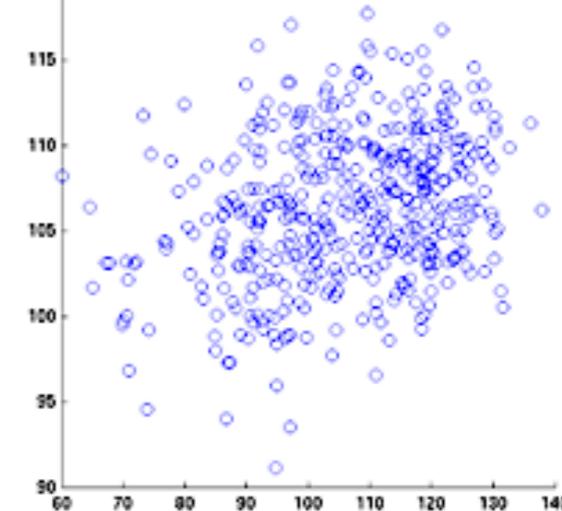
Correlation/prediction results for subject measure 207 (ReadEng_AgeAdj)

461 subjects had a valid ReadEng_AgeAdj measure.

Multivariate prediction (GLM-based, automatic feature selection, leave-one-family-out prediction)

Original data space: $r=0.29$ CoD=0.10 Deconfounded space: CoD=0.12

Scatterplot shows predicted-ReadEng_AgeAdj vs measured-ReadEng_AgeAdj (in original data space).



Univariate regression (regressing each netmat element independently against ReadEng_AgeAdj, correcting for multiple comparisons across elements, using PALM permutation testing, taking into account family structure).

Number of significantly correlated edges at $p < 0.05$ (two-tailed, FWE corrected) = 0 (minimum corrected $p = 0.0670$)

Number of significantly correlated edges at $p < 0.05$ (two-tailed, uncorrected) = 1456 (995 expected by chance)

Image shows edges (node-pairs) whose connection most strongly correlates with ReadEng_AgeAdj (in decreasing order), with "value"=t-statistic.

