LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

RESTING STATE FMRI

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Resting State fMRI

- The brain is always active, even in the absence of an explicit task.
- - According to certain etimates, task-related changes in neuronal metabolism only account for about 5% of the brain's total energy consumption.

- Resting state fMRI (rfMRI) is a relatively new approach used to identify synchronous BOLD changes in multiple brain regions while subjects lie in the scanner but do not perform a task.

Resting State fMRI

- In particular it has been shown that fluctuations in the low-frequency portion of the BOLD signal show strong correlations across spatially distant regions.
- - Thought to be caused by flucations in spontaneous neural activity.
- - The exact mechanims remain unclear.

- Neurosicentists are increasingly interested in studying the correlation between spontaneous BOLD signal across the brain to learn about its intrinsic functional connectivity.

Resting State fMRI

- Because of the lack of task, rfMRI is attractive as it removes the burden of experimental design, subject compliance, and training demands.
- - It is particularly attractive for studies of development and clinical populations.

- In addition, it is easy to add a resting state scan when performing task-based experiments.
- For these reasons the amount of available resting state data has exploded.

Resting State fMRI

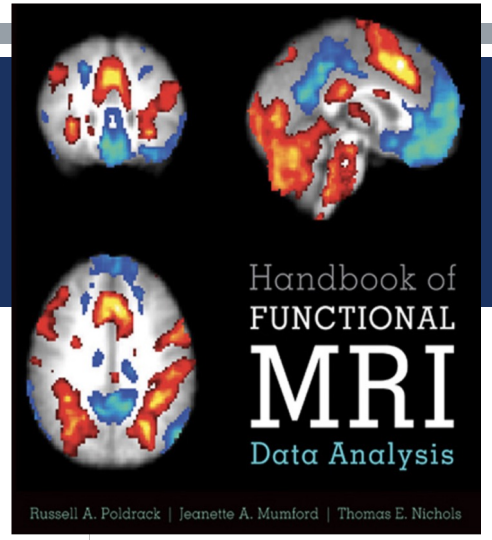
- One of the primary benefits with rfMRI is the ability to compare data across labs.
- - Experiments do not need to be synchronized.

- This has led to large data sharing initiatives (e.g., more than1000 Functional Connectomes Project).

Resting State Networks

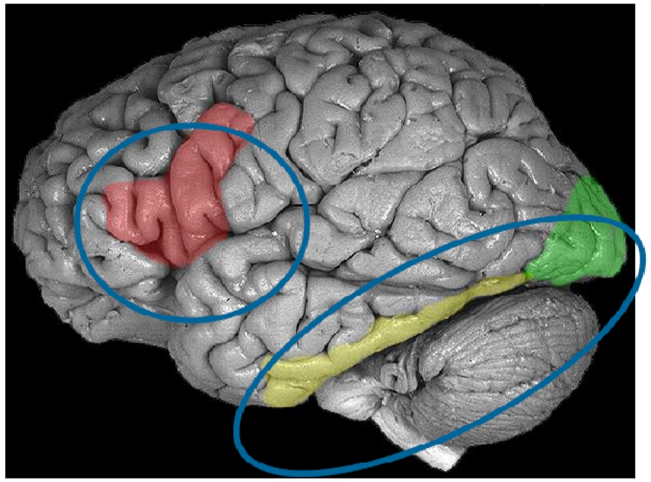
- Research has already revealed large-scale spatial patterns of coherent signal in the brain during rest, corresponding to functionally relevant resting-state networks (RSNs).
- - They are thought to reflect the neuronal baseline activity of the brain.
- A number of RSNs have been consistently observed both across groups of subjects and in repeated scanning sessions on the same subject.

Systems analysis in fMRI



Functional specialisation:

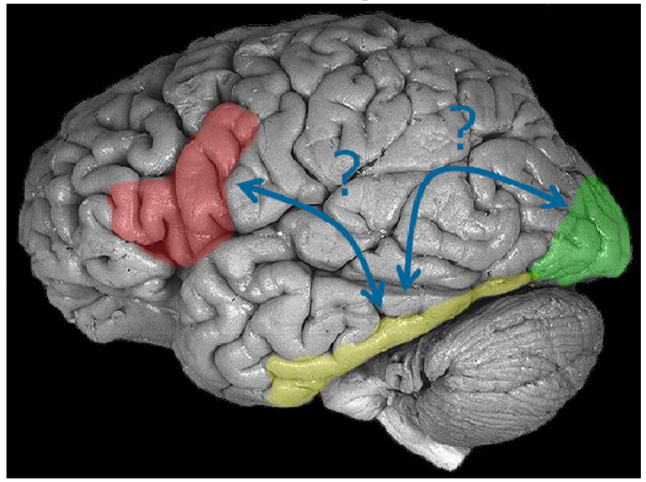
What regions respond to a particular experimental input?

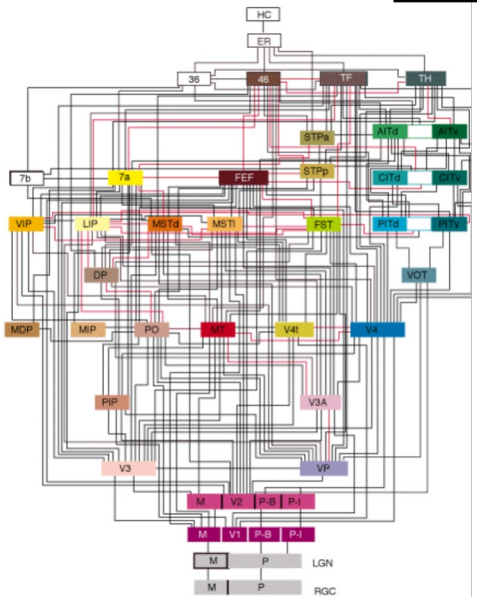


Functional integration:

How do regions influence each other?

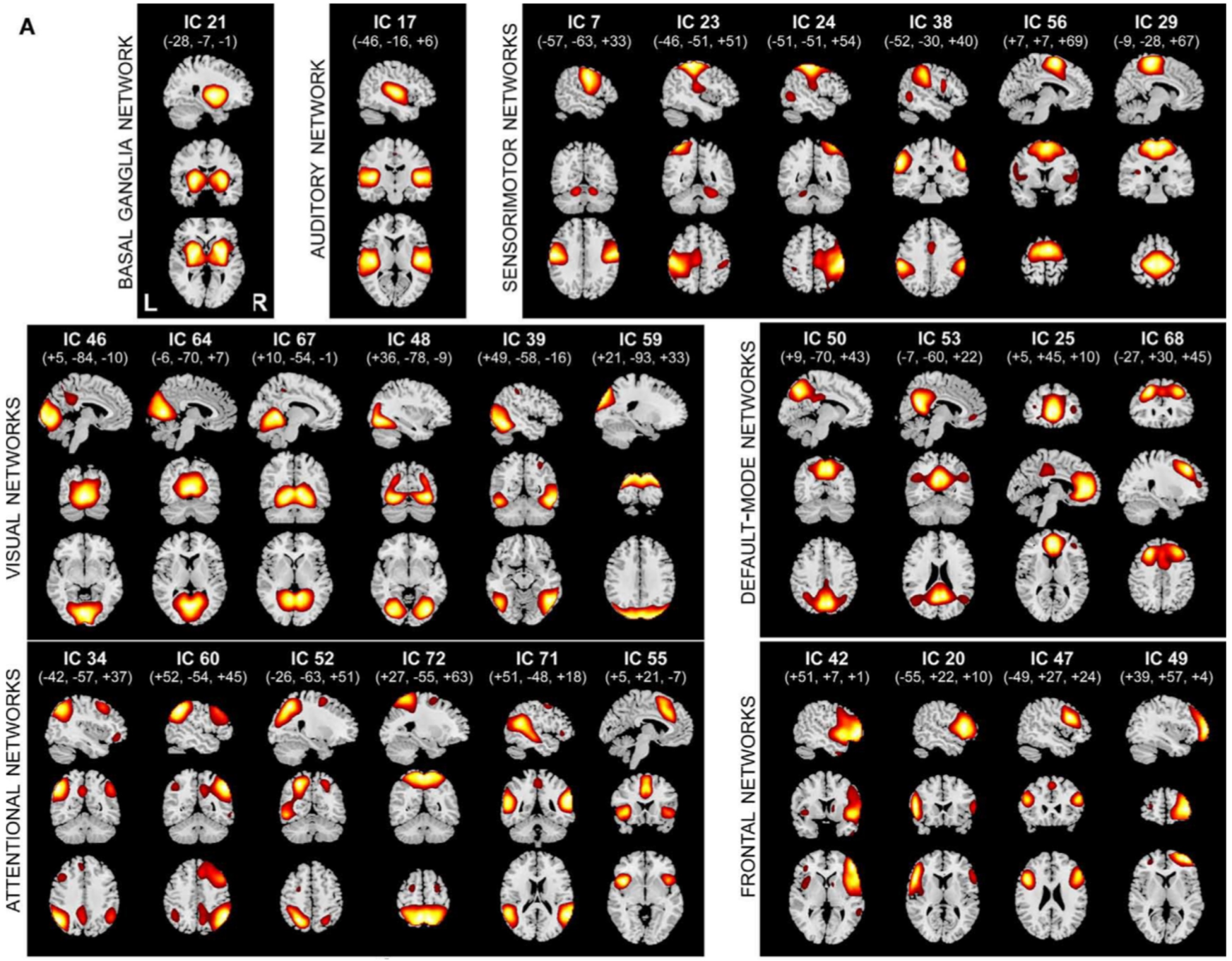
→ Brain Connectivity





Resting State Networks

- Resting-state networks (RSNs) are localized to grey matter, and are thought to reflect functional systems supporting core perceptual and cognitive processes.
- Regions that are co-activated during active tasks also show resting state connectivity.
- - Brain regions with similar functionality tend to express similar patterns of spontaneous BOLD activation.
- Sometimes subsets of RSNs appear to be either up or down-regulated during specific cognitive tasks.



- ICA algorithm search for components that are spatially independent.
- There is a large number of potentially independent networks in the brain, which might have similar timecourses during performance of a task.

Allen FrontSystNeurosci 2011

Resting State fMRI - low frequency fluctuations

- rfMRI is based on studying low-frequency BOLD fluctuations.
- Functionally relevant, spontaneous BOLD oscillations have been found in the lower frequency ranges (0.01-0.08 Hz).
- This is separable from respiratory (0.1-0.5 Hz) and cardiovascular (0.6-1.2 Hz) signal frequencies.

Resting State fMRI - data collection

- Typical resting experiments are of the order of 5-10 min, though the identification of an optimal duration of a resting fMRI session and the possible need for multiple sessions remains an open issue.

- In addition, there is no consensus as to whether data should be collected while subjects are asleep or awake, and with eyes open or closed.

Resting State fMRI – pre-processing

- Pre-processing of rfMRI data typically follows the same pipeline applied to standard task-related BOLD fMRI.
- However, there are a few important differences.
- - High pass temporal filtering applied to task fMRI data may be overly aggressive with respect to removing some of the relevant frequency information.
- - Often the data is band-pass filtered at 0.01-0.08 Hz.

Resting State fMRI – pre-processing

- It has been shown that non-neuronal physiological signals may interfere with resting state BOLD data.
- Removal of confounding signals, such as respiratory or cardiovascular noise considerably improves the quality of data attributed to neural activity.
- It has therefore become common practice in rfMRI research to monitor such signals, and retrospectively correct for their confounding effects post-acquisition.

Resting State fMRI – pre-processing

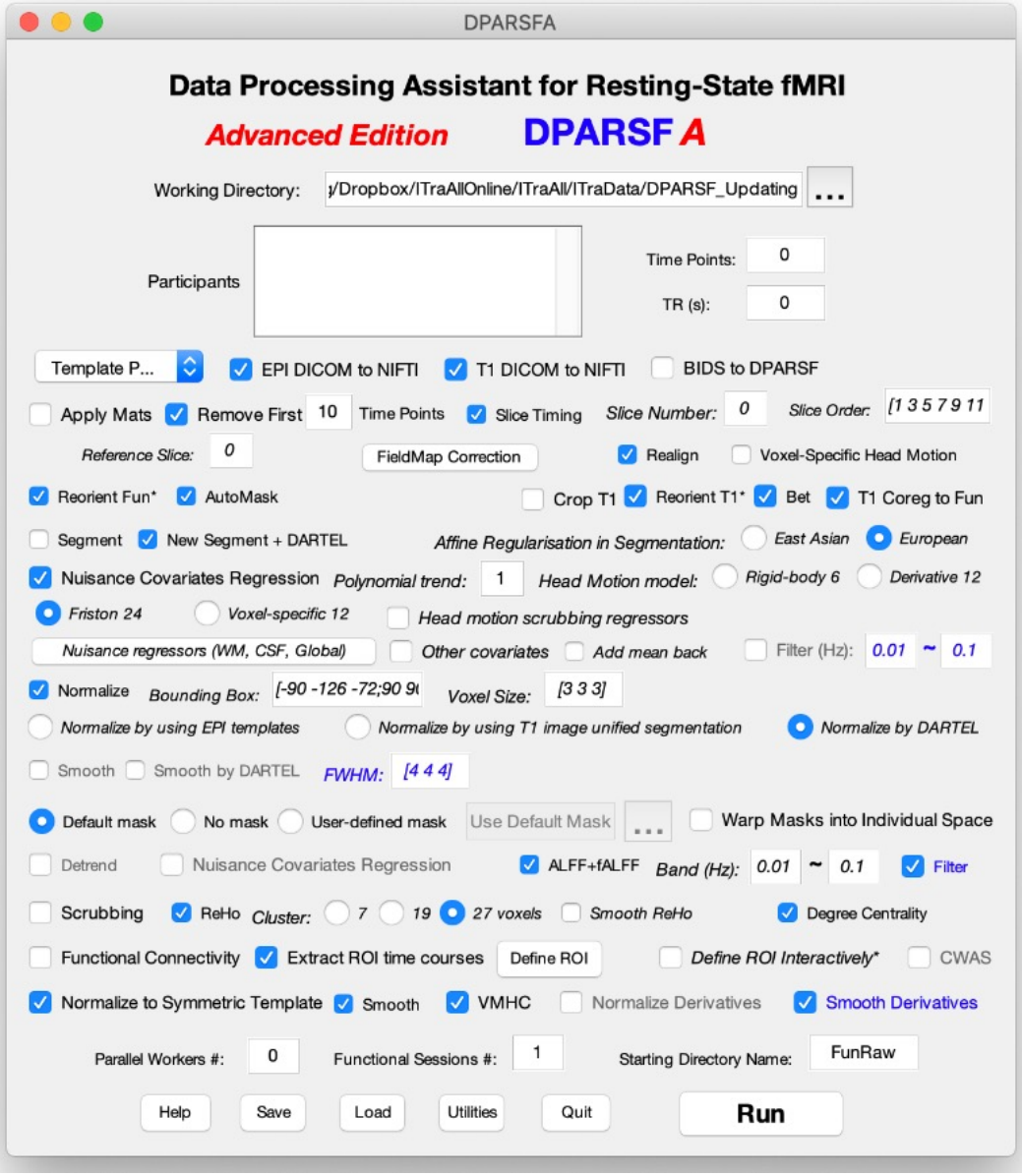
- Global mean signal, six motion parameters, the cerebrospinal fluid (CSF), and the white matter signals are also comonly removed as nuisance variables to reduce the effects of head motion and non-neuronal BOLD fluctuations.

- However, the removal of the global signal is particularly controversial.

- It is thought that global signal regression will induce a bias towards finding anti-correlations between RSNs.

Data Processing Assistant for Resting-State fMRI (DPARSF)

Submitted by YAN Chao-Gan on Mon, 08/18/2014 - 09:37



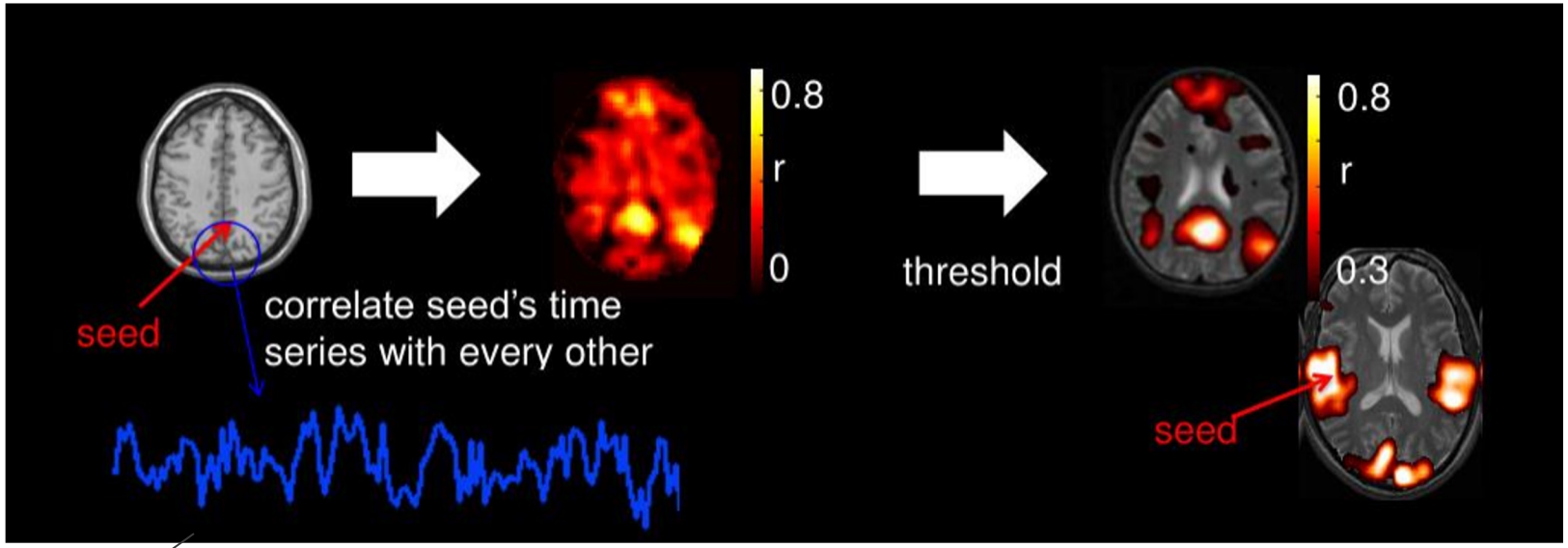
https://rfmri.org/DPARSF

Resting State fMRI – analysis

- Many traditional approaches toward analyzing fMRI data (e.g., the GLM) are not relevant for resting state data due to the inherent lack of task.
- Instead, more exploratory methods like seed analysis and independent components analysis (ICA) are popular.
- There are also specfic methdos tailored to rfMRI, such as amplitude of low frequency fluctuations (ALFF), fractional ALFF (fALFF), and regional homogeneity (ReHo).

Seed-based connectivity

- To test how a brain region (ROI) is functionally connected to other brain regions:
- extracting the timecourse (the first eigenvariate) from a seed voxel or seed region, which is determined based on some a priori hypothesis.
- computing its correlation with all of the voxels across the brain.



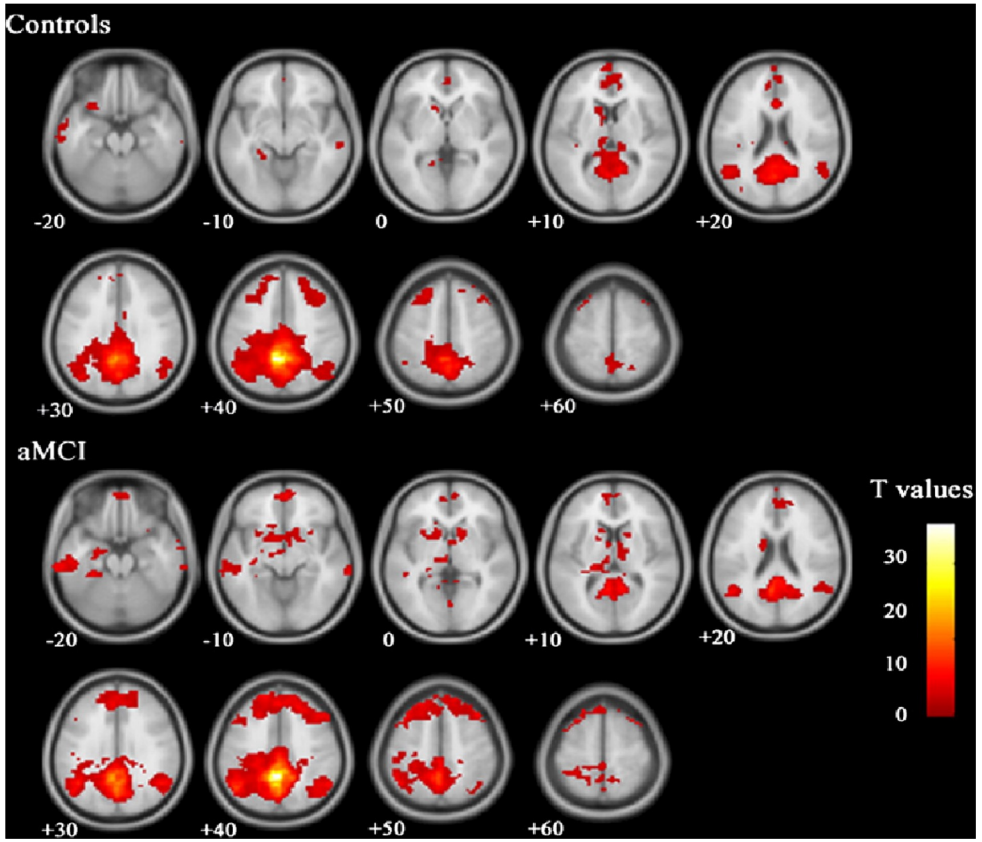
the first eigenvariate

Default mode network (DMN)

Precuneus (PCC), Posterior cingulate, Inferior parietal and Medial frontal cortex.

Higher activity during passive baseline conditions compared to tasks.

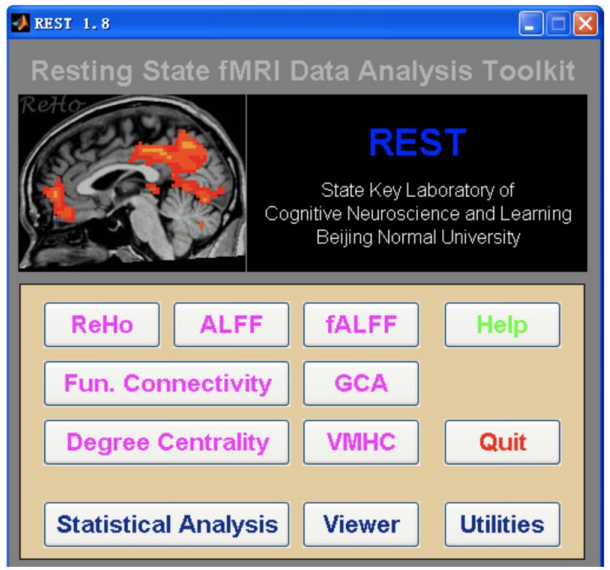
DMN dysfunction may underlie disease states including Alzheimer's disease, schizophrenia, ADHD, Parkinson's disease, depression and anxiety (Broyd et al., 2009) and autism (Assaf et al., 2010; Padmanabhan et al., 2017).



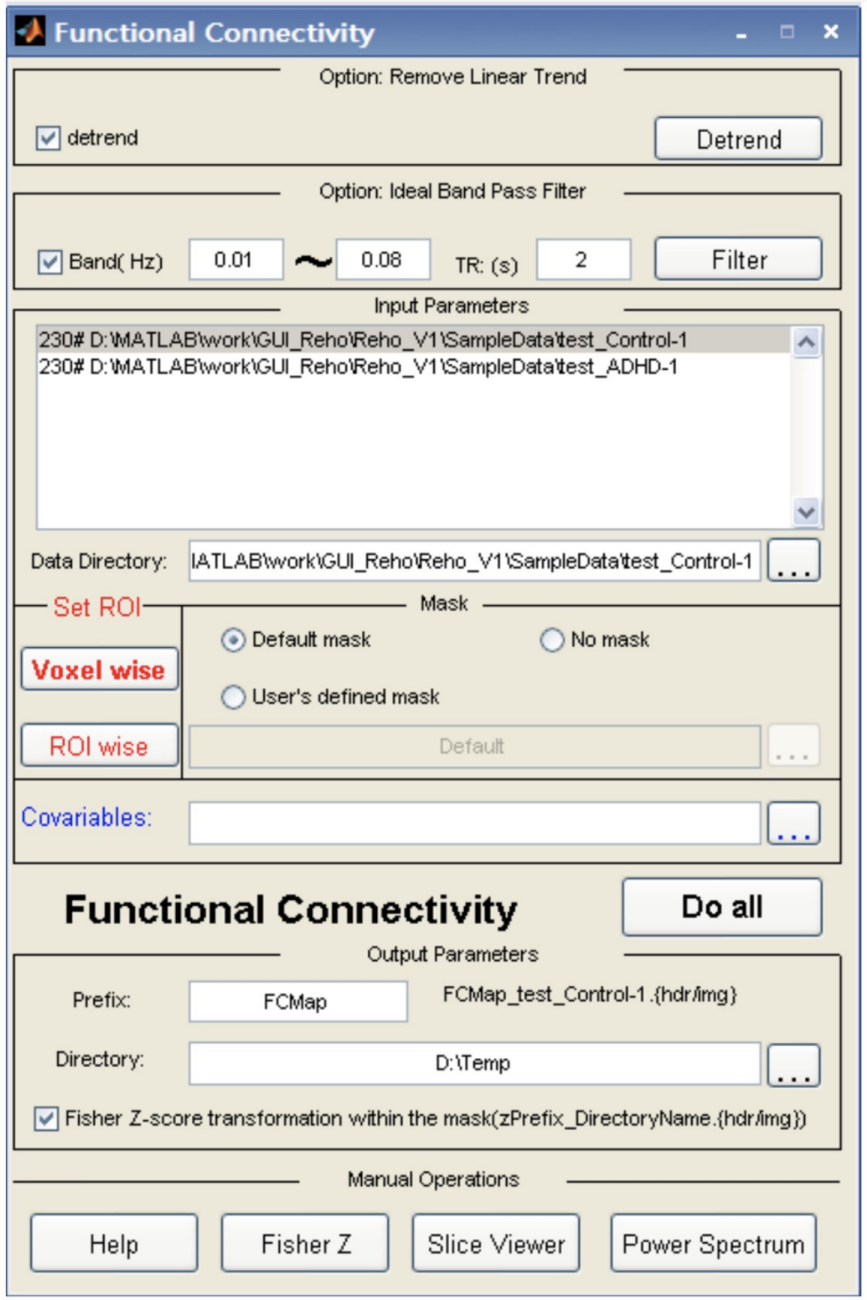
Bai et al., 2009

Preprocessed (in spm) resting-state fMRI files for each subject

REST



http://restfmri.net/forum/index.php?q=rest



SPM

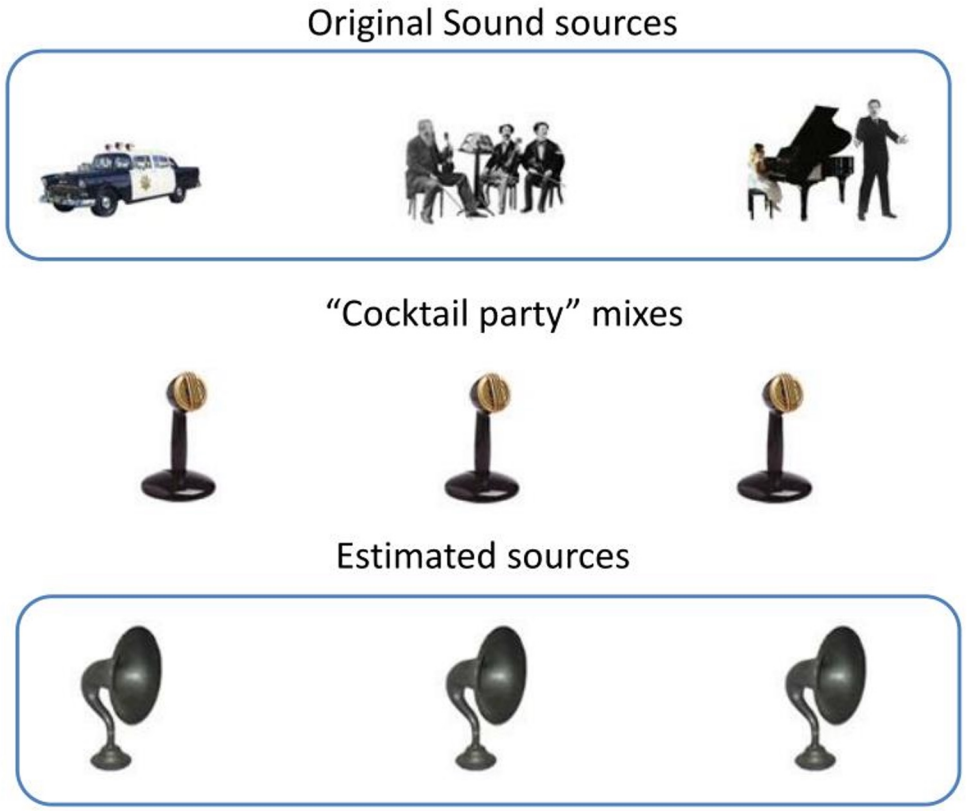
One sample T- test

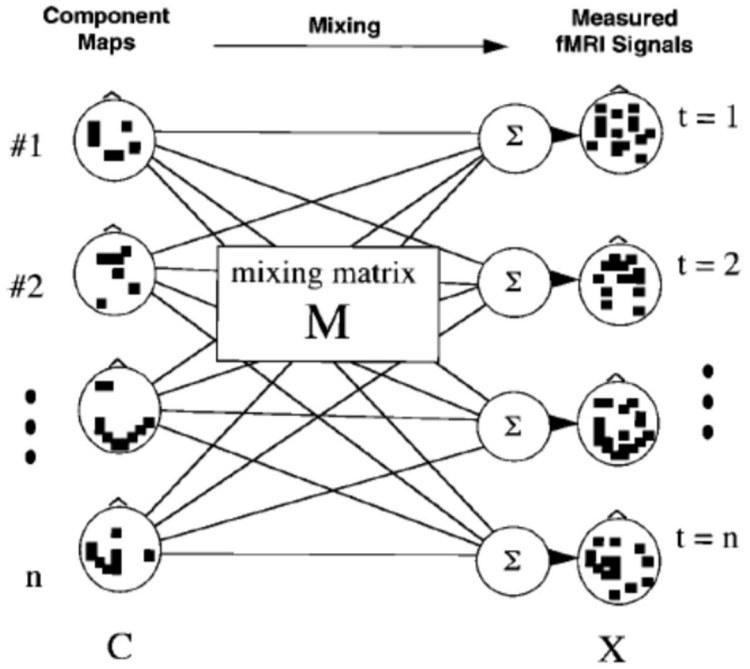
Include the FC maps of all subjects (use only the files that start with “zPCC…”)

ICA

$$x = As + e$$

x is the signal that we are trying to decompose, s is a set of unkonwn sources (or components), and A is the unknown mixing matrix that combines the components to obtain the observed signal.

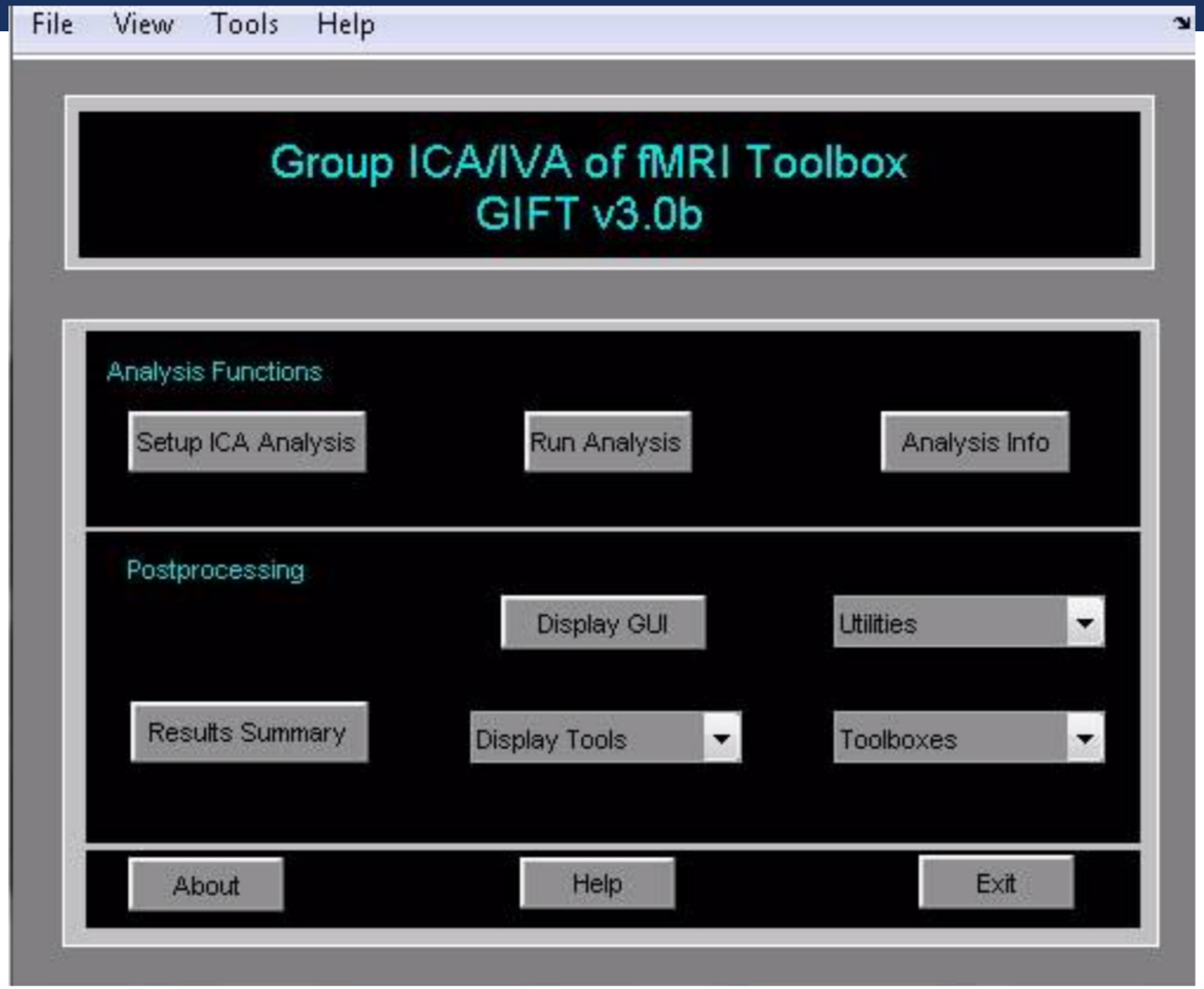




$$X = MC$$

The observed data is the sum of a set of inputs which have been mixed together in an unknown fashion. The goal of ICA is to discover both the inputs and how they were mixed.

GROUP ICA/IVA OF FMRI TOOLBOX (GIFT)



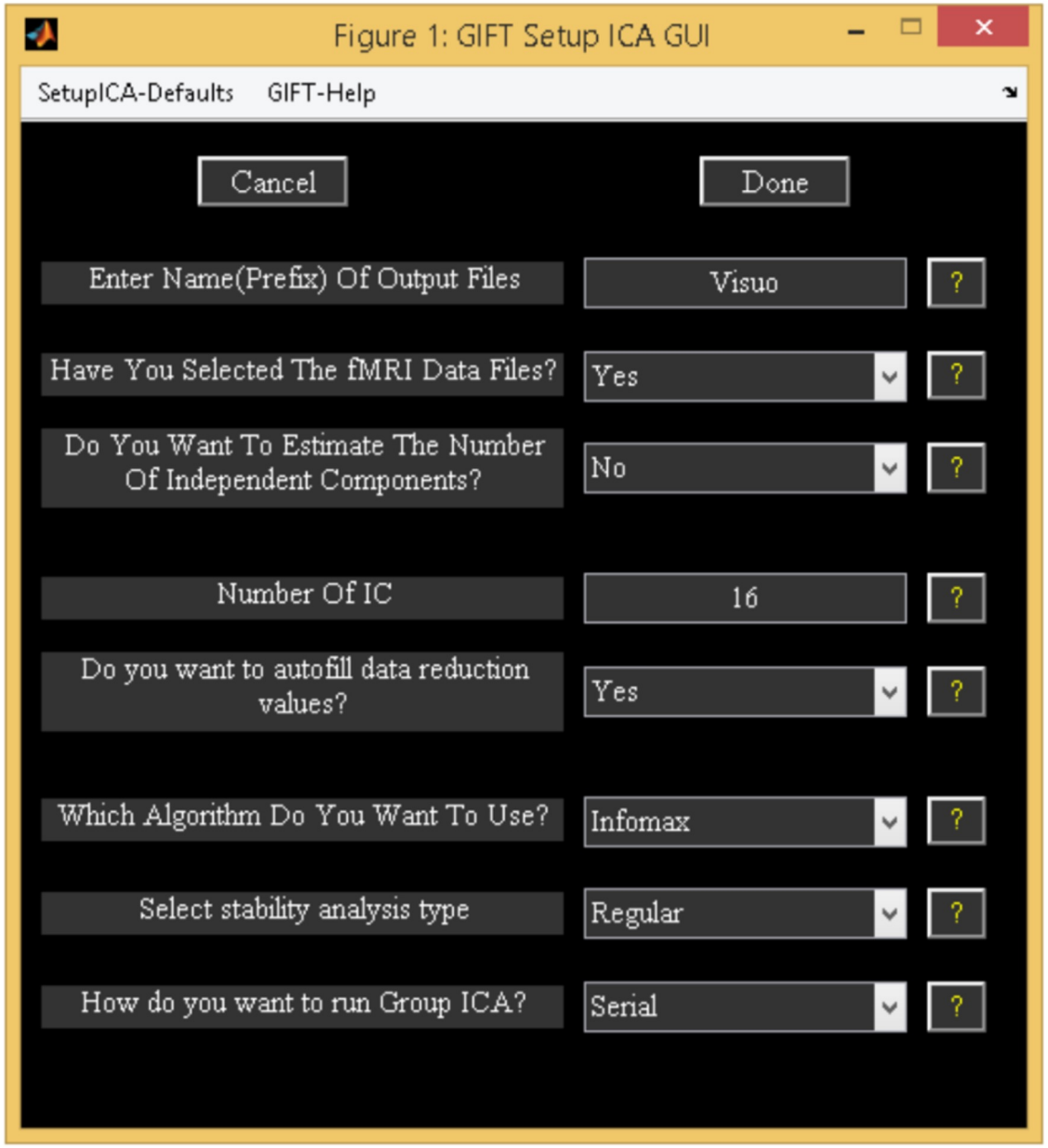


Figure 1: GIFT Setup ICA GUI
SetupICA-Defaults
GIFT-Help
Cancel
Done
Enter Name(Prefix) Of Output Files
Visuo
Have You Selected The fMRI Data Files?
Yes
Do You Want To Estimate The Number Of Independent Components?
No
Number Of IC
16
Do you want to autofill data reduction values?
Yes
Which Algorithm Do You Want To Use?
Infomax
Select stability analysis type
Regular
How do you want to run Group ICA?
Serial

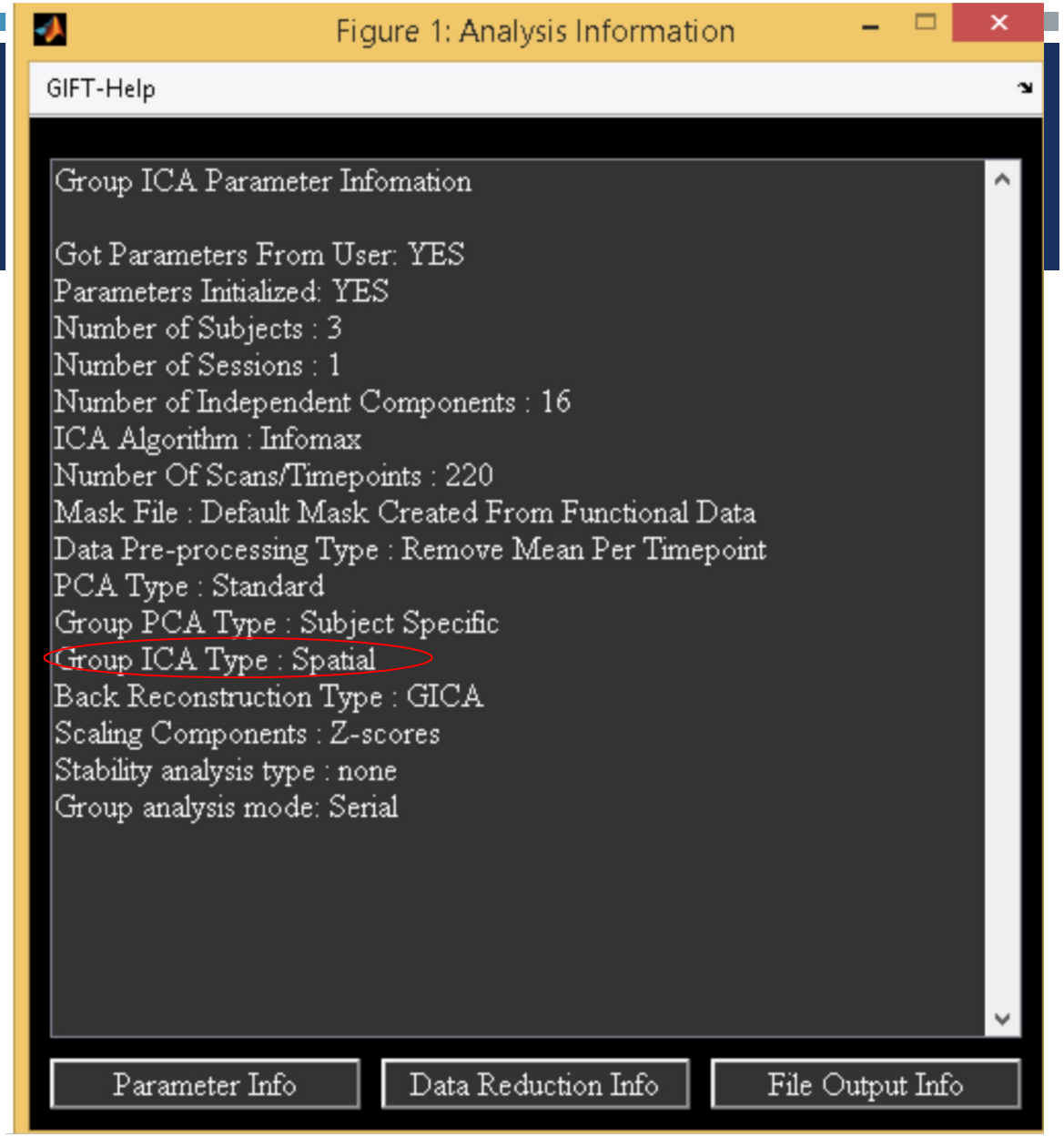
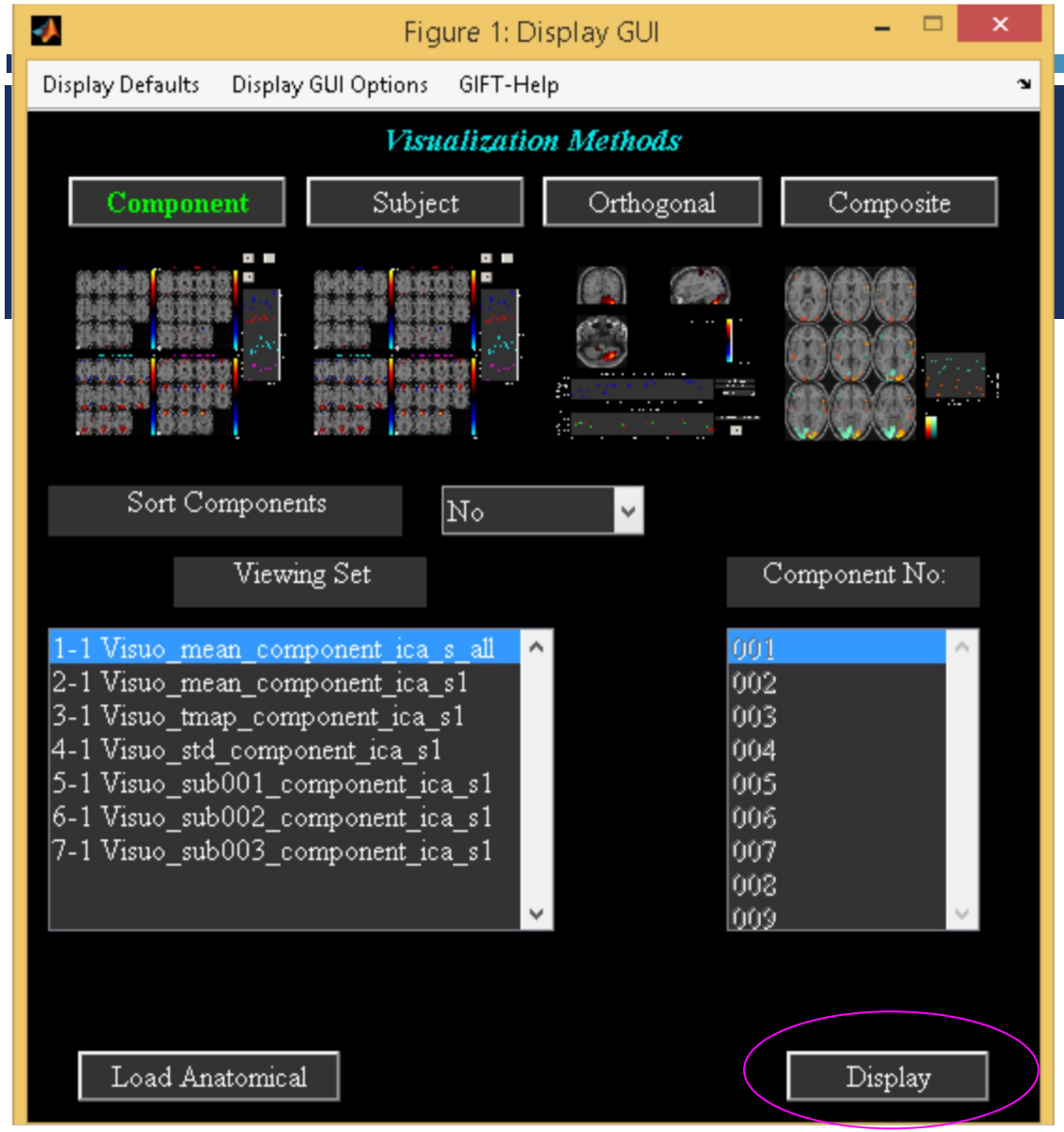
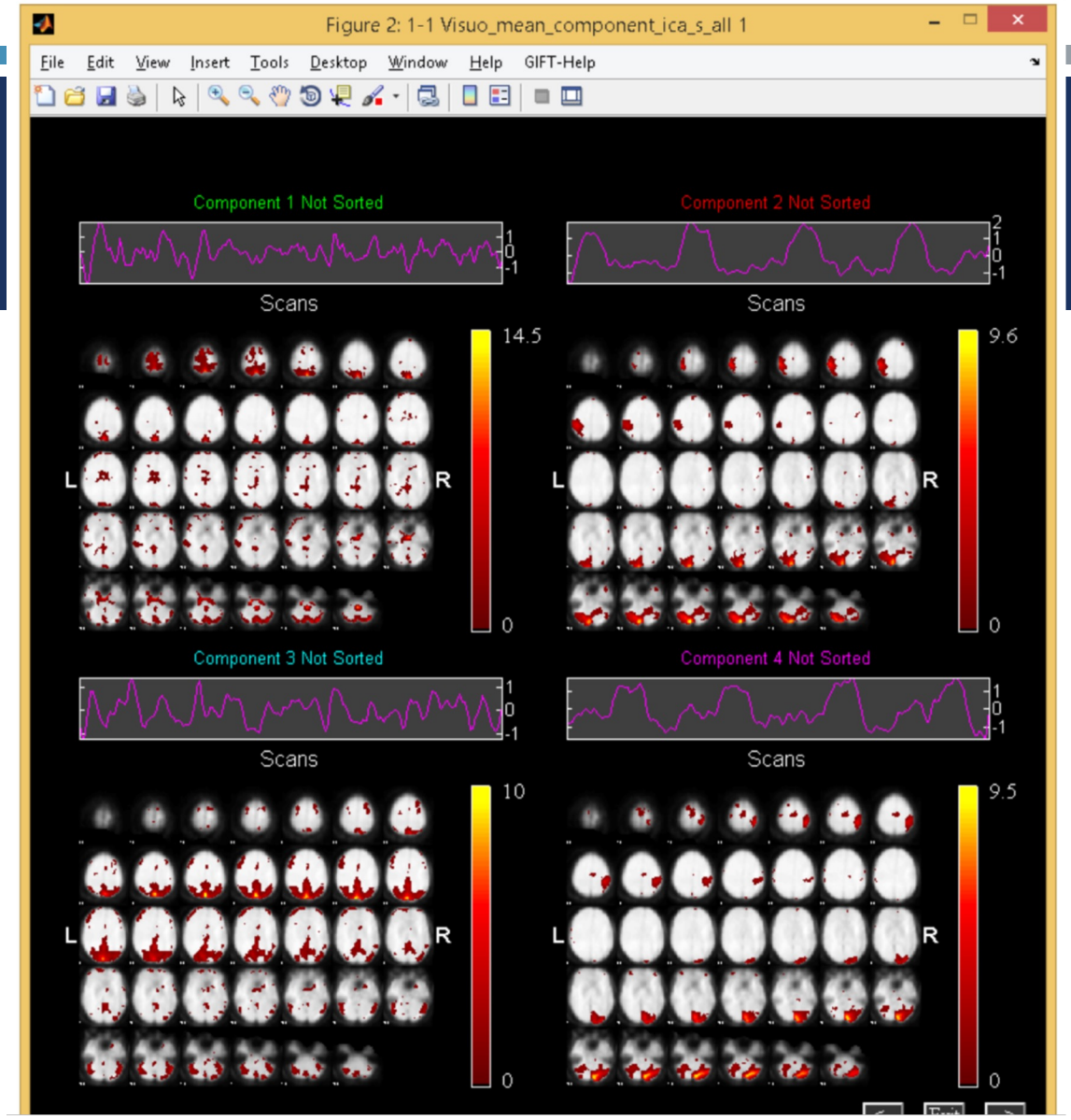
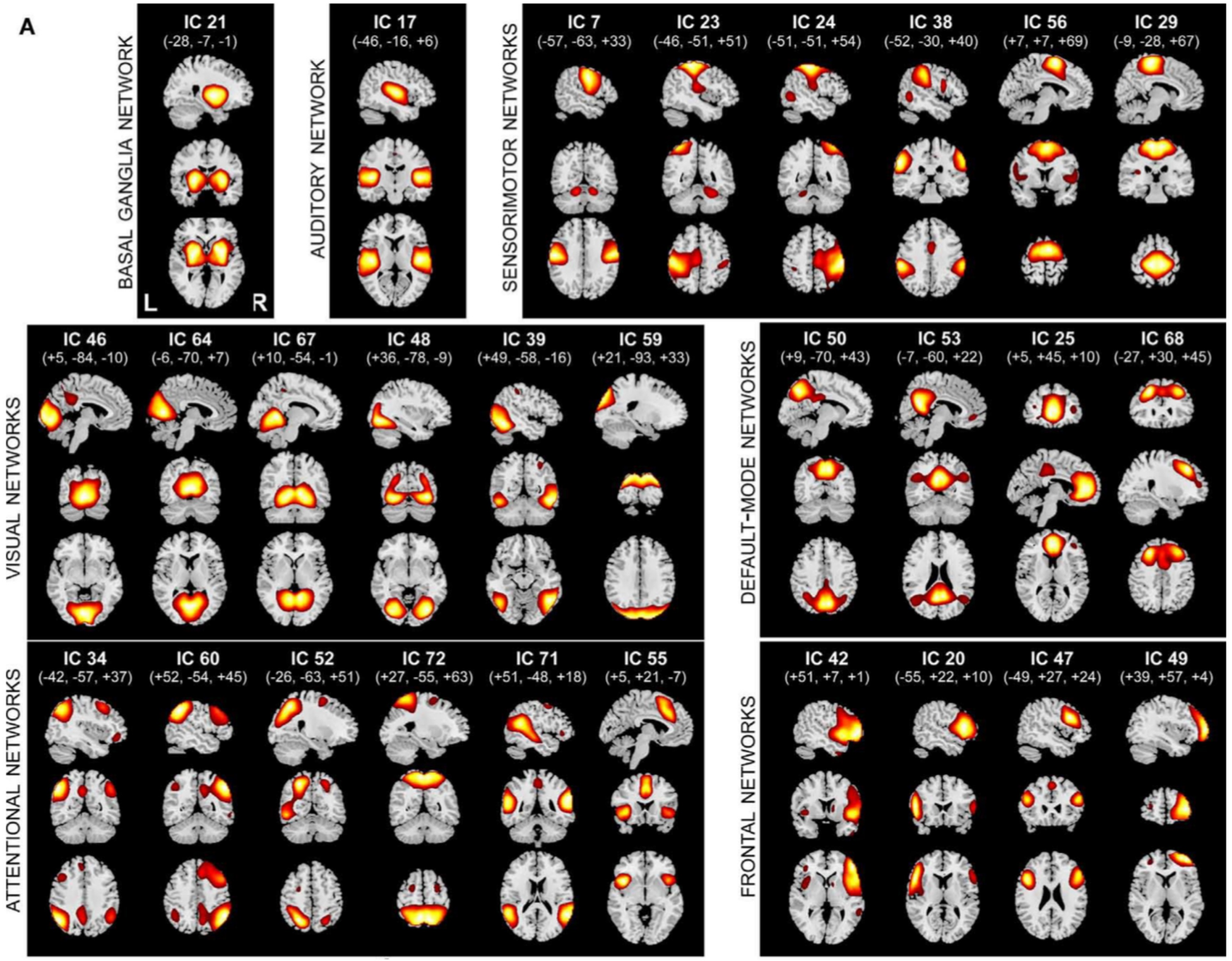


Figure 1: Analysis Information
GIFT-Help
Group ICA Parameter Infomation
Got Parameters From User: YES
Parameters Initialized: YES
Number of Subjects : 3
Number of Sessions : 1
Number of Independent Components : 16
ICA Algorithm : Infomax
Number Of Scans/Timepoints : 220
Mask File : Default Mask Created From Functional Data
Data Pre-processing Type : Remove Mean Per Timepoint
PCA Type : Standard
Group PCA Type : Subject Specific
Group ICA Type : Spatial
Back Reconstruction Type : GICA
Scaling Components : Z-scores
Stability analysis type : none
Group analysis mode: Serial
Parameter Info
Data Reduction Info
File Output Info





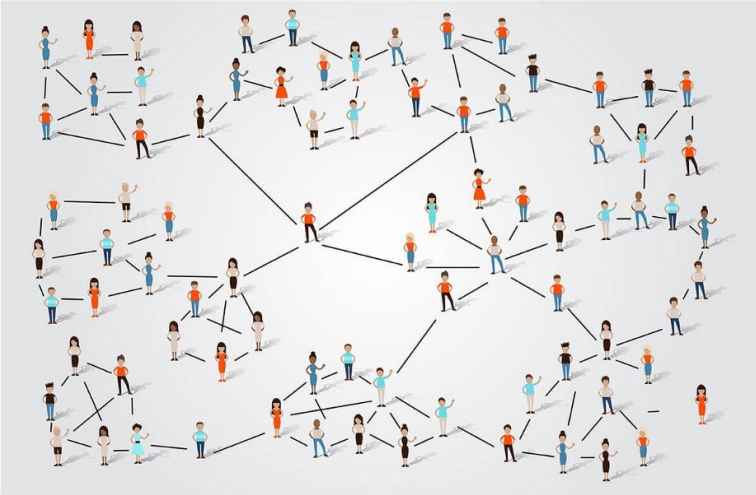
All the components of mean for all subjects and sessions
Identify the functional neural networks. E.g, DMN is IC#, Auditory is IC#



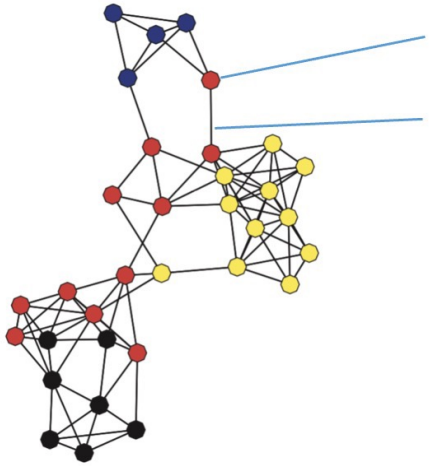
- ICA algorithm search for components that are spatially independent.
- There is a large number of potentially independent networks in the brain, which might have similar timecourses during performance of a task.

Allen FrontSystNeurosci 2011

Network analysis and graph theory - Small world networks



"six degrees of separation"



Node

Edge

the degree of a node = the number of edges

yellow: frontoparietal

black: cingulo-opercular

red: default mode

blue: cerebellar.

It has generally been applied to resting-state datas.

E.g. How the interactions between regions change over development

Metab Brain Dis (2017) 32:685–692
DOI 10.1007/s11011-016-9946-3

ORIGINAL ARTICLE

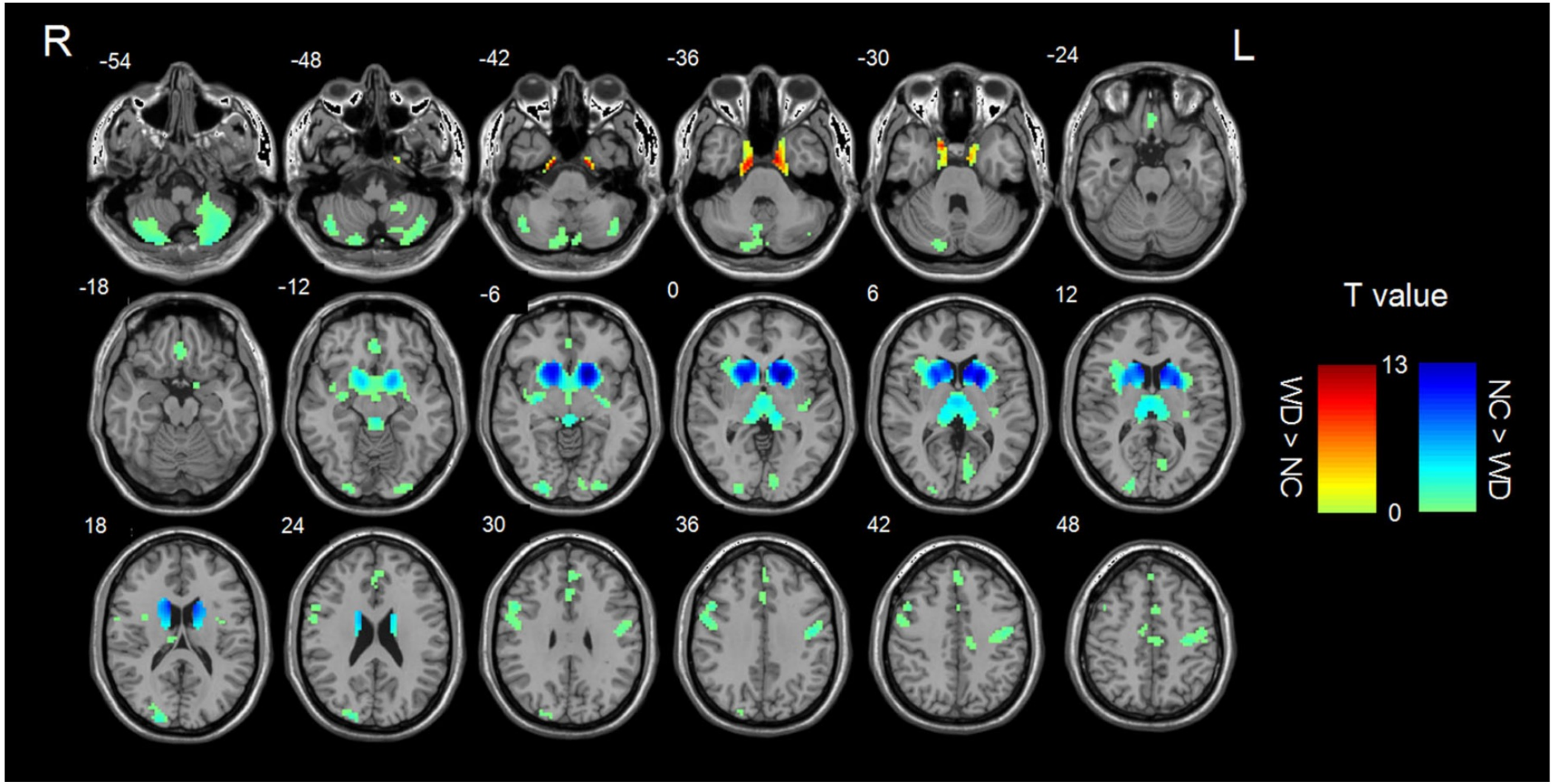
Frequency-dependent changes in the amplitude of low-frequency fluctuations in patients with Wilson's disease: a resting-state fMRI study

Xiaopeng Hu[1] · Siyi Chen[2,3] · Chang-Bing Huang[2] · Yinfeng Qian[1] · Yongqiang Yu[1]

Wilson disease (WD) is a rare inherited disorder in which an excessive amount of copper accumulates in the body. The buildup of copper leads to damage in the liver, brain, and eyes. Although copper accumulation begins at birth, symptoms of the disorder only appear later in life.

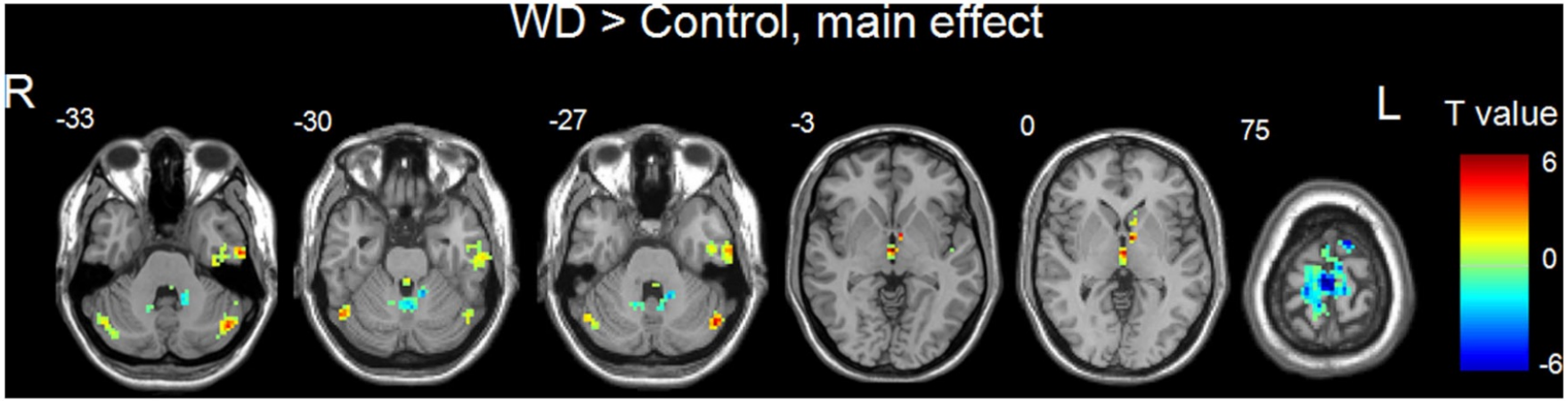
Twenty-eight neurological WD patients (18 males), with 21.43 ± 3.56 years (mean ± s.d.), were recruited from the Institute of Neurology at Anhui University of Chinese Medicine, Hefei, China.
Abnormal copper metabolism (decreased levels of serum ceruloplasmin: CP < 20 mg/dL; increased 24-h urinary excretion of copper: 24-h urinary Cu > 1.6 μmol/day.
Twenty-seven normal controls (NC; 15 males), aged 23.41 ± 2.65 years (mean ± s.d.), were recruited from the local community.

We performed a voxel-based morphometry (VBM) analysis for structural images (http://www.fil.ion.ucl.ac.uk/spm).

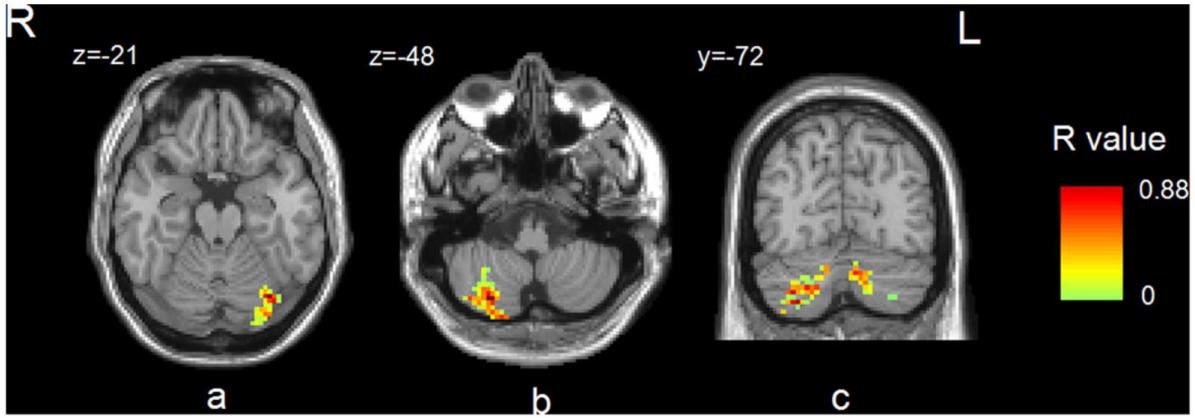


GM changes in WD patients as compared to normal controls (two-sample t-tests)

Abnormal ALFF activity in WD patients



Correlations between ALFF amplitudes and biochemical parameters



Areas showing correlation between **a,** Cu (μmol/day) and slow-5, **b,** CP (mg/dL) and slow-5, **c,** CP (mg/dL) and slow-4

Machine learning

AUTOENCODER MODEL

- Functional connectivity's (FCs) of ASD patients are widely disrupted throughout the entire brain and show uncertainties about the spatial distribution.

- In many autoencoder based brain disorder diagnosis algorithms, functional connectivity feature extraction (and/or selection) and classification are separately performed in different stages.

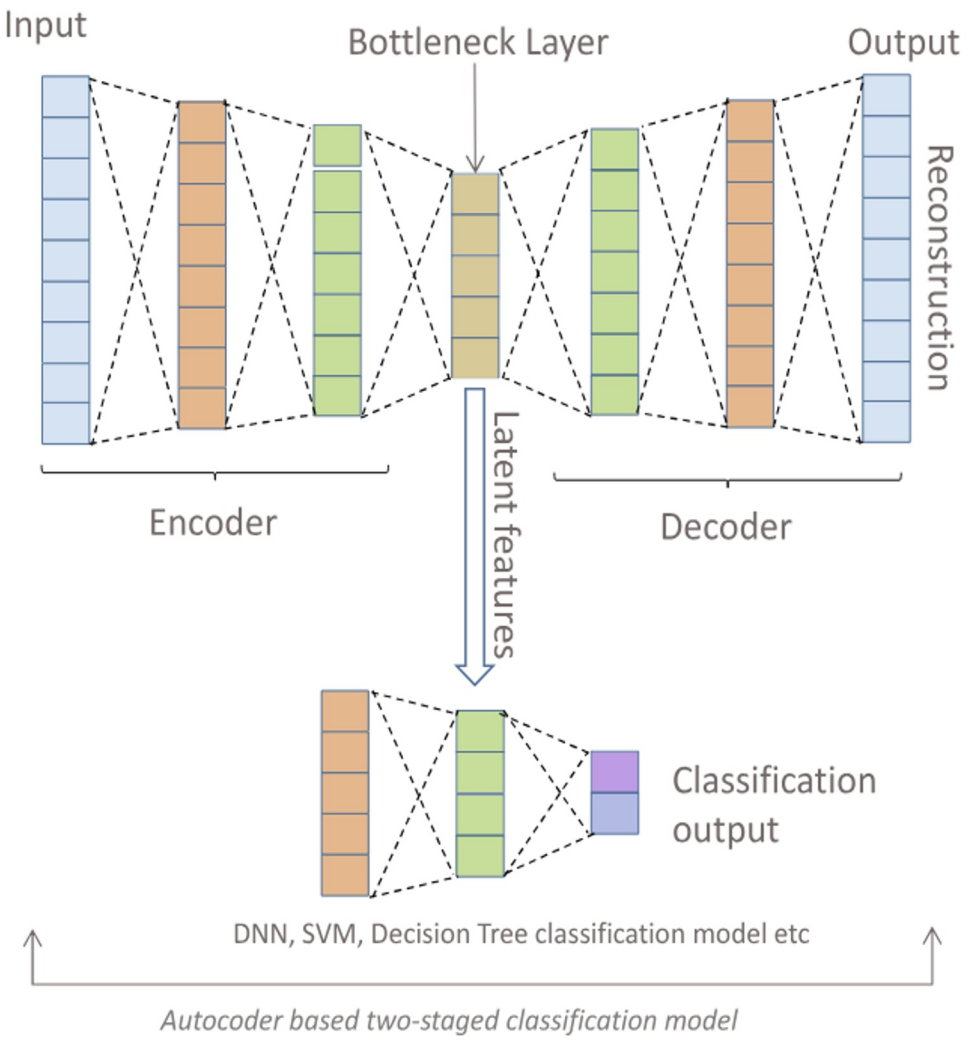


Fig. 1. A common autoencoder based two-staged classification model. The autoencoder and the classification models are trained separately in a sequential manner. The latent representation of the input data in the bottleneck layer is utilized as the input feature vector of the classification algorithms.

Journal of Computational Biology > Vol. 28, No. 2

Research Article | NO ACCESS | Published Online: 4 February 2021

Diagnosis of Autism Spectrum Disorder Based on Functional Brain Networks with Deep Learning

Authors: Wutao Yin, Sakib Mostafa, and Fang-xiang Wu | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Computational Biology • https://doi.org/10.1089/cmb.2020.0252

The classification accuracy comparison

Methods	Accuracy
Heinsfeld et al. [22]	70.0%
Eslami et al. [21]	70.1%
Xing et al. [31]	66.8%
Wong et al. [32]	71.1%
Mostafa et al. [24]	79.2%
The proposed method	87.2%

ABIDE I data set.

The preprocessing pipeline is normally standard.

Create a 264 ×264 connectivity matrix (PCCs) out of 264 ROIs, as the raw features for the SSAE model input

The label of each sample is given by the ABIDE dataset.

https://fcon_1000.projects.nitrc.org/indi/abide/

RECOMMEND SOURCES

- Resting-State fMRI Data Analysis Toolkit (REST)

  Functional Connectivity (FC), Regional Homogeneity (ReHo), Amplitude of Low-Frequency Fluctuation (ALFF), Fractional ALFF (fALFF), Gragner causality, degree centrality, voxel-mirrored homotopic connectivity (VMHC) and perform statistical analysis. You also can use REST to view your data, perform Monte Carlo simulation similar to AlphaSim in AFNI, perform Gaussian random field theory multiple comparison correction like easythresh in FSL, calculate your images, regress out covariates, extract ROI time courses, reslice images, and sort DICOM files.

  http://restfmri.net/forum/index.php?q=rest

RECOMMEND SOURCES

- BrainNet Viewers: Visualize your data

https://www.nitrc.org/frs/?group_id=504

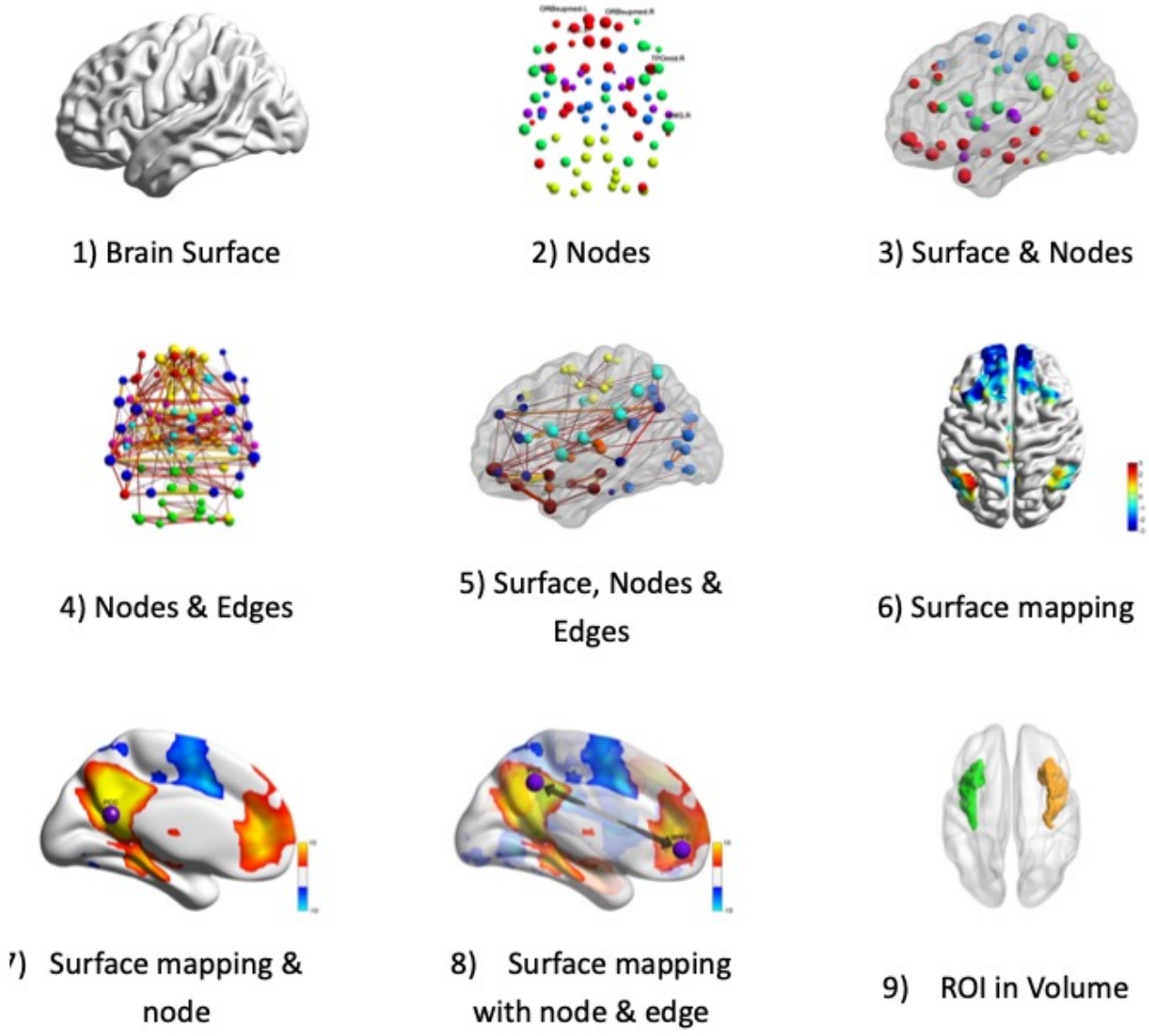


Fig. 2 Brain network pictures from different file combinations

RECOMMEND SOURCES

- HCP: a huge database
- https://www.humanconnectome.org/study/hcp-young-adult/data-releases

RECOMMEND SOURCES

- Neurosynth.org

Allows you to investigate brain functional connectivity patterns or brain activation patterns based on a huge set of imaging studies.

- Thank you for your attention!