Segmentation enhanced Resting-State fMRI for the Detection of Major Depression

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Pattern Recognition Lab (CS 5)

FRIEDRICH-ALEXANDER
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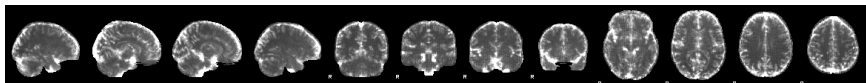ERLANGEN-NÜRNBERG

TECHNISCHE FAKULTÄT
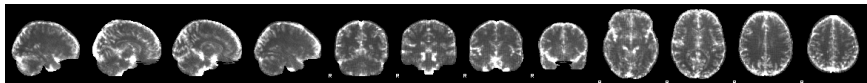
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Motivation

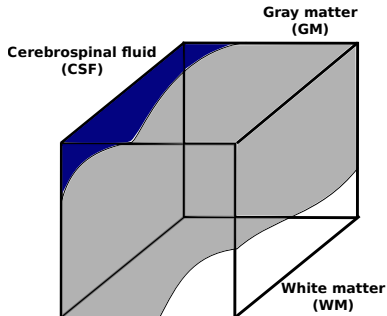# Where is signal source of the functional MRI?

Where is signal source of the functional MRI?

- Brain activity signal arises in gray matter brain tissue
- Signal from other tissue contributes to noise

Partial volume effect

- multiple tissue types in one voxel

- voxel signal is corrupted by noise

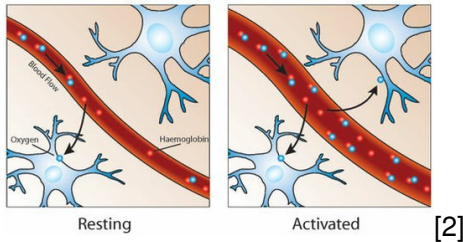⇒ usage of a segmentation approach may increase signal quality

Introduction

Physiological basis of functional MRI

Blood oxygen level-dependent (BOLD) images

- deoxygenated haemoglobin (Hb^-) = paramagnetic behaviour
- Hb^- decreases MRI signal contrast
- Increased blood flow during neuronal activation
- Increased O_2-concentration raises signal contrast

[2]

Functional connectivity

Definition

Temporal correlation between areas or voxels that are located in physically distant brain regions

Methods

- Independent component analysis (ICA)
- Regional Homogeinity (ReHo)
- Seed-based correlation analysis (SCA)

Meaning

Simultaneous activation of brain regions = brain network

The "Resting-state"

- Patient is at rest (eg. eyes closed, instructed to do nothing)
- Observation of spontaneous fluctuations in brain activity
- Low-frequency fMRI signal: 0.01 Hz - 0.08 Hz
- Activity can be found within the Default Mode Network (DMN)
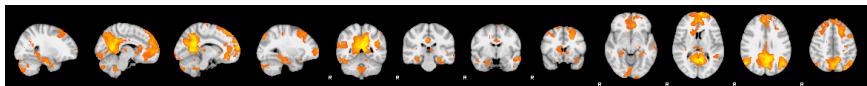
Mental disorders

Major depressive disorder (MDD)

- Defined within ICD-10 guidelines
- Symptoms:
  - Reduced capacity of enjoyment
  - Loss of concentration
  - Sleep disturbance and tiredness
  - Diminished appetite
  - Retardation of physical and emotional reactions
  - Reduced self-esteem and self-confidence
- Severity of the depression is determined by number of symptoms
- Moderate depressive episode: patient has difficulties in continuing with ordinary activities

Mental disorders

Seasonal affective disorder (SAD)

- Defined within DSM-IV guidelines
- Major depressive episode with a clear seasonal pattern
- Symptoms:
  - similar to MDD
  - increased need of sleep
  - increased appetite
- Affectation of the inner internal clock

Image Processing

Tools and code source

- FMRIB Software Library (FSL)

[5]

- Python Software Packages NiPy and SciPy

- Standard preprocessing and segmentation approach of [4]

- Processing pipeline provided by [4] was extended to 5D

[4]

Available image data

MPRAGE

- 3 dimensional
- Needed for:
  - localization of brain activity
  - segmentation
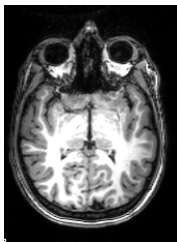


BOLD

- 4 dimensional
- Information on brain activity

MPRAGE preprocessing

| Face exclusion | Bias field correction | Registration | Segmentation |

MPRAGE preprocessing

Face exclusion and Registration

- Affine registration to standard space

  - Elimination of non brain tissue (e.g. face)
  - Preparation for non-linear registration
  - 12 degrees of freedom

- Non-linear registration standard space

  - Ensure comparability of different subjects
  - Transformation by a deformation field
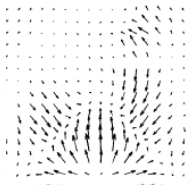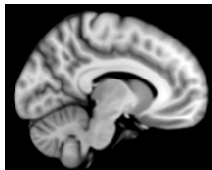
[3]

MPRAGE preprocessing

Bias field correction and Segmentation

The Bias field

Scanner artifact that causes alternating intensity values for equal tissue types.

- Segmentation and Bias field correction are engaged processes
- Initial Segmentation estimates probability values
- Bias field can be calculated out of tissue probabilities
- Bias field corrected image shows improved segmentation results

BOLD preprocessing

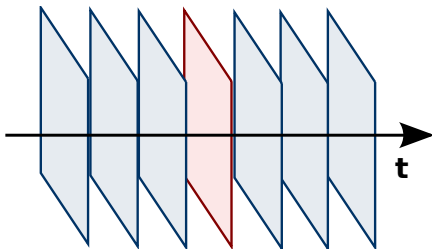Head motion correction → Registration → High-pass filtering → Nuisance Regression

MPRAGE preprocessing

Head motion correction and Registration

- Rigid-Body registration to reference image
- Rigid-Body registration to subject specific MPRAGE
- 6 degrees of freedom (rotation, translation)

BOLD preprocessing

Nuisance Regression and filtering

- High-pass filtering for signal detrending
- Nuisance signal regression for the correction of thermal and physiological signal noise
  - Setting up a general linear model (GLM)
  - Minimizing error term with least squares
  - Calculating the corrected image
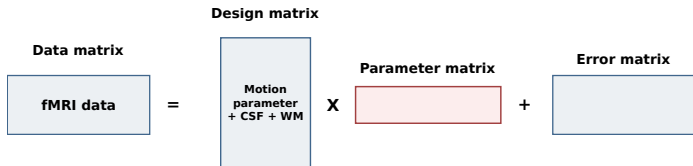
Smoothing methods

- General approach: Gaussian-kernel is applied
- Lenger et al.: linear equation system weighted by a Gaussian-kernel and extraction of gray matter tissue

$$
\begin{bmatrix} \mathbf{x_{GM}} \\ \mathbf{x_{WM}} \\ \mathbf{x_{CSF}} \end{bmatrix}_{\mathbf{i}} = \begin{bmatrix} [\mathbf{G} * (\mathbf{a_{GM}} \cdot \mathbf{a_{GM}})]_i & \dots & [\mathbf{G} * (\mathbf{a_{GM}} \cdot \mathbf{a_{CSF}})]_i \\ [\mathbf{G} * (\mathbf{a_{WM}} \cdot \mathbf{a_{GM}})]_i & \dots & [\mathbf{G} * (\mathbf{a_{WM}} \cdot \mathbf{a_{CSF}})]_i \\ [\mathbf{G} * (\mathbf{a_{CSF}} \cdot \mathbf{a_{GM}})]_i & \dots & [\mathbf{G} * (\mathbf{a_{CSF}} \cdot \mathbf{a_{CSF}})]_i \end{bmatrix}^{-1} \begin{bmatrix} [\mathbf{G} * (\mathbf{a_{GM}} \cdot \mathbf{B})]_i \\ \dots \\ [\mathbf{G} * (\mathbf{a_{CSF}} \cdot \mathbf{B})]_i \end{bmatrix} \tag{1}
$$

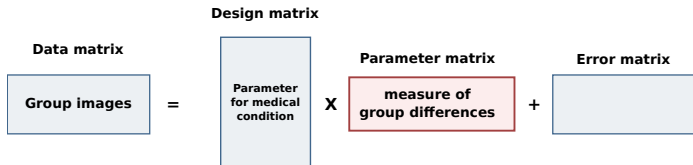| $\mathbf{a_x}$ | : | Partial volume map of tissue x from MPRAGE segmentation |
$\mathbf{B}$	:	subject specific BOLD image
$\mathbf{i}$	:	i-th voxel
$\mathbf{X_x}$	:	resulting voxel time course for each tissue type x
$\mathbf{G}$	:	Gaussian-kernel

Seed-based correlation analysis

Seed voxel within the posterior cingulate cortex (PCC)
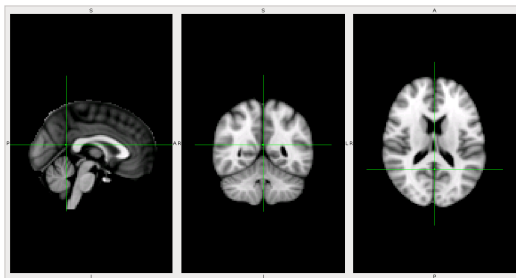
Univariate group analysis

- T-test on calculated parameters
- H_0: differences are due to chance

Contrast
HC - MDD
HC - SAD
MDD -SAD
male - female

Cluster-size based thresholding

- Too many false-positive results
- Thresholding decreases the number of errors
- calculate probability that:
  - one or more cluster
  - with a number of voxels $n > k$
  - voxels are above a certain threshold u
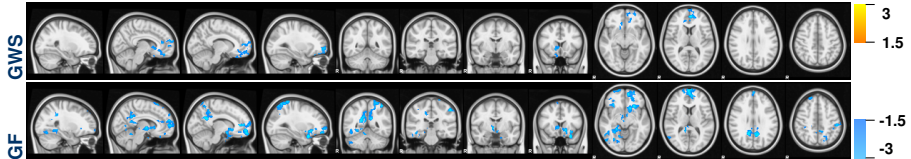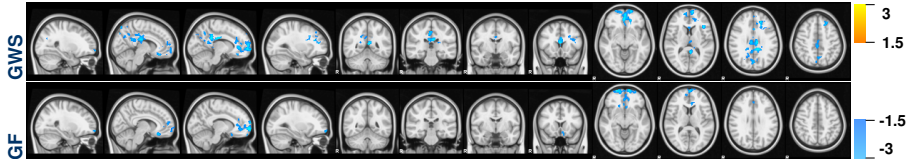
Results

Gender differences

- Female participants show increased connectivity compared to male
- Gaussian-weighted segmentation finds increased connectivity in male patients suffering SAD
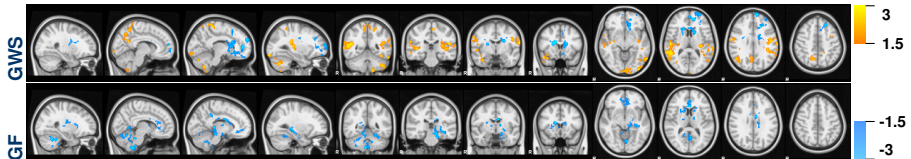- Gaussian-weighted segmentation finds additional cluster within MDD and SAD patients
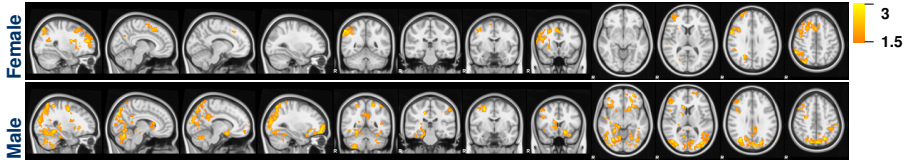
male > female - HC

GWS

GF

male > female - MDD

GWS

GF

male > female - SAD

GWS

GF

Univariate group inference

- Cerebellar structures $\rightarrow$ sensorimotor deficits [1]
- Occipital cortex $\rightarrow$ reduction of GABA neurotransmitter (attention-deficit)
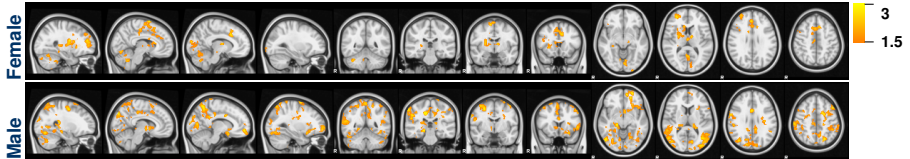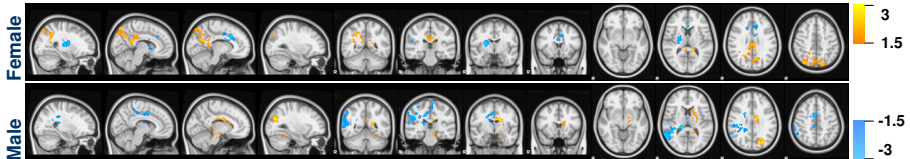- Regions are in agreement with literature
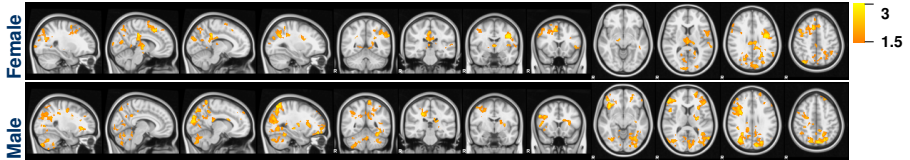
Gauss-filtered

MDD > HC — Female, Male
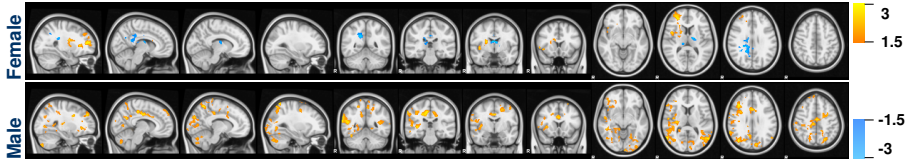SAD > HC — Female, Male
MDD > SAD — Female, Male

Segmentation

MDD > HC

Female

Male
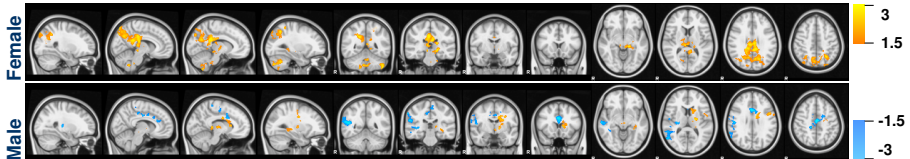
SAD > HC

Female

Male

MDD > SAD

Female

Male

Outlook

Further enhancements

- Usage of independent component analysis (ICA) for seed-voxel determination
- Usage of a combination of Gauss-filtering and Segmentation
- Improve cluster thresholding

Summary

Summary

- BOLD-signal is only a measure of the response to brain activity
- *Functional connectivity* is not yet fully understood
- Differences are observed within:
  - Male-Female groups
  - Groups with different medical conditions
  - Gauss-filtered and segmented images

Thank you for your attention.

References I

📄 Ahmed Abou Elseoud et al. "Altered resting-state activity in seasonal affective disorder." In: *Human brain mapping* 35.1 (Jan. 2014), pp. 161–72. ISSN: 1097-0193. DOI: 10.1002/hbm.22164. URL: http://www.ncbi.nlm.nih.gov/pubmed/22987670.

📄 University of Oxford The Oxford Centre for Functional MRI of the Brain Nuffield Department of Clinical Neurosciences. *FMRI- Functional MRI of the brain.* 2014. URL: http://www.fmrib.ox.ac.uk/research/education (visited on 11/18/2014).

References II

FSL and FreeSurfer Course. *Brain Extraction, Registration, Motion Correction and EPI Distortion*. 2014. URL: http://www.fsl.fmrib.ox.ac.uk/fslcourse/.

J. Lenger, K. Sembritzki, and S. Kreil. "Resting State Arterial Spin Labeling for Detection of Major Depression and Seasonal Affective Disorder". unpublished. 2014.

Analysis Group FMRIB Oxford UK. *FSL*. 2014. URL: http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL (visited on 11/18/2014).