fMRI data preprocessing and Functional connectivity (tutorial)
Outline

• Theoretical part
  – fMRI preprocessing with SPM
  – Functional connectivity with REST and GIFT

• Practical part
  – Demo of toolboxes

• Hands on session
  – Preprocessing of resting state data
  – Seed-based functional connectivity
  – Finding resting state networks with ICA
MRI data (convert DICOM into NIFTI format)
  - arranged in 3D structure \([X \times Y \times Z]\)
    - \([X \times Y]\) the size of the slice (usually 64x64 or 128 x 128)
    - \(Z\) – number of slices
Quality control
From image to time series

fMRI example: one voxel

Temporal series

fMRI

amplitude

time

voxel time course

Source: J-B. Poline
You have:

- your functional images are acquired throughout your TR
- You therefore sample the BOLD signal at different layers of the brain at different time points.

You want

- to have the signal for the whole brain from the same time point.
Preprocessing (1): Slice timing
Preprocessing (1) Slice-timing

- **Input**
  - Images (3D .nii or .img/.hdr)
  - Slice timing order of acquisition
    - Ascending or descending (slice order is sequential)
    - Interleave: even numbered slices acquired then odd numbered slices or vice versa
      
      Order of slice acquisition determines when in the hemodynamic response the signal for a slice is acquired
  - TR : repetition time
- **Output**
  - a*.nii
Slice Timing Correction

• Uses temporal interpolation to make it appear as though all of the slices were acquired at the same time

• Thus, HRF across slices are aligned
• In a perfect world, subjects would lie perfectly still in the scanner while you experimented on them

– MOTION REGISTRATION AND CORRECTION

Motion correction algorithms look across your images and try to "line up" each functional image with the one before it, so your voxels always sample the same location and you don't get blurring.
Preprocessing (2) - Realignment

• Coregister each volume in the run to a reference volume

• Possible reference volumes
  – First volume in the run
  – Middle volume in the run
Preprocessing (2) - Realignment

- Described by number of ways that one volume can be changed to match another (degrees of freedom)

- Rigid-body transform allows for translation in all 3 directions and rotation about all 3 axes (6 degrees of freedom)
Motion errors

- Examine the amount of motion in each run by looking at plots of motion
- Big spikes in motion plots problematic
- Run motion correction twice to see how much residual motion there was from first application of motion correction
How much motion is acceptable?

- **Ideal**
  - Less than 0.5-0.75 mm
  - Less than 0.5°
- **Patient population dependent**
  - Children, rare diseases, hard to recruit subjects, etc
• Putting anatomical data in-line with functional or vice versa

• Registering functional and structural data useful for both
  – looking at single subject results (e.g. overlaying statistical results onto that subject's structural scan)
  – Also used as precursor to warping subject into standard or atlas space for multi-subject analyses
Coregistration
Variations between individual brains is large:
- Overall size varies from 1100 cc to 1500 cc (30% variation)
- Even major landmarks such as central sulcus will vary considerably in position, branching, and length

Spatial normalization warps individual brains into a common reference space

Allows for examination of fMRI signal changes across individuals within a group or between groups of subjects
Talairach or MNI template
Disadvantages of Talairach

• Based on a single cadaver brain and not representative of younger living brains
• Left-Right hemispheric differences are ignored (assumed symmetric for spatial normalization)
• Cerebellum completely ignored
• Notorious problems (e.g. occipital lobe is much smaller in atlas than most brains)
• Non-European brains (e.g. Asian) do not fit well within the Talairach space
Suggestions:

- Register image of an individual brains to match a *template image* in a standard space, typically the MNI atlas

- Linear models incorporate parameters for scale and skew (12 degrees of freedom)
Normalization

• Can be done in two ways:
  – EPI template (EPI.nii)
  – Segmenting your anatomical image using Tissue probability maps (grey.nii, white.nii, csf.nii)
Normalization (+Segmentation)
Smoothing actually increases the ability to detect task-related signal changes (i.e. functional SNR increases)

Cost is of course reduced spatial resolution

Relies on spatial correlation of fMRI data (i.e. neighboring voxels have similar intensity and activation characteristics)
Smoothing & Statistical False Positives

Random dataset left is unsmoothed and right is smoothed
Similar to spatial filtering expect the data are processed across time

Some sources of temporal noise

- Transient jumps and drops in the global signal from timepoint to timepoint (i.e., overall brightness fluctuates)
- Drift in MRI signal over time
- Head movement
Linear Detrending
High-Pass Filtering

• Similar to linear detrending but higher order variations are also removed

• Types of signal variations that can be corrected are more complex

• All of the signal below a certain frequency is removed.
Quality Control in fMRI

- Very important to examine your data after each stage of preprocessing and statistics
  - Look at raw data for artifacts
  - Examine realignment plots
  - Examine how well spatial normalization worked (use Check Reg in SPM)
Brain Connectivity refers to a pattern of anatomical links ("anatomical connectivity"), of statistical dependencies ("functional connectivity") or of causal interactions ("effective connectivity") between distinct units within a nervous system. (Olaf Sporns)
• Functional connectivity is defined as the temporal correlation between spatially defined brain regions (Friston)

• Functional connectivity is defined as group of neurons that act together in a coherent fashion. (Aertsen and Preisssls, 1991)
Functional connectivity is defined as the study of temporal correlations between spatially distinct neurophysiological events (Friston et al., 1993b).
Pipeline of Functional connectivity

For preprocessed data:

1. Define ROIs
2. Extract Time Series (TS)
3. Functional Connectivity
Define ROI (region of interest)

- Voxel
- Anatomical region
- Functional region
- Combination of several regions
Extract time series!

- Peak voxel
- Average of the ROI
- Average over cluster
- ect
Relations

- Correlation
- Coherence
- Mutual information
- etc
fMRI data analysis

1. Seed-based or ROI-based FC mapping
2. Node-based global network analysis (graph theory)
3. The topology of functional connectivity networks using Independent Components Analysis
   - find resting state networks
     1. Default mode network
     2. Visual network
     3. Attention network
     4. Auditory network
     etc.
Resting state networks

(a) Biswal et al. (1995), (b) Beckmann et al. (2005), (c) De Luca et al. (2006), (d) Damoiseaux et al. (2006), (e) Salvador et al. (2005a), and (f) Van den Heuvel et al. (2008a)
Report analysis

• With full details!!!

• FAQ:
  http://mindhive.mit.edu/imaging
Let’s Put Hands On!