Imaging for Neuroscience

Homework – Group 2

The goal of this homework is to investigate the relationship between dynamic positron emission tomography and resting-state functional MRI data. The following scans were simultaneously acquired with a hybrid PET/MRI system on a healthy subject. The tracer is **irreversible**.

DATASET

Available at link:
https://drive.google.com/drive/folders/1LaK51OAIB6LonDEf_wV95aNQOutJtqCT?usp=share_link
Data are organized as follows.

The **PETdata.mat** file contains the following variables:

Cbnew = plasmatic tracer concentration, corrected for metabolites [kBq/ml]
Cpnew = whole blood concentration [kBq/ml]
delta = PET scan interval durations [min] gamma = PET
noise model constant
mask = Hammers anatomical atlas resampled in the PET images space
PET = 4D dynamic PET data
time = PET hemi-scan times [min]
tnew = arterial sampling acquisition timing [min]
The anatomical atlas consists of a matrix of integer values where each number refers to a specific anatomical region, as described in the HammersAtlas.pdf file. For example, regions 1 and 2 represent the right and left hippocampus, respectively.

Subject's **structural MRI data** (resampled in the PET images space): T1.nii.gz = T1w
structural image
CSF.nii.gz = Cerebrospinal fluid tissue probability map GM.nii.gz =
Grey matter tissue probability map
WM.nii.gz = White matter tissue probability map

Subject's **resting-state functional MRI data**:
fMRI.nii.gz = 4D dynamic data (TR=2.6)
RegMov.mat = estimated motion parameters (matrix 225x6)
The functional data are already motion-corrected (using a rigid spatial transformation) and resampled in the PET images space.

The **Matlab_tools** folder contains:
Nifti_toolbox: to load nifti files in matlab workspace
clustering_coef_bu.m: a code from the Brain Connectivity Toolbox, which can be used to derive the clustering coefficient of the graph nodes

AIMs of the study:

1. using a graphical approach, to quantify at the region of interest (ROI) and voxel-level the PET dynamic

2. to compute the subject's functional connectivity (FC) matrix
3. to investigate at the ROI level whether there is a relationship between the PET estimates and the computed connectivity measures.

PET analysis:

1. **Data Preprocessing:**
   a. Create a grey matter binary mask from the provided GM segmentation. Use a threshold equal to 0.3.
   b. Using the anatomical atlas and the grey matter mask, extract the average tissue time activity curve (TAC) of the grey matter of each atlas region.

2. **Graphical Methods**
   a. Based on the knowledge of the tracer kinetics, select the graphical method that better describes the PET data at the voxel level. If the Patlak method is used, estimate the net uptake (influx) rate constant (K_i). On the contrary, if the Logan method is used, estimate the tracer binding potential (BP) (consider the right and left cerebellum as a single reference region). In both cases, use the unweighted linear least square estimator.
   b. Select a single t* value for all the ROIs: provide a justification for the choice of t* and report an example of Logan/Patlak plot (i.e. plot(X,Y) for a representative ROI).
   c. Quantify PET data using the suitable graphical model (Platlak or Logan) both at the ROI and voxel level.
   d. Identify physiological estimates. How many ROIs show unreliable estimates? How many voxels are discarded due to this selection?
   e. Regarding the results at the voxel level: the physiological estimates of K_i or BP must be organized in a 3D matrix (same size of *mask* variable). Replace the unreliable estimates with zeros.
   f. Regarding the results at the ROI level: the physiological estimates of K_i or BP are close to those obtainable by averaging the Ki values of the voxels contained within each ROI? Provide a quantitative measure to evaluate the differences (at your choice, please motivate your choice)
   g. Within the same figure, visualize the 45th slice of K_i or BP matrix and of the Hammers atlas after masking only the grey matter. Discuss the results: is the spatial pattern of the estimates homogeneous among the regions?

Resting state fMRI analysis:

1. **Data Preprocessing:**
   a. WM and CSF signal calculation:
   These two signals will be used in the fMRI signal denoising step with the main aim to reduce partial volume effects.
   Threshold the provided tissue probability maps and create a binary mask for both the white matter and the cerebrospinal fluid. Erode the masks (*imerode* matlab function) by defining a proper structuring element . For both white matter and cerebrospinal fluid, derive and plot the 1st Principal Component from the WM and CSF voxel-wise fMRI time-series, and specify the percentage of the explained variance.
   Provide a justification of the employed threshold and of the erosion parameters.
   b. ROI time activity curve extraction:

Mask the Hammer atlas with the GM binary mask obtained during the preprocessing of PET data and for each GM ROI extract the mean fMRI signal.

2. **Data Denoising:**
   a. Noise regression:
      For each ROI, remove the non-neural undesired fluctuations from its temporal dynamic using a linear regression approach. Perform the regression using eight regressors: the six parameters estimated during the motion correction step (provided in the RegMov.mat file) and the PC1 signals of white matter and cerebrospinal fluid. Before being used, each regressor must be converted to Z scores. (Matlab functions: *zscore* and *lscov*)
      Visualize the regression matrix.
   b. Temporal filtering:
      To take the slow components out, filter the signals obtained at point 2.a. with a high pass filter choosing a reasonable cut-off frequency.
      Provide a justification of the selected filtering frequency cut-off.

3. **Check of preprocessing step**
   Plot the original time-course of the right hippocampus region and what was obtained after each denoising step. Do you see a drift in the original signal? If so, is the denoising able to remove it?

4. **FC Matrix Computation.**
   Compute the pairwise Pearson's correlation (and the relative *p*-value) between the time-series of the ROIs. Visualize the FC matrix after applying the Fisher's *z*- transform to the coefficients (*atanh* matlab function).

5. **Graph Measure: Clustering Coefficient**
   To summarize the functional connectivity in terms of functional segregation, for each ROI compute its clustering coefficient after binarizing the FC matrix by considering only the statistically significant functional connections. Use a level of significance equal to 0.05 and correct for multiple comparisons by dividing the p-value by the number of ROIs. In order to visualize the spatial pattern of the clustering coefficient, create a 3D map, with the same size of the atlas mask, where, for each ROI, the corresponding clustering coefficient is reported. Use the command implay() and a proper colormap to visualize the clustering coefficient across different slices.

PET/fMRI integration

1. **Visual inspection:**
   Visualize the scatterplot of ROIs clustering coefficient versus the Ki or BP (depending on the graphical analysis approach employed). Include in the scatterplot only ROIs with physiological estimates.

2. **Quantitative results:**
   Compute the Pearson's correlation between the ROIs clustering coefficient and PET estimates and the correlation p-value. Discuss the result: is there a statistically significant relationship between the two measures?

Submit you homework in the elearning page of the course in the Homeworks section. The submission MUST be completed one week before the day of the exam (for instance, if you want to do the exam on 6 September, you must upload the files by 29/8). You are required to do the homework in English (report, codes etc.).

In a .zip folder (named Hwnumber_Name_Surname) you are required to turn in a copy of your own commented Matlab code(s), as well as:

1) a brief and complete presentation in power point/pdf of the performed analysis (methods, problems and issues, results, discussions, …). Mandatory maximum 10 slides (excluding the first slide with title and your name)

2) A .mat file with the variables generated at points 2.e, 2.f of PET analysis, and the FC and degree values for the fMRI analysis