CS463/516 Final Project

Due: Friday August 11th at 11:59 PM *NO EXTENSIONS* as I must submit all grades by August 18th.

Title: Protecting the Aging Brain – Diet Study

Max group size = 4

Outline: in the final project, you will perform additional analysis to expand the results of this paper using the dataset 1 and dataset 2 that the authors have uploaded to OpenNeuro.

In the original publication (link above) the authors analyzed a larger dataset (lifespan dataset) acquired by other labs, as well as three smaller datasets acquired specifically for this study. Here, we will restrict our analysis to two of the smaller datasets. The datasets are as follows:

1. 12 participants scanned under 3 conditions:
    a. Standard diet (non-ketogenic)
    b. Standard diet followed by a 12-hour fast
    c. Ketogenic diet for 1-week
2. 30 participants scanned under 3 conditions:
    a. Standard diet followed by an overnight fast (12 hours) (pre-bolus)
    b. Breaking the 12-hour fast with a glucose drink bolus
    c. Breaking the 12-hour fast with a ketogenic drink bolus

There was also a 3rd dataset (case study, only one participant) that will not be used here.

The authors performed several types of analysis on these two datasets, to look for differences in resting state functional connectivity (RSFC) due to the brain switching energy source to ketones from glucose. In this project we will expand the analysis to include more RSFC metrics. You should proceed as follows:

Step 1: get the datasets from openneuro. You can create two separate folders (one for each dataset), and within each folder, give each subject their own folder, then put the T1 and BOLD images in each subject's individual folder.

Step 2: registration and preprocessing: for each of the 3 datasets, select a template subject and register the BOLD images to that template subject. You should use nonlinear registration with ANTs because each subject has their own unique brain shape. You will probably want to use some simple BASH scripting to help with this (instead of running a separate command for each subject). Be sure to visually inspect all registrations in AFNI with template subject as underlay. If the registration fails in any of the subjects, all subsequent results will be meaningless. The registration can be done by extracting the first volume from each BOLD image, registering it to the template subject, and then applying the transform to the full BOLD volume. You can then delete the original BOLD image if necessary to save space. Once all subjects are aligned, you can proceed with motion correction and bandpass filtering, as in assignment 3 (this is the basic denoising, you can also try more comprehensive denoising using the -censor and -ort options of 3dTproject, which will remove motion-corrupted time points and regress out physiological noise, respectively.

Step 3: compute RSFC metrics: the original paper looked only at the effects of ketones on two RSFC metrics: *network stability* and *ALFF*. Our goal is to expand this analysis to the following metrics:

a. REHO - https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dReHo.html
b. fALFF - https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dRSFC.html
c. RSFA - https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dRSFC.html
d. Global signal correlation map (similar to REHO, but for whole-brain instead of local coherence)
    i. Compute the global signal by averaging the fMRI signal across all voxels in the brain. Can use 3dmaskave for this.
    ii. Correlate the global signal with each voxel's time series separately. This will yield a correlation map show how strongly each voxel's time series matches the global signal. Can use 3dTcorr1D for this. This correlation map is the 4th RSC metric.

Step 4: statistical analysis: create the following T-value maps (we use T-value instead of correlation because we are comparing across two conditions, instead of 700+ time points like with assignment 3). Can use 3dttest++ for this, with the -paired option (each subject is paired across conditions).

a. Dataset 1: compute T-values for the following conditions for all 4 RSFC metrics outlined above:
    i. Standard diet minus 12-hour fast
    ii. Standard diet minus ketogenic diet
    iii. 12-hour fast minus ketogenic diet

    *****for all the above comparisons, combine all 4 BOLD runs from respective 'func' folders in 'ses-fast', 'ses-ket' and 'ses-std'. (motor, rest, and spanav 1,2). To combine the runs, you can either concatenate the BOLD volumes from all 4 runs *before* computing RSFC metrics, or, if RAM is an issue, average the 4 RSFC maps after computing them separately for each run.*****

b. Dataset 2: compute T-values for the following conditions for all 3 RSFC metrics outlined above:
    i. No bolus minus glucose drink (use run-1, run-2 in 'func' folder of 'ses-glc')
    ii. No bolus minus ketogenic drink (use run-1, run-2 in 'func' folder of 'ses-bhb')
    iii. Glucose drink minus ketogenic drink (use run-2 from 'ses-glc' and run-2 from 'ses-bhb')

At the end of step 4, you will have 3x4 (dataset 1) + 3x4 (dataset 2) = 24 separate T-value maps. You can also experiment with different -exblur values for 3dttest++.

Use 3dclustsim to extract significant clusters from all T-value maps (can also use as an option in 3dttest++, and then plot the significant clusters from each of the 24 maps separately using glass brain technique from nilearn or nipy.

Final output: show your 24 glass brains in a pdf report, along with all relevant code and afni commands used to produce the output. Write a short paragraph discussing what you found. **Do you notice any brain regions with overlapping significant clusters across multiple conditions, and if so what is the functional significance of these brain regions?** How do your results match those of the original paper? Do you think your results are suitable for publication?

I will contact the teams responsible for the best submissions about expanding it into a full-length article, if you are interested. We can work on it during the fall semester and hopefully submit something to NeuroImage by December '23.