A Technique to Detect Outliers Automatically in Multi-Site fMRI Data

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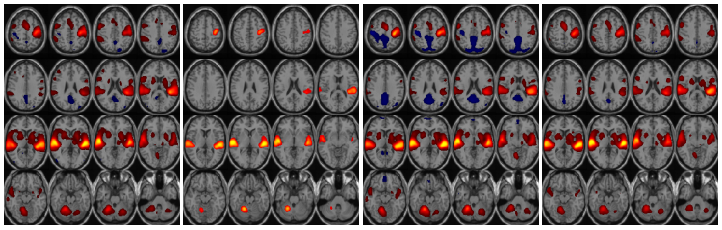
Introduction

Multisite brain image acquisition is required to collect data from a large number of subjects of a certain demographic group or to access a population with different demographic characteristics. Data from a large pool takes into account the biodiversity of human subjects and only from such studies can highly generalizable results be obtained or confirmed. However multisite studies are difficult to standardize due to differences in scanner vendors, pulse sequences, calibration parameters and combining multisite data is not easy [1]. Steps are taken to account for inter-site differences but it is almost impossible to keep all variables identical [2].

One of the problems with large scan studies is assessing the quality of the data, and specifically identifying outliers. There are multiple ways to detect outliers at an individual level. For example outliers can be removed based on motion parameters, behavioral data or by visual inspection of all subjects' brain images. These methods are important and help researcher to collect high-quality data, but they do not help to directly detect subjects who activate differently from the group mean. One approach which can be used is to spatially correlate the activation maps of individual subjects to that of the group mean. This method does not overcome two potential issues. The first is that if all voxels are included for the spatial correlation analysis it is possible that the most active, but few voxels, contribute positively towards the correlation and the less active, but many voxels, contribute negatively. In addition, by including the whole brain, non-task related voxels contribute towards the correlation. To overcome these issues, we can threshold the most active voxels and then calculate the spatial correlation. However, slight variations of voxels that pass the threshold can create incorrect correlations. In multisite data this issue can be further exacerbated since the threshold to select voxels can vary between sites. As an example in the adjoining figure we show the T maps (T>2) of an auditory sensorimotor task obtained from subjects across four different sites with a similar number of subjects. It can be seen that the number of voxels that pass the threshold is not the same for the different sites (even after accounting for different degrees of freedom). If the same threshold is applied to select subjects from different sites we observed that different numbers of voxels are selected. If we lower the threshold then voxels from non-task-related regions get selected for some sites. To overcome the issues explained above we introduce a technique that can help detect outliers more efficiently.

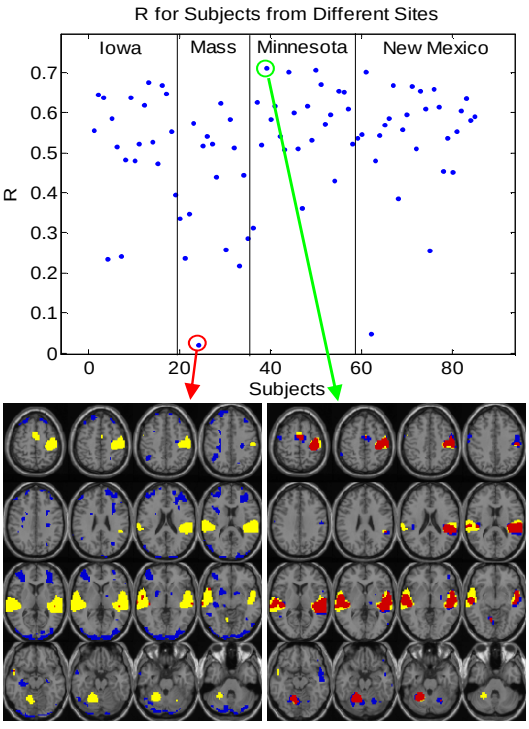


Subjects and Sites

Healthy subjects (number of subjects within parenthesis) were scanned at Iowa (19), Massachusetts (16), Minnesota (23) and New Mexico (27) as part of a large study (MCIC: MIND Clinical Imaging Consortium) designed to study schizophrenia. Each subject performed a sensorimotor (SM) task and activation maps from this task are used to demonstrate our technique. In the SM task ascending and descending pitched tones were presented and after each tone the subject is required to press a button with the right thumb. Scans were acquired with either a GE or Siemens scanner with EPI sequences at 3.0T, except at the New Mexico site where a 1.5T scanner was used. Pulse sequence = PACE-enabled, single shot, single echo EPI, scan plane = oblique axial, AC-PC, copy T2 in-plane prescription, FOV = 22 cm, 27 slices, slice thickness = 4mm, 1 mm skip, TR = 2 = 2000 ms, TE = 30ms (3.0T); 40ms (1.5T), FA = 90 degrees, BW = ±100 kHz =3126 Hz/Px, 64x64 matrix, 1 shot.

Method

Step1: Find the group mean T-maps of all subjects from all sites. Step2: Pick a threshold (*Th*) and construct a map (Mg) with the voxels that pass *Th* as ones and the rest of the brain as zeros. Step3: Find the number of voxels (*N*) in Mg. Step4: For each subject pick the *N* voxels with the highest T values and construct a map (Ms). Step5: Find the ratio (*R*) between the volume of spatial intersection between Mg and Ms and the volume of Mg. Step6: Select subjects based on *R*. In Step1 by averaging across subjects we remove inter-subject variability and increase the SNR. At step2 a researcher can select *Th* based on the level of significance needed or the activation regions desired. In step4 we select *N* highest T-valued voxels since our interest is on selecting the most task related voxels. The rationale behind this is that if the 'supposedly' highest task related voxels do not correspond to Mg then that subject can be considered as an outlier. At Steps2&3 we assign ones to remove variabilities that may exist in the active voxels. Finding *R* in Step5 is equivalent to finding the correlation between Mg and Ms. At Step6 the user can increase the fidelity of subjects to be selected by increasing *R*.



Results

In the adjoining Figure *R* values are indicated for a total of 85 different subjects from the 4 different sites found using a *Th* value of 3. We also indicate the subject with the lowest (red circle) and highest (green circle) *R* values. In the brain images below the plot, we show Mg in yellow, Ms in blue and the intersection of Mg and Ms in red. An 'outlier', as indicated in the left image has larger regions of blue and yellow and smaller regions of red. A 'good' subject has smaller regions of blue and yellow and larger regions of red. The blue regions indicate the locations of the most task relevant voxels in an individual subject outlier and yellow that of the group. In a 'good' subject these two regions should overlap as shown in the right figure. Artifacts in the left subject were probably caused by motion.

Discussion

We present a simple and efficient approach to detect outliers from multisite data. We point out the shortcomings of approaches used in outlier detection and address how they can be overcome by our technique. The method minimizes the human intervention of visually inspecting brain data to detect outliers.

References

[1] Styner et al, 'multi-site validation', SPIE 2002 [2] Friedman et al, 'Report on multicenter fMRI', Journal of MRI 2006

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