Group Analysis of fMRI Data based on fBIRN Traveling Human Phantom Study

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INTRODUCTION

Functional neuroimaging aims at finding brain regions specifically involved in the performance of cognitive tasks. In particular, functional MRI (fMRI) is based on the detection of task-related **Blood Oxygen-Level Dependent (BOLD)** effect in the brain. The method is based on MRI signal changes due to hemodynamic and metabolic responses at the sites of neuronal activation induced by external and internal stimuli to the brain. Using this methodology, it is possible to construct whole brain activation maps for sensory and mental functions.

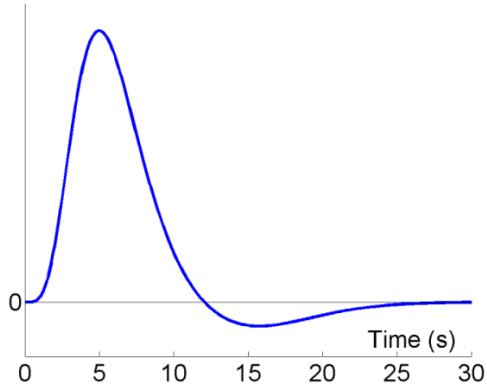


FIG.1 Typical BOLD response to neural impulse

In a basic block design paradigm, on-off states are alternated throughout the experiment to ensure that signal variation from small changes in scanner sensitivity, subject movement, or attention shifts have a similar effect on the signal responses associated with each of the different states. Such a paradigm for localization of the motor cortex, auditory and visual cortex was tested in a healthy subject.

Basic Block Design Paradigm

The five image datasets were obtained from the fBIRN traveling subjects human study database from **Scan Site : 13.** The block design task is a simple finger tapping task in time with 3Hz audio cue and watch 3Hz flashing checkerboard. The task began in the baseline "resting" state and the active state was bilateral finger tapping. Block durations were 15s on/off. 8 complete off/on cycles for a scan time of 240s, and an initial off-block. There are 17 blocks of 15 seconds (5 TRs). The T1 weighted anatomical data and four runs of sensory motor task data **SM1, SM2, SM3 and SM4** were analyzed.

- Format and Align the T1 weighted scan – convert NIFTI 4D format to AFNI .BRIK using following command.

```
% 3dcopy Native/Original__0001/NIFTI4D/f0001.nii  T1_at
```

- Transform T1 antomical dataset to match a template in TLRC space.

```
% @auto_tlrc -input T1+orig -base MNI_avg152T1+tlrc
```

- Format the BOLD imaging data Run1, Run2, Run3, Run4

```
% 3dcopy Native/Original__0001/NIFTI4D/f0001.nii  sm1
% 3dcopy Native/Original__0001/NIFTI4D/f0001.nii  sm2
% 3dcopy Native/Original__0001/NIFTI4D/f0001.nii  sm3
% 3dcopy Native/Original__0001/NIFTI4D/f0001.nii  sm4
```

- Put data together in a single Analysis directory

Outlier Removal - The program 3dDespike removes spikes from the fMRI data. Does a L1-fit smoothening to each voxel time series.

```
% 3dDespike -ssave sm1_Spikes -prefix sm1_Despike sm1+orig
% 3dDespike -ssave sm2_Spikes -prefix sm2_Despike sm2+orig
% 3dDespike -ssave sm3_Spikes -prefix sm3_Despike sm3+orig

% 3dDespike -ssave sm4_Spikes -prefix sm4_Despike sm4+orig
```

Motion Correction - The AFNI program 3dvolreg is used for this step.

Co-register the first time series to the first time point in the run

```
% 3dvolreg -verbose -prefix sm1_Coreg -base 0 sm1_Despike+orig
```

Co-register the second, third and fourth time series to the first run - first image

```
% 3dvolreg -verbose -prefix sm2_Coreg -base 'sm1_Despike+orig[0]' sm2_Despike+orig
% 3dvolreg -verbose -prefix sm3_Coreg -base 'sm1_Despike+orig[0]' sm3_Despike+orig
% 3dvolreg -verbose -prefix sm4_Coreg -base 'sm1_Despike+orig[0]' sm4_Despike+orig
```

Smooth Data - Spatially smooth the images to increase the SNR of the images and our ability to detect the BOLD response. The afni program 3dmerge is used for this step.

```
% 3dmerge  -doall  -prefix  sm1_Smooth  -1filter_mean 4 sm1_Coreg+orig
% 3dmerge  -doall  -prefix sm2_Smooth   -1filter_mean 4 sm2_Coreg+orig
% 3dmerge  -doall  -prefix sm3_Smooth   -1filter_mean 4 sm3_Coreg+orig
% 3dmerge  -doall  -prefix sm4_Smooth   -1filter_mean 4 sm4_Coreg+orig
```

Normalization Across Runs

3dTstat - generate mean image out of time series sm1.Used to edit 3D datasets in various ways (threshold, blur, cluster)and to merge multiple datasets. Generated a mean image of first time series.
3dAutomask - Will automatically guess where the brain is using some statistical and morphological operations.
3dcalc - Used to scale the images to a percentage change.
3dTcat - Concatenate the time series data from four runs.

```
% 3dTstat -mean -prefix sm_Mean sm1_Coreg+orig
% 3dAutomask -prefix sm_Mask sm_Mean+orig
% 3dTstat -prefix sm1_Mean sm1_Smooth+orig
% 3dcalc -a sm1_Smooth+orig -b sm1_Mean+orig -c sm_Mask+orig -expr "(a/b * 100) * c" -prefix
\sm1_Normalized
% 3dTstat -prefix sm2_Mean sm2_Smooth+orig
% 3dcalc -a sm2_Smooth+orig -b sm2_Mean+orig -c sm_Mask+orig -expr "(a/b * 100) * c" -prefix
\sm2_Normalized
% 3dTstat -prefix sm3_Mean sm3_Smooth+orig
% 3dcalc -a sm3_Smooth+orig -b sm3_Mean+orig -c sm_Mask+orig -expr "(a/b * 100) * c" -prefix
```

\sm3_Normalized
% 3dTstat -prefix sm4_Mean sm4_Smooth+orig
% 3dcalc -a sm4_Smooth+orig -b sm4_Mean+orig -c sm_Mask+orig -expr "(a/b * 100) * c" -prefix
\sm4_Normalized

Merge the Data Across Runs

% 3dTcat -prefix sm_ALL_Normalized sm1_Normalized+orig sm2_Normalized+orig sm3_Normalized+orig \sm4_Normalized+orig

Creating Hemodynamic Response Wave Defining the Experimental Design

This will perform a voxel-by-voxel cross-correlation with a defined time series. We generated using the AFNI command sqwave.

% sqwave -on 5 -off 5 -init 5 -length 85 -name blockDesign.1D

To visualize the design we use the following command.

% 1dplot blockDesign.1D

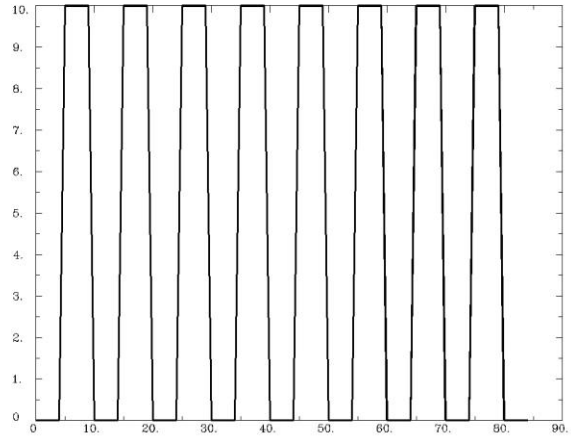


FIG.2 Time –series

Analyze the Data - Created a file that defines the start of each block

% echo "0 100" > runs.1D

Deconvolution Analysis

This was done for all normalized time series data using AFNI **3dDeconvolve** . The program models the system response as a sum of scaled and time delayed versions of the stimulus time series. The data itself determines the shape of the response function and each voxel will have a different response function Output consists of an AFNI 'bucket' type dataset containing the least squares estimates of the linear regression coefficients, t-statistics for significance of the coefficients, partial F-statistics for significance of the individual input stimuli, and the F-statistic for significance of the overall regression.

Maximum lag for stimulus response was 7.

% 3dDeconvolve -xout -input sm_ALL_Normalized+orig -num_stimts 1 -stim_file 1 blockDesign.1D
\-stim_label 1 sensorymotor -stim_minlag 1 0 -stim_maxlag 1 7 -iresp 1 sm_RF -concat runs.1D
\-full_first -fout -tout –bucket sm -polort 2 -mask sm_Mask+orig -progress 1000 -GOFORIT 3

Align with the AC-PC aligned T1 weighted image

% 3dAllineate –base ../t1_deface/T1_at+tlrc -1Dmatrix_save T1.aff12.1d -input sm_Mean+orig -warp aff -cost mi

% 3dAllineate –master ../t1_deface/T1_at+tlrc -1Dmatrix_apply T1.aff12.1d.aff12.1D -input sm+orig -float -final \quintic –prefix\ t1_deface/sm_Fit+tlrc

% cd ../t1_deface

Corrected the results for multiple comparisons – False Discovery Rate

% 3dFDR -list -cdep -input sm_Fit+tlrc -prefix sm_FDR > statTable.txt

Group Level Analysis

1. **Extraction of header information**
   For the AFNI bucket type datasets created for all 5 subjects, program 3dinfo prints out the label and statistical information for each sub-brick in the dataset.

   For Example – For dataset file 103_FDR+tlrc,

   %3dinfo -VERB 103_FDR+tlrc showed

   At sub-brick #17 'FDRz:SensoryMotor_Fstat' datum type is float: 0 to 6.71966
   statcode = fizt
   which implies that **sub-brick#17** contains statistical information of F-statistics.

2. **Program 3Dttest**

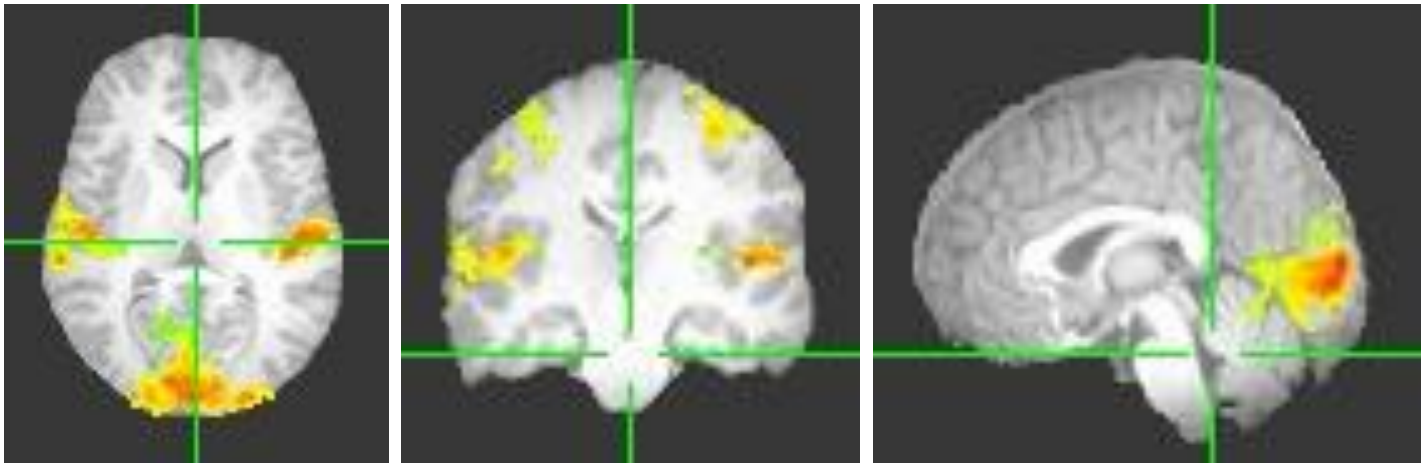
   %3dttest -base1 0 -set2 101_FDR+tlrc'[17]' 103_FDR+tlrc'[17]' 105_FDR+tlrc'[17]' 106_FDR+tlrc'[17]' 104_FDR+tlrc'[17]'

   It performs a t-test on all the five 3D datasets for sub-brick 17. The output is a single dataset created that is the voxel-by –voxel difference between the mean of set2 minus the mean of set 1 (set as 0). The output dataset is of intensity+ttest type **(tdif**). The t-statistic at each voxel can be used as an interactive thresholding tool in AFNI.

Visualization of Composite Activation Pattern on AFNI

- Underlay as **T1_at**
- Overlay as **tdif** and press **Set** button
- Set the threshold slider to corrected **p-value** =**0.0489**
- **Cluster volume = 200, radius = 0**

Views of Composite Activation Maps of Audio-Visual Cortex and Sensory Motor Cortices



a) Visual cortex on posterior auditory cortices on lateral sides

b) Coronal view -Sensory motor shown above auditory cortices.

c) Sagittal View – visual cortex

CONCLUSION

The goal of having a traveling subjects study is the measurement of image quality and temporal stability across centers, measurement of differences in task-evoked activation across a variety of scanners, and the measurement of test-retest reliability in subgroups of subjects. Traveling subjects data allow the simultaneous measurement of the effects of subjects, scanner and task on the BOLD signal changes.

The study of the healthy subjects targeted 'total brain coverage' in order to fully sample any possible area responding to the paradigm. Functional MR images satisfactorily visualized motor sensor spots and audio-visual centers. Motor activation elicited BOLD signal changes in the sensory motor cortex, permitting identification of primary motor and sensory cortical areas as shown. Furthermore, focal activation of different visual and auditory cortex was also seen.

The generation of composite activation pattern results in cancellation of many false-positives, which would otherwise show in individual subject response. Hence, the combined activation map obtained in this study has greater statistical relevance.