Summary, Question and Reflection on fMRI analysis 2004

Hanning Su

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In this paper, the author introduces fMRI data, its purpose of fMRI (functional magnetic resonance imaging) analysis and then outlines common steps involved such an analysis.

fMRI data is basically a time series of 4D images. In an experiment, some of the images are taken whilst stimulation and others whilst rest. An analysis of the series of volumns is useful for detecting which parts of the given brain have increased intensity.

Another way to look at fMRI data is times series of intensity levels associated with a single voxel (a little cube) within a given volume or image. fMRI analysis aims to identify which of the voxels has significant signal of interest (which voxels are activated by stimulation.)

There are certain data preprocessing techniques to align voxels across time and reduce noises, facilitating following statistical analysis.

Since GLM (generalized linear model) is ofen used in univariate setting, the author mainly introduces the basic technique to analyze over one voxel. For concreteness, he considers the case of square-wave block design. Some examples of models are shown below:

One stimulus model

$$y(t) = \beta_0 + \beta x(t) + e(t) \tag{1}$$

y(t) is a time series of intensity level of a voxel, for which one or more stimuli are applied. x(t) can be a times series of 0s and 1s.

Two stimuli model

$$y(t) = \beta_0 + \beta_1 x_1(t) + \beta_2 x_2(t) + e(t) \tag{2}$$

Multi-stimuli model in matrix notation

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \tag{3}$$

y is a column matrix of $y(t)$'s. The design matrix $\mathbf{X}$ has columns that are times series of $x(t)$. $\boldsymbol{\beta}$ is a vector of parameters including β_0

For these models, we can compute a "goodness of fit" index for each column of the design matrix so that we can find out which one of stimuli waveform has a better or worse fit to the response (voxel intensity).

To determine whether a stimulus has significant activation effect for a given voxel, we compute the T value, let p = number of parameters:

$$T = \frac{\hat{\beta}_i}{se(\hat{\beta}_i)} \quad i \in \{0, 1, 2, ..., n\} \tag{4}$$

Using this quantity, we can perform hypothesis testing on single parameters, describing how strongly each voxel is related to each EV.

The author goes one to describe general linear hypothesis testing in the following form:

$$H_0 : C\boldsymbol{\beta} = \boldsymbol{\delta}^* \text{ vs } H_1 : C\boldsymbol{\beta} \neq \boldsymbol{\delta}^* \tag{5}$$

where C is $r \times p$ **contrast** matrix and $\boldsymbol{\delta}^*$ is an $r \times 1$ vector of constants. In the paper discussed, we only consider cases where $r = 1$ and $\boldsymbol{\delta}^* = 0$, the examples are below:

Stimulus relevance in 2-stimulus model

For model (2), we have p = 3,

$$C = \begin{bmatrix} 0 & -1 & 1 \end{bmatrix}$$

Substitute these quantities into (5) and change the inequality sign to $>$. We can perform the resulting hypothesis test to answer the question "is the response to stimulus2 greater than the response to stimulus1 ?"

Stimuli interaction in 2-stimuli model

If we add the interaction term to model (2), we have:

$$y(t) = \beta_0 + \beta_1 x_1(t) + \beta_2 x_2(t) + \beta_3 (x_1(t) \times x_2(t)) + e(t) \tag{6}$$

We can then preform the hypothesis testing with p = 4, inequality sign changed to $>$, and contrast matrix

$$C = \begin{bmatrix} 0 & 0 & 0 & 1 \end{bmatrix}$$

change the inequality sign to $>$.answering whether the two stimulus have positive interaction. If we use $-C$ instead, we will answer whether negative interaction exists.

With general linear hypothesis testing, we can answer many question by setting C in certain ways, such as $\begin{bmatrix} 0 & -1 & 0 & 1 \end{bmatrix}$ or $\begin{bmatrix} 0 & 1 & -2 & 1 \end{bmatrix}$ We just need to make sure to correctly interpret the question encapsulated in C.

Our analysis above gives a statistic map consist of T for example. We then need to select a significance (p) threshold. Given a large number of voxels, we cannot directly consider a voxel activated simple because

p less than a certain significance level. Because purely by chance, some of them are activated without any stimulation. The general idea is that we need to supress p in some way. Bonferroni correction, Gaussain random field (GRF), and GRF cluster-based p value assignment, give different solutions to the supression issue.

So far we only consider single session statistics, we can also perform statistics over multiple sessions and subjects. Despite better potential generalizability of experiment result, there are several obstacles to overcome: First, we need to align all brain images. Second, we need to combine results across different sessions or subjects (could be using fixed-effects or mixed effects analyses) Third, we need to choose appropriate number of subjects.

The author then discusses registration, brain atlases and cortical flattening and finally gives a concrete example of conducting fMRI analysis. The content is too specific so I shall not further elaborate on them.