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ORIGINAL ARTICLE

Comparing classical nad bayesian GLM in the fMRI data for testing visual stimulation and face perception

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Abstract

OBJECTIVES: Classical and Bayesian GLM are the most common method to analyze Functional magnetic resonance imaging (fMRI) data in the study of human brain function. However, classical GLM and Bayesian model perform different approaches in handling spatial correlation of the fMRI data as well as estimation of the parameters. Consequently, they produce different results depending on the size of activation and variation in the data. In addition, the choice of prior in Bayesian analysis affect the statistical outcome. In this study we apply the classical GLM and Bayesian model with different priors to the fMRI dataset and compare their outcomes.

METHODS: This is a block design study in which 5 identical tasks were administrated based on pseudo-random order. In this single subject study, Classical and Bayesian GLM were applied to the fMRI data to test the visual stimulation and face perception. For Bayesian approach, UGL and LORETA prior were considered for parameters, and outcomes of Bayesian and classical GLM were compared.

RESULTS: In case of visual stimulation, despite the presence of some significant voxels in the GLM analysis, none of the voxels survive Bayesian analysis using either UGL or LORETA prior. For testing face perception, there are less significant voxels In GLM analysis than in Bayesian with LORETA prior; also, no significant activation was found using Bayesian analysis with the UGL prior.

CONCLUSION: Although the classical GLM is the most common method for analyzing fMRI data, in the case of small activation with large variation, the results should be interpreted with caution. Bayesian analysis can be done in parallel to have a clearer view of the outcomes.

Introduction

Functional magnetic resonance imaging (fMRI) is the most common method to study human brain function. In a typical task-related fMRI experiment, a subject performs a series of activities while the entire brain is scanned to obtain a time series of BOLD responses for each voxel of the brain. The temporal and spatial correlation among the voxels is an important feature of fMRI data (Poldrack *et al.* 2011).

To construct a model that can properly include spatial and temporal correlation structures, a range of classical and Bayesian methods have been proposed. The massive univariate technique known as the general linear model (GLM) is the classical statistical model for fMRI data (Friston *et al.* 1994). GLM models the association between each task or stimulus and the time series of BOLD responses at each voxel. For each voxel, T or F statistics are used to evaluate the hypothesis of task-related activation in that voxel. Also, Restricted Maximum Likelihood (ReML) was applied to show the significant voxels through the statistical parametric map (SPM). The area of task-related activation is determined by SPM thresholds at the specified significant level (Lazar 2008).

In classical GLM framework, the spatial nature of the BOLD response is taken into account by smoothing data as a part of preprocessing steps.

In the Bayesian framework, first a GLM model is considered for fMRI data on voxel level and then the spatial priors is defined for model coefficients. Variational Bayes is used to estimate parameters in a Bayesian GLM, and the posterior probability map (PPM) is used to represent the marginal probability of activation for a certain stimulus in each voxel(Lindquist 2008; Zhang *et al.* 2015).

Since classical GLM and Bayesian model perform different approach in handling spatial correlation of the fMRI data as well as estimation of the parameters, they produce different results depending on the size of activation and variation in the data.

In addition, the choice of prior in Bayesian analysis affect the statistical outcome.

In the present work we apply the classical GLM and Bayesian model with different priors to the fMRI dataset and compare their outcomes.

Materials and methods

Subjects

The experiment consisted of 16 volunteers from both sexes. All subjects were right-handed without any neurological or psychiatric conditions.

The brain image of subject 2 was selected for the present study. The data was obtained from the OpenfMRI database (https://doi.org/10.18112/openneuro.ds003548.v1.0.0). Its accession number is ds003548.

Study design

Psychological block-based task was implemented as shown in figure 1. There was 5 fMRI sequences and during each run, 5 identical tasks were administrated based on pseudo-random order. A total of six 30-s block classes were applied including happy faces, sad faces, angry faces, neutral faces, pseudo (scrambled) faces and low-stimulation. Each block shown for 30 seconds consisting of 10 images of the particular class and each block occurred twice per sequence. The data related to the first sequence was used for the present study.

Functional Magnetic Resonance Imaging

Scanning was conducted on a 3-Tesla General Electric Discovery MR750 scanner at the MR Unit at UNAM's Institute of Neurobiology. Echo-planar imaging (EPI) blood-oxygen level-dependent (BOLD) sequences for fMRI were acquired in 35 axial slices (TR=2000 ms, TE=30 ms, flip angle=$\pi/2$, filed of view [FOV] =64×64, voxel size=$(3mm)^3$). Five sequence were acquired each consisted of 185 volumes. High-resolution T1-weighted anatomic image was also acquired (TR=8.18 ms, TE=3.19 ms, flip angle=$3\pi/45$, filed of view[FOV]=256×256, voxel size=$(1mm)^3$) (David & Barrios 2021). The first functional run of second subject was selected for the analysis.

Data processing and statistical analysis

The data were preprocessed with regard to the pipeline in SPM manual (SPM manual) using the SPM12 software package (http://www.fil.ion.ucl.ac.uk/spm/software/ spm12/). Preprocessing includes motion realignment, segmentation, co-registration, and normalization. For classical GLM analysis, spatial smoothing was performed as the last step of preprocessing step. canonical hemodynamic response function was convolved with boxcar function for each time series to obtain the design matrix (Ashburner *et al.* 2014).

Statistical analysis

GLM model

Let T be the number of time points in the fMRI time series and V be the number of voxels in the brain V=1, 2…, v. The voxel-wise general linear model is presented as

$$Y_v = X_v \beta_v + e_v$$

Here, Y_v is T×1 response vector of time series data for voxel v, Xv is the T×P design matrix where P is the number of task under investigation.

$\beta_v = (\beta_{v,1}, \ldots, \beta_{v,p})$ T is a p×1 vector of regression coefficients and e_v is a T × 1 error vector.

Temporal modeling

Temporal modeling is applied through the autoregressive structure of order q (AR (q)) on e_v

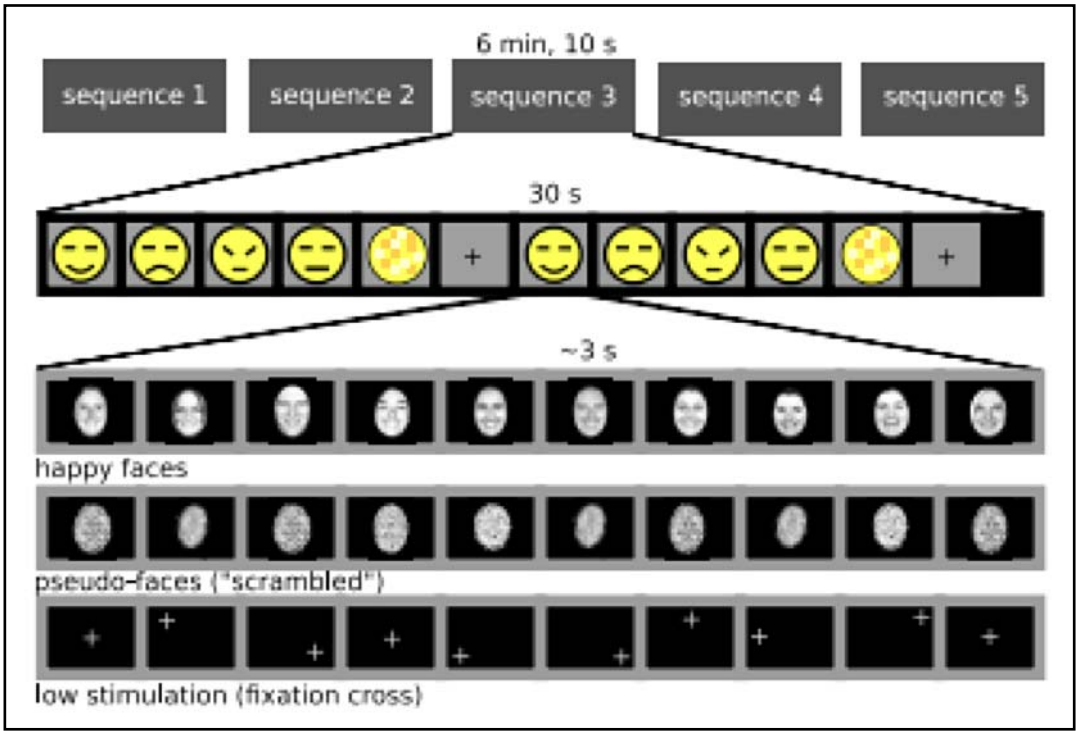

Fig. 1. Block -paradigm design to study visual stimulation and face perception

$$\varepsilon_{v,t} = \sum_{j=1}^{q} w_{v,j}\varepsilon_{v,t-j} + z_{v,t}$$

Where $w_v = (w_{v,1}, \ldots, w_{v,q})^T$ is a q×1 vector of AR coefficients and $z_{v,t}$ is a white noise. Classical GLM assumes the same error correlation structure at each voxel within each session. In Bayesian GLM, Voxel-wise AR models are fitted separately for each session of data. AR model order of 1 and 3 is used in this study for classical and Bayesian GLM, respectively.

Spatial modeling

For considering spatial dependencies between voxels in classical GLM analysis, spatial smoothing is implemented using Gaussian kernel size with full-width at half maximum (FWHM) of the Gaussian smoothing kernel. Smoothing kernel width of size 8 mm was applied in this study.

In Bayesian framework, spatial dependencies between voxels is entered to the model by imposing spatial priors on model parameters.

$$\beta'_p|\alpha \sim N(0, (\alpha_p D_\beta)^{-1}),$$

Where D is a fixed spatial precision matrix and α is the hyper-parameter to be estimated from the data.

There are several choice for prior on D, but this study considers Unweighted Graph-Laplacian (UGL) and Low resolution Tomography Prior (LORETA) to be applied for each $P = 0, \ldots, p$, where P is the number input stimuli(Pascual-Marqui *et al.* 1994).

UGL spatial prior constrains the regression coefficients at a given voxel to be similar to those at nearby voxels. LORETA prior is equivalent to UGL squared.

Computation

Restricted Maximum Likelihood (ReML) was applied to classical GLM to estimate the parameters. The T statistic is obtained by dividing a contrast of the ensuing parameter estimates by the standard error of that contrast. The statistical parametric map (SPM) then displays the significant voxels.

In the case of Bayesian GLM, the Variational Bayes was applied to the model to estimate the posterior probability of activations. An image of these posterior probabilities constitutes a posterior probability map (PPM) (Friston & Penny 2003; Friston *et al.* 2002a, 2002b).

Results

Classical GLM and Bayesian GLM were fitted to the fMRI data to test the visual stimulation and face perception, and the results were shown by SPM and PPM, respectively, as shown in figure 2 – 4.

In the case of visual stimulation, the contrast was defined as blank versus average of scrambled, happy, sad, angry and neutral. Also, face perception was tested by comparing scrambled with average of neutral, happy, sad and angry.

However, the significant voxel outcomes were different for classical GLM and Bayesian analysis. Figure 2 shows the result of GLM analysis comparing the visual stimulation vs blank. Despite the presence of some significant voxels in the GLM analysis, none

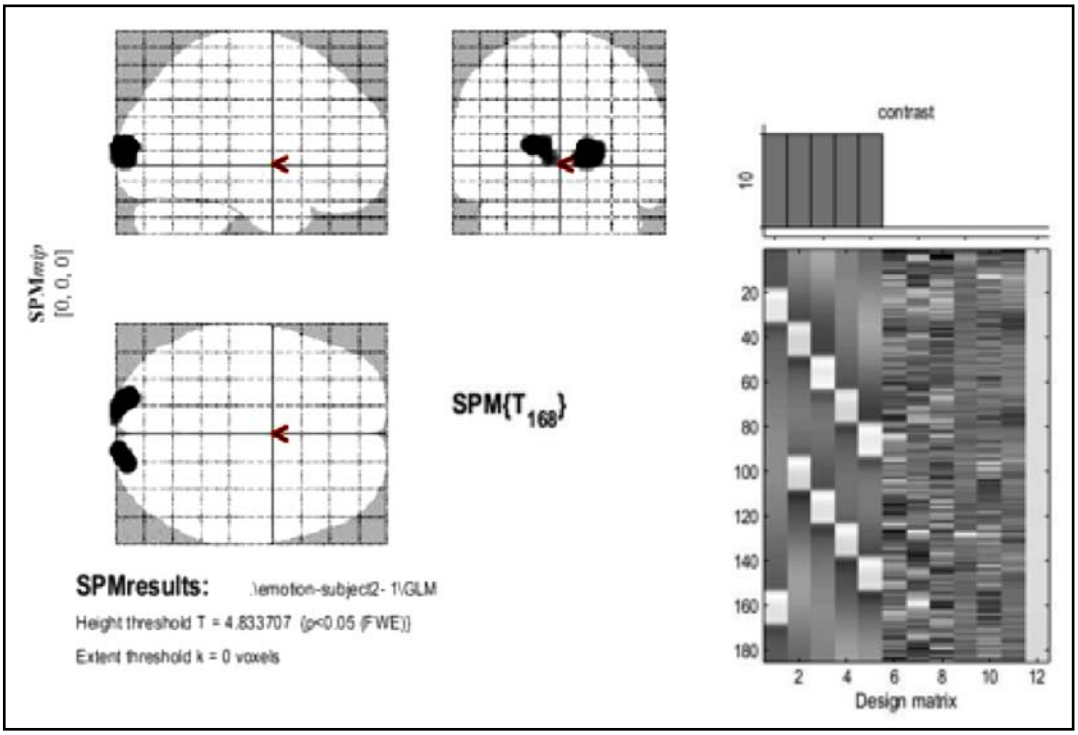

Fig. 2. SPM showing the result of GLM analysis for testing visual stimulation

of the voxels survive Bayesian analysis using either UGL or LORETA prior. Figure 3 displays the result of classical GLM with Bonferroni correction for testing face perception, and figure 4 shows the result of a Bayesian analysis using LORETA prior. In GLM analysis, there are less significant voxels than in Bayesian with LORETA prior, as shown in the figure. Again, no significant activation was found using Bayesian analysis with the UGL prior.

Discussion

In this study, the standard GLM with Bonferroni correction and the Bayesian GLM with two most commonly used prior was fitted to the fMRI data. The Bayesian technique indicated more meaningful activation than the traditional GLM. The activation is tested in classical analysis using hypothesis testing, and any non-zero activation can be significant (Lazar 2008).

The default Bayesian threshold, on the other hand, takes into account background noise and hence reports an activation as active if it is higher than the level of activation that is generic to the brain as a whole. As a result, tiny effects with low variation will pass the classical threshold but not the Bayesian, as seen in this study.

Conversely, when there is a large effect and large variation, the activation may pass the Bayesian but not the classical threshold. Furthermore, the nature of inference differs between the classical and Bayesian methods (Friston & Penny 2003; Friston *et al.* 2006).

In this study we used the Bonferroni method for addressing the multiple correction in classical GLM. Bonferroni method assumes that the tests are independent and consequently becomes conservative when there is strong correlation between tests, as there is with fMRI data (Poldrack *et al.* 2011).

Random Field Theory (RFT), which accounts for spatial interdependence between voxels, is another common approach to controlling the family-wise error rate (FWER) (Hayasaka & Nichols 2004; Worsley *et al.* 2004). Another method for addressing the multiple comparison problem in classical GLM is False Discovery Rate (FDR) (Genovese *et al.* 2002). The FDR is equal to the FWER if all of the null ,hypotheses are true (Lindquist 2008). FDR takes into consideration the spatial relationships between voxels and generates results that are more comparable to Bayesian analysis (Poldrack *et al.* 2011).

For Bayesian method, we must choose a prior for parameters and estimate the posterior probability of each parameter accordingly. The UGL and LORETA were the most common prior distributions for parameters in Bayesian analysis. The result of method based on LORETA prior indicate more significant activation than the results based on UGL prior. It can be associated with higher information that LORETA gains from the neighboring voxels. The LORETA prior is equivalent to UGL squared and consequently uses more information from the neighboring voxels(Ashburner *et al.* 2014). Other priors for regression parameters include Gaussian Markov Random Field (GMRF) (Woolrich *et al.* 2004) and uninformative prior (Penny *et al.* 2003). Uninformative prior is a flat prior in which no previous information is employed, and GMRF is equivalent to a normalized UGL (Ashburner *et al.* 2014).

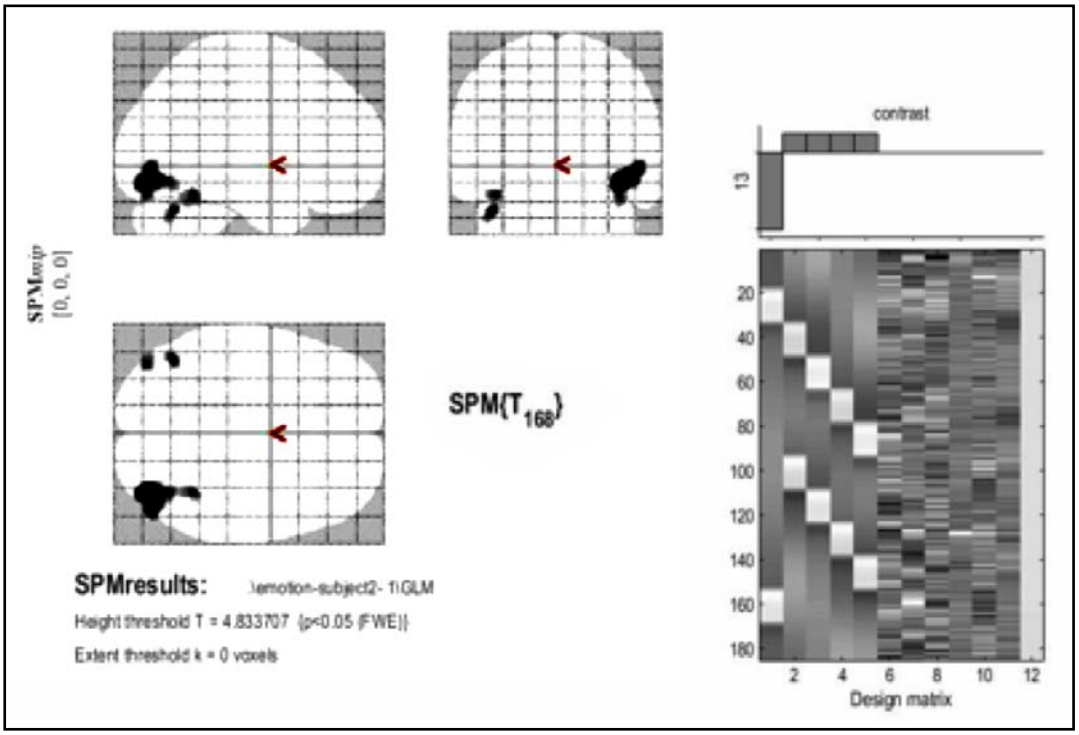

Fig. 3. SPM showing the result of classical GLM for testing face perception

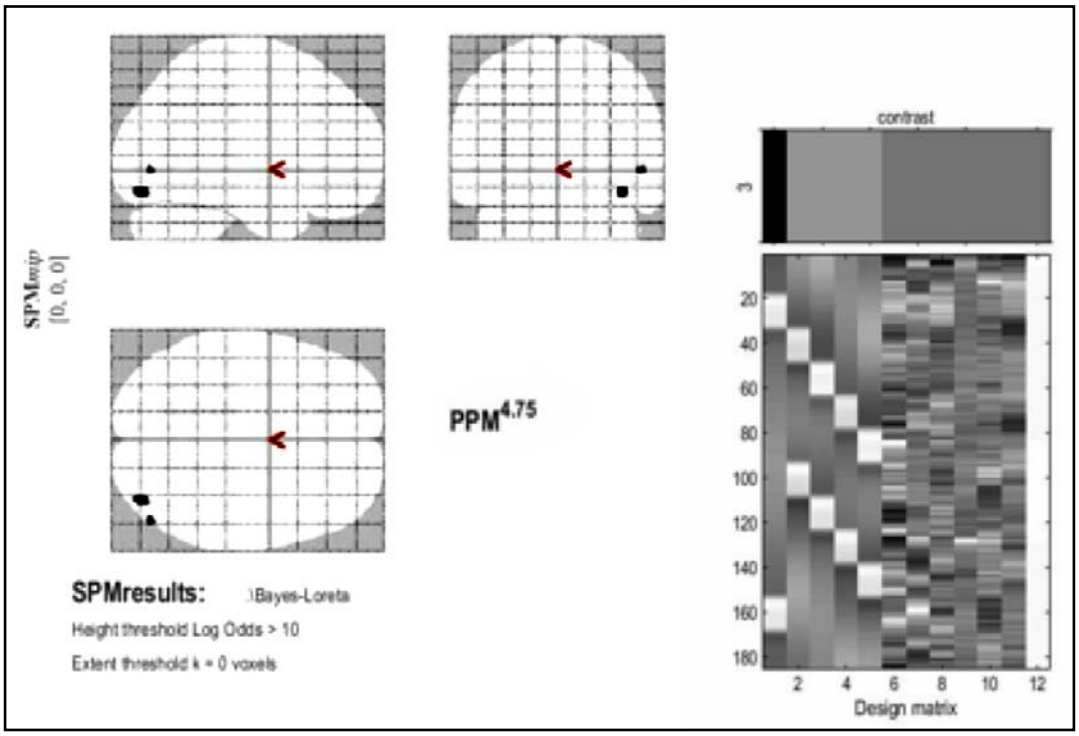

Fig. 4. PPM showing the result of a Bayesian analysis using LORETA prior for testing face perception

The outcome of Bayesian analysis depends on the activation threshold chosen. In this study, we set threshold that correspond to finding the activation greater than 1% of the activation in the whole brain mean signal. This threshold was chosen based of the study on visual data in the SPM manual (Ashburner *et al.* 2014).

In the Bayesian approach, Variational Bayes technique approximates the posterior density by factorizing the posterior distribution across model parameters, which is a less computationally expensive alternative to Markov Chain Monte Carlo algorithm (MCMC) and yields the posterior estimate in a shorter amount of time (Penny *et al.* 2003; Penny *et al.* 2005; Penny & Trujillo-Barreto 2005). Alternative methods for variational Bayes include spatial variational Bayes and integrated nested Laplace approximations (INLA) (Naseri *et al.* 2021; Sidén *et al.* 2017).

We performed single subject analysis in this study; the results of group analysis for these data sets are reported in the paper by David *et al.* and the GLM results are compared to SVM results (David & Barrios 2021). A simulation study is recommended to compare the outcomes of Classical and Bayesian GLM under different scenarios in terms of variation of fMRI data relative to the size of parameter of interest.

Conclusions

Although the classical GLM is the most common method for analyzing fMRI data, in the case of small activation with large variation, the results should be interpreted with caution. Bayesian analysis can be done in parallel to have a clearer view of the outcomes.

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Conflict of interest

The authors declare no conflicts of interest.

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