Mapping Pharmacological-Evoked fMRI Data Using Independent Component Analysis-Derived Pharmacodynamic Modeling

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INTRODUCTION

The rapid development in functional MRI (fMRI) field has created a large number of experimental paradigms and protocols, involving both hypothesis- and data-driven analysis techniques. The most popular method, the hypothesis-driven method, requires a *priori* model of hemodynamic response (HDR), and involves fitting a general linear model (GLM) whose functional form is based on the HDR function. The analysis results depend largely on how close the priori model is to the actual HDR. Recently, data-driven or exploratory approaches have also begun to be employed in brain imaging in order to identify and separate time courses of interest, along with their associated spatial patterns.

The modeling of pharmacological-evoked fMRI (phMRI) data is a relatively new application, and presents somewhat different challenges. fMRI measurements in response to neuropharmacological challenges produce a wealth of information contained with dynamic images of two or three spatial dimensions that evolve over a time course. Such information can be used to localize the spatial-temporal characteristics of the cerebral response to the stimuli. However, due to the complicated nature of neuronal responses to drug, it is difficulty to specify an exact model of data analysis [1] for phMRI measurement.

In this work, we developed a new method of phMRI data analysis that involves with both approaches. Specifically, ICA method is used to decompose the fMRI time series and distinctive pharmacodynamic profiles are derived [2, 3]. These ICA-derived pharmacodynamic profiles are used as the *priori* model (regressor) for statistical parametric mapping (SPM) of the fMRI data. We demonstrated this method of analysis in a phMRI study using D-amphetamine in a rat model, and satisfying fMRI maps were obtained.

MATERIALS AND METHODS

All the pharmacological-induced fMRI data were obtained using 7T small animal MRI scanner (Bruker Biospin Inc., Billerica, MA). Data were acquired using a single-shot EPI sequence with the following parameters: TR = 3000ms, TE = 28.92 ms, image matrix size = 64×64, FOV = 1.8×1.8cm, bandwidth = 200kHz. In total, 10 Sprague-Dawley rats (300-350 g) were used in this study. Animals were initially anesthetized with 3% isoflurane in O_2 at a rate of 3L/min and were maintained at 1.5% isoflurance at 1L/min during image acquisition via a face mask. The tail vein was cannulated with a 25–gauge needle for intravenous drug infusion. Typically, eight contiguous slices covered the whole rat brain with slice thickness 2 mm. The total imaging time was 40 minutes and total number of images was 400. Following 10-min of baseline acquisition after saline injection, D-amphetamine (3mg/kg) was manually injected over a 1-min interval; and images were continuously acquired for the rest of the time course. Data processing uses SPM2 along with Group ICA of fMRI Toolkit (GIFT v1.2c) [4] and customer-build Matlab codes. After motion correction, the time-series images were Gaussian smoothed to increase statistical analysis robustness.

RESULTS

Fig.1 showed the activation map and corresponding dynamic time course (pharmacodynamic profile) derived from the analysis using ICA method. This profile is then used as the *priori* model for statistical parametric modeling in SPM. The top row images in Fig.2 show the SPM result using boxcar alone as basic functions for analysis. The images in the bottom row of Fig. 2 show improved results of SPM analysis when added with prior model of pharmacodynamic profile derived from the ICA time course (in Fig.1 (b)).

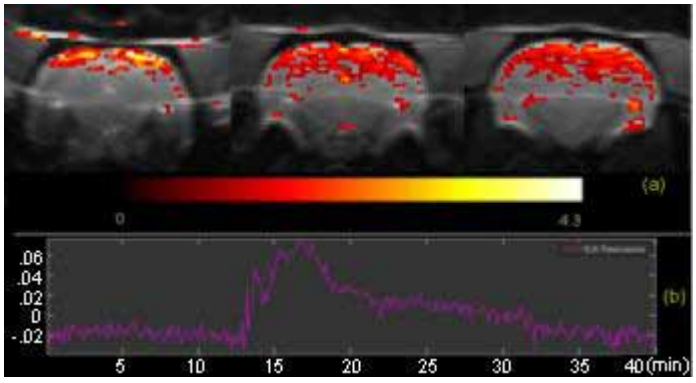

Fig.1 Prior modeling using ICA method (a) activation map; (b) dynamic time course.

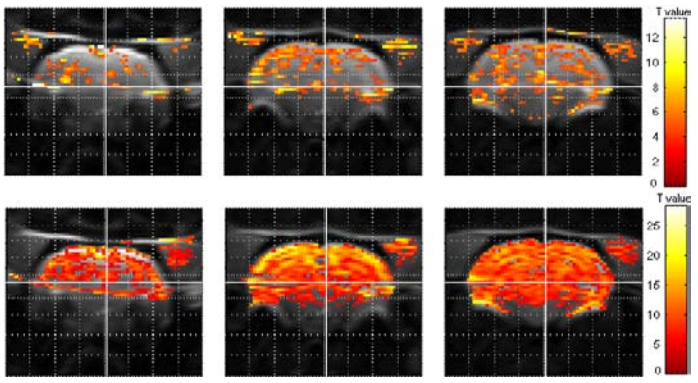

Fig.2 SPM results, p-value = 0.05.

DISCUSSIONS

Because the exact temporal modeling of BOLD responses associated with pharmacological challenge is unknown, the hypothesis-driven analysis method alone for fMRI data analysis in phMRI is difficulty. The pharmacodynamic profile derived from ICA method provides an excellent priori modeling for hypotheis-driven statistical analysis. Here we presented a new method that integrating the ICA time course into the SPM design matrix (as the priori regressor), and the results showed excellent improvement in analysis.

REFERENCES

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