Analysis of simultaneous fMRI and EEG data: a validation study

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Introduction

Simultaneous acquisition of functional magnetic resonance (fMRI) images and electroencephalograms (EEG) is used to explore the localisation of electrical discharges in epilepsy. EEG discharges or spikes are typically considered to be 'events' and entered into a typical event related analysis such as implemented in SPM99. One problem is how to deal with other signals in the EEG trace, such as atypical, potentially epileptiform EEG signal that could not clearly be considered an event, together with motion artefact. Whether or not to include the images that correlate with the timing of these ambiguous signals in the EEG trace is the subject of this study. We assess the extent to which the results of fMRI/EEG analysis are sensitive to how we deal with the scans acquired during ambiguous EEG signals.

Methods

Subjects consisted of 4 patients with epilepsy and frequent interictal discharges (spikes detectable in scanner using scalp electrodes) plus 4 healthy controls. Two "standard" methods of analysis of fMRI/EEG data were compared. They were: a) labelling the spike timings as events, and ignoring all other EEG events (all scans), and b) excluding the data during EEG events that were not considered spikes, and only analysing spikes and the "resting state" when no atypical EEG activity is present (artefact removed). For each of these approaches, we considered the effect of modelling the expected haemodynamic response function (HRF) as a canonical form versus explicitly fitting the response of each voxel using a freer model consisting of a set of Gamma basis functions. In order to assess the ability of each method to detect the assumed ground truth of cortical activity associated with the spikes, we assessed the potential of 20 randomly selected time periods, labelled as 'false spikes' to result in significant 'activation' in both patients and controls. The true maximum T (or F) statistic was compared to the distribution of maximum T statistics in the set of 20 "false" or random spikes. All analysis approaches were performed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm).

Results

Results are presented for one patient-control pair in the Table. Columns compare the canonical HRF and fitting with Gamma basis functions, as well as considering all scans, or removing scans containing artefact. The first data row shows the number of randomisations (of a possible 20) where voxels reached above the $p<0.05$ corrected threshold. The mean of the 20 maximum brain T/F scores (across randomisations) is then presented, followed by the threshold equivalent to $p<0.05$ corrected for comparison. The mean T/F max did not reach this threshold in any of the methods used, and was slightly lower in the control subject than the patient. Finally the maximum statistic for the "true" spike timings is presented for the patient. For all methods used, the true max T/F is above the threshold indicated in the line above. The number of standard deviations above the mean T/F obtained using 'false spikes', indicates that true spikes were best detected using basis functions with artefact removal. The figure shows the response detected using a free model (basis functions) applied to the complete dataset, where artefactual events remain in the data.

	Patient 1				Control 1			
	Canonical HRF		Basis functions		Canonical HRF		Basis functions	
	all scans	Artefact removed	all scans	Artefact removed	all scans	Artefact removed	all scans	Artefact removed
# randomisations with false pos. voxels	**2/20**	0	**2/20**	0	**1/20**	0	**2/20**	0
Mean random T/Fmax	4.27	3.94	10.07	8.56	3.79	3.66	8.23	7.52
0.05 corrected	4.75	4.75	10.59	10.59	4.75	4.75	10.59	10.59
True Max T/F	5.86	6.24	13.67	18.74				
# SD above mean	**2.72**	**6.53**	1.81	**9.93**				

Discussion/conclusions

Our findings indicate that fMRI/EEG results are quite sensitive to analysis strategy. In each case, the inclusion of all fMRI scans in the analysis without modelling explicitly for artefact leads to unacceptable levels of false positives, even at the $p<0.05$ (corrected) level. This is especially true in the case where we include all scans, and fit the spikes with a flexible model of basis functions. This yields results as shown in the figure, where we see an atypical haemodynamic response: most likely artefactual rather than reflecting the biology of spike activations. This approach may lead to artefactual variance being wrongly assigned as spike-related cortical activity. In contrast, in the reduced dataset, where fMRI data associated with confounding EEG events is removed, the flexible basis functions provide a more robust measure of the true response (9.93 SDs above the mean of max statistics for the "false" spikes) than the canonical model (6.53 SDs).