Model fitting and power in fast event-related designs

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Introduction

Event-related (ER) experiments are now standard in FMRI. Recent theoretical work has suggested that fast ER designs, with many events during an FMRI run, can give high statistical power to detect and estimate event responses. These predictions have been based on the assumption that event responses add up in a linear fashion, even when an event is very close to another in time. Fast ER designs are likely to lead to many short interstimulus intervals (ISIs), and there is much evidence to suggest that event responses are not linear at very short ISIs. Non-linearities can lead to a reduction in statistical power, and changes in the the shape of the haemodynamic response function (HRF), which will cause problems for standard statistical models. We have therefore investigated the theoretical predictions in a real FMRI experiment.

Methods

Events
One visual event was the onset of a checkerboard that reversed 3 times at 66 ms intervals, followed by fixation. The subject responded to the visual event by a button press with the right hand.

Conditions
7 conditions, with a mean ISI of 1, 2, 3, 4, 6, 8 and 10 seconds.
ISIs were generated from random exponential distributions with the required mean and a minimum of 0.59 sec.
The order of the ISI conditions was randomized across subjects.

Scanning
13 normal right-handed subjects
3T Bruker scanner
Standard EPI sequence
16 slices; 3.9 x 3.9 x 5mm voxels
2 second TR.
138 scans = ~280 seconds per run
One run per condition

Analysis
2 subjects excluded due to high rates of omitted responses

Preprocessing: SPM2
- standard (sinc) slice-time correction
- realignment to first image in the run
- 8mm FWHM smoothing

Definition of region of interest: SPM99
For each subject we defined a region of interest (ROI) in visual cortex using a standard SPM analysis of the ISI = 3 condition: 60s high pass filter, HRF low pass, event modelled by convolution with the canonical haemodynamic response function (HRF) and its temporal derivative (HRF-TD). The ROI was defined by voxels in the occipital cortex with p<0.0001 uncorrected for an F test including the HRF and HRF-TD. The figure shows a typical ROI.

Figure 1: Typical functional ROI defined from ISI=3

Region of interest analysis: MarsBaR
We extracted mean time courses within ROI for each condition other than ISI=3:
□ISI=1,2,4,6,8,10

Time courses were adjusted for mean signal across sessions, and high-pass filtered at 60 seconds.

HRF convolution model:
Events modelled by delta function at visual stimulus onset, convolved with canonical HRF and its TD

Deconvolution model:
Events modelled with finite inpulse response basis set, to derive estimated haemodynamic response

Canonical HRF analysis

Ordinary Least Squares (OLS) analysis
Events modeled with canonical HRF and TD.
No low-pass filter, no autocorrelation model.
Figure 2 shows the parameter estimates for HRF and TD; the t statistic for the HRF parameter, and the root mean squared residual error across the ISI conditions. All showed condition effects at p<0.01.

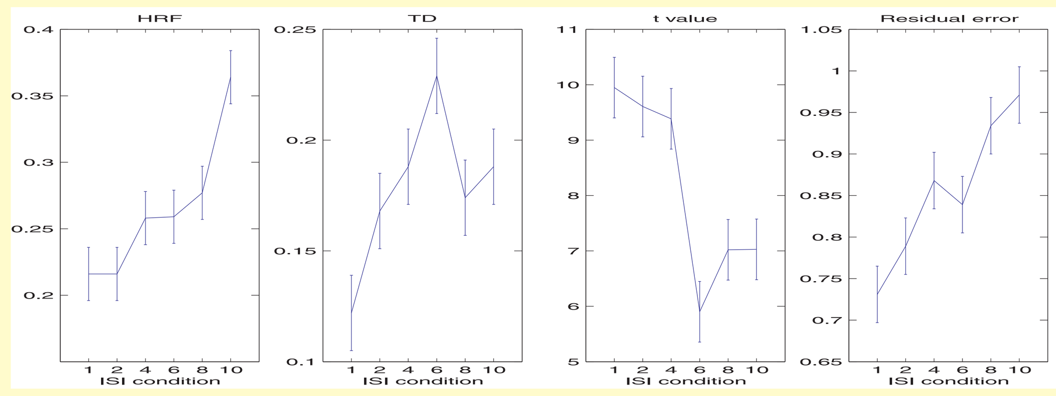

Figure 2: Parameters for OLS analysis; bars show standard error.

As predicted by the models, power (as measured by the t statistic) increases with faster event rate. However, the effect size for the canonical HRF decreases, suggesting either that the response per event is reduced, or that the canonical HRF is a less accurate model at fast event rates.

AR(3) model
We were interested to see if the fast event rates resulted in changes in the autocorrelation structure of the time course.
We used the same model as for OLS, with AR(3) model for autocorrelation fitted using ReML.
Comparison of the AR(1,2,3) parameters across ISI condition was not significant.

Deconvolution analysis

The canonical HRF analysis suggested that the amplitude or shape of the HRF response had changed for the short ISI conditions. We investigated the shape of the HRF response using a deconvolution (finite impulse response) model.

Finite Impulse Response (FIR) model with a single event type; FIR used 10 2 second time-bins. The results of the FIR analysis are shown in figure 3.

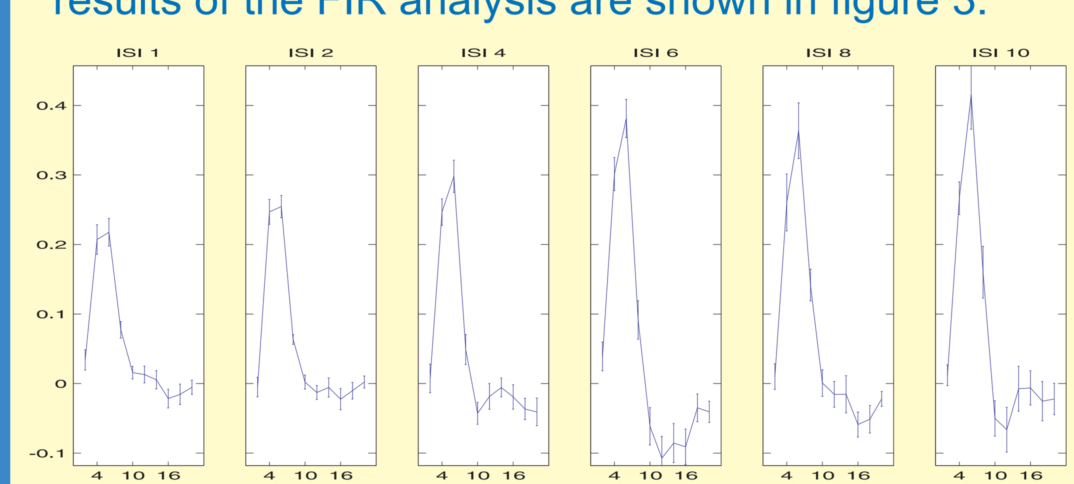

Figure 3: FIR estimation of HRF across ISI condition

The amplitude of the estimated HRF is reduced for the shorter ISI conditions, matching the HRF amplitude from the canonical model. The response shape also appears to change across conditions.

We wanted to address whether the apparent differences in response could be adequately explained by difference in scaling of a standard HRF shape.

To do this we did a singular value decomposition on the estimated HRFs; the first component represented a standard HRF shape across all runs (figure 4A). Scores for this component differed significantly across condition (figure 4B).

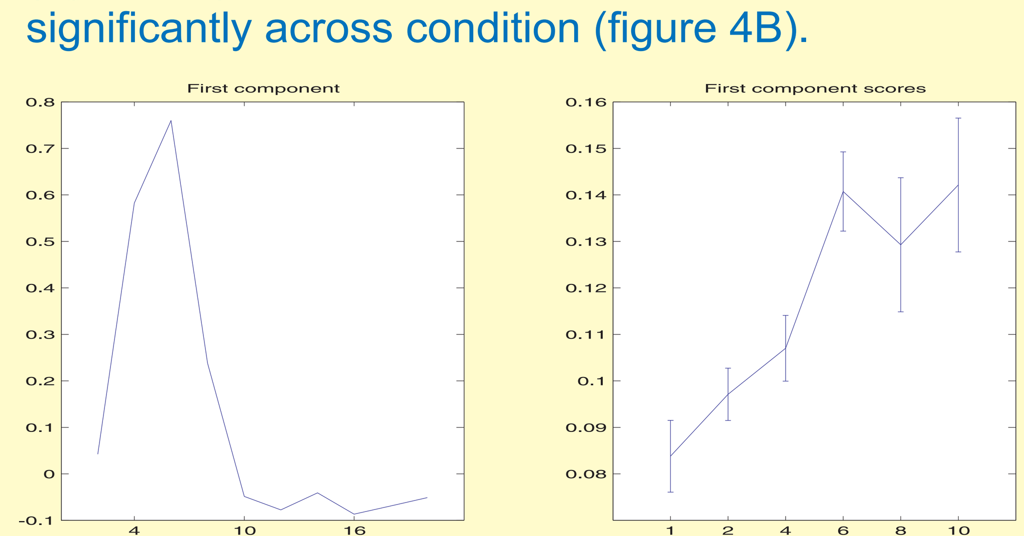

Figure 4: First component from SVD of FIR analysis

To look for changes in HRF shape over and above the scaling represented by the first component, we used a multivariate ANOVA across condition on the scores for components 2 to 10. This was highly significant, suggesting that there is also a change in HRF shape across condition.

Deconvolution - continued

Figure 3 suggests that events in the short ISI conditions have a lower HRF peak and less marked undershoot. If this HRF is characteristic of events which closely follow other events, the same shape should also be seen for short ISI events within the longer ISI conditions. We therefore restricted our analysis to the 6, 8 and 10 mean ISI conditions, and categorized events as being 1) the first event in the run; 2) a short ISI event - where the event has occurred less than 2 seconds after a previous event; 3) a long ISI event, occurring 2 seconds or more after the previous event. We modeled each type of event with its own FIR basis set. Figure 5 shows the estimated HRF for these event types.

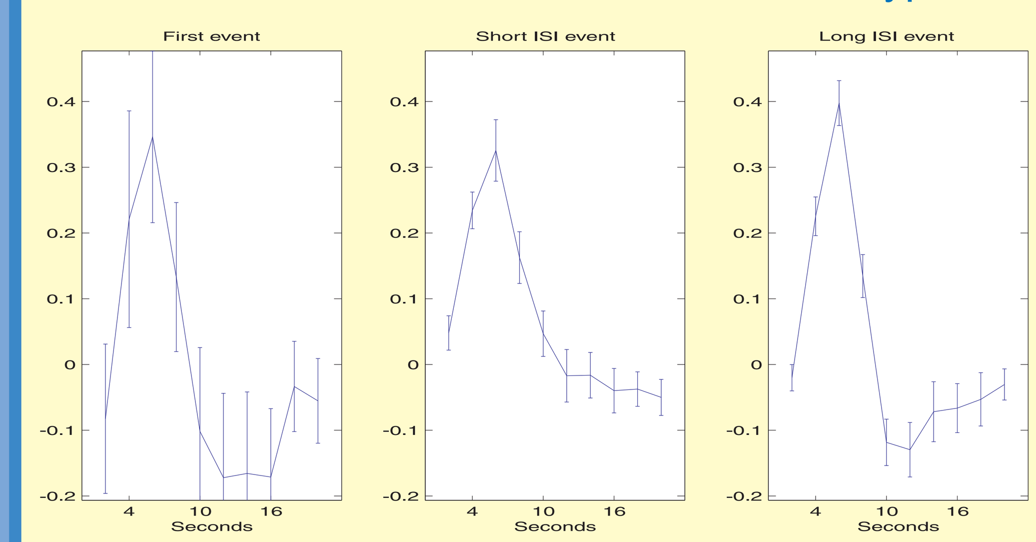

Figure 5: HRF estimates for first and short, long ISI events, within longer ISI conditions (mean ISI = 6,8,10)

HRF shapes for short and long ISI events within the longer ISI conditions resemble the HRF shapes from the short and long mean ISI conditions respectively (see figure 3).

Summary & conclusions

Fast ER designs lead to short ISIs, and short ISIs can lead to non-linearities of the HRF. Events which occur less than 2 seconds after a previous event may have a reduced peak amplitude and less undershoot than those that are more widely spaced.

Despite these non-linearities, shorter mean ISIs gave greater statistical power, even down to a mean ISI of 1 second. However, because of the reduced HRF amplitude, and possibly because of changes in HRF shape, the estimated effect size for short ISIs is reduced.

The differences in estimated HRF amplitude mean that it may be difficult to directly compare events with different ISI distributions; if there is a difference in the number of short ISIs between events, this may lead to differences in the apparent response amplitude, which are in fact due to HRF non-linearities.

The changes in HRF shape suggest that it may be necessary to adapt our model of the expected HRF to the context of the event; although the canonical HRF may be a good fit for widely spaced events, another HRF shape may be better for events which are close in time.

References

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Friston KJ, Zarahn E, Josephs O, Henson RN, Dale AM. (1999) Stochastic designs in event-related fMRI. *Neuroimage;*10(5):607-19.