An efficient method for obtaining subject-specific HRF estimates in event-related fMRI

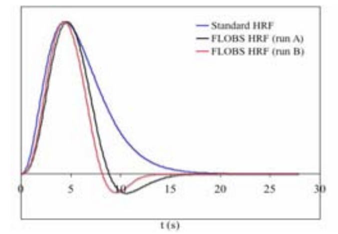
H. Devlin[1], J. T. Devlin[1], M. Woolrich[1], K. L. Miller[1], P. Jezzard[1]

[1]Clinical Neurology, University of Oxford, Oxford, Oxon, United Kingdom

Introduction It has previously been shown that there is significant variability in the shape of the haemodynamic response function (HRF) across individuals[1,2]. In light of these findings, Aguirre et al.[1] suggested that greater sensitivity to activation might be achieved by using subject-specific estimates of the HRF in functional analyses rather than using a standard HRF. However, the extra scan time required to explicitly measure subject-specific HRFs has prevented this suggestion from being widely adopted. Recent advances in linear optimised basis sets (FLOBS[3]) enable the HRF to be fit from (non-sparse) functional data. This suggests the possibility of using FLOBS fitting to derive an HRF from one functional data set (A), which can then be applied to the analysis of another independent data set (B) collected in the same subject, and vice versa (B to A). The resultant method would have the benefits of HRF subject-specificity without requiring additional scan time.

Experimental 16 participants performed a lexical decision task where they indicated with a button press whether a letter string was a real English word (e.g. "govern") or not ("xrftg"). An event-related jittered design was used for the word presentation with delay between trials ranging from 1.2-6.2s. Two runs (A and B), separated by twenty minutes, were carried out within the same scanning session. The order of A and B was randomised across subjects.
A FLOBS[3] analysis of run B data sets was performed using three basis functions to model the HRF. Prior constraints were applied to bias the fits against nonsensical HFF shapes. The FLOBS analysis generated an estimate of the HRF at every voxel along with a z-statistic for quality of fit. Weighted averages of the HRF, given by $HRF_{average} = \Sigma z_i^2 HRF_i$, were derived for each subject within anatomically defined ROIs corresponding to the visual, motor and language areas (Fig 1). Run A was then analysed using firstly the standard HRF (a gamma function with a lag of 6s and standard deviation of 3s) and secondly the FLOBS-derived $HRF_{average}$ from run B. In both cases the temporal derivative was also included in the model. A comparison was made between the sensitivity to activation for the two methods. All functional analyses were performed using the FSL software package[4].

(a)



(b)

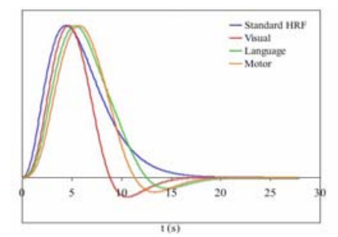
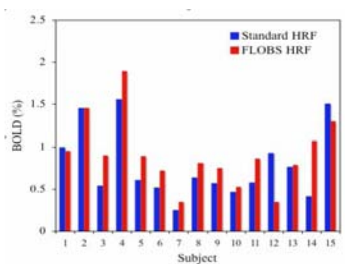


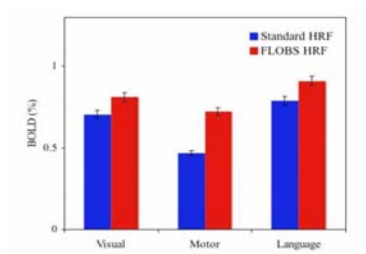
Figure 1. Standard HRF compared to FLOBS-derived HRFs for subject #4 in (a) the visual area from runs A and B (b) the visual, motor and language areas from run A.

Results Data from one subject was excluded due to excessive motion (maximum displacement=12mm).
There was generally good agreement between HRFs derived from common ROIs in runs A and B (Figure 1(a)), whilst the shape of HRF estimates tended to vary within subject across brain regions (Figure 1(b)).

(a)



(b)



(c)

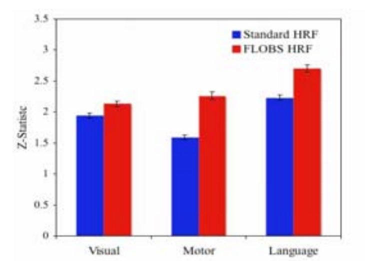


Figure 2. (a) BOLD (%) activation in the language area for all 16 subjects (b) group average BOLD (%) activation in the visual, motor and language areas (c) group average z-statistics in the visual motor and language areas.

In the language area twelve out of fifteen subjects showed an increase in BOLD (%) activation when using the empirically derived HRF estimate (Fig 2a). The three subjects who showed no improvement were those with the worst motion artefacts, all having a maximum displacement greater than 3mm. Similar results were found in the visual and motor areas. Over all subjects and all brain areas average increases of 24% in BOLD (%) change (Fig 2b) and 23% in the z-statistic (Fig 2c) were observed.

Discussion and Conclusions This study demonstrates that improved modelling of the HRF can significantly increase sensitivity to BOLD activation. As HRF estimates were obtained from independent data sets and averaged over an ROI it is unlikely that the observed improvement results from fitting to noise, which can occur when fitting basis functions on a voxel-by-voxel basis. The particular advantage of the method described is that the HRF is estimated from the functional data itself. In this study the functional data from run B was ignored, but in practice an estimate of the HRF derived from A could also be applied to run B. So for experiments divided into two or more runs, an increase in sensitivity to BOLD can be achieved without the time penalty normally associated with acquiring subject-specific HRF estimates. Finally, the statistics obtained when using an HRF derived from an independent data set can be carried up to group level analyses in the same way as when using a standard HRF across all subjects.

[1] Aguirre et al. NeuroImage 8 (1998) 360-369. [2] Handwerker et al. NeuroImage 21 (2004) 1639-1651. [3] Woolrich et al. NeuroImage 21 (2004) 1748-1761. [4] Smith SM, *et al*. Neuroimage 2004;23:S208-9