Optimising TR for fitting single trial HRFs

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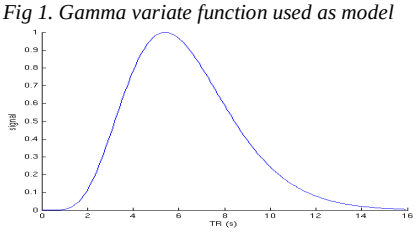
INTRODUCTION: With the increase in magnetic field strength of human clinical MRI scanners, single trial fMRI (mapping the response to a single stimulus) opens up the possibility of quantifying trial-by-trial variations in the response to stimulation, for instance during learning paradigms. To characterize variations in the response it is necessary to perform a trial-by-trial fit to features of the haemodynamic response function (HRF) such as the delay and amplitude. However it can be difficult to fit noisy, undersampled data to the shape of the HRF, and jittering is not possible for single trial data. Increasing the sampling rate (reducing TR) gives more degrees of freedom in the fit, but reducing TR reduces the signal-to-noise ratio (SNR) due to T_1 suppression. This work aims to determine the optimum TR at which to acquire single trial data in order to fit the data to determine trial-by-trial variations in response amplitude and delay. This was done using Monte Carlo simulations with experimental confirmation at 7 T.

Fig 1. Gamma variate function used as model



SIMULATIONS: An event related HRF (response to a short stimulus) was modeled as a gamma variate function [1,2]

$$H(t) = K\left(\frac{t-\Delta}{A}\right)^{\alpha} \exp\left[-\frac{t-(A+\Delta)}{\beta}\right] \quad \text{where} \quad \beta = \frac{W^2}{A8\log 2} \quad \text{and} \quad \alpha = 8\frac{A^2}{W^2}\log 2 \qquad [1]$$

For simulations the time to peak was A = 5.4 s, the full-width-at-half-maximum was W = 5.2 s, the initial onset time was Δ = 0 s, and the scaling factor was K = 1 with an ISI of 16 s, yielding the simulated HRF shown in Figure 1. *H(t)* was sampled regularly according to the TR being simulated, and then random noise was added. Assuming that the flip angle in the EPI sequence is set to the Ernst angle, and neglecting physiological noise for now, then as TR increases the SNR increases according to

$$SNR(TR) = M_0\sqrt{1-\exp\left[-\frac{2T_R}{T_1}\right]}\left\{\exp\left[-\frac{2T_R}{T_1}\right]+1\right\}^{-1}. \qquad [2]$$

Therefore Gaussian noise (mean = 0; standard deviation = 0.01 M_o) scaled with TR according to Eq.[2] was added to the simulated data. Monte Carlo modeling performed in Matlab (MathWorks Massachusetts) was used to assess the effect of varying TR on the systematic and random errors produced by performing a 2 parameter {amplitude (K) and onset time (Δ)} or 3 parameter {amplitude (K), onset time (Δ) and width (W)} fit to a gamma variate. The mean and standard deviation of the fitted parameters over 10000 repeats with different noise samples was found. The process was repeated for TR = 0.1 to 4 s in 0.1 s steps. The standard error in the fitted parameters was verified using an analytical approach based on the covariance matrix [3].

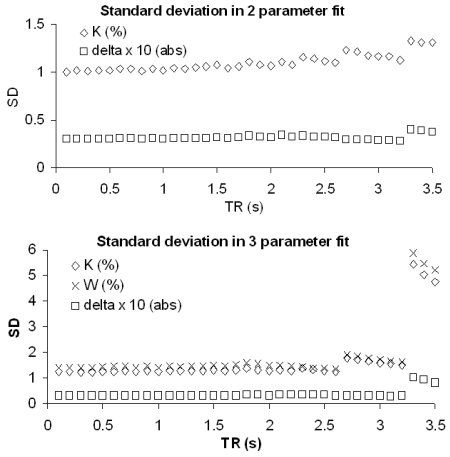


Fig 2: Simulation results for 2 and 3 parameter fitting.

EXPERIMENTAL: 2 subjects, age 25.5 ± 0.7 (mean ± stdev) were scanned using a Philips 7 T MRI scanner. The fMRI paradigm consisted of a visually cued single finger tap repeated with a 16 s ISI. The number of slices varied from 1 to 20 depending on TR. TE = 25 ms, matrix size = 96x96 and voxel size = 2x2x2 mm^3 with slice gap = 0.5 mm. The TR = 2 s data acquisition was run first so real time BOLD analysis could be used to ensure correct slice placement for the single slice data (where TR = 0.1 s). fMRI BOLD data was acquired using single shot EPI with TR = 0.1, 0.2, 0.4, 0.8, 1.0 or 2.0 s. The nominal flip angle was set according to the Ernst equation assuming T_1 grey matter = 2 s [4], although variation in flip angle across the field of view at 7 T will occur. **Analysis:** SPM was used to determine the location of the region activated by finger tapping by modeling the data as an event convolved with HRF and temporal derivative (FWE P < 0.01 corrected). The signal time course was extracted from a 3 mm radius sphere centered on the maximally activated voxel within the motor cortex and averaged across trials. The resulting average data was fitted for W, K, A and baseline and assuming Δ = 0, to provide an individualized canonical HRF. The data was then fitted on a trial-by-trial basis to this individualized canonical HRF by performing a 2 parameter or 3 parameter fit. The mean and standard error of the fitted parameters between trials was estimated. This process was repeated for each TR.

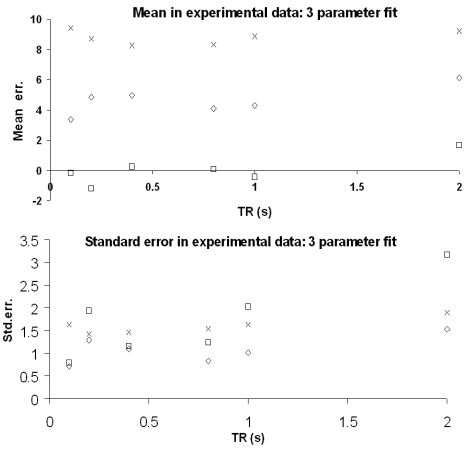


Fig 3: Mean and standard error in fitted parameters for 10 trials for 3 parameter model fitting, ◊ = K (% change); x = W (s); □ = delta (s).

RESULTS: Figure 2 shows Monte Carlo results for standard errors of the 2 and 3 parameter fits of simulated data. The random error was relatively constant for TR values up to approximately the time to peak of the HRF. The discontinuities in the curves depend on how close a sample point falls to the peak of the HRF for a given value of TR and probably depend on the fitting algorithm since the covariance matrix results did not show such sharp discontinuities. The mean values for the 2 and 3 parameter fit were K = 1, Δ = 0 and W = 5.2 respectively across the range of TR's. The results were independent of noise level for signal to noise levels in M_o of up to 10 %. The experimental results show similar trends with a slight tendency for the errors to increase at long TR relative to the simulations.

DISCUSSION: Single trial data can be fitted for features describing important aspects of the shape of the HRF (delay, amplitude and width). Simulations and experimental data indicate that if the flip angle is set to the Ernst angle then the errors in fitting the HRF for parameters describing its shape, are relatively independent of TR provided TR is shorter than the time-to-peak of the HRF. This analysis neglected physiological noise which is largely signal independent (except for inflow effects at short TR with a small number of slices). This may be the reason for the observed increase in the standard error in the fitted parameters for the experimental data at TR = 2 s, where physiological noise will start to dominate over thermal noise. The general independence of the results on TR suggests that the choice of TR can be a trade off between the need to obtain more slices in a given TR and the need to oversample the data to allow investigation of features of the single trial HRFs such as the post-stimulus undershoot.

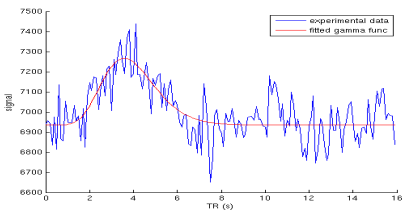


Fig 4: Single trial response to finger tap at TR= 100ms with fitted response.

REFERENCES [1]Worsley et. al. Neuroimage. 2002 Jan;15(1):1-15. [2] Cohen. Neuroimage. 1997 6:93-103 [3] WH Press *et al.* Num. Rec. in C (2nd Ed.) [4] P J Wright et. al. 921, ISMRM 2006. *This work was supported by the MRC and EPSRC*