

Spatial Dependence of the Nonlinear BOLD Response at Short Stimulus Duration

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Non-linearities in the measured BOLD data were found for the response integral and width. With the high sensitivity at 7T, a voxel-based analysis was feasible and was used to investigate the spatial dependence of the non-linearities at high spatial resolution. Correlation between response onset and non-linearity suggests that the origin of the observations are a tissue-specific phenomenon. Comparison with 4T and 1.5T data also indicates a field dependence. The observed non-linearity at short stimulus duration (SD) has likely a considerable hemodynamic contribution and thus must be accounted for in event-related fMRI paradigms.

Introduction Most fMRI studies use linear models to predict the measured response by convolution of the impulse response with the stimulus profile [1]. Using short stimuli, non-linear effects were reported for amplitude and width [e.g.,1-3]. In this study, high temporal and spatial resolution was used to explore non-linear effects and investigate their spatial dependence.

Methods Single-shot EPI with a voxel size of $1.2 \times 1.2 \times 2 \text{ mm}^3$ was performed on a 7T/ 90 cm system using a 7-cm quadrature T/R coil pair (TE 20 ms, TR 125 ms, sagittal plane). With a zoomed imaging technique, BISTRO [4], the FOV was reduced to $4.8 \times 15.4 \text{ cm}^2$. Event-related fMRI studies were performed on four volunteers (visual stimuli with LED goggles at 8 Hz). With inter-stimulus intervals fixed at 18 s, stimulus duration (SD) took values of 0.25, 0.5, 1, and 2 s. 16 trials were executed per series (5 min). The integral and width of the BOLD response were determined with *single-voxel analysis*. For both parameters, a non-linearity index (NL^{INT} and NL^{WIDTH}) was defined as the normalized difference $[R^{exp}(SD=0s) - R^{theo}(SD=0s)] / R^{exp}(SD=2s)$ between experimental and theoretical values, obtained by extrapolation to $SD=0s$. Also, a corresponding NL^{INT} map was computed. Cross correlation was used to determine activation maps and onset lag.

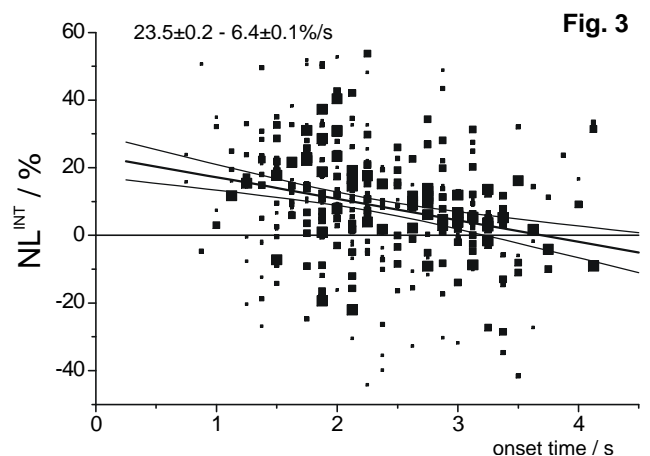
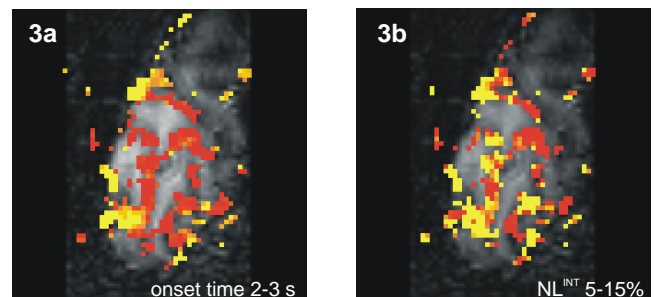
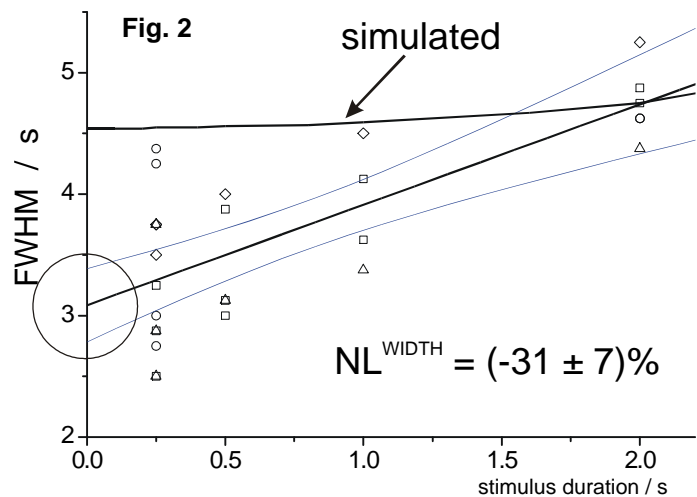
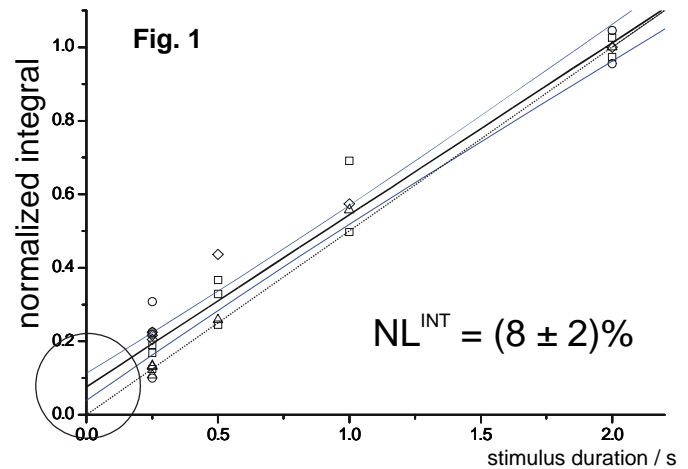
Results Non-linearities were observed for the amplitude and the integral of the BOLD response (positive component). The deviation from the linear model increased with decreasing SD (Fig. 1). NL^{INT} was determined from the intercept of a linear fit and found to be $(8 \pm 2)\%$ (4 subjects) for the averaged time course (voxel and epoch average). Comparable experiments at 4T using $3.1 \times 3.1 \times 6 \text{ mm}^3$ resolution [3], revealed a significantly higher NL^{INT} of $(30 \pm 3)\%$ (5 subjects). A motor study at 1.5 T reported a NL^{INT} of 40% [1]. These observations indicate a magnetic field dependence of the non-linearity in the response integral.

Previously reported non-linearities in the *width* (study at 4T [3]) were also observed in the present study at 7T using higher spatial resolution. NL^{WIDTH} was -31% (Fig. 2), indicating that the FWHM at short SD is much smaller than expected from a linear model (simulated curve in Fig. 2).

Maps of NL^{INT} and onset time are shown in Fig. 3a, 3b, demonstrating that the NL is clustered in patterns that are virtually identical to those in the onset map. With the spatial non-linearity information resolved, NL^{INT} was found to be up to 40%. Most important, significant linear correlation between NL^{INT} and onset was found (CC-weighted linear fit). Responses with a later onset revealed less non-linearity.

In summary, a significant spatial dependence of non-linearities was found, which is hypothesized to be tissue-type specific. Signal-to-noise gains at 7T provided sufficient sensitivity for simultaneously high temporal and high spatial resolution. The dependence of NL^{INT} on the magnetic field and the demonstrated non-linearity in the width supports the argument that the source of the non-linearity at short SD is not only of neuronal origin, but has also a considerable hemodynamic contribution. Understanding the

non-linearities in the BOLD response is significant for modeling event-related and single-trial fMRI experiments.



References 1. Glover GH *Neuroimage* 9:416;1999. 2. Vazquez AL *Neuroimage* 7:108;1998. 3. Pfeuffer J *ISMRM* 988;2000. 4. Garwood M, *MRM* 1095;2001.

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