Insights into the dynamics of hemodynamic response to millisecond stimulus duration: A fMRI and VEP combination study

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Introduction

In a previous study, we have shown that in human subjects, it is possible to detect blood oxygenation level dependent (BOLD) signal changes evoked by a visual stimulus presented only for 5ms [1]. Moreover, we observed that at this ultrashort stimulus duration a) the response was highly non-linear compared to 50ms, 250ms and 1s stimulus, and b) the extrapolated intercept at 0ms stimulus duration was not zero. Thus, below specific stimulus duration, the hemodynamic response remained constant [2]. In this study, we have expanded our previous investigation on the temporal behavior of the BOLD response by zooming into the time scale of stimulus durations as short as 0.1 to 5ms, in order to evaluate if there is indeed a minimum hemodynamic response. Moreover, in order to gain insights about the dynamics of neural response at ultra-short stimulus durations, we also performed VEP recordings to complement the fMRI data.

Methods

Measurements were made on a 3T Siemens/Trio scanner [TE=40ms; TR=0.5s; voxel-size=3x3x3.5mm^3; 7 slices, 560 repetitions]. Customized white light emitting diode goggles were used for the stimulation of visual field. Ultrashort stimulus pulses (0.1, 1, 3, 5ms) were presented to 4 human subjects. In each run, 8 stimuli were presented with randomized interstimulus intervals (30 to 35s). All experimental runs were performed twice to investigate the reproducibility of the responses. Motion correction, high pass filtering and statistical analysis were done using FSL software [3]. The time series of the most activated voxels were averaged and normalized to the mean of the baseline period.

The EEG was recorded using a 64 channel electrode cap (BrainProducts). Electrode placement followed the International 10-20 System [4], and were all referenced to a frontal central electrode (FCz). An electrode placed at AFz was used as the common ground. Inter-electrode impedances were kept below 15k. EEG recordings were digitally recorded at 5000Hz together with a 50Hz notch filter and stored for off-line analysis. Visual Evoked Potential (VEP) epochs (-100 – 500ms temporal range) were created based on the onset of triggers recorded during the session. The data was bandpass filtered within 1-40Hz and then averaged. In the end, each stimulus condition (1, 3 & 5ms) consisted of 320 sweeps, which is far greater than the minimum number of sweeps required for VEP analysis [5]. The amplitude of the first prominent VEP deflection (N75) was then recorded for each stimulus condition.

Result

Averaged BOLD time courses for the different stimulus durations (0.1 to 5ms) with corresponding activation maps are shown in fig. 1. Activation maps are in good agreement with each other. Hemodynamic responses to all stimulus durations were highly reproducible (data not shown). Shorter stimuli responses possessed smaller positive signal changes. In addition, weaker post stimulus undershoots were observed with decreasing stimulus duration. As shown in fig 2. BOLD response still decreases in integral for stimulus durations shorter than 5ms. The response integrals are highly non-linear with respect to each other, e.g. although the 1ms stimulation is only 20% in duration compared to 5ms, the BOLD response integral is ~75%. VEP amplitude increases monotonically with increasing stimulus duration (fig. 3). The VEP amplitude exhibit also non-linearities.

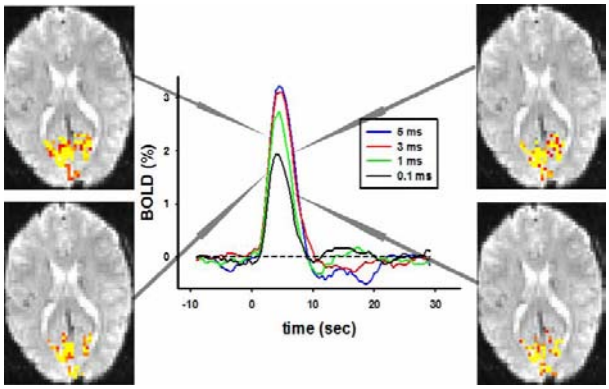

Figure 1

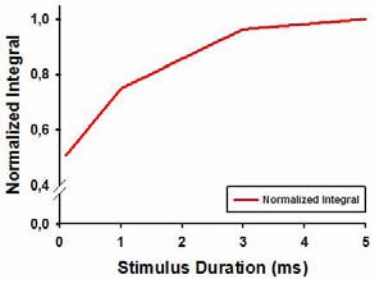

Figure 2

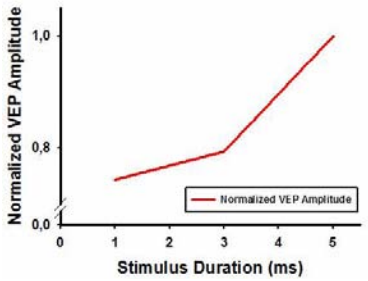

Figure 3

Discussion

We have been able to detect, for the first time, a hemodynamic response to 0.1ms visual stimulation. As Ogawa et al. [6] and we in a previous study [1] have already pointed out, this offers a new possibility to probe neural activity and interactions in even millisecond range despite the temporal blurring effect of hemodynamic response. The BOLD responses to different stimulus durations can be easily differentiated from each other (fig. 1). This suggests that the hemodynamic response is dependant on stimulus duration down to 0.1ms. Moreover, these data provide evidence that processes responsible for the positive response and the negative post-stimulus response are dissociated. Both BOLD integral and VEP amplitude increase monotonically with increasing stimulus duration. However, non-linearities in VEP amplitude can not account for all non-linearities observed in BOLD response even at these very short stimulus durations, indicating that vascular and/or metabolic effects must play a role in the non-linearities observed in the BOLD response.

References

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