Dynamics of ERP and Hemodynamic Responses at Very Short Stimulus Durations

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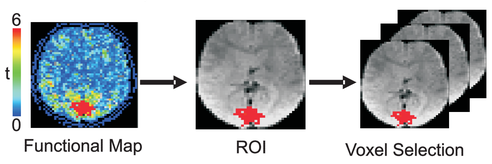
Introduction

Complementary non-invasive imaging methods on human subjects such as EEG and fMRI can provide new insights into the functioning of the brain and into neurovascular coupling. Particularly, short stimulus durations rather than commonly used standard durations in fMRI experiments are suitable to study the relationship between electrophysiological and vascular measures because of reduction of non-linearities of the hemodynamic response [1].

In this study, using measurements with fMRI and EEG we studied the dynamic behavior of hemodynamic and neural responses at very short stimulus durations (0.1 ms to 5 ms) and their relationship with each other.

Methods

fMRI: 3T Siemens Tim Trio Scanner; 10 human subjects
Sequence: T2* - weighted gradient-echo EPI
TE = 30ms; **TR** = 0.5 s; **voxel size** = 3x3x3mm^3; 560 repetitions
Stimulation of visual field: White LED (light emitting diode) goggles
Stimulus durations (SD): 0.1,1, 3 and 5 ms **Stimulus Intensities:** 20, 50, 100, 500 cd/m^2
In each run: 12-16 visual stimuli **Inter stimulus interval:** 30 - 35 s
Software: FSL, Matlab



Based on statistical map of 5ms stimulus experiment 50 most activated (highest t-scores) voxels were chosen and their time series were averaged. Responses normalized to the peak amplitude of 5ms response. Positive integral calculated as sum of positive values on BOLD signal and post-stimulus undershoot integral as sum of negative values.

EEG: 64 Channel Electro Cap, International 10-20 System; 9 human subjects
Inter-electrode impedances: below 15kΩ
Recorded: at 5000Hz together with a 50Hz notch filter
Bandpass filter: within 1- 40 Hz
Stimulus durations (SD): 0.1,1, 3 and 5 ms **For each stimulus duration:** 400 repetitions
Event related responses were calculated for each subject and stimulus duration. N2 and P2 VEP components were determined as the negative and positive peak occurring ~90 and 120 ms after stimulus onset respectively.

RESULTS

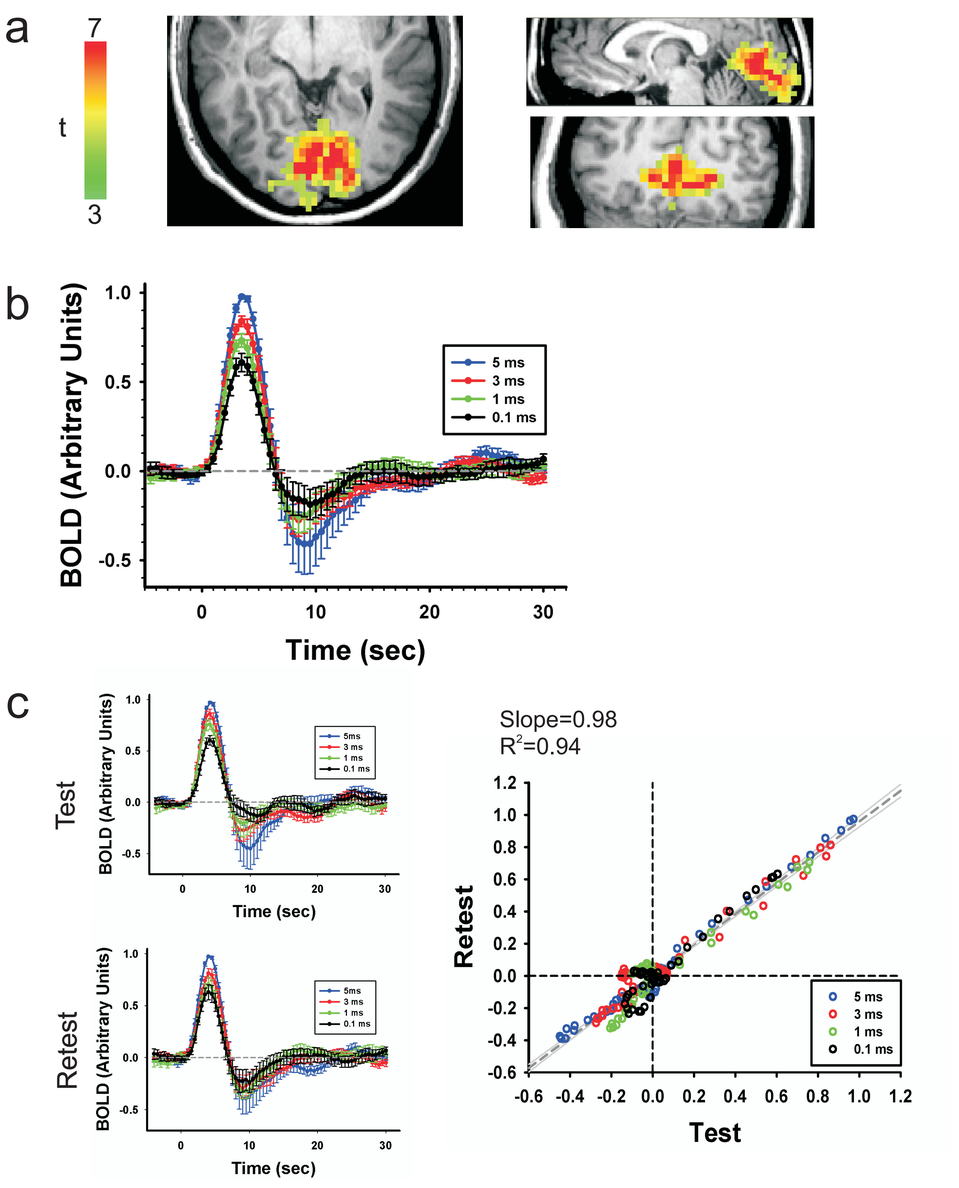


Figure 1: a) Color coded activation maps (Subject R.K.)
b) Averaged BOLD signal time courses (10 Subjects)
c) Test Retest reliability

- Robust activations in early visual areas in most of the subjects (Fig.1a)
- Shorter stimuli responses possess smaller positive signal changes (Fig. 1b)
- Weaker post-stimulus undershoots with decreasing stimulus duration (Fig. 1b)
- Test Retest reliability is very good (Fig. 1c)
- At very short stimulus durations, as stimulus duration increase post-stimulus undershoot tends to increase faster than positive response (data not shown)

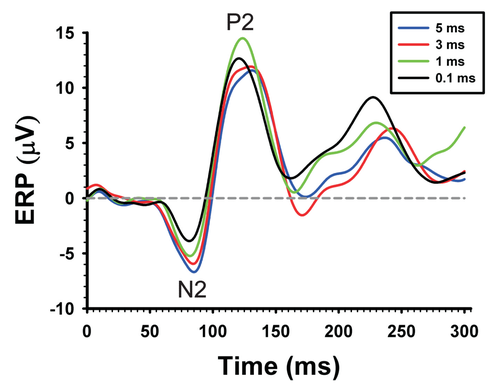


Figure 2: Examplary VEP time courses

- Amplitude of the N2 VEP component increases with increasing stimulus duration (Fig. 2)
- Amplitude of the P2 VEP component has no trend (data not shown)

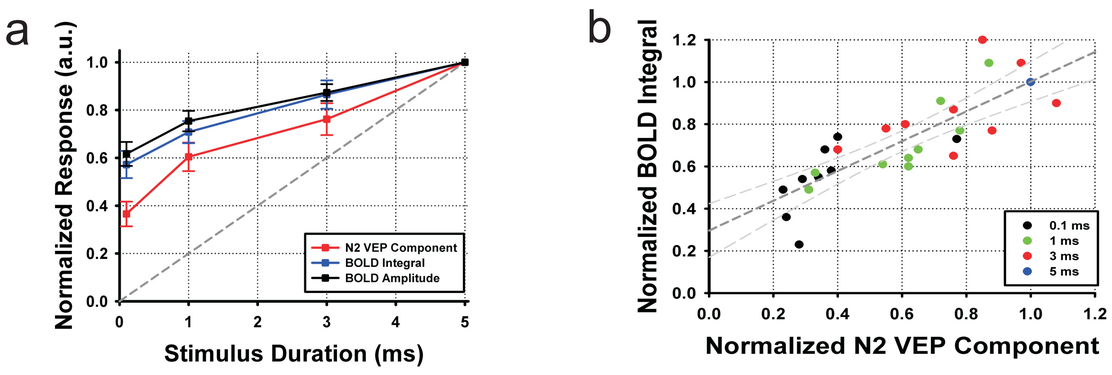


Figure 3: a) Normalized BOLD and N2 VEP responses v.s. Stimulus duration
b) Normalized BOLD integral v.s. normalized N2 VEP amplitudes

- BOLD and N2 VEP responses increase monotonically with stimulus duration (N2 VEP response increases faster than BOLD Integral) (Fig. 3a)
- Both responses exhibit non-linearities (although differently) with respect to SD
- N2 VEP component correlates well with BOLD response (Fig. 3b - consistent with [4])
- Intercept of the regression line is not zero (Fig. 3b - consistent with [2])

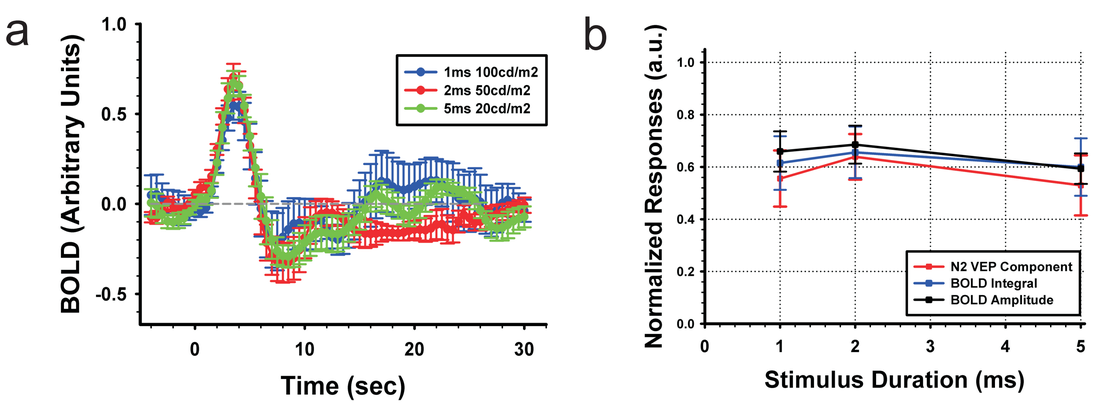


Figure 4: Equal stimulus energy (stimulus duration X stimulus energy = 100 ms.cd/m^2)
a) Averaged BOLD Signal time courses (6 Subjects)
b) Normalized BOLD and N2 VEP responses v.s. Stimulus duration

- At equal energy levels BOLD and N2 VEP responses remain approx. constant (Fig. 4a, b)

Discussion

- We have been able to detect, for the first time, a hemodynamic response to 0.1ms visual stimulation on human subjects at 3T.
- Interestingly, post stimulus undershoot relative to positive response increases with stimulus duration (consistent with [3]). This can be explained either by increase of neural inhibition or by cerebral blood volume (CBV) non-linearities.
- In agreement with previous studies, our results show that the N75 VEP component correlates well with the BOLD response [4].
- At the limit of zero VEP response, the hemodynamic response has a non-zero value. Similar results, correlating local field potentials with BOLD response, obtained also by Logothetis [2].
- N2 VEP and BOLD responses to equal energy stimuli remained nearly constant which is in consistence with the temporal integration theorem. However, at constant stimulus intensity we have observed that BOLD signal does not change linearly with stimulus duration. Furthermore, the non-linearies in VEP amplitude could not account for all non-linearities observed in BOLD response. These findings indicate that vascular and/or metabolic effects must play a role in case of non-linearities observed in BOLD signal.
- These results have the important implication that VEP and BOLD signal - although related - are non-reducible measures of brain activity.

References

[1]Buxton, Neuroimage (2004), [2]Logothetis, Nature (2001), [3]Shmuel, Nature (2006), [4]Whittingstall, Hum.Brain Mapp. (2006)