The Linearity of CBV Response in Rat Whisker Barrel Cortex

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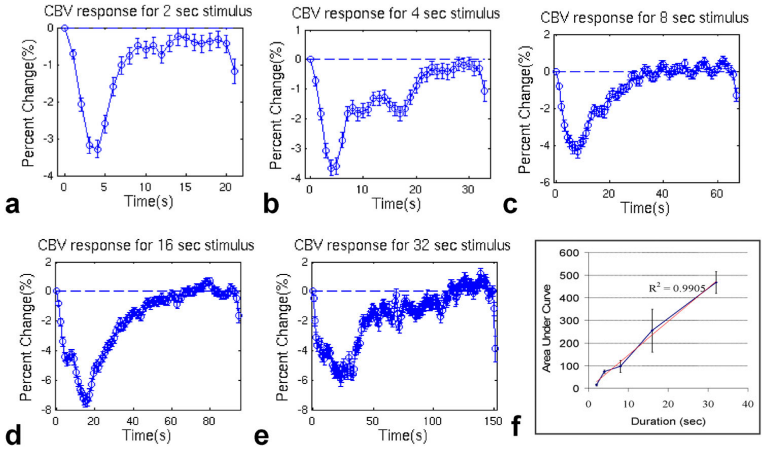
INTRODUCTION CBV-weighted fMRI using iron oxide contrast agent has superior sensitivity to BOLD contrast (1). More importantly, CBV-fMRI has the potential of detecting vascular response close to the foci of neuronal activity because the smallest vessels (10-20 μm) exhibit the greatest volume changes (2,3). Thus, CBV-fMRI can be a very useful tool for investigating neurovascular coupling *in vivo*. The linearity of CBV-fMRI response to stimulus is a fundamental issue regarding quantitative interpretation of CBV-fMRI data as well as paradigm design, but has not been well investigated. In the present study, we investigate the linearity of CBV response to different stimulus durations in rat whisker barrel cortex. Results (n = 3) suggest that CBV response is linear between the stimulus durations of 2 - 32 sec, and the area-under-curve of the CBV response (y) to stimulus duration (x) can be fit with $y = 14.78x$ ($R^2 = 0.99$).

THEORY and METHODS **Theory:** For a linear time-invariant system, the output $g(t)$ can be expressed as: $g(t) = \int_{-\infty}^{\infty} f(\tau)h(t-\tau)d\tau$, where $f(t)$ is the input function and $h(t)$ is the impulse response function. If $f(t) = 1$ for $T_1 < t < T_2$ and $f(t) = 0$ for $t < T_1$ and $t > T_2$, then $\int_{-\infty}^{\infty} g(t)dt = (T_2 - T_1) \cdot H$, where $H = \int_{-\infty}^{\infty} h(t)dt$. Thus, the area-under-curve (AUC) of the output function $g(t)$ is proportional to the stimulation period. We use AUC as an index to evaluate the linearity of CBV response in rat barrel cortex. **Method:** Three α-chloralose anesthetized rats were artificially ventilated and scanned in a 3T scanner equipped with a high efficiency local gradient coil (20 G/cm/100A along X and Y, 40 G/cm/100A along Z) and RF coils. A homemade computer-controlled whisker stimulator was used for *bilateral* whisker stimulation. The stimulus was set at 3mm displacement and 12 Hz throughout the experiments. A water-heating pad was used to maintain rat body temperature. CBV-fMRI experiment: TR 1 sec, TE 27 ms, FOV 3.5 cm, slice thickness 2 mm. MION was injected at 12 mg/kg. **Paradigm:** block design with the stimulus duration (SD) of 2, 4, 8, 16 or 32 sec with the off-periods (OP) changed correspondingly (SD = 2 sec, OP = 20 sec; SD = 4 sec, OP = 30 sec; SD = 8 sec, OP = 60 sec; SD = 16 sec, OP = 80 sec; SD = 32 sec, OP = 120 sec). Due to the slow response of CBV-fMRI signal, long off-periods were employed to ensure that the fMRI signal returned to baseline before the succeeding stimulus started. **Data Analysis:** active pixels were identified by cross-correlation method in AFNI (4,5). For each stimulus duration, time courses of active pixels were normalized to baseline signal and averaged., and the AUC was calculated.

RESULTS

Figures a-e show fMRI responses for different stimulus durations from one rat. Both the peak values and response periods increase with the stimulus durations. Significant fMRI response (high contrast to noise ratio) was observed at 8 sec SD. In this study, activation maps from 16 sec SDs were very similar to that of 32 sec SDs. The AUC values were calculated; data from three rats were averaged and are shown in Fig. f. It appears that the AUC values increase linearly with stimulus durations, and this trend can be fit with $y = 14.78x$ ($R^2 = 0.99$).



DISCUSSION **1.** With the MION dose of 12 mg/kg, intravascular BOLD contamination is minimal since blood signal has decayed away at the echo time due to dramatically reduced T_2* by iron oxide contrast. Thus, the fMRI response reflects primarily CBV changes. **2.** It is somewhat surprising that CBV response appears to be linear at a wide range of stimulus durations (n = 3, SD = 2 ~ 32 sec). It is noted that CBV response does not plateau at an SD of 32 sec. A previous study (6) showed that CBV response starts to plateau at an SD of 64 sec in this model. It is desirable to further explore the behavior of the CBV response at both longer and shorter SDs.

REFERENCES

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