Coupling between simultaneously recorded BOLD response and neuronal activity in the rat somatosensory cortex under different anesthetics

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Introduction

Many studies have addressed the issue of neural and hemodynamic coupling, although only a few performed simultaneous measurements of BOLD fMRI and local evoked field potentials in animals (Brinker et al., 1999, Shmuel et al., 2006) and none so far under urethane anesthesia. Although measurements from separate experiments provide an idea of the information processing in the brain, only simultaneous measurements provide unequivocal results for directly comparing the neural activity and BOLD contrast. Furthermore, the effect of different anesthetics on the interaction between nervous system activation and hemodynamics is poorly understood.

Materials and Methods

During surgery, a tungsten wire electrode was inserted to the somatosensory cortex of a rat (n=10, 394 ± 41 g). Either urethane (1.25 g/kg, i.p, n=7) or alpha-chloralose (60 mg/kg, i.v., n=3) was administered immediately after the halothane anesthesia was discontinued. Electrical stimulus to the forepaw of the rat was delivered with varying stimulus frequency (1-15 Hz). The signal from the electrode was amplified (1000 times), band-pass filter (0.1 Hz - 5 kHz) and resampled at 1 kHz.

The MRI experiments were performed in a 4.7 T horizontal scanner (Magnex Scientific) interfaced with a Varian UnityInova console. A quadrature surface coil with two 1.8 cm loops was used for signal transmission and reception. Anatomic images were acquired using double spin-echo sequence with adiabatic radiofrequency pulses (TR 2.5 s, TE 60 ms, 256 × 256, FOV 2.5 cm). Based on sagittal pilot scans, the functional imaging slice was positioned coronally to the somatosensory cortex at bregma within 1 mm of the electrode. Functional MR data were acquired using a single-shot spin-echo echo-planar-imaging sequence with an adiabatic BIR-4 refocusing pulse (TR 2 s, TE 60 ms, slice thickness 1.5 mm). The field of view was 1.5 cm × 2 cm with an acquisition matrix of 90 × 64 pixels in both the read out and phase encoding directions.

fMRI data were collected with 30 s baseline followed by 30 electrical stimuli to the forepaw, which was then repeated. Data were analyzed with FSL-program. The mean BOLD response was calculated as an average in the activated area in from 34 to 64 s. Integrated neural activity was defined as the sum of amplitudes of all the evoked potentials during stimulation.

Results

Electrophysiological recording showed high frequency transient peaks in the baseline field potential activity in alpha-chloralose-anesthetized rats, which is consistent with previous studies (Peeters et al., 2001). Consistent with evoked local field potential measurements, BOLD activity was observed in somatosensory cortex only at 1 and 3 Hz in the alpha-chloralose-anesthetized animal. Mean BOLD responses were 2.1 ± 1.0 % and 3.7 ± 0.1 %, respectively. Under urethane anesthesia, however, BOLD responses were observed above the 1 Hz frequency, even though electrical activity responses were observed at all stimulation frequencies. Mean BOLD responses varied between 1.7 % and 4.8 %, with the highest response being 4.8 ± 0.5 % at the 11 Hz frequency.

Under urethane anesthesia, both BOLD responses and summated field potentials increased almost linearly as a function of frequency, leveling off at 9 to 11 Hz. Under alpha-chloralose anesthesia, the frequency dependency was completely different, as no hemodynamic activity was observed at frequencies above 3 Hz. BOLD responses were highly correlated ($r=0.97$, $p<0.001$) with the integrated neural activity under urethane anesthesia, as shown in Figure 1. In alpha-chloralose-anesthetized animals, there was also a good correlation ($r=0.89$, $p<0.01$).

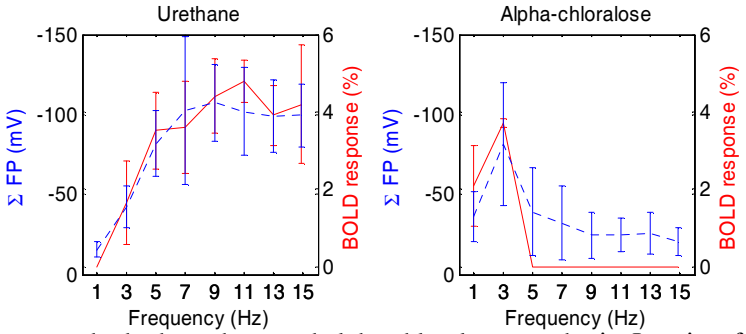

Figure 1. Tight coupling between hemodynamic (BOLD, red line) responses and integrated neural activity (summated local field potentials, blue dashed line) were observed under both anesthetic conditions. The correlated responses were different, however, under these anesthetic conditions. Error bars denote standard errors of means.

Discussion

There is a linear coupling between the neuronal and BOLD responses under both urethane and alpha-chloralose anesthesia. In spite of tight coupling under both anesthetics, the activation pattern as a function of frequency was clearly different. These results have implications for both understanding brain function and for designing fMRI paradigms in anesthetized animals.

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References

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