

# Effects of Low-dose Sevoflurane on Regional CBF and BOLD Responses to Auditory Stimulation of Varying Rate and Volume

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**Introduction** Task-induced neuronal activity in the presence of general anesthesia is the result of two counteracting factors: the anesthetic and the task. The former is supposed to suppress neuronal activity in general, while the latter is commonly used in fMRI and usually stimulates focal neuronal activity. It has been demonstrated in a limited number of animal models that the total amount of energy consumed by neurons or the level of neuronal activity in the sensorimotor region must reach the same level regardless of how deep the animal was anesthetized in order to accomplish certain task [1,2]. However this result has not been observed in humans [3], where the auditory and visual regions were examined in the presence of 0.25 MAC sevoflurane. Among many differences between these experiments, several issues remain to be clarified: e.g., will the strength of the functional stimulus affect the outcome? Will a strong functional stimulus dominates the observed changes in neuronal activity by emphasizing the primary projection against secondary associations? How the level of anesthesia affects the observation? The study was designed to address those issues.

**Materials and Methods** Seventeen consenting healthy subjects (ASA I, 19-40yrs) were recruited. Subjects on psychoactive drugs or any centrally acting medication were excluded. Imaging was performed on a 3T whole-body scanner Trio (Siemens Medical Systems, Erlangen, Germany) using a circularly polarized head coil. Simultaneous BOLD/CBF arterial spin labeling (ASL) imaging was performed. The auditory stimulus consisted of randomly presented pure tones presented through MR compatible headphones. The tones were presented at 2 rates (low: duration=250ms, ISI=250ms; high: duration=250ms, ISI=750ms) and 2 sound pressure levels/volumes. The high volume was adjusted for each subject to the maximum that the subject felt comfortable with; the low volume was adjusted low but the subject could still hear each tone clearly. Stimulation consisted of blocks in 40 seconds, and each was either low or high in rate, or high or low in volume. Stimulation blocks were presented to the subject in a random order, alternating with 40-s control periods when no tones were delivered. Total 3 functional runs were performed during each of the awake, 0.25MAC anesthesia, and 0.5MAC anesthesia sessions and each run lasted about 10 min. It should be noted that the signal change due to the change in rate comes from convolution of the same population of neurons but more frequently activated, while the signal volume involves recruiting more activated neurons.

**Results and Discussion** The auditory region of interest was defined based on the task-induced BOLD changes by auditory stimulation regardless of rate and volume (Fig. 1, pooled subject data). A Generalized linear model was employed to analyze the task-induced changes in BOLD and CBF in different conditions (Fig. 2). In the awake condition, task-induced changes in both BOLD and CBF increased when the rate or volume was increased, exhibiting a nice coupling relationship. During anesthesia, task-induced changes showed discrepancies in BOLD and CBF – with increased volume, task-induced changes in BOLD decreased while those in CBF increased. Because of the discrepancies observed, it is difficult to decide whether the intensified (high volume) auditory stimulus actually dominated the observed changes in neuronal activity. With increasing dose of sevoflurane, task-induced changes in CBF decreased progressively, while during 0.5 MAC, more BOLD activation was observed, which means that unit change in CBF brought about more change in BOLD during deep anesthesia. This is consistent with the observation in the previous study [3], indicating that during 0.5MAC sevoflurane this effect is more pronounced. Though interpretation of these effects in terms of neuronal activity is difficult due to the altered coupling and the epiphenomenal nature of BOLD, observations during 0.5 MAC sevoflurane were more likely consistent to those during 0.25 MAC sevoflurane [3].

**Conclusion** Because of changes in coupling between task-induced changes in BOLD and CBF, it remains difficult to determine whether the stimulus intensity was responsible for the observed discrepancies between [1] and [3]. Compared to the awake and 0.25 MAC anesthesia, we observed a mismatch between the BOLD and CBF changes during 0.5 MAC sevoflurane anesthesia, indicating that altered neurovascular coupling was more pronounced than the previously observed under 0.25 MAC sevoflurane anesthesia.

**References** [1] Hyder et al 2002, PNAS 99:10771-76. [2] Smith et al 2002, PNAS 99:10765-70. [3] Qiu et al 2008, MRM 60:987-96.



Figure 1 Regions of interest

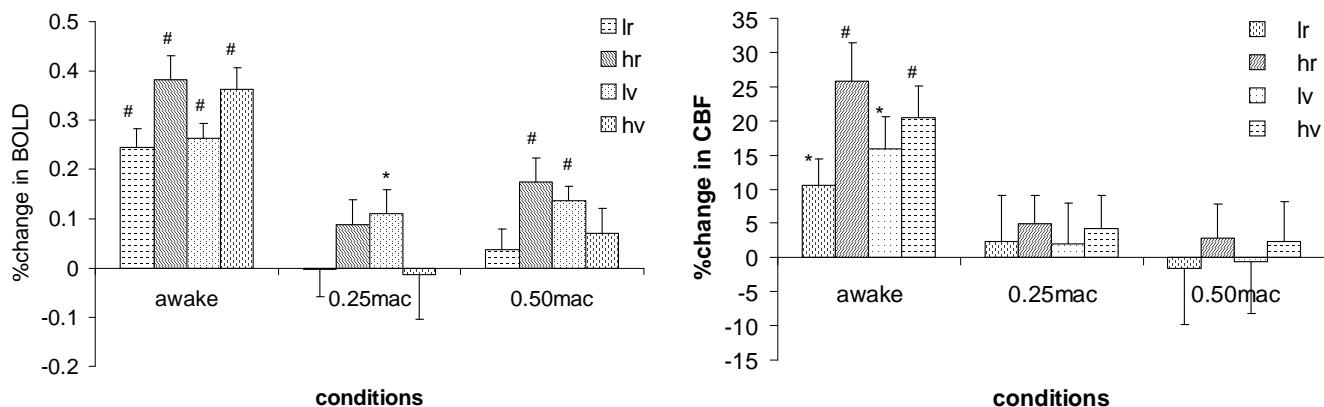


Figure 2 BOLD and CBF activation. \*: p<0.05; #: p<0.01.