Anesthesia: Regional Effects on Baseline and Activation Levels in Human Cortex

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ABSTRACT

fMRI[1] and PET[2] experiments have begun to explore the mechanisms of anesthetic agents and the impact of these agents on regional brain activation. Considerable interest exists in this topic both from a clinical perspective and from a basic science perspective. The latter is of interest because of the impact such studies may have on understanding brain function, the impact of baseline activity levels on the BOLD signal change, and ultimately what it may tell us about consciousness. This work demonstrates that sevoflurane lowers the overall BOLD activation amplitude, with higher order activation regions dropping below significance levels prior to primary regions[1], in tasks involving sensory/motor, visual, and auditory cortical stimulation.

INTRODUCTION

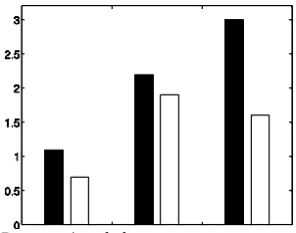
There is much interest in the impact baseline brain activity levels may have on functional activity detected using BOLD based fMRI. It remains an open question as to whether incremental activity is required for function or whether a specific absolute level of activity is required. Furthermore, the mechanisms of anesthesia are not well understood and little is known about the regional effects of anesthetic agents. This experiment was designed to test two hypotheses: 1) That the incremental BOLD signal change is affected by changes in baseline levels of brain activity, and 2) That anesthetic agents may differentially impact different cortical regions, and that higher order cognitive regions will be the most vulnerable. Such an approach can identify functional regions maximally altered by anesthetic agents, allowing these regions to be targeted with cognitive paradigms expected to be vulnerable to interruption of these circuits[1].

METHOD

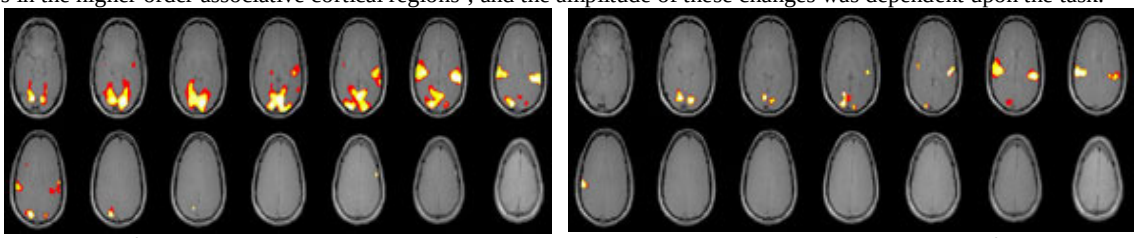
All imaging was performed on a 3T Siemens Trio with approval from the University IRB. A visually cued motor paradigm, a flashing checkerboard stimulation and an auditory stimulus, were presented in blocks alternating with fixation intervals under conditions of baseline/anesthesia/baseline/ anesthesia/baseline. This on/off repeated experimental design ensured that there were no order effects present and that the signal changes were not due to fatigue over the long course of these experiments. A single run lasted for 4:20min and 2 runs were performed under each condition. Sevoflurane was administered through a mask at a low dose of end-tidal concentration of 0.4% such that the subjects were always awake. BOLD imaging was performed using a gradient echo EPI sequence (α/TE/TR=80/30/1500msec, 64x64 matrix, FOV=22cm) and CBF imaging using a modified QUIPSSII approach (same coverage), were used in order to allow CMRO2 to be calculated[3]. Comparisons were made between activation maps collected under conditions of baseline and anesthesia, in addition to overall comparisons collapsing across a complete run in order to assess global changes in BOLD, CBF, and CMRO2.

RESULTS and DISCUSSION

The results indicate that sevoflurane anesthetic regionally affects both the baseline activities and the activation amplitude. Overall, non-task related signal changes (brain baseline effects) moving from baseline to the anesthetic condition are most pronounced in the frontal lobes. The activation data demonstrates a more complicated pattern with an overall decrease in the level of activity in the primary visual, motor, and auditory cortical regions. Furthermore, there are decreases in the higher order associative cortical regions[3], and the amplitude of these changes was dependent upon the task.



Percent signal change (baseline=white, sevo=black) for motor, auditory, and visual stimulation.



Thie middle 14 of 28 slices showing auditory and visual cortical activation during the baseline state with no anesthetic on board (left) and under 0.4% sevo (right) demonstrating a decrease in visual activation and only a mild decrease in auditory cortex. Both maps are displayed at the same statistical threshold (t=8, p<0.0001)

CONCLUSIONS

The results, consistent with the work of Heinke and Schwarzbauer, indicate that the incremental BOLD signal is altered with administration of sevoflurane (changes in baseline state), and varies according to the type of stimulus ranging from small changes for auditory input (12%) to up to 50% change for visual cortex. By using this approach to identify regional activations impacted by anesthetic agents, it will be possible moving forward to design paradigms to specifically test theories of network behavior in cognitive neuroscience.

REFERENCES: 1. Heinke W, Schwarzbauer C, *Anesthesiology*, 94: 973-981, 2001. 2. Kaisti KK, et al, *Anesthesiology*, 99: 603-613, 2003. 3. Hyder F, et al, *NMR in Biomedicine*, 14: 413-431, 2001.

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