Effects of 0.25MAC Sevoflurane on Functional Magnetic Resonance Imaging - In-Vivo Study of Normal Human Subjects and Implications to Data Interpretation

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Introduction: Changes in the blood oxygen level dependent (BOLD) contrast and the regional cerebral blood flow (rCBF) can be used as indices of underlying neuronal activity or metabolism. Under most circumstances increased neuronal activity is associated with a disproportionate increase in rCBF that overcompensates for the increase in oxygen consumption [1,2]. Quantification fMRI uses BOLD and CBF mapping to obtain relative changes in oxidative metabolism (cerebral metabolic rate for O2, CMRO2) [3-5]. This approach is needed to investigate the functionally related activity in the presence of different levels of "baseline" activity induced by anesthetic agents [6,7]. However, it is not clear in these models how this empirical relationship between flow and function is affected by anesthetics. This work presents results demonstrating altered coupling of rCBF, BOLD and CMRO2 in the presence of visual and auditory stimuli during anesthesia with 0.25 *MAC* sevoflurane using simultaneous BOLD and CBF fMRI techniques [8].

Methods: Sixteen consenting healthy human volunteers (19-30yrs old) were given 0.25 *MAC* end-tidal sevoflurane. Visual and auditory activation tasks were presented simultaneously in 30 second on/off blocks and BOLD and rCBF weighted images were acquired (*TR=3s*) across three 20 minute awake cycles and two 20 minute anesthesia cycles. Agent-induced changes in the resting condition (anesthetized vs awake) and stimulus-induced changes in rCBF and BOLD (during both anesthetized and awake) were calculated from the BOLD and rCBF weighted images. Within the visual and auditory regions of interest (ROIs, Fig 1) pooled voxel-wise changes in rCBF and BOLD were extracted and these are plotted in Fig 2 a and b (ΔBOLD the abscissa and ΔCBF along Y) along with linear regression (LR) results.

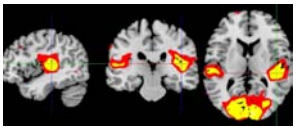

Fig 1 Visual and auditory ROIs on the normalized brain.

Results and Discussions: Several observation we might have from Fig 2: 1) For stimulus-induced changes in both visual and auditory ROIs the slope of the LR line decreased for anesthesia (green) compared to awake (blue), showing statistically unit change in rCBF brought about a bigger change in BOLD, indicating that the oxygen extraction fraction decreased; 2) The LR equations of changes during awake were also different for visual and auditory ROIs, indicating the rCBF, BOLD and CMRO2 coupling varied across cortical regions; 3) The decreased correlation coefficient (*R*) for the auditory ROI during anesthesia compared to awake showed that introduction of an agent may deteriorate the coupling relationship within some of cortical regions; 4) The LR lines for agent-induced changes in resting baseline suggested the effect of an agent on neuronal activity as revealed by CBF and BOLD differed from stimulation – same changes in CBF and/or BOLD induced by an agent and by a stimulus do not necessarily mean same changes in neuronal activity [6] and the CBF/BOLD-CMRO2 mapping has to be recalibrated, which is very important in baseline-related functional component quantification [5,7] to get unbiased results. These results suggest that calibration experiments must be performed in each cortical area of interest and under the same anesthetic conditions that will be used for the experimental conditions if accurate CMRO2 maps are to be obtained. Without taking into account these drug- and tissue- specific effects, quantification of basal neuronal activity and the related brain functions from fMRI data, or analysis of drug effects using fMRI could be biased.

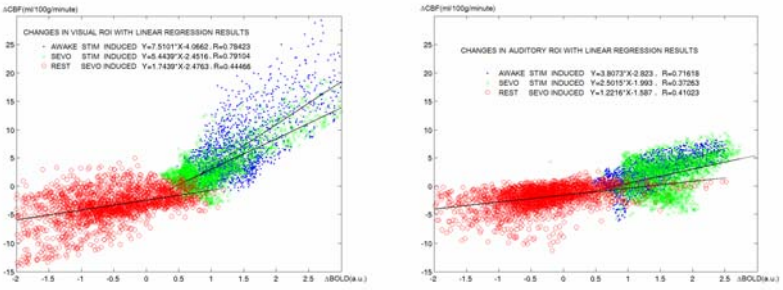

Fig 2 a & b Within visual and auditory ROIs, change in the slop of the LR lines indicates the resetting of the model of inferencing the underlying neuronal activity/metabolism from fMRI data. Mapping from rCBF and BOLD to neuronal activity is not an additive mapping.

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