Spatial Non-Uniformity of the CBF Response to Sevoflurane: Implications for fMRI

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Introduction: Function MRI has been widely used in studying neurophysiological changes associated with brain, and recently a handful of studies have attempted to quantitatively assess the impact of anesthetic agents on baseline brain activity levels [1-3], and the impact of these baseline changes on the functional component of the task induced neuronal activity. Quantitative measures of the change in CMRO2, can be obtained through models relating regional cerebral blood flow (rCBF) and blood oxygen level dependent (BOLD) contrast [2,3,5]. This abstract presents results from a study showing the complicated effects of an anesthetic agent on basal neuronal activity. Most important for fMRI studies, the spatial-specificity of the drug-induced incremental changes in rCBF and the confounding vascular effect of the agent, are investigated.

Methods: Twenty-two consenting healthy human volunteers (19-30yrs old) were given 0.25 *MAC* end-tidal sevoflurane. Arterial spin labeling (simultaneous CBF/BOLD) MRI [6] was performed during awake and the steady-state anesthesia while the subject lay resting with their eyes open and fixating on the "+" presented. The scanning room was darkened so that only a small amount of ambient light was present. Absolute CBF was estimated from perfusion weighted images for the anesthesia and awake periods, and the drug-induced incremental change in rCBF was obtained by comparing the resting periods with and without sevoflurane. The intensity in T2* weighted images of the resting brain was altered by 0.25 MAC sevoflurane relative to awake, and this agent-induced change was also estimated by comparing the resting periods with and without sevoflurane. Considering the agent as a "stimulus", we also call it "change in BOLD", or ΔBOLD in the following discussion.

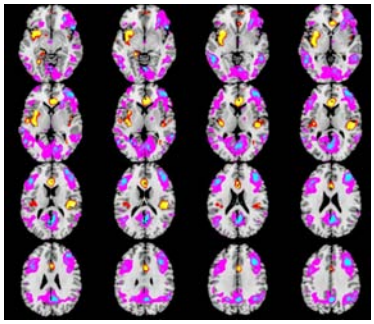

Fig 1 Regions of significant change ($p<0.0001$, t-test) in rCBF induced by 0.25 MAC Sevoflurane.

Results and Discussions: As shown in Fig 1, changes in rCBF during anesthesia compared to the resting baseline was region-specific, both significant increases and decreases in rCBF are seen in different brain regions, resulting in no significant change in global CBF; Increases in rCBF were most likely seen in the vicinity of subcortical structures, ventricles, and insula, while decreases in neocortical regions. In the literature, the spatial non-uniformity of the effects of volatile anesthetics on rCBF and the relation of these changes in rCBF to metabolism remain contradictory, even for low dose sevoflurane anesthesia [4,7]. It is generally believed that changes (either increases or decreases) in rCBF induced by an agent, represent equally well the changes in the underlying neuronal activity. MRI allows not only BOLD imaging but also changes in CBF (ΔCBF, an index of change in oxygen supply) induced in the resting brain by an anesthetic agent. Simultaneously monitoring ΔBOLD and CBF provides an index of change in the tissue oxygen content. Plots of ΔCBF versus ΔBOLD provide information about change in the underlying oxidative metabolism of the resting brain due to an agent. Two sets of regions of interest (ROIs) were defined based on agent-induced changes in rCBF: ROI1, where rCBF was significantly increased (warm in Fig 1), and ROI2, where rCBF was significantly decreased (cool in Fig 1) ($p<0.0001$, t-test). For voxels within ROI1 and ROI2, incremental ΔCBF and ΔBOLD are plotted in Fig 2 (ΔBOLD the abscissa and ΔCBF along Y) along with linear regression (LR) results (blue for ROI1, red for ROI2, respectively). The slopes of the 2 LR lines are almost the same, but their intercepts with Y are different, with a significant shift along Y for ROI1 relative to ROI2. We posit that this was due to a direct vascular dilating effect of the agent, and that the causes for drug-induced increases and decreases in rCBF might be different: in ROI2 (red, where rCBF was decreased) the CBF change was dominated by vasomotor products of metabolism but less disturbed by the direct vascular dilating effect of the agent, while increases in rCBF (in ROI1, blue) were mainly due to direct vascular dilating effect of the agent and less affected by metabolism. When exposed simultaneously to an agent and a stimulus [2,5], ΔCBF and ΔBOLD in a brain region are coupled, and these results indicate that such coupling is regionally dependent.

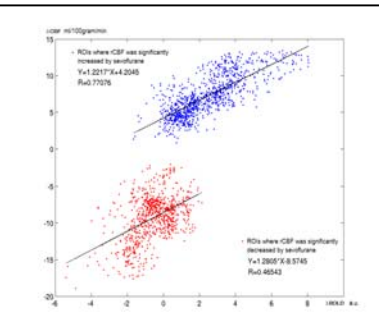

Fig 2 The relationship between anesthetic-induced changes in rCBF and BOLD: blue for SROI1 where rCBF was significantly increased and red for SROI2 where rCBF was significantly decreased.

References: [1] Hoge RD, et al. Proc Natl Acad Sci U S A. 1999 Aug 3; 96(16):9403-8. [2] Hyder F, et al. NMR Biomed. 2001 Nov-Dec; 14(7-8):413-31. [3] Kim SG, et al. Magn Reson Med. 1999 Jun; 41(6):1152-61. [4] Heinke W, et al. British Journal of Ananesthesia 2004; 92(5):641-50. [5] Shulman RG, et al. Proc Natl Acad Sci U S A. 2001 May 22; 98(11):6417-22. [6] Wong EC, et al. Magn Reson Med. 1998 May; 39(5):702-8. [7] Schlunzen L, et al. Acta Anaesthesiol Scand 2004; 48: 1268-1276.

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