Comparison of Anesthetic Effects on the Resting-State CBF between Sevoflurane and Propofol: Similarities, Discrepancies, and their Implications

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Introduction The anesthetic effects of different agents on regional neuronal activity, as reflected by regional cerebral blood flow, have been investigated in recent years, however, variability in results among the studies exists and no consensus has been reached yet. In this study, we use the same techniques, pulsed arterial spin labeling (PASL) MRI, with the similar experiment protocols, to assess the regional CBF changes in healthy human volunteers induced by sevoflurane and propofol. Our hypothesis is, in the presence of an anesthetic, the observed regional CBF is the interplay among local neuronal activity that contributes to the regional changes in CBF via the neurovascular coupling, the distributions of the neuroceptors as the molecular targets of the agent, the neurophysiology of the brain, i.e., the subsystems of the brain that the anesthetic progressively suppressed, and the vascular structure of the brain.

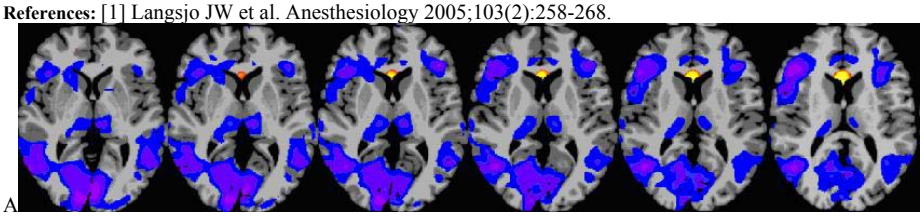
Materials and Methods Total 50 healthy control subjects (19-35 years) underwent pulsed arterial spin-labeling MRI for the resting-state absolute CBF with and without sevoflurane (0.25 MAC) or propofol (2 μg/ml plasma concentration) anesthesia. Magnetic resonance imaging data were acquired on a 3T whole-body scanner Trio (Siemens Medical Systems, Erlangen, Germany) with a 12-channel phased-array head coil. Pulsed arterial spin labeling imaging was used to measure perfusion-induced changes in image signal intensity during the resting state. A 20-slice ASL acquisition was implemented and all slices were AC-PC angled and positioned to fully cover the brain cortex. The ASL acquisition parameters were: field of view FOV = 256×256 mm^2; matrix = 64×64; bandwidth = 2004 Hz/pixel; slice thickness = 5 mm, and inter-slice gap = 2.5 mm. The repetition time was TR = 3000 ms; the echo time was TE = 26 ms. The subjects stayed still with eyes closed in the scanner during the MRI experiment. Two PASL runs, each of 200 volumes, were acquired for the awake condition and for the anesthesia conditions, respectively. BioImage Suite was used for multi-subject quantification.

Results and Discussion Physiological parameters such as end-tidal CO2, heart rate, and mean blood pressure (MAP) and global CBF was not affected by either anesthetics. The spatial patterns of regional CBF changes induced by both anesthetics show certain similarity (Figs. A & B). Suppression of regional CBF occurred extensively in the neocortical regions, whereas increases were limited primarily to some sub-cortical structures. More specifically, for sevoflurane anesthesia (Fig. 1), the middle/inferior frontal gyrus (BA 6-10, 44-47), middle temporal gyrus (Fusiform), primary visual cortex and associative areas, and posterior cingulate gyrus are among the regions with most suppressed regional CBF; for propofol anesthesia (Fig. 2, the middle frontal gyrus (BA 8-11, BA 46 and 47), primary visual cortex and associative areas and thalamus are among the regions where regional CBF was most suppressed. Brain areas around the anterior cingulate and corpus callosum, hippocampus and hippocampal gyrus are where regional CBF was found to increase significantly during both sevoflurane and propofol anesthesia. To further appreciate the similarity of the spatial patterns of regional CBF changes induced by both agents, voxel-based spatial correlation and regression were performed (Fig. C). All changes in regional CBF, whether significant or not, was considered in these plots. The CBF data were resampled into larger "voxels" of ~1.35 cm^3 and the mean CBF values within these regridded "voxels" were used for the X- and Y- coordinates to plot the data. There corrected R = 0.3, reaching a significance of $p < 0.001$. Though the 2 agents we used were different in terms of their vasoactivity – sevoflurane is vasodilative and propofol vasoconstrictive, we observed similar spatial patterns of agent-induced CBF changes. We speculate that these increases in regional CBF are a result of the interplay among several local and global factors. Some authors indicated that some anesthetics would increase regional CBF in excess of the local metabolic demands in the brain [1]. There are several "global" factors that can contribute to this spatial similarity: 1) Anesthetic endpoints have different sensitivities to anesthetics. Autonomic nervous sub-systems, such as cardiovascular responses to anesthetic exposure are very resistant, and require anesthetic concentrations well above those needed to ensure immobility. It has been found that the anterior and posterior hypothalamus, bilateral amygdala, hippocampus, insular cortex, mid/posterior cingulate cortex, right ventral frontal cortex, and temporal and frontal cortices of the brain mediated the automatic nervous system such as cardiovascular abnormality. CBF in these brain areas responsible for the normal functioning of the autonomic nervous sub-systems is less likely affected by anesthetics; and 2) since there were no significant changes in global CBF observed at the concentrations of anesthetics given to the subjects in this study, but we have observed significant decreases in regional CBF, it is not surprising the regions of significantly increased regional CBF coexist in the same time. Local variability in the spatial patterns of CBF changes induced by both agents was related to neuronal activity affected. But for regions with increase CBF, the most likely situation is, local neuronal activity does not necessitate these increases, in other words, increases in regional CBF are not demanded by local neuronal activity but rather "forced" to flow into those regions where regional CBF increases.

Conclusion Interactions between anesthetics and their molecular targets and the distribution of these molecular targets account for local CBF changes and the spatial variability induced by different anesthetics. Spatial resemblance in the CBF changes induced by both anesthetics observed in this study is largely due to the global factors, which have been ignored by researchers in similar studies. Redistributions of flow overshadow the local components in regional CBF especially in subcortical regions where regional CBF is increased during anesthesia. Regional CBF changes should be more representative of changes in local neuronal activity in most of the neocortical regions.

References: [1] Langsjo JW et al. Anesthesiology 2005;103(2):258-268.

A



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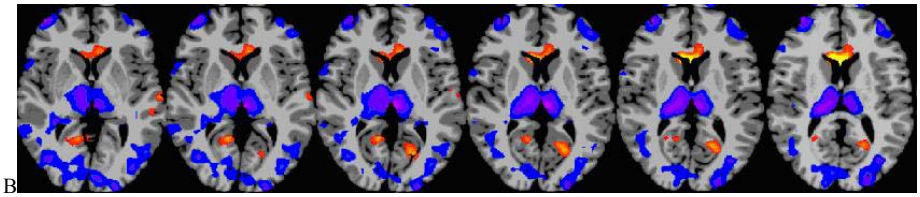

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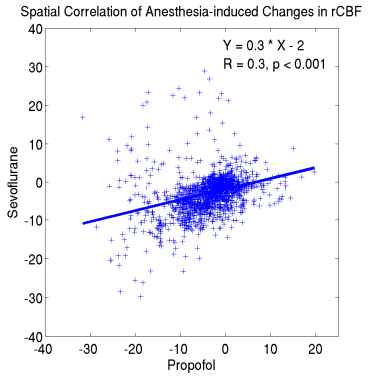

Figs. CBF significantly changed by sevoflurane (A) and by propofol (B), $p<0.05$, and the spatial correlation between regional CBF changes induced by both agents.