Anesthetic Effects of Sevoflurane and Propofol on Regional CBF: a Comparative MRI Study on Normal Subjects and Implications

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Introduction The way by which general anesthetics produce unconsciousness is unclear. Neural imaging techniques have been increasingly used to probe the mechanism that underlies general anesthesia [1,2]. The anesthetic effects on rCBF have been investigated in humans and animals but these investigations have failed to resolve the question of how rCBF is affected [2,3]. Interpretation of observed data has turned out to be even more challenging [4]. Using the arterial spin labeling (ASL) imaging, we have measured agent-induced changes in resting rCBF/perfusion on 37 normal subjects during administration of sevoflurane and propofol. Sevoflurane- and propofol-induced rCBF/perfusion changes are compared and discussed below. The results indicate that anesthetic molecular actions, local vaso-active effects of drug, the brain's global vasculature and auto-regulation should be taken into consideration for a proper data interpretation.

Materials and Methods Thirty-seven consenting healthy subjects (ASA, physical status class I), aged 19-40yrs, were divided into two groups: S-group, 22 subjects under administration of 0.25 MAC sevoflurane, and P-group, 15 subjects given a continuous propofol iv infusion of 120-150μg/kg/minute after 3-minute induction iv infusion of 1~2mg/kg. Subjects on psychoactive drugs or any centrally acting medication were excluded. All the subjects fixated on a white "+" presented against a black background. The scan room was darkened so that only a small amount of ambient light was present. For S-group, two anesthesia sessions were interleaved with 3 anesthesia free sessions, with approximate 10 minutes in between to allow the end-tidal sevoflurane concentration to reach a steady state. Each of the P-group subjects paid two visits for MR imaging: one for propofol anesthesia and the other for anesthesia free and only perfusion images were acquired. Imaging was performed on 3T Trio (S-group) and 1.5T Sonata (P-group) whole-body scanners (Siemens Medical Systems, Erlangen, Germany) with circularly polarized head coils. ASL imaging was performed to measure rCBF during both awake and anesthesia sessions. The maps of drug-induced changes were first estimated for each subject and then a multiple-subject integration process was performed to obtain the composite map for each group.

Results Typical slices of drug-induced rCBF/perfusion changes are shown in Figure 1. Significant changes in global CBF were not observed. Some similarity can be observed for both agents at the given doses: increased rCBF was restricted in the anterior cingulate and bilateral insula; decreased rCBF was found in the posterior cingulate and neocortical regions. Maps of changes in rCBF/perfusion were first low-pass filtered a 2D Gaussian kernel of FWHM 20mm and the whole brain region-based correlation between sevoflurane- (along Y-axis) and propofol-(along X-axis) induced rCBF/perfusion changes (R=0.4, p<0.001) is shown in Figure 2.

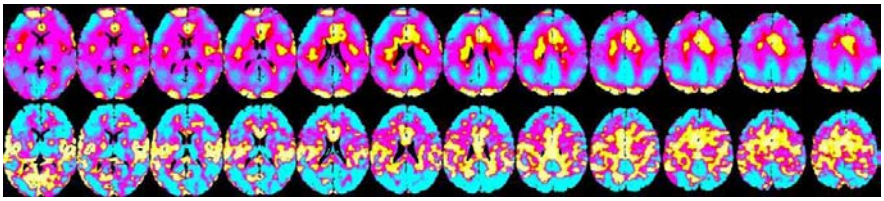

Figure 1 Maps of sevoflurane-(top) and propofol-(bottom) induced rCBF/perfusion changes (positive: red/yellow; negative: pink/blue).

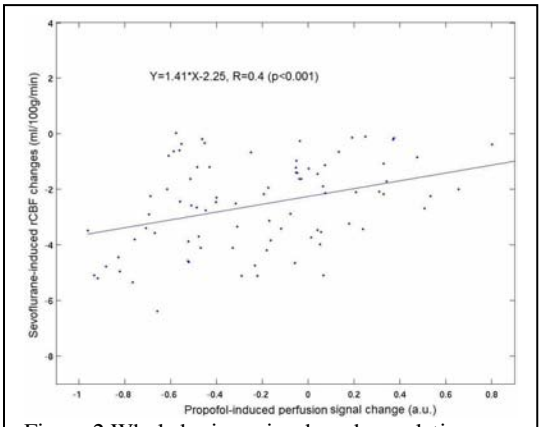

Figure 2 Whole brain region-based correlation between sevoflurane-(Y-axis) and propofol-(X-axis) induced changes (p<0.001).

Discussion It is well known that sevoflurane and propofol have distinctive vaso-active effects: the former is vaso-dilative while the latter vaso-constrictive. When rCBF is measured in the presence of an agent, the rCBF-metabolism coupling is very likely altered because of the direct vaso-active effect of the agent. There has been little evidence showing that in the regions where rCBF is elevated neuronal activity also increases. Therefore the association of functional changes in specific brain regions with resting state regional CBF changes induced by an agent ignores potential changes in the coupling of flow and metabolism and may not be an appropriate way to interpret the data [2]. Since different anesthetics act on different neural receptors [5], it is unlikely that the similar patterns reflect similar molecular actions of both agents, nor does it indicate a unified model as proposed by Alkire et al [6]. It is most likely that the similarity has a non-neuronal origin. We posit that drug-induced changes are balanced, at low dose anesthesia, by the auto-regulatory system, which is least impaired and focused on minimizing global CBF changes, such that significant changes in regional CBF must be accompanied by opposing regional CBF changes in other brain regions. The auto-regulatory system exerts its influence on changes in rCBF and the redistribution of rCBF is constraint by the brain anatomical/vascular structure.

Conclusion Sources for drug-induced changes in rCBF are multiple and include both global and regional control factors. Except for components from changes in neuronal activity and in the local vascular system, the global vasculature of the brain likely exerts a global constraint through the auto-regulatory system, such that some similarity in rCBF maps of changes induced by different anesthetics could be observed.

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