

## **ASA Residents' Research Essay Contest**

Title: EVIDENCE FOR PERSISTENT FLOW-METABOLISM COUPLING DURING HALOTHANE VS ISOFLURANE ANESTHESIA  
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**Introduction.** In the conscious state, changes in cerebral blood flow (CBF) parallel changes in cerebral metabolic rate (CMR). While volatile anesthetics are believed to "uncouple" this relationship(1), recent evidence suggests that anesthetic effects on metabolism may modulate their effects on blood flow(2). The current study was thus designed to further examine the relationship between regional CBF and CMR during halothane (Halo) vs isoflurane (Isof) anesthesia in the rat.

**Methods.** Sprague Dawley rats were anesthetized with either 1 MAC Isof (1.38%) or Halo (1.05%) in 33% O<sub>2</sub>/N<sub>2</sub>. Intubation and insertion of vascular catheters required 35 min. Anesthetic concentrations were then held stable 35 min more while MAP was held at 90-100 mmHg with blood. Temperature (36.8-37.0°C), PaCO<sub>2</sub> (38-42 mmHg), and PaO<sub>2</sub> (110-130 mmHg) were controlled. Local CMRg was then determined by infusion of <sup>14</sup>C-2-deoxyglucose (100 µCi/kg) over 30 sec with timed arterial plasma sampling over the next 45 min. Serial coronal autoradiographs obtained from frozen sections of the brain were analyzed for local CMRg(3) on a computerized image analysis system. At 8 anatomically standardized intervals, hemispheric, neocortical, and subcortical CMRg was determined along with a cortex/subcortex (C/S) CMRg ratio. In addition, current CMRg films, and autoradiographs of CBF obtained under identical experimental conditions(4), were re-examined. A total of eighty 500<sup>2</sup> pixel unit areas were identified over the 8 section levels in each brain sampling a total of 49 anatomic regions. CBF and CMRg values were determined for each area. Mean CBF values for each area within an anesthetic group were plotted vs anatomically corresponding mean CMRg values. Regression analysis of CBF vs CMRg plots was performed and resulting equations compared between anesthetics using an indicator variables statistic.

**Results.** No differences were seen between groups for MAP, pH, PaCO<sub>2</sub>, PaO<sub>2</sub>, or temp. Mean hemispheric, neocortical, and subcortical CMRg as well as the calculated C/S CMRg ratio, were greater during halothane compared to isoflurane anesthesia (Table). This pattern matched that seen for CBF(4). Regression analysis of CBF vs CMRg plots for each anesthetic showed two distinct lines (Halo:  $y = 2.19x - 24$ ,  $r = .84$ ; Isof:  $y = 1.90x + 47$ ,  $r = .78$ ) (Figure). The two lines had distinct Y intercepts ( $p < .001$ ), but similar slopes ( $p = .22$ ).

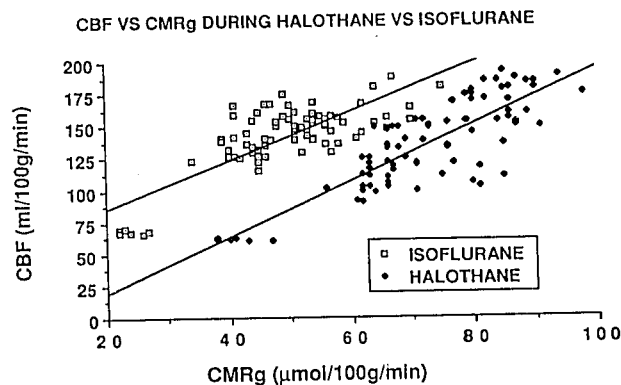
**Discussion.** At 1 MAC levels of Isof or Halo anesthesia in the rat, we have shown a strong correlation between CMR and CBF within individual anatomic regions which is persistent over a wide spectrum of metabolic values. Furthermore, the

cortical and subcortical patterns of CBF distribution for the two drugs reflects the pattern seen for CMRg (although CMRg during Isof was lower). In addition, at a given value for CMRg, CBF during Isof is higher than with Halo. This suggests that CBF and CMR remain coupled and that at a given level of CMRg, isoflurane may possess greater cerebral vasodilating capabilities than halothane.

**References.** 1. Kuramoto T, Oshita S, Takeshita H: *Anesthesiology* 51:211-217, 1979. 2. Drummond JC, Todd MM, Scheller MS, Shapiro HM: *Anesthesiology* 65:462-467, 1986. 3. Sokoloff L, Revich M, Kennedy C et al.: *J Neurochem* 28:897-916, 1986. 4. Hansen TD, Warner DS, Todd MM: (Abstract) *Anesthesiology* 67:A574, 1987.

Region	Halothane (n=8)	Isoflurane (n=8)
Hemisphere	72 ± 9**	49 ± 7
Subcortex	66 ± 10**	47 ± 7
Neocortex	84 ± 9**	54 ± 7
Cortex/Subcortex ratio	1.26 ± .07**	1.16 ± .08
Caudate nucleus	98 ± 7**	64 ± 6
Substantia nigra	75 ± 10**	51 ± 6
Lateral spetal nucleus	62 ± 9**	43 ± 5
Thalamus	81 ± 9**	53 ± 8
Amygdala	64 ± 6**	47 ± 7
Hippocampus	90 ± 10**	66 ± 7
Globus pallidus	62 ± 9**	45 ± 6

**Table:** CMRg (mean±S.D.; µmol/100g/min) in selected regions during 1 MAC Halo vs 1 MAC Isof. Values above the line were area-weighted over eight brain sections. All values are significant (Halo vs Isof).



**Figure:** Flow-metabolism relationships for 80 selected regions during 1 MAC isoflurane vs halothane anesthesia.