Laboratory Investigations

A comparison of the cerebral pressure-flow relationship for halothane and isoflurane at haemodynamically equivalent end-tidal concentrations in the rabbit

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The cerebral pressure-flow relationship for halothane and isoflurane was studied at end-tidal concentrations which resulted in similar baseline mean arterial pressure (MAP). Two groups of New Zealand white rabbits (n = 8; each group) were studied with five regional blood flow determinations in each animal. Blood flow was determined by injecting radioactive microspheres during the following conditions: injection 1: after stable 2.05 per cent end-tidal isoflurane (1.0 MAC) Group I; or after stable 0.74 ± 0.04 per cent end-tidal halothane (0.53 MAC) Group H. Injections 2–5: after MAP was increased 20, 40, 60, and 80 per cent respectively above baseline MAP by phenylephrine infusion. Baseline MAP was the same for both groups (64.3 ± 3.1 vs 67.2 ± 2.0 mmHg; mean ± SEM; Group I and H respectively). Baseline total CBF (tCBF; 0.68 ± 0.03 vs 0.86 ± 0.05) and hemispheric CBF (hCBF; 0.64 ± 0.03 vs 0.96 ± 0.06) were significantly greater in Group H; no significant difference between groups was seen for baseline posterior fossa CBF (pCBF; 0.79 ± 0.06 vs 0.75 ± 0.04). For each experiment a pressure-flow curve was generated by curvilinear regression analysis. Significantly greater phenylephrine concentrations were required for injections 2–5 in Group H. Mean slopes and intercepts were derived for each group. Within each group comparison of the pressure-flow curves for hCBF vs MAP and pCBF vs MAP showed autoregulation was less impaired in posterior fossa structures (cerebellum and brain stem) for both anaesthetic agents ($P \leq 0.05$). For all regions examined, the slope of the pressure-flow curve was significantly less steep during 1.0 MAC isoflurane anaesthesia, indicating cerebrovascular autoregulation was less impaired with isoflurane.

Key words
ANAESTHETICS, VOLATILE: isoflurane, halothane;
BRAIN: blood flow;
SYMPATHETIC NERVOUS SYSTEM, PHARMACOLOGY: phenylephrine.

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Chez deux groupes de huit lapins blancs de la Nouvelle-Zélande anesthésiés avec soit 2,05 pour cent (1,0 MAC) d'isoflurane ou 0,74 ± 0,04 pour cent (0,53 MAC) d'halothane (mesurés en fin d'expiration) de façon à obtenir une pression artérielle moyenne de départ semblable (64,3 ± 3,1 vs 67,2 ± 2,0 mmHg; moyenne ± erreur-type), nous avons mesuré le débit sanguin cérébral (DSC) par injection de microsphères radioactives. Nous avons ensuite répété cette mesure quatre fois sous perfusion de phényléphrine alors que la pression artérielle s'élevait à 120, 140, 160 et 180 pour cent de sa valeur de base. Au départ, le DSC global était plus faible avec l'isoflurane (0,68 ± 0,03 vs 0,86 ± 0,05 $ml \cdot g^{-1} \cdot min^{-1}$) tout comme le DSC hémisphérique (0,64 ± 0,03 vs 0,96 ± 0,06) tandis que le DSC de la fosse

postérieure était semblable dans les deux groupes (0,79 ± 0,06 vs 0,75 ± 0,04). On du utiliser plus de phényléphrine pour augmenter la pression sous halothane que sous isoflurane. Pour chaque groupe, nous avons pu établir la pente et l'origine moyennes des courbes pression-débit générées par régression curvilinéaire. Ces courbes nous ont permis de constater que dans les deux groupes, l'autorégulation était moins altérée dans les structures de la fosse postérieure (cervelet et tronc cérébral) que dans celles des hémisphères ($P < 0,05$). Par ailleurs, dans toutes les structures étudiées, et aux doses employées, l'autorégulation cérébrovasculaire était mieux conservée avec l'isoflurane qu'avec l'halothane.

If mean arterial pressure (MAP) is supported by vasopressor administration, cerebral blood flow (CBF) increases with increasing end–tidal anaesthetic concentration. In addition, cerebrovascular autoregulation becomes increasingly impaired, i.e., the autoregulatory curve shifts upward and to the left.[1] Animal studies have conclusively shown that when halothane and isoflurane are compared at 1.0 MAC, CBF is greater with halothane.[2–4] The cerebrovascular effects of these two agents are characteristically compared at the same MAP as supported by vasopressor infusion. In these studies, animals administered halothane have consistently required greater vasopressor concentrations to achieve the same baseline MAP.[2–4] Thus, the interpretation of the differences seen in CBF with the two volatile agents may be confounded by how the vasopressor itself influences CBF. If the vasopressor chosen for a given pressure-flow study had no direct influence on cerebrovascular tone then different vasopressor concentrations are of no consequence. However, if the chosen vasopressor resulted in cerebrovasoconstriction or indirect cerebrovasodilatation then true CBF during halothane anaesthesia would respectively be greater or less than observed. Baseline CBF or pressure-flow characteristics for these two volatile agents have not been compared at end–tidal concentrations that result in similar unsupported MAP. When compared in this fashion the confounding influence of the vasopressor on CBF is thereby eliminated.

In this study we have compared regional CBF and cardiac output in rabbits under two circumstances (1) 1.0 MAC isoflurane and (2) 0.53 MAC halothane. These end–tidal concentrations resulted in similar unsupported MAP in both groups. We also assessed regional cerebrovascular autoregulation in both groups during phenylephrine-induced increases in MAP. The MAP was increased up to 80 per cent above baseline values in both groups in incremental increases of 20 per cent to determine if cerebrovascular autoregulation was better maintained with either agent at haemodynamically equivalent end–tidal concentrations.

Methods

These experiments were approved by the Animal Care Committee of the University of Manitoba. New Zealand white rabbits (2.5–3.5 kg) were placed in a plexiglass box and anaesthetized with a free flow of either five per cent isoflurane in oxygen (Group I) or five per cent halothane in oxygen (Group H) at 6 $L \cdot min^{-1}$. The animals were then paralyzed with succinylcholine, 40 mg IM, their tracheas intubated and lungs ventilated with either 1.0 MAC end–tidal isoflurane (2.05 per cent)[4] or halothane (1.40 per cent)[4] as continuously monitored by an infrared anaesthetic agent analyzer (Beckman LB-2). Both agents were delivered from calibrated agent specific vaporizers (Ohio Medical Products). End–tidal CO_2 was continuously monitored by a Puritan-Bennett 223 CO_2 monitor and maintained at 35–40 mmHg. Rectal temperature was maintained at 38 ± 1° C by a servo-controlled heat lamp. A polyethylene catheter (PE-90) was inserted into each femoral artery for pressure monitoring or blood withdrawal. Normal saline (6 $ml \cdot kg^{-1} \cdot hr^{-1}$) was infused via a femoral vein catheter. A left thoracotomy was performed and a left atrial (LA) catheter inserted for radioactive microsphere injection. The animals were turned prone and the head secured in the sphinx position in a stereotactic head frame. A dorsal neck skin incision was made and a 22-gauge paediatric spinal needle was inserted by micromanipulator into the cisterna magna for continuous intracranial pressure (ICP) monitoring. Blood pressure and ICP were recorded at end–expiration using calibrated Gould P23 transducers referenced to the level of the cisterna magna. Left atrial pressure (LAP) was recorded at end expiration at mid-chest level.

Following surgery of approximately 45 min duration, all wound edges were infiltrated with 0.25 per cent bupivicaine and pancuronium 2 mg IV was administered for muscle paralysis. In Group I ($n = 8$) isoflurane (1.0 MAC end–tidal) was administered for one hour prior to the first injection of radioactive microspheres. In Group H ($n = 8$) halothane concentration was decreased until baseline MAP was similar to that seen in Group I. This end–tidal concentration was maintained until one hour had elapsed prior to microsphere injection.

Data were recorded on paper by a Gould oscillograph and on hard disk using an IBM PC-AT computer-based digital acquisition system (Dataq Instruments). Arterial blood gases (ABG) and haemoglobin concentration were measured immediately before and after radioactive microsphere injection.

Five microsphere injections were made in each animal. Injection 1: 1.0 MAC isoflurane (Group I), or a stable end–tidal halothane concentration (Group H) that resulted in a similar MAP as in Group I; Injections 2–5: after MAP was increased to 20, 40, 60 and 80 per cent respectively

above baseline MAP by infusion of phenylephrine (120 $\mu g \cdot ml^{-1}$) at constant end-tidal anaesthetic concentration. To achieve each 20 per cent increase in MAP, the phenylephrine infusion rate was increased over ten minutes then maintained at this level for five to ten minutes prior to injection of radioactive microspheres.

Regional blood flows were determined by LA injection of approximately 300,000–500,000 (15 μm diameter) microspheres of either ^{46}Sc, ^{85}Sr, ^{141}Ce (3M Company) or ^{95}Nb, ^{113}Sn (New England Nuclear).[5,6] The selection of microspheres was randomized. Total counts $\cdot min^{-1}$ in each syringe before and after microsphere injection were measured by gamma counter (LKB Compugamma). Using a Harvard pump, blood (3.0 ml) was withdrawn from the femoral artery over 120 seconds starting 20 seconds before each microsphere injection.

After the fifth microsphere injection, the ventilator was disconnected and the animal decapitated. The brain was removed and the pia mater stripped from the surface. The right and left frontal, parietal and occipital cortex, cerebellum, and brain stem were weighed in glass vials. The organ and blood samples were placed in the gamma counter. Counts $\cdot min^{-1}$ were converted to regional blood flow ($ml \cdot g^{-1} \cdot min^{-1}$) and cardiac output (CO) ($ml \cdot min^{-1}$) by computer as previously described.[7]

Total brain blood flow (tCBF) in $ml \cdot g^{-1} \cdot min^{-1}$ was determined by summing weighted flows to all brain regions and dividing by total brain weight. Similarly, hemispheric CBF (hCBF) and posterior fossa CBF (pCBF) were determined by the summation of weighted flows to the cerebral hemispheres and posterior fossa structures (cerebellum and brain stem) respectively. Cerebral perfusion pressure (CPP) was calculated as MAP–mean ICP.

Statistical methods

Time-related changes for each group were evaluated by analysis of variance (ANOVA) for repeated measures. Within and between group comparisons were made using the least squares means test. Bonferroni's correction was applied ($P \leq 0.05/n$; where n = number of comparisons) when multiple comparisons were made. The corrected P-value was considered statistically significant. Data is presented as mean ± SEM, $n = 8$ for each group.

For each experiment, curvilinear regression analysis of the raw data relating pressure to flow yielded curves of the form $y = Ae^{Bx}$ (Figure 1a and b). In all instances the data could be successfully fit to the equation shown. The correlation coefficient was higher for the majority of curves analyzed in this fashion than by linear regression analysis. The mean slope (B) and mean intercept (A) of tCBF vs MAP, hCBF vs MAP and pCBF vs MAP were derived for each group. Within and between group comparisons of the mean slopes and intercepts were made by Tukey's studentized range test; $P \leq 0.05$ was considered significant.

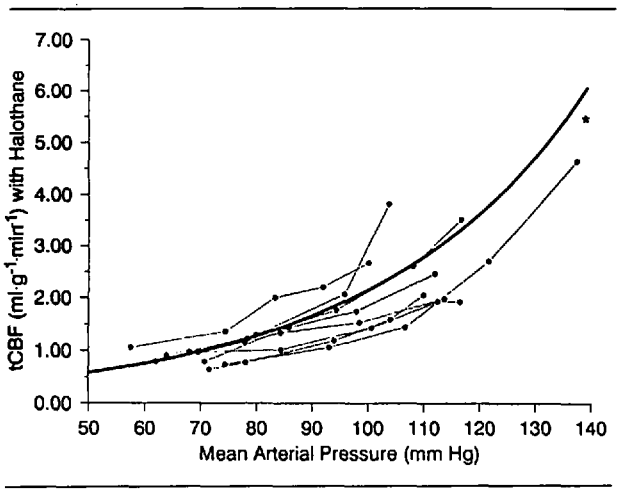

FIGURE 1a Plot of tCBF vs MAP of the raw data from the eight experiments in group H. The equation of the solid line is $y = 0.16e^{0.026x}$ as derived from curvilinear regression analysis of pressure-flow data from the eight experiments; $*P \leq 0.05$ vs mean slope in Figure 1b.

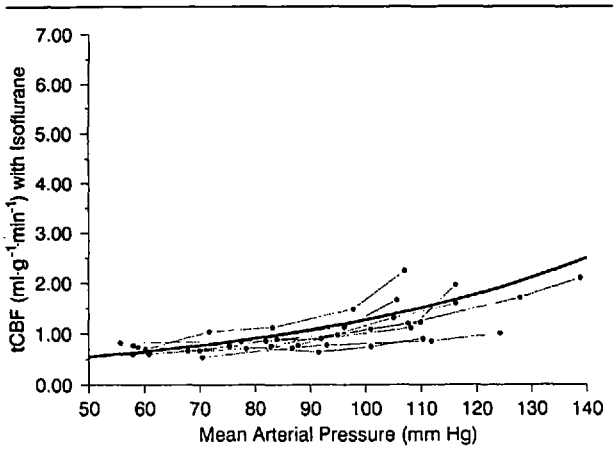

FIGURE 1b Plot of tCBF vs MAP of the raw data from the eight experiments in Group I. The equation of the solid line is $y = 0.23e^{0.016x}$ as derived from curvilinear regression analysis of pressure-flow data from the eight experiments.

Results

The experimentally controlled variables are shown in Table I. An end-tidal concentration of 2.05 per cent (1.0 MAC) isoflurane resulted in a baseline MAP of 64.3 ± 3.1 mmHg. An end-tidal concentration of 0.74 ± 0.04 per cent (0.53 MAC) halothane resulted in a similar MAP of 67.2 ± 2.0 mmHg. There were no differences in MAP or $PaCO_2$ between groups at any time period. For both groups ICP increased for the latter injection periods.

TABLE I Experimentally controlled variables: Group I vs Group II

Variable		*Baseline*	*Flow 2*	*Flow 3*	*Flow 4*	*Flow 5*
MAP (mmHg)	I	64.3 ± 3.1	79.2 ± 3.8†	89.6 ± 3.2†	105.4 ± 3.9†	116.6 ± 4.3†
	H	67.2 ± 2.0	81.5 ± 2.1†	94.7 ± 2.8†	106.6 ± 3.2†	115.8 ± 5.1†
ICP (mmHg)	I	2.9 ± 0.5	3.1 ± 0.5	3.4 ± 0.4	3.7 ± 0.3	5.0 ± 0.7*†
	H	2.1 ± 0.6	2.4 ± 0.5	3.6 ± 0.6	5.1 ± 0.9†	6.7 ± 1.1†
CPP (mmHg)	I	61.4 ± 3.0	76.1 ± 3.8†	86.2 ± 3.2†	101.7 ± 3.8†	111.7 ± 4.4†
	H	65.5 ± 2.4	79.5 ± 2.2†	91.5 ± 2.9†	102.0 ± 3.9†	109.8 ± 5.6†
LAP (mmHg)	I	1.1 ± 0.2	1.7 ± 0.2	2.1 ± 0.2	2.8 ± 0.3	4.1 ± 0.7
	H	1.9 ± 0.7	5.3 ± 1.3	10.4 ± 3.5*†	12.1 ± 1.3*†	16.2 ± 1.8*†
HGB (gm %)	I	13.6 ± 0.3	13.3 ± 0.4	13.1 ± 0.4	13.0 ± 0.4	12.6 ± 0.4†
	H	13.2 ± 0.6	12.7 ± 0.6	12.2 ± 0.5*†	11.3 ± 0.6*†	10.2 ± 0.8*†
$PaCO_2$ (mmHg)	I	37.1 ± 0.4	36.8 ± 0.4	36.9 ± 0.5	37.0 ± 0.6	37.5 ± 0.5
	H	38.0 ± 0.4	37.4 ± 0.6	37.7 ± 0.4	37.5 ± 0.6	37.6 ± 0.4
pH	I	7.41 ± 0.02	7.38 ± 0.02	7.35 ± 0.02†	7.32 ± 0.02†	7.29 ± 0.02†
	H	7.36 ± 0.01	7.35 ± 0.02	7.31 ± 0.02*†	7.26 ± 0.03*†	7.17 ± 0.04*†
PE infusion	I		8.5 ± 0.7	12.8 ± 1.2	16.9 ± 1.3	21.1 ± 1.5
	H		15.3 ± 2.0*	28.6 ± 8.1*	63.5 ± 26.1*	137.2 ± 30.9*
CO ($ml \cdot min^{-1}$)	I	472 ± 46	385 ± 36	388 ± 46	341 ± 32	325 ± 42
	H	506 ± 58	363 ± 40	263 ± 25*†	226 ± 22*†	150 ± 32*†

I = 1.0 MAC isoflurane.
H = 0.53 MAC halothane.
Mean ± SEM, $n = 8$ for each group except for Flow 5 with H, $n = 6$.
PE = phenylephrine in $\mu g \cdot kg^{-1} \cdot min^{-1}$.
*$P \leq 0.05$ between groups.
†$P \leq 0.05$ within groups vs baseline.

However, a significant difference in ICP between groups was only present for the final comparison being higher in Group H. At all times a significantly higher infusion rate of phenylephrine was needed in Group H. Significantly lower haemoglobin concentrations and arterial pH were seen in Group H for the latter injection periods. The acidosis was not treated. The CO was lower for the last three flow measurements in Group H indicating a failing left ventricle as evidenced by increased LAP. Only six observations were obtained for Flow 5 in this group as MAP could not be increased to the required level in two of eight animals despite massive doses of phenylephrine.

Baseline rCBF data for both groups are shown in Table II. The baseline tCBF and hCBF were significantly higher with halothane than isoflurane. No difference was seen between groups for baseline pCBF.

The raw pressure-flow data from each experiment were analyzed using curvilinear regression analysis to obtain a slope and intercept. The raw pressure-flow tCBF data for each experiment for the two volatile agents and the derived mean exponential curves are shown in Figure 1a and b. Figures 2 and 3 show the derived mean exponential curves for halothane and isoflurane for cerebral hemispheric and posterior fossa blood flow respectively. In all regions studied, the slope of the regression line for animals anaesthetized with isoflurane was less steep ($P \leq 0.05$, Tukey's studentized range test) indicating that cerebrovascular resistance (CVR) was greater with isoflurane at a given MAP than with halothane. The distribution of rCBF was markedly different for the two anaesthetic agents (Figures 4 and 5). For isoflurane baseline pCBF was higher than hCBF but the reverse with higher MAP. In contrast, with halothane, hCBF was always greater than pCBF.

TABLE II Baseline regional cerebral blood flows

Agent	*tCBF*	*hCBF*	*pCBF*
I	0.68 ± 0.03	0.64 ± 0.03	0.79 ± 0.06
H	0.86 ± 0.05*	0.96 ± 0.06*	0.75 ± 0.04

I: 1.0 MAC Isoflurane, $n = 8$.
H: 0.53 MAC Halothane, $n = 8$.
Mean ± SEM.
All flows are in $ml \cdot g^{-1} \cdot min^{-1}$.
tCBF: total cerebral blood flow.
hCBF: cerebral hemispheric blood flow.
pCBF: posterior fossa cerebral blood flow.
*$P \leq 0.05$ between groups.

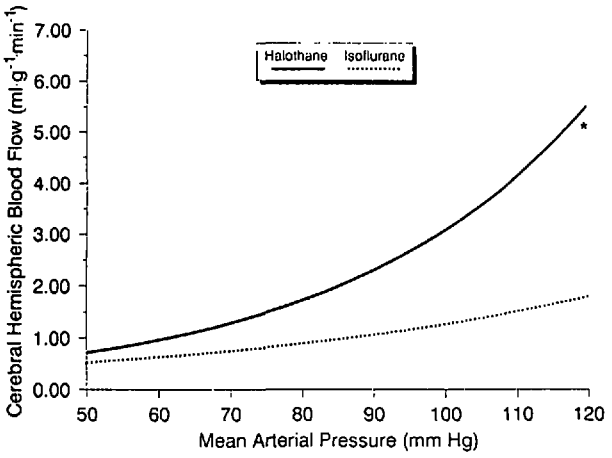

FIGURE 2 Plot of hCBF vs MAP of the derived exponential equations for Group H and I; the equation of the line for Group H is $y = 0.17e^{0.029x}$ and for Group I is $y = 0.21e^{0.018x}$; $*P \leq 0.05$ comparison of mean slopes.

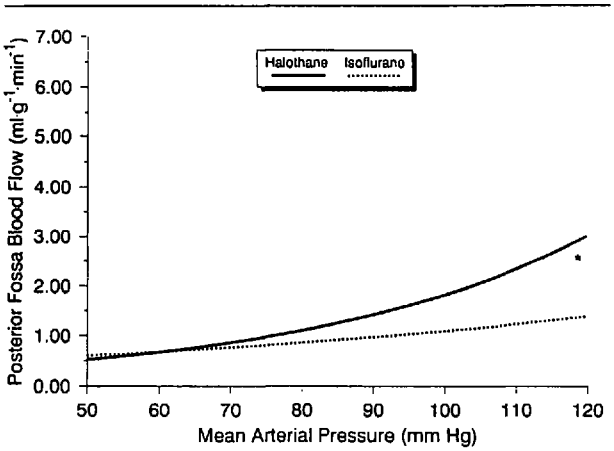

FIGURE 3 Plot of pCBF vs MAP of the derived exponential equations for Group H and I; the equation of the line for Group H is $y = 0.15e^{0.025x}$ and for Group I is $y = 0.33e^{0.012x}$; $*P \leq 0.05$ comparison of mean slopes.

Discussion

In this study in rabbits, we have compared the regional blood flow effects of 1.0 MAC isoflurane and 0.53 MAC halothane (end–tidal concentrations which resulted in the same baseline MAP unsupported by vasopressor). We have specifically administered the two volatile agents in oxygen to avoid confounding influences of N_2O or fixed anaesthetic agents. We have demonstrated that baseline tCBF is significantly higher with 0.53 MAC halothane than for 1.0 MAC isoflurane. Although impaired with both agents, cerebrovascular autoregulation was better

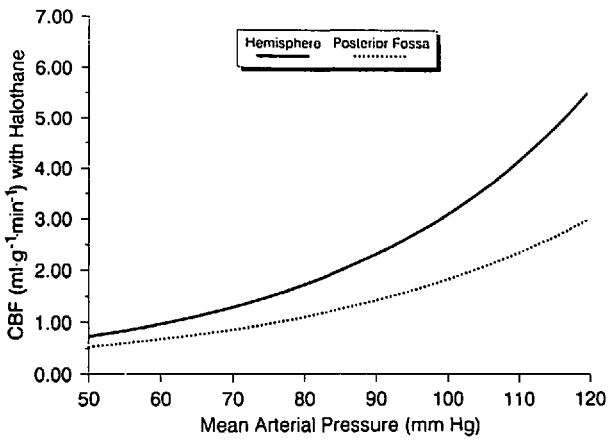

FIGURE 4 Plot of hCBF vs MAP and pCBF vs MAP with halothane; $*P \leq 0.05$ comparison of mean slopes.

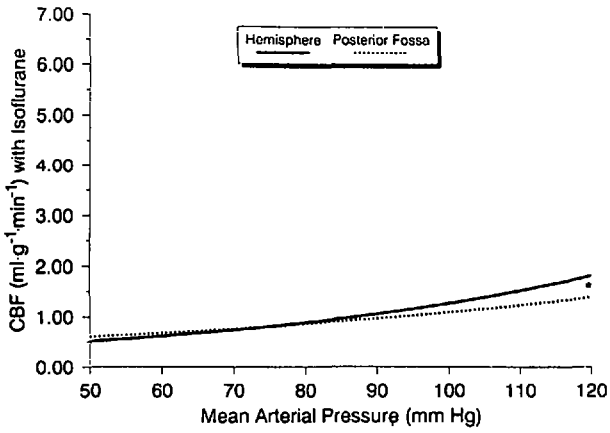

FIGURE 5 Plot of hCBF vs MAP and pCBF vs MAP with isoflurane; $*P \leq 0.05$ comparison of mean slopes.

preserved with 1.0 MAC isoflurane for all regions examined. In addition significant differences in supratentorial vs infratentorial rCBF were seen with autoregulation better preserved in posterior fossa structures for both anaesthetic agents. We have also demonstrated that 0.53 MAC halothane is a more potent myocardial depressant than 1.0 MAC isoflurane in the rabbit. This effect became manifest when MAP was increased by phenylephrine infusion and probably accounts for the greater vasopressor concentrations required in animals receiving halothane when the cerebrovascular effects of 1.0 MAC halothane and isoflurane were compared at similar MAP in previous experiments.[2–4] We have been unsuccessful in our attempt to eliminate the confounding influence of different vasopressor concentrations despite comparing

halothane and isoflurane at haemodynamically equivalent end–tidal concentrations.

However, baseline tCBF was 26 per cent higher with halothane independent of vasopressor effects. In a pilot study we found that rabbits anaesthetized with 1.0 MAC halothane in oxygen had a tCBF of 0.89 ± 0.07 $ml \cdot g^{-1} \cdot min^{-1}$ (mean ± SEM; $n = 5$) at an unsupported MAP of 36.5 ± 6.9 mmHg with $PaCO_2$ of 38.2 ± 0.8 mmHg. This MAP is below the autoregulatory threshold in the awake rabbit[8] suggesting CBF would be pressure passive at 1.0 MAC halothane. Thus, with MAP supported by vasopressor, CBF during 1.0 MAC halothane would be significantly higher than with 1.0 MAC isoflurane. Others have demonstrated such findings when equal anaesthetic concentrations of isoflurane and halothane were compared at equal supported MAP. In these studies higher concentrations of vasopressors were required in the group of animals anaesthetized with halothane.[2–4] It is possible that the differences in CBF seen may have been influenced by the requirement for vasopressor administration as recent evidence indicates some vasopressors have direct cerebrovascular effects.[9–11] Our results allow us to conclude that in the rabbit, in the presence of volatile agents, phenylephrine causes minimal vasoconstriction of the cerebral vasculature even when infused in massive doses. However, we cannot eliminate the possibility of indirect cerebral vasodilatation during phenylephrine infusion.

A consistent finding of greater CBF with halothane vs isoflurane with or without vasopressor support in our study suggests that the lower CVR seen with halothane is a consequence of the drug itself. In this study, baseline CBF was lower with 1.0 MAC isoflurane at an end–tidal concentration nearly double that for halothane at similar MAP and $PaCO_2$. Such differences may be a consequence of lower CMR_{oxygen} with 1.0 MAC isoflurane and closer CBF/CMR_{oxygen} coupling with this agent.[4] Another explanation for higher rCBF with 0.53 MAC halothane may be on the basis of arousal. The EEG was not monitored in this study so the presence of cortical arousal has not been assessed. Such arousal would presumably be associated with increased sympathetic outflow. The observation that baseline MAP and heart rate (290 ± 9 and 292 ± 6 for Group I and H respectively) were identical for the two groups of animals suggests little difference in sympathetic activity. In the latter injection periods significant decreases in haemoglobin concentration would presumably have contributed to higher tCBF in the group administered halothane (a consequence of decreased viscosity and oxygen delivery). However, for the first two injection periods the haemoglobin concentration was not different between groups. Decreased pH in the latter injection periods in Group H may in part explain the large doses of phenylephrine required.[12]

Indirect cerebrovasodilatation secondary to centrally mediated effects of phenylephrine cannot be ruled out by our study. Such effects could be due to direct neuronal stimulation following blood brain barrier (BBB) disruption or stimulation of central adrenergic pathways. The possibility of BBB disruption seems unlikely for a number of reasons. In this experiment the elevations in MAP were relatively modest (at most 50 mmHg). Elevations of MAP of greater than 80 mmHg are necessary to compromise the BBB in rabbits.[13] The MAP increases were gradual (over 5–10 mins) and only abrupt increases in MAP are associated with BBB compromise. Halothane anaesthesia does not effect BBB function.[14] As well, central stimulation of the CNS by catecholamines is felt to be a β-effect,[15] an effect not likely with the α-agonist phenylephrine. Recent evidence suggests that α-agonists contribute to increased CBF during hypoxia, an effect which may be centrally mediated.[16] If such were the case, in our experiments we might anticipate similar percentage increases in CBF at similar phenylephrine concentrations in the two groups, an effect not seen.

Regional blood flow to the cerebral hemispheres was consistently lower with 1.0 MAC isoflurane than with 0.53 MAC halothane regardless of MAP. These results conflict with work recently published by Hansen *et al.*[17] Using an autoradiographic technique they demonstrated higher neocortical blood flow with 1.0 MAC halothane vs 1.0 MAC isoflurane in rats, but global hemispheric blood flow was not different. Differences in species, anaesthetic depth, blood viscosity and technique used to assess CBF may account for the differences seen.

With both anaesthetic agents autoregulation was better preserved in posterior fossa structures (cerebellum and brain stem) or alternatively phenylephrine may have preferentially increased cerebrovascular tone in this vascular bed. Well preserved autoregulation was especially evident with isoflurane. Previous workers have documented higher cerebellar blood flow with isoflurane anaesthesia[18–20] and have speculated that cerebellar autoregulation could be impaired.[19] Our results suggest that such is not the case. If applicable to the clinical setting these findings suggest isoflurane may be especially suitable for posterior fossa surgery (high basal flow to these vital structures with well preserved cerebrovascular autoregulation). Well preserved autoregulation is to be preferred as marked fluctuations in MAP are common during posterior fossa surgery. Additional work in at least a primate model seems necessary to confirm the clinical implications of this finding.

Despite greater tCBF in Group H, ICP was significant-

ly higher in animals administered halothane only for the final between-group comparison. We propose that these findings can be explained by different relative changes in the inflow and outflow resistance for halothane vs isoflurane. Thus, inflow and outflow resistances were essentially changing in concert with halothane as minimal changes in ICP occurred despite marked increases in tCBF with increased MAP. In contrast, isoflurane had demonstrably less effect on inflow resistance but appears to have an even smaller effect on outflow resistance, thereby accounting for larger capacitive changes with resultant higher ICP at lower CBF. Todd and Drummond have previously documented in cats that at equal anaesthetic doses of isoflurane and halothane (from 0.5–1.5 MAC) ICP was not different despite significantly higher parietal cortical CBF with halothane.[2] These authors have also demonstrated that 0.5 MAC halothane and 1.0 MAC isoflurane resulted in identical cerebral cortical protrusion (an indirect assessment of cerebral blood volume).[21] In dogs cerebral blood volume increased 9–11 per cent with 1.0 MAC isoflurane[22] and 11–12 per cent with 1.0 MAC halothane.[23] Our results suggest that the differences these agents induce in intracranial compliance only become manifest with significant increases in MAP in normal brain at the concentrations, MAP and $PaCO_2$ levels tested. The possible implications of this finding must be tempered by the fact that isoflurane results in a steeper CO_2 response curve[2] and our comparison was during normocapnia in normal brain.

In conclusion, using radioactive microsphere methodology we have examined the cerebral pressure-flow relationship for halothane and isoflurane at haemodynamically equivalent end–tidal concentrations. We have demonstrated that 1.0 MAC isoflurane is associated with significantly lower total CBF than 0.53 MAC halothane at similar MAP unsupported by vasopressors. Cerebrovascular autoregulation was better maintained in posterior fossa structures than in the cerebral hemispheres for both agents. At the end–tidal concentrations examined, cerebrovascular autoregulation was better maintained with 1.0 MAC isoflurane than with 0.53 MAC halothane for all regions examined.

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