Laboratory Investigation

Haemodynamic and organ blood flow responses to sevoflurane during spontaneous ventilation in the rat: a dose-response study

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To determine the systemic haemodynamic and organ blood flow responses to the administration of sevoflurane during spontaneous ventilation, heart rate, cardiac index, mean arterial pressure, arterial blood gases, and blood flows to the brain, spinal cord, heart, kidneys and splanchnic organs were measured awake (control values) and after 30 min of anaesthesia with 0.5, 1.0, 1.2 or 1.5 MAC sevoflurane in rats. Cardiac output and organ blood flows were measured using radiolabelled

microspheres. The MAC (mean $\pm$ SEM) of sevoflurane was found to be $2.30 \pm 0.05\%$. At each concentration, haemodynamic variables were similar to awake values with the exception of a 12% reduction in mean arterial pressure at 1.5 MAC ($P < 0.01$). Arterial PCO_2 increased in a dose-related fashion. Cerebral and spinal cord blood flows increased at 1.2 and 1.5 MAC whereas coronary and renal blood flows did not change significantly. Portal tributary blood flow and preportal vascular resistance were unaffected. Hepatic arterial flow increased by 63% at 1.5 MAC ($P < 0.05$) but total liver blood flow remained unchanged compared with awake values. In conclusion, the administration of sevoflurane during spontaneous ventilation produces a high degree of cardiovascular stability and maintains blood flow to major organs in the rat.

Key words

ANAESTHETICS, VOLATILE: sevoflurane;

BRAIN: blood flow;

HEART: blood flow, myocardial, cardiac output;

KIDNEY: blood flow;

LIVER: blood flow;

MEASUREMENT TECHNIQUES: blood flow, microspheres;

POTENCY, ANAESTHETIC: MAC;

SPINAL CORD: blood flow.

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Supported in part with grants from the Medical Research Council of Canada and Maruishi Pharmaceuticals Inc, Osaka, Japan.

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Accepted for publication 7th October, 1991.

Afin de déterminer les réponses de l'hémodynamique systémique et du débit sanguin aux organes face à l'administration de sévo-flurane sous ventilation spontanée, la fréquence cardiaque, l'index cardiaque, la tension artérielle moyenne, les gaz sanguins artériels, et les débits sanguins au cerveau, à la moëlle épinière, au coeur, aux reins et aux organes splanchniques ont été mesurés chez les rats éveillés (valeur de contrôle) et après 30 minutes d'anesthésie avec 0,5, 1,0, 1,2 et 1,5 MAC de sévo-flurane. Le débit cardiaque et les débits sanguins aux organes ont été mesurés en utilisant des microsphères marquées aux radioisotopes. Le MAC (moyenne $\pm$ SEM) du sévo-flurane a été évalué à $2,30 \pm 0,05\%$. A chaque concentration, les variables hémodynamiques étaient semblables aux variables en état d'éveil, à l'exception d'une réduction de 12% de la tension artérielle moyenne à 1,5 MAC ($P < 0,01$). La PCO_2 artérielle augmentait proportionnellement à la dose. Les débits sanguins cérébraux et de la moëlle épinière augmentaient à 1,2 et 1,5 MAC, tandis que les débits sanguins coronariens et rénaux n'ont

pas changé de façon significative. Le débit sanguin tributaire portal et la résistance vasculaire préportale n'étaient pas affectés. Le débit sanguin hépatique augmentait de 63% à 1,5 MAC ($P < 0,05$) mais le débit sanguin hépatique total demeurait inchangé comparativement aux valeurs en état d'éveil. En conclusion, l'administration de sévoflurane sous ventilation spontanée produit un haut degré de stabilité cardiovasculaire et maintient le débit sanguin aux organes majeurs chez le rat.

In the quest for the ideal inhalational anaesthetic, the halogenated ethers continue to be investigated. Sevoflurane (fluoromethyl 2,2,2-trifluoro-1-[trifluoromethyl] ethyl ether) is a halogenated methyl-isopropyl ether which is undergoing phase-3 clinical trials in Canada and the United States, and is marketed for clinical use in Japan. Sevoflurane provides a rapid and smooth inhalational induction of anaesthesia.¹ This property is particularly desirable in paediatric anaesthetic practice and is attributed to the low blood gas partition coefficient of 0.6² and non-irritating odour of this anaesthetic agent.

The haemodynamic and organ blood flow responses to the administration of sevoflurane during spontaneous ventilation remain unclear. Although one study has reported the effects of sevoflurane on organ blood flows in spontaneously breathing swine,³ awake haemodynamic values in that study were elevated compared with other reported values for swine.^{4,5} Another study reported the cardiovascular effects of sevoflurane in animals ventilated to maintain normocarbia.⁶ However, the results of that study cannot be extrapolated to the spontaneously breathing animal since both positive pressure ventilation^{7,8} and elevated levels of carbon dioxide^{8,9} have considerable haemodynamic effects.

The present study was designed to determine the haemodynamic and organ blood flow responses to the administration of MAC multiples of sevoflurane during spontaneous ventilation in the rat.

Methods

With approval from the University of Toronto animal care committee, Sprague-Dawley rats (Charles River Breeding Laboratories, St. Constance, Quebec, Canada) weighing 260–320 g were studied. The rats were housed in a temperature- and humidity-controlled environment with a 12-hour light/dark cycle and were fasted overnight with water available *ad libitum*.

Minimal alveolar concentration (MAC) determination

MAC for sevoflurane was determined in eight rats using a tail-clamp technique.¹⁰ Responses to tail clamp were assessed following incremental changes of 10% in inspired anaesthetic concentration. Gross, purposeful movement of

the head, extremities or body in response to the supra-maximal stimulation was considered a positive response. MAC was bracketed while increasing and decreasing the anaesthetic concentration. MAC was the concentration midway between the highest concentration that allowed movement and the lowest concentration that prevented movement. Temperature was monitored with rectal probes and normothermia was maintained using overhead radiant heating lamps. Inspired anaesthetic concentration was monitored continuously using an infrared medical gas analyzer (SensorMedics LB 2, Anaheim, CA) that was calibrated before use in 1% increments from 0 to 4% sevoflurane using standards prepared in air.

Surgical preparation

During ether anaesthesia, lasting 20–25 min, polyethylene catheters (Tygon, PE-50) were inserted into: (1) the left femoral artery for blood pressure monitoring, blood sampling and reference sample withdrawal, and (2) the left ventricle via the right common carotid artery for injection of radioactive microspheres, as described previously.¹¹ Placement of the catheter in the left ventricle was verified by monitoring the blood pressure waveform. Incisions were infiltrated with 1% lidocaine and the catheters were capped with rubber injection ports and tunnelled subcutaneously to the midback of the rat where they were brought to the skin surface. Following the operative procedure, the rats were allowed to recover unrestrained in a temperature-controlled environment for four hours. There was no obvious evidence of stress or pain during recovery. In previous studies, we showed that indices of stress such as blood glucagon levels, arterial pressures, and heart rates remain unchanged following surgical preparation.¹¹

Experimental design

After recovery, the rats were placed in cylindrical plexiglas chambers through which oxygen was administered to prevent rebreathing of exhaled gases (flow rate 5 L · min⁻¹). After 20 min of haemodynamic stability, awake heart rate, blood pressure and arterial blood gases were recorded, and cardiac output and organ blood flows were determined using cobalt-57 (⁵⁷Co) labelled microspheres. The rats were then randomly assigned to receive 0.5, 1.0, 1.2 or 1.5 MAC sevoflurane. Thirty minutes after the onset of anaesthesia, heart rate, systemic arterial pressure and arterial blood gases were recorded, and scandium-46 (⁴⁶Sc) labelled microspheres were injected to determine cardiac output and organ blood flows. All measurements were made during haemodynamic stability. In separate studies, we found that the injection of the second set of microspheres (⁴⁶Sc) reproduced the values for cardiac output and organ blood flows that were obtained after

injection of the first set of microspheres (^{57}Co) (Carmichael *et al.*, unpublished). Throughout the study, ventilation was spontaneous and normothermia was maintained using overhead radiant heating lamps. Rectal temperatures taken after organ blood flow measurements were $37.1 \pm 0.4^\circ\text{C}$.

Haemodynamic and organ blood flow measurements

Mean arterial pressure was measured with a pressure transducer and recorded continuously using a physiograph (Narco Biosystems MK-1 Houston, Texas). Heart rate was determined from the blood pressure waveform. Cardiac output and organ blood flows were measured using $16.5 \pm 0.1\ \mu\text{m}$ diameter, radiolabelled microspheres (New England Nuclear, Boston, MA). The microspheres, prepared as previously described,¹² were suspended in 10% dextran containing one drop of Tween-80, agitated for ten minutes using a Vortex mixer, and aspirated into polyethylene tubing for gamma scintillation counting (Nuclear Chicago counter, model 1185, Chicago, IL) before infection. Approximately 30,000 microspheres were then infused into the left ventricle over 20 sec using an infusion pump (Sage Instruments, White plains, NY). A 0.6 ml reference sample, which contained 300–400 microspheres, was obtained from the femoral artery using a withdrawal pump that began to aspirate blood ten seconds before the infusion of microspheres and continued for 60 sec. An equal volume of ficoll (0.6 ml, 13% w/v; Sigma Chemical, St. Louis, MO), a non-ionic synthetic polymer of sucrose, was flushed through the microsphere infection tubing to replace the volume of blood sampled. The infusion of microspheres and the withdrawal of the reference sample had no demonstrable effect on monitored haemodynamic variables. The net counts infused was the difference between the counts obtained before injection into the left ventricle and those remaining in the polyethylene tubing. At the termination of the study, rats were killed with *iv* KCl and the following organs were removed and placed in saline-containing vials for analysis of radioactivity: brain, spinal cord, heart, lungs, liver, right kidney, left kidney, spleen, stomach, omentum, pancreas, small intestine, and large intestine. All organs were analyzed intact, with the exception of the liver and small intestine which were each subdivided into five sections. The mixing of microspheres in the circulation was considered to be adequate if the difference between the right and left renal blood flows was less than 15%. Three rats were deleted from the study on the basis of this criterion.

Calculations

Corrections for overlap during counting of the radioisotopes were made. Cardiac index, $\dot{Q}_t$ ($\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ body weight), was calculated by the equation:

$$\dot{Q}_t = \frac{C_i \cdot R}{C_r \cdot w}$$

where C_i = net counts injected, R = reference sample withdrawal rate, C_r = net counts in reference sample and w = body weight (kg). Organ blood flow, $\dot{Q}_o$ ($\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ body weight), was calculated by the equation:

$$\dot{Q}_o = \frac{\dot{Q}_t \cdot C_o}{C_i}$$

where C_o = net counts in organ. Systemic vascular resistance ($\text{mmHg} \cdot \text{ml}^{-1} \cdot \text{min} \cdot \text{kg}^{-1}$) was calculated as the quotient of the mean arterial pressure and cardiac index. Central venous pressure was assumed to approximate zero. Stroke volume index ($\text{ml} \cdot \text{kg}^{-1}$) was calculated as the quotient of cardiac index and heart rate. Organ vascular resistances ($\text{mmHg} \cdot \text{ml}^{-1} \cdot \text{min} \cdot \text{kg}^{-1}$) were calculated as the quotient of the mean arterial pressure and organ blood flow.

Portal tributary blood flow was calculated as the sum of the blood flow to the spleen, stomach, omentum, pancreas, small intestine, and large intestine. The contribution of blood flows from the pancreas and omentum, which cannot be readily isolated in the rat, is included in the flows to the small and large intestines. The accuracy of this method as an estimate of portal blood flow is well validated.^{12–14} Hepatic arterial blood flow was determined from the net counts within the liver. Total liver blood flow was calculated as the sum of the portal tributary and hepatic arterial blood flows.

Cardiac output, stroke volume, organ flows and vascular resistances were indexed to body weight (kg). Since the relationship of organ weight to body weight did not change throughout the study period, there are no differences in the conclusions derived when this form of expression is used as opposed to blood flows expressed per gram organ.

Data are presented as mean values $\pm$ SEM. Statistical significance ($P < 0.05$) was determined using one-way analysis of variance. Intergroup differences were determined by the least significant difference method.¹⁵

Results

The MAC value (mean $\pm$ SEM) of sevoflurane was $2.30 \pm 0.05\%$.

After recovery from surgery, rats appeared comfortable in the chambers. Awake haemodynamic and organ blood flow measurements were in agreement with values obtained by a variety of other investigators using the microsphere technique.^{12–14,16–18} The data from the four control groups were similar and were therefore pooled (Table I). Heart rate, cardiac index, stroke volume index

FIGURE 1 Effects of 0, 0.5, 1.0, 1.2, and 1.5 MAC sevoflurane on cerebral and spinal cord blood flows (means $\pm$ SEM). * P < 0.05 compared with awake values. ** P < 0.01 compared with awake values.

FIGURE 2 Effects of 0, 0.5, 1.0, 1.2, and 1.5 MAC sevoflurane on hepatic arterial and portal tributary blood flows (means $\pm$ SEM). * P < 0.05 compared with awake values. ** P < 0.01 compared with awake values.

TABLE I Demographic and physiologic measurements at 0, 0.5, 1.0, 1.2, and 1.5 MAC sevoflurane

Variable	Awake	0.5 MAC	1.0 MAC	1.2 MAC	1.5 MAC
Number of rats	36	7	10	12	7
Weight (kg)	0.29 $\pm$ 0.01	0.29 $\pm$ 0.01	0.31 $\pm$ 0.01	0.25 $\pm$ 0.01	0.30 $\pm$ 0.01
Heart rate (min ⁻¹)	360 $\pm$ 15	367 $\pm$ 10	370 $\pm$ 12	379 $\pm$ 7	392 $\pm$ 12
CI (ml $\cdot$ min ⁻¹ $\cdot$ kg ⁻¹)	244 $\pm$ 12	253 $\pm$ 16	244 $\pm$ 8	228 $\pm$ 18	225 $\pm$ 5
MAP (mmHg)	104 $\pm$ 3	106 $\pm$ 3	101 $\pm$ 5	99 $\pm$ 6	88 $\pm$ 2†
SV index (ml $\cdot$ kg ⁻¹)	0.67 $\pm$ 0.04	0.69 $\pm$ 0.06	0.71 $\pm$ 0.03	0.60 $\pm$ 0.04	0.72 $\pm$ 0.04
SVR (mmHg $\cdot$ ml ⁻¹ $\cdot$ kg $\cdot$ min ⁻¹)	0.44 $\pm$ 0.02	0.43 $\pm$ 0.03	0.44 $\pm$ 0.02	0.46 $\pm$ 0.03	0.39 $\pm$ 0.01
Arterial PCO ₂ (mmHg)	38 $\pm$ 4	39 $\pm$ 3	46 $\pm$ 4	51 $\pm$ 2*	56 $\pm$ 3*

Data represent the mean $\pm$ SEM determination for the number of rats shown in each column. CI = cardiac index; MAP = mean arterial pressure; SV = stroke volume; SVR = systemic vascular resistance. * P < 0.05 compared with awake values. † P < 0.01 compared with awake values.

TABLE II Organ blood flow measurements at 0, 0.5, 1.0, 1.2, and 1.5 MAC sevoflurane

Variable	Awake	0.5 MAC	1.0 MAC	1.2 MAC	1.5 MAC
Coronary BF	7.44 $\pm$ 0.7	8.93 $\pm$ 1.7	9.02 $\pm$ 0.4	9.09 $\pm$ 0.7	8.34 $\pm$ 0.5
Renal BF	41.5 $\pm$ 3.1	39.3 $\pm$ 3.9	44.6 $\pm$ 3.6	41.1 $\pm$ 3.8	39.2 $\pm$ 4.0
Stomach BF	3.41 $\pm$ 0.3	3.56 $\pm$ 0.3	2.54 $\pm$ 0.2*	2.30 $\pm$ 0.3†	2.34 $\pm$ 0.46*
Splenic BF	4.81 $\pm$ 0.4	4.72 $\pm$ 0.5	3.82 $\pm$ 0.4	3.31 $\pm$ 0.5*	4.75 $\pm$ 0.6
Small intestinal BF	23.9 $\pm$ 1.8	25.7 $\pm$ 2.5	26.4 $\pm$ 2.8	23.1 $\pm$ 2.2	26.2 $\pm$ 3.0
Large intestinal BF	8.2 $\pm$ 0.7	11.1 $\pm$ 1.6	7.01 $\pm$ 1.1	8.3 $\pm$ 0.7	5.7 $\pm$ 1.20
Total liver BF	50.6 $\pm$ 2.4	59.9 $\pm$ 5.3	53.1 $\pm$ 3.8	53.4 $\pm$ 2.8	56.2 $\pm$ 5.2

Data, in ml $\cdot$ min⁻¹ $\cdot$ kg⁻¹ body weight, represent the mean $\pm$ SEM determination. BF = blood flow. * P < 0.05 compared with awake values. † P < 0.01 compared with awake values.

and systemic vascular resistance during sevoflurane anaesthesia did not differ from awake values, with the exception of a 12% reduction in mean arterial pressure at 1.5 MAC compared with awake values (P < 0.01) (Table I). Arterial PCO₂ increased in a dose-related fashion from 38 $\pm$ 4 mmHg in awake rats to 56 $\pm$ 5 mmHg at 1.5 MAC sevoflurane (P < 0.05) (Table I). Arterial PO₂, at each MAC multiple, did not differ from awake values.

Cerebral blood flow increased by 61% at 1.2 MAC (P < 0.01) and by 120% at 1.5 MAC (P < 0.01), while spinal cord blood flow increased by 102% (P < 0.05) and 170% (P < 0.01) respectively (Figure 1). Coronary and renal blood flows did not change over the range of sevoflurane concentrations studied (Table II). The changes in cerebral and spinal cord blood flows were accompanied by reductions in vascular resistances (Table III). Blood flow

TABLE III Vascular resistances at 0, 0.5, 1.0, 1.2, and 1.5 MAC sevoflurane.

Variable	Awake	0.5 MAC	1.0 MAC	1.2 MAC	1.5 MAC
Coronary VR	14.6 ± 1.2	14.8 ± 2.6	12.2 ± 0.8	11.7 ± 1.3	10.7 ± 0.5
Renal VR	2.48 ± 0.3	2.90 ± 0.4	2.55 ± 0.24	2.54 ± 0.2	2.27 ± 0.2
Cerebral VR	26.9 ± 1.2	21.7 ± 2.7	23.7 ± 1.8	18.7 ± 2.4†	11.2 ± 1.5†
Spinal Cord VR	103 ± 15	101 ± 9	96 ± 9	48 ± 7†	36 ± 3†
Hepatic arterial VR	13.8 ± 1.6	10.1 ± 4.2	8.4 ± 0.8*	8.2 ± 2.1*	7.5 ± 1.0*
Portal tributary VR	2.58 ± 0.1	2.38 ± 0.2	2.83 ± 0.2	2.86 ± 0.3	2.42 ± 0.2
Splenic VR	20.3 ± 1.3	23.9 ± 2.0	31.2 ± 3.4*	36.1 ± 4.8†	20.8 ± 3.0
Stomach VR	32.5 ± 2.7	30.0 ± 1.9	44.5 ± 3.4	51.8 ± 7.3†	49.0 ± 4.8*
Small intestinal VR	4.50 ± 0.3	4.27 ± 0.4	4.49 ± 0.5	5.36 ± 0.8	3.68 ± 0.5
Large intestinal VR	13.4 ± 1.0	10.2 ± 1.2	16.5 ± 2.0	13.1 ± 1.3	18.1 ± 2.7

Data, in mmHg · ml⁻¹ · min · kg⁻¹ body weight, represent the mean ± SEM determination. VR = vascular resistance. **P* < 0.05 compared with awake values. †*P* < 0.01 compared with awake values.

to the lungs did not differ in awake and anaesthetized rats, suggesting that arteriovenous shunting of microspheres did not occur in the presence of sevoflurane.

Portal tributary blood flow (Figure 2) and preportal vascular resistance (Table III) were unaffected over the range of sevoflurane concentrations studied. Gastric blood flow decreased by 25% at 1.0 MAC (*P* < 0.05) and by 31% at 1.5 MAC (*P* < 0.05) (Table II). Small and large intestinal blood flows did not change (Table II). On the other hand, hepatic arterial blood flow increased by 47% at 1.0 MAC (*P* < 0.05) and by 63% at 1.5 MAC (*P* < 0.05) sevoflurane, with corresponding changes in vascular resistance of 39% and 46% respectively (Figure 2). These changes, however, did not increase total hepatic blood flow (Table II).

Discussion

Since sevoflurane has desirable anaesthetic induction characteristics, we sought to determine the haemodynamic and organ blood flow responses to the administration of sevoflurane during spontaneous ventilation. The administration of an inhalational anaesthetic during spontaneous ventilation produces haemodynamic effects that may be attributed not only to its direct pharmacological effects but also to an elevation in carbon dioxide tension in the blood. The results of the present study must therefore be interpreted in light of the dose-related increase in arterial carbon dioxide. Nonetheless, these data demonstrate that, during spontaneous ventilation, the administration of sevoflurane produces minimal haemodynamic disturbance.

The value for the MAC of sevoflurane in the present study is similar to that reported previously for dogs (2.36 ± 0.46%)¹⁹ and humans (2.05 ± 0.08%).²⁰ In other species, the MAC of sevoflurane has been reported to range from 1.4% in mice² to 3.7% in rabbits.²⁰ Although the MAC of an inhalational anaesthetic is species-dependent, it has been suggested that the MAC ratio, or relative

potency, of any pair of anaesthetics remains relatively constant from species to species.²¹ To test the validity of this statement, the ratio of sevoflurane MAC to halothane MAC was calculated for Sprague-Dawley rats and for humans. Our MAC value, together with that reported previously for halothane,¹⁰ indicate that the MAC ratio in Sprague-Dawley rats is 2.1. This value is similar to the ratio of sevoflurane MAC²⁰ to halothane MAC²² in humans (2.6).

Inspired, rather than end-tidal, concentrations of sevoflurane were measured in the present study. At each inspired concentration, measurements were obtained at least 30 min after the onset of anaesthesia. This time period is approximately five times greater than the reported time-constant for sevoflurane in the vessel-rich group.²³ Commensurate with principles of anaesthetic uptake and distribution,²⁴ it is likely therefore that the experimental data were collected when equilibration of sevoflurane with the tissues of the vessel-rich group was greater than 95%.

Systemic haemodynamics

Awake haemodynamic variables in the present study were similar to those reported in a number of previous studies that employ the microsphere technique.^{12-14,16-18} After administration of sevoflurane, haemodynamic variables were affected minimally despite a dose-related increase in arterial PCO₂. These results are in agreement with those found in piglets²⁵ but differ from those reported for spontaneously ventilating mature swine.³ Although species variation must be considered, the discrepancy between the present study and that in swine may be attributed, in part, to the elevated haemodynamic values reported for the awake swine. In another study in which ventilation was controlled to maintain normocarbida, sevoflurane produced reductions in stroke volume, systemic vascular resistance, and mean arterial pressure which were similar in magnitude to those reported for isoflurane.⁶ When interpreting

the results of that study, however, the haemodynamic effects of positive pressure ventilation^{7,8} must be considered.

Organ blood flows

The increase in cerebral blood flow at 1.2 and 1.5 MAC sevoflurane in the present study was of similar magnitude to that produced by hypercarbia during isoflurane anaesthesia in the rat.²⁶ Studies in normocarbic animals showed that sevoflurane has either no effect²⁷ or decreases³ cerebral blood flow. These findings suggest that the increase in cerebral flow found in the present study may be related to an effect of hypercarbic rather than to a pharmacological effect of sevoflurane.

The absence of an effect on coronary blood flow and vascular resistance suggests that myocardial oxygen requirement and coronary vascular tone were unaffected under the conditions of the present study. Coronary blood flow has been reported either to increase³ or to decrease⁶ after the administration of sevoflurane to normocarbic animals. Although species variation and differences in experimental technique must be considered, other factors may account for these differences. The decrease in coronary blood flow in swine may have been related to the hyperdynamic state of the swine at the onset of anaesthesia. In addition, the increase in coronary blood flow found in dogs may be attributed, in part, to an increase in myocardial oxygen requirement as suggested by a 60% increase in heart rate at 1.2 MAC compared with awake animals.

Both portal tributary blood flow and preportal vascular resistance were unaffected under the conditions of the present study. These findings are consistent with the observation that volatile anaesthetics can attenuate the increase in liver blood flow which is known to accompany hypercarbia.²⁸ Alternatively, a hypercarbia-induced increase in portal tributary blood flow might have obscured a decrease in flow in response to sevoflurane. Further studies are required to determine the effect of sevoflurane on the portal circulation.

Two observations suggest that a pharmacological effect of sevoflurane, rather than hypercarbia, was responsible for the increase in hepatic arterial flow observed in the present study. Firstly, hypercarbia has been reported to have either no effect^{29,30} or to decrease³¹ hepatic arterial blood flow. Secondly, sevoflurane has also been reported to increase hepatic arterial blood flow in normocarbic animals.^{3,32} Given that hepatic arterial blood flow increased without a concomitant reduction in portal tributary blood flow, the results of the present study suggest that the administration of sevoflurane during spontaneous ventilation would enhance hepatic oxygen supply. Similar independent, non-reciprocal alterations in hepatic arterial

and portal tributary blood flow have recently been described to occur under a number of other conditions.³³

In conclusion, these data demonstrate that the administration of sevoflurane during spontaneous ventilation produces a high degree of cardiovascular stability and maintains blood flow to major organs in the rat.

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