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Cardiac and Regional Hemodynamic Interactions between Halothane and Nitric Oxide Synthase Activity in Dogs

Jacques E. Chelly, M.D., Ph.D., Marie-Francoise Doursout, Ph.D.,† Thierry Lechevalier, M.D.,‡ Yang Yan Liang,§ Frank Chelly,‖ Craig Hartley, Ph.D.,# Robert G. Kilbourn, M.D., Ph.D.***

Background: ***In vitro,*** **halothane appears to affect the role played by nitric oxide in the regulation of vascular tone and cardiac function.** ***In vivo,*** **the results of the interactions between halothane and the nitric oxide pathway remain controversial. The authors investigated the effects of halothane on the cardiac and regional hemodynamic properties of N-methyl-L-arginine (NMA), a specific nitric oxide synthase inhibitor, in dogs.**

Methods: **Twenty-five dogs were chronically instrumented. Aortic pressure, the first derivative of left ventricular pressure, cardiac output, heart rate, and carotid, coronary, mesenteric, hepatic, portal and renal blood flows were continuously recorded. N-methyl-L-arginine was infused intravenously at 20 mg/kg over 1 min in awake dogs (n = 11) and in 1.2% halothane-anesthetized dogs (n = 10). As a control group, the remaining four dogs were studied awake and during 1.2% halothane for 2 h in the absence of NMA.**

Results: **In awake dogs, NMA produced a sustained pressor response (34%) and systemic vasoconstriction (40%) associated with a decrease in cardiac output (16%). Regional circulation changes included an immediate and transient increase in carotid (43%) and coronary (237%) blood flows and a subsequent decrease in carotid blood flow (25%). Hepatic and mesenteric blood flows also decreased, by 43% and 16%, respectively. Except for the coronary circulation, regional vascular resistance increased significantly. Halothane did not affect the pressor response to NMA but did blunt the cardiac output changes. Consequently, the systemic vasoconstriction after nitric oxide synthase inhibition was of shorter duration and of lesser magnitude during halothane anesthesia. Halothane also blunted the carotid, mesenteric, and renal vasoconstriction induced by NMA. Finally, in 1.2% halothane-anesthetized dogs, NMA induced a coronary vasoconstriction.**

Conclusions: **Halothane minimally interferes with the systemic and regional hemodynamic consequences of nitric oxide synthase blockade. The nature and magnitude of the interaction depend on the territory in which they occur. (Key words: Anesthetics, gases: nitric oxide. Anesthetics, volatile: halothane. Interactions: hemodynamic. Nitric oxide synthase blocker: N-methyl-L-arginine.)**

* Professor, Department of Anesthesiology, The University of Texas Health Science Center, Medical School at Houston, Houston, Texas.

† Assistant Professor, Department of Anesthesiology, The University of Texas Health Science Center, Medical School at Houston, Houston, Texas.

‡ Research Fellow, Department of Anesthesiology, The University of Texas Health Science Center, Medical School at Houston, Houston, Texas.

§ Research Technician II, Department of Anesthesiology, The University of Texas Health Science Center, Medical School at Houston, Houston, Texas.

‖ Research Technician, Department of Genitourinary Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas.

Professor, Department of Internal Medicine, Baylor College of Medicine, Houston, Texas.

** Assistant Professor, Department of Genitourinary Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas.

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Address reprint requests to Dr. Chelly: Department of Anesthesiology, The University of Texas Health Science Center, Medical School at Houston, Room 5020, 6431 Fannin, Houston, Texas 77030.

MULDOON *et al.* observed that halothane attenuated endothelium derived relaxing factor-mediated vasodilation of rat aorta.[1] Halothane inhibits both receptor and nonreceptor-mediated endothelium derived relaxing factor/nitric oxide-dependent vasodilation,[2] and it inhibits the increase in cyclic guanosine monophosphate associated with the receptor-mediated vasodilation.[3] More recently, Hart *et al.* found that the inhibition appears to be related to an interaction with smooth muscle guanylyl cyclase.[4]

In vivo data on halothane and the nitric oxide pathway are more limited. In rats, Wang *et al.* found that the increase in blood pressure associated with the inhibition of nitric oxide synthase (NOS) activity was markedly attenuated (96%) by 1.5% halothane; no significant effect occurred when the experiment was conducted with other anesthetics (pentobarbital, chlora-

lose, ketamine, althesin, urethane, enflurane).[5] Sigmon *et al.* showed that 1% halothane administered to rats blocked 71% of the blood pressure response to a NOS inhibitor, barbiturate did not have a significant effect.[6] In contrast, data reported by Greenblatt *et al.* suggest that the magnitude of the pressor response induced by N-methyl-L-arginine (NMA), a specific NOS blocker, may be only slightly affected by halothane anesthesia in Wistar Kyoto rats: in separately published reports, they described a 24% increase in blood pressure after NMA in the presence of 1.2% halothane[7] compared with a 40% increase recorded in awake rats.[8,9] In both awake and halothane-anesthetized rats, the administration of NOS blockers has been reported to decrease blood flow in the gastrointestinal tract, kidney, and liver; such deleterious consequences on regional circulation in rats have led Moncada *et al.*[10] to question the therapeutic potential value of NOS blockers. However, we recently demonstrated that renal blood flow and total hepatic blood flow were preserved in conscious dogs treated with NMA.[11]

The current study was therefore designed to examine the cardiac and regional hemodynamic consequences of NOS inhibition during halothane anesthesia in dogs. We hypothesized that halothane would minimally affect the pressor response to NMA and that regional blood flow would be maintained; such results would support the use of an NOS inhibitor as a vasopressor during halothane anesthesia. Further, we expected that the regional interaction between halothane and NOS inhibition would depend on the local circulation. Because we have previously demonstrated, using Doppler flowmetry, that cardiac and regional hemodynamic changes after NOS inhibition may be biphasic and may occur at different times according to the circulatory bed,[11] measurement of blood flow in the current study was continuous. Most previous studies of the effects of halothane on cardiac output and regional blood flow after NOS inhibition have been conducted using the microsphere method,[6–9] in which limited number of blood flow measurements can be obtained.

Methods

Instrumentation

Twenty-five mongrel dogs of either sex, heartworm free, weighing 25–34 kg, were instrumented as follows. Animals were anesthetized with intravenous 30 mg/kg thiopental and tracheally intubated. Anesthesia was maintained using a mixture of halothane, nitrogen, and oxygen. Lungs were ventilated with a Harvard ventilator (Harvard Apparatus, South Natick, MA). Under aseptic conditions, a Tygon catheter was inserted into the iliac artery *via* the abdominal aorta. A left thoracotomy between the fourth and fifth intercostal spaces was performed, the pericardium incised, the circumflex coronary artery dissected free and a 20-MHz pulsed Doppler flow probe (2.5–3.5 mm, Baylor College of Medicine, Houston, TX) was applied. A miniature pressure transducer (7.0 mm, Konigsberg Instruments, Pasadena, CA) was inserted into the left ventricle through an apical stab wound. A precalibrated ultrasonic flow probe (14–16 mm, Transonic Systems, Ithaca, NY) was positioned around the pulmonary artery, and a Tygon catheter was inserted into the left atrium. After a median laparotomy, 20-MHz pulsed Doppler flow probes were positioned around the hepatic artery (3.0–3.5 mm), the portal vein (8.0–8.5 mm), and the mesenteric artery (4.0–4.5 mm). After appropriate incisions, 20-MHz pulsed Doppler flow probes were positioned around the left carotid and renal arteries (3.5–4.0 mm). Probe functions were carefully checked *in vitro* and *in vivo* before the incisions were closed. All transducer leads and catheters were tunneled subcutaneously to the dorsum of the neck and secured after the thoracotomy was closed.

Postoperative analgesia was induced by infiltrating bupivacaine subcutaneously as necessary. Antibiotic prophylaxis was initiated before surgery and was maintained until the 7th postoperative day. Catheters were flushed twice weekly with heparin (1,000 units/ml). A specially designed jacket protected the catheters and the implanted instruments.

Measurements

This experimental preparation allowed continuous measurements of phasic and mean aortic pressures; the first derivative of left ventricular pressure; heart rate; cardiac output; and carotid, coronary, hepatic, portal, mesenteric, and renal blood flows. Systemic vascular resistance was calculated as the ratio of mean arterial pressure to cardiac output; regional vascular resistance was calculated as the ratio of mean arterial pressure to regional blood flow. Pressures were measured *via* the aortic and left atrial catheters using a Statham P23 DB pressure transducer (Gould, Cleveland, OH). Cardiac output was recorded using a Transonic flowmeter (T202-S). The ultrasonic flow dimension system enabled simultaneous measurements of pressures and

flows.[12] All hemodynamics were recorded on a 16-channel Gould brush polygraph. The miniature Konigsberg pressure transducer was calibrated both after implantation and before each study, using the aortic and mean left atrial pressures as reference. The pulsed Doppler flow signals are calibrated in terms of Doppler frequency shift. Baseline zero and the linear relationship between volume flow and frequency shift have been previously established *in vivo*.[13]

Experimental Protocol

The protocol was approved by The University of Texas Animal Welfare Committee. Dogs were carefully nursed through the first 24 postoperative hours and on subsequent days were trained to lie quietly on the laboratory floor. The dogs were studied no less than 10 days after surgery, when hematocrit was >30% and when body temperature, appetite, and general appearance were normal.

Body weight, body temperature, arterial blood gases, and hematocrit were routinely measured before each experiment. The experiments were conducted on fasted dogs. Animals were distributed randomly into three groups. N-methyl-L-arginine was administered either awake (group 1, n = 11) or during 1.2% halothane anesthesia (group 2, n = 10). Group 3 animals (n = 4) were studied awake and during 1.2% halothane for 2 h to confirm that hemodynamic values were stable over time in the absence of NMA injection. Halothane anesthesia was induced by mask. When anesthesia was deep enough, the trachea was intubated and the lungs were ventilated using an Ohmeda 7000 ventilator (Madison, WI). Tidal volume (10–15 ml/kg) and rate of ventilation were adjusted to maintain arterial partial pressure of carbon dioxide equal to those in awake dogs. A mixture of nitrogen and oxygen was used to maintain arterial oxygen tension at approximately the same level as in awake dogs. Blood gases were monitored during anesthesia. The concentration of halothane was monitored with an Ohmeda 5250 respiratory gas monitor to maintain 1.2% end-tidal concentration.

N-methyl-L-arginine was administered intravenously at 20 mg/kg through a filter over 1 min into a peripheral vein. In group 1, hemodynamic parameters were recorded before NMA injection, and for 2 h after NMA injection in awake dogs. In group 2, hemodynamic parameters were recorded for 45 min before anesthesia, for 30 min after steady-state 1.2% end-tidal halothane, before NMA injection, and for an additional 2 h thereafter. Previous studies from our laboratory have demonstrated that 20 mg/kg intravenous NMA produced the maximum pressure response in awake dogs.[14] In group 3, hemodynamic values were recorded for 2 h in awake and in 1.2% halothane-anesthetized dogs.

Data Analysis

Data obtained in awake conditions and during halothane anesthesia were analyzed using an analysis of variance for repeated measures in each group. When differences were significant, multiple within-comparisons to the control value obtained before NMA injections were performed using Dunnett's *t* test.[15] In addition, when changes from control and steady-state halothane were significant, the magnitude of changes produced by NMA in each experimental condition was compared using an unpaired *t* test. A *P* value less than 0.05 was considered significant. Data are presented as mean ± SEM.

Results

Baseline cardiac and regional hemodynamic values recorded before the administration of NMA in awake (group 1) and 1.2% halothane (group 2) anesthetized dogs are presented in table 1. As previously published, 1.2% halothane induced significant hypotension, tachycardia and decreases in the first derivative of left ventricular pressure, cardiac output, and portal and mesenteric blood flows[16] (table 1). Moreover, in the absence of NMA, hemodynamic values remained essentially unchanged for 2 h in awake and 1.2% halothane-anesthetized dogs (table 2).

In awake dogs, the inhibition of NOS activity by NMA resulted in a significant pressor response (29 ± 4 mmHg) and a significant systemic vasoconstriction (18 ± 3 dyn · s · cm^{-5}) that lasted 2 h and 1 h, respectively (fig. 1). Although cardiac output initially increased by 0.26 ± 0.19 l · min^{-1}, a significant secondary decrease (0.32 ± 0.08 l · min^{-1}) was recorded between 10 and 60 min. N-methyl-L-arginine injections were also followed by immediate and transient significant increases in heart rate (25 ± 5 beats · min^{-1}) and the first derivative of left ventricular pressure (457 ± 169 mmHg · s^{-1}; figs. 1 and 2). The effects of NMA on local circulation consisted of an immediate but transient significant increase in coronary blood flow (82 ± 17

Table 1. Cardiac and Regional H

MAP (mmHg)	
HR (beats · min^{-1})	
CO (L · min^{-1})	
dP/dt (mmHg · s^{-1})	
SVR (units)	
Car BF (ml · min^{-1})	
Cor BF (ml · min^{-1})	
Por BF (ml · min^{-1})	
Hep BF (ml · min^{-1})	
Mes BF (ml · min^{-1})	
Ren BF (ml · min^{-1})	

CO = cardiac output; HR = heart rate
* $P < 0.05$, 1.2% halothane *versus* aw

ml · min^{-1}) and significant
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increased by 50 ± 1 ml ·
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Table 2. Hemodynamic Valu

MAP (mmHg)	Awake
	Haloth
HR (beats · min^{-1})	Awake
	Haloth
CO (L · min^{-1})	Awake
	Haloth
dP/dt (mmHg · s^{-1})	Awake
	Haloth
Car BF (ml · min^{-1})	Awake
	Haloth
Cor BF (ml · min^{-1})	Awake
	Haloth
Por BF (ml · min^{-1})	Awake
	Haloth
Hep BF (ml · min^{-1})	Awake
	Haloth
Mes BF (ml · min^{-1})	Awake
	Haloth
Ren BF (ml · min^{-1})	Awake
	Haloth

CO = cardiac output; HR = heart r
* $P < 0.05$, 1.2% halothane *versus*

Table 1. Cardiac and Regional Hemodynamic Values prior to NMA Injection (20 mg · kg^{-1} iv)

	Awake Group 1	Awake Control Group 2	1.2% Halothane Group 2
MAP (mmHg)	90 ± 4 (11)	95 ± 5 (10)	63 ± 6* (10)
HR (beats · min^{-1})	85 ± 3 (11)	93 ± 3 (10)	108 ± 4 (10)
CO (L · min^{-1})	1.9 ± 0.1 (9)	2.1 ± 0.2 (8)	1.8 ± 0.2* (8)
dP/dt (mmHg · s^{-1})	3,175 ± 162 (11)	3,235 ± 307 (8)	1,564 ± 211* (8)
SVR (units)	48 ± 3 (9)	46 ± 3 (8)	37 ± 2* (8)
Car BF (ml · min^{-1})	116 ± 8 (10)	159 ± 27 (8)	150 ± 21 (8)
Cor BF (ml · min^{-1})	35 ± 6 (7)	34 ± 8 (6)	25 ± 7 (6)
Por BF (ml · min^{-1})	343 ± 7 (8)	422 ± 52 (7)	276 ± 49* (7)
Hep BF (ml · min^{-1})	130 ± 12 (7)	118 ± 15 (7)	105 ± 19 (7)
Mes BF (ml · min^{-1})	158 ± 34 (6)	146 ± 17 (7)	97 ± 16* (7)
Ren BF (ml · min^{-1})	116 ± 7 (7)	131 ± 22 (6)	122 ± 25 (6)

CO = cardiac output; HR = heart rate; MAP = mean arterial pressure.
* $P < 0.05$, 1.2% halothane *versus* awake control.

ml · min^{-1}) and significant decreases in hepatic (56 ± 16 ml · min^{-1}) and mesenteric (31 ± 7 ml · min^{-1}) blood flow. Carotid blood flow initially significantly increased by 50 ± 16 ml · min^{-1} during the first minute after NMA injection and subsequently significantly decreased by 29 ± 6 ml · min^{-1} between 5 and 60 min. Total hepatic blood flow decreased by 87 ± 25 ml · min^{-1} between 1 and 45 min (figs. 3 and 4). The concomitant changes in mean arterial blood pressure and regional blood flow resulted in significant carotid, mesenteric, and renal vasoconstrictions as well as an immediate but significant transient coronary vasodilation (1.72 ± 0.70 dyn · s · cm^{-5}). Carotid, mesenteric, and renal vascular resistance increased by 0.43 ± 0.08, 0.39 ± 0.12, and 0.30 ± 0.08 dyn · s · cm^{-5}, respectively. Although the carotid vasoconstriction occurred 5 min after NMA injection and lasted 120 min, increases in renal and mesenteric vascular resistance were im-

Table 2. Hemodynamic Values Recorded for 2 Hours in Awake and 1.2% Halothane-anesthetized Dogs (Group 3)

		0	15 min	30 min	45 min	60 min	120 min
MAP (mmHg)	Awake	99 ± 12	99 ± 11	98 ± 10	101 ± 11	100 ± 10	99 ± 10
	Halothane	67 ± 5*	68 ± 3*	68 ± 3*	68 ± 3*	68 ± 3*	70 ± 1*
HR (beats · min^{-1})	Awake	80 ± 4	80 ± 4	80 ± 4	80 ± 4	80 ± 4	80 ± 4
	Halothane	95 ± 6*	95 ± 6*	95 ± 6*	95 ± 6*	95 ± 6*	95 ± 6*
CO (L · min^{-1})	Awake	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.3	1.7 ± 0.3	1.8 ± 0.3
	Halothane	1.3 ± 0.2*	1.3 ± 0.2*	1.3 ± 0.1*	1.3 ± 0.1*	1.3 ± 0.2*	1.3 ± 0.1*
dP/dt (mmHg · s^{-1})	Awake	3,565 ± 341	3,544 ± 307	3,544 ± 307	3,544 ± 308	3,544 ± 308	3,563 ± 288
	Halothane	1,552 ± 111*	1,507 ± 87*	1,507 ± 87*	1,507 ± 87*	1,507 ± 87*	1,568 ± 74*
Car BF (ml · min^{-1})	Awake	102 ± 12	104 ± 12	104 ± 12	104 ± 12	104 ± 12	104 ± 12
	Halothane	146 ± 30	146 ± 26	145 ± 25	150 ± 31	152 ± 31	155 ± 28
Cor BF (ml · min^{-1})	Awake	48 ± 9	49 ± 8	49 ± 8	49 ± 8	50 ± 9	48 ± 9
	Halothane	33 ± 6	32 ± 5	32 ± 5	32 ± 5	33 ± 6	33 ± 6
Por BF (ml · min^{-1})	Awake	352 ± 36	352 ± 36	352 ± 36	352 ± 36	357 ± 37	357 ± 37
	Halothane	240 ± 40*	240 ± 40*	240 ± 40*	240 ± 40*	240 ± 40*	235 ± 42*
Hep BF (ml · min^{-1})	Awake	81 ± 10	81 ± 10	81 ± 10	81 ± 10	81 ± 10	76 ± 10
	Halothane	50 ± 3	50 ± 3	48 ± 3	46 ± 3	45 ± 3	44 ± 5
Mes BF (ml · min^{-1})	Awake	109 ± 4	107 ± 5	107 ± 5	107 ± 5	107 ± 5	110 ± 5
	Halothane	83 ± 8*	83 ± 8*	83 ± 8*	84 ± 8*	84 ± 8*	83 ± 8*
Ren BF (ml · min^{-1})	Awake	117 ± 37	117 ± 37	117 ± 37	117 ± 37	117 ± 37	117 ± 37
	Halothane	104 ± 17	104 ± 17	104 ± 17	103 ± 18	103 ± 18	103 ± 18

CO = cardiac output; HR = heart rate; MAP = mean arterial pressure.
* $P < 0.05$, 1.2% halothane *versus* awake (n = 4).

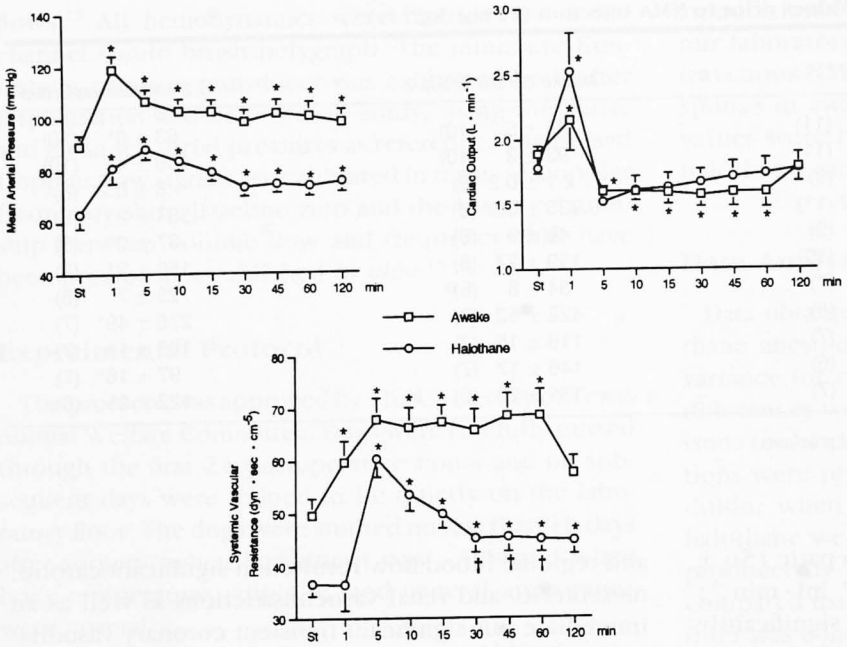

Fig. 1. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on mean arterial pressure, cardiac output, and systemic vascular resistance in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P < 0.05$ *versus* control. †$P < 0.05$ *versus* the magnitude of changes induced by N-methyl-L-arginine in awake dogs.

mediate and lasted 60 and 120 min, respectively. During the first 5 min after NMA injection, portal and hepatic vascular resistance significantly increased by 0.12 ± 0.04 and 1.49 ± 0.44 dynes · second · centimeter^{-5}, respectively (figs. 5 and 6). The magnitude and the duration of the effects of NMA on mean arterial blood pressure, heart rate, and the first derivative of left ventricular pressure in halothane-anesthetized dogs were essentially the same as those reported in awake dogs. Although cardiac output initially increased, no secondary decrease occurred in the presence of halothane anesthesia. As compared with awake dogs, the NMA-induced systemic vasoconstriction was of similar duration but the magnitude of the response was significantly reduced between 30 and 60 min after NMA administration in halothane-anesthetized dogs (fig. 1). Furthermore, inhibition of NOS activity by NMA did not affect carotid blood flow (fig. 3). However, a more prolonged decrease in hepatic blood flow, lasting 30 min was recorded in halothane-anesthetized dogs (fig. 4). Although the magnitude of the vasoconstriction induced by NMA on the mesenteric and hepatic circulation was not affected by halothane, the effects of NMA on carotid vascular resistance were less pronounced and of shorter duration (figs. 5 and 6). Finally, in halothane-anesthetized dogs, NMA produced a significant secondary increase in coronary vascular resistance that lasted 30 min (fig. 5).

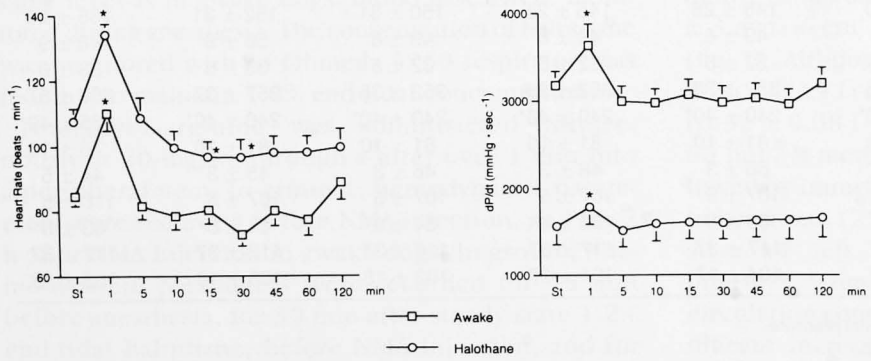

Fig. 2. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on heart rate and the first derivative of left ventricular pressure in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P < 0.05$ *versus* control.

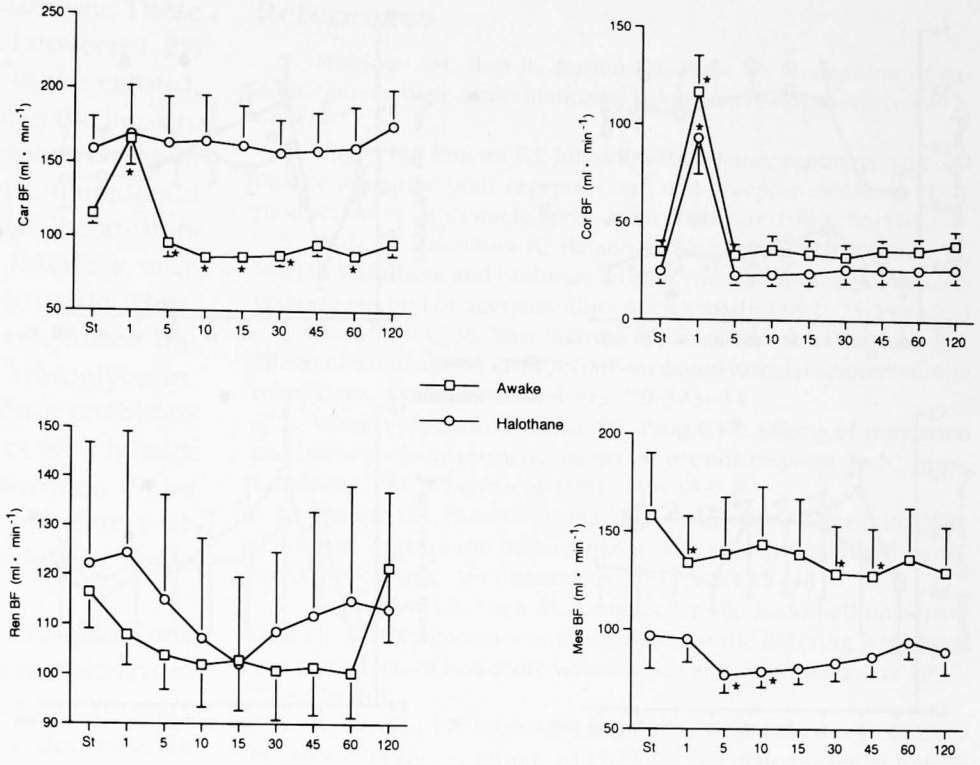

Fig. 3. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on carotid, coronary, mesenteric, and renal blood flows in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P < 0.05$ *versus* control.

Discussion

The current study of the effects of halothane on cardiac and regional hemodynamic consequences of NOS inhibition by NMA in chronically instrumented dogs entailed continuous assessment of the effects of each drug alone and the drugs in combination. Previous reports on the effects of halothane on regional blood flow changes mediated by the blockage of NOS activity did not use continuous hemodynamic measurements. Furthermore, they were conducted in the rat, a species in which the inhibition of NOS activity has been associated

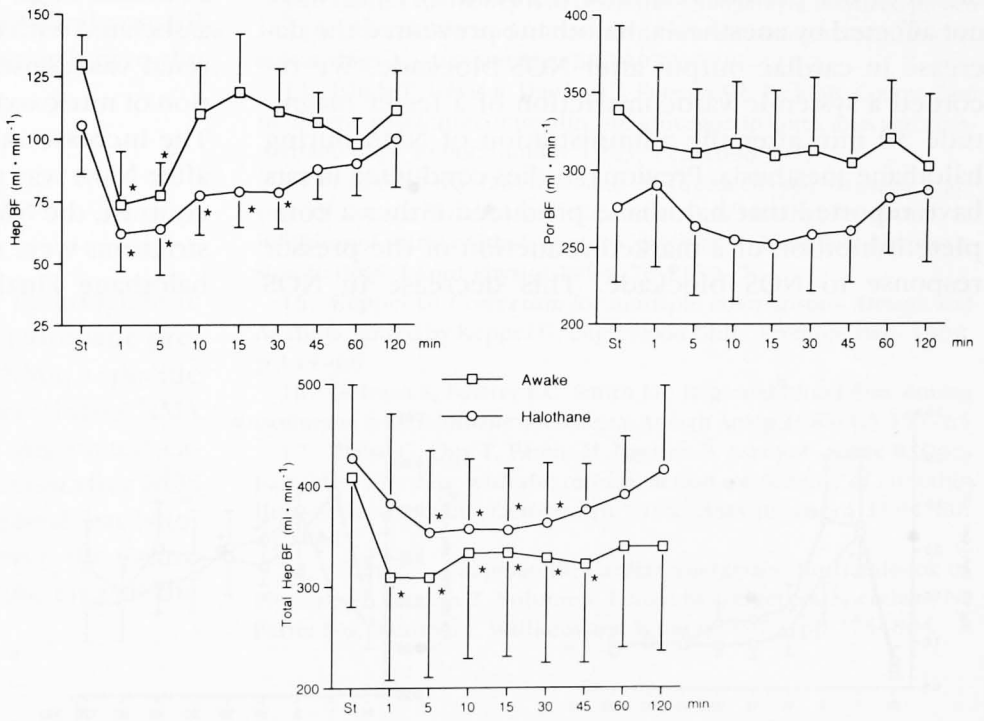

Fig. 4. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on hepatic, portal, and total hepatic blood flows in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P < 0.05$ *versus* control.

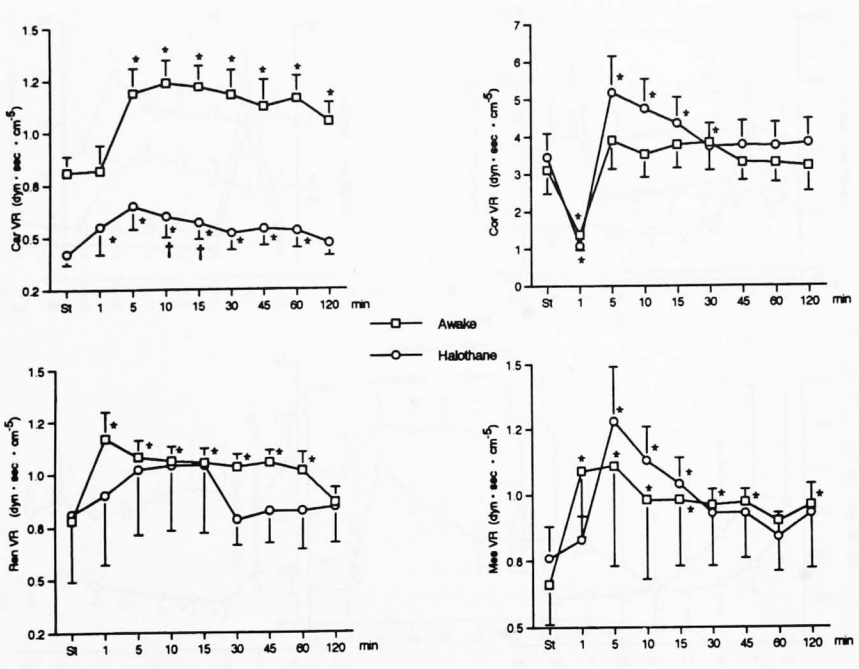

Fig. 5. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on carotid, coronary, mesenteric, and renal vascular resistance in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P <$ 0.05 *versus* control. †$P < 0.05$ *versus* the magnitude of changes induced by N-methyl-L-arginine in awake dogs.

with marked decreases in coronary, cerebral, renal, and mesenteric blood flows in the absence of anesthetics. Using continuous measurements, we previously demonstrated that regional blood flows are essentially preserved after administration of NMA in conscious dogs.

Our data demonstrate that the peak pressor response after the administration of NOS blocker was not affected by 1.2% halothane. Although the magnitude and duration of the pressor response induced by NMA were not affected by anesthesia, halothane prevented the decrease in cardiac output after NOS blockade. We recorded a systemic vasoconstriction of a lesser magnitude 30 min after the administration of NMA during halothane anesthesia. Previous studies conducted in rats have reported that halothane produced either a complete inhibition or a marked reduction of the pressor response to NOS blockade. This decrease in NOS blockage pressor response has been associated with either a decrease in cardiac output and systemic vasoconstriction of similar magnitude[7] or no change in cardiac output and a reduction of the increase in systemic vascular resistance.[6]

Halothane interfered with the role played by nitric oxide in the modulation of local vascular tone, but its effect seems to vary according to the vascular territory. In awake dogs, the administration of NOS blocker was associated with carotid, hepatic, portal, mesenteric, and renal vasoconstriction, suggesting an active contribution of nitric oxide to the maintenance of vascular tone. The increase in hepatic and portal vascular resistance after NMA was essentially unaffected by halothane. In contrast, the NMA-mediated carotid and renal vasoconstrictions were markedly attenuated by the presence of halothane. Finally, the mesenteric vasoconstriction was

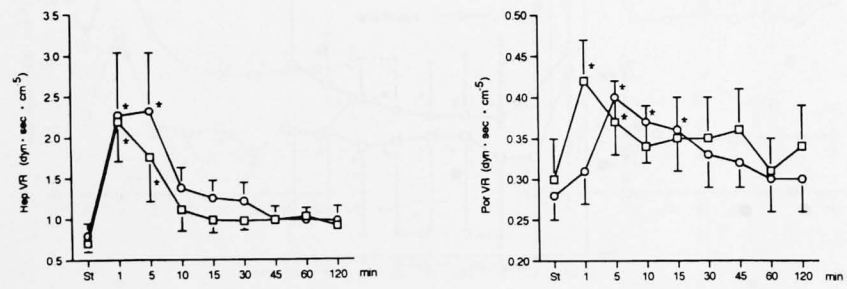

Fig. 6. Effects of N-methyl-L-arginine (20 mg/kg intravenous) on hepatic and portal vascular resistance in awake dogs (□) and anesthetized with 1.2% halothane (○). St = Steady − state control before N-methyl-L-arginine injection; *$P < 0.05$ *versus* control.

of shorter duration during halothane anesthesia. These findings suggest a significant interaction between 1.2% halothane and the nitric oxide pathway in the carotid, mesenteric, and renal circulations but not in the hepatic and portal territories. Muldoon *et al.*[1] reported that *in vitro,* halothane attenuated the endothelium-mediated vasodilation of the canine carotid artery. The authors further postulated that halothane may interfere with the synthesis, release, or transport of nitric oxide. Thus, halothane attenuated the effects of acetylcholine but did not affect the relaxation induced by nitroglycerin. Our experimental design, however, did not enable us to draw any conclusions about the level at which halothane interferes with the nitric oxide pathway. Blaise *et al.*[17] reported that halothane did not interfere with the release and transport of nitric oxide in bovine aortic endothelial cells.

Although NMA did not increase coronary vascular tone in awake dogs in our study, a coronary vasoconstriction was recorded during halothane anesthesia. Coronary vasoconstriction is often indicative of a decrease in myocardial oxygen demand.[18] It is unlikely that the NMA-induced coronary vasoconstriction recorded in the presence of halothane was metabolically correlated because NMA induced a similar increase in blood pressure and heart rate in awake and anesthetized dogs. Our data suggest that in the presence of halothane, the nitric oxide system is involved in the control of coronary vascular tone. Because NMA did not produce an increase in coronary resistance in awake dogs, it appears that the role played by nitric oxide in the local control of the coronary circulation also varies according to the experimental conditions.

Conclusion

In comparison with the cardiac and hemodynamic effects of NMA recorded in awake dogs, halothane preserved the pressor response induced by NMA, a specific NOS blocker. Cardiac output was preserved after NMA injection during anesthesia. Halothane attenuated carotid, mesenteric, and renal vasoconstriction after NOS inhibition. Therefore, we have demonstrated that halothane interferes with NOS activity. However, the nature of the interaction depends on the specific area of the circulation.

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