

The Response of the Feline Cerebral Circulation to P_{aCO_2} during Anesthesia with Isoflurane and Halothane and during Sedation with Nitrous Oxide

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The reduction in cerebral blood flow (CBF) caused by hypocapnia is an important element of neuroanesthetic techniques. While it has been demonstrated previously that the CO_2 response of the cerebral circulation ($CO_2 \cdot R$) is enhanced (*i.e.*, greater $\Delta CBF / \Delta P_{aCO_2}$) during halothane administration, the effect of isoflurane on $CO_2 \cdot R$ has not been evaluated completely. Accordingly, the authors examined $CO_2 \cdot R$ in cats during anesthesia with 1.0 MAC isoflurane (with 75% N_2O) and compared it with $CO_2 \cdot R$ during anesthesia with 1.0 MAC halothane (with 75% N_2O) and with $CO_2 \cdot R$ during the administration of 75% N_2O alone.

$CO_2 \cdot R$ during anesthesia with isoflurane- N_2O was enhanced relative to that observed during administration of both halothane- N_2O ($P < 0.025$) and N_2O alone ($P < .001$). $CO_2 \cdot R$ during anesthesia with halothane- N_2O was, in turn, greater than that observed during the administration of N_2O alone ($P < 0.025$). Furthermore, at similar levels of hypocapnia (P_{aCO_2} , 18-20 mmHg), CBF was significantly lower ($P < 0.01$) during administration of isoflurane- N_2O ($29.0 \pm 4.5 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$) than during administration of either N_2O ($40.6 \pm 5.5 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$) or halothane- N_2O ($39.6 \pm 7.8 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$). CBF values during administration of the N_2O alone and halothane- N_2O were not different during hypocapnia.

The results of this study indicate that $CO_2 \cdot R$ in cats not only is preserved during administration of 1.0 MAC isoflurane (with 75% N_2O) but is enhanced relative to that observed during anesthesia with 1.0 MAC halothane (with 75% N_2O) and during sedation with N_2O alone. In addition, the induction hypocapnia (P_{aCO_2} , 18-20 mmHg) resulted in a reduction of CBF to lower levels during the administration of isoflurane- N_2O than during administration of halothane- N_2O or N_2O alone. If the cerebral circulation of anesthetized humans responds similarly to that of the cat, these results suggest that the induction of hypocapnia during the administration of isoflurane (with N_2O) may facilitate a greater reduction in CBF, and therefore perhaps ICP, than will occur at a comparable P_{aCO_2} during anesthesia with halothane (with N_2O) or during the administration of N_2O alone. (Key words: Anesthetics, gases: nitrous oxide. Anesthetics, volatile: halothane; isoflurane. Brain: blood flow; CO_2 response.)

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THE REDUCTION in cerebral blood flow (CBF) that occurs in response to hypocapnia is a central element of anesthetic techniques for neurosurgery as well as for nonneurologic surgery in patients with reduced intracranial compliance. Accordingly, the impact of anesthetic agents on the CO_2 responsiveness of the cerebral circulation has important implications with regard to anesthetic selection.

The available information regarding the effects of isoflurane on CBF, cerebral metabolism,^{1,2} and autoregulation^{2,3} suggests that this agent may be more appropriate for use in neurosurgery than the other currently available volatile agents. However, the impact of isoflurane on the CO_2 responsiveness of the cerebral circulation has not been evaluated fully. Cucchiara *et al.*¹ have demonstrated that CO_2 response is present during 1.1 MAC isoflurane anesthesia in dogs, and Adams *et al.*⁴ have shown that lumbar cerebrospinal fluid pressure decreases with the induction of hypocapnia in neurosurgical patients anesthetized with isoflurane. However, there have been no direct comparisons of CO_2 response during isoflurane anesthesia with that seen in either an awake state or during anesthetic regimens not including other volatile agents. We therefore examined CO_2 response in cats during anesthesia with isoflurane and compared it with CO_2 response during sedation with 75% nitrous oxide. CO_2 response during the administration of halothane also was examined. A comparison of the CO_2 response of the cerebral circulation of normal humans during anesthesia with halothane (1.2% inspired), during sedation with nitrous oxide and in the awake state is already available,⁵ and those data indicate that halothane increases the slope of the P_{aCO_2} -CBF relationship in humans, whereas nitrous oxide has no effect. Halothane therefore was included in the present study as a means of assessing the potential relevance to human anesthesia of results obtained in our feline model.

Methods

Eleven mongrel cats of either sex (weight 3.5 ± 0.6 kg) were studied. Anesthesia was induced in a plexiglass

box by the administration of 4% halothane in oxygen. The animals were paralyzed with pancuronium (0.5 mg/kg), intubated, and ventilated (tidal volume 15 ml/kg; rate 20 breaths/min). Anesthesia was maintained with an inspired gas mixture of 1% halothane in 75% N₂O and oxygen, and carbon dioxide was added to the inspired mixture to maintain normocapnia (Pa_{CO₂} ca. 30 mmHg in the cat⁶) during surgical preparation. Relaxation was maintained with increments of pancuronium (ca. 0.5 mg/h), and normal saline was administered at 6 ml · ml · kg⁻¹ · h⁻¹. Esophageal temperature was servo-controlled (heat lamp) to 37° C. Catheters were placed in the abdominal aorta and the right atrium via femoral vessels and in the right lingual artery. The animal then was placed in the sphinx position, with the head secured in a stereotactic frame such that the interaural line was 12 cm above the table surface. Extracranial soft tissues were resected from brow toinion and to the zygomatic arches laterally. A catheter for measurement of intracranial pressure (ICP) was placed in the subarachnoid space via a burr hole over the left parietal area. The dura was sealed with cyanoacrylate cement, and the skull defect was closed with dental acrylic.

At the conclusion of surgical preparation, wound margins were infiltrated with 0.25% bupivacaine and the halothane was discontinued. (75% N₂O was continued throughout all subsequent phases of the study.) Noise and contact with the animal were avoided. A 90-min halothane "washout" period ensued, and in all animals end-tidal halothane concentration was less than 0.06% for at least 20 min prior to the ensuing CO₂ response determinations. During subsequent study, blood pressure and ICP (both referenced to head level), end-tidal carbon dioxide concentration, and end-tidal volatile agent concentration (Beckman LB II infrared analyzers) were recorded continuously. Arterial blood gas and cerebral blood flow (CBF) determinations were made intermittently. CBF was calculated (T_{1/2} method) from a washout curve recorded over the right posterior parietal area after injection of approximately 300 μCi of xenon¹³³ in saline via the right lingual artery catheter. A xenon blood-to-brain partition coefficient of 1.0 was assumed, and the first 15 s of the washout curve was discarded.⁷

At the beginning of each CO₂ response determination, the volatile agent under study was introduced and the end-tidal concentration was increased to the 1.0 MAC‡ level (halothane 1.19%; isoflurane 1.61%⁸) over 5 min by the use of over-pressure. Angiotension II was infused

where necessary to maintain mean arterial pressure (MAP) between 110 and 125 mmHg. Note that MAP in the domestic cat is high by comparison with the human and that anesthesia with 1.0 MAC halothane and isoflurane not infrequently results in an unsupported MAP in this range. When the end-tidal volatile agent concentration had been maintained at the 1.0 MAC level for 15 min, the inspired CO₂ concentration was reduced and Pa_{CO₂} was lowered to 18–20 mmHg using end-tidal CO₂ as a guide and ABG determination for confirmation. Cerebral blood flow was measured; and thereafter, Pa_{CO₂} was increased and CBF determinations were repeated at Pa_{CO₂}'s of 29–31, 39–41, and 47–50 mmHg. In each instance, the target Pa_{CO₂} was maintained for 5 min prior to flow determination. After the last flow measurement (Pa_{CO₂} 47–50 mmHg), the volatile agent was discontinued (N₂O continued) and normocapnia was restored. A 45-min "washout" ensued before the next CO₂ response determination. The intervals were identical for subsequent CO₂ response determinations, though for CO₂ response determination during N₂O sedation no volatile agent was introduced.

In each of the first six animals studied, a single CO₂ response curve was generated (two each for isoflurane–N₂O, halothane–N₂O, and N₂O alone.) Because of the cardiovascular and metabolic stability evident in these six studies, each of the subsequent five animals was exposed to all three anesthetic regimens in systematically varied sequences. In each of these five animals, a CO₂ response curve for each of the three anesthetic regimens was generated. Thus, for each anesthetic regimen, a total of seven CO₂ response curves were obtained.

Cerebral blood flow, intracranial pressure, carbon dioxide tension, and mean arterial blood pressure for each of the four Pa_{CO₂} ranges were compared by an analysis of variance and, where differences were detected, pair-wise comparisons were performed using Student's *t* test for unpaired data with the Bonferroni correction for multiple comparisons.

For the comparison of CO₂ response, the expression of the general form log_e CBF = a + b · Pa_{CO₂}, which best described the Pa_{CO₂}–CBF relationship for each of the three anesthetic regimens was determined using the least-squares method. The slopes of the three regression equations were examined by an analysis of covariance, and pairwise comparisons were performed using the Newman-Keul multiple range test.

Results

The Pa_{CO₂}, MAP, ICP, and CBF data are presented in table 1. There were no intergroup differences in the mean Pa_{CO₂} levels at which CBF comparisons were performed. There also were no differences in MAP

‡ The expression "1.0 MAC" will be used throughout this communication to refer to the concentration of the volatile agent in question without allowance for the anesthetic contribution of simultaneously administered nitrous oxide.

TABLE 1. Mean Arterial Blood Pressure (MAP), Arterial Carbon Dioxide Tension (P_{aCO_2}), Intracranial Pressure (ICP), and Cerebral Blood Flow (CBF) during Anesthesia with 1.0 MAC Isoflurane (with 75% N_2O), and 1.0 MAC Halothane (with 75% N_2O) and during Sedation with 75% N_2O

P_{aCO_2} Range	Halothane (with N_2O)	Isoflurane (with N_2O)	N_2O	ANOVA*
18-20				
$P_{aCO_2} \dagger$	19 \pm 1	18 \pm 1	18 \pm 1	NS
MAP \dagger	126 \pm 5	124 \pm 6	151 \pm 22	$P < 0.001$
ICP \dagger	6 \pm 3	8 \pm 4	7 \pm 4	NS
CBF \ddagger	40 \pm 8	29 \pm 5	41 \pm 6	$P < 0.01$
29-31				
P_{aCO_2}	30 \pm 1	30 \pm 1	30 \pm 1	NS
MAP	122 \pm 6	122 \pm 6	161 \pm 23	$P < 0.001$
ICP	10 \pm 3	11 \pm 4	8 \pm 4	NS
CBF	62 \pm 16	50 \pm 9	50 \pm 8	NS
39-41				
P_{aCO_2}	40 \pm 1	40 \pm 1	40 \pm 1	NS
MAP	121 \pm 5	124 \pm 7	157 \pm 24	$P < 0.001$
ICP	14 \pm 3	15 \pm 6	10 \pm 3	NS
CBF	123 \pm 31	126 \pm 32	85 \pm 15	$P < 0.05$
47-50				
P_{aCO_2}	48 \pm 1	48 \pm 2	48 \pm 1	NS
MAP	121 \pm 5	119 \pm 6	164 \pm 26	$P < 0.001$
ICP	18 \pm 4	19 \pm 5	15 \pm 7	NS
CBF	169 \pm 35	174 \pm 33	129 \pm 25	$P < 0.05$

* Analysis of variance. The results of pairwise comparisons are given in the text.

\dagger mmHg.

\ddagger $ml \cdot 100 g^{-1} \cdot min^{-1}$.

between the halothane and the isoflurane groups. The doses of angiotensin II ($ug \cdot kg^{-1} \cdot min^{-1} \pm SD$) required to maintain MAP during administration of the two volatile agents were small but were slightly greater ($P < 0.05$) for halothane (0.17 ± 0.1 , range 0-0.31) than for isoflurane (0.12 ± 0.1 , range 0-0.23). Mean arterial pressure in the nitrous oxide group was significantly ($P < 0.001$) higher than in the other two groups.

The P_{aCO_2} -CBF relations are presented graphically in figure 1. The equations defining the regressions for each anesthetic regimen were as follows: 1.0 MAC isoflurane (with 75% N_2O): $\log_e CBF = 2.17 + 0.06 P_{aCO_2}$, $r = 0.95$; 1.0 MAC halothane (with 75% N_2O): $\log_e CBF = 2.68 + 0.05 P_{aCO_2}$, $r = 0.94$; 75% N_2O : $\log_e CBF = 2.89 + 0.04 P_{aCO_2}$, $r = 0.92$.

The analysis of covariance indicated that there were significant differences ($P < 0.001$) among the slopes of the three regressions. The pairwise comparisons demonstrated that the halothane P_{aCO_2} -CBF regression was steeper than that observed during the administration of nitrous oxide alone ($P < 0.025$) and that the isoflurane P_{aCO_2} response curve was, in turn, significantly steeper than that for either halothane ($P < 0.025$) or nitrous oxide ($P < 0.001$).

The statistical comparisons of CBF at each P_{aCO_2} level (table 1) were as follows: for P_{aCO_2} 18-20 mmHg, CBF in the isoflurane group was less than in both the halothane ($P < 0.01$) and N_2O ($P < 0.01$) groups; at P_{aCO_2} 29-31 mmHg there were no differences; and at P_{aCO_2} 39-41 and 47-50 mmHg, CBF in the nitrous oxide group was significantly less than CBF in both the halothane ($P < 0.05$) and isoflurane ($P < 0.05$) groups.

The differences in intracranial pressure (table 1) with the three anesthetic regimens were small and an apparent trend toward higher ICP at normocapnia and hypercapnia during the administration of the two volatile agents (as compared with the nitrous oxide group at similar P_{aCO_2} 's) was not statistically significant.

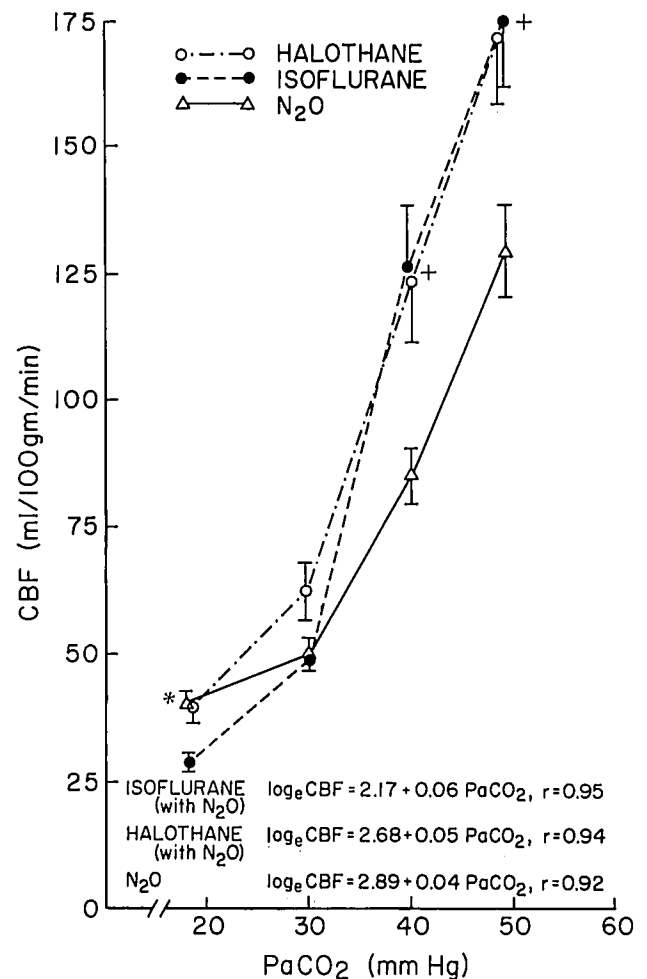


FIG. 1. The relationship between arterial carbon dioxide tension (P_{aCO_2} , mmHg) and cerebral blood flow (CBF, $ml \cdot 100 g^{-1} \cdot min^{-1}$) during anesthesia with 1.0 MAC halothane (with 75% N_2O), 1.0 MAC isoflurane (with 75% N_2O), and during sedation with 75% N_2O . The equations describing the P_{aCO_2} -CBF regressions are shown. * $P < 0.01$ for halothane and N_2O versus isoflurane. + $P < 0.05$ for halothane and isoflurane versus N_2O .

Discussion

Earlier human investigations have demonstrated that, during halothane anesthesia, the CO₂ responsiveness of the cerebral circulation is enhanced (*i.e.*, greater $\Delta\text{CBF}/\Delta\text{PaCO}_2$) relative to an awake or to a nitrous oxide sedated state.⁵ The results of the present study are consistent with the previously observed effect of halothane and indicate that feline CO₂ responsiveness during anesthesia with 1.0 MAC isoflurane (with 75% N₂O) also is enhanced relative to a nitrous oxide sedated state.

In the human studies cited above, the PaCO₂-CBF regressions for halothane (1.2% inspired) and for nitrous oxide converged to a similar CBF values at a PaCO₂ of approximately 20 mmHg. The relationship of the halothane and the nitrous oxide regressions in the present study was comparable. However, the isoflurane regression presented a departure from this pattern in that the CBF observed during hypocapnia (PaCO₂ 18–20 mmHg) was significantly *less* than that observed with either halothane (with nitrous oxide) or with nitrous oxide alone. The observation that, at the same level of hypocapnia, CBF actually may be lower during the administration of isoflurane than during administration of N₂O without a volatile agent may be intuitively difficult to accept for those many clinicians who were trained to minimize or avoid the use of volatile agents in neurosurgery. The phenomenon appears to be the result of the interaction of two effects. First, 1.0 MAC isoflurane anesthesia at normocapnia resulted in only a very small (nonsignificant) increase in CBF relative to the nitrous oxide sedated state (Table 1). This confirms an observation made previously in this laboratory.² And second, as noted above, the slope of the CO₂ response curve was increased during isoflurane administration. The result of these two effects is that the CO₂ response curves for the isoflurane and N₂O groups intersect near normocapnia. Thus, CBF during anesthesia with isoflurane is lower relative to CBF in the nitrous oxide group during hypocapnia and higher during hypercapnia. Note that this implies a two-edged sword. While a greater reduction in CBF can be achieved with hypocapnia during isoflurane administration, the CBF and ICP consequences of inadvertent hypercapnia might be more deleterious than would be the case in the absence of isoflurane.

If the results of this feline study are applicable to anesthetized humans, they suggest that a greater reduction in CBF (and hence cerebral blood volume⁹ and therefore perhaps ICP) can be achieved during hypocapnic (PaCO₂ 18–20 mmHg) isoflurane-nitrous oxide anesthesia than during a comparable degree of hypocapnia induced in conjunction with the administration of halothane-nitrous oxide or nitrous oxide alone. This

inference cannot be confirmed by currently available human data, as only normocapnic studies have been performed. However these normocapnic data are supportive. Murphy *et al.*⁸ demonstrated that CBF was lower during administration of 1.1 and 1.6 MAC isoflurane than during anesthesia with equi-MAC concentrations of halothane. If the relative relationships of the slopes of the CO₂ response curves for halothane, nitrous oxide, and isoflurane are similar in humans and the cat with the human isoflurane curve offset toward the lower CBF values observed by Murphy *et al.*, then CBF during hypocapnic isoflurane administration should be less, in fact, than that attainable during administration of either halothane or nitrous oxide alone. Whether the CBF values achieved during hypocapnia with an isoflurane-nitrous oxide anesthetic also would be lower than those that would occur during administration of nitrous oxide supplemented with a narcotic (a so-called nitrous-narcotic technique), is a relevant question not answered by this study. In humans, neither nitrous oxide¹⁰ nor a narcotic in large doses (morphine 1.0 and 3.0 mg · kg⁻¹)¹¹ administered with 70% N₂O altered normocapnic CBF with respect to awake values. Therefore, it might be anticipated that the position of a PaCO₂-CBF regression generated during a nitrous-narcotic regimen would be similar at normocapnia to that of a curve for nitrous oxide alone. However, the effect of narcotics on the slope of the PaCO₂-CBF regression (*i.e.*, what CBF would be above and below normocapnia) is less certain. While it has been demonstrated in pentobarbital anesthetized dogs by McPherson and Traystman,¹² that CO₂ response is present after the administration of moderately large doses of a narcotic (fentanyl, 25 and 100 μg · kg⁻¹), there have been no comparisons of CO₂ response during administration of nitrous oxide with and without a narcotic. Accordingly, we cannot predict the effect of narcotic supplementation on the slope of the nitrous oxide CO₂ response curve. If CO₂ response is not changed, in fact, by these agents, then it might be anticipated that CBF during hypocapnia with isoflurane-nitrous oxide anesthesia also might be less than that occurring with a nitrous-narcotic technique. Clarification will require further study.

It should be noted that the foregoing observations regarding lower CBF values during hypocapnic isoflurane administration are based on CBF determinations made at only one hypocapnic PaCO₂ level (18–20 mmHg). It

§ Murphy FL Jr, Kennell EM, Johnstone RE, Lief PL, Jobs DR, Tompkins BM, Gutsche BB, Behar MG, Wollman H: The effects of enflurane, isoflurane, and halothane on cerebral blood flow and metabolism in man. Abstracts of Scientific Papers, Annual Meeting of the American Society of Anesthesiologists, 1974, pp 61–62.

is possible that at lower P_{aCO_2} values, the three P_{aCO_2} -CBF regressions would converge to a common value and that the CBF differences reported herein no longer would be evident. Examination of the graphic presentation of the P_{aCO_2} -CBF relationships for the three anesthetic regimens (fig. 1) does not support this suggestion, particularly with respect to nitrous oxide alone. However, the present data cannot exclude the possibility.

In spite of the significant differences in cerebral blood flow that were observed during both hypocapnia and hypercapnia, there were no significant differences in intracranial pressure between the three anesthetic regimens. For example, the significantly lower CBF observed during administration of isoflurane at P_{aCO_2} 18–20 mmHg was not accompanied by a lower ICP than those observed in the halothane–nitrous oxide or nitrous oxide groups at the same P_{aCO_2} . We suspect that this reflects the highly compliant intracranial space of normal animals studied in a head-up posture. However, we recognize that while CBF (via its effect on cerebral blood volume⁹) is an important determinant of the volume of the intracranial contents (and hence ICP), other factors, *e.g.*, alterations in CSF dynamics^{13–15} may be involved in determining the ICP observed during a particular anesthetic regimen. In order to determine whether the CBF differences observed in this study will “translate” into clinically important differences in ICP, a comparison in a model of impaired compliance will be required.

There are several methodologic considerations that merit comment. The CBF determinations always began with hypocapnia and progressed stepwise to normocapnia and finally to the hypercapnic levels. This constant sequence presented the possibility of the intrusion of some time-related variable. Nonetheless, it was deemed preferable for two reasons. First, we sought to optimize the conditions under which the most clinically relevant P_{aCO_2} level, *i.e.*, hypocapnia, was examined and therefore performed the hypocapnic studies first. Second, it is possible that there is a degree of hysteresis in the P_{aCO_2} -CBF relationship and it was felt that increasing the scatter of the CBF results in a small population (by randomizing sequence) might have served to obscure meaningful differences between the groups. We doubt, in fact, that this constant sequence has any important impact on the results. We have observed prolonged stability of baseline (*i.e.*, N_2O sedated) CBF values in other experiments² and therefore feel that a progressive deterioration of the preparation during individual CO_2 response determinations is unlikely to have been a factor. Another possible time-related variable is the change in the cerebral vascular effects of the volatile agents that occurs with time. Specifically, CBF is known

to decrease during prolonged exposure to constant concentrations of both halothane¹⁶ and isoflurane.¹⁷ However, it is unlikely that this phenomenon had any material influence herein because the duration of exposure to a given agent was relatively brief in this protocol.

In order to avoid the potential interaction of differing and undefined effects of halothane and isoflurane on autoregulation, blood pressure was maintained at a similar level in the two groups by the administration of angiotensin II. The average infusion rate required in the halothane group ($0.17 \mu g \cdot kg^{-1} \cdot min^{-1}$) was greater than that required during isoflurane administration ($0.12 \mu g \cdot kg^{-1} \cdot min^{-1}$). The possibility of some influence of angiotensin on the results of this study must be considered. The CBF effects of angiotensin II in the cat have not been evaluated. However, in humans, angiotensin infused directly into the carotid artery at rates up to $0.21 \mu g \cdot kg^{-1} \cdot min^{-1}$ was found to have no effect on CBF.¹⁸ While we cannot unequivocally exclude an effect of angiotensin (given intravenously in this study) on the observed cerebral blood flows, the foregoing human observations would suggest that the impact if any, was small. Furthermore, any cerebral vasoconstrictive effect of angiotensin would have served to cause a greater reduction in CBF values in the halothane group (in which larger doses of angiotensin were used). This would have resulted in an *underestimation* of the CBF differences between halothane and isoflurane during hypocapnia, which we observed and report herein.

While MAP in the halothane and isoflurane groups was similar, it was significantly higher (approximately 25 mmHg) in the nitrous oxide group. It is difficult to be certain whether this difference interferes with the comparison of the CBF- P_{aCO_2} relationships. It would have been desirable to eliminate the disparity, but pilot studies indicate that it was not feasible to increase pressure pharmacologically in the isoflurane and halothane groups to the N_2O group levels without on occasion producing an unacceptable degree of cardiovascular instability. Lowering MAP in the nitrous oxide group was contemplated but excluded on the basis of reports indicating that substantial reduction of MAP, whether by hemorrhage,¹⁹ halothane,²⁰ trimethaphan,^{21,22} or sodium nitroprusside,^{21,22} reduces the slope of the CO_2 regression.

The mechanism by which volatile agents including isoflurane (present study), halothane,⁵ ether,⁵ and cyclopropane⁵ increase the slope of the P_{aCO_2} -CBF relation is unknown. Cerebral reactivity to carbon dioxide is thought to be mediated by CO_2 -related changes in extracellular pH (see Kagstrom *et al.*²³ for a recent

† Assumes 70-kg subjects.

discussion and references) and it is not obvious why volatile agents should alter this relationship. However, Sprague *et al.*²⁴ have demonstrated that both halothane and isoflurane result in increases in cyclic AMP levels in the vascular smooth muscle of rat aorta, and the effects of halothane and isoflurane on CO₂ response may be related to their impact on this second messenger system. This possibility, however, must be viewed as a matter of speculation both because the vessels studied by Sprague *et al.*²⁴ were noncerebral and because there are no data to confirm that cyclic AMP actually is involved in CO₂-related changes in cerebral vascular tone.

In summary, the results of this study indicate that in cats, the CO₂ responsiveness of the cerebral circulation not only is preserved but is enhanced during the administration of 1.0 MAC isoflurane (with 75% N₂O). Furthermore, CBF values observed at comparable levels of hypocapnia (PaCO₂ 18–20 mmHg) during isoflurane anesthesia (with 75% N₂O) were less than those observed during administration of either 1.0 MAC halothane (with 75% N₂O) or nitrous oxide alone. If CBF is an important determinant of ICP when intracranial compliance is abnormal, then these data suggest that greater reductions in ICP might be achieved with induction of hypocapnia during isoflurane–nitrous oxide administration than with halothane–nitrous oxide or with nitrous oxide alone. The nitrous oxide sedation in this study was not supplemented with narcotics or other intravenous agents, and therefore these data cannot predict whether isoflurane–nitrous oxide anesthesia also would result in a lower CBF (or ICP) than would occur at a comparable level of hypocapnia during a nitrous–narcotic anesthetic regimen. The resolution of that question will require further study. In the interim, this study constitutes a contribution to the growing body of animal data, which suggest that isoflurane may be more suitable for use in neuroanesthesia than previously available volatile agents.

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