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TITLE: Preserved Coupling of CNS Blood Flow and Metabolism During Halothane Anesthesia

AUTHOR: M.D. Szabo, M.D. and G. Crosby, M.D.
AFFILIATION: Department of Anesthesia, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114

Because volatile anesthetics decrease metabolism but increase flow[1], they are generally presumed to uncouple the normally close relationship between metabolic demand and blood flow in the CNS. Although recent indirect evidence indicates that some relationship between flow and metabolism is maintained during inhalation anesthesia[2], no study has directly evaluated whether a change in metabolism causes a change in flow. Accordingly, we tested the hypothesis that volatile anesthetics do not abolish flow:metabolism coupling by measuring the spinal cord blood flow (SCBF) response to metabolic stimulation during halothane anesthesia.

Ten male, Sprague-Dawley rats were anesthetized with halothane-$N_2$0-O_2 for bilateral femoral artery and vein cannulation, tracheostomy, and isolation of one femoral nerve. Following surgery, N_2O was discontinued and the inspired halothane concentration, measured with an agent analyzer, was adjusted to and maintained at 0.9%. Ventilation, arterial blood gases, rectal temperature, and MAP were controlled within normal physiologic limits. Following equilibration at 0.9% halothane for at least 30 min, electrical stimulation (20 v, 10 Hz, 0.5 ms) of the femoral nerve was begun. One minute later, regional spinal glucose utilization (n=4) or blood flow (n=6) measurements were begun with administration of 2-[^{14}C]deoxy-glucose or [^{14}C]-iodoantipyrine, respectively. The rates of SCBF or glucose utilization in the lumbar spinal cord ipsi- and contralateral to the stimulating electrode were compared with a paired t-test.

Stimulation produced large, statistically significant increases in both metabolic rate and SCBF in the ipsilateral dorsal horn (laminae I-III and IV-VI) of the spinal cord (Table). The 21-41% increase in glucose utilization in the ipsilateral dorsal horn was associated with a corresponding 27-43% increase in SCBF.

SCBF and Metabolism During Stimulation

		Glucose Utilization (4) ($\mu mol \cdot 100g^{-1} \cdot min^{-1}$)	SCFB (6) ($ml \cdot 100g^{-1} \cdot min^{-1}$)
LAMINA(E)			
I-II	I	45 ± 3 *	166 ± 4 ***
	C	32 ± 1	94 ± 5
IV-VI	I	40 ± 0.4 **	223 ± 12 ***
	C	33 ± 1	162 ± 11
VIII	I	35 ± 2	214 ± 15 *
	C	35 ± 2	191 ± 13
IX	I	34 ± 2	189 ± 8 *
	C	33 ± 2	175 ± 11

Data are mean ± SEM. I = ipsilateral, C = contralateral to stimulating electrode. * P < 0.05; ** P < 0.01; *** P < 0.001

Preserved flow:metabolism coupling during halothane anesthesia has been inferred from the recent observation that brain regions with higher metabolic rates tend to have higher flows than those less metabolically active[2]. This study, however, demonstrates that a stimulation-induced increase in metabolic rate causes a comparable increase in SCBF and thereby provides direct evidence that coupling remains intact during halothane anesthesia.

1. Anesth Analg 63:143-174, 1985
2. J Cerebral Blood Flow Metab 9:323-328, 1989

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TITLE: EFFECT OF HALOTHANE AND ISOFLURANE ON CANINE CEREBRAL ARTERIES IN VITRO

AUTHORS: J. E. Brian, Jr., M.D., R. H. Kennedy, Ph.D.
AFFILIATION: University of Arkansas for Medical Sciences, 4301 W. Markham, Slot 515, Depts. of Anesthesiology and Pharmacology, Little Rock, AR 72205-7199

Mechanisms by which halothane (H) and isoflurane (I) induce increased cerebral blood flow are unclear. To further elucidate mechanisms by which these inhaled anesthetics may alter cerebrovasomotor tone, we studied the effect of 1 and 2 MAC halothane and isoflurane on serotonin (5-HT) induced contractility in endothelium-intact (+) and -denuded (-) canine middle cerebral (MCA) and basilar arteries (BA) in vitro.

MATERIALS AND METHODS: BA and MCA were obtained as described elsewhere (1), cut into 4 to 5 mm segments and mounted for isometric tension recording. All segments were adjusted to and maintained at 1 gm resting tension. After 120 minutes of equilibration, a baseline cumulative 5-HT dose-response curve was obtained, following which the preparations were exposed to 1 or 2 dog MAC H (0.9% and 1.8%) or I (1.4% and 2.8%), and a second 5-HT curve obtained. One hour later, a recovery curve was obtained, followed by exposure to the alternate concentration of the same anesthetic, and a final recovery curve. Tmax and ED50 values were obtained for each curve, and Tmax responses adjusted to 100% of the baseline value. The n reported represents the number of animals in each group.

RESULTS: Prior to exposure to halothane, baseline values for Tmax were BA+ 1100 ± 209 mg (n=3), BA- 2269 ± 219 mg (n=4), MCA+ 650 ± 91 mg (n=3) and MCA- 1022 ± 73 mg (n=4). During exposure to both 1 and 2 MAC H, significant decreases in Tmax values ($p < 0.05$) ocurred in BA+, BA-, MCA+, and MCA- preparations. There were no differences between the amount of depression seen at 1 or 2 MAC (see table 1). Recovery from both levels of H was less than complete. No ED50 values were altered by halothane. Prior to exposure to isoflurane, baseline values for Tmax were BA+ 1075 ± 104 mg (n=3), BA- 2088 ± 238 mg (n=4), MCA+ 658 ± 145 mg (n=3) and MCA- 1025 ± 141 mg (n=4). There were no differences induced by I in Tmax in any of the groups, although there was a tendency for Tmax to be increased in both MCA+ and MCA- (table 1). ED50 values were significantly increased to the right during exposure to 2 MAC I in both BA- and MCA- groups. Baseline ED50 values in these BA and MCA groups were $3.73 \pm 0.43 \times 10^{-8}$ and $3.35 \pm 0.38 \times 10^{-8}$, which increased to $6.89 \pm 1.28 \times 10^{-8}$ and $5.62 \pm 0.23 \times 10^{-8}$.

DISCUSSION: Although there was a tendency for H to produce more depression at 2 MAC, these values were not different from 1 MAC, indicating a lack of dose-dependency at these levels. Additionally, there were no differences between (+) and (-) groups, indicating that the effects of H are not mediated by the endothelium. I produced no significant change in Tmax in any group, indicating that alterations in tone may be mediated by non-direct mechanisms.

REFERENCES: 1. Conner HE Br J Pharmacol 96:170-178, 1989.

	1 MAC	RECOVERY	2 MAC	RECOVERY
HALOTHANE				
BA+	73±4*	94±6	70±3*	87±8*
BA-	62±4*	86±2*	54±4*	87±4*
MCA+	77±5*	103±14	61±5*	95±7
MCA-	67±4*	87±4*	58±4*	94±5
ISOFLURANE				
BA+	92±13	109±7	105±16	103±8
BA-	103±6	106±8	104±5	101±5
MCA+	118±5	133±12	112±9	134±11
MCA-	117±2	128±4	115±3	121±3

Table 1 Tmax values expressed as % of baseline T_{max}. Values are mean ± SEM. * $p < 0.05$ as compared to baseline T_{max}.