Title: DIFFERENT 1.2 MAC COMBINATIONS OF NITROUS OXIDE-ENFLURANE PRODUCE SPECIFIC METABOLIC RESPONSES IN RAT SPINAL CORD.

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Introduction: Nitrous oxide (N_2O) and enflurane have been observed to have different neurophysiologic properties. This difference has led to hypotheses that these two anesthetics act at different sites or have distinct mechanisms of action.[1] In order to identify possible spinal cord interactive effects of N_2O and enflurane (E), we studied the effect three different 1.2 MAC combinations of N_2O and E had upon the local spinal cord metabolism of glucose (ISCMRg).

Methods: With prior approval by the Animal Studies Subcommittee, male, Sprague-Dawley rats (n = 30) of similar ages and weights were separated into three 1.2 MAC anesthetic groups. Following anesthetic induction and orotracheal intubation each rat was randomly placed on one of three 1.2 MAC anesthetic protocols: 1) 0% N_2O-2.76% enflurane, 2) 30% N_2O-2.28% enflurane, or 3) 60% N_2O-2.12% enflurane. An additive 1.0 MAC value for each N_2O/E combination was determined in previous studies in our lab, and the remaining 0.2 MAC of anesthesia was delivered as an E MAC fraction. A 120 minute anesthetic stabilization period was begun with equilibration of anesthetic gases verified by mass spectrometry sampling of end-tidal gases. Physiological variables (pH, PaO_2, $PaCO_2$, hematocrit, mean arterial pressure, and temperature) were monitored and maintained within normal limits. At the conclusion of the stabilization period 100 uCi/kg of 2-14C-deoxyglucose was administered and ISCMRg was determined by quantitative autoradiography.[2] Statistical analysis was performed on the physiological data and the metabolic values using Dunnett's t-test comparing treatment groups to control (0% N_2O). $P<0.05$ was used as significant.

Results: There were no significant differences between groups in any of the physiological variables. The metabolic data are summarized in Table 1. As N_2O was increased from 0-30% (with E concomitantly reduced) there was an observed homogeneous activation of spinal cord metabolism, with a return to control values as N_2O was further increased from 30-60%.

Discussion: The methodology of this study resembles the clinical use of N_2O as a MAC fraction of E was replaced with an equal MAC fraction of N_2O. However, with iso-MAC anesthetic combinations of N_2O and E it is not possible to ascribe ISCMRg changes specifically to either drug. In previous studies when N_2O was added to deepen an existing state of anesthesia a general increase in glucose metabolism was observed.[3] However, little effect upon glucose metabolism was observed when N_2O was evaluated alone at anesthetic levels inadequate to attain surgical depths of anesthesia.[4]

Studied in the context of comparing iso-MAC combinations of anesthetic agents, we observed a biphasic response in the metabolic interaction between N_2O and E in the spinal cord, in the rat. This may have clinical implications in choosing the optimal anesthetic regimen for surgical procedures during which the spinal cord is a risk for injury. Thus, further studies are necessary to determine if this interaction is present in humans, and to elucidate similar interactions between N_2O and other commonly used volatile anesthetic agents. If this concept is verified, the anesthetist may have more information to aid in decisions regarding combinations of N_2O and volatile anesthetic agents that have favorable effects upon spinal cord metabolism.

CERVICAL

GRAY MATTER	0% N2O	30% N2O	60% N2O
Sub Gelat	58.7 ± 4.6	67.7 ± 5.3*	54.7 ± 6.0
Dorsal Horn	64.0 ± 5.0	74.6 ± 6.0*	63.5 ± 5.7
Ventral Horn	62.7 ± 5.0	74.1 ± 5.9*	62.1 ± 5.2
WHITE MATTER			
Dorsal	39.1 ± 3.7	50.9 ± 5.3*	37.6 ± 6.0
Lateral	43.0 ± 4.3	56.1 ± 6.1*	41.8 ± 4.7
Ventral	41.0 ± 4.0	51.6 ± 5.3*	37.9 ± 4.4

THORACIC

GRAY MATTER	0% N2O	30% N2O	60% N2O
Sub Gelat	53.0 ± 5.1	64.1 ± 5.2*	50.3 ± 7.1
Dorsal Horn	55.4 ± 5.2	68.8 ± 6.3*	57.1 ± 5.4
Ventral Horn	56.9 ± 5.1	69.5 ± 6.2*	57.5 ± 5.1
WHITE MATTER			
Dorsal	38.0 ± 4.7	48.5 ± 5.7*	37.9 ± 4.8
Lateral	37.5 ± 5.0	49.6 ± 5.6*	37.1 ± 4.7
Ventral	40.3 ± 6.0	50.6 ± 5.3*	39.0 ± 5.0

LUMBAR

GRAY MATTER	0% N2O	30% N2O	60% N2O
Sub Gelat	63.5 ± 6.1	72.4 ± 5.0*	60.9 ± 6.3
Dorsal Horn	69.7 ± 6.0	79.9 ± 4.9*	71.8 ± 5.8
Ventral Horn	68.2 ± 6.0	80.7 ± 5.7*	73.1 ± 5.6
WHITE MATTER			
Dorsal	43.2 ± 5.7	56.0 ± 5.9*	42.5 ± 5.2
Lateral	52.9 ± 5.1	64.6 ± 6.0*	53.9 ± 6.3
Ventral	51.2 ± 6.3	61.7 ± 5.0*	52.4 ± 5.8

Table 1 -Local Spinal Cord Metabolism of Glucose umol/100g/min (mean ± SD).
-* difference from control ($P<0.05$).

References:
1. Stevens JE, et al: Effects of nitrous oxide on the epileptogenic property of enflurane in cats. Br J Anaesth 55:145, 1983.
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3. Sakabe T, et al: Local cerebral glucose utilization during nitrous oxide and pentobarbital anesthesia in rats. ANES 63:262, 1985.
4. Ingvar M, Siesjo BK: Effect of nitrous oxide on local cerebral glucose utilization in rats. J of Cereb Blood Flow and Metab 2:481, 1982.