TITLE: NITROUS OXIDE IS A MORE POTENT CEREBRAL VASODILATOR THAN EITHER HALOTHANE OR ISOFLURANE

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Introduction. Because volatile anesthetics (VA) are known to increase cerebral blood flow (CBF), N_2O is frequently used during neuroanesthesia to permit a reduction in concentrations of VA used. However, N_2O can also increase CBF(1), but the relative effects of increasing the concentration of VA vs adding N_2O are not well known(2). Therefore, we examined both the global and regional CBF effects of adding 0.5 MAC (66%) N_2O to a 0.5 MAC background of either halothane (Halo) or isoflurane (Isof), and have compared this with the effects of simply increasing VA concentrations to 1 MAC (no N_2O).

Methods. Sprague Dawley rats were anesthetized with either Halo or Isof in 33% O_2/N_2, intubated and ventilated. Femoral arterial and venous catheters were inserted. 35 min after induction, the rats were assigned to one of 6 anesthetic groups:

A) 0.5 MAC Halo (0.55%) in 66% N_2/O_2
B) 0.5 MAC Isof (0.7%) in N_2/O_2
C) 1 MAC Halo (1.1%) in 66% N_2/O_2
D) 1 MAC Isof (1.4%) in N_2/O_2
E) 0.5 MAC Halo + 0.5 MAC (66%) N_2/O_2
F) 0.5 MAC Isof + 0.5 MAC N_2/O_2

VA concentrations were assessed by measurement of mixed expired gases. These conditions, along with normothermia (37°C) and normocarbia ($PaCO_2 \approx 40$ mmHg) were maintained for an additional 55 min, during which time MAP was kept at 90-100 mmHg using autologous blood. CBF was then determined using 14C iodoantipyrine (75μCi/kg injected over 45 sec). Animals were killed, the brains removed, and coronal autoradiographs were made from frozen sections. These were digitized using a computerized image processing system. 8 anatomically standardized sections were selected, and a CRT-based cursor system was used to outline hemispheric, neocortical, and subcortical areas in each section. The areas (expressed in pixels) and mean CBF values (3) for each region were calculated. Area weighted values were used to calculate whole brain averages, as well as a cortical/subcortical (C/S) CBF ratio. Values were compared by ANOVA and Newman-Keuls testing.

Results. There were no intergroup differences in MAP, blood gases, or temp. CBF results are shown in the Table and Figure. As expected, 1 MAC concentrations of VA alone (Grps C & D) resulted in higher CBF values (all regions) than did 0.5 MAC concentrations of VA alone (Grps A & B). However, animals breathing Isof + N_2O (Grp F) had higher flows (all regions) than animals breathing an equi-MAC concentration of Isof alone (Grp D). A similar N_2O effect was noted only for cortical flows in animals breathing Halo (Grp E vs C). Inspection of the C/S ratio (which describes the distribution of CBF between cortex and subcortex, and which increased with both agents) suggests that N_2O is producing a selective increase in cortical CBF.

Discussion. The data obtained in this study suggest that adding N_2O to a VA background may result in higher CBF values than would be obtained by simply increasing the concentration of VA. Of particular interest was the fact that CBF during Isof + N_2O was greater than during Halo + N_2O - a reversal of the pattern seen with VA alone (1 MAC). In addition, our results suggest that N_2O is producing a relatively selective increase in cortical CBF when using in combination with a VA. The reasons for these effects and their clinical implications obviously require far more study.

References. 1. Drummond JC, et al. Anesth Analg 66:1083, 1987. 2. Manohar M, Parks C. Cardiovasc Res 18:344, 1984. 3. Sakurada O, et al. Amer J Physiol 324:H59, 1978.

Anesthetic	Hemispheric	Cortical	Subcortical	C/S
A. 0.5 MAC Hal + N2 (n=8)	120 ± 16 (C,D,E,F)	139 ± 20 (C,D,E,F)	113 ± 14 (C,D,E,F)	1.23 ± .06 (C,D,E)
B. 0.5 MAC Iso + N2 (n=7)	119 ± 10 (C,D,E,F)	125 ± 11 (C,D,E,F)	116 ± 10 (C,D,E,F)	1.08 ± .04 (A,C,E,F)
C. 1.0 MAC Hal + N2 (n=8)	150 ±16 (A,B,F)	185 ± 16 (A,B,D,E,F)	139 ± 17 (F,B,A)	1.36 ± .14 (A,B,D,F)
D. 1.0 MAC Iso + N2 (n=7)	147 ± 12 (A,B,F)	153 ± 19 (A,B,E,F)	144 ± 12 (A,B,F)	1.07 ± .06 (A,C,E,F)
E.0.5 MAC Hal + N2O (n=8)	162 ± 12 (A,B,F)	210 ± 15 (A,B,C,D)	146 ± 12 (A,B,F)	1.45 ± .12 (A,B,D,F)
F. 0.5 MAC Iso + N2O (n=8)	185 ± 14 (A,B,C,D,E)	214 ± 22 (A,B,C,D)	174 ± 12 (A,B,C,D,E)	1.24 ± .08 (B,C,D,E)

Table. CBF (mean±SD ml/100gm/min) in hemispheric, cortical, and subcortical regions and the C/S ratio for the various groups. Letters in parentheses indicate a significant difference ($p<0.05$) vs the group designated by the letter.

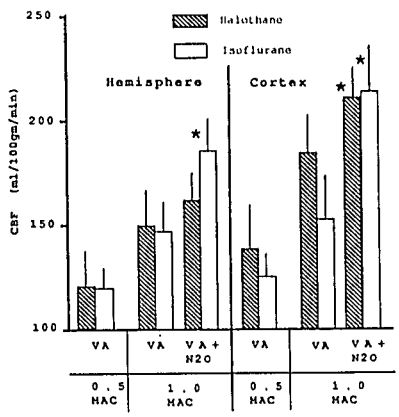

Figure. Hemispheric and cortical CBF values for the groups. * indicates a significant difference ($p<0.05$) between VA + N_2O (1 MAC total) vs VA alone (1 MAC).