Brain-surface Oxygen Tension and Cerebral Cortical Blood Flow during Hemorrhagic and Drug-induced Hypotension in the Cat

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Cerebral blood flow (CBF) is higher during drug-induced hypotension than during hypotension resulting from hemorrhage and, among the hypotensive drugs, CBF may be higher during nitroprusside (SNP) than during trimethaphan (TMP) administration. Increased perfusion of the brain does not guarantee better tissue oxygen supply, since perfusion of the capillary microcirculation may be inhomogeneous. In such a situation, minute areas of ischemia may exist while CBF values are normal. In this study, regional cerebral blood flow (rCBF) was measured in circles of parietal cortex approximately 1.5 cm in diameter in the cat. In addition, oxygen tension values ($P_{B_{O_2}}$) were measured in minute areas of cortical surface by use of 15-μm platinum oxygen electrodes. Control measurements were made during light anesthesia; blood pressure (BP) was then decreased to 30–35 torr by hemorrhage, TMP, or SNP. In the animals rendered hypotensive with TMP or SNP, a beta blocker, practolol, was also administered. It was found that rCBF was higher with SNP (68 ml/100 g/min) than with TMP (45 ml/100 g/min). $P_{B_{O_2}}$ values showed a marked hypoxic shift during hemorrhagic hypotension, but no shift from control during SNP-induced hypotension. The $P_{B_{O_2}}$ pattern with TMP was intermediate between the SNP and hemorrhage patterns. $P_{B_{O_2}}$ were less than 10 torr in 25 per cent of cortical areas examined during hemorrhage, 12 and 7 per cent of areas examined during TMP-induced hypotension (two studies) and only 1 per cent of areas examined during SNP-induced hypotension. These results agree with those of others in showing higher rCBF during SNP-induced than during TMP-induced hypotension. The $P_{B_{O_2}}$ values showed that the well-maintained cerebral perfusion during SNP administration was associated with homogeneous perfusion of the microcirculation. Therefore, brain tissue oxygen availability is greater during SNP-induced than during either TMP-induced or hemorrhagic hypotension. (Key words: Anesthetic techniques, hypotension, induced: trimethaphan; nitroprusside. Anesthetics, volatile: halothane; methoxyflurane. Brain: blood flow; oxygenation; metabolism. Blood pressure, hypotension.)

CEREBRAL BLOOD FLOW (CBF) is maintained at higher levels during hypotension induced by drugs than following hemorrhage to the same mean blood pressure.[1] Among the drugs intravenously administered for inducing hypotension, sodium nitroprusside (SNP) maintains CBF better than does trimethaphan (TMP).[2,3] Higher CBF during hypotension may be associated with better oxygenation of brain tissue, but this is not necessarily so when perfusion of the microcirculation becomes inhomogeneous. Under such circumstances, small areas of ischemia may coexist with satisfactory values of CBF measured over relatively large regions of the brain. In the experiments described below, cerebral perfusion was measured on the cortical surface of the cat during hypotension induced by hemorrhage, SNP or TMP, and the homogeneity of microcirculatory oxygen supply was determined by measuring P_{O_2} at multiple sites on the parietal cortical surface.

Methods

Cats of either sex, with a mean weight of 2.6 kg (range 2.1–3.6 kg) were anesthetized rapidly in a cage, using nitrous oxide–oxygen and halothane, 5 per cent. Succinylcholine, 75 mg, was administered intramuscularly and the trachea intubated. Normocapnic ventilation was maintained with a Starling ventilator during muscular paralysis with pancuronium, 1 mg, intramuscularly, every 30 min. Anesthesia was continued with nitrous oxide–oxygen and halothane, 0.7 per cent (Series I) or nitrous oxide–oxygen and methoxyflurane, 0.2 per cent (Series II). The N_2O/O_2 ratio was approximately 2:1, but it was adjusted to maintain the arterial blood P_{O_2} close to 160 torr throughout. Rectal temperature was held at 38 C.

Blood pressure (BP) was measured electronically from a catheter inserted in the abdominal aorta, which was also used for blood sampling. Catheters in the inferior vena cava allowed infusion of maintenance fluids (Hartmann's solution, 5 ml/kg/hr) and administration of drugs. A catheter was inserted in the right lingual artery and advanced so that its tip lay at the junction of this vessel with the common carotid artery and, through this catheter, [85]Kr dissolved in saline solution was injected for measurement of CBF.

The dura was reflected over an area 1.5 cm in diameter of the parietal cortex and the brain covered with plastic sheeting (Melinex®—I.C.I.), which was removed intermittently for the application of the oxygen electrode.

After completion of the surgical procedure, the cat was placed prone with the head in a holder and with

TABLE 1. Values for Mean Blood Pressure, Arterial Blood pH, Hemoglobin, Blood Halothane Concentration, and Rectal Temperature (Mean ± 1 SD) in Series I*

	$\overline{BP}$ (torr)	pH	Hemoglobin (g/dl)	Blood Halothane (mg/dl)	Rectal Temperature (C)	Heart Rate (Beats/Min)
A. Control (N_2O + O_2 + halothane)	118 ± 18	7.37 ± 0.07	11.8 ± 1.9	8.3 ± 1.2	38.0 ± 0.3	226 ± 22
B. Hemorrhage	30 ± 2	7.00† ± 0.10	6.7† ± 1.5	5.9† ± 0.8	37.7† ± 0.4	231§ ± 17
C. Trimethaphan	31 ± 2	7.31§ ± 0.14	11.5§ ± 1.8	7.2 ± 1.2	37.8 ± 0.7	169‡ ± 13

* Comparison of hypotension produced by hemorrhage with that produced by trimethaphan and practolol.
  Statistically significant difference ($P < 0.05$) between groups:

† A–B.
‡ A–C.
§ B–C.

supports under pelvis and thorax. The blood pressure transducer was zeroed at the level of the exposed area of cerebral cortex.

After a two-minute period of ^{85}Kr injection into the carotid artery, rCBF was measured by following, with a Geiger-Müller tube, the clearance of beta radiation from the exposed area of cerebral cortex.[4] CBF was obtained from the equation CBF = λ loge $2/T_{1/2}$ in which $T_{1/2}$ is the time to half-clearance of radioactivity and λ is the blood:brain partition coefficient of krypton, which was corrected for the measured hematocrit.[5]

Brain-surface oxygen measurements were made with a multi-wire P_{O_2} electrode designed by Lübbers and colleagues.[6] This gave seven channels of P_{O_2} from seven platinum cathodes each 15 μm in diameter. The electrodes were covered with an inner layer of 12 μm cellophane and an outer membrane of 12 μm Teflon® and calibration was performed with a zero P_{O_2} solution containing sodium sulfite in borax (Radiometer, Ltd.) and with air-equilibrated saline solution. The linearity of the electrode response was checked using saline solution equilibrated with oxygen, 10 per cent. The temperature of the calibrating liquids was held at 38 C and the liquids were continuously agitated to minimize boundary effects. Following sacrifice of the animal at the conclusion of the experiment it was confirmed that the reading of each O_2 electrode decreased to zero. Drifts of the O_2 electrode over 56 min when exposed to halothane, 0.5 per cent, were +15.3 ± 8.3 torr at P_{O_2} 147 torr, +8.2 ± 5.7 torr at P_{O_2} 67 torr, and +6.2 ± 2.2 at zero P_{O_2}, for all measurements except the first exposure of the day to halothane, when drift was considerably greater. For this reason, the electrode was not used to measure P_{BO_2} during the first exposure of the day to halothane. Drift during exposure to methoxyflurane, 0.2 per cent, over the same period was +10.1 ± 4.5 torr at P_{O_2} 147 torr. Zero and air calibration were performed immediately before and after each period of measurement on the brain surface, and results were discarded when the

drift exceeded 30 torr. When the drift was less than this, the brain surface P_{O_2} readings were corrected, assuming linear drift with time, an assumption that was shown to be correct when tested in vitro (unpublished data).

The multi-wire oxygen electrode was mounted in a gimballed, counterbalanced arm so that the pressure on the brain surface was less than 10 mg over a surface area of 80 sq mm. The output from each of the wires was amplified and converted to a digital signal, which was recorded on magnetic tape. Subsequently a programmable calculator printed out mean P_{O_2} values with standard deviations for each cathode for each minute of measurement. Arterial blood halothane concentrations were measured with a gas chromatograph using a flame ionization detector.

Two series of experiments were performed. In the first, cats anesthetized with nitrous oxide–oxygen and halothane, 0.7 per cent, were subjected to hypotension to a BP of 30–35 torr, induced either by controlled hemorrhage (five cats) or by TMP infusion, the latter combined with a beta blocker, practolol (five cats). In the second series, which was conducted during anesthesia with nitrous oxide–oxygen and methoxyflurane, hypotension to a BP of 30–35 torr with TMP–practolol (five cats) was compared with SNP–practolol-induced hypotension (five cats). In all animals four sets of measurements of rCBF and P_{BO_2} were made during light anesthesia and normocapnia, followed by similar measurements made during hypotension.

In the cats subjected to hemorrhagic hypotension, the amount of blood removed to produce BP 30 torr was 34.0 ± 7.1 ml/kg. In the drug-induced hypotension experiments, practolol was used to produce some beta blockade; 0.2 mg/kg was administered intravenously at the start of hypotension, and thereafter 0.1 mg/kg was given at 30-min intervals. TMP was infused at the rate needed, but with a maximum rate of 10 mg/kg/hr. SNP was also given by continuous infusion to a maximum total dosage of 1.0 mg/kg. The

total duration of hypotension to 30–35 torr was limited to 90 min. In the animals subjected to drug-induced hypotension it was necessary to remove small amounts of blood to obtain the desired hypotension. For this purpose, 9.2 ± 3.9 ml/kg blood were removed from the TMP-treated animals anesthetized with halothane and 21.1 ± 9.2 ml/kg from the TMP- and SNP-treated animals anesthetized with methoxyflurane. In the second series of animals, in which hypotension from TMP and hypotension from SNP were compared, venous blood samples from the superior sagittal sinus were used to calculate cortical oxygen uptake from arterial and venous oxygen content measurements by the method of Linden et al.[7]

Differences between groups were considered significant when $P < 0.05$.

Results

SERIES I (COMPARISON OF HEMORRHAGIC HYPOTENSION WITH TRIMETHAPHAN-INDUCED HYPOTENSION DURING HALOTHANE ANESTHESIA)

Arterial blood P$_{O_2}$s were 157 ± 15 torr (SD) during control conditions and 163 ± 25 and 152 ± 22 torr

TABLE 2. Values for Cerebral Cortical Blood Flow and Cerebral Cortical Vascular Resistance (Mean ± 1 SD) in Series I*

	CBF (ml 100 g⁻¹ min⁻¹)	CVR (torr ml⁻¹ 100 g⁻¹ min⁻¹)
A. Control (N$_2$O + O$_2$ + halothane)	66 ± 10	1.83 ± 0.34
B. Hemorrhage	42† ± 17	0.87† ± 0.44
C. Trimethaphan	40‡ ± 10	0.84‡ ± 0.34

* Comparison of hypotension produced by hemorrhage with that produced by trimethaphan and practolol.
Statistically significant difference ($P < 0.05$) between groups:
† A–B.
‡ A–C.
§ B–C.

during hypotension with hemorrhage and TMP, respectively. P$_{CO_2}$ was held close to 30 torr, which represents normocapnia in the cat. There was no significant difference between the groups in any of the blood-gas measurements. The hemorrhagic group developed metabolic acidosis and anemia during the hypotensive period, while the TMP-treated group did not (table 1). The lower value for blood halothane during hemorrhage may be due to a decrease in plasma albumin concentration.[8] Mean rectal tempera-
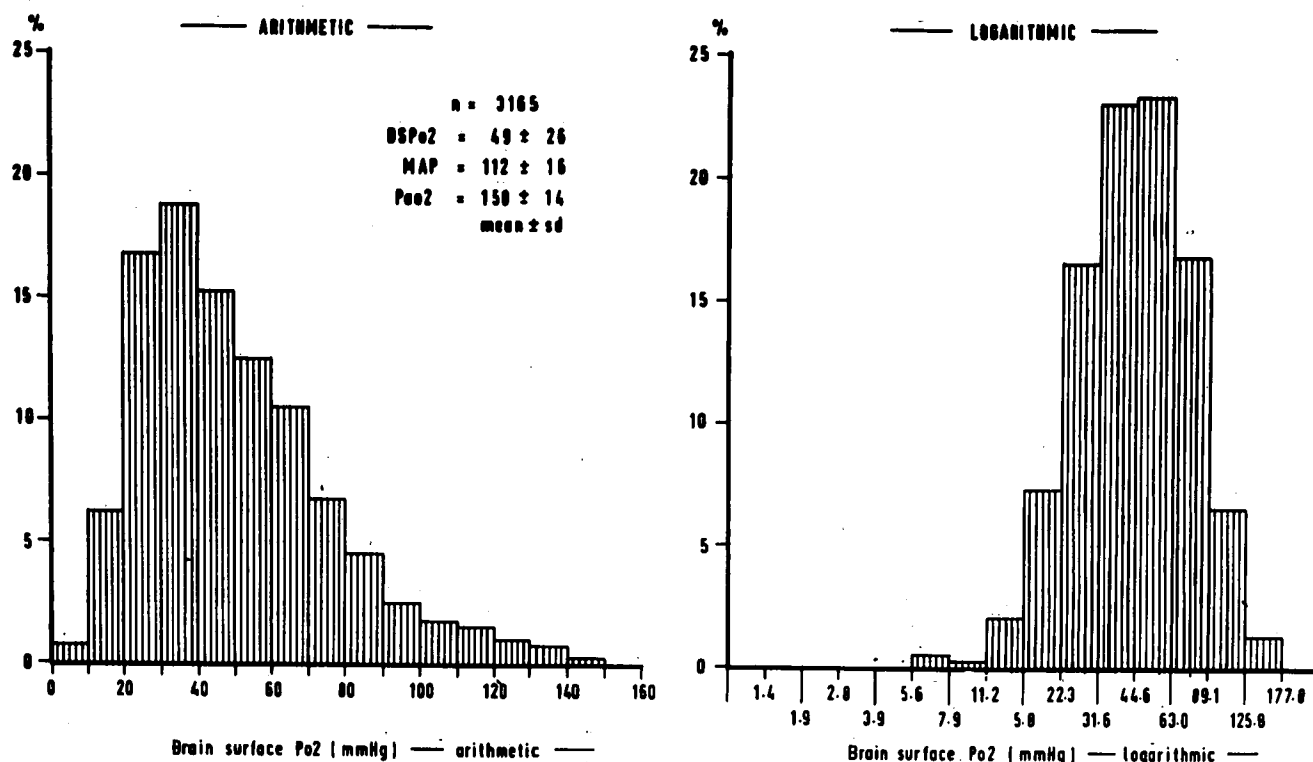

FIG. 1. Frequency histograms of brain-surface P$_{O_2}$ during normotension with light anesthesia with either nitrous oxide–oxygen and halothane, 0.7 per cent, or nitrous oxide–oxygen and methoxyflurane, 0.2 per cent. The x axis of the left histogram is in arithmetic form and that of the right histogram in logarithmic. The right histogram illustrates how closely the distribution of brain-surface P$_{O_2}$ conforms to a log-normal distribution. n = number of studies; BSP$_{O_2}$ = brain-surface oxygen tension (torr); MAP = mean arterial blood pressure (torr); Pa$_{O_2}$ = arterial oxygen tension (torr).

TABLE 3. Values for Mean Blood Pressure, Arterial Blood pH, Hemoglobin, Blood Methoxyflurane Concentration,
and Rectal Temperature (Mean ± 1 SD) in Series II*

	BP (torr)	pH	Hemoglobin (g/dl)	Blood MOF (mg/dl)	Rectal Temperature (C)	Heart Rate (Beats/Min)
A. Control (N_2O + O_2 + MOF)	106 ± 13	7.39 ± 0.04	12.1 ± 1.5	11.7 ± 2.8	38.2 ± 0.3	221 ± 26
B. Trimethaphan	32 ± 2	7.21† ± 0.12	9.6† ± 1.6	12.4 ± 1.8	37.9† ± 0.3	171† ± 14
C. Nitroprusside	33 ± 1	7.31‡§ ± 0.07	9.2‡ ± 1.5	13.7 ± 2.7	38.1 ± 0.3	178‡ ± 18

* Comparison of hypotension produced by trimethaphan-practolol with that produced by nitroprusside-practolol.
Statistically significant difference ($P < 0.05$) between groups:

† A-B.
‡ A-C.
§ B-C.

ture decreased by 0.3 C in the hemorrhagic group. In the TMP-treated group practolol decreased heart rate significantly. CBF and cerebrovascular resistance decreased to approximately 60 and 50 per cent of control, respectively, during hypotension with hemorrhage and TMP, and there was no significant difference between the groups (table 2).

The frequency histograms of P_{BO_2} obtained during administration of halothane, 0.7 per cent (Series I), did not differ from that found during methoxyflurane, 0.2 per cent, administration in Series II, and therefore all control values have been incorporated in figure 1. The modal value for P_{BO_2} during light

anesthesia with these volatile agents lies in the range 30–40 torr, with other values ranging from zero to near arterial blood P_{O_2} in a log-normal distribution (fig. 1).

At BP 30 torr the frequency histogram of P_{BO_2} was significantly shifted to lower oxygen values with both hemorrhage and TMP-induced hypotension (fig. 2). The modal value during hemorrhage was in the 0–10-torr block, while during TMP it was higher at 20–30 torr, and the percentages of areas with less than 10 torr were 23 with hemorrhage and 7 with TMP ($P < 0.01$) (fig. 3). The frequency histograms of P_{O_2} distribution were all statistically significantly different
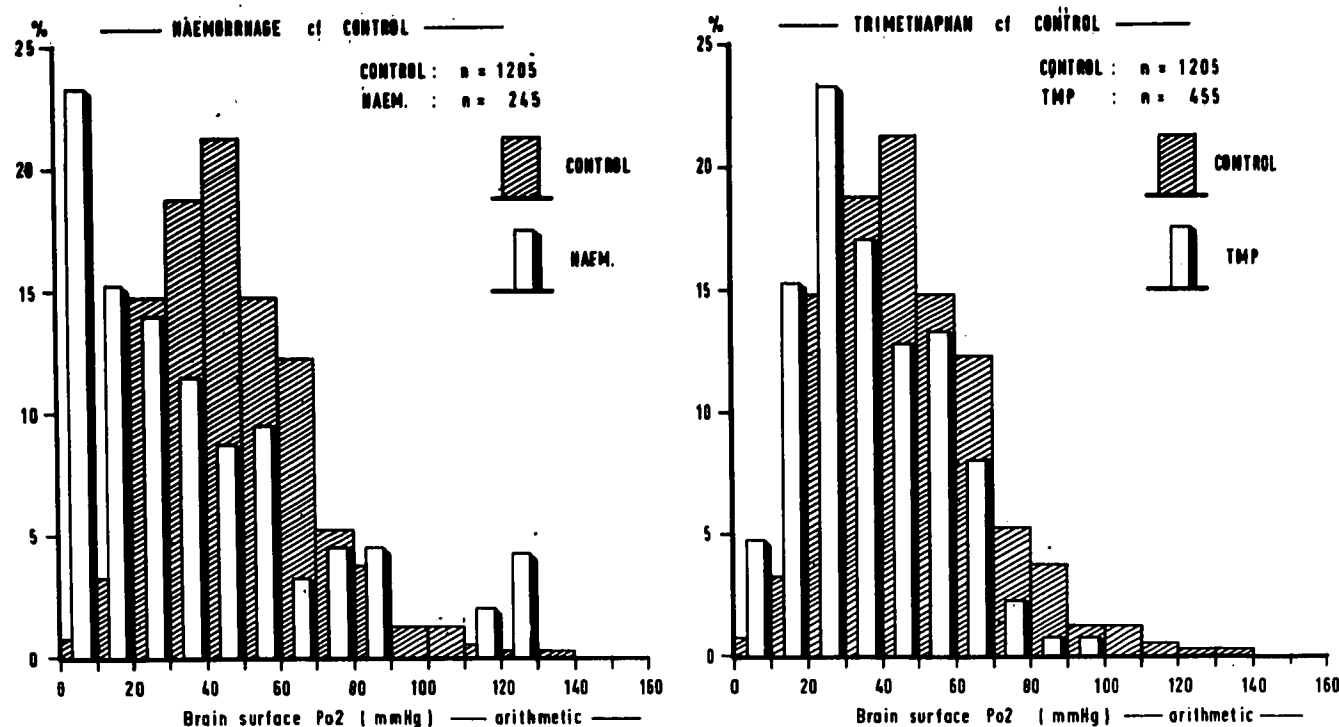

Fig. 2. Histograms of brain-surface P_{O_2} during control conditions of light anesthesia with nitrous oxide–oxygen and halothane, 0.7 per cent, and during hypotension to a mean pressure of 30–35 torr by hemorrhage on the left and by trimethaphan on the right (Series I).

TABLE 4. Values for Cerebral Cortical Blood Flow and Cerebral Vascular Resistance (Mean ± 1 SD) in Series II,* Oxygen Contents of Arterial and Sagittal Sinus Venous Blood, and Cerebral Cortical Oxygen Uptake

	CBF (ml 100 g^{-1} min^{-1})	CVR (torr ml^{-1} 100 g^{-1} min^{-1})	C_{aO_2} (ml/dl)	C_{vO_2} (ml/dl)	CMR_{O_2} (ml 100 g^{-1} min^{-1})
A. Control (N$_2$O + O$_2$ + MOF)	76 ± 13	1.43 ± .31	14.6 ± 2.1	6.7 ± 2.4	5.9 ± 1.1
B. Trimethaphan	45† ± 9	.72† ± .14	12.4† ± 1.1	1.2† ± 1.6	4.9 ± .6
C. Nitroprusside	68§ ± 14	.49‡§ ± .11	11.5‡ ± 1.6	4.3‡§ ± 1.3	4.7‡ ± .6

* Comparison of hypotension produced by trimethaphan-practolol with that produced by nitroprusside–practolol. Statistically significant difference ($P < 0.05$) between groups:

† A–B.
‡ A–C.
§ B–C.

(control cf. hemorrhage; control cf. TMP, and hemorrhage cf. TMP).

(SERIES II) (COMPARISON OF TMP-INDUCED HYPOTENSION WITH SNP-INDUCED HYPOTENSION DURING ANESTHESIA WITH METHOXYFLURANE)

Arterial blood P_{O_2} were 159 ± 13 torr during control conditions and 154 ± 21 and 165 ± 11 torr during TMP- and SNP-induced hypotension, while Pa_{CO_2} was held at 29 ± 3 torr. Metabolic acidosis developed in both groups, but was more severe with TMP (table 3). Hemoglobin decreased equally in the two groups, as did heart rate, under the influence of practolol. There was a 0.3-C decrease in rectal temperature in the TMP-treated group.

Cerebral blood flow and cerebrovascular resistance decreased with TMP to 60 per cent and 50 per cent, as in the TMP-treated animals of Series I (table 4). With SNP, CBF was markedly higher and did not differ significantly from control. This remarkable autoregulation of CBF with SNP is emphasized by the decrease in cerebrovascular resistance to only 34 per cent of control. In keeping with the CBF values, the sagittal sinus oxygen content was higher during SNP-induced hypotension. There was a 20 per cent decrease in cortical oxygen uptake with both hypotensive techniques, but only that with SNP reached statistical significance. There was, however, no statistically significant difference between cortical oxygen uptakes when the two hypotensive groups were directly compared.

The frequency histogram of $P_{B_{O_2}}$ during TMP-induced hypotension shows a shift of the modal value from 30–40 torr to 10–20 torr (fig. 4). There was an increase in the areas with $P_{B_{O_2}}$ less than 10 torr from 1 per cent in the control situation to 12 per cent during hypotension (fig. 3). During SNP-induced hypotension there was no statistically significant shift of the frequency histogram from control, and no significant increase in the number of areas with $P_{B_{O_2}}$ less than

10 torr. Direct statistical comparison of the hypotensive histograms shows that TMP produced a significantly lower pattern of $P_{B_{O_2}}$ than SNP.§

Discussion

Cerebral cortical perfusion was higher during hypotension with SNP than with TMP, in agreement with the results of Stoyka and Schutz[2] and Michenfelder and Theye.[3] It does not follow, however, that perfusion of the microcirculation was better maintained merely because rCBF was greater during SNP-induced hypotension. The ^{85}Kr-clearance technique, as used here, gives values that relate to an area of cerebral cortex approximately 1.5 cm in diameter. Within this area there may have been small areas of the capillary circulation with very low, or even absent, flow during hypotension, despite maintained values for Kr clearance. Relevant to this point are the results of Eklof and co-workers,[9] who demonstrated a more severe derangement of tissue metabolites in the rat brain when CO$_2$ was administered during hemorrhagic hypotension, although rCBF was greater during hypercapnic hypotension. They ascribed this finding to inhomogeneous capillary blood flow produced by the combination of low BP and increased Pa_{CO_2}.

Our measurements of cortical surface P_{O_2} give direct information about the homogeneity of capillary flow, since multiple P_{O_2} measurements were made with

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§ In Series I, measurements were also made at mean BP 50 torr during hemorrhage and during TMP-induced hypotension. The histograms of brain P_{O_2} showed the same trend, and the differences were significant. For histograms and tables of Results at BP 50 torr see NAPS document no. 03463, consisting of five pages of supplementary material. Order from ASIS/NAPS, Microfiche Publications, P.O. Box 3513, Grand Central Station, New York, number. Institutions and organizations may use purchase orders when ordering; however, there is a billing charge for this service. Make checks payable to Microfiche Publications. Photocopies are $3.00 each. Outside the United States and Canada, postage is $3.00 for photocopy of $1.00 for fiche.
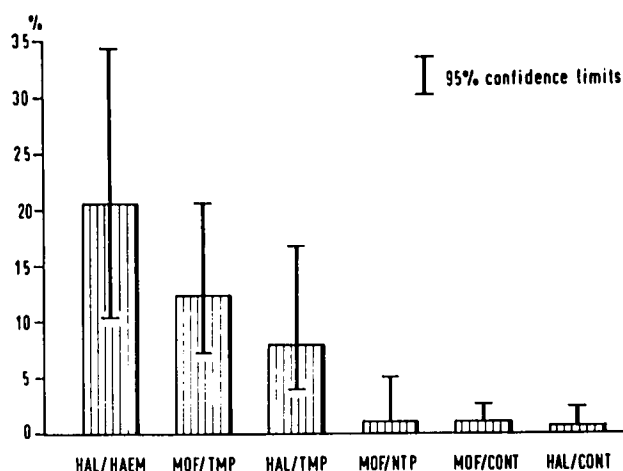
Fig. 3. Probability of brain-surface P_{O_2} less than 10 torr. Numbers of areas with P_{O_2} less than 10 torr expressed or percentages of areas examined under the different experimental conditions. HAL/HÆM = hemorrhagic hypotension during light halothane anesthesia; MOF/TMP = trimethaphan hypotension during light methoxyflurane anesthesia; HAL/TMP = trimethaphan hypotension during light halothane anesthesia; MOF/NTP = nitroprusside hypotension during light methoxyflurane anesthesia; MOF/CONT = control readings during light methoxyflurane anesthesia; HAL/CONT = control measurements during light halothane anesthesia.

electrodes 15 μm in diameter, compared with the average intercapillary distance in the cat cerebral cortex of 50–60 μm.[10] The evidence presented here is

the first demonstration of better-maintained perfusion of the microcirculation during SNP-induced as compared with TMP-induced hypotension. Indeed, the tissue oxygen supply during SNP was not significantly different from that observed during light anesthesia without hypotension. By contrast, during controlled hemorrhage, not only was there a hypoxic shift in the surface P_{O_2} measurement, but the distribution of these measurements was altered by the appearance of a separate population of very low values, probably indicating actual cessation of flow in areas of the microcirculation.

Lübbers and colleagues[6] have published histograms of brain-surface P_{O_2} similar to those shown here. However, modal P_{O_2} values during normotension were lower than ours (*i.e.*, 25–30 torr, compared with 30–40 torr in this study), partly because they used barbiturate anesthesia instead of nitrous oxide–halothane or methoxyflurane, and partly because the lungs of their animals were ventilated with air and those of ours, with a higher inspired oxygen concentration. It is well known that nitrous oxide, halothane, and methoxyflurane increase CBF, and that halothane and methoxyflurane depress cerebral oxygen uptake. The barbiturates, in contrast, decrease flow and oxygen uptake equally. When a logarithmic transformation was performed, it was shown that the frequency distribution of $P_{B_{O_2}}$ was log-normal (fig. 1). This facili-
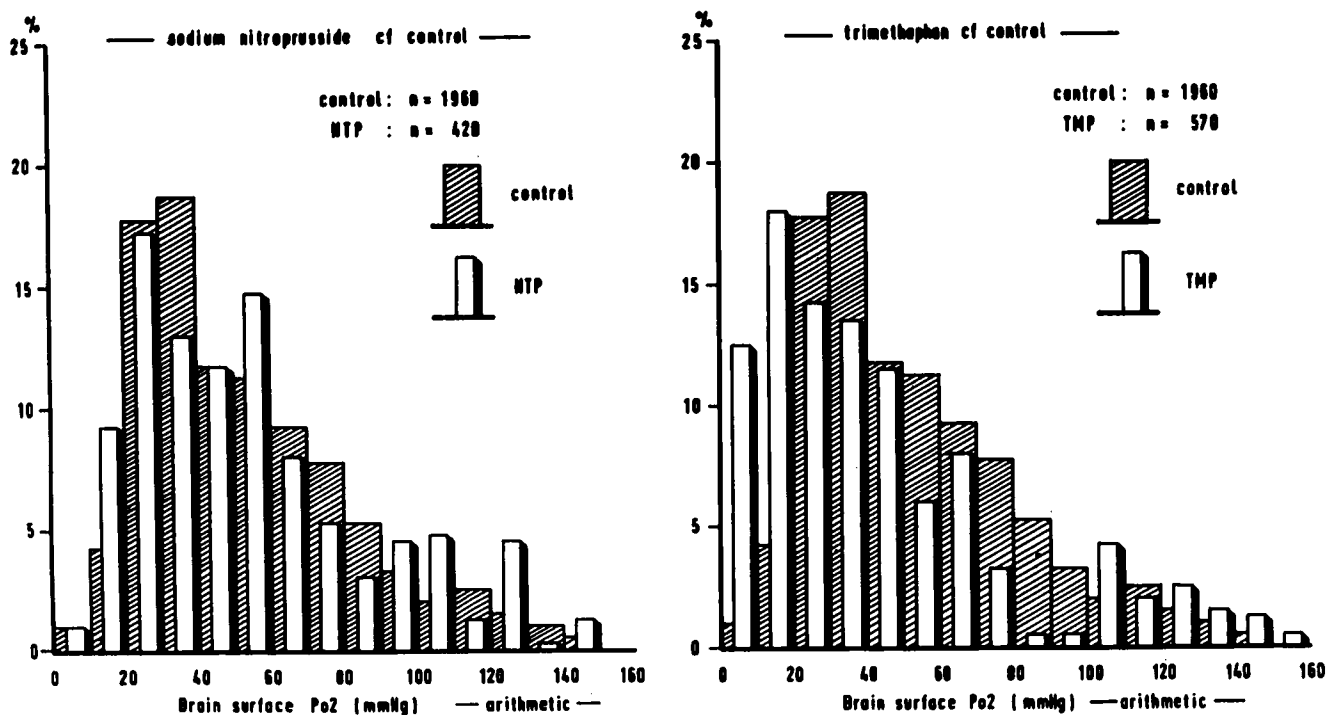

Fig. 4. Histograms of brain-surface P_{O_2} during control conditions of nitrous oxide–oxygen and methoxyflurane, 0.2 per cent, and during hypotension to a mean pressure of 30–35 torr by nitroprusside on the left and by trimethaphan on the right (Series II).

tated the statistical comparisons of the frequency histograms obtained under different experimental conditions.

The low values of brain-surface P_{O_2} during hemorrhagic hypotension are in agreement with the findings of Gygax and Wiernsperger,[11] and can probably be accounted for by the lower values of CBF during hemorrhage, compared with drug-induced hypotension, as described by Fitch and colleagues,[1] and also by the dilutional anemia that occurs very rapidly in the cat in response to hemorrhage.[12] Fitch and colleagues[1] ascribe the difference in perfusion between hemorrhage and drug-induced hypotension to the sympathetically induced vasoconstriction of large extracranial and medium-sized brain surface arteries during hemorrhage. Such sympathetic activation does not occur during the two types of drug-induced hypotension—TMP and deep halothane anesthesia—studied by these investigators. SNP-induced hypotension is associated with increased levels of catecholamines,[3] but the direct effect of SNP on the vascular smooth muscle appears to be the predominant influence.

There were almost identical decreases in calculated CMR_{O_2}s of the cerebral cortex with TMP and SNP, which amounted to 20 per cent of the control value, although only the result with SNP reached statistical significance. There was no statistically significant difference between the CMR_{O_2} values obtained during hypotension in the two groups. Since the dosage of SNP was limited to 1 mg/kg, the decrease in oxygen uptake cannot have been due to cyanide toxicity. Michenfelder and Theye reported decreases in CMR_{O_2} in dogs made hypotensive with both SNP and TMP, but only the TMP-induced changes were statistically significantly different from control.[3] It is difficult to explain these decreases in CMR_{O_2} when both perfusion and oxygenation were adequate, especially during SNP-induced hypotension. It is possible that a modest decrease in oxygen uptake occurs during hypotension, even in the presence of an adequate oxygen supply. However, possible sources of technical error should also be considered. Contamination of the sagittal sinus with blood draining extracranial tissues would tend to decrease calculated CMR_{O_2} because of the lesser oxygen extraction of non-brain tissues. It might be postulated that SNP, by dilating extracranial tissues, produces an increase in contamination of sagittal sinus blood and therefore a decrease in calculated CMR_{O_2}. This seems to the authors to be an unlikely source of error because communicating channels between the signal sinus and extracranial tissues are rarely encountered in the cat, unlike the dog. It is important to remember that the rCBF method used

records flow from only one area of cortex, whereas blood in the sagittal sinus has drained from both hemispheres. It follows that when cortical flow is unevenly distributed, errors will arise in the calculation of CMR_{O_2}. It is known that cortical flow is evenly perfused over the cortical surface during general anesthesia, but this is not true during induced hypotension when boundary zones are less well perfused than areas of cortex closer to the origins of the anterior, middle and posterior cerebral arteries. The area of parietal cortex monitored in the present studies would be expected to be in the region of the boundary zone, as found in other species by Brierley and colleagues.[13] Consequently, well-maintained though the measured rCBF was during SNP-induced hypotension, it may have been less than in other areas of cortex draining into the sagittal sinus.

Michenfelder and Theye[3] studied the metabolic disturbances produced in the cerebral cortex of the dog during induced hypotension and concluded that at mean BP 40 torr at brain level "halothane- or SNP-induced hypotension appears superior to that produced by TMP or hemorrhage." However, when they made their measurements at mean BP 30 torr, brain tissue lactate, lactate–pyruvate ratio, adenosine triphosphate, and creatine phosphate were equally disturbed by all hypotensive techniques, despite the fact that CBF was significantly greater during SNP. They therefore further concluded that at very low perfusion pressures the "deleterious cerebral metabolic effects that occur are unaffected by the technique used for inducing hypotension or by differences in total flow to the brain." We believe that another interpretation of their data is possible.[3] The dogs in their study received as much as 2.5 mg/kg SNP, but subsequent analysis of their data led them to conclude that doses greater than 1.0 mg/kg were toxic in the dog. When they divided their cerebral metabolic results into those from dogs receiving more than 1 mg/kg and those receiving less, it became clear that when SNP toxicity was avoided, brain lactate and lactate–pyruvate ratios were lower than with any of the other techniques of inducing hypotension, although adenosine triphosphate and phosphocreatinine levels were similar. There is therefore some evidence from their paper that, even at the lowest blood pressures, SNP showed advantages over TMP.

The present results would appear to indicate that during induced hypotension, SNP maintains cerebral perfusion and oxygenation better than does TMP. However, Turner and colleagues[14] have shown that at moderate degrees of hypotension (70–90 per cent of control BP values) SNP increases intracranial pressure (ICP), probably because of expansion of the intra-

cranial blood volume, while TMP has no such effect. SNP might therefore lead to ICP gradients in the presence of advanced intracranial compression when it is used to produce minor hypotension while the dura is still closed. TMP does not have this disadvantage during modest hypotension. On the other hand, when major decreases in BP are needed, SNP has the advantage of maintaining cerebral perfusion and brain-tissue P_{O_2} more effectively than does TMP. Dinmore[15] has suggested a hypotensive technique that starts with TMP and progresses to SNP for the brief period of the operation during which extreme hypotension is needed. The present results could be interpreted as supporting this approach.

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