Cerebral Metabolism and Electroencephalogram during Anesthesia

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ABSTRACT

The effects of halothane, diethyl ether, N_2O, and enflurane on the cerebral metabolic rate for oxygen ($CMRo_2$) and EEG were studied in forty-four dogs. With halothane, the $CMRo_2$ progressively decreased, being accompanied by irregular slow-wave activity of the EEG. With diethyl ether, the $CMRo_2$ did not change significantly, but the EEG showed slow-wave activity. With N_2O the $CMRo_2$ significantly increased, also accompanied by slow-wave activity. The increase in the $CMRo_2$ with N_2O was completely blocked by pretreatment of thiamylal. With enflurane the $CMRo_2$ decreased as anesthesia deepened. Deep enflurane anesthesia produced seizure-activity of the EEG. These results indicated that the effects of anesthetics on the $CMRo_2$ are divergent and an increased, decreased or unchanged $CMRo_2$ may be observed during anesthesia. There was no universal relationship between $CMRo_2$ and EEG.

Key Words: *brain*; *metabolism*; *EEG, anesthetics*

INTRODUCTION

Until recently it was believed that the general anesthetic state was accompanied by depression of neural function, the depression of cerebral metabolism, and electroencephalographic slowing and reduction of cerebral blood flow (CBF)[1]. There is increasing evidence which suggests differential effects of anesthetics on cerebral metabolism and electrical activity of the brain[2-4]. If one accepts the belief that alteration in cerebral metabolism in response to anesthetics is a net reflection of altered neural function, measurement of cerebral metabolism related to electrical activity of the brain during anesthesia may provide a better understanding of the anesthetic state. Accordingly, the present study was designed to examine the effects of anesthetics on the cerebral metabolic rate for

oxygen ($CMRo_2$) related to electroencephalogram (EEG). This study revealed considerable differences between different agents.

METHOD

Forty-four dogs were used in the present study. The CBF was measured by the direct method described by Michenfelder et al.[5]. Briefly, this requires exposure and occlusion of all of the diploic channels communicating with the sagittal sinus, and exposure and cannulation of the posterior of the sinus. Flow in measured by timed collection in a reservoir at the level of the sinus. Units of flow are converted from ml/min to ml/100 g/min by percentage of the total brain weight drained by the cannula. It is determined by injection of vinyl acetate into the cannula at the completaion of each experiment. This method was validated by Michenfelder et al.[5]. and in our own laboratory[6,7]. In this preparation, cerebral autoregulation and cerebrovascular response to the alteration of CO_2 were maintained. For $CMRo_2$ measurements, samples of arterial and sagittal sinus blood were taken before and after flow measurements and analyzed for oxygen content. The $CMRo_2$ was calculated as the product of the arterial-sagittal sinus blood difference of oxygen content and the CBF. The EEG was recorded using frontoparietal bipolar silver-silver chloride electrodes.

The responses of $CMRo_2$ to a variety of anesthetics administered in varying concentration were tested. The anesthetics investigated include halothane, diethyl ether, N_2O and enflurane. With N_2O, the effects of the addition of 60 per cent N_2O to 0.8 per cent halothane and prior administration of thiamylal (8 mg/kg) were investigated.

In all of these studies, the surgical preparation necessitated the continual presence of an anesthetic agent. Halothane was selected for this purpose and was used for both the induction and maintenance of anesthesia. The 0.2 per cent expired concentration of halothane was adequate for control anesthetic circumstance. Except as required by the specific circumstance to be studied, variables known to affect CBF and $CMRo_2$ were carefully controlled. Brain temperature was mainteined at $37.0 \pm 0.2°C$, $PaCO_2$ at 39 ± 2 Torr, PaO_2 at 173 ± 38 Torr and Hb at 12 ± 1 g. A normal buffer base was also maintained by administration of sodium bicarbonate as needed. End-tidal CO_2 was monitored with an infrared CO_2 analyzer and anesthetic concentrations of the blood or end-tidal gas were analyzed by gas chromatography. Statistical significance was tested by the paired t-test ($P<0.05$ being considered significant).

RESULTS

The effects of individual anesthetics on $CMRo_2$ and EEG are summarized in Tables 1 and 2.

Table 1 Effects of anesthetics on canine $CMRo_2$

	Anesthetic concentration in sagittal sinus blood (mg/dl) (mean±SE)		$CMRo_2$ (ml/100 g/min) (mean±SE)
Halothane	control	2±0.1	5.54±0.3
(n = 8)	light	5±0.2	5.18±0.3*
	moderate	10±0.4	4.80±0.4*
	deep	16±0.5	4.63±0.3*
Diethyl ether	control	0	5.44±0.2
(n = 7)	light	47±3.1	6.29±0.4
	moderate	98±3.9	5.86±0.3
	deep	160±5.4	5.58±0.3
N_2O	control	0	5.43±0.1
(n = 7)	end-tidal %	60	6.45±0.2*
Enflurane	control	5±0.5	6.1 ±0.2
(n = 8)	light	11±0.5	5.3 ±0.2*
	moderate	18±0.5	5.0 ±0.2*
	deep	27±1.3	4.3 ±0.2*

* Significantly different from control ($P < 0.05$)
Depth of anesthesia was arbitrarily classified as light, moderate or deep, according to the anesthetic concentrations in the sagittal sinus blood.
Control of the anesthetic circumstance is 0.2%expired concentraion of halothane, except with enflurane.

Table 2 Summary of the effects of individual anesthetics on $CMRo_2$ and EEG

Anesthetic	$CMRo_2$*	EEG
Halothane	−13%	slow
Diethyl ether	+8%	slow
N_2O	+21%	slow
Halothane+N_2O	+8%	slow
Thiamylal+N_2O	−7%	slow
Enflurane		
Moderate	−17%	slow, spikes
Deep	−29%	seizures

* %changes in $CMRo_2$ with halothane and diethyl ether are taken at a moderate depth of anesthesia.

Halothane

With halothane the $CMRo_2$ decreased to 94, 87 and 84 per cent of control at light (5 ± 0.2 mg/dl, halothane concentration), moderate (10 ± 0.4 mg/dl) and deep (16 ± 0.5 mg/dl) anesthesia, respectively. The reductions in the $CMRo_2$ at different anesthetic depths were statistically significant[8]. Halothane produced irregular slow-wave activity of the EEG which paralleled changes in the $CMRo_2$. A representative EEG with corresponding values of $CMRo_2$ is shown in Figure 1[8].

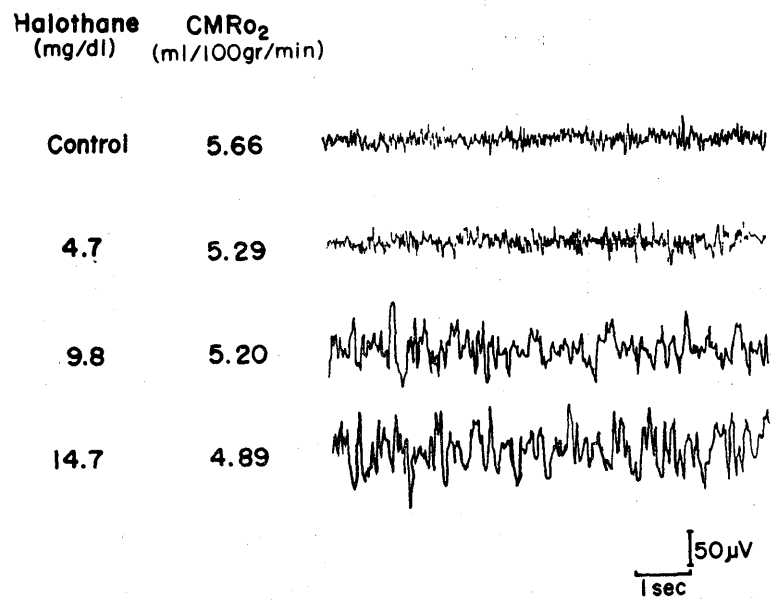

Fig. 1 Representative EEG pattern during halothane anesthesia with corresponding values of $CMRo_2$.

Diethy ether

With ether, the $CMRo_2$ was 116, 108 and 103 per cent of control in light (47 ± 3.1 mg/dl, ether concentration), moderate (98 ± 3.9 mg/dl) and deep (160 ± 5.4 mg/dl) anesthesia, respectively. These changes were not statistically significant. There war no relation between the changes in the $CMRo_2$ and EEG[8]. A representative EEG with corresponding values of $CMRo_2$ during ether anesthesia is shown in Figure 2[8]

Nitrous oxide

With N_2O (60 per cent end-tidal), $CMRo_2$ maximally increased by 21 per cent. The EEG showed low-voltage slow-wave activity (Fig. 3). During 0.8 per cent halothane anesthesia, addition of 60 per cent N_2O

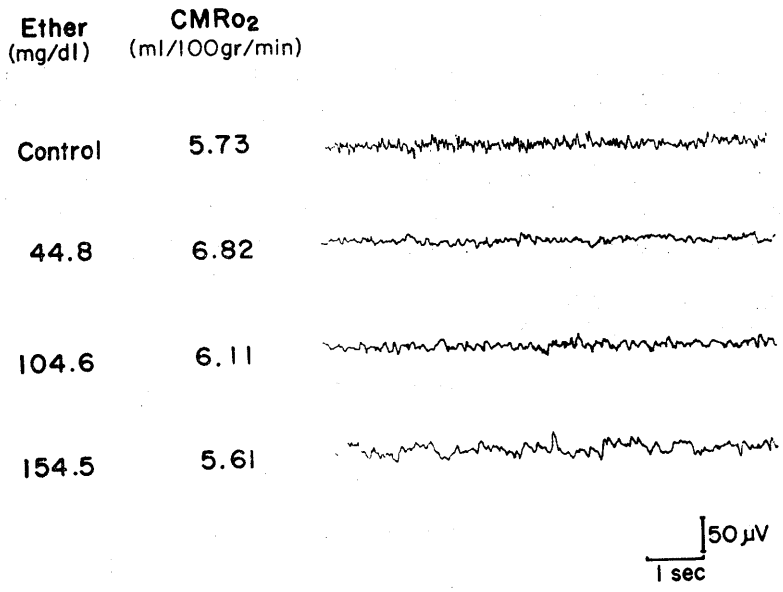

Fig. 2 Representative EEG pattern during diethyl ether anesthesia with corresponding values of $CMRo_2$.

maximally increased the $CMRo_2$ by 8 per cent. Slow activity in EEG became more predominant. After administration of thiamylal, 60 per cent N_2O decreased the $CMRo_2$ by 7 per cent during the initial 15 min, but thereafter this value increased above control level, when EEG changed from a high voltage irregular slow-wave to a low voltage slow-wave typical for N_2O[9].

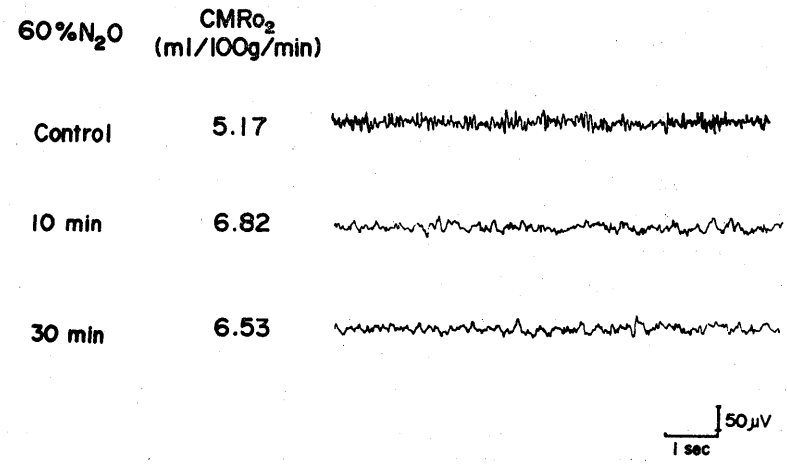

Fig. 3 Representative EEG pattern during N_2O anesthesia with corresponding values of $CMRo_2$.

Enflurane

The $CMRo_2$ decreased by 12, 17 and 29 per cent in light (11 ± 0.5 mg/dl, enflurane concentration), moderate (18 ± 0.5 mg/dl) and deep (27 ± 1.3 mg/dl) anesthesia, respectively. During moderate anesthesia spikes appeared in the EEG. The mean $CMRo_2$ decreased further in deep anesthesia with typical EEG seizures[10]. A representative EEG with corresponding value of $CMRo_2$ is shown in Figure 4[10].

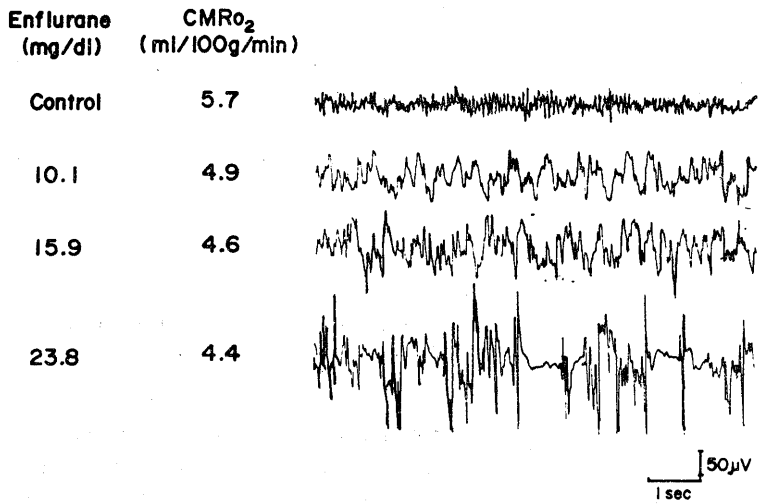

Fig. 4 Representative EEG pattern during enflurane anesthesia with corresponding values of $CMRo_2$.

DISCUSSION

Halothane caused significant decreases in the $CMRo_2$ which were accompanied by irregular slow-wave activity. The effects of halothane on cerebral metabolism in experimental animals have been studied by three laboratories including ours[8,11,12]. In the dog. Theye and Michenfelder[12] noted a 17 per cent decrease in the $CMRo_2$ at near 1 MAC. McDowall[11] found a significant decrease in the $CMRo_2$ when halothane in 70 per cent N_2O was increased from 0.5 to 2.0 per cent. Michenfelder and Theye[13] have reported that the lack of change in the $CMRo_2$ between 0.7 and 2.3 per cent did not correlate with the EEG, which showed progressive changes consistent with functional depression, and suggested that functional depression in one area of the brain may be matched by a degree of excitation in another area of the brain, resulting in no net change in $CMRo_2$. However, they found that over 4 per cent halothane produces a progressive decrease in the $CMRo_2$ even after abolition of cerebral function (flat EEG). Apparently, the degree and dose-response

of the depression of the $CMRo_2$ in halothane are still not clear. Our study indicates that depression of cerebral metabolism with clinical concentrations of halothane was accompanied by EEG slowing parallel to the change in the $CMRo_2$. Varying degrees of $CMRo_2$ changes with ether indicate the complete lack of correlation between cerebral metabolic response and EEG pattern. The latter showed progressive slowing, being characterized by a slow-wave. N_2O has been believed to be capable of producing anesthesia with only slight alteartion of cerebraa metabolism[14]. However, cerebral metabolic stimulation of N_2O was first reported by Theye and Michenfelder[15] in dogs. They found an 11 per cent increase in the $CMRo_2$, whereas our results showed a 21 per cent increase. The quantitative difference between the studies might be due to the fact that the dogs received total spinal anesthesia, vagotomies and cervical sympathetectomies in the study by Theye and Michenfelder[15]. One may believe that cerebral stimulation with N_2O is a reflection of excitement during light anesthesia. Our study showed that 0.8 per cent halothane alone decreases the $CMRo_2$ by 14 per cent. The observed change in the $CMRo_2$ with addition of N_2O to 0.8 per cent halothane was 8 per cent. Thus, it is perhaps more than coincidental that the effects of halothane and N_2O on the $CMRo_2$ are competitive. Even in this circumstance, EEG slowing became predominant. Nahrwold and Cohen[16] reported an additive effect of halothane and N_2O on mitochondrial respiration. It is well-known that addition of N_2O to halothane reduces the alveolar concentrations of halothane required to prevent response to surgical incision[17]. However, cerebral oxygen consumption during combined N_2O-halothane anesthesia is not additive in our preparation. Therefore, there is no relation between anesthetic depth and cerebral metabolic change. The results obtained in dogs with prior administration of thiamylal are also indicative of a lack of correlation between anesthetic depth and cerebral metabolic depression. Similar effects of barbiturate in blocking the cerebral metabolic response to ketamine have been reported by Dawson et al.[18]. Enflurane causes a striking decrease in the $CMRo_2$ in deep anesthesia which is accompanied by spikes or spikes-and-waves in the EEG[10]. Michenfelder and Cucchiara[19] observed an increase in the $CMRo_2$ above the control during deep enflurane anesthesia accompanied by seizure activity and myoclonic jerks. It must be emphasized that electrical activity usually seen in the convulsive state appears during depressed $CMRo_2$ under anesthesia. In summary, the effects of anesthetics on the $CMRo_2$ are divergent and an increased, decreased or unchanged $CMRo_2$ may be observed during anesthesia. There is no universal relationship between $CMRo_2$, EEG, anesthetic concentration in the blood and anesthetic depth.

At the present time the anesthetic state may be best defined as a complex altered state, perhaps an alteration in the balance between excitation and inhibition, and the generalization that the anesthetic state is accompanied by reduced cerebral metabolism and a slowing of EEG, as observed particularly in thiopental anesthesia, cannot be applied to all anesthetic circumstances.

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