Title : HYPERCARBIA REDUCES CEREBRAL METABOLISM IN THE ISOLATED CANINE BRAIN

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Introduction. There has been little agreement regarding the effects of hypercarbia on the cerebral metabolic rate for oxygen ($CMRO_2$). Artru and Michenfelder recently reported that the $CMRO_2$ was reduced by 10 percent in dogs having a $PaCO_2$ of 100 torr, and found no reduction at a $PaCO_2$ of 80 torr[1]. Siesjö, in an accompanying editorial, raised several questions concerning this study and earlier investigations into the effects of hypercarbia on cerebral metabolism and blood flow[2]. Among these questions were: 1) What were the effects of anesthetics? 2) Were there drug interactions? 3) Were there species differences in the response to CO_2? 4) Did the effects of hypercarbia vary in the presence of drugs? 5) Were there problems with determining blood flow measurement and the measurement of arteriovenous oxygen content difference in the presence of high cerebral blood flows? and 6) Do the various techniques used to measure $CMRO_2$ yield similar results? We have investigated this problem in the isolated perfused canine brain preparation. This has several advantages over other models, in that many of the questions posed by Siesjö do not apply because drugs are absent from the perfusate. The remaining methodologic problems are less prominent due to the more direct methods used to measure cerebral blood flow and oxygen content.

Materials and Methods. The brains of 15 unpremedicated fasting dogs were isolated in a manner previously described[3]. Anesthesia was induced and maintained with halothane. Following isolation, the brain was perfused by means of a double roller pump-membrane oxygenator system. During the initial 45 min of perfusion the halothane remaining in the system evaporated from the oxygenator. Arterial and venous blood gases were measured with an Instrumentation Labarotories model 313 blood gas analyzer. Blood oxygen content was determined with an oxygen fuel cell (Lex-O_2 Con) which had been calibrated with a Van Slyke blood gas apparatus. Cerebral blood flow (CBF) was measured directly by a timed collection of venous blood in a graduated cylinder. CBF was maintained at a constant normal level throughout the experiments. The control perfusate was blood having a normal pH, PaO_2, glucose, electrolytes, a $PaCO_2$ of 40 torr, and an hematocrit of 30%. Following several measurements of arteriovenous oxygen content difference and CBF, perfusion was changed to the second pump oxygenator system which contained blood identical to the control system except that the $PaCO_2$ was varied, while maintaining the pH at 7.4. During a 15 min perfusion with hypercarbic blood, 3 measurements of arteriovenous oxygen difference and CBF were made. A 6 lead EEG was continuously recorded. $CMRO_2$ (ml O_2/100 gm/min) and cerebral vascular resistance ((CVR) in torr/ml CBF/min/100 gm) were then calculated. Each dog served as its own control. Student's t-test for paired data was used to assess the significance of results. Experiments were performed at PaCO s of 60, 80 and 100 torr.

Results. The results are presented in Table I. Hypercarbia produced a dose related decrease in both $CMRO_2$ and CVR in the isolated perfused canine brain.

Discussion. The cerebrovasodilatory properties of hypercarbia have been well documented. This study confirms the depressive effect of hypercarbia on whole brain metabolism even at levels as low as 60 torr. There are no anesthetic effects or drug-CO_2 interactions. The cerebral blood flow was maintained constant, and at a normal level. The decrease in $CMRO_2$ may be a result of inhibited neuronal function since at high partial pressures CO_2 has an anesthetic effect. CO_2 also rapidly crosses the blood brain barrier. Therefore, it may cause a rapid change in pH in the vicinity of critical enzymes resulting in a slowing of oxidative phosphorylation and a decrease in oxygen utilization. In this model, with CBF constant, hypercarbia may result in the selective opening of vascular channels causing a "steal" phenomenon from marginally perfused tissues, and a "luxury" perfusion of other vascular beds. In the absence of other drugs and sympathetic stimulation it is clear that hypercarbia does result in a reduction of $CMRO_2$.

Table I

PCO_2 (torr)	N	$CMRO_2$	CVR
60	5	↓ 8.8%±2.0*	↓18.4%±2.2*
80	5	↓17.4%±8.6*	↓21.4%±3.8*
100	10	↓18.6%±3.3*	↓34.6%±4.4*

*$p < 0.05$ compared to control

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