

TITLE: BRAIN pH DURING RESPIRATORY ACIDOSIS AND ALKALOSIS, A  $^{31}\text{P}$  NMR STUDY

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**INTRODUCTION:** Phosphorus Nuclear Magnetic Resonance ( $^{31}\text{P}$  NMR) Spectroscopy permits simultaneous measurement of pH and high energy phosphates in brain with the skull intact. A good nondestructive technique for pH measurement in intact tissue is lacking. The measurement of brain pH by  $^{31}\text{P}$  NMR promises to fill this important methodological gap. We report the preliminary results of studies performed in dogs to determine the intracellular pH in the intact brain. Changes in ventilation were used to perturb brain  $\text{pCO}_2$  and pH, a model which has been well studied<sup>1-4</sup>.

**METHODS:** Beagle dogs were anesthetized with halothane in oxygen, intubated and mechanically ventilated. The femoral artery and vein were cannulated, and the animal was positioned in a stereotactic head holder within a plexiglass cylinder. To avoid muscle artifact, the skull was exposed surgically and a surface coil placed thereon. In two animals the sagittal sinus was cannulated through a small burr hole which was then sealed. Subsequently the animal was positioned within a 1.5 Tesla (23.4 MHz for  $^{31}\text{P}$ ) magnet so that the brain lay within the homogeneous field at the center. Anesthesia was converted to 70%  $\text{N}_2\text{O}$ /30%  $\text{O}_2$ /0.375% isoflurane 2 hours prior to study. Field homogeneity was optimized.  $^{31}\text{P}$  NMR data were acquired at a 4 second pulse interval and averaged over 15 minutes beginning 15 minutes after a change in ventilation. pH was determined from the frequency shift (distance) between the phosphocreatine and inorganic phosphate peaks<sup>5</sup>. These techniques have been described in detail elsewhere (In-Vivo Time Resolved Brain Phosphorus Nuclear Magnetic Resonance, J. Cereb. Blood Flow and Metab, 1984, In Press). Hypocapnia was induced by hyperventilation. Hypercapnia was achieved by increasing inspired  $\text{CO}_2$  concentrations from normocapnia. Studies were rejected if peak resolution was poor,  $^{31}\text{P}$  NMR signal:noise was low, or if the arterial pressure declined more than 10% from control. Variables were corrected for each animal by subtracting the average of values determined at 35 mmHg  $\leq \text{PaCO}_2 \leq 45$  mmHg from the observed values.

**RESULTS:** Sixty-one data sets from 5 animals were analyzed. Hypercapnia was associated with a progressive decline in brain intracellular pH in 5 animals. Two responses to hypocapnia emerged: brain pH remained normal in three (Fig 1), and increased in two. The discrepancy in hypocapnia between changes in arterial pH and in brain pH could be striking (Fig 2). In two animals arterial and sagittal sinus lactate levels increased 75% above control values at  $\text{PaCO}_2$  23-25 mmHg, one of these is shown in Fig 2, the other had poor NMR data, and was excluded from analysis.

**DISCUSSION:** The  $^{31}\text{P}$  NMR measurement of brain intracellular pH showed a decline in brain pH of 0.15 units as  $\text{PaCO}_2$  increased from 37 to 81 (0-50

in Fig 1) a result essentially identical to that reported by others<sup>2,4</sup>. The plateau in brain pH during hypocapnia seen in three animals suggested lactic acidosis due to hypoxia induced by cerebral vasoconstriction; the rise in blood lactate levels in two dogs tended to confirm this. Changes reported during hypocapnia differ from those previously reported; the use of barbiturate anesthesia in other studies may account for these differences<sup>3</sup>. The  $^{31}\text{P}$  NMR measurement of intracellular pH is nondestructive, suitable for repetitive measurement in individual animals, and may be used in humans.

FIG 1 BRAIN pH VS  $\text{PaCO}_2$

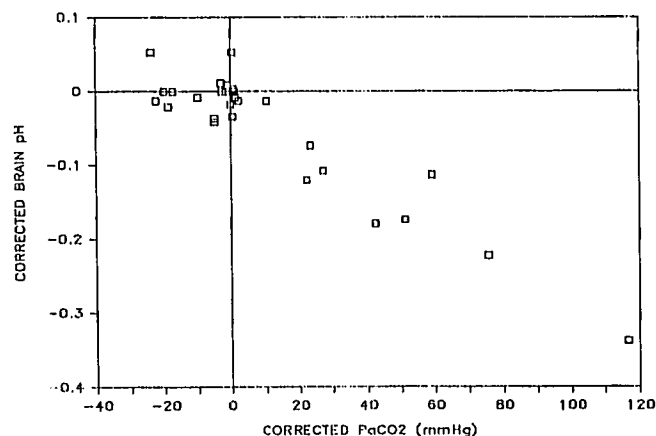
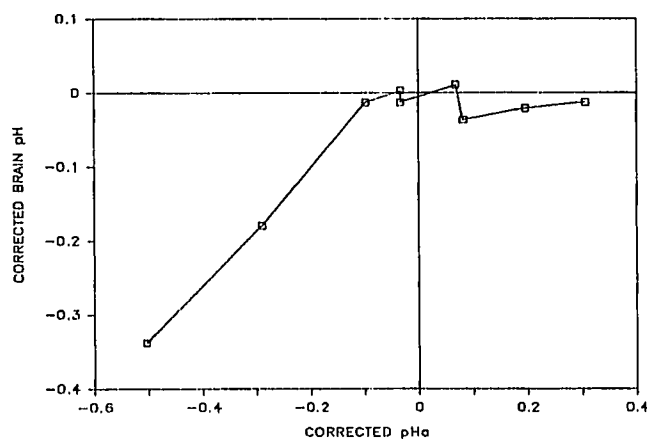


FIG 2 BRAIN pH VS  $\text{pH}_a$



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