Title: REGIONAL CBF AND CMRO₂, CBF Gl, AND BRAIN METABOLITE LEVELS DURING N₂O OR HALOTHANE: COMPARISON TO THE AWAKE STATE.

Authors: D. A. Felligrino, Ph.D., D. J. Miletich, Ph.D., W. E. Hoffman, Ph.D., and R. F. Albrecht, M.D.

Affiliation: Dept. of Anesthesiology, Michael Reese Hospital and Medical Center, Chicago, Illinois 60616

Introduction. N₂O and halothane are commonly utilized anesthetics in experimental animals and are often employed (in artificially ventilated and paralyzed animals) under a variety of physiological and pathophysiological conditions where measurements of CBF, CMRO₂, Gl, and brain metabolic levels are required. A number of studies have suggested that N₂O (60-70%) can increase CBF, CMRO₂ and Gl, and dose-related reductions in brain high energy phosphate levels and increases in the lactate/pyruvate ratio (L/P). However, no information regarding N₂O effects on brain tissue metabolite profiles is currently available. Halothane may increase CBF and have been associated with decreases in CMRO₂ and Gl and dose-related reductions in brain high energy phosphate levels and increases in the lactate/pyruvate ratio (L/P). Interpretations of results regarding halothane (≤5%) and N₂O effects on all of the above mentioned parameters are complicated by the lack of appropriate controls (i.e., unanesthetized and spontaneously breathing animals) where the influences of immobilization (and sampling) stress are minimized. In the present study we employed techniques in the awake goat which allowed us to: a) serially obtain rapidly frozen cerebral cortical tissue samples and b) measure CMRO₂, Gl, and total and local CBF. Thus with each animal utilized as its own control, we studied both N₂O and halothane effects on the above.

Methods. Five female goats (25-35 kg) were used. Two to four determinations of the effects of 60 min. of either N₂O (70% via a mask) or halothane (1% and 3% with paralysis and artificial ventilation) on cerebral metabolite profiles, CBF, CMRO₂ and Gl were performed on each animal. All animals were surgically prepared 7-8 days prior to use with an acrylic "cranial window" (for tissue sampling), femoral arterial and venous catheters and a sagittal sinus catheter. Two goats were additionally fitted with a left atrial catheter for injection of microspheres for use in local CBF determinations. In the other 3 goats an electromagnetic flow probe was implanted on the internal maxillary artery (following elimination of extra-cerebral flow) for estimation of total CBF. CMRO₂ and Gl were calculated via the Fick equation. For awake determination, goats were placed in a stanchion which prevented head movement. Serial tissue samples (50-200 mg) were obtained using a razor on a freezing apparatus. Preparing time was < 0.5 sec. Up to 5 samples were taken from the cranial window site (2-3 awake). Additional samples (under halothane) were obtained from the opposite hemisphere on the day of sacrifice. Frozen samples were extracted (HCl-methanol, perchloric acid) and metabolites analyzed using fluorometric enzymatic techniques. The metabolites measured were ATP, ADP, AMP, PCr, glucose-6-P, fructose-6-P, lactate, pyruvate, citrate and ß-KG. Plasma epinephrine (E) and norepinephrine (NE) were also analyzed throughout. Body temp remained between 39-40°C in all

animals. Paco₂ did not vary by more than ±3 mm Hg from control (X=34±1±3 mm Hg) during N₂O or halothane. Paco₂ was >80 mm Hg in all animals.

Results. Plasma E and NE were not altered by halothane. Plasma E and NE were not altered by fixation of the animal's head, nor following brain biopsy, thus suggesting lack of immobilization or sampling stress. No appreciable changes from control in any of the measured metabolites were found when animals were exposed to either N₂O or halothane (1% and 3%). A rather large increase in CBF could be noted during halothane administration and was primarily confined to cortical tissue (+20%). N₂O was also associated with increases in cortical CMRO₂ (15%) and Gl (12%). Whole brain analysis showed little or no increase in CMRO₂, a similar increase in Gl (20%) and a smaller increase in CBF (15%). These N₂O associated changes could not be related to increases in plasma E or NE, which remained constant throughout.

Halothane anesthesia increased CBF only at 3%. However, regional flow values indicated much greater increases (>200% in most regions) than whole brain flows (140%). This is probably a result of a much smaller fall in MAP at 3% halothane in the microsphere injected animals (~22 mm Hg) as opposed to animals with flow probes (~55 mm Hg). Both 1% and 3% halothane were associated with similar but marked falls in CMRO₂ and Gl (~40% and ~70% of control respectively).

Discussion. This study represents the first attempts in experimental animals to relate N₂O and halothane effects on CBF and cerebral metabolism to various anesthetic states. Present results indicate that N₂O can have a profound effect on cortical CBF and can lead to increases in oxygen and glucose consumption as well. These results confirm those of Sakabe et al. (1) in dogs and Ingvar et al. (2) in rats. Results also suggest that even 1% halothane can lead to marked falls in CMRO₂ and Gl. Although tissue metabolite profiles were not altered by N₂O or halothane anesthesia when interpreting changes in CBF and cerebral metabolism from studies using N₂O or halothane anesthetized animals.

References: