Title: EFFECT OF HALOTHANE ON THE NEUROTTRANSMITTER CHANGES CAUSED BY CO2 IN DISCRETE BRAINSTEM NUCLEI

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Introduction. Halothane depresses the ventilatory response to inhaled CO2 in a dose-dependent fashion.1-3 We investigated whether CO2 affected the neurotransmitter content in brainstem nuclei associated with respiratory control, and, if so, what effect halothane would have on these changes.

Methods. Male Sprague-Dawley rats (200-250 g, 8-12 per group) were given room air with or without 1.05% halothane with either 0%, 5%, or 10% CO2. Ninety minutes after initiation of anesthesia and/or exposure to CO2 and in a random sequence, animals were decapitated and their brains rapidly frozen. Using a cryostat (at -10°C) we prepared 300 um coronal brain slices beginning at the level of pyramidal decussation and advancing rostrally. Micropellets of tissue from eight brain nuclei, fiber tracts, or terminal regions were removed with stainless steel cannulae (method of Palkovits).4 The eight micro-dissected areas were the nucleus (n.) commissuralis, the n. reticularis medullae oblongata, the n. tractus solitarius (caudal and central to the area postrema) (N.T.S.), the n. reticularis gigantocellularis, the n. reticularis paramedialis, the lateral reticular n. (AL) and the A5 area (Palkovits and Jacobowits, 1975).5 Protein (Lowry) and norepinephrine, epinephrine and dopamine content (radioenzymatic assay) were measured. Statistical analysis included least mean-squares regression, multivariate analysis and one- and two-way analysis of variance with repeated measures.

Results. In the nucleus (n.) commissuralis the caudal (NTS), and the n. gigantocellularis, the content of dopamine varied directly with the dose of CO2 when given without halothane. In the n. gigantocellularis, the correlation coefficients of content of dopamine, epinephrine and norepinephrine were 0.93, 0.87 and 0.93 respectively, all (p < 0.01). No relationship existed between CO2 dose or content in blood and content of norepinephrine, epinephrine or dopamine in any brainstem region when halothane was administered.

Discussion. The NTS and n. commissuralis were studied because they receive input from the peripheral chemoreceptors and include the dorsal medullary respiratory group. The n. gigantocellularis has a cardiaclacceleratory and vasoconstrictor action.6 This study demonstrates that CO2 alters the catecholamine content of several hindbrain nuclei associated with respiratory control, but that halothane ablates that relationship. Moreover, destruction or microelectrode studies will be needed to evaluate the relative importance of these changes, and to determine whether release, or decreased metabolism, causes neurotransmitters to accumulate in these areas after administration of CO2.

In summary, previous work indicates that halothane disturbs the ventilatory response to CO2. Our results indicate that changes in neurotransmitter content in specific brainstem nuclei may be critical to this effect of halothane.

References: