

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

Authors: M.F. Roizen, M.D., C. Helke, Ph.D., E.I. Eger II, M.D., B. Frazer, B.A., P. Feustel, Ph.D., B. Johnson, A.B.

Affiliation: Departments of Anesthesia, Medicine and Pharmacology, University of California at San Francisco, School of Medicine, San Francisco, California 94143 and the Department of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, Maryland 20014

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 μm 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 (N.T.S.) the n. reticularis gigantocellularis, the n. reticularis paramedicalis, the lateral reticular n. (A1) and the A5 area (Palkovits and Jacobowitz, 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 cardigacceleratory and vasoconstrictor action.^{6,7} This study demonstrates that CO₂ alters the catecholamine content of several hindbrain nuclei associated with respiratory control but that halothane ablates that relationship. Turnover, destruction or microelectrode studies will be needed to evaluate the relative importance of these changes, and determine whether increased synthesis, decreased 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.

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