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THE EFFECT OF HALOTHANE, HYPOXEMIA AND RESPIRATORY ACIDOSIS AS ISOLATED VARIABLES ON SEROTONIN METABOLISM IN REGIONAL AREAS OF RAT BRAIN. T.H. McCoy* and M.A. Medina, Univ. Tex. Hlth Sci. Cntr., San Antonio, Texas 78284

The secondary effect of halothane-induced respiratory acidosis and hypoxemia on 5-hydroxytryptamine (5-HT) metabolism in rat brain cortex, midbrain, medulla-pons and striatum was studied. With respiratory control the primary effects of halothane on 5-HT metabolism were obtained. Hypothermia was prevented. Hypoxemia as an isolated variable in mechanically-ventilated, halothane-treated rats decreased 5-HT turnover and 5-hydroxyindoleacetic acid (5 HIAA) content, leaving 5-HT content unchanged, probably by combined block of 5-HT synthesis and oxidation, since both are oxygen-requiring. Respiratory acidosis, produced by mechanical hypoventilation in halothane-treated rats, slightly increased 5-HT turnover. Probenecid-induced respiratory acidosis increased 5 HIAA accumulation when compared to a probenecid-treated control group receiving compensatory hyperventilation, possibly via an increased free plasma tryptophan. When hypoxemia and respiratory acidosis were controlled, halothane increased 5-HT turnover in the medulla-pons. Increased serotonergic activity in the brainstem raphe terminals could suppress the adjacent reticular activating system, producing anesthesia.

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ISOLATED NERVES AS A TEST ORGAN TO STUDY THE RECEPTOR ACTIONS OF ANESTHETICS AND OTHER CENTRALLY ACTIVE AGENTS. B. Diamond*, H.S. Haydala*, and H.C. Sabelli. Mt. Sinai Hosp., Chicago, Ill. 60608 and Chicago Med. Sch., Chicago, Ill. 60612.

Electrically-excitabile axonal membranes are chemically excitable: (i) neurotransmitters can enhance or decrease selectively conduction block by centrally active agents (Sabelli & Gorosito, Int. J. Neuropharmacol., 1969); (ii) iontophoresis of neurotransmitters can elicit or inhibit action potentials in corpus callosum fibers and in frog nerves (Sabelli & May, Experientia, 1975). We have now observed in isolated frog sciatics, that large concentrations (2-5 mM) of neurotransmitters [catecholamines, serotonin, histamine, gamma amino butyric acid (GABA), etc.] reduce action potential height. Their effect is selectively blocked by the corresponding blockers; e.g. LSD-25 (0.25 mM) vs serotonin (5 mM), atropine (0.5 mM) vs bethanechol (5 mM), picrotoxin (0.5-1.0 mM) vs GABA (10 mM), hexamethonium (5 mM) vs nicotine (5 mM), phen-tolamine (3-5 mM) vs norepinephrine (3 mM) and propranolol (0.9 mM) vs isoproterenol (2.6 mM). The usefulness of hardy, simple nerve preparations to test on neural tissue the receptor activity of drugs will be exemplified for anesthetics, barbiturates and tranquilizers.
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EFFECTS OF HALOTHANE ON CONTRACTION OF ISOLATED SKELETAL MUSCLE. Henry Rosenberg* (SPON: C. P. Bianchi), University of Pennsylvania, Philadelphia, Pa. 19104

The inhalation anesthetic halothane (H) potentiates caffeine (caff.) contracture in skeletal muscle. The effects of H on potassium chloride (KCl) contracture has not been systematically investigated. This information will help clarify the site(s) of action of H in normal skeletal muscle. Strips of muscle (approx. 12 mm. by 2 mm.) were dissected from rat diaphragm held under resting tension in a muscle clamp. The strips were suspended in Human Krebs (2.5 mM CaCl_2), at 37°C, at a resting tension of 0.5 gm. Isometric tension in response to caff. (0.25, 0.5, 1, 2.4, 8 mM) and KCl (10, 20, 40, 50, 70, 80, 200 mM) were recorded + H vaporized in 95% O_2 - 5% CO_2 . 1% H lowered the threshold for caff. contracture to 0.125 mM from 1 mM and potentiated tension developed at each caff. concentration (max. at 2 mM caff.). One percent H potentiated tension at 10, 20 mM KCl, but depressed tension at other KCl concentrations. 3%, 5% H significantly depressed tension at all KCl concentrations. The threshold for contracture was raised from 20 to 50 mM KCl. With 1% H the threshold for maximum slope of tension increase was raised to 50 mM KCl also. H may therefore have a biphasic effect on KCl contracture depending on H dose.

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LOCAL ANESTHETIC SCREENING: A NEW METHOD USING ELECTRIC SHOCK. Philip W. Wirth*, James R. Parsons*, Ronald F. Borne*, and James C. Murphy* (SPON: W.M. Davis) Research Institute of Pharmaceutical Sciences and School of Pharmacy, University of Mississippi, University, MS 38677.

A sensitive *in vivo* method for detecting local anesthetic activity was developed using tail withdrawal elicited by electric shock. Advantages of this method over existing methods are increased sensitivity, and objective measurement of the aversive stimulus and the response.

The compounds tested were procaine, cocaine, morphine, meperidine, pentobarbital, saline and distilled water. Constant current electric shock was applied to a test site on the rats tail via a bipolar subcutaneous electrode before and after subcutaneous injection of 0.1 ml of the test and control substances. The shock was incremented between 0 to 2 ma until a tail withdrawal response of 100 g. of force occurred. The response automatically terminated the shock and the current level was recorded. Of the compounds tested, only the local anesthetics immediately inhibited the contractile response.