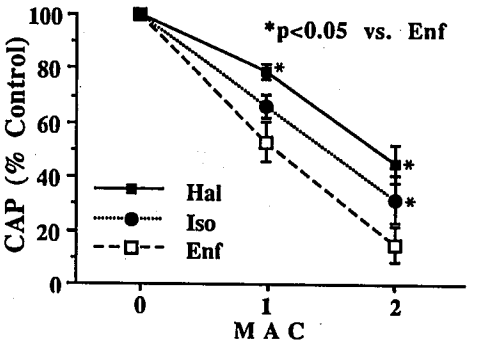
Title: DIFFERENTIAL EFFECTS OF INHALATIONAL ANESTHETICS ON SYMPATHETIC GANGLIONIC TRANSMISSION

Authors: ZJ Bosnjak PhD, HK Schedewie MD PhD, N Boban MD and JP Kampine MD PhD

Affiliation: Department of Anesthesiology, The Medical College of Wisconsin, Milwaukee, WI 53226

Inhalational anesthetics can cause significant impairment of cardiovascular stability and reflex regulation.[1] This depression is mediated by both central and peripheral sites of action. One of the important peripheral effects is the depression of synaptic transmission;[2,3] however, the degree of depression by various anesthetics remains to be quantified. The purpose of this study was to examine the differential effects of halothane (H), enflurane (E) and isoflurane (I) on synaptic ganglionic transmission using the isolated canine stellate ganglion (SG) *in vitro*. Eight SG were isolated from adult mongrel dogs after pentothal anesthesia, desheathed and superfused with Krebs solution equilibrated with 97% O_2-3% CO_2 mixture and maintained at 37°C and pH 7.4. The preganglionic T_3-ramus and postganglionic ventral ansa subclaviae were placed on bipolar tungsten electrodes for stimulating and recording purposes, respectively. Ganglionic transmission was measured by recording the compound action potential (CAP) under conditions of supramaximal electrical stimulation at 0.5 Hz. The percent CAP depression from control was measured 15 minutes after SG exposure to 1 and 2 MAC of H, E and I in random order. Control measurements of CAP were performed between each anesthetic exposure and the controls were averaged. At the end of the experiment the synaptic nature of the CAP was verified by blocking the synaptic transmission with hexamethonium. Vaporized anesthetic concentrations were measured by mass spectrometry, while SG bath concentrations were measured by gas chromatography. The following vaporizer settings were found to yield these corresponding superfusate concentrations: 0.7% H = 0.25mM, 1.3% H = 0.53mM; 1.7% E = 0.6mM, 3.3% E = 1.2mM; 1.1% I = 0.46mM and 2.2% I = 0.7mM. While the conduction velocity was not affected by any of the above anesthetic concentrations synaptic transmission was depressed as reflected by a decrease in CAP amplitude (see figure). CAP depression was dose-dependent and readily reversible, and the order of potency was E>I>H. The depression of synaptic transmission by inhalational anesthetics most likely involves both a decrease in ACh release and postsynaptic sensitivity to ACh, as previously shown for H.[3]

References: 1) Effects of Anesthesia, Baltimore & Easton, Waverly Press, 1985, p 149; 2) *Anesthesiology* 57:473, 1982; 3) *Anesthesiology* 69:500, 1988.



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Title: PREOPTIC REGION THERMOSENSITIVE SINGLE UNIT NEURONAL ACTIVITY IS REDUCED BY HALOTHANE

Authors: KA Poterack, M.D., JP Kampine, MD, PhD, and WT Schmeling, MD, Ph.D

Affiliation: Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI 53226

The volatile anesthetic agents, including halothane, have been previously demonstrated to disrupt normal thermoregulatory function by actions on the end-organ mediators of thermoregulation (i.e. behavior, shivering, vasomotor changes, etc.) as well as altering normal thermoregulatory responses modulated at the preoptic region (POR) of the anterior hypothalamus.[1] The purpose of the present investigation was to examine the action of halothane (H) on thermosensitive single units (TSSU) in the POR. Thirty-eight cats were anesthetized with intraperitoneal alpha-chloralose (60 mg/kg) and urethane (600 mg/kg). Bilateral thermodes, a thermocouple, and a tungsten single-unit microelectrode were implanted stereotaxically in the POR (Horsely-Clark coordinates A = 14.5 L = 2.5 D = -4.0). During maintenance of constant core temperature one hundred forty-eight single units were isolated, subjected to local heating and cooling and responses quantitated. Data was recorded on FM tape and digitized on-line *via* a microcomputer.

Eighteen percent (n=27) of all single units were found to be TSSU by accepted criteria (i.e. Δ firing rate (FR)/Δ 1.0°C°>0.8 or <-0.6).[2] Fifty-two percent (n=14) of all TSSU exhibited a maximal increase in FR over a narrow change (2-3°C) in temperature and were identified as heat-sensitive (HS). Twenty-six percent (n=7) responded with a constant increase in FR over the entire range of temperature change and were identified as linear (L), while twenty-two percent (n=6) exhibited a maximal decrease in FR over a narrow temperature change and were identified as cold-sensitive (CS). Sixty-three percent (n=17) of all TSSU were subjected to graded (0.25%, 0.5%, 0.75%, and 1% end-tidal) concentrations of H and thermal challenge repeated. H produced a dose-dependent decrease in spontaneous firing rate at 37°C (SFR 37) and thermosensitivity (Δ firing rate/Δ 1.0 C°). At 0.75% H, the SFR 37 of HS units was 29±11% of control and the SFR 37 of L units was 16.1±20.4% of control, both statistically significant ($p<0.05$) compared to control. At 1% H, the SFR 37 of HS units was 20.7±7.5% of control and the thermosensitivity was 5.5±6.3% of control ($p<0.05$). L units at 1% H displayed an SFR 37 of 13.4±10.6% of control, significant at $p<0.05$. Mean SFR 37 and thermosensitivity for all types of units returned toward control upon discontinuation of H. The dose-dependent decreases in SFR and thermosensitivity of POR TSSU may contribute to the alterations in thermoregulation produced by the volatile anesthetics.

References: 1) Schmeling WT, Kampine JP, Warltier DC: *Anesthesiology* 71(3A):A638, 1989
2) Schmeling WT, Hosko MJ: *Brain Res* 17:431-442, 1980