TITLE: MYOCARDIAL DEPRESSION BY NITROUS OXIDE: MECHANISM OF ACTION

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Introduction. We investigated the mechanism of action of the depressant effects of nitrous oxide (N_2O) in isolated ventricular myocardium by determining N_2O-induced changes in intracellular [Ca^{2+}] detected with the Ca^{2+}-regulated photoprotein, aequorin.

Methods. Multiple superficial cells of eight ferret right ventricular papillary muscles were microinjected with aequorin. Muscles contracted isometrically in a HEPES-buffered physiological salt solution (pH 7.24-7.40, 30°C, 4 sec stimulus interval). Peak developed force (DF) and aequorin luminescence were measured in isometric twitches in 20%, 30%, and 50% N_2O in 50% O_2 and N_2. Each exposure to N_2O was preceded and followed by equilibration in 50% O_2-50% N_2. Aequorin luminescence was compared (n=5) in twitches of equal amplitude in the absence (50% O_2-50% N_2) and presence of N_2O (50% O_2-50% N_2O with raised extracellular [Ca^{2+}]). Values (mean±SD) in N_2O were compared to the average value of the control immediately before and after exposure to N_2O with Student's paired t-test.

Results. 30% and 50% N_2O significantly decreased DF and aequorin luminescence (Fig. 1,2). At equal developed force, light signals in 50% N_2O were not different from control signals in 50% O_2-50% N_2 (Fig. 3).

Discussion. N_2O decreases developed force and intracellular [Ca^{2+}] but has no effect on myofibrillar Ca^{2+} responsiveness.

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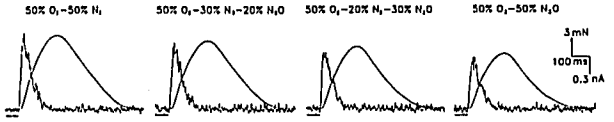


Figure 1

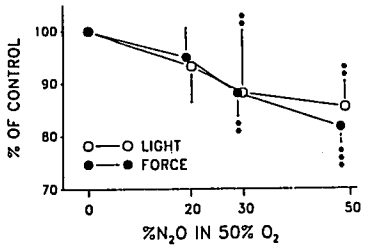
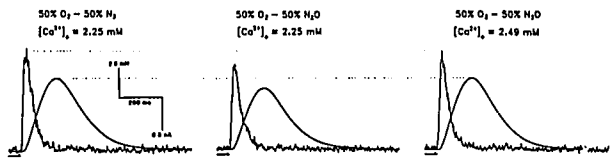


Figure 2

**p<0.01
***p<0.001

Figure 3



A576

Title: **EFFECTS OF HALOTHANE AND EPINEPHERINE ON AUTOMATICITY OF DOMINANT AND SUBSIDIARY ATRIAL PACEMAKERS**

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Wandering atrial pacemaker and ectopic atrial rhythm disturbances precede ventricular arrhythmias which result from exposure to epinephrine (EPI) during halothane (H) anesthesia.[1] The mechanism for such cardiac rhythm disturbances is not known, but could involve enhanced automaticity in subsidiary atrial pacemakers (SAP)[2] since H antagonizes the positive chronotropic action of EPI on sinoatrial (SA) node fibers.[3] The present study examined the effects of EPI and H on automaticity of the SA node and SAP's using a perfused canine right atrial preparation.

Twenty-four canine right atrial preparations were perfused via the sinoatrial (SA) node artery with Krebs solution (36.0±0.5°C) equilibrated with 97% O_2-3% CO_2. Bipolar extracellular recordings were made from the SA node region and distal sites (approximately 1, 2 and 3 cm) located along the sulcus terminalis to determine the site of earliest activation (SEA) during exposure to EPI (1, 2, 5 μg/L) and 1 or 2% H (perfusate concentrations 0.50±0.02 and 0.80±0.04 mM). Control (C) was no EPI or H, heart rate data are given as means±SEM, and statistical comparisons were done by ANOVA or paired t tests.

Control heart rate was decreased from 85±3 to 77±2 beats/min during experiments which lasted 4-5 hrs. H decreased heart rate (regardless of SEA) and opposed the action of EPI to increase rate ($p<0.05$, ANOVA). During C, SEA was the SA node. Pacemaker shifts (from SA node to more distal site) per number of SA node preparations examined, severity scores (sum of shifts to sites 1, 2 or 3), and normalized scores (severity scores/number of preparations) with EPI w/wo 1 or 2% H are tabulated.

EPI (μg/L)	Shifts/SA nodes (severity score)			Normalized score		
	EPI	1% H	2% H	EPI	1% H	2% H
0	0	1/24 (2)	3/24 (6)	0	0.08	0.25
1	0/15 (0)	1/17 (3)	3/19 (6)	0	0.17	0.31
2	4/17 (7)	4/20 (7)	7/22 (12)	0.41*	0.35*	0.54*
5	6/19 (11)	4/22 (7)	5/24 (9)	0.57*	0.31*	0.37*

* $p<0.05$ vs. Control

EPI increases the rate of SA node and SAP's, which increase is opposed by H. EPI also produces shifts in pacemaker location from the SA node to SAP's, which action is neither prevented nor augmented by H. We conclude that pacemaker shifts to SAP's may account for wandering atrial pacemaker or atrial ectopic rhythm disturbances early during the course of halothane-epinephrine sensitization.

References: 1. Anesthesiology 57: 285, 1982. 2. Am. J. Physiol, 238: H788, 1980. 3. Anesthesiology 33: 602, 1970.