TITLE: EFFECTS OF NITROUS OXIDE ON CONTRACTILITY AND RELAXATION OF ISOLATED MAMMALIAN VENTRICULAR MYOCARDIUM

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Introduction. The purpose of this study was to define the effects of N_2O on contractility and relaxation in isolated ventricular myocardium.

Methods. Eight ferret right ventricular papillary muscles contracted in a HEPES-buffered physiological salt solution (pH 7.24-7.4 at 30°C, 4 sec stimulus interval). Peak force (DF), time to peak force (TPF), maximal rate of force decline (-dF/dt), time to half isometric relaxation ($RT_{½}$) in isometric twitches, peak shortening (DL), time to peak shortening (TDL) in isotonic twitches, and maximum unloaded velocity of shortening (MUVS) in zero-load clamped twitches were measured 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. Isometric relaxation in 50% O_2-50% N_2O was compared with that in twitches of equal amplitude in 50% O_2-50% N_2 with aliquots of 0.2 M EGTA added. Values (mean±SD) were compared to the average control value measured immediately before and after exposure to N_2O with Student's paired t-tests.

Results. 30% and 50% N_2O significantly decreased DF, DL, MUVS, TPF and TDL (Fig. 1, 2). Isometric relaxation (-dF/dt, $RT_{½}$) in 50% O_2-50% N_2O was not significantly different from that in twitches of equal amplitude in 50% O_2-50% N_2 + EGTA (Fig. 3).

Discussion. N_2O is a direct myocardial depressant, yet does not alter isometric relaxation.

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Figure 1

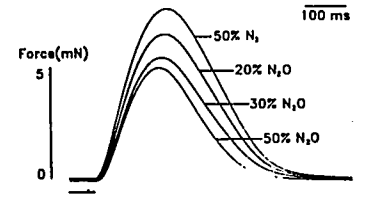
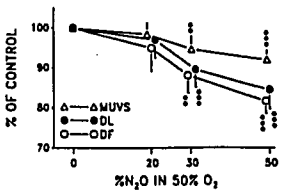
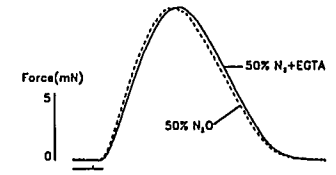


Figure 2



**p<0.01
***p<0.001

Figure 3



TITLE: THE EFFECT OF INSULIN INFUSION ON BRAIN AND BLOOD GLUCOSE IN HYPERGLYCEMIC DIABETIC RATS

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Introduction. Increases in brain glucose will worsen neurologic injury following global brain ischemia(1). The present study examined whether insulin therapy of diabetic hyperglycemia to normoglycemic values would result in brain glucoses similar to those of normoglycemic non-diabetic subjects.

Methods. Subjects were 66 Sprague-Dawley rats, 42 which had streptozocin-induced diabetes. Rats were anesthetized with halothane (1.3% inspired) in N_2 and O_2, intubated, and ventilated. Temperature, blood gases, and acid-base status were maintained within normal physiologic range. Following a 20 min stabilization period, the arterial blood was sampled for glucose (YSI 23A glucose analyzer) in 6 non-diabetic and 6 diabetic rats. Concomitantly, the brains were frozen in situ with liquid N_2. The cerebral cortex glucose subsequently was measured(1). An additional 18 non-diabetic and 18 diabetic rats were given i.v. saline infusions, 2 $ml \cdot h^{-1}$. The brains of these rats were frozen in situ at either 60, 90, or 120 min after the start of the infusions (n=6 for all groups). An additional 18 diabetic rats were treated with saline plus 0.75 $U \cdot h^{-1}$ of regular insulin. Data were compared using ANOVA, F-tests, and unpaired t-tests. $P<0.05$ was considered significant.

Results. In the non-diabetic controls, blood and brain glucose were 88 ± 9.5 $mg \cdot dl^{-1}$ and 2.07 ± 0.28 $\mu mol \cdot g^{-1}$, respectively. In diabetic controls, blood and brain glucose were 285 ± 19 $mg \cdot dl^{-1}$ and 8.11 ± 1.09 $\mu mol \cdot g^{-1}$, respectively. Saline had no effect on either brain or blood glucose in either diabetic or non-diabetic rats when compared to their respective controls. Blood glucose in insulin-treated diabetic rats decreased to normoglycemia in 120 min (109 ± 36 $mg \cdot dl^{-1}$). Brain glucose also significantly decreased with insulin treatment ($p<0.05$); however, at 120 min, brain glucose was significantly greater than in non-diabetic rats treated with saline ($p<0.05$). Brain to blood glucose ratio in all diabetic rats, irrespective of the type of infusion or time interval, was always significantly greater than in non-diabetic rats.

Discussion. The present data demonstrate that the use of an insulin infusion to restore normoglycemia in diabetic subjects will result in brain glucose values that are elevated when compared to normoglycemic non-diabetic subjects. This implies that the risk for worsened neurologic injury, in the event of cerebral ischemia, may be greater in normoglycemic diabetic subjects than in normoglycemic, non-diabetic subjects.

Reference.

1. Anesthesiology 66:39-49, 1987