small are consistent with both of the earlier studies. It is not yet clear whether these are biologically negligible.

Such findings could be interpreted as denials of the active transport hypothesis for follicular fluid formation, at least during the more rapid phase of preovulatory expansion. They also show that the specific electrical resistance of the follicle wall (including the granulosa and ovarian surface epithelia) is low and, therefore, electro-chemical gradients are unlikely to be stable. It can be concluded then that the results are not in conflict with the hypothesis which will require other methods for further testing. The near or complete absence of a measurable PD and short-circuit current across the follicle wall is not particularly surprising since the same properties are encountered in other 'leaky' epithelia, e.g. gallbladder, choroid plexus, renal proximal tubule, small intestine [5]. In these cases, the cell membrane resistance typically exceeds the transepithelial resistance by a large margin [24] and the linear current-voltage relationship indicates that current is being conducted paracellularly, a conclusion which agrees with the absence of morphologically recognisable 'tight' junctions between granulosa cells [25]. Consequently, it is probable that the major pathway for entry of water into the antrum is paracellular, although the forces involved, whether active transport and/or transudation, require further clarification.

Acknowledgments. We thank Robert Nichol and Carol McLeod for technical assistance, Dr Jane Langridge-Smith for advice and equipment. The Wellcome Trust and the Agriculture and Food Research Council financed the research.

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0014-4754/88/030212-03$1.50 + 0.20/0

Ventricular fibrillation threshold during acute ischemia in hypertrophied rat hearts

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Received 17 August 1987; accepted 10 November 1987

Summary. Ventricular fibrillation threshold was significantly lower in hypertrophied hearts than in normal hearts. Ischemia produced by coronary occlusion reduced fibrillation threshold in both normal and hypertrophied hearts, but the maximum reduction in fibrillation threshold was observed earlier in hypertrophied hearts.
Key words. Ventricular fibrillation threshold; cardiac hypertrophy; pressure overload; ischemia.

Left ventricular hypertrophy is associated with an increased risk of sudden cardiac death in coronary artery disease [1, 2]. The mechanisms responsible for this high incidence of sudden death are still obscure. One possible explanation is an increased vulnerability to ventricular tachyarrhythmias, especially ventricular fibrillation (VF), during ischemia in hypertrophied hearts [3]. Ventricular fibrillation threshold (VFT) has long been used to assess vulnerability to arrhythmias in experimental animals [4]. Using this technique, we compared VFT changes during ischemia between normal and hypertrophied rat hearts.

Methods. Left ventricular hypertrophy was created by partial occlusion of the abdominal aorta to produce chronic pressure overload. Male Sprague-Dawley rats (370–485 g) were anesthetized with sodium pentobarbital (35 mg/kg, i.p.). A polyethylene cannula and a small animal respirator were used to provide mechanical ventilation. Under aseptic conditions, a 4-cm midline incision was made terminating at the xiphoid process. The abdominal aorta (between the diaphragm and celiac artery) was exposed and looped with 3–0 silk suture. The suture was tightened around a 25-gauge needle, and then the needle was withdrawn. The rats were placed in an incubator until they regained consciousness, and kept in colonies until the day of study. At terminal study, 6–8 weeks after surgery, the animals were weighed, anesthetized, and treated with heparin sodium (300 μg/kg, i.p.). Age-matched normal rats were treated in the same way to provide control data. Systemic blood pressure was recorded through a polyethylene catheter inserted in the carotid artery. After thoracotomy, the hearts were quickly excised and placed in preoxygenated Tyrode's solution. Each heart was mounted by the Langendorf method on a perfusion apparatus by cannulation of the aorta, and perfused retrogradely with Tyrode's solution from a reservoir at a constant pressure of 95 cm H_2O in hypertrophied hearts, and of 65 cm H_2O in normal hearts. These perfusion pressures were deter-

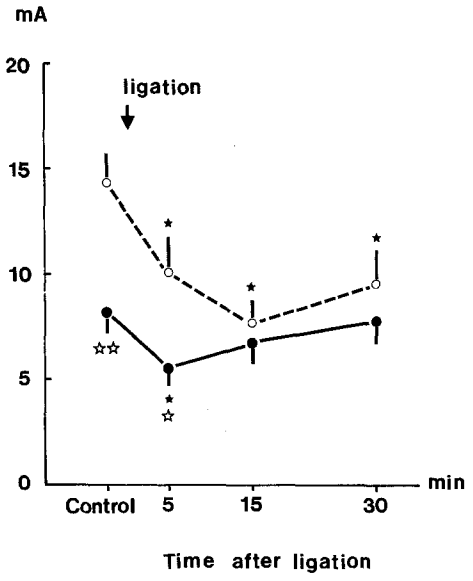
mined by preliminary studies in which pressure was adjusted to achieve similar coronary flow in normal and hypertrophied hearts (i.e., approximately 10 ml/g left ventricular weight/min). Flow was measured by collecting the coronary efflux for 1-min periods. The composition of the Tyrode's solution was (mM): NaCl 129, KCl 4, $MgCl_2$ 0.5, NaH_2PO_4 1.8, $CaCl_2$ 2.7, $NaHCO_3$ 20, and dextrose 5.5. The perfusate was gassed with 95% O_2 and 5% CO_2 (pH 7.30, 37 °C). Bipolar silver wire electrodes were implanted into the right ventricle to record a surface electrogram which was displayed on an oscilloscope and recorded with a polygraph. The sinoatrial node was crushed and the hearts were driven at a constant rate of 260 beats/min with 2-ms pulses delivered at twice diastolic threshold through bipolar electrodes implanted in the right ventricle. VFT was obtained by a train method. The cathode was placed on the base of left ventricle, which would be within the 'normal' perfused zone during ischemia; the anode was placed on the right ventricle in the region of the pulmonary conus. Trains of constant current stimuli (frequency: 100 Hz, pulse duration: 2 ms, train length: 150 ms) were delivered from a Grass S-88 stimulator through a constant current isolation unit. The trains were initiated with a 10-ms delay after the basic pacing cycle at every 10th basic drive stimulus. Beginning with zero current, the strength of the train was increased by 1 mA increments until VF occurred. Current strength was read from the oscilloscope using the principle of voltage drop across a known resistor. VFT was defined as the least amount of current required to produce VF. VF was defined as repetitive arrhythmias with irregular and varying morphology which persisted for more than six cycles. VF usually terminated spontaneously in this model. When VF persisted, electrical defibrillation (20 mA) was carried out, and repeated measurements were not made for at least 10 min after defibrillation. After 30 min equilibration, the left anterior coronary artery was occluded. VFT was measured before and 5, 15, and 30 min after coronary artery occlusion. At the end of the experiment, Evans blue dye (Sigma) was added to the perfusate. After the removal of the atria and right ventricle, the left ventricle was cut transversely into slices of approximately equal thickness (3 mm). Each slice was then photographed with magnification, and the perfused area and non-perfused area (risk area) were traced on a transparent sheet and measured using a computerized planimeter. The percentage of the risk area was then calculated. Results were expressed as mean values ± SE. Statistical analyses were performed using Student's unpaired t-test or analysis of variance with repeated measurements, where appropriate. P values < 0.05 were considered to be significant.

Results. The table summarizes the characteristics of the animals used in this study. Systolic blood pressure and the ratio of left ventricular weight to body weight were significantly higher in animals with aortic banding than in normal animals ($n = 11$ for each group, $p < 0.001$), while there was no difference in body weight between two groups. The mean VFT before ischemia was significantly lower in hypertrophied hearts (8.1 ± 0.7 mA) than in normal hearts (14.3 ± 1.1 mA) ($p < 0.001$). The figure shows the time course of changes in VFT during a 30-min period of coronary artery occlusion. In normal hearts, VFT decreased significantly and reached a minimum level 15 min after coronary occlusion, and then increased slightly. In hypertrophied hearts, VFT reached a minimum level 5 min after coronary occlusion, and then began to increase. The difference in the minimum values of VFT during ischemia between normal and hypertrophied hearts (7.7 ± 0.8 mA for normal and 5.5 ± 0.5 mA for hypertrophied hearts) was significant ($p < 0.05$). Coronary efflux (ml/g left ventricular weight/min) before and during a 30-min period of coronary occlusion did not differ between normal and hypertrophied heart groups. The mean value of the risk area was 55.7 ± 3.0% for normal hearts and 56.6 ± 1.6% for hypertrophied hearts. These values were not significantly different.

Characteristics of experimental animals

	BW (g)	LVW/BW (mg/g)	SBP (mm Hg)
Normal (n = 11)	429 ± 16	2.20 ± 0.03	130 ± 2
Hypertrophy (n = 11)	468 ± 13	3.14 ± 0.08*	232 + 8*

n = number of preparations. BW, body weight; LVW/BW, left ventricular weight/body weight; SBP, systolic blood pressure. Values are shown as the mean ± SE. * indicates significant difference at the level of $p < 0.001$.



Time course of the ventricular fibrillation threshold (VFT) prior to and after coronary artery occlusion in the normal heart group (n = 11, open circles) and the hypertrophied heart group (n = 11, closed circles). Each point is expressed as the mean ± SE. Solid asterisks indicate a statistical difference from the preocclusion values of each group at the level of *$p < 0.01$. Open asterisks indicate a statistical difference between two groups at the level of $p < 0.01$.

Discussion. VFT has been frequently used as a quantitative estimate of the susceptibility to VF in experimental animals. The time course of changes in VFT during coronary occlusion has been extensively studied and it is well established that VFT decreased during acute ischemia [5–7]. The present study showed that VFT in normal rat hearts was maximally reduced 15 min after coronary occlusion. These findings are similar to those previously reported [8].

The present study also showed that VFT was significantly lower in hypertrophied hearts than in normal hearts even before ischemia. Versailles et al. [9] noted that VFT was lower in spontaneously hypertensive rat hearts than in normotensives, although the degree of ventricular hypertrophy, if any, was not reported in their study. To our knowledge, there have been no reports on changes in VFT during ischemia in hypertrophied hearts. Our data showed that the minimum level of VFT observed during 30 min of coronary occlusion was significantly lower in hypertrophied hearts than in normal hearts, and the maximum reduction in VFT during ischemia was observed earlier in the hypertrophied hearts. In addition, VFT in hypertrophied hearts began to return to the preischemic level earlier than in normal hearts. The reason for this phenomenon is uncertain. VFT probably would increase with time if the electrodes used to induce fibrillation

were located in the ischemic area, as shown by Roland et al.[10]. However, in our study, we confirmed, using Evans blue perfusion at the end of each experiment, that the electrodes were within the normal zone during ischemia. Fisher et al.[11] have shown the VFT increases with worsening ischemia. Thus, it is likely that the degree of ischemia progressed more rapidly and severely in hypertrophied hearts than in normal hearts.

Many factors are known to influence VFT including the activity of the sympathetic and parasympathetic autonomic nervous system[12,13]. Although such neural activity is excluded from the present study in which isolated perfused hearts were used, the role of endogenous stores of catecholamine in nerve endings is unclear. Coulson et al.[14] report that catecholamine is depleted in pressure overloaded hypertrophied cat hearts. Thus, the lower VFT in hypertrophied hearts cannot be explained by increased myocardial catecholamine content. Coronary flow also may influence VFT, and cardiac hypertrophy reduces coronary vasodilator reserve[15,16]. However, in our study we adjusted perfusion pressure to achieve similar coronary flow in normal and hypertrophied hearts, and coronary efflux did not differ between the two groups even after coronary occlusion. The risk area was not different in the two groups, and the hearts were paced at a constant rate.

It has been reported that VFT reflects the degree of inhomogeneity of the excitability and recovery properties of the myocardium[17,18]. These inhomogeneities, which tend to enhance reentrant activity, reflect differences in the transmembrane potentials, including differences in the rate, amplitude, and length of depolarization. In this regard, it is noteworthy that Aronson[19] has reported that action potential duration is significantly longer in hypertrophied rat heart cells due to renal hypertension than in normal cells. Furthermore, Keung and Aronson[20] showed that action potential prolongation in such renal hypertension-induced hypertrophied heart cells is not uniform at various recording sites. These studies suggest that hypertrophied ventricles are more likely to suffer a greater risk of reentrant tachyarrhythmias. Furthermore, considering that ischemia per se produces dispersion of action potential duration and refractoriness, it is conceivable that electrical inhomogeneities during ischemia are even greater in hypertrophied hearts than in normal hearts.

Acknowledgment. Supported by Grants HL 19044 and HL 21735 from the National Heart, Lung, and Blood Institute, and by Grants-in-Aid from the American Heart Association, Florida Affiliate and Greater Miami Chapter.

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0014-4754/88/030214-03$1.50 + 0.20/0

Feeding induced by blockade of histamine H_1-receptor in rat brain

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Received 7 July 1987; accepted 17 December 1987

Summary. Histamine antagonists were infused into the third ventricle of the cerebrum in rats. All the H_1-, but none of the H_2-antagonists tested, induced initial feeding during the early portion of the light phase when histamine level was highest. No periprandial drinking was observed. Ambulation increased during feeding. The effect on feeding was attenuated when brain histamine was normally low during the early portion of the dark phase, or was decreased by α-fluoromethylhistidine. Hypothalamic neuronal histamine may suppress food intake through H_1-receptors, and diurnal fluctuations of food intake may mirror neuronal histamine levels.
Key words. Antihistamine; H_1-receptor; feeding elicitation; α-fluoromethylhistidine; hypothalamic neuronal histamine.

Histamine and the activity of its specific synthesizing and catabolizing enzymes are unevenly distributed in the brain. The highest levels are in the hypothalamic nuclei[1], the subcellular location is predominantly synaptosomal[2]. The regional distribution of histamine H_1-receptors is also uneven[3]. These receptors are relatively dense on discrete neurons in the hypothalamus[3], including areas related to food intake, such as the ventromedial hypothalamus (VMH) and the paraventricular nucleus[3]. It has been reported that histamine or its precursor amino acid, histidine, reduced or increased food intake[4,5]. However, exogenous histamine did not mimick the physiological role of endogenous histamine,