Delayed afterdepolarizations and triggered activity induced in feline Purkinje fibers by \( \alpha \)-adrenergic stimulation in the presence of elevated calcium levels

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ABSTRACT We studied the ability of \( \alpha \)-adrenergic stimulation to induce delayed afterdepolarizations and triggered activity in Purkinje fibers from cat hearts in the presence of an elevated \( \text{Ca}^{2+} \) concentration. Delayed afterdepolarizations could not be induced at drive cycle lengths of 200 to 500 msec in the presence of extracellular \( \text{Ca}^{2+} \) concentrations of 2.7 to 8.1 mM. However, the addition of \( 10^{-5} \text{M} \) phenylephrine in the presence of \( 5 \times 10^{-5} \text{M} \) propranolol elicited delayed afterdepolarizations in eight of 10 preparations at a \( \text{Ca}^{2+} \) concentration of 8.1 mM; nondrive-triggered action potentials were recorded from three of the preparations. These afterpotentials were completely suppressed by \( 5 \times 10^{-4} \text{M} \) prazosin or \( 10^{-4} \text{M} \) phentolamine. In the presence of \( 5 \times 10^{-5} \text{M} \) propranolol, \( 10^{-3} \text{M} \) phenylephrine prolonged action potential duration and this effect was suppressed by \( 5 \times 10^{-4} \text{M} \) prazosin. Methoxamine, at a concentration of \( 5 \times 10^{-6} \text{M} \), was also observed to potentiate delayed afterdepolarizations in all of three preparations studied. These results demonstrate that \( \alpha \)-adrenergic stimulation can induce afterpotentials in the presence of elevated \( \text{Ca}^{2+} \) levels in cat hearts. Stimulation of \( \alpha \)-adrenoceptors may be responsible for arrhythmias under \( \text{Ca}^{2+} \)-loaded conditions such as ischemia and coronary reperfusion.

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DELAYED AFTERDEPOLARIZATIONS and triggered activity have been studied in cardiac tissues under a variety of experimental conditions, including the presence of toxic levels of cardiac glycosides or \( \text{Na}^+ \) free, \( \text{Ca}^{2+} \) rich solutions used to superfuse canine Purkinje fibers,1–5 hypertrophied rat myocardium,6 and human atrial fibers.7 Recently, triggered ventricular rhythms were also demonstrated to occur in dogs with 1-day-old myocardial infarctions.8 Results of the previous studies on digitalis-induced delayed afterdepolarizations and triggered activity suggest that the intracellular calcium load plays an important role in the development of these afterpotentials.9,10

In other studies \( \alpha \)-adrenergic blockers have been reported to prevent the accumulation of intracellular calcium and to attenuate ventricular arrhythmias during acute ischemia and reperfusion in cats.11,12 These findings raise the possibility of a relationship between \( \alpha \)-adrenergic activity, intracellular calcium load, and the induction of arrhythmias during ischemia and reperfusion.

The present study was carried out to evaluate the involvement of \( \alpha \)-adrenergic receptors in the induction of arrhythmias under a calcium-loaded condition such as might occur during ischemia and coronary reperfusion. We examined the induction of delayed afterdepolarizations and triggered activity during pharmacologic stimulation of \( \alpha \)-adrenergic receptors in calcium-loaded Purkinje fibers of the cat.

Methods

Adult domestic cats of both sexes weighing 2.3 to 3.6 kg were anesthetized with sodium pentobarbital (30 mg/kg ip). The heart of each was rapidly removed, and the left ventricle was opened through an incision in the free wall in cool, oxygenated Tyrode's solution of the following composition (mM): \( \text{NaCl} \) 129, \( \text{KCl} \) 4.0 \( \text{NaHCO}_3 \) 20, \( \text{NaH}_2\text{PO}_4 \) 1.8, \( \text{MgCl}_2 \) 0.5, \( \text{CaCl}_2 \) 2.7, dextrose 5.5, and ascorbic acid 0.054. Preparations consisting of one free-running false tendon and the left ventricular
muscle attached at both ends were mounted in a Lucite tissue bath and superfused with warmed (37°C) Tyrode's solution gassed with 95% O₂ and 5% CO₂ at a rate of 10 ml/min. The pH of the superfusate was 7.35 ± 0.05.

The preparations were electrically stimulated at a cycle length of 500 msec through close bipolar silver-wire electrodes that were Teflon coated except at their tips. Pulse duration was 2 msec and current strength was 1.5 times diastolic threshold. Transmembrane potentials of Purkinje fibers were recorded by standard microelectrode techniques previously reported in detail. The glass microelectrodes, filled with 3M AgCl (Ehrenberg, 1954), were connected through Ag-AgCl junctions to a high-impedance electrometer with input capacity neutralization (WPI, KS-700). The first derivative of action potential upstroke was obtained by electronic differentiation. The amplifier outputs were displayed on a dual-beam oscilloscope (Tektronix, 564) and recorded on Polaroid film and with a two-channel pen recorder (Gould, Brush 220).

After a 60 min equilibration period, the preparations were superfused with Tyrode's solution containing 5 × 10⁻⁷M propranolol throughout the remainder of the protocol. In the presence of propranolol, the calcium concentration of the Tyrode's solution was increased from 2.7 to 8.1 mM. After 30 min of exposure to high-Ca⁺ Tyrode's solution, the preparations were stimulated by trains of 20 impulses at different drive cycle lengths ranging from 500 to 200 msec, separated by 10 sec quiescent periods to examine whether delayed afterdepolarizations could be induced. The same protocol was repeated after the addition of 10⁻⁵M phenylephrine. When delayed afterdepolarizations and triggered activity were induced, an α-adrenergic blocker, either 5 × 10⁻⁷M prazosin or 10⁻⁶M phentolamine, was added to the superfusate to determine whether these drugs prevented the induction of the afterpotentials under the experimental conditions described. In three experiments a very specific α-adrenergic agonist, methoxamine, was used in place of phenylephrine. Finally, to examine the ability of β-adrenergic stimulation to induce delayed afterdepolarizations and triggered activity in this cat preparation, norepinephrine (10⁻⁶ to 10⁻⁴M) was used in normal as well as high-calcium solutions.

In the second series of experiments, the effect of α-adrenergic stimulation on action potential characteristics of Purkinje fibers were examined. After a 60 min equilibration period, control measurements of maximum diastolic potential, action potential amplitude, action potential duration, and maximum upstroke velocity of phase zero (V₉₀max) were recorded. Action potential duration was measured at 50% and 90% of repolarization. Thereafter the preparations were superfused with Tyrode's solution containing 5 × 10⁻⁷M propranolol for 30 min. In the presence of propranolol, 10⁻⁵M phenylephrine and 5 × 10⁻⁷M prazosin were added to the superfusate, separated by 15 min intervals, and the measurements were repeated. In some experiments the effects of prazosin and phentolamine on action potential characteristics were also examined in normal and high-calcium solutions.

The definitions of the terms used are as follows: Delayed afterdepolarization is an afterpotential that occurs after completion of repolarization and carries the membrane potential to a level more than that recorded later in diastole and triggered activity is nondriven electrical activity initiated by one or more driven action potentials. All data are presented as mean ± SD. Statistical analyses were performed by repeated-measures analysis of variance and the Newman-Keuls multiple comparison procedure or Student's paired t test to compare drug-induced changes in action potential characteristics. Differences with p values of <.5 were considered significant.

The drugs used in this study were chemically pure 1-phenylephrine hydrochloride (Sigma Chemical), dl-propranolol hydrochloride (Sigma), prazosin hydrochloride (Sigma), methoxamine hydrochloride (Burroughs Wellcome Co.), and dl-norepinephrine hydrochloride (Sigma). The phenolamine mesylate (Regitine, Ciba-Geigy Corp.) was lyosiphylized and contained 1 mg of lactose for each milligram of phenolamine mesylate.

**Results**

Delayed afterdepolarizations and triggered activity induced by α-adrenergic stimulation. After a 60 min equilibration period and 30 min of superfusion with 5 × 10⁻⁷M propranolol, delayed afterdepolarizations and triggered activity were not recorded at drive cycle lengths of 500 through 200 msec in any of 10 preparations. Even after the extracellular calcium concentration was elevated from 2.7 to 8.1 mM, no clearly discernible delayed afterdepolarizations were recorded. However, after 10 to 15 min of exposure to 10⁻⁴M phenylephrine following 30 min of superfusion with high-Ca⁺ solution, delayed afterdepolarizations were induced at a drive cycle length of 250 or 200 msec in eight of the 10 preparations, and nondriven triggered action potentials were recorded in three of the eight preparations that displayed delayed afterdepolarizations. The delayed afterdepolarizations and triggered activity induced by phenylephrine in the presence of propranolol were almost completely suppressed by the addition of either 5 × 10⁻⁷M prazosin (n = 5) or 10⁻⁶M phentolamine (n = 3) (figure 1).

A typical experiment at a drive cycle length of 200 msec is shown in figure 1. Delayed afterdepolarizations were not recorded at drive cycle lengths of 500 through 200 msec, even at a calcium concentration of 8.1 mM (figure 1, A). After 10 min of exposure to 10⁻⁴M phenylephrine in the presence of 5 × 10⁻⁷M propranolol, a discernible delayed afterdepolarization was recorded (figure 1, B), and a nondriven triggered action potential occurred after another train of stimuli (figure 1, C). These afterpotentials were suppressed by 15 min of superfusion with 5 × 10⁻⁷M prazosin (figure 1, D). Figure 2, which illustrates recordings from another experiment, demonstrates that the delayed afterdepolarizations observed after the addition of phenylephrine could also be suppressed by 10⁻⁶M phentolamine.

In a separate preparation, subthreshold delayed afterdepolarizations were seen at a drive cycle length of 250 msec after 30 min of superfusion with high-calcium Tyrode's solution in the presence of propranolol (figure 3, A). The addition of phenylephrine resulted in the induction of clearly discernible delayed afterdepolarizations, and finally gave rise to nondriven action potentials (figure 3, B). These triggered action poten-
2. The suppression of phenylephrine-induced afterdepolarizations and triggered activity by phenylephrine in the presence of propranolol (5 × 10^{-7}M). Drive cycle length is 200 msec. A, No delayed afterdepolarizations at a Ca^{2+} concentration of 8.1 mM. B, Delayed afterdepolarizations induced by 10 min of exposure to 10^{-5}M phenylephrine. C, Nondriven triggered action potential after another train of stimuli. D, Suppression of phenylephrine-induced afterpotentials by 15 min of exposure to 5 × 10^{-7}M prazosin.

Figure 1. The induction of delayed afterdepolarizations and triggered activity by phenylephrine in the presence of propranolol (5 × 10^{-7}M). Drive cycle length is 200 msec. A, No delayed afterdepolarizations at a Ca^{2+} concentration of 8.1 mM. B, Delayed afterdepolarizations induced by 10 min of exposure to 10^{-5}M phenylephrine. C, Nondriven triggered action potential after another train of stimuli. D, Suppression of phenylephrine-induced afterpotentials by 15 min of exposure to 5 × 10^{-7}M prazosin.

Phenylephrine-induced afterdepolarizations were suppressed by prazosin (figure 3, C). Since this preparation failed to consistently follow stimuli at a drive cycle length of 200 msec, the effect of this rate of stimulation could not be studied. The data in figure 3 also show that, as the preceding drive cycle length decreased, the amplitude of the delayed afterdepolarizations increased and the coupling interval decreased.

Figure 4 illustrates recordings that separate effects of the number of stimuli from effects of rate of stimulation and of chemical interventions in the preparation in which delayed afterdepolarizations were induced by phenylephrine. As the number of driven action potentials increased, the amplitude of the delayed afterdepolarizations increased and the coupling interval decreased, finally leading to the induction of a nondriven triggered action potential at a critical number of stimuli. The rate of stimulation (cycle length, 200 msec) and conditions of superfusion remained constant.

In three experiments, the threshold concentration of phenylephrine that induced afterpotentials was examined in the presence of propranolol (5 × 10^{-7}M) and high Ca^{2+} (8.1 mM). In one preparation, 10^{-6}M phenylephrine produced delayed afterdepolarizations at a cycle length of 200 msec, and increasing the concentration to 10^{-5}M augmented the delayed afterdepolarizations and induced nondriven action potentials, as shown in figure 5. However, in the other two preparations no afterpotentials were observed at concentrations of phenylephrine less than 10^{-6}M.

We also determined the external Ca^{2+} concentra-
tion required for $10^{-5}$M phenylephrine in the presence of $5 \times 10^{-7}$M propranolol to induce afterpotentials. Delayed afterdepolarizations were not induced by phenylephrine at a Ca++ concentration of 2.7 mM in any of four preparations, but were induced in one of three preparations at a Ca++ concentration of 5.4 mM, and in eight of 10 preparations at a Ca++ concentration of 8.1 mM.

To confirm the hypothesis that delayed afterdepolarizations and triggered activity can be induced by the stimulation of $\alpha$-adrenergic receptors at a high Ca++ concentration, methoxamine was used in three other preparations. As shown in figure 6, 15 min of exposure to $5 \times 10^{-5}$M methoxamine potentiated a delayed afterdepolarization at a drive cycle length of 200 msec at a Ca++ concentration of 8.1 mM (figure 6, B), and this potential was suppressed by the addition of $5 \times 10^{-7}$M prazosin (figure 6, C). Nondriven triggered action potentials were not recorded.

Although 30 min of exposure to high-Ca++ Tyrode’s solution (Ca++ concentration 8.1 mM) with or without propranolol ($n = 10$ and $n = 7$, respectively) did not induce afterpotentials, we further examined the effects of 60 min of superfusion with high-Ca++ solution in three other preparations to exclude the possibility that long exposure to high-Ca++ solution itself could induce afterpotentials. No changes in electrical activity were found after 60 min of exposure to high-Ca++ solution.

In the absence of $\alpha$-adrenergic agonists, no delayed afterdepolarization or triggered activity was recorded at the Ca++ concentrations of 2.7, 5.4, and 8.1 mM. With the addition of either phenylephrine or methoxamine, no activity was induced at a Ca++ concentration of 2.7 mM, while activity was induced in 11 of 13 experiments at a Ca++ concentration of 8.1 mM. Afterpotentials were induced by phenylephrine in only one of three experiments at a Ca++ concentration of 5.4 mM. Thus, simply elevating external Ca++ concentration, in the absence of $10^{-7}$M-adrenergic agonists, did not permit the induction of afterpotentials. Furthermore, elevation of external Ca++ concentration was required for the induction of afterpotentials by $\alpha$-adrenergic agonists.

Delayed afterdepolarizations and triggered activity induced by $\beta$-adrenergic stimulation. We also examined the ability of $\beta$-adrenergic stimulation to induce delayed afterdepolarizations and triggered activity in preparations in normal and high-Ca++ Tyrode’s solutions. Norepinephrine at concentrations of $10^{-7}$M to $10^{-9}$M enhanced automaticity in four preparations studied in normal Tyrode’s solution (Ca++ concentration 2.7

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mM). In addition, rapid stimulation further enhanced automaticity after exposure to norepinephrine, as previously reported. Therefore, we could not evaluate the ability of norepinephrine to induce delayed afterdepolarizations and triggered activity at this Ca\(^{++}\) concentration. However, at a high Ca\(^{++}\) concentration (8.1 mM) this enhanced automaticity was not observed in three of four preparations, and 10\(^{-7}\)M to 5 x 10\(^{-4}\)M norepinephrine produced delayed afterdepolarizations and nondriven triggered action potentials in each of these three preparations (figure 7). When 5 x 10\(^{-7}\)M prazosin was added to the superfusate of the three preparations that could be studied, induction of afterpotentials was not affected, but inducibility was then suppressed by the addition of 5 x 10\(^{-7}\)M propranolol to the superfusate. The threshold concentration of norepinephrine to induce delayed afterdepolarizations was 10\(^{-7}\)M in two preparations (figure 8) and 5 x 10\(^{-6}\)M in the other preparations.

**Effects of \(\alpha\)-adrenergic agonist and antagonists on action potential characteristics in Purkinje fibers.** The effects of phenylephrine on action potential characteristics of Purkinje fibers in the presence of propranolol are summarized in table 1. Propranolol at a concentration of 5 x 10\(^{-7}\)M slightly shortened action potential duration, but did not affect any other parameters. In the presence of 5 x 10\(^{-7}\)M propranolol, action potential duration was prolonged by 15 min of exposure to 10\(^{-3}\)M phenylephrine. The prolonged action potential duration returned to the original value after 15 min of exposure to 5 x 10\(^{-7}\)M prazosin.

The effects of prazosin and phentolamine at the concentrations used in this study on action potential characteristics of Purkinje fibers in normal and high-Ca\(^{++}\) Tyrode’s solution were also evaluated. As shown in table 2, none of the action potential parameters were affected by 30 min of exposure to 5 x 10\(^{-7}\)M prazosin in normal (Ca\(^{++}\) concentration 2.7 mM) solution. In additional preparations, 30 min of superfusion with 5 x 10\(^{-7}\)M prazosin in a high Ca\(^{++}\) concentration (8.1

**FIGURE 4.** The effects of the number of preceding driven action potentials on the amplitude of delayed afterdepolarizations induced by phenylephrine (10\(^{-5}\)M) in the presence of propranolol (5 x 10\(^{-7}\)M). Ca\(^{++}\) concentration was 8.1 mM and drive cycle length was 200 msec. The amplitude of delayed afterdepolarizations increased as the number of driven beats increased (A and B) until a single nondriven action potential was developed at a critical number (C).

**FIGURE 5.** The threshold concentration of phenylephrine to induce afterpotentials in the presence of 5 x 10\(^{-7}\)M propranolol and 8.1 mM Ca\(^{++}\). There were no afterpotentials at a concentration of 10\(^{-7}\)M. Increasing the concentration of phenylephrine to 10\(^{-6}\)M induced delayed afterdepolarizations at a cycle length of 200 msec, and nondriven action potentials occurred at a concentration of 10\(^{-5}\)M. BCL = basic cycle length; Phe = phenylephrine; Pz = prazosin.
mM) also did not affect the action potential characteristics. Superfusion with $10^{-6}$M phentolamine for 30 min did not change the action potential characteristics in normal solution either.

**Discussion**

In this study, we have demonstrated that delayed afterdepolarization and triggered activity were not induced by elevating external calcium concentration from 2.7 to 8.1 mM, even at a drive cycle length of 200 msec. However, the addition of $10^{-5}$M phenylephrine in the presence of $5 \times 10^{-7}$M propranolol elicited delayed afterdepolarizations in eight of 10 preparations and nondriven triggered action potentials were developed in three of them. The delayed afterdepolarizations and triggered activity induced by phenylephrine were completely suppressed by either $5 \times 10^{-7}$M prazosin or $10^{-6}$M phentolamine, which alone did not affect action potential characteristics. Furthermore, in the presence of $5 \times 10^{-7}$M propranolol, $10^{-5}$M phenylephrine prolonged action potential duration, and this effect was suppressed by $5 \times 10^{-7}$M prazosin.

The stimulation of $\alpha$-adrenergic receptors is known to prolong action potential duration, whereas $\beta$-adrenergic stimulation shortens it.\textsuperscript{15,16} Our results with regard to prolongation of action potential duration by phenylephrine are consistent with those of previous
studies. From these data and the finding that prazosin suppressed phenylephrine-induced prolongation of the action potential duration, it can be assumed that the α-adrenergic–stimulating effects of phenylephrine were operative under the conditions of this study. Therefore, the induction of delayed afterdepolarizations and triggered activity can be ascribed to the α-adrenergic mechanism. This assumption is further supported by the observation that methoxamine, a specific α-adrenergic agonist, also potentiated delayed afterdepolarization in three other preparations.

One might argue that long exposure to the high-calcium solution itself potentiated delayed afterdepolarizations. However, we observed no afterpotentials after 30 to 60 min of superfusion with the high-calcium solution in any of 20 preparations in the presence or absence of propranolol (n = 10 for each). Furthermore, the finding that delayed afterdepolarizations recorded after the addition of phenylephrine were suppressed by either prazosin or phentolamine excludes the possibility that exposure to the calcium solution alone induced afterpotentials.

Afterpotentials and triggered rhythms have been shown in bovine Purkinje fibers and human atrial fibers in the presence of epinephrine. The present study revealed that delayed afterdepolarizations and triggered action potentials were also induced by norepinephrine at a high concentration of Ca++. Although norepinephrine has both α- and β-adrenergic–stimulating actions, prazosin did have little effect on the afterpotentials induced by norepinephrine and the addition of propranolol suppressed them. These findings indicate that β-adrenergic stimulation by norepinephrine is responsible for the induction of the afterpotentials. The involvement of the α-adrenergic mechanism might be masked by the dominant β-adrenergic–stimulating effect of norepinephrine.

Delayed afterdepolarizations induced by phenylephrine in the presence of propranolol became larger as the stimulation frequency or number of preceding driven beats was increased, as shown in figure 3 and 4. In addition, triggered activity arising from delayed afterdepolarizations occurred at a critical drive cycle length or after a critical number of driven beats. These features are similar to the electrical activity reported to occur in cardiac Purkinje fibers exposed to toxic concentrations of cardiac glycosides. The results of previous studies on delayed afterdepolarizations and triggered activity induced by cardiac glycosides have shown that the magnitude of delayed afterdepolarizations is augmented by increasing Ca++ concentration and is suppressed by Ca++ channel–blocking agents, suggesting that intracellular Ca++ overload is involved in the genesis of the afterpotentials.

Cardiac glycosides, increased stimulation, elevation

<table>
<thead>
<tr>
<th>TABLE 1</th>
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<tbody>
<tr>
<td>Effects of propranolol, phenylephrine, and prazosin on action potential characteristics in Purkinje fibers</td>
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<tr>
<td></td>
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<tr>
<td>Control</td>
</tr>
<tr>
<td>Propranolol, 5 × 10⁻⁷M</td>
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<tr>
<td>Phenylephrine, 10⁻⁷M</td>
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<td>Prazosin, 5 × 10⁻⁷M</td>
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</table>

Data are presented as the mean ± SD; n = 5.

MDP = maximum diastolic potential; APA = action potential amplitude; APD₅₀ and APD₉₀ = action potential duration measured at 50% and 90% of repolarization, respectively; V_max = maximum upstroke velocity of phase zero of action potential.

*p < .05 vs the values after superfusion with propranolol and control values.

*p < .05 vs the values after superfusion with phenylephrine.
of external Ca\(^{++}\) concentration, and \(\beta\)-adrenergic stimulation, which are known to augment or induce delayed afterdepolarizations, increase Ca\(^{++}\) uptake by cardiac cells and have positive inotropic influences. The stimulation of \(\alpha\)-adrenergic receptors has been demonstrated to increase the force of contraction in most mammalian cardiac muscles including those of cats, without an increase in cyclic AMP levels. Furthermore, there is evidence to suggest that Ca\(^{++}\) influx is enhanced by \(\alpha\)-adrenergic stimulation, although it remains controversial whether slow inward Ca\(^{++}\) current is increased by stimulation of \(\alpha\)-adrenergic receptors. It is possible that intracellular Ca\(^{++}\) overload is aggravated by the \(\alpha\)-adrenergic–stimulating effect of phenylephrine, giving rise to delayed afterdepolarizations and triggered activity, as seen in this study.

An increase in intracellular Ca\(^{++}\) concentration occurs during ischemia and coronary reperfusion. Recently, \(\alpha\)-adrenergic blockers were reported to prevent the accumulation of intracellular Ca\(^{++}\) during coronary reperfusion in cats. In addition, Sheridan et al. demonstrated that the number of premature ventricular complexes was reduced by \(\alpha\)-adrenergic blockade with either phentolamine or prazosin during ischemia and reperfusion in cats. These findings suggest that \(\alpha\)-adrenergic stimulation may play a role in the induction of arrhythmias by enhancing intracellular Ca\(^{++}\) overload. From the observations described above and our current data, it is reasonable to speculate that \(\alpha\)-adrenergic stimulation can initiate triggered activity as a result of aggravation of the intracellular Ca\(^{++}\) load during ischemia and reperfusion. Although the extent to which triggered activity has a role in the genesis of cardiac arrhythmias during ischemia remains unknown, a recent experimental study did show that delayed afterdepolarizations and triggered ventricular rhythms are developed in dogs with 1-day-old myocardial infarction. Since the number of \(\alpha\)-adrenergic receptors is increased in ischemic myocardium, the results of our study raise the possibility that not only \(\beta\)- but also \(\alpha\)-adrenergic stimulation by catecholamines, released by ischemic myocardium, can produce triggered activity and play a role in the induction of arrhythmias during ischemia and reperfusion.

We are grateful to Mrs. Thelma L. Gottlieb for administrative and secretarial support.

### References

### Table 2

<table>
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<tr>
<th></th>
<th>MDP (mV)</th>
<th>APA (mV)</th>
<th>APD(_{90}) (msec)</th>
<th>APD(_{99}) (msec)</th>
<th>(V_{\text{max}}) (V/sec)</th>
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<tr>
<td>Control</td>
<td>88.0 ± 4.8</td>
<td>129.0 ± 3.4</td>
<td>158.0 ± 25.2</td>
<td>215.8 ± 17.4</td>
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<td>Prazosin, 5 (\times 10^{-7})M</td>
<td>87.5 ± 5.0</td>
<td>129.0 ± 5.4</td>
<td>155.0 ± 28.6</td>
<td>218.8 ± 21.4</td>
<td>433.8 ± 81.8</td>
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<td>Control</td>
<td>84.8 ± 3.4</td>
<td>122.8 ± 3.0</td>
<td>161.0 ± 19.0</td>
<td>230.5 ± 13.3</td>
<td>435.0 ± 55.1</td>
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<td>Ca(^{++}), 8.1 mM</td>
<td>85.8 ± 2.5</td>
<td>125.0 ± 3.9</td>
<td>155.3 ± 29.2</td>
<td>233.5 ± 7.5</td>
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<td>Prazosin, 5 (\times 10^{-7})M</td>
<td>86.0 ± 2.0</td>
<td>124.3 ± 3.7</td>
<td>150.8 ± 30.3</td>
<td>236.3 ± 10.3</td>
<td>410.0 ± 52.9</td>
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<td><strong>Experiment 3 (n = 3)</strong></td>
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<td>Control</td>
<td>86.0 ± 3.0</td>
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<td>Phentolamine 10(^{-6}) M</td>
<td>88.3 ± 3.2</td>
<td>131.7 ± 6.4</td>
<td>162.3 ± 21.5</td>
<td>233.7 ± 23.3</td>
<td>472.0 ± 95.2</td>
</tr>
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</table>

Data are mean ± SD; abbreviations are as in table 1.
None of the comparisons revealed statistically significant differences.
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