LABORATORY INVESTIGATION
ARRHYTHMIA

Automaticity, triggered activity, and responses to adrenergic stimulation in cat subendocardial Purkinje fibers after healing of myocardial infarction

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ABSTRACT  We studied automaticity, triggered activity, and responses to α- and β-adrenergic stimulation in subendocardial Purkinje fibers overlying healed infarct scars (infarct preparation) and from remote normal zones (noninfarct preparation) of cat left ventricles. The preparations were studied 2 to 4 months after ligation of multiple distal tributaries of the left anterior descending and circumflex arteries. Subendocardial Purkinje fibers from corresponding areas of normal hearts served as control samples (control preparation). Transmembrane action potential characteristics and rates of automaticity (spontaneous phase 4 depolarization) did not differ among control, noninfarct, and infarct preparations. However, overdrive at cycle lengths of less than 400 msec suppressed automaticity to a greater degree in Purkinje fibers of infarct preparations than those of control and noninfarct preparations. Changes in automatic rate during superfusion with isoproterenol (10^-6M to 10^-4M) were not different among the three groups of preparations, but exposure to phenylephrine (10^-6M to 10^-7M) in the presence of 5 × 10^-7M propranolol reduced the automatic rate to a greater degree in Purkinje fibers of infarct preparations than those of control or noninfarct preparations. Triggered activity arising from delayed afterdepolarizations was recorded in 10 of 29 infarct preparations (34%), but in 12 control and 10 noninfarct preparations. These afterpotentials were augmented by increasing extracellular Ca^2+ concentration, 10^-7M isoproterenol, and 10^-5M phenylephrine in the presence of 5 × 10^-7M propranolol. We conclude that Purkinje fibers overlying healed infarct scars have altered physiology of spontaneous automaticity, enhanced responses to α-adrenergic interventions, and a tendency to triggered activity, and that both α- and β-adrenergic effects may result in worsening of arrhythmias by augmentation of afterpotentials in healed myocardial infarction.


PREVIOUS studies have suggested that several mechanisms may be responsible for arrhythmias occurring 24 hr after experimental acute myocardial infarction. These include enhanced automaticity of subendocardial Purkinje fibers surviving myocardial infarction,¹⁻⁴ triggered activity arising from delayed afterdepolarizations,⁵ and reentry.⁶ The infarct zones of canine hearts studied 24 hr after infarction have demonstrated enhanced rate responses to epinephrine.⁷ These findings lead to the question of whether abnormal automaticity, triggered activity, or both persist into the healing or chronic phase of the experimental infarction, and whether the response to adrenergic stimulation is altered after healing of myocardial infarction. Although Lazzara et al.⁸ reported that dogs with chronic infarction (2 weeks to 3 months) had no arrhythmias and no enhanced automaticity, our studies using a different infarction technique have demonstrated long-term electrophysiologic changes after healing of myocardial infarction in cats.⁹⁻¹¹ In man, lethal arrhythmias commonly occur in the presence of healed myocardial infarction, without an identifiable acute myocardial infarction.¹²,¹³ This combination of observations led us to design this study to evaluate auto-
ticity, triggered activity, and their responses to pharmacologic α- and β-adrenergic stimulation in the subendocardial Purkinje fibers of the cat healed myocardial infarction.

Methods

Preparation and solution. Adult domestic cats of both sexes weighing 2.5 to 4.0 kg were anesthetized with sodium pentobarbital (30 mg/kg ip). Under sterile conditions, acute myocardial infarction involving the anterior papillary muscle and adjacent area was created by single-stage ligation of multiple distal tributaries of the left anterior descending and circumflex arteries.3-11 On the day of terminal study, 2 to 4 months after coronary artery ligation, the cats with healed myocardial infarction (n = 29) were anesthetized with sodium pentobarbital (30 mg/kg ip), and the heart of each was removed through a thoracotomy. The atria and right ventricle were excised, and the left ventricle was opened in cool, oxygenated Tyrode’s solution by an incision through the free wall. The healed infarct zone (approximately 8 mm × 8 mm) was excised from the left ventricle (infarct preparation, n = 29) for isolated tissue studies. Only one infarct preparation was obtained from each infarcted heart. For some experiments, a normal zone consisting of the posterior papillary muscle and adjacent area was excised from the infarcted left ventricle (noninfarct preparation, n = 10). Control preparations from 12 normal hearts consisted of the anterior papillary muscle and adjacent area, corresponding in size and location to the infarct zone (control preparation, n = 12). The preparations were placed with endocardial surface up in a tissue bath, and were superfused at a rate of 15 ml/min with warm (37°C) Tyrode’s solution equilibrated with 95% O₂ and 5% CO₂. The composition of Tyrode’s solution was (in mM): NaCl 129, KC1 4, NaHCO₃ 20, NaH₂PO₄ 1.8, MgCl₂ 0.5, CaCl₂ 2.7, dextrose 5.5, and ascorbic acid 0.054. The pH of the superfusate was 7.30.

Electrical stimulation and recording. The preparations were stimulated at a basic cycle length of 800 msec with bipolar Teflon-coated silver wire electrodes placed on the endocardium near the tip of the anterior papillary muscle. Pulse duration was 2 msec and current intensity was twice late diastolic threshold. By conventional microelectrode techniques, transmembrane action potentials were recorded from subendocardial Purkinje fibers near the junction of the anterior papillary muscle and the anterior division of the left bundle branch. Glass microelectrodes, filled with 3M KC₁ (resistance 10 to 30 MΩ), 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 electrical differentiation. The amplified output was displayed on a dual-beam oscilloscope (Tektronix 565) and photographed on Polaroid film and recorded on a polygraph (Grass, model 79).

Experimental protocol. After a 45 to 60 min equilibration period, transmembrane action potentials were recorded. The spontaneous automatic rate was measured during a 5 min period without stimulation. The preparations were then stimulated by trains of 20 stimuli at drive cycle lengths ranging from 1000 to 200 msec, separated by 10 sec quiescent periods. In 10 of the 29 infarct preparations, delayed afterdepolarizations and triggered activity were induced during the pacing protocol described above. These 10 preparations were used for the afterpotential studies described below, and were not used for the recovery time and adrenergic stimulation studies, because triggered activity may influence the properties of spontaneous automaticity. Twelve of the 19 remaining infarct preparations had regular automatic rhythms at rates ranging from 30 to 50 impulses/min, and were used for the recovery time and adrenergic stimulation studies. There were no differences in spontaneous automatic rates among control, noninfarct, and infarct preparations (see Results). Therefore, control and noninfarct preparations with the same automatic rates (30 to 50 impulses/min) were used for the recovery time and adrenergic stimulation studies to compare the responses of the three groups.

Recovery cycle lengths were measured after 15 sec of pacing at cycle lengths ranging from 1000 to 250 msec. The recovery cycle length was measured from the upstroke of the last driven action potential to the upstroke of the first spontaneously firing action potential. Pacing at each cycle length was performed after the automatic rate and resting potential returned to the predrive level. This procedure was repeated twice, and the average value was used as the recovery cycle length at each drive cycle length. Since it has been shown that the recovery cycle length after cessation of overdrive pacing is proportional to the predrive cycle length,14-15 we corrected the recovery cycle length by subtracting the predrive cycle length and expressed the data as the corrected recovery cycle length.

The effects of α- and β-adrenergic stimulation on the rate of automaticity of Purkinje fibers were examined after determination of recovery cycle lengths. Isoproterenol was used as the β-adrenergic agonist, and phenylephrine was used in the presence of 5 × 10⁻⁴M propranolol as the α-agonist, as previously reported.16 The preparations were allowed to beat spontaneously to avoid overdrive suppression by pacing. After the automatic rate became stable, the preparations were exposed to a series of increasing concentrations of isoproterenol or phenylephrine ranging from 10⁻⁴M to 10⁻⁵M. The automatic rate was measured after 15 min of superfusion with the drugs at each concentration since preliminary studies indicated that new stable levels were obtained after this period of exposure to the drugs. In phenylephrine experiments, the preparations were superfused with 5 × 10⁻⁷M propranolol for 40 min before exposure to phenylephrine and throughout the remainder of the phenylephrine protocol.

In the 10 infarct preparations in which delayed afterdepolarizations and triggered activity were recorded, the effects of Ca²⁺, isoproterenol, and phenylephrine in the presence of propranolol were studied. A delayed afterdepolarization was defined as an afterpotential occurring after completion of repolarization and carrying the membrane potential to a level less negative than that recorded later in diastole, and triggered activity was defined as nondriven electrical activity initiated by one or more driven action potentials.17 The measurements of the amplitude and coupling interval of delayed afterdepolarizations were made in a manner similar to that described by Rosen and Danilo.18 The amplitude was measured from the most negative level recorded during repolarization to the peak positive level reached by the delayed afterdepolarization. The coupling interval was measured from the upstroke of the last driven action potential to the peak positive level of the delayed afterdepolarization.

Drugs. The drugs used in this study were dl-isoproterenol hydrochloride (Sigma), l-phenylephrine hydrochloride (Sigma), dl-propranolol hydrochloride (Sigma), and phentolamine hydrochloride (Ciba-Geigy).

Statistical analysis. All data are presented as mean ± SE. Statistical analyses were performed by analysis of variance with repeated measures or Student’s unpaired t test, where appropriate. Differences with p values < .05 were considered significant. The data on the effects of adrenergic agonists on automaticity are presented as percent changes from the control (before exposure to the drugs). However, calculation for statistical analysis was made with use of the absolute values.
TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>MDP (mV)</th>
<th>APA (mV)</th>
<th>APD50 (msec)</th>
<th>APD90 (msec)</th>
<th>Vmax (V/sec)</th>
<th>SR (impulses/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>84.7 ± 0.6</td>
<td>119.0 ± 1.6</td>
<td>169.2 ± 4.8</td>
<td>236.8 ± 3.9</td>
<td>310.0 ± 17.0</td>
<td>42.4 ± 8.7</td>
</tr>
<tr>
<td>Infarct</td>
<td>83.0 ± 0.6</td>
<td>113.1 ± 1.0</td>
<td>156.0 ± 4.2</td>
<td>248.1 ± 6.5</td>
<td>281.4 ± 16.9</td>
<td>38.4 ± 8.4 (26)</td>
</tr>
<tr>
<td>Noninfarct</td>
<td>84.5 ± 1.0</td>
<td>115.4 ± 1.8</td>
<td>165.5 ± 6.5</td>
<td>231.1 ± 4.5</td>
<td>325.3 ± 17.7</td>
<td>40.3 ± 7.1</td>
</tr>
</tbody>
</table>

Data are mean ± SE. None of the comparisons between the three groups showed statistically significant differences. Data on spontaneous rate from three infarct preparations were discarded because of development of triggered rhythms.

MDP = maximum diastolic potential; APA = action potential amplitude; APD50 and APD90 = action potential duration measured at 50% and 90% repolarization, respectively; Vmax = maximum upstroke of phase 0 of action potential; SR = spontaneous rate.

Results

Action potential characteristics and automaticity. Data on action potential characteristics and spontaneous automatic rates recorded from subendocardial Purkinje fibers of control, infarct, and noninfarct preparations are summarized in Table 1. Although action potential duration at 50% repolarization tended to be shorter and action potential duration at 90% repolarization tended to be longer in infarct preparations, there were no statistically significant differences in action potential variables in control, infarct, and noninfarct preparations. Spontaneous automatic rate also was not different in the three groups. Previous studies have shown that enhanced automaticity in isolated ischemic preparations is observed during the first 20 min of study in the tissue bath, and that automaticity is gradually decreased by continuous superfusion. Therefore, stimulation was interrupted every 5 to 10 min during equilibration periods to determine whether enhanced automaticity was present. Spontaneous automatic rates of 90 to 100 impulses/min were recorded in only three of 29 infarct preparations and the rates remained almost constant through the 60 min equilibration periods. Either no automaticity or automaticity at a frequency of less than 5 impulses/min was observed in eight of 29 infarct preparations. The automatic rates of the remaining infarct preparations ranged from 20 to 60 impulses/min. The mean spontaneous rate of infarct preparations (38.4 ± 8.4 impulses/min) was not different from that of control or noninfarct preparations (42.4 ± 8.7 and 40.3 ± 7.1 impulses/min, respectively).

Recovery cycle length. The corrected recovery cycle length at different pacing rates in eight control, eight infarct, and seven noninfarct preparations is shown in Figure 1. The corrected recovery cycle length was significantly longer in infarct preparations than in control and noninfarct preparations at drive cycle lengths of less than 500 msec. Overdrive at cycle lengths of 320 and 250 msec was associated with marked prolongation of recovery cycle lengths in infarct preparations. In two of eight infarct preparations, the correct recovery cycle length was longer than 30 sec at a drive cycle length of 250 msec.

Effect of β-adrenergic agonist. Figure 2 shows the concentration-response curves for the effect of isoproterenol on automatic rates of Purkinje fibers in six control, five infarct, and five noninfarct preparations. The response to isoproterenol at concentrations of 10^-8 M to 10^-6 M was nearly identical in the three groups.

Effect of α-adrenergic agonist. Figure 3 shows the effects of phenylephrine in the presence of 5 × 10^-7 M...
propranolol on automatic rates of Purkinje fibers in six control, six infarct, and five noninfarct preparations. Exposure to $5 \times 10^{-7}$M propranolol tended to decrease the automatic rates in all three groups. During subsequent exposure to phenylephrine at concentrations of $10^{-5}$M to $10^{-6}$M, the automatic rate remained unchanged in two of six control and one of five noninfarct preparations. In the remainder of the control and noninfarct preparations, the automatic rate decreased, but the change overall did not reach statistical significance. On the other hand, in all six infarct preparations the automatic rate decreased during exposure to phenylephrine. At a concentration of $10^{-5}$M of phenylephrine, the decrease in automatic rate was significantly greater in infarct preparations than in control and noninfarct preparations. In addition, automaticity was completely abolished by longer (30 min) exposure to $10^{-5}$M phenylephrine in two of six infarct preparations, whereas none of the control or noninfarct preparations became quiescent. Suppression of automaticity by combined phenylephrine and propranolol was almost completely antagonized by 30 min of superfusion with $10^{-6}$M phenolamine.

Delayed afterdepolarizations and triggered activity. Delayed afterdepolarizations and triggered activity were recorded in 10 of 29 (34%) infarct preparations. None of 12 control or 10 noninfarct preparations developed afterpotentials. We compared the automatic rates of the infarct Purkinje fibers developing afterpotentials to

**FIGURE 2.** Concentration-response curves showing the effect of isoproterenol on automatic rates of Purkinje fibers of control (filled circles, $n = 6$), noninfarct (open circles, $n = 5$), and infarct (open squares, $n = 5$) preparations. Data are expressed as the mean ± SE. The response to isoproterenol was not different among the three groups. C = before exposure to the drug.

**FIGURE 3.** Concentration-response curves showing the effect of phenylephrine in the presence of $5 \times 10^{-7}$M propranolol on automatic rates of Purkinje fibers from control (filled circles, $n = 6$), noninfarct (open circles, $n = 5$), and infarct (open squares, $n = 6$) preparations. Data are expressed as the mean ± SE. The reduction in automatic rate during exposure to phenylephrine was greater in infarct preparations than in control and noninfarct preparations. C = before exposure to the drugs; Prop = propranolol ($5 \times 10^{-7}$M); Phent = phenolamine ($10^{-6}$M). $\star$ p < .05 vs control and noninfarct preparations.
those without afterpotentials to identify differences in automaticity; there were no differences in automatic rates (41.6 ± 8.6 and 36.9 ± 8.5 impulses/min in the infarct preparations with and without afterpotentials, respectively).

Figure 4 illustrates results of three experiments in which delayed afterdepolarizations and triggered activity were initiated by changes in intrinsic automaticity. The amplitude of the delayed afterdepolarizations increased progressively as the rate of intrinsic automaticity increased. Finally, the delayed afterdepolarizations reached threshold and induced triggered activity, which persisted for several seconds to a few minutes and then stopped spontaneously. A subthreshold delayed afterdepolarization was recorded after the last action potential of the triggered activity, and then the intrinsic automaticity resumed after a 1.8 sec pause. As the rate of intrinsic automaticity increased to a critical level, triggered activity resulting from delayed afterdepolarizations developed again. The automatic rhythm due to phase 4 depolarization appeared after cessation of triggered activity and then reinduced triggered activity as the increasing automatic rate produced afterpotentials that reached threshold.

We studied the characteristics of delayed afterdepolarizations recorded from the infarct preparations (figures 5 and 6). The amplitude of delayed afterdepolarizations increased and their coupling intervals decreased as the stimulation frequency or number of preceding driven beats was increased (figure 5). The relationships of the amplitude and coupling interval of the delayed afterdepolarizations to the stimulation frequency are shown in figure 6.

We also studied the effects of Ca²⁺ (n = 2), isoproterenol (n = 5), and phenylephrine in the presence of propranolol (n = 5) on delayed afterdepolarizations observed in infarct preparations. As previously demonstrated in digitalis-induced delayed afterdepolarizations, the amplitude of afterpotentials increased when the extracellular Ca²⁺ concentration was elevated from 2.7 to 5.4 mM (figure 7). This effect was reversed by washout with 2.7 mM Ca²⁺ Tyrode’s solution.

The effect of 10⁻⁷M isoproterenol on delayed afterdepolarizations in infarct preparations is shown in figure 8. Initial superfusion with 10⁻⁷M isoproterenol for 15 min augmented delayed afterdepolarizations and induced nondriven triggered action potentials. Subsequent superfusion with isoproterenol plus 5 x 10⁻⁷M propranolol for 30 min blocked this response. Figure 9, A, demonstrates that 10⁻⁷M isoproterenol shifted the curve representing the relationship between the amplitude of delayed afterdepolarizations and the stimulation frequency in an upward fashion.

The effect of 10⁻⁵M phenylephrine in the presence of 5 x 10⁻⁷M propranolol on delayed afterdepolarizations in infarct preparations is shown in figure 10. Phenylephrine augmented delayed afterdepolarizations and induced nondriven triggered action potentials in a manner qualitatively similar to that in the experiments with isoproterenol. However, as shown in figure
FIGURE 5. A, The effect of the drive cycle length on the amplitude of delayed afterdepolarizations recorded from infarct preparations. The amplitude of delayed afterdepolarizations increased as the drive cycle length shortened and finally a nondriven triggered action potential was induced, as indicated by the star. B, The effect of the number of driven action potentials on the amplitude of delayed afterdepolarizations recorded from infarct preparations. The amplitude of delayed afterdepolarizations increased as the number of driven action potentials increased and finally a nondriven action potential was induced. The preparations in panels A and B are different. DCL = drive cycle length.

FIGURE 6. The relationships of the amplitude and coupling interval of delayed afterdepolarizations to the stimulation frequency (n = 7). Data are expressed as the mean ± SE. The amplitude increased and the coupling interval shortened as the stimulation frequency increased. DAD = delayed afterdepolarization.

9, B, phenylephrine shifted the curve of delayed afterdepolarization amplitude to a lesser extent than isoproterenol. Phenylephrine induced triggered activity only at short cycle lengths.

Finally, we studied the effect of the combination of $5 \times 10^{-7}$M propranolol and $10^{-6}$M phentolamine on the upstroke of action potentials to exclude the possibility of the local anesthetic effects of these adrenergic blockers on delayed afterdepolarizations induced by phenylephrine. As summarized in table 2, the amplitude and upstroke velocity of action potentials were not changed by 30 min of exposure to propranolol and phentolamine at the concentrations used. Only action potential duration was slightly prolonged by the combination of the drugs.

Discussion

In these experiments, we observed that enhanced automaticity was absent in the majority of healed infarct preparations and that automaticity of Purkinje fibers of infarct preparations was markedly suppressed by overdrive at cycle lengths of 400 msec or less. In addition, phenylephrine in the presence of propranolol suppressed automaticity to a greater degree in Purkinje fibers from infarcted hearts, whereas the positive chronotropic response to isoproterenol was almost identical in infarct and normal preparations. Finally,
the chronic stage of myocardial infarction, we have previously demonstrated that long-term electrophysiological instability is present in the cat preparation of myocardial infarction that we used.\(^9\)\(^-\)\(^11\) In the clinical setting it has been shown that lethal arrhythmias often occur in the patient with a healed myocardial infarction in the absence of an identifiable acute myocardial infarction.\(^12\)\(^-\)\(^13\) However, based on our observations it is unlikely that automaticity contributes in a major way to tachyarrhythmias in the presence of healed myocardial infarction.

Automaticity of Purkinje fibers from healed infarct preparations was shown to be suppressed by overdrive to a greater degree than that of fibers from control or noninfarct preparations. This finding might provide some insight into possible mechanisms of bradyarrhythmic events. However, the extent to which Purkinje fibers overlying areas of healed infarction interact with those elsewhere in the heart in situ and their role in the initiation of the impulse formation and cardiac arrhythmias is not known at this time. Further studies are needed to clarify this question.

![Figure 7](http://circ.ahajournals.org/)

**FIGURE 7.** The effect of extracellular \(Ca^{++}\) concentration on delayed afterdepolarizations recorded from infarct preparations. When the extracellular \(Ca^{++}\) concentration was increased from 2.7 to 5.4 mM, the amplitude of delayed afterdepolarizations increased and nondriven action potentials were induced. This effect was reversed by washout with 2.7 mM \(Ca^{++}\) Tyrode's solution. Stars indicate nondriven action potentials.

FIGURE 8. The effect of isoproterenol on delayed afterdepolarizations recorded from infarct preparations. Isoproterenol (10\(^{-7}\)M) augmented delayed afterdepolarizations and induced triggered action potentials. This effect of isoproterenol was blocked by 5 \(\times\) 10\(^{-7}\)M propranolol. Iso = isoproterenol. Stars indicate nondriven action potentials.
Cameron and Han\textsuperscript{7} have demonstrated that epinephrine increases the automatic rate to a greater degree in infarcted Purkinje fibers than in noninfarcted fibers 24 hr after myocardial infarction in dogs, and these investigators emphasized the role of catecholamines in enhancement of arrhythmias at this stage of infarction. However, our data show that exaggerated responses to $\beta$-adrenergic stimulation do not occur in subendocardial Purkinje fibers after healing of myocardial infarction.

Previous investigations\textsuperscript{19,20} have shown that there is a biphasic response of automatic rate to phenylephrine and epinephrine in canine Purkinje fibers. A decrease in rate is mediated by $\alpha$-adrenergic effects, while an increase in rate is mediated by $\beta$-adrenergic effects. However, Rosen et al.\textsuperscript{20} pointed out that there are two

\begin{table}
\centering
\caption{The effect of the combination of propranolol ($5 \times 10^{-7}$M) and phentolamine ($10^{-6}$M) on action potential characteristics ($n = 4$)}
\begin{tabular}{llllll}
\hline
 & MDP (mV) & APA (mV) & APD$_{50}$ (msec) & APD$_{90}$ (msec) & $V_{\text{max}}$ (V/sec) \\
\hline
Control & 85.0 $\pm$ 0.8 & 117.3 $\pm$ 1.0 & 161.8 $\pm$ 5.7 & 230.5 $\pm$ 6.7 & 322.5 $\pm$ 16.0 \\
30 min & 84.3 $\pm$ 0.5 & 116.5 $\pm$ 0.5 & 151.8 $\pm$ 7.9\textsuperscript{a} & 247.8 $\pm$ 9.0\textsuperscript{a} & 312.5 $\pm$ 14.4 \\
\hline
\end{tabular}
\footnotesize{Data are mean $\pm$ SE.}
\footnotesize{Control = values obtained before exposure to the drugs; 30 min = values obtained after 30 min of exposure to the drugs.}
\footnotesize{Other abbreviations are as in table 1.}
\footnotesize{\textsuperscript{a}$p < .05$ vs control values when evaluated by paired $t$ test.}
\end{table}
suggests that the properties of α-adrenergic receptors may be modified in infarcted Purkinje fibers. Corr et al. have demonstrated an increase in the number of α-adrenergic receptors in acutely ischemic cat myocardium, although their infarct preparation was not comparable to ours. It is also possible that α-adrenergic effects on automaticity in infarcted Purkinje fibers are nonspecific, since automaticity was easily suppressed by overdrive as well. Another possibility is that conduction disturbances might result in reduction of automaticity, since an α-adrenergic agonist, methoxamine, has been shown to cause conduction block in depressed tissues. This is unlikely, however, because the automatic rate decreased gradually and diastolic threshold did not change even in the preparations in which automaticity was completely suppressed.

The present study revealed that 34% of the infarct preparations developed delayed afterdepolarizations and triggered activity. The delayed afterdepolarizations and triggered activity observed in our study were similar to those noted in other preparations. The amplitude and coupling interval of delayed afterdepolarizations were a function of the cycle length and number of preceding impulses, and were dependent on extracellular Ca²⁺ concentration (figures 5 to 7).

Triggered activity arising from delayed afterdepolarizations has been observed in various tissues under a number of experimental conditions, and there has been considerable speculation on the role of triggered activity in the genesis of cardiac arrhythmias. Furthermore, El-Sherif et al. have reported that triggered activity develops in 84% of subendocardial preparations from one-day-old canine infarcts. The present study raises the possibility that some arrhythmias that develop in the presence of healed infarction may result from triggered activity. However, extrapolation of our data on triggered activity to spontaneous arrhythmias in vivo should be done with caution in the absence of data on the effect of pacing on arrhythmias occurring at this stage of infarction in the intact cat.

Finally, the present study showed that delayed afterdepolarizations recorded from Purkinje fibers from preparations of healed infarction were augmented by both α- and β-adrenergic agonists. Epinephrine has been shown to induce or augment delayed afterdepolarizations, probably due to its β-effect. El-Sherif et al. demonstrated that epinephrine augmented delayed afterdepolarizations and induced triggered activity in subendocardial Purkinje fibers from dogs with 1-day-old infarcts. Our data on the effects of β-adrenergic agonists on afterpotentials are consistent with the results of these studies.
It has been recently demonstrated that afterpotentials may be induced through \(\alpha\)-adrenergic mechanisms under specific conditions such as hypoxia\textsuperscript{15}\textsuperscript{16} and exposure to high concentrations of \(Ca^{++}\).\textsuperscript{16} The observation that afterpotentials in Purkinje fibers from areas of healed infarction were augmented by \(\alpha\)-adrenergic stimulation without any other interventions suggests a possible \(\alpha\)-component among the mechanisms of arrhythmias in this preparation. Although \(\beta\)-adrenergic effects were dominant in the augmentation of afterpotentials, it appears that enhanced \(\alpha\)-adrenergic effects can also be a causal factor in the development of triggered activity in healed myocardial infarction.

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References

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