Transmembrane Potential Properties at the Core of Functional Reentrant Wave Fronts in Isolated Canine Right Atria

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Background—The characteristics of transmembrane potential (TMP) at the core of functional reentry in the atrium are not well understood.

Methods and Results—In protocol 1 (11 dogs), isolated perfused canine right atria were mapped from the endocardial surface while simultaneous TMPs were recorded from the epicardial surface. Episodes of reentry (n = 64) were induced in the presence of 1 to 5 μmol/L acetylcholine. Successful simultaneous TMP recordings and activation maps were made in 8 episodes. The TMP was “near the core” if it was within 3.2 mm of the core; otherwise, it was considered to be “in the periphery.” The mean cycle length of reentry was 110 ± 35 ms. The TMP amplitude, duration (90% repolarization), and (dV/dt) max near the core (n = 106) were 58 ± 22 mV, 46 ± 14 ms, and 33 ± 20 V/s, respectively, significantly less than those in the periphery (n = 241): 70 ± 8 mV, 94 ± 32 ms, and 55 ± 10 V/s (P < 0.001 for all). In 2 episodes of reentry, the cell at the core remained unexcited at its resting membrane potential. In protocol 2 (2 dogs), we performed simultaneous high-density mapping in 4 episodes of reentry and showed synchronous activation patterns on both surfaces with similar locations of the core.

Conclusions—During meandering functional reentry in isolated canine right atria, (1) TMPs of cells near the core have a reduced amplitude, duration, and (dV/dt) max , and (2) cells at the core may remain unexcited at their resting membrane potential. These findings are compatible with the spiral wave concept of functional reentry in the atrium. (Circulation. 1998;98:1556-1567.)

Key Words: waves ■ atrium ■ arrhythmia ■ tachycardia ■ electrophysiology

Functional reentry, a well-documented mechanism of cardiac arrhythmia,1 refers to propagation of an impulse around a core determined by the electrophysiological properties of the tissue. Allessie et al2 measured transmembrane potential (TMP) of stationary reentrant wave fronts in isolated rabbit atria. On the basis of the results of that study, they proposed the “leading circle” concept to explain the mechanisms of functional reentry in the atria. The maintenance of leading circle reentry (the absence of short-circuiting) was due to repetitive centripetal wavelets that kept the core in a constant state of refractoriness. The leading circle hypothesis also proposed that the head of a reentrant wave front bites its own tail, resulting in little or no excitable gap. In comparison, other investigators3,4 proposed that in addition to refractoriness, the wave front curvature is also important in the maintenance of functional reentry. The curvature of a reentrant wave front progressively increases as one approaches the central core. When a critical curvature is reached, propagation fails despite the presence of excitable tissue. The point at which propagation fails is the site of a wave break. The area encircled by the wave breaks is the core of reentry. According to this hypothesis, the core of functional reentrant wave front may remain excitable but unexcited. Compatible with the latter hypothesis, experimental data obtained from thin slices of ventricular tissues5,6 revealed that there was a progressive reduction of the amplitude of the action potential (AP) as the recording site moved from the periphery toward the core of reentry. At the core itself, the electrical activity had a very low amplitude.5 However, because optical mapping techniques used in the latter studies sample from a group of cells rather than a single cell and cannot give the value of resting potential of the cells, the excitability of the cells at the core of functional reentry remains unclear. We recently developed a model of functional reentry in isolated superfused canine atrial tissues in which the location of the core could be determined accurately with computerized mapping techniques.6 By analyzing extracellular bipolar electrogram recordings, we found that the core of stationary functional
reentry in this model remained excitable but unexcited. However, no TMP was recorded in that study, and therefore the TMP properties near the presumed excitable core could not be determined. To study the TMP properties of the core, we induced functional reentry in the isolated perfused canine right atrium using a model previously reported by Schuessler et al. The patterns of activation on the endocardial surface were registered with computerized mapping techniques while TMP was recorded simultaneously from an epicardial site with a standard glass microelectrode. With these methods, we could determine the relative location of the TMP electrode on the epicardium and the core of functional reentry on the endocardium. The purpose of the present study was to characterize the TMP profile of cells at the core of functional reentry in the canine right atrium to test the hypotheses that the core of functional reentry in atrial tissues is excitable but remains unexcited and that a large excitable gap is present near the core of functional reentry.

Figure 1. Recording methods. A, Schematic of experimental model. A 3.2×3.8-mm plaque electrode array (B) was fixed in a Plexiglas tissue bath superfused with oxygenated Tyrode’s solution. Vertical black bars at bottom of tissue bath represent bipolar electrodes, which protrude 2 to 3 mm from bottom. Not all bipolar electrodes are shown. Endocardial surface of isolated atria were gently placed on electrode plaque. S1 and S2 pacing electrodes and a bipolar recording electrode were placed on epicardial surface. A roving microelectrode was used to record TMPs. B, Location and channel numbers of recording electrodes. Same electrode numbers were used in all figures. C, Two plaque electrode arrays used to simultaneously map endocardial and epicardial surface during reentry. Length and width of plaques are not drawn to scale.

Methods

Tissue Preparation

The research protocol was approved by the institutional animal care and use committee of the Cedars-Sinai Medical Center and followed the guidelines of the American Heart Association. Thirteen mongrel dogs weighing between 9 and 23 kg (mean±SD, 19±5 kg) were anesthetized with sodium pentobarbital (30 to 35 mg/kg), intubated, and ventilated with room air by a respirator (Harvard Apparatus). The chest was opened through a median sternotomy, and the heart was rapidly removed. The right coronary artery was immediately cannulated and perfused at 10 mL/min with oxygenated and warmed (36.5°C) Tyrode’s solution. The atrial appendage and the free wall were then excised, along with the proximal portion of the right coronary artery. The distal portion of the right coronary artery was ligated, and branches to the residual right ventricular tissue were cauterized to enhance perfusion to the right atrium. The tissue was then placed in a tissue bath with dimensions of 10.2×7.2×2.7 cm, superfused with oxygenated Tyrode’s solution, and mounted on the mapping plaque with the endocardial surface down (Figure 1A). The details of this recording electrode array and the composition of the Tyrode’s solution were reported elsewhere. The temperature in the bath was maintained at 36.5°C and the pH at 7.4.
Protocol 1: TMP Characteristics During Reentry

Recording Electrodes
In protocol 1, we mapped the endocardium in 11 isolated canine right atria with a high-resolution electrode plaque while simultaneously recording TMP from the epicardial surface roving microelectrode. Figure 1B shows the recording plaque array. The recording plaque measured 3.2x3.8 cm and consisted of 509 electrodes. Because of technical difficulties, the first 32 electrodes were not used for recording; leaving a total of 477 recording bipolar electrodes available for the study. The interelectrode distance was 1.6 mm, and the interpolateral distance was 0.5 mm, measured from center to center. The recording electrodes were connected to a computerized mapping system (EMAP, Uniservices). The electrograms were filtered with a high-pass filter of 0.5 Hz and were acquired at 1000 samples per second with 16 bits of accuracy.

In each study, a bipolar electrode (interpolateral distance, 0.5 mm) was placed on the epicardial surface. This electrode was used to calculate activation differences between the epicardium and the endocardium. With the S1 or S2 stimulus used as a reference point, the activation times of the epicardial bipole and the corresponding endocardial bipole on the mapping plaque were recorded, and the difference was determined during pacing and during reentry.

TMP Recordings
TMPs were recorded from the epicardial surface (Figure 1A) with conventional machine-pulled, glass capillary electrodes filled with 3 mol/L of KCl with a tip resistance of ~20 MΩ. The electrodes were coupled by silver-silver chloride wire in a right-angle micropipette holder leading to a high-input impedance and variable-capacitance neutralization amplifier (IE-251, Warner Instrument Corp). The data were acquired by AxDON TL-1-A0 A/D acquisition hardware and Axoclamp-2A software (Axon Instruments, Inc) and were digitized at 1 kHz with 12 bits of accuracy. The sites of the TMP recordings were marked with insect pins that penetrated both the tissue and the recording plaque electrode array. At the end of the study, the tissue was lifted slightly to allow determination of the location of the pin on the recording electrode plaque (channel number). The tissue with the pin in place was then removed from the plaque and tissue bath.

Stimulation Protocol
A bipolar stimulating electrode (S1) was placed at the middle lower edge of the epicardial surface to deliver baseline pacing with 5-ms pulse widths at twice diastolic threshold current. After 8 beats at a cycle length of 300 ms, a premature stimulus was given at twice diastolic threshold current to determine the refractory period at the S1 site. Another pair of stimulation electrodes was placed 0.5 to 1.0 cm away from the S1 electrode, near the center of the mapping plaque, to give premature stimulation (S2) to induce reentry. After 8 S1 stimuli at a cycle length of 300 ms, an S2 stimulus was used as a reference point to determine the refractory period at the S1 site. If repetitive activations were not induced, the strength of S2 was increased until repetitive activations were induced, the S1 stimulus was used as a reference point to determine the refractory period at the S1 site. The recordings made at distances >3.2 mm from the core were considered in the “periphery” of the epicardium. The time of activation was taken as the time of the largest dV/dt, and the patterns of activation were displayed progressively faster pacing from the S1 site was routinely performed at baseline to detect areas of conduction slowing and conduction block. Figure 2 shows an isochronal map of activations during baseline S1 pacing from the middle lower edge of the isolated right atrial myocardium. Propagation proceeded without evidence of conduction block. Because of the heterogeneity in atrial tissue structure, the conduction velocity varied in both orthogonal directions. This phenomenon is manifested on the isochronal map by the variations of the distances between isochronal lines. Figure 2B shows bipolar recordings from selected (circled) channels during S1 pacing. No evidence of conduction block was observed in this tissue or in the remaining 10 tissues studied.

Electrophysiological parameters were measured at baseline and after perfusion with acetylcholine. The mean effective refractory period was 168±18 ms (n=11), with an S1-S1 interval of 300 ms. With the addition of 1 to 5 μmol/L acetylcholine, the mean effective refractory period decreased to 100±17 ms (n=11) compared with baseline (P<0.001). There was significant shortening of APD90 during acetylcholine infusion, 76±8 ms (n=11) compared with 180±16 ms (n=11) at baseline (P<0.001). The mean AP amplitude and (dV/dt)max at baseline were 78±17 mV and 68±4 V/s (n=11), respectively, after the addition of acetylcholine (P=NS for both comparisons). The mean epicardial-endocardial delay was 4±3 ms (n=11) during S1 pacing at 300 ms. During reentry, the epicardial-endocardial delay increased to 15±6 ms (n=24). The epicardial-endocardial delay during reentry was significantly greater than the delay during S1 pacing (P<0.001).

Protocol 2: Simultaneous Endocardial and Epicardial Mapping
In protocol 2, simultaneous endocardial and epicardial maps from 2 additional isolated canine atria were obtained during reentry. Two mapping electrode plaques were used (Figure 1C). One contained 416 electrodes and was used to map the endocardium in the manner described above. A second recording plaque (2.1x2.1 cm) consisting of 96 electrodes was placed on the epicardial surface to register simultaneous activations. TMP was not recorded in this protocol.

Data Analyses
A reentrant wave front was defined as a wave front that completed a circular pathway and reentered the area of origin. The approximate location of the core was identified by dynamic display as the area encircled by the reentrant wave front. TMP recordings near the “core” of reentry were defined as recordings within 2 bipolar electrodes (3.2 mm) of the core. The recordings made at distances >3.2 mm from the core were considered in the “periphery” of the reentry. The time of activation was taken as the time of the largest dV/dt, and the patterns of activation were displayed progressively faster pacing from the S1 site was routinely performed at baseline to detect areas of conduction slowing and conduction block. Figure 2 shows an isochronal map of activations during baseline S1 pacing from the middle lower edge of the isolated right atrial myocardium. Propagation proceeded without evidence of conduction block. Because of the heterogeneity in atrial tissue structure, the conduction velocity varied in both orthogonal directions. This phenomenon is manifested on the isochronal map by the variations of the distances between isochronal lines. Figure 2B shows bipolar recordings from selected (circled) channels during S1 pacing. No evidence of conduction block was observed in this tissue or in the remaining 10 tissues studied.

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Reentry was not inducible without acetylcholine. A total of 64 episodes of functional reentry (5.8±6 episodes per tissue; range, 0 to 17) were induced in the presence of acetylcholine. Successful simultaneous TMP recordings and activation maps were obtained in 8 of these 64 episodes of reentry. These 8 episodes were from 4 tissues. The 3 episodes in...
which the core of TMP was registered were from 2 different tissues.

**TMP Properties Near the Core of Reentry**

In 3 of the 8 episodes, the TMP recordings were within 3.2 mm of the core of reentry. These 3 episodes were from dogs 1 and 3. A total of 106 reentrant activations from these 3 episodes were analyzed (Table). Figure 3 displays a computerized dynamic activation display of 3 cycles of reentry during a sustained episode induced in dog 3. The activation wave front proceeds in a clockwise direction around the core denoted by the circle. Two complete rotations are displayed (panels A through H). The site of the TMP recording is indicated by an asterisk and is within 2.6 mm of the core of reentry.

Figure 4A displays slightly later activations of the same episode of reentry as that shown in Figure 3. Functional reentry continues in a clockwise direction. The core meanders slightly (1.6 mm) in the southeast direction from 4A through 4E. In 4E, the core visits the TMP recording site. The core then meanders in the northwest direction, then southeast once again to visit the recording site (4J) a second time. Figure 4B shows an endocardial bipolar electrogram recording at the core of functional reentry, showing characteristic double potentials.

The TMP recordings corresponding to the activations shown in Figures 4 and 5 are displayed in Figure 5 and labeled 1 to 13. In the squares at the bottom of the figure, we show the location of the core (ellipse), the site of TMP recordings (asterisk), and the site of epicardial bipolar recording (plus sign). This figure illustrates that TMP recordings near the core of reentry show marked variations in amplitude and duration. The amplitude and duration of the TMP depend

<table>
<thead>
<tr>
<th>Near Core (n=106)</th>
<th>Periphery (n=241)</th>
<th>P</th>
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<tbody>
<tr>
<td>AP amplitude, mV</td>
<td>58±22</td>
<td>70±8</td>
</tr>
<tr>
<td>APD90, ms</td>
<td>46±14</td>
<td>94±32</td>
</tr>
<tr>
<td>(dV/dt)max, V/s</td>
<td>33±20</td>
<td>55±10</td>
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<tr>
<td>Cycle length, ms</td>
<td>143±29</td>
<td>95±30</td>
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**Transmembrane Potential at the Core of Reentry**

AP indicates action potential; APD90, action potential duration measured from the onset of action potential to 90% repolarization.
on the relative proximity of the TMP recording to the core. When the 2 were close to each other (2 and 3), there was a significant reduction of TMP amplitude and duration. When the 2 overlapped (7 and 9), the TMP stayed at roughly $265\,\text{mV}$, indicating that it was excitable but remained unexcited. The simultaneously recorded epicardial bipolar electrogram (Figure 5, top) opposite channel 384 in the periphery of reentry showed minimal variations of activation cycle length.

The TMP from another episode of reentrant activity is shown in Figure 6A, from dog 3. This episode was registered immediately after the induction of reentry by the $S_1$-$S_2$ protocol. The TMPs labeled 1, 2, and 3 correspond to the $S_1$, $S_2$, and the first reentrant activation, respectively. During the second cycle of the induced reentry, no TMP was recorded (labeled 4). Simultaneous computerized mapping data (not shown) revealed that the core of reentry was visiting the TMP site. Figure 6B shows that TMP during pacing immediately after the episode in Figure 6A terminated. The AP amplitude was $>70\,\text{mV}$, indicating that the altered TMP characteristics were unrelated to recording instabilities. In a total of 5 instances, including the 3 shown in Figures 3 to 6, the impaled cell remained near resting membrane potential during reentry when the core approached the vicinity of the TMP recording site. In these 5 instances during 2 episodes of reentry, the TMP averaged $3.0\pm1.5\,\text{mV}$ above the maximum diastolic potential. These findings indicate that at least 1 cell at the core of functional reentry remained excitable but unexcited during reentry.

When TMP recordings were made near the core, the AP amplitude, $\text{APD}_{90}$, and $(\text{dV/dt})_{\text{max}}$ were significantly reduced compared with those in the periphery (Table). The presence of large diastolic intervals of the APs near the core implies that an excitable gap is present during functional reentry, consistent with our previous findings.$^{6,11}$. 

Figure 3. Computerized dynamic activation display during reentry. Red represents activation wave front. Color changes to yellow, green, light blue, and dark blue at 10-ms intervals before it returns to background color. Reentrant circuits proceed in clockwise direction as indicated by arrows. A, E, and H correspond to activations 1, 2, and 3 of Figure 5, respectively. *Epicardial TMP recording location; + bipolar electrogram recording location. Numbers below each panel indicate times of activation, with beginning of data collection as time zero.
Figure 4. Computerized dynamic display pattern corresponding to activations 6, 7, 8, 9, and 10 in Figure 5. A, Counterclockwise reentrant excitation as indicated by arrows. Ellipse indicates location of core. *Epicardial TMP recording location; +bipolar electrogram recording location. Numbers below each panel indicate times of activation, with beginning of data acquisition as time zero. B, Endocardial bipolar electrograms from contiguous electrodes at core of reentry. Bipolar electrograms show double potentials (arrowheads). Long arrows indicate direction of reentrant excitation. Site of TMP recording is directly opposite electrode 266, which has double potentials of equal size.
The TMP recordings at the periphery were registered in 5 episodes of sustained reentry from dogs 1, 8, and 10, for a total of 241 reentrant activations (Table). Figure 7A shows the dynamic activation display of an episode of functional reentry in dog 10. The reentrant wave front propagates in a clockwise direction in the far right upper quadrant. A single complete rotation around a stationary core (indicated by the ellipse) with a cycle length of 118 ms is displayed. The activation spreads peripherally from the core to activate the rest of the tissue. The activation wave front reaches the epicardial bipolar recording site (indicated by a plus sign) at 58 ms and the TMP site (indicated by an asterisk) at 66 ms during this rotation. The TMP site is in the periphery, 27.5 mm away from the core. The TMP recordings (Figure 7B) show a stable cycle length of reentry of 118 ms without cycle length variation. The AP amplitude, APD90, and (dV/dt)max for this episode remained constant and were 63 ± 1 mV, 100 ± 1 ms, and 58 ± 6 V/s. There were no variations in the cycle length or action potential characteristics in this episode and in the remaining 4 episodes of functional reentry.

Figure 7C displays selected endocardial bipolar electrograms located in the periphery of reentry. As the tip of the wave front propagates clockwise around the core, it sequentially activates sites a through f. A single rotation of the reentrant wave front is displayed. The arrows indicate the direction of wave propagation.

**Protocol 2: Simultaneous Endocardial and Epicardial Mapping**
To ensure that the core of reentry was in a similar location on both the endocardial and epicardial surfaces, we performed simultaneous mapping on both sides of 2 isolated atrial tissues. A total of 4 episodes were recorded. All showed that the reentrant wave front on the endocardium and epicardium propagated in the same direction, with the core at the same location. Figure 8A shows an example. A single counterclockwise reentrant wave front was present during sustained reentry with a cycle length of 115 ms. The upper sections of each panel display maps from the endocardial surface, and the lower sections display maps from the epicardial surface. The lower right panel shows the direction of wave propagation (arrows) and the locations of the core on both endocardial and epicardial surfaces. The core was at the same location on both surfaces of the atrium. Figure 8B shows the actual bipolar electrogram recorded during the same episode of reentry.

**Discussion**

**TMPs at the Core of Functional Reentry**
Using simultaneous computerized mapping and standard glass microelectrode recordings, we recorded TMPs near the core and at the periphery of functional reentry in isolated canine atria. A major finding of the present study is the demonstration of quiescent cells at the core during function-
ally based reentrant excitation, consistent with an excitable but unexcited state. In addition, APs of cells near the core of reentrant activity have a reduced amplitude, duration, and \( (dV/dt)_{\text{max}} \) compared with cells at the periphery. Although we were not able to register TMPs simultaneously from the core and from the periphery, only the TMP near the core showed large variations of amplitude, duration, and \( (dV/dt)_{\text{max}} \). Furthermore, excitable but unexcited cells were registered only at the core. These findings support the conclusion that there is reduced amplitude, duration, and \( (dV/dt)_{\text{max}} \) near the core and that the cells at the core remained unexcited.

In the Belousov-Zhabotinskii chemical reaction, which generates self-perpetuating spiral waves, light intensity modulations at the core are less than in the surrounding area, indicating an area of reduced activity. Pertsov et al. demonstrated a gradual decrease in AP amplitude as recordings approached the core during reentry in thin sheets of sheep ventricular tissue. Because optical mapping techniques register from a group of cells, the resting membrane potential of a single cell was not defined in that study. In the present study, we found that the TMPs at the core in the 5 recorded instances during 2 episodes of reentry were only 3.0\( \pm \)1.5 mV above the maximum diastolic potential. In some episodes, the cell at the core remained at its maximum diastolic potential. These findings clearly indicated that the cells at the core remained unexcited.

A second implication of these findings is that the excitable gap is larger near the core than in the periphery of the reentry. The diastolic interval, or the difference between the cycle length of reentry (110 ms) and the \( \text{APD}_{90} \) (46 ms), was 64 ms near the core. In comparison, the diastolic interval was <20 ms in the periphery. We have demonstrated in another study...
using isolated swine ventricular tissues that in a stable functional reentrant circuit, only a thin layer of activation, a few millimeters thick, was responsible for sustaining reentry. The activation in the periphery was due to outward propagation of the activation from this thin layer of reentrant excitation. If the results of the latter study are applicable to atrial tissues, then the excitable gap of reentrant activity in the atria should be determined by the diastolic interval near the core (≈50% of the cycle length) and not by the diastolic interval distant from the core (≈20% of the reentrant cycle length). The presence of a large excitable gap in functional reentry in the atria is incompatible with the leading-circle concept.

**Variation of Morphological Characteristics of TMP Near the Core**

A feature commonly observed in computer simulation and in experimental studies of functional reentry is the meandering nature of the spiral wave. The velocity of meandering determined whether the arrhythmia was compatible with tachycardia or fibrillation. In this study, we recorded TMP during episodes of atrial tachycardia, with a single reentrant wave front in the entire mapped region. The TMP registered distant from the core always demonstrated regular and consistent morphology. Conversely, the TMP near the core was irregular in cycle length, with variable morphology and amplitude. These findings are compatible with the spiral wave theory, which predicts that the path of a functional reentrant wave front often is not fixed but rather meanders slightly from activation to activation. However, the resolution of our mapping techniques did not allow us to determine whether or not the path of the reentrant waves had a distinct signature, as was demonstrated by computer simulations.

An additional factor that may contribute to meandering is the complex atrial structure. For example, the thickness of the atrium increases significantly at the site of pectinate muscle

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**Figure 7.** Activation at periphery of reentry. A, Activation during episode of functional reentry. Numbers below each panel indicate time of activation, with beginning of top left panel as time zero. Reentry proceeds in clockwise direction around a core indicated by ellipse. TMP recordings were obtained in periphery indicated by * and located above channel 276. Site of epicardial bipolar recording is indicated by + located above channel 153. Bottom right, Schematic of spread of activation. Black arrow indicates direction of reentry around core. Red arrows indicate direction of spread of activation. B, Epicardial bipolar electrogram, top; TMP, bottom. C, Electrograms during reentry. Sites a, b, c, d, e, and f correspond to channels 102, 184, 181, 119, 79, and 81, respectively. Cycle length of reentry is 118 ms. These selected electrograms are located several millimeters away from core of reentry and were selected to demonstrate presence of reentry.
Figure 8. Simultaneous endocardial and epicardial activation during reentry. A, Activation patterns on endocardial (ENDO) and epicardial (EPI) surfaces during episode of reentry. Reentrant wave front rotates in counterclockwise direction as indicated by arrows. Numbers below each panel represent time in milliseconds, with beginning of data acquisition as time zero. Bottom right, Schematic of activation pattern of reentry on both surfaces. Circle indicates location of core. B, Selected electrograms registered by electrodes several millimeters from core during same episode of reentry.
bundled. This variable thickness may result in significant source-sink mismatch and Wenckebach-like pattern of conduction block, as shown in Figure 5. However, we have examined our tissue specimen. The core of functional reentry shown in Figure 5 was not located at the site of a pectinate muscle. Therefore, we do not think that the pectinate muscle structure is responsible for the activation patterns shown in Figure 5.

Mechanism of Functional Reentry in Canine Atrial Tissues

Spiral wave theory predicts that the core is excitable yet remains unexcited.\(^5,^{14}\) Self-sustaining spiral waves are generated in myocardial tissues when 2 waves meet at a critical temporal and spatial location, inducing a wave break.\(^{5,8,23}\) The tip of the wave break has a pronounced curvature, which results in a very low margin of safety for propagation. Therefore, the tissue ahead is not excited, even though it is fully excitable. The wave front propagates around the unexcited area, the core, without invading or short-circuiting the core. In other words, the “source-sink mismatch”\(^{24–26}\) is the basis for cessation of propagation into the core, thereby preventing the short-circuiting and termination of reentry. A corollary to this hypothesis is that the core should remain excitable rather than refractory. It is therefore possible to excite the core of functional reentry by electrical stimulation\(^{16,27}\) or by a propagating wave front,\(^6,^{28}\) resulting in termination or displacement of the core. The demonstration of fully excitable cells (TMP at or near resting membrane potential) at the core of functional reentry by the present study further strengthens the hypothesis that source-sink mismatch resulted in the failure of propagation toward the core. Because (dV/dt)\(_{max}\) is proportional to the safety factor of propagation, these findings also support the hypothesis that failure of propagation may occur more easily near the core than away from the core. The results of the present study are compatible with a previous study that shows a quiescent core with extracellular recordings,\(^6\) and they support the spiral wave concept of functional reentry in the atria.

Limitations of the Study

The lack of action potential duration and effective refractory period measurements at the cycle length comparable to the reentrant cycles (110±35 ms) is a limitation of this study. However, during attempts to pace the atria at 110-ms cycle lengths, arrhythmia was often induced, making the testing of effective refractory period difficult. An alternative method is to give premature stimulus during the reentrant excitation and test the effective refractory period. This was done in our previous studies in the same animal model.\(^9\) For a reentrant excitation with a cycle length of 120 ms, the excitable gap was ∼38 ms. There was no postrepolarization refractoriness. Furthermore, regenerative action potentials were inducible during phase 3 repolarization. In Figure 7B of the present study, we also demonstrate that atrial cells were excitable almost as soon as they repolarized. These findings indicate that there was no postrepolarization refractoriness in the atria mapped. The quiescent phase 4 intervals shown in Figures 5 and 6 are not the result of postrepolarization refractoriness.

Although our results are not compatible with the leading circle concept of functional reentry, these results may be applicable only to the model used in this study. It is possible that in other animal models or in humans, the leading circle concept is still applicable to the reentry in atria. The number of episodes in which TMP recordings were successfully obtained was small. Therefore, the present study cannot provide a certain answer to whether the mechanism of reentry is, in general, spiral waves.

A third limitation is that, because of technical difficulties, the mapping was done on the endocardial surface, whereas the TMP was registered on the epicardial surface. Although we performed separate studies to show that the reentrant wave fronts mapped on both surfaces were of the same cycle length, had the same direction of rotation, and shared the same core, there is still a possibility that the TMP is not registered at or near the core of reentry in the reentrant episodes studied. This possibility and the small number of successful impalements at or near the core are important limitations of the study.

Conclusions

In this study, we registered TMP near the core and at the periphery of functional reentrant wave fronts in isolated, perfused canine atrial tissues. The TMP at the core showed large variations of amplitude and morphology, with long diastolic intervals, implying the presence of a significant excitable gap. The cells at the core were quiescent, with TMP near or at the maximum diastolic potential. These findings imply that the functional reentrant wave fronts in the atrial tissues are not leading circles. Rather, they exhibit the major characteristics observed in the spiral waves of excitation.

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References


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