Atrioventricular Nodal Conduction During Atrial Fibrillation
Role of Atrial Input Modification

Stéphane Garrigue, MD; Kent A. Mowrey, MS; Gerard Fahy, MD; Patrick J. Tchou, MD; Todor N. Mazgalev, PhD

Background—Posteroseptal ablation of the atrioventricular node (AVN) has been proposed as a means to slow the ventricular rate during atrial fibrillation (AF). The suggested mechanism is elimination of the AVN “slow pathway.” On the basis of the unpredictable success of the procedure, we hypothesize that, in fact, the slow pathway is preserved. Therefore, the slowing of the ventricular rate results from reduced bombardment of the AVN.

Methods and Results—In 8 rabbit heart atrial-AVN preparations, cooling of the posterior and/or the anterior AVN approaches revealed nonspecific effects on the slow and fast pathway portions of the AVN conduction curve. In 13 other preparations, simulated AF during posterior cooling (n = 6) prolonged the His-His (H-H) intervals but did not reveal specific slow pathway injury. In the remaining 7 preparations, AF was applied before and after posteroseptal surgical cuts. During AF with posterior origin, the cuts resulted in longer mean H-H along with slowing of the AVN bombardment rate. However, there was no change in the minimum observed H-H, suggesting an intact slow pathway. During AF with anterior origin, the mean and the shortest H-H remained unchanged before and after the cuts in all preparations. This was associated with the maintenance of high-rate AVN bombardment.

Conclusions—Posteroseptal ablation does not eliminate the slow pathway. Ventricular rate slowing can be obtained if the ablation procedure results in a posteroanterior intra-atrial block leading to a reduction of the rate of AV nodal bombardment. (Circulation. 1999;99:2323-2333.)

Key Words: atrioventricular node • fibrillation • electrophysiology • ventricles

The atrioventricular node (AVN) is the natural barrier limiting conduction of atrial impulses into the His-Purkinje system during atrial fibrillation (AF). Dependence of refractoriness on the impulse rate,1,2 concealed conduction,3,4 and annihilation and summation5,6 of wave fronts contribute to the complex pattern of impulse propagation within the AVN. It is well known that “slow pathway” (SP) ablation, which corresponds clinically to posterior atrial-AVN input ablation, suppresses the incidence of AV junctional reentrant tachycardia. Indeed, recent investigations7–11 suggest that posterior perinodal atrial tissues form a part of the reentrant circuit.

A similar ablative technique has been developed to slow and regularize the ventricular rate (VR) during AF.12,13 The presumed mechanism of this procedure is the elimination of the putative SP that has a short refractory period.14–16 This new technique for AVN modification showed encouraging clinical results, but with inconsistent success rates among different investigators.17,18 Recently, one study19 pointed out that such a technique could eliminate the SP but might also cause nonspecific injury of the AVN. To clarify the electrophysiological mechanisms involved in this particular ablative therapy for VR slowing, we examined the effect of posteroseptal ablation performed close to but away from the compact node in superfused rabbit preparations during simulated AF. The main objective of this study was to evaluate the involvement of the dual AVN pathway electrophysiology in the determination of the VR during AF and the feasibility of eliminating the SP with ablation of the posteroseptal AVN approach. For this purpose, we evaluated the contributions of both anterior and posterior AVN approaches by using reversible thermoelectric cooling and surgical dissociation of the AVN inputs during standard stimulation protocols with prematurity and during AF simulated by high-rate random atrial pacing.

Methods

Atrioventricular Nodal Preparation
The experiments were performed in vitro in 22 preparations obtained from the hearts of New Zealand rabbits of either sex weighing 2 to 2.2 kg and anesthetized by sodium pentobarbital injection (50 mg/kg) into an ear vein. After a midsternal incision, the heart was

Received September 24, 1998; revision received December 11, 1998; accepted December 30, 1998.
From the Department of Cardiology, the Cleveland Clinic Foundation, Cleveland, Ohio.
Correspondence to Todor N. Mazgalev, PhD, Department of Cardiology/Desk FFI-02, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195. E-mail mazgalt@cesmtp.ccf.org
© 1999 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

2323
removed and placed in an oxygenated room-temperature Tyrode’s solution (pH 7.30 to 7.35) previously described. After trimming, the final preparation contained right atrial tissues as shown in Figure 1A. The crista terminalis (CrT) divides this preparation into posterior (Figure 1A, left) and anterior (Figure 1A, right) sides. The preparations were pinned down on a thin silicon disk (endocardial surface up) and transferred into a thermostat-controlled glass chamber for superfusion at 35.5°C.

Electrical Stimulation and Recordings

Bipolar stimulating and recording electrodes (0.5-mm interelectrode distance) were custom-made from 0.20-mm Teflon-insulated platinum-iridium wire. Electrical stimuli (2 ms, twice diastolic threshold) were applied at different sites of the preparation (ellipses in Figure 1A), as explained later. Bipolar electrodes for recording surface electrograms (small circles in Figure 1A) were placed at the CrT and the interatrial septal (IAS) input sites of the AVN and at the bundle of His (H). All electrodes were positioned with micromanipulators (WI, M330). The stimulating electrodes were connected to optically isolated stimulator units (WI, A360). An 8-channel programmable stimulator (AMPI, Master-8) determined the stimulation sequence. The recording electrodes were connected first to high-resistance, differential-input probes and then to an 8-channel, programmable amplifier (Axon Instruments, CyberAmp 380). Signals were monitored on a storage oscilloscope (Tektronix 2216). They were also digitally recorded on tape (Vetter Digital, 4000A) for offline computer analysis (AxoScope, Axon Instruments).

Stimulation Protocols

The spontaneous mean sinus cycle length at the start of the experiments was 361±23 ms. The basic paced cycle length was 300 ms in all preparations, and the mean basic conduction time (CrT-to-His) was 69±5 ms. The compact AVN was localized by use of anatomic and functional criteria. Specifically, the exact location of the compact node (within 1 mm) was determined by mapping the apex of the triangle of Koch with subthreshold postganglionic vagal stimulation. The site at which maximum depression of conduction was achieved in response to this stimulation was assumed to be the compact AVN. Care was taken to avoid any damage to this area during cooling and surgical procedures.

Three groups of experiments (A, B, and C) were performed as explained below.

Experiments A (n=8) were performed to evaluate the effect of cooling of the anterior and posterior AVN approaches on dual-pathway electrophysiology during prematurity pacing protocols. Two thermoelectric cooling probes that used the Peltier effect (Novoste Corp) with 3.75-mm² tips were placed posteriorly at the isthmus between the tricuspid annulus and the coronary sinus (CS) ostium and at the low anterior IAS.

The stimulation protocol consisted of basic drive, followed by premature stimuli during control, followed by cooling. The basic drive consisted of 21 beats (S₁) and was performed by simultaneous stimulation at the IAS and CrT at a cycle length of 300 ms. The test beat (S₂) followed. The first S₁S₂ was 300 ms and was progressively decreased by 5 ms in each cycle until nodal or atrial refractoriness was encountered.

Experiments B (n=6 preparations) were performed to independently assess the role of the anterior and posterior AVN inputs on the VR during random high-rate atrial pacing. Two different ranges of coupling intervals (125 to 300 ms and 90 to 300 ms) were used for the random pacing in each preparation. For each range, the same AF run was repeated in control and during reversible cooling (15°C) applied consecutively at the posterior, anterior, and both AVN inputs.

Experiments C (n=7 preparations) were used to evaluate the role of surgical modification of the posterior approaches for slowing of the VR. A computerized, random, high-rate atrial pacing simulated AF (range, 75 to 150 ms). The same stimulation sequence was applied in random order at 6 atrial-pacing sites (ellipses in Figure 1A): 3 on the posterior side (high right atrium, mid right atrial appendage, and posterior AVN [PA] approaches) and 3 on the anterior side (musculae pectinatis, mp; crista terminalis, CrT; superior vena cava, SVC; inferior vena cava, IVC; tendon of Todaro, T; atrioventricular node, AVN; fossa ovalis, FO; interatrial septum, IAS; bundle of His, His; high right atrium, HRA; mid right atrial appendage, MRA; coronary sinus, CS; posterior approach to the AV node [crista terminalis input], PA; high right atrial septum, HS; anterior approach to the AV node [interatrial septal input], AA; and tricuspid valve, TV. Elliptical frames indicate 6 sites used for randomized pacing. C, Dissociation of AVN from posterior approach by a through-cut from TrV to T. C, Further modification of preparation from B to create a model of posteroanterior dissociation. See text for details.
anteroseptal side (high septum, above the CS, and anterior AVN approaches). Five hundred electrogram intervals measured at the bundle of His recording site (H-H) were analyzed in each episode.

Each of the 7 AVN preparations was studied in 3 morphological configurations. The intact AVN preparation represented the control (Figure 1A). In the second configuration, a surgical cut of the PA was performed (Figure 1B). This cut started at the septal leaflet of the tricuspid valve (TrV) and proceeded up to the ostium of the CS inside the triangle of Koch. The tendon of Todaro was kept intact. This configuration was called the CPA (“cut posterior approach”). In the third configuration (Figure 1C), a cut was initiated from the top of the preparation downward to the ostium of the inferior vena cava so that only a narrow isthmus remained between the posterior and anterior sides of the preparation. The isthmus could be cooled down to 15°C by thermoelectric probe.

In addition to the 21 preparations reported above, 1 additional preparation was used for confirmation of the reproducibility of the simulated AF pacing protocol (see Results).

Data Acquisition
Activation times at the 2 atrial recording sites, the CrT and the IAS inputs, and the bundle of His were determined with 1-ms precision. These activation times were used to plot conduction curves as well as to determine electrogram intervals measured at the posterior crista terminals input (CrT-CrT), the anterior interatrial septal input (IAS-IAS), and H-H intervals.

In experiments A, conduction curves $S_1S_2S_3$ were generated in control and after cooling of the inputs. In addition, the effective refractory period (ERP) of the AVN was defined as the minimum $S_3$ associated with AVN conduction.

In experiments B, the histogram distribution of the 500 recorded H-H intervals was analyzed in control and during 3 subsequent coolings in each preparation. A total of 48 episodes were analyzed by comparison of the H-H distributions between control and cooling.

In experiments C, for each simulated AF episode, CrT-CrT, IAS-IAS, and H-H intervals were measured and averaged. The ratio of the number of CrT-CrT intervals to the number of IAS-IAS intervals (N(CrT)/N(IAS)) and the ratio of the number of IAS-IAS intervals to the number of H-H intervals (N(IAS)/N(H)) were calculated before and after CPA. These parameters were used to quantify the degree of intra-atrial and AVN-His conduction, respectively.

In addition, the consecutive CrT-CrT, IAS-IAS, and H-H intervals were plotted as Lorenz plots, the abscissa representing the value of the nth interval and the ordinate representing the nth+1 interval. This method of presentation facilitated the visualization of the minimal observed intervals as well as the degree of interval dispersion. The latter was called a scattering index ($S(I/I)$) and was calculated as

$$S(I/I) = 1/n \cdot \sum_{i=1}^{n} \sqrt{(x_i - \bar{x})^2 + (y_i - \bar{y})^2}$$

where $x_i$ and $y_i$ are the current and next values of the intervals measured at the respective site II (ie, CrT, IAS, or bundle of His recording site, H), $n$ is the number of measured intervals, and $\bar{x}$ and $\bar{y}$ are the coordinates of the center of the scattergram.

Statistical Analysis
In experiments A, the ERP and the maximum achieved AVN conduction time were compared between control and cooling by use of the nonparametric paired Wilcoxon test. In experiments B, the H-H intervals were compared between control and cooling by use of a 4-level repeated-measures within-factor analysis. In experiments C, 84 consecutive AF episodes were analyzed before and after the CPA. Multifactorial ANOVA for repeated-measures studies was performed to evaluate the influence of each of the 6 pacing sites on the AVN conduction time measured before and after the CPA. Polynomial and linear correlation analyses were performed to assess the relationship between the CrT-CrT, IAS-IAS, and H-H before and after the CPA. A value of $P<0.05$ was considered to be statistically significant.

Results
Effect of Perinodal Input Cooling on the AVN Conduction Curve (Experiments A)
In all 8 preparations, “smooth” AVN conduction curves were generated in response to the baseline pacing protocol. Data are shown in Table 1. In 2 of the 8 preparations, posterior cooling away from the compact node resulted in AVN conduction time prolongation of short-coupled atrial beats only (Figure 2). In the remaining 6 preparations, the cooling probe had to be placed more anteriorly to observe $S_1S_2$ prolongation at short coupling intervals. This, however, was associated with a prolongation of $S_2H_2$ at long coupling intervals that was proportional to the temperature, suggesting some cooling of the compact node (Figure 3). In all preparations (Table 1), posterior cooling increased the AVN ERP (135±8 versus 103±4 ms) and decreased the maximum observed AVN conduction time (146±7 versus 180±14 ms).

With the cooling probe located at the apex of the triangle of Koch, it was impossible to identify an anterior region that, when cooled, caused specific effects only at long coupling

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Control 1</th>
<th>Posterior Cooling</th>
<th>Control 2</th>
<th>Anterior Cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum AVN Nodal Conduction Time, ms</td>
<td>1</td>
<td>…</td>
<td>162</td>
<td>180</td>
</tr>
<tr>
<td>2</td>
<td>144</td>
<td>124</td>
<td>144</td>
<td>162</td>
</tr>
<tr>
<td>3</td>
<td>248</td>
<td>176</td>
<td>232</td>
<td>209</td>
</tr>
<tr>
<td>4</td>
<td>195</td>
<td>144</td>
<td>172</td>
<td>175</td>
</tr>
<tr>
<td>5</td>
<td>202</td>
<td>163</td>
<td>195</td>
<td>218</td>
</tr>
<tr>
<td>6</td>
<td>166</td>
<td>156</td>
<td>165</td>
<td>181</td>
</tr>
<tr>
<td>7</td>
<td>142</td>
<td>124</td>
<td>142</td>
<td>202</td>
</tr>
<tr>
<td>8</td>
<td>162</td>
<td>135</td>
<td>162</td>
<td>168</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>180±14</td>
<td>146±7</td>
<td>172±10</td>
<td>187±7</td>
</tr>
<tr>
<td>$P$</td>
<td>0.009</td>
<td>0.18</td>
<td>0.07</td>
<td></td>
</tr>
</tbody>
</table>

Effect of Perinodal Input Cooling on the AVN Conduction Curve (Experiments A)
In all 8 preparations, “smooth” AVN conduction curves were generated in response to the baseline pacing protocol. Data are shown in Table 1. In 2 of the 8 preparations, posterior cooling away from the compact node resulted in AVN conduction time prolongation of short-coupled atrial beats only (Figure 2). In the remaining 6 preparations, the cooling probe had to be placed more anteriorly to observe $S_1S_2$ prolongation at short coupling intervals. This, however, was associated with a prolongation of $S_2H_2$ at long coupling intervals that was proportional to the temperature, suggesting some cooling of the compact node (Figure 3). In all preparations (Table 1), posterior cooling increased the AVN ERP (135±8 versus 103±4 ms) and decreased the maximum observed AVN conduction time (146±7 versus 180±14 ms).

With the cooling probe located at the apex of the triangle of Koch, it was impossible to identify an anterior region that, when cooled, caused specific effects only at long coupling
intervals (Figure 4). A variable effect on the AVN ERP was noted (Table 1), with an increase in 5 preparations, a decrease in 2, and no change in 1. This suggested that the area of the anterior AVN input was in close proximity to the compact node. Thus, it was difficult to avoid direct nodal cooling.

These data showed that localized cooling of the AVN inputs did not produce effects compatible with the presence of 2 distinct pathways/channels outside the compact node, which had discrete atrial attachments. Specifically, the SP appeared to receive a broader input wave front, not limited to the posterior approaches alone. However, the inevitable probability of some remote cooling effect on the compact node did not permit a conclusive rejection of the hypothesis of discrete posterior attachment of the SP.

Reproducibility of Interval Measurements During Simulated AF
The mean data from the preparation used to evaluate the reproducibility of interval measurements during AF are shown in Table 2. Each of the CrT-CrT, IAS-IAS, and H-H intervals was measured in 2 consecutive trials performed from each of the 6 pacing sites. The differences between the mean intervals in trials 1 and 2 did not exceed 3 ms. The intraclass correlation coefficients for the mean intervals ranged from 0.97 to 0.99. Thus, repetitive AF episodes were associated with a high degree of reproducibility of all measured time intervals. This permitted multiple comparisons in the subsequent studies.

H-H Histograms in AVN Preparations During AF and Selective Cooling of the Posterior and Anterior Inputs (Experiments B)
It has been hypothesized that a 2-peak H-H histogram could reveal the dual-pathway AVN electrophysiology during AF. The shorter H-H peak has been thought to represent the SP, whereas the longer H-H peak should correspond to the fast pathway. In our study, 10 of the 12 control AF episodes exhibited a 2-peak distribution (Table 3). We expected that, according to the above hypothesis, localized cooling of the AVN inputs would transform the 2-peak histograms into a single-peak (bell-shape) distribution.

Data in Table 3 illustrate that anterior input cooling did not change the mean H-H interval (262±22 versus 256±27 ms). In contrast, cooling of the posterior AVN input resulted in a significant mean H-H interval prolongation (327±29 ms). A similar effect was observed with cooling of both inputs (336±41 ms). However, transformation of the 2-peak histograms into a bell-shape distribution was seen in only 1 episode with posterior cooling and 3 episodes with simultaneous anterior and posterior cooling (Table 3). Figure 5 shows an example of a 2-peak histogram in control that remained with 2 peaks after the input cooling. Notice that the peaks were shifted to the right with posterior cooling, whereas they remained similar to control during anterior cooling. In addition, the cooling procedures did not eliminate the occurrence of the shortest H-H intervals (in this case, ~150 ms, arrows). Figure 6 illustrates the only case in which a control 2-peak H-H histogram was transformed into a histogram with 1 predominant peak after posterior cooling. However, there were 3 peaks after anterior cooling and 2 peaks after cooling of both inputs. There was no case in which cooling of a particular input resulted in elimination of 1 peak without influencing the other peak(s) of the histogram.

The above data did not exclude the possibility that bimodal H-H histograms during AF may result from dual-pathway electrophysiology. However, cooling of the proposed discrete atrial attachments of the pathways did not reveal a link between a particular peak and a pathway. This suggested that either the atrial connections of the pathways were not discrete

Figure 2. Effect of posterior cooling to 15°C on AVN conduction curve. Note that most marked prolongation of conduction time S2H2 was seen at shortest S1S2 intervals.

Figure 4. Effect of anterior cooling to 15°C on AVN conduction curve. Note a nondifferential effect on conduction time at long and short coupling intervals.
or/and that each peak resulted from a complex participation of both pathways.

**Observations During AF and Before and After the CPA (Experiments C)**

The reasoning to choose the microsurgical cut procedure (instead of cooling) was to dissociate the posterior approach while minimizing any indirect damaging effect on the compact AVN. On the basis of the effect produced by the CPA on the VR, the preparations were split into group 1 and group 2.

One preparation from group 1 is illustrated in Figure 7. The data were obtained with a PA pacing site (Figure 1A). Short CrT-CrT (112±628 ms, A), short IAS-IAS (195±41 ms, C), and longer H-H (330±108 ms, E) intervals were observed before CPA. After CPA, the CrT-CrT intervals remained unchanged (112±631 ms, B), as expected, because the cut was distal to the recording site (see Figure 1B). In contrast, both the IAS-IAS (524±181 ms, D) and the H-H (523±183 ms, F) intervals increased substantially. Similar results were observed in 4 preparations.

Different results were observed in the preparations from group 2, as shown in Figure 8. After CPA (B, D, and F), even though the CrT-CrT remained similar (112±625 ms), the IAS-IAS increased (232±647 versus 189±31 ms), and the H-H shortened (235±675 versus 265±660 ms).

### Table 2. Intraclass Correlation of Repeated Intervals Measurements in 1 Rabbit Heart Preparation

<table>
<thead>
<tr>
<th>Pacing Site</th>
<th>Mean Intervals, ms</th>
<th>CrT-CrT</th>
<th>IAS-IAS</th>
<th>H-H</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial 1</td>
<td>Trial 2</td>
<td>Trial 1</td>
<td>Trial 2</td>
</tr>
<tr>
<td>Posterior</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRA</td>
<td>117</td>
<td>121</td>
<td>140</td>
<td>144</td>
</tr>
<tr>
<td>MRA</td>
<td>123</td>
<td>126</td>
<td>134</td>
<td>132</td>
</tr>
<tr>
<td>PA</td>
<td>112</td>
<td>112</td>
<td>177</td>
<td>181</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>117±628</td>
<td>120±7</td>
<td>150±23</td>
<td>152±26</td>
</tr>
<tr>
<td>Ri–c</td>
<td>0.98</td>
<td>0.99</td>
<td>0.99</td>
<td></td>
</tr>
</tbody>
</table>

Ri–c indicates intraclass correlation coefficient; other abbreviations as in Figure 1.

### Table 3. Mean H-H Intervals and Their Distribution During Localized Cooling of the Posterior and Anterior AV Node Inputs

<table>
<thead>
<tr>
<th>AF Episodes</th>
<th>Mean H-H±SD, ms</th>
<th>Control</th>
<th>Anterior Cooling</th>
<th>Posterior Cooling</th>
<th>Both Inputs Cooling</th>
<th>Control</th>
<th>Anterior Cooling</th>
<th>Posterior Cooling</th>
<th>Both Cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>279±63</td>
<td>227±54</td>
<td>274±74</td>
<td>265±60</td>
<td></td>
<td>&gt;2</td>
<td>2</td>
<td>&gt;2</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>276±69</td>
<td>285±70</td>
<td>357±56</td>
<td>353±46</td>
<td></td>
<td>2</td>
<td>2</td>
<td>&gt;2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>215±61</td>
<td>255±66</td>
<td>333±80</td>
<td>373±65</td>
<td></td>
<td>2</td>
<td>2</td>
<td>&gt;2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>210±56</td>
<td>309±88</td>
<td>351±22</td>
<td>411±75</td>
<td></td>
<td>2</td>
<td>&gt;2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>272±59</td>
<td>264±58</td>
<td>294±61</td>
<td>301±75</td>
<td></td>
<td>2</td>
<td>2</td>
<td>&gt;2</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>268±72</td>
<td>260±65</td>
<td>330±87</td>
<td>356±113</td>
<td></td>
<td>2</td>
<td>&gt;2</td>
<td>2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>7</td>
<td>298±61</td>
<td>280±72</td>
<td>310±62</td>
<td>307±73</td>
<td></td>
<td>2</td>
<td>&gt;2</td>
<td>2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>8</td>
<td>276±79</td>
<td>265±81</td>
<td>321±69</td>
<td>315±82</td>
<td></td>
<td>2</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>9</td>
<td>242±64</td>
<td>250±66</td>
<td>337±76</td>
<td>315±85</td>
<td></td>
<td>2</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>10</td>
<td>253±61</td>
<td>240±62</td>
<td>304±83</td>
<td>326±97</td>
<td></td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>11</td>
<td>254±61</td>
<td>263±54</td>
<td>335±64</td>
<td>322±70</td>
<td></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>233±62</td>
<td>246±61</td>
<td>383±79</td>
<td>389±82</td>
<td></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>256±27</td>
<td>262±22</td>
<td>327±29</td>
<td>336±41*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P<0.05 vs control.
Qualitatively similar results were observed in 3 preparations.

Data obtained with all pacing sites were summarized in Tables 4 and 5. We will analyze first the data obtained with posterior pacing, then the observations obtained with anterior pacing.

**Effects of CPA During AF Initiated From the Posterior Sites**

As shown in Figure 9A, the mean H-H in group 1 significantly increased after CPA independently of the posterior pacing site (352 ± 26 versus 261 ± 7 ms, \( P < 0.01 \)). In contrast, in group 2 preparations (Figure 9B), there was a significant H-H shortening after CPA (275 ± 9 versus 298 ± 7 ms, \( P < 0.05 \)). One may speculate that the above results indicated elimination of the SP in group 1. However, the shortest observed H-H intervals (representing the refractory properties of the SP) increased only slightly in group 1 and even decreased in group 2 (Table 4). This suggested that the surgical procedure did not result in a selective elimination of the SP AVN conduction.

An important difference was found between the 2 groups when the IAS-IAS intervals before and after CPA were compared (Figure 10). In group 1, the increase of this interval reached 151 ± 78 ms, whereas in group 2, it was only 72 ± 37 ms (\( P < 0.01 \)). We interpreted this as an indication of a better intra-atrial conduction in group 2 over the remaining posteroanterior connections after the CPA. To test this hypothesis, we modified the preparations in group 2 by creating an isthmus between the posterior and anterior atrial sides (see Figure 1C). This procedure did not change the mean intervals (data not shown). Consequently, we cooled the isthmus, and the result was a dramatic IAS-IAS increase (Figure 10B, dashed line) from 72 ± 37 ms before the isthmus modification to 145 ± 81 ms thereafter (\( P < 0.01 \)). The H-H increased from 275 ± 9 ms after the CPA to 328 ± 18 ms after the cooling of the isthmus (\( P < 0.01 \), Figure 10B, dashed line). Thus, as in group 1, the slowing of the septal AVN bombardment resulted in slowing of the VR.

The role of the CPA-induced changes in the IAS-IAS intervals for the subsequent changes in the H-H intervals is further illustrated in Figure 11 by data combined from all preparations. There was a strong second-order polynomial correlation of 0.92 (\( P < 0.001 \)). Therefore, a small IAS-IAS increase (as in group 2 before the isthmus modification) induced H-H shortening, whereas an IAS-IAS increase beyond 150 ms (as in group 1) induced a significant H-H prolongation.

Detailed data obtained during pacing from all posterior sites in group 1 and group 2 preparations are summarized in
of intra-atrial block and the consequent presence of long IAS-IAS and H-H intervals (see also Figure 7). The changes in the S(IAS) and S(H) observed after the CPA in group 2 were much smaller (Table 4, \(P<0.01\)).

**Effects of CPA During AF Initiated From the Anterior Sites**

The different effects produced by the CPA in groups 1 and 2 during pacing from the posterior sites (see above) were no longer present when AF was initiated from the anterior sites of the preparations. This correlated well with the preserved level of anterior AVN bombardment before and after the CPA.

As shown in Figure 12, in contrast to the observations in Figure 9, there was no increase in the mean H-H interval in group 1 for each of the 3 anterior pacing sites. In group 2, there was a small shortening of the H-H (280±14 versus 306±23 ms, \(P<0.05\)). In both groups, there was no increase of the minimal H-H. In fact, the CPA produced some shortening of the minimal observed H-H intervals (Table 5). These observations argued against the hypothesis that the surgical cut entirely eliminated the slow AVN pathway.

Figure 13 summarizes the data for all mean intervals during anterior pacing before and after CPA. Importantly, the CPA did not result in a significant change of the mean IAS-IAS in both groups. Neither linear nor polynomial correlation was found (\(r=-0.18\) and \(r=-0.22\), respectively, \(P=NS\)) between the \(\Delta\)IAS-IAS intervals and the \(\Delta\)H-H intervals (Figure 14). Thus, the lack of change in the degree of anterior bombardment resulted in lack of change in the VR after the CPA.

As shown in Table 5, in contrast to the observations made during posterior site pacing (Table 4), the N(IAS)/N(CrT) ratio changed much less after the CPA. Similarly, the scattering index S(CrT) did not change significantly. This suggested that, although the CPA resulted in some intra-atrial block, the degree of the latter was much less in the anteroposterior direction.

**Discussion**

The present study was designed to evaluate what role modification of the atrial inputs to the AVN has on filtering during high atrial rates. In particular, we tested the hypothesis that posterior modification results in ablation (destruction) of the slow AVN pathway, which is considered the major conduction route for closely coupled atrial impulses. The results obtained in the present study demonstrate that a model based on the putative presence of channels (slow and fast pathways) providing discrete connections between the AVN and the atrium is not applicable during simulated AF. Surgical dissociation of the AVN from its posterior approach did not eliminate the shortest H-H intervals and did not guarantee slowing of the VR. Our data are compatible with the hypothesis that the slow and fast pathways are nodal structures that may remain intact even after ablative procedures. The VR during AF therefore depends on the complex interaction of wave fronts propagating via the slow and the fast pathways. Surgical or ablative procedures can modulate
the VR by altering the pattern of atrial bombardment reaching the posterior and anterior AVN inputs.

**Slow and Fast Pathways: Discrete Conduction Channels Versus Functional Nodal Entities**

Despite the attractiveness of the hypothesis of pathways/channels with discrete atrial connections, convincing morphological evidence for their existence is missing. It has been demonstrated that the atrial fibers form a complex multidirectional structure at the AVN approaches. Interestingly, successful AVN reentrant tachycardia ablation procedures may not affect the compact AVN at all. Conversely, characteristic posterior extensions of the AVN have been reported, and successful slow-pathway ablation has been attributed to damage inflicted on these extensions. The electrophysiological evidence is also conflicting. Electrical signals recorded in the region of the posterior AVN approaches (the “slow” potentials) appear to have an extranodal origin. To make the whole picture even more complex, recent experimental work described a third AVN pathway.

The observations in the present study, obtained with localized reversible cooling of the AVN inputs, did not reveal specific channel structures. Posterior cooling (Figures 2 and 3) was partially successful in differentially affecting the conduction time of short-coupled atrial beats. This effect could have resulted from depressed conduction in the posterior AVN extensions and confirms the importance of this atrial input for conduction at short coupling intervals. Cooling of the anterior atrial approaches (Figure 4) failed to produce a specific effect on the conduction (ie, only at long coupling intervals). It should be realized, however, that both the cooling and the clinical radiofrequency ablations may affect not only the putative discrete insertion of the SP but also the compact node itself.

We also tested the hypothesis that the discrete duality of AVN electrophysiology can be evaluated during AF by examination of H-H interval distribution, which was shown to exhibit 2-peak histograms in limited clinical studies. Our results did not support such a hypothesis.

In view of the above, it becomes logical to investigate whether the “SP modification” used for VR control in AF results in elimination of the SP conduction or rather in elimination of just 1 important connection between the pathway and the atrium.

**Alteration of the Filtering Role of the AVN During AF**

The results from the present study illustrate 2 contrasting outcomes of the CPA procedure (Figure 1). The latter was used to mimic clinically performed SP modification for ventricular slowing during AF. As in clinical studies, disinhibition of the connection between the AVN and the

### Table 4: Electrophysiological Data Before and After Cutting of the AVN Posterior Approach With Pacing From Posterior Atrial Sites

<table>
<thead>
<tr>
<th>Pacing Site</th>
<th>Intervals, ms</th>
<th>Blocking Index</th>
<th>Scattering Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CrT-CrT</td>
<td>N(CrT)/N(IAS)</td>
<td>S(CrT)</td>
</tr>
<tr>
<td></td>
<td>IAS-IAS</td>
<td>N(IAS)/N(H)</td>
<td>S(IAS)</td>
</tr>
<tr>
<td></td>
<td>H-H</td>
<td>S(H)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min H-H</td>
<td>2(CrT)/2(H)</td>
<td>2(IAS)/2(H)</td>
</tr>
</tbody>
</table>
posterior atrial approaches in the isthmus between the CS and TrV did not guarantee VR slowing in our preparations. Most importantly, however, the CPA had little effect on the shortest H-H intervals that are related to the SP (Figures 7 and 8). That is, even in those cases in which the CPA resulted in a prolongation of the mean H-H interval, the shortest H-H intervals were similar to those observed in control (Tables 4 and 5). Careful examination of the underlying mechanisms revealed that in the experimental model used in these studies, the CPA procedure resulted in dramatic changes of the atrial engagement of the AVN.

In group 1 preparations, the isthmus between the CS and the TrV was the major route through which the triangle of Koch was reached during pacing from the posterior sites. Cutting of this link proved to be critical because of the presence of substantial functional block across the CrT that...
prevented the high-rate AF to reach the node via the anterior
approaches. The result was a substantial slowing of the VR
(Figures 9 and 10). The reason for this slowing was the
marked prolongation of the mean IAS-IAS observed at the
site of the remaining intact anterior input. This dramatic
slowing of the atrial bombardment reaching the AVN permit-
ted a virtual 1:1 conduction to the bundle of His (Figure 7).
However, when the AF was initiated from the anterior sites,
the CPA procedure had no effect on the filtering properties
of the AVN in these preparations (Figures 12 and 13). Thus,
as long as the high-rate bombardment was present, the AVN
produced H-H rates similar to those before the CPA proce-
dure. This outcome would not be possible if the SP were
eliminated after the CPA.

In group 2 preparations, the CPA did not slow the VR
during posterior pacing (Figures 9 and 10). In fact, a small
acceleration was observed. In these preparations, accordingly,
there was a much smaller degree of posteroanterior functional
block. Further increase of the intra-atrial block in these
preparations by cooling (Figure 1C) produced effects that
were very similar to those described in group 1 (Figure 10).
Thus, the contrasting behavior observed in the 2 groups of
preparations can be explained without assuming success or
failure of the CPA procedure in eliminating the SP entirely. In
fact, the experimental data suggest that SP conduction was
intact in all preparations and that short H-H intervals contin-
ued to exist even after the CPA. The major difference

between the 2 groups of preparations was in the degree
of intra-atrial conduction block that was revealed after the CPA.

Although tempting, the results of the present study should
be extended to clinical observations with caution. There are
several reasons why the modification might result in success-
ful or unsuccessful slowing of the VR during AF. First, like
the mechanisms analyzed in the present study, the clinical
modification may result in substantial altering of the effective
rate of bombardment of the AVN. Second, because the
radiofrequency ablation is not strictly confined in space,
damage to the posterior extensions of the compact node and
even to the compact node cannot be ruled out. This may result
in successful VR slowing independent of the predominant
source(s) of fibrillatory waves.

Limitations of the Study
The limitations of this study are determined by the experi-
mental models and pacing protocols used. The high-rate
random atrial pacing was used to simulate AF. Although it
permitted us to initiate the same fibrillatory process multiple
times and therefore allowed multiple comparisons, the real
AF organization in the human heart may be different. The
intra-atrial blocks observed in this study may not be a feature
of the fibrillating human heart or may have different locations
and therefore exert different effects. However, by illustrating
the coexistence of cut posterior approaches and intact com-


![Figure 11](https://example.com/figure11.png)

**Figure 11.** Correlation between CPA-produced change in IAS-
IAS intervals and subsequent changes in H-H intervals in all
preparations studied with posterior pacing.

![Figure 12](https://example.com/figure12.png)

**Figure 12.** CPA-induced changes in H-H intervals in group 1 (A)
and group 2 (B) with 3 anterior pacing sites (CS, AA, and HS).
Abbreviations as in Figure 1. See Table 5 for detailed numerical
values. Note that the mean H-H intervals did not increase and
were even shortened in B. *P<0.05.

![Figure 13](https://example.com/figure13.png)

**Figure 13.** CPA-induced changes in H-H, IAS-IAS, and CrT-CrT
intervals in group 1 (A) and group 2 (B) with anterior pacing.
Note that, unlike cases with posterior pacing (Figure 10), here
IAS-IAS intervals remained unchanged. Consequently, there was
no prolongation of H-H intervals. Significant changes in the
mean intervals are indicated by * (P<0.05).

![Figure 14](https://example.com/figure14.png)

**Figure 14.** Relationship between CPA-produced change in IAS-
IAS intervals and subsequent change in H-H intervals in all
preparations studied with anterior pacing.
pact AVN, the present study strongly suggests that similar situations may be present during clinical AVN modification procedures.

Acknowledgments
This research was supported in part by grant 9807701 from the American Heart Association (Ohio Valley Affiliate). Dr Garrigue was a Visiting Research Fellow from Centre Hospitalier Universitaire de Bordeaux, Bordeaux-Pessac, France. The authors thank Dr D. Van Wagoner for his help with the final preparation of the manuscript.

References
2. Toivonen L, Kadashe M, Kow V, Morady F. Determinants of the ventricu-
7. Cox J.L., Holman W.I., Cain M.E. Cyrosurgical treatment of atrioventric-
11. Inoue S., Becker A.E. Posterior extensions of the human compact atrio-
ventricular node: a neglected anatomic feature of potential clinical signif-
12. Williamson B.D., Man K.C., Daoud E., Niebauer M., Strickberger S.A., Morady F. Radiofrequency catheter modification of atrioventricular con-
13. Feld G.K., Fleck R.P., Fujimura O., Prothro D.L., Bahnsen T.D., Ibarra M. Control of rapid ventricular response by radiofrequency catheter modifi-
18. Feld G.K. Radiofrequency catheter ablation versus modification of the AV node for control of rapid ventricular response in atrial fibrillation. J Car-
Atrioventricular Nodal Conduction During Atrial Fibrillation: Role of Atrial Input Modification
Stéphane Garrigue, Kent A. Mowrey, Gerard Fahy, Patrick J. Tchou and Todor N. Mazgalev

Circulation. 1999;99:2323-2333
doi: 10.1161/01.CIR.99.17.2323
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/99/17/2323

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/