Evidence of a Reentry Circuit in the Common Type of Atrial Flutter in Man

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SUMMARY To investigate the mechanism of atrial flutter (AF) in humans, we studied 13 patients during episodes of spontaneous common AF, with simultaneous multiple atrial endocavitary recordings and atrial programmed stimulation. In all patients, low paraseptal atrial activation preceded high right atrial activation, and the latter preceded mid- or low lateral right atrial activation (recorded in five patients). Programmed atrial stimulation resulted in early reset of the AF cycle, with an unchanged poststimulation AF activation pattern. The poststimulation cycle recorded from an even potential to the site of stimulation was always shorter than the basic flutter cycle length. The poststimulation cycle recorded at the site of stimulation was always equal to or longer than the flutter cycle length.

These results strongly favor the existence of a reentry circuit to which the extrastimulus has access.

THE MECHANISM of atrial flutter (AF), (ectopic focus1-3 vs reentry4-12) is controversial. Some experimental studies have demonstrated that a reentry circuit is the mechanism of induced13,14 or even spontaneous15 AF in animals. This has not been demonstrated in man.

We recently documented induction and termination of episodes of common AF in man by programmed atrial stimulation.16,17 Although this strongly favors reentry, it is not definitive evidence of it, because a triggered activity cannot be excluded.18 We studied the effects of programmed atrial stimulation on the basic AF cycle in man, and observed that the poststimulation cycle, recorded at the stimulation point, was equal to the basic AF cycle in some cases.16,17

In this paper we report the results of studies using simultaneous multiple atrial endocavitary recordings and atrial programmed stimulation.

Materials and Methods

The study population consisted of 13 patients, 11 males and two females, ages 32–72 years (mean 54.3 years).

The underlying heart disease was coronary athero-sclerotic heart disease in five patients, idiopathic cardiomyopathy in five and mitral valvular disease in two. One patient had no clinical evidence of heart disease except for the arrhythmia (table 1).

All patients gave written informed consent. They underwent atrial electrostimulation for treatment of a spontaneous episode of common AF.12,17 The diagnostic of common AF was based on the following electrocardiographic criteria:1,5,11,17,19: (1) regular, rhythmic atrial waves (variation of the cycle length not above 10% of the basic cycle); (2) sawtooth atrial waves, predominantly negative in L2, L3, aVf; (3) an atrial rate of at least 240 beats/min when drugs had not been previously administered; and (4) an atrioventricular (AV) conduction ratio different from 1:1 either spontaneously or after vagal stimulation. All were pretreated with antiarrhythmic drugs (table 1) to facilitate sinus rhythm resumption by atrial pacing.17,20,21

After diazepam, 10 mg i.m., at least two quadripolar catheters (1 cm between electrodes) were inserted for atrial endocavitary recordings and stimulation. Initially, all patients had one catheter positioned in the low paraseptal atrium (low right septal wall in eight and proximal coronary sinus in five) and another in the high right atrium (lateral wall in 10 and septal wall in three). These two sites were named points 1 and 2, respectively. The different catheter positions were chosen so as to attain a firm position with good atrial potentials and atrial capture during stimulation.

Programmed atrial stimulation was first performed at point 2, with a coupling interval progressively decreased by 10 msec until the atrial refractory period was attained. If the interruption or transformation of the arrhythmia was unsuccessful, the coupling interval of this extrastimulus was fixed at a slightly higher value than that of the effective atrial refractory period; a second extrastimulus was then given at progressively decreasing coupling intervals. In case of failure, a third extrastimulus was given in the same way.

In five cases, the same pattern of stimulation was repeated at point 1. In five others, recording and stimulation in another atrial site, called point 3 (midlateral right atrium in three, low lateral right atrium in two), were carried out after inserting a third catheter or after moving one of the first two.

The pattern of atrial activation and its behavior after programmed stimulation were studied in all cases, and the poststimulation trial cycle length was calculated at each recording point.

The stimulation output was 10 V and impulse duration 2 msec; a Devices MPS 4279 stimulator was used. The ECGs and bipolar electrograms were recorded on a Siemens-Elema Mingograph 804 at a paper speed of 50–100 mm/sec.
Results

Pattern of Atrial Activation

Low paraseptal atrial activation (point 1) preceded high right atrial activation (point 2) in all patients; the latter preceded mid- or low lateral right atrial activation (point 3) in the five patients in whom recordings were carried out at this site. The time course between atrial activation at points 1, 2, and 3 and the onset of the negative F wave in lead aVF is reported in table 2.

S. A. yrs 34.

L 1

\[ \text{aVF} \]

V 1

\[ \text{RASlo} \]

\[ \text{RALhi} \]

Programmed Single Atrial Stimulation

Irrespective of the stimulation point, AF persisted, but with an early reset of the cycle. The pattern of atrial activation in the poststimulation atrial complex did not change (figs. 1, 2, and 3).

The length of the poststimulation atrial cycle recorded proximal to the stimulation point (i.e., at points reached preemptively by the spreading AF wave) always decreased compared with the basic AF cycle and to the poststimulation cycle recorded at the stimulation point. However premature the stimulus was at point 2 and 3, it never modified the simultaneous activation time at point 1; however, the poststimulation atrial cycle recorded at point 1 was always shorter than both the basic AF cycle and the poststimulation cycle recorded at points 2 (table 2) and 3 (figs. 1, 2A, and 3).

The length of the poststimulation atrial cycle recorded at the stimulation point or distally (i.e., at points reached after the latter by the AF wave) either increased or remained unchanged in all but one patient (fig. 2A) compared with the basic AF cycle. In particular, using point 1 stimulation, the poststimulation cycle, both recorded at points 1 and 2 (table 2), was always equal to or longer (although never compensatory) than the basic AF cycle (fig. 2B).

In recordings made distal to the stimulation point, the atrial cycle sandwiching the stimulus was shorter than the basic AF cycle (figs. 2B and 3B).

Programmed Double or Triple Atrial Stimulation

The patterns observed after double and triple stimulation were the same as those seen after single stimulation: early reset of AF cycle and the unchanged activa-

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Heart disease</th>
<th>Antiarrhythmic treatment before atrial stimulation† (mg/day)</th>
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<tr>
<td>1</td>
<td>72</td>
<td>M</td>
<td>CHD</td>
<td>D 0.25 Q 1100</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>M</td>
<td>Id</td>
<td>D 0.25 Q 1100 Ad 600</td>
</tr>
<tr>
<td>3</td>
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<td>M</td>
<td>CHD</td>
<td>D 0.25 Ad (LTT) 200</td>
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<td>4</td>
<td>49</td>
<td>M</td>
<td>Id</td>
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</tr>
<tr>
<td>5</td>
<td>50</td>
<td>M</td>
<td>Id</td>
<td>D 0.20 Q 1100</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>M</td>
<td>O</td>
<td>D 0.25 Q 1100 Ad 600</td>
</tr>
<tr>
<td>7</td>
<td>71</td>
<td>F</td>
<td>CHD</td>
<td>D 0.25 Q 1100</td>
</tr>
<tr>
<td>8</td>
<td>47</td>
<td>M</td>
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</tr>
<tr>
<td>9</td>
<td>58</td>
<td>M</td>
<td>MVD</td>
<td>D 0.25 Q 1100 Ad 600</td>
</tr>
<tr>
<td>10</td>
<td>48</td>
<td>M</td>
<td>Id</td>
<td>D 0.10 Q 1100 Ad (LTT) 200</td>
</tr>
<tr>
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<td>70</td>
<td>M</td>
<td>CHD</td>
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<td>12</td>
<td>32</td>
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<td>D 0.25 Q 1100</td>
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<tr>
<td>13</td>
<td>69</td>
<td>F</td>
<td>CHD</td>
<td>D 0.20 Q 1100</td>
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</tbody>
</table>

Abbreviations: CHD = coronary heart disease; Id = idiopathic; O = no detectable heart disease; MVD = mitral valve disease; D = digoxin; Q = quinidine; Ad = amiodarone; Ad (LTT) = amiodarone long-term treatment.

Figure 1. Patient 2 — atrial flutter at a cycle length 250 msec. ECG leads I, aVF, and V1, and bipolar electrograms recorded at 100 mm/sec of right atrial low septal wall (RASlo) and high lateral wall (RALhi). Premature stimulation of the RALhi (arrow) lengthens the subsequent cycle (270 msec), while shortening that of RASlo (200 msec). Atrial flutter persists with same rate and activation pattern. At the bottom is a diagram of the events.
In patients 1, 4 and 13, direct termination of the AF by triple stimuli was observed (fig. 4). The respective sites of stimulation were the right atrial high and mid-lateral wall and proximal coronary sinus. A final, spontaneous, flutter-like atrial beat preceded AF termination in all patients.

In patient 8, double stimulation caused acceleration pattern of the poststimulation atrial complex in case of AF persistence; and the poststimulation cycle recorded proximal to the stimulation point was shorter than the basic AF cycle. At the stimulation point itself, the poststimulation cycle was longer or the same.

**TABLE 2. Electrophyslogic Data**

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Point 1</th>
<th>Point 2</th>
<th>Point 3</th>
<th>Time course (msec) between onset of negative F wave in aVF and</th>
<th>Last AF cycle preceding programmed stimulation (msec)</th>
<th>Coupling interval of maximally premature atrial stimulated complex at point 2 (msec)</th>
<th>Post stimulation cycle recorded at point 1 (msec)</th>
<th>Post stimulation cycle recorded at point 2 (msec)</th>
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<td>RALhi</td>
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<td>200</td>
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<td>310</td>
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<td>RALhi</td>
<td>—</td>
<td>—</td>
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<td>180</td>
<td>200</td>
<td>270</td>
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<td>RALhi</td>
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<td>240</td>
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<td>210</td>
</tr>
<tr>
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<td>CSpr</td>
<td>RALhi</td>
<td>RALmid</td>
<td>20 80 100</td>
<td>230</td>
<td>180</td>
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<td>RALhi</td>
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<td>RALhi</td>
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<td>RALhi</td>
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<td>RALhi</td>
<td>RALlo</td>
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</tr>
<tr>
<td>9</td>
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<td>20 50 110</td>
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<td>310</td>
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<tr>
<td>10</td>
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<td>RASHi</td>
<td>RALlo</td>
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<tr>
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<td>10 50 120</td>
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<td>RASHi</td>
<td>—</td>
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<tr>
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<td>0 40</td>
<td>280</td>
<td>210</td>
<td>270</td>
<td>340</td>
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</tbody>
</table>

Abbreviations: CSpr = coronary sinus proximally; RASlo = right atrium low septal wall; RASHi = right atrium high septal wall; RALhi = right atrium high lateral wall; RALmid = right atrium midlateral wall; RALlo = right atrium low lateral wall.

**FIGURE 2.** Patient 3 — atrial flutter at a cycle length of 220–240 msec. (A) Premature stimulation of right atrial high lateral wall (RALhi) (arrow), with results similar to those in figure 1. (B) Premature stimulation of right atrial low septal wall (RASlo) (arrow) foreshortens the RALhi cycle (190 msec). The subsequent cycle at both points (230 msec) is longer than the basic atrial flutter cycle. At the bottom is a diagram of events.
of the AF with spontaneous termination of arrhythmia 25 seconds later. The higher-rate AF had the same activation pattern as the lower-rate AF, but the atrial activation times, particularly in the low right atrium, were different.

In six patients, sinus rhythm restoration by programmed stimulation (double stimuli in four and triple in two) was preceded by a few seconds or minutes of atrial fibrillation. In three patients, programmed stimulation failed to terminate AF.

**Discussion**

Whether AF in humans is based on abnormal rapid impulse formation or on a reentrant mechanism is not settled. Our study, while supporting the reentrant theory, also permits speculation about the site and structure of the circuit itself.

**Electrophysiologic Mechanism of Atrial Flutter**

Endocavitary mapping in man and some experimental studies in animals have shown that right atrial activation in common AF spreads from low to high atrium, in a counterclockwise pattern.

In all of our patients, low paraseptal atrial activation (point 1) preceded high right atrial activation (point 2). It follows that if a focus mechanism (automaticity or triggered activity) is present, the impulse must arise in cells in the low atrium close to point 1.

If there was a single low atrial focus and premature high right atrial stimulation failed, as in our cases, to capture it, the subsequent low atrial cycle should equal that of the basic AF cycle without reset. However, in our cases, high atrial stimulation (point 2) always resulted in an early reset of the AF, with the poststimulation cycle recorded at the low atrium (point 1) less than the basic AF cycle.

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

**Figure 3.** Patient 10 — atrial flutter (AF) at a cycle length of 250–260 msec. (A) Premature stimulation (arrow) of the right atrial low lateral wall (RALlo) foreshortens (210 msec) the cycles recorded at the proximal coronary sinus (CSpr) and the high right atrial septal wall (RASHi) (These points are reached by the AF wave front in advance of the stimulation point.) After stimulation, the AF activation sequence is unchanged. (B) Premature stimulation of the RASHi (arrow) foreshortens the RALlo stimulus containing cycle (210 msec). The poststimulation cycle at CSpr (220 msec) is shorter than the basic AF cycle, while that of RASHi (250 msec) is not. At the bottom is a diagram of events. The paper recording speed is 100 mm/sec.
Even if we accept that the extrastimulus can depolarize or somehow influence the focus and temporarily accelerate its firing rate, the poststimulation cycle recorded in the low atrium (point 1) must have the same length irrespective of the stimulation site (high or low atrium). However, in the five patients in whom this was studied, the low atrial cycle after high right atrial stimulation was always less than that after low atrial stimulation (table 2). Thus, a low atrial abnormal impulse formation, including triggered activity, could be excluded.

If high atrial stimulation that is insufficiently premature to capture the low atrium can nevertheless influence the subsequent cycle of the latter, then the impulse must be propagated along a pathway extraneous to the spreading AF wave front. Otherwise, the two wave fronts would collide at some point in between.

If we acknowledge the existence of a reentry circuit to which the extrastimulus had access, in advance of the leading edge of the circus wave front, we can explain why high atrial stimulation produces a shortened low atrial cycle with subsequent unchanging AF cycles and activation pattern.

A careful examination of the surface ECG morphol-
ogy of the paced atrial complexes revealed a similarity to the AF waves or a fusion morphology during double and triple stimulation. These findings are similar to the so-called AF entrainment described by Waldo et al.,2,5 who documented that during rapid atrial pacing (at rates faster than the spontaneous AF rate) that failed to interrupt the AF, although the atrial rate increased to the pacing rate, the polarity and morphology of the atrial complexes in ECG lead II remained predominantly negative. This occurred although the atria were being paced from a site high in the right atrium, which should have produced positive atrial complexes in this ECG lead.

We cannot explain the mechanism of the poststimulation spontaneous atrial beat (fig. 4) and brief acceleration of AF rate in patient 8, which both preceded AF termination. These patterns were reported previously.16,17 We also pointed out the abrupt AF termination, which usually accounts for a reentry circuit. However, poststimulation tachycardia acceleration24 or a spontaneous final beat before conversion25 was also observed in triggered activity.

Type and Site of the Circuit

Experimental studies performed by Allessie et al.13,14 have documented that a reentrant circuit is the mechanism of induced AF. They believed that these circuits are not due to anatomic obstacles but are exclusively secondary to inhomogeneity of atrial refractory periods (leading circle). As a consequence, site and dimension of the circuit differ from case to case.

The experimental studies of Boineau et al.,15 some of which were performed during spontaneous AF in the dog, give somewhat different results. The AF reentry circuit seemed to be due to slow conduction in a hypoplastic right atrial myocardium with discontinuities of the crista terminalis and superior interatrial band. To support these data, Boineau et al. provoked AF episodes in animals after ligation of the crista terminalis. Pastelin et al.27 stressed the importance of preferential pathways for the induction and maintenance of experimental AF in the animal.

It is difficult to extrapolate these data to humans. If we accept for clinical AF the mechanism proposed by Allessie et al.,13 then it would appear odd that almost all patients have near identical flutter morphology in the ECG.

Furthermore, in the circuit described by Allessie et al.13 there is a tight fit between the crest and the tail of the wave front, without an excitable gap in the circuit. In our cases, however, there was an excitable gap that permitted access of stimuli of even moderate prematurity. This might be explained by the high output of the extrastimulus because a wave front (or stimulus) of greater efficacy than the circulating impulse could interfere with the latter in the leading circle.13 Recently, Inoue et al.,23 by overdrive and programmed stimulation, and Plumb et al.,28 by overdrive pacing, have documented an excitable gap in the AF of man.

In our patients, who all had the common type of AF, the decrease of the poststimulation cycle length compared with the basic AF cycle in sites proximal to the stimulation point, was observed not only by pacing the high right atrium but also the midlateral right atrium (three cases) and the low lateral right atrium (two cases). These patterns not only account for a right atrial site of the reentrant circuit (probably macroreentry), but also could suggest that the posterior internodal tract was part of it in the common type of AF.

As already speculated by Allessie et al.13 and Boineau et al.,15 intermingling of the various mechanisms observed in the experimental animal models could occur in spontaneous human AF. Prolonged atrial conduction,29 particularly along preferential pathways, together with inhomogeneity of atrial refractory periods, could constitute the electrophysiologic basis of spontaneous common AF in man.

We believe that the demonstration of a poststimulation low atrial recorded cycle less than the basic AF cycle after high atrial programmed stimulation strongly favors a reentry circuit as the mechanism of common AF in humans. While our results do not allow a precise identification of the site and type of the circuit, they are more compatible with macroreentry than microreentry in the right atrium.

References


Evidence of a reentry circuit in the common type of atrial flutter in man.
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