The mechanism of atrioventricular nodal re-entrant tachycardia (AVNRT) remains elusive.1,2 Both anatomic and functional models have been proposed. There has been electrophysiological evidence that the right and left inferior extensions of the human AV node and the atrionodal inputs they facilitate, which have been identified histologically, might provide the anatomic substrate for the slow pathway.3–6 Data indicating the potential anatomic site of the fast pathway are sparse. There is a histological evidence of multiple superior atrial inputs to the AV node,7–11 but the nature of fast pathway conduction, especially during atypical AVNRT of the fast–slow type, is poorly understood. We have previously reported data, suggesting that atypical fast–slow and typical slow–fast AVNRT do not seem to use the same limb for fast conduction.12 This evidence, however, was derived by observations on typical and atypical tachycardias recorded in different patients. We are not aware of data on patients who have exhibited both typical and atypical forms of this tachycardia. We compared conduction intervals during typical and atypical AVNRT that occurred in the same patient.

Methods

Patients

Data from adult patients with AVNRT undergoing catheter ablation at 5 centers, Beth Israel Deaconess Medical Center Boston, MA, and Rhode Island Hospital, Boston, MA (2009–2013); Athens Euroclinic, Athens, Greece (2007–2014); the Johns Hopkins Hospital, Baltimore, MD (2009–2013); and University of Michigan Health System, Ann Arbor, MI (2009–2013). From the Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA (D.G.K., A.E.B., M.E.J.); Rhode Island Hospital, Boston, MA (A.E.B.); Athens Euroclinic, Athens, Greece (D.G.K., T.Z.); Johns Hopkins Hospital, Baltimore, MD (J.E.M., T.T., H.C.); and University of Michigan Health System, Ann Arbor (R.L., S.H.S., F.M.). Correspondence to Demosthenes G. Katritsis, MD, PhD, Division of Cardiology, Beth Israel Deaconess Medical Center, 185 Pilgrim Rd, Baker 4, Boston, MA 02215.

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WHAT IS KNOWN

• The nature of fast pathway conduction, especially during atypical AVNRT of the fast-slow type, is poorly understood.
• There is evidence that atypical fast-slow and typical atrioventricular AVNRT do not utilize the same limb for fast conduction, but no data exist on patients who have presented with both typical and atypical forms of this tachycardia.

WHAT THE STUDY ADDS

• We investigated the nature of the fast pathway in patients displaying both slow-fast and, so-called, fast-slow AVNRT.
• Our data provide further evidence that typical slow-fast and atypical fast-slow AVNRT utilize different anatomical pathways for fast conduction.
• Anterograde fast conduction during atypical AVNRT is distinct from retrograde fast conduction during typical AVNRT.

MD (2011–2014); and the University of Michigan Health System, Ann Arbor, MI (2009–2014), were analyzed. The subjects of this study were the patients in whom both typical and atypical AVNRT were induced in the same procedure and in whom tracings suitable for evaluation were available. All patients were studied in the postsorptive state, under mild sedation, and after all antiarrhythmic agents had been discontinued for >5 half-lives. No patient had received amiodarone for the preceding 3 months. The study received approval from our institutional review boards.

Definitions

AVNRT was diagnosed by fulfillment of established criteria during detailed atrial and ventricular pacing maneuvers, and subsequent abolition of the tachycardia by anatomic ablation of the slow pathway. Typical (slow–fast) AVNRT was defined by an atrial-His/His-atrial ratio (AH/HA) >1 and HA interval of ≤70 ms. Atypical AVNRT was defined by delayed retrograde atrial activation with HA>70 ms. If the AH was <200 ms and the AH<HA, the atypical form was characterized as fast–slow. If AH>200 ms and AH>HA, the atypical form was considered slow–slow. Tachycardias with a prolonged AH interval of >200 ms but AH<HA, or with AH<200 ms and AH>HA, or with variable intervals during the same or different episodes, were classified as indeterminate. Details of our methodology for measurements of intervals during tachycardia have been described elsewhere.

Hypothesis

If the anatomic models are correct, AVNRT types that coexist in the same patient may use the same distinct limbs of the circuit regardless of the tachycardia type, and retrograde atrial and anterograde ventricular activation should use the same anatomical pathways in all forms of AVNRT. Therefore, conduction times such as the AH and HA intervals during types of tachycardia coexisting in the same patient can be calculated and used to provide data on the characteristics of the fast and slow circuit limbs.

Figure 1 depicts one of the proposed fixed, anatomic models of slow-fast and fast-slow AVNRT. According to this model, during AVNRT, the tachycardia circuit is confined within the AV node region, and activation of the atrium takes place after activation of the retrograde pathway. Thus, during typical slow–fast AVNRT, the HA interval represents the time difference between activation of the His bundle and activation of the atrium; this is HA=Fr+A–H, where Fr is the time the impulse travels retrogradely along the fast pathway, A is the time the impulse travels from the AV node to right atrium as recorded by the electrode positioned on the His bundle, and H is the time the impulse travels from the AV node to the His bundle. Similarly, the AH interval represents the time difference between activation of the right atrium as recorded by the catheter positioned on the His bundle and the next activation of the His bundle. This is AH=Sa+H–A, where Sa is the anterograde conduction along the slow pathway, H is the time the impulse travels from the AV node to the His bundle, and A the time the impulse travels from the AV node to right atrium. During atypical fast–slow AVNRT, HA=Sr+A–H, where Sr is the time required for the impulse to travel retrogradely along the slow pathway, A is the time the impulse travels from the AV node to right atrium, and H is the time the impulse travels from the AV node to the His bundle. AH=Pa+H–A, where Pa is the time required for anterograde conduction along the fast pathway.

Statistical Analysis

Data normality was assessed using the D’Agostino–Pearson test. Continuous, normally distributed variables were presented as mean±SD. Categorical data were expressed as frequencies (percentages). Statistical analysis was performed to compare the measured difference between Fr and Fa (Fr–Fa) to the anticipated difference considering the variability between repeated measurements on the same subject. To determine the maximum difference that could be attributed to between-measurement variability, we measured the AH interval, HA interval, and tachycardia cycle length during the typical form of AVNRT and computed Fr twice for each patient. The mean cycle length=AH+HA=Sa+F, by definition, derivation of the S interval can provide the value of F. If derived Fr values are significantly different than those for Fa, then the possibility of typical and atypical AVNRT using the same anatomic limb for fast conduction is unlikely.

Figure 1. Depiction of conduction and resultant AH and HA during typical and atypical atrioventricular nodal re-entrant tachycardia (AVNRT) types. A indicates conduction from the AV node to right atrium as recorded by the electrode positioned on the His bundle; AH, time difference between activation of right atrium and the next His; Fa, anterograde conduction over the fast pathway that is used by the fast–slow form; Fr, retrograde conduction over the fast pathway; H, conduction from the AV node to His bundle; HA, time difference between activation of the His bundle and right atrium; S, conduction over the slow pathway (anterogradely or retrogradely) (see text for details).
absolute value of the difference between these 2 measurements and its SE (3.69±0.44 ms) was used to estimate 95% confidence intervals for the between-measurement error (2.72–4.66 ms). Accordingly, using 1 sample \( t \) test, we compared the mean of the absolute values of \( F_r - F_a \) to the upper bound of the 95% confidence interval (4.7 ms). To further examine the relationship of measured \( F_r - F_a \) values to an expected between-measurement error, we have plotted measured \( F_r - F_a \) values together with 95% confidence intervals of between-measurement error, in a manner analogous to a Bland–Altman plot. Statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp, Armonk, NY). All tests were 2 tailed, and values of \( P < 0.05 \) were considered significant.

### Results

#### Patients

In total, 1299 patients with AVNRT were studied at Beth Israel Deaconess Medical Center, Boston, MA, and Rhode Island Hospital, Boston, MA (n=188); Athens Euroclinic, Athens, Greece (n=287); the Johns Hopkins Hospital, Baltimore, MD (n=271); and the University of Michigan Health System, Ann Arbor, MI (n=553). Using the criteria mentioned above, 20 patients had both typical and atypical AVNRT during the electrophysiology study. The mean age of all patients was 47.6±10.9 years (range, 32–75 years), and 11 patients (55%) were women. Among these 20 patients, 13 patients (65%) displayed atypical AVNRT with characteristics compatible with the fast–slow type according to both the \( \text{AH} \text{<HA} \) and the \( \text{AH} < 200 \text{ms} \), and 4 patients (20%) had slow–slow form of AVNRT. The remaining 3 patients (15%) could not be reliably classified because of inconsistent \( \text{AH} \) and \( \text{HA/AH} \) patterns or variable intervals. Conduction intervals during tachycardias are shown in Table 1. Typical anterograde conduction jumps during AV conduction curves were demonstrated in 11 of 20 patients. Typical retrograde conduction jumps were not demonstrated in any patient.

#### Mode of Induction and Earliest Atrial Retrograde Activation

Typical tachycardia induction during atrial pacing was seen in 8 of 20 patients, and in 2 of them only after isoproterenol infusion. Tachycardia induction with typical anterograde conduction jumps was seen in 9 patients. In 2 patients, typical AVNRT was induced with ventricular pacing and used 3 extrastimuli. Atypical AVNRT was induced by atrial pacing in 3 patients, and by ventricular pacing in 7 patients (in 1 patient with isoproterenol). No typical retrograde conduction jumps were seen at induction; in 1 patient, 2:1 retrograde conduction was noted at tachycardia induction. Atypical AVNRT was induced after atrial or ventricular ectopic beats in 2 patients. Earliest retrograde activation was variable and documented at the coronary sinus ostium in the majority of patients for both types of AVNRT. In all patients, both tachycardias were abolished after anatomic slow pathway ablation.

### Table 1. Conduction Intervals During Typical and Atypical AVNRT of All Types

<table>
<thead>
<tr>
<th>AVNRT Type</th>
<th>CL, ms</th>
<th>( \text{AH}_{\text{tachy}} ) (His), ms*</th>
<th>( \text{HA}_{\text{tachy}} ) (His), ms*</th>
<th>( \text{HA}_{\text{tachy}} ) (pCS),† ms</th>
<th>Earliest Retrograde Atrial Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical AVNRT</td>
<td>368.0±43.1</td>
<td>281.6±47.1</td>
<td>67.3±14.6</td>
<td>62.0±13.7</td>
<td>pCS (60%)</td>
</tr>
<tr>
<td>Atypical AVNRT</td>
<td>365.8±41.1</td>
<td>128.2±58.0</td>
<td>217.4±66.2</td>
<td>202.3±70.1</td>
<td>pCS (65%)</td>
</tr>
</tbody>
</table>

*\( \text{AH}_{\text{tachy}} \) indicates atrial to His interval during tachycardia; AVNRT, atrioventricular nodal re-entrant tachycardia; CL, tachycardia cycle length; \( \text{HA}_{\text{tachy}} \), His to right atrium interval during tachycardia; and pCS proximal coronary sinus.
†Measured in 17 patients.

### Table 2. Patients With Typical (Slow–Fast) and Atypical AVNRT of the Fast–Slow Type

<table>
<thead>
<tr>
<th>Pt No</th>
<th>Age, y</th>
<th>Sex</th>
<th>CL</th>
<th>( \text{AH}_{\text{tachy}} )</th>
<th>( \text{HA}_{\text{tachy}} )</th>
<th>Earliest Retrograde Atrial Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>M</td>
<td>410</td>
<td>320</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>F</td>
<td>395</td>
<td>325</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>F</td>
<td>345</td>
<td>248*</td>
<td>77*</td>
<td>Gt 1</td>
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<tr>
<td>4</td>
<td>47</td>
<td>M</td>
<td>380</td>
<td>313</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>44</td>
<td>M</td>
<td>370</td>
<td>300</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>M</td>
<td>400</td>
<td>310</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>M</td>
<td>325</td>
<td>229*</td>
<td>77*</td>
<td>Gt 2</td>
</tr>
<tr>
<td>8</td>
<td>48</td>
<td>M</td>
<td>410</td>
<td>305*</td>
<td>81*</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>32</td>
<td>F</td>
<td>280</td>
<td>211</td>
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</tr>
<tr>
<td>10</td>
<td>53</td>
<td>M</td>
<td>404</td>
<td>272*</td>
<td>95*</td>
<td>Gt 3</td>
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<tr>
<td>11</td>
<td>43</td>
<td>F</td>
<td>395</td>
<td>335</td>
<td>58</td>
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</tr>
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<td>12</td>
<td>55</td>
<td>F</td>
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<td>294</td>
<td>50</td>
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</tr>
<tr>
<td>13</td>
<td>58</td>
<td>F</td>
<td>376</td>
<td>289</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

*\( \text{AH}_{\text{tachy}} \) indicates atrial to His interval during tachycardia; AVNRT, atrioventricular nodal re-entrant tachycardia; CL, tachycardia cycle length; \( \text{HA}_{\text{tachy}} \), His to right atrium interval during tachycardia; and Pt, patient.
*Because of overlap of ventricular and atrial electrograms, the high right atrial electrogram was used for measurements.
Slow–Fast Versus Fast–Slow AVNRT

Using the strict criteria in this study, 13 patients had both slow–fast and fast–slow AVNRT according to our definitions. Patient characteristics and conduction intervals are presented in Table 2. Conduction times over the fast pathway during slow–fast AVNRT (Fr) and during fast–slow AVNRT (Fa) are presented for each patient in Figure 2A. The mean difference between Fr and Fa was 41.8±39.7 ms. This was significantly different when compared with the estimated between-measurement error (P=0.0055; Figure 2B).

Discussion

Our study represents the largest series of AVNRT cases with coexistence of both typical and atypical forms of which we are aware. Interestingly, in the majority of these patients, earliest retrograde atrial activation was detected at the coronary sinus ostium in both types of tachycardia. This is in keeping with previous observations on atypical AVNRT.12

Most patients with atypical AVNRT display the fast–slow variety. Our results argue against the conventional notion of a common anatomic fast pathway that supports both slow–fast and fast–slow AVNRT by conducting opposite directions. Derived Fr and Fa values were significantly different in our study, and this difference is unlikely to be because of a between-measurement error. Because tachycardia cycle length=F+S, and according to the fixed anatomic model, both types of AVNRT use the same slow pathway, an indirect comparison of fast pathway conduction during typical and atypical AVNRT could be also derived by comparing tachycardia cycle lengths. However, changes in autonomic tone, either spontaneously or after isoprenaline infusion, do not make such a comparison legitimate. Our method of deriving slow pathway values by taking into account both tachycardias in the same patient represents an attempt to overcome this limitation.

Considering the anatomic models of the AVNRT circuit, our results provide further evidence in support of our proposed scheme of re-entry along the posterior nodal extension in all forms of atypical AVNRT.12 Attempts to provide a functional circuit model have also been made by reference to contextual considerations, such as the anisotropic conduction properties of the transitional area between the atria and the AV node,15–20 and variability in the space constant of tissue and poor gap junction connectivity because of differential expression of connexin isoforms in the nodal area.21,22 Regardless of the nature of the re-entry circuit in AVNRT, our results suggest that anterograde fast conduction during atypical AVNRT is distinct from retrograde fast conduction during typical AVNRT.

Limitations

The main limitation of our study is that we considered a hypothetical model based on theoretical assumptions such as similar anterograde and retrograde conduction velocities for the slow and fast pathways in both types of AVNRT. Although studies on orthodromic and antidromic conduction of lateral accessory pathways do not indicate fundamental differences in conduction velocity, whether this is true also for decremental AV nodal pathways is not known. The comparison of AV nodal conduction properties with that of bypass tracts is complex. It is likely that much of the difference between anterograde and retrograde conduction properties relates to impedance mismatch between ventricular or atrial muscle and that of the bypass tract. This does not directly parallel the situation in the AV node, and there are no data to allow any definitive conclusion in this respect. In addition, retrograde atrial activation, in particular, may not take similar paths in all forms of AVNRT as accepted in purely anatomic models. Finally, one could argue that using the same data and the same formula, an investigator who believes that there is a single fast pathway can prove that there are discrete slow pathways. The fact that anatomic slow pathway ablation abolishes both typical and atypical AVNRT argues against such a hypothesis although it

Figure 2. A. Conduction times over the fast pathway during slow–fast atrioventricular nodal re-entrant tachycardia (AVNRT) (Fr) and during fast–slow AVNRT (Fa) for each patient. Corresponding values for each patient are connected with lines. B. Scatter plot of the difference in conduction times over the fast pathway during slow–fast AVNRT (Fr) and during fast–slow AVNRT (Fa) (Fr–Fa) against mean conduction time over the fast pathway for each patient. The 95% confidence intervals of the estimated between-measurement error are superimposed (dotted lines) for comparison.
cannot exclude the possibility of anatomically close, but discrete, slow pathways affected by anatomic ablation.

Conclusions
Our data provide further evidence that both slow–fast and fast–slow AVNRT do not use the same anatomic pathway for fast conduction.

Disclosures
None.

References
Coexistent Types of Atrioventricular Nodal Re-Entrant Tachycardia: Implications for the Tachycardia Circuit

Demosthenes G. Katritsis, Joseph E. Marine, Rakesh Latchamsetty, Theodoros Zografos, Tanyanan Tanawuttiwat, Seth H. Sheldon, Alfred E. Buxton, Hugh Calkins, Fred Morady and Mark E. Josephson

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