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Characterization of subforms of AV nodal reentrant tachycardia

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Abstract **Background** Different subforms of AV nodal reentrant tachycardia (AVNRT) have been described (''Slow/Fast'', ''Slow/Slow'' and ''Fast/Slow''). Our aim is to improve definition of these subforms, based on systematic evaluation, in a large cohort of patients, of the site of earliest atrial activation, timing intervals, and evidence for the presence or absence of a lower common pathway (LCP).
Methods and results In 344 patients, AVNRT using a slow pathway (SP) for antegrade conduction and earliest atrial activation at the superior septum (i.e. retrograde fast pathway) was present in 81.4% (Slow/Fast). AVNRT using an SP for antegrade conduction and earliest atrial activation at the inferior septum or proximal coronary sinus (i.e. retrograde slow pathway; Slow/Slow) was present in 13.7%. AVNRT with a short A-H interval and retrograde SP conduction (Fast/Slow) was present in 4.9%. All timing intervals during tachycardia are dependent on autonomic tone. H-A intervals during tachycardia (H-A_t) overlap in Slow/Slow and Slow/Fast AVNRT: Slow/Slow therefore may mimic Slow/Fast AVNRT. The H-A interval during pacing at the tachycardia cycle length (H-A_p) better discriminates both subforms. The difference between H-A_p and H-A_t (ΔH-A) was significantly longer in Slow/Slow compared with Slow/Fast AVNRT (isoprenaline 0.5 μg/min: 27 $\pm$ 18 ms vs. 1 $\pm$ 9 ms; $p<0.0001$). ΔH-A $>$ 15 ms had a specificity and sensitivity for Slow/Slow of 94% and 64%, respectively. A ΔH-A $>$ 15 ms, combined with other data, pointed to the presence of a long LCP in 36 of 43 evaluable Slow/Slow (84%) and all Fast/Slow, but in only 10% of Slow/Fast ($p<0.0001$). Retrograde conduction during ventricular pacing at the tachycardia cycle length was present in only 6% of Fast/Slow.
Conclusions AVNRT subforms can be distinguished based on a systematic evaluation of atrial activation sequence, timing intervals and evidence for the presence of an LCP.

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Introduction

The concept of dual AV nodal physiology as the underlying substrate for AV nodal reentrant tachycardia (AVNRT) is well established. The fast pathway (FP) forms the usual physiological conduction axis during sinus rhythm. During retrograde activation over the FP, earliest atrial activation is recorded at the superior (anterior) [1] aspect of the atrial septum, close to the site recording the His bundle potential [2–5], often above the tendon of Todaro and/or to its left [6]. In contrast, retrograde slow pathway (SP) conduction typically activates the inferior (posterior) [1] septum, between the tricuspid annulus and coronary sinus (CS) ostium or inferiorly inside the CS within 1–3 cm of the ostium [2,3,6,7]. The AVNRT circuit usually utilizes the SP for antegrade conduction and FP for retrograde conduction (''Slow/Fast'' AVNRT). Forms using an SP as the retrograde limb have also been described [6,8,9]. Depending on the A-H interval they have been subdivided into ''Slow/Slow'' or ''Fast/Slow'' AVNRT.

The impetus for our study was the observation that the terms ''Slow/Fast'', ''Slow/Slow'' and ''Fast/Slow'' AVNRT are used daily in every electrophysiology lab, but that the definitions of these subforms are ill-defined. This paper describes the characteristics of AVNRT in a large cohort of patients, being evaluated consistently and prospectively, including the site of earliest atrial activation during tachycardia and a systematic evaluation of the presence or absence of a lower common pathway (LCP). Our aim was to provide a better characterization scheme for this common arrhythmia and hence to improve definition of the AVNRT subforms.

Methods

Patients

All patients ($n = 344$) were admitted for ablation of AVNRT at the University Hospital Leuven. They underwent electrophysiological study in the fasting state, under deep sedation/anaesthesia with midazolam/fentanyl ($n = 5$) or propofol ($n = 339$). Antiarrhythmic drugs were discontinued for ≥ 5 half-lives. Multielectrode catheters were placed in the right atrial appendage, His bundle region, proximal CS and inferior atrial septum (between the tricuspid annulus and the CS ostium). AVNRT was induced at baseline ($n = 140$, 41%), or after the administration of isoprenaline at low dose ($n = 146$, 42%; 0.25 μg/min $n = 5$; 0.50 μg/min $n = 141$) or high dose (≥ 1 μg/min in 58, 17%). The relatively high proportion of patients needing isoprenaline was likely related to the heightened vagal tone at baseline as a result of anaesthesia. Sustained or nonsustained AVNRT (≥ 5 beats) was induced in all patients. Only data from patients with sustained tachycardia were used for comparative evaluation of timing intervals ($n = 293$).

Diagnostic evaluation

Electrophysiological testing consisted of:

(1) Atrial extrastimulus testing and decremental atrial pacing. A 50 ms increase in A_2-H_2 interval following a 10 ms decrease in atrial coupling interval (A_1-A_2) during atrial extrastimulus testing, or a 50 ms increase in A-H interval following a 10 ms decrease in pacing cycle length (CL) during decremental atrial pacing was interpreted as antegrade conduction block in the FP with continued conduction over the SP. In patients without an abrupt 50 ms increase (38%), A-H or A_2-H_2 intervals ≥ 200 ms were considered to represent conduction over the slow pathway. This value is based on prior studies examining the longest A-H interval over the FP in patients with a clear ''jump'' under similar circumstances [6].

(2) Ventricular extrastimulus testing and decremental ventricular pacing coupled with mapping the right atrium and CS to identify the site of earliest atrial activation at long and short pacing intervals. Ventricular pacing was performed from a ''para-Hisian'' position, i.e. close to the proximal right bundle branch without directly capturing the His bundle [10,11]. Pacing at this site delayed retrograde activation of the His bundle, separating the retrograde His bundle and atrial potentials from the ventricular potential. This allowed measurement of the H-A and H_2-A_2 intervals and clear identification of the retrograde atrial activation sequence. The retrograde His bundle electrogram was always validated by pacing at higher output, directly capturing the His bundle, resulting in advancement of retrograde atrial activation [10,11].

(3) Right atrial and CS mapping was performed during AVNRT to identify the site of earliest atrial activation (Fig 1A). When the atrial potentials were obscured by ventricular potentials, para-Hisian ventricular extrastimuli were delivered (without capturing the His bundle) to advance the ventricular potential without

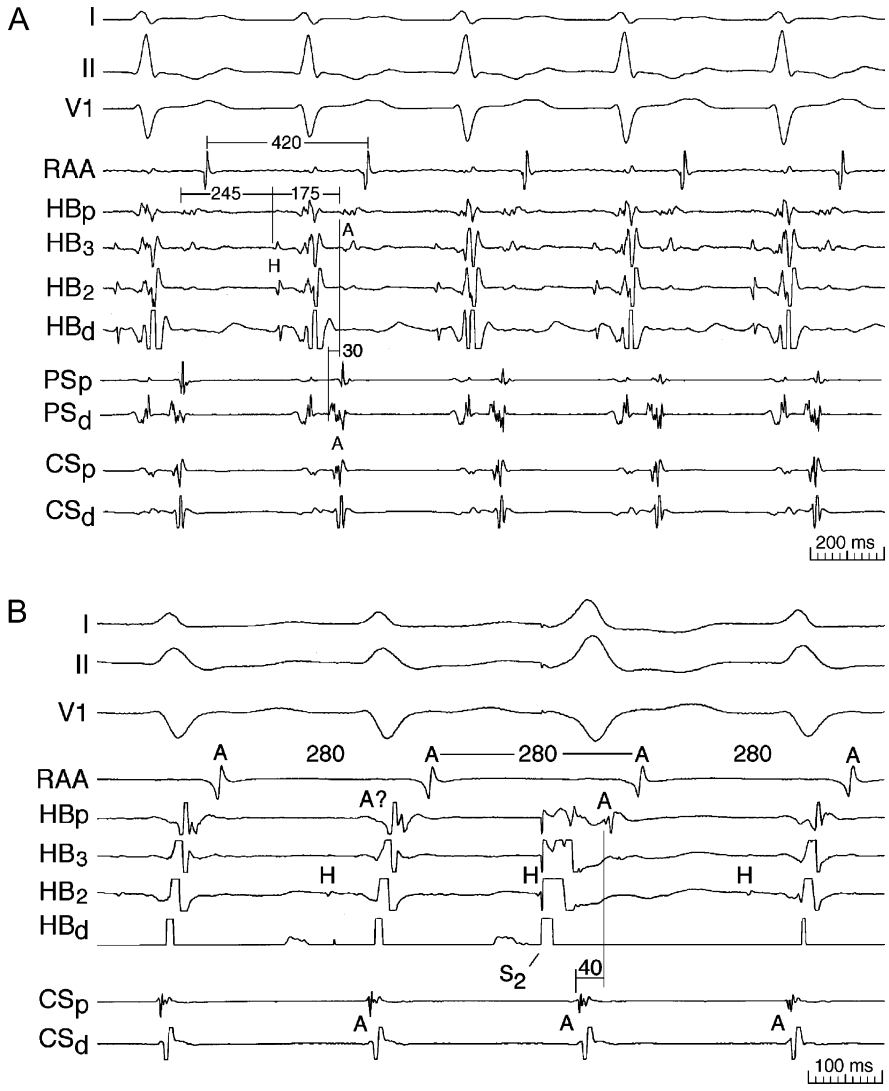

Figure 1 Atrial activation sequence in AVNRT using slow pathways for both antegrade and retrograde conduction (Slow/Slow AVNRT). A. Atrial activation (*A*) was recorded earliest at the inferoseptal (posteroseptal) region between CS ostium and tricuspid annulus (PS_d), followed by activation just inside the CS ostium (CS_p), and 30 ms later in the His bundle electrogram (HB_p). B. When atrial and ventricular potentials were superimposed (different patient), a ventricular extrastimulus (S_2) was delivered to the para-Hisian region [11] through the distal pair of electrodes on the His bundle catheter (HB_d) [10]. Advancing ventricular but not atrial activation allowed identification of the atrial potential in all electrograms, showing earliest activation in the proximal CS (CS_p). Without the ventricular extrastimulus, the tachycardia mimicked Slow/Fast AVNRT (long A-H and short H-A intervals, with overlapping atrial and ventricular potentials). RAA: right atrial appendage.

advancing the atrial potential and hence separate both (Fig. 1B). We used the new anatomical nomenclature as proposed by a recent ESC/NASPE experts consensus group [1]. The older nomenclature has been added in brackets for the sake of clarity. Earliest atrial activation recorded at the inferior (posterior) septum (between the CS ostium and the tricuspid annulus, or in the proximal and inferior CS) was considered indicative of retrograde conduction over a slow pathway, based on studies showing different sites of earliest atrial activation during retrograde conduction over the fast and slow pathways and selective ablation of them at these sites [5–7,12].

(4) Comparison of H-A interval during tachycardia ($H\text{-}A_t$) and ventricular pacing at the same CL ($H\text{-}A_p$) was used as a relative measure of the functional length of the lower common pathway (LCP), i.e. the conduction path between the distal turnaround point of the antegrade and retrograde conduction pathways and the

His bundle [13,14]. (For details of the methods, see Ref. [15].) H-A_t was measured after stabilization of tachycardia (usually >1 min). The tachycardia was terminated (typically with an atrial pacing burst) and ventricular pacing (at the same CL) was initiated immediately. H-A_p was measured as soon as the interval became stable. Therefore, measurements were separated by only a few seconds [14]. The retrograde atrial activation sequence during tachycardia and pacing was compared. H-A_t was measured from the *onset* of the most proximal His bundle potential to the beginning of the earliest atrial potential. H-A_p was measured from the *end* of the most proximal His bundle potential to the onset of the atrial potential in the same electrogram used to measure H-A_t (Fig. 2).

Statistical analysis

Data are listed as mean ± SD. Between and within group comparisons were based on ANOVA, followed by unpaired or paired Student's *t*-test for continuous variables (or nonparametric Kruskal–Wallis or Mann–Whitney testing for not normally distributed values), and chi-square analysis for nominal values. Bonferroni corrections were made to all calculations. Statistical significance was determined as $p<0.05$.

Results

In 327 (95%) of the 344 patients, antegrade conduction during tachycardia occurred over an SP, identified by initiation of tachycardia following abrupt prolongation of the A-H interval or an A-H interval >200 ms during tachycardia. Earliest atrial activation was recorded at the superior (anterior) septum, near the level recording the His bundle potential, indicating retrograde FP conduction (Slow/Fast AVNRT) in 278 (85% of 327 patients with AVNRT using an SP for antegrade conduction and 80.8% of all 344 AVNRT patients). In many of them, there was also early (but later) activation in the roof (superior portion) of the proximal coronary sinus, due to the left-sided insertion of the retrograde fast pathway. Also 2 patients with earliest activation in the mid-septum were considered as Slow/Fast AVNRT since the H-A interval during tachycardia (H-A_t) was very short (≤30 ms). They also did not have a lower common pathway (see below). Earliest atrial activation was recorded at the inferior (posterior) septum or proximal CS, indicating retrograde conduction over a second SP (Slow/Slow AVNRT, Fig. 1) in 44 (13.5% of AVNRT with antegrade SP conduction and 12.8% of all 344 AVNRT patients). In 3 patients, earliest atrial activation occurred simultaneously in the superior and inferior septum (outside the proximal CS or in its inferior part): they were considered as Slow/Slow AVNRT because of an H-A_t interval ≥80 ms. During further analysis they also had criteria for a lower common pathway (see below).

In 17 (4.9%) of 344 patients, the A-H interval during tachycardia was <200 ms (70–175 ms; 124 ± 33 ms). In all but one, earliest retrograde atrial activation was recorded at the inferior septum or proximal and inferior in the CS, indicating use of an SP for retrograde conduction (Fast/Slow AVNRT). A single patient had simultaneous breakthroughs in the superior and inferior septum.

Table 1 summarizes the timing intervals in patients with sustained AVNRT, either during baseline, or after the administration of a low dose (0.25–0.5 μg/min) or high dose (1 μg/min) isoprenaline. As expected, all intervals were longer if AVNRT was induced in the baseline state (sedated). The CL in Slow/Slow AVNRT was slightly longer than in Slow/Fast AVNRT, due to longer H-A_t intervals. However, values of H-A_t overlapped between the 2 subforms in the range of 60–95 m in baseline and −20 to 80 ms with 0.5 μg/min isoprenaline. Values of H-A_t ≤ 10 ms (including negative values) and ≥100 ms occurred only in Slow/Slow AVNRT. With 0.5μg/min isoprenaline, 108/111 (97%) of Slow/Fast AVNRT had an H-A_t ≤ 62 ms (mean + 2 SD), but this was also true in 8/14 (57%) of Slow/Slow AVNRT. These short H-A_t intervals, combined with overlapping atrial and ventricular potentials (masking the retrograde atrial activation sequence) cause Slow/Slow AVNRT often to mimic Slow/Fast AVNRT (Fig. 1B). Table 1 also shows that the conduction time over the retrograde slow pathway clearly shortens with isoprenaline in Slow/Slow AVNRT but not in Fast/Slow AVNRT.

During decremental atrial pacing in the baseline (sedated) state, the shortest pacing cycle length maintaining 1:1 antegrade FP conduction was similar in the three AVNRT subforms (Table 2). There was also no significant difference in the proportion of patients with 1:1 antegrade SP conduction (after Wenckebach block in the FP, 65–81%) or in the shortest CL maintaining 1:1 SP conduction. Retrograde 1:1 FP conduction was present during ventricular pacing at a long CL (usually 800 ms) in the baseline state in 94% of patients with Slow/Fast AVNRT but only in a minority of patients with Slow/Slow (13%) and Fast/Slow (29%) AVNRT

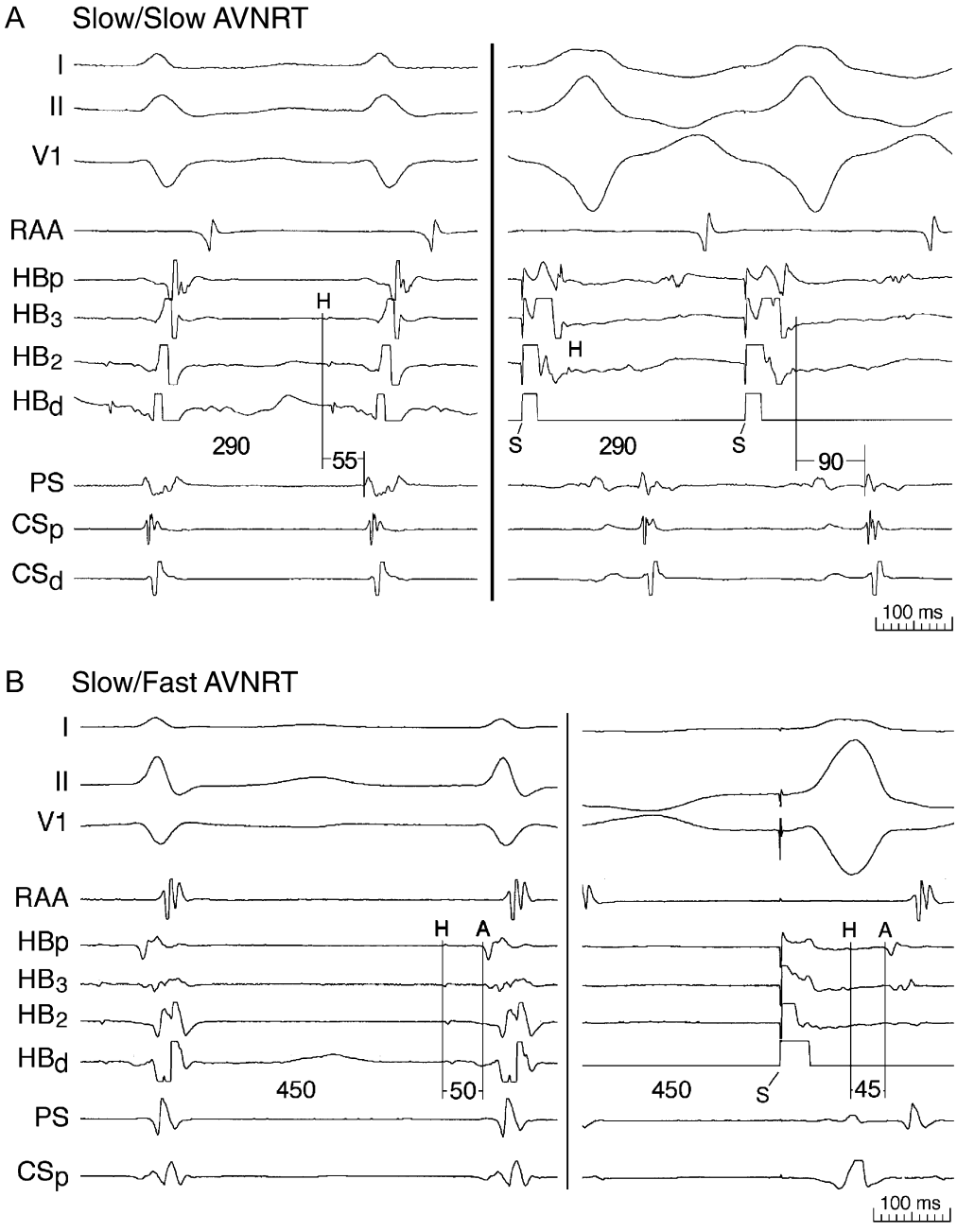

Figure 2 Measurement of H-A_t (left panels) and H-A_p (right panels) in patients with Slow/Slow AVNRT and Slow/Fast AVNRT. A. During Slow/Slow AVNRT (CL 290 ms), the interval from the beginning of the most proximal antegrade His bundle potential (*H*) to earliest atrial activation in the inferior septal area (*A*) was 55 ms (H-A_t). During right ventricular pacing at the same CL (right panel), the interval from the end of the most proximal retrograde His bundle potential (*H*) to earliest atrial activation was 90 ms (H-A_p). The retrograde atrial activation sequence was identical during tachycardia and pacing. ΔH-A was 35 ms, suggesting the presence of a long lower common pathway (LCP). *S*: pacing stimulus. B. Patient with Slow/Fast AVNRT. H-A_p (45 ms) was slightly shorter than H-A_t (50 ms) resulting in ΔH-A of −5 ms. The short H-A_p and negative ΔH-A suggest the absence of a long LCP.

($p<0.0001$). Ventricular pacing at the tachycardia CL (measured immediately after termination of tachycardia) resulted in 1:1 retrograde FP conduction in 144 (98%) of 147 Slow/Fast AVNRT patients tested. Retrograde 1:1 SP conduction was present at the tachycardia CL in 72% of Slow/Slow AVNRT tested but in only one Fast/Slow AVNRT (6%; $p<0.0001$).

Comparisons of the H-A interval during tachycardia (H-A_t) and the H-A interval during ventricular

Table 1 Timing intervals in different subforms of AV nodal reentrant tachycardia

	Tachycardia cycle length (ms)			Tachycardia AH AHt (ms)			Tachycardia HA HAt (ms)			Ventricular pacing HA HAp (ms)			ΔH-A (ms)		
	Baseline	Iso 0.5	Iso 1	Baseline	Iso 0.5	Iso 1	Baseline	Iso 0.5	Iso 1	Baseline	Iso 0.5	Iso 1	Baseline	Iso 0.5	Iso 1
Slow/Fast	408 ± 71 (285–670) $n = 93$	339 ± 49 (265–490) $n = 111$	324 ± 53 (255–510) $n = 28$	364 ± 71 (245–645) $n = 93$	300 ± 54 (215–475) $n = 111$	283 ± 55 (215–450) $n = 28$	45 ± 15 (20–95) $n = 93$	40 ± 11 (15–80) $n = 111$	41 ± 13 (25–75) $n = 28$	45 ± 18 (15–95) $n = 65$	41 ± 16 (15–95) $n = 69$	40 ± 18 (25–75) $n = 9$	−1 ± 7 (−15 to 25) $n = 65$	1 ± 9 (−10 to 30) $n = 69$	−1 ± 7 (−10 to 15) $n = 9$
Vs. baseline		$p < 0.0001$	$p < 0.0001$		$p < 0.0001$	$p < 0.0001$		$p < 0.01$	NS		NS	NS		NS	NS
Vs. Iso 0.5			NS			NS			NS			NS			NS
Slow/Slow	459 ± 65 (335–600) $n = 16$	349 ± 73 (265–560) $n = 16$	367 ± 59 (290–465) $n = 13$	323 ± 52 (200–400) $n = 16$	269 ± 44 (210–355) $n = 16$	292 ± 62 (215–435) $n = 13$	136 ± 65 (60–315) $n = 16$	80 ± 76 (−20 to 330) $n = 16$	75 ± 26 (30–125) $n = 13$	128 ± 52 (60–215) $n = 9$	97 ± 33 (50–170) $n = 11$	88 ± 29 (30–135) $n = 10$	13 ± 12 (0–30) $n = 9$	27 ± 18 (10–70) $n = 11$	16 ± 9 (0–30) $n = 10$
Vs. baseline		$p < 0.0001$	$p < 0.001$		$p < 0.01$	NS		NS	$p < 0.05$		NS	NS		NS	NS
Vs. Iso 0.5			NS			NS			NS			NS			NS
Fast/Slow	385 ± 79 (295–485) $n = 4$	354 ± 37 (305–400) $n = 7$	367 ± 63 (270–425) $n = 5$	135 ± 32 (100–175) $n = 4$	121 ± 32 (75–150) $n = 7$	118 ± 39 (70–175) $n = 5$	250 ± 89 (150–365) $n = 4$	232 ± 64 (160–320) $n = 7$	249 ± 50 (200–325) $n = 5$	–	380 – $n = 1$	–	–	–	–
Vs. baseline		NS	NS		NS	NS		NS	NS						
Vs. Iso 0.5			NS			NS			NS						
ANOVA	$p < 0.05$	NS	$p = 0.05$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	–	–	–	–	–	–
Slow/Fast vs. Slow/Slow	$p < 0.05$	NS	$p = 0.07$	NS	NS	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.001$	$p < 0.0001$	$p < 0.0001$	$p < 0.001$
Slow/Fast vs. Fast/Slow	NS	NS	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$						
Slow/Slow vs. Fast/Slow	NS	NS	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.05$	$p < 0.01$	$p < 0.001$						

Iso 0.5 and Iso 1: isoprenaline 0.25 ($n = 5$) and 0.5 ($n = 141$), respectively, 1 μg/min. Note that data are not paired (the same patient in baseline and with isoprenaline) but constitute different patients (with AVNRT induced during baseline or during 0.5 or 1 μg/min isoprenaline).

Table 2 Characteristics of different subforms of AV nodal reentrant tachycardia

Subform	*n* (%)		Women (%)	Age (years)	Earliest retrograde atrial activation[a]	Shortest cycle length with 1:1 antegrade FP conduction (baseline)	Demonstrable 1:1 antegrade SP conduction (baseline)	Shortest cycle length with 1:1 antegrade SP conduction (baseline)	Demonstrable 1:1 retrograde FP conduction (baseline)	1:1 retrograde SP conduction during ventricular pacing at tachycardia cycle length (immediately after tachycardia)	Evidence of lower common pathway
Slow/Fast	280 (81.4%)		78%	43 ± 16	Superior Septum	543 ± 139 (300–1300)	73%	442 ± 101 (270–1250)	94%	–	10%
Slow/Slow	47 (13.7%)		60%	44 ± 12	Inferior Septum	551 ± 157 (350–1200)	81%	448 ± 102 (290–800)	13%	72%	84%
Fast/Slow	17 (4.9%)		65%	35 ± 14	Inferior Septum	531 ± 210 (270–950)	65%	457 ± 165 (250–750)	29%	6%	100%
Total	344		75%	43 ± 15							
	Slow/Fast	vs. Slow/Slow	0.03	NS		NS	NS	NS	<0.0001	–	<0.0001
	Slow/Fast	vs. Fast/Slow	NS	0.04		NS	NS	NS	NS	<0.0001	NS
	Slow/Slow	vs. Fast/Slow	NS	0.01		NS	NS	NS	<0.0001	–	<0.0001

[a] Two Slow/Fast patients had earliest retrograde atrial activation at the mid-septum. Three Slow/Slow and 1 Fast/Slow patients had simultaneous retrograde breakthroughs in the superior and inferior septum. See Results section for description.

pacing at the tachycardia CL immediately after terminating the tachycardia (H-A_p) are shown for patients with Slow/Slow AVNRT and Slow/Fast AVNRT in Fig. 2. Fig. 3 plots the H-A_t (panel A), H-A_p (panel B) and their difference (ΔH-A, H-A_p − H-A_t, panel C) for Slow/Fast and Slow/Slow AVNRT induced during administration of 0.5 μg/min isoprenaline. H-A_p was similar to H-A_t in Slow/Fast AVNRT under all autonomic conditions (Table 1). In contrast, H-A_p was significantly longer than H-A_t in Slow/Slow AVNRT ($p<0.001$; ΔH-A in Table 1 and Fig 3C). H-A_p was <70 ms in 64/69 (93%) Slow/Fast AVNRT, vs. only 1/11 (9%) Slow/Slow AVNRT (Figs. 2 and 3). H-$A_p \geq 70$ ms had a positive predictive value for Slow/Slow AVNRT of 75%. The average difference between H-A_p and H-A_t (ΔH-A) was 27 ± 18 ms in Slow/Slow AVNRT compared with 1 ± 9 ms in Slow/Fast AVNRT ($p<0.0001$). The H-A was negative in 46 (34%) of 134 Slow/Fast AVNRT patients. Specificity and sensitivity for Slow/Slow AVNRT of ΔH-A $>$ 15 ms were 94% and 64%, respectively (PPV 64%). A reliable comparison of H-A intervals during tachycardia and pacing could be performed in 57% of patients with Slow/Fast AVNRT, 65% in Slow/Slow AVNRT and in only 1/17 Fast/Slow AVNRT. Nonsustained or unstable tachycardia prevented comparison in 37%, 11% and 18% of patients, respectively. A reliable proximal His bundle recording was absent in 3%, 0% and 0%, respectively. Absence of 1:1 retrograde conduction or a different atrial activation sequence during ventricular pacing at the tachycardia CL accounted for the remainder (3% Slow/Fast, 24% Slow/Slow and 76% Fast/Slow AVNRT).

Lower common pathway

Although the specific value of ΔH-A which indicates a long lower common pathway (LCP) is unknown, we arbitrarily chose a value $\geq$15 ms [14]. The ΔH-A was $\geq$15 ms in 21 (70%) of 30 Slow/Slow AVNRT in which ΔH-A could be measured. Other findings suggestive of an LCP (Table 3) were present in 15 of the remaining 22 Slow/Slow AVNRT (total 36 of 48, 84%), including: (a) absence of 1:1 retrograde SP conduction during ventricular pacing at the tachycardia CL immediately after terminating AVNRT (Fig. 4A) suggesting retrograde conduction block between the proximal His bundle and the retrograde limb of the tachycardia circuit, i.e. within the LCP (12/43, 28%); (b) retrograde atrial activation preceding antegrade His bundle activation (negative H-A_t; often during the initial beats of tachycardia, Fig. 4B) due to conduction delay

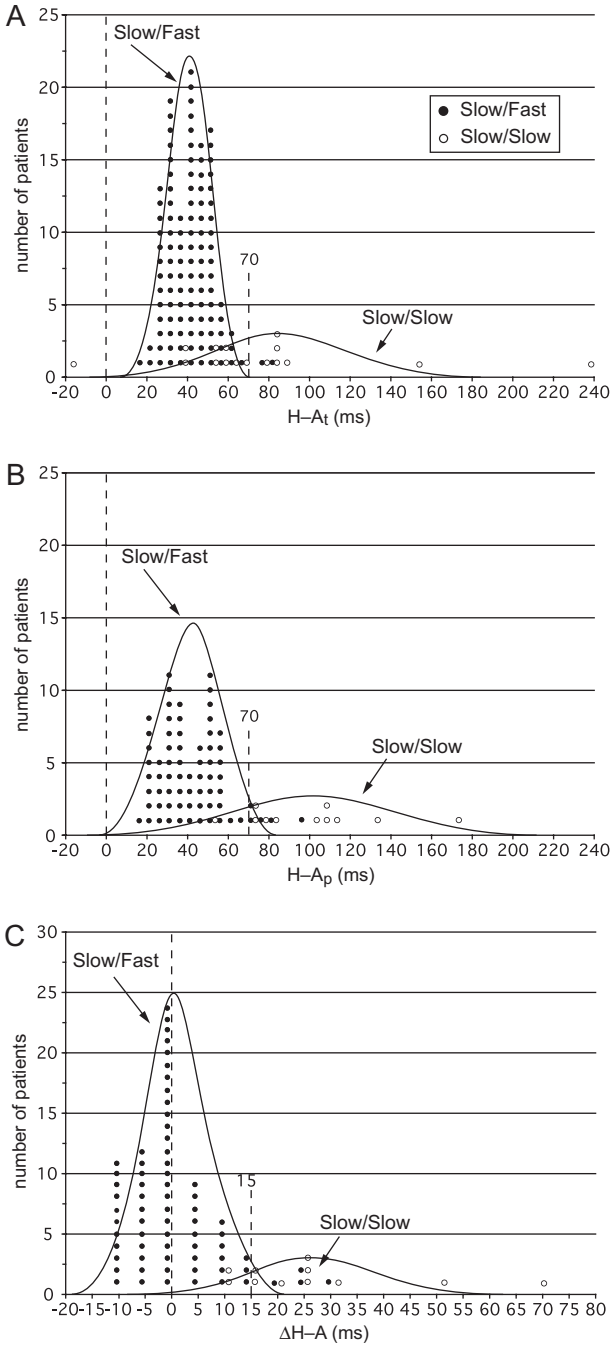

Figure 3 Distribution of H-A interval during tachycardia (panel A; H-A_t), H-A during ventricular pacing at the same cycle length immediately after terminating tachycardia (panel B; H-A_p) and their difference (panel C; ΔH-A = H-A_p − H-A_t) in patients with sustained Slow/Fast (filled circles; $n=111$ in A and 69 in B, C) and Slow/Slow (open circles; $n=14$ in A and 11 in B, C) AVNRT, during administration of 0.5 μg/min isoprenaline. A negative ΔH-A value was observed in none of 11 evaluable Slow/Slow AVNRT but in 23 of 69 Slow/Fast AVNRT (33%).

Table 3 Evidence of lower common pathway in different subforms of AV nodal reentrant tachycardia

Subform	Evaluable patients	ΔH-A ≥ 15 ms	Absent 1:1 retrograde conduction at tachycardia cycle length	''A-before-H''	2:1 Block proximal to His potential during AVNRT	Ventricular extrastimulus advance His potential by ≥20 ms	Total
Slow/Fast	$n = 147$	10 (7%)	3 (2%)	4 (3%)	2 (1%)	1 (0.5%)	15 (10%)
Slow/Slow	$n = 43$	21 (49%)	12 (28%)	4 (9%)	2 (5%)	1 (2%)	36 (84%)
Fast/Slow	$n = 16$	1 (6%)	15 (94%)	5 (3%)	2 (1%)	1 (0.5%)	16 (100%)

between the arrhythmia circuit and the proximal His bundle, i.e. within the LCP (4/43, 9%); (c) 2:1 atrioventricular block prior to His bundle activation during tachycardia (i.e. presumably in the LCP, 2/43, 5%); and (d) ventricular extrastimuli during tachycardia being able to advance the proximal His bundle potential by >15 ms without resetting of the tachycardia (which was formally evaluated in only 1 patient).

In contrast, evidence for an LCP was present in only 10% of tested Slow/Fast AVNRT ($p < 0.0001$; Table 3). Tachycardia with 2:1 atrioventricular block was present in 7 Slow/Fast AVNRT, but block occurred clearly after a proximal His bundle potential in 5 of 7 (Fig. 5) i.e. without evidence of a lower common pathway.

All evaluable patients with Fast/Slow AVNRT had evidence for a long LCP, including absence of 1:1 retrograde SP conduction at the tachycardia CL in 15 of 16 (94%) patients, and a ΔH-A of 60 ms in the remaining patient.

Discussion

Main findings

Our study shows that three subforms of AVNRT are distinguishable on the basis of: (1) atrial activation sequence; (2) timing intervals; and (3) presence or absence of an LCP. The site of earliest atrial activation may be masked in Slow/Fast and Slow/Slow AVNRT due to overlapping of atrial and ventricular potentials, but can be revealed by delivering a late ventricular extrastimulus to the para-Hisian region [10,11] to advance the ventricular potential without advancing the timing of His bundle or atrial activation (and without resetting the tachycardia; Fig. 1B). Defining the site of earliest atrial activation is crucial for identification of the AVNRT subform, since the H-A interval during tachycardia (H-A_t) may be misleading. The fact that earliest atrial activation was shown to be in the inferior septum, despite a short H-A_t interval, may explain a lower proportion of typical Slow/Fast AVNRT in our series than in others.

Evaluation of the ''lower common pathway'' (LCP) and timing intervals

The presence or absence of an identifiable LCP is a matter of ongoing debate [16,17]. The use of ΔH-A to assess the length of the LCP is based upon several assumptions, including that the retrograde conducting pathway and its conduction time are the same during pacing and tachycardia (which also implies a similar autonomic tone); and that the beginning of the most proximal antegrade His bundle potential during AVNRT and the end of the most proximal retrograde His bundle potential during pacing represent activation at the same anatomical site. It is possible that the most proximal antegrade ''His bundle potential'' may even be generated within the AV node, before retrograde activation of the FP during AVNRT. Moreover, the conduction velocity over the retrograde FP may be faster during ventricular pacing (due to activation of the retrograde FP by greater current from the rapidly conducting His bundle than from antegrade conduction over the SP and/or compact AV node) and the change in direction of activation during AVNRT may also lead to delay in activation of the retrograde FP. Any of these factors could account for the negative ΔH-A seen in 46 (34%) of 134 Slow/Fast AVNRT. The major finding, however, is that despite the considerations about the technique, the same methodology revealed no evidence for an LCP in most patients with Slow/Fast AVNRT in contrast to the majority of patients with Slow/Slow and Fast/Slow AVNRT (Table 3). Therefore, assessment of ΔH-A provides information that is useful for characterizing AVNRT subforms.

The large overlap in H-A_t limits its usefulness for distinguishing Slow/Slow from Slow/Fast AVNRT. H-A_p, however, is a better discriminator. The vast

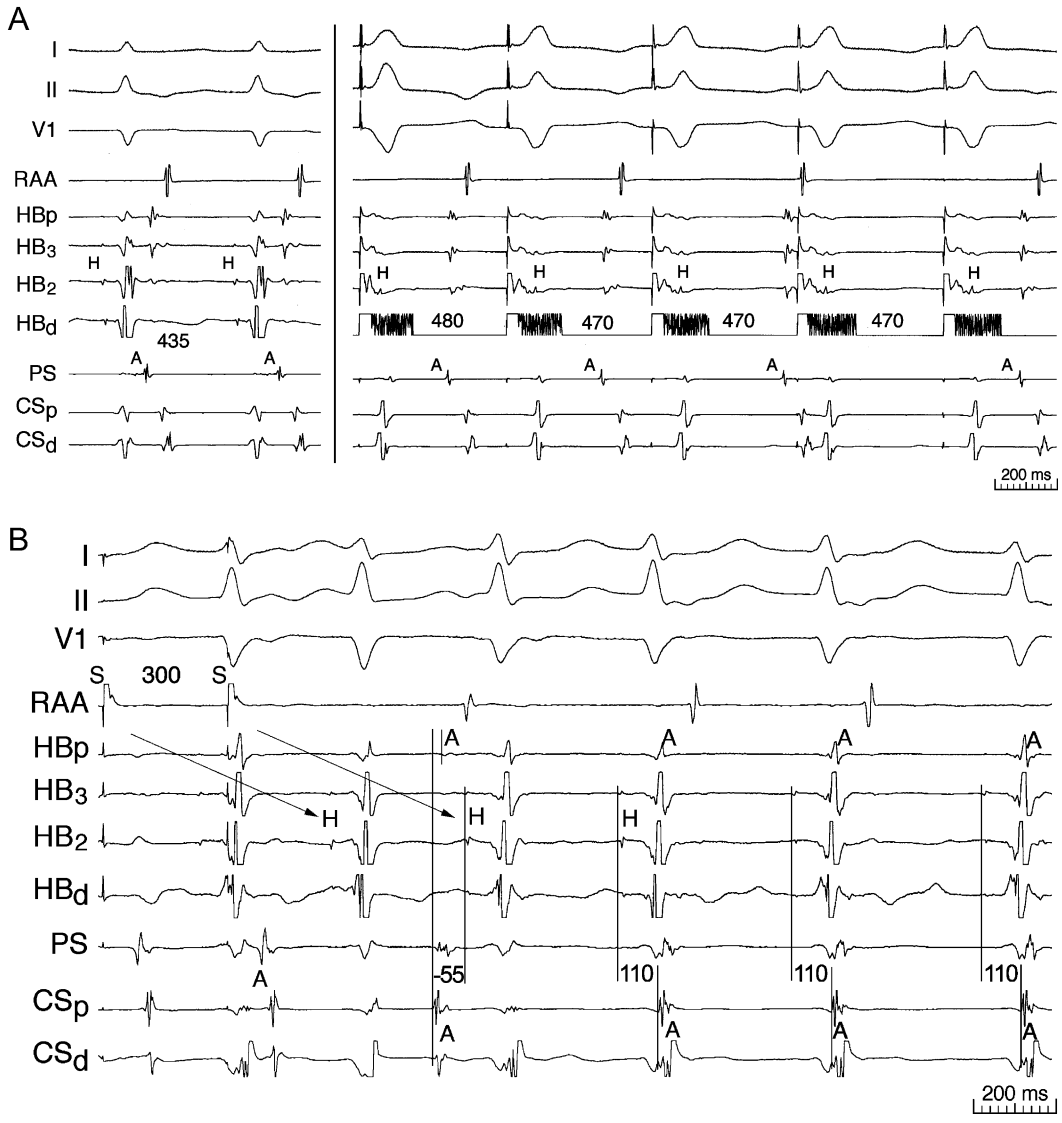

Figure 4 Observations suggesting the presence of a lower common pathway (LCP). A. Absence of 1:1 retrograde AV nodal conduction during ventricular pacing at a cycle length (CL) longer than the tachycardia CL in a patient with Slow/Slow AVNRT. The left panel shows tachycardia with a CL of 435 ms and earliest atrial activation in the inferior septal region. During decremental ventricular pacing with longer CL (480—470 ms) immediately after cessation of tachycardia, there is progressive lengthening of the stimulus-to-atrial interval and Wenckebach-type V-A block. The absence of 1:1 retrograde SP conduction during ventricular pacing is presumed due to delay or block, respectively, between the His bundle and tachycardia circuit, i.e. in the LCP, since the retrograde slow pathway is able to conduct in a 1-to-1 fashion at a CL of at least 435 ms. B. Induction of Slow/Slow AVNRT by rapid atrial pacing, resulting in progressively lengthening A-H intervals (Wenckebach sequence). The two last stimuli (*S*) of a burst of atrial pacing (CL 300 ms) are shown. Retrograde atrial activation of the first tachycardia beat (*A*) preceded antegrade His bundle activation (*H*). Conduction to the His bundle proceeded over the SP (A-H 450 ms), initiating Slow/Slow AVNRT as defined by earliest atrial activation in the proximal CS (CS_p). The first retrograde atrial potentials preceded antegrade His bundle (*H*) activation by 55 ms. In the subsequent beats, atrial activation (with the same activation sequence) followed His bundle activation by 110 ms. The negative initial H-A interval is the result of delay in the timing of His bundle activation (rather than early atrial activation) due to a prolonged conduction time through a long LCP.

majority of patients with an H-$A_p \geq 70$ ms had Slow/Slow AVNRT (sensitivity and specificity of 91% and 93%). Detailed mapping along the septum has shown that the atrial activation sequence may be different during tachycardia and pacing [18]. We only found clearly discordant sequences in 8.9% of the patients (albeit with less detailed mapping), excluding ΔH-A measurements.

Longer ΔH-A intervals for Slow/Fast AVNRT found in earlier studies [19] could be the result of

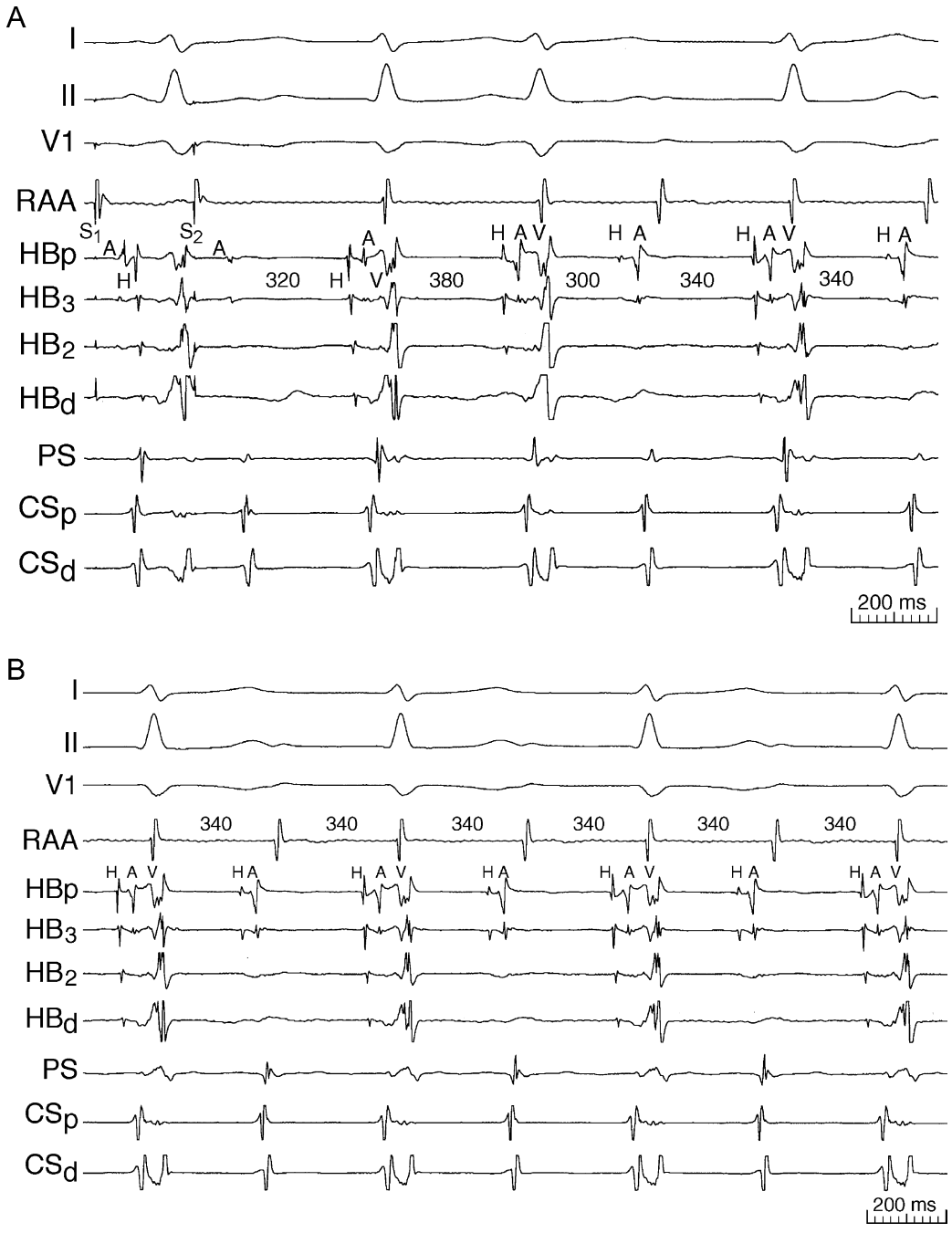

Figure 5 Slow/Fast tachycardia with 2-to-1 infra-His AV block. A. An atrial extrastimulus (S_2) during right atrial pacing (S_1) at CL 600 ms induces Slow/Fast AVNRT (earliest atrial activation at the anterior septum). Oscillations in the A-H interval lead to A-V block in the beats with shorter H-H intervals (beats 3 and 5 of the tachycardia). The proximal His bundle potential (*H*) is recorded in the blocked complexes. B. Later during tachycardia the CL stabilized but 2:1 block persisted. Recordings of the His bundle/proximal right bundle branch confirm the block distal to the proximal HB potential. C. A ventricular extrastimulus (*S*) results in early retrograde activation of the HB. The subsequent lengthened H-H interval (315 ms) enables resumption of 1:1 conduction (but with persistent left bundle branch block).

differences in methods. The further distal the end of the retrograde His bundle potential is measured during ventricular pacing, the larger the H-A_p, and therefore the larger the ΔH-A. During previous studies, pacing was performed in the RV apex: due to overlap with local ventricular activation, only a larger retrograde His bundle deflection can be discerned, which will often not be the most proximal electrogram. Pacing from the para-Hisian region provides the greatest separation of the retrograde His bundle potential from the local ventricular potential, allowing the recording of the

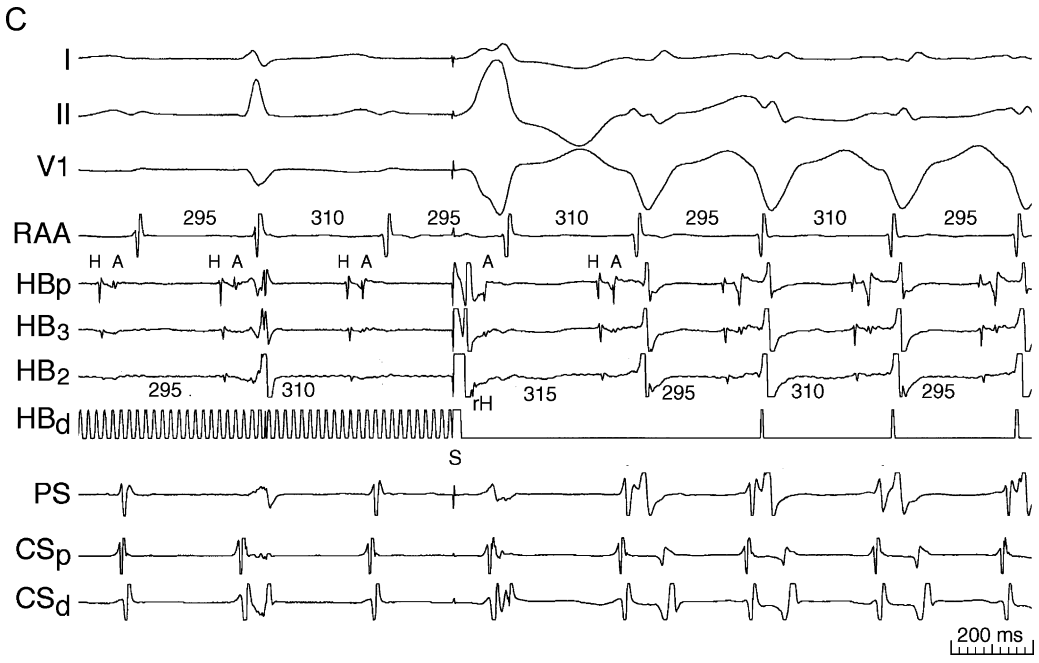

Figure 5 (*continued*).

end of the most proximal His bundle potential. We also initiated ventricular pacing immediately upon terminating AVNRT to minimize changes in autonomic tone, which may result in shorter H-A_p.

The findings in this study suggest the absence of an identifiable LCP is a classical finding in ''typical Slow/Fast AVNRT''. The presence of a long LCP in Slow/Slow AVNRT explains the frequent occurrence of a short H-A interval. It also demonstrates that Slow/Slow AVNRT is not a variant of Slow/Fast AVNRT with a inferior exit.

Although our findings help to distinguish different subforms of AVNRT, they cannot resolve the precise anatomical location of the reentrant circuits, and whether the differences are mainly due to anatomical or functional factors (like non-uniform anisotropy) [20]. Functional conduction slowing and block occur at the junctions between the different types of tissue in the AV nodal area and are highly dependent on the direction of activation of the compact node—transitional cell junction region [21]. Previous studies have shown that the superior septal input to the AV node is closer to the proximal His bundle than the inferior septal inputs [22]. For AVNRT with earliest atrial activation in the inferior septum, both antegrade and retrograde conduction may occur over separate (functional) slow pathways. The anatomical correlate for multiple slow pathways could be rightward and leftward inferior extensions of the AV node [7]. It is conceivable that when the arrhythmia circuit is comprised only of tissue in the inferior septal region (rightward and/or leftward) as in Slow/Slow AVNRT, it may be separated by more tissue (or more slowly conducting tissue) from the beginning of the His bundle (i.e. a longer LCP) than when the fast pathway forms the retrograde path.

An expanded definition scheme

Based on the observations mentioned above, the three AVNRT subforms can be better defined. An essential aspect in this scheme is that identification of the retrograde pathway during AVNRT is based on the site of earliest atrial activation and *not* on the H-A interval during tachycardia (H-A_t). H-A_t is a composite measurement: it does not only depend on the conduction time over the retrograde pathway but also on the antegrade conduction time over the LCP (for a scheme, see Ref. [15]). H-A_t can be confusingly short despite retrograde conduction proceeding over a slow pathway (like in Slow/Slow AVNRT). The described timing intervals are also dependent on autonomic tone and should be extrapolated cautiously, dependent on the electrophysiological measurement setting (type and degree of sedation, isoprenaline, atropine, ...).

Slow/Fast AVNRT: (1) antegrade conduction occurs over an SP, with an A-H interval during tachycardia of $\geq$200 ms; (2) retrograde conduction proceeds over the FP, manifest by earliest atrial activation in the superior septum, above the tendon of Todaro [6]; (3) H-A_p is $<$70 ms; and (4) there is

generally no evidence for an LCP. Using these criteria, 77% of the arrhythmias in our cohort would fit this definition.

Slow/Slow AVNRT: (1) antegrade conduction occurs over an SP (A-H interval $\geq$200 ms); (2) retrograde conduction over an SP with earliest atrial activation in the inferior septum or proximal CS; (3) H-A_p usually $\geq$70 ms; and (4) evidence for a significant LCP. AVNRT fitting these criteria comprised 11.6% of the present population.

Fast/Slow AVNRT: (1) an A-H interval $<$200 ms (indicating antegrade conduction over the FP); (2) earliest atrial activation at the inferior septum; and (3) the presence of an LCP (usually manifest by the absence of 1:1 retrograde SP conduction at the tachycardia cycle length). These tachycardias comprised 4.9% of our population. The reentrant circuit in Fast/Slow AVNRT has previously been thought to be the reverse of the circuit in Slow/Fast AVNRT. Reverse Slow/Fast would not be expected to incorporate a long LCP. However, in all patients with Fast/Slow AVNRT there was evidence for an LCP. This suggests that Fast/Slow AVNRT may not utilize the FP for antegrade conduction and therefore may be more closely related to Slow/Slow AVNRT. In support of the latter view is the observation that many episodes of Fast/Slow AVNRT are initiated following a sudden A-H prolongation (indicating antegrade conduction over a slow pathway) [23] which shortens during the ensuing beats. On the other hand, we noted that the conduction time over the retrograde SP shortened with isoprenaline in Slow/Slow AVNRT but not in Fast/Slow AVNRT. We have no clear explanation for this finding.

Finally, in 6.5% of the patients, inconsistent findings were observed. They comprised patients: (a) with antegrade conduction over an SP and earliest atrial activation at the inferior septum or proximal CS (like Slow/Slow AVNRT) but without evidence of an LCP; or (b) antegrade conduction over an SP and earliest atrial activation at the superior septum (like Slow/Fast AVNRT), but with evidence of a long LCP. Since these arrhythmias do not unambiguously fit any of the above categories, we prefer to list them as ''Undetermined'' (or truly atypical) AVNRT until more insight into the arrhythmia circuits emerges.

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