Corrected Sinus Node Recovery Time

Experimental Physiologic and Pathologic Determinants

By Kul D. Chadda, M.D., Vidya S. Banka, M.D., Monty M. Bodenheimer, M.D., and Richard H. Helfant, M.D.

SUMMARY

To determine the factors affecting reproducibility of sinus node recovery time, the effects of basic pacing rate, pacing duration, milliamperage, vagal and beta-adrenergic stimulation, and sinus node injury, as well as its instantaneous and daily reproducibility, were studied in 36 anesthetized dogs. Corrected sinus node recovery time (CSNRT) showed a mean variation of 9.8 ± 0.4 msec at an atrial pacing rate of 200 beats/min and 29.8 ± 8 msec at an atrial pacing rate of 140 beats/min (P < 0.05). CSNRT increased progressively from 55.4 ± 10 msec to 103.7 ± 13 msec with increase in pacing rate from 140 beats/min to 200 beats/min. It was reproducible when atrial pacing was carried out for 1–5 min, although a wide variation (10–30 msec) was seen from 7–60 minutes (P < 0.05). This measurement was reproducible on two consecutive days and was unaffected by changes in milliamperage. Vagal stimulation consistently prolonged the CSNRT while beta-adrenergic stimulation decreased it from 132.9 ± 34.5 msec to 50.0 ± 6.5 msec. Sinus node injury consistently prolonged CSNRT at all paced rates.

In summary, CSNRT is reproducible only if the same pacing rate and duration are utilized. Since vagal stimulation and sinus node injury prolong this measurement while beta-adrenergic stimulation shortens it, an "abnormal" CSNRT should be assessed in terms of the possible influence of the autonomic nervous system as well as sinus node dysfunction per se.

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SINCE THE ORIGINAL DEMONSTRATION that intact pacemakers are suppressed by tetanic stimulation,¹ the phenomenon has been studied in both isolated atrial tissue² and intact animals.³ More recently clinical studies have focused on the response of the human sinoatrial node to atrial pacing at rapid rates. Several investigators have used this method to determine the time required for a sinus beat to resume following cessation of atrial pacing. This "sinus node recovery time" has been utilized in the evaluation of sinoatrial node dysfunction in normal individuals,⁴ ⁵ and patients with "sick sinus" syndrome.⁶ ⁷ However, the methodology of these clinical studies has varied as have the results.

The present study was, therefore, undertaken to experimentally define both the physiologic and pathologic determinants and the reproducibility of sinus node recovery time in the intact dog heart.

Methods and Materials

Experiments were performed on 36 mongrel dogs weighing 15–30 kg anesthetized with pentobarbital sodium (30 mg/kg) intravenously. The trachea was intubated and positive pressure respiration employed using a Harvard pump. A bipolar electrode (#5 or #6 French) catheter was introduced percutaneously via the right or left femoral vein and positioned in the high right atrium.

All recordings were made utilizing a multichannel recorder at a paper speed of 100 mm/sec. Lead II of the surface electrocardiogram was recorded as a baseline and atrial pacing performed with a battery powered Medtronic model 5837 pacemaker.

The reproducibility of each observation was assessed by repeating each individual measurement three times. The mean of the variation in the three observations at each rate before sinus node injury was compared to the mean variation after sinus node injury. All measurements were performed either 15 minutes after the previous observation had been made or when the heart rate had returned to baseline values.

In all experiments determination of sinus node recovery time was made by measuring the time from the last paced atrial complex to the following spontaneous "sinus" beat. Corrected sinus node recovery time (CSNRT) was determined by subtracting the penultimate P-P cycle length from the sinus node recovery time.⁸

From the Division of Cardiology, Presbyterian-University of Pennsylvania Medical Center, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Dr. Chadda's present address is Mount Sinai Hospital Services, 7901 Broadway, Elmhurst, New York 11373.

Address for reprints: Richard H. Helfant, M.D., Chief, Division of Cardiology, Presbyterian-University of Pennsylvania Medical Center, 51 North 39th Street, Philadelphia, Pennsylvania 19104.

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Effect of Pacing Rate, Duration, and Milliamperage

After obtaining initial records, the effect of increasing heart rate on sinus node recovery time was assessed by atrial pacing with incremental increases from 140–200 beats/min. At each incremental increase in pacing rates atrial pacing was performed for 5 min at 2 ma; these variables were kept constant for each pacing rate. The effect of duration of pacing on sinus node recovery time was studied by pacing at 200 beats/min at 2 ma for periods of 1–60 minutes in successive experiments, with sinus node recovery time determined at the end of each time period. The effect of ma threshold was determined by atrial pacing at 200 beats/min for 5 min at ma ranging between 2–10.

Daily Reproducibility

Experiments were repeated on the same animal for two consecutive days to determine the daily variability and reproducibility of the results. The animals were allowed to recover after the study on the first day and were reanesthetized on the second day. Atrial pacing was performed at a rate of 200 beats/min for 5 min and 2 ma in each of these experiments.

Effect of Acute Sinus Node Injury

The effect of acute sinus node injury on the reproducibility of sinus node recovery time was also studied. During these experiments, the animal was anesthetized and intubated as described earlier. In addition, the chest was opened via midsternal incision and the pericardium incised to form a cradle. Sinus node recovery time determinations were made according to the previously indicated protocol followed by partial crush of the sinoatrial node with a clamp. Electrical injury to the sinus node was recognized to be present when sinus node crush resulted in the appearance of transient junctional rhythm persisting for 3–5 min. Sinus rhythm return after this time period was determined by the presence of similar P wave morphology and P-R interval as in the control electrocardiogram prior to the crush. Only those experiments in which sinus rhythm returned were included in the study.

Effect of Vagal Stimulation

The cervical vagi were exposed and transected in the neck. The distal portions were stimulated via two attached teflon-coated stainless steel wires. The effect of vagal stimulation was evaluated with atrial pacing at a rate of 200 beats/min for 5 min and 2 ma before and during vagal stimulation performed by an electrical stimulator, American Electronic Laboratories, Model No. 104A, which provided 9.0 mV stimuli at a frequency of 20/sec and an impulse duration of 2.5 msec to either one or both vagi.

Effect of Beta-adrenergic Stimulation

Effects of beta-adrenergic stimulation were evaluated by comparing the CSNRT determined by atrial pacing at 200 beats/min for 5 minutes at 2 ma in each study. Beta-adrenergic stimulation was produced by intravenous infusion of isoproterenol in a dose response fashion and the range (0.5 to 2.0 μg/min) was derived from the dosage used to achieve a clearcut heart rate increase of at least 20 beats/min. After stabilizing the heart rate for 5 min on isoproterenol, CSNRT was determined.

The effect of change in atrial pacing rate, duration of atrial pacing, and milliamperage was studied in the same group of 14 dogs. In ten of these 14 dogs, sinus rhythm returned after sinus node crush and the effect of sinus node injury was determined. Daily variation, vagal stimulation, and beta-adrenergic stimulation were performed in separate groups of animals.

Statistical analysis was performed by using Student's t-test for paired values.

Results

Effect of Atrial Pacing Rate (14 Experiments)

Figure 1 shows the effects of atrial pacing rate on the CSNRT both before and after sinus node injury. The control mean sinus rate was 142 ± 12 beats/min before and 150 ± 18 beats/min after partial sinus node crush. The mean CSNRT before sinus node injury was 55.4 ± 10 msec when atrial pacing was performed at a rate of 140 beats/min and it increased progressively to 103.7 ± 13 msec (P < 0.001) as atrial pacing rate was increased to 200 beats/min (fig. 1). A similar progressive increase in CSNRT from 107.5 ± 15 to 359 ± 94 msec (P < 0.001) occurred when experiments were repeated at similar pacing rates after partial sinus node crush (fig. 1). In addition the CSNRT after sinus node injury was significantly higher (P < 0.001) than that before sinus node crush at each pacing rate (fig. 1).

Reproducibility (Ten Experiments)

Reproducibility of CSNRT occurred with minimal variation at an atrial pacing rate at 200 beats/min...
both before and after sinus node injury. As shown in figure 2, the mean variation in CSNRT before sinus node injury was 9.8 ± 0.4 msec (maximum variation ± 12 msec) with atrial pacing rate at 200 beats/min. At the lowest atrial pacing rate tested (140 beats/min), the variation was much greater: 29.8 ± 8 msec (maximum variation ± 70 msec) with atrial pacing at 140 beats/min. This difference in reproducibility at the two extremes of pacing rates, which was statistically significant ($P < 0.05$), shows that variation is less when higher pacing rates are used.

When experiments were repeated after sinus node crush, the mean variation of these extremes of pacing rates was 9.8 ± 4 msec (maximum variation ± 30 msec) at 200 beats/min and 40.0 ± 16 msec (maximum ± 120 msec) at 140 beats/min. However, this difference was not statistically significant.

**Daily Variation and Reproducibility (Six Experiments)**

Figure 3 shows the effects of daily variation and reproducibility when experiments were repeated for two consecutive days on the same experimental animal. This ranged from no variation to a maximum of 60 msec. The mean CSNRT changed insignificantly from 104.7 ± 26.4 to 92.7 ± 30.6.

**Effect of Duration of Atrial Pacing (14 Experiments)**

Figure 4 shows the effect of duration of atrial pacing at 200 beats/min and 2 ma on CSNRT. With atrial pacing lasting from 1 to 5 min, the mean CSNRT remained 150 ± 34 msec. This was reproducible without any variation. However, there was a wide variation in the mean CSNRT with atrial pacing from 7-60 min ($P < 0.05$).

![Figure 2](http://circ.ahajournals.org/)

**Figure 2**

Variability of CSNRT before and after sinus node injury (SNI) in ten experiments. Open bars represent findings at an atrial pacing rate of 140 beats/min; striped bars, at 200 beats/min. The difference after SNI was not statistically significant. $I = $ Standard error of mean.

**Effects of Pacing Amperage (Five Experiments)**

With atrial pacing at 200 beats/min for 5 min and degree of stimulation varying from 2 to 10 ma, no significant change in CSNRT was noted.

**Effects of Vagal Stimulation (Nine Experiments)**

Figure 5 shows the effect of vagal stimulation in individual experiments. This intervention consistently prolonged the CSNRT both before and after sinus node injury. Before sinus node injury the CSNRT increased from 44.0 ± 12.1 to 52.1 ± 13.3 ($P < 0.05$). After sinus node injury it showed an increase from 122.5 ± 28.4 to 300.0 ± 35.8 ($P < 0.05$) msec.

**Effect of Beta-adrenergic Stimulation (Seven Experiments)**

Figure 6 demonstrates the effect of isoproterenol infusion on the CSNRT in individual experiments. Mean CSNRT decreased from 132.9 ± 34.5 msec to 50.0 ± 6.5 msec ($P < 0.05$). An increase in heart rate is indicated by simultaneous decrease in P-P interval from 484.3 ± 30.3 to 341.4 ± 8.8 msec ($P < 0.01$).
Discussion

Sick sinus syndrome comprises a wide spectrum of clinical, electrocardiographic, and pathological abnormalities. Although sinus bradycardia is a common manifestation of this syndrome, a normal or even rapid heart rate may also occur. The effects of various interventions including exercise, isoproterenol, and atropine, have been utilized in the diagnosis of sick sinus syndrome. More recently studies have focused on the value of CSNRT in making this diagnosis. The corrected sinus node recovery time, determined after a period of overdrive suppression, is based on the assumption that the first escape beat after pacing does in fact originate in the sinus node and not from another atrial focus. No direct evidence has been sought to support this assumption. In addition, since the sinus node is affected by various physiological as well as pathological influences, these factors could critically affect both CSNRT and the reproducibility of this measurement.

The results of the present study confirm that rapid atrial pacing suppresses sinus node activity. The finding in this study of a linear increase in CSNRT with increments in atrial pacing rate is also in agreement with a previously reported study but differs from another study, in man, that reported a rapid decline in sinus node recovery time at pacing rates of 150 beats/min. The explanation of this difference is unclear. It may reflect an increase in sympathetic tone in patients at this pacing rate.

Prior reports have not reported on the reproducibility of these data at varying pacing rates. As shown in figure 1 maximum suppression of sinus node activity occurs at the highest pacing rates. Of additional importance is the finding that the results obtained at these high rates are reproducible with minimal variation. At slower rates the CSNRT varied widely (fig. 2).

The linear increase in CSNRT with increments in atrial pacing rates persists after partial sinus node injury. However, the mean CSNRT after sinus node injury is longer with pacing at both 140 beats/min and 200 beats/min when compared with the results obtained at these rates before sinus node injury (fig. 1).

In a large series reported by Narula, CSNRT was reproducible after 7½ months in one of these patients. The results of the present study indicate that CSNRT is reproducible with minimal variation when studies are performed on consecutive days (fig. 3) in the same animal. CSNRT was also reproducible in successive experiments when the length of atrial pacing varied from 1–5 min. However at longer intervals of pacing — 7, 10, 15, 30, or 60 min — the values obtained for CSNRT varied widely (fig. 4). The reason for the difference of results obtained at 7 and 10 min of atrial pacing is unclear. The gradual decline in the mean CSNRT apparent with atrial pacing for 15, 30, or 60 min may be explained by a temporary resetting of the

Figure 5
Effect of vagal stimulation on CSNRT in individual experiments.

Figure 6
Effect of beta-adrenergic stimulation (isoproterenol infusion) on CSNRT in individual experiments. Mean CSNRT decreased from 132.9 ± 34.5 msec to 50.0 ± 6.5 msec (P < 0.05). Increase in heart rate is indicated by simultaneous decrease in P-P interval from 484.3 ± 30.3 to 341.4 ± 8.8 msec. (P < 0.01).
intrinsic pacemaker at a more rapid rate. The present study confirms the results of Mandel et al. that pacing amperage has no significant effect on the CSNRT.

Increased vagal tone is known to augment postdrive depression by its effect on pacemaker cells. In the present study a consistent prolongation of the CSNRT was induced by vagal stimulation in the normal as well as the injured sinus node (fig. 5). Recent studies by Spear and Moore have demonstrated that brief vagal stimuli inhibit sinus node pacemaker activity.

In conclusion, the results of the present study indicate that CSNRT is a reproducible measurement with minimum daily variability, particularly at high paced rates, in both the normal and injured sinus node. However this measurement is significantly affected by induced changes in vagal and beta-adrenergic tone, changes which are similar to those brought on by sinus node injury. These findings are of potential clinical significance. A finding of an "abnormal" CSNRT should be evaluated in terms of the influence of the autonomic nervous system before concluding that sinus node dysfunction per se caused the abnormality.

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