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COMPARISON OF DIRECT AND INDIRECT DETERMINATIONS OF THE SINUS NODE RECOVERY TIME

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High-frequency atrial stimulation is used in the diagnosis of the sick sinus syndrome [1, 5-7]. During atrial stimulation activity of the sinus node is considered to be suppressed and is not restored until a short time has elapsed after the end of stimulation [5, 6]. This time is called the sinus node recovery time (SNRT) and is regarded as an indicator of the functional capacity of the sinus node: In patients with a sick sinus syndrome SNRT is greater than normally. In clinical practice SNRT is determined indirectly from the atrial activity recovery time. Hence the great importance of the question of how correctly the atrial activity recovery time reflects the recovery time of the sinus node itself, how the sinus node functions during atrial stimulation, how the atrial activity recovery time depends on the character of activity of the sinus node during atrial stimulation with different frequencies. The investigation described below was devoted to a study of these problems.

EXPERIMENTAL METHOD

Experiments were carried out on the frog *(Rana temporaria)* heart. The sinus venosus was isolated together with the atria, unfolded to form a tissue slab, and placed in Ringer's solution, pH 7.2.

Electrical potentials were recorded by means of suction electrodes with a tip not more than 100 μ in diameter. The potentials were recorded on an ELKAR electrocardiograph. The atria were stimulated extracellularly by above-threshold square pulses 5 msec in duration from a "Physiovar" stimulator. The frequency of stimulation was higher than the spontaneous frequency of excitation of the preparation and was 37.5, 43, 50, 63, and 77 ± 4 beats/min. Stimulation at each frequency lasted 30-40 sec, after which the preparation was excited for 20-30 sec in its intrinsic rhythm.

The experimental results were analyzed by Student's t test.

EXPERIMENTAL RESULTS

In 11 experiments atrial stimulation was carried out as mentioned above. During atrial stimulation the imposed frequency was completely bound. In all experiments the sinus venosus continued to be excited during atrial stimulation (Fig. 1 and 2) but the frequency of its excitation varied depending on the frequency of atrial stimulation. The mechanism of changes in the frequency of the sinus venosus was examined previously [2].

During atrial stimulation at a frequency 20-30% higher than the intrinsic frequency of the preparation, the sinus venosus of all the preparations switched to the frequency of stimulation. An example of one such experiment is given in Fig. 1. The spontaneous frequency

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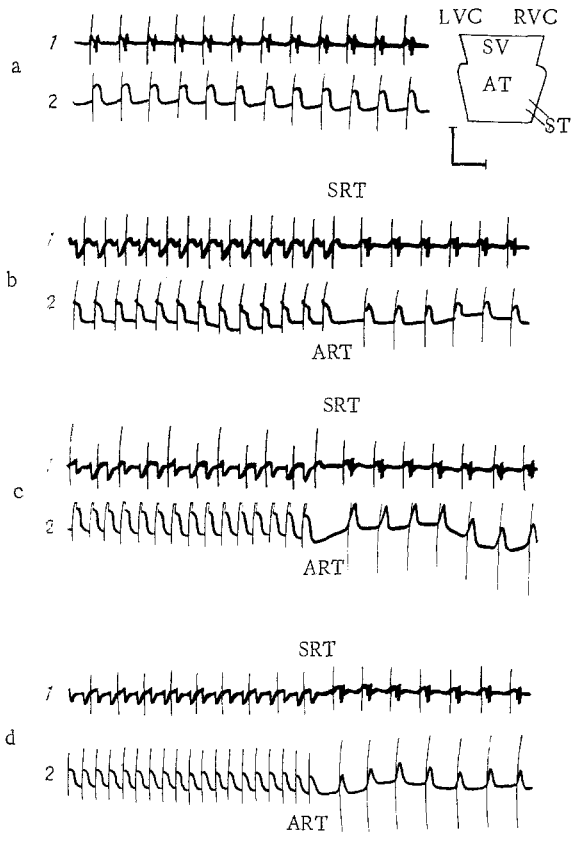

Fig. 1. Changes in frequency of sinus venosus and atrial recovery time (ART) during atrial stimulation at different frequencies. Traces of extracellular action potentials without stimulation (a, right hand sides of traces in b, c, d) and during stimulation with different frequencies (left hand sides of traces in b, c, d). 1, 2) Recording from sinus venosus and atria recpectively. LVC) Left vena cava; SV) sinus venosus; AT) atrium; ST) stimulating electrodes. Calibration: horizontally 2 sec, vertically 10 mV.

of excitation of the preparation was 34.7 beats/min (T = 1730 msec; see Fig. 1a). During atrial stimulation with a frequency of 50 beats/min excitation of the sinus venosus took place with the same frequency (see Fig. 1b).

If the frequency of stimulation exceeded the intrinsic frequency of the preparation by 30-60%, the sinus venosus of some preparations switched to an irregular rhythm, and of others to the frequency of stimulation. When the frequency of stimulation exceeded the spontaneous frequency by 70-90%, the sinus venosus of all preparations was excited irregularly. After a frequency of 63 beats/min had become bound on the atria (T = 950 msec) the sinus venosus changed to an irregular rhythm, and bigeminy developed: A long interval (1650 msec) was replaced by a short (1250 msec), and vice versa (Fig. 1c). For every three excitations of the atria, there were two of the sinus venosus.

If the frequency of stimulation exceeded the spontaneous frequency of the preparation by more than 100%, the sinus venosus of all preparations changed to a frequency which was only half that of the frequency of stimulation. Atrial stimulation with a frequency of 77 beats/min (T = 780 msec) caused the sinus venosus to switch to a frequency of 38.5 beats/min (Fig. 1d). After the end of stimulation the sinus venosus switched to its previous initial rhythm. The interval between the last excitation during stimulation and the first spontaneous excitation differed both from the period of stimulation and the period of spontaneous excitations. During this time there was evidently a reorganization of the structure of the automatic processes determining the frequency of the sinus venosus. This time interval may be called the sinus reorganization time (SRT). SRT is a basic parameter which it would be useful to know in clinical practice. However, it is impossible to measure SRT clinically because there are no methods capable of recording electrical activity of the sinus node during

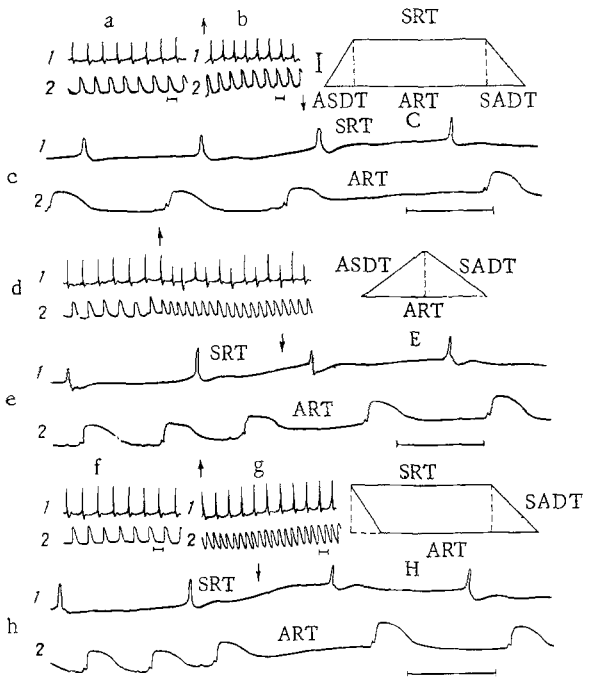

Fig. 2. Correlation between direct and indirect determination of SNRT. Traces of extracellular action potentials. Upward arrow — beginning of stimulation (b, d, g); downward arrow — end of stimulation (c, e, h). 1, 2) Recordings from sinus venosus and atria respectively. Calibration: horizontally 1 sec, vertically 10 mV.

atrial stimulation. It has been suggested that SNRT reflects SRT correctly. In clinical practice, the time interval between the last P wave arising during stimulation and the first spontaneous depolarization on the intra-atrial electrogram is taken as the SNRT [5]. Under the present experimental conditions, the time between the last atrial excitation evoked by stimulation and the first atrial excitation at the spontaneous rhythm, or the atrial recovery time (ART), corresponds to SNRT. Let us examine how correctly ART reflects SRT and what relationship exists between ART and SRT.

In the experiments changes in SRT were very small. The difference between the maximal and minimal values of SRT was not significant ($P > 0.05$), but the highest and lowest values of ART differed significantly ($P < 0.001$). In the experiment illustrated in Fig. 1, SRT was independent of the frequency of stimulation and remained at 1600 msec, whereas ART after atrial stimulation with a frequency of 50 beats/min was 2500 msec, after stimulation with a frequency of 63 beats/min it was 2700 msec, and with stimulation at a frequency of 77 beats/min it was 1800 msec. To understand what caused the sharp decrease in SRT in the last case, let us examine what are its components. If during stimulation the sinus venosus was excited with a frequency equal to the frequency of stimulation, for every excitation of the atria there must be one excitation of the sinus venosus. The interval between excitation of the atria and excitation of the sinus venosus can be called the atrium-sinus delay time (ASDT) (see the scheme in Fig. 2c). After the end of stimulation spontaneous activity of the sinus venosus was restored. The first spontaneous excitation of the sinus venosus was conducted to the atria during the sinus venosus—atrium delay time (SADT). It will be evident that

$$ART = ASDT + SRT + SADT. \quad (1)$$

In the example given in Fig. 2, in scheme C, it will be clear that SRT = 2350 msec: This was actually the sum of ASDT = 340 msec + SRT = 1560 msec + SADT = 440 msec. In this example the spontaneous frequency of excitation of the preparation before stimulation was 34 beats/min (Fig. 2a). Atrial stimulation with a frequency of 43 beats/min caused the sinus venosus to change to this frequency (Fig. 2b).

At higher frequencies of atrial stimulation the sinus venosus began to be excited irregularly, but with a further increase in frequency, for every two atrial excitations there was one excitation of the sinus venosus. ART under these circumstances began to depend on yet another parameter, namely the time when stimulation ceased. Cessation of stimulation before the occurrence of excitation of the sinus venosus led to shortening of ART, for the last excitation of the atria evoked by stimulation was not followed by excitation of the sinus venosus. The relationship (1) between ART and SRT was disturbed under these circumstances. In Fig. 2f the frequency of the preparation before stimulation was 34 beats/min and stimulation with a frequency of 77 beats/min led to a switch of the sinus venosus to a frequency of 38.5 beats/min (Fig. 2g). Stimulation was stopped at a moment before excitation of the sinus venosus occurred, and for that reason atrial excitation evoked by stimulation took place after excitation of the sinus venosus (Fig. 2h). As a result, ASDT = 360 msec became negative and had to be subtracted from the sum of SRT = 1660 msec + SADT = 560 msec, i.e.,

$$ART = SRT + SADT - ASDT. \quad (2)$$

This means that ART, with a value of 1860 msec, consisted of SADT and only part of SRT. Similar shortening of ART also was observed in the experiment illustrated in Fig. 1d.

A decrease in ART also was observed in cases when the sinus venosus was excited irregularly during stimulation. This irregularity was usually well described by a Wenckebach phenomenon. In this case, for every three atrial complexes there were two sinus complexes. The delay time ASDT assumed two values in succession, namely 430 and 800 msec, after which excitation of the sinus venosus occurred. When stimulation ceased the sinus venosus was excited 800 msec after its end, after the last atrial complex, but then this excitation was conducted with a delay of 600 msec to the atria (Fig. 2e). In that case ART = 1400 msec was equal to the sum of two delays: ASDT = 800 msec and SADT = 600 msec, and SRT = 1320 msec was not a component of ART at all, i.e.,

$$ART = ASDT + SADT. \quad (3)$$

It can be concluded from the results of these experiments that SRT characterized the process of recovery of the pacemaker node itself and is a stable value. Conversely, ART is composed of several parts (see equations 1, 2, and 3). The type of dependence of ART is determined by the character of working of the sinus venosus during stimulation. When the sinus venosus during atrial stimulation switches to the frequency of stimulation, ART is determined by equation (1). If, however, the sinus venosus was excited irregularly during stimulation or if for every two atrial excitations there was one excitation of the sinus venous, ART was determined by one of the equations (1, 2, or 3). Depending on the time when stimulation ceased, ART could assume different values and could distort information about SRT. It will be recalled that ART corresponds to SNRT, as measured under clinical conditions.

Since the experiments were conducted on an isolated preparation of pacemaker and atria, the influence of the extracardial nervous system on the values measured was ruled out. Our results provide no information on the role of the intracardial nervous system in the effects observed.

The view that in man also the frequency of activity of the sinus node is influenced by the rhythm of activity of lower regions of the heart is supported by a clinical observation described in the literature [3]. In 14 patients with complete AV block ventricular stimulation by means of an implanted pacemaker led to a switch of the sinus node to a frequency close to the frequency of stimulation. If the frequency of stimulation differed only very slightly from the frequency of the sinus node, a complete switch of the sinus node to the frequency of stimulation was observed.

Using this analogy we can explain a number of unexplained clinical observations: Mandel et al. [6] observed an unexpected decrease in SNRT during atrial stimulation with frequencies of over 130 beats/min. Thormann and Schlepper [7] observed a significant difference in SNRT in normal individuals during stimulation with frequencies of 90 and 170 beats/min ($P < 0.01$). It can be tentatively suggested that during atrial stimulation with frequencies exceeding the spontaneous frequency of the human sinus node by 50%, arrhythmia developed in the sinus node and the value of SNRT was determined, not by Eq. (1), but by Eq. (2) or (3), and for that reason SNRT was underestimated. Gupta et al. observed no lengthening of SNRT in patients with a sick sinus syndrome [4]. This was perhaps also linked with the onset of arrhythmia in the sinus node and, as a result, the value of SNRT was understated. If in the sick sinus syndrome SNRT was 70% or more higher than the period of spontaneous excitations of the sinus node, the effects which we observed would most probably not have any influence

on the diagnosis of the syndrome. However, they may distort the picture when SNRT in patients is close to normal.

The results of this investigation show that the true SNRT may differ considerably from SNRT measured indirectly under clinical conditions on the basis of recovery of atrial activity. This difference depends on the behavior of the sinus mode itself during atrial stimulation.

It can be recommended that atrial stimulation be carried out with frequencies close to the frequency of the sinus node, and during stimulation with higher frequencies repeated measurements of SNRT be made at the same frequency of stimulation.

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