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Circadian Rhythm of the Ventricular Fibrillation Threshold in Female Wistar Rats

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Summary

The circadian rhythm of ventricular fibrillation threshold (VFT) and its relation to the heart rate (HR) and the rectal temperature (RT) was studied in female Wistar rats. The animals were exposed to daily light-dark cycles of 12 h of light alternating with 12 h of darkness and were under pentobarbital anaesthesia (40 mg/kg i.p.). The experiments were performed on open chest animals and VFT was measured by direct stimulation of the myocardium. VFT in female rats showed a circadian rhythm with the acrophase −338° (at 22.53 h), with the mesor 2.58 mA and the amplitude 0.33 mA. HR was not significantly changed during the experiments and no dependence was found between VFT and HR during the whole 24-hour period (r=0.08). The acrophase of the circadian rhythm of HR (on −47°, i.e. at 03.08 h) was shifted to the acrophase of VFT. The circadian rhythms of RT before the application of the anaesthetic agent and under general anaesthesia before the operative interventions had a very similar course with the nearly corresponding acrophases as the circadian rhythm of VFT. It is concluded that the electrical stability of the rat heart measured by VFT shows the significant circadian rhythm in a parallel with the circadian rhythm of RT and probably without dependence on the changes of HR.

Key words

Circadian rhythm – Ventricular fibrillation threshold – Rat

Introduction

The electrical stability of the heart is influenced by the number of extra- and intracardiac factors. The tone of the autonomic nervous system is one of the important ones. It is presumed that the existence of the circadian variation in the cardiovascular reactivity is influenced by the functional state of the autonomic nervous system. Cinca *et al.* (1986) thus presumed that in normal healthy organism the sympathetic-parasympathetic tone is subject to daily rhythmic variations. It is thus conceivable that the electrophysiological properties of the heart may also follow a parallel circadian variability.

Methods

The experiments were performed during the whole year and the obtained results were averaged indepedently of the seasons. Female Wistar rats bred under specific pathogen-free conditions, 315±15 g body weight were used for the experiments. These rats were kept in light- and climate-controlled room for 4 weeks. The animals were exposed to daily light-dark cycles of 12 h of light alternating with 12 h of darkness with dark period from 18.00 to 06.00 h.

The experiments were performed on anaesthetized rats (Pentobarbital Spofa 40 mg/kg i.p.) in 3-hour periods during 24 hours. The first measurement of rectal temperature was performed immediately after short-term ether anaesthesia before pentobarbital administration. The rectal temperature and heart rate were recorded before the operative interventions, cca 20 min after the administration of the anaesthetic agent and then during the whole experiment. The heart rate was measured by the heart rate meter and maintained by radiant heat at the level cca ± 20 beats/min from the basic heart rate recorded

before the surgery and in the actual circadian dependence. Normal respiration was maintained through a tracheal cannula connected to an artificial respirator.

The cardiac stimulation was performed directly on the open chest. The stimulating electrodes (diameter 1 mm and 5 mm interelectrode distance) were placed at the border between the right atrium and right ventricle. The ventricular fibrillation threshold was obtained by stimulation with a train of rectangular pulses of 33 ms duration, 10 ms impulse length, duration of stimulation 400 ms. The current intensity was increased progressively by steps of 0.5 mA until ventricular fibrillation was obtained. The ventricular fibrillation threshold was estimated in 17 animals 5–7 times at each interval of the measurement.

Results are expressed as mean values ± S.D. and correlation coefficients are calculated for the linear regresion. The basic circadian characteristics are calculated using single and population mean cosinor tests (Nelson *et al.* 1979, Cornélissen *et al.* 1980).

Table 1
Ventricular fibrilation threshold (VFT), heart rate (HR) during the experiments, rectal temperature before the administration of the anaesthetic agent (RT1) and rectal temperature under general anaesthesia before the operative interventions (RT2) as well as the acrophases of the circadian rhythms of VFT, HR, RT1 and RT2 in female Wistar rats

Time	VFT	HR	RT1	RT2
09.00	2.64±0.99	359±31	36.8±0.5	35.0±0.7
15.00	2.51±0.69	358±25	36.4±0.4	35.1±0.8
18.00	2.46±0.64	354±35	36.8±0.4	35.3±0.8
21.00	2.45±0.84	359±27	37.5±0.5	35.9±0.7
24.00	2.99±0.73	349±23	37.5±0.5	35.9±0.7
03.00	3.02±0.65	356±24	37.5±0.6	35.5±0.9
05.00	2.57±0.83	342±22	37.1±0.4	35.5±0.8
09.00	2.64±0.99	353±40	36.6±0.4	35.3±0.6

	Acrophase in ° (confidence interval)	Acrophase in hours (confidence interval)
VFT	−338° (−288°; −7°)	22.53 (19.20; 00.28)
HR	−47° (− ; −)	03.08 (− ; −)
RT1	−344° (−339°; −349°)	23.30 (23.10; 23.50)
RT2	4° (−351°; −17°)	00.16 (23.24; 01.08)

Results and Discussion

The experimental results varied inter- and intraindividually in the relative wide range of the values at all intervals of the measurement. The rhythm of VFT was revealed after averaging the results of the individual measurement intervals (about 87 measurements at each interval) (Table 1), with the minimum values during the light phase from 12.00 to 18.00 h and maximum values during the dark phase of the daily regime from 24.00 to 03.00 h (Fig. 1-A). The significant circadian rhythm of VFT ($p<0.01$) with mesor 2.59 mA (i.e. the average value of the mathematically calculated oscillatory quantity), amplitude 0.33 mA (one half of the difference between the maximum and minimum value in the course of one cycle) and acrophase −338° (at 22.53 h) with its confidence intervals from −288° to −7° (from 19.20 to 0.28 h) was revealed using population mean cosinor. The acrophase represents the maximum value in the temporal or angular expression.

Heart rate reached nonsignificantly higher values during the dark phase of the daily regime (354±28 beats/min) in comparison with the light phase (352±30 beats/min) (Fig. 1-C). The calculated correlation coefficients show no dependence of VFT on HR either in the individual intervals, or during the light phase ($r=0.08$ from 423 pairs of the measurements), or during the dark phase of the daily regime ($r=0.06$ from 332 pairs of the measurements) and or during the

whole 24-h period, indepedently of the daytime ($r = 0.08$ from 755 pairs of the measurements). Our findings correspond to the conclusions Kujaník *et al.* (1985), who estimated VFT in rats during various types of ventilation, where this parameter was not dependent on HR. Our results are indirectly supported by Otsuka and Watanabe (1990), who estimated the circadian rhythms of the incidence of three kinds of bradyarrhythmias in the rat. The minimum incidence occurred during the activity, in dark phase of the day.

A number of studies (Han 1964, Abildskov 1985, Billman 1990) indicate that the increased sympathetic activity decreases VFT and thus increases ventricular vulnerability to the fibrillation in dog experiments, although they were not performed in circadian dependence. The relation revealed in the larger experimental animals is not valid for small experimental animals. Although HR was not changed significantly during the whole 24-h period, VFT showed more significant changes. The course and acrophase of the circadian rhythm of HR ($-47°$) did not correspond either to the course, or to the acrophase of the circadian rhythm of VFT ($-338°$) (Figs 1-A, 1-C, Table 1).

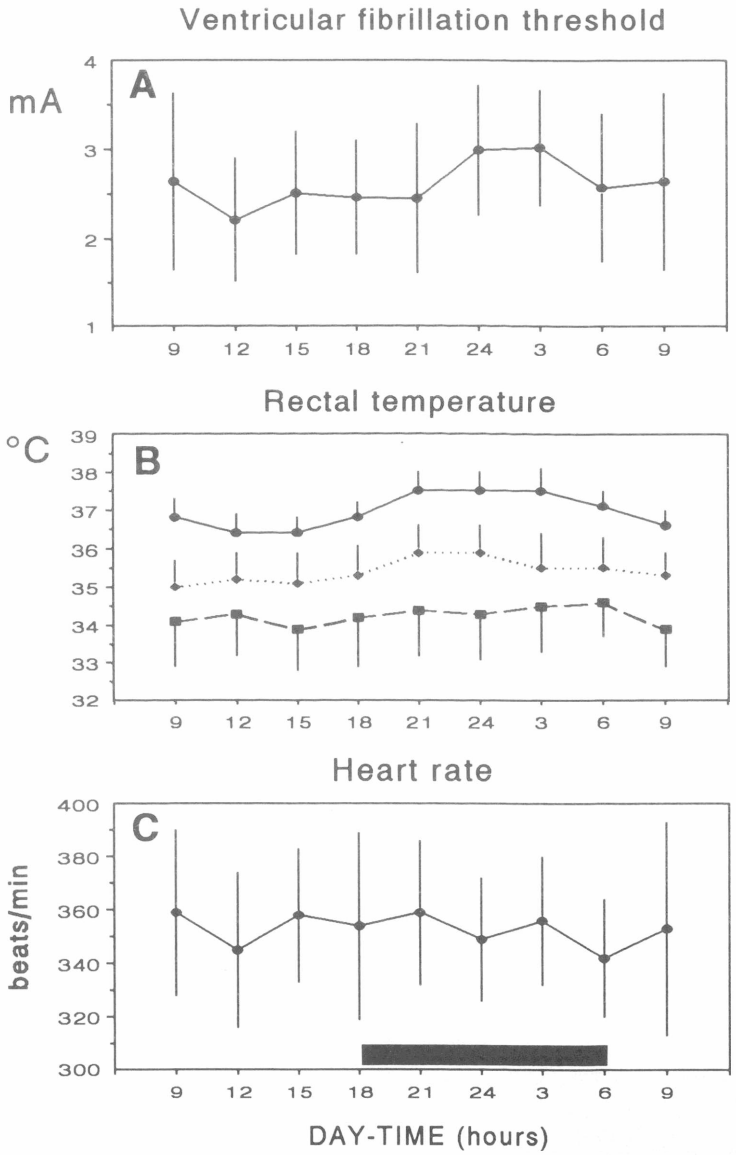

Fig. 1
The circadian rhythms of ventricular fibrillation threshold (A), of the rectal temperature (B) before the administration of the anaesthetic agent (RT1) (full line), of the rectal temperature under general anaesthesia before the operative interventions (RT2) (dotted line), of the rectal temperature during experiments (RT3) (broken line) (only for comparison with the courses of RT1 and RT2) and of heart rate (C) in the female Wistar rats. Data are mean values ± S.D.

A more significant relationship between the circadian rhythm of RT before the application of the anaesthetic agent (RT1) (the acrophase −344°), under general anaesthesia before the operative interventions (RT2) (−4°) and the circadian rhythm of VFT (−338°) was discovered. The acrophases of these rythms were not shifted and the courses were almost identical in character, but with the different amplitudes (Fig. 1-B).

It is concluded that the electrical stability of the heart measured by VFT in female Wistar rats shows a significant circadian rhythm, accompanying the circadian rhythm of RT in parallel and probably without dependence on HR.

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