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Features of the Structure of the Circadian Rhythm of Blood Pressure and Heart Rate under Genetically Determined Hypertension in the Experiment

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In SHR rats of different ages (22, 26, 30, 34, and 38 weeks), continuous 24-h telemetric monitoring of BP and HR was performed. The amplitude and power of oscillations of diastolic BP significantly decreased at the later stages of arterial hypertension (38 weeks), which was considered as a poor prognostic marker. We also observed a significant decrease in the mean daytime, nighttime, and maximum HR and mesor on weeks 30 and 34, but not on week 38, which can reflect triggering of the adaptive response followed by its exhaustion.

Key Words: *blood pressure; heart rate; circadian rhythm; arterial hypertension; spontaneously hypertensive rats (SHR)*

Currently, there are research problems that need to be solved by studying not only previously unknown causes of various pathological processes, but also their temporal organization [3]. In recent decades, chronomedical approach aimed at detection of rhythm abnormalities at different stages of the disease development was used more often as a methodology for assessing cardiovascular risk in essential arterial hypertension [1]. Importantly, biorhythms and the range of their variations are genetically determined, which determines the adaptive capacity of the organism [7]. The changes in the rhythmic component are probably the central component of AH pathogenesis and their further exploration will help to improve its treatment, prognosis, and prevention [2].

Significant progress in the field of experimental medicine and chronobiology has been made due to radiotelemetry technique for evaluating oscillatory processes in the cardiovascular regulation contour [4-6].

To assess the dynamics of the circadian profile of systolic and diastolic BP and HR, we conducted an experimental study on male Wistar and SHR rats using radiotelemetry technique.

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MATERIALS AND METHODS

The study was performed on SHR (n=5) and Wistar (n=5) male rats. The animals were kept and treated in accordance to the Order No. 755 of the Ministry of Health of the USSR (August 12, 1977) and European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986). BP and HR were monitored over 24 h using a Data Sciences International system. To this end, radiotelemetry transmitters for monitoring of abdominal aorta BP and ECG in standard lead II and transmissing the data (as radio signal) to the recorders with storage of BP and HR curves in computer's memory were implanted to Wistar rats aged 22 weeks and SHR rats aged 22, 26, 30, 34, and 38 weeks under general anesthesia. During monitoring, the animals were kept in individual cages at 12/12 h light/dark (07.00-19.00/19.00-07.00) cycle. The data were processed using DataquestA.R.T.4.2 Gold software. The mean systolic and diastolic BP (SBP and DBP) and HR were measured over 2 min with 15 min intervals.

The results were analyzed using Chronos-Fit software by linear and non-linear rhythm analysis [8]. Non-linear analysis is a combination of partial Fourier analysis and stepwise regression technique. The following parameters were obtained by linear analysis: mean daily SBP and DBP and mean daily HR (SBPd, DBPd, and HRd) and mean daytime and nighttime SBP, DBP, and HR (SBPdt, DBPdt, SBPnt, DBPnt, HRdt, and HRnt). When using non-linear analysis, the following parameters were calculated: mesor as the mean SBP, DBP, and HR over 24 h, maximum and minimum SBP, DBP, and HR over 1 day (SBPmax, SBPmin, DBPmax, DBPmin, HRmax, and HRmin), amplitude of oscillations as the difference between the maximum and minimum value of the parameter, and power of oscillations (% of rhythm) as chronobiological index reflecting percentage of oscillations (percentage of values of the investigated indicator with oscillatory distribution within 1 day).

The mean and error of the mean were calculated using Student's *t* test; the differences were significant at $p \leq 0.05$.

RESULTS

Mesor, maximum, and minimum SBP in SHR rats significantly exceeded the corresponding values in normotensive animals throughout the experiment (Table 1). The amplitude of oscillations did not significantly differ from that in the control group at any of the time points. At the same time, a strong trend was observed to a decrease in the power of oscillations (% of rhythm) from week 22 to 30. This parameter was below the control on week 34, while on week 38 this decrease was insignificant.

Comparison of mesor, SBPmax and SBPmin on week 26 to 38 with the corresponding initial values (week 22) indicated that SBP was stable throughout the 4-month experimental period; however, significant increase in mesor was recorded on week 26 and minimum SBP on week 26 to 30.

DBP (Table 2) was featured by a significant increase in mesor, maximum, and minimum levels in comparison with the controls similar to SBP. In this case, the values of these parameters did not differ significantly from baseline on week 26 to 38, which confirms the stable character of AH during this period. However, the amplitude of oscillations significantly decreased by week 38 in comparison with the control and baseline values. The power of oscillations (% of rhythm) significantly decreased in comparison with the baseline and showed a tendency to a decrease in comparison with the control. Thus, the signs of impaired

TABLE 1. Parameters of SBP in Wistar Rats (Normotensive Animals) and SHR Rats (*M*±*m*)

Parameter	Wistar rats (control)	SHR rats				
		week 22	week 26	week 30	week 34	week 38
Mesor	116.46±4.38	189.71±4.16*	202.09±3.29+*	200.13±3.73*	195.33±4.37*	201.06±4.08*
SBPmax	119.78±3.24	201.75±4.14*	215.82±6.07*	209.85±5.83*	206.42±4.48*	209.13±6.16*
SBPmin	99.60±3.34	178.14±4.23*	189.70±1.89+*	189.65±1.53+*	184.24±4.36*	191.30±5.50*
Range	20.17±0.10	23.62±1.71	26.12±5.12	20.20±4.48	22.18±1.27	17.83±3.05
% of rhythm	43.13±10.33	25.67±4.03	21.50±5.09	20.91±7.11	19.87±1.55*	20.51±6.53

Note. Here and in Tables 2, 3: $p \leq 0.05$ compared with *controls, +baseline (week 22).

TABLE 2. Parameters of DBP in Wistar Rats (Normotensive Animals) and SHR Rats (*M*±*m*)

Parameter	Wistar rats (control)	SHR rats				
		week 22	week 26	week 30	week 34	week 38
Mesor	86.98±2.84	136.17±6.23*	147.30±2.03*	143.01±3.03*	138.45±2.32*	145.07±4.07*
DBPmax	92.61±5.10	146.90±5.16*	156.46±4.88*	151.81±4.75*	148.27±3.23*	153.73±6.90*
DBPmin	75.71±5.95	125.68±7.22*	138.15±0.72*	133.91±1.68*	128.63±1.67*	141.97±7.23*
Range	16.90±0.85	21.21±2.12	18.30±4.43	17.90±4.07	19.65±2.20	11.75±0.33+*
% of rhythm	32.71±12.01	26.04±1.29	17.55±5.59	21.30±6.56	20.61±2.76	13.43±1.46+

TABLE 3. Parameters of HR in Wistar Rats (Normotensive Animals) and SHR Rats (*M*±*m*)

Parameter	Wistar rats (control)	SHR rats				
		week 22	week 26	week 30	week 34	week 38
HRd	312.07±21.89	328.52±17.81	335.47±11.35	276.43±4.35+	280.56±5.74+	299.22±10.99
HRdt	302.03±23.53	314.35±18.51	316.01±15.31	260.41±8.26+	262.29±7.39+	284.63±13.37
HRnt	321.70±20.35	342.11±17.17	354.13±7.94	291.79±3.50+	298.08±4.31+	313.21±8.96
Mesor	312.04±21.93	328.39±17.85	335.40±11.32	276.38±4.36+	280.48±5.73+	299.13±11.00
HRmax	351.07±18.84	372.57±12.45	370.48±11.48	319.58±5.52+	318.15±5.74+	338.60±11.96
HRmin	216.69±19.91	277.03±26.41	300.32±12.01*	236.48±6.03	243.17±6.72	259.66±17.45
Range	134.39±1.06	95.54±14.34	70.15±6.25*	83.10±8.29*	74.98±4.77*	78.94±20.29
% of rhythm	51.69±6.17	37.62±4.83	26.65±3.05*	41.23±0.77*	34.75±3.03*	28.78±7.66

rhythmic organization of DBP regulation appeared by week 38, which, in our opinion, is a marker of unfavorable development of AH.

HRd, HRdt, HRnt, mesor, and HRmax (Table 3) did not significantly differ from the corresponding parameters in normotensive animals throughout the experiment. The amplitude and power of oscillations (% of rhythm) significantly decreased in comparison with the control on weeks 26, 30, and 34.

Comparison of HRd, HRdt, HRnt, mesor, and HRmax with those in 22-week old SHR rats attested to pronounced decrease in these values on weeks 30 and 34. We can assume that deceleration of HR occurs as an adaptive response to long-term overload of the heart. The same parameters on week 38 did not significantly differ from those on week 22, which probably attests to exhaustion of this compensatory mechanism.

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