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Disturbances of Autonomic Regulation of Cardiovascular System at Different Working Regimes with Night Shifts

Aim To study temporal and spectral characteristics of heart rhythm variability (HRV) in night shift workers.

Material and methods Along with traditional risk factors, conditions of labor contribute to development of cardiovascular morbidity, including night shift work, which can be associated with disorders of the autonomic regulation detected by analysis of HRV. This study included 100 healthy men. 74 of them were engaged in shift work, including 53 men with rotating shift work, 21 men with fixed night shifts, and 26 men with day-time work. HRV was analyzed by data of 5-min electrocardiogram recording (background recording and orthostatic test).

Results Night-shift workers had decreases in total power of regulation (TP, SDNN) and in the parasympathetic branch (HF, pNN50). Rotating night-shift workers displayed significant decreases in SDNN and pNN50 and pronounced changes in the VLF/LF/HF ratio in the orthostatic test.

Conclusion In work with night shifts, the type of autonomic regulation differs from the "standard" functioning of the autonomic nervous system (ANS). This study showed different effects of night work regimens on HRV indexes. With the rotating shift work, the ANS dysregulation was more profound and was evident by a significant decrease in the ANS total tone and parasympathetic activity (SDNN, pNN50) compared to night shifts with fixed working hours. The excessive weakening of the parasympathetic component in the passive orthostatic test can be considered as an early marker for ANS maladaptation.

Keywords Heart rhythm variability; autonomic nervous system; adaptation; night shift; circadian rhythm; occupational medicine

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In the working-age population, more attention is increasingly being given to adverse work-related factors and the working environment, along with traditional cardiovascular risk factors, including smoking, blood pressure, cholesterol level, and other factors. Among these, working in shifts and, above all, working at night are of particular interest [1, 2]. Throughout the world, 20–25% of the working-age population work in shifts, including about 15% who regularly work at night. In some sectors, such as the transport and service sectors, more than 60% have night shifts [1, 3].

Recent studies have shown an increased risk of angina, hypertension, and metabolic disorders in people who work night shifts [4–7]. The negative impact of night shifts on the cardiovascular system is explained by circadian rhythm desynchronosis, which develops with such a work schedule [8–10]. Thus, the question arises as to how a person working night shifts adapts to rhythm desynchronosis.

Vegetative functions are modulated by direct and inverse connections of the autonomic nervous system (ANS). According to the theory of P. K. Anokhin, trophotropic and ergotropic regulatory mechanisms are based on reciprocal sympathetic and parasympathetic reactions The classical theory of Baevsky et al. [11] of a multi-level model of autonomic function regulation states that the best type of ANS functioning is the predominance of trophotropic regulation mechanisms, such as the parasympathetic part of the segmental ANS, over ergotropic, suprasegmental influences. A dysfunctional rearrangement of the ratio of tropho- to ergotropic autonomic effects during the adaptation to circadian rhythm desynchronosis can predict the onset and progression of a dysregulation pathology, mainly cardiovascular [12–14].

Heart rate variability (HRV) analysis remains the most informative method for assessing ANS function. Heart rate reflects changes in the ANS in response to external and internal factors [15–17]. Thus, ANS function can be evaluated using mathematical analysis of temporal and spectral parameters of HRV. By analyzing HRV, various studies showed that it is possible to assess the functional state of healthy subjects,

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astronauts, and professional athletes [18–21], as well as, individuals with various somatic diseases [17, 22]. Studies on HRV in subjects working night shifts have shown changes in the parasympathetic and sympathetic regulation of cardiac activity [23–26]. These changes become more pronounced with increasing years of night shift work [26, 27].

Night shift schedules can vary by differing in frequency, duration, regularity or randomness, rest time between shifts, and in other characteristics. Thus, the question arises as to whether the effect of night shifts on cardiac activity is universal. This problem is especially relevant for healthcare professionals who have shift schedules combined with exceptional professional stress and possible burnout syndrome.

Thus, with regard to health monitoring of the working-age population and to workflow safety, it is relevant to study ANS function in people working with different night shift schedules. By analyzing HRV, it may be possible to identify precursors of dysregulatory disorders [23].

Objective

The objective was to investigate temporal and spectral characteristics of HRV in individuals whose professional activity involved night shifts.

Material and Methods

This comparative cohort study included 100 subjects of working age (mean age 40.7 ± 8.5 yrs). Inclusion criteria were male sex, age from 22 to 55 yrs, work experience of at least 5 yrs, sinus heart rhythm, no cardiovascular diseases (CVDs), no pulmonary, endocrine and neurological diseases, no need for systematic use of cardio- or psychotropic drugs, signed informed consent to conduct the study. Exclusion criteria were female sex, lack of data on work schedule, functionally significant diseases, and heart rhythm disorders. The study was conducted according to the principles described in international conventions on legal and ethical principles of scientific research in human subjects.

All subjects were divided into two groups. The main group consisted of 74 subjects who regularly worked night shifts, and the comparison group included 26 employees who worked only in the daytime. Two subgroups were allocated in the main group: subgroup 1, individuals having night shift rotation schedule (flexible night shifts) e.g, locomotive crew members (n=53); subgroup 2, employees with a fixed night shift schedule who were allowed to sleep during night shifts, e.g., hospital-based physicians (n=21).

Examinations of the subjects during off-work hours confirmed their normal health state. These examinations included medical history, physical and neurological examination, clinical and biochemical blood tests, blood pressure (BP) measurement, and 12-lead electrocardiogram (ECG). The subject's work schedule and work nature of night shifts were analyzed from the subject's occupational history.

The ANS function was studied by analyzing HRV in the morning hours at least 36 hrs after the night shift. A short ECG was registered with a tilt table test using a VNS-micro device with corresponding software. A standard, baseline ECG was recorded for 5 min with the subject lying horizontal on a tilt table. A second 5-min ECG was performed immediately after the subject was passively positioned in a head-up vertical tilt.

ECGs were processed and interpreted with particular attention given to such temporal and spectral HRV characteristics as the standard deviation of regular sinus R – R intervals (SDNN, ms), the percentage of adjacent R – R intervals which differed by more than 50 ms (pNN50, %), the total spectral power of the cardiointervalogram (TP, ms^2/Hz) and the percentages of the spectral components, very low frequency (VLF), low (LF) and high frequency (HF).

Statistical analysis was performed using the Statistica 8.0 software suite. Parametric and nonparametric methods were used to analyze quantitative data depending on their distribution characteristics as determined by the Shapiro-Wilk test. Quantitative indicators are expressed as the mean (M) and standard deviation (SD) for normally distributed data, otherwise as the median (Me) and lower (LQ, lower 25%) and upper quartiles (UQ, upper 75%). The groups were compared by quantitative and categorical ordinal indicators using the Mann-Whitney U-test. The dependent characteristics reflecting the intensity of variables before and after diagnostic tests were compared using the Wilcoxon test. In all types of statistical analysis, two-sided hypotheses were tested; null hypotheses were rejected at the achieved significance level of $p<0.05$.

Results

Results of the HRV analysis are presented in Table 1. The analysis of temporal and spectral HRV characteristics of subjects who worked night shift showed decreased overall variability. For example, mean SDNN, pNN50, and TP before the tilt table test, i.e., the baseline record, were significantly lower than in the comparison group ($p=0.002$, $p=0.000$, $p<0.001$, respectively) and also lower than most common reference ranges [17, 22]. At the same time, there were no significant differences in the distribution of individual spectral components (VLF, LF, HF) of the total spectrum power (TR) of the night shift group versus the comparison group. These data reflect a general decrease in the ANS effect on heart rhythm regulation, particularly the parasympathetic component, which may correspond to a suboptimal, initial, functional state in the main group.

A comparative analysis of HRV parameters of the baseline recording of night shift workers based on their occupation revealed more significant changes in subgroup 1. For example, SDNN and pNN50 were significantly lower in locomotive drivers than in the subgroup of hospital-based physicians (p=0.037 and p=0.016, respectively). Since the subgroups did not differ in TP, particular attention was given to analyzing the spectral components of HRV. Median VLF/LF/HF percentages of TP were 45.7%/32.4%/17.7% in subgroup 1 and 50.3%/29.6%/19.1% in subgroup 2. These percentages did not fully correspond to an optimal regulation model with approximately equal distribution of HRV components [28]. However, no statistically significant differences were found between the subgroups and the comparison group when comparing the HRV spectral characteristics.

Analysis of the baseline HRV record revealed differences between the night shift group and the comparison group. This analysis established that in the subgroup with night shift rotation schedules, these differences were mainly due to a decrease in SDNN, pNN50, and TR. SDNN and pNN50 had the highest sensitivity as early markers of ANS dysregulation.

The tilt-table test revealed significant quantitative differences in ANS function between subgroups having flexible night shift schedules and the comparison group. This reflected a autonomic reactivity disorder and differences in autonomic support in the target subgroups. During the tilt table test, it was noted in the general group of subjects working night shifts that restructuring of ANS function was evident. This was seen from analysis of the percentages of the VLF/LF/HF HRV spectrum components, as well as from the differences in SDNN, pNN50, and TP compared to those of the comparison group (p=0.001). The median percentage values were 54.9%/32.4%/9.3% of TP, respectively. This indicated a significant increase in the VLF component (p=0.009 vs the comparison group) and a significant reduction in the HF component (p=0.002 vs the comparison group) with the LF component unchanged.

It is known that a change in ANS function during the tilt table test in healthy individuals increases the power of the LF component. This reflects the role of the sympathetic ANS in the vegetative support of cardiovascular function by reducing relative HF power and maintaining VLF power at the same level, as was confirmed in our study by significant changes of the corresponding median spectrum percentages in the comparison group (Table 1). LF increased from 31.2% to 38.9% (p<0.05), and HF decreased from 20.7% to 15.0% (p<0.01). The difference between the TP and VLF components during the baseline and the tilt table test recordings was insignificant (p=0.485 and p=0.809, respectively). In other words, the type of suboptimal functional state in the main group of night shift workers compared daytime workers changed qualitatively, thus reflecting the lack of sympathetic support of heart rhythm regulation during the tilt table test.

Analysis of the HRV spectrum ratio during the tilt table test between subgroups 1 and 2 produced the following results. The percentages of median VLF/LF/HF spectrum components in subgroup 1 were 60.0%/30.6%/8.0%, which indicated a significant increase in the VLF component

Table 1. Temporal and spectral HRV characteristics during the baseline and in the tilt table recordings

Recordingmode	Variable	Night shift group			Control group (n=26)
		Subgroup 1 (n=53)	Subgroup 2 (n=21)	Total (n=74)	
Horizontal position – baseline	SDNN, ms	36.0 [23.0; 48.0]	47.0 [34.0; 62.0]$^{\Delta}$	38.0 [26.0; 51.0]	53.5 [45.0; 66.0]**
	pNN50, %	1.8 [0.6; 4.6]	8.8 [2.6; 16.5]$^{\Delta}$	2.8 [0.7; 9.6]	10.6 [6.4; 20.3]**
	TP, ms²/Hz	933.0 [672.0; 1736.0]	1418.0 [891.0; 3970.0]	1208.0 [707.0; 2012.0]	2333.0 [1458.0; 3780.0]**
	VLF, %	45.7 [38.5; 57.0]	50.3 [46.7; 54.5]	47.6 [39.6; 56.3]	46.3 [34.5; 56.8]
	LF, %	32.4 [25.7; 40.2]	29.6 [25.9; 33.9]	31.5 [25.7; 40.1]	31.2 [22.7; 36.6]
	HF, %	17.7 [13.5; 24.0]	19.1 [15.7; 22.9]	18.3 [14.3; 24.0]	20.7 [16.8; 29.4]
Vertical position – tilt table test	SDNN, ms	34.0 [25.0; 46.0]	42.0 [31.0; 60.0]	35.0 [25.0; 47.0]	51.0 [43.0; 65.0]**
	pNN50, %	0.3 [0.0; 1.7]††	2.3 [0.7; 7.5]$^{\Delta\Delta\dagger\dagger}$	0.7 [0.0; 2.6]††	3.7 [1.7; 10.0]**††
	TP, ms²/Hz	1290.0 [645.0; 2229.0]	1366.0 [839.0; 5400.0]	1047.5 [659.0; 2779.0]	2594.5 [1255.0; 4582.0]**
	VLF, %	60.0 [44.3; 73.5]††	50.4 [36.0; 56.9]$^{\Delta}$	54.9 [42.7; 70.9]††	44.7 [33.4; 53.1]**
	LF, %	30.6 [17.3; 41.7]	35.5 [29.3; 53.3]†	32.4 [19.5; 45.2]	38.8 [32.4; 46.2]†
	HF, %	8.0 [5.0; 11.3]††	10.8 [8.7; 16.2]Δ††	9.3 [5.6; 15.2]††	15.0 [9.2; 18.3]**††

Data are median [LQ; UQ]. * and **, significance of differences of the night shift group from the control group according to the Mann–Whitney test at p<0.05 and p<0.01 respectively; $^{\Delta}$ and $^{\Delta\Delta}$, significance of differences in subgroup 1 and subgroup 2 according the Mann–Whitney test at p<0.05 and p<0.01, respectively; † and ††, significance of differences in the baseline record and tilt table record according to the Wilcoxon test at p<0.05 and p<0.01 respectively.

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and a reduction in the HF component in the subgroup with night shift rotation. In subgroup 2, these percentages were 50.4%/35.5%/10.8%, along with the revealed changes in the autonomic regulation type, i.e., a decrease in the total power of autonomic regulation. However, no significant changes affecting the suboptimal centralization of heart rhythm regulation were detected.

Discussion

The complexity of evaluating CVD risk involves studying various aspects. Concerning the working-age population, we should always keep in mind the possible impact of the working environment, including shift work. This is due to the high prevalence of traditional risk factors, such as, dyslipidemia, insulin resistance, increased body mass index, hypertension and coronary heart disease among workers with night shifts [4, 5, 27].

Previous studies indicate that analysis of HRV is informative in determining the role of the ANS in cardiovascular disorders. It was determined that night shift workers have changes in the temporal and spectral components of HRV at rest [24, 29, 30]. These changes were explained by the complex influence of altered circadian rhythmicity, time changes, and sleep duration [9, 29, 31–33]. In workers of this category, our findings confirmed significant changes in the main factors, which are a decrease in the total power of regulation (TP, SDNN) and the parasympathetic component (HF, pNN50).

It should be noted that brief, 5-min ECG records were used in the study. This technique was chosen for practical reasons since, in industrial medicine, a priority is to assess the employee's condition quickly. The consistency of our findings with previous studies by other authors who used HRV analysis of long-term, daily ECG recording [11, 17, 34] supports the use the brief-record analysis to monitor the ANS function in health assessment of the working-age population.

Our study included only male subjects since females are less likely to be involved in night shifts [3]. Sex uniformity is rare in studying the effects of night shifts on physiological parameters. Only a few trials also studied HRV in just male individuals [24]. In this regard, data on comparing HRV variables in groups divided by sex are of interest. According to such data, SDNN, VLF, and TP decrease significantly due to night shifts more in males than in females, while night work is associated only with a lower LF/HF ratio in female subjects [29]. Based on this, it is assumed that sympathetic activity is less predominant in females and changes in the ANS function are more complex in males working with similar night shift schedules [29]. This may be due to the observed lack of a clear relationship between BP levels and night shifts in females [4].

According to our findings, flexible and fixed night shifts have different effects on ANS function. The group with flexible night shifts showed significantly lower temporal values of SDNN and pNN50 at rest and significant changes in the VLF/LF/HF percentages of the median spectrum during the tilt table test.

However, variables of the spectral and temporal analysis were closer in fixed night shifts to those in the comparison group, which indicates an adequate autonomic response to changes in the body position. A significant relative decrease in HF with increased spectrum VLF component during the tilt table test in the subgroup of flexible night shift schedule without sleep, i.e., the locomotive drivers, indicates a high degree of imbalance in ANS regulation.

In this regard, it should be noted that work schedule has not been taken into account in previous assessments of changes of HRV variables during the tilt test. For example, the meta-analysis by Swai et al. [33], which combined the results of 20 studies of HRV with the tilt test and included 717 patients with postural orthostatic tachycardia syndrome and 641 healthy subjects, analyzed age, comorbidities, and other factors potentially associated with HRV changes, but not the factor of night shifts. Monteze et al. [34] studied the relationship of HRV components with obesity, BP, and age in night shift workers without analyzing the effect of shift schedules. In another study [26], the possible effect of working schedules was also not analyzed when evaluating HRV in night shift workers. However, as follows from our results, this factor contributes to autonomic regulation disorders. Thus, it cannot be ignored when interpreting HRV values obtained in the tilt table test of working-age subjects.

Conclusion

The adaptation of autonomic functions in individuals with flexible night shift schedules is achieved by intensive action of regulatory systems. The tilt table test revealed excessive weakening of the parasympathetic component, which can be an early marker of changes in the adaptability of the autonomic nervous system to circadian rhythm desynchronosis. The results showed that the night-shift autonomic regulation differs from the standard functioning of the autonomic nervous system in subjects who do not work at night. Heart rate variability analysis is a sensitive method to monitor autonomic nervous system function, since it detects changes in the main parameters of heart rate variability.

No conflict of interest is reported.

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