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## Sleep restriction progress to cardiac autonomic imbalance

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### ABSTRACT

Previous studies have shown that night shift work is thought to be a risk factor for cardiovascular disease and inadequate sleep is a common feature of night shift work. Since it's more difficult to maintain adequate sleep duration among night watchmen during their working schedule, hence the purpose of our present study was to investigate whether mental stress or fatigue over restricted sleep period in night shift, affects HRV, in order to elucidate on cardiac autonomic modulation among night watchmen. With the purpose of this, autonomic activity determined from the levels of the heart rate variability (HRV), and also measured, body mass index (BMI), body fat percentage from skin fold thickness (biceps, triceps, and sub-scapular, supra-iliac) among normal sleep watchmen (n = 28) and restricted sleep watchmen (n = 28) at first (1st) day, fourth (4th) day and seventh (7th) day of restricted sleep period. We observed that among restricted sleep individuals, sleepiness was significant increase at 4th day and 7th day when compare to normal sleep individuals, and, there was significant increase in, mean NN, VLF, LF, LF(nu), LF/HF AND significant decrease in SDNN, RMSSD, TSP, HF, and HF(nu) at 4th and 7th day of restricted sleep period. In addition to, this variable was more significant increase on 7th day, when compare with 4th day. As well as there was significant negative correlation between LF(nu) and HF(nu) at subsequent 4th day [ $r(48) = -0.84$ ;  $P = 0.01$ ] and 7th day [ $r(48) = -0.95$ ;  $P = 0.01$ ] of restricted sleep period. However we didn't observe any significant variation in BMI, and body fat percentage among restricted sleep individuals when compare to normal sleep individuals with in this restricted sleep periods. Hence we concluded that partial sleep loss may cause autonomic imbalance represented by increased sympathetic and decreased parasympathetic activity; as revealed by altered HRV indices observed in this study.

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### 1. Introduction

Inadequate sleep is a common feature of shift work. Sleep loss during shift work is a growing problem in our modern society and may become a major threat for health and wellbeing in the near future and supposed to be a threat for cardiovascular disease (CVD).<sup>1–5</sup> Sleep loss may be affecting stress system which plays a critical role in this adaptation.<sup>6</sup> Acute sleep loss may be associated with increased heart rate and blood pressure, and a shift of sympathovagal balance toward sympathetic dominance.<sup>7,8</sup>

The heart rate variability (HRV) analysis is a non-invasive diagnostic technique, has been proposed for the study of autonomic nervous system.<sup>9</sup> The heart rate (HR) is modulated by the combined effects of the sympathetic (SNS) and parasympathetic (PNS) nervous systems. Therefore, measurement of changes in HR

(heart rate variability or HRV) provides information about cardiac autonomic functioning.<sup>10</sup> Slower HRV rhythms (LF) specify increased sympathetic and/or lower vagal activity, whereas faster HRV rhythms (HF) SPECIFY lower sympathetic and/or increased vagal activity.<sup>10</sup> Hence, the variability in heart rate, (with reduced heart rate variation), has been proposed as an independent prognostic marker for an imbalance of normal cardiac autonomic control mechanisms.<sup>11</sup>

HRV is measured using: time-domain, frequency (spectral)-domain, and geometrical analysis methods. In time-domain, SD index and low frequency spectra can reflect a combination of sympathetic and parasympathetic activity while rMSSD, pNN50 and high frequency spectra represent the conditions of parasympathetic activity.

Frequency domain method is analyzed by studying the power spectral density. It provides information about the power distribution across frequencies.<sup>9</sup> The two key components are low-frequency band (LF) and high-frequency band (HF). LF is considered to be an indicator for sympathetic activity, in contradiction,

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HF is determined by vagal effect.<sup>9</sup> The LF/HF ratio has been derived from these values to show sympathovagal balance.<sup>9</sup>

The sympathetic activation is considered to be the main mechanism involved in the development of cardiovascular diseases in sleep impairment.<sup>12,13</sup> The impairment of HRV parameters with an increased incidence of adverse cardiovascular and metabolic disorders in sleep loss has been acknowledged.<sup>14–16</sup> However, only limited studies have conveyed upon the dynamics of the autonomic nervous system during partial sleep loss or restricted sleep.<sup>17–19</sup>

Thus, the purpose of our present study was to investigate whether mental stress or fatigue over restricted sleep period for the duration of night shift among night watchmen, affects HRV, in order to elucidate on cardiac autonomic modulation.

## 2. Methods

### 2.1. Ethics declaration

The study was approved by the local research advisory committee of People College of Medical Science and Research Center (PCMS/OD/2015/1056). The study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from each subject before the start of the study, and all evaluations were performed at completion of first (1st) day, fourth (4th) day and seventh (7th) day of restricted sleep period.

### 2.2. Study design

The study population consisted of 50 healthy good sleepers, night watch men ranging in age from 18 to 35 years and underwent a medical interview to ensure that they had a regular sleep/wake schedule. None of the subjects had cardiovascular complication such as hypertension, diabetes mellitus, and hyperlipidemia. The participants were divided into two groups.

Group I-(Normal sleep) (n = 28) - Twenty-eight watchman working in day time and used to have normal sleep in night ( $\geq 8$  h).

Group II-(Restricted sleep) (n = 22) - Twenty-two watchman working in night time and used to have restricted sleep in night ( $\leq 3$  h).

### 2.3. Protocol

#### 2.3.1. Sleep schedule assessment

The participants were instructed to maintain a regular sleep-wake schedule and were monitored. No stimulant of any kind was allowed during the study. For the tests obtained in normal rested condition, instructed to participants to maintain normal sleep in night every day. In sleep restriction condition, participants were also instructed to sleep in night less than three hours ( $< 3$  h) for one week in their night shift schedule. All the participants were not allowed to sleep in day time. Participants slept at home and completed scheduled sleep diaries, regularly while at home, the duration of sleep was self-monitored. Total time in bed was recorded with a click button by the subject when getting into and out of bed. Participants reported less sleep during study duration which was also confirmed by monitors. After completion of one week study period, participants visited to the laboratory on the morning at 09:00 a.m for assessment. Each participant was tested after a normal sleep night and after a restricted sleep night in random order. The study was conducted in the department of physiology, peoples college of medical science and research center, Bhopal; India. All the measurement was assessed in the normal resting state, with abstinence from alcohol and caffeine at first

(1st) day, fourth (4th) day and seventh (7th) day of restricted sleep period. All laboratory assessments were done in triplicate, at the end of study period.

The following clinical data were recorded: the Karolinska Sleepiness Scale (KSS),<sup>20</sup> body mass index (BMI)<sup>21</sup> and the percentage of body fat<sup>22</sup> was determined from the sum of the thickness of four skinfolds (biceps, triceps, suprailiac and subscapular) by using a Harpenden Skinfold Caliper (British Indicators, Burgess Hill, UK).

### 2.4. Measurement of HRV indices

To study the HRV, we performed 5-min of consecutive digitized electrocardiographic (ECG) signals recording after completion of restricted sleep periods at first (1st) day, fourth (4th) day and seventh (7th) day. All obtained beats (QRS complexes) were amplified further and reviewed on the analyzer screen to avoid any artificial labeling of the QRS complex. The analysis of HRV was performed by the Kubios HRV (version 1.1, Finland) software after research and correction of artifacts, in accordance with the guidelines issued by the European Society of Cardiology and The North American Society of Pacing and Electrophysiology in 1996.<sup>9</sup> We analyzed in time-domain variables: mean NN was the mean of RR intervals of normal sinus beats (mean RR, ms), and RMSSD was the square root of the mean of the sum of the squares of differences between adjacent RR intervals. The standard deviation of the RR-intervals (SDNN, ms), and the root mean square of the difference between successive normal intervals (RMSSD, ms).

In frequency domain analysis, the total spectral power (TSP) was calculated for very-low frequency (VLF, 0.00330.04 Hz), low-frequency (LF, 0.040.15 Hz), and high-frequency bands (HF, 0.15 0.40 Hz). The LF/HF ratio was also included in the statistics. Normalized values of HF (nuHF) and LF (nuLF) bands had been recalculated using the formulas of nuLFLF/HFLF and nuHFHF/HFLF.

## 3. Statistical analysis

Data are expressed as Mean  $\pm$  Standard deviation (SD). All data were analyzed with the SPSS for windows statistical package (version 20.0, SPSS Institute Inc., Cary, North Carolina. Statistical significance between the different groups was determined by the independent student 't' test and the significance level was fixed at  $p \leq 0.05$  (95% confidence intervals). Finally, Pearson correlation coefficient was used to find correlation between two variables.

## 4. Results

### 4.1. Effect of restricted sleep on sleepiness and BMI

The data are summarized in (Fig. 1) with mean  $\pm$  SD. Among all normal and restricted sleep individuals, KSS score was comparable on 1st day of restricted sleep. However at subsequent on 4th day and 7th day of restricted sleep, there was significant increase in KSS score in restricted sleep individual when compare to normal sleep individuals indicating higher levels of sleepiness. In addition to, sleepiness level on 7th day was more significant increase, when compare with 4th day of restricted sleep period.

### 4.2. Effect of restricted sleep on BMI, skin fold and body fat percentage

The data are summarized in (Table 1) with mean  $\pm$  SD. Among all normal and restricted sleep individuals, however, we didn't observe any significant variation in BMI, skin fold (biceps, triceps, and sub-scapular, supra-iliac) and body fat percentage among restricted sleep individuals when compare to normal sleep individuals with in this restricted sleep periods.

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