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Shift work is associated with reduced heart rate variability among men but not women

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ABSTRACT

Background: Imbalance in the autonomic nervous system due to a disrupted circadian rhythm may be a cause of shift work-related cardiovascular diseases.
Objective: We aimed to determine the association between shift work and cardiac autonomic activity in blue-collar workers.
Methods: The study included 665 blue-collar workers aged 18–68 years in different occupations from two Danish cohort studies. Time and frequency domain parameters of heart rate variability (HRV) were measured during sleep using the Actiheart monitor, and used as markers of cardiac autonomic function. Multiple linear regression analyses were used to investigate differences in HRV between day and shift workers.
Results: Shift workers had no significantly different HRV parameters than day workers, except for a lower VLF (B: 0.21; 95% CI: −0.36–0.05). The lower VLF was only present among non-night shift workers ($p < 0.05$) and not among night shift workers ($p > 0.05$). Results differed significantly by gender (p for interaction < 0.10): among men, shift work was negatively associated with RMSSD (B: −7.83; 95% CI: −14.28–1.38), SDNN (B: −7.0; 95% CI: −12.27–1.78), VLF (B: −0.27; 95% CI: −0.46–0.09) and Total Power (B: −0.61; 95% CI: −1.20–0.03), while among women, shift work was only associated with the LF/HF ratio (B: −0.29; 95% CI: −0.54–0.03).
Conclusion: Shift work was particularly associated with lower HRV during sleep among men. This indicates that shift work causes imbalance in the autonomic nervous system among men, which might increase their risk of cardiovascular diseases.

1. Introduction

More than twenty percent of the working population in the European Union reports working shifts [1], and this will further increase as the societal demand for the provision of goods grows [2,3]. Reviews and meta-analyses show that working in rotating shifts, and even more when night shifts are included, increases the risk of chronic diseases, such as type 2 diabetes [4–7] and cardiovascular diseases (CVD) [8,9].

Evidence suggests different interrelated pathways of shift work leading to CVD [9–11]. Working in shifts may lead to behavioral changes, such as smoking, a poor diet, and less physical activity, which increases the risk of CVD [10,12]. Another theory is that shift work leads to desynchronization of the circadian rhythm and biological clock [10]. Hereby, the ability of the cardiovascular system to adapt to external influences decreases, which results in tissue damage and an increased risk of CVD [12,13]. A third theory suggests that disruption of the circadian rhythm due to shift work to cause imbalanced autonomic regulation of the cardiovascular system [14,15]. Autonomic imbalance is an established risk factor for CVD and can be measured by heart rate variability (HRV), the variation in time interval between successive heartbeats [16]. A low HRV at rest is associated with an increased risk of 32–45% for a first cardiovascular event [17]. It is also associated with poor general health status and greater cardiovascular morbidity and mortality [14,15].

The systematic review of Togo et al. showed inconsistent results in the relation between shift work and HRV during rest or work across relatively small studies (n = 6–240) [9]. More recent studies suggested that working in rotating night shifts is adversely related to HRV [13,18–20].

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However, three of the four studies included only male shift workers and did not compare shift workers to day workers [13,18,20], which is optimal to examine the long-term chronic effects of shift work. Kunikullaya et al. compared day workers with night shift workers and showed a trend towards an increased sympathetic activity among night shift workers, but did not find statistically significant differences [19]. Moreover, none of the previous studies distinguished between night shift workers and non-night shift workers [13,18–20], nor investigated differences by age and gender [13,18–20]. This is significant because research has shown that HRV largely depends on age and gender [21,22].

The aim of this study was to determine the association between shift work (with and without night shifts) and cardiac autonomic activity during sleep in blue-collar workers, and to investigate differences by age and gender. We hypothesized that shift workers, particularly those with night shifts, have lower HRV during sleep than day workers.

2. Methods

2.1. Population

Cross-sectional data were used from two Danish cohort studies: the New method for Objective Measurements of physical Activity in Daily living (NOMAD) and the Danish Physical ACTivity cohort with Objective measurements (DPhacto) [23,24]. In the NOMAD study, 358 blue-collar workers from 7 Danish workplaces were invited to participate in the study, all primarily recruited via contact with trade unions and safety representatives. The workers were aged 18–65 years and data collection was conducted between October 2011 and April 2012. In DPhacto, 2107 blue-collar workers from 15 different workplaces were invited. Workers were aged 18–68 years and data collection took place between April 2012 and May 2013. Details of the study designs have been described elsewhere [23,24]. Exclusion criteria for the present study were being white-collar worker, working less than 20 h/week, occupations in which nobody works in irregular shifts, pregnancy, pacemaker, history of CVD, allergy to adhesive tape, reporting fever, and missing data on shift work, HRV or covariates. All workers gave written informed consent prior to the study and the regional Ethics Committee in Copenhagen, Denmark (journal number H-2-2011-047 and H-2-2012-011).

2.2. Variables

2.2.1. Shift work

In both NOMAD and DPhacto, workers were asked about their shift work using a question: "At which time of the day do you usually work in your main occupation?". This is a validated question used by the National Research Center for the Working Environment in Denmark in their National working environment and health questionnaire in 2012 [25]. In the NOMAD study, the response options were "fixed day work", "fixed evening work (mostly between 15:00 and 24:00)", "fixed night work (mostly between 24:00 and 05:00 h)", "varying working hours with night shifts", "varying working hours without night shifts", and "other". In the DPhacto study, response options were "day work", "night or varying working hours with night shifts", and 'other'. In line with our previous study [26], data from both studies were merged into day work and shift work, subdivided into night shift work (i.e. workers with fixed and/or varying night shifts) and non-night shift work (i.e. shift workers without night shifts).

2.2.2. HRV

Objective data on HRV were collected for four consecutive days, during 24 h per day using the Actiheart monitor [23,24]. This is a small and water resistant device for recordings over multiple days [27]. Measurement of HRV using the Actiheart was found technically reliable and valid when compared to state-of-the art clinical measurements (Holter monitoring) [27]. According to the guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [16], non-overlapping five-minute windows were used to measure inter-beat-interval (IBIs). HRV parameters in both the time and frequency domains were derived from these IBIs. The calculated time domains were: the Standard Deviation of Normal to Normal IBIs (SDNN) and the Root Mean Square of Successive Differences (RMSSD). The four calculated frequency domain parameters were: very low-frequency spectral power (VLF: 0.003–0.04 Hz), low-frequency spectral power (LF: 0.04–0.15 Hz), high-frequency spectral power (HF: 0.15–0.4), and the ratio between low- and high-frequency components (LF/HF ratio) [23]. Total power was calculated by the sum of VLF, LF, and HF. SDNN and Total Power are expressions of global HRV; RMSSD and HF reflect parasympathetic cardiac activity; LF is considered as a quantitative marker for sympathetic modulations, but is also as a reflection of both sympathetic and parasympathetic activity; LF/HF is an indicator of sympathetic-to-parasympathetic balance; and VLF possibly reflects sympathetic function though its physiological origin is controversial [16,28,29].

In the present study, HRV during sleep was analyzed to assess the autonomic nervous system at rest, using the three five-minute intervals in which the highest average IBIs (lowest heart rate) were detected. This could occur at any time of the day and was detected by the combination of data from the diary (sleep times) and accelerometer (Actigraph GT3X+). In line with the study of Hallman et al. [23], we applied the following cleaning criteria for HRV measurement during sleep: 1) data from the first 30 and last 15 min were removed to avoid transient periods, such as falling asleep or waking up; 2) intervals for which trunk movement occurred or the posture was not classified as "lying" were removed; and 3) periods where the percentage of erroneous IBIs was higher than 5% were removed.

2.3. Covariates

Workers completed a questionnaire at baseline on sociodemographic and lifestyle factors. Smoking status was dichotomized into current smoker (yes daily/yes sometimes) and non-smoker (no/former smoker). Alcohol use was dichotomized into none/moderate drinker (i.e. ≤1 drink/day for women and ≤2 drinks/day for men) and heavy drinker [30]. Present occupational sector was categorized into: cleaning, manufacturing, transportation, and other (i.e. health services, assemblers, and garbage collectors). Working hours was asked by "how many hours per week do you work in your main occupation, including extra hours?" (continuous). Furthermore, objectively measured body weight and body height were used to calculate BMI in kg/m^2 (continuous). Data on occupational physical activity and leisure-time physical activity (percentage time spent in moderate-to-vigorous physical activity) were collected from accelerometer recordings using the Actigraph GT3X as described elsewhere [26].

2.4. Data analysis

Multiple linear regression models were fitted to estimate regression coefficients for the association between shift work and HRV parameters. Gender, age, BMI, smoking, alcohol and objectively measured physical activity at work and leisure time were included in the models as potential confounders based on literature [15,21]. We tested whether inclusion of occupational sector and working hours changed the regression coefficient of the crude models by ≥10% [31]. As this was not the case, we did not include them as covariates in the models. The independent variable was shift work (shift work with and without night shifts versus day work) and the dependent outcome variables were HRV parameters: IBI, RMSSD, SDNN, VLF, LF, HF, LF/HF, and Total Power. VLF, LF, HF, LF/HF ratio as well as Total Power were log-transformed because the residuals did not follow a normal distribution. In additional analyses, shift work status was categorized into three categories (day work, night shift work, and non-night shift work) to investigate whether HRV parameters of night shift workers were more affected than those of non-night shift workers. Age and gender were a priori selected as potential effect modifiers and tested in the primary models [21,22]. Due to limited statistical power for testing interaction effects, we considered an interaction term between shift work and age or gender as statistically significant if $p < 0.10$. If significant, stratified analyses were carried out. Analyses were carried out using SPSS version 22, and a two-sided p-value smaller than 0.05 was considered statistically significant.

3. Results

3.1. Participants

Of the 1355 participating workers, we excluded 215 white-collar workers, 27 workers who worked less than 20 h per week, 56 who worked in an occupational sector without shift workers, eight with a history of CVD, two with a pacemaker, 51 workers with missing values on shift work or covariates, and 331 workers without valid HRV measurements (Suppl. Fig. 1). Baseline characteristics of workers with and without valid HRV measurement were comparable (data not shown). This led to a study population of 543 day workers and 122 shift workers, consisting of 74 night shift workers and 48 non-night shift workers.

Of the 665 blue-collar workers, 56.1% were male, 30.4% reported being a smoker, and 18.5% being a heavy drinker (Table 1). Compared to day workers, night shift workers were statistically significantly more often male, worked less often in cleaning, and more in transportation and manufacturing. Non-night shift workers were statistically significantly more often smokers and worked more in cleaning and transportation than day workers. Means and standard deviations for HRV parameters during sleep are presented in Table 2.

3.2. Association between shift work and HRV during sleep

The linear regression models adjusted for age, gender, BMI, smoking, and alcohol showed that shift work was not associated with HRV parameters, except for ln VLF (B: −0.21; 95% CI: −0.36–0.05) (Table 3). This means that VLF is 23% lower in shift workers than in day workers (formula: $100 * (\text{Exp}(B) - 1)\%$). Non-night shift workers