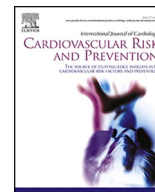




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Is there an association between socioeconomic status and the degree of diurnal variation in heart rate?

Benjamin P. van Nieuwenhuizen^{a,*}, Paul de Goede^{b,c}, Hanno L. Tan^{d,e},
 Bert-Jan van den Born^{a,f}, Anton Kunst^a

^a Department of Public and Occupational Health, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

^b Laboratory of Endocrinology, Amsterdam University Medical Center, University of Amsterdam, Amsterdam Gastroenterology, Endocrinology, and Metabolism, Amsterdam, the Netherlands

^c Hypothalamic Integration Mechanisms Group, Netherlands Institute for Neuroscience (NIN), An Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands

^d Department of Clinical and Experimental Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

^e Netherlands Heart Institute, Utrecht, the Netherlands

^f Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

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ABSTRACT

Background: Disruption in circadian rhythms is associated with cardiovascular disease and may play a role in socioeconomic differences in cardiovascular disease prevalence. However, it is unclear whether low SES is associated with a lower diurnal rhythm in autonomic activity markers. We investigated the association between SES and the amplitude of the daily fluctuation of heart rate.

Methods: We included data of 450 participants of a HELIUS sub-study in Amsterdam, the Netherlands. Participants wore an Actiheart monitor (CamNtech), a chest-worn monitor which measures heart rate every 15 s for several days. Cosinor analysis was performed on the time series of heart rate within each participant. We analyzed the association between the cosinor parameters (amplitude, midline and peak time of the diurnal HR rhythm) and SES indicators (education, occupational class and a proxy of income) in multivariate linear regression models, adjusting for age, sex and ethnicity.

Results: There was a clear diurnal rhythm in the average heart rates, with a peak between noon and 18:00 and a trough between 04:00 and 06:00. This rhythm was present for all categories of education, occupation and income proxy. The estimates for the cosinor parameters did not differ consistently and significantly between categories of education, occupation or income proxy.

Conclusions: We did not find any consistent evidence to support our hypothesis of a diminished amplitude in the diurnal variation of heart rate in individuals with lower SES. Future studies should explore SES differences in the diurnal variation in markers of autonomic activity other than heart rate.

1. Introduction

There are large socioeconomic disparities in cardiovascular disease (CVD) morbidity and mortality [1]. How socioeconomic disparities in CVD arise is incompletely understood. Although behavioural factors are known to explain part of the association between socioeconomic status (SES) and CVD, e.g. coronary heart disease, other mechanisms have been

postulated to also play a role [2]. Further understanding of the mechanisms explaining this association is likely to expose novel targets for primary prevention and treatment for high risk subpopulations.

SES differences in cardiovascular disease are thought to be partially mediated by alterations in autonomic nervous system activity [2]. In this proposed psychobiological pathway, raised psychosocial risk factors, associated with low SES (e.g. stress), stimulate increased, sustained

Abbreviations: CVD, cardiovascular disease; SES, socioeconomic status; HRV, heart rate variability; BRS, baroreflex sensitivity; HELIUS, Healthy life in an urban setting study.

* Corresponding author. Department of Public and Occupational Health, Amsterdam University Medical Center, Location AMC, Meibergdreef 15, 1105 AZ, Amsterdam, the Netherlands.

E-mail address: b.p.vannieuwenhuizen@amsterdamumc.nl (B.P. van Nieuwenhuizen).

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sympathetic nervous system activity and/or decreased parasympathetic activity. This is supported by studies reporting an association between low heart rate variability (HRV) or baroreflex sensitivity and low SES [3–6], as well as evidence of an increased risk of CVD events in individuals with a reduced HRV [7].

Potential markers of cardiovascular autonomic nervous system (ANS) activity [8], such as heart rate (HR), blood pressure (BP) and heart rate variability oscillate with a regular, daily, periodic pattern [9, 10]. The diurnal rhythm in each of these measures indicates a relatively higher sympathetic activity and/or lower parasympathetic activity in the day time and the opposite at night. This has prompted the use of 24 h ambulatory recordings of HR and BP to measure the degree of variation across the day within a non-clinical, naturalistic setting. Diminished day-night differences in HR and nocturnal reduction in BP are associated with a greater risk for cardiovascular morbidity and mortality [11,12], independent of mean levels of HR and BP measured across the day.

The diurnal rhythm in ANS activity might also be relevant in triggering cardiovascular events. The frequency of events such as myocardial infarction and sudden cardiac death peak in the day and are least common at night. This frequency of cardiovascular events thus peaks, during the periods of relative predominance of sympathetic activity [13, 14]. Observational and experimental evidence suggest that the fluctuations in ANS activity are partially responsible for the diurnal fluctuations in CVD event frequency [15–19]. Moreover, experimental evidence suggests that circadian rhythm disruption can lead to cardiovascular pathology [16,18,19].

Given such evidence, SES differences in CVD might in part be attributable to SES differences in diurnal variation in HR and other measures of ANS activity. However, there is currently only limited evidence for SES differences in the amplitude of diurnal variation in HR or other markers of ANS activity. A lower nocturnal reduction in sympathetic activity has been observed in low SES groups alongside raised mean levels of sympathetic activity [20,21]. A greater morning rise in HR was observed in individuals with a low occupation level compared to those with a high occupation level in the Whitehall study [22]. Low SES has also been associated with a lower morning peak and lower nocturnal decline in salivary, urinary and serum cortisol [22–24]. A lower reduction in HR and blood pressure has been reported in African Americans compared to Americans from other ethnic groups [25].

We investigated whether low SES, measured by education, occupation and an income proxy, was consistently associated with a lower amplitude in the diurnal variation of HR. We investigated this hypothesis using a sample of 500 individuals living in Amsterdam, aged between 18 and 70.

2. Methods

We performed a cross-sectional analysis with data from the HEalthy Life in an Urban Setting (HELIUS) study, conducted in Amsterdam, the Netherlands. HELIUS has been described in detail elsewhere [26]. In brief, the baseline data collection took place between 2011 and 2015. Participants aged 18–70 years and living in Amsterdam, were sampled randomly from the municipality register after stratification by the following ethnic groups: Dutch, Surinamese, Ghanaian, Turkish and Moroccan. These are the largest ethnic groups residing in Amsterdam. The HELIUS study was conducted in accordance with the Declaration of Helsinki and has been approved by the Amsterdam Medical Center Ethical Review Board. All participants provided written informed consent.

Participants that had indicated willingness to participate in future sub-studies, were invited for further data collection on physical activity. This sub-study has been described previously [27]. In brief, this study aimed to include 500 participants, with equal distributions between ethnicity and sex. Only Dutch, Moroccan, Surinamese and Turkish participants were invited; Ghanaian participants were excluded from this sub-study because of funding limitations. Data were collected between

November 2012 and November 2013 using the Actiheart combined heart rate (electrocardiogram) and accelerometry monitor (version 4, CamNtech Ltd, UK) [28]. Each recording contained between one and five days heart rate in beats per minute (BPM) every 15 s. The data for 462 successful recordings were available for analysis. After visual inspection of time series of heart rates, the recordings of 9 participants were excluded due to obvious artefactual measurement throughout the recording or more than 20% of the recording comprising of missing values. As a result we analyzed the data of 453 participants.

2.1. Study variables

SES indicators were studied separately as is advised in the epidemiological literature due to the variation in the association between SES and health according to the combination of outcome and SES indicator chosen [29]. Education was based on the highest qualification attained, either in the Netherlands or in the country of origin, and was categorized into four groups: (1) never been to school or elementary schooling only, lower vocational schooling or lower secondary schooling, (2) intermediate vocational schooling or intermediate/secondary schooling, or (3) higher vocational schooling or university. Occupation was defined according to the Dutch Standard Occupation classification of Statistics Netherlands, based on job title and description. Occupation was categorized into the following four groups: (1) elementary or low, (2) intermediate, (3) high or academic profession. Income proxy was based on answers to the question “Do you have trouble to make ends meet”: (1) no difficulty or no, but I do have to be careful how I spend my money, (2) yes, some difficulty, (3) yes, great difficulty.

A participant was defined as belonging to the Dutch (majority) ethnic group if the participant was born in the Netherlands and whose parents were born in the Netherlands. A participant was defined as one of the ethnic minority groups if the participant was born in the specified country and had at least one parent that was born in the same country (first generation), or was born in the Netherlands but both parents were born abroad (second generation). After data collection, Surinamese subgroups were further classified according to self-reported ethnic origin (South-Asian or African). Age was defined as years since date of birth. Sex was defined as assigned sex at birth. Physical activity level was recorded as counts by the tri-axial accelerometer within the Actiheart monitor every 15 s. For each individual, activity level was determined by calculating the mean number of counts over the entire recording. Individuals with an activity level over 1 SD above the mean activity level in the whole study sample were defined as having a ‘high activity level’.

2.2. Diurnal variation in heart rate

We checked for differences in recording length, proportion of missing values, proportion of weekend and weekdays and mean activity level across age, sex, ethnicity, education, occupation and income proxy groups.

Values of heart rate above 150 or below 30 were assumed to be due to measurement error and were set as missing. After visual inspection of the time series of heart rate, sections of the recordings of at least a 24 h length, free of measurement artefact and with less than 20% missing values were used for analysis. Before analysis, the data was smoothed with a moving median filter with a width of 1 h. For each data point (x) a median is calculated for all the data points within 30 min either side of x . The first and last hours of each recording were not used for analysis.

Chronobiological analysis was chosen over simple day-night differences because using average values for day and night is likely to underestimate the diurnal variation. Chronobiological analysis is a more detailed assessment of available data and thus provides a closer estimate of the magnitude of diurnal variation [30,31]. Cosinor analysis (=cosine regression) was chosen as it is the most standard approach in chronobiological research due to its relative simplicity in application and interpretation [31]. Cosine curves were fitted to the HR data for each

recording using sigma plot 14 (systat software inc.), as this software package is capable of taking repeated measures into account. Daily rhythmicity of HR profiles were assessed using cosinor analysis determining mesor (midline estimating statistics of rhythm), amplitude and acrophase of the considered measure. The mesor is the midline of the fitted cosine curve and thus represents the harmonic mean; this is the average HR over the entire recording. The amplitude is the height of the cosine curve, calculated as the difference between the midline and the peak; this represents the degree of diurnal variation in HR. The acrophase is the time of day when the fitted cosine curve peaks. Data was fitted to the following regression: $y = A + B \cdot \cos(2\pi(x - C)/24)$, where A is the midline, B the amplitude and C the peak time of the rhythm. Such a curve was calculated per individual in the study sample. The amplitude, midline and peak time were calculated for each curve. These cosinor parameters for each individual were subsequently used in the subgroup analyses.

2.3. Analysis

Descriptive characteristics (age, sex, ethnic group, education, occupation and income proxy) and activity level were provided in means and standard deviations for continuous variables or percentages for categorical variables. Mean heart rates per 2 h were calculated, stratified by categories of education, occupation and income proxy. These 2 h averages were graphically represented. Unadjusted means and standard deviations were given by SES variable category. Using multivariate linear regression models, the associations between amplitude, midline and peak time and education, occupation and income proxy were assessed, adjusting for age, sex and ethnicity.

We carried out several additional analyses. First, due to the likelihood of a less regular diurnal rhythm in the weekend, we repeated our analyses, using only cosinor parameters calculated from data collected on weekdays. Second, during periods of strenuous physical activity HR is acutely raised. As physical activity could thus affect the measurement of circadian parameters, we chose to repeat our subgroup analyses after exclusion of individuals with an average high activity level. Third, to check consistency of our analysis method for diurnal rhythm (cosinor), we repeated our subgroup by comparing day-night differences in heart

rate. For each individual an average heart rate was calculated for the nighttime (12:00–08:00) and the daytime (08:00–12:00). The difference between these two values was then used as the dependent variable in our subgroup analyses.

All data processing and analysis, aside from the calculation of the cosine parameters, were performed using R version 3.4.3. A p-value of <0.05 was used to define statistical significance.

3. Results

Descriptive statistics of the study sample have been described in [Table 1](#). Levels of high physical activity, a potential determinant of diurnal rhythm parameters, differed across sociodemographic variables, with higher levels in lower education and occupation categories, while the opposite was observed for income proxy.

[Supplement 1a](#) shows the mean heart rate per 2 h in the study sample, demonstrating a clear diurnal rhythm with the trough between 04:00 and 06:00 and the peak between 12:00 and 14:00. When stratified by education level, all three groups showed a very similar rhythm, although in the lower education group HR appeared to be consistently lower at all times in the day than the two higher education groups ([Supplement 1b](#)). A similar pattern was seen across occupation level groups ([Supplement 1c](#)). For income proxy groups, the diurnal fluctuation of heart rate also appeared similar ([Supplement 1d](#)).

The observed mean amplitude was slightly lower in the lowest education group (10.4 BPM) compared to the highest education group (11.0 BPM; [Table 2](#)). Similarly, the lowest occupation group had a lower mean amplitude (9.5 BPM) compared to the highest occupation group (10.8 BPM). In contrast, the lowest income proxy had a higher amplitude (11.1 BPM) compared to the highest income proxy group (10.6 BPM). The lowest education and occupation groups had a lower midline (72.0 BPM) and 71.7 BPM than the highest education and occupation groups (76.7 BPM and 76.4 BPM). In contrast, the lowest income proxy group had a higher midline than the lowest income proxy group (76.9 BPM). The peak time was an hour later in the lower and intermediate occupation level groups (14.1 h) compared to the lower occupation level group (13.1 h), while this differed by less than 0.7 h in education level groups and less than 0.4 h in income proxy groups. When only

Table 1
Descriptive statistics of the study population.

Descriptive variables	n = 450		Activity mean (SD) ^a	High activity [†] (%)
Age category (years)	18–39	107 (23.8)	8.9 (4.4)	18.1
	40–49	131 (29.1)	7.9 (3.5)	12.4
	>50	212 (47.1)	7.7 (3.9)	13.5
Sexn (%)	Women	238 (52.9)	7.6 (3.4)	9.9
	Men	212 (47.1)	8.5 (4.4)	19.1
Ethnicityn (%)	Dutch	108 (24.3)	8.6 (3.9)	19.4
	South-Asian Surinamese	95 (21.3)	7.6 (3.8)	11.2
	African Surinamese	81 (18.2)	8.0 (4.2)	13.9
	Turkish	89 (20.0)	7.9 (3.9)	11.4
	Moroccan	72 (16.2)	8.2 (3.9)	15.3
	Missing	5	5.2 (2.5)	0.0
Education leveln (%)	Higher	184 (41.3)	7.9 (3.8)	10.5
	Intermediate	123 (27.6)	7.9 (3.8)	13.3
	Lower	138 (31.0)	8.4 (4.2)	20.0
	Missing	5	8.9 (3.0)	20.0
Occupation leveln (%)	Higher	159 (41.4)	7.9 (3.8)	12.7
	Intermediate	115 (29.9)	8.2 (4.0)	14.3
	Lower	110 (28.6)	8.3 (4.0)	17.6
	Missing	66	7.8 (4.0)	12.5
Income proxyn (%)	Higher	132 (29.9)	8.4 (4.3)	19.4
	Intermediate	144 (32.6)	8.0 (3.6)	11.3
	Lower	166 (37.6)	7.8 (3.9)	12.9
	Missing	8	7.9 (3.0)	12.5

^a Physical activity was measured in counts by the tri-axial accelerometer in the actiheart monitor. The second column shows the mean of the counts over the entire recording length. The third column shows the percentage of individuals with an average count over 1 SD above the average number of counts in the whole population. [†]High activity was defined as having a physical activity level over one SD above the mean activity level of the whole study population.

Table 2

Descriptive unadjusted group (SES) means (and SD) of diurnal parameters (amplitude, mesor and acrophase).

		All days			Weekdays only		
		Amplitude	Mesor	Acrophase	Amplitude	Mesor	Acrophase
Education level	Higher	11.0 (4.0)	76.7 (7.8)	13.6 (7.3)	11.3 (4.4)	76.9 (7.8)	12.8 (7.9)
	Intermediate	10.7 (4.3)	77.4 (9.6)	13.4 (7.6)	11.4 (4.9)	77.7 (9.6)	11.3 (9.4)
	Lower	10.4 (3.8)	72.0 (7.9)	14.1 (6.3)	10.6 (4.3)	72.2 (8.1)	12.8 (8.1)
Occupation level	Higher	10.8 (4.0)	76.4 (7.6)	13.1 (7.7)	11.1 (4.2)	76.5 (7.8)	12.3 (8.5)
	Intermediate	11.5 (4.6)	77.6 (8.4)	14.1 (6.5)	12.4 (5.3)	77.9 (8.2)	12.3 (8.1)
	Lower	9.5 (3.3)	71.7 (7.5)	14.1 (6.4)	9.7 (4.1)	71.9 (7.8)	12.6 (8.5)
Income proxy	Higher	10.6 (4.2)	73.2 (7.9)	13.5 (7.1)	10.5 (4.5)	73.3 (8.0)	12.9 (7.8)
	Intermediate	10.5 (3.9)	76.1 (9.6)	13.9 (6.8)	11.1 (4.5)	76.4 (9.7)	11.8 (9.1)
	Lower	11.1 (3.8)	76.9 (8.0)	13.7 (7.2)	11.7 (4.5)	77.0 (8.2)	12.6 (8.1)

The amplitude is the difference in heart rate from the midline of the cosine wave to the peak. The Acrophase is the time of the peak in the cosinor models.

considering data measured on weekdays, the pattern of results was nearly identical (Table 2).

In age, sex and ethnicity adjusted linear regression analyses, the amplitude did not differ significantly or with a consistent pattern across education, occupation or income proxy groups (Table 3, 1st column). For example, the intermediate occupation group had a slightly higher amplitude (0.81; CI: 0.17, 1.79) and the lower occupation group had a slightly lower amplitude (-0.93 CI: -2.00, 0.13) compared to the lower occupation group. None of these differences in amplitude were significantly different. When considering only weekdays (Table 3, column 2), there were also no substantial differences in amplitude across SES groups. Only the intermediate occupation group had a statistically significant higher amplitude compared to the highest occupation group (1.50 BPM; CI: 0.38, 2.63; $p = 0.01$). Similarly, small differences were observed in the analyses excluding individuals with a high average activity level (Table 3, column 3).

The adjusted midline was significantly lower in the lower education group (-3.90 BPM; CI: -5.88, -1.91) and the lower occupation group (-3.69 BPM; CI: -5.69, -1.68) than the higher education and occupation groups, respectively (Table 4). In contrast, the midline was higher in lower income proxy groups, with a 1.99 BPM (-0.01, 3.99) rise in the intermediate group and a 2.39 BPM (0.38, 4.41) rise in the lower group compared to the higher income proxy group. Both were a statistically significant difference. The peak time did not differ substantially across SES groups.

Additional analyses on day-night differences in heart rate showed similarly small group differences compared with the cosinor derived parameters (Supplements 2b and 2c).

4. Discussion

4.1. Key findings

We showed clear diurnal patterns in heart rate using ambulatory

Table 3

Amplitude of cosinor model by education level, occupation level and income proxy, adjusted for age, sex and ethnicity.

		Main	Weekdays	Excluding high activity
		β (CI) p value	β (CI) p value	β (CI) p value
Education	Higher	1	1	1
	Intermediate	-0.40 (-1.31, 0.50) 0.38	-0.20 (-1.24, 0.84) 0.71	-0.30 (-1.21, 0.61) 0.52
	Lower	-0.03 (-0.98, 0.92) 0.95	-0.37 (-1.48, 0.74) 0.51	0.02 (-0.93, 0.98) 0.96
Occupation level	Higher	1	1	1
	Intermediate	0.81 (-0.17, 1.79) 0.11	1.50 (0.38, 2.63) 0.01	1.16 (0.17, 2.15) 0.02
	Lower	-0.93 (-2.00, 0.13) 0.09	-1.06 (-2.30, 0.19) 0.10	-0.45 (-1.52, 0.62) 0.41
Income proxy	None	1	1	1
	Careful	-0.21 (-1.15, 0.72) 0.65	0.46 (-0.63, 1.55) 0.41	0.33 (-0.63, 1.29) 0.50
	Difficulty	-0.10 (-1.04, 0.84) 0.83	0.68 (-0.42, 1.78) 0.23	0.52 (-0.45, 1.48) 0.29

The amplitude is the difference in heart rate from the midline of the cosine wave (mesor) to the peak of the wave. All days refers to data from week and weekend days used for analyses. Weekdays refers to models not using data recorded on Saturday or Sunday. Excluding high activity refers to models after the exclusion of individuals with a high average activity level.

Table 4

Mesor and acrophase of the cosinor models by education level, occupation level and income proxy, adjusted for age, sex and ethnicity.

		Mesor		Acrophase	
		β	(CI) p value	β	(CI) p value
Education	Higher	1		1	
	Intermediate	0.87	(-1.02, 2.76) 0.37	-0.14	(-1.81, 1.52) 0.87
	Lower	-3.90	(-5.88, -1.91) 0.00	0.77	(-0.97, 2.52) 0.39
Occupation level	Higher	1		1	
	Intermediate	1.10	(-0.74, 2.94) 0.24	1.09	(-0.68, 2.86) 0.23
	Lower	-3.69	(-5.69, -1.68) 0.00	1.07	(-0.87, 3.00) 0.28
Income proxy	Higher	1		1	
	Intermediate	1.99	(-0.01, 3.99) 0.05	0.35	(-1.37, 2.07) 0.69
	Lower	2.39	(0.38, 4.41) 0.02	0.24	(-1.49, 1.97) 0.79

Mesor is the midline (harmonic mean) of the cosinor wave, i.e. the overall median heart rate. Acrophase is the time of the peak in the cosinor models, therefore this shows how much earlier or later the daily HR peak in intermediate and lower SES groups compared to the higher (reference) groups, for each SES indicator respectively. Models presented in Table 4 were conducted in the whole study sample (not excluding individuals with high activity) and all recording days (including weekend days) were included.

occupations are associated with irregular work times and sleep disturbance, which may both contribute to a raised heart rate during the day [22,35]. Unfortunately, we did not have data available on sleeping patterns or on the level of physical demands of work. Thus, we were not able to exclude manual laborers or other physically demanding occupations from our sample, which the Whitehall study did. Such a mechanism could have increased day-night differences in heart rate in low SES groups, perhaps nullifying the opposite (hypothesized) effect of greater diurnal variation in high SES groups.

The observed higher midline in lower income proxy groups followed an expected pattern, while this was not the case for education and occupation level. A raised HR is associated with cardiovascular disease morbidity and mortality [36]. Other autonomic activity markers such as heart rate variability and blood pressure are associated with low SES, although it is unclear if this is also the case for HR [3–6]. Thus, a raised midline in the diurnal variation of HR may be expected to be associated with low SES. It is unclear why the lower education and occupation groups had a lower midline than the higher education and occupation groups.

Diurnal variation in heart rate may have a more complex relationship with autonomic activity than other markers of cardiovascular autonomic activity (e.g. blood pressure) that are measured in standard protocols [8,10]. Heart rate exhibits a distinct circadian rhythm [37,38]. Black et al. review evidence for the role of the autonomic nervous system in maintaining the circadian rhythm in heart rate [19]. Studies using pharmacological blockade of autonomic input into the heart and genetic knockout studies of beta adrenergic receptors result does not abolish circadian rhythm in heart rate [19]. Referencing the lack of association between heart rate and muscle sympathetic nerve activity within cardio-metabolic risk populations, Grassi argues that heart rate does not fully reflect the excess sympathetic activity associated with cardio-metabolic disease states [39]. However, studies have found associations between HR and CVD risk factors [39]. HR may thus have a more complex association with autonomic function than other more direct indicators such as blood pressure and heart rate variability.

4.3. Limitations

The current sub-study of the HELIUS study was selected by asking HELIUS participants if they were willing to participate in further data collection. Potentially, the response rate may have differed according to SES. However, two SES indicators, average property value and percentage on minimum income of the area of residence, were similar with, for example, 9.1% of the Dutch participants and 11.1% of the Dutch non-participants earning the minimum wage. It is however uncertain how this could have influenced on the relative differences in diurnal rhythms

between SES groups.

Recording parameters such as the length of recording, the relative proportions of week and weekend days within recordings, and proportion of missing observations may be both associated with demographic and socioeconomic variables and cosinor parameters. However, we observed that conditioning on these factors in the linear regression analyses did not significantly improve the models (data not shown). Use of antihypertensive medications such as β blockers are likely to affect the diurnal variation of HR and may differ by socioeconomic group. We checked the proportion of antihypertensive medication use across categories of socioeconomic indicators, which did not show substantial differences. Additionally, conditioning on the use of antihypertensive medication use in the main analyses did not change our results (data not shown).

5. Conclusion

We observed a clear diurnal rhythm in HR in all SES groups. We did not find evidence to support the hypothesis that lower SES groups would exhibit a lower amplitude in the diurnal rhythm of HR. This may suggest that the diurnal rhythm of HR does not contribute to the known SES differences in CVD morbidity and mortality. However, HR might not be a sufficiently sensitive marker of circadian variation in autonomic activity in a naturalistic/non-experimental study setting using ambulatory measurements. This may be elucidated in future studies by assessing SES differences in other markers of autonomic activity such as blood pressure or heart rate variability.

Credit author statement

Benjamin van Nieuwenhuizen: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing review and editing, Visualisation, Project administration. Paul de Goede: Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing, Hanno L. Tan: Conceptualization, Writing – review & editing, Bert-Jan van den Born: Conceptualization, Writing – review & editing, Anton Kunst: Conceptualization, Methodology, Project administration, Writing – review & editing.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcrp.2021.200118>.

References

- [1] G.A. Mensah, A.H. Mokdad, E.S. Ford, K.J. Greenlund, J.B. Croft, State of disparities in cardiovascular health in the United States, *Circulation* 111 (10) (2005) 1233–1241.
- [2] A. Steptoe, M. Marmot, The role of psychobiological pathways in socio-economic inequalities in cardiovascular disease risk, *Eur. Heart J.* 23 (1) (2002) 13–25.
- [3] H. Hemingway, M. Shipley, E. Brunner, A. Britton, M. Malik, M. Marmot, Does autonomic function link social position to coronary risk? The Whitehall II study, *Circulation* 111 (23) (2005) 3071–3077.
- [4] R. Lampert, J. Ickovics, R. Horwitz, F. Lee, Depressed autonomic nervous system function in African Americans and individuals of lower social class: a potential mechanism of race- and class-related disparities in health outcomes, *Am. Heart J.* 150 (1) (2005) 153–160.
- [5] R.P. Sloan, M.H. Huang, S. Sidney, K. Liu, O.D. Williams, T. Seeman, Socioeconomic status and health: is parasympathetic nervous system activity an intervening mechanism? *Int. J. Epidemiol.* 34 (2) (2005) 309–315.
- [6] B.P. van Nieuwenhuizen, D. Collard, H.L. Tan, M.T. Blom, B.J.H. van den Born, A. E. Kunst, et al., Socioeconomic differences in sympathovagal balance: the HELIUS study, *Psychosom. Med.* 83 (1) (2020) 16–23.
- [7] S. Hillebrand, K.B. Gast, R. de Mutsert, C.A. Swenne, J.W. Jukema, S. Middeldorp, et al., Heart rate variability and first cardiovascular event in populations without known cardiovascular disease: meta-analysis and dose-response meta-regression, *Europace* 15 (5) (2013) 742–749.
- [8] F. Leys, A. Fanciulli, J.-P. Ndayisaba, R. Granata, W. Struhal, G.K. Wenning, Cardiovascular autonomic function testing in multiple system atrophy and Parkinson's disease: an expert-based blinded evaluation, *Clin. Auton. Res.* 30 (3) (2020) 255–263.
- [9] M.N. Jarczok, H. Guendel, J.J. McGrath, E.M. Balint, Circadian rhythms of the autonomic nervous system: scientific implication and practical implementation, *Chronobiol. Sci. Biol. Time Struct.* (2019).
- [10] P. Guaraldi, G. Barletta, F. Baschieri, G. Calandra-Buonaura, F. Provini, P. Cortelli, Testing cardiovascular autonomic function in the COVID-19 era: lessons from Bologna's Autonomic Unit, *Clin. Auton. Res.* 30 (4) (2020) 325–330.
- [11] A.M. Birkenhäger, A.H. van den Meiracker, Causes and consequences of a non-dipping blood pressure profile, *Neth. J. Med.* 65 (4) (2007) 127–131.
- [12] T.W. Hansen, L. Thijs, J. Boggia, Y. Li, M. Kikuya, K. Bjorklund-Bodegard, et al., Prognostic value of ambulatory heart rate revisited in 6928 subjects from 6 populations, *Hypertension* 52 (2) (2008) 229–235.
- [13] C.J. Morris, J.N. Yang, F.A. Scheer, The impact of the circadian timing system on cardiovascular and metabolic function, *Prog. Brain Res.* 199 (2012) 337–358.
- [14] M.C. Cohen, K.M. Rohtla, C.E. Lavery, J.E. Muller, M.A. Mittleman, Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death, *Am. J. Cardiol.* 79 (11) (1997) 1512–1516.
- [15] R.W. Peters, J.E. Muller, S. Goldstein, R. Byington, L.M. Friedman, B.S. Group, Propranolol and the morning increase in the frequency of sudden cardiac death (BHAT Study), *Am. J. Cardiol.* 63 (20) (1989) 1518–1520.
- [16] N. Takeda, K. Maemura, Circadian clock and cardiovascular disease, *J. Cardiol.* 57 (3) (2011) 249–256.
- [17] F. Scheer, G. Ter Horst, J. van Der Vliet, R. Buijs, Physiological and anatomic evidence for regulation of the heart by suprachiasmatic nucleus in rats, *Am. J. Physiol. Heart Circ. Physiol.* 280 (3) (2001) H1391–H1399.
- [18] R.D. Rudic, D.J. Fulton, Pressed for time: the circadian clock and hypertension, *J. Appl. Physiol.* 107 (4) (2009) 1328–1338.
- [19] N. Black, A. D'Souza, Y. Wang, H. Piggins, H. Dobrzynski, G. Morris, et al., Circadian rhythm of cardiac electrophysiology, arrhythmogenesis, and the underlying mechanisms, *Heart Rhythm* 16 (2) (2019) 298–307.
- [20] C.J. Rodriguez, Z. Jin, J.E. Schwartz, D. Turner-Lloveras, R.L. Sacco, M.R. Di Tullio, et al., Socioeconomic status, psychosocial factors, race and nocturnal blood pressure dipping in a Hispanic cohort, *Am. J. Hypertens.* 26 (5) (2013) 673–682.
- [21] D.A. Hickson, A.V.D. Roux, S.B. Wyatt, S.Y. Gebreab, G. Ogedegbe, D.F. Sarpong, et al., Socioeconomic position is positively associated with blood pressure dipping among African-American adults: the Jackson Heart Study, *Am. J. Hypertens.* 24 (9) (2011) 1015–1021.
- [22] A. Steptoe, S. Kunz-Ebrecht, N. Owen, P.J. Feldman, G. Willemsen, C. Kirschbaum, et al., Socioeconomic status and stress-related biological responses over the working day, *Psychosom. Med.* 65 (3) (2003) 461–470.
- [23] A. Hajat, A. Diez-Roux, T.G. Franklin, T. Seeman, S. Shrager, N. Ranjit, et al., Socioeconomic and race/ethnic differences in daily salivary cortisol profiles: the multi-ethnic study of atherosclerosis, *Psychoneuroendocrinology* 35 (6) (2010) 932–943.
- [24] J.B. Dowd, A.M. Simanek, A.E. Aiello, Socio-economic status, cortisol and allostatic load: a review of the literature, *Int. J. Epidemiol.* 38 (5) (2009) 1297–1309.
- [25] M.L. Jehn, D.J. Brotman, L.J. Appel, Racial differences in diurnal blood pressure and heart rate patterns: results from the Dietary Approaches to Stop Hypertension (DASH) trial, *Arch. Intern. Med.* 168 (9) (2008) 996–1002.
- [26] M.B. Snijder, H. Galenkamp, M. Prins, E.M. Derks, R.J.G. Peters, A.H. Zwinderman, et al., Cohort profile: the healthy life in an urban setting (HELIUS) study in Amsterdam, The Netherlands, *BMJ Open* 7 (12) (2017), e017873.
- [27] M. Nicolaou, M.G. Gademian, M.B. Snijder, R.H. Engelbert, H. Dijkshoorn, C. B. Terwee, et al., Validation of the SQUASH physical activity questionnaire in a multi-ethnic population: the HELIUS study, *PLoS One* 11 (8) (2016), e0161066.
- [28] K. Hinde, G. White, N. Armstrong, Wearable devices suitable for monitoring twenty four hour heart rate variability in military populations, *Sensors* 21 (4) (2021), 1061.
- [29] B. Galobardes, J. Lynch, G.D. Smith, Measuring socioeconomic position in health research, *Br. Med. Bull.* 81 (1) (2007) 21.
- [30] G. Cornelissen, F. Halberg, K. Otsuka, R. Singh, C.-H. Chen, Chronobiology predicts actual and proxy outcomes when dipping fails, *Hypertension* 49 (1) (2007) 237–239.
- [31] G. Cornelissen, Cosinor-based rhythmometry, *Theor. Biol. Med. Model.* 11 (1) (2014) 1–24.
- [32] C.J. Stepnowsky Jr., R.A. Nelesen, D. DeJardin, J.E. Dimsdale, Socioeconomic status is associated with nocturnal blood pressure dipping, *Psychosom. Med.* 66 (5) (2004) 651–655.
- [33] F. Euteneuer, P.J. Mills, M.A. Pung, W. Rief, J.E. Dimsdale, Neighborhood problems and nocturnal blood pressure dipping, *Health Psychol.* 33 (11) (2014), 1366.
- [34] T.M. Spruill, W. Gerin, G. Ogedegbe, M. Burg, J.E. Schwartz, T.G. Pickering, Socioeconomic and psychosocial factors mediate race differences in nocturnal blood pressure dipping, *Am. J. Hypertens.* 22 (6) (2009) 637–642.
- [35] L. Golden, Irregular work scheduling and its consequences, *Econ. Pol. Instit. Brief. Pap.* 394 (2015).
- [36] P. Palatini, S. Julius, Elevated heart rate: a major risk factor for cardiovascular disease, *Clin. Exp. Hypertens.* 26 (7–8) (2004) 637–644.
- [37] J.-P. Degautte, P. Van De Borne, P. Linkowski, E. Van Cauter, Quantitative analysis of the 24-hour blood pressure and heart rate patterns in young men, *Hypertension* 18 (2) (1991) 199–210.
- [38] G. Vandewalle, B. Middleton, S.M. Rajaratnam, B.M. Stone, B. Thorleifsdottir, J. Arendt, et al., Robust circadian rhythm in heart rate and its variability: influence of exogenous melatonin and photoperiod, *J. Sleep Res.* 16 (2) (2007) 148–155.
- [39] G. Grassi, F. Arenare, F. Quarti-Trevano, G. Seravalle, G. Mancina, Heart rate, sympathetic cardiovascular influences, and the metabolic syndrome, *Prog. Cardiovasc. Dis.* 52 (1) (2009) 31–37.