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Dipping and Variability of Blood Pressure and Heart Rate at Night are Heritable Traits

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Abstract

Background: Blunted nocturnal blood pressure dipping (NBPD) as well as high variability of blood pressure (BPV) and low variability of heart rate (HRV) are

associated with increased cardiovascular morbidity and mortality. The aim of this study was to test if these traits are heritable.

Methods: We studied 260 healthy siblings without antihypertensive drugs from 118 Swedish families. BPV and HRV were defined as the standard deviation of blood pressure and heart rate values recorded during 24-hours, daytime (06am-10pm) and nighttime (10pm-06am). NBPD was defined as the ratio between nighttime and daytime blood pressure. Heritability was estimated with a maximum likelihood method implemented in "Solar" software package with and without adjustment for significant covariates.

Results: At night, significant heritability was found for systolic (33%, $P<0.05$), diastolic (36%, $P<0.05$) and mean (42%, $P<0.01$) BPV. After covariate adjustment the corresponding heritability values were 23% ($P=0.08$), 29% ($P<0.05$) and 37% ($P<0.05$). Daytime BPV was not heritable. The heritability of NBPD was 38% ($P<0.05$) for systolic, 9% ($P=0.29$) for diastolic and 36% ($P<0.05$) for mean blood pressure but after adjustment only systolic NBPD was significant (29%, $P<0.05$). Heart rate was highly heritable both during daytime (57%, $P<0.001$) and nighttime (58%, $P<0.001$) but the variability of heart rate, after adjustment, was only significant at night (37%, $P<0.05$).

Conclusions: Our data suggest that BPV and HRV are partially under genetic control and that genetic loci of importance for these traits could be mapped by linkage analysis.

Key Words: ambulatory blood pressure, dippers, variability, heritability, genetics of hypertension.

Introduction

Ambulatory blood pressure (ABP) monitoring is a validated and accurate method to evaluate blood pressure during 24 hours [1,2]. It has been shown that ABP better predicts cardiovascular morbidity and mortality than office blood pressure (OBP) [3]. Intra-arterial blood pressure monitoring is required for beat-to-beat analysis of BPV [4] and continuous ECG recording is needed to assess beat-to-beat HRV.[5-7] However, ABP permits a non-invasive estimation of both BPV and HRV. Several studies have investigated the prognostic value of BPV and HRV measured by ABP monitoring in hypertensive patients. In particular, 24-hour standard deviation (SD), daytime SD, and nighttime SD of blood pressure have been independently related to cardiovascular events [8,9] and structural damages [10,11]. Furthermore, non-dippers and inverted-dippers, who do not have the physiologic decrease in blood pressure between day and night, are at augmented risk of mortality [12] and target organ impairments [13-15] as compared to dippers. More recently, extreme dippers have been recognized to be at augmented risk for clinical and silent cerebrovascular disease [16,17]. Decreased HRV measured by ECG recordings has been shown to be a strong predictor of future cardiac events whether [5,6] or not [7] preceded by a myocardial infarction.

At the population level BPV is related to left ventricular mass index [18] and, interestingly, both BPV and HRV measured by ABP were recognized as independent predictors of cardiovascular mortality in a Japanese cohort study independently of hypertensive state and precedent cardiovascular events, underlining the prognostic value also in normotensive subjects [19].

It is well established that blood pressure and heart rate are heritable traits [20,21] and in the "Malmö family collection for the study of Macrovascular and Hemodynamic Genetics" ("MMHG") material we recently found that ABP is more heritable than office blood pressure, especially at night [22]. However, little is known about heritability of BPV and HRV. In the Framingham study it was demonstrated that HRV analyzed by spectral analysis of 2 hours continuous electrocardiogrphic recording has a heritability of 13-23% [23]. In the same cohort, a genome wide scan (GWS) for HRV has been performed, pointing out loci linked to this trait on chromosome 15 and 2 [24]. Recently another study [25] analyzing ECG recording during 24-hours found significant estimates for genetic contribution to different indices of HRV ranging from 35% to 48% in different periods of the day. As the heritability of BPV and HRV, measured by ABP monitoring, has not been investigated previously, the aim of this study was to test whether BPV and HRV phenotypes are heritable traits in a family material consisting of siblings free from a history of hypertension and antihypertensive medication.

Methods

Subjects

All study participants gave written informed consent. The Ethics Committee of the Medical Faculty of Lund University approved the study. The procedures were in accordance with the institutional guidelines.

Between September 2000 to March 2002, we collected 118 families from Malmö, Sweden which form the "Malmö family collection for the study of Macrovascular and Hemodynamic Genetics" ("MMHG") [22]. The probands of the families were ascertained from the population based "Malmö Diet and Cancer Study" [26] and the

"Malmö Preventive Project" [27]. We focused the collection on siblings receiving no antihypertensive medication (n=260). Siblings with one or two parents with diagnosed and pharmacologically treated primary hypertension were primarily included. Thus 91% of the included subjects, who were without a history of hypertension and free from antihypertensive treatment, had ≥1 first degree relative with diagnosed primary hypertension. In total we had 104 sib-ships consisting of 2 siblings, 16 sib-ships with 3 siblings and 1 sib-ship with 4 siblings. The mean age of the 260 subjects included was 38.3 ± 8.6 years, body mass index (BMI) 25.2 ± 4.0 kg/m^2, heart rate 68.6 ± 10 beats per minute, 49% were male and 22% were smokers. ABP and heart rate phenotypes are shown in Table 1. The degree of NBPD expressed as night to day ratio was [median (inter quartile range)] 91 (86-95) % for systolic, 85 (79-90) % for diastolic and 88 (83-92) % for mean blood pressure.

Phenotyping

Fasting blood samples were drawn (30 mL) for analysis of metabolic and endocrine parameters as well as for DNA isolation, 24-hour urine samples were collected and a standardized questionnaire, concerning medical history, was completed by all subjects. BMI was calculated after height and weight were recorded in light clothing without shoes. Smoking was defined as being a current smoker. At the end of the visit an ABPM 90207 device (Spacelabs Medical Inc, Redmond, WA, USA) was applied on the left arm for ABP measurement. Two different cuff sizes were used depending on the arm circumference (24-32 cm and 32-42 cm, respectively) of the study subjects. Daytime (one recording every 20 minutes) was defined as 06 a.m.-10 p.m. and nighttime (one recording every 60 minutes) as 10 p.m.-06 a.m. ("long clock-time periods"). As this

definition of day and night is not always equivalent to the subjects´ actual awake- and sleeping times, we also analyzed "short clock-time periods" with 00 a.m. - 06 a.m. defined as nighttime and 10 a.m. - 08 p.m. as daytime [9,28] in an attempt to avoid the risk that some actual nighttime measurements are recorded as daytime measurements and vice versa.

Study subjects were advised to maintain the left arm relaxed along the body during each measurement. None of the subjects were night-workers or had a shift of the ordinary day-night cycle for any other reason. None reported having smoked at night. BPV and HRV were defined as the SD of blood pressure and heart rate recordings during daytime, nighttime and 24-hours. As an additional measure of BPV and HRV we used the coefficient of variation (CV) (SD/average blood pressure or heart rate x 100). NBPD was defined the night to day ratio (nighttime blood pressure/daytime blood pressure x 100). None of the NBPD phenotypes (systolic, diastolic and mean blood pressure) were normally distributed and we therefore used the logarithm of the night to day ratio as NBPD phenotype throughout in the heritability calculations.

Statistics

Descriptive measurements are presented as means ± SD if not otherwise specified. For normally distributed continuous variables t-test was used to compare group means, whereas Mann Whitney test was used otherwise. χ^2-test was used for comparisons of group frequencies. Comparison of different blood pressure phenotypes within the same subject was performed by paired t-test. Before calculating the heritability of BPV, NBPD and HRV, we screened for significant covariates in multiple linear regression analyses. Potential covariates for BPV included in the regression analyses were age, sex, BMI,

NBPD (only for 24-hour BPV), smoking and at the corresponding measurement period the mean blood pressure (systolic, diastolic or mean depending on the BPV phenotype), pulse pressure and HRV. Potential covariates for NBPD were age, sex, BMI, 24 hour blood pressure and pulse pressure, HRV and smoking; and for HRV age, sex, BMI, smoking and at the corresponding measurement period pulse pressure and heart rate. Each heritability analysis for BPV, NBPD and HRV was performed without and with adjustment for significant covariates. Variables for which a normal distribution of the residuals in the regression model was not achieved were transformed in logarithmic scale. All these analyses were performed using NCSS statistical software (version 6.0.21, Statistical Solutions Limited, Cork, Ireland).

Heritability estimates of each phenotype was performed using standard quantitative genetic variance component analysis using the "SOLAR" software package [29] (South-West Foundation for Biomedical Research, San Antonio; TX; USA).

Results

In accordance with a previous population based study [30] we found that age, sex, BMI, HRV and either the corresponding (measurement period and type of blood pressure) blood pressure or pulse pressure were significant covariates for most of the BPV and NBPD phenotypes in the multiple regression analyses (supplementary material, available upon request) and we also confirmed that NBPD was an independent determinant of 24-hour BPV [30]. For most of the HRV phenotypes the significant covariates were heart rate, age, sex and smoking (supplementary material, available upon request), which is also inline with previous reports [31,32]. None of the models accounted for more than 49% of total phenotype variance (range 4-49%).

When analyzed by “long clock-time periods” the heritability of NBPD was significant for systolic and mean blood pressure but after full adjustment the heritability was significant only for systolic NBPD (Table 2). Raw and adjusted heritability estimates for BPV are shown in table 2 and for heart rate and HRV in table 3. The heritability of unadjusted nighttime BPV and that after partial adjustment (that is, for the classical blood pressure co-variates age, sex and BMI) was significant for systolic, diastolic and mean blood pressure (Table 2). After full adjustment, including blood pressure indices, BPV heritability decreased somewhat but remained significant for diastolic and for mean blood pressure (Table 2). No heritability was found for daytime BPV (Table 2). Heart rate was heritable both during day and night but after full adjustment significant HRV was only found at night (Table 3).

In the supplementary analyses of heritability (table 4) using “short clock-time periods” (in contrast to the “long clock-time periods”; table 2-3) the indices of heritability of daytime BPV were higher, although not significant, whereas some of the indices of heritability of nighttime BPV were lower. All the indices of heritability of NBPD resulted to be higher and systolic and mean NBPD heritabilities were significant. The heritability indices of HRV both during daytime and nighttime increased somewhat but only nighttime HRV was significant.

Discussion

The key finding of this study is that nighttime diastolic and mean BPV, as well as HRV, are significantly heritable after adjustment for all significant covariates whereas BPV and HRV during the day are not.

A likely explanation for the day-night discrepancy could be that one proportion of variance in BPV and HRV, which is related to varying degree of emotional stress and physical activity, is not genetically mediated whereas another proportion of BPV and HRV variance, which is determined by autonomous physiological systems, is partially under control of genetic factors. Supporting this hypothesis, at least for HRV, Kupper and colleagues [25] found higher heritability for HRV during nighttime ECG recordings than during daytime when considering specific genetic components. Obviously, the environmental influence of physical activity and emotional stress as well as the influence of other life style factors such as caffeine and alcohol intake, that are hard to quantify and therefore to appropriately adjust for, is greater during the day than at night, thereby diluting the genetic component of daytime BPV and HRV. Thus, although BPV and HRV seems to be clearly more heritable at night than during the day, it cannot be ruled out that a larger study sample than the present one may be able to detect a significant heritability also of daytime BPV and HRV. Furthermore, we defined the nighttime period arbitrarily in order to be able to pre-program the device with fewer measurements at night in an attempt not to disturb night sleep. However, it could well be that we have underestimated both daytime and nighttime BPV and HRV heritability by defining the nighttime arbitrarily rather than as the subjects´ actual sleeping times [33]. In an attempt to exclude the influence on BPV and HRV in subjects whose sleeping times deviated from the ones defined by the “long-clock time periods” we also analysed heritability of BPV and HRV measured during “short clock time periods”. The higher heritabilities for daytime BPV and NBPD may be a consequence of less influence on daytime variability of subjects getting up late or going to bed early. On the other hand some of the

heritability indices of nighttime BPV decreased somewhat. As blood pressure recordings were less frequent at night than during the day, in order not to disturb night sleep, the nighttime phenotypes may be more vulnerable than daytime phenotypes to reducing the number of measurement points. One potential explanation for the reduction in some of the nighttime heritability indices during the "short clock-time period" could thus be lower accuracy of the measured phenotypes when compared to those measured at night during the long clock-time period.

We recently found significant heritability for ABP blood pressure phenotypes, especially for systolic, diastolic and mean blood pressure at night and for pulse pressure regardless of measurement period [22]. As the heritability estimates for nighttime BPV in the present study decreased somewhat after BPV adjustment for significant covariates, including blood pressure and pulse pressure (Table 2), it is likely that part of the heritability of nighttime BPV reflects co-heritability with blood pressure and pulse pressure. This hypothesis is supported by similar heritability estimates for the unadjusted nighttime BPV phenotype of CV, which by definition is normalized for blood pressure, as for the nighttime BPV expressed as SD after full adjustment (Table 2). However, diastolic and mean nighttime BPV remained significant supporting existence of genetic factors controlling these BPV phenotypes, which are separate from those controlling blood pressure.

The reason why systolic nighttime BPV heritability decreased more after adjustment than did diastolic and mean nighttime BPV heritability suggests relatively stronger co-heritability between systolic nighttime BPV and nighttime pulse pressure. Nighttime pulse pressure was a strong determinant of all nighttime BPV:s and the correlation

between nighttime pulse pressure and systolic nighttime BPV was stronger than those between nighttime pulse pressure and diastolic and mean nighttime BPV, respectively (supplementary material, available upon request). In addition, the heritability value of systolic, as compared to diastolic and mean nighttime BPV, was slightly lower both before and after adjustment (Table 2). As emotional stress increases systolic blood pressure more than diastolic and mean blood pressure [34], this may be a consequence of relatively higher environmental heritability dilution of nighttime systolic BPV caused by factors such as intermittent emotional stress during sleep.

In accordance with previous work on the general population [30] we found that HRV and pulse pressure were strong determinants of BPV, indicating that baroreceptor function and arterial stiffness are important determinants of raw BPV. Recent studies have found high heritability for baroreflex function [35] and pulse pressure [22], but the fact that nighttime diastolic and mean BPV heritability remained significant after adjustment for HRV and pulse pressure suggests that there are also genetic factors that affect these BPV phenotypes via pathways unrelated to baroreceptor function and arterial stiffness.

In contrast to the situation with nighttime BPV heritability, systolic NBPD heritability was significant after adjustment for significant covariates, whereas diastolic and mean NBPD were not. Importantly NBPD, which reflects the degree of day to night blood pressure reduction, is a very different variability measure than BPV, which rather reflects constantly ongoing phasic changes in blood pressure. Generally, increased NBPD and BPV, respectively, have opposite relationships with future cardiovascular risk, further underlining the distinct nature of these two phenotypes. The finding of significant

systolic NBPD heritability, indicating a genetic effect, may be clinically meaningful as systolic NBPD has been most strongly related to future cardiovascular risk [12,16,17]. Our finding of significant heritability of nighttime HRV, measured by ABP monitoring, is in accordance with previous studies performed with ECG recordings demonstrating that some measures of HRV, such as frequency and time domain variables, are heritable. [23,25]. Similar to our findings on BPV, daytime HRV was not significant. In part, this discrepancy may have a similar explanation as the lack of heritability of daytime BPV, i.e. dilution of the heritability by environmental influences. However, the studies based on ECG recordings reported significant HRV heritability also during daytime periods [23,25] and it is important to remember that ABP monitoring is not as accurate as ECG to measure HRV. In any case, it seems clear that nighttime HRV has a significant heritability, independently of known HRV determinants [31,32], suggesting the existence of genetic factors that determine HRV via pathways that are yet to be discovered.

BPV and HRV measured with ABP, like the more exact beat-to-beat measures of BPV and HRV recorded intra-arterially and by continuous ECG, have been shown to predict cardiovascular events [5-8] but the molecular mechanisms that determine these traits are unknown. Our finding of significant heritability of systolic NBPD and nighttime measures of BPV and HRV, independently of known covariates, suggests that it may be possible to map genes of importance for these cardiovascular risk phenotypes by linkage analysis thereby to unravel new pathophysiological mechanisms for cardiovascular disease.

To date, there are no clear guidelines of how to use the information on NBPD, BPV and HRV in clinical practice and, in particular, if, when and how it is worth treating them.

Recently, a study in spontaneously hypertensive rats have shown that nitrendipine as compared with hydralazine could decrease significantly BPV inducing organ protection, despite the same blood pressure reduction [36] suggesting that additional cardiovascular risk reduction may be achieved by monitoring and specifically treating BPV. In conclusion, the present study shows that systolic NBPD and nighttime BPV and HRV are heritable independently of known covariates, suggesting that genetic factors controlling these cardiovascular risk factors may be mapped by linkage analyses. Discovery of genetic factors for NBPD, BPV and HRV could be helpful in identifying novel pathophysiological pathways for cardiovascular disease and in the development of new more specific drugs for cardiovascular prevention.

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Supplementary Table 1: Linear Regression of 24-hour BPV for SBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	14.18052	2.992779	8.314783	20.04626	0.0000	4.7382	0.000004
Gender *	-0.7576607	0.2778238	-1.302185	-0.213136	-0.1367	-2.7271	0.006843
Age, year	$7.946672 \cdot 10^{-02}$	$1.579091 \cdot 10^{-02}$	$4.851711 \cdot 10^{-02}$	0.1104163	0.2482	5.0324	0.000001
BMI, Kg/m^2	$-7.482674 \cdot 10^{-03}$	$3.438444 \cdot 10^{-02}$	$-7.487494 \cdot 10^{-02}$	$5.990959 \cdot 10^{-02}$	-0.0107	-0.2176	0.827905
Smoking habit†	0.3474595	0.3177931	-0.2754035	0.9703224	0.0524	1.0934	0.275296
SD of 24-hour HR, bpm	0.1765463	$4.017262 \cdot 10^{-02}$	$9.780943 \cdot 10^{-02}$	0.2552832	0.2142	4.3947	0.000016
24-hour PP, mmHg	0.1747279	$2.744705 \cdot 10^{-02}$	0.1209326	0.2285231	0.3801	6.3660	0.000000
24-hour SBP,mmHg	$1.759013 \cdot 10^{-02}$	$1.848945 \cdot 10^{-02}$	$-1.864853 \cdot 10^{-02}$	$5.382879 \cdot 10^{-02}$	0.0604	0.9514	0.342344
NBPD of SBP, ratio	-19.2288	2.218505	-23.57699	-14.88061	-0.4038	-8.6675	0.000000
Model	r^2 0,49						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;
NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 2: Linear Regression of 24-hour BPV for DBP (SD) measured by ABP and possible covariates. (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	9.687281	2.116669	5.538685	13.83588	0.0000	4.5767	0.000007
Gender *	-0.402649	0.2247225	-0.8430969	3.779897E-02	-0.1063	-1.7918	0.074385
Age, year	9.259392E-03	1.261299E-02	-1.546161E-02	0.0339804	0.0423	0.7341	0.463569
BMI, Kg/m^2	4.516682E-02	2.768823E-02	-9.101112E-03	9.943474E-02	0.0949	1.6313	0.104099
Smoking habit†	1.987992E-03	0.2560312	-0.499824	0.5037999	0.0004	0.0078	0.993811
SD of 24-hour HR, bpm	0.1436215	3.234694E-02	8.022263E-02	0.2070203	0.2550	4.4400	0.000014
24-hour PP, mmHg	6.610819E-02	0.0184933	2.986199E-02	0.1023544	0.2105	3.5747	0.000421
24-hour DBP,mmHg	2.852355E-02	0.0151294	-1.12953E-03	5.817663E-02	0.1107	1.8853	0.060553
NBPD of DBP, ratio	-8.513275	1.34408	-11.14762	-5.878926	-0.3435	-6.3339	0.000000
Model	r^2 0,28						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 3: Linear Regression of 24-hour BPV for MBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	10.64899	2.38468	5.975099	15.32287	0.0000	4.4656	0.000012
Gender *	-0.2213641	0.2339179	-0.6798348	0.2371067	-0.0518	-0.9463	0.344897
Age, year	$3.882886 \cdot 10^{-02}$	$1.350711 \cdot 10^{-02}$	$1.235541 \cdot 10^{-02}$	$6.530231 \cdot 10^{-02}$	0.1574	2.8747	0.004394
BMI, Kg/m^2	$5.345047 \cdot 10^{-02}$	0.0294035	$-4.179331 \cdot 10^{-03}$	0.1110803	0.0995	1.8178	0.070292
Smoking habit†	0.0473144	0.2732915	-0.4883271	0.5829558	0.0093	0.1731	0.862691
SD of 24-hour HR, bpm	0.1406289	0.0345545	$7.290338 \cdot 10^{-02}$	0.2083545	0.2214	4.0698	0.000063
24-hour PP, mmHg	$8.034945 \cdot 10^{-02}$	$1.991908 \cdot 10^{-02}$	$4.130877 \cdot 10^{-02}$	0.1193901	0.2268	4.0338	0.000073
24-hour MBP,mmHg	0.0363064	$1.557058 \cdot 10^{-02}$	$5.788632 \cdot 10^{-02}$	$6.682418 \cdot 10^{-02}$	0.1321	2.3317	0.020513
NBPD of MBP, ratio	-13.10198	1.674314	-16.38357	-9.820385	-0.4024	-7.8253	0.000000
Model	r^2 0,35						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 4: Linear Regression of Daytime BPV for SBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	-2.152201	2.188084	-6.440767	2.136365	0.0000	-0.9836	0.326259
Gender *	-0.5986348	0.2849916	-1.157208	-0.0400615	-0.1218	-2.1005	0.036680
Age, year	0.0707295	$1.611852 \cdot 10^{-02}$	$3.913779 \cdot 10^{-02}$	0.1023212	0.2487	4.3881	0.000017
BMI, Kg/m^2	$5.202778 \cdot 10^{-03}$	$3.510937 \cdot 10^{-02}$	$-6.361033 \cdot 10^{-02}$	$7.401589 \cdot 10^{-02}$	0.0084	0.1482	0.882314
Smoking habit†	0.329165	0.3262597	-0.3102923	0.9686224	0.0559	1.0089	0.313992
SD of Daytime HR, bpm	0.2007744	$4.172787 \cdot 10^{-02}$	0.1189893	0.2825595	0.2701	4.8115	0.000003
Daytime PP, mmHg	0.1628472	$2.775736 \cdot 10^{-02}$	0.1084438	0.2172506	0.4066	5.8668	0.000000
Daytime SBP,mmHg	$7.85314 \cdot 10^{-04}$	$1.809775 \cdot 10^{-02}$	-3.468562•10-02	$3.625625 \cdot 10^{-02}$	0.0032	0.0434	0.965423
Model	r^2 0,29						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 5: Linear Regression of Daytime BPV for DBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	4.475127	1.919009	0.7139378	8.236316	0.0000	2.3320	0.020492
Gender *	-0.3654143	0.2499454	-0.8552982	0.1244697	-0.0939	-1.4620	0.144999
Age, year	$7.032693 \cdot 10^{-03}$	$1.413638 \cdot 10^{-02}$	$-2.067409 \cdot 10^{-02}$	$3.473948 \cdot 10^{-02}$	0.0312	0.4975	0.619280
BMI, Kg/m^2	$7.182283 \cdot 10^{-02}$	$3.079187 \cdot 10^{-02}$	$1.147186 \cdot 10^{-02}$	0.1321738	0.1465	2.3325	0.020464
Smoking habit†	-0.1099246	0.2861386	-0.670746	0.4508969	-0.0235	-0.3842	0.701181
SD of Daytime HR, bpm	0.1724828	3.659648•10-02	0.100755	0.2442105	0.2929	4.7131	0.000004
Daytime PP, mmHg	$4.551172 \cdot 10^{-02}$	2.023907•10-02	$5.84388 \cdot 10^{-03}$	$8.517956 \cdot 10^{-02}$	0.1434	2.2487	0.025399
Daytime DBP,mmHg	$-1.066234 \cdot 10^{-02}$	1.587222•10-02	$-4.177132 \cdot 10^{-02}$	$2.044663 \cdot 10^{-02}$	-0.0428	-0.6718	0.502353
Model	r^2 0,14						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 6: Linear Regression of Daytime BPV for MBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	0.3585084	1.958399	-3.479882	4.196899	0.0000	0.1831	0.854897
Gender *	-0.1048244	0.2572103	-0.6089473	0.3992985	-0.0254	-0.4075	0.683956
Age, year	$3.670141 \cdot 10^{-02}$	$1.487755 \cdot 10^{-02}$	$7.541958 \cdot 10^{-03}$	$6.586087 \cdot 10^{-02}$	0.1535	2.4669	0.014297
BMI, Kg/m^2	$8.369715 \cdot 10^{-02}$	$3.205756 \cdot 10^{-02}$	$2.086549 \cdot 10^{-02}$	0.1465288	0.1608	2.6108	0.009575
Smoking habit†	$-9.550794 \cdot 10^{-02}$	0.2985464	-0.6806481	0.4896322	-0.0193	-0.3199	0.749303
SD of Daytime HR, bpm	0.1880103	$3.822552 \cdot 10^{-02}$	0.1130896	0.2629309	0.3008	4.9184	0.000002
Daytime PP, mmHg	$6.317186 \cdot 10^{-02}$	$2.141343 \cdot 10^{-02}$	$2.120231 \cdot 10^{-02}$	0.1051414	0.1876	2.9501	0.003477
Daytime MBP,mmHg	$7.294576 \cdot 10^{-03}$	$1.655156 \cdot 10^{-02}$	$-2.514588 \cdot 10^{-02}$	$3.973503 \cdot 10^{-02}$	0.0286	0.4407	0.659796
Model	r^2 0,16						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 7: Linear Regression of Nighttime BPV for SBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	-6.863777	3.377912	-13.48436	-0.2431919	0.0000	-2.0320	0.043215
Gender *	-1.502233	0.4837244	-2.450315	-0.5541509	-0.1843	-3.1056	0.002118
Age, year	$8.568691 \cdot 10^{-02}$	$2.682861 \cdot 10^{-02}$	$3.310379 \cdot 10^{-02}$	0.13827	0.1820	3.1939	0.001584
BMI, Kg/m^2	-0.0391986	$5.975066 \cdot 10^{-02}$	-0.1563077	$7.791055 \cdot 10^{-02}$	-0.0382	-0.6560	0.512404
Smoking habit†	0.1964447	0.5530645	-0.8875418	1.280431	0.0201	0.3552	0.722744
SD of Nighttime HR, bpm	0.1253002	$6.535523 \cdot 10^{-02}$	$-2.79366 \cdot 10^{-02}$	0.2533942	0.1094	1.9172	0.056350
Nighttime PP, mmHg	0.1510134	$4.635107 \cdot 10^{-02}$	$6.016697 \cdot 10^{-02}$	0.2418598	0.2234	3.2580	0.001277
Nighttime SBP,mmHg	$7.264186 \cdot 10^{-02}$	$2.685653 \cdot 10^{-02}$	$2.000404 \cdot 10^{-02}$	0.1252797	0.1869	2.7048	0.007304
Model	r^2 0,24						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 8: Linear Regression of Nighttime BPV for DBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	-1.402272	2.881155	-7.049232	4.244689	0.0000	-0.4867	0.626894
Gender *	-0.7654234	0.4137411	-1.576341	4.549433•10-02	-0.1171	-1.8500	0.065493
Age, year	$4.626329•10^{-03}$	$2.287574•10^{-02}$	$-4.020929•10^{-02}$	$4.946195•10^{-02}$	0.0123	0.2022	0.839896
BMI, Kg/m^2	$-3.185793•10^{-02}$	0.0502229	-0.130293	$6.657714•10^{-02}$	-0.0388	-0.6343	0.526445
Smoking habit†	1.781172•10-02	0.4658533	-0.895244	0.9308674	0.0023	0.0382	0.969531
SD of Nighttime HR, bpm	0.1530043	$5.513406•10^{-02}$	0.0449435	0.261065	0.1666	2.7751	0.005935
Nighttime PP, mmHg	$8.300596•10^{-02}$	$3.418798•10^{-02}$	$1.599876•10^{-02}$	0.1500132	0.1531	2.4279	0.015892
Nighttime DBP,mmHg	$9.915214•10^{-02}$	$2.539676•10^{-02}$	0.0493754	0.1489289	0.2418	3.9041	0.000122
Model	r^2 0,16						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 9: Linear Regression of Nighttime BPV for MBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	-5.478824	2.963473	-11.28712	0.3294764	0.0000	-1.8488	0.065670
Gender *	-0.6563076	0.4222791	-1.483959	0.1713442	-0.0959	-1.5542	0.121401
Age, year	$3.438697 \cdot 10^{-02}$	0.0236221	$-1.191149 \cdot 10^{-02}$	$8.068544 \cdot 10^{-02}$	0.0870	1.4557	0.146727
BMI, Kg/m^2	$-1.108117 \cdot 10^{-02}$	$5.188851 \cdot 10^{-02}$	-0.1127808	$9.061844 \cdot 10^{-02}$	-0.0129	-0.2136	0.831066
Smoking habit†	0.161376	0.4818494	-0.7830315	1.105784	0.0197	0.3349	0.737974
SD of nighttime HR, bpm	0.1663589	$5.692299 \cdot 10^{-02}$	$5.479185 \cdot 10^{-02}$	0.2779259	0.1730	2.9225	0.003790
Nighttime PP, mmHg	0.1009758	$3.580325 \cdot 10^{-02}$	$3.080269 \cdot 10^{-02}$	0.1711489	0.1779	2.8203	0.005183
Nighttime MBP,mmHg	$9.534997 \cdot 10^{-02}$	$2.584417 \cdot 10^{-02}$	$4.469633 \cdot 10^{-02}$	0.1460036	0.2301	3.6894	0.000276
Model	r^2 0,18						<0,001

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 10: Linear Regression of 24-hour BPV for SBP (VC) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	20.3763	2.375997	15.71943	25.03316	0.0000	8.5759	0.000000
Gender *	-0.6022361	0.220567	-1.03454	-0.1699327	-0.1451	-2.7304	0.006778
Age, year	$6.167429 \cdot 10^{-02}$	$1.253655 \cdot 10^{-02}$	0.0371031	$8.624548 \cdot 10^{-02}$	0.2572	4.9196	0.000002
BMI, Kg/m^2	$-5.035185 \cdot 10^{-03}$	$2.729814 \cdot 10^{-02}$	$-5.853856 \cdot 10^{-02}$	$4.846819 \cdot 10^{-02}$	-0.0096	-0.1845	0.853809
Smoking habit†	0.2829291	0.252299	-0.2115679	0.777426	0.0569	1.1214	0.263196
SD of 24-hour HR, bpm	0.1466894	$3.189343 \cdot 10^{-02}$	$8.417942 \cdot 10^{-02}$	0.2091994	0.2377	4.5994	0.000007
24-hour PP, mmHg	0.1376151	$2.179048 \cdot 10^{-02}$	$9.490651 \cdot 10^{-02}$	0.1803236	0.3998	6.3154	0.000000
24-hour SBP,mmHg	$-5.701902 \cdot 10^{-02}$	$1.467896 \cdot 10^{-02}$	$-8.578924 \cdot 10^{-02}$	$-2.824879 \cdot 10^{-02}$	-0.2615	-3.8844	0.000132
NBPD of SBP, ratio	-15.45962	1.761292	-18.91169	-12.00755	-0.4335	-8.7774	0.000000
Model	r^2 0,41						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 11: Linear Regression of 24-hour BPV for DBP (VC) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	25.44398	2.783954	19.98753	30.90043	0.0000	9.1395	0.000000
Gender *	-0.5057856	0.2955667	-1.085086	$7.351449 \cdot 10^{-02}$	-0.0966	-1.7112	0.088282
Age, year	$1.122916 \cdot 10^{-02}$	$1.658926 \cdot 10^{-02}$	$-2.128519 \cdot 10^{-02}$	$4.374351 \cdot 10^{-02}$	0.0371	0.6769	0.499102
BMI, Kg/m^2	$5.980925 \cdot 10^{-02}$	0.036417	-1.156676•10-02	0.1311852	0.0909	1.6423	0.101781
Smoking habit†	$6.275382 \cdot 10^{-02}$	0.3367456	-0.5972553	0.722763	0.0100	0.1864	0.852319
SD of 24-hour HR, bpm	0.1949782	$4.254438 \cdot 10^{-02}$	0.1115928	0.2783637	0.2505	4.5829	0.000007
24-hour PP, mmHg	$8.887582 \cdot 10^{-02}$	$2.432335 \cdot 10^{-02}$	$4.120292 \cdot 10^{-02}$	0.1365487	0.2047	3.6539	0.000315
24-hour DBP,mmHg	-0.1311212	$1.989897 \cdot 10^{-02}$	-0.1701225	$-9.211992 \cdot 10^{-02}$	-0.3680	-6.5893	0.000000
NBPD of DBP, ratio	-11.24496	1.767805	-14.70979	-7.780128	-0.3282	-6.3610	0.000000
Model	r^2 0,34						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 12: Linear Regression of 24-hour BPV for MBP (VC) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	22.81762	2.60421	17.71346	27.92178	0.0000	8.7618	0.000000
Gender *	-0.2445672	0.2554521	-0.7452441	0.2561098	-0.0534	-0.9574	0.339299
Age, year	$4.179631 \cdot 10^{-02}$	$1.475056 \cdot 10^{-02}$	$1.288575 \cdot 10^{-02}$	$7.070687 \cdot 10^{-02}$	0.1580	2.8335	0.004981
BMI, Kg/m^2	$6.102416 \cdot 10^{-02}$	$3.211035 \cdot 10^{-02}$	$-1.910969 \cdot 10^{-03}$	0.1239593	0.1060	1.9005	0.058529
Smoking habit†	$9.449215 \cdot 10^{-02}$	0.2984504	-0.4904598	0.6794441	0.0172	0.3166	0.751805
SD of 24-hour HR, bpm	0.1542652	3.773554•10-02	8.030487•10-02	0.2282255	0.2266	4.0881	0.000059
24-hour PP, mmHg	$8.524193 \cdot 10^{-02}$	0.0217528	$4.260723 \cdot 10^{-02}$	0.1278766	0.2245	3.9187	0.000115
24-hour MBP,mmHg	$-8.212914 \cdot 10^{-02}$	1.700399•10-02	-0.1154563	$-4.880194 \cdot 10^{-02}$	-0.2789	-4.8300	0.000002
NBPD of MBP, ratio	-14.293	1.828449	-17.8767	-10.70931	-0.4096	-7.8170	0.000000
Model	r^2 0,33						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 13: Linear Regression of Daytime BPV for SBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	6.083055	1.704742	2.741821	9.424288	0.0000	3.5683	0.000430
Gender *	-0.4489211	0.2220377	-0.8841071	$-1.373515 \cdot 10^{-02}$	-0.1234	-2.0218	0.044256
Age, year	$5.210565 \cdot 10^{-02}$	$1.255798 \cdot 10^{-02}$	$2.749246 \cdot 10^{-02}$	$7.671883 \cdot 10^{-02}$	0.2474	4.1492	0.000046
BMI, Kg/m^2	$5.653718 \cdot 10^{-03}$	$2.735381 \cdot 10^{-02}$	$-4.795876 \cdot 10^{-02}$	$5.926619 \cdot 10^{-02}$	0.0123	0.2067	0.836421
Smoking habit†	0.2601204	0.2541898	-0.2380825	0.7583233	0.0596	1.0233	0.307136
SD of Daytime HR, bpm	0.1599824	0.0325103	$9.626338 \cdot 10^{-02}$	0.2237014	0.2906	4.9210	0.000002
Daytime PP, mmHg	0.1226187	$2.162583 \cdot 10^{-02}$	$8.023281 \cdot 10^{-02}$	0.1650045	0.4135	5.6700	0.000000
Daytime SBP,mmHg	$-5.817855 \cdot 10^{-02}$	0.0141	$-8.581405 \cdot 10^{-02}$	$-3.054305 \cdot 10^{-02}$	-0.3218	-4.1261	0.000050
Model	r^2 0,21						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 14: Linear Regression of Daytime BPV for DBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	15.72694	2.410758	11.00194	20.45193	0.0000	6.5236	0.000000
Gender *	-0.3915366	0.3139941	-1.006954	0.2238806	-0.0731	-1.2470	0.213576
Age, year	$4.485694 \cdot 10^{-03}$	$1.775884 \cdot 10^{-02}$	$-3.032099 \cdot 10^{-02}$	$3.929237 \cdot 10^{-02}$	0.0145	0.2526	0.800792
BMI, Kg/m^2	$9.286218 \cdot 10^{-02}$	$3.868232 \cdot 10^{-02}$	$1.704622 \cdot 10^{-02}$	0.1686781	0.1376	2.4006	0.017095
Smoking habit†	-0.0410056	0.359462	-0.7455381	0.6635269	-0.0064	-0.1141	0.909270
SD of Daytime HR, bpm	0.22134	$4.597436 \cdot 10^{-02}$	0.1312319	0.3114481	0.2731	4.8144	0.000003
Daytime PP, mmHg	$6.341593 \cdot 10^{-02}$	$2.542535 \cdot 10^{-02}$	$1.358317 \cdot 10^{-02}$	0.1132487	0.1452	2.4942	0.013268
Daytime DBP,mmHg	-0.1448911	$1.993949 \cdot 10^{-02}$	-0.1839718	-0.1058104	-0.4230	-7.2665	0.000000
Model	r^2 0,28						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 15: Linear Regression of Daytime BPV for MBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	9.489928	2.051742	5.468589	13.51127	0.0000	4.6253	0.000006
Gender *	$-6.900736 \cdot 10^{-02}$	0.2694696	-0.5971582	0.4591435	-0.0157	-0.2561	0.798094
Age, year	$3.488747 \cdot 10^{-02}$	$1.558665 \cdot 10^{-02}$	$4.338196 \cdot 10^{-03}$	$6.543675 \cdot 10^{-02}$	0.1367	2.2383	0.026079
BMI, Kg/m^2	0.0922496	3.358551•10-02	0.0264232	0.158076	0.1661	2.7467	0.006456
Smoking habit†	-5.663837•10-02	0.3127759	-0.669668	0.5563912	-0.0107	-0.1811	0.856449
SD of Daytime HR, bpm	0.1972371	4.004746•10-02	0.1187455	0.2757287	0.2957	4.9251	0.000002
Daytime PP, mmHg	$6.507569 \cdot 10^{-02}$	$2.243405 \cdot 10^{-02}$	$2.110575 \cdot 10^{-02}$	0.1090456	0.1811	2.9008	0.004053
Daytime MBP,mmHg	$-8.786031 \cdot 10^{-02}$	$1.734045 \cdot 10^{-02}$	-0.121847	$-5.387365 \cdot 10^{-02}$	-0.3228	-5.0668	0.000001
Model	r^2 0,19						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 16: Linear Regression of Nighttime BPV for SBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	2.815248	2.882468	-2.834285	8.464781	0.0000	0.9767	0.329672
Gender *	-1.377488	0.4127757	-2.186513	-0.5684625	-0.2097	-3.3371	0.000975
Age, year	$7.219437 \cdot 10^{-02}$	$2.289362 \cdot 10^{-02}$	$2.732371 \cdot 10^{-02}$	0.117065	0.1903	3.1535	0.001811
BMI, Kg/m^2	$-2.793809 \cdot 10^{-02}$	$5.098693 \cdot 10^{-02}$	-0.1278706	$7.199446 \cdot 10^{-02}$	-0.0338	-0.5479	0.584218
Smoking habit†	0.1694907	0.4719456	-0.7555057	1.094487	0.0216	0.3591	0.719800
SD of Nighttime HR, bpm	0.1081386	$5.576947 \cdot 10^{-02}$	$-1.167577 \cdot 10^{-03}$	0.2174447	0.1172	1.9390	0.053623
Nighttime PP, mmHg	0.1316859	$3.955268 \cdot 10^{-02}$	$5.416403 \cdot 10^{-02}$	0.2092077	0.2418	3.3294	0.001002
Nighttime SBP,mmHg	$-1.335912 \cdot 10^{-02}$	$2.291743 \cdot 10^{-02}$	$-5.827647 \cdot 10^{-02}$	$3.155823 \cdot 10^{-02}$	-0.0427	-0.5829	0.560470
Model	r^2 0,14						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 17: Linear Regression of Nighttime BPV for DBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	10.73307	4.174381	2.551434	18.91471	0.0000	2.5712	0.010715
Gender *	-1.285497	0.5994515	-2.4604	-0.1105932	-0.1413	-2.1445	0.032961
Age, year	$1.035201 \cdot 10^{-02}$	$3.314366 \cdot 10^{-02}$	$-5.460836 \cdot 10^{-02}$	$7.531239 \cdot 10^{-02}$	0.0197	0.3123	0.755044
BMI, Kg/m^2	$-4.213924 \cdot 10^{-02}$	$7.276578 \cdot 10^{-02}$	-0.1847576	0.1004791	-0.0368	-0.5791	0.563038
Smoking habit†	$-2.773229 \cdot 10^{-02}$	0.6749547	-1.350619	1.295155	-0.0025	-0.0411	0.967259
SD of Nighttime HR, bpm	0.2321216	$7.988135 \cdot 10^{-02}$	$7.555707 \cdot 10^{-02}$	0.3886862	0.1816	2.9058	0.003991
Nighttime PP, mmHg	0.1243233	$4.953347 \cdot 10^{-02}$	$2.723948 \cdot 10^{-02}$	0.2214071	0.1648	2.5099	0.012710
Nighttime DBP,mmHg	$-4.382467 \cdot 10^{-02}$	$3.679627 \cdot 10^{-02}$	-0.115944	$2.829469 \cdot 10^{-02}$	-0.0768	-1.1910	0.234780
Model	r^2 0,09						<0,001

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary table 18: Linear Regression of Nighttime BPV for MBP (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	4.114815	3.508547	-2.761811	10.99144	0.0000	1.1728	0.241993
Gender *	-0.9240946	0.4999492	-1.903977	$5.578795 \cdot 10^{-02}$	-0.1197	-1.8484	0.065729
Age, year	0.0441297	$2.796694 \cdot 10^{-02}$	$-1.068449 \cdot 10^{-02}$	$9.894388 \cdot 10^{-02}$	0.0990	1.5779	0.115848
BMI, Kg/m^2	$-7.110251 \cdot 10^{-03}$	$6.143241 \cdot 10^{-02}$	-0.1275156	0.1132951	-0.0073	-0.1157	0.907951
Smoking habit†	0.1922197	0.5704764	-0.9258934	1.310333	0.0208	0.3369	0.736440
SD of Nighttime HR, bpm	0.2023366	$6.739289 \cdot 10^{-02}$	$7.024892 \cdot 10^{-02}$	0.3344242	0.1866	3.0023	0.002951
Nighttime PP, mmHg	0.1219588	$4.238857 \cdot 10^{-02}$	$3.887876 \cdot 10^{-02}$	0.2050389	0.1905	2.8772	0.004359
Nighttime MBP,mmHg	$-1.557709 \cdot 10^{-02}$	$3.059771 \cdot 10^{-02}$	-0.0755475	$4.439332 \cdot 10^{-02}$	-0.0333	-0.5091	0.611136
Model	r^2 0,10						<0,05

BPV Blood Pressure Variability; CV, Coefficient of Variation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 19: Linear Regression of Night to day Dipping in SBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	0.9223496	0.0622605	0.8003212	1.044378	0.0000	14.8144	0.000000
Age, year	$-1.274329 \cdot 10^{-03}$	$4.428967 \cdot 10^{-04}$	$-2.142391 \cdot 10^{-03}$	$-4.062676 \cdot 10^{-04}$	-0.1895	-2.8773	0.004358
BMI, Kg/m^2	$-9.898157 \cdot 10^{-04}$	$9.782371 \cdot 10^{-04}$	$-2.907125 \cdot 10^{-03}$	$9.274938 \cdot 10^{-04}$	-0.0676	-1.0118	0.312595
Gender *	$4.979855 \cdot 10^{-03}$	$7.913989 \cdot 10^{-03}$	$-1.053128 \cdot 10^{-03}$	$2.049099 \cdot 10^{-02}$	0.0428	0.6292	0.529762
Smoking habit†	$3.352644 \cdot 10^{-03}$	$9.057224 \cdot 10^{-03}$	$-1.439919 \cdot 10^{-02}$	$2.110448 \cdot 10^{-02}$	0.0241	0.3702	0.711575
SD of 24-hour HR, bpm	$-8.137437 \cdot 10^{-04}$	$1.144092 \cdot 10^{-03}$	$-3.056122 \cdot 10^{-03}$	$1.428635 \cdot 10^{-03}$	-0.0470	-0.7113	0.477588
24-hour PP, mmHg	$5.897867 \cdot 10^{-05}$	$7.824568 \cdot 10^{-04}$	$-1.474608 \cdot 10^{-03}$	$1.592566 \cdot 10^{-03}$	0.0061	0.0754	0.939976
24-hour SBP,mmHg	4.289617•10-04	$5.264022 \cdot 10^{-04}$	-6.027677•10-04	$1.460691 \cdot 10^{-03}$	0.0702	0.8149	0.415909
Model	r^2 0,04						n.s.

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 20: Linear Regression of Night to day Dipping in DBP (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	78.68221	8.723735	61.58401	95.78042	0.0000	9.0193	0.000000
Age, year	$-4.150636 \cdot 10^{-02}$	$6.275649 \cdot 10^{-02}$	-0.1645068	0.0814941	-0.0442	-0.6614	0.508973
BMI, Kg/m^2	-0.1109953	0.1376847	-0.3808525	0.1588618	-0.0543	-0.8062	0.420919
Gender *	0.1080091	1.118732	-2.084666	2.300684	0.0066	0.0965	0.923164
Smoking habit†	0.6611134	1.275697	-1.839206	3.161433	0.0340	0.5182	0.604751
SD of 24-hour HR, bpm	-0.2972537	0.1610745	-0.6129539	$1.844651 \cdot 10^{-02}$	-0.1229	-1.8454	0.066156
24-hour PP, mmHg	$1.608635 \cdot 10^{-02}$	$9.211347 \cdot 10^{-02}$	-0.1644527	0.1966254	0.0119	0.1746	0.861507
24-hour DBP,mmHg	$9.840413 \cdot 10^{-02}$	0.0753682	-4.931482•10-02	0.2461231	0.0889	1.3056	0.192873
Model	r^2 0,04						n.s.

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 21: Linear Regression of Night to day Dipping in MBP (SD) measured by ABP and possible covariates. (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* $H_0:B=0$	*P*
Intercept	88.03785	7.323404	73.68424	102.3915	0.0000	12.0214	0.000000
Age, year	$-8.018711 \cdot 10^{-02}$	$5.450677 \cdot 10^{-02}$	-0.1870184	$2.664419 \cdot 10^{-02}$	-0.0982	-1.4711	0.142511
BMI, Kg/m^2	-0.1277086	0.1189836	-0.3609121	0.105495	-0.0719	-1.0733	0.284158
Gender *	$-2.964244 \cdot 10^{-02}$	0.948306	-1.888288	1.829003	-0.0021	-0.0313	0.975088
Smoking habit†	0.1800531	1.108473	-1.992515	2.352621	0.0106	0.1624	0.871096
SD of 24-hour HR, bpm	-0.2951554	0.1398319	-0.5692208	$-2.108989 \cdot 10^{-02}$	-0.1405	-2.1108	0.035784
24-hour PP, mmHg	$1.636586 \cdot 10^{-02}$	$8.075798 \cdot 10^{-02}$	-0.1419169	0.1746486	0.0140	0.2027	0.839571
24-hour MBP,mmHg	$4.045804 \cdot 10^{-02}$	$6.314943 \cdot 10^{-02}$	$-8.331256 \cdot 10^{-02}$	0.1642286	0.0445	0.6407	0.522323
Model	r^2 0,04						n.s.

BPV Blood Pressure Variability; SD, Standard deviation; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index; NBPD, Nocturnal Blood Pressure Dipping; SBP, Systolic Blood Pressure; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 22: Linear Regression of 24-hour HRV (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	8.690538	2.54834	3.695884	13.68519	0.0000	3.4103	0.000756
Gender *	-0.7557813	0.4029888	-1.545625	$3.406231 \cdot 10^{-02}$	-0.1124	-1.8754	0.061893
Age, year	$-8.442537 \cdot 10^{-02}$	$2.197381 \cdot 10^{-02}$	-0.1274933	$-4.135748 \cdot 10^{-02}$	-0.2173	-3.8421	0.000155
BMI, Kg/m^2	-0.2021116	$5.122697 \cdot 10^{-02}$	-0.3025146	-0.1017085	-0.2390	-3.9454	0.000103
Smoking habit†	1.002877	0.4692943	$8.307725 \cdot 10^{-02}$	1.922677	0.1245	2.1370	0.033566
24-hour HR, bpm	0.130041	$2.249083 \cdot 10^{-02}$	$8.595975 \cdot 10^{-02}$	0.1741222	0.3550	5.7820	0.000000
24-hour PP,mmHg	$2.827093 \cdot 10^{-02}$	$3.414175 \cdot 10^{-02}$	$-3.864567 \cdot 10^{-02}$	$9.518754 \cdot 10^{-02}$	0.0507	0.8280	0.408431
Model	r^2 0,22						<0,001

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 23: Linear Regression of Daytime HRV (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	6.898113	2.475864	2.045509	11.75072	0.0000	2.7861	0.005740
Gender *	-0.3119799	0.3938553	-1.083922	0.4599624	-0.0472	-0.7921	0.429037
Age, year	$-8.632277 \cdot 10^{-02}$	$2.171275 \cdot 10^{-02}$	-0.128879	$-4.376656 \cdot 10^{-02}$	-0.2256	-3.9757	0.000092
BMI, Kg/m^2	-0.1662938	$4.993752 \cdot 10^{-02}$	-0.2641695	$-6.841805 \cdot 10^{-02}$	-0.1997	-3.3300	0.000998
Smoking habit†	0.9649711	0.4647295	$5.411804 \cdot 10^{-02}$	1.875824	0.1217	2.0764	0.038869
Daytime HR, bpm	0.1183558	$2.055123 \cdot 10^{-02}$	$7.807612 \cdot 10^{-02}$	0.1586355	0.3491	5.7591	0.000000
Daytime PP,mmHg	$3.190506 \cdot 10^{-02}$	$3.278955 \cdot 10^{-02}$	$-3.236127 \cdot 10^{-02}$	9.617139•10-02	0.0592	0.9730	0.331474
Model	r^2 0,21						<0,001

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 24: Linear Regression of Nighttime HRV (SD) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	5.841937	2.642721	0.6622989	11.02157	0.0000	2.2106	0.027967
Gender *	-1.330427	0.4493421	-2.211121	-0.4497326	-0.1869	-2.9608	0.003362
Age, year	$-7.065292 \cdot 10^{-02}$	$2.480411 \cdot 10^{-02}$	-0.1192681	$-2.203776 \cdot 10^{-02}$	-0.1718	-2.8484	0.004758
BMI, Kg/m^2	-0.0864886	$5.810198 \cdot 10^{-02}$	-0.2003664	$2.738919 \cdot 10^{-02}$	-0.0966	-1.4886	0.137857
Smoking habit†	0.3802568	0.5203998	-0.6397082	1.400222	0.0446	0.7307	0.465643
Nighttime HR, bpm	0.1085973	$2.517303 \cdot 10^{-02}$	0.0592591	0.1579356	0.2804	4.3140	0.000023
Nighttime PP,mmHg	$1.743831 \cdot 10^{-02}$	3.547326•10-02	$-5.208801 \cdot 10^{-02}$	$8.696464 \cdot 10^{-02}$	0.0310	0.4916	0.623439
Model	r^2 0,12						<0,01

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 25: Linear Regression of 24-hour HRV (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	26.2493	3.486529	19.41583	33.08278	0.0000	7.5288	0.000000
Gender *	-0.9824353	0.551352	-2.063065	$9.819466 \cdot 10^{-02}$	-0.1112	-1.7819	0.075980
Age, year	-0.1222974	$3.006363 \cdot 10^{-02}$	-0.1812211	$-6.337381 \cdot 10^{-02}$	-0.2397	-4.0680	0.000064
BMI, Kg/m^2	-0.2666596	$7.008654 \cdot 10^{-02}$	-0.4040267	-0.1292926	-0.2401	-3.8047	0.000178
Smoking habit†	1.476257	0.6420683	0.2178265	2.734688	0.1396	2.2992	0.022314
24-hour HR, bpm	$-2.472908 \cdot 10^{-02}$	$3.077098 \cdot 10^{-02}$	$-8.503909 \cdot 10^{-02}$	$3.558093 \cdot 10^{-02}$	-0.0514	-0.8036	0.422360
24-hour PP,mmHg	$4.530425 \cdot 10^{-02}$	$4.671127 \cdot 10^{-02}$	$-4.624817 \cdot 10^{-02}$	0.1368567	0.0618	0.9699	0.333041
Model	r^2 0,15						<0,001

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table.26: Linear Regression of Daytime HRV (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	22.17113	3.249622	15.80199	28.54027	0.0000	6.8227	0.000000
Gender *	-0.388187	0.5169432	-1.401377	0.625003	-0.0471	-0.7509	0.453397
Age, year	-0.1195461	$2.849843 \cdot 10^{-02}$	-0.175402	-0.0636902	-0.2504	-4.1948	0.000038
BMI, Kg/m^2	-0.2105246	$6.554402 \cdot 10^{-02}$	-0.3389885	$-8.206071 \cdot 10^{-02}$	-0.2026	-3.2120	0.001490
Smoking habit†	1.37854	0.609967	0.1830266	2.574053	0.1394	2.2600	0.024674
Daytime HR, bpm	$-2.210399 \cdot 10^{-02}$	$2.697391 \cdot 10^{-02}$	$-7.497188 \cdot 10^{-02}$	$3.076391 \cdot 10^{-02}$	-0.0522	-0.8195	0.413300
Daytime PP,mmHg	$4.849423 \cdot 10^{-02}$	$4.303695 \cdot 10^{-02}$	$-3.585665 \cdot 10^{-02}$	0.1328451	0.0721	1.1268	0.260897
Model	r^2 0,13						<0,001

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Supplementary Table 27: Linear Regression of Nighttime HRV (CV) measured by ABP and possible covariates**.** (n=260)

Variable	*Regression Coefficient*	*Standard Error*	*C.L* lower *limit*	*C.L.* upper *limit*	Standardized Coefficient	*T-value* H_0*:B=0*	*P*
Intercept	19.2131	3.952523	11.4663	26.9599	0.0000	4.8610	0.000002
Gender *	-1.882702	0.6720477	-3.199892	-0.5655128	-0.1803	-2.8014	0.005484
Age, year	-0.1096369	$3.709767 \cdot 10^{-02}$	-0.182347	$-3.692678 \cdot 10^{-02}$	-0.1818	-2.9554	0.003420
BMI, Kg/m^2	-0.1329771	$8.689884 \cdot 10^{-02}$	-0.3032956	$3.734155 \cdot 10^{-02}$	-0.1013	-1.5303	0.127214
Smoking habit†	0.5187852	0.7783236	-1.006701	2.044271	0.0415	0.6665	0.505677
Nighttime HR, bpm	$5.346889 \cdot 10^{-03}$	$3.764945 \cdot 10^{-02}$	$-6.844468 \cdot 10^{-02}$	$7.913845 \cdot 10^{-02}$	0.0094	0.1420	0.887180
Nighttime PP,mmHg	$3.095508 \cdot 10^{-02}$	$5.305474 \cdot 10^{-02}$	-0.0730303	0.1349405	0.0375	0.5835	0.560111
Model	r^2 0,08						<0,05

CV, Coefficient of Variation; HRV Heart Rate Variability; ABP, Ambulatory Blood Pressure; BMI, Body Mass Index;; PP, Pulse Pressure; HR Heart rate. C.L., Confidence limit at 95%; n.s. non significant; * (1 male, 2 female) † (1 not smoker, 2 smoker)

Table 1 Blood pressure and heart rate phenotypes measured by ABP monitoring (n=260)

ABP phenotype	24-hour	Daytime	Nighttime	*P* §
SBP, mmHg	123 ± 10	127 ± 10	115 ± 11	<0.001
DBP, mmHg	76 ± 7	80 ± 8	68 ± 8	<0.001
MBP, mmHg	92 ± 8	96 ± 8	83 ± 8	<0.001
HR, bpm	73.4 ± 9.2	76.8 ± 9.7	65.7 ± 9.2	<0.001
SD of SBP, mmHg	11.3 ± 2.7	10.1 ± 2.5	9.8 ± 4.1	n.s.
SD of DBP, mmHg	10.3 ±1.9	9.0 ± 2	8.6 ± 3.3	<0.05
SD of MBP, mmHg	10.5 ± 2.2	9.3 ± 2.1	8.7 ± 3.4	<0.01
SD of HR, bpm	11.3 ± 3.4	10.7 ± 3.3	7.4 ± 3.6	<0.001

ABP, Ambulatory Blood Pressure; SD, Standard Deviation; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; HR, Heart Rate; § daytime in comparison with nighttime

Table 2 Heritability (%) of BPV and NBPD measured by ABP monitoring (n=260) analyzed by "long-clock time periods".

Blood pressure phenotype (%)	SBP unadjusted	DBP	MBP	SBP § partial adjustment	DBP	MBP	SBP † full adjustment	DBP	MBP
24-hour SD	46***	12	30**	32**	12	28**	21	15	14
Daytime SD	8	0	0	8	0	0	0	0	0
Nighttime SD	33**	36**	42***	29**	39***	42***	23	29**	37**
24-hour VC	33**	5	16	19	7	16	9	9	14
Daytime VC	0	2	0	0	1	0	0	0	0
Nighttime VC	28**	26	36**	24	26	36**	21	25	33**
NBPD	38**	9	36**	29**	9	29**	29**	9	24

BPV, blood pressure variability; NBPD, nocturnal blood pressure dipping; ABP, Ambulatory Blood Pressure; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; SD Standard Deviation; VC: Variation Coefficient;

§ adjustment for age, gender and body mass index;

† BPV phenotypes were adjusted for age, gender, body mass index, smoking, the corresponding (measurement period and type) blood pressure, pulse pressure and heart rate variability (for 24-hour BPV also NBPD), whenever significant.

NBPD phenotypes were adjusted for age, gender, body mass index, corresponding 24-h blood pressure, pulse pressure and heart rate variability, whenever significant; *P < 0.05, **P < 0.01, ***P < 0.001

Table 3 Heritability (%) of HR and HRV measured by ABP monitoring (n=260) and analyzed by long clock-time periods.

HR and HRV phenotype (%)	HR	HRV		HR	HRV		HR	HRV	
	Unadjusted			*partial adjustment			† full adjustment		
		SD	VC		SD	VC		SD	VC
24-hour	58***	35**	29**	61***	25	13	53***	15	15
Daytime	57***	24	23	57***	13	1	53***	1	1
Nighttime	58***	27	38**	58***	24	37**	54***	37**	37**

ABP, Ambulatory Blood Pressure; HR, Heart Rate; HRV, Heart Rate Variability; SD, Standard Deviation; VC, Variation Coefficient;

§ adjustment for age, sex and body mass index; † HR was adjusted for age, gender, body mass index and smoking whereas HRV was adjusted for age, gender, body mass index, HR and smoking, whenever significant; *P < 0.05, **P < 0.01, ***P < 0.001

Table 4 Heritability (%) of BPV, HRV and NBPD measured by ABP monitoring and analyzed by short clock-time period (n=260)

Phenotypes (%)	SBP † full adjustment	DBP	MBP	HR
Daytime SD	20	12	11	5
Nighttime SD	19	31 *	23	48 **
Daytime VC	22	22	11	6
Nighttime VC	15	27	22	48 **
NBPD	35 *	20	39 *	n.a.

ABP, Ambulatory Blood Pressure; NBPD, nocturnal blood pressure dipping; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; HR, Heart Rate; SD, Standard Deviation; VC, Variation Coefficient; n.a. not applicable

Heritability was calculated after "full adjustment" (see methods and tables 2-3)

*P < 0.05, **P < 0.01, ***P < 0.001