



## Research Article

# Association between Irritable Affective Temperament and Nighttime Peripheral and Central Systolic Blood Pressure in Hypertension

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## ABSTRACT

**Background:** Affective temperaments (depressive, anxious, cyclothymic, irritable and hyperthymic) have important role in psychopathology, but cumulating data support their involvement in vascular pathology, especially in hypertension as well. The aim of our study was to evaluate their associations with 24-h peripheral and central hemodynamic parameters in untreated patients who were studied because of elevated office blood pressure.

**Methods:** The oscillometric Mobil-O-Graph was used to measure the 24-h peripheral and central parameters. Affective temperaments, depression and anxiety were evaluated with Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire, Beck and Hamilton Anxiety Scale (HAM-A) questionnaires, respectively.

**Results:** Seventy four patients were involved into the study (45 men). In men after the adjustment for age, irritable affective temperament score was associated with nighttime peripheral and central systolic blood pressure ( $\beta = 1.328$ , std. error = 0.522,  $p = 0.015$  and  $\beta = 1.324$ , std. error = 0.646,  $p = 0.047$ , respectively). In case of nighttime peripheral systolic blood pressure this association remained to be significant after further adjustment for smoking, alcohol consumption, sport activity and body mass index and became non-significant after adjustment for Beck and HAM-A scores. In case of nighttime central systolic blood pressure the association lost its significance after the adjustment for smoking, alcohol consumption and sport activity.

**Conclusion:** Irritable affective temperament can have an impact on nighttime peripheral and central systolic blood pressures in untreated men with elevated office blood pressure.

## HIGHLIGHTS

- Affective temperaments can have importance in vascular pathology.
- Associations were evaluated between temperaments and ABPM and hemodynamic parameters.
- In men irritable temperament correlated with nighttime peripheral and central SBP.
- Affective temperaments can have an impact on 24-h blood pressure patterns.

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## 1. INTRODUCTION

As an inherited part of personality, temperament represents a stable core of emotional reactivity [1]. Affective temperaments (depressive, anxious, cyclothymic, irritable and hyperthymic) determine the basic level of mood, energy and emotional reactivity of an individual

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and also can be the antecedents of minor and major mood disorders [2]. Each temperament possesses both positive and negative aspects. Depressive temperament is sensitive to suffering, self-denying and striving to live in harmony with others. Subjects with pronounced anxious temperament can best be described by exaggerated worries especially toward family members. Cyclothymic temperament shows intense emotions and affective instability with rapid mood shifts, while irritable temperament incorporates critical and skeptical traits. Finally, hyperthymic temperament is characterized by overconfident, over-energetic and upbeat traits [3]. Besides their importance in psychopathology, affective temperaments are likely influence somatic disorders as well. Recently an association has been demonstrated between cyclothymic affective temperament

score and peripheral systolic blood pressure [4] and dominant cyclothymic temperament was found to be associated with chronic hypertension and with acute coronary events in hypertensive patients [5,6]. In contrast, hyperthymic temperament was associated with better augmentation index, which is a pulse wave reflection parameter [4] and patients with higher hyperthymic score showed lower propensity for coronary atherosclerosis [7]. It is also important to note, that sex differences are present in the pattern of affective temperaments [8].

Hypertension, as an independent disease has the highest impact on Cardiovascular (CV) mortality. High blood pressure is the leading cause of death and disability-adjusted life years [9]. In the United States hypertension accounted for more CV deaths than any other modifiable CV Disease (CVD) risk factor and was second only to cigarette smoking as a preventable cause of death for any reason [10,11].

Ambulatory Blood Pressure Monitoring (ABPM) is a recommended method for the diagnosis of hypertension for those patients, who has elevated office blood pressure [12]. It provides the average of blood pressure readings over a defined period, usually 24 h. ABPM is a proper tool for discrimination essential hypertension from white-coat hypertension and it is a better predictor of hypertension-mediated target organ damage than office blood pressure [13]. Recently new oscillometric devices were developed, which are, besides that validated ABPMs, also provide 24-h data on central blood pressure and arterial stiffness parameters [14]. No data is available so far neither with traditional ABPM nor with the novel 24-h central hemodynamic devices about their possible associations with affective temperaments.

The aim of our study was to discover associations between affective temperaments and 24-h peripheral and central blood pressure and arterial stiffness indexes in untreated patients who were under investigation because of elevated office blood pressure. We hypothesized a positive association between different hemodynamic parameters and cyclothymic and irritable temperaments and an inverse association with hyperthymic temperament.

## 2. MATERIALS AND METHODS

### 2.1. Patients

In this cross-sectional study Caucasian patients were involved, who did not have hypertension in the history, but had elevated office blood pressure (>140/90 mmHg) during repeated measurements of a family physician visit. The study was performed in a general practitioner praxis in Budapest, Hungary, between November 2014 and December 2018. Exclusion criteria were the ongoing treatment of hypertension, dementia potentially interfering with the completion of questionnaires or the denial of the consent.

For the involved patients with elevated office blood pressure, within 2 weeks after the screening visit an appointment was agreed for 7 a.m. for ambulatory peripheral and central hemodynamic and arterial stiffness measurement and also for blood sampling. During the screening visit an autoquestionnaire was handed out to them with a written informed consent and with a questionnaire for the evaluation of family and personal history, anxiety, depression and affective temperaments. Patients were asked to bring back the autoquestionnaires for the morning of the clinical measurements.

In the morning of the clinical measurements, after 5 min of rest, blood pressure was evaluated twice on each arm with a validated oscillometric device Omron M3 (Omron Corporation, Japan). The average of the higher side was further used during the study. Next, anxiety was evaluated by the examiner with the used questionnaire and the 24-h ABPM device was taken on the patient, with the cuff placed on the left arm and blood sample was taken from the right arm. The 24-h ABPM device was brought back on the following day, when its results and also of the blood sample were discussed with the patient.

The study was approved by the Scientific and Research Ethics Committee of the Medical Research Council, the Hungarian Ministry of Health (ETT TUKEB 570/2014) and was carried out in accordance with the tenets of the Declaration of Helsinki.

### 2.2. Evaluation of Affective Temperaments, Depression and Anxiety

The Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A) was used to assess affective temperaments on depressive, cyclothymic, hyperthymic, irritable and anxious subscales, requiring ‘yes’ (score 1) or ‘no’ (score 0) answers [15]. TEMPS-A contains 110 items (109 in the version for males) and the questions of the various temperament types are grouped together as follows:

1. Depressive temperament: questions 1–21 (21 points).
2. Cyclothymic temperament: questions 22–42 (21 points).
3. Hyperthymic temperament: questions 23–63 (21 points).
4. Irritable temperament: questions 64–84 (21 points in women, 20 in the men’s version).
5. Anxious temperament: questions 85–110 (26 points).

Temperament evaluation of Memphis, Pisa, Paris and San Diego autoquestionnaire has been extensively studied, translated into more than 25 languages and validated in several of the latter. Similarities and differences were also found in national samples which suggest that distribution of affective temperaments has both universal and cultural-specific characteristics [8].

The Beck Depression Inventory (BDI), created by Beck, is a 21-question multiple-choice self-report questionnaire and is one of the widely used instruments for measuring depression severity. Participants are asked to make ratings on a four point scale, where a higher score correlates with more severe depression [16].

The Hamilton Anxiety Scale (HAM-A) was used to study the severity of anxiety. The scale consists of 14 items, each item is scored on a scale of 0 (not present) to 4 (severe anxiety) and it is evaluated by the examiner [17].

### 2.3. Evaluation of 24-h Peripheral and Central Blood Pressure and Arterial Stiffness

Twenty-four-hour ambulatory peripheral and central blood pressures, arterial stiffness and wave reflection parameters were registered by the Mobil-O-Graph NG device (I.E.M. GmbH, Germany). This is an oscillometric device, whose brachial blood pressure detection unit was validated according to standard protocols [18,19]. For the registration

of pulse wave curves, after the registration of brachial blood pressure, the cuff is kept inflated at the level of diastolic blood pressure for approximately 8 s. During our study for the calibration of brachial pulse waveforms we used the mean arterial pressure–central systolic blood pressure method. Mobil-O-Graph uses the ARCSolver algorithm with generalized transfer function to evaluate aortic pulse waveform [20,21]. Among various indexes, the device, as normal ABPMs measures peripheral (brachial) systolic blood pressure, peripheral diastolic blood pressure and heart rate. Moreover, the device calculates pulse wave velocity, central systolic blood pressure, central diastolic blood pressure and augmentation index normalized for the heart rate of 75 beats/min. The device was monitoring the above parameters every 15 min during the day (7 a.m. to 10 p.m.) and every 30 min during the night (10 p.m. to 7 a.m.) for 24 h. Measurements were used for the analysis if >80% of recordings were valid. Previous validation studies in healthy and hypertensive subjects showed acceptable agreement of Mobil-O-Graph parameters with the parameters of “gold standard” noninvasive and invasive methodologies [21–24]. Twenty-four-hour, daytime and nighttime parameters were studied separately.

## 2.4. Statistical Analysis

Descriptive data are expressed as mean  $\pm$  standard deviation or mean with interquartile ranges or percentages. Normality of continuous parameters was tested with the Kolmogorov–Smirnov test. For the comparison of the different parameters and sexes unpaired Student’s *t*-test or Mann–Whitney *U* test for data failing tests of normality were used.

Based on literature data, sex differences in the association between affective temperaments and the studied hemodynamic or arterial stiffness parameters were expected [8]. It is also well-known, that age is an important predictor of blood pressure parameters. Based on these facts, age and sex were both included into our multiple linear regression models, when the association of affective temperaments and hemodynamic parameters were studied in the whole population. Next, the associations were studied separately in the two sexes with adjustment for age and when a significant association was found, with adjustment for further potential confounders. A two-sided  $p < 0.05$  was considered to be significant. SPSS 22 for Windows (IBM Ltd., USA) was used for all calculations.

## 3. RESULTS

A total of 74 subjects were included. Baseline characteristics of the study participants, including the demographic data, laboratory measurements, psychometric and hemodynamic parameters are included in Table 1. As in many psychometric and hemodynamic parameters significant differences were present between men and women, in Table 1. The data of the whole cohort and the two sexes separately are both demonstrated. Table 1 also demonstrates the result of the ABPM analyses for the confirmation of the diagnosis of hypertension. In men higher proportion of the subjects were confirmed to be hypertensive, while in women the diagnosis of white-coat hypertension was more frequent. Irritable temperament score was equal in those, who regularly drink alcohol [4.5 (2–6) and 3 (1–6) for drinkers and non-drinkers, respectively,  $p = 0.254$ ] and in those, who regularly make sport activity [4 (1.5–6) and 4 (2–6) for sportsman and sedentary, respectively,  $p = 0.631$ ], but it

was significantly higher in those, who smoke [5 (3.5–6) and 3 (1–6) for smokers and non-smokers, respectively,  $p = 0.048$ ].

After the adjustment for age and sex, in the whole population irritable temperament score had an association with borderline significance with nighttime peripheral systolic blood pressure ( $\beta = 1.292$ , std. error = 0.673,  $p = 0.059$ ), and with nighttime central systolic blood pressure ( $\beta = 1.373$ , std. error = 0.752,  $p = 0.072$ ). These associations were missing in women ( $\beta = 1.216$ , std. error = 1.641,  $p = 0.466$  and  $\beta = 1.513$ , std. error = 1.766,  $p = 0.400$  in case of nighttime peripheral and central systolic blood pressure, respectively). Table 2 demonstrates the associations of these two parameters with irritable temperament score in men. Irritable temperament was associated with nighttime peripheral systolic blood pressures after multiple adjustments with potential confounders, like age, smoking, alcohol consumption, sport activity and Body Mass Index (BMI). The association became non-significant after further adjustment for depression and anxiety. In case of nighttime central systolic blood pressure the association became non-significant after the adjustment of smoking, alcohol consumption and sport activity, however, the model improvement was only marginal.

## 4. DISCUSSION

In our study we analyzed first the association between affective temperaments and 24-h, daytime and nighttime peripheral and central blood pressure parameters and found that irritable affective temperament is an independent predictor of nighttime peripheral and central systolic blood pressure in men. Our findings give additional knowledge to the complex psychosomatic relationship between affective temperaments and CV pathology.

Irritable affective temperament shows similarities with anger and hostility traits. Subjects with pronounced hostility have been found to produce exaggerated catecholamine and cortisol secretion in response to anger-provoking stimuli [25] and they secrete extended levels of cortisol during daily living as well [26]. Hostility in healthy young adults is inversely associated with the high frequency component of heart rate variability power spectrum [27], which is regulated by the parasympathetic system [28,29]. These results suggest the overactivation of the sympathetic nervous system in hostility and presumably in subjects with marked irritable temperament, which can lead to the development of hypertension.

This association between hostility and CV pathology is probably indirect, as the reduction of hostility failed to improve autonomic nervous system activity [30] and in other studies behavioral factors, like smoking, alcohol consumption, increased BMI and decreased physical activity suggested to be the mediators between hostility and increased CV risk [31,32]. There are also data in the literature about the association between irritable affective temperament and CV risk factors suggesting similar mediator pathways with hostility. Previously it has been demonstrated that patients with marked irritable and cyclothymic temperaments show higher propensity for smoking [33]. In relation of morbid obesity dominant irritable, cyclothymic and anxious temperaments were found with higher prevalence compared with healthy controls [34]. In case of alcohol dependency, alcoholics scored higher on irritable, cyclothymic and depressive scales [35]. Furthermore, irritable and cyclothymic scores were found to be higher in alcoholics in another study as well [36]. In line with the literature in our study, the association between irritable temperament score and nighttime central

**Table 1** | Baseline characteristics, psychometric and hemodynamic parameters and the confirmation of the diagnosis of hypertension in the whole cohort and in men and women separately

	Whole cohort	Men	Women
N	74	45	29
Age (years)	50 ± 1.76	49.6 ± 16.1	50.5 ± 12.6
Smoking (%)	13 (17.6)	8 (17.8)	5 (17.2)
Alcohol consumption (%)	36 (46.2)	21 (46.7)	15 (51.7)
Regular sport activity (%)	29 (37.2)	17 (37.8)	12 (41.4)
Diabetes (%)	1 (1.3)	1 (2.2)	0
BMI (kg/m <sup>2</sup> )	26.9 ± 3.8	27.5 ± 3.7	25.9 ± 12.2
Glucose (mmol/l)	5.3 (5–5.8)	5.3 (5–5.8)	5.2 (4.8–5.7)
GFR-EPI (mmol/l)	98.1 ± 17	100 ± 18.1	95.3 ± 9.2
Uric acid (μmol/l)	321.5 ± 72.2	355.4 ± 58.9	270.6 ± 59.7*
Cholesterol (mmol/l)	5.75 ± 1.28	5.8 ± 1.4	5.7 ± 1.1
Triglyceride (mmol/l)	1.46 ± 0.72	1.5 ± 0.6	1.3 ± 0.8
Psychometric parameters: TEMPS-A, BDI, HAM-A			
Depressive	6 (4–8)	6 (4–7)	7 (4.5–10)*
Cyclothymic	3 (1–6)	3 (1–6)	3 (0.5–6)
Hyperthymic	12.13 ± 0.73	12.5 ± 3.8	9.6 ± 4.5*
Irritable	4 (2–6)	5 (2.5–6)	3 (1–5.5)
Anxious	4 (1–7)	3 (1–6)	5 (2–8.5)*
BDI	5 (2–8)	3 (2–7)	6 (3–10)*
HAM-A	6.5 (4–13)	6 (3–10.5)	8 (4–15)*
Hemodynamic parameters			
Office SBP (mmHg)	141.6 ± 15.6	145.3 ± 13.7	136 ± 16.9*
Office DBP (mmHg)	86.1 ± 10.1	87.5 ± 11.1	83.9 ± 8
Office HR (1/min)	75.7 (68.2–86)	74.5 (68–86.2)	83.5 (73–85.7)
24-h pSBP (mmHg)	126.5 (121.7–132)	129 (124.5–137)	123 (118–128)*
Daytime pSBP (mmHg)	130.5 (124–137.2)	132 (127.5–140)	126 (122–131.5)*
Nighttime pSBP (mmHg)	113.5 (107–122)	117 (109–125)	109 (105–118)*
24-h pDBP (mmHg)	79 (74–87.5)	82 (76–89)	76 (71.5–81.5)*
Daytime pDBP (mmHg)	84.2 ± 9.8	86.5 ± 10.6	80.8 ± 9.6*
Nighttime pDBP (mmHg)	69 (64–76.2)	71 (64–80)	66 (62.5–69)*
24-h cSBP (mmHg)	127.5 (123–137)	131 (126–138)	124 (120–128)*
Daytime cSBP (mmHg)	130 (124–137.5)	133 (128.5–140)	125 (122–131)*
Nighttime cSBP (mmHg)	122 (115.7–136)	126 (119–139.5)	118 (110.5–124.5)*
24-h cDBP (mmHg)	80.5 (75–90)	83 (78–90)	77 (73.5–82.5)*
Daytime cDBP (mmHg)	85.9 ± 10.5	88.3 ± 10.5	82.2 ± 9.6*
Nighttime cDBP (mmHg)	69 (64.5–78)	73 (65.5–81.5)	67 (62.2–70.5)*
24-h HR (1/min)	74 (68.7–82)	72 (67–82)	76 (70–81)
Daytime HR (1/min)	76.5 (71–85)	76 (71–86)	79 (73.5–84.5)
Nighttime HR (1/min)	63 (59–68)	62 (57.5–69)	65 (61–68)
24-h Aix75 (%)	21.8 ± 6.9	18.5 ± 5.8	26.7 ± 5.3*
Daytime Aix (%)	22.6 ± 7.4	18.9 ± 6.3	28.1 ± 5.4*
Nighttime Aix (%)	19.2 ± 10.6	17.3 ± 9.7	21.9 ± 11.4
24-h PWV (m/s)	7.1 (6.3–8.6)	7.2 (6.3–9.2)	7.1 (6.2–8.5)
Daytime PWV (m/s)	7.3 (6.3–8.7)	7.4 (6.3–9.2)	7.2 (6.4–8.6)
Nighttime PWV (m/s)	6.6 (5.8–8.1)	6.6 (5.8–8.9)	6.7 (5.6–8)
Outcome			
Essential HT/white-coat HT	37/37	27/18	10/19

\* $p < 0.05$ . Data are presented as mean ± SD or median (interquartile range). BMI, body mass index; GFR-EPI, glomerular filtration rate assessed by the chronic kidney disease epidemiology collaboration glomerular filtration rate equation; TEMPS-A, temperament evaluation of Memphis Pisa, Paris and San Diego questionnaire; BDI, beck depression inventory score; HAM-A, Hamilton Anxiety Scale; SBP, systolic blood pressure; pSBP, peripheral SBP; cSBP, central SBP; DBP, diastolic blood pressure; pDBP, peripheral DBP; cDBP, central DBP; HR, heart rate; PWV, pulse wave velocity; Aix75, augmentation index normalized for the heart rate of 75 beats/min; HT, hypertension.

systolic blood pressure in men has become to be non-significant after the adjustment for smoking, alcohol consumption and regular sport activity suggesting their mediator role in this association. In contrast, in case of nighttime peripheral systolic blood pressure the association in men with irritable temperament has remained to be significant even after the adjustment for these confounders plus BMI as well, suggesting the presence of other mediators. These were depression and anxiety, which are also known risk factors of CV diseases [37,38].

In our study we have found that in men irritable affective temperament was associated with nighttime peripheral and central systolic blood pressures. The importance of nighttime peripheral systolic blood pressure in the relation with the prediction of CV outcome is well-known and was also confirmed in a recent study on more than 11,000 subjects [39]. As the measurement of ambulatory central blood pressure is a relatively new methodology with <10 years of history, only a few data is available about

**Table 2** | Predictive values of irritable affective temperament scores on nighttime peripheral systolic blood pressure and on nighttime central systolic blood pressure in different models in men. Other significant predictors of the final models are also demonstrated

	$\beta$	Std. error	Std. beta	<i>p</i>	<i>R</i> <sup>2</sup>
Nighttime peripheral systolic BP					
Model 1 (Age)					0.134
Irritable temp. score	1.328	0.522	0.376	0.015*	
Model 2 (Model 1 + smoking, alcohol consumption, sport activity)					0.249
Irritable temp. score	1.259	0.511	0.356	0.018*	
Model 3 (Model 2 + BMI)					0.250
Irritable temp. score	1.243	0.523	0.352	0.023*	
Model 4 (Model 3 + BDI, HAM-A)					0.272
Irritable temp. score	1.154	0.621	0.326	0.072	
Sport activity	-7.958	3.427	-0.372	0.026*	
Nighttime central systolic BP					
Model 1 (Age)					0.122
Irritable temp. score	1.324	0.646	0.304	0.047*	
Model 2 (Model 1 + smoking, alcohol consumption, sport activity)					0.150
Irritable temp. score	1.346	0.669	0.310	0.051	

\**p* < 0.05. BP, blood pressure; Irritable temp. score, irritable affective temperament score; BMI, body mass index; BDI, beck depression inventory; HAM-A, Hamilton Anxiety Scale.

its clinical importance and no data is provided about the predictive value of nighttime central blood pressure yet. Twenty-four-hour central systolic blood pressure was better associated with left ventricular mass than peripheral office systolic blood pressure in a population with suspected hypertension, but free of antihypertensive medication [40]. In contrast, in hemodialysis patients 48-h central systolic blood pressure failed to predict all-cause mortality [41]. However, the associations of irritable temperament with nighttime peripheral and central systolic blood pressure in our present study in line with previous findings in hypertensive patients confirms the importance of the identification of affective temperaments not only in psychopathology but also in CV disorders.

There are some limitations of our study. The relatively low number of the involved patients limited the detailed analysis and the involvement of more confounders into the multiple regressions. Although standardized autoquestionnaires were used and patients with dementia were excluded, but a complete exclusion of mistakes or misinterpretations by patients was not possible. Additionally, a limitation stems from the cross-sectional design of the study which precludes causal inference. Finally, the characteristics of the involved patients, as all were examined because of elevated office blood pressure, limits the generalizability of our findings, although it was a clinically realistic selection.

In conclusion, this is the first study which evaluated associations between affective temperaments and 24-h peripheral and central hemodynamic parameters and discovered positive associations between irritable affective temperament score and nighttime peripheral and central systolic blood pressure in men. Our new data support the hypothesis, that affective temperaments have complex psychosomatic impact and their evaluation may help in the identification of subjects with higher risk both for psychopathological and CV disorders.

## CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

## AUTHOR'S CONTRIBUTION

BK, DB and JN conceptualized the study. BK, DB, JN, AL and MVN planned the investigation. XG and ZR contributed to methodology. XG, ZR, AL, MVN wrote (review and editing) the manuscript. JN performed the formal analysis and wrote (original draft) the manuscript.

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