Twenty-four-Hour Blood Pressure and Heart Rate Profiles in Humans

A Twin Study

Jean-Paul Degaute, Eve Van Cauter, Philippe van de Borne, Paul Linkowski

Abstract  To delineate the relative roles of genetic and environmental factors on physiological variations of blood pressure and heart rate, we performed 24-hour ambulatory blood pressure monitoring with simultaneous polygraphic sleep recordings in 28 monozygotic and 16 dizygotic healthy young male twin pairs investigated in a standardized physical and social environment. Blood pressure and heart rate were measured every 10 minutes for 24 hours. A best-fit curve based on the periodogram method was used to quantify changes in blood pressure and heart rate over the 24-hour span. Surprisingly, monozygotic twins as a group tended to have higher blood pressure values than dizygotic twins, and this difference reached the level of significance for daytime systolic blood pressure (P<.005). Although environmental influences largely controlled the mean levels and characteristics of the 24-hour systolic blood pressure variations, significant genetic effects were demonstrated for the mean levels and 24-hour patterns of diastolic blood pressure and heart rate. For both diastolic blood pressure and heart rate, the genetic effects concerned largely the same characteristics of the 24-hour profiles: the 24-hour mean, the daytime mean, the value of the evening acrophase, and the value of the major acrophase. Moreover, there was a strong genetic influence for the amplitude of the 24-hour rhythm of heart rate. (Hypertension. 1994;23:244-253.)

Key Words  • genetics  •  blood pressure  •  heart rate  •  blood pressure monitoring  •  circadian rhythm  •  twins

The recent development of noninvasive ambulatory blood pressure recorders has shown the existence of a wide intraindividual and interindividual variability of blood pressure in humans.1 Twin studies, based on casual blood pressure recordings, have indicated that resting blood pressure levels are more concordant among monozygotic (MZ) than dizygotic (DZ) twins. This finding suggests that a significant component of the variability in blood pressure levels is of genetic origin.2-5 However, casual blood pressure measurements also partially reflect the well-known reaction to the clinical setting usually referred to as the "white coat" effect.6 A genetic contribution for cardiovascular reactivity, studied by various environmental stressors, has been demonstrated by several investigators,7-10 but estimations of the relative importance of this genetic component have been variable across studies. Thus, at the present time, the relative importance of genetic and environmental factors in controlling resting blood pressure, resting heart rate, and cardiovascular reactivity in healthy humans remains to be determined.

There are several approaches for the evaluation of the inheritance of blood pressure, including familial aggregation of blood pressure in adults and children, adoption studies, and twin studies. Generally, the estimates of genetic variance derived from twin studies are higher than estimates derived from other study designs. This is probably due to the greater extent of shared environment in MZ twins, which gives rise to an upwardly biased estimate of genetic variance.11 Nevertheless, the twin model has been used extensively in medical research for more than half a century.12

We have previously described the normal diurnal variations in blood pressure and heart rate using a computerized method for characterization of 24-hour temporal variations and polygraphic sleep recordings.11,13 In the present study, groups of young male MZ and DZ twins were investigated using a similar methodology to delineate the relative roles of genetic and environmental factors on physiological variations of blood pressure and heart rate levels under standardized social and physical conditions.

Methods

The Twin Sample

Procedures used for recruitment and selection of twins have been previously described.4,15 Briefly, the twins were selected from the Twins Registers of the Universiteit Antwerpen and the Vrije Universiteit Brussel and from the computer files of the student and alumni population of five major Belgian universities in the cities of Brussels (Université Libre de Bruxelles and Vrije Universiteit Brussel), Louvain (Université Catholique de Louvain), Liège, and Mons. A total of 509 twin pairs were invited by phone to participate in the study. Eighty-three pairs agreed to come to the hospital for a detailed interview and physical examination. Forty-four pairs of young male twins aged 16 to 36 years, including 28 MZ pairs (mean age, 23.4±5.2 years) and 16 DZ pairs (mean age, 23.9±4.8 years), were finally selected.

Subjects suffering from current or past major somatic, psychiatric, or sleep pathology as well as shift workers were excluded. We also noted whether subjects were living together (ie, cohabiting) or apart (ie, noncohabiting). There were 17
cohabiting pairs among the 28 pairs of MZ twins and 9 cohabiting pairs among the 16 pairs of DZ twins. These proportions of cohabiting pairs were not significantly different between the two groups of twins.

On admission, all subjects underwent a physical examination and routine laboratory tests. They gave informed consent and were paid for their participation in the study.

Twin zygosity was determined after analysis of different blood markers including ABO, Rh, MNSs, Kk, Lea, Leb, Fya, Fyb, Jka, Jkb, and Pi blood groups. For twin pairs who were identical in all the genetic markers but judged themselves to be dizygotic or were considered as physically different by the principal investigator, zygosity was confirmed using DNA acid fingerprinting with the M13 probe (five pairs).16

Experimental Protocol

All twins were studied in the Sleep Laboratory of the Department of Psychiatry, Hôpital Erasme, Université Libre de Bruxelles, Belgium. The protocol was approved by the Ethics Committee. Both members of each pair were studied simultaneously but in separate rooms. After one night of habituation to the laboratory environment, polygraphic sleep recordings were performed during four consecutive nights. During the day preceding the fourth night of recording, ambulatory blood pressure was monitored with a noninvasive device based on the auscultatory method of measuring blood pressure (Medilog, Oxford Medical Ltd). The subjects were equipped with the device between 8 and 9 AM. Blood pressure and heart rate were measured automatically every 10 minutes during a 24-hour period. The arm cuff was positioned on the nondominant arm (ie, left arm for right-handed subjects and right arm for left-handed subjects). Other details of the experimental protocol were as described in our previous study on 24-hour blood pressure patterns in young men.1 The 31 volunteers included in this previous analysis were one randomly selected member of the first 31 of the total of 44 twin pairs included in the present study.

During the daytime, the subjects were free to ambulate inside the hospital but were required to take two 1-hour walks, one in the morning and one in the afternoon. Recumbency and naps were not allowed. The subjects were asked to refrain from movement and to keep their arm immobile during each cuff deflation. Standard mixed meals of identical composition were served at fixed hours.

Data Analysis

For all recordings, the first hour of measurement was not included in the analysis to eliminate possible artifacts related to the beginning of the experiment. All measurements that corresponded to a pulse pressure below 15 mm Hg or represented an isolated increase by more than 50% over the previous measurement were considered to be technical artifacts and were deleted. Deleted data points were replaced by linear interpolation between the previous and following measurements. For each subject, at least 80% of valid blood pressure and heart rate measurements had to be obtained for inclusion in the study.

For each profile of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate, the 24-hour mean level was calculated as the mean of all measurements obtained during the 24-hour study period. The sleep mean was defined as the mean of all measurements obtained after sleep onset and before morning awakening as determined from electroencephalographic recordings. The daytime mean was defined as the mean of all measurements obtained between 9 AM and 9 PM, ie, a period during which all subjects were awake and ambulatory.

The 24-hour variations of SBP, DBP, and heart rate were quantitatively characterized by a best-fit curve obtained by repeated periodogram calculations.15 The asymmetric nature of the resulting best-fit curve, with one nocturnal nadir and one in the morning and one in the afternoon. Recumbency and naps were not allowed. The subjects were asked to refrain from movement and to keep their arm immobile during each cuff deflation. Standard mixed meals of identical composition were served at fixed hours.

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The 24-hour variations of SBP, DBP, and heart rate were quantitatively characterized by a best-fit curve obtained by repeated periodogram calculations.15 The asymmetric nature of the resulting best-fit curve, with one nocturnal nadir and two daytime acrophases, has been confirmed using a totally different analytic approach.17 Thus, the periodogram procedure appears to be superior to methods based on a single sinusoid curve, such as the cosinor.18-20 Using this methodology, we have previously shown that 24-hour blood pressure and heart rate profiles are adequately described by a best-fit curve including two periodogram components—one with a period between 23 and 24 hours, and one with a period between 11 and 12 hours.1 Thus, to standardize the analysis of the blood pressure and heart rate profiles within and among twin pairs, the best-fit curve included these two periodogram components, with period lengths minimizing the sum of squared residuals. Such best-fit curves may be unimodal (ie, characterized by a single acrophase) or bimodal (ie, characterized by two acrophases). The acrophases and nadirs were defined as, respectively, the times of occurrence of maxima and minima in the best-fit curve. The amplitude of the best-fit curve was defined as 50% of the difference between its maximum and minimum. The level of an acrophase (nadir) was defined as the level of the best-fit curve at the time of occurrence of the acrophase (nadir). An example of a 24-hour blood pressure profile and the corresponding best-fit curve obtained in a representative subject is illustrated in Fig 1. The 24-hour blood pressure and heart rate profiles are typically bimodal, with a morning acrophase (around 10 AM), a modest afternoon nadir (around 3 PM), an evening acrophase (around 8 PM), and a profound nocturnal nadir (around 3 AM).

For determination of which component of the 24-hour pattern was significantly affected by genetic factors, each parameter quantifying the 24-hour variation of SBP, DBP, and heart rate (ie, 24-hour mean, daytime mean, sleep mean, amplitude of the 24-hour variation, timing and value of the daytime acrophases, and timing and value of the nocturnal nadir) was submitted separately to the analysis of genetic variance described below. When the best-fit curve was unimodal rather than bimodal, the single acrophase was considered as a "morning" acrophase if it occurred in the morning or in the early afternoon (ie, before 3 PM) and as an "evening" acrophase if it occurred after 3 PM. For determination of whether genetic factors influence the overall daily maxima of blood pressure and heart rate, irrespective of their times of occurrence, the major acrophase, ie, the acrophase with the highest value in the case of bimodal profiles or the single acrophase in the case of unimodal profiles, was also submitted to the analysis of genetic variance.

For each parameter, the analysis of genetic variance was performed according to the methodology developed by Christian and associates.21-23 When applied to twin samples such as those in the present study, this analysis is relatively sensitive to outlying values. Therefore, for each parameter, outliers were
identified using a two-tailed test described by Grobb and Beck. This procedure tests the significance of the standardized deviation of the smallest \((X_i)\) or largest \((X_i)\) observation in a normal sample of \(n\) observations [ie, \((X-X)/S\) or \((X-X)/S\), where \(X\) is the sample mean and \(S\) is the sample standard deviation] against the null hypothesis. If necessary, the analysis was repeated after excluding the outlying pair or pairs. A first step in the analysis of Christian et al is a test of the differences between twin means for the trait studied, further analysis being valid only if the means do not differ significantly. If the first condition is fulfilled, the second step consists of calculating two independent estimates of the genetic variance: the “within-twin pair estimate” and the “among-twin pair component estimate.” The within-twin pair estimate, \(G_{WT}\), is \(G_{WT}=M_{W_{DZ}}-M_{W_{MZ}}\) (\(M_{W_{DZ}}\) and \(M_{W_{MZ}}\) being the mean squares for within-pair variation in DZ and MZ twins, respectively). The significance of \(G_{WT}\) is tested by a one-tailed \(F=\frac{M_{W_{DZ}}}{M_{W_{MZ}}}\). The among-twin pair component estimate, \(G_{AT}\), is \(G_{AT}=G_{WT}+G_{ATR}\), with \(G_{WT}\) being the within-twin pair estimate and \(G_{ATR}=M_{D_{DZ}}-M_{D_{MZ}}\) (\(M_{D_{DZ}}\) and \(M_{D_{MZ}}\) being, respectively, the mean squares for among-twin pair variation in MZ and DZ twins). The significance of \(G_{CT}\) is tested by a one-tailed \(F=\frac{M_{D_{DZ}}+M_{D_{MZ}}}{M_{D_{DZ}}+M_{D_{MZ}}}\). The third step is a test of equality of the variances of the trait under study for the MZ and DZ groups. The genetic variance is significant whenever (1) the variances of the MZ and DZ twins are not significantly different and the within-twin pair estimate is significant at the 5% level or (2) the variances are not equal and the among-twin pair component estimate is significant at the 5% level. These estimates of genetic variance are appropriate if there are no MZ-DZ differences in environmental covariation. This possible greater environmental covariation in MZ twins is detected by a screening \(F\) test of \(M_{W_{DZ}}/M_{W_{MZ}}\). If an estimate of genetic variance is significant and this \(F\) ratio is not appreciably greater than 1.0, then the possibility of greater environmental covariation for MZ twins should be suspected. Among the outputs of the analysis are the intraclass coefficients of correlation, which are a measure of the similarity in the parameter of interest in the MZ and DZ twin pairs. The existence of a significant genetic effect is typically reflected in a higher intraclass correlation in the MZ than the DZ group. However, if there is a significant intraclass correlation in the MZ group but not in the DZ group, the existence of a higher environmental covariation in the MZ group, rather than of a genetic effect, should be suspected, because a genetic effect should be reflected in a significant level of correlation among the DZ twins, who are genetically related as siblings. It is also possible that relatively small DZ intraclass correlations may reflect the presence of gene interactions.27

Results

Anthropometric Characteristics

There were no significant differences between MZ and DZ twins concerning their body weight (70.4 ± 9.7 versus 71.1 ± 9.8 kg, respectively), height (1.80 ± 0.07 versus 1.80 ± 0.06 m), and body mass index (22.1 ± 2.8 versus 21.8 ± 2.7 kg/m²). As expected, the estimates of genetic variance were significant for these anthropometric features (respectively, within-pair estimate: 19, \(P<.001\); among-component estimate: 240, \(P<.003\); within-pair estimate: 3, \(P<.005\)).

Systolic Blood Pressure

Mean Levels Over the 24-Hour Span, During the Daytime, and During Sleep

The top panel of Fig 2 illustrates the mean 24-hour profiles of SBP in MZ and DZ twins. Unexpectedly, mean SBP levels were consistently higher by approximately 5 mm Hg in MZ than in DZ twins except during the early morning. This difference was statistically significant during the daytime period only (\(P<.005\)), and the analysis of genetic variance could not be applied to this parameter. Table 1 gives the results of the analysis of genetic variance for all parameters characterizing the SBP profiles. For the 24-hour mean levels, the estimations of intraclass correlations and genetic variance showed that there was a predominant environmental effect. The same conclusion could be drawn for the mean levels during sleep. The distribution around the line of identity of individual values for the mean daytime level is shown in the top left panels of Fig 3 for both groups of twins.

Quantitative Characteristics of the 24-Hour Profiles

Table 2 gives the proportion of unimodal and bimodal best-fit curves obtained for the SBP profiles and the concordance of subtype of best-fit curve within twin pairs. The overall proportion of individual SBP profiles for which the best-fit pattern was bimodal was 86%, ie, a proportion similar to that observed in our previous study (87%).1 The analysis of genetic variance did not indicate the existence of a genetic control for the amplitude of the
24-hour SBP variation. Indeed, because the intraclass correlation in the DZ group was not different from zero, the significant intraclass correlation in the MZ group indicated a greater environmental covariance in this group rather than a genetic effect. Scatterplots showing the distribution of individual values for the amplitude of the diurnal variation in SBP in MZ and DZ twins are presented in the top left panels of Fig 4.

As far as the values of the morning acrophases were concerned, there was an outlier in the DZ group. When this DZ pair was excluded, the difference in mean values of the morning acrophases between MZ and DZ twins became significant, and thus the analysis of Christian et al.\textsuperscript{21-23} could not be applied. However, an environmental effect for the value of the morning acrophase, based on significant intraclass correlations for both groups of twins, was suggested. For the times of occurrence of the morning acrophases, neither genetic nor environmental effects were found to be significant.

For the evening acrophases, the analysis of genetic variance indicated the existence of an environmental effect on their values. The interpretation of the findings regarding the times of occurrence of the evening acrophases is unclear. Indeed, the estimate of genetic variance was statistically significant, but the intraclass correlation in the DZ group was significantly negative. This combination may reflect greater environmental covariance in MZ twins or the effects of gene interaction.\textsuperscript{24} The analysis of genetic variance for the value of the major acrophase indicated the existence of a predominant environmental effect. The top left panels of Fig 5 show the distribution around the line of identity of individual values of the major acrophase of SBP in MZ and DZ twins.

When the characteristics of the nocturnal nadirs were examined, environmental effects appeared to be predominant for their values, whereas for their timings the analysis indicated the existence of a greater environmental covariance in MZ twins.

### Diastolic Blood Pressure

The results of the analysis of genetic variance of the mean DBP levels and of the characteristics of the 24-hour DBP patterns are summarized in Table 3.

#### Mean Levels Over the 24-Hour Span, During the Daytime, and During Sleep

The middle panel of Fig 2 shows the mean DBP profiles in both groups of twins. As was observed for SBP, mean DBP levels appeared to be higher in MZ than in DZ twins, but in the case of DBP this difference was not significant during either the daytime or the nighttime. The analysis of genetic variance showed that both the 24-hour and daytime mean levels were influenced by genetic factors (Table 3). Indeed, the existence of a greater environmental covariance in MZ twins...
FIG 3. Scatterplots show day mean of systolic blood pressure, diastolic blood pressure, and heart rate in one member of each twin pair versus the same parameter in the other member of the same twin pair. For each parameter, the distribution of values around the line of identity is represented in the left panels for the monozygotic group (MZ) and in the right panels for the dizygotic group (DZ).

could be reasonably excluded ($P=.07$ and $.17$, respectively). On the contrary, the possibility of a larger environmental covariance in MZ twins for the mean DBP level during sleep could not be excluded ($P=.66$). The distribution of the individual values of the mean daytime DBP levels around the line of identity is presented for both groups of twins in the top right panels of Fig 3.

**Quantitative Characteristics of the 24-Hour Profiles**

The proportion of unimodal and bimodal best-fit curves obtained for the DBP profiles and their concordance within twin pairs are given in Table 2. The overall proportion of individual DBP profiles for which the best-fit pattern was bimodal was 67%. In our previous study, 81% of the DBP profiles disclosed a bimodal pattern. In the remaining 57 volunteers who completed the whole study population of the present report, a similar proportion of bimodal profiles was observed (60%, $P=\text{NS}$, $\chi^2$ test).

No significant outlier was detected for any of the parameters characterizing the 24-hour DBP variation. However, for the value of the nocturnal nadir, one MZ twin pair was almost qualified as an outlier with a probability level of .08. When this MZ pair was maintained in the group, the difference between the means of MZ and DZ twins for the values of the nocturnal nadirs was significant, and thus the analysis of Christian

<table>
<thead>
<tr>
<th>Subtype of Best-Fit Curve</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both twins, bimodal</td>
<td>21/28 = 75.0%</td>
<td>14/16 = 87.5%</td>
<td>17/28 = 60.7%</td>
</tr>
<tr>
<td>Both twins, unimodal</td>
<td>2/28 = 7.1%</td>
<td>0/16 = 0%</td>
<td>4/28 = 14.3%</td>
</tr>
<tr>
<td>One twin unimodal, one twin bimodal</td>
<td>4/28 = 14.3%</td>
<td>1/16 = 6.3%</td>
<td>5/28 = 17.9%</td>
</tr>
<tr>
<td>No significant best-fit curve in one twin</td>
<td>1/28 = 3.6%</td>
<td>1/16 = 6.3%</td>
<td>1/28 = 3.6%</td>
</tr>
<tr>
<td>No significant best-fit curve in both twins</td>
<td>0/28 = 0%</td>
<td>0/16 = 0%</td>
<td>1/28 = 3.6%</td>
</tr>
</tbody>
</table>

BP Indicates blood pressure; MZ, monozygotic twins; and DZ, dizygotic twins. The differences in proportions of concordant subtypes of best-fit curves between MZ and DZ twins were not significant ($\chi^2$ test).
FIG 4. Scatterplots show amplitude of systolic blood pressure, diastolic blood pressure, and heart rate variation in one member of each twin pair versus the same parameter in the other member of the same twin pair. For each parameter, the distribution of values around the line of identity is represented in the left panels for the monozygotic group (MZ) and in the right panels for the dizygotic group (DZ).

et al.21-25 could not be applied. For examination of the possible existence of genetic influences on this parameter, the analysis of genetic variance was applied after this borderline outlying pair was removed from the MZ sample.

When the amplitude of the 24-hour DBP variation was examined, the intraclass correlations indicated a positive correlation in the MZ group but not in the DZ group. Therefore, the significant within-pair estimate of genetic variance needed to be interpreted as reflecting a difference in environmental covariance between MZ and DZ twins. The top right panels of Fig 4 show the distribution around the line of identity of individual values of the amplitude of the 24-hour variation of DBP in MZ and DZ twins.

For the morning acrophases, the examination of the intraclass correlations and of the estimates of genetic variance demonstrated a predominant environmental effect for both their values and times of occurrence (Table 3). Concerning the evening acrophases, there was a trend for a genetic influence for their values (P = .09), whereas neither a genetic nor an environmental effect could be evidenced for their timings. A weak trend for a genetic influence on the values of the major acrophases was also apparent. The top right panels of Fig 5 illustrate the distribution around the line of identity of individual values of the major acrophases of DBP in MZ and DZ twins.

When the values of the nocturnal nadirs were examined, there was a significant intraclass correlation in the MZ group but not in the DZ group. The within-pair estimate of genetic variance had a probability level of .16, and the probability level for the existence of an MZ-DZ difference in environmental covariance was .14. These ambiguous results do not allow us to conclude in favor of either genetic or environmental effects on this parameter. Because of the absence of significant intraclass correlations in both groups of twins, genetic or environmental effects did not seem to influence the timings of the nocturnal nadirs.

Heart Rate

A summary of the results of the analysis of genetic variance for the various parameters quantifying the characteristics of the 24-hour heart rate profiles is given in Table 4.

Mean Levels Over the 24-Hour Span, During the Daytime, and During Sleep

The bottom panel of Fig 2 shows the mean 24-hour profiles of heart rate in MZ and DZ twins. In contrast to the mean profiles of SBP and DBP, the mean heart rate profiles were entirely superimposable throughout the 24-hour cycle. A trend for a genetic influence was evident for the 24-hour and daytime mean levels (Table 4). For the mean levels during sleep, environmental effects seemed to be predominant. The distribution of the individual daytime mean heart rate values around the line of identity is presented for both groups in the bottom panels of Fig 3.
Quantitative Characteristics of the 24-Hour Profiles

The proportion of unimodal and bimodal best-fit curves obtained for the heart rate profiles and their concordance within twin pairs are given in Table 2. The overall proportion of individual heart rate profiles for which the best-fit pattern was bimodal was 83%, i.e., a proportion similar to that observed in our previous study (84%).

The within-pair estimate of genetic variance for rhythm amplitudes was significant, indicating the existence of a genetic effect on this parameter. The bottom panels of Fig 4 illustrate the distribution around the line of identity of individual values for the amplitude of the 24-hour variation in heart rate in MZ and DZ twins.

The estimate of genetic variance was nonsignificant for the values of the morning acrophases of heart rate, and because the intraclass coefficients of correlation were positive in both the MZ and DZ groups, the results suggest the existence of environmental effects. For the times of occurrence of the morning acrophases, neither a genetic nor an environmental effect could be demonstrated.

A trend for a genetic influence for the values of the evening acrophases was apparent. For the times of occurrence, no evidence for either a genetic or an environmental effect was obtained.

A highly significant estimate of genetic variance for the values of the major acrophases strongly indicated the existence of a genetic influence on this parameter of the 24-hour heart rate profile. The bottom panels of Fig 5 show the distribution around the line of identity of individual values of the major acrophase of heart rate in MZ and DZ twins.

The analysis indicated the existence of a predominant environmental effect for the values of the nocturnal nadirs. Concerning the times of occurrence of the nadirs, the intraclass correlations in the two groups of twins are indicative of a greater environmental covariance in the MZ group, because the intraclass correlation in the DZ group was not significantly different from zero. Indeed, a greater environmental covariance in the MZ group could not be excluded (P = .45).

Discussion

Our study demonstrates that, although environmental influences largely control the mean levels and characteristics of the 24-hour SBP variation, significant genetic effects are evidenced for the nycterohemeral DBP and heart rate variations or their mean levels. Genetic influences were particularly dominant for the daytime mean and maximum daytime level of DBP and heart rate.

To our knowledge, this is the first 24-hour ambulatory blood pressure analysis performed in healthy young twins. Up to now the twin model has been used extensively to test the inheritance of blood pressure based on casual blood pressure recordings. All these studies clearly indicated that the level of blood pressure, which exhibits a continuous distribution in the population, is, in an individual, the result of a complex interaction between genetic and environmental factors, a genetic effect having been shown either for SBP or for DBP or for both SBP and DBP. Some studies
revealed that the genetic influence was more pronounced for resting DBP than for resting SBP, whereas others established a comparable genetic component or a greater heritability of resting SBP. The genetic variation of resting heart rate has been less investigated. Although a significant genetic influence has been suggested, a more recent work did not confirm these preliminary observations. All the above studies indicate that a genetic influence could be demonstrated on either resting blood pressure or heart rate levels as measured by casual blood pressure recordings. The reasons for discrepancies among studies are unclear, but differences in the populations studied, the various experimental protocols, or the mathematical procedures used to analyze the data could probably play a confounding role.

In our study, it is noteworthy that the significant genetic effects detected for DBP and heart rate concerned largely the same parameters of the 24-hour profiles: the 24-hour mean, the daytime mean, the value of the evening acrophase, and the value of the major acrophase. In addition, there was a strong genetic influence for the rhythm amplitude of the heart rate. This latter observation could be related to the more pronounced influence of an endogenous rhythm for the 24-hour heart rate variation than for the 24-hour blood pressure variation, as we have previously reported.

### Table 3. Quantitative Characteristics of 24-Hour Profiles of Diastolic Blood Pressure in Monozygotic and Dizygotic Twins and Results of the Analysis of Genetic Variance

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>MZ, mean±SD</th>
<th>r</th>
<th>n</th>
<th>DZ, mean±SD</th>
<th>r</th>
<th>Within-Pair</th>
<th>Among-Component</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-Hour mean, mm Hg</td>
<td>28</td>
<td>59.9±8.1</td>
<td>.81*</td>
<td>16</td>
<td>57.1±5.5</td>
<td>.36†</td>
<td>...</td>
<td>43 (P=.008)</td>
<td>Genetic</td>
</tr>
<tr>
<td>Daytime mean, mm Hg</td>
<td>28</td>
<td>63.0±8.8</td>
<td>.83*</td>
<td>16</td>
<td>60.4±6.2</td>
<td>.25</td>
<td>...</td>
<td>56 (P=.004)</td>
<td>Genetic</td>
</tr>
<tr>
<td>Sleep mean, mm Hg</td>
<td>28</td>
<td>53.6±7.6</td>
<td>.67*</td>
<td>16</td>
<td>50.9±7.7</td>
<td>-.11</td>
<td>46 (P=.002)</td>
<td>...</td>
<td>Greater environmental covariance in MZ</td>
</tr>
<tr>
<td>Amplitude, mm Hg</td>
<td>28</td>
<td>7.7±3.6</td>
<td>.61*</td>
<td>16</td>
<td>8.1±3.7</td>
<td>-.38†</td>
<td>15 (P=.0008)</td>
<td>...</td>
<td>Greater environmental covariance in MZ</td>
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<td><strong>Morning acrophase</strong></td>
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<tr>
<td>Value, mm Hg</td>
<td>26</td>
<td>67.1±7.6</td>
<td>.57*</td>
<td>13</td>
<td>63.9±6.5</td>
<td>.39†</td>
<td>1 (NS)</td>
<td>...</td>
<td>Environmental</td>
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<tr>
<td>Timing</td>
<td>26</td>
<td>11:16 AM±02:12</td>
<td>.35†</td>
<td>13</td>
<td>12:12 AM±02:28</td>
<td>.82*</td>
<td>-.7515 (NS)</td>
<td>...</td>
<td>Environmental</td>
</tr>
<tr>
<td><strong>Evening acrophase</strong></td>
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<tr>
<td>Value, mm Hg</td>
<td>17</td>
<td>69.1±8.2</td>
<td>.83*</td>
<td>9</td>
<td>64.2±6.1</td>
<td>.35</td>
<td>13 (P=.09)</td>
<td>...</td>
<td>Trend for genetic effect</td>
</tr>
<tr>
<td>Timing</td>
<td>17</td>
<td>7:58 PM±01:20</td>
<td>-.09</td>
<td>9</td>
<td>7:32 PM±01:54</td>
<td>.10</td>
<td>...</td>
<td>-.780 (NS)</td>
<td>Neither genetic nor environmental effect</td>
</tr>
<tr>
<td>Value of major acrophase, mm Hg</td>
<td>26</td>
<td>68.3±7.5</td>
<td>.70*</td>
<td>14</td>
<td>64.3±6.6</td>
<td>.37†</td>
<td>10 (P=.16)</td>
<td>...</td>
<td>Trend for genetic effect</td>
</tr>
<tr>
<td>Nocturnal nadir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value, mm Hg</td>
<td>25</td>
<td>51.1±6.4</td>
<td>.52*</td>
<td>14</td>
<td>48.0±6.5</td>
<td>.29</td>
<td>11 (P=.16)</td>
<td>...</td>
<td>Neither genetic nor environmental effect</td>
</tr>
<tr>
<td>Timing</td>
<td>26</td>
<td>3:05 AM±01:33</td>
<td>.04</td>
<td>14</td>
<td>3:19 AM±01:09</td>
<td>-.21</td>
<td>...</td>
<td>1307 (NS)</td>
<td>Neither genetic nor environmental effect</td>
</tr>
</tbody>
</table>

r indicates number of pairs included in analysis and takes into account the number of outliers as well as cases for which it was not possible to estimate the parameter under consideration (eg, only one acrophase can be estimated in monomodal profiles); MZ, monozygotic twins; DZ, dizygotic twins; and NS, not significant.

**Trend for genetic effect**

**Neither genetic nor environmental effect**

**Greater environmental covariance in MZ**

**Environmental effect**

### Conclusion

Genetic influences on the mean DBP and heart rate levels are stronger for the mean daytime values, whereas environmental factors are predominant for the mean sleep values. As a consequence, for both variables the genetic effects on the 24-hour mean levels are slightly less pronounced than those on the daytime mean. At first sight, the greater genetic influence on daytime mean levels could seem rather unexpected, as environmental factors may be thought as more prevalent during the daytime. However, sleep quality may be markedly influenced by environmental factors that then influence blood pressure indirectly. In previous reports, we have shown that regulation of some sleep stages such as rapid eye movement sleep is more controlled by environmental rather than genetic effects. We thus could consider that sleep quality during the night of recording is an environmental influence.

The trend toward greater blood pressure levels (especially for SBP) throughout the 24-hour span in MZ twins was an unexpected finding. This difference does not appear to be related to the most important confounding factors known to interfere with mean blood pressure levels. Indeed, no significant differences in age, sex, and body mass index between the MZ and DZ groups were observed. Great care was exercised in the selection procedure of our twin sample. Nevertheless, because of the difficulties inherent in the recruitment of volunteers for this type of study, moderate users of
alcohol and/or tobacco as well as twins with a family history of hypertension were not excluded. Retrospective analysis of our data revealed that these factors cannot explain the observed trend for differences in blood pressure between MZ and DZ twins. There were 3 DZ pairs with a known family history of hypertension compared with only 1 MZ pair with such a history. Concerning drinking and smoking habits, the proportions were, respectively, 3 of 28 MZ versus 2 of 16 DZ twins and 8 of 28 MZ versus 4 of 16 DZ twins. Concerning social status, most of our twins were students (12 of 26 in the MZ group versus 8 of 16 in the DZ group). There were no differences in the reported level of physical exercise. A tentative explanation for the trend toward greater blood pressure values in MZ twins could be an increased level of sympathetic activity contributing to the trend toward greater blood pressure values in MZ twins. 2'5'7'10-29'30

In conclusion, ambulatory blood pressure monitoring performed in a limited population of young male twins demonstrated genetic influences on various parameters characterizing the 24-hour DBP and heart rate profiles and their mean levels, whereas mainly environmental factors were evidenced for SBP. An unexpected but clear tendency for higher blood pressure levels in MZ twins compared with DZ twins was evidenced. This latter finding clearly needs further investigation.

Acknowledgments

We gratefully thank Dominique Detroux for analyzing the electroencephalographic sleep recordings, Bernard Jacques

TABLE 4. Quantitative Characteristics of 24-Hour Profiles of Heart Rate in Monozygotic and Dizygotic Twins and Results of the Analysis of Genetic Variance

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MZ, mean±SD</th>
<th>DZ, mean±SD</th>
<th>r</th>
<th>n</th>
<th>Within-Pair</th>
<th>Among-Component</th>
<th>Conclusion</th>
<th>r</th>
<th>n</th>
<th>Within-Pair</th>
<th>Among-Component</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-Hour mean, bpm</td>
<td>66.9±9.1</td>
<td>68.2±7.6</td>
<td>.39†</td>
<td>13</td>
<td>(P=.15)</td>
<td></td>
<td>Trend for genetic effect</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Daytime mean, bpm</td>
<td>73.5±11.1</td>
<td>74.6±9.7</td>
<td>.38†</td>
<td>26</td>
<td>(P=.06)</td>
<td></td>
<td>Trend for genetic effect</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Sleep mean, bpm</td>
<td>56.6±6.8</td>
<td>56.7±5.8</td>
<td>.35‡</td>
<td>4</td>
<td>(NS)</td>
<td></td>
<td>Environmental</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Amplitude, bpm</td>
<td>14.5±4.7</td>
<td>14.3±4.8</td>
<td>.32</td>
<td>8</td>
<td>(P=.04)</td>
<td></td>
<td>Genetic effect</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Morning acrophase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value, bpm</td>
<td>79.9±13.0</td>
<td>79.9±10.8</td>
<td>.35</td>
<td>22</td>
<td>(NS)</td>
<td></td>
<td>Environmental</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Timing</td>
<td>10:55 AM±00:48</td>
<td>11:04 AM±01:32</td>
<td>.48‡</td>
<td>22</td>
<td>(NS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evening acrophase</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value, bpm</td>
<td>73.6±9.6</td>
<td>75.6±10.2</td>
<td>.35</td>
<td>31</td>
<td>(P=.11)</td>
<td></td>
<td>Trend for genetic effect</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Timing</td>
<td>7:28 AM±01:01</td>
<td>7:18 PM±01:18</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value of major acrophase, bpm</td>
<td>78.3±19.4</td>
<td>80.1±11.1</td>
<td>.47‡</td>
<td>273</td>
<td>(P=.002)</td>
<td></td>
<td>Genetic effect</td>
<td>.03</td>
<td>15</td>
<td>11:04 AM±01:32</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Nocturnal nadir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Value, bpm</td>
<td>51.6±6.8</td>
<td>52.3±5.7</td>
<td>.52‡</td>
<td>-2</td>
<td>(NS)</td>
<td></td>
<td>Environmental</td>
<td>.03</td>
<td>15</td>
<td>3:32 AM±01:17</td>
<td></td>
<td>.48‡</td>
</tr>
<tr>
<td>Timing</td>
<td>3:32 AM±01:17</td>
<td>3:22 AM±01:00</td>
<td>.03</td>
<td>2108</td>
<td>(P=.006)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n indicates number of pairs included in analysis and takes into account the number of outliers as well as cases for which it was not possible to estimate the parameter under consideration (eg, only one acrophase can be estimated in monomodal profiles); MZ, monozygotic twins; r, intraclass coefficient of correlation; DZ, dizygotic twins; bpm, beats per minute; and NS, not significant.

*P<.05, **P<.01, †P<.10.
Blood Pressure and Heart Rate Profiles in Twins

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