

Blood Pressure and Heart Rate Variabilities in Normotensive and Hypertensive Human Beings

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SUMMARY. Blood pressure and heart rate variabilities were studied in 89 ambulant normotensive or essential hypertensive subjects in whom blood pressure was recorded intra-arterially for 24 hours (Oxford method) under standardized living conditions. Data were analyzed beat to beat by a computer to provide mean values of the 48 half hours of the 24-hour period. Variabilities were assessed by the standard deviation and variation coefficients separately obtained for each half hour, as well as by the standard deviations and variation coefficients obtained by averaging the 48 mean values. In each subject, blood pressure and heart rate varied markedly either among or within half hours, indicating the existence of relatively long- and short-term variabilities during the 24 hours. When averaged for all subjects, the long-term variabilities showed only one systematic component, i.e., the marked reduction occurring during sleep. Sleep was further responsible for a marked reduction in the short-term blood pressure and heart rate variabilities. These variabilities showed marked (though nonsystematic) modifications, even outside sleep, which were positively related to the blood pressure and heart rate means. Modifications in blood pressure and heart rate means and short-term variabilities were also positively related to each other. All these features were common to normotensives and hypertensives. In hypertensives, the absolute long and short-term blood pressure variabilities were greater than in normotensives, but the percent blood pressure variabilities were similar. Heart rate variabilities (both absolute and percent) were similar in normotensive and hypertensive subjects. Heart rate variabilities were also similar whether the subjects had impaired or preserved baroreflex control of heart rate (vasoactive drug technique). These findings uncover a number of factors that are associated with and responsible for blood pressure and heart rate variabilities in human beings. The nature of these factors suggest a primary role of central nervous mechanisms in the production of these phenomena and in the overall cardiovascular modulation, with no substantial difference between conditions of normal and chronically elevated blood pressure. (*Circ Res* 53: 96-104, 1983)

BLOOD PRESSURE is known to be spontaneously variable in human beings. Techniques that make prolonged blood pressure recordings possible have recently offered a way to quantify this phenomenon, which has since been studied for two main purposes: (1) to diagnose hypertension more accurately, predict the risk, and check the effectiveness of treatment (Littler et al., 1975a; Sokolov et al., 1980; Littler et al., 1975b; Mancia et al., 1979, 1981, 1982b, 1982a), and (2) to obtain an insight into the main factors that modulate circulation in daily life under physiological and pathophysiological conditions (Clement et al., 1977, 1979; Littler et al., 1978; Watson et al., 1979; Mancia et al., 1980).

Although considerable knowledge has been gained, several important features of blood pressure variability have never been described. For example, while attention has been directed to the blood pressure changes associated with day and night rhythm (Bevan et al., 1969; Littler et al., 1978, 1979), little information has been collected on the brief but pronounced blood pressure variations that may take

place within short-term intervals. Also, limited knowledge has been gained of the factors that are responsible for blood pressure variability, and in particular of the central and reflex mechanisms that may be involved in determining the magnitude of this phenomenon. Finally, no agreement has been reached as to whether blood pressure variability is different in normotensive and hypertensive subjects and whether it undergoes a modification with aging (Shaw et al., 1963; Richardson et al., 1964; Clement et al., 1977; Goldberg et al., 1978; Birkenhäger et al., 1978; Watson et al., 1980).

We have addressed these unexplored or unsolved questions by a detailed analysis of 24-hour blood pressure and heart rate recordings in a large number of ambulant subjects widely differing in average blood pressure and age, all studied under standardized living conditions. Our results provide a quantitative description of the short-term blood pressure variations that characterize human beings. They define the relationship of several factors (time of the day, blood pressure means, heart rate variability,

etc.) to blood pressure variability and suggest that central mechanisms may play an important role in the production of this phenomenon. Finally, our results show percent blood pressure variability to be similar in subjects with different blood pressure values and to be increased only by age.

METHODS

We studied 89 hospitalized subjects of either sex (55 male, 34 female) who had been clinically classified as normotensive or as having an established or suspected essential hypertension. The subjects were admitted to the study if (1) no major disease apart from hypertension was present and (2) no treatment with cardiovascular drugs had been given in the preceding 3 weeks. Consent to the study was obtained after description of its nature and purpose.

Blood Pressure Recording

Arterial blood pressure was measured invasively by means of the Oxford technique (Goldberg et al., 1976; Stott et al., 1976). A small catheter (1.3 mm inside diameter, 11 cm length) was inserted in a radial artery after local anesthesia with 2% procaine solution. The catheter was connected via a rigid polyethylene tube to a small and light plexiglass box fastened to the subject's thorax at the level of the heart. The box contained a 40-ml saline reservoir-pump (operated by a battery) which provided the catheter with a constant slow perfusion to keep it patent for 24 hours. It also contained a blood pressure transducer which was connected to an amplifier and a battery-operated mini-tape recorder (fastened to the subject's waist) on which the 24-hour blood pressure signals were stored. The method is known for providing a faithful blood pressure recording because of the stability of the zero signal, the linearity of the transducer from 50 to 250 mm Hg, and the frequency-response of the whole set of equipment (tubing-transducer-amplifier) that is optimal up to 10 Hz (Stott et al., 1976). In each patient, these features were checked before and after the 24 hours to be sure that the recording had been properly obtained throughout. The recordings were performed while the subjects were hospitalized, which allowed their environmental and living conditions to be relatively well standardized. For example, all subjects underwent a similar diet, had meals at similar times, were allowed night rest of a similar length, and could move within the hospital area engaging in the social activities of the hospital inpatients (TV watching, playing cards, visits with relatives, etc.) which were allowed at fixed times of the day. In each subject, the recording was begun during the early evening and continued without interruption until completion of the 24-hour period. In no subject did the procedure cause pain or discomfort.

Analysis of Data Obtained by Continuous Recording

Data analysis was made in the manner described in a previous report (Di Rienzo et al., 1982). Briefly, the blood pressure tracing was visually examined at high speed on an oscilloscope to determine the good quality of the signal throughout the 24-hour recording. The signal then was sent to a digital computer (PDP 11/34) that had been programmed (1) to sample the blood pressure value every 60 msec and provide one average every 3 seconds, and

(2) to determine the highest and the lowest blood pressure values, and the number of pulse pressure waves during each 3-second interval. In this way, 3-second average values of mean arterial pressure, systolic and diastolic blood pressures, and heart rate were calculated and stored on a magnetic disk.

For each of the above-mentioned variables, further analysis of the stored data provided the mean value of the 24-hour recording period, and the mean values, the standard deviations, and the variation coefficients (i.e., standard deviation as percent of the mean) of each of the 48 half-hour sub-periods in which the 24 hours could be subdivided. From these values, two different measures of variability were obtained: (1) the 48 standard deviations and variation coefficients were averaged and the results taken as the variability that occurred within half hours; (2) the mean of the 48 mean values was also calculated and its standard deviation and variation coefficient taken as the variability that occurred among half hours. These two measures allowed estimation of a relatively short-term and of a long-term variability within the 24-hour recording time (Fig. 1). Absolute values, standard deviations, and variation coefficients were also separately calculated for a period of wakefulness (taken from 2-hour periods in the morning, afternoon, and evening) and for a period of 2 hours of night sleep (taken approximately between midnight and 4 a.m.) when the hemodynamic effects of this condition were most pronounced.

To examine the relationship between blood pressure variability and blood pressure mean, the subjects were assigned to three preselected groups: a group in which the average blood pressure recorded during the 24 hours was less than 100 mm Hg, a group in which this blood pressure was between 101 and 115 mm Hg, and a group in which it was above 115 mm Hg. According to the standard criteria these groups might be defined as "normotensive," "mild hypertensive," and "severe hypertensive." The subjects were also classified into two groups according to age, one group including subjects younger than 38 years and

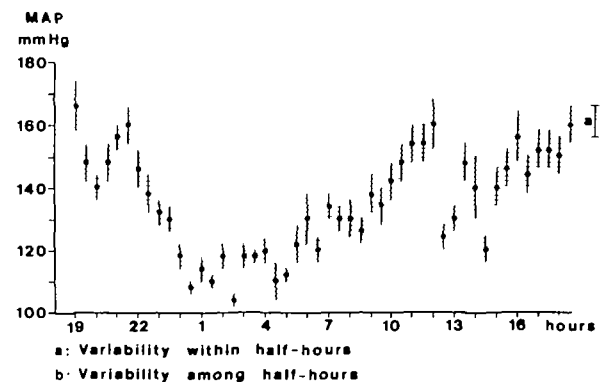


FIGURE 1. Computer analysis of a 24-hour intra-arterial blood pressure recording in a hypertensive subject. Black points refer to average mean arterial pressure (MAP) values obtained separately for each of the 48 half hours of the recording period, the vertical lines representing the corresponding standard deviations; "a" represents the average of the 48 standard deviations (one for each half hour) and is referred to as variability within half hours or short-term MAP variability; "b" represents the standard deviation obtained by averaging the 48 average MAP values (one for each half hour) and is referred to as variability among half hours or long-term MAP variability. The horizontal line at the bottom indicates the time during the recording.

the other those older than 48 years. Subjects whose age was between 38 and 48 years were excluded from this analysis in order to have the two age groups more clearly separated.

Study of Baroreflexes

In 38 normotensive, mild and severe hypertensive subjects of our series, the invasive blood pressure recording was prolonged to study the arterial baroreflexes. This study was performed by means of the classical vasoactive drug technique which allows one to obtain information on the heart rate control exerted by the arterial baroreceptors (Gribbin et al., 1971; Pickering et al., 1972). Briefly, phenylephrine (100 μ g) and trinitroglycerine (100 μ g) were diluted in a small volume of saline and injected iv as boluses to cause, respectively, a 20–30 mm Hg rise and fall in arterial blood pressure. During the ramp phase of the blood pressure changes, each systolic blood pressure value was related to the R-R interval of the subsequent cardiac cycle (ECG recording). Significant linear regressions ($r > 0.80$) were always obtained for this relationship, which allowed the regression coefficients to be taken as measures of the baroreflex sensitivity. Either phenylephrine and trinitroglycerine were injected twice, the two regression coefficients obtained being averaged. Injections were separated by 15-minute intervals. The study was conducted with the subjects supine.

Statistical Analysis

The following statistical analysis was performed. Data on normotensive, moderate, and severe hypertensive subjects were compared by one-way analysis of variance (ANOVA). Data of two different blood pressure or age groups were compared by the *t*-test for unpaired observations. The *t*-test for paired observations was used to perform within subject comparison, respectively, of day and night values and of different half-hour values. In each subject, half-hour values were also analyzed in terms of correlations (systolic vs. diastolic blood pressure, blood pressure vs. heart rate, and blood pressure mean vs. blood pressure standard deviation, etc.). To this purpose, use was made of the nonparametric test of Smirnov (Smirnov, 1948; Lehman, 1959) which allowed evaluation of the tendency of the half-hour values to vary systematically in similar or in opposite directions. Finally, the unpaired *t*-test was used again to compare the baroreflex sensitivities of the severe hypertensive subjects with those of the normotensive and mild hypertensive subjects. In all instances, a *P* value of less than 0.05 was taken as the level of statistical significance. Throughout the text the symbol \pm refers to the standard error of the mean.

RESULTS

Blood Pressure and Heart Rate Variabilities in the Whole Series of Patients

The 24-hour variabilities of systolic, diastolic, and mean arterial pressure, and of heart rate, are shown in Figure 2, as average values from all 89 subjects. The long-term variabilities were always greater than the short-term ones, except for the percent systolic pressure variability. The absolute variabilities were significantly greater for systolic than for diastolic blood pressure, but the reverse was the case for the long-term (though not for the short-term) percent

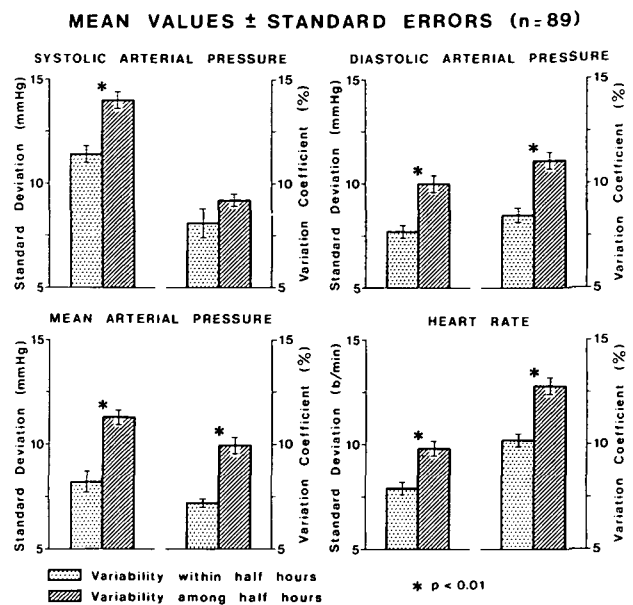


FIGURE 2. Absolute and percent short and long-term variabilities (variabilities within and among half hours) of systolic, diastolic, mean arterial pressure, and of heart rate. Data are shown as means (\pm SE) of all 89 subjects. Each asterisk refers to the statistical significance of the difference between the short and long-term variabilities. Lack of asterisk indicates lack of statistical significance.

variability. The percent heart rate variabilities significantly exceeded the percent variabilities of both systolic and diastolic blood pressures.

The blood pressure and heart rate values for each of the 48 consecutive half-hour subperiods into which the 24-hour recording was subdivided are shown in Figure 3, again as averages of all 89 subjects. Figure 3 shows that (1) there was a marked

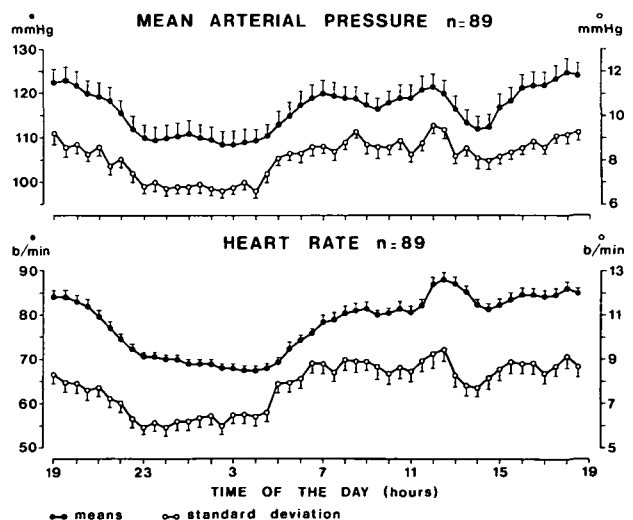


FIGURE 3. The black points represent the mean arterial pressure and heart rate values separately obtained for the 48 half hours of the recording. The open circles represent the corresponding absolute variabilities (standard deviations). The scales for the mean values are on the left, those for the variabilities on the right. Data are shown as means (\pm SE) of all 89 subjects.

reduction in blood pressure during the night and a more moderate reduction during the early afternoon, both reductions being related to the occurrence of sleep; (2) there was no systematic difference in blood pressure in periods outside sleep; (3) changes in blood pressure variability closely paralleled changes in mean blood pressure with a marked reduction during sleep and no systematic difference outside sleep; (4) there was a close parallelism between changes in blood pressure and heart rate, which involved both their mean values and their variabilities.

The parallelism between blood pressure and heart rate was also examined in individual subjects. In the large majority of subjects, half-hour values of blood pressure and heart rate did vary strictly in the same direction. The nonparametric test of Smirnov (see Methods) showed that blood pressure and heart rate means were linked by a significant positive relationship in 74 of the 89 subjects and, for blood pressure and heart rate standard deviations, that this occurred in 77 of the 89 subjects. In no instance was a negative correlation found between blood pressure and heart rate values.

Also, the parallelism between blood pressure and its variability was examined, and confirmed, in individual subjects. The test of Smirnov showed that half-hour blood pressure means and standard deviations or variation coefficients were linked by a significant positive relationship in 66 of the 89 subjects, most of the remaining subjects falling just short of statistical significance. As a result of this relationship, differences in half-hour blood pressure means were paralleled by similar differences in blood pressure absolute or percent variabilities. This is exemplified in Figure 4, which represents a selection of three half hours from each subject: the half hour with the lowest blood pressure mean, the half hour with the highest mean, and the half hour with a mean approximately equidistant between these two extremes. It is clear that these different mean blood

pressure values were accompanied by similar differences in blood pressure standard deviations and variation coefficients.

A further striking parallelism was found between systolic and diastolic blood pressure. The test of Smirnov showed that half-hour systolic and diastolic mean values, and half-hour systolic and diastolic standard deviations were linked by significant positive relationship in 89 and 88 subjects, respectively. The correlation coefficients were usually close to unity. This implies that changes in pulse pressure are effectively minimized during the 24 hours.

Blood Pressure and Heart Rate Variabilities in Normotensive and Hypertensive Subjects

Table 1 shows the 24-hour blood pressure variabilities in the three groups defined as normotensive, mild, and severe hypertensive subjects. The 24-hour average values of mean arterial pressure was 88 ± 2 mm Hg in the normotensive group, $108 \pm$ mm Hg in the mild hypertensive group, and 138 ± 3 mm Hg in the severe hypertensive group. The average ages of the three groups were relatively well matched (see footnote to Table 1). For systolic, diastolic, and mean arterial pressures, the absolute short- and long-term variabilities were lowest in normotensive subjects and often greatest in severe hypertensive subjects. In contrast, the percent short- and long-term blood pressure variabilities were similar among the three groups, or lower in the severe hypertensive, compared with the mild hypertensive or normotensive subjects. These were also the results obtained when wakefulness and sleep periods were analyzed separately. Wakefulness and sleep were characterized by large differences in blood pressure variability (see preceding section). Yet, under both conditions, the absolute variabilities were smallest in normotensives and greatest in severe hypertensives, whereas the percent variabilities were similar among the normotensive and hypertensive groups (Table 2).

Heart rate data in normotensive, mild, and severe hypertensive subjects are also shown in Table 1 (24-hour values) and Table 2 (values for wakefulness and sleep). Twenty-four-hour average heart rate values were 75 ± 2 beats/min in the normotensive group, 77 ± 2 beats/min in the mild hypertensive group, and 79 ± 1 beats/min in the severe hypertensive group. These values were not significantly different. The three groups also shared similar absolute and percent short- and long-term variabilities. This was also found when wakefulness and sleep data (respectively characterized by a higher and a lower heart rate variability) were analyzed separately.

Study of arterial baroreceptor control of heart rate performed in the 38 normotensive, mild, and severely hypertensive subjects of our series allowed information on the mechanisms of heart rate variability to be obtained also. As shown in Figure 5,

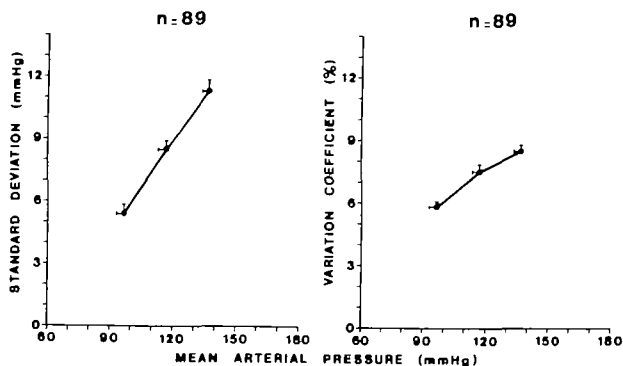


FIGURE 4. Absolute (standard deviations) and percent (variation coefficient) variabilities of mean arterial pressure at different average mean arterial pressures. Data refer to the three of the 48 half hours which, in each subject, showed the lowest mean arterial pressure mean, the highest mean, or a mean approximately equidistant between these two extremes. Averages (\pm SE) from all 89 subjects are shown.

TABLE 1
Blood Pressure and Heart Rate Variabilities in Normotensive, Mild, and Severe Hypertensive Subjects

	Systolic blood pressure				Diastolic blood pressure			
	Short-term variabilities		Long-term variabilities		Short-term variabilities		Long-term variabilities	
	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)
Normotensives (n = 22)	9.5 ±0.4	7.8 ±0.3	12.0 ±0.7	10.0 ±0.6	6.1 ±0.4	9.3 ±0.8	8.3 ±0.4	12.6 ±0.7
Mild hypertensives (n = 26)	11.3 ±0.4	7.8 ±0.3	14.6 ±0.8	10.1 ±0.6	7.4 ±0.2	8.9 ±0.3	10.3 ±0.6	12.3 ±0.8
Severe hypertensives (n = 41)	12.2 ±0.5	6.7 ±0.2	14.7 ±0.6	8.0 ±0.4	9.0 ±0.5	8.3 ±0.4	10.8 ±0.6	10.0 ±0.5
P (ANOVA)	*	*	†	*	*	‡	*	*

	Mean arterial pressure				Heart rate			
	Short-term variabilities		Long-term variabilities		Short-term variabilities		Long-term variabilities	
	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)
Normotensives (n = 22)	6.5 ±0.3	7.4 ±0.3	9.5 ±0.5	10.8 ±0.6	8.2 ±0.9	10.9 ±0.6	8.7 ±0.7	12.3 ±1.1
Mild hypertensives (n = 26)	8.1 ±0.3	7.5 ±0.3	12.2 ±0.7	11.3 ±0.7	7.9 ±0.5	10.2 ±0.6	10.2 ±0.6	13.3 ±0.8
Severe hypertensives (n = 41)	9.2 ±0.4	6.7 ±0.3	11.8 ±0.5	8.5 ±0.4	8.0 ±0.6	10.0 ±0.6	10.1 ±0.5	12.8 ±0.6
P (ANOVA)	*	*	*	*	*	*	*	*

Data are shown as means (\pm SE) for the three groups of subjects. Average age of the normotensive group was 39 ± 3 years, of the mild hypertensive group was 40 ± 2 years and of the severe hypertensive group 45 ± 2 years. SD: standard deviation; VC: variation coefficient; P: values from F values obtained by one-way analysis of variance (ANOVA).

* $P < 0.01$, † $P < 0.02$; ‡ $P < 0.05$ Absence of symbol means absence of statistical significance.

either when tested by the phenylephrine or by the trinitroglycerine method, the sensitivity of the arterial baroreceptor-heart rate control showed a significant and marked reduction in the severe hypertensive subjects as compared to the normotensive and mild hypertensive subjects combined. This reduction was in contrast with the heart rate variability values of the two groups which were, in all instances (long- and short-term, absolute and percent), not significantly different.

Blood Pressure and Heart Rate Variabilities in Relation to Age

Table 3 shows the results obtained when blood pressure variability was analyzed in the two groups of subjects classified according to age. These groups were relatively well matched for 24-hour blood pressure values (see footnote to Table 3). The absolute and percent long-term variabilities were similar, but the absolute and percent short-term variabilities were greater in the older than in the younger group. This was the case for systolic and mean arterial pressure. It was also the case for diastolic blood pressure, although in this instance only the difference in absolute short-term variability attained statistical significance.

Table 3 also shows data on heart rate variabilities

according to age. The absolute and percent variabilities were markedly less in the older than in the younger subjects, this being the case both for the short- and the long-term variabilities. Thus, in contrast to arterial blood pressure, heart rate variability underwent a reduction rather than an increase with age. Similar results were obtained when wakefulness and sleep data of younger and older subjects were separately compared.

Discussion

There are several features of blood pressure and heart rate variabilities described in the present study that deserve a comment. These features will be discussed under separate sections following the order adopted under Results.

Blood Pressure and Heart Rate Variabilities in the Whole Series of Subjects

The first contribution of our study is the observation that blood pressure and heart rate vary markedly during the 24-hour period, and that a large part of these phenomena is accounted for by the different blood pressure and heart rate average values that can occur at different half hours. An important part of blood pressure and heart rate variability is there-

TABLE 2
Blood Pressure and Heart Rate Means and Variabilities during Wakefulness and Sleep in Normotensive, Mild and Severe Hypertensive Subjects

	Wakefulness			Sleep		
	MAP (mm Hg)	SD (mm Hg)	VC (%)	MAP (mm Hg)	SD (mm Hg)	VC (%)
Normotensives (n = 22)	94.2 ±2.3	7.0 ±0.4	7.4 ±0.4	74.0 ±1.9	4.9 ±0.3	6.6 ±0.4
Mild hypertensives (n = 26)	113.4 ±1.9	8.4 ±0.4	7.5 ±0.4	92.4 ±1.8	6.2 ±0.4	6.7 ±0.3
Severe hypertensives (n = 41)	141.4 ±3.5	9.9 ±0.4	7.0 ±0.4	122.8 ±2.9	7.2 ±0.4	5.9 ±0.3
P (ANOVA)	*	*		*	*	
	HR (beats/min)	SD (beats/min)	VC (%)	HR (beats/min)	SD (beats/min)	VC (%)
Normotensives (n = 22)	81.1 ±2.6	10.0 ±1.1	12.3 ±1.1	69.5 ±1.7	5.6 ±0.5	8.1 ±0.7
Mild hypertensives (n = 26)	82.8 ±2.8	8.5 ±0.8	10.3 ±0.9	66.3 ±2.0	5.3 ±0.4	8.0 ±0.6
Severe hypertensives (n = 41)	84.3 ±1.9	8.2 ±0.7	9.7 ±0.7	70.2 ±1.5	6.2 ±1.0	8.8 ±0.8
P (ANOVA)						

Data are shown as means (\pm SE) of the three groups of subjects of Table 1. For each subject, the wakefulness period represents the average values of 2 hours of the morning, the afternoon, and the evening. The sleep period represents the average values of 2 hours of night sleep. Differences between wakefulness and sleep values were always significant at $P < 0.01$ or 0.05 . MAP: mean arterial pressure; HR: heart rate; all other symbols as in Table 1.

fore represented by rather sustained or "long-term" blood pressure and heart rate changes occurring at different times during day and night. In this regard, our results show that the only systematic and by far the most important of these changes is the reduction in blood pressure and in heart rate that occurs during sleep, regardless of its appearance during the day (which in our setting reflected the Italian habit of "siesta") or during the night. This confirms, in a large sample, the pronounced cardiovascular effects of sleep that have been described by other investigators (Richardson et al., 1964; Bevan et al., 1969; Littler et al., 1975, 1978) and by ourselves (Mancia and Zanchetti, 1981). Furthermore, it sheds light on the controversial issue as to whether a circadian rhythm affects the human cardiovascular system, with a systematic blood pressure surge during early morning and a subsequent progressive decline (Millar-Craig et al., 1979; Rowlands et al., 1980). In our subjects, both blood pressure and heart rate averages were not higher in the early morning, and all half-hour averages measured during waking were substantially similar. This allows one to conclude against the existence of a circadian rhythm capable of clearly shaping the 24-hour blood pressure profile and prevailing over the influence of various behaviors that affect circulation in human beings. It should be emphasized that the large number of subjects of our series and the fact that they were studied while living under relatively standardized environmental conditions strengthens this conclusion.

The second contribution of our study is that not only "long-term" but also "short-term" blood pressure and heart rate oscillations characterize the 24-hour time in human beings. Several interesting aspects of these "short-term" variations deserve to be mentioned. First of all, short-term variations represent a very important phenomenon whose magnitude is between two-thirds and three-fourth of the magnitude of the long-term variations. Incidentally, this has obvious implications for the reproducibility of blood pressure measurements by the cuff or other current non-invasive methods. Second, "short-term" variations are not uniform, but show large differences in magnitude during the various half-hour periods of the 24 hours. Interestingly, a factor that is strictly related to the modification of "short-term" blood pressure variability is the concomitant mean arterial pressure value. In our subjects, when this value was increased, so was the "short-term" blood pressure variability and vice versa. This provides at least one element to predict the short-term blood pressure variability profile.

The third interesting feature of the short-term blood pressure and heart rate variabilities is the marked systematic reduction that both phenomena showed during sleep. This permits discussion of another aspect of our data, i.e., the mechanisms responsible for spontaneous variability. The fact that a neural phenomenon like sleep (Jouvet, 1967) so markedly affected blood pressure and heart rate variabilities suggests that variabilities can be neur-

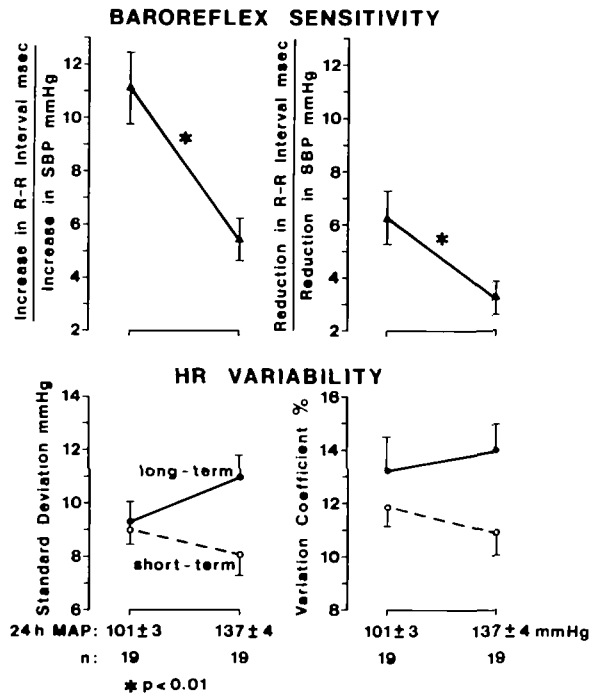


FIGURE 5. Sensitivity of the arterial baroreceptor-heart rate control and absolute and percent short- and long-term heart rate variabilities in 38 of the 89 subjects shown in the preceding figures. The baroreflex sensitivities have been separately assessed by the phenylephrine (left upper panel) and the trinitroglycerine method (right upper panel). The 38 subjects have been subdivided into two even groups of 19 normotensive and mild hypertensive subjects and of 19 severe hypertensive subjects. Twenty-four-hour average mean arterial pressures of the two groups were, respectively, 100.6 ± 2.8 mm Hg and 137.0 ± 4.2 mm Hg. Respective 24-hour average heart rates were 76.8 ± 2.0 and 79.1 ± 2.2 beats/min. Each asterisk refers to the statistical significance ($P < 0.01$) of the difference between the two groups. Lack of asterisk indicates lack of statistical significance.

ally modulated and that the origin of this modulation may be largely within the central nervous system. This interpretation is supported by two other findings. One, in severe hypertensive subjects, marked impairment of the arterial baroreceptor-heart rate control was associated with no modification at all in heart rate variabilities. This indicates that the buffering action of these reflexes (Cowley et al., 1973; Ito and Scher, 1978; Watson et al., 1979) may have only a minor role in determining the magnitude of some variability phenomena in humans. Two, in most subjects, blood pressure and heart rate means, and blood pressure and heart rate "short-term" variabilities, varied directionally in a similar manner during the 24 hours. This parallelism shows that there are influences acting consensually on blood vessels and the heart which prevail over reflex homeostatic mechanisms (i.e., the baroreflexes) which would determine opposite changes in vascular and cardiac targets. It is reasonable to assume that these prevailing influences are central in origin and thus that central nervous mechanisms

play a primary role in cardiovascular modulation during the 24 hours.

Blood Pressure and Heart Rate Variabilities in Normotensive and Hypertensive Subjects

Absolute blood pressure variability increased from the subjects with a normal 24-hour blood pressure to the subjects with essential hypertension of moderate or severe degree. This phenomenon involved both short- and long-term variabilities. It affected both systolic and diastolic blood pressures. It was visible not only during wakefulness but also during sleep, despite the fact that—in the latter condition—variability values were markedly reduced. However, the increase in absolute blood pressure variability that characterized essential hypertension was proportional to the elevation in the 24-hour blood pressure mean, for which reason percent blood pressure variability was not greater in the hypertensive condition than that displayed at normal blood pressure. This differed from the disproportionate increase in absolute blood pressure variability, with an increase also in its percent value, that occurred in each subject when blood pressure rose during a half-hour period (see Fig. 4). Such a difference may suggest that the mechanisms that produce transient pressor events are not the same as those that are responsible for maintaining the enduring pressure rise characterizing hypertension. It may alternatively suggest, however, that on transition from an acute to a chronic blood pressure rise, a readjustment of cardiovascular control mechanisms takes place which brings back variability to percent values similar to those typical of lower blood pressures.

Percent blood pressure variability was not the only feature that made the hypertensive subjects of our series similar to the normotensive ones. Normotensive, mild, and severe hypertensive subjects had similar 24-hour mean heart rates. They had similar absolute and percent short- and long-term heart rate variabilities. Furthermore, the correlation between systolic and diastolic blood pressure, and between blood pressure and heart rate, were not limited to the normotensives, but were typical of the large majority of subjects, including severe hypertensives. All these similarities show that cardiovascular events that take place in life may not differ at normal and chronically elevated blood pressures, and suggest that cardiovascular modulation may not be impaired in hypertension. Because of its paramount importance, this may apply in particular to the modulating influence played by central nervous mechanisms.

Blood Pressure and Heart Rate Variabilities and Age

In subjects older than 48 years, absolute and percent blood pressure variabilities were greater than in subjects younger than 38 years. This phe-

TABLE 3
Blood Pressure and Heart Rate Variabilities in Younger and Older Subjects

	Systolic blood pressure				Diastolic blood pressure			
	Short-term variabilities		Long-term variabilities		Short-term variabilities		Long-term variabilities	
	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)
Younger subjects (n = 31)	10.2 ±0.4	7.2 ±0.3	13.6 ±0.7	9.7 ±0.6	7.2 ±0.3	9.0 ±0.6	9.8 ±0.5	11.9 ±0.6
Older subjects (n = 26)	12.7 ±0.5	8.0 ±0.2	15.1 ±0.7	9.5 ±0.5	8.8 ±0.7	10.0 ±0.8	10.4 ±0.5	11.9 ±0.6
P	*	‡			†			

	Mean arterial pressure				Heart rate			
	Short-term variabilities		Long-term variabilities		Short-term variabilities		Long-term variabilities	
	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)	SD (mm Hg)	VC (%)
Younger subjects (n = 31)	7.6 ±0.3	7.1 ±0.3	11.2 ±0.5	10.5 ±0.6	9.8 ±0.7	11.7 ±0.6	11.0 ±0.6	14.4 ±0.9
Older subjects (n = 26)	9.2 ±0.4	8.0 ±0.3	12.1 ±0.6	10.5 ±0.5	6.8 ±0.4	8.9 ±0.6	9.0 ±0.6	11.7 ±0.7
P	*	‡			*	*	‡	†

Data are shown as means (\pm SE) of a group of subjects younger than 38 years (mean 30 ± 1) and a group of subjects older than 48 years (mean 54 ± 1). P refers to statistical significance of the differences between the two groups; 24-hour average values of mean arterial pressure were 110 ± 4 mm Hg for the younger and 117 ± 4 mm Hg for the older group. Respective 24-hour average heart rate were 78 ± 2 and 77 ± 2 beats/min. Symbols as in the Table 1.

nomenon was limited to the short-term variability, whereas the long-term variability did not show any significant difference between the older and the younger group. The increased variability of the older subjects, though more evident and consistent for systolic and mean arterial pressure, was observed for diastolic blood pressure as well. These results offer a scientific ground to the well-known clinical impression that blood pressure is more labile in elderly people, and demonstrate that this involves the short-lived blood pressure oscillations.

As to the mechanisms of the increased blood pressure variability of older subjects, our observations rule out an involvement of cardiac events because both the short- and the long-term heart rate variabilities were remarkably reduced in the elderly subjects, presumably as a result of the impairment of sinus node responsiveness that occurs with aging (Lakatta, 1979). Vascular factors must therefore be responsible for this phenomenon. It is likely that one factor is anatomical, i.e., the stiffening of the largest arteries that occur with aging and cause greater blood pressure excursions in response to given alterations in stroke volume. It is also likely, however, that another factor is functional, i.e., the age-related reduction in baroreflex sensitivity (Gribbin et al., 1971; Korner et al., 1974). This factor might explain why diastolic as well as systolic blood pressure variability shows an increase with age, a finding that suggests that not merely the larger but also the smaller arteries are involved.

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