Influence of aging on cardiac baroreflex sensitivity determined non-invasively by power spectral analysis

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ABSTRACT
Aging reduces cardiac baroreflex sensitivity. Our primary aim in the present study was to assess the effects of aging on cardiac baroreflex sensitivity, as determined by power spectral analysis (α index), in a large population of healthy subjects. We also compared the α indexes determined by power spectral analysis with cardiac baroreflex sensitivity measured by the phenylephrine method (BSphen). We studied 142 subjects (79 males/63 females; age range 9–94 years), who were subdivided into five groups according to percentiles of age (25, 50, 75 and 95). Power spectral analysis yields three α indexes: an α low-frequency (LF) index of cardiac baroreflex sensitivity that ranges around 0.1 Hz; an α high-frequency (HF) index reflecting cardiac baroreflex sensitivity corresponding to the respiratory rate; and α total frequency (α TF), a new index whose spectral window includes all power in the range 0.03–0.42 Hz. Spectra were recorded during controlled and uncontrolled respiration. Under both conditions, all three α indexes were higher in the youngest age group (≤ 34 years old) than in the three oldest groups. Notably, α TF was significantly higher in younger subjects than in the three oldest groups [14 ± 1 ms/mmHg compared with 9 ± 1 (P < 0.05), 8.1 ± 1 (P < 0.001) and 8.1 ± 1 (P < 0.05) ms/mmHg respectively]. BSphen showed a similar pattern [12 ± 1 ms/mmHg compared with 8 ± 0.5 (P < 0.001), 6 ± 0.5 (P < 0.05) and 6 ± 1 (P < 0.05) ms/mmHg respectively]. No significant differences were found for cardiac baroreflex sensitivity among the three oldest groups. All α indexes were correlated inversely with age. The index yielding the closest correlation with BSphen was α TF (r = 0.81, P < 0.001). Cardiac baroreflex sensitivity in normotensive individuals declines with age. It falls predominantly in middle age (from approx. 48 years onwards) and remains substantially unchanged thereafter. The elderly subjects we selected for this study probably had greater resistance to cardiovascular disease that is manifested clinically, with preserved cardiac baroreceptor sensitivity.

INTRODUCTION
Cardiac baroreflex sensitivity, assessed by measuring reflex variations in heart rate during the infusion of vasoactive drugs (including phenylephrine and nitroprusside), is increasingly gaining acceptance as a tool for stratifying the risk of mortality under clinical circumstances associated with altered autonomic cardiovascular control. Recent evidence shows that, in heart failure and myocardial infarction, diminished cardiac baroreflex sensitivity calculated by the phenylephrine method; DBP, diastolic blood pressure; HF, high-frequency; LF, low-frequency; SBP, systolic blood pressure; α TF, α total frequency (α index from 0.03 to 0.42 Hz).

Key words: aging, autonomic nervous system, baroreflex sensitivity, power spectral analysis, sudden death.
Abbreviations: α index, cardiac baroreflex sensitivity or gain calculated by power spectral analysis; BSphen, cardiac baroreflex sensitivity calculated by the phenylephrine method; DBP, diastolic blood pressure; HF, high-frequency; LF, low-frequency; SBP, systolic blood pressure; α TF, α total frequency (α index from 0.03 to 0.42 Hz).
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sensitivity is associated with poor survival [1–4]. An alternative, non-invasive tool for determining cardiac baroreflex sensitivity is power spectral analysis [5–8], a technique that has the advantage of requiring neither the infusion of vasoactive drugs nor the collaboration of the subject.

The aim of the present study was to assess the effects of aging on cardiac baroreflex sensitivity or gain calculated by power spectral analysis (\(\alpha\) index) and by phenylephrine infusion (BS\(_{\text{phen}}\)) [1–4,9]. Because power spectral analysis measures the power of the individual spectral components of R–R interval and systolic blood pressure (SBP) variabilities, it distinguishes \(\alpha\) indexes for the low-frequency (LF) component oscillating around 0.1 Hz and for a high-frequency (HF) component around 0.3 Hz [7,8]. We have also calculated a new index, \(\alpha\) total frequency (\(\alpha\) TF), obtained from the power from 0.03 to 0.42 Hz (see Figure 1). Because the experimental condition yielding the best correlation between power spectral analysis and BS\(_{\text{phen}}\) is controlled breathing [8], we determined all the \(\alpha\) indexes under conditions of uncontrolled breathing (rest) and controlled breathing (resp).

**METHODS**

**Study subjects and protocol**

Subjects were recruited from people attending our outpatient clinic for a medical follow-up, and from staff of the clinic and their family members. Because the study evaluated the effects of age on cardiac baroreflex sensitivity, all recruits underwent meticulous screening to exclude medical illnesses. Because recent observations have shown that levels of high anxiety can influence spectral components, all subjects were given a brief questionnaire designed to assess anxiety (Cornell Anxiety Subscale) [10]. Eligible subjects had to have an SBP of \(< 140\) mmHg and a diastolic blood pressure (DBP) of \(< 90\) mmHg, measured on at least three separate occasions. The criteria for selection and the study protocol have been described in detail elsewhere [11–14]. Subjects were excluded if they had total cholesterol values exceeding 220 mg/dl (5.7 mmol/l) and triacylglycerol values greater than 150 mg/dl (1.6 mmol/l). Other criteria for exclusion were the presence of glycosuria or fasting glycaemia greater than 110 mg/dl (6.1 mmol/l) or those with two values exceeding 140 mg/dl (7.8 mmol/l) during the 2 h after oral glucose loading. Subjects with a body mass index of greater than 27 kg/m\(^2\) and smokers were also excluded.

All selected subjects underwent three short-term simultaneous recordings: ECG, beat-to-beat blood pressure (Finapres) and respiratory activity (strain-gauge belt), as well as measurement of BS\(_{\text{phen}}\). All recordings were obtained at baseline (rest) and during controlled breathing (20 breaths/min), and were used for off-line spectral analysis. All participants gave their informed consent to the procedures, and the local ethical committee approved the study.

**Measurement of BS\(_{\text{phen}}\)**

Cardiac baroreflex sensitivity was determined with the method originally proposed by Smyth et al. [9] and used by Mortara and colleagues [1–3]. A bolus of phenylephrine (2 \(\mu\)g/kg) was given to raise SBP by 15–40 mmHg; if this dose failed to raise SBP sufficiently, it was increased to 3 or 4 \(\mu\)g/kg. The R–R intervals were plotted against the preceding arterial pulse, and the points were subjected to linear regression analysis. Only re-
gression lines with a $P$ value of $<0.05$ were accepted for the analysis. The mean of at least three tests (the final slope) was considered to be an index of cardiac baroreflex sensitivity (ms/mmHg).

**Offline analysis of heart rate and blood pressure variability**

An autoregressive algorithm was used to compute power spectral densities from the ECG and beat-to-beat blood pressure recordings. Spectral power was calculated as follows, from a series of 512 consecutive beats [11–15].

For R–R interval and SBP we calculated the following spectral components: HF component (from 0.16 to 0.42 Hz) and LF component (from 0.03 to 0.15 Hz).

Respiratory spectra were analysed on the signal sampled once every cardiac cycle. These spectra were used as a reference to identify heart rate oscillations caused by respiratory sinus arrhythmia. The R–R interval and respiratory signal recordings were also used for cross-spectral analysis.

Software for data acquisition and storage and for spectral analysis were designed according to the guidelines of the Taskforce of the European Society of Cardiology and the North American Society of Pacing [11–15].

**Cardiac baroreflex sensitivity determined by power spectral analysis**

The $\alpha$ index was calculated by dividing the square root of the spectral density of the heart rate by the square root of the corresponding spectral density of arterial pressure (PAS) [5–8,10]:

\[
\alpha_{LF} = \sqrt{LF_{RR}} / \sqrt{LF_{PAS}} \\
\alpha_{HF} = \sqrt{HF_{RR}} / \sqrt{HF_{PAS}}.
\]

Because heart rate variations induced by cardiac baroreflex activity during uncontrolled breathing can fall within the 0.03–0.42 Hz frequency range, we also calculated an $\alpha$ index in this frequency range ($\alpha$ TF):

\[
\alpha_{TF} = \sqrt{RR(0.03–0.42\text{ Hz})} / \sqrt{SBP(0.03–0.42\text{ Hz})}.
\]

Other investigators have determined this index (termed the $\alpha$ mean) by calculating the mean of $\alpha_{LF}$ and $\alpha_{HF}$ [8]. The two indexes yield similar results.

The coherence function of the various spectral components was then estimated. Coherence expresses the fraction of power at a given frequency in either time series that can be explained as a linear transformation between the two signals. Recordings showing less than 0.5 coherence in LH and HF [7,8] between the pressure signal and R–R interval variability were discarded.

**Data and statistical analysis**

All data were evaluated by use of the database SPSS-PC+ (SPSS-PC+ Inc., Chicago, Ill., U.S.A.). All results are expressed as means ± S.E.M. and as 5% and 95% confidence intervals.

Subjects were subdivided into five groups according to age percentiles (25, 50, 75 and 95): subjects aged $\leq 34$ years (group I), $> 35$ to $\leq 47$ years (group II), $> 48$ to $\leq 62$ years (group III), $> 63$ to $\leq 78$ years (group IV) and $> 79$ years (group V). One-way ANOVA and Bonferroni’s test were used to compare the general characteristics, spectra data and cardiac baroreflex sensitivity in the five groups. Repeated-measures ANOVA was used to evaluate the differences between spectral variables measured at rest and during controlled respiration. Pearson’s correlation coefficients were calculated to compare the $\alpha$ indexes at rest and during controlled respiration, and to compare the $\alpha$ index and the BS$_{mean}$. Linear regression analysis was used to determine a possible relationship between age and any single $\alpha$ index. The limits of agreement were calculated using the method of Bland and Altman [16,17]. Possible associations between age and other continuous variables (including heart rate, SBP, DBP and $\alpha$ index) were studied by stepwise multiple-regression analysis. A $P$ value of $<0.05$ was considered to indicate statistical significance.

**RESULTS**

Over 5 years, we tested more than 800 subjects; of these we selected for study 142 subjects (79 males/63 females), with an age range of 9–94 years. Group I comprised 40 subjects (23 males/17 females; age range 9–34 years, mean age 27.7 ± 1 years); group II comprised 34 subjects (21 males/13 females; age range 35–47 years, mean age 40.0 ± 0.6 years); group III comprised 33 subjects (17 males/16 females; age range 48–62 years, mean age 53.8 ± 0.7 years); group IV comprised 28 subjects (16 males/12 females; age range 63–78 years, mean age 67.1 ± 0.8 years); and group V comprised seven subjects (four males/three females; age range 79–94 years, mean age 84.3 ± 1.9 years). The main criteria for exclusion were arterial hypertension (189 subjects), obesity (154 subjects), diabetes mellitus (121 subjects) and high blood levels of cholesterol (64 subjects). In particular, 54 subjects were excluded owing to changes in the cardiac repolarization phase during exercise testing; 23 subjects were excluded because they stopped exercise testing without reaching the required heart rate. Finally, 53 subjects (42 in group V and 11 in group III) met the selection criteria, but were excluded because one or both spectral components showed less than 0.5 coherence or the regression line for BS$_{mean}$ failed to reach acceptable statistical significance. Coherence of less than 0.5 indicates a poor correlation between the variables studied. A low correlation arises mainly from artefacts due to
Table 1  General characteristics of study subjects
Values are means ± S.E.M. Significance of differences (one-way ANOVA and Bonferroni test): * P < 0.05 for group I compared with Group III; † P < 0.001 for group I compared with group IV; ‡ P < 0.05 for group I compared with group V; § P < 0.05 for group II compared with group IV.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (≤ 34 years)</th>
<th>Group II (≥ 35 to ≤ 47 years)</th>
<th>Group III (≥ 40 to ≤ 62 years)</th>
<th>Group IV (≥ 63 to ≤ 78 years)</th>
<th>Group V (≥ 79 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>40</td>
<td>34</td>
<td>33</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.6 ± 1.6</td>
<td>72.3 ± 1.8</td>
<td>69.8 ± 1.8</td>
<td>67.0 ± 2.6</td>
<td>68.9 ± 2.1</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.69 ± 0.02</td>
<td>1.71 ± 0.01</td>
<td>1.65 ± 0.01</td>
<td>1.65 ± 0.02</td>
<td>1.64 ± 0.02</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.6 ± 0.2</td>
<td>24.5 ± 0.2</td>
<td>25.6 ± 0.2</td>
<td>24.6 ± 0.2</td>
<td>25.6 ± 0.1</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>69.3 ± 1.6</td>
<td>66.3 ± 1.4</td>
<td>66.7 ± 1.8</td>
<td>64.5 ± 1.8</td>
<td>69.4 ± 4.1</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>108.5 ± 1.8†</td>
<td>113.7 ± 1.8</td>
<td>116.4 ± 1.9</td>
<td>120.2 ± 2.1</td>
<td>119.3 ± 3.5</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>70.0 ± 1.2</td>
<td>70.6 ± 1.1</td>
<td>70.8 ± 1.4</td>
<td>71.2 ± 1.6</td>
<td>70.7 ± 4.3</td>
</tr>
<tr>
<td>BSphen (ms/mmHg)</td>
<td>12.1 ± 0.8†‡</td>
<td>9.8 ± 0.7§</td>
<td>8.5 ± 0.5</td>
<td>6.4 ± 0.5</td>
<td>6.3 ± 0.7</td>
</tr>
</tbody>
</table>

Table 2  Power spectral data for the 142 study subjects
Indexes were measured under conditions of controlled breathing. Values are means ± S.E.M.; values in parentheses are 5–95% confidence intervals. Significance of differences (one-way ANOVA and Bonferroni test): * P < 0.05 for group I compared with group III; † P < 0.001 for group I compared with group IV; ‡ P < 0.05 group I compared with group V; § P < 0.05 for group II compared with group IV; || P < 0.05 for group II compared with group V.

<table>
<thead>
<tr>
<th>Spectral variable</th>
<th>Group I (≤ 34 years)</th>
<th>Group II (≥ 35 to ≤ 47 years)</th>
<th>Group III (≥ 40 to ≤ 62 years)</th>
<th>Group IV (≥ 63 to ≤ 78 years)</th>
<th>Group V (≥ 79 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LF</td>
<td>11.4 ± 1.1††</td>
<td>9.9 ± 0.7§</td>
<td>7.2 ± 0.8 (5.6–8.8)</td>
<td>6.1 ± 0.7 (4.6–7.5)</td>
<td>6.4 ± 0.9 (4.1–8.7)</td>
</tr>
<tr>
<td>Hf</td>
<td>16.3 ± 1.3††</td>
<td>13.7 ± 1.2 (11.2–16.1)</td>
<td>10.6 ± 1.1 (8.4–12.8)</td>
<td>9.3 ± 1.0 (7.1–11.4)</td>
<td>9.8 ± 2.3 (4.1–15.5)</td>
</tr>
<tr>
<td>LF</td>
<td>13.9 ± 1.1††</td>
<td>11.8 ± 0.8§</td>
<td>8.9 ± 0.8 (7.2–10.6)</td>
<td>7.7 ± 0.7 (6.1–9.2)</td>
<td>8.1 ± 1.6 (4.2–12.0)</td>
</tr>
</tbody>
</table>

Involuntary movements or poor-quality recordings. No significant differences were found between the various groups for weight, height, body mass index, level of anxiety, heart rate or DBP. Groups III and IV had higher SBP values than group I (Table 1). BSphen was significantly higher in groups I and II than in the other groups (P < 0.001) (Table 1).

All the spectral indexes of R–R interval variability determined at rest and during respiration were significantly higher in the youngest age group (group I) than in the other groups. These data are not reported here because they confirm results from two previous studies [17,18]. Spectral indexes of arterial pressure variability recorded at rest remained unchanged during controlled breathing.

No significant difference was found for the central LF and HF components in the five groups, or between LF values at rest and during respiration (0.0866 Hz and 0.0868 Hz respectively). However, the HF component differed significantly in subjects at rest and during controlled breathing (rest, 0.29 ± 0.003 Hz; controlled breathing, 0.32 ± 0.001 Hz; P < 0.001).

Recordings at rest and under conditions of controlled breathing yielded significantly higher α LF and α TF values in the two younger groups than in the oldest group (P < 0.001) (Table 2). However, α HF was significantly higher only in the comparison between the youngest
Cardiac baroreflex sensitivity in the elderly

Figure 4 Effect of age on $\alpha$ TF

Figure 5 Effect of age on BS$_{phen}$

Figure 6 Plot of the difference between BS$_{phen}$ and $\alpha$ TF against the average of the two tests

Shown is a Bland and Altman plot, with the 95% limits of agreement (broken lines) and the regression line (solid line) indicated.

No significant differences were found for spectral data, other clinical data or $\alpha$ indexes between males and females.

Linear regression analyses indicated that age was correlated inversely with all the $\alpha$ indexes recorded under conditions of both uncontrolled and controlled respiration (Figures 2–4), and with BS$_{phen}$ (Figure 5).

Multiple regression analysis highlighted a significant association of age with SBP, heart rate and $\alpha$ TF obtained during controlled breathing (Table 3), and between age, SBP, heart rate and BS$_{phen}$ (Table 4). Age was also significantly associated with $\alpha$ TF measured at rest (uncontrolled breathing).

All $\alpha$ indexes were correlated significantly with BS$_{phen}$. Correlations reached higher significance during controlled than during uncontrolled breathing ($\alpha$ LF, $r =$

Table 3 Multiple regression for age, $\alpha$ index and other variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Partial regression coefficient</th>
<th>Standard error</th>
<th>Standardized regression coefficient</th>
<th>t-test</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$ TF (ms/mmHg)</td>
<td>-1.4</td>
<td>0.2</td>
<td>-0.4</td>
<td>-5.4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>0.4</td>
<td>0.1</td>
<td>0.2</td>
<td>3.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>-0.4</td>
<td>0.1</td>
<td>-0.2</td>
<td>-2.8</td>
<td>0.005</td>
</tr>
<tr>
<td>Intercept</td>
<td>45.4</td>
<td>18.8</td>
<td></td>
<td>2.4</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Table 4 Multiple regression for age, BS$_{phen}$ and other variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Partial regression coefficient</th>
<th>Standard error</th>
<th>Standardized regression coefficient</th>
<th>t-test</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS$_{phen}$ (ms/mmHg)</td>
<td>-1.8</td>
<td>0.2</td>
<td>-0.5</td>
<td>-6.4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
<td>2.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>-0.3</td>
<td>0.1</td>
<td>-0.2</td>
<td>-2.6</td>
<td>0.009</td>
</tr>
<tr>
<td>Intercept</td>
<td>50.9</td>
<td>17.2</td>
<td></td>
<td>2.9</td>
<td>0.004</td>
</tr>
</tbody>
</table>
0.75 and 0.62 respectively, \( P < 0.0001; \alpha \text{HF}, r = 0.54 \) and 0.52 respectively, \( P < 0.0001; \alpha \text{TF}, r = 0.81 \) and 0.63 respectively, \( P < 0.0001 \). All spectral components showed low concordance with \( \text{BS}_{\text{phen}} \), (at rest: \( \alpha \text{LF}, \text{from } 8.7 \text{ to } -7.7; \alpha \text{HF}, \text{from } 26.9 \text{ to } -9.2; \alpha \text{TF}, \text{from } 11.1 \text{ to } -7.5; \) during controlled breathing: \( \alpha \text{LF}, \text{from } 6.5 \text{ to } -7.1; \alpha \text{HF}, \text{from } 15.4 \text{ to } -8.6; \alpha \text{TF}, \text{from } 6.5 \text{ to } -5.6 \) (Figure 6) [16].

**DISCUSSION**

All investigators agree that the spectral HF component obtained from heart rate and arterial pressure oscillations corresponds to respiratory-associated variations in intrathoracic pressure. Hence the HF power of R–R variability is a marker of sinus vagal modulation [15], whereas the HF power of arterial pressure variability reflects pressure oscillations induced by respiratory mechanics. The ratio between the square root of HF R–R and that of SBP HF (\( \alpha \text{HF} \); see the Methods section) gives an index of cardiac baroreflex sensitivity and vagal function. Pressure oscillations related to respiratory events induce changes in heart rate (respiratory arrhythmia) by activating a baroreflex that uses parasympathetic afferent and vagal efferent pathways. Conversely, the physiological meaning of the LF component remains debatable. Whereas some investigators consider LF power to be a marker of vascular and sinus sympathetic modulation [7,15], others argue in favour of a sympathetic and parasympathetic influence [18,19]. Despite this controversial issue, pharmacological studies show that the LF component, like the HF component, reflects vagal and cardiac baroreflex function [20]. In other words, these findings suggest that the cardiac baroreflex response to pressure variations may not be concentrated in a single spectral peak [21], but can be distributed over a wider-frequency band not necessarily within the HF range (0.15–0.42 Hz). Hence, from a physiological point of view, in determining cardiac baroreflex sensitivity by power spectral analysis we consider it appropriate to consider a single wide band encompassing both the LF and HF spectral components. Other investigators recommend using the mean of the two values [8,22]. Arithmetically, the two calculations yield identical results.

As others have observed in a study comparing the two techniques of power spectral analysis and the phenylephrine method [8], the relatively wide limits of concordance make it impossible to regard the techniques as interchangeable. The two methods express two distinct and non-overlapping features of the cardiac baroreflex response. Accordingly, with the phenylephrine method, the cardiac baroreflex is evoked by pressure variations greater than 15 mmHg, whereas with power spectral analysis variation in frequency is induced by pressure changes of no more than a few mmHg. Therefore the phenylephrine-induced reflex is the result of a strong, albeit submaximal, pressure stimulation, whereas the \( \alpha \) index-induced reflex is influenced primarily by pressure oscillations related to respiration. The two tests of cardiac baroreflex sensitivity therefore lie at opposite ends of the ideal cardiac baroreflex sensitivity curve. Finally, we confirm controlled breathing as the preferred experimental condition, because it yields a more accurate evaluation of the upper spectral boundaries (approx. 0.42 Hz), namely the HF component. An irregular breathing rate could result in higher-frequency oscillations that would be difficult to assess.

The fact that aging decreases cardiac baroreflex sensitivity explains why we found a significant correlation of age with the various \( \alpha \) indexes. Interestingly, the influence of age seems to differ in the various age decades. This accounts for the significant but low \( r \) values (Table 3). The \( \alpha \) indexes determined during controlled breathing – the condition yielding the closest correlation with \( \text{BS}_{\text{phen}} \) – specify that cardiac baroreflex sensitivity diminished markedly between groups I/II and the older groups (older than 48 years) (Table 2), whereas in the three older groups it remained unchanged (Table 2). Other investigators reached the same conclusion with the \( \text{BS}_{\text{phen}} \) method [23–25], and our data seem to agree (Table 1).

The earliest published papers investigating cardiac baroreflex sensitivity using traditional techniques or spectral analysis recruited few subjects and rarely included the very elderly. Gribbin et al. in 1971 [23] in their original report describing \( \text{BS}_{\text{phen}} \), followed by Duke et al. in 1976 [24], considered only a small number of subjects 60 years of age or older. Similarly, Shimada et al. in 1986 [25], and more recently James et al. in 1996 [26], studied subjects of 80+ years of age, but again included few normotensive subjects. The distinctive feature of our present study is that we assessed a wide age range, extending even to healthy individuals of 90 years of age or older. Previous age-related data for power spectral analysis are practically non-existent. The only published study to date addressed normotensive subjects with a mean age of 31 years, with the upper age limit (deduced from a Figure) being 65 years [22]. Ours is therefore the only study that has compared indexes of cardiac baroreflex sensitivity determined by the \( \text{BS}_{\text{phen}} \) technique and by power spectral analysis in normotensive elderly subjects. Confirming the earlier report by James et al. [26], we provide evidence in a larger population that the most conspicuous decrease in cardiac baroreflex sensitivity takes place not in old age, but in middle age. A cross-sectional study design, such as this, generally makes it difficult to separate the effects of aging from the effects of atherosclerosis or other coronary risk factors that might adversely affect cardiac baroreflex sensitivity. Selecting a study population without coronary risk...
factors and with negative exercise tests allowed us to be reasonably certain that none of our subjects had coronary artery disease. Hence the decreased cardiac baroreflex sensitivity that we found arose exclusively from the effects of aging. Undoubtedly the largest bias arises from the middle-aged group with low cardiac baroreflex sensitivity, who tend to have higher mortality. This difference tends to produce a survival bias in the older groups. Presumably the elderly individuals we studied were phenotypically exceptionally strong. Despite advancing age, they remained free of cardiovascular disease and hence, as we noted in previous studies on R–R variability [27,28], they had a younger biological age than true age. In these healthy elderly people, either the age-related reduction in cardiac baroreflex sensitivity proceeds slowly or their cardiac baroreflex sensitivity levels were already high when they were younger. To understand the true mechanism, we must await a longitudinal study assessing the effects of aging on cardiac baroreflex sensitivity.

One of the most hotly debated topics in this area is whether the diminished cardiac baroreflex sensitivity associated with aging arises from a reduction in the neural part of the reflex, or reflects age-related changes in vascular compliance. This latter hypothesis receives no support from our data. We found no significant differences in the spectral components of arterial pressure variability in the different age ranges. This finding implies that the vascular component of the power spectrum (the denominator; see the Methods section), a component linked also to vascular compliance [29], is uninfluenced by aging. Hence we attribute the low α indexes as being due mainly to a decrease in the spectral components of R–R variability (the numerator). Overall, rather than supporting the postulated role of reduced compliance, our findings seem to agree with conclusions reached by other studies [26]. Other investigators who observed decreased sympathetic baroreflex control in elderly dogs attributed the effect to a central autonomic nervous system dysregulation rather than to diminished arterial elasticity [30–32]. Others reached similar conclusions in studies conducted in humans, reporting no difference in cardiac baroreceptor sensitivity in elderly subjects with combined hypertension and those with isolated systolic hypertension, although the latter had reduced vascular compliance [26]. However, not all investigators agree. Some, in studies conducted in athletes and hypertensive individuals, reach diametrically opposite conclusions [33]. The question therefore remains open. Accordingly, the multiple regression analysis detected an inverse relationship between age and cardiac baroreflex sensitivity, but a positive relationship with SBP. Hence the elderly subjects we studied had significantly higher arterial pressures than those younger than 34 years. This age-related rise in pressure probably resulted in decreased baroreflex sensitivity.

REFERENCES


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