Vasomotor instability preceding tilt-induced syncope: does respiration play a role?

LEWIS A. LIPSITZ,1,2,3 RAYMOND MORIN,1 MARGARET GAGNON,1 DAN KIELY,1 AND AHARON MEDINA1,3,4
1 Hebrew Rehabilitation Center for Aged Research and Training Institute, Boston, Massachusetts 02131; 2 Beth Israel/Deaconess Medical Center Department of Medicine, and 3 Harvard Medical School, Boston, Massachusetts 02131; and 4 Bikur Cholim Hospital, Jerusalem, 91004 Israel

Many years ago, several investigators observed that subjects frequently yawned, sighed, and hyperventilated before the development of neurally mediated syncope (5, 8, 31). In 1968, Epstein and colleagues (5) observed phasic oscillations in arterial BP at a frequency of 4–9 oscillations/min before the development of syncope during head-up tilt. Furthermore, they demonstrated that the amplitude of these oscillations could be enhanced by increasing the depth of respiration. Therefore, we asked whether arterial BP Mayer wave oscillations during upright tilt are affected by controlled breathing in subjects who subsequently develop syncope and whether alterations in vasomotor control in these subjects may be related to changes in spontaneous respiration. If vasomotor instability before syncope were related to abnormal respiratory cycles, specific breathing exercises might be designed to avert syncope in susceptible patients.

METHODS

Subjects. A total of 52 healthy subjects participated in the study. These subjects were divided into a subgroup of 27 who developed syncope or presyncope during head-up tilt, and a subgroup of 25 who remained asymptomatic during the procedure.

Healthy subjects were recruited from the local community through newspaper advertisements and the subject registry of the Harvard Cooperative Program on Aging. Subjects were carefully screened with a medical history, physical examination, electrocardiogram (ECG), and, if they were ≥40 yr of age, a graded-exercise stress test. Potential subjects were excluded if they had evidence of cardiovascular or other diseases, smoking tobacco products, drank alcohol, took medications other than oral contraceptives, or were obese [body mass index (BMI) > 30 kg/m²] or hypertensive [systolic BP (SBP) > 140]. None of the subjects had experienced syncope within the past 5 yr.

The study was approved by the Institutional Review Board of the Hebrew Rehabilitation Center for the Aged, and all subjects provided informed consent.

Instrumentation. Subjects reported to the Clinical Research Center at the Hebrew Rehabilitation Center for the Aged at 7:30 AM on the morning of the study in the fasting state and after an overnight rest. Premenopausal women were carefully screened with a medical history, physical examination, complete blood count, chemistry screen, lipid profile, electrocardiogram (ECG), and, if they were >40 yr of age, a graded-exercise stress test. Potential subjects were excluded if they had evidence of cardiovascular or other diseases, smoked tobacco products, drank alcohol, took medications other than oral contraceptives, or were obese [body mass index (BMI) > 30 kg/m²] or hypertensive [systolic BP (SBP) > 140]. None of the subjects had experienced syncope within the past 5 yr.

The study was approved by the Institutional Review Board of the Hebrew Rehabilitation Center for the Aged, and all subjects provided informed consent.

Neurally mediated syncope is a common and potentially dangerous abnormality in blood pressure (BP) regulation that often can be provoked in healthy individuals by the orthostatic stress of head-up tilt (13). We and others have observed high-amplitude low-frequency heart rate (HR) (13, 27) and arterial BP (Mayer wave) (11, 29) oscillations preceding the onset of neurally mediated syncope. These observations suggest that alterations in beat-to-beat HR and arterial BP dynamics may be indicative of maladaptive arterial BP control mechanisms that predispose people to syncope.

Low-frequency Mayer wave and HR oscillations (centered at 0.1 Hz) are thought to represent baroreflex-feedback control of vasomotor activity or cardiac chronotropy, respectively (2). However, there may be several mechanisms capable of producing these oscillations, none of which is currently well understood. For example, respiratory cycles can influence low-frequency arterial BP and cardiac interval (R-R) fluctuations (9, 12, 19).
tion of the Colin monitor, was attached to the upper right arm.

A continuous respiration signal was recorded by an induc-
tive plethysmograph (Respirac, Ambulatory Monitoring, Ardsley, NY) from two elastic respiratory transducer bands: one around the midchest and the other around the abdomen. The Respirac output was calibrated according to the proce-
dure of Sackner et al. (23), by having subjects exhale and inhale to fill, and empty an 800-ml spirometer bag. Minute ventilation (V) [respiratory rate \( \times \) average tidal volume (Vt)] was calculated during 3 min of spontaneous breathing during supine rest and was subsequently held constant during periods of paced breathing by having the subject adjust his or her depth of respiratory excursion according to a marker on an oscilloscope screen. During paced breathing, respiratory frequency was controlled by having subjects follow a taped-
recorded auditory signal and line on the oscilloscope screen.

Experimental protocol. After equipment hook up and cali-
bration, subjects rested supine for 30 min to reach equilib-
rium. Continuous ECG, BP, and respiratory data were then collected during 30 min of supine rest, and 45 min of 60° head-up tilt. During a 10-min supine period, and between minutes 5 and 15 after the initiation of tilt, subjects were instruct-
ed to breathe at a fixed rate of 15 breaths/min (0.25 Hz), as described above. While they were in the upright position, subjects were carefully observed and questioned for signs and symptoms such as dizziness, nausea, sweating, other discomfort, yawning, or near syncope. If subjects be-
came symptomatic or hypotensive (SBP <80 mmHg) during tilt, they were returned immediately to the supine position.

Data processing. All data were digitized at 250 Hz and displayed in real time by using commercially available data acquisition software (WinDaq, Dataq Instruments, Akron, OH) on a personal computer. Continuous ECG and BP data recorded before and during tilt were visually inspected and edited offline for artifact and ectopy, with the use of an automated program to detect arrhythmias. Eight-minute segments of stationary data (without trends or abrupt changes in the mean over time) during paced and spontaneous breath-
ing in the supine and tilted positions were used for analysis. Data segments obtained during the tilt were analyzed from the initial 5–15 min while subjects were performing paced breathing and from 15–25 min while they were breathing spontaneously. Because 13 subjects developed syncope before the spontaneous breathing segment could be obtained, and 5 fainted before completion of paced breathing, their data were not available for the tilt component of the analysis. All data segments used in the analysis for syncopal subjects were obtained while the subjects were asymptomatic, at least 1 min before the onset of symptoms.

Beat-to-beat R-R intervals were determined from the R-
wave of the ECG, and SBP and diastolic BP (DBP) were derived from the maximum and minimum of the arterial BP waveform. HR was calculated as the reciprocal of the R-R interval (in s), multiplied by 60. The means \( \pm SD \) for R-R interval, HR, SBP, and DBP were calculated from the beat-to-
beat values averaged over 30 s. Each R-R interval, HR, SBP, DBP, and respiratory time series was resampled at 2 Hz to obtain equidistant time intervals. The resampled series were analyzed by using a fast Fourier transform algorithm as previously described (18). The areas under the power spectra in the Mayer wave and respiratory frequencies (defined as 0.04–0.15 and 0.15–0.50 Hz, respectively) were integrated and used for statistical comparisons.

Data analysis. Baseline characteristics of the two groups of subjects were compared by using analysis of covariance (ANCOVA) and Student’s t-tests. Supine and tilt cardiovascu-
lar variables and spectral powers were compared between the groups by using two different methods to handle missing data. The first was a two-way repeated-measures ANCOVA (to examine group and time effects), removing those subjects with incomplete data. The second analysis employed an unbalanced repeated-measures model with structured covariance matrices (proc mixed; see Ref. 24) that is useful in unbalanced repeated-measures experiments in which there are missing observations. Because both methods yielded the same results, only the proc-mixed analysis is reported. All spectral data were natural log transformed to normalize their distributions and were adjusted for age effects. Data are expressed as untransformed means \( \pm SE \).

The respiratory time series was further analyzed by computing histograms of breathing frequencies (breaths/min) and Vt (ml) for each subject during upright tilt. The means of these distributions were compared between groups of sub-
jects using Student’s t-tests. We also compared V (average frequency \( \times \) volume) and the percentage of breaths below 0.15 Hz.

To identify a possible linear relation, and the strength of that relation between respiratory (input signal) and arterial BP (output signal) fluctuations and between arterial BP (input) and R-R interval (output) fluctuations in the low-
frequency range (0.04–0.15 Hz) during upright tilt, we calcu-
lated the coherence and transfer magnitudes between the signals by using the technique of Saul et al. (25). All analyses were performed with DaDisp software on a personal com-
puter. Coherence was calculated from the cross spectra and autospectra of the time series, according to the formula

\[
\text{Coherence} = \frac{(cross \text{ spectra})^2}{(output \text{ signal autospectra}) \times (input \text{ signal autospectra})}
\]

The signals were considered coherent over the frequencies at which coherence values exceeded 0.5 (25). Transfer magni-
tudes and phases were calculated for each subject over the frequency range meeting this criterion. Transfer magnitudes were determined by dividing the cross spectrum by the input autospectrum. For all analyses, the phase was negative, indicating that respiration led arterial BP, and arterial BP led R-R interval changes.

RESULTS

Symptomatic responses to tilt. Of the 52 healthy subjects, 27 developed presyncope or syncope within 4–39 min of the onset of upright tilt. These episodes were usually preceded by a brief period of yawning and restlessness. BP then began to fall as the subjects
developed pallor, diaphoresis, and dizziness or syncope. Relative bradycardia followed the decline in BP. All subjects recovered spontaneously on return to the supine position. As shown in Table 1 descriptive and baseline supine cardiovascular characteristics of symptomatic subjects were the same as those of asymptomatic subjects.

Arterial BP dynamics. Examination of individual arterial BP time series during upright tilt revealed striking high-amplitude, low-frequency SBP and DBP oscillations in many of the healthy subjects who subse-
sequently developed syncope. The amplitude of SBP oscillations in these subjects was occasionally as large as 60–70 mmHg. These large amplitude oscillations
were observed only during spontaneous breathing and were less striking in the asymptomatic subjects (Fig. 1). Power spectral analysis of spontaneous breathing segments of the study showed that both symptomatic and asymptomatic subjects had similar low-frequency (0.04–0.15 Hz) SBP and DBP power in the supine position, and increased both systolic and diastolic power significantly during tilt ($P = 0.0001$, time effect for both pressures; Figs. 2 and 3). However, subjects with subsequent syncope had significantly greater increases in low-frequency systolic and diastolic power during tilt than the asymptomatic subjects ($P = 0.01$, time by group interaction, Figs. 2 and 3). This difference was not present during the paced breathing segments of the study.

High-frequency (0.15–0.50 Hz) SBP and DBP power also increased significantly during tilt ($P = 0.0001$), but only the diastolic power response was significantly greater in syncopal subjects than asymptomatic subjects ($P = 0.04$). Again, this difference was not seen during paced breathing (Figs. 2 and 3).

R-R and HR dynamics. Low-frequency R-R interval power was unchanged during tilt, whereas high-frequency power decreased significantly ($P = 0.0001$) in both the symptomatic and asymptomatic groups of healthy subjects (Fig. 4). There were no differences in responses between the two groups of subjects. In contrast, low-frequency HR power increased to a significantly greater extent in syncopal subjects than in asymptomatic subjects ($P = 0.008$; Fig. 5). There were no differences in high-frequency HR power.

During paced breathing, both high-frequency R-R interval power was unchanged during tilt, whereas high-frequency power decreased significantly ($P = 0.0001$) in both the symptomatic and asymptomatic groups of healthy subjects (Fig. 4). There were no differences in responses between the two groups of subjects. In contrast, low-frequency HR power increased to a significantly greater extent in syncopal subjects than in asymptomatic subjects ($P = 0.008$; Fig. 5). There were no differences in high-frequency HR power.

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Health Subjects</th>
<th>Healthy Subjects Without syncope</th>
<th>With syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 ± 4</td>
<td>44 ± 3</td>
</tr>
<tr>
<td>Men/women (n)</td>
<td>10/15</td>
<td>13/14</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.2 ± 0.6</td>
<td>24.0 ± 0.5</td>
</tr>
</tbody>
</table>

Supine characteristics

<table>
<thead>
<tr>
<th>n</th>
<th>SBP, mmHg</th>
<th>DBP, mmHg</th>
<th>HR, beats/min</th>
<th>Respir. rate, breaths/min</th>
<th>Vt, ml</th>
<th>Vl/min</th>
<th>%Breaths &lt; 0.15 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>122 ± 3</td>
<td>121 ± 3*</td>
<td>66 ± 2</td>
<td>16 ± 1</td>
<td>297 ± 27</td>
<td>4.5 ± 0.3*</td>
<td>14 ± 3</td>
</tr>
</tbody>
</table>

Tilt characteristics

<table>
<thead>
<tr>
<th>n</th>
<th>SBP, mmHg</th>
<th>DBP, mmHg</th>
<th>HR, beats/min</th>
<th>Respir. rate, breaths/min</th>
<th>Vt, ml</th>
<th>Vl/min</th>
<th>%Breaths &lt; 0.15 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>114 ± 3</td>
<td>107 ± 2*</td>
<td>66 ± 2</td>
<td>17 ± 1</td>
<td>345 ± 27</td>
<td>5.6 ± 0.4*</td>
<td>13 ± 2</td>
</tr>
</tbody>
</table>

Values are means ± SE. BMI, body mass index; n, no. of subjects; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; respir., respiration; Vt, tidal volume; Vl, minute ventilation. *P ≤ 0.03, supine to tilt; †n = 14.
Respiratory dynamics. As shown in Table 1, average VT, respiratory rate, and V˙ during tilt did not differ significantly between symptomatic and asymptomatic subjects. Furthermore, the proportion of breaths in the low-frequency range, 0.15 Hz (Table 1) and both low- and high-frequency respiratory power under all conditions were similar between these two groups of subjects. Low- and high-frequency respiratory power during spontaneous breathing increased to a similar extent in response to tilt in subjects with and without syncope (Fig. 6). There was no relationship between the change in SBP power and change in respiratory power for either group of subjects.

Paced breathing at 0.25 Hz reduced low-frequency respiratory power (P = 0.0001) and increased high-frequency power (P = 0.0001) for both groups, but it did not distinguish symptomatic from asymptomatic subjects.

Potential influence of respiration on arterial BP dynamics. Although respiratory dynamics were similar between groups, it was possible that high-amplitude low-frequency breaths had a greater influence on arterial BP in syncopal than in nonsyncopal subjects. Therefore, we examined the transfer functions between respiration and SBP in subjects with and without syncope during tilt (Table 2). Eight-minute segments of artifact-free tilt data were available from 21 healthy nonfainters and 14 healthy fainters.

During upright posture, low-frequency respiratory and SBP signals were coherent (>0.50), in the range of 0.10–0.15 Hz, in 9 of the 14 (64%) fainters and 12 of the 21 (57%) nonfainters. The transfer magnitudes were also similar (22.9 ± 2.9 and 22.7 ± 2.9, respectively).

There was no coherence between respiration and R-R interval fluctuations in the low-frequency range.

Potential influence of the cardiac vagal baroreflex on arterial BP dynamics. We also asked whether cardiovascular baroreflex buffering of low-frequency SBP oscillations might be less effective in fainters than nonfainters, and we examined the coherence and transfer magnitude between SBP and R-R interval oscillations in the low-frequency range. These signals were coherent in 13 of 14 (93%) fainters and 18 of 21 (86%) nonfainters in the range of 0.06–0.12 Hz (Table 2). The transfer magnitudes were similar (5.53 ± 0.73 and 5.92 ± 0.72, respectively).

DISCUSSION

There are three principal findings from this study. 1) Healthy individuals who develop neurally mediated syncope...
syncope during head-up tilt demonstrate exaggerated low-frequency arterial BP and HR oscillations before the onset of syncope while they are still asymptomatic. 2) Although the difference in these oscillations between syncopal and nonsyncopal subjects disappears during paced breathing, the oscillations do not appear to be related to respiration. 3) The oscillations are not associated with alterations in the cardiovagal baroreflex. What is the origin of these low-frequency oscillations and their physiological significance?

Rhythmic fluctuations of systemic arterial BP were described as early as 1733 by the physiologist Stephen Hales (6). Subsequent investigators, including Traube in 1865 (30) and Hering in 1869 (7), attributed these “blood pressure waves” to respiration. In 1876, Sigmund Mayer (17) described in rabbits spontaneous low-frequency arterial BP waves that were independent of the respiratory rhythm. Since that time, there has been considerable controversy over the origin of low-frequency arterial BP oscillations. This controversy has been fueled in part by differences in nomenclature and oscillation period for the pressure waves, different stimuli used to evoke them, and the different animal models used to study them. Proposed mechanisms are of two types: 1) phasic feedback loops from peripheral baro- or chemoreceptors to brainstem centers that produce oscillating sympathetic output to the vasculature and 2) a central rhythm generator that operates independently of phasic feedback (22). High-amplitude arterial BP oscillations with a frequency between 0.04 and 0.15 Hz can be generated in mammals by hypotensive hemorrhage (22), coronary artery occlusion (14), upright posture (4, 21), and intravenous nitroglycerin infusion (21), suggesting that they represent the vasomotor response to sympathoexcitation. This notion is supported by the fact that this response can be prevented by bilateral stellatectomy (21), peripheral α-adrenergic blockade with phentolamine mesylate (22), or sympathetic vasomotor blockade by epidural anesthesia (26).

Respiration also modulates HR and arterial BP (9, 19). Periodic breathing caused by congestive heart failure, sleep apnea, and high-altitude exposure has been shown to influence low-frequency HR oscillations (12). The attenuation of Mayer wave oscillations in healthy syncopal subjects during paced breathing at 0.25 Hz suggested to us that low-frequency respiratory cycles before syncope might be responsible for the vasomotor fluctuations we observed. However, after comparison of respiratory rates, VT, spectral powers, and respiratory-to-arterial BP transfer magnitudes in fainters and nonfainters, this did not appear to be the case. The damping effect of paced breathing on low-frequency oscillations of systemic arterial BP and HR are shown in Fig. 4. As can be seen, the mean power of low-frequency oscillations was significantly lower in the paced condition than in the spontaneous condition. This finding is consistent with the notion that low-frequency respiratory cycles contribute to vasomotor instability before syncope.

Fig. 4. Low-frequency (0.04–0.15 Hz; A) and high-frequency (0.15–0.50 Hz, B) R-R interval power in supine and tilt positions, during spontaneous and paced breathing, for healthy nonfainters (solid bars) and fainters (open bars). Statistical analyses were performed on age-adjusted, natural log-transformed data, by using proc-mixed procedure.

Fig. 5. Low-frequency (0.04–0.15 Hz; A) and high-frequency (0.15–0.50 Hz, B) HR power in supine and tilt positions, during spontaneous and paced breathing, for healthy nonfainters (solid bars) and fainters (open bars). Statistical analyses were performed on age-adjusted, natural log-transformed data, using the proc mixed-procedure.
frequency arterial BP oscillations may have been due to partial entrainment of arterial BP rhythms at the higher breathing frequencies (9) or to suppression of sympathetic activity by the relaxation response. Alternatively, it is possible that enhanced Mayer wave amplitude occurs only at a time more proximal to syncope and, therefore, was not present during the initial phase of tilt when paced breathing was performed. We did not randomize the order of paced and spontaneous breathing because we wanted to maximize the chance of acquiring controlled breathing data during tilt, before subjects became symptomatic. If subsequent studies confirm that paced breathing not only reduces vasomotor instability but also prevents the development of syncope, paced breathing may prove to be a useful intervention in otherwise healthy individuals who are at risk of fainting during prolonged standing.

We also explored the possibility that an exaggerated Mayer wave response to tilt represented impaired cardiovagal baroreflex buffering of arterial BP. To investigate the cardiovagal baroreflex, we examined the transfer magnitudes between SBP and R-R intervals and found that they did not differ between healthy subjects with and without symptoms during tilt. This analysis implies a causal direction of change from low-frequency arterial BP to R-R interval. Although it is possible that a causal change can occur in the opposite direction, the analysis was limited to the tilted position, which increases low-frequency arterial BP variability, even when R-R interval variability is eliminated by cardiac pacing (28). The negative phase relation between these signals also supports the notion that arterial BP led R-R interval changes.

It is notable that the analysis of R-R variability yielded different results depending on whether HR or interbeat interval was used as the unit of measure. R-R interval is linearly related to cardiac vagal outflow, whereas HR is inversely related to R-R interval and reflects minute-to-minute systemic hemodynamic adjustments to physiological stimuli (1, 10). The finding that R-R interval variability during tilt did not differ between symptomatic and asymptomatic subjects, but that HR variability did, suggests that vasomotor instability in the syncopal subjects was probably not related to alterations in cardiovagal activity preceding syncope but was related to abnormalities in hemodynamic control of the circulation. Hemodynamic alterations that would predispose healthy subjects to syncope include inadequate cardiac output or systemic vascular resistance during upright tilt. A recent study (20), showing large-amplitude, low-frequency arterial BP oscillations when cardiac output was held constant by computer control of cardiac rate, suggests that our findings probably reflect beat-to-beat changes in systemic vascular resistance rather than cardiac output.

If Mayer waves indeed reflect sympathetic outflow to the vasculature, then a heightened sympathetic response to tilt might be the cause or effect of hemodynamic changes associated with syncope. One possible physiological explanation for our findings is that an excessive reduction in venous return during tilt in subjects prone to syncope resulted in heightened sympathetic activity, vigorous contraction of a relatively empty cardiac ventricle, stimulation of afferent vagal C fibers in the ventricular wall, and subsequent provocation of the Bezold-Jarisch reflex (16). This is consistent with the observation that Mayer wave oscillations increased before the onset of hypotension and bradycardia. Unfor-

---

Table 2. Respiration, SBP, and interbeat interval (R-R) coherence analysis for healthy subjects with and without tilt-induced syncope

<table>
<thead>
<tr>
<th>Coherence Analysis</th>
<th>Without syncope (n = 21)</th>
<th>With syncope (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-frequency respiration to SBP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with coherence &gt; 0.5 (%)</td>
<td>12 (57%)</td>
<td>9 (64%)</td>
</tr>
<tr>
<td>Coherence</td>
<td>0.64 ± 0.01</td>
<td>0.64 ± 0.03</td>
</tr>
<tr>
<td>Frequency range, Hz</td>
<td>0.11–0.15</td>
<td>0.10–0.14</td>
</tr>
<tr>
<td>Transfer magnitude</td>
<td>22.7 ± 2.9</td>
<td>22.9 ± 2.9</td>
</tr>
<tr>
<td>Low-frequency SBP to R-R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with coherence &gt; 0.5 (%)</td>
<td>18 (86%)</td>
<td>13 (93%)</td>
</tr>
<tr>
<td>Coherence</td>
<td>0.62 ± 0.02</td>
<td>0.66 ± 0.02</td>
</tr>
<tr>
<td>Frequency range, Hz</td>
<td>0.06–0.12</td>
<td>0.06–0.11</td>
</tr>
<tr>
<td>Transfer magnitude</td>
<td>5.92 ± 0.72</td>
<td>5.53 ± 0.73</td>
</tr>
</tbody>
</table>

Values are means ± SE for coherence and transfer magnitude; n, no. of subjects.
fortunately, we were unable to measure venous return or stroke volume in the present study.

Limitations. There are several limitations to the present study. As discussed above, we did not randomize the sequence of paced and spontaneous breathing data collection periods during upright tilt. Therefore, we cannot be certain that lower Mayer wave amplitude during paced breathing was not due to a temporal effect. However, this limitation would not affect the principal analysis of respiratory dynamics during periods of spontaneous breathing when Mayer wave amplitude was heightened.

Also, this study did not examine hemodynamic changes associated with syncope. Instead, we focused specifically on the role of respiration and the cardiovascular baroreflex on beat-to-beat cardiovascular dynamics. Additional studies are needed to examine potential relationships between beat-to-beat changes in stroke volume or systemic vascular resistance and arterial BP in both health and disease.

The number of syncopal subjects with complete data during upright tilt was relatively small, because syncope occurred before data collection could be completed. This attrition of subjects decreased the power of the study to detect differences in respiration and may have biased the study by removing those with the most maladaptive response to tilt. Nevertheless, the symptomatic subjects who remained in the sample still demonstrated exaggerated Mayer wave oscillations during tilt, without a corresponding increase in the number or amplitude of low-frequency respiratory cycles. Therefore, we believe our findings are valid.

Finally, it is unlikely that high-amplitude Mayer wave oscillations are a fixed characteristic of syncopal prone subjects and thus could be used for diagnostic purposes. Both the occurrence of these oscillations and the syncopal response to tilt are highly variable within individuals. However, their coincident relationship suggests that the emergence of highly periodic BP rhythms may be indicative of an unstable physiological control network that predisposes individuals to circulatory collapse. Similar cyclic variations in vasomotor activity are seen in other conditions leading to cardiovascular decompensation such as hemorrhage (15), sinoaortic denervation (3), and myocardial ischemia (14).

The authors are grateful to Roberta Rosenberg for assistance with subject recruitment, Dr. J. Andrew Taylor for his insightful suggestions, and Dr. Adrienne Cupples for help with the statistical analysis. Address for reprint requests: L. A. Lipsitz, Hebrew Rehabilitation Center for Aged, 1200 Centre St., Boston, MA 02131 (E-mail: Lipsitz@Mail.HRC.Harvard.edu).

Received 16 December 1996; accepted in final form 31 March 1997.

REFERENCES


