Dynamic Regulation of Middle Cerebral Artery Blood Flow Velocity in Aging and Hypertension

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Background and Purpose—Although aging and hypertension may predispose hypertensive elderly subjects to cerebral hypoperfusion during orthostatic stress, their effects on the acute cerebral autoregulatory response to hypotension are not known.

Methods—Continuous middle cerebral artery blood flow velocity (BFV) (transcranial Doppler ultrasound) and mean arterial pressure (MAP, Finapres) were measured in response to (1) acute hypotension during standing, (2) steady-state sitting and standing, and (3) hypercarbia during CO2 rebreathing in 10 healthy young subjects (age 24±1 years), 10 healthy elderly subjects (age 72±3 years), and 10 previously treated hypertensive elderly (age 72±2 years) subjects. CO2 reactivity was computed as the slope of cerebrovascular conductance (CVC=BFV/MAP) versus end-expiratory CO2. Coherence, transfer magnitudes, and phases between low-frequency MAP and BFV signals were computed from their autospectra during 5 minutes of sitting and standing.

Results—MAP fell to a similar extent in all groups by an average of 21 to 26 mm Hg (22% to 26%) within 30 seconds of standing. Mean BFV also fell in all subjects but significantly less in the older subjects (−4.7±0.7 cm/s in hypertensives and −5.3±1.2 cm/s in normotensives, P=NS) compared with younger subjects (−10.1±1.1 cm/s, P<0.05). CO2 reactivity was greater in the young subjects (0.19±0.01) compared with normotensive (0.14±0.01, P<0.05) and hypertensive elderly subjects (0.11±0.02, P<0.05) (P=NS between elderly groups). Fewer hypertensive subjects had coherence between MAP and BFV signals; for subjects with coherence, there were no significant group differences in phase or transfer magnitudes in either sitting or standing positions.

Conclusions—Despite reduced CO2 reactivity, elderly normotensive and previously treated hypertensive subjects retain cerebral autoregulatory capacity in response to acute orthostatic hypotension. (Stroke. 2000;31:1897-1903.)

Key Words: autoregulation | cerebral blood flow | hypotension, orthostatic | spectrum analysis

Both aging and hypertension impair arterial blood pressure (BP) regulation, potentially making hypertensive elderly subjects vulnerable to cerebral hypoperfusion and syncope during orthostatic stress. Hypertension has been shown to elevate the threshold for cerebral autoregulation1 and reduce the cerebrovascular response to changes in the arterial partial pressure of CO2.2 However, the effects of age, with and without concomitant hypertension, on the acute cerebrovascular autoregulatory response to hypotension are not well understood. The availability of transcranial Doppler ultrasonography for the noninvasive measurement of beat-to-beat changes in cerebral blood flow velocity (BFV) has made it possible to assess cerebral autoregulation under both steady-state and dynamic conditions. Therefore, in this study we used TCD to evaluate changes in middle cerebral artery (MCA) BFV in response to (1) acute hypotension during standing, (2) spontaneous BP oscillations during steady-state sitting and standing, and (3) hypercarbia during CO2 rebreathing in groups of healthy young, healthy elderly, and hypertensive elderly subjects. We hypothesized that age and hypertension would impair dynamic autoregulation, resulting in relative cerebral hypoperfusion during acute hypotensive stress.

Subjects and Methods
Ten healthy young subjects (age 24±1 years), 10 normotensive elderly subjects (age 72±3 years), and 10 hypertensive elderly subjects (age 72±2 years) were recruited from among laboratory personnel, volunteers responding to newspaper advertisements, and members of the Harvard Cooperative Program on Aging subject registry. All subjects were carefully screened with a medical history, physical examination, and ECG to exclude acute medical conditions other than hypertension. A carotid Doppler study was performed on hypertensive subjects to rule out significant carotid artery stenosis. Subjects were also evaluated for an adequate temporal window for insonation of the MCA. Antihypertensive medications were tapered.
over 1 to 2 weeks, then withheld for ≥1 week before the experimental protocol was conducted. The study was approved by the hospital institutional review board, and all subjects provided informed consent.

**Experimental Protocol**

**Instrumentation**
Subjects reported to the cardiovascular laboratory in the postabsorptive state, ≥2 hours after their last meal. Three ECG leads were attached to the chest for measurement of the R-R interval, and the finger cuff of a photoplethysmographic noninvasive arterial pressure monitor (Finapres) was placed on the middle finger of the right hand to measure beat-to-beat arterial pressure. The hand was supported by a sling at the level of the right atrium to eliminate hydrostatic pressure effects. Finapres measurements were initially corroborated by standard measurements of arterial pressure with an oscillometric cuff on the upper arm (Dinamap). Respiration was measured continuously with an inductive plethysmograph (Respiracar) attached to two elastic respiratory transducer bands, one around the mid chest and the other around the abdomen. This was used to assess breath-to-breath breathing frequency and tidal volume during the protocol.

TCD ultrasonography was used to measure the changes in MCA BFV in response to BP changes during sitting and standing and end-tidal CO2 changes during CO2 rebreathing. The 2-MHz probe of a Nicolet Companion portable Doppler system was placed over the temporal bone just above the zygomatic arch between the frontal process and the front of the ear to insonate the MCA. The MCA BFV signal was identified according to the criteria of Aaslid et al3 and recorded at a depth of 50 to 65 mm. Once an optimal signal was obtained, the probe was strapped to the subject’s head and locked in position with a Mueller-Moll probe fixation device. The envelope of the velocity waveform, derived from a fast-Fourier analysis of the Doppler frequency signal, was digitized at 500 Hz, displayed continuously during the final 1 minute of sitting and 1 minute of standing, and then divided into 5 equal raw waveforms for each individual during the period of sitting to standing. Data were collected during 5-minute periods of steady-state sitting and standing.5–7

**Standing Protocol**
During pilot studies to determine an appropriate orthostatic stress with which to assess cerebral autoregulation, we tested the head-up tilt procedure but often lost the TCD signal because of apparent movement of the brain within the cranial vault. Therefore we used an active sit-to-stand procedure, which produced immediate orthostatic hypotension without altering the spatial relation between the Doppler probe and MCA. The initial fall in arterial pressure during active standing is due to leg muscle vasodilation and is not normally seen during passive head-up tilt.4

After instrumentation, subjects sat in a straight-backed chair with their legs elevated at 90 degrees in front of them on a stool. For each of 2 active stands, subjects rested in the sitting position for 5 minutes, then stood upright for 1 minute. The initiation of standing was timed from the moment both feet touched the floor. Data were collected continuously during the final 1 minute of sitting and 1 minute of standing. After these 2 active stands, a third sit-to-stand procedure was performed for the transfer function analysis of BP and cerebral BFV signals. For this procedure, data were collected during 5 minutes of sitting and 5 minutes of standing. Respiration was paced at 0.25 Hz during all data collection periods to control end-tidal CO2, and to permit the calculation of low-frequency BP-to-BFV transfer functions, without the influence of respiratory cycles.

**CO2 Reactivity Protocol**
Changes in MCA BFV were measured during alterations in end-tidal CO2 to determine whether impairments in autoregulation represented a generalized abnormality in cerebrovascular reactivity or a specific abnormality in response to changes in perfusion pressure. During each of 2 tests, cerebral BFV was measured continuously while subjects sat in a chair and breathed a mixture of 5% CO2 and 95% air through a 5-L rebreather bag at 15 breaths per minute (0.25 Hz) for 1 minute. Inspired oxygen concentration was found to remain stable over this time period. Cerebrovascular conductance (mean cerebral BFV/mean arterial BP) was determined for each R-R interval and plotted against end-tidal CO2 for the breath coinciding with that interval. The slope of this relation was used as an index of CO2 reactivity. The average of 2 trials is reported, except in 4 cases in which 1 trial had to be discarded because of technical problems with the Doppler signal or CO2 delivery that disrupted the linear relation between CO2 and BFV. Results from 1 young subject could not be used because neither trial was technically adequate.

**Data Processing and Analysis**
All data were displayed and digitized in real time at 500 Hz with commercially available data acquisition software (Windaq, Dataq Instruments) on a personal computer (NEC Pentium 90 MHz). Beat-to-beat R-R interval, systolic and diastolic pressures, and systolic and diastolic BFVs were determined from the R wave of the ECG and the maximum and minimum of the arterial pressure or BFV waveforms.

To evaluate the beat-to-beat dynamics of arterial BP and cerebral BFV responses to acute posture change, we visually examined the raw waveforms for each individual during the period of sitting to standing. To quantify and compare changes in systolic, diastolic, and mean pressures and velocities, we computed the difference between the mean sitting value (averaged over a period of 50 seconds) and the standing value at the time of the diastolic BP nadir (average of 5 values surrounding the nadir) for each trial, then averaged the values for each group. The change in flow velocity relative to the change in pressure was determined by dividing individual changes in flow velocity by the associated change in pressure, then averaging these ratios for each subject group. Although it is generally thought that the absolute change in BP within a given range is the stimulus for the autoregulatory blood flow response, it is possible that similar absolute changes in pressure could represent different homeostatic stresses, depending on the initial BP. Therefore, we also computed blood flow changes as a function of the percent change in BP. Since this provided similar results, we chose to present cerebral BFV changes divided by the percent change in BP as an index of cerebral autoregulation.

We also assessed the autoregulatory response to transient orthostatic hypotension by determining the absolute and percent change in cerebrovascular resistance (CVR = MAP/BFV) from the sitting position (average of 50 seconds data) to the BP nadir during standing (average of 5 values). Finally, as described below, we computed coherence, transfer magnitudes, and phases between continuous MAP and BFV signals from their autospectra during 5-minute periods of steady-state sitting and standing.5–7

**Coherence and Transfer Function Analysis**
All data segments were visually inspected and edited for artifact and ectopy, and only stationary data were used for this analysis. Frequency domain analysis was performed on beat-to-beat mean arterial pressures (MAPs) and cerebral BFVs. A power spectrum analysis technique based on the Welch algorithm of averaging periodograms was used. The time series were interpolated at 4 Hz to obtain equidistant time intervals and then divided into 5 equal overlapping segments. Each segment was detrended, Hanning filtered, and fast-Fourier transformed to its frequency representation squared. The periodograms were averaged to produce the spectrum estimate. Coherence between low-frequency mean arterial BP and BFV was calculated from the cross-spectra and autospectra of stationary data segments in the sitting and standing positions. Coherence was computed as (cross-spectra/√(input signal autospectrum) √(output signal autospectrum)). The signals are considered coherent over the frequencies at which coherence values exceeded 0.5. Transfer magnitudes and phases were calculated for each subject over the frequency range meeting this criterion, with MATLAB software. Transfer functions were determined by dividing the cross-spectrum by the input autospectrum.

**Statistical Analysis**
All variables were compared within and between groups by means of 2-way repeated-measures ANOVA. The results of each trial were entered into the analysis. There were no significant intra-individual
differences in the results from the 2 standing or CO2 rebreathing trials. Data are presented in tables and graphs as mean ± SEM.

Linear regression was used to compute the slope of the relation between end-tidal CO2 and cerebrovascular conductance. Each regression except the 6 excluded (see above) had good linear fits, with $R^2$ values ≥0.64.

## Results

### Subject Characteristics

Subject characteristics are summarized in Table 1. Hypertensive elderly subjects had higher systolic and diastolic pressures than the other 2 groups. There were no significant differences in BP between the young and normotensive elderly subjects.

### Hemodynamic Responses to Posture Change

Representative BP and cerebral BFV waveforms during sitting and the first 25 seconds of standing are shown for a subject from each group in Figure 1. Average sitting and standing MAP, BFV, cerebral vascular resistance, and heart rate and their changes during standing are shown for each group in Table 2. Mean BFV was lower and CVR was higher in both elderly groups compared with the young group in both sitting and standing positions. CVR was higher in hypertensive compared with normotensive elderly subjects only in the sitting position.

### Table 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normotensive</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>Hypertensive</th>
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<td>Young</td>
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<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Cilostazol</td>
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</table>

MBFV indicates mean BFV; MABP, mean arterial BP.

*P<0.05 compared with Young.
†P<0.05 compared with Normotensive Elderly.

### Table 2. Hemodynamic and Cerebrovascular Responses to Standing and CO2 Rebreathing

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>Hypertensive</th>
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<td></td>
<td>Sitting</td>
<td>Elderly</td>
<td>Elderly</td>
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<tr>
<td>Mean arterial BP</td>
<td>94.1±2.2</td>
<td>87.2±2.9</td>
<td>116±3.8†</td>
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<tr>
<td>Mean BFV</td>
<td>52.2±2.2</td>
<td>35.5±2.3*</td>
<td>34.7±1.2*</td>
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<tr>
<td>CVR</td>
<td>1.9±0.1</td>
<td>2.7±0.2*</td>
<td>3.5±0.2*†</td>
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<tr>
<td>Heart rate</td>
<td>69±3</td>
<td>62±1</td>
<td>75±2</td>
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<tr>
<td></td>
<td>Standing</td>
<td>Elderly</td>
<td>Elderly</td>
<td></td>
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<tr>
<td>Mean arterial BP</td>
<td>70.0±2.6</td>
<td>66.2±2.9</td>
<td>90.1±3.2†</td>
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<tr>
<td>Mean BFV</td>
<td>42.1±1.6</td>
<td>30.2±2.4*</td>
<td>30.0±1.4*</td>
<td></td>
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<tr>
<td>CVR</td>
<td>1.6±0.1</td>
<td>2.4±0.2*</td>
<td>2.8±0.2*</td>
<td></td>
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<tr>
<td>Heart rate</td>
<td>95±3</td>
<td>73±1*</td>
<td>82±2*</td>
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<tr>
<td>Change</td>
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<tr>
<td>∆Mean arterial BP</td>
<td>−24.3±2.1</td>
<td>−21.0±2.2</td>
<td>−26.2±1.9</td>
<td></td>
</tr>
<tr>
<td>%∆Mean arterial BP</td>
<td>−25.7±2.2</td>
<td>−24.0±2.6</td>
<td>−22.4±1.5</td>
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<tr>
<td>∆Mean BFV</td>
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<td>−5.3±1.2*</td>
<td>−4.7±0.7*</td>
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<td>%∆Mean BFV</td>
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<tr>
<td>∆MBFV/%∆MABP</td>
<td>0.41±0.05</td>
<td>0.19±0.04*</td>
<td>0.22±0.03*</td>
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<tr>
<td>∆CVR</td>
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<td>−0.29±0.05</td>
<td>−0.72±0.10†</td>
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<tr>
<td>%∆CVR</td>
<td>−14.9±3.0</td>
<td>−14.8±2.6</td>
<td>−26.7±3.4†</td>
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</tr>
<tr>
<td>∆Heart rate</td>
<td>26±1</td>
<td>11±1*</td>
<td>11±1*</td>
<td></td>
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</tbody>
</table>

CO2 reactivity 0.19±0.01 0.14±0.01* 0.11±0.02*

MBFV indicates mean BFV; MABP, mean arterial BP.

Figure 1. Continuous BP (top panels) and MCA blood flow velocity (bottom panels) waveforms during 15 seconds of sitting and 25 seconds of standing for a young subject (left), normotensive elderly subject (middle), and hypertensive elderly subject (right). Arrow in each panel marks the initiation of standing when both feet touched the floor.
All subjects had similar declines in systolic, diastolic, and mean arterial BP during the initial standing period. MAP fell an average of 21 to 26 mm Hg (22% to 26%) by 30 seconds after the initiation of standing. Cerebral BFV also fell in all subjects, but the response differed quantitatively between the young and both elderly groups. Systolic BFV increased to a greater extent in the young subjects (14.1 ± 1.8 cm/s) compared with elderly normotensive (7.4 ± 1.1 cm/s, P < 0.05) and elderly hypertensive (6.9 ± 0.9 cm/s, P < 0.05) subjects. Diastolic BFV fell to a greater extent in the young (−23.3 ± 1.3 cm/s) compared with elderly normotensive (−16.9 ± 1.2 cm/s, P < 0.05) and hypertensive (−12.9 ± 0.6 cm/s, P < 0.05) subjects. There were no differences in systolic or diastolic BFV changes between the 2 elderly groups. Mean BFV (Table 2) fell to a similar extent in both groups of older subjects (−4.7 ± 0.7 cm/s in hypertensives and −5.3 ± 1.2 cm/s in normotensives, P = NS) and to a greater extent in the young (−10.1 ± 1.1 cm/s, P < 0.05, compared with each elderly group).

The change in mean BFV relative to the percent change in MAP was used as an index of autoregulation. Lower values represent smaller changes in BFV for a given change in BP. This index was significantly lower in normotensive (0.19 ± 0.04) and hypertensive (0.22 ± 0.03) elderly subjects compared with the young (0.41 ± 0.05, P < 0.05, see Table 2). There were no significant differences in this index of autoregulation between the 2 elderly groups.

CVR fell during posture change in all groups. The absolute and relative decrease during standing was significantly greater in the hypertensive elderly subjects compared with the normotensive elderly and young subjects (Table 2).

We also examined the relation between changes in BFV relative to the percent change in BP (the index of autoregulation) and the BP nadir during standing (Figure 2). For all subjects combined, there was no significant relation between this index of autoregulation and the BP nadir. However, during mean arterial BP declines to similarly low pressure ranges in young and normotensive elderly subjects, the young demonstrated greater declines in cerebral BFV than the elderly group.

Changes in heart rate during standing were greater in the young subjects compared with normotensive and hypertensive elderly subjects (Table 2). There were no differences in the heart rate response between the 2 elderly groups of subjects.

**CO2 Reactivity**

There was a linear relation between end-tidal CO2 and cerebrovascular conductance. The slope of this relation, representing CO2 reactivity, was greater in the young group (0.19 ± 0.01) compared with the other 2 groups (0.14 ± 0.01 in normotensive and 0.11 ± 0.02 in hypertensive elderly, P < 0.05 compared with young, Table 2). There were no differences in CO2 reactivity between the 2 groups of elderly subjects. Furthermore, there were no sex differences in CO2 reactivity (0.16 ± 0.01 in women versus 0.14 ± 0.01 in men, P = 0.38).

**Transfer Function Analysis of Spontaneous Autoregulation**

Representative power spectra for mean arterial BP and mean cerebral BFV time series during 5 minutes of sitting and 5 minutes of steady-state standing are shown in Figure 3, along with the corresponding coherence, phase, and gain (transfer magnitude) relations between the 2 signals at each frequency of interest (0.05 to 0.30 Hz). Highly coherent respiratory oscillations in both signals are evident at the paced breathing frequency near 0.25 Hz. The signals also appear to oscillate together with high coherence in the low-frequency (Mayer wave) region between 0.05 and 0.15 Hz. Consistent with the high-pass filter model of cerebral autoregulation, the positive phase of 45 to 90 degrees in the lower frequencies moves closer to zero degrees in the high-frequency range >0.15 Hz. The transfer magnitude falls in the lower frequencies, where
autoregulation of cerebral blood flow appears to damp low-frequency oscillations in BP.

Table 3 summarizes the average low-frequency BP and BFV powers (between 0.05 and 0.15 Hz) and the average coherence, phase, and transfer magnitudes over low frequencies, where coherence exceeded 0.50 for the 3 groups of subjects. BFV power was attenuated with both age and hypertension, particularly in the standing position. Fewer hypertensive elderly subjects had coherence between BP and BFV than subjects in the other 2 groups (7 versus 10 subjects in each of the other groups, \(P = 0.06\)). For those subjects who had coherence between the signals, there were no significant group differences in coherence, phase, or magnitude in either the sitting or standing position. Despite a lower transfer magnitude in the normotensive elderly group and higher phase in both elderly groups during standing compared with sitting, there were no significant intragroup changes in these variables during posture change for any group (Table 3).

**Figure 3.** Transfer function analysis for 1 subject in the sitting (left) and standing (right) positions. Top panel shows power spectra for mean arterial BP (MABP) and mean BFV (MBFV). Note the presence of low-frequency (0.05 to 0.15 Hz) and high-frequency (0.22 to 0.26 Hz) peaks in both signals. The higher-frequency peak is due to paced breathing at 0.25 Hz. The second panel shows coherence between BP and BFV signals at each frequency. The signals are coherent (>0.50) over most frequencies where spectral power is present. The third panel shows the corresponding phase relation between the 2 signals at each frequency. In the low frequencies, BFV leads BP by \(\approx 90^\circ\) degrees, whereas at the respiratory frequency, signals are in phase with 0-degree shift between them. This is characteristic of a high-pass filter. The lowest panel shows the transfer magnitude between signals. Transfer magnitude declines in the low-frequency range, suggesting that autoregulation is damping the transmission of low-frequency BP oscillations to BFV.

**Discussion**

The results of this study highlight several important characteristics of MCA circulatory dynamics and provide new insights into the effects of aging and hypertension on cerebral autoregulation. First, contrary to our hypothesis, we have shown that in response to an immediate orthostatic fall in BP, elderly normotensive and hypertensive subjects retain cerebral autoregulatory capacity, manifest by a reduction in cerebral vascular resistance and relative preservation cerebral BFV. The presence of normal autoregulation in our hypertensive subjects could be due to their previous treatment, which may have improved cerebral autoregulatory function.

Second, our data show no age-related or hypertension-related differences in the transfer magnitude (gain) between spontaneous BP and cerebral BFV changes, suggesting that cerebral autoregulation is intact in elderly and previously treated hypertensive subjects.

Finally, we found a reduction in \(\mathrm{CO}_2\) responsiveness in normotensive and hypertensive elderly subjects compared with young subjects. Taken together, the study results suggest there is a dissociation between small-vessel reactivity to \(\mathrm{CO}_2\) and cerebral hemodynamic responses to transient hypotension.

Examination of the raw cerebral BFV waveforms (Figure 1) indicates that the systolic velocity increases and diastolic velocity decreases in response to acute orthostatic hypoten-
sion. This response appears to be exaggerated in the young compared with the elderly subjects. An increase in peak systolic flow velocity associated with a decline in end-diastolic velocity is characteristic of a shift from a low-resistance to a high-resistance arterial system. However, our data show a decline in CVR in all subjects, consistent with normal autoregulation.

In experimental rabbits, Czosnyka et al also demonstrated an increase in flow velocity pulse amplitude in response to a decrease in perfusion pressure. The typical velocity profile noted during the fall in perfusion pressure was a decrease in diastolic flow velocity and a decrease or no change in systolic velocity. Although we found an increase in systolic flow velocity, both studies found that the increase in pulse amplitude was associated with a decline in CVR.

There are several possible explanations for the observed changes in the cerebral BFV waveform during orthostatic hypotension. Amplification of the systolic pressure wave is not only associated with peripheral vasoconstriction and enhanced wave reflection at arterial-arteriolar junctions but also a short cardiac ejection duration. The larger cardiovascular seen in young subjects may have resulted in greater systolic wave pulse amplification by shortening cardiac ejection duration. Kroeker and Wood and O’Rourke have shown that brachial pulse pressure pulse amplification during head-up tilt is very sensitive to changes in the duration of ventricular ejection, whereas Bos et al have shown this to be true of pulse amplification between the brachial and finger arteries. The well-known age-associated impairment in cardiovascular during orthostatic stress may have diminished pulse amplification in elderly subjects.

Another factor that may explain the observed flow velocity profiles during standing is a collapse of downstream vascular pressure as diastolic pressure falls below the critical closing pressure of cerebral blood vessels. If younger subjects have more compliant and collapsible vessels, they may have a greater diminution in blood flow and increase in pulsatility as cerebral perfusion pressure reaches this critical closing pressure. Elderly subjects with stiffer vessels may be able to maintain small-vessel patency at similar pressures. As demonstrated in Figure 2, hypertensive elderly subjects may not have declines in BP to levels below the critical closing pressure.

A variety of methods have been used for the measurement of cerebral autoregulation with use of TCD ultrasonography. Our standing procedure corresponds most closely to the leg cuff method of Aaslid et al, in which the sudden deflation of bilateral leg cuffs (inflated to above systolic pressure) results in an abrupt BP reduction similar to that seen in Figure 1. We preferred using the standing method because it was more physiological and less uncomfortable for our subjects. Since at a normal heart rate there are only 2 to 3 physiological points with which to plot CVR over the first 2.5 seconds of hypotension, we could not determine a reliable “rate of regulation” as Aaslid et al proposed. Instead, we determined the absolute change in mean BFV, normalized by the change in MAP at its nadir.

An alternative method to assess cerebral autoregulation is to compute the phase relation or transfer magnitude, between arterial pressure and cerebral blood flow during stationary conditions. These techniques are based on a high-pass filter model of cerebral autoregulation, which assumes that spontaneous variations in cerebral blood flow caused by changes in arterial pressure are effectively damped in the low-frequency range but not in the high-frequency range, where changes in pressure are directly transferred to changes in cerebral blood flow. Consistent with this model, phase angles were larger and transfer magnitudes were lower for low-frequency oscillations in these signals (0.04 to 0.15 Hz) than for high-frequency (0.15 to 0.40 Hz) oscillations (see Figure 3). Using the transfer function method, we were not able to show differences in autoregulation between the 3 groups of subjects. This could be due to the fact that spontaneous fluctuations in BP remained within the normal range of cerebral autoregulation for all subjects. Relatively few hypertensive elderly subjects had adequate coherence between arterial pressure and cerebral BFV signals to compute the transfer functions. This may be consistent with intact autoregulation, if the relation between low-frequency systemic pressure and cerebral blood flow oscillations is reduced to the point that signal coherence is no longer present. The absence of coherence in the hypertensive subjects also may have been due to the low spectral power of these signals. Although the transfer function analysis does not permit us to draw conclusions about cerebral autoregulation in older hypertensive subjects, it does provide evidence that spontaneous autoregulation remains intact with healthy aging.

Finally, we measured CO2 reactivity to assess age-related and hypertension-related changes in microvascular sensitivity to hypercarbia. Our findings suggest an effect of age but not hypertension on the cerebral vasodilatory response to CO2. Previous studies by Kastrup et al and Matteis et al, who used 5-minute CO2 inhalation or 30-second breath-holding, respectively, showed age-related reductions in CO2 reactivity in women but not in men. Hormone replacement therapy appeared to improve CO2 reactivity in postmenopausal women. We did not find sex differences in our study. It is difficult to compare our results with others because previous studies examined younger subjects, used different techniques, and did not use repeated measurements to account for the variability of response that is inherent in the measurement of CO2 reactivity.

In conclusion, the present study suggests that despite a decline in CO2 reactivity, elderly normotensive and hypertensive subjects retain cerebral autoregulatory capacity in response to acute orthostatic hypotension.

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References


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