Muscle Tensing During Standing
Effects on Cerebral Tissue Oxygenation and Cerebral Artery Blood Velocity

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Background and Purpose—When standing up causes dizziness, tensing of the leg muscles may alleviate the symptoms. We tested the hypothesis that leg tensing improves orthostatic tolerance via enhanced cerebral perfusion and oxygenation.

Methods—in 10 healthy young adults, the effects of leg tensing on transcranial Doppler–determined middle cerebral artery (MCA) mean blood velocity (\(V_{\text{mean}}\)) and the near-infrared spectroscopy–determined frontal oxygenation (O\(_2\)Hb) were assessed together with central circulatory variables and an arterial pressure low-frequency (LF) (0.07 to 0.15 Hz) domain evaluation of sympathetic activity.

Results—Standing up reduced central venous pressure by (mean \(\pm\) SEM) 4.3 \(\pm\) 2.6 mm Hg, stroke volume by 49 \(\pm\) 7 mL, cardiac output by 1.9 \(\pm\) 0.4 L/min, and mean arterial pressure at MCA level by 9 \(\pm\) 4 mm Hg, whereas it increased heart rate by 30 \(\pm\) 4 beats per minute (\(P<0.05\)). MCA \(V_{\text{mean}}\) declined from 67 \(\pm\) 4 to 56 \(\pm\) 3 cm/s, O\(_2\)Hb decreased by 7 \(\pm\) 2.8%, and LF spectral power increased (\(P<0.05\)). Leg tensing increased central venous pressure by 1.4 \(\pm\) 2.7 mm Hg and cardiac output by 1.8 \(\pm\) 0.4 L/min with no significant effect on blood pressure, whereas heart rate decreased by 11 \(\pm\) 3 beats per minute (\(P<0.05\)). MCA \(V_{\text{mean}}\) increased to 63 \(\pm\) 3 cm/s and O\(_2\)Hb increased by 2.1 \(\pm\) 2.6%, whereas LF power declined (\(P<0.05\)). Within 2 minutes after leg tensing, these effects had disappeared.

Conclusions—During standing, tensing of the leg muscles attenuates a reduction in cerebral perfusion and oxygenation as it stabilizes central circulatory variables and reduces sympathetic activity. (Stroke. 2001;32:1546-1551.)

Key Words: Fourier analysis • orthostatic • spectroscopy, near-infrared • syncope • ultrasonography, Doppler, transcranial
Standing and Leg Tensing Protocol
Instrumentation occurred at 9 AM in a room at 22°C and was followed by a test run and baseline recordings after 30 minutes. The subjects then stood up, and after 5 minutes, they tensed their muscles by crossing the legs and pressing them against each other for 2 minutes, followed by 2 minutes of free standing.12 After 10 minutes of supine rest, the protocol was repeated.

Measurements
The proximal segment of the right MCA was ionsoned (Multidop X; DWL Sipplingen) through the posterior temporal “window.”13 Once the optimal signal-to-noise ratio was obtained, the probe was covered with an adhesive ultrasonic gel (Tensive; Parker Laboratories Inc) and secured with a headband. MCA Vmean was the integral of the maximal frequency shifts over 1 heartbeat.

Cerebral oxygenation was monitored by NIRS, and changes in absorption of mainly oxyhemoglobin (O2Hb) and deoxyhemoglobin (Hb) were recorded with the light source and the sensing optode positioned on the forehead below the hairline (INVOS 3100 cerebral oximeter; Somanetics [with light at 808.75 and 732.50 nm]).14 With continuous light, the chromophore content is not determined because the path length of light is unknown but the NIRS-determined oxygenation changes in parallel with cerebral blood flow.15 Changes in O2Hb are given relative to supine rest.

Mean arterial pressure (MAP) was measured with a Finapres (model 5; Netherlands Organization for Applied Scientific Research, Biomedical Instrumentation, TNO-BMI).16,17 The cuff was applied to the midphalanx of the middle finger of the dominant arm placed at heart level. Central venous pressure (CVP) was recorded with a catheter (1.7 mm ID, 16 gauge) introduced percutaneously through the basilic vein of the nondominant arm and advanced to the superior caval vein under continuous ECG recording. Correct catheter positioning was confirmed by monitoring of the pressure waveform. CVP was recorded from a transducer (Bentley) referenced to the level of the right atrium and connected to a monitor (8041; Simonsen & Weel). A catheter (1.0 mm ID, 19 gauge) in the brachial artery of the nondominant arm was used for blood sampling.

Thoracic electrical impedance (TI) was measured with skin electrodes (Blue Sensor; Medicotest) with 10 mA at 100 kHz (Caspersen & Nielsen) as an index of the thoracic blood volume.18 Two pairs of electrodes were positioned with an internal distance of 5 cm behind the right sternocleidomastoid muscle, and another pair was placed at a similar distance in the left midaxillary line at the level of the xiphoid process. The outer electrodes served for current, and TI was recorded by the inner pair.

Changes in stroke volume (SV) of the heart were computed from the arterial pressure waveform by simulation of a nonlinear, time-varying model of the aortic input impedance. The relation between the cross-sectional area of the human thoracic aorta and the distending pressure is described by an arctangent equation.19 The aortic characteristic impedance and arterial compliance are derived from this pressure-area equation.20 SV is tracked from peripheral arterial pressure in patients with cardiovascular disease20 and septic shock,21 and replacement by the finger arterial pressure wave as input to the model enhances the model during orthostatic stress compared with a thermodilution-based estimate.22 CO was the product of SV and heart rate (HR). To obtain absolute values, model CO was calibrated by a Fick-determined CO as estimated from the arterial and central venous O2 content and the pulmonary O2 uptake (VO2) averaged over 4 minutes of standing.

Breath-to-breath online gas analysis was performed using a MedGraphics CPX/D metabolic cart. Respiratory gas was sampled continuously from a mouthpiece, and partial gas pressures were obtained from a Zirconia oxygen analyzer (accuracy ±0.03% O2) and a nondispersive infrared sensor for CO2 (accuracy ±0.05% CO2) that delivered VCO2 and end-tidal CO2 tension (PETCO2). Arterial and venous blood was sampled (5850; Radiometer) for blood gas variables and analyzed immediately (ABL-4 and OSM-3 apparatus; Radiometer). PaCO2 was measured at 2 and 1 minute before standing up, at 2 minutes, and at the end of standing, after 1 minute of leg tensing and 1 minute after uncrossing of the legs.

Data Processing and Analysis
Blood pressure and MCA Vmean values were analog-to-digital converted at 100 Hz and stored on a hard disk. O2Hb and TI were recorded every 15 seconds. MAP and CVP were the integral over 1 beat. MAP at the level of the MCA (MAPmean) took into account the finger-to-Doppler probe distance. The inverse of the interbeat pressure interval was HR, and systemic vascular resistance was calculated from MAP, CO, and CVP. The influence of tensing on the MCA Vmean-PaCO2 relationship was analyzed in 8 subjects in whom satisfying simultaneous recordings of PaCO2 and MCA Vmean were made. Sequences of consecutive MCA Vmean values for ≥5 cardiac cycles at 5 minutes of standing and 1 minute of leg tensing were taken, and their averages were related to the corresponding PaCO2 values. The steady-state CO2 reactivity was calculated from the change in MCA Vmean and corresponding PaCO2 from standing to tensing and expressed as their ratio. The LF component of oscillations of arterial pressure was taken to reflect changes in sympathetic activity.23 During standing and leg tensing, oscillations in arterial pressure were analyzed by fast Fourier transformation, and spectral power was expressed as the integrated area in the LF (0.07 to 0.15 Hz) range.24,25

Statistical Analysis
Data were transformed to equidistantly resampled data at 2 Hz (PetCO2 data at 0.25 Hz accounting for respiratory rate) by polynomial interpolation. Data that fit a normal distribution are expressed as mean and SEM and otherwise as median with range. Changes over time were examined by repeated measures ANOVA, and differences were determined by the Student-Newman-Keuls test. Differences in responses between body positions were examined by t test or Wilcoxon signed rank test. P<0.05 was considered to indicate a statistically significant difference.

Results
Standing Up
One subject developed syncope symptoms during free standing with a 22% fall in O2Hb accompanied by a 25% reduction in MCA Vmean, and the experiment was terminated. In the other subjects, CVP decreased by 4.3±2.5 mm Hg and TI increased from 45.3±3.2 to 48.9±4.0 Ω after 1 minute and to 49.9±3.8 Ω after 5 minutes. After 1 minute of standing, HR had increased by 30±4 beats per minute, whereas SV remained reduced by 49±7 mL and CO was reduced by 1.9±0.4 L/min.

At 2 and 1 minute before the subjects stood up, PaCO2 was 5.24±13 and 5.34±0.18 kPa, respectively (P=0.145). After the subjects stood up, ventilation increased (Table 1) and PaCO2 fell to 4.68±0.13 kPa at 2 minutes and then remained stable until the end of standing (4.64±0.17 kPa). The SaO2 did not change, but the Svo2 continued to decrease. After 8 seconds of standing, a reduction in MAPmean coincided with a fall in MCA Vmean by 20±3 cm/s, followed by a recovery and an overshoot with a peak after 15 seconds and similar changes in blood pressure (Figure 1). After 30 minutes, MAPmean had decreased by 9±4 mm Hg, Vmean stabilized at 84±5% of the level established during rest, and cerebral oxygenation decreased by 7.2±2.6% (Figures 2 and 3). LF variability in MAP increased from 3.4±3.5 to 16.9±7.8 mm Hg2/Hz.
Muscle Tensing

After 2 seconds, CVP increased by 1.4 ± 2.7 mm Hg, whereas TI did not change significantly. The MAP response was biphasic with a 7 ± 4 mm Hg increase after 2.5 seconds, a nadir at −6 ± 4 mm Hg after 8 seconds, and then a recovery after 14 seconds (Figures 2 and 3). Apart from these initial changes, MAPmca was not significantly different from the values during free standing.

After 9 seconds, CO was elevated by 1.8 ± 0.4 L/min, followed by a decline as HR decreased 11 ± 4 beats per minute. MCA $V_{\text{mean}}$ increased to ≈62 cm/s during the first 70 seconds and to ≈59 cm/s until muscle tensing was terminated (Figures 2 and 3). $O_2$Hb increased by 2.1 ± 2.5% after 2 minutes. The TI was maintained at 49.8 ± 3.8 Ω during tensing. With muscle tensing, $Paco_2$ increased to 4.90 ± 0.13 kPa, although ventilation did not change significantly and the “$CO_2$ reactivity” of the $V_{\text{mean}}$ was elevated (Table 2). Leg tensing reduced the LF variability from 16.9 ± 7.8 to 9.8 ± 5.7 mm Hg/Hz ($P<0.01$) (Figure 4).

During the first 2 minutes after the cessation of muscle tensing, CVP, CO, MCA $V_{\text{mean}}$, $Paco_2$, and $O_2$Hb fell to the level of 5 minutes of free standing.

Discussion

When humans stand up, the gravitational displacement of blood from the chest to lower parts of the body reduces venous return within seconds, resulting in a fall in cardiac filling volume and a reduction in cerebral perfusion and oxygenation. The new finding of the present study is that tensing of the leg muscles attenuates the orthostatic reduction in MCA $V_{\text{mean}}$ and in cerebral oxygenation.

We did not evaluate how leg tensing enhances cerebral perfusion or oxygenation during standing, but pressing the legs against each other modified central circulatory variables.

![Figure 1](https://stroke.ahajournals.org/)

**Figure 1.** MCA blood velocity and mean arterial pressure (MAP) responses to standing. Thin lines indicate individual values; thick line, averaged response (n=10).

![Figure 2](https://stroke.ahajournals.org/)

**Figure 2.** Cerebrovascular and cardiovascular responses to leg tensing. For $PETCO_2$/ $Paco_2$, line indicates $PETCO_2$ dots, $Paco_2$. SVR indicates systemic vascular resistance; dotted lines, supine reference level.

### Table 1. Ventilatory Responses to Standing Up and Leg Tensing

<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Standing: 5 min</th>
<th>Leg Tensing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>60 s</td>
</tr>
<tr>
<td>$SaO_2$, %</td>
<td>97 (0.3)</td>
<td>98 (0.2)*</td>
<td>98 (0.2)</td>
</tr>
<tr>
<td>$SvO_2$, %</td>
<td>78 (1)</td>
<td>62 (2)*</td>
<td>64 (1)</td>
</tr>
<tr>
<td>$V_t$, L/min</td>
<td>7.7 (4.7–9.4)</td>
<td>9.5 (6.5–15.0)*</td>
<td>9.8 (7.2–13.8)</td>
</tr>
<tr>
<td>$f$, f/min</td>
<td>17 (1.2)</td>
<td>16 (1.0)</td>
<td>16 (1.3)</td>
</tr>
<tr>
<td>$PETCO_2$, kPa</td>
<td>5.31 (4.80–5.60)</td>
<td>4.83 (3.67–5.31)*</td>
<td>5.07 (4.05–5.45)</td>
</tr>
<tr>
<td>$Paco_2$, kPa</td>
<td>5.34 (0.18)</td>
<td>4.64 (0.17)*</td>
<td>4.90 (0.13)†</td>
</tr>
</tbody>
</table>

$V_t$ indicates ventilation; $f$, respiratory frequency. Values given as mean ± SEM; significant difference ($P<0.05$).

*Standing vs supine.
†Leg tensing vs standing.
Leg tensing increased CVP without affecting the central blood volume, as indicated by an unchanged TI, which suggests a reduced central venous compliance. Whether or not the central blood volume was increased, apparently more blood was provided to the heart as CO increased. First, during standing, the increase in HR results from an enhanced sympathetic activity rather than from vagal withdrawal. Conversely, when leg tensing attenuates the increase in HR elicited by standing up, the reduction is likely to be by way of reduced sympathetic outflow. Furthermore, during standing, the integrated area of muscle sympathetic bursts and the spectral power of LF arterial pressure oscillations increase in proportion to the degree of orthostatic stress. We found an increased arterial pressure LF spectral power during standing but a reduction during leg tensing. 

The MCA $V_{mean}$ was chosen for evaluation of cerebral perfusion because it allows for a time resolution corresponding to 1 heartbeat, with the assumption that changes in MCA $V_{mean}$ are representative of changes in cerebral blood flow. During craniotomy, Giller et al found that the diameter of the large cerebral vessels did not change with large changes in arterial pressure, and a reduced cerebral perfusion pressure in the upright position renders an increase in cerebral vessel diameter unlikely. Orthostatic stress as simulated by lower body negative pressure does not alter the MCA diameter as determined with MRI, supporting the assumption that under the conditions of this study, the changes in MCA $V_{mean}$ represent changes in cerebral blood flow. The postural reduction in MCA $V_{mean}$ was attenuated for as long as leg tensing was maintained with no significant change in MAP, and an increase in cerebral blood flow was supported by an increase in cerebral oxygenation.

Postural stress, either by active standing or mimicked by lower body negative pressure, induces a reduction in cerebral blood flow velocity. Harms et al showed that postural stress reduces cerebral oxygenation and MCA $V_{mean}$ in both healthy subjects and patients with sympathetic failure, although the decline in these variables was more profound in the patients. There also is evidence for the notion that cerebral vasoconstriction in subjects with orthostatic intolerance is amplified by hypocapnia related to postural hyperventilation. The 15% orthostatic reduction in MCA $V_{mean}$ on standing is comparable to data from Bode and Levine et al and even larger than noted for elderly subjects with the NIRS-determined cerebral oxygenation following this pattern, indicating that the postural reduction in cerebral perfusion in the young is substantial.

$Paco_2$ is an important determinant for the cerebral perfusion. At the levels of hypocapnia and hypercapnia attained in this study, the MCA diameter remains stable and a reduction in $Paco_2$ is followed by a decline in cerebral blood flow and equally in MCA $V_{mean}$. The lower $Paco_2$ during standing has been ascribed to an increase in breathing rate and an improved ventilation-perfusion relationship, which in
values found were considerably larger than the normal standing and after 1 minute of leg tensing (Table 2). The cerebral oxygenation.14 Pa CO\textsubscript{2} and equally in P\textsubscript{ET} CO\textsubscript{2} by 19.5%/kPa or 2.6%/mm Hg.44 The observed increase in "Figure 2) could explain a 11% increase in MCA \textsubscript{V}\textsubscript{mean} was associated with a gradual rise in the P\textsubscript{et} CO\textsubscript{2} with a time course of 4 seconds to attain the maximal value (Figure 2). In contrast, the increase in MCA \textsubscript{V}\textsubscript{mean} by leg tensing was of immediate onset, whereas the contribution of Paco\textsubscript{2} would be expected to be manifest later. We examined an effect of an elevated CO\textsubscript{2} tension on MCA \textsubscript{V}\textsubscript{mean} at the later stages of tensing and analyzed the steady-state MCA \textsubscript{V}\textsubscript{mean}-Paco\textsubscript{2} relationship at standing and after 1 minute of leg tensing (Table 2). The values found were considerably larger than the normal cerebrovascular response to CO\textsubscript{2} reported in healthy subjects (≈19.5%/kPa or 2.6%/mm Hg).44 The observed increase in Paco\textsubscript{2} and equally in P\textsubscript{et}CO\textsubscript{2} by ≈0.3 kPa (Table 1 and Figure 2) could explain a ≈6% rise in MCA \textsubscript{V}\textsubscript{mean} and probably less when accounting for the smaller slope of the MCA \textsubscript{V}\textsubscript{mean}-Paco\textsubscript{2} relationship during orthostatic stress.44 It is therefore likely that the produced increase in Paco\textsubscript{2} is not the only factor for the increase in cerebral perfusion and oxygenation.

Besides an influence of Paco\textsubscript{2}, it is to be considered whether sympathetic activity influenced cerebral perfusion and oxygenation. In the sequence from supine rest to free standing, standing with the legs pressed against each other and again to free standing, the changes in MCA \textsubscript{V}\textsubscript{mean} and NIRS-determined cerebral oxygenation followed the indices of sympathetic activity in that they decreased as the indices of sympathetic activity increased. MCA \textsubscript{V}\textsubscript{mean} and sympathetic activity are also inversely related during exercise in that MCA \textsubscript{V}\textsubscript{mean} decreases when the ability to increase CO is limited by cardioselective β-blockade,45 and under those conditions, the reduction in MCA \textsubscript{V}\textsubscript{mean} is blunted by sympathetic blockade at the level of the neck.46

In conclusion, the orthostatic reduction in cerebral perfusion and oxygenation is attenuated by pressing the legs against each other, suggesting that leg tensing alleviates the symptoms sometimes associated with postural stress by stabilizing central circulatory variables at a reduced sympathetic activity.

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