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

Johannes J. van Lieshout, MD, PhD; Frank Pott, MD; Per Lav Madsen, MD; Jeroen van Goudoever, MSc, PhD; Niels H. Secher, MD, PhD

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±SEM) 4.3±2.6 mm Hg, stroke volume by 49±7 mL, cardiac output by 1.9±0.4 L/min, and mean arterial pressure at MCA level by 9±6 mm Hg, whereas it increased heart rate by 30±4 beats per minute ($P<0.05$). MCA $V_{\text{mean}}$ declined from 67±4 to 56±3 cm/s, O$_2$Hb decreased by 7±2.8%, and LF spectral power increased ($P<0.05$). Leg tensing increased central venous pressure by 1.4±2.7 mm Hg and cardiac output by 1.8±0.4 L/min with no significant effect on blood pressure, whereas heart rate decreased by 11±3 beats per minute ($P<0.05$). MCA $V_{\text{mean}}$ increased to 63±3 cm/s and O$_2$Hb increased by 2.1±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

Assumption of the upright position is associated with a reduction in venous return and cardiac output (CO), and blood pressure is maintained with a sympathetically mediated increase in vascular resistance. In the upright position, the cerebral arteries are positioned 30 cm above the heart, and their perfusion pressure is reduced. Both the position of the cerebral circulation and the reduction in CO challenge cerebral blood flow, and although the postural reduction in cerebral perfusion and oxygenation is kept limited via cerebral autoregulatory mechanisms, orthostatic intolerance is not uncommon in healthy subjects. Leg tensing may relieve orthostatic symptoms, and we considered that when leg tensing alleviates the dizziness developed during standing, this occurs through the modulation of brain perfusion.

In the present study, we addressed the hypothesis that in the upright position, leg tensing enhances cerebral perfusion and oxygenation. To evaluate rapid changes in cerebral perfusion, we studied the transcranial Doppler ultrasonographically determined middle cerebral artery (MCA) mean blood velocity ($V_{\text{mean}}$) and near-infrared spectroscopy (NIRS)-indicated cerebral oxygenation (O$_2$Hb). In addition, we determined central circulatory variables and an arterial pressure low-frequency (LF) domain evaluation of sympathetic activity.

Subjects and Methods

Subjects
After informed consent was obtained, 11 healthy subjects (4 women, median age 27 years, age range 21 to 38 years, median weight 76 kg, weight range 50 to 85 kg, median height 180 cm, height range 162 to 191 cm) participated in the study as approved by the Ethics Committee of Copenhagen (KF 01-120/96).
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 insonated (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 (Tensite; Parker Laboratories Inc) and secured with a headband. MCA $V_{\text{mean}}$ was the integral of the maximal frequency shifts over 1 heartbeat.

Cerebral oxygenation was recorded by NIRS, and changes in absorption of mainly oxyhemoglobin ($O_2Hb$) 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 $O_2Hb$ are given relative to supine rest.

Mean arterial pressure (MAP) was measured with a Finapres (model S; Netherlands Organization for Applied Scientific Research, Biomedical Instrumentation, TNO-BMI).16,17 The cuff was applied to the midpoint of the fingers of the dominant arm placed at heart level. Central venous pressure (CVP) was measured 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 position was confirmed by monitoring of the pressure waveform. CVP was recorded from a transducer (Bentley) referenced to the midaxillary line at 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 relationship 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 model based on 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 $V_{\text{mean}}$–PaCO$_2$ relationship was analyzed in 8 subjects in whom satisfying simultaneous recordings of PaCO$_2$ and MCA $V_{\text{mean}}$ were made. Sequences of consecutive MCA $V_{\text{mean}}$ values for $\sim$15 cardiac cycles at 5 minutes of standing and 1 minute of leg tensing were taken, and their averages were related to the corresponding PaCO$_2$ values. The steady-state CO reactivity was calculated from the change in MCA $V_{\text{mean}}$ and corresponding PaCO$_2$ 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.22,23 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 (PetCO$_2$ 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 syncopal symptoms during free standing with a 22% fall in $O_2Hb$ accompanied by a 25% reduction in MCA $V_{\text{mean}}$ 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 $\Omega$ after 1 minute and to 49.9±3.8 $\Omega$ after 5 minutes. After 1 minute of standing, HR had increased by 30±4 beats per minute, whereas SV was 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, PetCO$_2$ was 5.24±13 and 5.34±0.18 kPa, respectively ($P=0.145$). After the subjects stood up, ventilation increased (Table 1) and PaCO$_2$ 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 $O_2$SO$_2$ did not change, but the $\text{SvO}_2$ continued to decrease. After 8 seconds of standing, a reduction in MAP$_{\text{mean}}$ coincided with a fall in MCA $V_{\text{mean}}$ 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). $\text{MAP}_{\text{mean}}$ had decreased by 9±4 mm Hg, $V_{\text{mean}}$ 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 Hg$^2$/Hz.
Muscle Tensing

After 2 seconds, CVP increased by $1.4 \pm 0.2$ mm Hg, whereas TI did not change significantly. The MAP response was biphasic with a $7 \pm 4$ mm Hg increase after 2.5 seconds, a nadir at $-6 \pm 4$ 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 $1.8 \pm 0.4$ L/min, followed by a decline as HR decreased $11 \pm 4$ beats per minute. MCA $V_{\text{mean}}$ increased to $\sim 62$ cm/s during the first 70 seconds and to $\sim 59$ cm/s until muscle tensing was terminated (Figures 2 and 3). $O_2$Hb increased by $2.1 \pm 2.5\%$ after 2 minutes. The TI was maintained at $49.8 \pm 3.8$ V during tensing. With muscle tensing, $P_a CO_2$ increased to $4.90 \pm 0.13$ 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 $16.9 \pm 7.8$ to $9.8 \pm 5.7$ mm Hg$^2$/Hz ($P<0.01$) (Figure 4).

During the first 2 minutes after the cessation of muscle tensing, CVP, CO, MCA $V_{\text{mean}}$, $P_a CO_2$, 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 volume1 and a reduction in cerebral perfusion3–6 and oxygenation.7–9 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.

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**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>$V_e$, 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>

$V_e$ indicates ventilation; $f$, respiratory frequency. Values given as mean $\pm$ 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.

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 the case, although 3 indices suggested a reduced sympathetic activity during leg tensing.

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.

Finally, the leg-tensing maneuver resulted in a reduced systemic vascular resistance with an elevation in CVP. A similar effect was observed by Ray et al when they examined muscle sympathetic nerve activity during 1-legged exercise in the upright position. They demonstrated that in the first minute of exercise, CVP became elevated and sympathetic nerve activity decreased.

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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 \( \approx 15\% \) 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 NIRSt-determined cerebral oxygenation following this pattern, indicating that the postural reduction in cerebral perfusion in the young is substantial.

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Tensing of the legs did not influence ventilation or the respiratory frequency, although arterial and end-tidal CO₂ tension increased. Changes in MCA V_{mean} induced by hypercapnia reflect changes in 133Xe clearance–determined cerebral blood flow, supporting that the increase in MCA V_{mean} by muscle tensing reflects changes in blood flow in the MCA territory. It should therefore be considered that an increase in PaCO₂ induces cerebral vasodilatation with a rise not only in cerebral blood flow but also in MCA V_{mean}. Poulin et al. analyzed the steady-state MCA V_{mean} to changes in end-tidal CO₂ and found that the onset of the MCA V_{mean} response was delayed ~4 seconds with time constants of ~7 and ~4 seconds for the MCA V_{mean} responses to a step decrease or increase in CO₂, respectively. During leg tensing, the ~11% increase in MCA V_{mean} was associated with a gradual rise in the P_{a}CO₂ with a time course of 16 seconds to attain the maximal value (Figure 2). In contrast, the increase in MCA V_{mean} by leg tensing was of immediate onset, whereas the contribution of PaCO₂ would be expected to be manifest later. We examined an effect of an elevated CO₂ tension on MCA V_{mean} at the later stages of tensing and analyzed the steady-state MCA V_{mean}-P_{a}CO₂ relationship at standing and after 1 minute of leg tensing (Table 2). The values found were considerably larger than the normal cerebrovascular response to CO₂ reported in healthy subjects (~19.5%/kPa or 2.6%/mm Hg). The observed increase in PaCO₂ and equally in P_{a}CO₂ by ~0.3 kPa (Table 1 and Figure 2) could explain a ~6% rise in MCA V_{mean} and probably less when accounting for the smaller slope of the MCA V_{mean}-P_{a}CO₂ relationship during orthostatic stress. It is therefore likely that the produced increase in PaCO₂ is not the only factor for the increase in cerebral perfusion and oxygenation.

Besides an influence of PaCO₂, 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 V_{mean} and NIRS-determined cerebral oxygenation followed the indices of sympathetic activity in that they decreased as the indices of sympathetic activity increased. MCA V_{mean} and sympathetic activity are also inversely related during exercise in that MCA V_{mean} decreases when the ability to increase CO is limited by cardioselective β-blockade, and under those conditions, the reduction in MCA V_{mean} is blunted by sympathetic blockade at the level of the neck.

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.

Acknowledgments

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