Wave reflection augments central systolic and pulse pressures during facial cooling

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Submitted 27 November 2007; accepted in final form 10 April 2008

Edwards DG, Roy MS, Prasad RY. Wave reflection augments central systolic and pulse pressures during facial cooling. Am J Physiol Heart Circ Physiol 294: H2535–H2539, 2008.—Cardiovascular events are more common in the winter months, possibly because of hemodynamic alterations in response to cold exposure. The purpose of this study was to determine the effect of acute facial cooling on central aortic pressure, arterial stiffness, and wave reflection. Twelve healthy subjects (age 23 ± 3 yr; 6 men, 6 women) underwent supine measurements of carotid-femoral pulse wave velocity (PWV), brachial artery blood pressure, and central aortic pressure (via the synthesis of a central aortic pressure waveform by radial artery applanation tonometry and generalized transfer function) during a control trial (supine rest) and a facial cooling trial (0°C gel pack). Aortic augmentation index (AI), an index of wave reflection, was calculated from the aortic pressure waveform. Measurements were made at baseline, 2 min, and 7 min during each trial. Facial cooling increased (P < 0.05) peripheral and central diastolic and systolic pressures. Central systolic pressure increased more than peripheral systolic pressure (22 ± 3 vs. 15 ± 2 mmHg; P < 0.05), resulting in decreased pulse pressure amplification ratio. Facial cooling resulted in a robust increase in AI and a modest increase in PWV (AI: −1.4 ± 3.8 vs. 21.2 ± 3.0 and 19.9 ± 3.6%; PWV: 5.6 ± 0.2 vs. 6.5 ± 0.3 and 6.2 ± 0.2 m/s; P < 0.05). Change in mean arterial pressure but not PWV predicted the change in AI, suggesting that facial cooling may increase AI independent of aortic PWV. Facial cooling and the resulting peripheral vasoconstriction are associated with an increase in wave reflection and augmentation of central systolic pressure, potentially explaining ischemia and cardiovascular events in the cold.

artrial stiffness; augmentation index; blood pressure; cold

Epidemiologic studies have demonstrated that there is an increase in cardiovascular events and deaths in the winter months (10, 13, 26, 27, 39). Additionally, exposure to cold has been reported to make symptoms of angina more severe in those with cardiovascular disease (14, 21). Identifying the mechanisms by which cold exposure increases cardiovascular events and myocardial ischemia is important in understanding this phenomenon, potentially leading to countermeasures to minimize risk in those with cardiovascular disease.

It has been suggested that increased sympathetic activation and blood pressure in response to cold exposure may contribute to cardiovascular events in the cold (9, 27). Sympathetic activation could lead to an increase in peripheral arterial stiffness via vasoconstriction (4) and passively increase central elastic arterial stiffness via changes in arterial pressure (29). An increase in arterial stiffness can elevate central systolic pressure due to an inability to absorb pulsations from the heart and an increase in wave reflection from the periphery (30).

Central pressure is the pressure that the left ventricle must overcome, thus determining left ventricular workload (31, 44). Additionally, central systolic and pulse pressures are clinically important because they have been shown to be markers of disease (3, 33, 42) and predictors of cardiovascular outcomes (34, 35, 45).

We have demonstrated (11) that full-body cold exposure for 30 min at 4°C increased aortic augmentation index (AI), a measure of wave reflection, leading to augmented central systolic pressure, indicating that cold-induced increases in arterial stiffness and wave reflection may be an important underlying mechanism explaining the high prevalence of cardiovascular events in cold environments. Facial cooling results in sympathetic activation, vasoconstriction, and increased systolic and diastolic peripheral blood pressure (5, 18, 20) similar to whole body cooling in a cold environment. Facial cooling may be a more appropriate model to examine the effects of cold-induced sympathetic activation on vascular function given that individuals are typically properly clothed in cold weather and cold exposure is restricted to smaller body regions such as the face. Thus, studying the effects of facial cooling may be a better model for examining the effects of cold exposure. Additionally, assessment of aortic stiffness should be included in studies of cold exposure since an acute change in arterial stiffness is one mechanism by which cold may increase wave reflection; however, the contribution of acute changes in aortic stiffness to increased wave reflection during cold exposure has yet to be studied. The purpose of this study was to determine the effects of facial cooling on central blood pressure, wave reflection, and aortic stiffness. We hypothesized that facial cooling would result in increased central blood pressure, wave reflection, and aortic stiffness.

METHODS

Subjects. Twelve apparently healthy men (n = 6) and women (n = 6), as assessed by medical history questionnaire, participated in this study (age 23 ± 3 yr; mass 68 ± 9 kg; height 171 ± 9 cm; body mass index 23 ± 2 kg/m²). Subjects were nonsmokers, were asked to refrain from caffeine, alcohol, and exercise for at least 24 h before testing, and reported to the lab at least 4 h after eating. All procedures were reviewed and approved by the Institutional Review Board, and all subjects gave written informed consent.

Study design. Testing involved two visits to the lab, where subjects underwent two trials under either facial cooling or control conditions. The two trials consisted of measurement of either arterial stiffness (carotid-femoral pulse wave velocity, PWV) or central pressures and wave reflection (pulse wave analysis, PWA). Two trials were per-
formed because our lab only has two tonometers; therefore, assessment of carotid-femoral PWV and radial artery tonometry could not be performed simultaneously. The order of trials (PWV or PWA) and selection of conditions (facial cooling or control) were randomized, with the remaining condition performed during the second visit. Visits were performed within 5 days of each other at the same time of day. All testing in female subjects was completed within 5 days of the onset of their menstrual cycle.

Experimental protocol. Control trials involved supine rest, and facial cooling trials involved applying a cold gel pack (0°C) to the forehead with a damp paper towel forming a barrier between the gel pack and forehead. The gel pack was secured in place with an ACE bandage. Gel packs were kept in a thermostat-controlled standard freezer. Baseline measurements were performed after 15 min of supine rest. Measurements were repeated after 2 min of facial cooling/control and again 5 min later (7 min total), with the same procedures as baseline measurements. Two minutes was chosen for the first measurement because peak sympathetic nervous system activity has been observed at 90 s and peak systolic and diastolic pressure by 2 min of ice on forehead facial cooling (19). The measurement at 7 min was taken to evaluate the effects of prolonged facial cooling. After 4 min of facial cooling, the gel pack was replaced with a new gel pack for the remainder of the protocol to maintain the cold stimulus. Subjects rested for 20 min between trials to allow heart rate and blood pressure to return to baseline values.

Physiological measures. Baseline blood pressure was assessed in triplicate and averaged with oscillometric sphygmomanometry (Dash 2000, GE Medical Systems) and heart rate with three-lead ECG telemetry (Dash 2000, GE Medical Systems) after subjects were lying quietly in a supine position for 15 min. Carotid-femoral PWV was measured with the use of applanation tonometry to record both carotid artery and femoral artery waveforms simultaneously, by clamping high-fidelity strain gauge transducers (Millar Instruments, Houston, TX) in place over the right carotid and femoral arteries. These data were continuously collected during the facial cooling or control protocol (BIOPAC Systems, Goleta, CA). External distances were measured proximally from the carotid measurement site to the sternal notch and distally from the sternal notch to the femoral measurement site via the navel. Aortic distance was calculated by subtracting the carotid to sternal distance from the sternal to femoral distance. Carotid-femoral PWV was calculated by dividing the measured aortic distance by the average measured time delay between the initial upstrokes of 10 consecutive corresponding carotid and femoral waveforms. Carotid-femoral PWV is a regional measurement of aortic stiffness (40).

Applanation tonometry was used to record a radial arterial waveform by clamping a high-fidelity strain gauge transducer in place over the radial artery (Millar Instruments). Applanation tonometry has been shown previously to record a pressure wave that does not differ from waveforms obtained from intra-arterial measurements (23). The radial waveform was calibrated from the brachial high-fidelity strain gauge transducers (Millar Instruments, Houston, TX) in place over the right carotid and femoral arteries. These data were continuously collected during the facial cooling or control protocol (BIOPAC Systems, Goleta, CA). Aortic distance was calculated by subtracting the carotid to sternal distance from the sternal to femoral distance. Carotid-femoral PWV was calculated by dividing the measured aortic distance by the average measured time delay between the initial upstrokes of 10 consecutive corresponding carotid and femoral waveforms. Carotid-femoral PWV is a regional measurement of aortic stiffness (40). The waveform was synthesized from the measured radial artery pressure waveform with the SphygmoCor Px system (AtCor Medical, Sydney, Australia), which uses a transfer function and is FDA approved. The use of a transfer function to approximate the central pressure wave from the radial wave has been validated with both intra-arterially (7, 22, 32) and noninvasively (15) obtained radial pressure waveforms. Central systolic and pulse pressures derived with this system have also been shown to agree well with estimates using carotid recordings (1). We chose to record radial waves instead of carotid because they are easier to obtain. Central pressures, AI, and the time delay of the reflected wave (T\(_R\)) were obtained from the synthesized waveform. AI is defined as the ratio of reflected wave amplitude and pulse pressure, or AI = (P\(_R\) - P\(_D\))/(P\(_R\) - P\(_D\)), where P\(_R\) is peak systolic pressure, P\(_D\) is end-diastolic pressure, and P\(_D\) is an inflection point marking the beginning upstroke of the reflected pressure wave. T\(_R\) is the travel time of the forward wave from the heart to the major reflecting site and back. Additional calculations derived from the synthesized aortic pressure wave were the systolic pressure time index (STI), the diastolic pressure time index (DTI), and the subendocardial viability ratio (SEVR). STI, the area under the systolic portion of the curve, has been shown to be related to systolic load or the work of the heart and oxygen consumption, and DTI, the area under the diastolic portion of the curve, is associated with coronary perfusion (6). SEVR is the ratio of DTI to STI expressed as a percentage and an index of subendocardial perfusion (6).

Pulse pressure amplification ratio was calculated as brachial pulse pressure/central pulse pressure. Mean arterial pressure (MAP) was calculated over the cardiac cycle from the calibrated radial pressure waveform.

Statistical analysis. A 2 × 3 (condition × time) analysis of variance (ANOVA) with repeated measures was used to compare differences among trials. Bonferroni adjusted post hoc analyses were performed to determine differences within and between conditions. Pearson correlations were determined between change in AI and change in PWV, STI, and DTI. MAP did not change during control or facial cooling trials. MAP did not change during control trials but was increased (P < 0.05) above baseline at both 2 and 7 min of each facial cooling trial. Peripheral systolic and diastolic blood pressure did not change during control trials and were increased (P < 0.05) at 2 and 7 min of each facial cooling trial. Similarly, central aortic systolic and diastolic blood pressures did not change during control trials but increased (P < 0.05) during facial cooling. Facial cooling induced an average increase of 22 ± 3 mmHg in central aortic systolic pressure from baseline to 2 min, compared with only a 15 ± 2 mmHg increase in brachial systolic pressure (P < 0.05; Fig. 1). Brachial pulse pressure remained unchanged throughout both control and facial cooling trials, whereas central aortic pulse pressure did not change during control trials but increased (P < 0.05) above baseline at both 2 and 7 min of each facial cooling trial. Pulse pressure amplification ratio (brachial pulse pressure/central pulse pressure) was decreased (P < 0.05) below baseline at both 2 and 7 min of facial cooling but remained unchanged during control trials.

AI was increased at 2 and 7 min of facial cooling (P < 0.05; Table 1). There was an increase in carotid-femoral PWV and a decrease in T\(_R\) at 2 and 7 min of facial cooling (P < 0.05; Table 1). STI and DTI both increased at 2 and 7 min of facial cooling (P < 0.05; Fig. 2, A and B). Facial cooling did not elicit any changes in SEVR compared with baseline (Fig. 2C). There were no changes in AI, carotid-femoral PWV, STI, DTI, or SEVR during control trials.

Pearson correlations between change in AI and change in MAP, PWV, and T\(_R\) after 2 min of facial cooling revealed that only change in MAP was significantly correlated with change in AI (r = 0.796, R\(^2\) = 0.63, P = 0.002). Furthermore, multiple linear regression revealed that only change in MAP was a significant predictor of change in AI.
Table 1. Hemodynamic variables

<table>
<thead>
<tr>
<th></th>
<th>PWA Trial</th>
<th>PWV Trial</th>
<th>PWA Trial</th>
<th>PWV Trial</th>
<th>Facial Cooling</th>
<th>PWV Trial</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>2 min</td>
<td>7 min</td>
<td>Baseline</td>
<td>2 min</td>
<td>7 min</td>
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<tr>
<td>Heart rate, beats/min</td>
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<td>55±3</td>
<td>57±3</td>
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<tr>
<td>Peripheral SP, mmHg</td>
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<td>112±3</td>
<td>111±3</td>
<td>115±3</td>
<td>116±3</td>
<td>117±3</td>
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<tr>
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<td>Peripheral PP, mmHg</td>
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<td>Mean arterial pressure, mmHg</td>
<td>79±2</td>
<td>78±3</td>
<td>77±3</td>
<td>78±2</td>
<td>96±2*†</td>
<td>96±3*†</td>
</tr>
<tr>
<td>Central SP, mmHg</td>
<td>93±3</td>
<td>94±3</td>
<td>93±3</td>
<td>94±3</td>
<td>96±4*†</td>
<td>116±4*†</td>
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<tr>
<td>Central DP, mmHg</td>
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<td>63±2</td>
<td>63±3</td>
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<td>72±2*†</td>
<td>78±2*†</td>
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<td>Central PP, mmHg</td>
<td>28±2</td>
<td>31±2</td>
<td>30±2</td>
<td>28±2</td>
<td>39±2*†</td>
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<td>Carotid-femoral PWV, m/s</td>
<td>1.75±0.5</td>
<td>1.64±0.4</td>
<td>1.65±0.5</td>
<td>1.69±0.3</td>
<td>1.38±0.7*†</td>
<td>1.44±0.6*†</td>
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<td>Augmentation index, %</td>
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<td>0.3±3.8</td>
<td>-0.7±3.2</td>
<td>-1.4±3.8</td>
<td>21.2±3.0*†</td>
<td>19.9±3.6*†</td>
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<td>Ta, ms</td>
<td>156±5</td>
<td>155±7</td>
<td>151±2</td>
<td>163±7</td>
<td>143±3*†</td>
<td>148±6*†</td>
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<tr>
<td>Carotid-femoral PWV, m/s</td>
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<td>5.5±0.15</td>
<td>5.5±0.15</td>
<td>5.6±0.18</td>
<td>6.4±0.27*†</td>
<td>6.2±0.24*†</td>
</tr>
</tbody>
</table>

Values are means ± SE. SP, systolic pressure; DP, diastolic pressure; PP, pulse pressure; PWV, pulse wave velocity; PWA, pulse wave analysis; T_a, time delay of the reflected wave. Mean arterial pressure was obtained from the radial pressure wave. *P < 0.05 vs. baseline; †P < 0.05 vs. control; ‡P < 0.05 vs. 2 min.

Fig. 1. Change in systolic pressure induced by facial cooling. Values are means ± SE. *P < 0.05 vs. baseline.
increases wave reflection by altering the amplitude and timing of the reflected wave (29). An increase in wave reflection can result from alterations in the arterial system via changes in PWV (29). Interestingly, only the change in MAP was correlated with the change in AI following 2 min of facial cooling. This suggests that facial cooling may increase AI independent of aortic PWV and that increased smooth muscle tone in resistance vessels is potentially the primary determinant of increased wave reflection during facial cooling-induced sympathetic activation. In support of this, Kelly et al. (24) demonstrated that AI can change independently from aortic PWV during administration of nitroglycerin or angiotensin II, which have primarily peripheral effects. These authors observed relatively small changes in aortic PWV (<1 m/s) in the presence of large changes in AI during both angiotensin II and nitroglycerin administration (24). These findings are similar to the small change in PWV and the large change in AI observed in the present study. Acute increases in stiffness of elastic arteries, such as the aorta as observed in the present study, are thought to be passive (29). As MAP increases higher levels of wall stress are supported by stiffer collagen fibers, causing a stiffer arterial wall, as opposed to a more compliant arterial wall at lower pressures when elastin fibers predominate (9). Indeed, aortic stiffness is unaltered during sympathetic activation induced by lower body negative pressure when MAP does not change (37).

In addition to PWV, AI may depend on alterations in tone of small arteries and arterioles determining the amplitude and site of wave reflections (24). We could not calculate vascular resistance since we did not measure cardiac output; however, we did not observe any change in heart rate, and it was previously reported that facial cooling does not alter cardiac output (25, 36). Therefore, the rise in MAP would indicate that smooth muscle tone increased in resistance vessels as a result of facial cooling. Given the statistical relationship between MAP and AI in the present study, we speculate that the primary mechanism of increased wave reflection during facial cooling is alteration in the amplitude and site of wave reflections as a result of sympathetic activation. Previous observations of increased wave reflection during handgrip exercise (12) or CPT (17) may be due to the same mechanism.

We also examined systolic and diastolic time indexes (STI and DTI) as well as SEVR. STI and DTI were both increased during facial cooling, resulting in no change in SEVR. In the present study, normal coronary perfusion would be expected even during increased demand on the heart (STI), because of a parallel increase in perfusion pressure (DTI). It has been demonstrated that normal coronary arteries dilate in response to cold stimulus with CPT (28), aiding coronary blood supply in young healthy individuals. Atherosclerotic coronary arteries have been shown to constrict in response to cold-induced sympathetic outflow with CPT (28), potentially altering the balance between myocardial oxygen supply and demand. Constriction of the coronary arteries may reduce myocardial oxygen supply even under conditions of increased diastolic perfusion pressure, as observed in the present study, increasing the likelihood of myocardial ischemia.

It should be noted that our study involved direct application of cold to the forehead and therefore may not be the best representation of environmental exposure to cold. Others have investigated the effect of blowing cold air on the face and found that peripheral systolic and diastolic pressures increased to varying degrees depending on the temperature and wind speed used (8, 16, 38, 43); however, the pressure increases observed in the present study are within the range of observed values found in those studies. Future work could examine the effects of facial exposure to cold air and wind on arterial stiffness and wave reflection.

In summary, facial cooling resulted in a greater increase in central systolic pressure compared with peripheral systolic pressure. The greater change in central systolic pressure can be attributed to the observed increase in wave reflection. Thus facial cooling and the resulting augmentation in central systolic pressure might play a role in the occurrence of ischemia and
cardiovascular events in the cold. Future investigations should examine the effect of cold exposure on arterial stiffness, wave reflection, and myocardial oxygen demand in older or cardiovascular disease populations.

REFERENCES


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