Acute effects of cold exposure on central aortic wave reflection

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Edwards, David G., Amie L. Gauthier, Melissa A. Hayman, Jesse T. Lang, and Robert W. Kenefick. Acute effects of cold exposure on central aortic wave reflection. J Appl Physiol 100: 1210–1214, 2006. First published October 13, 2005; doi:10.1152/japplphysiol.01154.2005.—The purpose of this study was to determine the effects of acute cold exposure on the timing and amplitude of central aortic wave reflection and central pressure. We hypothesized that cold exposure would result in an early return of reflected pressure waves from the periphery and an increase in central aortic systolic pressure as a result of cold-induced vasoconstriction. Twelve apparently healthy men (age 27.8 ± 2.0 yr) were studied at random, in either temperate (24°C) or cold (4°C) conditions. Measurements of brachial artery blood pressure and the synthesis of a central aortic pressure waveform (by noninvasive radial artery applanation tonometry and use of a generalized transfer) were conducted at baseline and after 30 min in each condition. Central aortic augmentation index (AI), an index of wave reflection, was calculated from the aortic pressure waveform. Cold induced an increase (P < 0.05) in AI from 3.4 ± 1.9 to 19.4 ± 1.8%. Cold increased (P < 0.05) both brachial and central systolic pressure; however, the magnitude of change in central systolic pressure was greater (P < 0.05) than brachial (13 vs. 2.5%). These results demonstrate that cold exposure and the resulting peripheral vasoconstriction increase wave reflection and central systolic pressure. Additionally, alterations in central pressure during cold exposure were not evident from measures of brachial blood pressure.

arterial stiffness; blood pressure

SYMPTOMS OF ANGINA have been reported to become more severe when patients with cardiovascular disease are exposed to a cold environment (8, 13). Additionally, there is epidemiological evidence that seasonal variation exists in the incidence of cardiac events and deaths, with an increase in winter months (6, 7, 20, 21, 34). Identifying mechanisms by which cold exposure increases the reported incidences of myocardial ischemia may be helpful in explaining this phenomena and assessing possible risk for individuals with cardiovascular disease.

The body’s compensatory responses to cold exposure are aimed at heat conservation for survival. Cold exposure is accompanied by sympathetic activation and cold-induced vasoconstriction (CIVC). CIVC lowers the temperature gradient between the skin and environment, decreasing heat loss and helping to maintain core temperature. While serving to maintain core temperature, CIVC may also lead to an increase in the stiffness of the arterial system. Arterial stiffness is known to increase systolic blood pressure as a result of an inability to absorb pulsations from the heart and an increase in wave reflection from the periphery increasing myocardial oxygen demand (24). Pressure waves generated by the heart are buffered by the aorta and large elastic arteries. As pressure waves travel through the arterial system they encounter bifurcations and the arteriole beds, which reflect these waves back to the heart. If the reflected wave arrives early in systole it will add to the pressure generated by the heart and increase systolic and pulse pressures. Because larger elastic arteries buffer pulsations from the heart, muscular arteries can alter the speed of travel of pressure waves along their length and determine when reflected waves return back at the heart, and arterioles serve as major reflecting sites (23, 29), alterations in the stiffness of the arterial system resulting from CIVC may have dramatic effects on the central pressure wave.

The speed and amplitude of reflected waves affect peak central systolic pressure but not peripheral pressure (35). Thus measures of brachial cuff blood pressure will not reveal these effects. Central pressure, the pressure that the left ventricle must overcome, influences wall tension and is a better indicator of myocardial oxygen demand. Therefore, the effect of cold exposure on blood pressure (and myocardial oxygen demand) may be greater than previously thought. The purpose of this study was to determine the effects of acute cold exposure on the timing and amplitude of central aortic wave reflection and central pressure. We hypothesized that cold exposure would result in an early return of reflected pressure waves from the periphery and an increase in central aortic systolic pressure as a result of CIVC.

METHODS

Subjects. Twelve apparently healthy men, as assessed by medical history questionnaire, participated in this study (age 27.8 ± 2.0 yr; weight 81.5 ± 2.3 kg; height 175.4 ± 1.8 cm). All subjects were nonsmokers and refrained from caffeine and ethanol for at least 12 h before testing. All procedures were reviewed and approved by the Institutional Review Board, and all subjects gave written informed consent.

Study design. Testing involved 30 min of rest in two treatment conditions consisting of cold exposure (4°C and wind speed of 6.1 m/s) and temperate exposure (24°C). The environmental treatment protocols were randomly assigned and separated by at least 7 days.

Experimental protocol. A urine specific gravity (USG) of <1.019 (3) was used to verify adequate hydration before each trial. After a seated 20-min equilibration period at 24°C baseline measurements were made. Subjects then entered the environmental chamber and rested in a seated position for 30 min in either the temperate or cold condition.

Physiological measures. During the experimental trials, core (rectal) and mean weighted skin (27) temperatures and oxygen uptake (V˙O2, V˙max 229 metabolic cart, SensorMedics, Yorba Linda, CA) were monitored every 10 min. Brachial blood pressure was assessed by sphygmomanometry in triplicate and averaged at baseline and 30 min.

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EFFECTS OF COLD EXPOSURE ON WAVE REFLECTION

wave reflection and a manifestation of overall systemic arterial stiffness. AI is defined as the ratio of reflected wave amplitude and pulse pressure, or $AI = (P_s - P_i)/(P_s - P_d)$, where $P_s$ is peak systolic pressure, $P_d$ is end-diastolic pressure, and $P_i$ is an inflection point marking the beginning upstroke of the reflected pressure wave. The $\Delta t$ is a measure of the time it takes for the reflected wave to travel to the periphery and back to the heart and is defined as the time delay from the foot of the pressure wave and the inflection point on the central waveform. A stiffer arterial system results in faster wave travel and quicker return of the reflected wave and thus a lower $\Delta t$.

Statistical analyses. A $2 \times 2$ (condition $\times$ time) analysis of variance with repeated measures was used to compare differences among the trials. A Newman-Keuls post hoc analysis was used to determine significant differences within and between conditions. Paired $t$-tests were used to compare $V_{O_2}$ and skin and core temperatures between conditions. An $\alpha$-level of $P < 0.05$ was required for significance, and all data are presented as means $\pm$ SE.

RESULTS

All subjects completed each experimental trial. There were no differences in baseline measurements between conditions. Additionally, subjects were in a well-hydrated state at baseline for both the cold (USG: 1.010 $\pm$ 0.002) and temperate (USG: 1.009 $\pm$ 0.002) conditions.

Thermoregulatory responses. The thermoregulatory responses to cold and temperate exposure are shown in Table 1. During the 30-min rest period, $V_{O_2}$ was elevated ($P < 0.05$) in the cold condition compared with the temperate condition. Mean weighted skin temperature was lower ($P < 0.05$) in the cold vs. the temperate condition, and core temperature in the cold condition was higher ($P < 0.05$) than the temperate condition.

Hemodynamic responses. Heart rate and blood pressure responses are shown in Table 2. After 30 min of exposure, brachial systolic pressure was higher in the cold compared with the temperate condition ($P < 0.05$). Cold exposure resulted in an increase ($P < 0.05$) in central systolic pressure, and this increase was different from both baseline and 30-min central systolic pressure in the temperate condition ($P < 0.05$). Cold induced an average increase of 13% in central systolic pressure compared with only 2.5% in peripheral systolic pressure ($P < 0.05$, Fig. 2). Consistent with the change in central systolic pressure, central pulse pressure also increased in response to cold exposure ($P < 0.05$) and was greater than both baseline and 30-min central pulse pressure in the temperate condition ($P < 0.05$).

AI significantly increased after 30 min of exposure to the cold (3.4 $\pm$ 3.3 vs. 19.4 $\pm$ 4.4%, $P < 0.05$, Fig. 3). This response was also significantly different compared with the temperate condition (Fig. 2). There was a significant decrease in the $\Delta t$ from baseline to rest in both the cold and temperate conditions ($P < 0.05$); however, $\Delta t$ was lower in the cold condition at 30 min compared with the temperate condition ($P < 0.05$).

Table 1. Physiological variables

<table>
<thead>
<tr>
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<th>Temperate</th>
<th>Cold</th>
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<tr>
<td>$V_{O_2}$ ml kg$^{-1}$ min$^{-1}$</td>
<td>3.3 $\pm$ 0.2</td>
<td>6.0 $\pm$ 0.4*</td>
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<tr>
<td>Mean skin temperature, $^\circ$C</td>
<td>31.4 $\pm$ 0.2</td>
<td>18.8 $\pm$ 0.5*</td>
</tr>
<tr>
<td>Core temperature, $^\circ$C</td>
<td>36.6 $\pm$ 0.2</td>
<td>37.3 $\pm$ 0.1*</td>
</tr>
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</table>

Values are means $\pm$ SE. $V_{O_2}$, oxygen uptake. *$P < 0.05$ vs. temperate.
due to shivering and nonshivering thermogenesis in response to
crease in core temperature. An increase in core temperature
shivering response was, in part, responsible for a 0.7°C in-
significantly elevated after 30 min of cold exposure. Addition-
reflection and indicator of systemic arterial stiffness, was
The major findings demonstrate that AI, a measure of wave
reflection and central blood pressure.

Fig. 2. Percent change in systolic pressure induced by cold. Values are
means ± SE. *P < 0.05 vs. peripheral.

DISCUSSION
The purpose of this study was to examine the effect of acute
cold exposure on wave reflection and central blood pressure.

whole body cooling has been reported by others (36). These
data confirm a cold response to the 4°C climate.

Fig. 3. Augmentation index and time to wave reflection at baseline and after
30 min in the temperate and cold conditions. Values are means ± SE. *P <
0.05 vs. baseline; †P < 0.05 vs. baseline temperate; ‡P < 0.05 vs. 30-min temperate.

Hemodynamic responses. Wave reflection, as assessed by
AI, was increased in the cold condition and was responsible for
the greater change in central systolic pressure compared with
peripheral systolic pressure. Additionally, central pulse pressure
was significantly greater after 30 min of cold exposure as a
result of the increase in wave reflection and central systolic
pressure. Geleris and colleagues (11) have also reported a
significant increase in AI after cold exposure; however, these
authors used the cold pressor test (CPT). The CPT is a method
of experimentally inducing pain (22) rather than a true cold
response. The whole body cooling in the current study may be
more physiologically relevant.

The observed increase in AI is a manifestation of an increase
in the stiffness of the arterial system during cold exposure.
Because an increase in wave reflection affects central, but not
peripheral, systolic pressure, the effect of cold exposure was
not readily apparent from measurement of brachial cuff pressure.
Under conditions of acute increase in arterial stiffness, as in
the present study, peripheral systolic pressure changes very
little. Due to this small change in systolic pressure, the effects
of an increase in central pressure will not be reflected in
estimates of myocardial oxygen demand (heart rate × periph-
eral systolic blood pressure).

CIVC is the likely mechanism by which cold exposure
increases the stiffness of the arterial system and subsequently
wave reflection and central systolic pressure. Δt was signifi-
cantly lower in the cold condition, indicating that the reflected
pressure wave returned earlier from the periphery. CIVC likely
leads to a decrease in diameter of muscular arteries and arterioles,
speeding pressure wave travel and potentially altering the site of wave reflection. However, dysfunction of the
endothelial nitric oxide pathway may also play a role in the
increase in AI. Carnio and Branco (4) observed that the
increased pressure in response to acute cold exposure in rats is

Table 2. Hemodynamic variables

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<thead>
<tr>
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<th>Temperate</th>
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<tr>
<td></td>
<td>Baseline</td>
<td>30 min</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>72 ± 3</td>
<td>73 ± 3</td>
</tr>
<tr>
<td>Peripheral SP, mmHg</td>
<td>132 ± 4</td>
<td>129 ± 3</td>
</tr>
<tr>
<td>Peripheral DP, mmHg</td>
<td>85 ± 2</td>
<td>85 ± 2</td>
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<tr>
<td>Peripherial PP, mmHg</td>
<td>47 ± 2</td>
<td>44 ± 2</td>
</tr>
<tr>
<td>Central SP, mmHg</td>
<td>112 ± 2</td>
<td>114 ± 3</td>
</tr>
<tr>
<td>Central DP, mmHg</td>
<td>86 ± 2</td>
<td>86 ± 2</td>
</tr>
<tr>
<td>Central PP, mmHg</td>
<td>26 ± 2</td>
<td>27 ± 2</td>
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</table>

Values are means ± SE. SP, systolic pressure; DP, diastolic pressure; PP, pulse pressure; MAP, mean arterial pressure. *P < 0.05 baseline cold; †P <
0.05 vs. baseline temperate; ‡P < 0.05 vs. 30-min temperate.

Fig. 2. Percent change in systolic pressure induced by cold. Values are
means ± SE. *P < 0.05 vs. peripheral.
ischemia in persons with cardiovascular disease. The increase in arterial stiffness may shorten time to CAD (19). When considering the results of Kingwell et al. with bandaging (37) or stiff plastic tube bypass (15, 28) to increase central systolic pressures increased with cold exposure; however, the magnitude of the cold-induced change in central systolic pressure was greater than the change in brachial systolic pressure. This is attributable to cold-induced increases in wave reflection and stiffness of the arterial system and suggests that the magnitude of the hemodynamic response to cold exposure cannot be determined with traditional brachial cuff measurements. Cold exposure may increase myocardial oxygen demand through an increase in central systolic pressure secondary to increased arterial stiffness and wave reflection. The present study provides new insight into the cardiovascular and hemodynamic responses to environmental stress. Future research should be aimed at examining the effect of cold exposure on wave reflection and central pressure in an aging and/or CAD populations, to determine clinical significance.

REFERENCES