Responses to mild cold stress are predicted by different individual characteristics in young and older subjects

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DeGroot, David W., George Havenith, and W. Larry Kenney. Responses to mild cold stress are predicted by different individual characteristics in young and older subjects. J Appl Physiol 101: 1607–1615, 2006.—Older individuals’ ability to maintain core temperature during cold stress is impaired; however, the relative importance of individual characteristics that influence this response are unknown. The purpose of this study was to determine the relative influence of individual characteristics on core temperature and tissue insulation (Iₜ) during mild cold stress. Forty-two young (23 ± 1 yr, range 18–30 yr) and 46 older (71 ± 1 yr, range 65–89 yr) subjects, varying widely in muscularity, adiposity, and body size, underwent a transient cooling protocol during mild cold stress (11, 17, 25). However, one difficulty in interpreting these studies is the confounding influence of body size and composition differences within an age cohort and between age cohorts. Most previous research concerning the thermoregulatory responses due to body composition differences have used the approach of testing two distinct subject populations, matched for all but one relevant individual characteristic, such as muscle mass (20, 38). While this experimental design is useful, it is also flawed in that subjects may also differ in other characteristics, such as surface area (A₉)-to-mass ratio (A₉/mass), that may be relevant for cold stress responses (37). Efforts to match young and older subject groups for body composition fail to incorporate changes intrinsic to the aging process (22). An alternative approach is the use of multiple-regression analysis, in which a large, heterogeneous subject population that varies in several anthropometric parameters is tested and the relative contribution of individual and combined predictors of Tₑ are determined (21–24).

Previous studies have shown that Tₑ may be maintained, decreased, or even slightly increased in response to cold stress (11, 37, 40). Young subjects tend to adequately defend Tₑ during mild (11) but not more severe (37) cold stress. We recently reported that older subjects fail to adequately defend Tₑ during mild cold stress, while young subjects’ Tₑ actually increased slightly (11). The increase in Tₑ in the absence of shivering during cold stress is likely due to peripheral vasoconstriction and redistribution of body heat to the core. Interindividual variability in the Tₑ response is likely due to body composition characteristics (38, 40), as well as age.

During resting cold stress, there are several plausible variables that may contribute to the Tₑ response. For example, muscle mass accounts for a large portion of tissue insulation (Iₜ) (13) and, therefore, contribute to the defense of Tₑ (20, 38). The term “sarcopenia” is applied to those individuals whose muscle mass, often quantified as appendicular skeletal muscle mass (ASMM), is >2 SD below a reference population mean, and the prevalence of sarcopenia increases with age (3). The development of sarcopenia with advancing age may predispose an individual to a cold-induced Tₑ drop due to reduced Iₜ (28), although supporting data are lacking. Similarly, the relation between adiposity and thermoregulation is well known, as individuals with greater subcutaneous fat have a higher Tₑ (2) and lower metabolic (7) response to cold stress than individuals with relatively less subcutaneous fat, although others have suggested that leaner individuals may compensate with a greater metabolic rate to maintain Tₑ (19). Due to the redistribution of body fat with aging (33, 43), whether percent fat or subcutaneous adiposity explains a greater portion of the Tₑ or Iₜ variance in older subjects is unknown. While a few studies have noted sex differences in response to cold stress (40), these are likely due to sex-related body composition differences (7, 30, 37). Finally, the thyroid hormones triodo-
thyroxine (T₃) and thyroxine (T₄) may also influence the cold stress response through their effects on metabolic rate (34). Mean thyroid hormone concentrations tend to be similar in young and older subjects, although hypothyroidism prevalence increases with aging (5, 31). When considering the literature regarding cold stress, it is important to note that cold air and cold water impose different physiological stresses, but limited literature in this area precludes limiting the discussion to only cold air exposure studies.

In addition to the normal interindividual variations in muscle mass and adiposity within an age cohort, there are well-known longitudinal changes in muscle and fat mass that occur with aging. The prevalence of obesity increases with aging (9), and an increase in adiposity may provide a protective effect that offsets a decrease in muscle mass. Limited longitudinal data suggest that individuals lose muscle mass and gain fat mass at similar rates so that body weight remains stable over time (18). The relative importance of these changes on the response to cold stress is unknown.

The purpose of the present investigation was to determine the individual characteristics that influence the response to cold stress, as assessed by esophageal temperature (Tₑₓₐₑ), in heterogeneous young and older subject groups and to determine the relative contributions of the predictors to the response. The individual predictors considered included sex, age in years, weight, ASMM, Aᵩ/mass, sum of skinfolds, percent fat, and serum [T₃] and [T₄] (where brackets denote concentration). Because Tₑₓₑ is one of the variables used to calculate Iₑ, it may be inappropriate to analyze the contribution of the latter on the former. Therefore, an additional purpose was to separately determine the individual characteristics that influence Iₑ and determine the relative contributions of these characteristics. We hypothesized that the individual predictors of Tₑₓₑ and Iₑ would differ between age groups, as would the relative contributions of predictors to the explained variance.

METHODS

Subjects

Forty-two young (18–30 yr; 21 men, 21 women) and 46 older (65–89 yr; 24 men, 22 women) subjects participated in the study after verbal and written, informed consent were obtained. The protocol was approved in advance by The Pennsylvania State University Institutional Review Board. All subjects were normotensive, nonsmokers, and not taking any medications that might alter the cardiovascular or thermoregulatory responses to cooling. Young women were eumenorrheic, not taking oral contraceptives, and were tested during days 2–10 of the menstrual cycle. All older women were postmenopausal and not taking hormone replacement therapy. All subjects abstained from alcohol and caffeine for 12 h before reporting to the laboratory on the day of the experiment.

Preliminary Testing

Subjects underwent a standardized medical screening, including a resting electrocardiogram, blood chemistry analysis (CHEM-24, complete blood count, and thyroid hormone analysis, Quest Diagnostics), and a physical exam. Body composition (%fat) was determined via dual-energy X-ray absorptiometry (DXA; model QDR 4500W, Hologic, Waltham, MA). ASMM was taken as the sum of the arm and leg lean masses determined via DXA and expressed relative to height in meters squared (kg/m²), as proposed by Baumgartner et al. (3), to eliminate differences in muscle mass due to height differences. Skinfold thickness was measured at the chest, midaxillary, tricep, subscapular, abdominal, suprailiac, and mid thigh sites by the same investigator as an estimate of subcutaneous adiposity. Body Aₒ was estimated according to Dubois and Dubois (12), and the Aₒ/mass was calculated.

Experimental Protocol

Subjects arrived at the laboratory between 0800 and 0900, and a copper-constantin thermocouple sealed in a pediatric feeding tube was inserted through the naris a distance equal to one-fourth of the subject’s standing height for measurement of Tₑₓₑ (41). The subject then entered the environmental chamber [dry-bulb temperature (Tₘᵢₜ) = 26.5°C] and was positioned in a semirecumbent position, dressed only in shorts (men) or shorts and a sports bra (women). Baseline Tₘᵢₜ was maintained for 20 min; Tₘᵢₜ was then decreased at a rate of 0.2°C/min for 20 min and 0.05°C/min thereafter. The protocol was terminated when visible, sustained shivering was observed by the investigators and/or reported by the subject. Temperature data were recorded and stored as 1-min averages using computer software (LabView) and a data-acquisition system (National Instruments, Austin, TX). F (°C·m²·W⁻¹) was calculated as (Tₑₓₑ – Tₘᵢₜ)/(MLX – S), where Tₑₓₑ is mean weighted skin temperature (°C), MLX (W/m²) is metabolic rate corrected for respiratory heat losses, and S (W/m²) is heat storage, which is typically negative during cold exposure.

Statistics

Data were analyzed using Student’s t-test for subject characteristics. Considering that the time to shivering varied greatly for each age group, Tₑₓₑ and Iₑ at 60 min were used as the response variables. This approach standardized the exposure time and conditions, avoiding the difficulty of varying time and environmental conditions had data just before shivering onset been used, and is consistent with the methodology of previous thermoregulation studies using the multiple-regression technique described below (21–24). To determine the relative influence of subject characteristics, multiple-regression analysis was performed (Minitab statistical software, version 14, State College, PA) in an interactive manner (21–24). All regression analyses were conducted separately for each age group. The first step was to determine which individual predictors correlated with Tₑₓₑ or Iₑ at 60 min. The following individual predictors were considered: sex, age in years, weight, ASMM, Aₒ, Aₒ/mass, sum of skinfolds, percent fat, and serum [T₃] and [T₄]. The predictor with the highest Pearson correlation coefficient was introduced into the regression equation first, and the residual variance was calculated and saved. Next, the remaining predictors were correlated with the residual variance of the regression equation, and the predictor with the highest Pearson correlation coefficient was regressed against the residual variance. This process was repeated until no significant predictors remained. In effect, a forward stepwise regression analysis was conducted manually, which gave the authors control over the entry of a given predictor into the equation, based on statistical and physiological relevance and independence from other predictors. This process lead to one regression equation for each age group, but there was more than one combination of predictors, resulting in similar explanatory power, and these alternatives were explored. Normal probability plots and residual vs. fitted value plots were obtained for each regression equation to assess normality of the data, and a variance inflation factor (VIF) statistic was calculated to test for colinearity among the predictors. If VIF was >4.0, colinearity among predictors was suspected (16). To further compare predictor variables between age groups, a cross-validation of the predictors was performed. In this cross-validation, a combination of significant predictors for one age group was applied to the other group, regardless of whether the Pearson correlation coefficients were significant or not.

Once the regression models were obtained, standardized regression coefficients were calculated. This enabled the comparison of the
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young (n = 42)</th>
<th>Older (n = 46)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>23 ± 1 (18–30)</td>
<td>71 ± 1 (65–89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.73 ± 0.02 (1.55–1.99)</td>
<td>1.69 ± 0.01 (1.56–1.89)</td>
<td>0.13</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>68.1 ± 1.9 (48–104)</td>
<td>69.2 ± 1.8 (46–99)</td>
<td>0.68</td>
</tr>
<tr>
<td>ASMM, m²</td>
<td>1.80 ± 0.03 (1.48–2.34)</td>
<td>1.79 ± 0.03 (1.43–2.22)</td>
<td>0.76</td>
</tr>
<tr>
<td>ASMM/m²</td>
<td>2.68 ± 0.03 (2.24–3.06)</td>
<td>2.62 ± 0.03 (2.24–3.13)</td>
<td>0.23</td>
</tr>
<tr>
<td>Fat, %</td>
<td>23.0 ± 1.3 (9.5–37.7)</td>
<td>26.9 ± 1.0 (13.8–43.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Skinfolds, mm</td>
<td>124 ± 7 (42–209)</td>
<td>124 ± 4 (69–199)</td>
<td>0.99</td>
</tr>
<tr>
<td>T₃, ng/dl</td>
<td>7.19 ± 0.21 (5.00–9.48)</td>
<td>6.90 ± 0.17 (5.05–9.36)</td>
<td>0.68</td>
</tr>
<tr>
<td>T₄, μg/dl</td>
<td>121 ± 6 (74–166)</td>
<td>112 ± 3 (83–149)</td>
<td>0.10</td>
</tr>
<tr>
<td>T₄, μg/dl</td>
<td>6.9 ± 0.3 (4.7–10.3)</td>
<td>6.5 ± 0.3 (2.3–13.7)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Values are means ± SE (range in parentheses); N, no. of subjects. ASMM, appendicular skeletal muscle mass; T₃, triiodothyronine; T₄, thyroxine.

relative contribution of individual predictors to the $r^2$ while controlling for the units of measurement and range of values for each predictor. The value of the standardized regression coefficient represents the change of the response variable expressed in units of its SD when the predictor variable changes by 1 SD. The relative contribution of each predictor to the variance explained was calculated as follows: (standardized regression coefficient for predictor/∑ all standardized regression coefficients in equation)×$r^2$. Absolute values were used, as standardized regression coefficients can be positive or negative. Adjusted $r^2$ values are given, i.e., $r^2$ corrected for the number of observations and the number of predictors in the analysis. Comparison of the magnitude of the residual (unexplained) variance between groups was conducted using the $\chi^2$ test.

RESULTS

Subject characteristics are presented in Table 1. Adiposity ranged from 10–44% fat, which includes the 10th–90th percentile of published normative values for both age groups (1). Seven young and 14 older subjects met the commonly accepted criteria for sarcopenia. There was a similarly large range for the calculated variables $A_d$ and $A_d$/mass. $T_3$ and $T_4$ were within the age- and sex-specific normal range for all subjects. There were no differences in baseline values for $T_{es}$ or $I_1$ ($T_{es}$: 37.05 ± 0.04 vs. 36.95 ± 0.04°C; $I_1$: 0.065 ± 0.002 vs. 0.065 ± 0.002 for young and older subjects, respectively; $P > 0.05$ for both comparisons), and skewness and kurtosis scores indicated that the data were normally distributed; therefore, correction for baseline differences by analyzing the change in $T_{es}$ or $I_1$ was not considered necessary. Additionally, using the absolute values of the response variables was consistent with previous studies using similar multiple-regression analysis designs (21–24). The $T_{db}$ at 60 min was virtually identical between groups (21.96 ± 0.09 vs. 21.99 ± 0.08°C for young and older subjects, respectively; $P = 0.77$); therefore, the cold stress was similar for both groups. The young subjects slightly increased $T_{es}$, while older subjects failed to maintain $T_{es}$ (Fig. 1 (11)). For the developed regression equations, there was no linearity among predictors, based on the VIF statistic.

The physiological responses of these subjects have been previously reported (11). Briefly, there were no differences for mean weighted skin temperature, calculated heat debt, or heat storage, while there was an attenuated cutaneous vasoconstrictor response in the older subjects [53 ± 4 vs. 42 ± 3 $ΔCVC_{base}$, i.e., cutaneous vascular conductance (CVD), determined via laser-Doppler flowmetry, expressed as percent change from baseline, $P < 0.01$]. Metabolic rate was lower (37.6 ± 0.9 vs. 41.0 ± 1.2 W/m², $P < 0.05$) and mean arterial pressure was higher (96.0 ± 1.2 vs. 86.9 ± 1.6 mmHg, $P < 0.01$) in older vs. young subjects. The correlation matrices for all of the possible predictors and the independent variables are shown in Table 2, top (young subjects) and bottom (older subjects). Table 3 contains the standardized regression coefficients for all of the subsequent equations, with the equation numbers given in the text corresponding to the equation numbers in Table 3.

$T_{es}$

Young subjects. Based on the high observed correlation coefficient with $T_{es}$, the sum of skinfolds was entered into the regression equation first. Correlation with the residual variance of this regression equation indicated that $T_3$ should be entered next. Once sum of skinfolds and $T_3$ were entered into the regression equation, no other individual characteristic was correlated with the residual variance. Considering that percent fat was also highly correlated with $T_{es}$, a second regression equation was developed, starting with this predictor. $T_3$ was again the second predictor, with no additional predictors correlated with the residual variance. Figure 2 presents the proportion of the variance explained by each term of Eq. 1 (A) and of Eq. 2 (B). Sum of skinfolds, percent fat, and $T_3$ were each positively associated with $T_{es}$. A greater proportion of the variance could be accounted for in Eq. 1 than Eq. 2, due to greater relative influence of sum of skinfolds than percent fat.
Table 2. Correlation matrices for young and older subjects

<table>
<thead>
<tr>
<th></th>
<th>T&lt;sub&gt;e&lt;/sub&gt;</th>
<th>I&lt;sub&gt;t&lt;/sub&gt;</th>
<th>Years</th>
<th>Weight</th>
<th>ASMM</th>
<th>A&lt;sub&gt;d&lt;/sub&gt;</th>
<th>Skinfolds</th>
<th>%Fat</th>
<th>[T&lt;sub&gt;3&lt;/sub&gt;]</th>
<th>[T&lt;sub&gt;4&lt;/sub&gt;]</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>0.43†</td>
<td>1.00</td>
<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td>0.09</td>
<td>−0.11</td>
<td>0.30</td>
<td>1.00</td>
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<tr>
<td></td>
<td>−0.32*</td>
<td>−0.49†</td>
<td>0.16</td>
<td>0.75†</td>
<td>1.00</td>
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<td></td>
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<tr>
<td></td>
<td>0.03</td>
<td>−0.13</td>
<td>0.27</td>
<td>0.96†</td>
<td>0.71†</td>
<td>1.00</td>
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<tr>
<td></td>
<td>−0.18</td>
<td>0.07</td>
<td>0.12</td>
<td>−0.90†</td>
<td>−0.71†</td>
<td>−0.77†</td>
<td>1.00</td>
<td></td>
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<tr>
<td></td>
<td>0.75†</td>
<td>0.43†</td>
<td>0.14</td>
<td>0.16</td>
<td>−0.30</td>
<td>−0.01</td>
<td>−0.39†</td>
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<td></td>
<td>0.65†</td>
<td>0.57†</td>
<td>−0.02</td>
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<td>−0.62†</td>
<td>−0.34*</td>
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<td></td>
<td>[T&lt;sub&gt;3&lt;/sub&gt;]</td>
<td>0.50†</td>
<td>0.03</td>
<td>0.33*</td>
<td>0.16</td>
<td>0.04</td>
<td>0.12</td>
<td>−0.20</td>
<td>0.33*</td>
<td>0.13</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>[T&lt;sub&gt;4&lt;/sub&gt;]</td>
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<td>0.28</td>
<td>−0.34*</td>
<td>−0.33*</td>
<td>−0.34*</td>
<td>0.24</td>
<td>0.29</td>
<td>0.26</td>
<td>0.65†</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
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<td>0.56†</td>
<td>−0.25</td>
<td>−0.65†</td>
<td>−0.85†</td>
<td>−0.69†</td>
<td>0.54†</td>
<td>0.34*</td>
<td>0.68†</td>
<td>−0.21</td>
</tr>
</tbody>
</table>

Older subjects. Percent fat, ASMM, and sex were all similarly correlated with T<sub>e</sub>; therefore, three regression equations were developed, starting with each of these predictors. After percent fat was included in the equation, A<sub>d</sub>/mass was correlated with the residual variance. After an equation was started with either ASMM or sex, no remaining predictor was correlated with the residual variance. Figure 2, C–E, shows the explained variance for the resulting equations. The residual variance was larger than in the young subjects (χ<sup>2</sup> = 5.78, P < 0.05), and ASMM was negatively associated with T<sub>e</sub>.

I<sub>t</sub>

ASMM, sum of skinfolds, percent fat, and age were the only predictors considered, as a theoretical basis relating other body composition characteristics to I<sub>t</sub> is lacking.

Young subjects. Based on the correlation coefficients, two regression equations were developed. When adiposity was expressed as percent fat, muscle mass was not correlated with the residual variance. However, when ASMM was entered first, sum of skinfolds was correlated with the residual variance. The relative contribution to the r<sup>2</sup> of each predictor is shown in Fig. 3, A (Eq. 6) and B (Eq. 7). The residual variance for each equation was greater than the residual variance for T<sub>e</sub> and muscle mass and percent fat had similar relative contributions to the r<sup>2</sup> as sum of skinfolds alone.

Older subjects. ASMM and percent fat were the predictors with the largest correlation coefficients, and two equations were developed. When ASMM was entered into the equation first, the sum of skinfolds was correlated with the residual variance. Alternatively, when percent fat was entered first,
ASMM had the highest correlation with the residual variance. Figure 3, C (Eq. 8) and D (Eq. 9), shows the relative contribution to the $r^2$ for each predictor. Percent fat accounted for a greater proportion of the residual variance than sum of skinfolds, and ASMM was negatively associated with $I_t$.

**Cross-validation of Predictors**

The results of the cross-validation analysis are shown in Table 4. For $T_e$, in the young subjects, ASMM, $A_d$/mass, and sex were nonsignificant predictors, while the relative importance of percent fat was unchanged. The sum of skinfolds explained 67% ($P < 0.001$) of the variance in young subjects but only 2% ($P > 0.05$) in the older subjects, and the contribution of $[T_3]$ dropped from 19–24% ($P < 0.001$) in young subjects to 3–7% ($P > 0.05$) in older subjects. Due to similar original predictors, there was little difference in the cross-validation of $I_t$ predictors. An exception was ASMM, which, when combined with percent fat in young subjects, was nonsignificant. The greater $r^2$ for $I_t$ ($\chi^2 = 20.49$, $P < 0.01$) in the older subjects was due primarily to a greater contribution from ASMM.

**DISCUSSION**

The major findings of the present study are 1) in young subjects, adiposity and $[T_3]$ explain most of the variance in the $T_e$ response to mild cold exposure; 2) in older subjects, either percent fat and $A_d$/mass or ASMM accounted for similar portions of the variability; and 3) due to similar explained variance, sex is interchangeable with body composition characteristics in older subjects. While residual (unexplained) variance in $T_e$ was greater in older subjects ($P < 0.01$), the residual variance of $I_t$ was greater in the young subjects.
ASMM explained a significant portion of the variance in older but not young subjects, although, unexpectedly, this was a negative relationship.

Previous studies regarding the effects of body composition and/or aging on Tc during cold exposure have either inadequately matched subject groups for relevant anthropometric characteristics (40) or failed in an attempt to match groups for all except one characteristic (37, 38). In contrast, in the present paper, we have applied multiple-regression analysis to a large heterogeneous subject population that varied across several characteristics. The use of multiple-regression analysis has been successfully employed to examine the relative influence of individual characteristics during heat stress (21-24); to our knowledge, the present study is the first application of this technique to cold stress. It is important to point out that the purpose of this multiple-regression analysis is not to attempt to globally predict Tex or It, as there are a number of models, ranging from simple to complex, aimed at predicting thermoregulatory responses to cold stress. Rather, this study attempted to quantify the relative contribution of individual characteristics to the determination of Tex and It and how these relationships differ between young and older subjects.

Adiposity had the largest contribution to the $r^2$ for Tex prediction in the young subjects, with sum of skinfolds explaining 33% more of the variance than percent fat, as determined by DXA. Conversely, sum of skinfolds was not correlated with Tex in older subjects, whereas percent fat was the best predictor. One possible explanation for this is the redistribution of body fat with aging. Cross-sectional studies of young and older subjects (33, 43) have demonstrated that total

Table 4. Cross-validation of models presented in Table 3

<table>
<thead>
<tr>
<th>Equation No.</th>
<th>Independent Variable</th>
<th>Constant</th>
<th>ASMM</th>
<th>%Fat</th>
<th>Skinfolds</th>
<th>[T3]</th>
<th>A/Mass</th>
<th>Sex</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (older)</td>
<td>Tex</td>
<td>37.33</td>
<td></td>
<td></td>
<td>0.16 (2)*</td>
<td>-0.28 (3)*</td>
<td>0.05*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (older)</td>
<td>Tex</td>
<td>36.84</td>
<td>0.42 (14)</td>
<td>0.20 (7)*</td>
<td>0.21</td>
<td></td>
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</tr>
<tr>
<td>3 (young)</td>
<td>Tex</td>
<td>37.13</td>
<td>0.64 (34)</td>
<td>-0.14 (7)*</td>
<td>0.41</td>
<td></td>
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<tr>
<td>4 (young)</td>
<td>Tex</td>
<td>37.61</td>
<td>-0.32 (8)*</td>
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<td>0.08*</td>
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</tr>
<tr>
<td>5 (young)</td>
<td>Tex</td>
<td>37.05</td>
<td></td>
<td>0.22 (2)*</td>
<td>0.02*</td>
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<td></td>
</tr>
<tr>
<td>6 (older)</td>
<td>It</td>
<td>0.043</td>
<td>0.68 (45)</td>
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<td>0.45</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>7 (older)</td>
<td>It</td>
<td>0.121</td>
<td>-0.77 (46)</td>
<td>0.35 (21)</td>
<td>0.67</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 (young)</td>
<td>It</td>
<td>0.076</td>
<td>-0.23 (11)*</td>
<td>0.43 (21)</td>
<td>0.32</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 (young)</td>
<td>It</td>
<td>0.089</td>
<td>-0.41 (17)</td>
<td>0.30 (13)</td>
<td>0.30</td>
<td></td>
<td></td>
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</tr>
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</table>

Significant predictors in the young subjects were used to develop regression equations and calculate standardized regression coefficients for the older subjects and vice versa. Table contents are standardized regression coefficients (percentage of total variance explained by that predictor in parentheses). The sum of the percentage of total explained variances equals the $r^2$. *$P > 0.05$. 

J Appl Physiol • VOL 101 • DECEMBER 2006 • www.jap.org
body and intra-abdominal fat increase with aging, while subcutaneous fat decreases and total body mass tends to remain stable. Similar results have been reported in longitudinal studies (26) of elderly men and women. In the present study, as a group, the older subjects had similar mean sum of skinfolds but a higher mean percent fat than the young subjects, which supports the notion of body fat redistribution. Additionally, analysis of limb vs. trunk fat mass from the DXA scans revealed that the older subjects had proportionally less limb fat than the young subjects (46.9 ± 1.0 vs. 49.9 ± 1.0%, P < 0.05). Therefore, the lack of a significant correlation between $T_{es}$ and sum of skinfolds in the older subjects was not surprising in light of this redistribution of body fat. These findings suggest that subcutaneous fat is more important than central or intra-abdominal fat during mild cold stress in older subjects, and proportionately less subcutaneous fat may be a disadvantage in older subjects, considering that these subjects failed to defend $T_c$ (Fig. 1).

Plasma $[T_3]$ explained a significant portion of the variance in $T_c$ in young but not older subjects; however, possible reasons for this difference are unclear. Thyroid hormones stimulate obligatory thermogenesis, i.e., the heat production due to biological processes such as Na$^+$-K$^+$-ATPase activity, and are essential for facultative (nonshivering) thermogenesis in brown adipose tissue in nonhuman mammals (34). Most of the variability in basal metabolic rate can be explained by differences in lean body mass, but it has been suggested that thyroid hormones may explain some of the remaining variability (42). Data from animal studies suggest a vasodilatory role for thyroid hormones in the hyperthyroid state, possibly leading to increased heat loss due to greater blood flow. Therefore, in euthyroid individuals, such as those in the present study, the predominant effect of thyroid hormones appears to be heat production.

An unexpected finding was a significant negative relationship between $T_{es}$ and ASMM in older subjects and between $I_1$ and ASMM in young and older subjects. Ducharme and Tikuisis (13) demonstrated that muscle mass may account for up to 92% of $I_1$ in the forearm of young subjects, and it has been hypothesized that loss of muscle mass with aging may lead to lower $I_1$ (28), with the assumption that lower $I_1$ would then lead to an impaired defense of $T_c$. $I_1$ is the result of the passive effects of adipose and muscle tissues coupled with the dynamic effects of skin and muscle blood flows (27). Either increased adiposity or muscle mass or decreased blood flow increases $I_1$. However, Jequier et al. (27) proposed that markedly obese subjects have less nonfat (i.e., muscle) insulation than normal-weight subjects and suggested that changes in blood flow may be the mediating factor.

In an effort to determine the role of blood flow on $I_1$, forearm vascular conductance (FVC, ml·100 ml$^{-1}$·min$^{-1}$·100 mmHg$^{-1}$, determined via strain gauge plethysmography) data (11) were correlated with ASMM. There were significant correlations between FVC and ASMM for young and older subjects ($r = 0.61$ and 0.57, $P < 0.01$ for young and older, respectively), suggesting that the increased $I_1$ expected due to larger muscle mass is more than offset by higher tissue perfusion, which decreases $I_1$. Similarly, Ducharme and Tikuisis (13) showed that, during forearm immersion in water $>30^\circ$C, there was a linear relationship between thermal conductivity (the inverse of $I_1$) and forearm blood flow, such that higher blood flow reduced $I_1$. Due to colinearity among FVC, ASMM, and adiposity, regression modeling of $I_1$ failed to yield a model incorporating all three parameters. Additionally, the relationship between $I_1$ and $T_c$ is difficult to determine, considering that $T_c$ is one of the terms in the numerator of the equation to estimate $I_1$.

Examination of the predictors included in each model and the relative contribution of each to the $r^2$ demonstrates the age dependence of the predictors. The only predictor that was significant for all models (except Eqs. 4 and 5) was adiposity, the relative contribution of which ranged from 13 to 67% of the total variance. The residual (unexplained) variance of the $T_{es}$ equations was considerably greater in the older subjects, suggesting greater variability in the responses of the older subjects. Our laboratory has previously documented greater variability in vasomotor responsiveness to exogenous norepinephrine infusion (35), which may be the result of differential aging, such that a given individual may show impaired physiological function at different chronological ages and at different rates. This phenomenon of differential aging occurs in the cardiovascular system (15) and in the thermoregulatory system as well. That the residual variance for $I_1$ was greater in the young subjects argues against this conclusion; however, this is difficult to interpret due to a lower relative influence of ASMM.

Numerous studies have suggested a relationship between core cooling and $A_d$/mass (29, 30, 32), whereby a larger $A_d$/mass (i.e., a smaller size) leads to greater decreases in $T_c$ during cold stress. Several studies reported that women having higher $A_d$/mass but similar adiposity cooled faster compared with men (29, 30). However, there was a strong inverse correlation between percent fat and $A_d$/mass ($r = -0.93$ and $-0.95$ for men and women, respectively) (30). A similar significant correlation was not evident in the present study. In contrast, others have suggested that $A_d$/mass has minimal effect on heat transfer in subjects matched for adiposity (38). Additionally, the inclusion of $A_d$/mass in models to predict the metabolic response during cold water immersion reduces model precision (36). In the present study, $A_d$/mass contributed only to the explained variance in $T_{es}$ in older subjects. Unexpectedly, this was a positive relationship, and the underlying mechanism for this relationship is not clear. In general, our results support the notion that $A_d$/mass has little individual relevance or sole predictive value during mild cold stress.

Sex showed the highest correlation with $T_{es}$ in the older subjects (Table 2). Others have shown that sex differences during cold stress are due to body composition differences (11, 30, 37). After sex was included in the regression equation, neither muscle mass nor adiposity was correlated with the residual variance. Conversely, when either ASMM or percent fat was entered first, sex was not correlated with the residual variance. Our data support the conclusion that sex differences can be explained by differences in body composition. Therefore, the inclusion of both sexes in the present study allowed for a larger sample size and a greater range of individual characteristics. Fitness level was not considered as a potential predictor, as other studies have argued against reduced aerobic capacity as a significant predictor of $T_c$ during resting cold stress (14), and there are no differences between young and older individuals for heat loss, heat production, or $I_1$ (6, 11), although one study did suggest an effect of aerobic capacity on metabolic rate during cold stress (4).
In summary, we have shown through multiple-regression analysis that the significant predictors as well as the relative contribution of those predictors to the \( r^2 \) varies by age group. Adiposity and \( |T_s| \) explain most of the variance in the \( T_{es} \) response to mild cold exposure in young subjects, whereas, in older subjects, either percent fat and \( A_d/mass \) or ASMM accounted for similar portions of the variability. Due to similar explained variance, sex is interchangeable with body composition characteristics in older subjects. While residual (unexplained) variance in \( T_{es} \) was greater in older subjects, the residual variance of \( I_1 \) was greater in the young subjects. ASMM explained a significant portion of the variance in older subjects, although, unexpectedly, this was a negative relationship, possibly due to higher tissue perfusion and therefore greater heat conductance in those with greater muscle mass, offsetting the increased passive insulation associated with greater muscle mass. Other individual characteristics, such as body mass, body mass index, and \( A_d \), were not significant predictors. Possibly due to differential aging, in which a given individual may show impaired physiological function at different chronological ages and at different rates, the residual (unexplained) variance for \( T_{es} \) was considerably greater in older vs. younger subjects.

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