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ORIGINAL ARTICLE

Validation of an individualised model of human thermoregulation for predicting responses to cold air

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Abstract Most computer models of human thermoregulation are population based. Here, we individualised the Fiala model [Fiala et al. (2001) Int J Biometeorol 45:143–159] with respect to anthropometrics, body fat, and metabolic rate. The predictions of the adapted multisegmental thermoregulatory model were compared with measured skin temperatures of individuals. Data from two experiments, in which reclining subjects were suddenly exposed to mild to moderate cold environmental conditions, were used to study the effect on dynamic skin temperature responses. Body fat was measured by the three-compartment method combining underwater weighing and deuterium dilution. Metabolic rate was determined by indirect calorimetry. In experiment 1, the bias (mean difference) between predicted and measured mean skin temperature decreased from 1.8°C to −0.15°C during cold exposure. The standard deviation of the mean difference remained of the same magnitude (from 0.7°C to 0.9°C). In experiment 2 the bias of the skin temperature changed from 2.0±1.09°C using the standard model to 1.3±0.93°C using individual characteristics in the model. The inclusion of individual characteristics thus improved the predictions for an individual and led to a significantly smaller systematic error. However, a large part of the discrepancies in individual response to cold remained unexplained. Possible further improvements to the model accomplished by inclusion of more subject characteristics (i.e. body fat distribution, body shape) and model refinements on the level of (skin) blood perfusion, and control functions, are discussed.

Keywords Skin temperature · Body composition · Metabolic rate · Ambient temperature

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Introduction

Various detailed models of the human thermal system, predicting human thermoregulatory responses to the environment, clothing and/or different levels of activity, have been developed in the past three decades. Most of the models available today are based on the work of Stolwijk, who modelled the body as a composite of several cylinders representing the head, the corpus, and the upper and lower extremities (Stolwijk 1971). Useful refinements of this model have been implemented, among others by Gordon (1974), Lotens (1993), and Huizinga et al. (2001), and new thermoregulatory models have also been developed, e.g. by Wissler (1985) and Fiala et al. (1999). However, virtually all models are population based, i.e. they predict an average response of the population or use an average subject with standardized body characteristics.

In recent years, there has been growing interest in 'personalised' models capable of predicting the thermal behaviour of individuals or specific groups of populations.

The fields of application for such models include indoor climate and thermal comfort research (e.g. air conditioning systems in buildings and cars), biometeorology, textile research by the military (e.g. to assess exposure limits and the performance of protective clothing systems), health sciences (e.g. study of factors determining metabolic efficiency), risks under stressful conditions (e.g. heat stress, cold stress, strenuous exercise), and in clinical environment (e.g. neuroprotection, surgery, anaesthetics, recovery, accidental hypothermia).

Recently, some models that incorporate individual human characteristics have emerged (Havenith 2001; Zhang et al. 2001; Gonzalez 2004) but, although promising, the validation results remain limited. Such models predicted core temperatures during hot stress using an extended two-node model and concluded that, although model individualisation did improve the predictions, substantial error still remained. Zhang et al. (2001) used a multi-segmental model and implemented individualised body composition and energy expenditure characteristics. Body fat and resting metabolic rate (RMR) were derived from body length and weight (Zhang et al. 2001). However, it is important that the development and validation of individualised models is based on actually measured subjective characteristics such as body composition and RMR.

Even in modern western societies, humans are frequently exposed to environments that deviate from thermo-neutral conditions. Moreover, transient changes in ambient temperature, air velocity, and other environmental parameters are typical. Disturbances from thermo-neutral conditions lead to temporal changes in body heat content and to adjustments of the thermoregulatory system. In this respect, large differences between subjects have been documented (Marken Lichtenbelt et al. 2002; van Ooijen et al. 2004). Despite the fact that moderate conditions appear to be more relevant to our daily lives, most studies have focussed on extreme (severe cold or heat stress) conditions. Inter-individual differences in thermoregulatory responses to severe cold have been linked to age, body composition and gender (Matsumoto et al. 1999; Kaciuba-Uscilko and Grucza 2001; Van Someren et al. 2002). Comparatively little information is available on thermoregulatory responses under mild cold; however, even under such conditions, individuals may differ considerably in their physiological response (Dauncey 1981; Marken Lichtenbelt et al. 2001, 2002; van Ooijen et al. 2004). Recent research seems to indicate that body composition is a factor contributing to these individual differences (van Ooijen et al. 2004).

The purpose of this study is to examine to what extent a 'personalised' multi-segmental mathematical model can improve the capability of predicting the temperature responses of individuals. For this purpose we used a detailed computer model of human thermoregulation (Fiala et al. 1999, 2001), which is based on the analysis of a large number of independent experimental data. The original model was developed to simulate a 'standard' person with a body weight of 73.5 kg, 1.71 m in height (Dubois area 1.86 m^2), body fat content of 14.4%wt, and basal metabolism of 87.1 W. Experimental data, collected when reclining subjects were suddenly exposed to a moderate cold environment, were used to study the effect on dynamic skin temperature responses. Two different experiments were designed: one used mild cold conditions with an air temperature of 15°C, where no shivering was observed (Marken Lichtenbelt et al. 2004; Ooijen et al. 2004). In the other study, the subjects were exposed to the same ambient temperature but with less clothing, which caused shivering after 83 min on average (Ooijen et al. 2005). In this trial the focus was on body temperature and metabolic responses as well as the duration of the non-shivering interval (NSI).

After carrying out a sensitivity analysis using the original model, the above-mentioned data sets were used to validate both the original and the individualised model incorporating the independently measured subject characteristics, i.e. body composition and metabolic rate.

Materials and methods

Model

The thermoregulatory responses of the test subjects were modelled using the Fiala model (Fiala et al. 1999, 2001, 2003). In the original model used in this study, the human body was subdivided into 14 cylinders representing the lower and upper torso, neck, shoulders, and the lower and upper extremities, and a combination of a cylinder for the face and a sphere for the head (Fig. 1). Every cylinder and sphere was built of five (face, thorax and abdomen) or four layers (other body elements) that represented different tissue materials: brain, lung, viscera, bone, muscle, fat, and skin. Furthermore, the cylinders were divided spatially into three sectors (anterior, posterior, and interior) by which asymmetric boundary conditions can be modelled (such as inhomogeneous radiant fields, or extra insulation caused e.g. by an operating-room table). The body elements exchanged heat with each other via arterial blood delivered from the central blood pool located in the thorax. After passing counter-current heat exchanges, heat was delivered to local tissues via blood perfusion (Gordon 1974; Wissler 1985; Lotens 1993; Fiala et al. 1999; Huizinga et al. 2001).

The dynamic model consisted of passive and active components. The passive component modelled heat transfer phenomena and heat redistribution within the body, including the thermal effects of blood circulation, heat generation, accumulation and conduction in tissue layers. The model interacted with the environment by convection,

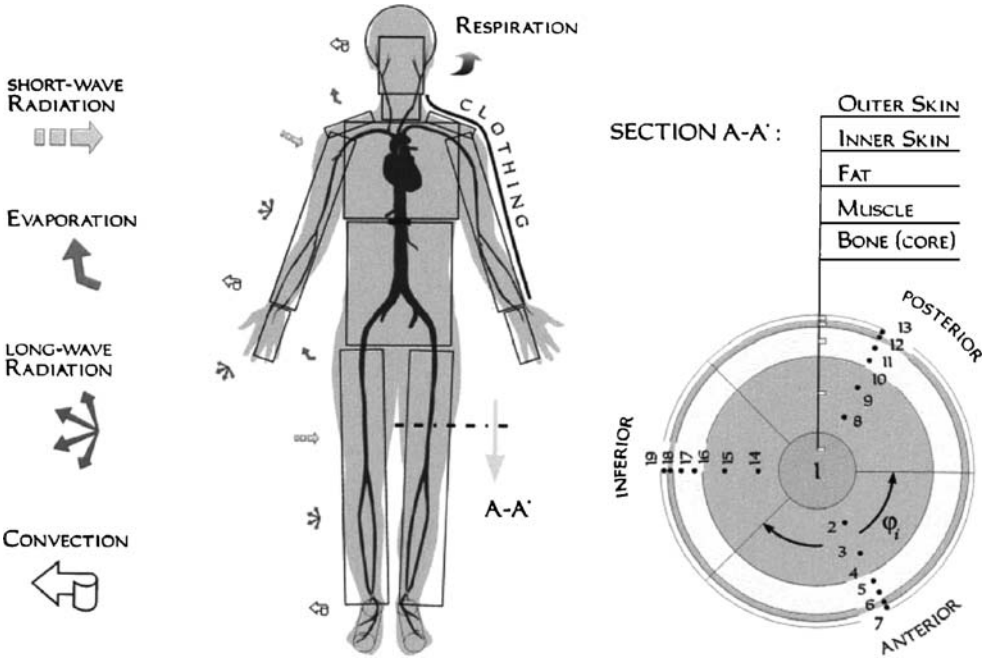

Fig. 1 Schematic view of the human body model (Fiala et al. 1999)

(short-wave and long-wave) radiation, respiration, skin evaporation and water vapour diffusion. In this original model, the insulative effect of clothing was considered by adapting local heat transfer coefficient U^*_{cl} according to the method described in Fiala et al. (1999):

$$U^*_{cl} = \frac{1}{\sum_{j=1}^{n} I^*_{cl} + \frac{1}{f^*_{cl}\left(h_{c,mix}+h_R\right)}} \quad (1)$$

where j and n represent the running and total number of clothing layers covering a body part, respectively, I^*_{cl} is the local insulation value, f^*_{cl} the area of the body element covered by clothing, and $h_{c,mix}$ and h_R the local values predicted for convection and radiation, respectively. The values for I^*_{cl} were derived by converting overall clothing characteristics obtained from the literature (McCulloch et al. 1985, 1989) by accurately simulating the experimental procedures (Fiala et al. 1999). A similar approach was also used to calculate the clothing's local evaporative resistance (Fiala et al. 1999).

The active component represents the actual thermoregulatory system. The body responds to temperatures and changes in temperature by extra heat production produced by shivering, sweating and vasomotion. The thermoregulatory system was developed based on regression analysis of measured responses using a large number of published experiments with volunteers. The model mimics the response of a standard healthy, unacclimatised person.

Individualisation

In this research we compared the results of the "standardised" person with predictions from the individualised model in which the anthropometric and basal metabolism data were adjusted according to the personal characteristics obtained from test-subjects in our experiments. Except for the head, the length of the body elements was scaled by a factor, f, which was the ratio of the height of the individual to the height of the average person. The head was scaled by the square root of f. The thickness of the skin layers of all body parts was kept unchanged. The radii of the core, bone, muscle, and fat layers of the modified model were adjusted to reflect the measured total mass and body fat content of the individual test subjects. The heat generation rates of the model were converted from the measured whole body metabolic rates.

Sensitivity analysis

To obtain information on how body temperatures are affected by individual characteristics (body height, body weight, fat percentage and metabolic rate), we first compared the results of the standard human model of Fiala et al. (1999) with temperatures predicted by an adapted model representing an average Dutch man and woman (Visscher and Seidell 2004). The data for the mass, height and body mass index (BMI) are listed in Table 1. The body fat percentage (BF%) was calculated by:

$$\text{BF\%} = 1.20 \times \text{BMI} + 0.23 \times \text{age} - 10.8 \times \text{sex} - 5.4 \quad (2)$$

Table 1 Literature values: mean (standard deviation) for Dutch men and women aged 20–59 years. *BMI* Body mass index, *BF* body fat, *RMR* resting metabolic rate

	Men	Women
Mass (kg) [a]	80.9 (12.2)	67.7 (11.7)
Height (m) [a]	178.3 (7.4)	165.7 (6.8)
BMI (kg/m^2) [1)]	25.4 (3.6)	24.7 (4.3)
BF (%) [b]	24.6 (4.3)	34.6 (5.2)
RMR (MJ/day) [c]	7.53 (0.59)	5.84 (0.40)

[a] From Visscher and Seidell (2004)
[b] BF% =1.20×BMI+0.23×age−10.8×sex−5.4 at age=45 years. From Deurenberg et al. (1991)
[c] From WHO (2004)

where age=45 years, sex=1 for males and 0 for females (Deurenberg et al. 1991). The RMR (in MJ/day) was obtained as in WHO (2004):

$$\mathrm{RMR} = 0.048^{*}\mathrm{weight} + 3.653 \text{ for men} \quad (3)$$

$$\mathrm{RMR} = 0.034^{*}\mathrm{weight} + 3.538 \text{ for women} \quad (4)$$

In the simulations, the subjects wore sweatpants (0.28 clo), a sweater (0.37 clo), socks (0.02 clo), and underwear (0.04 clo). The simulations were carried out for the following boundary conditions: thermo-neutral initial conditions (according to Fiala et al. 2001), followed by a 100-min exposure to ambient temperature of 21.5°C and 200 min to 16.5°C. The simulation was run with an air speed of 0.1 m/s and relative humidity of 50%. These conditions were similar to the conditions of experiment 1 described below. The simulation results are shown in Table 2.

In the simulations, the onset of shivering was predicted to occur after 170 to 300 min of exposure. We therefore chose to analyse skin temperatures at t=160 min, i.e. just before any shivering occurred. The simulations showed that the mean skin temperatures of an average man or woman would differ from the standard person by up to 1.5°C (Table 2). This indicates the importance of the actual body composition and RMR on predicted skin temperatures.

In order to evaluate the effect of individual body composition parameters and RMR relevant to the population under study, these parameters were then changed keeping the other parameters in the model constant. The time of onset of shivering, the rectal temperature and some skin temperatures were compared for both the 5th percentile and the 95th percentile of Dutch men with the values obtained for the average person. The body composition and RMR values for the 5th percentile and the 95th percentile of Dutch men were defined as their mean values plus or minus twice their standard deviation, respectively (Table 1). The simulation results are listed in Table 3.

The analysis revealed that the impacts of body mass, body fat percentage and RMR on the mean skin temperature are of comparable order of magnitude (1.2°C to 1.5°C) whereas the impact of body height is less pronounced (0.4°C). The effect on local skin temperatures in the extremities was found to be even more significant, again clearly indicating the importance of actual body composition and RMR in the response of the individuals to be modelled.

Experimental investigations

Two types of experiments were carried out to validate the model. Experiment 1 involved subjects resting for 1 h at a comfortable temperature followed by a 3-h exposure to mild cold. Mild cold means that no shivering occurred during the entire duration of the test. In experiment 2, cold exposure was enhanced by using less clothing. Also, this experiment started with a1-h exposure to thermally comfortable conditions followed by cold exposure until shivering occurred. The tests were terminated 30 min after the onset of shivering.

Measurements

The volunteers in both experiments were given detailed information regarding the purpose and the methods used in the study, before written consent was obtained. The Ethics Committee of Maastricht University approved the studies.

The body composition of all subjects was determined in a separate session, which took place within 1 week before the actual trials. Body composition was calculated using the three-compartment model according to Siri (1956). For this

Table 2 Simulated time to shiver and temperatures (*T*) at 160 min for the standard man according to Fiala et al. 1999, and the average Dutch man and the average Dutch woman (Visscher and Seidell 2004)

	Time to shiver (min)	Mean T_{skin}(C)	T_{rectal} (°C)	T_{leg} (anterior) (°C)	T_{hand} (posterior) (°C)	T_{foot} (anterior) (°C)	T_{chest} (anterior) (°C)
Standard man	230	30.0	36.73	30.06	28.40	24.41	32.94
Average Dutch man	240	29.3	36.66	28.92	27.83	24.47	32.18
Average Dutch woman	260	28.5	36.01	28.14	26.92	23.43	31.46

Table 3 Time to shiver and temperatures (T) for the average man and the 5th percentile and 95th percentile Dutch man with respect to mass, height, body fat percentage and basal metabolism. When a parameter is changed to the 5th or 95th percentile value, all other parameters are kept at the average value. Temperatures are at t=160 min

		Time to shiver (min)	T_{skin} (°C)	T_{rectal} (°C)	T_{leg} (anterior) (°C)	T_{hand} (posterior) (°C)	T_{foot} (anterior) (°C)	T_{chest} (anterior) (°C)
Average man		240	29.3	36.66	28.92	27.83	24.47	32.18
Mass	5th %	300	29.5	36.04	28.85	28.30	24.05	31.96
	95th %	170	28.0	37.74	24.88	26.47	22.05	33.65
Height	5th %	260	29.5	36.87	29.05	28.04	24.55	32.32
	95th %	230	29.1	36.48	28.77	27.65	24.09	32.06
Fat %	5th %	240	29.9	36.92	29.59	28.39	25.00	32.90
	95th %	250	28.7	36.31	28.22	27.25	23.83	31.69
RMR	5th %	210	28.3	36.98	25.68	26.91	22.63	32.92
	95th %	280	29.5	36.75	29.35	28.00	24.10	32.31

calculation, the body density and the total body water content were determined using underwater weighing and deuterium dilution (Westerterp et al. 1995).

During the tests, O_2 consumption and CO_2 production were measured by indirect calorimetry, using a ventilated hood system. Metabolic rate was calculated from these data according to Weir (1949). RMR was defined as the metabolic rate of subject who were awake and lying still while exposed to thermoneutral conditions.

Rectal temperature was measured continuously using a thermistor-probe (YSI probes, series 402, Yellow Springs Instruments, Ohio) inserted for 10 cm. Skin temperatures were measured using surface thermistors (YSI probes, series 409B, Yellow Springs Instruments) at the hand posterior, upper arm posterior, chest at the m. pectoralis, abdomen anterior, back sub scapula, thigh anterior, and foot posterior. In experiment 2 measurements of skin temperature of the posterior forearm and the calf were also included. Temperatures were recorded continuously for 50 s out of each minute and saved every minute. The mean skin temperature was calculated as proposed by Ramanathan (1964) and Mitchell and Wyndham (1969).

Shivering was detected using electromyography (EMG) (Tiretherm, Maastricht Instruments, Maastricht University, The Netherlands) placed on the skin above the m. pectoralis major. This site was chosen based on earlier findings of Tikuisis et al. (1991), who found that shivering starts in the upper trunk region in people with a normal amount of fat and in the upper trunk and leg regions in lean people, before propagating towards the extremities. In addition, the subjects were asked every 15 min if they felt they were shivering, and this condition was also checked visually by the investigator.

The subjects arrived at the laboratory by car or public transport and had fasted for at least 4 h in order to avoid any effects of activity or diet. They were instructed not to perform any strenuous activity the day before the experiment.

Experiment 1

Ten male and ten female subjects, all healthy non-smokers, participated in these tests. Participants were between 19 and 36 years of age, with an average height of 1.74±0.09 m (mean±SD), weight 71.1±14.4 (range 51.2–107.2) kg, and a BF% of 22.5±8.4 (range 8.2–36). Their average basal metabolic rate was 6.59±1.01 MJ/day.

The trials took place at the end of the summer, in August and September. The subjects attended the laboratory for an overnight stay including the following morning to participate in the experiment. The subjects were instructed to perform no exercise the day before the measurement and they fasted from the moment they entered the chamber for the whole duration of the experiment. They stayed quietly in the laboratory for 1.5–2 h at 22°C before the actual measurements started. The measurements took place in the morning. Metabolic rate (MR), intestinal, rectal and skin temperatures were measured for 1h at an ambient temperature of 22°C followed by 3 h during which the subjects were exposed to 15°C. The subjects were lying supine on a stretcher. The clothing consisted of sweatpants (0.28 clo), a sweater (0.37 clo), socks (0.02 clo), and panties and a bra for women and briefs for men (0.04 clo). During the experiment, the face, hands and ankles were uncovered.

Experiment 2

Ten women and seven men participated in this study. All were healthy and non-smokers. The subjects were 19–31 years old, 1.78±0.12 m tall, weighed 66.9±8.4 (range 54.7 79.5) kg, and had a BF% of 21.2±2.2 (9.6–40.4). Their basal metabolic rate averaged 6.64v±1.28 MJ/day.

In the experiment the subjects were lying supine, the head slightly tilted, on a stretcher, in an environment with an air temperature of 15°C. Other environmental parameters were the same as in experiment 1. The clothing had a total estimated insulative value of 0.18 clo (0.028 m^2°C W^{-1}) and consisted of pants (0.1 clo), a singlet (0.04 clo) and panties and a bra for women and briefs for men (0.04 clo). Subjects stayed quietly in the laboratory for 1.5–2 h at 22°C before the actual measurements started. The measurements took place in the morning. The subjects were initially covered with a duvet (375 g /m^2) to simulate thermoneutral conditions. Cold was then induced after 30 min by removing the duvet. The test was terminated 30 min after the onset of shivering. The interval between removing the duvet and the onset of shivering was defined as the non-shivering interval (NSI). The interval between the onset of shivering and the termination of the test was termed the shivering interval (SI). MR, body temperatures and EMG were measured continuously.

Model-measurement comparisons and statistical analysis

We initially compared the predictions obtained using the standard subject with measured individual thermoregulatory responses to mild cold. In the second stage, the model was adapted by including the individualised body composition (BC) data (i.e. height, weight and BF%) and/or RMR or actual measured MR to simulate the cold exposure tests.

We calculated the differences between predicted and measured results for each 1-min interval for each individual. These data were used to calculate the mean differences and standard deviations. In Tables 4 and 5, the results averaged over the whole group are given as mean±SD over 30-min time intervals, i.e. the last 30 min or 10 min in comfort (exp 1: 31–60 min; exp 2: 21–30 min), during early cold exposure (exp 1: 91–120 min; exp 2: 51–80 min), and the last 30 min in the cold (exp 1: 211–240 min; exp 2: 81–110 min). The 30-min mean values were used to test significance by two-tailed paired *t*-tests between model predictions and measurements with and without inclusion of subject characteristics. The *t*-tests were calculated using the absolute differences between model and measurements. Absolute values are used because positive and negative change in errors should not cancel each other out.

Linear regression analyses was employed to evaluate the relationship between the predicted and observed times between the start of cold exposure and the onset of shivering. Any differences were considered statistically significant at $P<0.05$.

Results

Experiment 1

A typical example of measured results is shown in Fig. 2a. The data refers to a female subject. During the first hour of comfort the rectal and chest temperatures were constant and the temperatures of the thigh, hand and foot showed a small decline. During the 3 h of cold exposure, all measured

Table 4 Experiment 1. Mean temperature difference (°C) ± standard deviation between model and measurement for mean skin temperature and at four body locations. Time interval in the cold: 61–240 min; 20 subjects

Interval (min)	Model input	*T* skin mean	*T* leg anterior	*T* hand posterior	*T* foot anterior	*T* chest
31–60	Standard	0.86±0.59	0.64±0.80	1.62±2.05	−1.17±1.53	0.14±1.02
91–120		1.63±0.74	1.68±0.99	3.74±3.28	1.47±1.89	0.45±1.37
211–240		1.78±0.67	1.93±1.07	5.26±2.76	2.63±1.67	0.08±1.71
31–60	RMR	0.87±0.58 ns	0.60±0.78 ***	1.68±2.05 ns	−1.20±1.53 ns	0.16±1.02 ns
91–120		1.61±0.74 **	1.52±0.98 ***	3.75±3.27 ns	1.40±1.86 **	0.51±1.36 ns
211–240		1.67±0.66 ***	1.56±1.04 ***	5.13±2.78 ***	2.48±1.62***	0.14±1.70 ns
31–60	MR	0.14±0.59 **	−0.37±0.81 ns	1.23±1.97 *	−1.86±1.52 ***	0.20±1.02 ns
91–120		0.51±0.74 ***	0.06±1.00 ***	3.00±3.17 **	0.31±1.88 *	0.83±1.37 ns
211–240		0.61±0.68 ***	−0.21±1.08 ***	3.99±2.55 ***	1.14±1.66 **	1.07±1.72 ns
31–60	BC	0.12±0.76 *	−0.33±1.01 ns	0.87±2.08 ns	−1.98±1.51 **	−0.56±1.26 ns
91–120		0.84±0.92 ***	0.65±1.26 **	2.92±3.15 ***	0.70±1.88 **	−0.27±1.65 ns
211–240		0.86±1.03 ***	0.68±1.29 **	4.27±2.58 ***	1.87±1.63 **	−0.81±2.09 *
31–60	BC, RMR	0.12±0.77 *	–0.37±1.01 ns	0.90±2.09 ns	−1.93±1.53 **	−0.53±1.24 ns
91–120		0.84±0.92 ***	0.53±1.28 **	2.93±3.14 ***	0.71±1.88 *	−0.17±1.61 ns
211–240		0.79±1.03 ***	0.37±1.36 **	4.16±2.59 ***	1.80±1.64 ***	−0.68±2.04 *
31–60	BC, MR	−0.58±0.75 ns	−1.28±0.98 ns	0.04±2.10 ns	−2.59±1.49 ***	−0.47±1.25 ns
91–120		−0.20±0.89 ***	−0.82±1.20 ns	1.47±3.16 **	−0.31±1.86 ns	0.17±1.62 ns
211–240		−0.15±0.89 ***	−1.18±1.10 ns	1.98±2.54 ***	0.62±1.60 **	0.38±2.01 **

* $P<0.05$, ** $P<0.01$, *** $P<0.001$, ns not significant; compared to standard model input

Table 5 Experiment 2. Mean temperature difference (°C) ±standard deviation between model and measurement for mean skin temperature and at four body locations. Time interval in the cold: 31–110 min; 11 subjects

Interval (min)	Model input	*T* skin mean	*T* leg anterior	*T* hand posterior	*T* foot anterior	*T* chest
21–30	standard	0.62±0.87	−1.00±1.09	2.23±2.66	−2.38±1.79	0.04±1.22
51–80		2.05±1.00	2.24±1.62	6.57±1.18	0.73±2.21	1.37±1.55
81–110		2.00±1.09	2.51±1.54	7.59±0.95	1.42±2.50	1.31±1.60
21–30	RMR	0.56±0.82 *	−1.08±1.05 ns	2.19±2.64 ns	−2.43±1.78 *	0.07±1.22 ns
51–80		2.02±0.98 ns	2.08±1.56 **	6.53±1.17 ns	0.66±2.17 *	1.52±1.63 ns
81–110		1.98±1.07 *	2.30±1.45 *	7.55±0.94 *	1.34±2.46 *	1.53±1.73 ns
21–30	MR	0.55±0.82 *	−1.10±1.04 ns	2.18±2.64 *	−2.45±1.77 **	0.06±1.22 ns
51–80		2.00±0.98 *	2.09±1.54 *	6.51±1.17 *	0.64±2.17 *	1.45±1.62 ns
81–110		1.98±1.06 *	2.36±1.40 ns	7.55±0.93 ns	1.35±2.45 *	1.44±1.69 ns
21–30	BC	0.03±0.54 **	−1.65±0.91 *	1.73±2.42 **	−2.87±1.35 *	−0.63±1.31 ns
51–80		1.39±0.86 **	1.47±1.35 **	5.97±0.99 **	0.23±1.80 **	0.68±1.30 ns
81–110		1.28±0.91 *	1.62±1.22 **	6.89±0.87 **	0.91±2.11 ***	0.59±1.39 ns
21–30	BC, RMR	−0.03±0.53 **	−1.73±0.95 *	1.69±2.41 **	−2.92±1.36 **	−0.60±1.30 ns
51–80		1.35±0.89 **	1.35±1.38 **	5.92±1.03 **	0.17 ± 1.79 **	0.85±1.35 ns
81–110		1.28±0.92 **	1.47±±1.24 **	6.84±0.90 **	0.85±2.09 ***	0.85±1.45 ns
21–30	BC, MR	−0.04±0.53 **	−1.76±0.95 *	1.67±2.41 **	−2.49±1.35 **	−0.61±1.30 ns
51–80		1.34±0.89 **	1.35±1.37 **	5.90±1.03 **	0.15±1.79 **	0.78±1.33 ns
81–110		1.27±0.93 **	1.52±1.22 *	6.84±0.91 **	0.85±2.08 ***	0.75±1.41 ns

* $P<0.05$, ** $P<0.01$, *** $P<0.001$, ns not significant; compared to standard model input

temperatures decreased, except for the rectal temperature, which exhibited a slight increase as the exposure continued. The most prominent decrease in temperature was observed for the hands and feet. The individualised model (with body composition and the metabolic rate adjusted) showed very similar trends (Fig. 2b) including all skin temperatures as well as rectal temperature. In the model, the slight increase in the rectal temperature resulted from a massive peripheral vasoconstriction predicted as a response to the cool environment.

Considering the skin temperatures from all subjects (Table 4), the differences between predictions using the standard person model and actual measurements were substantial, i.e. during the final 30 min interval, the prediction-measurement discrepancy of the mean skin temperature was 1.78±0.67°C, and that of the back of the hand 5.3±2.8°C. The mean deviation between the predicted and measured mean skin temperature is plotted over time in Fig. 3 (line A). Adopting individual body composition characteristics and the actual MR of the subjects in the model notably improved the predictions of skin temperature for most body parts. The error decreased from 1.8°C to −0.15°C ($P<0.001$) and 5.26°C to 1.98°C ($P<0.001$) for the mean skin temperature and the back of the hand skin temperature, respectively, during the final 30 min of exposure (Table 4; for *T* skin Fig. 3 line B).

The most significant improvements in skin temperature predictions were achieved when both BC and MR data were adopted. In contrast, the effect of RMR on predicted skin temperatures was relatively small.

The predicted skin temperature of the chest was found to be less sensitive to variations of individual characteristics (Table 4). The results for the posterior thorax and the anterior abdomen showed similar results (data not shown).

During the state of comfort (time interval: 31–60 min) the predictions were not much improved by adopting individual characteristics, except for hand skin temperature. However, for some subjects the differences between predicted and measured skin temperatures (see e.g. foot in Table 4) increased during this interval as a result of the inclusion of personal characteristics. Overall, considering all subjects and body parts, the standard deviation was not decreased significantly by the introduction of individual characteristics (compare Fig. 3, standard deviations of lines A and B).

Experiment 2

In this experiment, shivering was elicited, on average, after about 83 min of cold exposure. Since we were only interested in metabolic and temperature responses prior to shivering, only data from 11 subjects and for times up to 110 min of exposure was analysed, thus excluding subjects ($n=12$) who started shivering earlier. There were generally considerable inter-individual differences in the measured times of onset of shivering, which ranged from 20 to 148 min.

Analysis of the results indicated that the differences between predictions obtained using the standard model and actual measurements were only slightly larger than those obtained for experiment 1 (Table 5, Fig. 4a for *T* skin). The

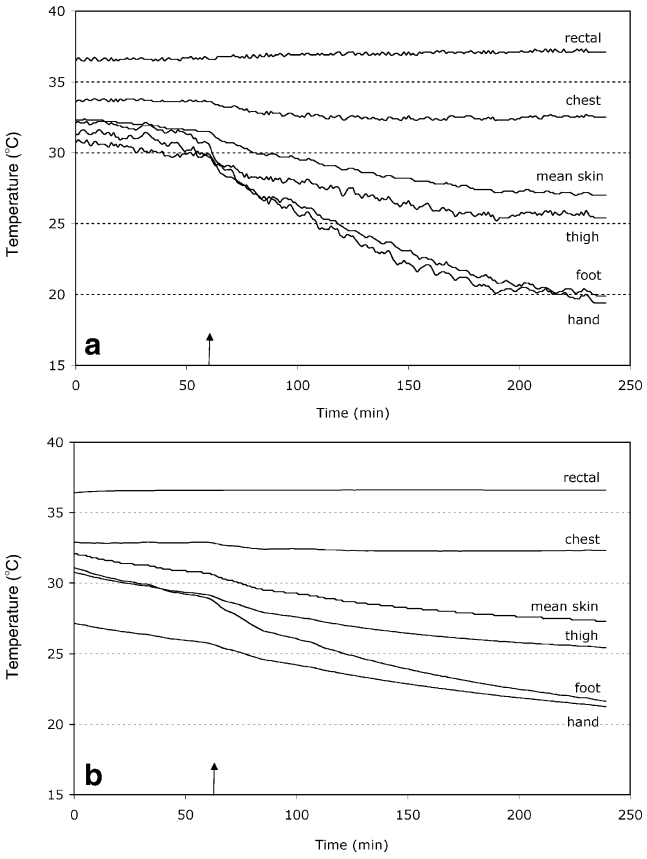

Fig. 2 **a** Example of temperature measurements from experiment 1. Data from one subject. **b** Example of temperature model results of experiment 1. Data from the same subject as in **a**

discrepancies ranged from 2.0±1.1°C for the mean skin temperature to 7.6±1.0°C for the hand skin temperature during the final 30 min interval. Introducing individual characteristics led to better agreement with measurements to some extent for all measured body sites during the final 30 min of cold exposure (Table 5). In contrast to experiment 1, however, the improvement was rather limited and there were virtually no differences between predictions obtained by including the measured RMR or including the actual measured MR. Nevertheless, the inclusion of both measured MR and BC data showed significant improvements with experimental observations (Table 5; *T* skin: Fig. 4).

During the 'comfort' state (baseline values from 21–30 min) the adapted model also showed improved predictions for all body parts when both BC and MR data were included. Here, however, it was mainly the input of the personal BC data that provided the largest improvements. As already observed in experiment 1, the standard deviations of predicted skin temperatures were only marginally affected by the introduction of individual subject characteristics (Table 5; Fig. 4).

Finally, the predicted and measured times of the onset of shivering correlated significantly (with inclusion of both BC and resting metabolic values: R^2=0.47 and P<0.05). However, the modelled time intervals ranged from 130 to 150 min (range 20 min), while the actual observed range amounted to 80–190 min (range 110 min).

Discussion

Adapted versus standard model

The predictions of the multisegmental thermoregulatory model of Fiala et al. (2001) were compared with measured skin temperatures of individuals during exposure to thermally comfortable and (mild) cold conditions. Analysis of the results showed that the deviations between the predictions and individual measurements were substantial, but that the

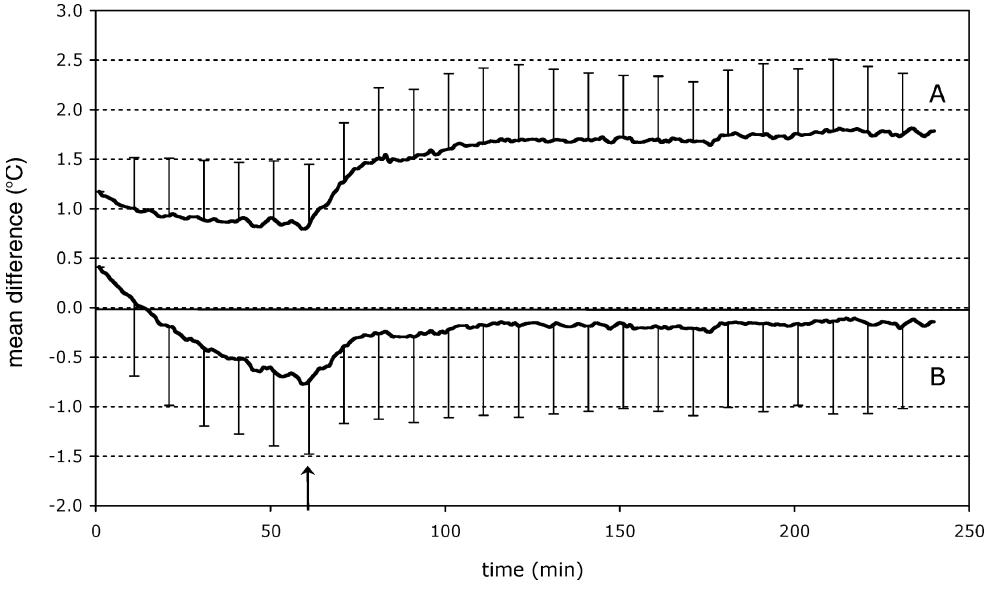

Fig. 3 Comparison of model predictions and measurements in experiment 1. Mean difference (*bold lines*) with SD (*vertical lines*) between modelled and measured skin temperatures plotted against time, using the standard subject in the model (*line A*), and with input in the model of subject characteristics [body composition (BC) and metabolic rate (MR)] (*line B*). The *arrow* indicates the change the air temperature from 22°C to 15°C

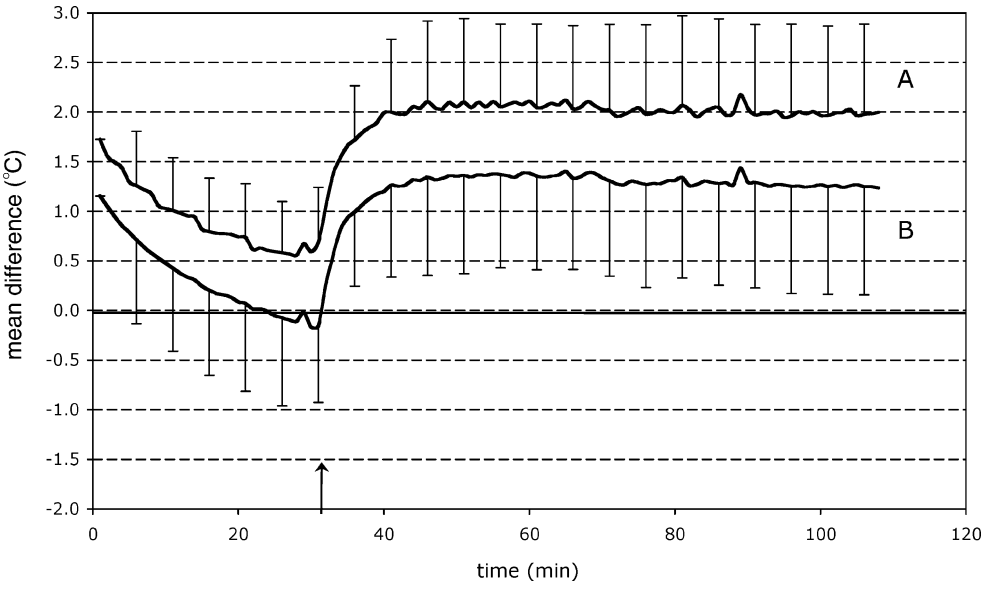

Fig. 4 Comparison of model predictions and measurements of experiment 2. Mean difference (*bold lines*) with SD (*vertical lines*) between modelled and measured skin temperatures plotted against time, using the standard subject in the model (*line A*), and with input in the model of subject characteristics (BC and MR) (*line B*). The *arrow* indicates the change the air temperature from 22°C to 15°C

agreement with measured data improved significantly on a group level (bias decreased) when individual characteristics were incorporated. The deviations on an individual level (standard deviations), however, remained large. The inclusion of individual characteristics thus improved the predictions for an individual and led to a smaller systematical error. However, a large part of the discrepancies in individual response to cold remained unexplained.

Individual characteristics

The effect of the following individual characteristics was studied: body composition, resting metabolic rate, and actual measured metabolic rate. All three characteristics did improve the predictions; however, this study did not clarify which of these characteristics is the most important for predicting skin body temperature.

The sensitivity analysis of the model indicated that variations in the body composition of the Dutch population (range 5th and 95th percentile) caused changes in the mean skin temperature of up to 3.1°C. The normal range of RMR in the Dutch population resulted in a variation in the mean skin temperature of 1.2°C. It follows that the effect of body composition is two to three times as large as the effect of adapted metabolic rates.

Considering the results of both experiments, the difference between measured and predicted temperatures was indeed decreased much more by the input of body composition characteristics than by the input of the metabolic rate. As expected, individualisation of body composition plus the resting metabolic rate reduced the differences between measured and predicted skin temperatures even more.

It appeared that, in experiment 1, the model predictions agreed best with measured data when body composition and actual metabolic rate instead of RMR were incorporated. One reason for this might be that by using the measured MR the model was dynamically adapted as exposure progressed. The model would thus benefit from improved predictions of metabolic responses to mild cold. In experiment 2, inclusion of both RMR and MR provided comparable improvements.

Finally, the model shows a much smaller variation in the time interval between the start of cold exposure and the onset of shivering than did actual measurements. Once model individualisations can provide higher accuracy in predicting skin temperatures, then individual differences in the time of onset of shivering may be better predicted. In the current model, shivering thermogenesis is governed by skin temperature, and the rate of change in skin temperature, and is affected, to a lesser degree, by the level of the body core temperature. However, different formulations have been proposed (Tikuisis et al. 1988). The influence of peripheral and central thermoreception on shivering might, however, not be simply additive as implied in the original model. There is some experimental indication for possible cross-correlations, when the strength of signals from one body side (body core) could affect the sensitivity of the central nervous system to signals from other body sites (skin) when eliciting shivering. Such cross-correlations could have important implications for modelling metabolic responses to cold in obese and lean subjects, who typically show notable differences in their core/skin-temperature ratios.

Model time response

It was expected that, during the comfort period, subjects would have reached thermal steady state. During the

experiments this was almost the case, but the model predictions still showed a gradual decline in skin temperature even during the last minutes of comfort in both experiments. This explains that the bias was not constant during comfort (see Figs. 3 and 4). During exposure to cold, the measurements showed a faster temperature response than that predicted by the model in both experiments, explaining the large shift in the mean difference between model and measurement at the onset of cold exposure. After 10–20 min the bias then levelled off.

The time response may also explain the deviations between model prediction and measurement in experiment 2, which were generally larger than in experiment 1. The important difference between the two experiments was the severity of the exposure. That the model responded slower to changes in environmental conditions is in line with the relatively large deviations between model and measurements during the shorter and colder exposure in experiment 2.

Comparison with other individualised models

This study considered individual characteristics such as anthropometrical data, body fat content, and resting metabolic rate. Other individualised models include "Scenario", which includes anthropometrical, VO_2max, menstrual cycle and circadian rhythm data (Gonzalez 2004), the "Berkeley comfort model", which includes anthropometrics, body fat, gender, skin colour, and resting metabolic rate data (Huizinga et al. 2001; Zhang et al. 2001), and the model described by Havenith (2001), which includes information on the anthropometrics, body fat layer thickness, VO_2max, and the acclimatisation state.

Only Havenith (2001) published a validation study of his model, using independently measured characteristics. The results from that study focussed on rectal temperatures, which were predicted with and without incorporating subjective characteristics. No skin temperature results were presented. Compared to our study on skin temperatures, the inclusion of individual characteristics decreased the systematic error of the rectal temperature predictions during heat exposure. In contrast to our results, the mean squared error also decreased significantly. Havenith concludes however, just as we do, that a substantial part of the differences of individual responses remains unexplained.

Possible improvements

These results indicate that knowledge of the inter-individual differences is still limited and that (1) further characteristics may play a role and/or (2) further model refinements and/or development might be necessary to better represent individuals or population groups.

Further characteristics

Further subjective characteristics, in addition to total body fat content, height, weight and MR, might be important. Here, the most influential characteristics could include, e.g., the distribution of body fat specific to individuals, training status, and gender. Cold acclimatisation could play a role, although experiment 1 took place at the end of the summer and thus any acclimatisation effects to cold were expected to be at a minimum at that time of year in the Netherlands. Individual differences in sympathetic nervous system function and its sensitivity might be important, causing individual variations in the metabolic response and, importantly, in the heat distribution over the body controlled by the peripheral vasoconstriction. It is furthermore assumed that skeletal muscles might play an important role in cold-induced thermogenesis, apart from shivering. Therefore, muscle mass (in addition to the effect of training) could be a further variable that needs closer consideration.

Model refinements and further development

With respect to the above mentioned subjective characteristics (body fat distribution, training status, gender) only body fat distribution can be modelled in some detail using the original Fiala et al. (2001) model. Further refinements, such as those incorporated in the latest model version, i.e. the introduction of further cylinders for upper and lower legs and arms, will improve the prediction of local skin temperatures regarding personal differences in the distribution of body fat and/or muscle mass.

Another improvement could involve connecting the different blood pathways in their natural order. In the current circulatory model, the blood pathways to individual body segments are linked to the central blood pool via counter-current heat exchangers. This approach recognises the fact that even the arterial blood temperature is not homogeneous over the body. A more realistic approach would be to link, e.g., the hands with lower arms, rather than with the central blood pool.

With respect to the thermoregulatory component, the model was developed based on regression analysis using a large number of published experiments to mimic 'average' human thermoregulatory behaviour. The simulation of the thermoregulatory behaviours of individuals and/or specific groups of the population will require further modelling research efforts. To this end, the prediction of the above mentioned vasomotor responses to cold might be of paramount importance. To this end, a model implementing individualised, physiological principles of human thermoregulation should, at least in part, replace the original statistical regression approach of predicting an average

response. Aspects such as training status and gender would also have to be included in the definition of a new, personalised thermoregulatory system.

We conclude that inclusion of individual characteristics can substantially improve model predictions but a significant error remains. The objectives for future research are therefore to improve the models and gain more knowledge of the physiological processes and individual characteristics. Individual characteristics could include more detailed anatomy. On the other hand the model can be improved, e.g., by introducing a more detailed treatment of blood vessels and pathways in the extremities, further subdivisions of the extremities, and the development of individualised, physiologically based control-mechanisms in the model.

As our knowledge of the causes of inter-individual differences is still scant, further research employing both modelling and experiment seems to be necessary to enhance our understanding of the nature of the individual characteristics and physiological principles governing human thermoregulation.

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