questionnaire is subjective, and the measures for PA depend on the observer. An objective measurement approach using an accelerometer may avoid these limitations of a questionnaire, as an accelerometer can count movements in sedentary to vigorous activities (9).

Accelerometers can be used to predict EE and to classify levels of PA (9–12). Validation studies of accelerometers have been performed in both children and adults; however, such studies for classification of PA in young children have only recently been reported (13,14). The principal purpose of the study by Reilly et al. (13) was only to determine cut-off values for accelerometry output. They validated the same type of accelerometer (Actigraph, CSA/MTI) against the DLW method later (15) and indicated that the accelerometer was not appropriate to estimate total EE in preschool-age children. Pfeiffer et al. (14) calibrated an accelerometer (Actical) for use with preschool children during rest, slow and brisk walking, and jogging. However, light to moderate intensity lifestyle activities, except for rest, were not included in the study. These lifestyle activities are known to be underestimated using uniaxial or a single summary measure of the triaxial acceleration counts in adults (12). In these studies (13–15), uniaxial and omniaxial accelerometers were used, respectively. Because the nature of PA in young children is different from that in older children and adults (11), triaxial accelerometry may provide more useful information in young children than uniaxial accelerometry. We are unaware of any data regarding the validity of triaxial accelerometry for assessment of PA intensity in young children, although Hoos et al. (16) validated the triaxial accelerometer (Tracmor2) in 6.9 ± 2.2-year-old children for the estimation of total EE against the DLW method. Some studies have evaluated the validity of the accelerometer in older children (11,17); however, the modeling equations used in these studies assumed a linear relationship between accelerometer counts and EE, while a non-linear model using vertical and horizontal acceleration counts independently may be more appropriate (10,18).

The purpose of the present study was to derive the best models using linear or non-linear equations that estimate EE and physical activity ratio (PAR) from triaxial accelerometer counts in young children.

Research Methods and Procedures

Subjects

Subjects were 5- to 6-year-old Japanese girls (n = 11) and boys (n = 16) (mean age, 6.0 ± 0.3 years), living in the Tokyo metropolitan area, and going to kindergarten. All of the subjects reported being in good health, without any anamnesis affecting EE, such as abnormal thyroid gland function. The sample size was determined based on the results of similar studies published previously. Informed consent was obtained from a parent, and the Ethical Committee of the J.F. Oberlin University approved the study protocol.

Measurement Items and Methods

Body height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. EE was assessed for nine activities using indirect calorimetry by the Douglas bag method. The 27 subjects performed the nine activities while wearing a 57-gram triaxial accelerometer (ActivTracer, GMS, Tokyo, Japan) (19) on the left side of the waist and a mask for collecting expired air using the Douglas bag method. An ActivTracer recorded triaxial acceleration every 5 seconds. The triaxial accelerometer obtained three-dimensional accelerations every 40 ms with a sensitivity of 2 mG and with a band-pass filter of 0.3 to 100 Hz. The acceleration count was calculated as the average of the absolute values for acceleration in each direction for a given interval (5 seconds). Anteroposterior (x-axis), mediolateral (y-axis), vertical (z-axis), and synthetic (synthesized triaxes as vector) accelerations were obtained from the triaxial accelerometer during the nine activities. The acceleration data were uploaded to a personal computer. In addition, because the triaxial accelerometer could shift horizontally during measurements, the x- and y-axes were synthesized as "horizontal acceleration" for the analysis.

For a subgroup of subjects, another accelerometer (actigraph, model RC; Ambulatory Monitoring, Inc., Ardsley, NY), which weighs about 9 g, was worn on the wrist of the dominant arm (n = 14). The actigraph is designed to detect a wide range of limb movements related to sleep/wake behavior and PA. The actigraph was set to operate in "Proportional Integral Mode" (low) to record the number of movements within a 1-minute interval. Calculations were performed with Action-W software, version 2.0 (Ambulatory Monitoring, Inc.). The activity counts during each PA were calculated as an average while the EE for the PA was determined.

The measurements began approximately 2 hours after breakfast to limit additional variability in EE due to the thermic effect of food. Subjects were permitted only drinking water during the experiment. The selected activities were resting while lying down, watching a video while sitting and standing, line drawing for coloring-in, playing blocks, walking at personal normal speed, stair climbing (up and down) at personal normal speed, performing a ball toss, and running at personal normal speed. These nine activities were chosen as representative activities of daily life, based on our observations in a preliminary study using the activity records of observers of 4- to 6-year-old children in a nursery school. Moreover, the selected activities in the present study were able to be conducted with a facemask and Douglas bag attached to 5- to 6-year-old children.

Initially, subjects were attached to a facemask connected to the Douglas bag and lay resting to determine resting metabolic rate. Oxygen consumption measurements were made for 10 minutes, from 30 to 40 minutes after resting. Subsequently, watching a video while sitting and standing, line drawing for coloring-in, and playing blocks were performed, and respiratory measurements were made during the last 5 minutes of each activity after the steady states were obtained. The walking and playing ball toss activities were performed for 4 minutes, and respiratory measurements were made during the last 2 minutes. Stair climbing (up and down) was performed three times using stairs with 32 steps in one direction; the first up-down was performed to obtain a steady state, and then respiratory measurements were made during the second and third up-downs (for ~2 minutes). Running was performed twice over a distance of 220 m, at an interval time of ~5 seconds between each run. Measurements of EE were made during the second set (for ~2 minutes). These procedures were determined so that the steady states for respiratory measurements could be obtained, based on the results in young children.

Expired air volume was measured with a certified dry gas meter (SHINAGAWA DC-5, Tokyo, Japan). Expired air was sampled and the O_2 and CO_2 concentrations were measured using a gas analyzer (Minato Medical Co., AE-300S, Tokyo, Japan). EE was calculated from O_2 consumption and CO_2 production using Weir's equation (20). Before each measurement, the gas analyzer was calibrated using room air and a certified gas. In addition, PAR was calculated as EE during each activity divided by the predicted basal metabolic rate (BMR) (21–23). The predicted BMR was estimated using the resting EE with an assumption that the thermic effect of food is 10% of BMR. The equation for predicted BMR was: predicted BMR = (resting EE/1.1).

Statistics

Statistical analyses were performed with SPSS version 14.0J for Windows (SPSS, Inc., Chicago, IL). All results are shown as the mean ± standard deviation. The relationship between two variables was evaluated by Pearson's correlation. Linear and non-linear regression models were used to develop equations predicting EE or PAR from accelerometer counts. The non-linear regression equation using accelerations individually was as follows:

$$EE = a + b1 \times (\sqrt{Ax^2 + Ay^2})^{p1} + b2 \times Az^{p2}$$

Ax and Ay: these counts were combined to represent acceleration in the horizontal plane; Az: the vertical acceleration counts; a, b1, b2, p^1, p^2: the coefficients. Non-linear regression equations were developed using one of the vertical, horizontal, or synthetic accelerations.

$$EE = a + b \times A^p$$

Table 1. Physical characteristics of subjects (n = 24)

Variable	Mean ± standard deviation
Age (yrs)	6.1 ± 0.3
Height (cm)	113.4 ± 4.8
Weight (kg)	20.3 ± 3.5
BMI (kg/m^2)	15.8 ± 2.0
Predicted basal metabolic rate (MJ/d)*	3.75 ± 0.59

* Predicted from observed resting energy expenditure in the supine position.

A: vertical, horizontal, or synthetic acceleration.

The percentage difference was calculated as [(predicted value − observed value)/observed value] × 100. A multiple linear stepwise regression model was used to consider the contribution of two accelerometers to EE, and the standard error of estimate (SEE) was calculated. A stepwise discriminant analysis was conducted to discriminate different types of medium-intensity activities using 1) vertical and horizontal acceleration counts or 2) synthetic acceleration counts and the vertical/horizontal counts ratio. The F critical value for entry into the equation was set at 0.05, and the F critical value for removal from the equation was set at 0.10. Using the best model obtained in the above process, thresholds for classifying accelerometer counts into light and moderate-to-vigorous PA were determined. PAR of moderate to vigorous PA was defined as 3 or more. Sensitivity (true positives/true positives + false negatives) and specificity (true negatives/true negatives + false negatives) were calculated. All statistical tests were regarded as significant when the probabilities were <0.05.

Results

The physical characteristics of the subjects are shown in Table 1. Most of the subjects in the present study were of normal weight. The numbers of overweight girls and boys based on BMI (24) were one and two, respectively.

Observed EE, PAR, and accelerometer counts for each activity are shown in Table 2. Correlation coefficients between the predicted and observed EE or PAR were 0.878 to 0.932 for EE and 0.859 to 0.920 for PAR in all activities. Pearson correlation coefficients were not significant for resting and watching a video while standing. In general, horizontal accelerometer counts provided a slightly better EE or PAR assessment than vertical accelerometer counts. There were no gender differences, so the following analyses were performed using the combined data.

Table 2. Observed energy expenditure, physical activity ratio, and accelerometer counts for each activity

Activity	Energy expenditure		Physical activity ratio		Accelerometer counts (per 5 secs)			
	n	(kJ/kg per min)	*n*		*n*	Synthetic	Vertical	Horizontal
Resting while lying down	24	0.140 ± 0.022			24	5 ± 2	1 ± 1	3 ± 2
Watching television while sitting	25	0.144 ± 0.023	22	1.14 ± 0.09	27	8 ± 6	1 ± 2	6 ± 5
Watching television while standing	24	0.147 ± 0.025	21	1.16 ± 0.12	26	13 ± 8	3 ± 3	10 ± 6
Line drawing for coloring-in	24	0.175 ± 0.029	21	1.39 ± 0.14	24	30 ± 13	5 ± 3	25 ± 11
Playing blocks	26	0.190 ± 0.028	23	1.51 ± 0.17	26	67 ± 20	10 ± 5	60 ± 18
Walking	27	0.327 ± 0.055	24	2.60 ± 0.47	27	315 ± 79	213 ± 73	163 ± 44
Stair climbing (up and down)	27	0.513 ± 0.074	24	4.10 ± 0.63	25	356 ± 66	256 ± 55	179 ± 29
Performing a ball toss	27	0.463 ± 0.084	24	3.64 ± 0.82	27	266 ± 59	144 ± 53	173 ± 27
Running	26	0.706 ± 0.104	23	5.58 ± 1.27	26	945 ± 150	780 ± 131	380 ± 75

Figure 1 shows the relationship between PAR and synthetic acceleration counts. When linear and non-linear regression models were applied to the data of all activities, these equations underestimated EE by ~30% or more for stair climbing (up and down) and performing a ball toss. Therefore, linear and non-linear regression equations were calculated for all activities except these two activities, and then evaluated for all activities. Table 3 shows the results of the regression equations for EE and PAR for all activities except these two activities. The linear and non-linear regression equations demonstrated a comparable relationship between the accelerometer counts and EE. In non-linear equations

$$EE = a + b1 \times (\sqrt{Ax^2 + Ay^2})^{p1} + b2 \times Az^{p2} \text{ or}$$

$$EE = a + b \times A^p$$

p Values were near 1. SEE values were slightly better for models with synthetic or "vertical and horizontal" counts than for those with only vertical or horizontal counts.

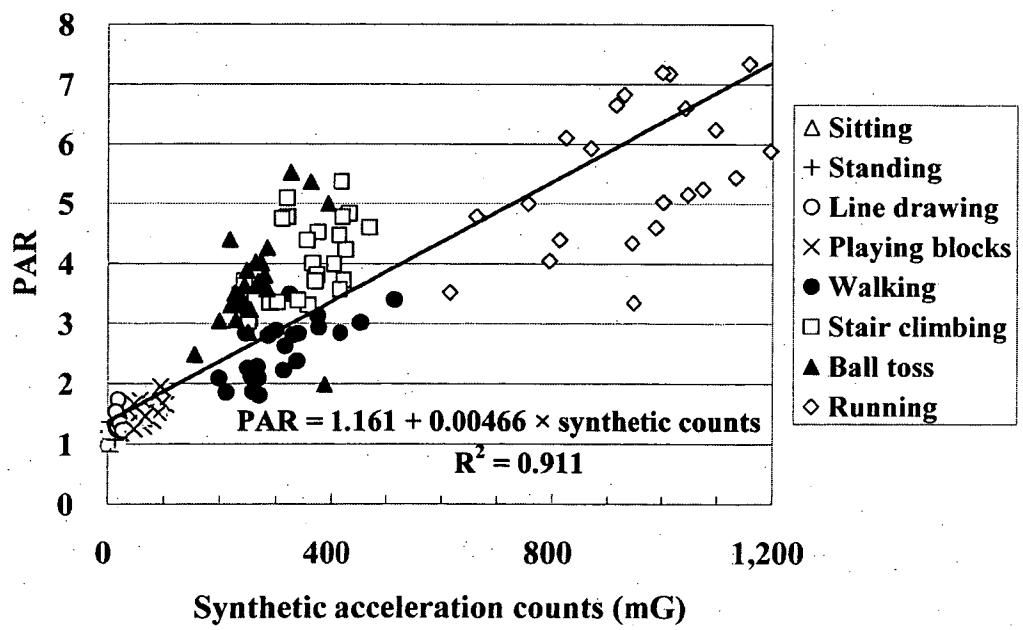

Figure 1: Relationship between predicted PAR and synthetic acceleration counts. The regression line is obtained from all activities except stair climbing and performing a ball toss.

Table 3. Regression equations of energy expenditure and PAR for all activities except stair climbing and performing a ball toss

	Regression equations	SEE (kJ/kg per min)	R^2	p
Energy expenditure (kJ/kg per min)				
Linear				
Synthetic	kJ/kg per min = 0.1453 + 0.000586 × synthetic accelerometer counts	0.0454	0.948	<0.05
Vertical and horizontal	kJ/kg per min = 0.1432 + 0.000369 × vertical accelerometer counts +0.000698 × horizontal accelerometer counts	0.0459	0.947	<0.05
Vertical	kJ/kg per min = 0.1610 + 0.000694 × vertical accelerometer counts	0.0520	0.931	<0.05
Horizontal	kJ/kg per min = 0.1281 + 0.001435 × horizontal accelerometer counts	0.0531	0.928	<0.05
Non-linear				
Synthetic	kJ/kg per min = 0.1383 + 0.00109 × synthetic accelerometer counts$^{0.910}$	0.0450	0.949	<0.05
Vertical and horizontal	kJ/kg per min = 0.1373 + 0.00027 × vertical accelerometer counts$^{1.054}$ + 0.00164 × horizontal accelerometer counts$^{0.850}$	0.0460	0.948	<0.05
Vertical	kJ/kg per min = 0.1506 + 0.00271 × vertical accelerometer counts$^{0.797}$	0.0498	0.938	<0.05
Horizontal	kJ/kg per min = 0.1361 + 0.00080 × horizontal accelerometer counts$^{1.098}$	0.0528	0.930	<0.05
Physical activity ratio				
Linear				
Synthetic	PAR = 1.161 + 0.00466 × synthetic accelerometer counts	0.503	0.911	<0.05
Vertical and horizontal	PAR = 1.117 + 0.00253 × vertical accelerometer counts +0.00638 × horizontal accelerometer counts	0.503	0.911	<0.05
Vertical	PAR = 1.313 + 0.00547 × vertical accelerometer counts	0.555	0.892	<0.05
Horizontal	PAR = 0.992 + 0.01148 × horizontal accelerometer counts	0.539	0.898	<0.05
Non-linear				
Synthetic	PAR = 1.127 + 0.00653 × synthetic accelerometer counts$^{0.951}$	0.504	0.912	<0.05
Vertical and horizontal	PAR = 1.179 + 0.00453 × vertical accelerometer counts$^{0.907}$ + 0.00194 × horizontal accelerometer counts$^{1.200}$	0.505	0.913	<0.05
Vertical	PAR = 1.238 + 0.01650 × vertical accelerometer counts$^{0.836}$	0.547	0.896	<0.05
Horizontal	PAR = 1.116 + 0.00405 × horizontal accelerometer counts$^{1.172}$	0.530	0.902	<0.05

PAR, physical activity ratio; SEE, standard error of the estimate.

Table 4. Percent differences between the predicted and the observed physical activity ratio

	Linear				Non-linear			
		Vertical and horizontal				Vertical and horizontal		
Physical activity ratio	Synthetic		Vertical	Horizontal	Synthetic		Vertical	Horizontal
Total activities	−6.6 ± 19.9	−5.8 ± 19.1	−6.8 ± 23.8	−4.2 ± 19.2	−6.5 ± 19.4	−6.0 ± 19.5	−6.2 ± 21.6	−4.6 ± 19.0
Light	1.4 ± 9.7	0.5 ± 9.4	5.3 ± 14.2	−0.9 ± 13.0	0.4 ± 9.4	1.5 ± 9.8	1.8 ± 12.5	1.7 ± 10.5
Moderate	−19.8 ± 21.5	−16.5 ± 22.5	−25.5 ± 21.9	−9.4 ± 23.7	−18.3 ± 21.9	−18.1 ± 22.1	−19.2 ± 23.8	−14.2 ± 22.5
Vigorous	3.4 ± 22.4	2.5 ± 21.3	3.7 ± 23.4	−0.5 ± 21.0	2.9 ± 22.2	2.3 ± 21.2	3.3 ± 23.1	0.4 ± 21.6
Watching television while sitting	5.5 ± 7.0	2.1 ± 6.8	16.0 ± 8.1	−6.3 ± 6.9	3.3 ± 6.8	5.8 ± 7.0	10.4 ± 7.3	1.5 ± 6.8
Watching television while standing	5.9 ± 9.4	3.1 ± 9.1	15.3 ± 10.7	−3.9 ± 9.0	4.2 ± 9.2	6.1 ± 9.4	10.6 ± 9.9	2.3 ± 9.1
Line drawing for coloring-in	−5.8 ± 8.6	−6.6 ± 8.9	−2.7 ± 8.7	−7.5 ± 10.7	−6.5 ± 8.7	−6.3 ± 8.5	−5.5 ± 8.3	−6.3 ± 9.4
Playing blocks	−0.9 ± 9.2	2.7 ± 9.8	−8.4 ± 9.0	13.7 ± 12.5	−0.2 ± 9.3	−0.3 ± 9.3	−9.5 ± 8.5	8.7 ± 11.3
Walking	2.3 ± 14.7	4.8 ± 18.9	−3.5 ± 16.7	11.3 ± 20.8	4.2 ± 15.0	2.8 ± 18.5	4.6 ± 18.7	5.2 ± 19.6
Stair climbing (up and down)	−29.6 ± 9.8	−27.4 ± 10.3	−32.4 ± 9.3	−23.8 ± 11.4	−28.4 ± 10.0	−28.8 ± 10.2	−26.9 ± 10.0	−27.8 ± 11.0
Performing a ball toss	−32.1 ± 18.9	−26.8 ± 19.7	−40.6 ± 17.8	−15.7 ± 21.6	−30.8 ± 19.2	−28.4 ± 19.4	−35.5 ± 19.2	−20.2 ± 20.7
Running	3.4 ± 22.4	2.5 ± 21.3	3.7 ± 23.4	−0.5 ± 21.0	2.9 ± 22.2	2.3 ± 21.2	3.3 ± 23.1	0.4 ± 21.6

Table 4 shows the percentage differences between the predicted and observed PAR. Similar results were obtained for EE. Linear and non-linear regression equations using vertical acceleration counts overestimated PAR for very low intensity activities and underestimated PAR for stair climbing and ball tossing more than the other models. In general, the other models demonstrated a good prediction of PAR for light to vigorous activities. However, all models underestimated EE and PAR, while stair climbing and ball tossing were underestimated to the same degree, as shown in Table 4. Therefore, an additional analysis was applied to discriminate these activities from walking. In a stepwise discriminant analysis using synthetic acceleration counts and vertical/horizontal acceleration counts ratios as independent variables, only the vertical/horizontal acceleration ratio was entered. As a result, the obtained classification criteria were as follows:

- Walking: vertical/horizontal ratio: 1.19 or more
- The other two activities: vertical/horizontal ratio: <1.19.

Performing a ball toss was correctly classified in 26 of 27 cases, whereas climbing stairs was misclassified as walking in many cases. In the case of a linear model with synthetic acceleration counts, after adjustment of EE using the average percentage difference, the obtained average percentage difference was improved from −32.1 ± 18.9% to −4.7 ± 15.5% for performing a ball toss, while that for climbing stairs did not change (−29.6 ± 9.8% to −29.7 ± 12.9%). In the other cases using the stepwise discriminant analysis with both the vertical and horizontal acceleration counts or for PAR, similar results were obtained (data not shown). The obtained thresholds between light and moderate and moderate and vigorous activities for activities, except activities identified as ball toss or climbing stairs, were 395 mG and 1038 mG, respectively. The sensitivity and specificity to discriminate light and moderate intensity were 77% and 94%, respectively, when using the synthetic acceleration counts and the criterion of vertical/horizontal acceleration counts.

In a subgroup of subjects (n = 15), the correlation coefficient between EE and Actigraph counts for all activities was 0.788 (n = 141, $p < 0.05$), while those between EE and horizontal and vertical acceleration counts by ActivTracer were 0.919 and 0.863, respectively. A stepwise regression analysis of the original data indicated that horizontal accelerometer counts obtained by ActivTracer alone explained 84.3% of EE variance, while Actigraph added only 1.4% of EE variance.

Discussion

This study developed regression equations to predict EE and PAR from three-dimensional accelerometer counts in young children. Because EE correlates closely with body

size, PA must be evaluated after adjustment for body size. For this reason, we examined EE/kg and PAR (EE divided by the BMR) as measurements of PA. Significant correlations were found between synthetic, vertical, and horizontal accelerometer counts and observed EE or PAR for all activities using a linear regression model. Although many studies have utilized accelerometry to assess PA in adults and children (11,12,25), few studies to validate the estimation of PA intensity have been conducted in young children (13,14). Based on correlation coefficients or the other statistics, the relationship between accelerometer counts and observed EE in young children appears better than in previous reports in adolescents and adults (25).

Many previous studies have addressed the question of whether multiaxis accelerometers provide more valid assessments of EE than do single axis accelerometers. Eston et al. (17) showed that three-dimensional accelerometers may provide a better evaluation of children's free-play activities than uniaxial accelerometers. The triaxial or omnidirectional accelerometer-based monitor may capture total body movement better than uniaxial devices (10,12,25).

The degree of underestimation and overestimation by accelerometers depends on the type of activity (12,26,27). In the present study, EE and PAR for most activities were relatively correctly predicted. Moreover, prediction errors obtained using linear and non-linear regression equations were comparable. In non-linear equations, p values were near 1, which indicated that the relationship between EE and acceleration counts was almost linear in all activities except two medium intensity activities, and non-linear equations are not needed, at least for young children. Although this result is inconsistent with that of Chen and Sun (18) and Campbell et al. (28), for adults, it is similar to that of Bouten et al. (29), who showed that the quadratic relationship between EE and the accelerometer output was inferior to the linear relationship in adults. The difference in activities may explain the diverse results. Thus, this result indicates that a non-linear model is not needed for prediction of EE and PAR, at least in young children.

In general, horizontal, synthetic, and combined vertical and horizontal accelerometer counts provided a comparable assessment of predicted EE. However, the prediction error obtained by vertical accelerometer counts using linear regression equations was larger than that obtained by horizontal accelerometer counts for resting while lying down, watching TV while sitting and standing, climbing stairs, and performing a ball toss. Variation of vertical acceleration counts was larger than that of horizontal counts, particularly in higher intensity activities. This may be related to the overestimation of EE for low intensity activities. EE of low intensity activities is not high, but these activities are likely observed very frequently. Therefore, the prediction errors obtained by vertical acceleration counts may cause a significant problem. Thus, the present study indicates that the prediction of EE and PAR using vertical acceleration counts is inferior to prediction using horizontal counts in young children. On the other hand, the prediction errors for playing with blocks and walking that were obtained by horizontal acceleration counts were slightly larger than those obtained by synthetic acceleration counts, in addition to slightly higher SEE values of linear and non-linear regression models that did not include ball toss and stairs climbing. Thus, the synthetic acceleration counts may be slightly better to use, and the linear equation using synthetic counts is recommended, in combination with a criterion of the vertical/horizontal counts ratio for better discrimination of medium intensity activities.

The most significant problem we found was the underestimation of EE for climbing stairs and ball tossing, due to the different balance of vertical and horizontal acceleration counts for these activities and the different relationship of the acceleration counts with EE. While performing these activities, horizontal acceleration counts increase compared with vertical acceleration counts. Increases in horizontal acceleration are associated much more with increases in EE than are increases in vertical acceleration. Therefore, based on the results from discriminant analysis, the large prediction error for performing a ball toss could be reduced. Moreover, similar types of activities, including lifestyle activities and playing, might be adjusted using the classification functions. On the other hand, the large underestimation of EE for climbing stairs would persist. The time for this activity is likely short, probably several minutes a day, although this is a representative activity in daily life. For example, if climbing stairs costs 16 kJ (4 kcal)/min and the time spent in this activity is 5 minutes, then the predicted underestimation of EE is ~80 kJ (20 kcal). Thus, the obtained prediction error would result in a small prediction error for total EE. Therefore, a combination of vertical and horizontal acceleration counts may be needed for discrimination of medium intensity activities and a slight improvement in EE or PAR prediction, although synthetic or even horizontal acceleration counts alone can predict EE for most activities.

In some previous studies, subjects were asked to perform activities at a set pace. Puyau et al. (30) pointed out that treadmill walking/running has the advantage of being precisely controlled and reproducible: it does not reflect all torsional accelerations associated with free-living activities. R^2 values are actually higher while walking and running on a treadmill (30,31) than in lifestyle conditions (9,17,27,32). Fewer researchers have allowed subjects to perform activities at a self-selected pace. It is likely that a self-selected pace more precisely reflects actual EE or the accelerometer counts of young children doing the activities in the real world, as children do not perform activities at predetermined speeds. Therefore, each activity in the present study was performed at a self-selected pace, except for the ball toss, which was conducted with a researcher.

For some applications, categorizing levels of PA in children and adults is of interest (9,12,30). The threshold counts for each activity can be calculated using an equation presented in the present study and then used to classify each PA into light, moderate, or vigorous activity for young children. Although it is difficult to compare the sensitivity and specificity values between studies because types of PA are different, the obtained values, particularly specificity, are good.

Previous studies have shown that waist-worn accelerometers underestimate the EE of free-living individuals (10). One of the reasons for underestimation may be a failure to detect the additional EE resulting from other kinds of movements. Thus, in the present study, the wrist-worn accelerometer was used to detect simultaneous upper body movement measurements, and the combined model further improved the accuracy of EE prediction. The combined quantification of trunk movement with an accelerometer on the waist and upper limb movement with an accelerometer on the wrist is a unique approach, as previous papers typically measured trunk movement only with a uniaxial accelerometer on the waist (25). Melanson and Freedson (33) validated Computer Science and Applications, Inc. monitors on the ankle, hip, and wrist in adults on a treadmill. The contributions of the uniaxial accelerometers on the hip and wrist were comparable for overall and each intensity PA. However, our results showed that waist-worn accelerometer counts were superior to wrist-worn accelerometer counts. A stepwise regression analysis in the present study indicated that the wrist-worn accelerometer counts explained just 1.4% of the variance in EE. Our data revealed that waist-worn accelerometer counts were highly correlated with EE and that wrist-worn accelerometer counts added minor contributions. The different results between Melanson and Freedson's study (33) and our study may be due to the types of performed PA (on treadmill vs. various kinds of PA), in addition to the different age groups studied (adults vs. young children). The degree to which the wrist acceleration counts explain the variance in EE depends on the chosen activities. Moreover, it should be carefully noted that different accelerometers were used to detect movements of the waist and wrist. In general, however, it is likely that the detection of wrist movements does not contribute significantly to more accurate predictions of PAR and EE.

The sample size of this study was not large. However, the high correlation coefficients found between acceleration counts and EE or PAR, and mean and standard deviation values of % differences of prediction in various activities, suggest that the findings of the present study are robust. The more important limitation of the present study may be that there are relatively small numbers of data points, in particular between 500 and 800 counts of synthetic acceleration. In addition, only running was examined as a vigorous activity. This selection of a single activity could have led to less robust results for predictions of moderate to vigorous activities.

The triaxial accelerometer used in this study provided valid measures of young children's EE and PAR and can be used to discriminate light, moderate, and vigorous levels of PA. Our results also suggest that even a linear model contributes to the assessment of daily EE when horizontal or synthetic acceleration counts combined with the vertical/horizontal counts ratio are used for better discrimination of medium intensity activities. Future studies are required to further validate accurate predictions of EE and PAR under free-living conditions. Our results will make it possible to objectively and accurately assess PA in young children and thereby contribute to the prevention of childhood obesity.

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References

1. **Matsushita Y, Yoshiike N, Kaneda F, Yoshita K, Takimoto H.** Trends in childhood obesity in Japan over the last 25 years from the national nutrition survey. *Obes Res.* 2004;12:205–14.
2. **Bhargava SK. Sachdev HS, Fall CH, et al.** Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. *N Engl J Med.* 2004;350:865–75.
3. **Abbott RA, Davies PS.** Habitual physical activity and physical activity intensity: their relation to body composition in 5.0–10.5-y-old children. *Eur J Clin Nutr.* 2004;58:285–91.
4. **Trost SG, Sirard JR, Dowda M, Pfeiffer KA, Pate RR.** Physical activity in overweight and nonoverweight preschool children. *Int J Obes Relat Metab Disord.* 2003;27:834–9.
5. **Levine JA.** Non-exercise activity thermogenesis (NEAT). *Nutr Rev.* 2004;62(suppl):82–97.
6. **Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C.** Determinants of 24-hour energy expenditure in man: methods and results using a respiratory chamber. *J Clin Invest.* 1986;78:1568–78.
7. **Levine JA, Eberhardt NL, Jensen MD.** Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science.* 1999;283:212–4.
8. **Zurlo F, Ferraro RT, Fontvielle AM, Rising R, Bogardus C, Ravussin E.** Spontaneous physical activity and obesity: cross-sectional and longitudinal studies in Pima Indians. *Am J Physiol.* 1992;263:E296–300.
9. **Treuth MS, Schmitz K, Catellier DJ, et al.** Defining accelerometer thresholds for activity intensities in adolescent girls. *Med Sci Sports Exerc.* 2004;36:1259–66.

10. **Chen KY, Bassett DR Jr.** The technology of accelerometry-based activity monitors: current and future. *Med Sci Sports Exerc.* 2005;37(suppl):490–500.
11. **Freedson P, Pober D, Janz KF.** Calibration of accelerometer output for children. *Med Sci Sports Exerc.* 2005;37(suppl): 523–30.
12. **Matthew CE.** Calibration of accelerometer output for adults. *Med Sci Sports Exerc.* 2005;37(suppl):512–22.
13. **Reilly JJ, Coyle J, Kelly L, Burke G, Grant S, Paton JY.** An objective method for measurement of sedentary behavior in 3- to 4-year olds. *Obes Res.* 2003;11:1155–8.
14. **Pfeiffer KA, McIver KL, Dowda M, Almeida MJ, Pate RR.** Validation and calibration of the Actical accelerometer in preschool children. *Med Sci Sports Exerc.* 2006;38:152–7.
15. **Reilly JJ, Kelly LA, Montgomery C, et al.** Validation of Actigraph accelerometer estimates of total energy expenditure in young children. *Int J Pediatr Obes.* 2006;1:161–7.
16. **Hoos MB, Plasqui G, Gerver WJ, Westerterp KR.** Physical activity level measured by doubly labeled water and accelerometry in children. *Eur J Appl Physiol.* 2003;89:624–6.
17. **Eston RG, Rowlands AV, Ingledew DK.** Validity of heart rate, pedometry, and accelerometry for predicting the energy cost of children's activities. *J Appl Physiol.* 1998;84:362–71.
18. **Chen KY, Sun M.** Improving energy expenditure estimation by using a triaxial accelerometer. *J Appl Physiol.* 1997;83: 2112–22.
19. **Iwashita S, Takeno Y, Okazaki K, et al.** Triaxial accelerometry to evaluate walking efficiency in older subjects. *Med Sci Sports Exerc.* 2003;35:1766–72.
20. **Weir JB.** New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol.* 1949;109: 1–9.
21. **Food and Agriculture Organization of the United Nations/ World Health Organization/United Nations University.** Human Energy Requirements: Report of a Joint FAO/WHO/ UNU Expert Consultation, FAO Food and Nutrition Technical Report [Series 1]. Rome, October 17–24, 2004.
22. **Institute of Medicine of the National Academies.** *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids.* Washington, DC: National Academies Press; 2005, pp. 880–935.
23. **Puyau MR, Adolph AL, Vohra FA, Butte NF.** Validation and calibration of physical activity monitors in children. *Obes Res.* 2002;10:150–7.
24. **Cole TJ, Bellizzi MC, Flegal KM, Dietz WH.** Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ.* 2000;320:1240–3.
25. **Trost SG, McIver KL, Pate RR.** Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc.* 2005;37(suppl):531–43.
26. **Bray MS, Wong WW, Morrow JR Jr, Butte NF, Pivarnik JM.** Caltrac versus calorimeter determination of 24-h energy expenditure in female children and adolescents. *Med Sci Sports Exerc.* 1994;26:1524–30.
27. **Schmitz KH, Treuth M, Hannan P, et al.** Predicting energy expenditure from accelerometry counts in adolescent girls. *Med Sci Sports Exerc.* 2005;37:155–61.
28. **Campbell KL, Crocker PR, McKenzie DC.** Field evaluation of energy expenditure in women using Tritrac accelerometers. *Med Sci Sports Exerc.* 2002;34:1667–74.
29. **Bouten CV, Westerterp KR, Verduin M, Janssen JD.** Assessment of energy expenditure for physical activity using a triaxial accelerometer. *Med Sci Sports Exerc.* 1994;26:1516–23.
30. **Puyau MR, Adolph AL, Vohra FA, Zakeri I, Butte NF.** Prediction of activity energy expenditure using accelerometers in children. *Med Sci Sports Exerc.* 2004;36: 1625–31.
31. **Trost SG, Ward DS, Moorehead SM, Watson PD, Riner W, Burke JR.** Validity of the computer science and applications (CSA) activity monitor in children. *Med Sci Sports Exerc.* 1998;30:629–33.
32. **Eisenmann JC, Strath SJ, Shadrick D, Rigsby P, Hirsch N, Jacobson L.** Validity of uniaxial accelerometry during activities of daily living in children. *Eur J Appl Physiol.* 2004;91: 259–63.
33. **Melanson EL Jr, Freedson PS.** Validity of the Computer Science and Applications, Inc. (CSA) activity monitor. *Med Sci Sports Exerc.* 1995;27:934–40.

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ORIGINAL ARTICLE

Interindividual variability in sleeping metabolic rate in Japanese subjects

AA Ganpule[1,2], S Tanaka[1], K Ishikawa-Takata[1] and I Tabata[1]

[1]*Health Promotion and Exercise Program, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjuku-ku, Tokyo, Japan and* [2]*Diabetes Unit, KEM Hospital and Research Centre, Pune, Maharashtra, India*

Introduction: Basal metabolic rate (BMR) or sleeping metabolic rate (SMR) is the largest component of total energy expenditure (EE). An accurate prediction of BMR or SMR is needed to accurately predict total EE or physical activity EE for each individual. However, large variability in BMR and SMR has been reported.
Objectives: This study was designed to develop prediction equations using body size measurements for the estimation of both SMR and BMR and to compare the prediction errors with those in previous reports.
Methods: We measured body size, height, weight and body composition (fat mass and fat-free mass) from skinfold thickness in adult Japanese men ($n=71$) and women ($n=66$). SMR was determined as the sum of EE during 8 h of sleep (SMR-8h) and minimum EE during 3 consecutive hours of sleep (SMR-3h) measured using two open-circuit indirect human calorimeters. BMR was determined using a human calorimeter or a mask and Douglas bag.
Results: The study population ranged widely in age. The SMR/BMR ratio was 1.01 ± 0.09 (range 0.82–1.42) for SMR-8h and 0.94 ± 0.07 (range 0.77–1.23) for SMR-3h. The prediction equations for SMR accounted for a 3–5% larger variance with 2–3% smaller standard error of estimate (SEE) than the prediction equations for BMR.
Discussion: SMR can be predicted more accurately than previously reported, which indicates that SMR interindividual variability is smaller than expected, at least for Japanese subjects. The prediction equations for SMR are preferable to those for BMR because the former exhibits a smaller prediction error than the latter.
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Keywords: sleeping metabolic rate; basal metabolic rate; prediction; variability; body size; Japanese

Introduction

There are three principal components of energy expenditure (EE) in humans: basal metabolic rate (BMR), thermic effect of food and EE of physical activity. The FAO/WHO/UNU expert panel (1985) adopted the principle of expressing the energy requirements of adults in terms of multiples of BMR. Thus, BMR is used to estimate 24-h EE and physical activity level (24-h EE divided by BMR).

Sleeping metabolic rate (SMR), similar to BMR, is approximately 60% of the total EE. Although both are measured in the supine position, SMR is measured during sleep whereas BMR is measured in the postabsorptive state when the subject is awake. They thus involve slightly different thermogenic processes. EE is lower during sleep than under BMR conditions (Garby *et al.*, 1987; Goldberg *et al.*, 1988; Seale and Conway, 1999; Zhang *et al.*, 2002), probably due to the absence of arousal and maybe to less body movement. Moreover, EE gradually increases after awakening (Kashiwazaki, 1990). Therefore, SMR, not BMR, should be the minimum EE for humans. SMR may be measured more accurately than BMR as it is measured during sleep when there is no arousal. Also, SMR can be measured using equipment (e.g., a human calorimeter) that gives highly reproducible and accurate results (Murgatroyd *et al.*, 1993).

Many equations have been developed to estimate BMR or SMR from body size measurements (Cunningham, 1991; Frankenfield *et al.*, 2005), which can be helpful when actual metabolic measurements are not available. Their accuracy and applicability to specific ethnic groups must be considered. The body size of Japanese differs from that of other ethnicities (Popkin and Doak, 1998; WHO, 1998). Most

Correspondence: Dr S Tanaka, Health Promotion and Exercise Program, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8636, Japan.
E-mail: tanakas@nih.go.jp
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equations currently available apply to Caucasians (Frankenfield *et al.*, 2005). Studies have found that they are not applicable to nonwhite groups (Liu *et al.*, 1995; Case *et al.*, 1997; Yamamura and Kashiwazaki, 2002).

We studied the association of SMR and BMR with body size and composition (anthropometry) in adult Japanese men and women who ranged widely in age. The purpose of this study was to develop simple-to-use prediction equations for both SMR and BMR and to compare the variability in prediction errors after adjustment for body size and composition with those found in previous studies.

Methods

Subjects

The data used for the current analysis were collected from different experimental studies that followed a similar methodology. All 137 apparently healthy Japanese subjects (71 male and 66 female subjects; $\geqslant$20 years) residing in the Tokyo metropolitan area were volunteers approached through personal contact, internet communication or poster advertisement. None had diseases that might affect metabolic rates. The study protocol was explained in advance to the subjects, who were instructed to eat a normal diet and do normal, but not vigorous, physical activity beginning 1 day before monitoring.

All studies were carried out in the National Institute of Health and Nutrition (Tokyo). The study protocol was approved by the Ethics Committee of the National Institute of Health and Nutrition. All of the subjects signed an informed consent form.

Study protocol

The indirect human calorimeter (IHC) data for SMR and BMR were obtained from several studies conducted at the National Institute of Health and Nutrition in Japan. Subjects entered the IHC at 1800–1900 on the study day, had dinner at 1830 or 1900, went to bed at 2300 after sedentary activities and slept until 0700 the following morning. Each subject was provided a standardized dinner to meet EE during the chamber stay using predicted BMR and an assumed physical activity level of 1.5. Energy intake at dinner was set as a third of the total energy. BMR was measured in the supine position and in the postabsorptive state (about 12 h after the last meal).

Measurements

SMR was defined as the average EE of all EEs at 15-min intervals between 2300 and 0700 over an 8 h of sleep (SMR-8h) and the minimum EE during 3 consecutive hours of sleep (SMR-3h) (Schrauwen *et al.*, 1997; Westerterp-Plantenga *et al.*, 2002). Two open-circuit IHCs were used to evaluate SMR. Details of the IHC are shown elsewhere (Futami *et al.*, 2003). In brief, the two respiratory chambers were airtight rooms (20 000 and 15 000 l, respectively) containing a bed, desk, chair, TV, etc. The temperature and relative humidity in the room were controlled at 25°C and 55%, respectively. The O_2 and CO_2 concentrations of the air supply and exhaust were measured by mass spectrometry. For each experiment, a gas analyser (ARCO SYSTEM Inc., ARCO-1000A-CH, Kashiwa, Japan) was initially calibrated using a certified gas mixture and atmospheric air. The flow rate exhausted from the chamber was measured by a pneumotachograph (ARCO SYSTEM Inc., FLB1, Kashiwa, Japan). The flow meter was calibrated before each measurement, and the flow rate was fixed in both chambers. VO_2 and VCO_2 were determined from the flow rate exhausted from the chamber and the concentrations of the inlet and outlet air of the chamber, respectively (Futami *et al.*, 2003). The values of VO_2 and VCO_2 were expressed under standard temperature, pressure and dry air conditions. EE was estimated from VO_2 and VCO_2 using Weir's equation (Weir, 1949). The accuracy and precision of the IHC for measuring EE, as evaluated by the alcohol combustion test, were $99.2\pm0.7\%$ in 6 h and $99.2\pm3.0\%$ in 30 min, respectively.

BMR was determined in the postabsorptive state (12 h or more after the last meal) and in a supine position. The measurement was performed using a human calorimeter from 0715 to 0800, or using a mask and Douglas bag for 20 min with a minute of intermission. The detailed protocol is described in Yamamura *et al.* (2003). To examine whether slightly different conditions caused a significant difference in the observed BMR, analysis of covariance with BMR as the dependent variable and gender, age, stature and body weight as covariates was employed. No significant effect of the measurement conditions was observed.

Anthropometric measurements. Body weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm using a stadiometer. Measurements were performed in light clothing and underwear. The light clothing was weighed and subtracted from the total to obtain body weight with minimal clothing (underwear). Triceps, subscapular and umbilicus skinfold thicknesses were measured by two trained observers using a standardized protocol and a Holtain caliper (Holtain Ltd, Crosswell, Crymych, Dyfed, UK). There were no significant inter-observer differences in any of the measurements. BMI was calculated as weight (kg)/height (m^2).

Tahara's equations (2002) for Japanese adults were used to predict body density from the sum of skinfold thickness measurements, and the Brozek equation (1963) was used to estimate body fat percentage (% FAT) from the predicted body density.

Statistics. Results are presented as the mean$\pm$standard deviation (s.d.). The relationship between SMR, BMR and body size and composition measurements was examined using Pearson's correlation. Age and sex were adjusted for in

partial correlation analysis. Stepwise multiple regression analysis was done to examine the predictors of metabolic rate. Statistical significance was set at $P<0.05$ for all predictors. Gender was treated as a binomial variable (1 for male subjects, 2 for female subjects). The % difference in prediction error was calculated as the residual divided by the measured value for each subject. Statistical analyses were performed using SPSS for Windows (version 11.0; SPSS Inc., Chicago, IL, USA). Statistical significance was set at $P< 0.05$.

Results

The study population consisted of adult Japanese men ($n=71$) and women ($n=66$) of a wide range of ages (Table 1). The average height and weight of subjects in each age and gender group were similar to national standard heights and weights (The National Nutrition Survey in Japan, 2002). Although the age range was wide, variability in body size and composition was small.

BMR and SMR were highly correlated (Figure 1). The SMR/BMR ratio was 1.01 ± 0.09 (range 0.82–1.42) for SMR-8h and 0.94 ± 0.07 (range 0.77–1.23) for SMR-3h, which was not gender sensitive. On the other hand, the ratios (SMR-8h/BMR and SMR-3h/BMR) were weakly correlated with age ($r=0.38$ and 0.36, respectively). SMR-3h was significantly lower than SMR-8h and BMR, whereas SMR-8h was not significantly different from BMR. In most cases, SMR-3h was observed during the latter part of the sleep cycle (2300–0700), around 0300–0600. The phase of the menstrual cycle did not affect BMR and SMR in women (data not shown).

Metabolic rate was strongly correlated with body size and body composition irrespective of age and gender. Metabolic rate was positively correlated with body weight ($r=0.83$, 0.85 and 0.79 for SMR-8h, SMR-3h and BMR, respectively). The strongest correlation of metabolic rate was with fat-free mass ($r=0.85$, 0.87 and 0.79, for SMR-8h, SMR-3h and BMR, respectively) after adjustment for age and gender.

Table 1 Basic characteristics, body size, composition and metabolic rates

	Males (71) *Mean±s.d.*	*Females (66)* *Mean±s.d.*
Age (years)	36±16	37±16
Stature (cm)	170.5±7.1	159.1±5.6
Weight (kg)	68.3±11.5	54.0±9.2
BMI (kg/m^2)	23.4±3.1	21.4±3.3
Fat mass (kg)	12.9±6.4	14.2±5.2
Fat-free mass (kg)	55.3±7.4	39.8±5.1
SMR-8h (MJ/day)	6.376±0.749	4.929±0.607
SMR-3h (MJ/day)	5.954±0.736	4.552±0.548
BMR (MJ/day)	6.368±0.916	4.837±0.569

Abbreviations: BMI, body mass index; BMR, basal metabolic rate; s.d., standard deviation; SMR, sleeping metabolic rate.

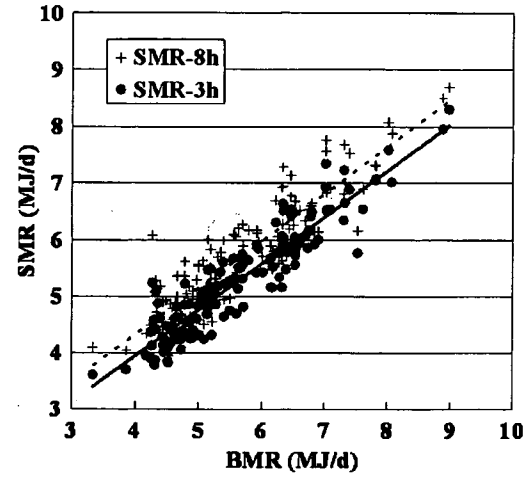

Figure 1 Relationship between SMR and BMR. Regression lines between SMR-8h (dashed line) or SMR-3h (straight line) and BMR.

Table 2 Stepwise regression of BMR, SMR-8h and SMR-3h with body size measurements

Outcome	*Predictors*	*Un std coefficients*		*Change in % R^2*	*SEE (MJ/day)*
		B	*Standard error*		
SMR-8h	Constant	1.2142	1.1912		
	Weight	0.0498***	0.0038	75.9	0.494
	Gender	−0.5590***	0.0967	8.2	0.402
	Stature	0.0146*	0.0071	1.1	0.389
	Age	−0.0046*	0.0021	0.4	0.385
	Total			85.6	
SMR-3h	Constant	0.1004	1.0439		0.000
	Weight	0.0469***	0.0033	74.9	0.456
	Gender	−0.4925***	0.0845	9.6	0.368
	Stature	0.0197**	0.0063	2.5	0.343
	Age	−0.0050**	0.0021	0.8	0.339
	Total			87.8	
BMR	(Constant)	0.1238	1.4054		0.000
	Weight	0.0481***	0.0046	65.4	0.619
	Stature	0.0234**	0.0084	11.8	0.510
	Age	−0.0138***	0.0025	2.9	0.485
	Gender	−0.5473***	0.1138	3.3	0.448
	Total			83.4	

Abbreviations: BMR, basal metabolic rate; SMR, sleeping metabolic rate; SEE, standard error of estimate; Un std coefficients, unstandardized coefficients. *$P<0.05$; **$P<0.01$; ***$P<0.001$.

A stepwise multiple regression analysis of predictors of metabolic rate (including height, weight, age and gender) revealed that weight was the strongest predictor of metabolic rate (Table 2). Age, gender and height were additional predictors. These models accounted for 85.6% of the variance in SMR-8h (prediction error 6.7%) and 87.8% of the variance in SMR-3h (prediction error 6.2%). Adjustment for the predictors reduced the variance from 0.996 MJ/day to 0.385 MJ/day (238–92 kcal/day) in SMR-8h and 0.958–0.339 MJ/day (229–81 kcal/day) in SMR-3h. Adjustment for all predictors accounted for 83.4% of the variance in BMR

Table 3 Stepwise regression of BMR, SMR-8h and SMR-3h with body composition measurements

Outcome	*Predictors*	*Un std coefficients*		*Change in % R^2*	*SEE (MJ/day)*
		B	*Standard error*		
SMR-8h	Constant	1.8175	0.3678		
	Fat-free mass	0.0812***	0.0054	86.3	0.368
	Fat mass	0.0213***	0.0067	0.9	0.360
	Gender	−0.2125*	0.1063	0.4	0.356
				87.6	
SMR-3h	Constant	0.8878	0.1372		
	Fat-free mass	0.0874***	0.0029	88.3	0.331
	Fat mass	0.0151**	0.0046	0.8	0.318
				89.1	
BMR	Constant	2.3958	0.5602		
	Fat-free mass	0.0787***	0.0079	82.2	0.460
	Age	−0.0109***	0.0029	0.6	0.452
	Fat mass	0.0268**	0.0088	0.5	0.448
	Gender	−0.3314*	0.1477	0.6	0.439
				84.0	

Abbreviations: BMR, basal metabolic rate; SMR, sleeping metabolic rate; SEE, standard error of estimate; Un std coefficients, unstandardized coefficients. *$P<0.05$; **$P<0.01$; ***$P<0.001$.

(prediction error 7.3%) and reduced the variance from 1.084 MJ/day to 0.448 MJ/day (259–107 kcal/day).

Fat-free mass was the strongest predictor of metabolic rate in stepwise multiple regression analysis using metabolic rate as the independent variable and fat mass, fat-free mass, age and gender as the dependent variables (Table 3). Fat-free mass, fat mass and gender accounted for 86.7% of the total variation in SMR-8h (difference for prediction error 6.2%). Adjustment for the predictors reduced variance in SMR-8h from 0.996 MJ/day to 0.356 MJ/day (238–85 kcal/day). For SMR-3h, fat-free mass and fat mass accounted for 89.1% of the variation (difference in prediction error 5.9%) and adjustment for the predictors reduced variance in SMR-3h from 0.958 to 0.318 MJ/day (229–76 kcal/day). Adjustment for fat-free mass, fat mass, age and gender predicted 84.0% of the variance in BMR (difference in prediction error 7.6%) and reduced the variance from 1.084 MJ/day to 0.439 MJ/day (259–105 kcal/day).

The mean difference between predicted BMR using FAO/WHO/UNU equations and observed BMR was $+0.519\pm0.494$ MJ/day ($+0.565\pm0.556$ MJ/day for male subjects and $+0.469\pm0.414$ MJ/day for female subjects).

Discussion

This study was performed to develop predictive equations for SMR-3h and SMR-8h that predict SMR with much lower prediction errors than previously reported (Tataranni and Ravussin, 1995; Weyer *et al.*, 1999; Nielsen *et al.*, 2000; Henry, 2005). The findings indicate that interindividual variability in SMR after adjustment for body size or body composition is much smaller than expected, at least in healthy Japanese adults.

BMR and SMR are measured in a similar manner, but BMR is slightly larger as SMR is measured only in part during sleep (SMR/BMR, 0.88–0.95) (Garby *et al.*, 1987; Goldberg *et al.*, 1988; Seale and Conway, 1999; Zhang *et al.*, 2002; Kumahara *et al.*, 2004). The SMR-3h/BMR ratio in this study was in good agreement with those previous values, whereas SMR-8h was found to be slightly higher than the BMR. In the first hour of sleep, the metabolic rate was higher than BMR by an average of 20%, probably due to sleeping status and diet-induced thermogenesis. In addition, the metabolic rate during periods when body movements were observed using a radar system was excluded from the SMR calculation in some of the previous studies. Thus, evaluation methods appear to affect the slight discrepancy of the ratio between studies. BMR is measured in the morning hours when heat production increases after awakening (Garby *et al.*, 1987) and causes gradual increases in resting EE (Kashiwazaki, 1990). BMR and SMR (although measured in a similar manner) thus might represent different thermogenic processes.

Metabolic rates can be predicted using equations that involve body size and composition measurements. Many prediction equations are available for estimating metabolic rates, but their applicability to other ethnic groups is uncertain (Hayter and Henry 1993; Frankenfield *et al.*, 2005). In the present study, FAO/WHO/UNU equations overestimated BMR by more than 0.45 MJ/day on average, with a prediction error comparable to previously published reports.

We developed two types of equations using stepwise regression to predict metabolic rates in adult Japanese subjects ranging widely in age. The first equation uses weight and height, which are simple body size measurements that can be easily obtained in clinical as well as epidemiological settings. In this equation, body weight accounted for 65–75% of the variation in metabolic rates. Age, gender and height were additional predictors. The second equation uses fat-free mass, which is a more valid predictor than body mass of resting metabolic rate (RMR) because it is associated with a much higher rate of resting EE (Elia, 1992). Sophisticated methods can be used to provide more insight into the metabolically active components of fat-free mass, such as the liver, heart and kidney, in relation to energy metabolism (Muller *et al.*, 2002), but their applicability to epidemiological studies is restricted. Anthropometry, a relatively simpler technique used to predict RMR, has an accuracy rate similar to that of more complicated techniques (Van der Ploeg *et al.*, 2001). In our equations, fat-free mass (measured using skinfold thickness) accounted for 84–89% of the variation in SMR, which is better than previously reported (Ravussin *et al.*, 1990; Toubro *et al.*, 1996; Weyer *et al.*, 1999). In addition, results for the BMR equations are in good agreement with those of others (Cunningham, 1991; Ravussin and Bogardus, 1989; Tataranni and Ravussin, 1995). After fat-free mass, fat mass predicted metabolic rate, but accounted for less than 1% of variation in SMR. The relationship of age and gender with

metabolic rates disappeared after adjustment for fat mass and fat-free mass, except for SMR-8h. Similar results have been reported showing that the effect of age and gender on metabolic rates is mainly due to fat-free mass (Ravussin *et al.*, 1986; Astrup *et al.*, 1990; Cunningham, 1991; Nelson *et al.*, 1992) and fat mass (Dionne *et al.*, 1999).

Relatively smaller variations in body size and composition are observed in Japanese than in Caucasians or African Americans. Although the subjects varied widely in age (20–50 years), the variance (s.d.) in their weights were 11.5 kg (male subjects) and 9.2 kg (female subjects). These variations were much lower than reported in other studies. For example, although Weyer *et al.* (1999) worked with subjects with a smaller age range than in this study, the s.d. values of their weights were 25.9 kg (male subjects) and 26.3 kg (female subjects). A larger percentage of explained variance in metabolic rate calculated from an equation can be due to large variance in the body size of the study subjects. The percentage of explained variance thus does not necessarily indicate better prediction. Therefore, the two measures used to compare prediction errors were standard error of estimate (SEE) and percentage difference in the residuals. The SEE of both equations was lower than that reported by other studies, even those using sophisticated techniques.

The smaller prediction error indicates that variation in minimum metabolic rate (measured as SMR or BMR after adjusting for body size or composition) may be smaller than previously indicated. In general, the reported interindividual CV is about 8–13% (Shetty *et al.*, 1996, Muller *et al.*, 2004). For our SMR equations, the SEE was much lower than the SEE reported by Weyer *et al.* (1999), which was based on fat-free mass measured using sophisticated methods. In Weyer's equation, age, impaired glucose tolerance and waist-to-thigh ratio were additional predictors. In the equation, the SEE was 0.611 MJ/day (146 kcal/day) and fat-free mass accounted for 0.808 MJ/day (193 kcal/day) of the total 1.347 MJ/day (322 kcal/day) variance. Similarly, the new Oxford equations (Henry, 2005) for prediction of BMR in tropical regions have reported an SEE of 0.5–0.7 MJ/day in age group and gender-specific equations, which is higher than our SMR equations. Tataranni and Ravussin (1995) also reported a higher SEE (0.703 MJ/day (168 kcal/day)) in BMR prediction equations, with fat-free mass accounting for 0.268 MJ/day (64 kcal/day) of the total 1.318 MJ/day (315 kcal/day) variance. A similarly high SEE of 0.753 MJ/day (180 kcal/day) in men and 0.628 MJ/day (150 kcal/day) in women was reported by Nielsen *et al.* (2000), who developed equations that used dual-energy X-ray absorptiometry (DXA) measurements of fat-free mass. Bader *et al.* (2005) reported that s.d. of BMR adjusted for fat-free mass was from 0.81 to 0.92 MJ/day. Thus, most researchers have indicated larger interindividual variability in SMR or BMR compared to the SEE in the present study, particularly for SMR. Although the reasons are unclear, ethnicity may be an explanation. In addition, measurement of SMR using a human calorimeter is very accurate, particularly prolonged measurements (99.2±0.7% in 6 h), and may have contributed to the lower prediction error in our study.

One of the limitations of the present study was that a different method was used for measurement of BMR. This might partially explain why the SEE was greater for the BMR equation than the SMR equation. However, the study by Soares *et al.* (1989) showed that the energy outputs were comparable using different methods (e.g., whole-body indirect calorimetry) to measure metabolic rates. In the present study, the method used for measurement of BMR was also found to have no statistically significant effect on the metabolic rates and s.d. values for the difference between different BMR measurement groups were within 1%. Another limitation was the method of determining body composition using skinfold thicknesses. More sophisticated measures of body composition would have produced better results.

In conclusion, our equations, which use body size and body composition, are useful for estimating metabolic rates in the Japanese population. The prediction error of SMR was smaller than reported for BMR or SMR, which indicates small interindividual variability in SMR after adjustment for body size or body composition. When metabolic rates are needed to estimate 24 h EE or physical activity level, prediction equations of SMR (or, if necessary, the SMR/BMR ratio) should be used rather than BMR because SMR correlates very well with BMR and the SMR/BMR ratio is fairly constant.

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References

Astrup A, Astrup A, Thorbek G, Lind J, Isaksson B (1990). Prediction of 24-h energy expenditure and its components from physical characteristics and body composition in normal-weight humans. *Am J Clin Nutr* **52**, 777–783.

Bader N, Bosy-Westphal A, Dilba B, Muller MJ (2005). Intra- and interindividual variability of resting energy expenditure in healthy male subjects – biological and methodological variability of resting energy expenditure. *Br J Nutr* **94**, 843–849.

Brozek J, Grande F, Anderson JT, Keys A (1963). Densitometric analysis of body composition: revision of some quantitative assumptions. *Ann NY Acad Sci* **110**, 113–140.

Case KO, Brahler CJ, Heiss C (1997). Resting energy expenditures in Asian women measured by indirect calorimetry are lower than

expenditures calculated from prediction equations. *J Am Diet Assoc* **97**, 1288–1292.

Cunningham JJ (1991). Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. *Am J Clin Nutr* **54**, 963–969.

Dionne I, Despres JP, Bouchard C, Tremblay A (1999). Gender difference in the effect of body composition on energy metabolism. *Int J Obes Relat Metab Disord* **23**, 312–319.

Elia M (1992). Organ tissue contribution to metabolic rate. In: Kinney JM, Tucker HN (eds.) *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press, 61–79.

FAO/WHO/UNU (1985). Energy and protein requirements. *Report of a joint FAO/WHO/UNU expert consultation* WHO Tech Rep Ser **724**, 1–206.

Frankenfield D, Roth-Yousey L, Compher C (2005). Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. *J Am Diet Assoc* **105**, 775–789.

Futami J, Tanaka S, Yamamura C, Oka J, Ishikawa-Takata K, Kashiwazaki H (2003). Measurement of energy expenditure by whole-body indirect human calorimeter – evaluation of validity and error factors – nippon eiyo shokuryo gakkaishi. *J Jpn Soc Nutr Food Sci* **56**, 229–236.

Garby L, Kurzer MS, Lammert O, Nielsen E (1987). Energy expenditure during sleep in men and women: evaporative and sensible heat losses. *Hum Nutr Clin Nutr* **41**, 225–233.

Goldberg GR, Prentice AM, Davies HL, Murgatroyd PR (1988). Overnight and basal metabolic rates in men and women. *Eur J Clin Nutr* **42**, 137–144.

Hayter JE, Henry CJ (1993). Basal metabolic rate in human subjects migrating between tropical and temperate regions: a longitudinal study and review of previous work. *Eur J Clin Nutr* **47**, 724–734.

Henry CJ (2005). Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr* **8**, 1133–1152.

Kashiwazaki H (1990). Seasonal fluctuation of BMR in populations not exposed to limitations in food availability: reality or illusion? *Eur J Clin Nutr* **44** (Suppl 1), 85–93.

Kumahara H, Yoshioka M, Yoshitake Y, Shindo M, Schutz Y, Tanaka H (2004). The difference between the basal metabolic rate and the sleeping metabolic rate in Japanese. *J Nutr Sci Vitaminol* **50**, 441–445.

Liu HY, Lu YF, Chen WJ (1995). Predictive equations for basal metabolic rate in Chinese adults: a cross-validation study. *J Am Diet Assoc* **95**, 1403–1408.

Muller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M *et al.* (2004). World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. *Am J Clin Nutr* **80**, 1379–1390.

Muller MJ, Bosy-Westphal A, Kutzner D, Heller M (2002). Metabolically active components of fat-free mass and resting energy expenditure in humans: recent lessons from imaging technologies. *Obes Rev* **3**, 113–122.

Murgatroyd PR, Shetty PS, Prentice AM (1993). Techniques for the measurement of human energy expenditure: a practical guide. *Int J Obes Relat Metab Disord* **17**, 549–568.

Nelson KM, Weinsier RL, Long CL, Schutz Y (1992). Prediction of resting energy expenditure from fat free mass and fat mass. *Am J Clin Nutr* **56**, 848–856.

Nielsen S, Hensrud DD, Romanski S, Levine JA, Burguera B, Jensen MD (2000). Body composition and resting energy expenditure in humans: role of fat, fat-free mass and extracellular fluid. *Int J Obes Relat Metab Disord* **24**, 1153–1157.

Popkin BM, Doak CM (1998). The obesity epidemic is a worldwide phenomenon. *Nutr Rev* **56**, 106–114.

Ravussin E, Bogardus C (1989). Relationship between genetics, age, and physical fitness to daily energy expenditure and fuel utilization. *Am J Clin Nutr* **49**, 968–975.

Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C (1986). Determinants of 24-hour energy expenditure in man: methods and results using a respiratory chamber. *J Clin Invest* **78**, 1568–1578.

Ravussin E, Zurlo F, Ferraro R, Bogardus C (1990). Energy expenditure in man: determinants and risk factors for body weight gain. In: Omomura Y, Tarui S, Inoue S, Shimazu T (eds.) *Proceedings in Obesity Research 1990: Proceedings of the 6th International Congress on Obesity.* Libbey: London, pp 175–182.

Schrauwen P, van Marken Lichtenbelt WD, Westerterp KR (1997). Energy balance in a respiration chamber: individual adjustment of energy intake to energy expenditure. *Int J Obes Relat Metab Disord* **21**, 769–774.

Seale JL, Conway JM (1999). Relationship between overnight energy expenditure and BMR measured in a room-sized calorimeter. *Eur J Clin Nutr* **53**, 107–111.

Shetty PS, Henry CJ, Black AE, Prentice AM (1996). Energy requirements of adults: an update on basal metabolic rates (BMRs) and physical activity levels (PALs). *Eur J Clin Nutr* **50**, S11–S23.

Soares MJ, Sheela ML, Kurpad AV, Kulkarni RN, Shetty PS (1989). The influence of different methods on basal metabolic rate measurements in human subjects. *Am J Clin Nutr* **50**, 731–736.

Tahara Y, Moji K, Aoyagi K, Tsunawake N, Muraki S, Mascie-Taylor CG (2002). Age-related pattern of body density and body composition of Japanese men and women 18–59 years of age. *Am J Human Biol* **14**, 743–752.

Tataranni PA, Ravussin E (1995). Variability in metabolic rate: biological sites of regulation. *Int J Obes* **19**, S102–S106.

The National Nutrition Survey in Japan (2002): Ministry of Health, Labor and Welfare, Japan.

Toubro S, S¢rensen TIA, R¢nn B, Christensen NJ, Astrup A (1996). Twenty-four-hour energy expenditure: the role of body composition, thyroid status, sympathetic activity, and family membership. *J Clin Endocrinol Metab* **81**, 2670–2674.

Van der Ploeg GE, Gunn SM, Withers RT, Modra AC, Keeves JP, Chatterton BE (2001). Predicting the resting metabolic rate of young Australian males. *Eur J Clin Nutr* **55**, 145–152.

Weir JB (1949). New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol* **109**, 1–9.

Westerterp-Plantenga MS, van Marken Lichtenbelt WD, Strobbe H, Schrauwen P (2002). Energy metabolism in humans at a lowered ambient temperature. *Eur J Clin Nutr* **56**, 288–296.

Weyer C, Snitker S, Rising R, Bogardus C, Ravussin E (1999). Determinants of energy expenditure and fuel utilization in man: effects of body composition, age, sex, ethnicity and glucose tolerance in 916 subjects. *Int J Obesity* **23**, 715–722.

World Health Organization (1998). A World Health Organization consultation on obesity. *Obesity Preventing and Managing the Global Epidemic.* WHO: Geneva.

Yamamura C, Kashiwazaki H (2002). Factors affecting the post-absorptive resting metabolic rate of Japanese subjects: reanalysis based on published data. *Jpn J Nutr Diet* **60**, 75–83.

Yamamura C, Tanaka S, Futami J, Oka J, Ishikawa-Takata K, Kashiwazaki H (2003). Activity diary method for predicting energy expenditure as evaluated by a whole-body indirect human calorimeter. *J Nutr Sci Vitaminol* **49**, 262–269.

Zhang K, Sun M, Werner P, Kovera AJ, Albu J, Pi-Sunyer FX *et al.* (2002). Sleeping metabolic rate in relation to body mass index and body composition. *Int J Obes* **26**, 376–383.

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REVIEW

A dose–response relation between aerobic exercise and visceral fat reduction: systematic review of clinical trials

K Ohkawara, S Tanaka, M Miyachi, K Ishikawa-Takata and I Tabata

Health Promotion and Exercise Program, National Institute of Health and Nutrition, Shinjuku-ku, Tokyo, Japan

Objective: It has been suggested that exercise has preferential effects on visceral fat reduction. However, the dose–response effect remains unclear because of limited evidence from individual studies. The purpose of this study was to systematically review the current literature to establish whether reduction of visceral fat by aerobic exercise has a dose–response relationship.
Methods: A database search was performed (PubMed, 1966–2006) with appropriate keywords to identify studies exploring the effects of aerobic exercise as a weight loss intervention on visceral fat reduction. Visceral fat reduction was expressed as the percentage of visceral fat change per week (%ΔVF/w). The energy expenditure by aerobic exercise was expressed as ∑(metabolic equivalents × h per week (METs · h/w)).
Results: Nine randomized control trials and seven non-randomized control trials were selected. In most of the studies, the subjects performed aerobic exercise generating 10 METs · h/w or more. Among all the selected groups (582 subjects), visceral fat decreased significantly ($P<0.05$) in 17 groups during the intervention, but not in the other 4 groups. There was no significant relationship between METs · h/w from aerobic exercise and %ΔVF/w in all the selected groups. However, when subjects with metabolic-related disorders were not included (425 subjects), METs · h/w from aerobic exercise had a significant relationship with %ΔVF/w ($r=-0.75$). Moreover, visceral fat reduction was significantly related to weight reduction during aerobic exercise intervention, although a significant visceral fat reduction may occur without significant weight loss.
Conclusion: These results suggest that at least 10 METs · h/w in aerobic exercise, such as brisk walking, light jogging or stationary ergometer usage, is required for visceral fat reduction, and that there is a dose–response relationship between aerobic exercise and visceral fat reduction in obese subjects without metabolic-related disorders.
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Keywords: central obesity; metabolic-related disorder; clinical trial; METs · h/w; aerobic exercise

Introduction

Obesity is a widespread and growing problem around the world, with a population of more than 1 billion overweight adults, of which at least 300 million are clinically obese.[1] Excess adipose tissue, especially visceral adipose tissue, releases inflammatory cytokines that increase insulin resistance in skeletal muscles.[2] Furthermore, central obesity, which is defined as a state of excessive visceral fat accumulation, is associated with a decreased production of adiponectin, an adipose-specific molecule with anti-diabetic, anti-atherosclerotic and anti-inflammatory functions.[3] In recent years, central obesity has been defined as a predominant risk factor for metabolic syndrome,[4,5] a condition for which a collection of cardiovascular biomarkers are correlated with an increased probability of heart disease, stroke and diabetes. These biomarkers include high plasma triacylglycerol, low high-density lipoprotein cholesterol, high plasma blood glucose, and high blood pressure.

Numerous studies have investigated the effects of diet, drugs and exercise on reduction in weight, total fat mass and/or visceral fat mass.[6,7] Generally, diet therapy is the most effective method for decreasing weight and total fat mass rapidly, because it easily results in a negative energy balance, as compared with exercise or drug therapies.[8] However, it has been suggested that aerobic exercise has specific effects on decreasing visceral fat mass as it may lead

Correspondence: Dr K Ohkawara, Health Promotion and Exercise Program, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjuku, Tokyo 162-8636, Japan.
E-mail: ohkawara@nih.go.jp
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to increased sympathetic tonus, thereby increasing lipolysis especially in abdominal fat.[9] For that reason, exercise therapy is expected to be one of the most effective methods for improving central obesity.

Several investigators have reviewed the effects of physical activity (or aerobic exercise) on the reduction in body weight, total fat mass and/or visceral fat mass.[10–14] Ross and Janssen[13] suggested that physical activity was associated with a reduction of total fat, in a dose-dependent manner, within 16 weeks. However, the effects of physical activity on visceral fat reduction were unclear. Kay and Fiatarone Singh[10] also reviewed the influence of physical activity on abdominal fat. Although they concluded that physical activity had a beneficial influence on visceral fat reduction, a dose–response relationship was not examined. After Ross and Janssen[13] reviewed the dose–response relationship between physical activity and visceral fat reduction, several papers were published.[15–25] In the present study, we systematically reviewed the literature to clarify whether aerobic exercise for weight loss is positively associated with visceral fat reduction, and to determine the minimal amount of aerobic exercise required to achieve visceral fat reduction.

Materials and methods

Data collection

A PubMed (1966–May 2006) database search was performed to identify studies examining the effects of aerobic exercise as a weight loss intervention on visceral fat reduction using the following keywords: (physical activity, exercise, (physical and training), sports, physical education, or physical fitness) and (((abdominal, abdomen, or visceral) and (fat or adipose)) or ((waist, abdominal, or abdomen) and (girth or circumference))). The searches were limited to humans and clinical trials. Several studies were selected from reference lists cited in the selected studies.

Study selection

Studies were selected if they met the following criteria: (1) they involved clinical trials (that is, randomized controlled or non-randomized); (2) they must have included at least one group of aerobic exercise alone; (3) the age of subjects was between 18 and 65; (4) subjects had a mean body mass index (BMI) of $<25\,kg/m^2$, or a mean BMI of $\geqslant 25\,kg/m^2$, but with a small amount of visceral fat (if the mean plus s.d. of the visceral fat area (VFA) in a group was less than $100\,cm^2$ (in which case, only 16% of the subjects are estimated to have over $100\,cm^2$ of visceral fat), that group was considered not to need to reduce visceral fat) were excluded;[15,26–28] (5) the studies used computed tomography (CT) or magnetic resonance imaging (MRI) as a measurement of visceral fat; (6) the subjects were instructed to maintain energy intake before and during the intervention; and (7) the exercise amount and change in visceral fat could be calculated by the procedures described. Only groups that were instructed to practice aerobic exercise without weight loss by additional energy intake, which corresponded to the increased energy expenditure (EE) by prescribed aerobic exercise, were included.[22,29] We excluded data from studies using drug therapy, but included data from their control groups with aerobic exercise therapy alone.[17] Resistance training groups were also excluded, because calculation of their EE is difficult and the mechanism of decreasing visceral fat during resistance training may be different to that for aerobic exercise. Furthermore, if we identified two studies that used approximately the same research subjects, the study containing the least amount of information was excluded. Within these criteria-matched studies, groups that were not instructed to practice exercise during the intervention were employed as the control group for the degree of visceral fat reduction compared to the aerobic exercise groups.[15,19,21–23,29] Eligible studies were reviewed independently by two of the authors to assess inclusion suitability and data extraction accuracy.

Conversion to %ΔVF/w

In the selected studies, several units (for example, cm^2, cm^3, kg) were used for expressing the quantity of visceral fat. VFA was measured at either the 3rd-4th lumbar or 4th-5th lumbar vertebrae. Kvist *et al.*[30] and Shen *et al.*[31] have shown a strong correlation between the 4th-5th lumbar VFA, or the 3rd-4th lumbar VFA, and total visceral fat volume, respectively. However, they have also reported that the actual values do not accurately match between the 4th-5th and 3rd-4th lumbar VFA as well as VFA measured by CT vs MRI in the same region.[32] Therefore, we converted the visceral fat amount reported in each study to a percentage of visceral fat change per week (%ΔVF/w), which enabled us to directly compare the groups.

Conversion to METs · h/w

Aerobic exercise amounts during the intervention were converted to ∑(metabolic equivalents × h per week (METs · h/w)), which adjusted the EE for body size. Weekly EE by aerobic exercise during the intervention was acquired using the following criteria: (1) if an actual value was shown, that value was used;[22,29] (2) if an estimated or instructed value by authors was stated, that value was used;[16,19,24] (3) if values were not expressed,[9,15,17,18,20,21,23,25,27,33,34] EE was calculated using exercise intensity, exercise time, exercise frequency, body weight and VO2max/VO2peak as follows:[35]

$$EE\,(kcal/week) = (V \times I)/1000 \times 5 \times F \times T \times W \text{ or}$$
$$= (3.5 + (V - 3.5) \times I')/1000 \times 5 \times F \times T \times W,$$

where 3.5 ml/kg/min is resting metabolic rate, 5 kcal/l is EE for oxygen consumption per liter, V is VO2max or VO2peak (ml/kg/min), I is exercise intensity (for example, if exercise was done by 70%VO2max, the value is 0.7.), I′ is exercise intensity (if exercise was done by 70% heart rate reserve, the

value is 0.7.), F is exercise frequency (times/week), T is exercise time (min/session) and W is body weight (kg).

For the exercise intensity and time used in the EE calculation, the values decided by authors in each study were used. For studies that gradually increased exercise intensity and time, final target values were used. In cases where only the number of daily steps was shown,[20] 100 steps was calculated as one minute of exercise,[36] and intensity was assumed to be that for normal walking (3.5 METs).[37] If only the percentage of the heart rate maximum (%HRmax) for exercise intensity was shown, the exercise intensity by %HRmax was converted into exercise intensity by percentage of heart rate reserve. For the EE calculation, we did not include exercise volume during warm-up and cool-down (for example, stretching) periods, since several studies described this information, while others did not. Following these calculations, EE by aerobic exercise/week in each study was converted to METs · h/w using the following equation:[35]

$$\text{METs} \cdot \text{h/w} = \text{EE}/((\text{W} \times 3.5 \times 5/1000) \times 60),$$

where W is body weight (kg).

Data analysis

The amount of visceral fat decrease in each group was considered to be statistically significant if the *P*-value was less than 0.05. Correlations between METs · h/w and %ΔVF/w in selected groups, with or without the metabolic-related disorders, such as type 2 diabetes and dyslipidemia, were assessed by weighted Pearson's correlation coefficients (*r*) for the number of subjects. The Kruskal–Wallis test and the Mann–Whitney's *U*-test for *post hoc* comparisons were applied for comparing the mean %ΔVF/w values between the control and exercise groups that had been divided into tertiles by METs · h/w amount. We also analyzed these correlations in several categorized groups (for example, groups with only women or men, and groups with more or less than 16-week interventions). Furthermore, the relationship between METs · h/w and %ΔWeight/w, and between %ΔVF/w and %ΔWeight/w, were expressed by weighted *r* values for the number of subjects. Because %ΔVF/w and METs · h/w were calculated from mean values in each study, only these variables and the number of subjects were available for analyses. Therefore, specific analytic programs for meta-analysis could not be used, although the number of subjects was weighted for.

Results

Two hundred and fifty-five studies were selected from PubMed (1966–May 2006) with the appropriate keywords. From these papers, plus the added references collected from the cited literature, nine randomized control trials (RCT)[9,15,16,19,22–24,29,33] and seven non-randomized control trials (nRCT)[17,18,20,21,25,27,34] were selected according to our criteria (Table 1). The studies included 13 RCT groups and 8 nRCT groups examining solo aerobic exercise interventions (Table 2). The subjects of six groups in four of the studies were diagnosed as having metabolic-related disorders.[9,16,24,33] In all of the selected studies, the calculated METs · h/w ranged from 5.9 to 47.1, and the %ΔVF/w ranged from −6.062 to 0.078, including four groups that did not show any significant changes in VF during the intervention period.

Correlation coefficients between METs · h/w and %ΔVF/w are shown in Figure 1. METs · h/w had a significant correlation with %ΔVF/w in the groups that did not include subjects with metabolic-related disorders ($r = -0.75$), although there was no significant correlation when all groups were selected ($r = -0.28$). The selected groups without metabolic-related disorders were divided into tertiles by their METs · h/w amount. %ΔVF/w values in the 1st, 2nd and 3rd exercise groups were significantly higher than that of the control group, although these exercise groups were not significantly different from each other (Figure 2). Significant correlations were also observed in the women-only group, while there was no significant correlation in the men-only group (Table 3). Groups were also categorized by their duration of either shorter or longer than the 16-week intervention period (short-term or long-term intervention duration). Only in the short-term intervention groups, without metabolic-related disorder subjects, did METs · h/w exhibit a significant correlation with %ΔVF/w ($r = -0.81$).

For analysis of the relationship between %ΔWeight/w and METs · h/w or %ΔVF/w, the two groups[22,29] that did aerobic exercise without weight loss, were excluded. As a result, METs · h/w had a significant correlation with %ΔWeight/w in all of the selected groups ($r = -0.79$), as well as the groups without metabolic-related disorder subjects ($r = -0.87$) (Figure 3). Furthermore, %ΔVF/w had a strong relationship with %ΔWeight/w in the groups not including metabolic-related disorder subjects ($r = 0.93$), even though there was a significant correlation in all the selected groups ($r = 0.64$) (Figure 4).

Discussion

Dose–response relationship between aerobic exercise and visceral fat reduction

The present study indicates aerobic exercise volume has a dose–response relationship with visceral fat reduction in subjects without metabolic-related disorders. There are several excellent reviews for investigating the relationship between diet and exercise interventions and weight and/or visceral fat reduction.[6,7,10–14] Ross and Janssen[12] suggested that physical activity with or without weight loss was associated with a reduction in visceral adipose tissue, although insufficient evidence limited their reaching a definitive conclusion. Based on this research, Ross and Janssen[13] also reviewed dose–response relationships between

Table 1 Characteristics of selected studies in this paper

Reference	*RCT or nonRCT*	*Intervention*		*Subject*			
		Duration	*Type of group*	*Gender*	n	*Age (year)*	*Specific characteristics*
Despres *et al.*[34]	NonRCT	6 months	A	F	13	38.8±5.3	—
Donnelly *et al.*[15]	RCT	16 months	A	F	25	24±5	—
			C	F	18	21±4	—
			A	M	16	22±4	—
			C	M	15	24±4	—
Green *et al.*[17]	nonRCT	20 weeks	Dr+A	F	30	56.4±5.4	Estrogen replacement therapy (ERP), postmenopausal
			A	F	18	52.3±6.3	Non ERP, postmenopausal
Halverstadt *et al.*[18]	nonRCT	24 weeks	A	M+F	83 (34+49)	57.9±0.6	Combined LIPG (endothelial lipase gene) genotype CC and CT/TT
Irwin *et al.*[19]	RCT	12 months	A	F	87	61.0 (59.6–62.5)	Menopausal
			C	F	86	60.6 (59.1–62.1)	Menopausal
Miyatake *et al.*[20]	nonRCT	1 year	A	M	31	(32–59)	—
Park *et al.*[21]	nonRCT	24 weeks	C	F	10	43.1±1.67	—
			A	F	10	42.2±1.91	—
			A+R	F	10	43.4±1.04	—
Ross *et al.*[22]	RCT	14 weeks	Di	F	15	43.9±4.9	—
			A	F	17	43.2±5.1	—
			A[a]	F	12	41.3±7.2	—
			C	F	10	43.7±6.4	—
Ross *et al.*[29]	RCT	12 weeks	Di	M	14	42.6±9.7	—
			A	M	16	45.0±7.5	—
			A[a]	M	14	44.7±7.6	—
			C	M	8	46.0±10.9	—
Schwartz *et al.*[27]	nonRCT	27 weeks	A	M	13	28.2±2.4	—
			A	M	15	67.5±5.8	—
Short *et al.*[23]	RCT	16 weeks	A	M+F	65	40.5±1.1	—
			C	M+F	37	40.7±1.4	—
Wilund *et al.*[25]	nonRCT	12 weeks	A	M+F	16 (6+10)	56±1	CETP (cholesteryl ester transfer protein) genotype (B1B1)
			A	M+F	14 (8+6)	56±1	CETP (cholesteryl ester transfer protein) genotype (B1B2)
Boudou *et al.*[33]	RCT	8 weeks	A	M	8	42.90±5.20	Type 2 diabetics
Giannopoulou *et al.*[16]	RCT	14 weeks	Di+A	F	11	57.4±1.7	Diabetics, menopausal
			Di	F	11	58.5±1.7	Diabetics, menopausal
			A	F	11	55.5±1.7	Diabetics, menopausal
Mourier[1]*et al.*[9]	RCT	8 weeks	A	M+F	10	45±2	Diabetics
			C	M+F	11	46±3	Diabetics
Slentz *et al.*[24]	RCT	32 weeks	A[b]	M+F	40	54.0±5.5	Dyslipidemia, postmenopausal
			A[b]	M+F	46	53.0±7.0	Dyslipidemia, postmenopausal
			A[b]	M+F	42	51.5±5.3	Dyslipidemia, postmenopausal
			C	M+F	47	52.3±7.65	Dyslipidemia, postmenopausal

Abbreviations: A, aerobic exercise therapy; A[a], aerobic exercise therapy without a weight loss; A[b], three different types of aerobic exercise therapy in the study; C, control; Di, diet therapy; Dr, drug therapy; F, female subjects; M, male subjects; *n*, number of subjects (number of males+number of females); R, resistance training therapy; RCT, randomized control trials. Age expressed by mean±s.d. (range).

Table 2 Summary of aerobic exercise groups in this paper

Reference	*Subjects*				*Aerobic exercise*	
	Gender	*Age (yr)*	*BMI (kg/m^2)*	*% fat (%)*	*Session time and intensity*	*Mode or used exercise instrument*
Despres *et al.*[34]	F	38.8	34.5	47.0	90 min, 55%HRmax	Walking
Donnelly *et al.*[15]	M	22	29.7	28.3	45 min, 70%VO2max	Treadmill
Green *et al.*[17]	F	56.4	29.3	40.8	75%VO2max	Ergometer
Halverstadt *et al.*[18]	M+F	57.9	—	36.0	70%VO2max	—
Irwin *et al.*[19]	F	61	30.5	47.6	Mean 81%HRmax	Treadmill walking and stationary bicycling in Lab, and aerobic exercise (e.g. walking, aerobics, bicycling) at home
Miyatake *et al.*[20]	M	32–59	28.6	29.3	7012→8839 steps/day (plus 1827 steps/days)	Normal walking
Park *et al.*[21]	F	42.2	25.3	42.2	60–70%HRmax	Fast walking
Ross *et al.*[22]	F	43.2	32.8	—	Mean 80%HRmax	Brisk walking or light jogging on treadmill
	F	41.3	32.9	—	Mean 82%HRmax	Brisk walking or light jogging on treadmill
Ross *et al.*[29]	M	45	32.3	—	Mean 77%HRmax	Brisk walking or light jogging on treadmill
	M	44.7	31.3	—	Mean 77%HRmax	Brisk walking or light jogging on treadmill
Schwartz *et al.*[27]	M	67.5	26.2	24.7	45 min, 85%HRreserve	Walking/jogging
Short *et al.*[23]	M+F	40.5	26.6	31.4	80%HRmax	Stationary bicycling
Wilund *et al.*[25]	M+F	56	—	38.0	40 min, 70%VO2max	—
	M+F	56	—	34.0	40 min, 70%VO2max	—
Boudou *et al.*[33]	M	42.9	28.3	—	1) 2 times/week, 45 mi n, 75%VO2peak, 2) 1 time/week, 10 min, 85%VO2peak, and 12 min, 50%VO2peak	Ergometer
Giannopoulou *et al.*[16]	F	55.5	35.9	—	60 min, 65–70%VO2max, energy expenditure: 250.95–298.75 kcal/session	Walking
Mourier *et al.*[9]	M+F	45	30.4	24.4	1) 2 times/week, 45 min, 75%Vo2peak, 2) 1 time/week, 10 min, 75%VO2peak, and 12 min, 50%VO2peak	Ergometer
Slentz *et al.*[24]	M+F	54	29.8	—	40–55%VO2max, 14 kcal/kg/wk (12 miles/week)	Treadmill walking
	M+F	53	29.7	—	65–80%VO2max, 14 kcal/kg/wk (12 miles/week)	Treadmill jogging
	M+F	51.5	29.1	—	65–80%VO2max, 23 kcal/kg/wk (20 miles/week)	Treadmill jogging

Table 2 (Continued)

Aerobic exercise					Weight						Visceral fat							
VO2max (baseline)	*Frequency (times/ week)*	*Time (min/ session)*	*Energy expenditure (kcal/week)*	*METs·h/w*	*Before (kg)*	*After (kg)*	*Δ (kg)*	*%Δ (%)*	*%Δ (%/ week)*	*Sig[1]*	*Before*	*After*	*Δ*	*Unit*	*%Δ (%)*	*%Δ (%/ week)*	*Sig[2]*	*Method*
	4–5	90	1913	20.2	90.0	86.3	−3.7	−4.11	−0.069	*	124.7	121.3	−3.4	cm^2	−2.73	−0.045	NS	CT
	5	45	3300	33.4	94.0	85.2	−8.8	−9.36	−0.136	*	97.9	75.5	−22.4	cm^2	−22.88	−0.334	*	
21.3±4.0	3	50	920	11.4	76.8	76.9	0.1	0.13	0.007	NS	121.6	117.8	−3.8	cm^2	−3.13	−0.156	NS	CT
25.2±0.5	3	40	853	10.1	80.6	79.5	−1.1	−1.36	−0.057	*	127.8	113.4	−14.4	cm^2	−11.27	−0.469	*	CT
20.1 (19.3–20.9)	3.5	176/week	1051	12.3	81.6	—	−1.3	−1.59	−0.031	*	147.6	—	−8.5	cm^2	−5.76	−0.113	*	CT
	7	18.27	507	5.9	82.0	79.0	−3.0	−3.66	−0.091	*	108.7	87.0	−21.7	cm^2	−19.96	−0.499	*	CT
34.2±3.2	6	60	1908	28.5	63.7	59.0	−4.7	−7.38	−0.307	*	195.0	112.4	−82.6	cm^2	−42.36	−1.765	*	CT
	7	64	3668 (524±52/session)	40.2	86.9	80.9	−6.0	−6.90	−0.493	*	2.3	1.6	−0.7	kg	−30.43	−2.174	*	MRI
	7	63	3619 (517±58/session)	39.1	88.1	87.6	−0.5	−0.57	−0.041	NS	2.2	1.8	−0.4	kg	−18.18	−1.299	*	
	7	60.4	4886 (698/session)	45.8	101.5	94.0	−7.5	−7.39	−0.616	*	186.0	134.0	−52.0	cm^2	−27.96	−2.330	*	MRI
	7	63.3	4844 (692/session)	47.1	97.9	97.4	−0.5	−0.51	−0.043	NS	191.0	159.0	−32.0	cm^2	−16.75	−1.396	*	
29.1±4.4	4.44±0.43	45	2009	24.0	79.6	77.1	−2.5	−3.14	−0.131	*	144.5	109.0	−35.5	cm^2	−24.57	−1.024	*	
25.6 (40.5±1.1/ FFM)	4	40	1166	14.0	79.2	78.7	−0.5	−0.63	−0.039	*	133.0	124.0	−9.0	cm^2	−6.77	−0.423	*	CT
25±1	3	40	882	10.0	84.0	83.2	−0.8	−0.95	−0.079	NS	146.0	130.0	−16.0	cm^2	−10.96	−0.913	*	CT
26±1	3	40	863	10.4	79.0	77.8	−1.2	−1.52	−0.127	*	128.0	109.0	−19.0	cm^2	−14.84	−1.237	*	
23.45±3.60	3	1) 45, 2) 22	836	9.2	86.9	85.0	−1.9	−2.19	−0.273	NS	153.3	84.2	−69.1	cm^2	−45.06	−5.632	*	MRI
	3–4	60	962	9.9	92.9	91.2	−1.7	−1.83	−0.131	NS	5204.0	4675.0	−529.0	cm^3	−10.17	−0.726	*	MRI
23.0±1.2	3	1) 45, 2) 22	795	8.9	85.3	83.8	−1.5	−1.76	−0.220	NS	156.1	80.4	−75.7	cm^2	−48.49	−6.062	*	MRI
	3.5	178	1232	6.9	88.0	—	—	−0.70	−0.022	*	173	—	—	—	1.70	0.053	NS	CT
	3.1	120	1190	13.3	85.0	—	—	−0.80	−0.025	*	154	—	—	—	2.50	0.078	NS	
	3.6	173	1971	21.9	85.7	—	—	− 2.60	−0.081	*	168	—	—	—	−6.90	−0.216	*	

Abbreviations: CT; computed tomography; F, female subjects; M, male subjects; METs·h/w, ∑(metabolic equivalents × hour) per week; MRI, magnetic resonance imaging; Sig[1], a significant weight change was observed during the intervention ($P<0.05$); Sig[2], a significant visceral fat change was observed during the intervention ($P<0.05$); Δ, change. Results expressed by mean (range) or mean±s.d.