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Age-related changes in resting energy expenditure in normal weight, overweight and obese men and women

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ABSTRACT

Objectives: Aging is associated with changes in resting energy expenditure (REE) and body composition. We investigated the association between age and changes in REE in men and women stratified by body mass index (BMI) categories (normal weight, overweight and obesity). We also examined whether the age-related decline in REE was explained by concomitant changes in body composition and lifestyle factors.
Study design: Cross-sectional.
Main outcome measures: 3442 adult participants (age range: 18–81 y; men/women: 977/2465) were included. The BMI range was 18.5–60.2 kg/m^2. REE was measured by indirect calorimetry in fasting conditions and body composition by bioelectrical impedance. Regression models were used to evaluate age-related changes in REE in subjects stratified by sex and BMI. Models were adjusted for body composition (fat mass, fat free mass), smoking, disease count and physical activity.
Results: In unadjusted models, the rate of decline in REE was highest in obese men (slope = −8.7 ± 0.8 kcal/day/year) whereas the lowest rate of decline was observed in normal weight women (−2.9 ± 0.3 kcal/day/year). Gender differences were observed for the age of onset of REE adaptive changes (i.e., not accounted by age related changes in body composition and lifestyle factors). In women, adaptive changes appeared to occur in middle-age (~47 y) across all BMI groups whereas changes seemed to be delayed in obese men (~54 y) compared to overweight (~43 y) and normal weight (~39 y) men.
Conclusions: Sex and BMI influenced the rate and degree of the age-related decline in REE. Critical age windows have been identified for the onset of putative mechanisms of energy adaptation. These findings require confirmation in prospective studies.

1. Introduction

Aging appears to be caused by the accumulation of molecular damage [1] which results in a progressive decline of physiological and metabolic functions and changes in tissue architecture, organ size and function [2]. In particular, aging is associated with smaller mass for a number of important organs contributing to energy metabolism [3] and with reciprocal changes in lean body mass (decline) and adipose tissue (increase) [4]. These body composition changes are gender-specific since the rate of decline of lean body mass is faster and occurs at younger ages in men [5]

Abbreviations: BMI, body mass index; REE, resting energy expenditure; TEE, total energy expenditure; AEE, activity energy expenditure; TEF, thermic effect of food; IPAQ, International physical activity questionnaire; BIA, bioelectrical impedance; FM, fat mass; FFM, fat free mass; METs, metabolic equivalents time; BLSA, Baltimore Longitudinal Study of Aging; Health ABC, Health, Aging, and Body Composition Study.

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whereas changes in body shape and composition in women are almost coincidental with the onset of menopause [6,7].

These age-related changes in body size and composition co-occur with modifications of total energy expenditure (TEE) and its sub-components [(i.e., resting energy expenditure (REE), activity energy expenditure (AEE) and thermic effect of food (TEF)] [8]. REE accounts for ~60–70% of TEE and several cross-sectional and longitudinal studies have reported a progressive decline in REE of about 1–2% per decade [8–14]. This decline has been explained largely by body composition changes (85–95%), while the remainder of these adaptive changes (5–15%) has been attributed to reduced cellular metabolism driven by adjustments of sympathetic tone, thyroid function, mitochondrial efficiency, protein turnover and/or maintenance of cellular electrolyte gradients [8,9,11,15,16]. Further, it has also been suggested that the onset of these REE changes may depend on sex, degree of adiposity and lean body mass [17–20].

Here, we hypothesized that the rate and degree of the age-related decline in REE may be influenced by sex and body mass index (BMI). We tested this hypothesis in a large sample of 3442 adults with detailed assessment of body composition, REE, health status and physical activity. We specifically aimed to investigate the following questions: (1) Are age-related trajectories of REE modified by sex and body size (categorized by canonical BMI groups)? and (2) Is the age of onset of adaptive changes in REE different in men and women stratified by BMI?

2. Methods

2.1. Participants

Participants were recruited consecutively among subjects attending the International Center for the Assessment of Nutritional Status (ICANS, University of Milan) for clinical and nutritional evaluation between February 2010 and September 2013. The sample comprises adult Caucasian men and women (age ≥18 years) with a body mass index (BMI) ≥18.5 kg/m^2. Subjects were not excluded from the primary analyses based on clinical diagnosis or medication use to enhance sample representativeness. A sensitivity analysis was conducted after exclusion of subjects with medical conditions that could have influenced energy expenditure.

2.2. Study procedures

All measurements were performed in the morning after an overnight fast. 3442 subjects (male/female: 977/2465) were included in the final analysis. The higher prevalence of females is representative of the higher number of females attending our outpatient nutritional clinic. The study procedures were approved by the University of Milan Ethical Committee and all participants gave written informed consent. The STROBE statement for cross-sectional studies was adopted to provide detailed information on the study design and sample characteristics.

2.2.1. Smoking, physical activity and health status

Current smoking habits were recorded as current smokers, never smoked or former smokers. A detailed medical interview was conducted and self-reported diagnosis of medical conditions was collected. Disease count including major chronic diseases, such as cancer, thyroid and adrenal disorders, systemic inflammatory diseases (i.e., Crohn's disease, Ulcerative Colitis, Sjögren's syndrome, Systemic lupus erythematosus, Systemic sclerosis), HIV, and acute and chronic kidney failure, was calculated for each subject. Physical activity level was assessed using the short version of the International physical activity questionnaire (IPAQ) [21].

2.2.2. Anthropometry

Anthropometric measurements were collected by the same observer, according to standardized procedures. Body weight (WT, Kg) and height (HT, cm) were measured to the nearest 0.1 kg and 0.5 cm, respectively. Body mass index (BMI) was calculated as [weight/height^2] and classified using the WHO criteria (18.5–24.9 kg m^{-2} – normal weight, 25.0–29.9 kg m^{-2} – overweight and ≥30 kg m^{-2} – obese).

2.2.3. Bioelectrical impedance (BIA)

Impedance (Z) was measured using a tetrapolar 8-point tactile electrode system (InBody 720, Biospace, Seoul, Korea) at 1, 5, 50, 250, 500 and 1000 kHz. The system measured the impedance of the participant's right arm, left arm, trunk, right leg and left leg. Total body impedance value was calculated by summing the segmental impedance values. Participants stood on the scale platform of the instrument and grasped the handles of the device, to provide contact with a total of eight electrodes (two for each foot and for each hand). Manufacturer's equations were used to estimate body composition variables. The intra-examination coefficient of variation for BIA was 0.8%.

2.2.4. Measured REE

An open-circuit ventilated-hood indirect calorimetry system was used (Sensor Medics 29, Anaheim, CA, USA). Resting VO_2 and VCO_2 measurements were measured in the early morning, after an overnight fast, under standardized conditions, with the person lying awake and emotionally undisturbed, completely at rest and comfortably supine on a bed, their head under a transparent ventilated canopy, in a thermally neutral environment (24–26 °C). When relevant, the participant was asked to abstain from smoking on the morning of the measurement. Respiratory gas samples were taken every minute for 30–40 min and data collected during the first 5–10 min were discarded, as recommended by Isbell et al. [22]. This time period allowed the subjects to acclimatize to the canopy and instrument noise. The calorimeter was calibrated daily before starting the tests, using a two-point calibration method based on two separate mixtures of known gas content. The flow rate was calibrated with a 3-L syringe, according to the calorimeter manufacturer's instructions. The average of the last 20 min of measurements was used to determine 24 h REE according to the standard abbreviated Weir equation [23].

2.2.5. Predicted REE

REE was calculated using predictive equations including FM, FFM, sex and lifestyle factors (smoking, disease count and physical activity) as independent variables. Specifically, FFM (kg), FM (kg), sex (female = 0, male = 1), smoking (0 = smoker; 1 = non-smoker; 2 = ex-smoker), disease count (range: 0–13) and physical activity (Total METs) were entered as independent variables into a stepwise multiple regression model. The following predictive equation was obtained: REE (kcal/day) = 407.2 + 70.5 * Sex + 17.2 * FFM(kg) + 7.7 * FM(kg) − 7.5 * Disease Count − 8.3 * Smoking, $R^2 = 0.82$, $p < 0.001$. This equation was then used to calculate REE and the difference between measured and predicted REE was obtained as a measure of adaptive changes in REE.

2.3. Statistical analyses

The data are reported as mean ± SD (continuous variables) and frequency and percentage (categorical variables). Groups stratified by sex and BMI groups were compared using univariate analysis of variance entering sex (S) and BMI categories (BMI-C) as between-subjects factors. A sex-BMI categories (S*BMI-C) interaction term was added to the model. Linear regression models were used to

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assess the relationship between age and REE after stratification by BMI and sex. Unadjusted models were run first to assess the association between age and REE; next, models were adjusted for body composition (FM, FFM), smoking, disease count and IPAQ-physical activity level to estimate age-related decrease in REE not accounted for by modifications of body composition and lifestyle factors (i.e., adaptive changes). Intercepts (α) and regression coefficients (β) are reported.

In addition, the association between predicted and measured REE with age was evaluated by fitting linear regression models to sex and BMI stratified groups. The intersection point between the measured and predicted regression lines was calculated to provide an estimate of the age of onset of adaptive changes in REE (X-Intersection Point). The intersection point was identified using the following formula:

2.4. X-intersection point: (intercept 1–intercept 2)/(slope 1–slope 2)

The residuals of the measured and predicted REE were regressed against measured REE to examine the age- and BMI-specific onset of adaptive changes in REE. The specific value is indicated by the y-intercept of the regression line. A zero-difference between measured and predicted indicated a lack of adaptive changes whereas negative residuals indicated a lower measured REE which was not explained by co-occurring changes in body composition and lifestyle factors. Changes in measured REE per decade (18–29.9 y, 30.0–39.9 y, 40.0–49.9 y, 50.0–59.9 y, 60.0–69.9 y, ≥70 y) were also assessed in the sample stratified by sex and BMI groups. The difference between measured and predicted REE was expressed as absolute (kcal/day) and percent (%) values.

Sensitivity analyses were conducted after exclusion of subjects with medical conditions likely to influence energy expenditure (e.g., cancer, systemic inflammatory disorders, acute and chronic kidney failure, HIV, thyroid and adrenal disorders). The results of these sensitivity analyses have been reported in the online supplementary material. Analyses were conducted using Excel for Windows and STATISTICA v.10 for Windows. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptives

These analyses are based on a convenient sample of 2465 women and 977 men with an average age of 45.1 ± 12.7 y (age range: 18–80 y) and 47.2 ± 12.4 y (age range: 18–81 y), respectively. A histogram of the age distribution by sex is shown in Fig. S1 of the Supplementary Material. In addition, the description of the confounding factors (smoking, physical activity and disease count) stratified by sex and BMI categories is provided in Table S1. Obese subjects were significantly older than normal weight and overweight subjects (BMI-C: $p < 0.001$) but age was not different between men and women (S: $p = 0.18$; S*BMI-C: $p = 0.72$). Men and women were matched for BMI (S: $p = 0.36$) but significant body composition differences were found between men and women and BMI groups. FMI (fat mass index) was significantly higher in women across the three BMI groups (S*BMI-C: $p < 0.001$) whereas FFMI (fat free mass index) was higher in men and increased with BMI (S*BMI-C: $p < 0.001$). The differences in FFMI may also explain the higher REE in men and the direct association with BMI (S*BMI-C: $p < 0.001$). However, differences between sex and BMI categories were no longer significant after the adjustment of REE for FFM (S*BMI-C: $p = 0.77$) (Table 1).

Table 1
Sample characteristics stratified by sex and body mass index (BMI) categories.

	Men			Women			
	Normal weight	Overweight	Obesity	Normal weight	Overweight	Obesity	
N	78	382	517	690	935	840	Factorial ANOVA *P*
Age (years)	42.0 ± 11.8 (18–75)	46.2 ± 12.2 (18–77)	48.8 ± 1.4 (18–81)	41.4 ± 11.8 (18–75)	45.7 ± 12.5 (18–80)	47.5 ± 13.1 (18–80)	S: 0.18 BMI-C: <0.001 S*BMI-C: 0.72
Weight (kg)	71.6 ± 5.7 (58.9–88.0)	85.8 ± 7.6 (62.3–112.4)	106.1 ± 15.5 (75.3–177.8)	60.8 ± 5.7 (43.7–81.2)	71.6 ± 6.3 (52.9–94.4)	89.8 ± 13.2 (61.4–165.1)	S: <0.001 BMI-C: <0.001 S*BMI-C: <0.001
Height (cm)	175.5 ± 5.5 (165.3–188.2)	175.4 ± 6.5 (151.3–196.4)	175.0 ± 6.6 (157.7–198.2)	162.8 ± 6.2 (145.1–186.5)	161.4 ± 6.2 (142.9–181.6)	160.3 ± 6.4 (140.3–182.3)	S: <0.001 BMI-C: <0.001 S*BMI-C: 0.06
BMI (kg/m²)	23.2 ± 1.4 (19.3–24.9)	27.8 ± 1.3 (25.0–29.9)	34.6 ± 4.2 (30.0–54.9)	22.9 ± 1.4 (18.7–24.9)	27.4 ± 1.4 (25.0–29.9)	34.9 ± 4.5 (30.0–60.1)	S: 0.36 BMI-C: <0.001 S*BMI-C: 0.01
Fat mass (kg)	13.0 ± 4.0 (4.3–22.2)	22.3 ± 4.8 (6.4–36.2)	37.6 ± 11.0 (18.2–88.1)	17.5 ± 3.7 (7.2–29.5)	26.6 ± 3.9 (9.3–40.6)	41.5 ± 9.2 (24.6–85.4)	S: <0.001 BMI-C: <0.001 S*BMI-C: 0.72
Fat free mass (kg)	58.5 ± 5.1 (45.3–73.6)	63.4 ± 6.5 (39.6–81.5)	68.5 ± 8.6 (38.6–103.3)	43.3 ± 4.6 (30.9–64.2)	45.0 ± 5.0 (30.0–63.0)	48.3 ± 6.2 (29.6–79.7)	S: <0.001 BMI-C: <0.001 S*BMI-C: <0.001
Fat mass index (kg/m²)	4.2 ± 1.3 (1.2–7.1)	7.2 ± 1.5 (2.0–11.6)	12.2 ± 3.6 (6.2–27.2)	6.6 ± 1.4 (2.6–11.1)	10.2 ± 1.5 (3.7–15.8)	16.1 ± 3.5 (9.4–32.7)	S: <0.001 BMI-C: <0.001 S*BMI-C: <0.001
Fat free mass index (kg/m²)	18.9 ± 1.0 (16.4–20.9)	20.5 ± 1.2 (16.8–24.5)	22.3 ± 1.7 (12.5–27.8)	16.2 ± 1.0 (12.7–20.1)	17.2 ± 1.0 (13.2–23.5)	18.7 ± 1.6 (12.1–29.0)	S: <0.001 BMI-C: <0.001 S*BMI-C: <0.001
REE (kcal/day)	1549.9 ± 144.8 (1241.0–1885.0)	1706.7 ± 162.6 (1222.0–2221.0)	1937.5 ± 264.7 (1311.0–3170.0)	1280.9 ± 120.0 (798.0–1810.0)	1363.2 ± 137.3 (952.0–1843.0)	1527.2 ± 191.3 (1003.0–2273.0)	S: <0.001 BMI-C: <0.001 S*BMI-C: <0.001
REE/FFM	26.5 ± 1.8 (22.6–31.3)	27.0 ± 2.3 (21.0–37.4)	28.3 ± 2.8 (18.4–45.1)	29.7 ± 2.5 (22.2–36.9)	30.4 ± 2.9 (22.7–45.7)	31.7 ± 3.1 (19.7–46.7)	S: <0.001 BMI-C: <0.001 S*BMI-C: 0.77

Data is presented as mean ± SD. Range in parentheses. *N* = number of subjects. REE = resting energy expenditure; FFM = fat free mass. S = sex; BMI-C = BMI categories.

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Table 2
Linear regression models to evaluate the association between age and resting energy expenditure (REE (kcal/day), dependent variable) in subjects stratified by sex and body mass index categories.

	Male			Female		
	Normal weight	Overweight	Obese	Normal weight	Overweight	Obese
Model 1						
Intercept	1743.7 ± 56.6	1923.8 ± 30.5	2363.2 ± 43.1	1402.3 ± 16.0	1604.3 ± 14.8	1780.1 ± 23.1
R^2	0.14	0.12	0.16	0.08	0.23	0.13
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Age (years)						
Slope	−4.6 ± 1.2	−4.6 ± 0.6	−8.7 ± 0.8	−2.9 ± 0.3	−5.2 ± 0.3	−5.3 ± 0.4
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Model 2						
Intercept	476.6 ± 163.7	774.8 ± 76.9	626.8 ± 71.0	602.1 ± 39.5	728.5 ± 40.4	638.4 ± 39.6
R^2	0.56	0.47	0.70	0.46	0.51	0.63
P	0.002	<0.001	<0.001	<0.001	<0.001	<0.001
Age (years)						
Slope	−3.0 ± 1.1	−3.2 ± 0.6	−4.7 ± 0.6	−2.0 ± 0.3	−3.8 ± 0.2	−3.1 ± 0.3
P	0.01	<0.001	<0.001	<0.001	<0.001	<0.001
FM (kg)						
Slope	4.3 ± 3.3	7.4 ± 1.3	10.0 ± 0.6	4.3 ± 0.9	6.7 ± 0.7	7.1 ± 0.4
P	0.22	<0.001	<0.001	<0.001	<0.001	<0.001
FFM (kg)						
Slope	19.1 ± 2.3	14.3 ± 0.9	16.5 ± 0.8	15.7 ± 0.7	14.0 ± 0.6	15.2 ± 0.7
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Variability of intercept and slope expressed as ±SEM. R^2 = explained variance; FM = fat mass; FFM = fat free mass. Model 2 was adjusted for smoking, disease count and physical activity.

3.2. Age-related changes in REE

REE showed a greater decrease in men ($\beta = -5.0 \pm 0.6$ kcal/day/year) compared to women ($\beta = -3.2 \pm 0.3$ kcal/day/year). The rate of decline was higher in obese men ($\beta = -8.7 \pm 0.8$ kcal/day/year), whereas the lowest value was observed in normal weight women ($\beta = -2.9 \pm 0.3$ kcal/day/year) (Table 2). The rate of decline per decade was directly associated with BMI and was overall greater in obese men compared to obese women (−84.4 vs −55.0 kcal/day/decade, respectively) (Fig. S2A, Online Supplementary Material). We also calculated changes in REE for each decade, stratified by BMI and sex, relative to the youngest age group (<30 years). The energy gap was age-dependent as it became progressively larger in older subjects and it was, again, greater in obese men (−434.5 kcal/day) and obese women (−278.6 kcal/day) (Fig. S2B, Online Supplementary Material).

The decline in REE was modified by the adjustment of the regression models for body composition, smoking, physical activity and disease count. Yet, obese men and normal weight women showed the greatest (−4.7 ± 0.6 kcal/day/year) and lowest (−2.0 ± 0.3 kcal/day/year) decrease, respectively (Table 2).

3.3. REE and adaptive changes

The residuals of the fully adjusted models presented in Table 2 were calculated to (1) assess the magnitude of adaptive changes in REE and (2) to identify BMI and sex-specific values for the onset of the adaptive changes. The association between residuals and measured REE was consistently significant (R^2 range = 0.36–0.60, $p < 0.001$). The identification of the intersection point appeared to be influenced by BMI and age in both women (Fig. 1) and men (Fig. 2). The values of these intersection points for each BMI, age and sex group are presented in Fig. 3A. Young obese men were characterized by a greater intercept (1980 kcal/day) compared to older male subjects (1802 kcal/day). A difference of approximately 400 kcal/day was observed between obese men and obese women.

3.4. Age and adaptive changes

Overall, the rate of REE decline was greater for measured compared to predicted REE but the intersection of the two regression lines appeared to differ between sex and BMI groups (Fig. 4). A distinct gender-difference was observed for the age of onset of adaptive changes. In women, these appeared to occur in middle-age (∼47 years) across all BMI groups whereas adaptive changes seemed to occur later in obese (∼54 years) compared to overweight (∼43 years) and normal weight (∼39 years) men (Figs. 3B and 4).

3.5. Sensitivity analysis

The exclusion of 623 subjects with medical conditions potentially influencing REE did not modify the results. The regression coefficients and the explained variance (R^2) of the unadjusted and adjusted regression models remained essentially unchanged (Table S3, Online Supplementary Material). Similarly, the absolute and percent differences between predicted and measured REE are comparable to the values obtained in the entire sample (Table S4, Online Supplementary Material). These sensitivity analyses have also shown that the age-related decline in REE per decade did not change and a greater decline was again observed in obese men (Fig. S3, Online Supplementary Material). We also found a similar age of onset of adaptive changes in both men (normal weight: ∼38 years; overweight: ∼43 years; obese: ∼52 years) and women (normal weight: ∼48 years; overweight: ∼47 years; obese: ∼46 years).

4. Discussion

The present analyses showed that the rate and degree of age-related decline in REE may be influenced by sex and BMI. Obese men experienced an average decline per decade of −84 kcal/day compared to −38 kcal/day of normal weight women. In addition, the age of onset of adaptive changes was different between women and men, which seemed to coincide with the menopausal phase in the former whereas a greater adiposity appeared to delay the

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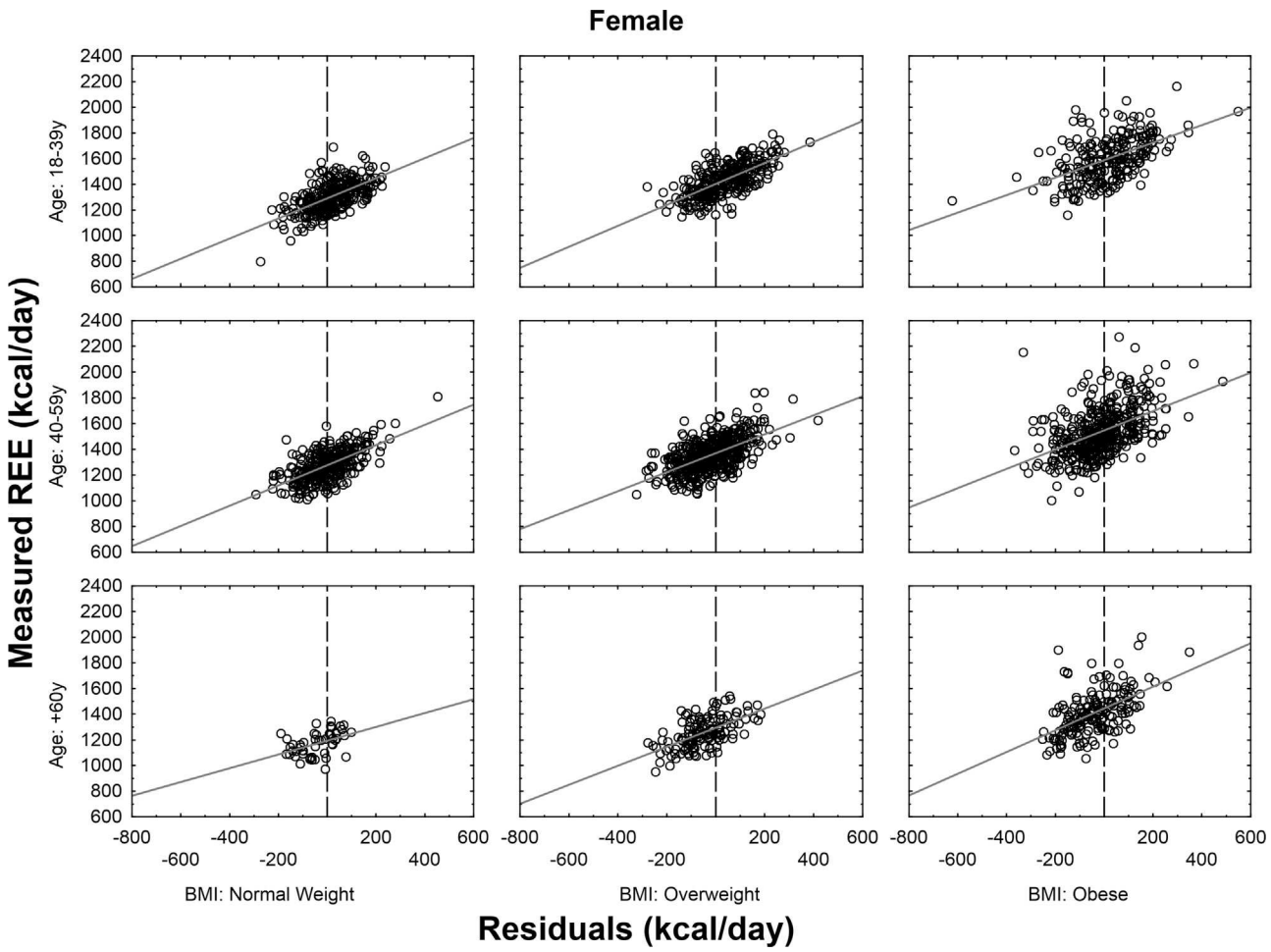

Fig. 1. Evaluation of age-related adaptive changes in REE by fitting linear regression models between age (years, independent variable (x)) and measured and predicted REE (kcal/day, dependent variables (y)). Analyses were stratified by sex and BMI categories. The regression equations (y = constant + slope * x) are showed separately for measured and predicted REE. The greater decline in measured REE suggested the presence of adaptive changes not explained by changes in body composition and lifestyle factors. Predicted REE was calculated using a predictive equation for REE (dependent variable) based on fat mass (kg), fat free mass (kg), sex, smoking and disease count as independent variables (see Section 2 for more details).

onset of adaptive changes in the latter. These results emphasize the physiological impact of hormonal changes occurring during the menopause transition on energy metabolism. The magnitude of these adaptive changes increased with age as it was higher in older subjects and ranged from −1.4% (50–59 y, normal weight women) to −7.5% (≥70 y, overweight women) (Table S2, Online Supplementary Material).

The cross-sectional design is an important limitation of the study, which may impact on the ascertainment of the causality of the associations as well as on the evaluation of age-related trajectories of REE, which warrant further investigations in longitudinal studies. However, longitudinal studies investigating life course trajectories of energy expenditure are rare. To our knowledge the only study recording changes in REE over a period of 40 years is the Baltimore Longitudinal Study of Aging (BLSA); however, longitudinal changes were assessed only in men showing that the rate decline of REE accelerated from 0.07 kcal/m^2/h per year between the age of 40 and 50 years to 0.15 kcal/m^2/h per year between the age of 70 and 80 years [13]. Longitudinal changes in REE in an aging population were investigated in the GISELA [12] and Health, Aging, and Body Composition (Health ABC) [14] studies. The former showed a significant decline in REE with increasing age which was significantly different between women and men [12]. The latter showed a decrease in REE of 79 kcal/day in men and 36 kcal/day in women over the 7-year follow up period. In addition, changes in REE was positively correlated with changes in FFM for men but not for women [14]. Cross sectional studies provide therefore a simpler approach to obtain a life course snapshot of age-related changes in REE and, to our knowledge, our study represents one of the largest life course collection of REE and body composition measurements. This has provided an adequate power to investigate the modulating effects of sex and body size on age-trajectories of REE. Our results should not be generalized to the "oldest old," since this age group was not properly represented in our sample. Measurements of REE were not standardized by menstrual phase in younger women. Finally, this is a self-selected, convenient clinical sample and therefore prevalent estimates of lifestyle and risk factors might not be representative of the general population.

The concept of critical age windows in the onset of an accelerated decline in REE is not a novel finding. A faster decline in REE was observed in younger men (41 y) compared to women (50 y). Furthermore, these studies found that the rate of decline was greater in men (−10.9 kcal/day/year) than in women (−5.5 kcal/day/year), suggesting that sex may be an important modifier of both the onset and the rate of decline in REE [20,24,25]. However, these studies did not investigate whether these age-related trajectories were also modified by BMI. Conversely, our analyses confirmed the modifying effects of sex on the onset to REE decline, which appeared to interact with body size. Further, we have identified specific "metabolic windows" indicating the REE thresholds beyond which adaptive

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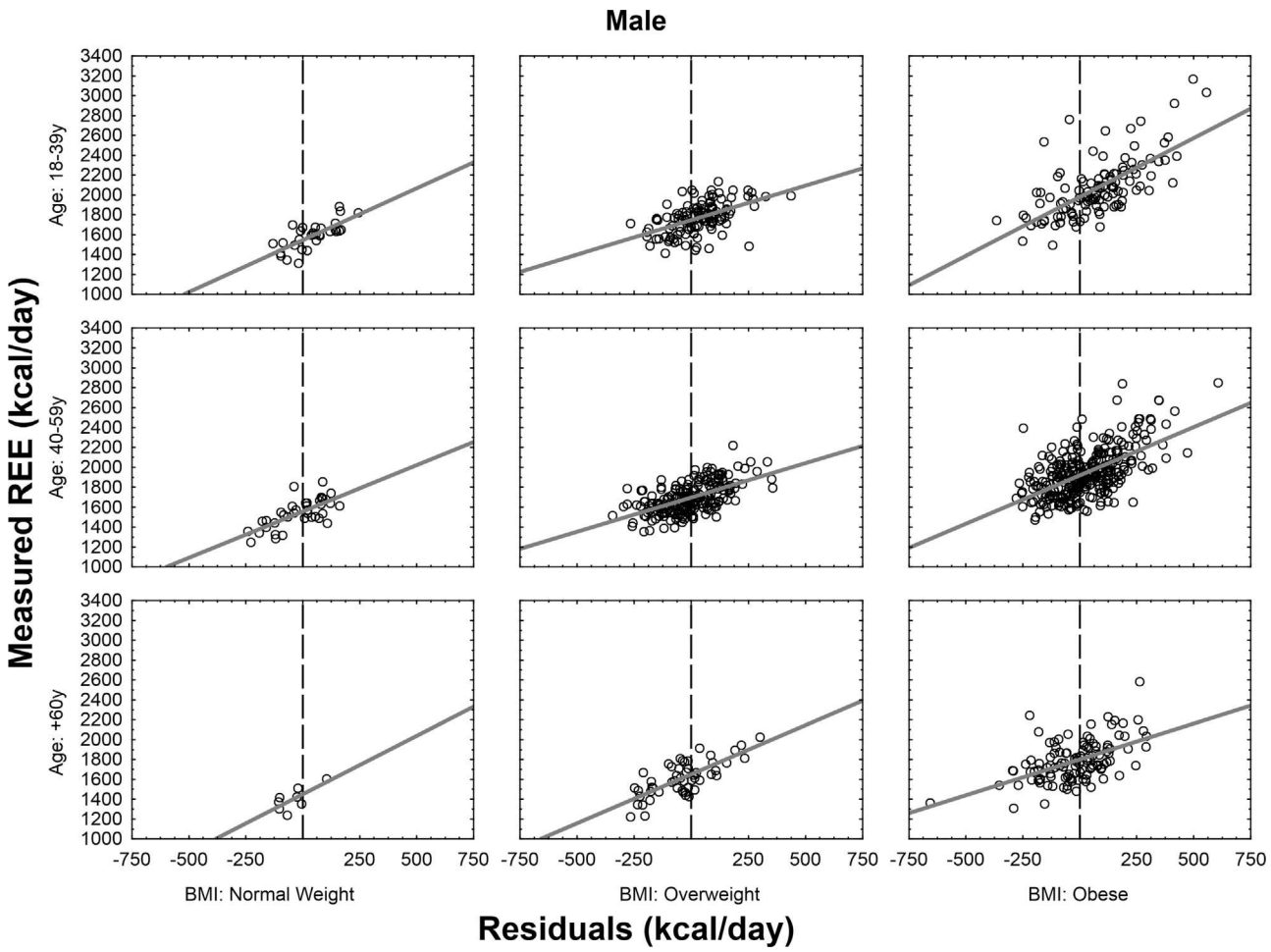

Fig. 2. Association between REE residuals with measured REE in female subjects. The residuals are calculated as the difference between predicted and measured REE; negative residual values indicate the presence of adaptive changes not explained by body composition, smoking, physical activity and health status. The y-intercept crossing the dashed line (residual value = 0) indicates the REE value associated with no adaptive changes.

mechanisms are likely to take place. In this case, the role of sex and BMI on the magnitude of the adaptation was less prominent as differences varied between 3.0 and 4.0% (50–60 kcal/day).

Our findings have important implications for the estimation of energy requirements and prevention of weight gain. The accuracy of predictive equations may be age-dependent which could result in a decreased accuracy and consequent mis-calculation of energy requirements. Hall et al. [26] have recently demonstrated that the obesity epidemic is largely attributed to small accrual of energy (~8 kcal/day) over periods of decades; therefore a measurement error of ~50 kcal/day on the overall energy balance of an individual can have a significant impact on the control of energy balance.

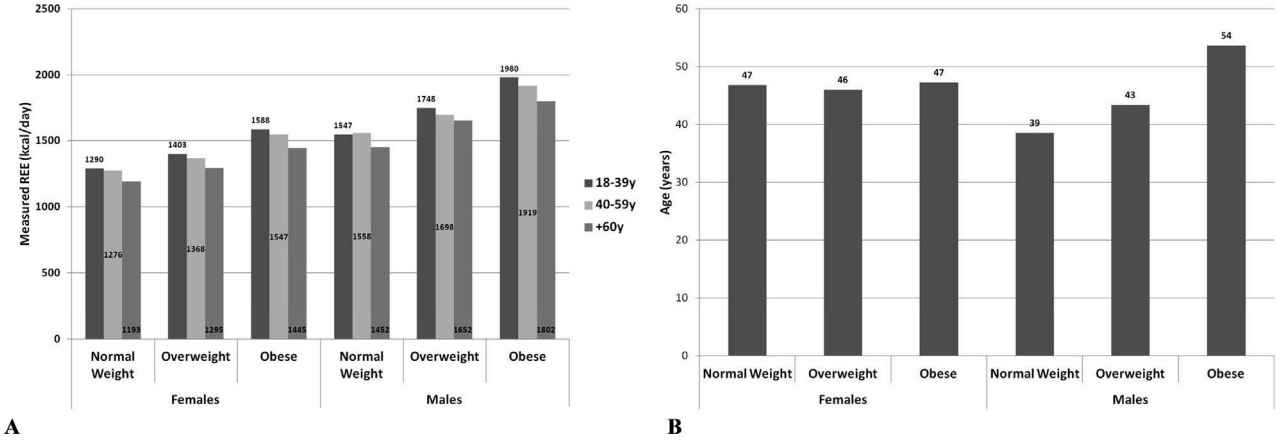

Fig. 3. Association between REE residuals with measured REE in male subjects. The residuals are calculated as the difference between predicted and measured REE; negative residual values indicate the presence of adaptive changes not explained by body composition, smoking, physical activity and health status. The y-intercept crossing the dashed line (residual value = 0) indicates the REE value associated with no adaptive changes.

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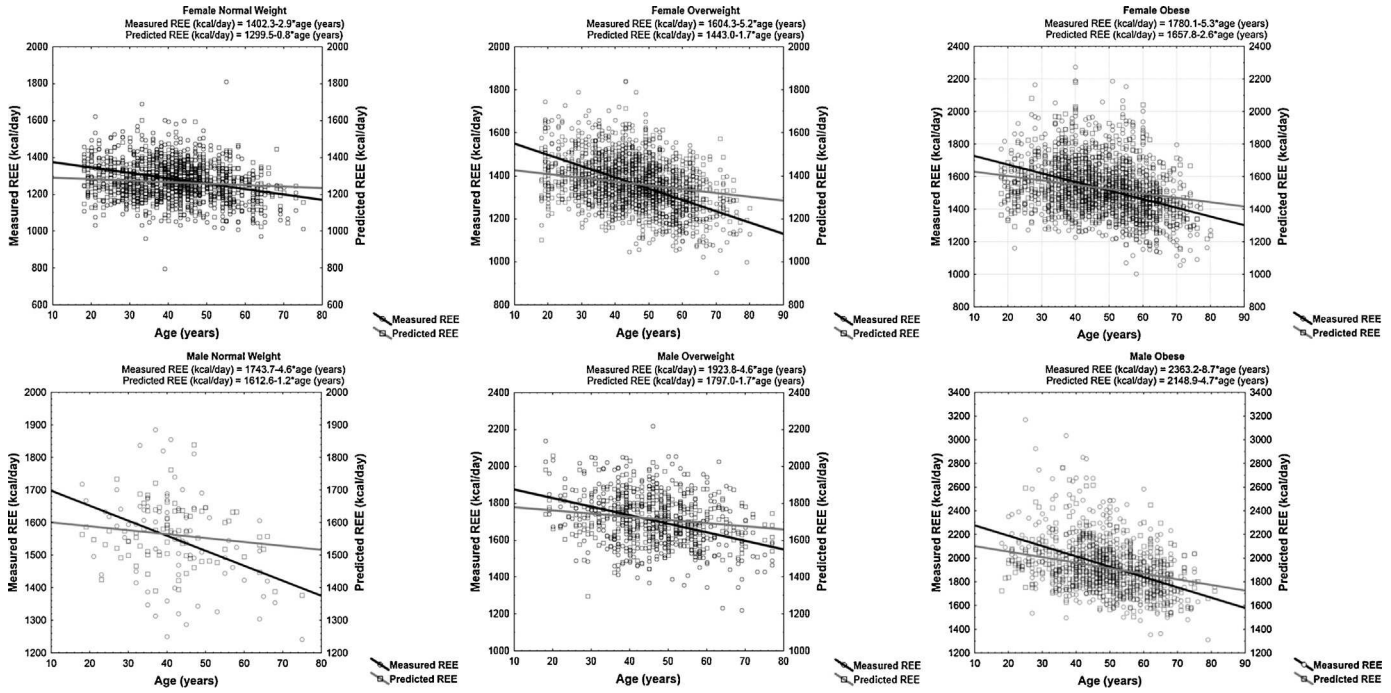

Fig. 4. Identification of age and REE metabolic windows. (A) It shows the specific cut off values for measured REE below which the residual analyses (Figs. 1 and 2) suggest the presence of adaptive changes in REE. (B) It shows the age at which adaptive changes in REE occurred in male and female subjects with different BMI (Fig. 1).

The mechanisms underpinning these metabolic adaptive changes are still largely undetermined. Overall, previous studies have found a lower REE adjusted for body composition (i.e. decrease of about 5%), which is in agreement with our results [15,24]. This decline in energy expenditure could be explained by a reduced metabolic rate of lean tissues. In addition, Gallagher et al. [27] demonstrated that the assumed stability of the metabolic rate attributed to individual organs and tissues across the adult age span is probably incorrect and that the theoretical values of organ tissue-specific metabolic rates, which are largely based on young adults, may not be applicable to older subjects.

5. Conclusions

In summary, we conclude that sex and degree of adiposity may influence the rate and level of age-related decline in REE. Critical age windows have been identified for the onset of an accelerated decline in REE not explained by changes in body composition and lifestyle factors. If confirmed in future studies, this information may provide the opportunity for timely interventions to minimize the onset of adaptive metabolic mechanisms and play a role in the maintenance of a healthy body composition phenotype.

Contributors

The manuscript was conceived by MS who analyzed the data and wrote the first draft of the manuscript. Data were collected by AL, SB, AB and AT. All authors contributed to critical interpretation subsequent of results. All authors contributed to the final revision of the manuscript. The corresponding author (MS) is the guarantor for the manuscript and had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis reported in the manuscript.

Competing interest

All authors have no conflicts of interest to declare.

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Ethics

The study procedures were approved by the University of Milan Ethical Committee and all participants gave written informed consent.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.maturitas.2014.12.023.

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