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Short Communication

Grade of adiposity affects the impact of fat mass on resting energy expenditure in women

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Body fat mass (FM) adds to the variance in resting energy expenditure (REE). However, the nature and extent of this relationship remains unclear. Using a database of 1306 women and a linear regression model, we systematically analysed the contribution of FM to the total variance in REE at different grades of adiposity (ranges of body %FM). After adjusting for age, the relative contribution of FM on REE variance increased from low (≤10 %FM) to normal (>10– ≤30 %FM) and moderately elevated (>30– ≤40 %FM) grades of adiposity but decreased sharply at high (>40– ≤50 %FM) and very high (>50 %FM) grades of adiposity according to the ratio between regression coefficients. These data suggest that the specific metabolic rate of fat tissue is reduced at high adiposity. This should be considered when REE is normalized for FM in obesity.

Resting energy expenditure: Fat mass: Fat-free mass: Women

Understanding the determinants of interindividual variance in resting energy expenditure (REE) is indispensable for interpreting (i.e. normalizing) or even predicting metabolic rate. Fat-free mass (FFM) explains 70–80 % of variance in REE. This is plausible because in a two-compartment model FFM is viewed as a surrogate for the metabolically active, oxygen-consuming body cell mass. By contrast, fat mass (FM) resembles the metabolically inert lipid compartment of the body. However, a number of studies also showed an independent contribution of FM (in kg) to the variance in REE[1–9]. The contribution of FM to REE is generally explained by the energy requirement of adipose tissue. When compared with the specific metabolic rate of lean tissue (ranging from 54 kJ/kg for skeletal muscle to 1841 kJ/kg for heart and kidney, respectively[10]), the specific metabolic rate of adipose tissue is low (11·3–14·3 kJ/kg lipid[11]). In contrast to these *in vitro* results, regression equations from population analyses reveal different relationships between the effect of either FFM or FM on REE, i.e. the ratio between the regression coefficients of FFM and FM on REE ranged between 1·5:1[1] and 7:1[4], suggesting that each kg of lean tissue exerts a 1·5–7 times greater effect on REE than did each kg of fat tissue. These discrepant results might be caused by differences in (1) age between study populations and/or (2) the degree of adiposity which might affect the secretion of metabolically active adipose tissue-derived hormones such as leptin, resitine or adiponectin. The contribution of the grade of adiposity on the relationship between REE and FM is currently unknown. The present study offers a systematic analysis of the relationship between REE, FFM,

Abbreviations: FFM, fat-free mass; FM, fat mass; REE, resting energy expenditure.

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FM and age using data of a large population of healthy women with a wide BMI range stratified by degree of adiposity.

Subjects and methods

A detailed description of the study population recruited in seven German research centres as well as the assessment of body composition and REE have been published previously[9]. Children and adolescents were excluded because of the impact of growth and maturity status on body composition and energy expenditure. In addition, men were omitted because of insufficient sample sizes in low and very high BMI groups. Finally, a subgroup of 1306 non-pregnant and non-lactating Caucasian women, with large range in age (18·0–91·2 years) and BMI (12·4–67·1 kg/m^2) served as the basis of the study. All subjects were investigated under clinically stable conditions and no subject took medications known to influence REE. Smoking was not considered as an exclusion criteria. Written informed consent was obtained from each subject at the beginning of the study, which was approved by the responsible local Ethic Committees.

Anthropometric data and body composition

Body weight was measured in underwear to the nearest 0·1 kg and standing height without shoes to the nearest 0·5 cm. Body composition was assessed by either bioelectrical impedance analysis (*n* 1079 subjects) or skinfold measurements (*n* 227 subjects). A single tetrapolar bioelectrical impedance analysis measurement of resistance and reactance was taken between the right wrist and ankle while in a supine position. Bioelectrical impedance analysis devices and algorithms are reported elsewhere[9]. Triceps, subscapular and supraileacal skinfolds were measured on the right side of the body to the nearest 0·5 mm by a Lange Skinfold Caliper as a mean of three measurements taken by the same investigator (see Müller *et al.* [9] for respective equations).

Assessment of resting energy expenditure

REE was obtained by indirect calorimetry using different ventilated hood systems, or a respiratory chamber (see Müller *et al.* [9] for description of the individual measurement procedures, technical devices and calibration). Continuous gas exchange measurements were taken in the morning after an overnight fast. REE (kJ) was calculated by using the Weir equation (ventilated hood) or by $16{\cdot}18\ V_{O2} + 5{\cdot}02\ V_{CO2} - 5{\cdot}99\ N_{excretion}$ (respiratory chamber).

Statistics

Stepwise linear regression analysis (SPSS version 13.0; SPSS Inc., Chicago, IL, USA) was used to model the relationship between REE and body composition at varying grades of adiposity. Study centre was not a significant covariate in these models. REE was adjusted for age and body composition using linear regression analysis. Adjustment for age was performed because of the age-dependent decrease in the relative contribution of high metabolic rate organ mass to FFM[12] and mitochondrial dysfunction in the elderly[13] that both contribute to a lower REE per FFM with age. Differences between

Table 1. Characteristics of the study population by grade of adiposity (percentage fat mass)
(Mean values and standard deviations)

	Age (years)		BMI (kg/m^2)		FFM (kg)		FM (kg)		FM (%)		REE (MJ/d)		REE_{adj1} (MJ/d)		REE_{adj2} (MJ/d)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
All (*n* 1306)	45·0	17·8	27·3	7·5	47·5	10·4	26·8	12·9	34·4	9·6	6·13	1·32	6·13	1·00	6·13	0·87
%FM groups																
⩽ 10 (*n* 23)	24·5	3·6	15·8	2·9	40·7	4·7	5·1	5·0	5·9	2·5	4·55	0·72	5·03	0·57	5·62[a]	0·49
> 10– ⩽ 30 (*n* 386)	35·3	14·7	22·0	5·8	45·4	9·7	15·4	5·5	24·5	4·6	5·65	1·05	5·78	0·75	6·15[b]	0·74
> 30– ⩽ 40 (*n* 519)	46·1[a]	16·8	28·0	5·5	49·7	10·2	27·2	6·6	35·2	2·9	6·26	1·24	6·08	1·02	6·15[b]	0·96
> 40– ⩽ 50 (*n* 344)	55·4	15·9	31·7	6·5	46·9[a]	11·0	36·9	8·7	44·1	2·6	6·44	1·44	6·54	0·93	6·15[b]	0·88
> 50 (*n* 34)	47·9[a]	19·0	41·2	8·3	47·2[a]	9·0	62·5	21·6	55·9	5·9	7·49	1·53	7·53	1·07	5·86[a]	0·72

FFM, fat-free mass; FM, fat mass; REE, resting energy expenditure; REE_{adj1}, REE adjusted for age and FFM; REE_{adj2}, REE adjusted for age, FFM and FM.
[a,b]Mean values within a column with a common superscript letter were not significantly different.

Table 2. Age-adjusted covariate effects of fat-free mass (FFM) and fat mass (FM) on resting energy expenditure (REE) by grade of adiposity (%FM)*

	K1 FFM†	K2 FM†	K1/K2	Intercept	R^2	SEE
All (*n* 1306)	12·1	11·2	1·08	744·1	56·7	207·9
%FM groups						
≤ 10 (*n* 23)	15·4	17·9	0·86	356·3	62·4	113·1
> 10– ≤ 30 (*n* 386)	11·8	14·4	0·82	629·2	52·7	173·0
> 30– ≤ 40 (*n* 519)	5·5	19·3	0·28	926·3	42·6	225·4
> 40– ≤ 50 (*n* 344)	12·0	10·4	1·15	886·0	63·3	210·8
> 50 (*n* 34)	11·5	7·1	1·62	1097·2	80·5	169·3

K1, K2, regression coefficients; R^2, covariate variance; SEE, standard error of the estimate.
* REE (kcal/d) = K1 × FFM (kg) + K2 × FM (kg) + intercept.
† All regression coefficients were significant: $P<0·001$.

categories of %FM are analysed by ANOVA with Bonferoni's *post hoc* test.

Results

Subject characteristics for the total study population are shown in Table 1 stratified into five subgroups according to the grade of adiposity (defined by %FM). REE as well as REE adjusted for age and FFM increased with increasing %FM. These differences disappeared after further adjustment for FM in a range between >10 and ≤50 %FM. By contrast, REE adjusted for age, FFM and FM was significantly lower at ≤10 %FM and >50 %FM.

Multivariate linear regression models with measured REE as dependent variable, and age, FFM and FM as independent variables as well as regression coefficients (K1 and K2) are shown in Table 2. At both a very low (≤10 %FM) and a very high grade of adiposity (>50 %FM) the variance in REE was mainly (46·5 and 64·5 %) explained by FM in kg whereas at intermediate %FM categories it was 3·4, 12·4 and 1·4 %. The ratio between K1 and K2 decreased with increasing adiposity from ≤10 %FM to >10– ≤30 %FM and >30– ≤40 %FM. Thus, the relative impact of FM on REE variance increased with increasing %FM with a concomitant decrease in the relative contribution of FFM. By contrast, at high (>40– ≤50 %FM) as well as at very high (>50 %FM) grade of adiposity, the K1/K2 ratio sharply increased to values >1, suggesting a lower impact of FM *v.* FFM in obese subjects.

Discussion

We have shown that the effect of absolute FM on the variance in REE depends on the grade of adiposity. Up to a FM of 40 % it increased with increasing adiposity, but decreased with a further increase in %FM. There may be at least two explanations for this finding. First, a lower specific metabolic rate of adipose tissue in obesity may be explained by greater adipocytes and obesity-associated mitochondrial dysfunction and degeneration. This phenomenon has been shown in human skeletal muscle[14] and also occurs in adipocytes of obese *db/db* mice[15]. Moreover, *in vitro* the specific metabolic rate of adipose tissue decreased with increasing grade of obesity[11]. Alternatively, a lower relative contribution of FM to REE may be explained by a higher specific metabolic rate of FFM. In obesity, metabolic alterations associated with insulin resistance have been shown to correlate with an elevated REE[16]. The latter explanation is contradicted by our finding of a significantly lower REE adjusted for age, FFM and FM in subjects with >50 %FM (Table 1). The present observation indicates an overestimation of the specific metabolic rate of adipose tissue rather than an underestimation of the energy requirement of FFM. Although both effects may be present simultaneously, an underestimation of the specific metabolic rate of FFM only partly compensates the overestimation in the energy requirement of adipose tissue.

In severely obese subjects (>50 %FM) FM explained the main variance in REE (see Results). This is in line with other studies showing a higher 'impact' of FM on REE in obese populations[1,2,4,5,8] but a lower or even absent effect in lean subjects[17]. These earlier findings were explained by the low specific metabolic rate of adipose tissue because adipose tissue mass has to become large before significantly contributing to REE[4]. However, this interpretation may be misleading because the coefficient of determination for FM was also higher at a very low FM (see Results). A steep relationship between REE and FM in underweight females with anorexia nervosa has been observed previously in our group[18]. This relationship is lost after weight gain (i.e. gain in FM) of about 8–10 kg body weight. Although in the underweight patients the relationship was confirmed for REE *v.* serum leptin levels, it was unlikely to be explained by leptin secretion, because it remained no longer significant after adjusting FM for leptin levels (V Haas *et al.*, unpublished results).

The present finding of a lower impact of FM on REE at high adiposity (>40 %FM) remains causally enigmatic, but may be consistent with the finding that (1) the coefficient of FM in the REE prediction equation was even negative in severely obese subjects[19] and (2) REE is systematically overestimated in obese subjects by standard prediction equations[20–22]. Part of the 'thermic effect' of FM may be explained by adipocyte secretory activity (e.g. leptin was considered a thermogenic hormone[23]). However, human data are equivocal and future studies are needed to investigate the impact of adipokine secretion on the 'thermic effect' of FM in lean *v.* obese subjects. Low sample sizes in the lowest and highest category of FM are a limitation of the present study. Further studies in the extremes of body composition are needed to confirm the present results.

In conclusion, the impact of FM on the variance in REE depends on the grade of adiposity. The impact of FM on REE increased up to 40 %FM. At higher grades of adiposity the

impact of FM on REE was reduced. This decrease cannot be sufficiently explained by the metabolic rate of adipose tissue. Adjusting REE for FM by an equation derived from lean or overweight subjects may lead to spurious conclusions in obesity.

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