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Computing DIT from energy expenditure measures in a respiratory chamber: a direct modeling method

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Abstract

The possibility of computing Diet Induced Thermogenesis (DIT) is an important feature of metabolic investigations. However, methodological problems have affected the determination of DIT in the indirect calorimetric chamber. DIT has been commonly estimated by regressing energy expenditure on a measure of physical activity. Although used for many years as the only feasible approach to calculate DIT in a respiratory chamber, this traditional method has been criticized because of an apparent underestimation of the DIT, but no alternative method has been suggested so far. The present work proposes to estimate DIT directly by means of a mathematical model. This approach also allows to simultaneously estimate other parameters, namely resting energy expenditure (REE), physical activity (PA) and physical exercise (PE).

Keywords: Energy Expenditure; Diet Induced Thermogenesis; Mathematical Model; Obesity

1. Introduction

The best approach to measure long-time energy expenditure (EE), also including the contribution of physical activity to the total EE is the indirect calorimetry in a respiratory chamber or the double-labeled water technique [1–3]. The human respiratory chamber, an experimental structure that offers the advantage to closely mimic physiological conditions over an extended period of time while regular meals are consumed throughout the day, is used for 24-h assessment of EE and its components as well as substrate (fat and carbohydrate) oxidation. These measures are

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important for nutrient and energy balance studies in both normal and disease states, including determination of factors contributing to obesity, effects of normal life processes such as aging or pregnancy on energy balance, and effects of various treatments for obesity on substrate oxidation and EE. Indirect calorimetry techniques can also be used to assess the factors contributing to daily energy expenditure, such as frequency and intensity of physical activity or exercise, thermic effect of food, drug treatments, etc. Total energy expenditure includes: resting Energy Expenditure (REE), Diet-Induced Thermogenesis (DIT), and EE due to physical activity (PA) and, eventually, to physical exercise (PE).

In the literature, Resting Metabolic Rate (RMR) and Basal Metabolic Rate (BMR) often replace REE. DIT defines the increase in heat production by the body after eating. It is due to both the metabolic energy cost of digestion (the secretion of digestive enzymes, active transport of nutrients from the gut, and gut motility) and the energy cost of forming tissue reserves of fat, glycogen, and protein. It is usually expressed as a percentage of the energy intake.

Methodological problems have affected the study of DIT in the respiratory chamber. Schutz et al. [4] proposed to calculate DIT over a 15-h period (disregarding the sleeping hours) using a regression of energy expenditure on some measure of physical activity (like the microwave-sensor-derived measurement index). Although used for many years as the only feasible approach to the computation of DIT in a respiratory chamber, the method of Schutz et al. has been criticized by Tataranni et al. [5] because of an apparent underestimation of the DIT. These authors [5] report that, when DIT was calculated as the difference of 24-h EE in the same subjects studied twice, in fed or fasted state, it resulted to be significantly higher ($12 \pm 5\%$ of energy intake versus $5 \pm 7\%$ of energy intake, $p < 0.01$) than using the regression method [4]. However, they did not suggest any different method for calculating DIT in the respiratory chamber. It is conceivable that subjects fasted for one day may already show downward adaptation of their basal energy expenditure, and therefore that the observed difference between fed and fasted energy expenditure may exceed the simple contribution of DIT.

However, the question remains open, in the lack of some alternative way of computing DIT from indirect calorimetric data. Furthermore, a subpopulation of subjects frequently studied by means of indirect calorimetry, namely the morbidly obese patients ($\mathrm{BMI} > 40\ \mathrm{kg/m^2}$), typically show very little movement within the chamber, due to the static behavior induced by extreme body size. In these subjects, the fundamental assumption of co-variation of EE with movement is difficult to maintain since movement varies very little. In these cases, in fact, the regression employed by the traditional Schutz's method has very small slope, with a very large relative variability, and is of limited usefulness.

The present work proposes to estimate DIT directly from the EE measurements obtained throughout a single day in the respiratory chamber by means of a mathematical modeling approach in a sample of morbidly obese individuals. In this way other parameters, namely resting energy expenditure (REE), physical activity energy expenditure (PA) and physical exercise energy expenditure (PE) may be simultaneously obtained. A comparison between the DIT values obtained using the method proposed by Schutz et al. [4] and those computed by the present model is reported.

Although the units for EE and REE represent power (kcal/24 h) instead of energy (kcal), we will use the terms "Energy Expenditure" and "Resting Energy Expenditure" without mentioning "over 24 h", in order to be consistent with the literature.

2. Materials and methods

2.1. Subjects

Twenty morbidly obese subjects (6 men and 14 women) were included in the study. Anthropometrical characteristics of the study subjects are given in Table 1. None had diabetes mellitus or any other endocrine or non-endocrine disease. At the time of the study, all subjects were on an *ad lib* diet, with the following average composition: 55% carbohydrate, 30% fat, 15% protein (at least 1 g/kg of body weight). This dietary regimen was maintained for one week prior to the study. The Institutional Review Board approved the study protocol; the nature and purpose of the study were carefully explained to all subjects before they provided their written agreement to participate. The protocol guidelines of the hospital Ethics Committee were followed.

2.2. Body composition

On the day preceding the study, body weight was measured to the nearest 0.1 kg by a beam scale and height to the nearest 0.5 cm using a stadiometer (Holatin, Crosswell, Wales, UK).

2.3. Total body water (TBW) measurement

TBW was determined using 0.19 Bq of tritiated water in 5 ml of saline solution administered as an intravenous bolus injection [6]. Blood samples were drawn before and 3 h after the injected dose. The dpm were counted in duplicate on 0.5 ml of plasma using a Beta-scintillation counter (Canberra-Packard, Model 1600TR, Meriden, CT, USA). Corrections were made (5%) for non-aqueous hydrogen exchange [2] and water density at body temperature was assumed to be 0.99371 kg/l. TBW (kg) was computed as $3H_2O$ dilution space (liters) $\times$ 0.95 $\times$ 0.99371. The within-person day-by-day CV reported for this method is 1.5% [7]. The plasma tritium values have been adjusted for dilution by plasma solids constant, namely TBW = dpm/g water = dpm/g plasma/0.94.

2.4. Respiratory Chamber

The Respiratory Chamber protocol has been the following. Subjects spent a day (starting at 8:00 AM) in the respiratory chamber (volume 23.6 m^3) at the Metabolism Unit of the Catholic

Table 1
Anthropometrical characteristics of the study subjects

Subjects (n)	20
Sex (M/F)	7/13
Age (yr)	40 $\pm$ 12
Height (cm)	162 $\pm$ 12
Weight (kg)	130 $\pm$ 29
Body Max Index-BMI (kg/m^2)	49.4 $\pm$ 7.8
Fat Free Mass-FFM (kg)	63 $\pm$ 21
Fat Mass-FM (kg)	66 $\pm$ 14

University School of Medicine in Rome. Twenty-four-hour energy expenditure (24-h EE) and resting energy expenditure (REE) were measured as previously described [8]. Briefly, the carbon dioxide (CO_2) concentration was measured by a 2% full-scale (0–2%) infrared absorption analyzer (URAS 3G, Hartmann & Braun, Frankfurt, Germany), while the oxygen (O_2) concentration was assessed by a 2% full-scale (19–21%) paramagnetic analyzer (Magnos 4G, Hartmann & Braun, Frankfurt, Germany). Both gas analyzers operated with a precision of 0.02 vol%. The zero values of both analyzers were calibrated by allowing fresh air to flow through the sample and the reference lines simultaneously, whereas the span values were calibrated using commercially available gas mixtures (Rivoira, Torino, Italy). The composition of the gas mixture used to calibrate the O_2 analyzer was 19.48% O_2 in N_2. The composition of the gas mixture used to calibrate the CO_2 analyzer was 1.5% CO_2 in N_2. The calibration procedure was made every day at the beginning of each experimental session. The algorithm used for computing O_2 consumption (V_{O_2} ml/min) and CO_2 production (V_{CO_2} ml/min) approximated the gas consumption/production during a time interval by adding two independent quantities: dynamic (open) and static (closed) gas production [6], consumption being negative production. Values were corrected for temperature, barometric pressure and humidity. Energy expenditure was calculated according to Ferrannini [9]. Protein oxidation was determined from 24-h urinary nitrogen excretion (BUN Analyzer, Beckman Instruments, Fullerton, CA); carbohydrate and lipid oxidation rates were determined from the non-protein respiratory quotient (npRQ). Calibration procedures, precision, and variability of the respiratory chamber have been reported elsewhere [10,11]. Physical activity was monitored by means of two orthogonal ultrasound sensors: the sensitivity of the receivers was set so that respiratory movements were not detected.

2.5. Exercise testing

On the day preceding the experimental session, the patients entered the Energy Metabolism Research Unit at 08:00 AM after an overnight fast. They were allowed to practice walking on the motorized treadmill until they were able to walk without holding on to the railings in order to become familiar with the testing equipment. During the day spent in the calorimetric chamber, the patients performed a physical exercise session at 04:00 PM by walking for 30 min at a constant speed of 3 km/h up a 10% grade. So PA refers to the Physical Activity or normal movements of the patient during the 24 h, while PE refers to the Physical Exercise on the motorized treadmill (only 30 min in the 24 h).

2.6. Diet in the respiratory chamber

During the day spent in the respiratory chamber, all subjects were assigned a diet with an energy content of 30 kcal/kg of fat-free mass (kg_{FFM}) consisting of 55% carbohydrate, 30% fat and 15% protein. This amount was divided as follows: 20% at breakfast, 40% at lunch, 10% as an afternoon snack, and 30% at dinner. A dietician using common foods such as meat, fish, vegetables, bread, fruit, etc prepared the 4 meals served in the chamber. The food given and returned was weighed to the nearest gram on precision scales (KS-01, Rowenta, Berlin, Germany). The nutrient content of all food items was calculated by using computerized tables (Food Processor II, Hesha Research, Salem, OR, modified according to the food Tables of the Istituto Nazionale di Nutrizione, Italy).

The energy content of food was computed as follows: 4.3 kcal/g for protein, 4.2 g for starch (or starch equivalent), and 9.3 kcal/g for fat.

2.7. 24-h nitrogen and lipid output

Twenty-four-hour urine collection was carried out during the day spent in the calorimetric chamber. The BUN Analyzer analyzed total urinary nitrogen.

3. Mathematical modeling and statistical analysis

The EE time course during the 24 h spent in the calorimetric chamber was modeled with a generalized linear model in the parameters: it is a mixture of lognormal functions plus a linear/quadratic contribution which takes into account the mobility of the subject.

The mathematical model is the following:

$$\begin{aligned}\mathrm{EE}(t) = {} & \mathrm{REE} + (\rho_1 \mathrm{radar}(t) + \rho_2(\mathrm{radar}(t))^2) \\ & + \mathrm{DIT}\left(\sum_{i=1}^{4}[w\, kal_i\, \mathrm{Lognormal}(\mu, \sigma^2; t - \tau_i)]\right) \\ & + \gamma\, \mathrm{Lognormal}(\mu, \sigma^2; t - \tau_e)\end{aligned}$$

where

- $\mathrm{EE}(t)$ (kcal/24 h) is energy expenditure;
- t (min) is time;
- REE (kcal/24 h) is the constant Resting Energy Expenditure;
- $\mathrm{radar}(t)$ [a.m.u.: arbitrary movement unit] is the sum of the two microwave radar measures at time t;
- ρ_1 [(kcal/24 h)/a.m.u.] expresses the linear effect of the monitored mobility of the subject over the day on the EE time course;
- ρ_2 [(kcal/24 h)/(a.m.u.)^2] explains the quadratic effect of the monitored mobility of the subject over the day on the EE time course;
- DIT [fraction of the caloric intake] is Diet-Induced Thermogenesis;
- w (kg) is subject's fat-free mass (FFM);
- γ (kcal/24 h) the EE due to PA;
- τ_i (min) ($i = 1, 2, 3, 4$) the starting time of the meals;
- τ_e (min) is the starting time of the exercise
- kal_i (kcal/24 h/kg) (i=1, 2, 3, 4) are the caloric amount coefficients. They were obtained as follows:

(i) Set k (kcal/24 h/kg) as the total caloric intake per kg FFM per day, where $k = k_{\mathrm{LP}} + k_{\mathrm{CD}} + k_{\mathrm{PD}}$ with $k_{\mathrm{LD}} = 0.3k$, $k_{\mathrm{CD}} = 0.55k$ and $k_{\mathrm{PD}} = 0.15k$, respectively the amount of ingested (D: dietary) nutrients (L = lipids, C = carbohydrates and P = proteins).

(ii) Correct the amounts of ingested proteins as follows: $k_{\mathrm{PD}}^{\mathrm{corrected}} = (k_{\mathrm{PD}} - 4.2\mathrm{N}_2)$, where N_2 (g/24 h) is the daily urinary excretion of nitrogen.

(iii) Re-calculate the total caloric intake as $k^{\text{corrected}}=k_{\text{CD}}+k_{\text{PD}}^{\text{corrected}}+k_{\text{LD}}$ and $Kal_1=0.2k^{\text{corrected}}$, $Kal_2=0.4k^{\text{corrected}}$, $Kal_3=0.1k^{\text{corrected}}$, $Kal_4=0.3k^{\text{corrected}}$, following the proportions of administered calories in the four meals.

- μ (min) is the mean of the lognormal functions;
- σ^2 (min^2) is the variance of the lognormal functions;

The last lognormal function, Lognormal$(\mu,\sigma^2;t-\tau_e)$, takes into account the effect of physical exercise on the EE time course. It has the same shape (same parameters) of the others but, of course, different starting time and different amplitude (γ).

The mathematical formulation of the lognormal functions is as follows:

$$\text{Lognormal}(\mu,\sigma^2;t-\tau)=\begin{cases}0, & t\leqslant\tau\\ \dfrac{1}{\sigma\sqrt{2\pi(t-\tau)}}\exp\left\{-\dfrac{1}{2}\left(\dfrac{\log(t-\tau)-\mu}{\sigma}\right)^2\right\}, & t>\tau\end{cases}.$$

The reason why lognormal functions were employed is because EE arises after food is ingested, reaches quickly a peak and slowly decreases, reaching basal levels. Both qualitative data analysis and physiological considerations suggest to model EE meal time behavior by means of lognormal functions where the slope of the increasing EE is higher (in absolute value) with respect to the slope of the decreasing EE. Lognormal function parameters, namely μ, σ^2, are assumed to be independent from τ_i $(i=1,2,3,4)$ and τ_e. This in order to reduce the number of parameters to be estimated and because the shape of the five lognormal functions may be considered the same for all meals and PE, except for a constant magnitude which takes in account the actual caloric intake (kal_i, $i=1,2,3,4$, known constants) or caloric expenditure due to physical exercise (γ, parameter to be estimated). The parameters to be estimated are thus: REE, ρ_1, ρ_2, DIT, μ, σ^2, γ. The aim of the model is to differentiate the effects on Energy Expenditure due respectively to:

(1) Resting Energy Expenditure (REE),
(2) Global Physical Activity (ρ_1 radar + ρ_2 radar^2);
(3) Diet Induced Thermogenesis (DIT)
(4) Physical exercise (γ Lognormal$(\mu,\sigma^2;t-\tau_e)$).

The model is thought as an additive scheme, where if no physical exercise is performed the fourth term is neglected. Yet, kal_i, $i=1,2,3,4$, can be modified accordingly to different diet regimens.

3.1. Schutz method

The Schutz method has been applied following the descriptions given in the literature [4]. The EE time-course during the 24 h spent in the calorimetric chamber has been modeled by a linear regression relationship between EE and PA (by means of radars monitorizing the measurable degree of physical activity). The regression equation is calculated after having preprocessed the data relating to EE and PA. REE is measured by averaging the EE between 3 h after the dinner and 1 h before the subject wakes up. The method to measure DIT depends on simultaneous continuous measurement of both the activity level by radar and the energy expenditure by the respiratory chamber over

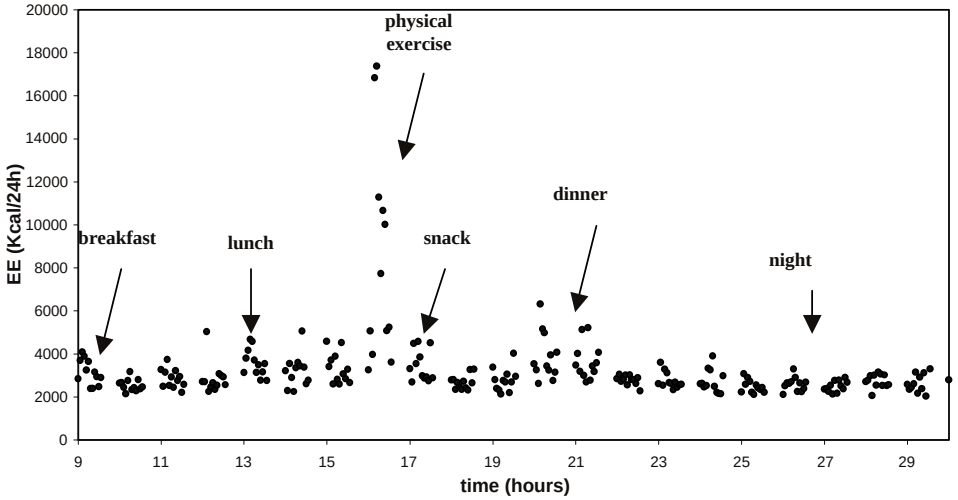

Fig. 1. Sample plot of 24 h Energy Expenditure time course. Meal-times are also shown.

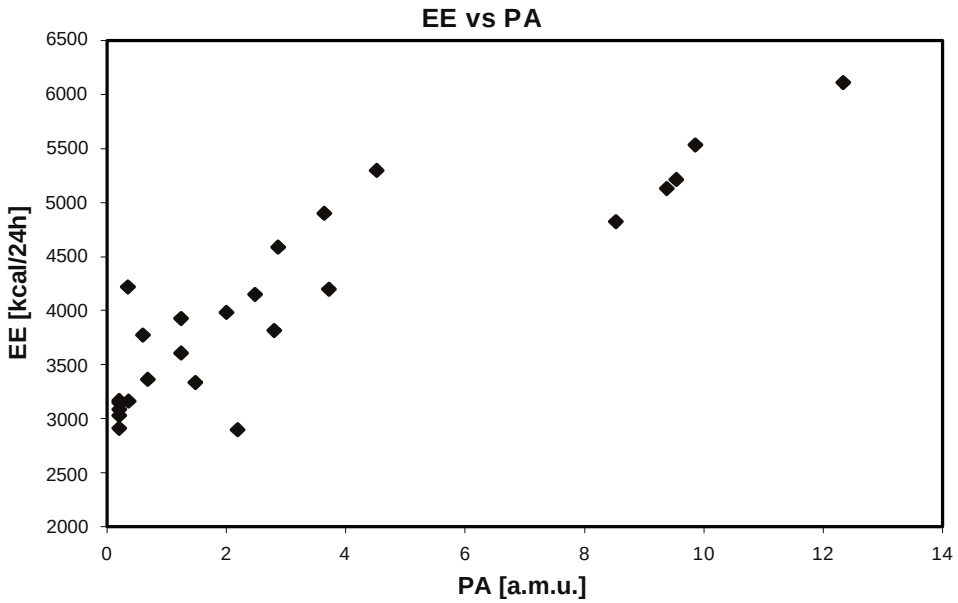

Fig. 2. Scatter diagram of EE versus PA by Schutz method (each point represents measures averaged over 30 min both for EE and radars).

a 14–15 h period, i.e. from 8:30 AM to approximately bed time (10:30 to 11:30 PM). A typical pattern of energy expenditure over one day is plotted in Fig. 1. The corresponding relationship between the physical activity (PA) averaged over 30 min periods, and the energy expenditure (EE), averaged over the same periods of time, is shown in Fig. 2. The intercept of the regression line at zero activity, EE_0, represents the energy expenditure in the inactive state. The value of EE_0 includes

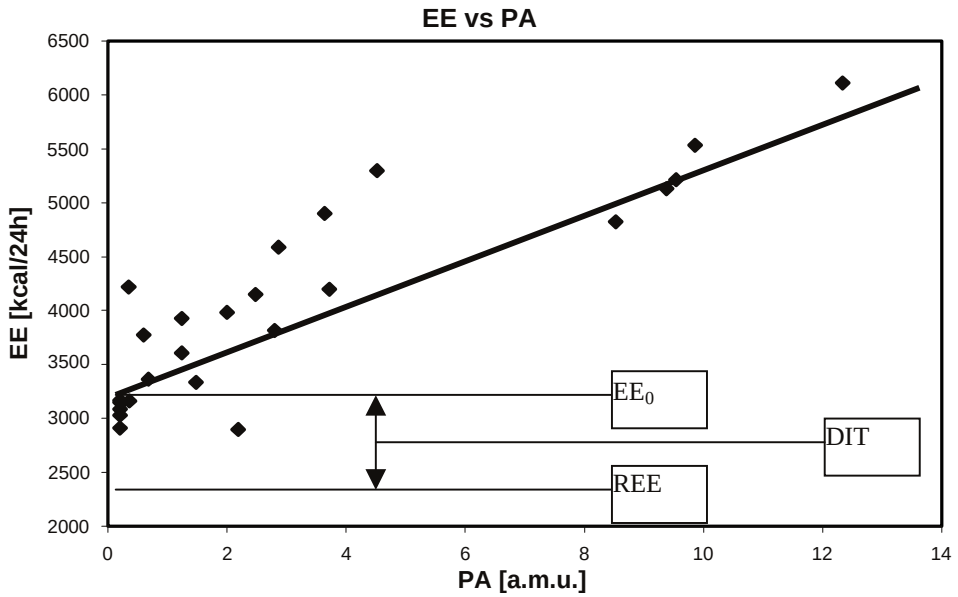

Fig. 3. Example of DIT computation by Schutz method. The solid regression line is also shown.

REE and DIT. Therefore, the difference between EE_0 and REE is supposed to represent the DIT coefficient (Fig. 3). The value of DIT is expressed as a fraction of the total energy ingested during the day. The net response over 14 h is obtained by subtracting REE from EE_0 and by dividing the results by the total energy content, E_{intake} of the four meals (assumed to be the only source of calories over the 24 h), i.e.

$$\text{DIT} = \frac{\text{EE}_0 - \text{REE}}{E_{\text{intake}}}$$

where EE_0 and REE and E_{intake} have all dimension of kcal/24 h. The measurements of energy expenditure during exercise have been discarded in computing DIT coefficients.

3.2. Parameter estimation techniques

SAS Statistical Analysis System software and procedures have been used to perform parameter estimation. The Schutz model has been estimated by a standard linear regression procedure (Proc Reg) while our model parameter estimation has been performed by a standard non-linear regression analysis (Proc NLin). Model fitting was performed by unweighted least squares with a standard Levenberg–Marquardt algorithm and an Armijo line-search technique. The parameter estimation was obtained on each individual subject. On the model parameter estimates thus obtained, sample mean and sample standard error have been computed and measures of goodness of fit (R^2) are displayed. All results are expressed as mean ± standard error, unless otherwise specified. The comparisons between groups were performed by Student's *t*-test for samples of different variance.

4. Results

Tables 2 and 3 show, respectively, our model and Schutz method parameter estimation results. In Table 2 are reported the patient label, the estimate of DIT, the asymptotic standard error of the estimate of DIT and the estimate of the remaining model parameter, namely REE, the lognormal function parameters (μ and σ), γ, ρ_1 and ρ_2, Further, the energy intake and the R^2 of the model fit are reported for each patient. Minimum, maximum and average values are calculated for each parameter. The coefficient of variation of the sample of DIT estimates resulted to be 42.7%. Fig. 4 shows the EE predicted by the model against the experimental measures. Meals times are indicated as well as the time when physical exercise is performed.

Table 3 reports the patient label, the estimate of the DIT, the standard error of the estimate of DIT, the estimate of the REE, the estimate of the EE_0, the standard error of the estimate of the REE. Further, the energy intake and the R^2 of the model fit are reported for each patient. Minimum, maximum and average values are calculated. The coefficient of variation of the sample of DIT estimates resulted to be 151.7%.

Table 2
Our model parameter estimation results

PAT	DIT fraction	SE_{DIT}	REE	μ	σ	γ	ρ_1	ρ_2	Energy intake	R^2
1	0.071	0.030	1484	2.97	0.15	3547	46.5	−0.1	1798	0.76
2	0.293	0.060	1984	2.18	1.95	34986	59.6	−0.2	1277	0.84
3	0.183	0.060	2297	2.76	0.42	47909	72.9	−0.9	1294	0.73
4	0.257	0.092	2122	2.20	1.35	30063	110.1	−1.2	1083	0.72
5	0.068	0.085	3151	2.80	0.39	32968	131.1	−0.8	2661	0.83
6	0.113	0.030	3396	2.55	0.93	37993	61.5	−0.2	2420	0.61
7	0.086	0.017	2910	3.32	0.34	49515	39.6	0.0	2666	0.84
8	0.071	0.030	2481	3.11	0.29	30612	61.6	−0.4	1424	0.60
9	0.202	0.020	2748	2.86	0.52	105646	55.5	−0.7	2029	0.86
10	0.192	0.020	2450	2.77	1.23	47383	155.3	−2.8	1434	0.53
11	0.190	0.034	2582	2.52	1.18	44292	58.5	−0.3	1331	0.55
12	0.250	0.089	2145	2.91	2.77	2034	162.2	−1.9	1218	0.47
13	0.125	0.020	2784	2.94	0.75	64452	78.1	0.0	2605	0.82
14	0.169	0.040	2065	2.93	0.58	55527	41.2	−0.2	1424	0.83
15	0.268	0.073	2326	2.36	1.42	98203	−70.3	11.3	1451	0.82
16	0.115	0.021	3353	2.74	0.67	91657	127.0	−0.7	3243	0.84
17	0.209	0.103	3069	2.60	1.07	40502	84.9	−0.2	1730	0.68
18	0.288	0.048	2342	3.06	0.65	79577	92.8	−0.2	1427	0.89
19	0.295	0.043	1996	4.40	1.55	31416	56.2	−0.2	1372	0.81
20	0.232	0.066	2502	2.56	1.36	76255	27.9	0.0	1278	0.74
Min	0.068	0.017	1484	2.18	0.15	2034	−70.3	−2.8	1083	0.47
Max	0.295	0.103	3396	4.40	2.77	105646	162.2	11.3	3243	0.89
Average	0.184	0.049	2509	2.83	0.98	50227	72.6	0.015	1758	0.74

Table 3
Schutz method parameter estimation results

PAT	DIT fraction	SE_{DIT}	REE	EE_0	SE EE_0	Energy intake	R^2
1	0.100	0.025	1407	1586	44	1798	0.49
2	0.071	0.046	1901	1992	59	1277	0.64
3	0.194	0.135	2125	2376	175	1294	0.28
4	0.048	0.088	2036	2088	95	1083	0.63
5	0.107	0.043	3108	3392	115	2661	0.57
6	−0.136	0.057	3649	3322	138	2420	0.53
7	−0.034	0.071	2773	2683	189	2666	0.60
8	0.139	0.094	2531	2729	134	1424	0.41
9	0.119	0.059	2626	2866	120	2029	0.28
10	0.073	0.049	2493	2597	70	1434	0.55
11	0.105	0.074	2534	2674	99	1331	0.47
12	0.226	0.083	2071	2346	101	1218	0.65
13	0.101	0.072	2714	2977	188	2605	0.28
14	−0.025	0.085	2083	2048	122	1424	0.55
15	−0.104	0.085	2298	2147	124	1451	0.48
16	0.033	0.039	3228	3336	126	3243	0.72
17	0.218	0.114	3040	3416	198	1730	0.10
18	0.171	0.126	2249	2492	179	1427	0.25
19	0.013	0.050	2107	2125	69	1372	0.68
20	0.606	0.104	2209	2983	133	1278	0.11
Min	−0.136	0.025	1407	1586	44	1083	0.10
Max	0.606	0.135	3649	3416	198	3243	0.72
Average	0.101	0.075	2459	2609	124	1758	0.46

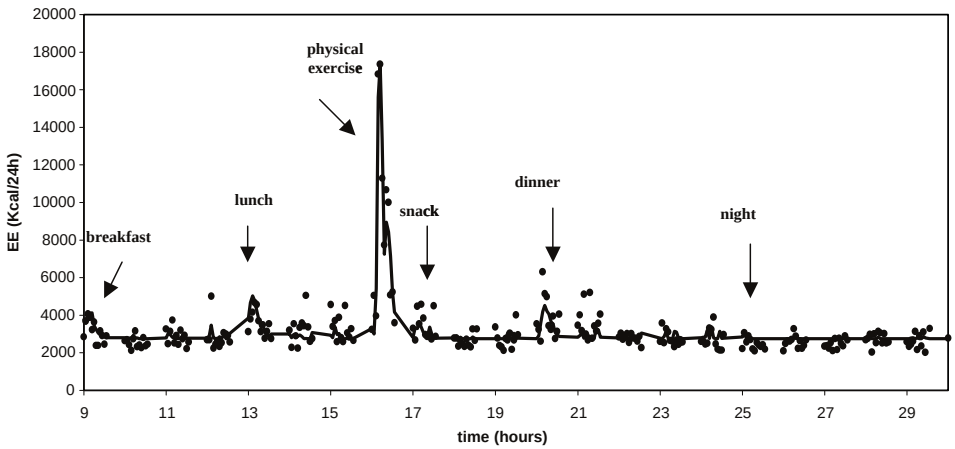

Fig. 4. Theoretical 24 h Energy Expenditure time course predicted by our model (solid line) versus observed data (dots). Meal-times are also shown.

5. Discussion

The mathematical formulation proposed in the present study represents the first attempt to model raw data resulting from indirect calorimetry measures and it allows the estimation of various components of EE during 24 h. The suggestion, postulated in the literature [5,11] that DIT computation by Schutz method may give rise to underestimation seems to agree with the results obtained in the present study. In our series Schutz method gives an average DIT of 0.101 ± 0.034 which is significantly lower ($p < 0.05$) than 0.184 ± 0.018, which is our model's average value.

Of course the real value of DIT is not known. However, further arguments support the greater reliability of the new model with respect to the traditional Schutz method: average standard error of the estimates was almost halved (0.049% against 0.075%) using our model. Yet the precision of the new formulation in estimating DIT is confirmed by the whole-sample coefficient of variation which was reduced by more than two thirds (42.7% versus 151.7%) and from the fact that, in some patients, negative values (patients 6, 7, 14, 15) or excessively high values (patient 20) result. Finally our model formulation gives generally good results in terms of goodness of fit (R^2 ranges from 0.47 to 0.89) and generally consistent and reliable results, both in terms of DIT values (all values between 0.068 and 0.295) and in terms of the standard error of each estimate.

One possible explanation for unreliability of the application of the traditional method in our series might be its main assumption: it presupposes a significant relationship between EE and radar, i.e. that there exists a positive covariance between EE and radar and that this is significantly different from zero. However, if the measured physical activity of the subject is low (for example in obese subjects, or when the mobility of the patients in the respiratory chamber is limited), the above assumption fails. Moreover, the postulated relationship can easily result quite unstable and non-robust estimates can result because of leverage and masking effects due to outliers [12,13]. Data preprocessing is adopted to prevent or weaken the presence of these outliers but it results in loss of information, which is particularly damaging when the covariance between EE and radar is near zero. The key point is that the patient within the respiratory chamber is an intrinsically non-linear dynamical system: any attempt to approximate it with a static linear relationship will cause loss of information, great uncertainty and unreliability in estimating relevant parameters, such as DIT. Our model formulation explicitly includes time in modeling the EE time course and suitable non-linear terms are utilized in order to overcome the above shortcomings. Although the new model has more parameters to be estimated, it has many degrees of freedom because no data preprocessing is performed and parameter estimation is conducted on the original data set (from 180 to 230 observations each subject).

In conclusion, the traditional Schutz method underestimates DIT in the average and appears to estimate DIT with excessive variation at least in obese subjects, who show little movement in the chamber. The proposed modeling procedure overcomes these drawbacks and can also give quantitative information regarding physical activity (PA), resting energy expenditure (REE) and physical exercise (PE) of subjects undergoing the respiratory chamber protocol.

6. Summary

The possibility of computing Diet Induced Thermogenesis (DIT) is an important feature of metabolic investigations. DIT defines the increase in heat production by the body after eating. It

is due to both the metabolic energy cost of digestion (the secretion of digestive enzymes, active transport of nutrients from the gut, and gut motility) and the energy cost of forming tissue reserves of fat, glycogen, and protein. It is usually expressed as a percentage of the energy intake. Total Energy Expenditure (EE) includes: Resting Energy Expenditure (REE), Diet-Induced Thermogenesis (DIT), and EE due to physical activity (PA) and, eventually, to physical exercise (PE).

The best approach to measure long-time energy expenditure (EE) is the indirect calorimetry in a respiratory chamber or the double-labeled water technique. The human respiratory chamber is an experimental structure that closely mimics physiological conditions over an extended period of time. It is used for 24-h assessment of EE and its components as well as substrate (fat and carbodydrate) oxidation. These measures are important for nutrient and energy balance studies in both normal and disease states (obesity, diabetes).

The standard method to calculate DIT [4] uses a regression of EE on some measure of PA. Although used for many years as the only feasible approach to the computation of DIT in a respiratory chamber, this method has been criticized because of an apparent underestimation of the DIT [11].

This present work represents the first attempt to build an alternative model of raw data resulting from indirect calorimetry measures. The EE time course during the 24 h spent in the calorimetric chamber was modeled with a generalized linear model in the parameters: it is mixture of lognormal functions plus a linear/quadratic contribution which takes into account the mobility of the subject. Parameter estimation results strengthen the idea that DIT computation by Schutz method gives rise to underestimation. In our series the classical method gives an average DIT of 10.1 ± 3.4 which is significantly lower ($p < 0.05$) than 18.4 ± 1.8, our model's average value. The precision of the new formulation in estimating DIT is confirmed by both the almost halved average standard error of the estimates (0.049% against 0.075%) and the whole-sample coefficient of variation which was reduced by more than two thirds (42.7% versus 151.7%), as well as from the fact that, in some patients, negative values or excessively high values result. Finally our model gives generally good results in terms of goodness of fit (R^2 from 0.47 to 0.89) and generally consistent and reliable results, both in terms of DIT values (all values between 0.068 and 0.295) and in terms of the standard error of each estimate.

In conclusion, the traditional method underestimates DIT in the average and appears to estimate DIT with excessive variation at least in obese subjects, who show little movement in the chamber. Our model overcomes these drawbacks and can also give quantitative information regarding PA, REE and PE of subjects undergoing the respiratory chamber protocol.

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