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SHORT REPORT

A low resting metabolic rate is associated with metabolic syndrome

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KEYWORDS
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Summary
Background & aims: The metabolic syndrome is associated with central accumulation of fat. Previous studies showed that some obese subjects are characterized by a sparing energy metabolism. The aim of this study was to investigate whether obese subjects with metabolic syndrome have a lower resting metabolic rate than obese subjects without metabolic syndrome.
Methods: Forty obese subjects were divided into three groups according to the presence of metabolic syndrome and type 2 diabetes; 15 non-obese healthy control subjects were also enrolled. Body composition (bio-impedance analysis) and resting metabolic rate (indirect calorimetry) were performed.
Results: The group with metabolic syndrome exhibited a significantly lower resting metabolic rate adjusted for fat-free mass with respect to the control group and the obese group without metabolic syndrome (respectively: 108 ± 3 vs. 118 ± 3, $p < 0.01$ and 123 ± 3 kJ/kg fat-free mass 24 h, $p < 0.01$; mean $\pm$ sem). The obese group with metabolic syndrome and type 2 diabetes (T2D) had a not different adjusted resting metabolic rate (114 ± 6 kJ/kg fat-free mass 24 h) with respect to other groups.
Conclusions: An energy sparing condition seems to characterize non-diabetic obese subjects with metabolic syndrome.

Abbreviations: BIA, bioimpedance analysis; BMI, body mass index; FFM, fat-free mass; FM, fat mass; HOMA-IR, homeostasis model assessment of insulin resistance; MS, metabolic syndrome; RMR, resting metabolic rate; RQ, respiratory quotient; T2D, type 2 diabetes

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Introduction

The metabolic syndrome is invariably associated with overweight or frank obesity with central distribution of body fat. Evidences have been accumulated that a sparing energy metabolism, probably due to genetic factors, characterizes some obese subjects.[1] Resting metabolic rate (RMR) is the main component of daily energy expenditure, accounting for about 70% of total daily energy expenditure in most adult sedentary individuals and it is a predictive factor for the development of future body weight gain.[2,3] A recent study showed also that RMR variability was associated with some genetic traits that overlapped regions previously linked to the metabolic syndrome; furthermore, a significant association between RMR and metabolic syndrome was observed.[4] Therefore, subjects predisposed to the metabolic syndrome might also be characterized by a lower energy expenditure that facilitate body weight gain. In the present study we investigated the RMR in different groups of obese subjects distinguished on the basis of the presence or less of the metabolic syndrome with or without diabetes.

Materials and methods

Forty obese subjects (24 males, 16 females; range of age: 30–60 years; range of BMI: 30–39.9 kg/m^2) were recruited among the obesity outpatients seen at the Department of Internal Medicine and Cardiovascular and Kidney Diseases of the University of Palermo. They were divided into three groups according to the presence (MS+) or less (MS−) of the metabolic syndrome, with or without type 2 diabetes (T2D). A group of 15 (9 males and 6 females) normal weight subjects was also recruited as control. Both diabetes and hypertension (when these conditions occurred) were diagnosed for the first time when subjects were enrolled in the study. All participants in the study had their body weight stable for at least the last 3 months and nobody habitually assumed any drug. Before starting the study, body weight was registered in two occasions with a 7–10 days interval, subjects whose body weight changed ± 0.5 kg were excluded from the study. Metabolic syndrome was defined according to the diagnostic criteria of the NCEP-ATPIII, T2D according to the criteria of the American Diabetes Association. The physical and clinical characteristics of the studied groups are reported in Table 1. The study protocol was approved by the ethical committee of our institute; before taking part in the study all subjects were informed of its aims and methods and gave their voluntary written consent. Each patient was tested in the morning after about 10 h of overnight fasting. A blood venous sample was obtained to determine chemical and C-peptide (radioimmunoassay) data; an oral glucose tolerance test was performed in all subjects and blood concentrations of glucose and insulin (radioimmunoassay) were measured before and 2 h after the assumption of a 75 g glucose load. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to Matthews et al.[5] Fat mass (FM, % body weight) and fat-free mass (FFM, kg) were estimated as previously described[6] by means of bioelectrical impedance analysis (BIA; BIA-103, RJL, Detroit, USA/Akern Florence, Italy). Body circumferences were measured at the umbilicus (waist circumference) and at the most prominent buttock level (hip circumference). The RMR and the fasting respiratory quotient (RQ; VCO_2/VO_2: an indirect measurement of the mixture of carbohydrate and lipid oxidation) were obtained by means of the indirect calorimetry method. A ventilated hood system of indirect calorimetry was employed (2900 MMC, Sensormedics; Yorba Linda, CA, USA/Bilthoven, The Netherlands). Respiratory gas exchanges were continuously measured for about 1 h, data were obtained from at least 30 min of stable measurements. The RMR was expressed both in absolute value (kJ/24 h) and adjusted for FFM size (kJ/kg-FFM 24 h). Alternatively, due to the positive intercept in the relationship between RMR and FFM, a regression-based approach was considered in order to adjust RMR for FFM size.[7]

All data are expressed as mean $\pm$ sem. The statistical comparisons between the groups were calculated by means

Table 1 Main characteristics of control subjects and obese groups defined according to the presence (+) or less (−) of metabolic syndrome (MS) and type 2 diabetes (T2D) (mean $\pm$ sem).

	Control	MS−	MS+	MS+/T2D
M/f	9/6	9/6	8/5	7/5
Age (years)	39 ± 2	42 ± 3	42 ± 4	46 ± 3^{b}
Body weight (kg)	64.8 ± 2.2	87.4 ± 3.2^{c}	$100.3 \pm 4.3^{c,d}$	99.5 ± 6.0^{c}
BMI (kg/m^2)	23.5 ± 0.5	31.4 ± 0.7^{c}	$35.0 \pm 0.9^{c,d}$	$35.3 \pm 1.9^{c,d}$
Fat mass (%)	23.6 ± 1.8	33.9 ± 2.5^{c}	33.2 ± 1.9^{b}	33.1 ± 2.3^{b}
Waist circumference (cm)	85 ± 2	94 ± 4^{a}	$116 \pm 2^{c,d}$	$119 \pm 4^{c,d}$
Systolic blood pressure (mmHg)	105 ± 2	122 ± 8	139 ± 10^{a}	151 ± 7^{a}
Diastolic blood pressure (mmHg)	72 ± 1	81 ± 5	86 ± 4^{a}	91 ± 5^{c}
Blood concentration of:				
Total cholesterol (mmol/l)	3.76 ± 0.23	4.38 ± 0.21^{a}	5.31 ± 0.52^{a}	$5.39 \pm 0.36^{b,d}$
HDL cholesterol (mmol/l)	1.24 ± 0.21	1.17 ± 0.10	$0.82 \pm 0.08^{a,d}$	$0.96 \pm 0.16^{a,d}$
Triglycerides (mmol/l)	0.96 ± 0.14	0.99 ± 0.11	$1.77 \pm 0.42^{a,d}$	$2.43 \pm 0.50^{b,e,f}$

Significance level vs. control group: $^{a}p<0.05$; $^{b}p<0.01$; $^{c}p<0.001$.
Significance level vs. MS− group: $^{d}p<0.05$; $^{e}p<0.01$.
Significance level vs. MS+ group: $^{f}p<0.05$.

of Student's unpaired *t*-test. A *p* value of less than 0,05 was considered as statistically significant. The SPSS statistical software (release 6.0; SPSS Inc.; Chicago, IL, USA) was utilised to perform all the statistical analysis.

Results

Anthropometric, clinical and biochemical characteristics, energy expenditure and RQ are reported in Tables 1 and 2. The RMR in absolute value (kJ/24 h) was significantly correlated to the FFM-kg ($r = 0,84$; $p < 0,0001$; Figure 1) as described by the following equation:

$$RMR(kJ/24\,h) = 1420 + 21.9FFM\text{-}kg.$$

The RMR, adjusted for FFM according to the Ravussin procedure (7), was significantly lower in the MS+ group with respect to the MS− group (6472 ± 197 vs. 7205 ± 193 kJ/24 h; $p < 0.01$); no differences were observed with other studied groups (control group: 6719 ± 101; MS+/T2D: 6849 ± 335 kJ/24 h; *p* n.s.). A positive correlation between fasting plasma glucose and RMR adjusted for FFM (kJ/FFM-kg) was observed in the diabetic group but the statistically significance level was not reached ($r = 0.51$; $p = 0.07$).

Discussion

This study investigated three groups of subjects that were similar as far as sex distribution, age and anthropometric characteristics were concerned. However, some differences need to be pointed out. As expected, the diabetic group was slightly but significantly older than the control group; both MS+ and MS+/T2D groups had a significantly higher BMI than the MS− group; body fat size was comparable between the groups but waist circumference was significantly higher in the groups with MS. The RMR expressed in absolute value (kJ/24 h) did not differ between the obese groups, however it resulted significantly lower in the MS+ group when adjusted for FFM (kJ/FFM-kg 24 h). This result is in accordance with the hypothesis that obese subjects with MS have an energy sparing metabolism. The FFM is commonly considered as the metabolically active body compartment and it is strongly correlated with RMR. However, to a lesser extent, other factors are able to influence the RMR as suggested by the positive intercept (1420 kJ in this study) of the regression line relating FFM to RMR. Therefore, it has been proposed to adjust the RMR for FFM taking into consideration the positive intercept in the linear regression between these two variables.[7] Even when the RMR was adjusted according to this procedure, the same conclusions were reached and the MS+ group had a

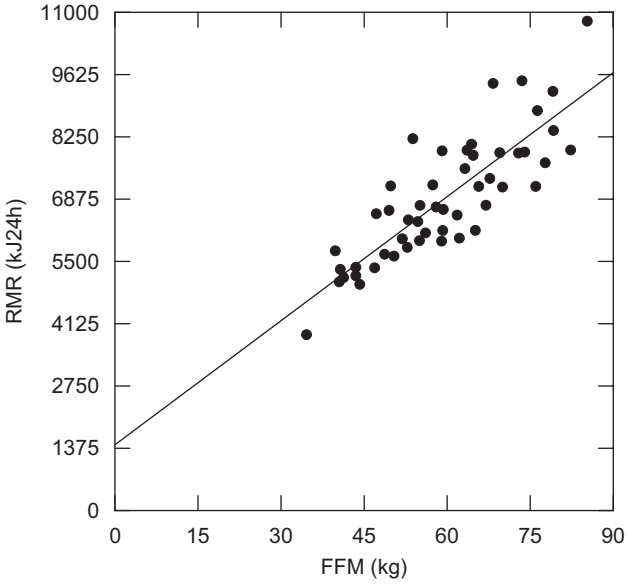

Figure 1 Correlation between resting metabolic rate (RMR) and fat-free mass (FFM).

Table 2 Basal or after oral glucose (g 75) load blood concentrations of glucose, insulin and C-peptide, HOMA-IR, resting metabolic rate and respiratory quotient in control subjects and obese groups defined according to the presence (+) or less (−) of metabolic syndrome (MS) and type 2 diabetes (T2D) (mean ± sem).

	Control	MS−	MS+	MS+/T2D
Blood concentration of:				
Basal glucose (mmol/l)	4.8 ± 0.2	4.3 ± 0.1	5.0 ± 0.3[e]	9.3 ± 0.6[c,f,i]
2 h post-load glucose (mmol/l)	4.9 ± 0.2	5.6 ± 0.3	9.1 ± 0.9[a,e]	14.8 ± 2.8[c,f,h]
Basal insulin (pmol/l)	66.0 ± 6.3	74.3 ± 6.3	100.0 ± 10.4[a,d]	147.2 ± 22.9[c,f,i]
2 h post-load insulin (pmol/l)	279.9 ± 50.7	352.8 ± 43.8	663.2 ± 97.9[a,d]	341.7 ± 96.5
Basal C-peptide (μg/ml)	1.86 ± 0.17	2.19 ± 0.14	2.79 ± 0.15[c,e]	3.69 ± 0.44[c,f]
HOMA-IR	2.01 ± 0.24	2.03 ± 0.26	3.20 ± 0.34[a]	8.79 ± 1.81[c,f,i]
Resting metabolic rate:				
kJ/24 h	5856 ± 256	7092 ± 373[b]	7226 ± 331[b]	7616 ± 423[c]
kJ/kg-FFM···24 h	118 ± 3	123 ± 3	108 ± 3[b,e]	114 ± 6
Basal RQ (VCO_2/VO_2)	0.87 ± 0.02	0.82 ± 0.02	0.79 ± 0.02[b]	0.87 ± 0.02[d,g]

FFM: fat-free mass; RQ: respiratory quotient:
Significance level vs. control group: [a]$p < 0.05$; [b]$p < 0.01$; [c]$p < 0.001$.
Significance level vs. MS− group: [d]$p < 0.05$; [e]$p < 0.01$; [f]$p < 0.001$.
Significance level vs. MS+ group: [g]$p < 0.05$; [h]$p < 0.01$; [i]$p < 0.001$.

significantly lower RMR than the MS− group. Furthermore, the same conclusions are obtained even when the RMR is considered in absolute value. In fact, the RMR expressed in absolute terms was not significantly different between the MS− and the MS+ groups despite the latter group had a significantly higher body weigh of about 13 kg.

The value of adjusted RMR in the MS+/T2D group was about 6% higher than that of the MS+ group and comparable to that of both the control and the MS− groups. This result is contradictory only in appearance and is in accordance with previous studies that demonstrated an increased RMR in diabetic subjects.[8] The physiological mechanisms responsible for the increased RMR in individuals with T2D are poorly understood and several mechanisms have been proposed. Gluconeogenesis is increased in T2D and contributes to hyperglycaemia; this is known to be an energy-consuming metabolic pathway. The observed positive correlation between fasting plasma glucose and RMR (despite the level of significance was not fully reached) is highly suggestive of this possibility. Diabetic subjects exhibited a higher RQ with respect to both MS+ and MS− groups thus suggesting a higher post-absorptive glucose oxidation; this might be a compensatory mechanism that limits the accumulation of glucose from the enhanced neoglucogenesis.[9]

The results of this observational study show that subgroups of obese subjects different for the presence of metabolic syndrome or diabetes have a quite different RMR. Therefore, obesity is not the main element that determine the decreased energy expenditure of the MS+ group; in this case, obesity seems, at least in part, the consequence of an increased energy efficiency. Different pathogenetic mechanisms could explain a lower energy expenditure in MS+ obese subjects including the lipotoxic hypothesis, lower mitochondrial levels of uncoupling proteins and genetic polymorphism in these proteins,[10] however they were not investigated in this study.

In conclusion, these results might contribute to explain the propensity of subjects affected by MS to obesity. Further studies are necessary to investigate other components of energy expenditure and total daily energy expenditure in subjects with MS. Similarly, the metabolic abnormalities and underlying mechanisms associated with a lower energy expenditure in individuals with MS remain to be elucidated.

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Statement of authorship

S.B.: Participated in the conception and design of the study, carried out the resting metabolic rate and the body composition, participated in drafting of the manuscript.

S.V.: Participated in the design of the study, participated in data collection, performed the statistical analysis and participated in drafting of the manuscript, provided significant advice and consultation.

G.C.: Participated in the design of the study and in drafting of the manuscript, provided significant advice and consultation.

G.C.: Participated in the conception and design of the study, in its coordination and in drafting the manuscript.

Conflict of interest statement

None to be declared.

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