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Original

Increased resting energy expenditure by fat-free mass in children and teenagers with constitutional leanness

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Abstract

Background/objectives: **To compare the resting energy expenditure (REE) and the REE/Fat-free-mass (FFM) quotient in children with constitutional leanness (CL) and children with normal body weight, and to describe the within-family clustering of CL.**

Subjects/methods: **We have studied 18 children and teenagers with CL, 10 girls and 8 boys, and 18 gender and age matched normal controls, with the same pubertal stage. All were recruited from the outpatient pediatric clinic nutrition unit. None of the children with CL showed symptoms of chronic illness, they had normal laboratory results, they had a normal caloric food intake, and they did not agree with the DSM-IV-TR criteria for anorexia nervosa. We describe the body mass index (BMI) of children and their parents. The children were classified according to Cole's recently published BMI cut-offs for thinness: under 18.5 points in CL group, stable at least in the last year, and between 18.5 and 25 cutt-offs in the control group. The body composition was calculated by anthropometric methods (skinfold thickness measurements). In addition REE was measured using fasting indirect calorimetry.**

Results: **The CL group had a higher mean percentage of FFM, and a mean FM significantly less, relative to controls ($p < 0.001$). The average absolute REE was significantly lower in the CL group (1,106.55 ± 240.72 kcal) than the control group (1,353.33 ± 270.01 kcal/día) ($p < 0.01$). However, the REE adjusted for FFM showed a mean significantly greater in the CL group (41.39 ± 2.26 kcal/kg FFM) (Mean confidence interval (CI) 95 %: 40.33-42.45) than the controls (37.37 ± 3.06 kcal/kg FFM) (Mean CI 95 %: 35.93-38.81) ($p < 0.001$). Finally, in the family study, the mean BMI of fathers of CL group was significantly lower ($p < 0.01$), but there were not any differences in the mean BMI of mothers. Among parents with BMI known, 8 of 35 parents of CL group**

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INCREMENTO DEL GASTO ENERGÉTICO EN REPOSO POR MASA LIBRE DE GRASA EN NIÑOS Y ADOLESCENTES CON DELGADEZ CONSTITUCIONAL

Resumen

Objetivos: **Comparar el gasto energético en reposo (GER) y el cociente GER/masa libre de grasa (MLG) entre niños con delgadez constitucional (CL) y niños con peso normal, y describir la agregación familiar de la DC.**

Material y métodos: **Hemos estudiados 18 niños y adolescentes con DC, 10 niñas y 8 niños, y 18 controles pareados con aquellos por edad, sexo y mismo estadío puberal. Todos fueron captados en la consulta externa de la Unidad de Nutrición clínica infantil. Ninguno de los niños con DC mostraba síntomas de enfermedad crónica, todos presentaban hallazgos de laboratorio normales, tuvieron una ingesta calórica normal, y no cumplieron en ningún caso criterios de anorexia nerviosa según la DSM-IV-TR. Se describe el índice de masa corporal (IMC) de los niños y de sus padres. Los niños fueron clasificados según los puntos de corte de IMC para definición de delgadez recientemente publicados por Cole: inferior al punto 18.5 en el grupo de DC, estable durante al menos un año, y entre los puntos de corte 18.5 y 25 en el grupo control. La composición corporal fue calculada por métodos antropométricos (medida de pliegues cutáneos). Además, el GER fue determinado mediante calorimetría indirecta en ayunas.**

Resultados: **El grupo de DC tuvo un porcentaje de MLG medio mayor, y una masa grasa (MG) media significativamente menor, en relación con los controles ($p < 0,001$). El GER absoluto medio fue significativamente más bajo en el grupo con DC (1.106,5 ± 240,72 kcal) que en el grupo control (1.353,3 ± 270,01 kcal/día) ($p < 0,01$). Sin embargo, el GER ajustado por MLG mostró una media significativamente mayor en el grupo de DC (41,39 ± 2,26 kcal/kg MLG) (Intervalo de confianza (IC) de la media al 95%: 40,33-42,45) que en los controles (37,37 ± 3.06 kcal/kg MLG) (CI 95%: 35,93-38,81) ($p < 0,001$). Finalmente, en el estudio familiar, el IMC medio de los padres del grupo con DC fue significativamente más bajo ($p < 0,01$), pero no hubo ninguna diferencia entre el IMC de las madres. Entre los padres con IMC conocido, 8/35 padres del grupo con DC presentaron un IMC menor de 18,5, por sólo 2/36 padres del grupo control ($p < 0.05$).**

had an BMI lower 18.5, and only 2 of 36 parents in the control group ($p < 0.05$).

Conclusions: **This increased energy expenditure-to-FFM ratio differentiates between CL and controls. These metabolic differences are probably genetically determined.**

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Key words: *Resting energy expenditure. Fat-free mass. Constitutional leanness. Children. Teenagers.*

Conclusiones: **El incremento en el GER por MLG diferencia niños con DC de controles. Estas diferencias metabólicas podrían estar determinadas genéticamente.**

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Palabras clave: *Gasto energético en reposo. Masa libre de grasa. Delgadez constitucional. Niños. Adolescentes.*

Introduction

Despite the obesity trend in developed countries, some individuals usually maintain low weight for many years.[1] Constitutional leanness (CL) is generally defined as a thinness not secondary to organic disease or anorexia nervosa. Body weight and body mass index (BMI) have always been in the lower percentiles for age and gender, without any hormonal abnormality.[2] The mechanisms underlying the development and maintenance of this condition remain unknown,[3] but seem to have a common familial aggregation.[4]

Little is known nor has been written about the characteristics of persistently thin individuals, despite the frequency of this condition.[1] The recent development of new growth charts in different countries, using the pattern of children of today, shows overweight and obesity prevalence has decreased and that thinness has increased, although this prevalence depends on the references used.[5,6]

The BMI is the most widely used weight/height index since the 60's. International BMI cut-offs to assess overweight and obesity in adults and more recently in children, were developed previously, but the concept of thinness in children was not clearly established. However, the published references of Cole et al. for this condition, available since 2007,[7] based on data from six countries, are useful for comparative studies, and they also establish three degrees of thinness below the cut-off 18.5.[5]

The body weight regulation is carried out by different factors, but a negative energy balance may lead to weight loss and growth delay. In this sense, several hypotheses have been established to try to explain the CL. An abnormality in food intake control, a high level of physical activity, or a constitutional increase in resting energy expenditure (REE) may be involved.[3,8]

Regarding this matter, REE is the largest component of metabolic rate in children, and contributes to about two-thirds (60-70%) of the total daily energy expenditure;[9] the remaining third is the sum of that related to physical activity, thermogenesis, and growth.[10] Up to 80% of the variance in energy intake and energy expenditure is explained by body composition.[11] Fat-free mass (FFM) and fat mass (FM) are both determinants of REE, but the contribution of lean mass to REE is three to five times greater per kg than fat mass, and there is a good correlation between REE and lean mass.[8,12] However, there may be differences in the REE of individuals with similar characteristics of age, gender and lean body mass, which can reach up to 30%.[13] Therefore, similar people require different energy intake to maintain body weight.

It the obese, a lower resting metabolic rate adjusted for fat-free mass with respect to the control group has been observed,[14] which is considered a risk factor for weight gain and obesity.[15] However, in other cases no differences were found either in children[9] or young women,[15] among the obese and the non-obese also adjusting REE for FFM.

Several studies, all performed on young adult women with CL, show a higher REE, when corrected for FFM, than in control subjects.[2,3,16] The only study conducted on children does not confirm these findings, and found a decrease in REE adjusted for FFM. The authors conclude that children with CL have a low resting metabolic rate, probably adaptive.[8]

The objective of our study was to compare the resting energy expenditure (REE) and the REE/FFM quotient in children and teenagers with CL and children with normal body weight, taking advantage of recent international references for thinness, and to describe the within-family clustering of constitutional leanness.

Material and methods

In this observational cross-sectional study, we have studied 18 children with CL, 10 girls and 8 boys, and 18 gender and age matched normal controls, with the same pubertal stage (Tanner).[17] All patients and controls were caucasian subjects, and they were recruited from the outpatient pediatric clinic nutrition unit.

The children with CL, all of whom wished to gain weight, were selected from patients evaluated for thinness. The evaluation included a detailed medical history and physical examination and the following additional tests: basic laboratory tests (erythrocyte, leukocyte and platelet counts; plasma hemoglobin, erythrocyte sedimentation rate, and routine biochemical studies), always

including thyroid hormones and IgG/IgA antigliadin and IgA tissue transglutaminase antibodies determination. None of the children with CL showed symptoms of chronic illness, they had normal laboratory results, they had a normal caloric food intake (above the 80% of RDA for their age, in a three day prospective survey, including one at the weekend), and they did not agree with the DSM-IV-TR criteria for anorexia nervosa (refusal to maintain body weight at or above a minimally normal weight for age and height; intense fear of gaining weight or becoming fat, even though underweight; disturbance in the way in which one's body weight or shape is experienced, and finally, in postmenarcheal females, amenorrhea, with the absence of at least three consecutive menstrual cycles).[18]

Anthropometric measurements of both children and their parents, were always carried out in the same clinic office, using standard techniques. We describe the weight, height and body mass index (BMI) of children and their parents. BMI was defined as the ratio weight/height^2 (in kg/m^2). The children were classified according to Cole's recently published BMI cut-offs for thinness: under 18.5 points in CL group, stable at least in the last year, and between 18.5 and 25 cutt-offs in the control group.[7]

The body composition was calculated by anthropometric methods (skinfold thickness measurements to determine the subcutaneous fat layer, using a Holtain Skinfold Caliper), at the biceps, triceps, subscapular and suprailiac sites. All skinfold thickness measurements were done in triplicate by the same person. Fat-free mass and fat mass were first calculated using the Brook formula up to the age of 11, and Durnin and Womersley formula for those over 12 years.[19,20] Once body density is obtained, the body fat percentage is determined by applying the Siri equation, based on the two compartment model.[21]

In addition REE was measured using fasting indirect calorimetry with a canopy system (Deltatrac calorimeter), in standardized conditions, lying down on a bed, in a quiet environment. Oxygen consumption (VO2) and carbon dioxide production (VCO2) were continuously recorded for at least 30 minutes, using an open-circuit indirect calorimeter.

Statistical analyses. All results are expressed as mean and standard deviation (SD). The Student t test was carried out for between-groups comparison of means, after checking normal distribution of variables (Kolmogorov-Smirnov test), and for qualitative variables we used the Chi-square test, by SPSS software (v. 15). Informed consent was obtained from parents of all patients and controls before their participation.

Results

We have studied 18 children, 10 girls and 8 boys, with CL (6.8-19 years), with an average age of 12.29 ± 2.63 years (6.8-19 y), and 18 gender, age and pubertal stage matched normal controls, with an average age of 12.54 ± 2.24 years (8-17 y). Their characteristics are summarized in table I.

Obviously, there was no difference between groups in mean age (about 12 years-old), sex or mean height, among children with CL and the control group chosen matched with that.

However, there was a significant difference in weight and BMI, which were obviously lower in the group with CL. The children with CL had a BMI cut-off between 17-18.5 in 6 cases, 16-17 in 9 cases, and lower than 16 in 3 cases. All control children were among those cut-offs 18.5 and 25 for their age and sex.

The CL group had a higher mean percentage of FFM, and a mean FM significantly less, relative to controls ($p < 0.001$).

With regard to the study of the basal metabolic rate by indirect calorimetry, the average absolute REE was significantly lower in the CL group (1,106.5 ± 240.72 kcal) than the control group (1,353.3 ± 270.0 kcal/día) ($p < 0.01$). However, the REE adjusted for FFM showed a mean significantly greater in the CL group (41.39 ± 2.26 kcal/kg FFM) (Mean confidence interval (CI) 95%: 40.33-42.45) than the controls (37.37 ± 3.08 kcal/kg FFM) (Mean CI 95%: 35.93-38.81) ($p < 0.001$).

Finally, in the family study, the mean BMI of fathers of CL group was significantly lower ($p < 0.01$), but there were not any differences in the mean BMI of mothers. Among parents with BMI known, 8 of 35 par-

Table I
Physical characterisics of patients with CL and controls

	Total	*Age (y)*	*Height (cm)*	*Weight (kg)*	*BMI kg/m²*	*FFM kg*	*FFM %*	*FM kg*	*REE kcal*	*REE/ kg FFM*
CL	x	12.29	146.65	31.28	14.23	26.93	86.48	4.35	1,106.5	41.39
	SD	2.63	15.41	8.09	1.02	6.57	3.31	1.84	240.72	2.26
Controls	x	12.54	155.62	47.36	19.16	36.54	77.79	10.93	1,353.3	37.37
	SD	2.24	13.15	11.73	2.32	7.92	6.05	4.56	270.0	3.06
P		**0.76**	**0.069**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**0.007**	**< 0.001**

Abbreviations: CL: Constitutional Leanness; BMI: Body Mass Index; FFM: Fat-Free-Mass; FM: Fat Mass; REE: Resting Energy Expenditure; X: Mean; SD: Standard Deviation.

Table II
Within-family clustering of constitutional leanness

		BMI fathers	*BMI mothers*	*Fathers with BMI < 18.5*	*Mothers with BMI < 18.5*	*Total parents BMI < 18.5*
CL	X	21.26	20.92	3/17	5/18	8/35
	SD	2.13	2.19			
Controls	X	25.36	22.16	1/18	1/18	2/36
	SD	3.85	2.79			
P		**0.001**	0.232			**0.046**

Abbreviations: CL: Constitutional Leanness; BMI: Body Mass Index; X: mean; SD: Standard Deviation.

ents of CL group had an BMI lower 18.5 (3 fathers and 5 mothers), and only 2 of 36 parents in the control group (1 father, 1 mother) (p = 0.046) (table II).

Discussion

The recently published references on thinness, based on a large historical sample of nationally representative surveys of six countries (Brazil, United Kingdom, Hong Kong, The Netherlands, Singapore and the United States), have allowed us to gain some universal criteria for the same.[7] Curves were defined based on BMI < 18.5, 17 and 16 at the age of 18 y, providing definitions of thinness grades 1, 2, and 3 in children and adolescents consistent with the World Health Organization adult definitions. The cut-off 17 gave mean BMI close to a z score of -2.

The proposed cut-off points may help to provide a better distinction between different grades of undernutrition, specially for comparative studies of the prevalence rates of thinness in children and teenagers, rather than as standards for recommended body mass index by age and sex in each country.[22] We have used the cut-off 18.5 as criteria for inclusion in our study of children with CL.

Constitutional leanness seems a non-pathological condition, and some authors believe that persistent thinness appears to be associated with greater well-being,[1] even with better health indicators.[23] However, it has been reported that young women with CL present bone mineral density significantly lower than in controls (like patients with anorexia nervosa),[24,25] and a level of oxidative stress in prepubertal children with CL similar to the obese was found.[26]

Among other possible mechanisms, it has been proposed that an increase in REE could be involved in the CL.[3,8] For example, fasting REE is depressed in patients with anorexia nervosa for an adaptation mechanism,[27] but it is higher in obese subjects.[3,28] However, it seems more useful to express the REE in terms of free-fat mass. Most studies in this area do not find differences, with similar values of REE expressed per kg FFM between obese and non-obese subjects,[9,15,29-33] and there is only some communication that reports a lower REE adjusted for FFM in obese patients.[14]

However, in constitutional thinness, several studies found a significantly higher REE when corrected for kg of FFM than in control subjects,[2,3,16] although the only carried out on children does not confirm these findings.[8] In our study, absolute REE was significantly lower in the CL group than the controls. However, REE/kg FFM ratio was greater in the CL than the control group, in keeping with most of the previous reports. This increased energy expenditure-to-FFM ratio differentiates between CL and controls, and could account for the resistance to weight gain observed in this condition.[2]

Marra et al. report similar findings to ours in young women with CL, but also they find that fidgeting, or spontaneous muscle contractions, was significantly increased in comparison to the obese and controls, and this can significantly increase energy expenditure above standard levels.[3] The three main components of energy expenditure are resting metabolic rate, the thermic effect of food, and activity thermogenesis, that usually accounts for 10-15% of daily energy expenditure, including the latter exercise related and non-exercise related activity thermogenesis (NEAT).[34] NEAT is a significant component of energy balance, and these authors believe that increased fidgeting represents a facilitating factor for thinness and appears to be a biological marker of constitutional leanness.[3]

These metabolic differences observed in CL subjects with regard to the controls are probably genetically determined.[27,35,36] In fact, within-family clustering, both of obesity and CL, is common,[4] as we have noted in our study, despite the small sample size. Genetic studies of thinness or obesity resistance could complement the genetic advances in obesity.[37]

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