British Journal of Nutrition (1992), **68**, 593–602

Energy supplementation reverses changes in the basal metabolic rates of chronically undernourished individuals

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(*Received 12 March 1991 – Accepted 17 December 1991*)

The objective of the present study was to examine the influence of energy supplementation and its cessation thereafter on the basal metabolic rates (BMR) of chronically undernourished individuals. Seven apparently healthy males were supplemented daily with 3·35 MJ (15 g protein, 35 g fat, 105 g carbohydrate) for 12 weeks. The average gain in body-weight was 1·9 kg (body fat, 58 %; fat-free mass (FFM), 42 %). The rise in BMR exceeded that accounted for by the increases in FFM during the 12 weeks of supplementation and was attributed to increases in the amount and activity of the visceral tissue as well as to an added cost of lipogenesis. At 12 weeks after cessation of the supplement, body-weights and FFM had decreased to presupplementation levels. BMR at this stage were significantly lower than at the 12th week of supplementation, when expressed per kg FFM or when adjusted for FFM using an analysis of covariance. These results suggest an increase in the metabolic efficiency during this negative energy balance period. The study demonstrates that, in the chronically undernourished, the changes in BMR are reversible and, hence, physiologically important to the process of adaptation to low-energy intakes.

Basal metabolic rate: Body composition: Metabolic efficiency: Chronic undernutrition: Energy supplementation

Individuals adapt to a sustained deficit in energy intake by a reduction in the basal metabolic rate (BMR). When the decrease in BMR exceeds that explained by the concomitant loss of the active tissue mass or fat-free mass (FFM), an apparent increase in the 'metabolic efficiency' of the residual tissues is said to exist. If such changes in BMR are to be considered as being physiologically important during periods of energy deprivation, they must demonstrate a reversibility on energy supplementation (Waterlow, 1985). Individuals habituated to low energy intakes over prolonged periods exhibit changes in BMR that suggest an increase in the metabolic efficiency (Shetty, 1984). More recently, however, we were unable to demonstrate a lower BMR expressed per kg FFM in similar individuals. We concluded that the ability to uncover a metabolic efficiency in those who are chronically undernourished may well depend on several factors including the manner of expression of BMR, its mode of analysis, as well as the degree of undernutrition at the time of investigation (Soares & Shetty, 1991). Hence, the present study was carried out to examine whether supplementation of energy and its cessation thereafter would help uncover physiological responses of BMR to acute perturbations in energy intake in chronically undernourished individuals.

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* For reprints.

EXPERIMENTAL

Experimental design

This longitudinal study was conducted to assess the changes in BMR and body composition of a group of free-living undernourished men who received a daily supplement of 3·35 MJ (800 kcal) for 12 weeks. Measurements were made before, during and 12 weeks after the cessation of supplementation.

Materials and methods

Subjects. Seven apparently healthy, chronically undernourished male volunteers aged between 18 and 30 years were investigated. All subjects underwent a complete clinical assessment before recruitment. They were selected, as previously described (Soares & Shetty, 1991), on the basis of their body mass index (weight/height^2; BMI $<$ 18·5) and their lower socio-economic class (class IV–V; Kuppuswamy, 1984).

Dietary supplement. The dietary supplement provided 3·35 MJ (800 kcal)/d and consisted of maize, soya-bean meal, sugar and maize oil (15 g protein, 34·5 g fat and 105 g carbohydrate). The nutrient composition and energy content were calculated from standard food tables (Gopalan *et al.* 1985). The supplement was served each day, under supervision, as two isoenergetic snacks, once each in the morning and evening for twelve consecutive weeks. The supplement was palatable and acceptable to all subjects and was administered without fail throughout the supplementation phase.

Dietary intakes. Subjects were instructed to maintain their normal dietary intakes and eating habits for the duration of the dietary supplementation. Dietary recalls (24 h) of the preceding day's energy and protein intakes were obtained in each phase of the study as detailed elsewhere (Piers *et al.* 1992*a*). While two random recalls were conducted before the supplementation and three recalls in the week after supplementation, a single recall every 8–10 d was obtained during the 12 weeks of supplementation. In order to cross check the 24 h dietary recalls of these subjects, 24 h dietary weighings were made in six of seven subjects, using the self-weighing procedure.

BMR and body composition. All measurements of BMR were made on a Hartmann & Braun Metabolator that had been validated earlier (Soares *et al.* 1989). The instrument measured ventilation volumes, and oxygen and carbon dioxide concentrations from which the respiratory quotients (RQ) could be calculated. BMR were measured under standard conditions early in the morning after an overnight sleep in the laboratory. Measurements were made in duplicate for 10 min each with a 10 min rest between measurements. Duplicates within ±3% of their means were considered technically valid. Nutritional status was assessed by anthropometry, i.e. body-weight (kg), height (m) and mid-upper arm circumferences (MAC). Body fat was estimated from the sum of four skinfold thicknesses (biceps, triceps, subscapular and suprailiac) using the age-specific equations of Durnin & Womersley (1974). Corrected arm muscle areas (CAMA) were calculated from the equations of Heymsfield *et al.* (1982).

BMR and body composition were measured before the start of supplementation and then serially during the 3rd, 6th, 9th and 12th week of supplementation. At the end of the period of supplementation five subjects agreed to further serial measurements. They were measured on days 2, 4, 6, and 8 post supplementation. A final measurement was made 12 weeks after the cessation of supplementation in these five subjects.

Statistical analysis

The dietary intakes were analysed by a two-way analysis of variance (ANOVA) with replicates, for differences between occasions as well as between methods. All metabolic and body composition data were examined on the basis of an ANOVA for repeated measures, with F ratios considered significant at $P < 0{\cdot}05$ level. Where F ratios were significant, univariate F tests were used to test for differences between occasions. Adjusted BMR were compared using an analysis of covariance (ANCOVA) with FFM as covariate (Dowdy & Wearden, 1983).

Ethical approval

The study was approved by the Human Investigation Committee of the Medical College and all subjects gave written informed consent.

RESULTS

During supplementation. The mean dietary recalls before, during and after supplementation were similar for unsupplemented energy intakes (8·44 (SE 1·77), 8·61 (SE 1·79), 8·75 (SE 1·29) MJ (2017 (SE 422·1), 2060 (SE 426·9), 2093 (SE 308·3) kcal)/d respectively) and protein intakes (51 (SE 12·1), 57·8 (SE 14·7), 56·9 (SE 11·4) g/d respectively). A two-way ANOVA detected a significant subject × period interaction for energy intakes (df 12, 68; F 2·69; $P < 0{\cdot}001$) but not for protein intakes (df 12, 68; F 1·72; $P > 0{\cdot}05$). There were, however, no differences between the periods, for either energy intakes (df 2, 12; F 0·11; $P > 0{\cdot}05$) or protein intakes (df 2, 68; F 2·4; $P > 0{\cdot}05$). During supplementation, neither energy (8·61 (SD 1·81) *v.* 8·61 (SD 1·80) MJ (2060 (SD 432·3) *v.* 2059 (SD 429·6) kcal)/d nor protein intakes (58·1 (SD 13·5) *v.* 57·6 (SD 16·0) g/d appeared to be different between the first 6 weeks and the last 6 weeks of this 12-week period (energy df 1, 41; F 0·013; $P > 0{\cdot}05$; protein df 1, 41; F 0·002; $P > 0{\cdot}05$).

An ANOVA of the dietary intake as estimated by the 24 h dietary recall and 24 h weighing method, also showed no differences between methods in energy intake (df 1, 5; F 0·08; $P > 0{\cdot}05$) or in protein intake (df 1, 24; F 2·67; $P > 0{\cdot}05$). There was, however, a significant interaction between subject and method in energy intakes (df 5, 24; F 6·69; $P < 0{\cdot}005$).

The results of changes in body composition and BMR are summarized in Table 1. On using an ANOVA for repeated measures there were significant increases (df 4, 24; $P < 0{\cdot}005$ for all variables) in body-weight (F 11·9), body fat (F 5·0), FFM (F 4·95), RQ (F 5·07), BMR (F 12·76), BMR/kg body-weight (F 8·71) and BMR/kg FFM (F 11·15). The overall increases in body-weight (about 1·9 kg) during the period of supplementation were due to significant percentage increases in body fat and FFM, in the ratio 58:42. By the 3rd week, subjects had gained 68% (1·3 kg) of their total weight gain (46% fat:54% FFM). Body-weights had reached a plateau by the 6th week with the remainder of the body-weight (0·6 kg), being gained as 83% fat and 17% FFM. No changes in CAMA could be demonstrated during the 12-week supplementation period (F 1·54; $P > 0{\cdot}05$).

On initiation of supplementation, the fasting RQ rose from the 3rd week onwards, returning to presupplementation levels by the 12th week. BMR were significantly higher (over baseline values) from the 3rd week and remained so until the 12th week. The total increase in BMR by the 12th week was 22% above baseline (presupplementation) values. BMR, expressed per kg body-weight, and FFM showed similar trends, with the increase in BMR per kg FFM during the 12th week being about 20% higher than presupplementation values.

There were no differences in BMR adjusted for FFM (df 1, 32; F 2·73) between the well-

Table 1. *Body composition and basal metabolic rates (BMR) of seven chronically undernourished subjects, before and during supplementation*

(Mean values with their standard errors)

	Presupplementation		Period of supplementation (week)							
			3rd		6th		9th		12th	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Body-wt (kg)	43·5	0·8	44·8***	1·0	45·4***	1·0	45·3*	0·9	45·3	1·1
Fat (kg)	4·8	0·3	5·4*	0·4	5·9**	0·4	5·9	0·5	5·8	0·6
FFM (kg)	38·7	0·8	39·4**	0·9	39·5*	0·8	39·4	0·7	39·5	0·9
Corrected arm muscle area (cm^2)	28·6	1·1	29·3	0·9	29·8	1·0	29·8	1·3	29·3	1·2
RQ	0·97	0·03	1·08	0·04	1·17*	0·06	1·13	0·04	0·98*	0·04
BMR: MJ/d	4·81	0·11	5·21***	0·10	5·43**	0·10	5·65***	0·08	5·89*	0·28
kJ/kg body-wt per d	110·5	2·5	116·4*	2·4	119·7*	3·0	125·0***	3·0	129·8*	5·4
kJ/kg FFM per d	124·3	2·3	132·3**	2·2	137·5***	2·9	143·4***	2·4	148·5*	5·2

FFM, fat-free mass; RQ, respiratory quotient.

Mean values were significantly different from those of preceding measurements (univariate F test; overall significance was assessed using an ANOVA for repeated measures): * $P < 0·05$, ** $P < 0·01$, *** $P < 0·005$.

nourished (n 28; reported previously by Soares & Shetty, 1991) and the supplemented undernourished in the present study. The latter values were, however, significantly higher than the presupplemented BMR of the same subjects using an ANOVA with FFM as covariate (12th week 5·82 (SE 0·17) MJ/d *v.* presupplemented 4·88 (SE 0·17) MJ/d; df 1, 11; F 15·66; $P < 0{\cdot}005$).

Post-supplementation. The results of five subjects who volunteered for measurements after the supplementation period are given in Table 2. Since there was one missing value on day 2, we omitted all measurements for this time-point. On using an ANOVA for repeated measures, there were significant differences after cessation of supplementation (df 4, 16; $P < 0{\cdot}05$ for all variables). There were decreases in body-weight (F 5·96), FFM (F 3·67), BMR (F 4·07) and BMR/kg FFM (F 3·4) but no statistical differences in body fat (F 1·65), RQ (F 0·94) and BMR/kg body-weight (F 2·71). The mean coefficients of variation (CV) of within-group changes in body-weight and BMR were 0·92 and 2·3% respectively for the first week following cessation of supplementation. At 12 weeks after the termination of the supplement, body-weights were lower and had returned closer to presupplementation values. The loss in body-weight 12 weeks after the cessation of supplementation amounted to 1·4 kg of which 36% was fat and 64% was FFM. BMR, in absolute terms and when expressed per kg FFM, were significantly lower at this point than during the preceding period (Table 2). On adjusting for FFM using an ANCOVA, BMR were significantly lower than values at the 12th week of supplementation (post cessation 5·13 (SE 0·12) MJ/d *v.* 12th week 5·65 (SE 0·12); df 1, 7; F 9·29; $P < 0{\cdot}05$). There were no changes in the CAMA following the cessation of supplementation. Compared with the presupplementation values, BMR and BMR/kg FFM were still significantly higher in these five subjects (Table 2).

DISCUSSION

Shetty (1984) demonstrated a lower BMR per kg FFM in chronically undernourished individuals when compared with well-nourished subjects. This metabolic efficiency was not apparent in recent studies from this laboratory, with BMR per kg FFM being invariably higher in the undernourished (Kurpad *et al.* 1989; Soares & Shetty, 1991; Piers *et al.* 1992*b*). However, using more appropriate analysis (like ANCOVA) we have shown that chronically undernourished males have a significantly lower BMR adjusted for FFM (Soares & Shetty, 1991). The objective of the present study was to examine whether the documented metabolic changes in the BMR of chronically undernourished subjects were reversible with an improvement in energy intake. We, therefore, studied the changes in BMR and body composition of chronically undernourished subjects before, during and following a period of supervised dietary supplementation.

The subjects in the present study were free living. An analysis of the 24 h dietary recalls showed a significant subject × period interaction suggesting that all subjects were not uniform in their energy intakes over these three periods, an expected drawback of a free-living study. However, overall there appeared to be no differences in the unsupplemented energy and protein intakes between these phases. In addition, the method was comparable with the more accurate method of weighed intakes in these subjects. Despite these results the occurrence of a certain degree of 'substitution' cannot be excluded, given the nature of the study design. That a successful dietary augmentation did occur, however, is confirmed from the increases in body-weight due, in turn, to increases in both body fat and FFM.

The equations of Durnin & Womersley (1974) have not been validated in these undernourished subjects. In the present study, however, we were only concerned with the repeatability of the skinfold method in the assessment of body composition. The precision of the skinfold method using the Durnin & Womersley (1974) equations varies between 0·2

Table 2. *Body composition and basal metabolic rates (BMR) of five chronically undernourished subjects, measured up to 12 weeks after cessation of supplementation*

(Mean values with their standard errors)

	Presupplementation		12th week of supplementation		Period post-cessation of supplementation							
					Day 4		Day 6		Day 8		12th week	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Body-wt (kg)	43·7	1·2	46·0	1·5	45·9	1·4	45·6	1·3	45·6	1·2	44·6*	1·2
Body fat (kg)	4·8	0·4	6·2	0·8	6·3	0·7	6·0	0·7	6·1	0·7	5·7	0·6
FFM (kg)	38·9	1·2	39·8	1·3	39·6	1·2	39·6	1·2	39·5	1·3	38·9*	1·1
CAMA (cm^2)	27·9	1·4	28·9	1·5	—		—		—		28·8	1·7
RQ	0·95	0·04	0·98	0·04	0·99	0·08	0·94	0·04	0·95	0·04	0·88	0·02
BMR: MJ/d	4·78	0·14	5·74	0·33	5·69	0·31	5·56	0·25	5·74	0·30	5·05*†	0·13
kJ/kg body-wt per d	109·4	2·8	124·5	4·9	124·2	5·4	122·0	5·3	125·7	5·3	113·3	1·9
kJ/kg FFM per d	122·9	2·3	143·7	4·4	143·5	4·4	140·3	3·9	145·0	4·4	129·8*†	0·9

FFM, fat-free mass; CAMA, corrected arm muscle areas; RQ, respiratory quotient.

Overall significance following cessation of supplementation, tested using an ANOVA for repeated measures: * $P < 0{\cdot}05$.

Mean presupplementation value was significantly different from that 12 weeks post-cessation of supplementation (paired *t* test): † $P < 0{\cdot}05$.

and 0·3 kg body fat (Hill *et al.* 1978; Burkinshaw, 1985). Moreover, this method has been used with reasonable accuracy to monitor the serial changes in body composition of subjects with anorexia nervosa undergoing refeeding (Melchior *et al.* 1989), as well as to quantify short-term fat changes in hospitalized patients on intravenous nutrition (Burkinshaw, 1985; King, 1985).

The results of the present study indicate that during supplementation nearly 70% of the total increase in body-weight occurred within the first 3 weeks, with almost equal proportions of fat and FFM being gained. The increase in BMR by the 3rd week was, however, significantly higher than that accounted for by the increase in FFM, a feature which persisted throughout the 12 weeks (Table 1). Similar conclusions were reached on adjusting for the increased FFM using an ANCOVA. There were no changes in CAMA throughout the study. Also, creatinine excretions (24 h) in the same subjects did not show any significant increases with supplementation (R. N. Kulkarni and P. S. Shetty, unpublished results) suggesting that muscle mass did not contribute to the observed increases in FFM during this period. Hence, the increase in FFM seemed to be the consequence of significant increases in visceral (organ) tissue. This, together with possible increases in the activity of such tissues, could account for the higher BMR of the undernourished during supplementation. Grande (1964) has suggested that much of the increase in BMR on refeeding semi-starved individuals could be ascribed to an increase in both the activity and amount of visceral (liver) tissue, and that the tissues which were lost first on underfeeding were the earliest to show increases on supplementation. Animal studies also suggest that the amount of visceral tissue can be the major determinant of the basal metabolism. Koong & Ferrel (1990) have demonstrated that in animals reared to achieve similar body-weights those with a higher fasting heat production following a higher plane of nutrition had significantly greater visceral masses. The added observations in the present study that following supplementation the BMR adjusted for FFM appear comparable with those of well-nourished subjects would reinforce our view of an increase in the activity of the visceral tissue.

We have earlier, on several occasions, reported a high RQ in chronically undernourished subjects (Shetty, 1984; Kurpad *et al.* 1989; Piers *et al.* 1992*b*), a feature previously noted by others (Ramanamurthy *et al.* 1962). An interesting observation during the 12 weeks of supplementation was a further and significant increase in RQ, with values greater than 1·0 from the 3rd to 9th week (Table 1). Both animal and human studies have shown that the provision of extra amounts of carbohydrate result in greater amounts of carbohydrate oxidation in the fasted (post-absorptive) state (Flatt, 1985). Massive increases in carbohydrate intake resulted in higher RQ (i.e. > 1·15), with up to 25% of the increase in BMR due to the cost of lipogenesis which continued even in the post-absorptive state (Schutz *et al.* 1982). Estimates of substrate oxidation rates support these observations, with an increase in carbohydrate oxidation and a net lipogenesis in the fasting state in these energy-supplemented undernourished subjects (Piers *et al.* 1992*a*). The added cost of lipogenesis from carbohydrate sources would, therefore, in part account for the higher BMR seen in the supplementation phase. Although BMR continued to increase beyond the 6th week, body-weights were stable suggesting that these individuals came into energy balance at this higher plane of nutrition. This could have resulted from changes in dietary intake or an increase in non-BMR energy expenditure, i.e. physical activity, the increase in BMR accounting for less than 0·5 MJ/d. Since dietary recalls in the last 6 weeks of supplementation were not different from the initial weeks, a change in dietary intake can be excluded. Perhaps, with the benefit of supplementation, there was an increase in discretionary activities that matched the raised intake in this period. Interestingly, associated with the rise in RQ > 1, an increase in body fat could be demonstrated and when

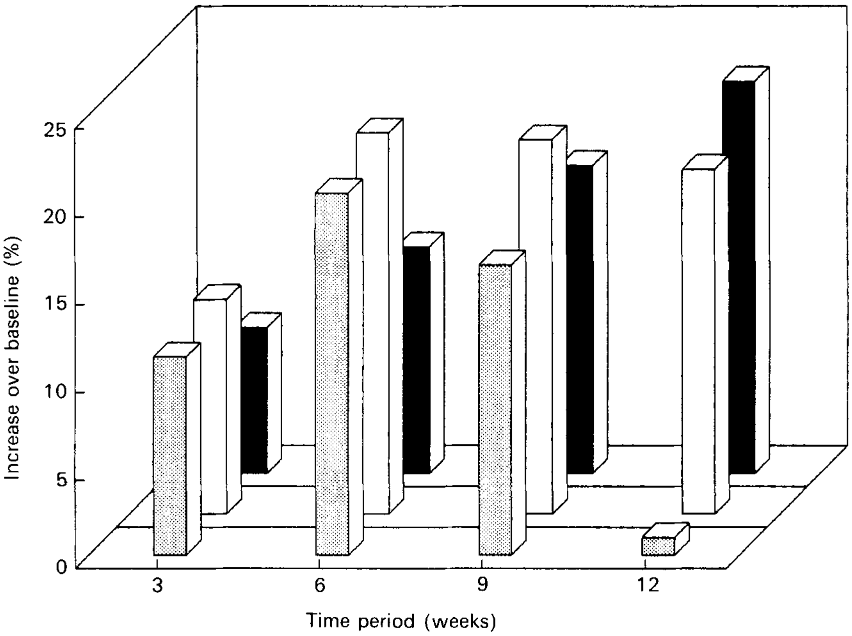

Fig. 1. Changes in RQ, body fat and BMR during supplementation. ▨, RQ; □, body fat; ■, BMR.

energy balance was achieved, with no demonstrable further increases in body fat (i.e. 6th week), the fasting RQ declined (Table 2; Fig. 1).

On restricting energy intake, BMR begins to fall by the 4th–9th day in both lean and obese individuals (Grande *et al.* 1958; Bray, 1969; Shetty, 1980). The absence of a decrease in BMR in the first week following the cessation of supplementation in the present study is possibly a carry-over effect. In addition, the habitual dietary intakes of these individuals may have been slow to return to presupplementation levels, since the subjects in the present study were free living, with no control on their habitual intakes. The low CV of both body-weight and BMR changes in this first week would suggest random changes, well within the documented CV of 3% for intra-individual variations in BMR of free-living individuals (Shetty & Soares, 1988). However, 12 weeks after cessation of supplementation there is a loss in FFM and a decrease in BMR compared with the preceding measurements (Table 2). The trend towards lower RQ would suggest a greater utilization of fat and protein at this stage. The significantly lower BMR when expressed per kg FFM or on adjusting for FFM differences (using an ANCOVA) denotes a reduction in the metabolic activity of FFM. Such a ‘metabolic efficiency’ would benefit these subjects as an acute adaptive response to the negative energy balance during this phase. These results are in agreement with those obtained on individuals undergoing semi-starvation (Keys *et al.* 1950; Grande, 1964). The higher BMR and BMR/kg FFM at this stage, compared with pre-supplementation values, suggests that the effects of supplementation were still to subside.

The present study indicates a reversibility of BMR when chronically undernourished individuals are energy supplemented. It has been shown previously in the same individuals that there were no changes in the thermogenic response to either infused norepinephrine or to a standard meal during supplementation (Naz *et al.* 1991; Piers *et al.* 1992*a*). Although we do not have a record of the type or time spent in physical activity, there were no changes in maximum O_2 consumption during supplementation (R. N. Kulkarni & P. S. Shetty, unpublished results). Hence, these processes are unlikely to have contributed to the change in energy expenditure in achieving energy balance. The continued rise in BMR in the present study over and above the increases in FFM would in turn limit further gain in body-weight, since both the gross cost of physical activity and the 24 h energy expenditure would proportionately increase during this period. Coupled with a certain degree of substitution in energy intakes, these observations possibly account for the rather modest total gains in body-weight seen in the present study. The results do not appear to be specific to the undernourished and are similar to observations made earlier following overfeeding of human subjects (Goldman *et al.* 1975).

In conclusion, reductions in BMR of chronically undernourished individuals are indeed 'adaptive' in nature and, together with the reduced body size, are physiologically and mechanistically important in the process of attaining energy balance. Future studies employing controlled dietary conditions, with longer periods of supplementation, are desirable to examine the extent of this 'reversibility' in BMR and to establish the nature of the changes in body composition on refeeding individuals habituated to low intakes over prolonged periods.

This study was supported by the United Nations University, Tokyo and the Indian Council of Medical Research (ICMR), New Delhi. L.S.P. is the recipient of a Senior Research Fellowship from the ICMR. The authors thank Thilaka Baskaran, Jennifer Sequeira & Chacko Thomas for their assistance in this study.

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Printed in Great Britain