Energy metabolism in free-living, 'large-eating' and 'small-eating' women: studies using $^2H_2{}^{18}O$

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The doubly-labelled water ($^2H_2{}^{18}O$) technique was used to assess the long-term rates of energy expenditure and, after accounting for any changes in body composition, the derived rates of energy intake in weight-stable 'large-eating' (*n* 6) and 'small-eating' (*n* 6) women. The self-reported energy intakes (approximately 11·2 *v.* 5·6 MJ/d) and energy expenditures (approximately 8·5 *v.* 12·4 MJ/d) for the 'large-eating' and 'small-eating' groups respectively, should not be sustainable without significant body-weight changes. $^2H_2{}^{18}O$-assessed rates of energy expenditure for the 'large-eaters' (approximately 8·5 MJ/d) and 'small-eaters' (approximately 11·3 MJ/d) were in close agreement with the results obtained using 5 d, self-reported activity diaries but the derived rates of energy intake for the 'large-' (approximately 8·5 MJ/d) and 'small-eaters' (approximately 10·8 MJ/d) were markedly different from those obtained using self-reported, weighed food diaries. When two 'small-eaters' were supplied with their self-reported energy intakes (approximately 5 MJ/d) for up to 28 d both subjects lost about 0·75 kg body-weight/week. These results provide no support for the existence of 'metabolically efficient' women in the community.

Energy metabolism: Doubly-labelled water: Eating disorders

There is convincing evidence linking obesity with many different health problems; these range from physical limitations to diabetes and ischaemic heart disease (Department of Health and Social Security/Medical Research Council, 1976). Whatever the underlying reason(s) for the development of the extra adipose tissue, be it genetic, hormonal, metabolic and/or psychological, the basic problem is an energy intake which has exceeded energy expenditure over a considerable time period. Despite the self-evidence of this tenet there are numerous anecdotal reports, as well as some scientific studies, which suggest that some people are able to consume excessive amounts of food yet stay slim ('large-eaters') while others appear to fast constantly in order not to become obese ('small-eaters'; Rose & Williams 1961; Widdowson, 1962; Morgan *et al.* 1982; McNeill *et al.* 1989; George *et al.* 1989, 1991; Clark *et al.* 1992, 1993). If these two quite distinct groups of people do exist they should provide an excellent model for studying metabolic efficiency and the aetiology of obesity.

To date there have been five comprehensive investigations dealing with energy metabolism in normal-weight subjects who consider themselves either 'large-eaters' or 'small-eaters' (Rose & Williams, 1961; Morgan *et al.* 1982; McNeill *et al.* 1989; Clark *et al.* 1992, 1993); all of these studies reported that 'large-eaters' appeared to be consuming nearly twice as much energy per day as their matched, normal-weight 'small-eaters' yet only one of these investigations found significant differences in laboratory-assessed rates of energy expenditure (J/kg fat-free mass (FFM) per min) between the 'large-' and 'small-eating' subjects (Clark *et al.* 1992). In female, but not male, 'large-eaters', energy expenditure at rest was 10 to 35% higher than that of the 'small-eaters'. It was also reported that the higher metabolic rate of these 'large-eating' subjects accounted for only a small proportion of the apparent difference in energy intake between the 'large-' and 'small-eating' subjects (Clark *et al.* 1992). An additional complicating finding in this study was that the self-reported activity diaries indicated that the 'small-eaters' were apparently expending approximately 6·3 MJ/d more than the energy intake suggested from their weighed food diaries (Clark *et al.* 1992). This very large negative energy balance is obviously not sustainable without appreciable weight loss. Possible explanations for the disparity between energy intake and energy expenditure data for 'large-' and 'small-eaters' have been presented previously (Rose & Williams 1961; McNeill *et al.* 1989; Clark *et al.* 1992). It is now accepted that dietary information from groups of subjects who are concerned with weight, nutrition and/or exercise should be treated with caution (Southgate, 1986; Livingstone *et al.* 1990; Mulligan & Butterfield, 1990; Clark *et al.* 1992; Ludbrook & Clark 1992).

In the present study we have used $^{2}H_{2}{}^{18}O$ to determine the long-term rates of energy expenditure and energy intake in free-living 'large-' and 'small-eating' women and to assess the accuracy of self-reported food and activity diaries in these two groups of subjects. The resting energy requirements of these volunteers had been assessed, in previous studies, using indirect calorimetry (Clark *et al.* 1992; D. Clark, F. Tomas, R. T. Withers, M. Brinkman, C. Chandler, C. Doherty, M. Dewar, F. J. Ballard and P. Nestel, unpublished observations).

METHODS

Subjects

The fourteen subjects selected to take part in this study were drawn from female volunteers, in the normal weight range, who had participated in earlier studies in our laboratory. At that time they were placed into 'large-eating' and 'small-eating' groups on the basis of self-reported energy intake and energy expenditure diaries (see Clark *et al.* 1992) and then underwent measurements of their energy expenditure by indirect calorimetry (Clark *et al.* 1992). Six of these 'large-eating' females, who had relatively high resting metabolic rates (RMR; J/kg FFM per min) and six 'small-eating' subjects who had relatively low RMR were chosen for the first part of the present study on the basis that they were most likely to have been drawn from population subgroups with differing efficiencies of energy use. The research was approved by the Human Ethics Committee, CSIRO Division of Human Nutrition and by the Committee of Clinical Investigation, Flinders Medical Centre. All subjects gave their written informed consent before commencing the study.

Protocol

The subjects reported to the laboratory before 09.00 hours after a 12 h fast, on day 0, 3–7 d after menstrual flow ceased. A mid-stream urine (approximately 25 ml) and a sub-lingual saliva (approximately 1·5 ml) sample were collected for baseline measurements and the unclothed weight of each subject was obtained. Labelled water (approximately 100 ml) containing ^{2}H (originally 99·75% purity by weight from the Australian Institute of Nuclear Science and Engineering, Sydney, NSW and ^{18}O (initially 10·4% enrichment, supplied by Isotec Inc., Miamisburg, OH, USA) at respective doses of 0·12 and 0·3 g/kg total body water (TBW) was taken orally. The dose was followed by three 33 ml water rinses of the container. A total urine sample was collected, weighed and sub-sampled at 2 h. Additional mid-stream urine and sub-lingual saliva samples were obtained at 3 h after which each volunteer was given a light meal and allowed to resume usual daily activities except that mid-stream urine samples were collected, usually between 09.00 and 12.00 h, on days 1, 3, 5, 7, 10, 14, 17, 21 and 24. These were labelled with the time and date of collection and were immediately frozen. At the completion of the measurement period (day 28) the protocol outlined for day 0 was repeated except that the labelled water drink contained only ^{2}H (at a dose of 0·06 g/kg TBW).

During the final week of the measurement period (days 21 to 28), 5 d, self-reported, weighed food and activity diaries (Clark *et al.* 1992) were maintained by each volunteer from Friday to Tuesday inclusive.

Two additional 'small-eating' females repeated the above protocol but were given a controlled diet similar in composition and total energy (approximately 5 MJ/d) to that indicated by several 5- and one 50-d self-reported, weighed food diaries. Body composition was determined by ^{2}H dilution (Schoeller *et al.* 1982, 1986) and densitometry (Meneely & Kaltreider, 1949; Goldman & Buskirk, 1961; Siri, 1961) at the beginning and end of the experimental period.

Isotope analyses

The ^{2}H and ^{18}O isotope abundances in the two dosing solutions (solution I for subject numbers 022 to 298 inclusive; solution II for the remaining eight subjects, numbers 004, 301 and 419 to 510 inclusive) and in the urine samples collected at 0 and 3 h and on days 3, 7, 14, 21 and 28 were analysed separately on a VG Micromass 602D mass spectrometer (V.G. Isotopes Ltd, Winsford, Cheshire), at the CSIRO (Australia), Division of Water Resources, Adelaide, South Australia. Before analysis each sample (urine or saliva) was centrifuged, and a portion of the supernatant distilled azeotropically with toluene as the solvent (Cuthbertson *et al.* 1989). Water (25 μl) from urine or saliva was reduced to H_2 by circulating over uranium heated to 800° for 5·0 min using a specially designed vacuum line. A portion of the gas was transferred to the mass spectrometer and the ^{2}H:H ratio was measured. This value was compared with that of H_2 gas made from water of known isotopic composition (Leaney *et al.* 1985). The Taylor (1973) description of the Epstein & Mayeda (1953) procedure was followed for the analysis of ^{18}O. Water (5·0 ml) was equilibrated with CO_2 of known isotopic composition at 30° for 15 h. Subsamples of CO_2 were removed, dried and purified before being analysed. These samples were also compared with standards of known isotopic composition. The ^{2}H and ^{18}O analyses were made relative to existing natural abundance and enriched International Atomic Energy Agency standards. All samples were analysed in the order of expected increasing enrichment.

Calculations

Rates of CO_2 production were calculated using equation A6 of Schoeller *et al.* (1986) which assumes that the ^{18}O and ^{2}H dilution spaces differ from TBW by 1 and 4% respectively, and that only expired water vapour, breath CO_2 and insensible cutaneous water loss are isotopically fractionated. As multiple urine samples were collected over the 28 d measurement period, ^{2}H and ^{18}O elimination rates were derived from the slopes of the appropriate regression lines for the log transformations. Food quotient (FQ) values, estimated from the 5 d weighed food diaries which were maintained during the final week of the experimental period, were used in the calculations of free-living energy expenditures (Black *et al.* 1986).

Table 1. *Physical characteristics and body composition† of 'large-eating' and 'small-eating' subjects‡*

(Values in parentheses are results from studies conducted 2–3 years previously)

Subject no.	Age (years)	Weight (kg) Initial		Final	Height (m)	Total body water§ (kg)	Fat-free mass‖ (kg)	Body fat¶ (%)
'Large-eaters'								
228	29	46·30	(46·93)	46·15	1·66	26·12	35·78	22·7
215	41	48·70	(48·30)	48·70	1·61	26·17	35·85	26·4
135	37	44·25	(45·20)	44·85	1·64	22·19	30·39	31·3
510	27	58·10	(56·69)	58·20	1·65	30·16	41·32	28·9
439	51	50·55	(51·76)	50·25	1·63	24·72	33·89	33·0
469	39	57·45	(56·59)	58·10	1·73	29·42	40·31	29·8
Mean	37·3	50·89*	(50·91)	51·04	1·65	26·46*	36·26*	28·7
SE	3·6	2·35	(2·01)	2·38	0·02	1·21	1·66	1·5
'Small-eaters'								
298	43	52·55	(50·48)	51·25	1·54	28·94	39·65	24·5
022	36	58·70	(60·23)	58·85	1·66	31·14	42·66	27·3
245	43	62·25	(59·65)	61·20	1·59	30·65	41·98	32·6
430	45	52·65	(52·50)	53·13	1·61	26·55	36·37	30·9
425	39	59·05	(59·68)	60·25	1·64	33·02	45·24	23·4
419	32	74·10	(71·97)	73·73	1·67	41·77	57·21	22·8
Mean	39·7	59·88	(59·09)	59·74	1·62	32·01	43·85	26·9
SE	2·0	3·25	(3·08)	3·24	0·02	2·15	2·94	1·7

Mean values were significantly different from those for 'small-eaters' (Student's *t* test): * $P < 0·05$.

† For details of procedures, see pp. 22–23.

‡ For details of subjects, see p. 22.

§ From ^2H dilution space (saliva sample/1·04).

‖ From total body water/0·73.

¶ From total body water assuming that body fat = body-weight − total body water/0·73.

Statistical analysis

All results are presented as mean values with their standard errors. Differences between groups were calculated using dependent or independent Student *t* tests as appropriate.

RESULTS

The physical characteristics, TBW (assessed from saliva ^2H data), FFM and percentage body fat of the six 'large-eating' and the six 'small-eating' female subjects are shown in Table 1. The sub-group of 'large-eaters' used in this study were selected on the basis of their relatively high rates of energy expenditure at rest (RMR) normalized to FFM and, likewise, the sub-group of 'small-eaters' were selected on the basis of their relatively low FFM-normalized RMR (see Table 3). For this reason no attempt was made to match the physical characteristics of these 'large-eaters' and 'small-eaters'. Although the heights of the two groups were similar, FFM was 7·7 kg greater (approximately 21 %; $P < 0·05$) and body weight was 9·0 kg heavier (approximately 17 %; $P < 0·05$) in the 'small-eating' group (Table 1).

There were no statistically significant differences between the 'large-' and 'small-eating' females for the ^2H and ^{18}O elimination rate constants (Table 2). Neither was the divergence between these constants (k_o–k_H; Table 2), which is a measure of CO_2 production (Schoeller

Table 2. *Elimination rates of $H_2{}^{18}O$ and ${}^2H_2O$ in female 'large-eaters' and 'small-eaters'**

Subject no.	k_O*†	k_H†	k_O–k_H
'Large-eaters'			
228	0·0946	0·0734	0·0212
215	0·1191	0·0927	0·0264
135	0·1102	0·0846	0·0256
510	0·1094	0·0815	0·0279
439	0·1190	0·0906	0·0284
469	0·1485	0·1216	0·0269
Mean	0·1168	0·0907	0·0261
SE	0·0073	0·0068	0·0011
'Small-eaters'			
298	0·1116	0·0874	0·0242
022	0·1120	0·0866	0·0254
245	0·2296	0·1963	0·0333
430	0·1245	0·0964	0·0281
425	0·1676	0·1308	0·0368
419	0·1143	0·0858	0·0285
Mean	0·1433	0·1139	0·0294
SE	0·0193	0·0179	0·0044

* For details of subjects and procedures, see Table 1 and pp. 22–23.

† Mean, daily elimination rate constants for oxygen (k_O) and hydrogen (k_H) calculated from linear regressions between log of isotopic enrichments and time.

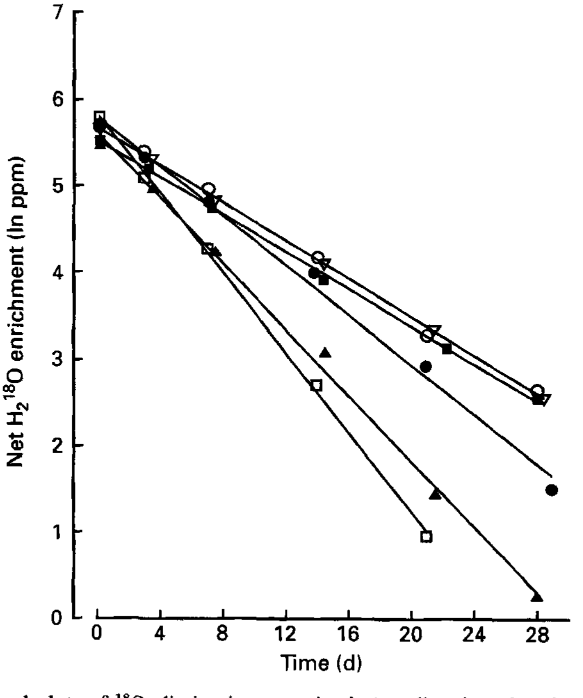

Fig. 1. Log transformed plots of ^{18}O elimination rates in six 'small-eating' female subjects. Only five plots are apparent as the subjects represented by the open circles (○) and the open triangles (▽) share the same regression line.

Table 3. *Comparisons of rates of energy metabolism in 'large-eating' and 'small-eating' females*
(Values in parentheses are results from studies conducted 2–3 years previously)

Subject no.	Energy balance (self-reported diary): Apparent energy intake‡ (MJ/d)		FQ	Apparent energy expenditure‡ (MJ/d)		BMR (calorimetry): (J/kg FFM per min)	(MJ/d)	Energy balance ($^2H_2{}^{18}O$): Expenditure§ (MJ/d)	Intake‖ (MJ/d)	TEE-BMR (MJ/d)	TEE: BMR
'Large-eaters'											
228	13·28	(12·73)	0·825	9·47	(7·89)	(97·6)	(5·06)	7·00	7·36	1·94	1·38
215	8·60	(11·07)	0·875	7·65	(7·83)	(108·0)	(5·61)	8·32	8·22	2·71	1·48
135	11·56	(9·49)	0·871	7·43	(7·31)	(112·2)	(4·93)	6·94	6·98	2·01	1·40
510	9·53	(11·51)	0·862	9·38	(9·17)	(99·7)	(5·96)	10·45	10·26	4·49	1·75
439	9·29	(11·01)	0·826	8·97	(9·21)	(102·2)	(5·01)	8·96	8·30	3·95	1·79
469	10·70	(11·57)	0·866	9·53	(9·90)	(102·6)	(6·00)	9·28	9·75	3·28	1·55
Mean	10·49***	(11·23)***	0·854	8·74***	(8·55)***	(103·7)***	(5·43)	8·49*	8·48*	3·06**	1·56***
SE	0·70	(0·43)	0·009	0·39	(0·41)	(2·2)	(0·20)	0·56	0·53	0·42	0·07
'Small-eaters'											
298	4·72	(4·25)	0·881	12·31	(10·46)	(76·2)	(4·37)	8·33	7·91	3·96	1·90
022	4·90	(5·54)	0·839	10·63	(11·61)	(81·2)	(5·03)	9·86	10·50	4·83	1·96
245	7·07	(6·69)	0·847	13·17	(13·60)	(81·2)	(4·94)	11·57	11·43	6·63	2·34
430	4·64	(4·69)	0·876	10·79	(10·22)	(89·2)	(4·70)	9·00	10·15	4·30	1·92
425	5·62	(5·78)	0·873	11·93	(11·93)	(88·3)	(5·80)	14·61	12·69	8·81	2·52
419	8·37	(6·84)	0·902	14·68	(16·47)	(85·4)	(7·08)	14·27	12·26	7·19	2·02
Mean	5·89	(5·63)	0·870	12·25	(12·38)	(83·6)	(5·32)	11·27	10·82	5·95	2·11
SE	0·62	(0·42)	0·009	0·62	(0·96)	(2·0)	(0·40)	1·10	0·71	0·78	0·11

FQ, food quotient; TEE, total energy expenditure; BMR, basal metabolic rate; FFM, fat-free mass.
Mean values were significantly different from those for 'small-eaters': * $P < 0{\cdot}05$; ** $P < 0{\cdot}01$: *** $P < 0{\cdot}001$.
† For details of subjects, and procedures see Table 1 and pp. 22–23.
‡ Results calculated from 5 d diaries.
§ Daily energy expenditure was calculated from rate of CO_2 production using the FQ value determined from the self-reported, weighed food diary.
‖ Derived daily energy intake was calculated as the sum of measured daily energy expenditure and the change in body energy stores over the measurement period.

Table 4. *Energy metabolism in two 'small-eating' females receiving a controlled energy intake to match that from self-reported diaries**

Subject no.	Age (years)	Weight (kg)	Height (m)	Energy intake (MJ/d)	Mass changes: Total (g/d)	Mass changes: Fat† (g/d)	Energy metabolism measurements: Expenditure‡ (MJ/d)	Balance (MJ/d)	Intake (MJ/d)
004	45	54·65	1·63	4·96	−127	−90	9·59	−3·33	6·26
301	23	56·80	1·59	4·92	−105	−103	7·41	−3·12	4·29

* For details of subjects and procedures, see pp. 22–23.
† Determined by densitometry.
‡ Determined using $^2H_2{}^{18}O$ over 28 d for subject 004 and 21 d for subject 301.

et al. 1986; Prentice, 1990), significantly different between the groups. Net enrichments of ^{18}O in the urine samples collected by the 'small-eating' subjects over the measurement period are shown in Fig. 1. Only one of the six decay curves had returned to pretest values within the 28 d measurement period.

Apparent daily energy intakes and apparent rates of energy expenditure, determined from 5 d, self-reported diaries for the 'large-' and 'small-eating' female subjects, are shown in Table 3. Also presented are: the FQ values, which were derived from the 5 d food diaries; the basal rates of energy expenditure determined by indirect calorimetry (see Clark *et al.* 1992); the rates of free-living energy expenditure assessed using $^2H_2{}^{18}O$; energy intakes derived from the $^2H_2{}^{18}O$-determined rates of energy expenditure and changes in body composition; total daily energy expenditures minus basal metabolic rates (BMR) and the energy expenditure:BMR ratios. All data presented in parentheses (Table 3) are results which were obtained for the same subjects during investigations on energy metabolism that had been conducted 2 to 3 years before the present study. There were significant differences ($P < 0·05$) between the two groups for all variables except BMR (MJ/d) and FQ (Table 3).

The average rates of energy expenditure assessed using $^2H_2{}^{18}O$ over the 28 d measurement period for both the 'large-eating' (8·49 (SE 0·56) MJ/d) and 'small-eating' (11·27 (SE 1·10) MJ/d) female subjects were within one-twelfth (not significant; paired Student *t* tests) of the values obtained using 5 d activity diaries during the final week of the isotope study (8·74 (SE 0·39) and 12·25 (SE 0·62) MJ/d respectively; Table 3). On the other hand, the rates of energy intake derived from the isotope data and changes in body composition for the 'large-eaters' (8·48 (SE 0·53) MJ/d) were nearly one-fifth ($P < 0·05$) lower than the diary-assessed intake rates for this group (10·49 (SE 0·70) MJ/d) and over 80% ($P < 0·001$) higher for the 'small-eating' subjects (10·82 (SE 0·71) *v.* 5·89 (SE 0·62) MJ/d respectively; Table 3).

Table 4 contains data for two 'small-eating' females whose rates of energy expenditure were determined using $^2H_2{}^{18}O$ while they were given approximately 5 MJ/d, an amount determined from their self-reported, weighed food diaries. Both subjects had appreciable weight losses while consuming this controlled level of energy intake. Their derived rates of energy intake are in reasonable agreement with the estimated energy content of the food eaten (Table 4).

DISCUSSION

Over the past 30 years there have been a number of studies on energy metabolism in matched groups of 'large-' and 'small-eating' humans (Rose & Williams, 1961; Morgan *et al.* 1982; McNeill *et al.* 1989; George *et al.* 1989, 1991; Clark *et al.* 1992, 1993). All of these studies have reported that the average daily energy intake of the selected 'large-eating' subjects was nearly double that of the 'small-eating' subjects who were matched for age, height, weight, and, in some cases, FFM. The maintenance of a two-fold difference in apparent daily energy intake between these groups of matched, normal-weight subjects is quite tenable as long as the 'large-eating' group leads a relatively active lifestyle and expends approximately twice the amount of energy as the 'small-eating' group.

Our investigations on energy metabolism in 'large-' and 'small-eaters' were initiated with the primary aim of determining whether we could demonstrate the presence of 'metabolically efficient' ('small-eaters') and/or 'metabolically inefficient' ('large-eaters') individuals in the free-living population (Clark *et al.* 1992). To accomplish this we determined not only the apparent daily energy intake of the volunteers who considered themselves to be 'large-eaters' or 'small-eaters' but also their apparent daily energy expenditures using self-reported activity diaries. A consistent finding in these studies was that the normal-weight 'large-eaters' appeared to be eating nearly one-third more energy per day (approximately 11·9 MJ/d) than they were expending (approximately 9·2 MJ/d) yet not gaining weight, while the 'small-eaters' appeared to be expending more than twice as much energy per day (approximately 12·1 MJ/d) as they were eating (approximately 5·3 MJ/d) without losing any weight (Clark *et al.* 1992). It is possible to provide a plausible mechanism for the maintenance of a stable body weight when the apparent, sustained energy balance is positive but not when it is negative (Clark, *et al.* 1992).

The questions raised by these studies call for the identification of the real rates of energy intake and energy expenditure in these normal-weight 'small-eating' women.

During the last decade the doubly-labelled-water method for measuring total energy expenditure in free-living humans has been successfully validated in over thirteen separate studies by four independent research groups (Prentice, 1990). As this research has demonstrated that the accuracy of this technique is generally in the order of 1 to 3% and the precision 2 to 8% (Prentice, 1990) we decided to use this method to determine the actual rates of energy expenditure in some of our 'large-' and 'small-eating' subjects.

The results obtained in the present investigation for apparent rates of energy intake and energy expenditure for the six selected 'large-eaters' and the six selected 'small-eaters', using the 5 d, self-reported, weighed food and activity diaries, gave similar results to those obtained during previous self-assessments of their energy metabolism (Table 3, results in parentheses; Clark *et al.* 1992). The apparent energy intake of the six selected 'large-eaters' (approximately 10·5 MJ/d) was only one-fifth greater than their apparent rate of energy expenditure (approximately 8·8 MJ/d) but the apparent intake of the selected 'small-eaters' (approximately 5·9 MJ/d) was less than half their apparent rate of energy expenditure (approximately 12·4 MJ/d, Table 3). These apparent rates of energy intake and energy expenditure were obtained during the final week of the month-long estimation of free-living energy expenditure using doubly-labelled water (see pp. 22–23).

The stable isotopes revealed that the energy expenditure of the 'large-eating' females averaged 8·6 MJ/d while that of the 'small-eating' females averaged 11·3 MJ/d (Table 3). Although the $^{2}H_{2}{}^{18}O$-assessed rates of energy expenditure for the groups of free-living, 'large-' and 'small-eaters' were the same as those obtained using 5 d activity diaries (Table 3), there were some large differences between these two methods in the estimation of rates of energy expenditure for some of the individual subjects (−2·7 to 4 MJ/d; Table 3). The mean of the absolute differences between these two methods was 0·8 MJ/d (r 0·481) for the 'large-eaters' and 1·9 MJ/d (r 0·581) for the 'small-eaters' (data derived from Table 3). These results indicate that self-reported, 5 d activity diaries can provide realistic estimations of the average rates of energy expenditure for groups of free-living humans but not necessarily for a specific individual (Table 3).

It is possible to estimate actual rates of energy intake in 'normally-occupied', free-living humans provided that their rates of energy expenditure have been accurately determined over a reasonably long (2 to 4 week) time period (Prentice, 1990). If there are no measurable changes in body composition over the experimental period then energy intake is equal to energy expenditure. If there have been changes in body composition over the measurement period, rates of energy intake can still be estimated as long as the body composition changes can be accurately appraised. In this case energy intake is equal to the sum of energy expenditure plus the change in body energy over the measurement period. We have applied this approach to determine actual rates of energy intake in the selected 'large-' and 'small-eating' females (Table 3).

Over the 4-week experimental period there was little variation in body weight (Table 1) or body composition (Table 3) in either group of subjects. Thus when the $^{2}H_2{}^{18}O$-assessed rates of energy expenditure (Table 3) were adjusted for the measured changes in body energy over the measurement period the derived energy intakes of the 'large-eaters' and 'small-eaters' (8·48 (SE 0·53) and 10·82 (SE 0·71) MJ/d respectively) were within 5% of their measured energy expenditures (Table 3). Not only do these derived estimates of energy intake indicate that the 'small-eaters' appear to be consuming nearly twice as much energy per day than that determined from their 5 d weighed food diaries (Table 3), but they also suggest that they were eating about one-fourth more energy per day than the 'large-eaters' (Table 3). Although it is difficult to determine changes in body composition and hence changes in body energy stores, especially when these changes are small, our derived rates of energy intake should be reasonably accurate. This is because the rates of energy expenditure assessed using $^{2}H_2{}^{18}O$ for the 'small-eating' females were determined using samples collected over a 28 d period and the subjects maintained stable body weights over this time (Table 1). In fact, most of these subjects had been weight stable over the preceding 2 or more years (Table 1).

The measures of energy intake based on the $^{2}H_2{}^{18}O$ method for the 'small-eating' females are markedly different from the self-reported, 5 d, weighed food diary results (Table 3) and further indicate that estimates of energy intake based on diaries kept by food conscious individuals should be treated with caution (Southgate, 1986; Livingstone *et al.* 1990; Mulligan & Butterfield, 1990; Clark, 1992; Ludbrook & Clark, 1992). This conclusion is supported by the results of the final experiment in this investigation (Table 4). When two 'small-eating' females were supplied with their self-reported daily energy intakes (approximately 5 MJ/d) for 21 (subject 301) or 28 d each lost about 0·75 kg body weight/week. This is close to the weight loss that would be predicted from the $^{2}H_2{}^{18}O$-assessed rate of energy expenditure and the supplied daily energy intake for subject 301 (Table 4), but subject 004 should have recorded a greater loss of fat mass to account for her energy imbalance of $-4{\cdot}6$ MJ/d (Table 4). As discussed above, this discrepancy probably reflects the difficulty in accurately assessing changes in the fat and the FFM of human subjects (Prentice, 1990).

The results obtained with the stable isotopes indicate that the 'small-eating' females had significantly higher rates of energy expenditure (total energy expenditure (TEE); TEE-BMR; TEE/BMR; Table 3) than the 'large-eating' females. The doubling of the rates of energy expenditure due to increased physical activity (TEE-BMR; Table 3) in the 'small-eaters' would increase the rates of formation of both CO_2 and water in this group due to an enhanced oxidation of carbohydrate and lipid. As a consequence of these increases there could be differences in isotope fractionation in breath CO_2, expired water vapour and insensible cutaneous water loss in the 'small-eating' females. Our results provide few data which address this problem. However, research from other groups has demonstrated that there are significant decreases in ^{2}H (6%; $P < 0{\cdot}01$) and ^{18}O (1%; $P < 0{\cdot}01$) fractionation between water vapour and liquid during exercise at 75% of maximal rates of O_2 consumption but no change in ^{18}O fractionation between CO_2 and water (1·035 *v.* 1·036, results from the Rowett group, cited by Prentice, 1990). Since the fractionation correction for water vapour loss depends on the difference between ^2H and ^{18}O fractionation rather than on the absolute values it was concluded that the doubly-labelled-water technique also provides accurate measurements of energy expenditure in subjects who lead physically active lifestyles.

Another factor which affects isotope fractionation is body temperature. The oral temperature of 'small-eating' females was 0·3° lower than that of the matched 'large-eaters' at rest, dropping to 0·7° lower during different walking activities (Clark *et al.* 1992). Unfortunately we cannot assess what effect this would have on isotope fractionation and the calculated rates of energy expenditure in the 'small-eating' females as we have no measurements of their core temperatures at rest and during exercise.

In conclusion, the results from these studies with $^2H_2{}^{18}O$ not only demonstrate the unreliability of energy intakes determined using self-reported, weighed food diaries in some food (weight) conscious people but also belie the existence of normal-weight, 'metabolically efficient' ('small-eating') females in the community.

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