Differences in energy metabolism between normal weight 'large-eating' and 'small-eating' women

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Nine 'large-eating' (approximately 12 MJ/d) and nine 'small-eating' (approximately 5·3 MJ/d) women were selected from the population on the basis of diet and activity diaries. At rest and in the post-absorptive state the rate of oxygen consumption ($\dot{V}_{O_2}$)/kg fat-free mass (FFM) and rate of carbon dioxide production ($\dot{V}_{CO_2}$)/kg FFM were 9–17% higher ($P < 0{\cdot}05$) in the 'large-eaters' than in the 'small-eaters'. As energy expenditure was increased by walking at 2·4, 3·9 and 5·4 km/h the differences between the two experimental groups for both $\dot{V}_{O_2}$/kg FFM and $\dot{V}_{CO_2}$/kg FFM were decreased to negligible values, but energy expended on a body-weight basis (MJ/kg per min) remained significantly higher (5–10%) in 'large-eaters'. Oral temperature was also consistently higher (up to 0·5°) in this group both at rest and during sitting, standing and walking activities. Although the average thermic effect of a standardized liquid meal tended to be higher (27%; not significant) in the 'small-eaters', the other results demonstrate that the 'large-eating' females had a markedly higher rate of energy expenditure at rest and during light physical activities.

Energy metabolism: Indirect calorimetry: Women

There is anecdotal evidence for the existence of people who eat excessively yet stay slim ('large-eaters') and also for people who appear constantly to restrict their energy intake in order not to gain weight ('small-eaters'). More substantial proof has arisen from data collected by interview, questionnaires or self-reporting food intake and daily activity diaries (Rose & Williams, 1961; Widdowson, 1962; McNeill *et al.* 1989); however, these methods of assessing energy intake and energy expenditure are not considered to be very accurate for small groups or for individuals (Marr, 1971; Acheson *et al.* 1980; Baghurst & Baghurst, 1981; McNeill *et al.* 1989; Livingstone *et al.* 1990). If these two quite distinct groups of people do exist in the population it should be possible to demonstrate either that the 'large-eaters' have higher metabolic rates or that the 'small-eaters' have depressed metabolic rates at rest or during different daily activities. This has not been accomplished to date in any comparative investigations with groups of 'large-eaters' or 'small-eaters': Rose & Williams (1961) found no differences in the rates of oxygen consumption, measured at rest and during different activities, in young, male 'large-eaters' (*n* 6) and 'small-eaters' (*n* 6) who were matched for age, height and weight. More recently McNeill *et al.* (1989) were unable to demonstrate any differences in basal metabolic rate (BMR) or in 24 h energy expenditure between their young male volunteers who were matched for age, height, weight and

percentage body fat (% BF; *n* 5 per group). We were also unable to demonstrate any differences in resting metabolic rate (RMR) in male volunteers matched for age, body mass index (BMI) and fat-free mass (FFM), but we did establish that 'large-eating' men had a 4–5% higher energy expenditure during different activities (sitting, standing and walking at slow to moderate speeds) compared with 'small-eaters' (D. Clark, F. Tomas & R. T. Withers, unpublished results).

The present paper describes our findings for normal weight, 'large-' and 'small-eating' women and demonstrates substantial differences in maintenance energy expenditure between these groups.

METHODS

Subjects

Subjects were recruited by advertising for healthy, 20–50 year-olds who regarded themselves either as being able to eat freely without weight gain ('large-eaters') or having to restrict their food intake in order to keep within the normal weight range ('small-eaters'). All female respondents (*n* 187) were sent a comprehensive, food-frequency dietary questionnaire (Baghurst & Baghurst, 1981) which was coded to determine the average daily energy intake of each subject. Questionnaire respondents who appeared to fall within the set limits of age, weight and health (*n* 120) were given self-reporting, 5 d weighed food and activity diaries and a set of 0–2 kg Soehnle digital scales with a taring function. In addition to detailed written instructions and a sample daily log, which were supplied with each diary, each subject was counselled on how to weigh and record all foods and beverages consumed. Food records were analysed with a computer program to determine the average daily energy intake of each volunteer (McCance & Widdowson, 1978). Daily activity was also recorded over the same 5 d period; Friday to Tuesday inclusive. Each day was divided into twenty-four 1 h periods and volunteers were asked to record, to the nearest 5 min, how long they spent sleeping, sitting relaxed, sitting erect, standing, strolling, walking, jogging, running or sprinting during each hour. Activities such as swimming, cycling, aerobics, vacuuming etc, which could not be listed under one of the nine major headings previously described, were itemized separately with an indication of the intensity of the activity. Written instructions and a sample daily record were also supplied with each diary. Daily energy expenditures were calculated using the subject's weight on that day and the appropriate energy expenditure values compiled by McArdle *et al.* (1986). A 24 h urine collection was made during the 5 d diary recording period. Dietary protein intake was estimated from the excretion of urinary nitrogen and was compared with that obtained from the food diary for the corresponding time period (Isaksson, 1980; Warwick *et al.* 1988).

Subjects at opposite extremes of the distribution for the apparent energy expenditure: apparent energy intake ratio (E:I) were selected to form the study groups of 'large-eaters' (low ratio) and 'small-eaters' (high ratio).

Ethical approval for the investigation was obtained from the Human Ethics Committee, CSIRO Division of Human Nutrition and from the Committee of Clinical Investigation, Flinders Medical Centre. Written informed consent was received from each volunteer before she proceeded with the study.

Protocol

Each selected subject (nine from each group) attended the Exercise Physiology Laboratory (EPL) four times at approximately monthly intervals, 3–7 d after menstrual flow ceased. The subject had fasted for at least 12 h before each visit, had refrained from strenuous physical activity for a minimum of 24 h and was driven to the laboratory so that she arrived

in a relaxed state at 08.20 hours. The subject then changed into a light, cotton hospital gown, voided and was weighed. She then rested supine for at least 45 min before the commencement of testing. RMR was measured by indirect calorimetry (see below) during the periods 50–60 and 70–80 min after the start of each of the four visits. Metabolic rate (MR) was measured during periods of sitting on a stool and standing erect at 20 and 40 min respectively, after the RMR measurements on the first and second visits. On day 1 this was followed by 20 min practice walking on a treadmill at 2·4, 3·9 and 5·4 km/h. MR during exercise was assessed on day 2 during the final 10 min of walking at each of the three different speeds (two 5·0 min collection periods at 2·4 and 3·9 km/h and two 3·0 min collection periods at 5·4 km/h). Percentage body fat (% BF) was determined by underwater weighing at the conclusion of the MR measurements on day 2 and the result obtained used to calculate the subject's fat mass (FM) and FFM.

The thermic effect of food (TEF) was assessed after the RMR measurements by determining the rates of O_2 consumption ($\dot{V}_{O_2}$; ml/kg FFM per min) and CO_2 production ($\dot{V}_{CO_2}$; ml/kg FFM per min) at rest starting 45 min after the commencement of a standard liquid meal (Ensure Plus (g/l): carbohydrate 533, fat 320, protein 147, 50 kJ/kg FFM which was consumed within 15 min) and then at 30 min intervals for the next 4 h. Half the women in each group completed the TEF measurements on day 3 and the other half on day 4. The same procedures were followed on the alternate control day except that the subjects remained fasted until the completion of the day's measurements (approximately 15.30 hours).

Whole-body protein turnover (see p. 34) was measured in fasted subjects over a 9 h period from approximately 07.00 hours on the control day for TEF measurements. Muscle protein breakdown rates (see p. 34) were estimated within 1 month of completing the calorimetric measurements.

Indirect calorimetry

All indirect calorimetric measurements were performed in the EPL which was maintained at $24 \pm 1°$ in the vicinity of the subject. There were no disturbances or interruptions after the commencement of each day's measurements (08.30 hours). Subjects breathed through a Hans Rudolph (model 2600) respiratory valve and the expirate was collected in a 150 l Douglas bag. Before each collection period there was a 4–5 min trial to ensure comfort but also to flush the Douglas bag with mixed expirate. The O_2 and CO_2 contents of dry expired gas were determined with an Electrochemistry S-3A and a Beckman LB-2 analyser respectively. These were calibrated before each reading using Lloyd-Haldane verified dry gas mixtures. Expired gas volumes were measured using a calibrated Singer DTM-325 gas meter with a digital read-out. $\dot{V}_{O_2}$ (ml/kg FFM per min) and respiratory quotient (RQ) values were determined using the classical Haldane (1912) transformation.

Densitometric analysis

Body density was determined by underwater weighing (Goldman & Buskirk, 1961) in a large cylindrical tank (1·5 m deep × 1·5 m wide) in which a light metal chair was suspended from a Western load cell. The weighing procedure was repeated at least seven times until the three heaviest readings were within 25 g of one another; the mean of these three readings was used in the calculation of body density. Residual lung volume was determined by the helium-dilution method (Meneely & Kaltreider, 1949) before and after the measurements of immersed mass, and the average value was used in the computation of body density. The Siri (1961) equation was used to convert body density to % BF.

Protein turnover

Whole-body protein turnover was determined using [^{15}N]glycine essentially as described by Fern *et al.* (1981). The [^{15}N]glycine (100 mg, 99% enrichment; MSA Isotopes) was administered orally in a gelatin capsule and the excretion of ^{15}N in urinary ammonia was used to calculate whole-body nitrogen flux (Fern *et al.* 1981). The rate of breakdown of muscle protein was assessed from the urinary excretion of N$^{\tau}$-methylhistidine and creatinine over a 48 h period 3 d after commencing a meat-free diet (Thompson & Tomas, 1987).

Urine N

Urine samples were assayed for N using a N analyser (NA 1500; Carlo Erba Instrumentazione, Milan, Italy). Protein intake (g) was estimated as (urinary N (g) + 2) × 6·25 (Isaksson, 1980).

Blood chemistry

Blood samples (approximately 40 ml) were collected from eight 'large-eaters' and eight 'small-eaters' after a 12 h overnight fast and 1–7 d after menstruation. The plasma was assayed for electrolytes, urea and creatinine in a Synchron CX-3 automated analyser (Beckman Instruments, Fullerton, CA, USA); lipids (total cholesterol, high-density-lipoprotein (HDL)-cholesterol and triacylglycerols) with Boehringer Mannheim reagents, (Boehringer Mannheim Australia Pty Ltd, Dulwich, South Australia) using a Cobas BIO centrifugal analyser (Roche Diagnostics, CH-4002 Basle, Switzerland); other metabolites (glucose, lactate, pyruvate, acetoacetate, hydroxybutyrate, glycerol and free fatty acids) by standard enzymic techniques (Bergmeyer, 1974) on neutralized perchloric acid extracts (free fatty acids were assayed on the unacidified plasma samples) in a Cobas FARA automated analyser (Roche Diagnostics, Basle); and trace elements (zinc and copper) by flame atomic absorption spectrophotometry with a Perkin-Elmer 5000 atomic absorption spectrophotometer (Perkin-Elmer Ltd, Melbourne). Insulin and glucagon were measured by radioimmunoassay of plasma obtained from blood collected in a tube containing EDTA and a proteinase inhibitor (Aprotinin 1000 U/ml: Boehringer Mannheim). Insulin was measured using a commercial kit (Phadeseph, Pharmacia Diagnostic Products) and glucagon using an antiserum specific for pancreatic glucagon (Oliver *et al.* 1976). Insulin-like growth factor-1 (IGF-1) was extracted from plasma with acid-ethanol (Daughaday *et al.* 1980) and diluted 10-fold with assay buffer. IGF-1 was measured by radioimmunoassay using rabbit antiserum raised against bovine (= human) IGF-1 (Francis *et al.* 1989). Recombinant human IGF-1 was used as the radioligand (approximately 80 Ci/g) and standard. Antibody-bound radioactivity was precipitated with donkey anti-rabbit serum. Testosterone, oestradiol and thyroid hormones in serum were measured with radio-immunoassay kits.

Statistical analyses

Descriptive data, including body composition, plasma measures and diary information for the groups were compared using the independent Student's *t* test. The indirect calorimetric measurements were assessed by analyses of variance. For measurements made during the assessment of (a) RMR on each of the 4 d and (b) MR in the control period for the TEF, each series of observations was analysed in a repeated-measures-design ANOVA. The relationships between diary and urinary N estimates of protein intake were examined by regression analyses.

RESULTS

The physical characteristics of the selected 'large-' and 'small-eating' female subjects, together with their apparent daily energy intakes, apparent daily energy expenditures and

E:I, are shown in Table 1. As there were only nine female volunteers who could be classified as 'large-eaters' (E:I < 0·9), and most of these subjects had BMI between 18 and 20, it was not possible to match these volunteers with nine 'small-eaters' whose BMI, in all but two cases, were greater than 21 (Table 1). This investigation was consequently performed with unmatched groups of 'large-eaters' and 'small-eaters'. However, the only physical characteristics which were significantly different between these two groups were height and BMI. On average the 'large-eaters' were 4% ($P < 0·05$) taller than the 'small-eaters' and their BMI was 18% ($P < 0·001$) lower (Table 1). FM, % BF and FFM were 28, 16 and 5% lower respectively in the 'large-eaters' but none of these differences attained statistical significance (Table 1).

Apparent daily energy intake in the 'large-eaters', as assessed by dietary questionnaires and by 5 d self-reported food diaries (see p. 32), appeared to be twice ($P < 0·001$) that of the 'small-eaters' although their apparent daily energy expenditure was 25% ($P < 0·001$) less than that of the 'small-eaters' (Table 1). In our selected groups the ratio of the two estimates of protein intake (urinary N excretion *v.* the diet diary) were 0·91 (SE 0·11) and 1·93 (SE 0·36) for 'large-' and 'small-eaters' respectively ($P < 0·025$) (Isaksson, 1980; Warwick *et al.* 1988).

Resting $\dot{V}_{O_2}$ measured on four separate days, at least 3–5 weeks apart (Table 2) or at 30 min intervals during the TEF control day, were 12–17% ($P < 0·05$) higher in the 'large-eaters' at each measurement period (Table 2). This difference was maintained during sitting, increased to 19% ($P < 0·01$) during standing, but while walking at 2·4, 3·9 and 5·4 km/h decreased to 7·5 (not significant (NS)), 2·4 (NS) and 0·8% (NS) respectively of the values obtained for the 'small-eaters' (Table 2). Similar results were obtained for $\dot{V}_{CO_2}$ which was 9–12% (NS) higher in the 'large-eaters' at rest.

The RQ averaged 0·784 (SE 0·004) for the 'large-eaters' and 0·829 (SE 0·048) ($P < 0·05$) for the 'small-eaters' during all the resting measurements (Table 2), and was further elevated in this latter group during walking at the three different speeds (Table 2). These values are indicative of a relatively greater metabolism of carbohydrate relative to fat in the 'small-eaters'.

A standardized liquid meal increased $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and RQ in both experimental groups (values not shown). RQ values increased to the same value (0·875) in both the 'large-eaters' and the 'small-eaters' 30 min after completion of the meal and then fell similarly to 0·825 at the end of the measurement period (285 min). The average TEF in the 'small-eaters' (5·75 (SE 0·91)% of the energy of the test meal) was 27·5% (NS) greater than that of the 'large-eaters' (4·51 (SE 1·14)%; Fig. 1).

The average resting oral temperature of the 'large-eaters' (36·15 (SE 0·04)°) was approximately 0·3° higher (NS) than that of the 'small-eaters' (Table 2). This difference increased to approximately 0·6° ($P < 0·05$) during exercise.

There were no significant differences in the rates of whole-body protein turnover or muscle protein breakdown between the 'large-eating' and 'small-eating' groups (Table 3).

Values for blood variables for the 'large-eaters' and the 'small-eaters' are shown in Table 4. Significant differences ($P < 0·05$) between the two groups were only found for plasma bicarbonate, acetoacetate and insulin concentrations.

DISCUSSION

Daily energy intake and expenditure

The apparent energy intake in the nine 'large-eating' women (12 MJ/d) was more than double that of the nine 'small-eating' women (5·3 MJ/d; Table 1). The 'large-eaters' (E:I < 0·91) appeared to be maintaining a positive energy balance (2·8 MJ/d) and the 'small-

Table 1. *Physical characteristics and energy balance in the nine, most extreme 'large-eating' and the nine, most extreme 'small-eating' female subjects*

Subject	Age (years)	Height (m)	Wt (kg)	BMI	Fat-free mass (kg)	Fat mass (kg)	Body fat (%)	Energy (MJ/d)			
								Intake (Int)		Expenditure (Exp)	
								Q	Diary	Diary	Exp:Int†
'Large-eaters'											
ja 228	27	1·66	46·93	17·03	38·15	8·78	18·7	10·19	12·72	7·86	0·62
mk 140	46	1·68	60·75	21·52	42·77	17·98	29·6	18·47	15·47	9·69	0·63
bk 215	39	1·61	48·30	18·63	32·57	15·73	32·6	10·16	11·06	7·82	0·71
gg 135	34	1·64	45·20	16·81	31·93	13·28	29·4	10·75	9·48	7·30	0·77
jt 159	41	1·69	53·20	18·63	40·71	12·49	23·5	8·59	11·72	9·33	0·80
ss 078	28	1·74	57·25	18·91	45·46	11·79	20·6	10·04	12·44	9·89	0·80
cp 147	37	1·66	53·23	19·32	43·71	9·52	17·9	14·72	12·90	10·86	0·84
dt 226	40	1·76	65·30	21·08	46·17	19·13	29·3	11·54	12·21	11·03	0·90
vm 240	45	1·66	51·68	18·75	38·55	13·13	25·4	9·22	9·64	8·76	0·91
Mean	37·4	1·68	53·62	18·96	40·00	13·54	25·2	11·52	11·96	9·17	0·78
SEM	2·2	0·02	2·16	0·52	1·73	1·17	1·8	1·05	0·61	0·45	0·04
		*		***				***	***	***	***
'Small-eaters'											
jl 156	32	1·69	60·93	21·33	46·49	14·44	23·7	8·40	4·77	13·07	2·74
eh 104	36	1·73	84·65	28·28	49·77	34·88	41·2	11·15	5·35	14·59	2·73
wg 235	30	1·64	55·95	20·80	36·12	19·83	35·4	5·62	4·69	12·23	2·60
cg 298	41	1·54	50·48	21·29	40·58	9·90	19·6	3·93	4·24	10·45	2·46
cd 301	21	1·60	50·50	19·73	37·57	12·93	25·6	4·07	4·78	10·16	2·13
sj 054	26	1·58	61·83	24·77	42·23	19·60	31·7	5·94	5·48	11·60	2·12
pc 022	35	1·66	60·23	21·86	45·53	14·70	24·4	5·88	5·53	11·60	2·10
fg 232	47	1·55	63·55	26·45	40·48	23·07	36·3	4·95	6·07	12·45	2·05
mr 245	41	1·59	59·65	23·59	40·87	18·78	31·5	3·50	6·68	13·59	2·03
Mean	34·3	1·62	60·86	23·12	42·18	18·68	29·9	5·94	5·29	12·19	2·33
SEM	2·7	0·02	3·36	0·96	1·46	2·44	2·4	0·81	0·25	0·48	0·10

BMI, body mass index (weight (kg)/height (m)^2); Q, questionnaire.
Mean values were significantly different from those for 'small-eaters': * $P < 0·05$, *** $P < 0·001$ (Student's t test).
† Diary results.

Table 2. *Indirect calorimetric measurements in groups of nine, non-smoking 'large-eating' (LE) and 'small-eating' (SE) female subjects*†

(Mean values with their standard errors)

		RMR												Walking					
		Day 1		Day 2		Day 3		Day 4		Sitting		Standing		2·4 km/h		3·9 km/h		5·4 km/h	
Variable	Group	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Oxygen consumption (ml/kg FFM per min)	LE	4·67*	0·19	4·75*	0·17	4·71*	0·23	4·62*	0·18	5·05*	0·19	5·32***	0·23	11·45	0·38	13·35	0·50	18·46	0·63
	SE	4·12	0·08	4·19	0·09	4·06	0·11	4·12	0·08	4·46	0·09	4·49	0·07	10·65	0·41	13·04	0·48	18·31	0·72
Respiratory quotient	LE	0·79	0·01	0·80	0·01	0·79	0·01	0·80	0·01	0·79	0·01	0·80	0·01	0·80	0·01	0·80	0·01	0·82*	0·01
	SE	0·82	0·02	0·83	0·03	0·84	0·03	0·82	0·02	0·82	0·01	0·84	0·02	0·87	0·03	0·85	0·02	0·87	0·02
Energy expenditure (J/kg FFM per min)	LE	93·8*	3·8	95·4*	3·7	94·6	5·0	92·9*	3·8	101*	3·9	107**	4·5	231	9	269	10	373	13
	SE	83·3	1·7	85·0	2·5	82·5	2·5	82·9	1·7	90·0	2·1	91·3	1·7	218	8	265	10	375	15
Oral temperature (°)	LE	36·3*	0·1	36·1	0·2	36·2	0·1	36·0	0·1	36·2	0·1	36·1*	0·1	35·5*	0·2	35·7*	0·2	35·6*	0·2
	SE	35·8	0·2	35·9	0·1	35·8	0·2	35·8	0·1	35·9	0·2	35·7	0·2	34·8	0·2	34·9	0·2	34·9	0·2

RMR, Resting metabolic rate; FFM, Fat-free mass.
Mean values were significantly different from those for 'small-eater': * $P < 0·05$, ** $P < 0·01$, *** $P < 0·001$ (Student's t test).
† For details of subjects, see p. 32 and Table 1.

Table 3. *Rates of whole-body protein turnover and muscle protein breakdown in groups of nine, non-smoking 'large-eating' and 'small-eating' female subjects*

(Mean values with their standard errors)

Variable	'Large-eaters'		'Small-eaters'	
	Mean	SE	Mean	SE
Whole-body protein turnover (g/kg FFM per 9 h)	1·43	0·12	1·21	0·14
Muscle protein breakdown (%/d)	0·87	0·03	0·89	0·03

FFM, fat-free mass.
* For details of subjects, see p. 32 and Table 1.

Table 4. *Blood variables (mmol/l) in groups of eight, non-smoking 'large-eating' and 'small-eating' female subjects*

(Mean values with their standard errors)

Variable	'Large-eaters'		'Small-eaters'	
Sodium	140·9	0·6	141·1	0·5
Potassium	4·23	0·11	4·36	0·15
Chloride	108·0	1·0	107·5	0·8
Bicarbonate	25·9*	0·3	26·8	0·2
Urea	4·90	0·32	4·08	0·38
Creatinine	0·071	0·003	0·073	0·004
Total cholesterol	5·48	0·48	5·20	0·33
HDL-cholesterol	1·66	0·12	1·49	0·13
Triacylglycerols	1·53	0·67	1·10	0·20
Free fatty acids	0·300	0·071	0·211	0·033
Glycerol	0·048	0·010	0·034	0·009
Acetoacetate	0·028*	0·006	0·013	0·003
Hydroxybutyrate	0·052	0·019	0·015	0·005
Glucose	4·35	0·10	4·59	0·20
Lactate	1·36	0·27	1·67	0·15
Pyruvate	0·058	0·008	0·068	0·006
Insulin (pmol/l)	29·6*	3·0	52·2	9·3
Glucagon (pmol/l)	41·6	3·1	36·9	7·7
Oestradiol (pmol/l)	314	107	174	43
Testosterone (nmol/l)	1·19	0·12	1·22	0·14
Total thyroxine (nmol/l)	112·8	9·8	109·0	8·4
Total triiodothyronine (nmol/l)	1·96	0·17	1·70	0·14
IGF-1 (nmol/l)	25·7	2·6	27·7	5·3
Zinc (μmol/l)	13·1	1·0	13·7	0·6
Copper (μmol/l)	22·0	1·9	20·7	1·3

HDL, high-density lipoprotein; IGF-1, Insulin-like growth factor-1.
Mean values were significantly different from those for 'small-eaters': * $P < 0·05$ (Student's t test).

eaters' (E:I > 2·0) a large negative energy balance (−6·9 MJ/d; Table 1). While these subjects considered that their daily energy intakes and daily energy expenditures were 'normal' for the 5 d during which they maintained food and activity diaries (see p. 32), such large discrepancies in energy balance are obviously not sustainable. Possible explanations for the disparity between energy intake and energy expenditure in 'large-

eaters' and 'small-eaters' have been presented previously (Rose & Williams, 1961; McNeil *et al.* 1989; see below).

Other workers have addressed the problem of apparent differences in the efficiency of energy use in man (Widdowson, 1947; Warwick, 1978; Garrow, 1985). Warwick (1978) measured the energy expended by one 'large-eating' (9·9 MJ/d) and one 'small-eating' (6·5 MJ/d) woman of similar age, weight and FFM. She found that the energy expended at rest and during light activities (sitting and standing) could differ by approximately 40% over 24 h in a whole-body calorimeter. Even this marked variation in metabolic rate could explain just approximately 75% of the apparent difference in energy intake between these two volunteers and some of the variation in energy intake must be attributed to error in the estimate of habitual energy intake (Garrow, 1985). This view is shared by Rose & Williams (1961) and by McNeill *et al.* (1989) who found no differences in energy expenditure between their 'large-eaters' and 'small-eaters' despite a 2-fold difference in reported energy intake.

Our findings comparing the estimates of protein intake obtained from both the weighed food diary and the urinary N excretion also supports the view that substantial error exists in the estimation of energy intake in such groups of people. However, our use of the diary information was directed towards the identification of potentially 'efficient' or potentially 'inefficient' subjects, or both, to form study groups for the subsequent objective metabolic measurements.

The present investigation also indicated large apparent differences in daily energy expenditure, as determined from activity diaries, between the two experimental groups (Table 1). This result is at variance with previous studies on energy metabolism in 'large-' and 'small-eaters' (Rose & Williams, 1961; McNeil *et al.* 1989). Furthermore, the 'small-eaters' appeared to expend more energy per d than the 'large-eaters' rather than less as may be expected from the energy intake data (Table 1). However, these results, obtained using self-reporting activity diaries, must reflect both the precision of each volunteer's recording and the accuracy of the energy expenditure values used for the different activities. In fact, our direct measurements of energy expenditure by our subjects during the performance of standard daily activities (Table 2) indicate that use of the published tables (Passmore & Durnin, 1955; McArdle *et al.* 1986) would overestimate energy expenditure and, importantly, to a relatively greater extent in 'small-eaters'. In order to obtain more realistic estimates of total daily energy expenditure, rates of energy expenditure for each subject should be measured during the performance of usual daily activities in the usual environment for those activities. These rates could then be used in conjunction with activity diaries to calculate daily energy expenditures. Alternatively, average daily energy expenditures could be determined using doubly-labelled water (Schoeller & Van Santen, 1982; James *et al.* 1988). This approach is now recognized as giving the most accurate measure of energy expenditure in free-living subjects. Notwithstanding the problems associated with assessing total daily energy expenditure in humans, our purpose was to use the data only as part of a selection index (which included apparent energy intake) to obtain the two disparate groups of people referred to as 'large-eaters' and 'small-eaters' (Rose & Williams, 1961) for studies on energy metabolism.

Our findings (Table 2) demonstrate substantial differences in the rates of energy expenditure (per kg FFM), under controlled conditions, between the 'large-eating' and 'small-eating' women but these differences appear to be confined to resting, sitting and standing activities (Table 2). However, unlike the previous studies with male 'large-' and 'small-eaters' (Rose & Williams, 1961: McNeil *et al.* 1989) our women were not matched for BMI. Weight has a bearing on energy expended during exercise and if the values obtained during the walking exercises are expressed as an increment above RMR per kg body-weight then the 'large-eaters' use an average of 6·3 J/kg per min more energy to

perform this task. The average 'small-eater' would, therefore, expend about 210 KJ less than a 'large-eater' in 1 h of walking. The question which now needs to be addressed is whether these differing rates of energy expenditure arise from higher than normal rates of metabolism in the 'large-eaters' or lower than normal rates of metabolism in the 'small-eaters' (see p. 41).

Resting energy expenditure

Two of our 'large eaters' had resting rates of O_2 consumption greater than 5·3 ml/kg FFM per min (subject bk 215 5·30 (SE 0·5), subject gg 135 5·57 (SE 0·16)) and three of the 'small-eaters' had rates less than 4·0 ml/kg FFM per min (mr 245 3·95 (SE 0·13), wg 235 3·91 (SE 0·08), cg 298 3·88 (SE 0·09)). These findings suggest that resting rates of O_2 consumption, even when expressed per kg FFM, can vary by up to 45% between normal weight women in the free-living population. This confirms and extends the findings of Warwick (1978).

There have been a number of comparative investigations on energy expenditure in normal-weight and obese women (Hoffman *et al.* 1979; Ravussin *et al.* 1982; Bessard *et al.* 1983; Blaza & Garrow, 1983; Felig *et al.* 1983; Schutz *et al.* 1984; Owen *et al.* 1986; Blair & Buskirk, 1987; for mini-review, see De Boer *et al.* 1987). These studies showed that resting $\dot{V}_{O_2}$ averaged 4·16 (SE 0·07; range 3·64–4·48) and 4·38 (SE 0·08; range 3·81–4·89) ml O_2/kg FFM per min in normal-weight and obese women respectively. Comparison of these results with those obtained with 'large-' and 'small-eating' women (Garrow, 1985; Table 2) suggests that resting $\dot{V}_{O_2}$ is indeed normal in 'small-eating' women (4·13 *v.* 4·16) but markedly higher in the 'large-eaters' (4·72 *v.* 4·16 ml O_2/kg FFM per min). These findings do not agree with those of Geissler *et al.* (1987) and Shah *et al.* (1988) who found that sixteen post-obese women had metabolic rates approximately 15% lower than their matched, lean controls at all levels of energy expenditure. The post-obese women certainly appeared to restrict their energy intake greatly (Shah *et al.* 1988) and, in addition, their physical characteristics matched those of our group of 'small-eaters'. It is difficult to explain why energy expenditure appears to be reduced in the post-obese (Geissler *et al.* 1987) but not in 'small-eating' females (see p. 35; Table 2). One possible explanation for these contradictory findings lies in the different experimental methodologies. The investigation on energy expenditure in post-obese women and their matched controls was performed over three separate 24 h sessions in a study/bedroom respirometer with each volunteer maintaining a reasonably normal life-style (Geissler *et al.* 1987). Care was taken to try to ensure customary energy, nicotine and caffeine intakes. This protocol is in marked contrast to that used for the present investigation (see pp. 32–33).

Thermic effect of food

The 'small-eating' women showed a 27% (NS) greater average TEF than the 'large-eating' women (Fig. 1). These findings support the results from our initial study with matched 'large-' and 'small-eating' males which demonstrated a 21% (NS) higher TEF in 'small-eating' men (D. Clark, F. Tomas and R. T. Withers, unpublished results). These results, although not attaining statistical significance, are contrary to expectations as other studies have demonstrated that post-prandial energy expenditure is increased during overeating (Miller *et al.* 1967; Rothwell *et al.* 1982) and reduced in subjects who are in negative energy balance (Dore *et al.* 1982; Rothwell *et al.* 1982), circumstances which to some extent could be extended to the groups in our study. A lack of proportionality between the size of the test meal and both the resting energy expenditure and apparent usual daily energy intake (Table 1) might explain some of the observed increase in postprandial thermogenesis in the 'small-eaters'. Nonetheless, it is obvious that the apparent differences in energy balance between the groups cannot be ascribed to differences in TEF.

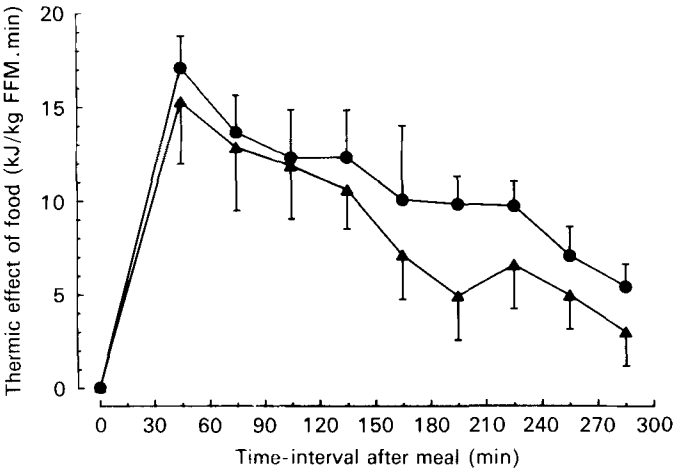

Fig. 1. Increments in energy expenditure in 'large-eating' (▲) and 'small-eating' (●) women after the consumption of a standardized liquid meal. Values are group means with their standard errors represented by vertical bars. FFM, fat-free mass. For details of subjects, see p. 32 and Table 1.

'*Large-eaters*' v. '*small-eaters*'

The two groups of subjects available for the present study could not be matched and had significantly different weight:height^2 ratios. Thus, the observed variations in energy expenditure (Table 2), although expressed per kg FFM, might reflect this dissimilarity rather than the differences in apparent daily energy requirements. However, studies which have compared rates of energy expenditure in lean (BMI 17–20), normal-weight (BMI 20–25) and obese females (BMI > 30) have shown that resting O_2 consumption (ml O_2/kg FFM per min) is either the same for the three groups (Owen *et al.* 1986) or perhaps depressed in lean volunteers (Ravussin *et al.* 1982; Segal & Gutin, 1983). These reported results support the view that the differences observed by us (Table 2) are indicative of altered energy metabolism in the 'large-eating' females.

It is possible, in theory at least, to explain how 'large-eaters' might be able to maintain an apparent positive energy balance (Table 1) yet not gain weight. It is now accepted that futile cycles such as the glucose:glucose-6-phosphate cycle in hepatic tissue (Clark *et al.* 1975; Katz & Rognstad, 1976) and the fructose-6-phosphate:fructose-1,6-diphosphate cycle in liver (Clark *et al.* 1974; Clark *et al.* 1975) and muscle (Newsholme, 1980), in addition to other potential energy-dissipating reactions such as protein, lipid and glycogen turnover, are capable of converting food energy to heat (Katz & Rognstad, 1976; Newsholme, 1980). While this assists in homeothermy, most of this energy is lost to the body rather than being used in anabolic metabolism. It is possible that 'large-eaters' or metabolically 'inefficient' people may have more active futile cycles than the metabolically 'efficient'. This would be reflected in higher rates of O_2 consumption at rest or during different activities. Although this was observed in the present investigation (Table 2), we cannot directly attribute the higher $\dot{V}_{O_2}$ to increased futile cycle activity as the only energy-dissipating reaction we measured, protein turnover in muscle and whole body, was not significantly different between the two experimental groups. On the other hand, the higher oral temperatures (0·3–0·5°) in the 'large-eaters' (Table 2) support the thesis of increased thermogenesis in these volunteers, but a similar difference in oral temperature was demonstrated between male 'large-' and 'small-eaters' (D. Clark, F. Tomas and R. T. Withers, unpublished results) when there was no disparity between rates of O_2

consumption. Until body (core) temperature measurements are made the actual significance of the higher oral temperatures cannot adequately be evaluated.

Comparative analyses of blood samples from the two experimental groups (Table 4) revealed few differences between the groups. Immunoreactive insulin was almost 2-fold higher in plasma from the 12 h post-absorptive 'small-eaters'. The other major difference was in the concentration of acetoacetate which was more than 2-fold higher in plasma from the 'large-eaters'. As insulin depresses the release of fatty acids from adipose tissue (Butcher *et al.* 1972; Fritz, 1972), the lower concentration of acetoacetate (and other lipids and lipid metabolites) in the plasma from the 'small-eaters' (Table 4) probably results from the higher concentration of this anabolic hormone. The insulin levels in turn probably reflect the 20% (NS) higher fat content of the 'small-eaters' (Segal *et al.* 1989) and an associated degree of insulin resistance.

Conclusions

The present investigation is the first study to show appreciable differences in metabolic rate between 'small-eating' and 'large-eating' subjects. Previously published research (Rose & Williams, 1961; McNeil *et al.* 1989) showed no or only minor differences in rates of energy expenditure between groups of male volunteers. In contrast, the present results, which demonstrate that rates of energy expenditure at rest and during light daily activities are substantially elevated in 'large-eating' women of stable body-weight, provide the first substantial evidence that there may be intrinsic differences in energy metabolism between free-living, normal-weight, 'large-' and 'small-eating' females.

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