

## Intra-individual variation in resting metabolic rate during the menstrual cycle

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Little information exists on the extent of day-to-day intra-individual variation in resting metabolic rate (RMR) in women. The present study has investigated the intra-individual variation in RMR of women during the menstrual cycle. Nineteen women (naturally cycling non-pill users) were recruited to the study. Anthropometric and RMR measurements were taken at least three times per week for the duration of one complete menstrual cycle; measurements were taken for a second, consecutive cycle in eight of the nineteen subjects. RMR was measured by indirect calorimetry using a ventilated hood system under standardized conditions. The measurements made throughout each complete menstrual cycle were averaged and the levels of inter- and intra-individual variation in RMR were assessed by determining the CV (%). Mean RMR of the group was 5686 (SD 674) kJ/d; inter-individual variation in RMR was 11.8%. There were wide differences in the intra-individual variation in RMR of women (CV range 1.7–10.4%). The CV in ten subjects was small (2–4%), while the CV in nine women was high (5–10%), indicating a significant variation in RMR during the menstrual cycle in certain subjects. Using statistical models, it has been shown that there was a significant effect on RMR due to a subject-specific level of variability; this was the case even when accounting for a possible training effect. In conclusion, the findings from our present study show that RMR cannot be assumed to be 'stable' in all women. The implications of intra-individual variation in RMR and its impact on energy balance needs further research.

### Resting metabolic rate: Intra-individual variation: Menstrual cycle

Throughout most of human history, weight gain and fat storage have been viewed as signs of health and prosperity (Bray, 1997). Today, obesity poses an increasing threat to the health of the nation. In the UK alone, >50% of the adult population are classified as overweight or obese (Erens & Primatesta, 1999). Obesity is defined as an excess accumulation of body fat. This condition can only arise if energy intake is greater than requirements, energy expenditure lower, or due to a combination of these two factors. Modest fluctuations in daily energy intake and expenditure could lead to a large imbalance in energy over time, leading to obesity.

Women have a greater degree of adiposity than men. This sexual dimorphism appears to be universal (James & Ralph, 1999). However, there is currently no widely accepted explanation for women's susceptibility to gain more body fat than men.

The Food and Agriculture Organization/World Health Organization/United Nations University (1985) report on energy and protein requirements recommended the use of energy expenditure rather than energy intake as the basis for determining energy requirements in human subjects. The largest component of total energy expenditure is RMR.

Previous research has indicated that the RMR of an individual is markedly stable over time (Shetty & Soares, 1988; Henry *et al.* 1989). Indeed, the biological 'stability' of RMR underpinned its use to estimate energy requirements. However, these observations have been largely made in men, and little information exists on the intra-individual variation in RMR in women.

Previous studies investigating RMR in women have had conflicting results. Some studies suggest that RMR changes with the menstrual cycle (Wakeham, 1923; Hitchcock & Wardwell, 1929; Solomon *et al.* 1982; Meijer *et al.*

**Abbreviation:** RMR, resting metabolic rate.

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1992), whereas other studies have shown no demonstrable difference (Blunt & Dye, 1921; Wiltshire, 1921; Howe *et al.* 1993; Weststrate, 1993; Piers *et al.* 1995). More recently, it has been suggested that the menstrual cycle might influence RMR in some individuals (Curtis *et al.* 1996a). Many of the previous studies were performed on a limited number of female subjects. In light of this, the aim of our present study was to investigate the intra-individual variation in RMR in a larger number ( $n = 19$ ) of women (naturally cycling non-pill users) during the menstrual cycle. In particular, the question of interest was to assess whether there was a subject-specific component of variance, i.e. whether the variation of RMR during the menstrual cycle for each subject was different.

## Methods

### Subjects

Nineteen women were recruited to the study. Subjects were staff and students (undergraduate and postgraduate) from Oxford Brookes University and were healthy, premenopausal women. None of the subjects were using oral contraceptive pills. Ethical approval for the study was obtained from the Ethics Committee at Oxford Brookes University and written informed consent was obtained from all subjects before participation in the study.

### Anthropometric measurements

All anthropometric measurements were made in the fasting state. Height was recorded to the nearest centimetre using a stadiometer (Seca Ltd, Birmingham, UK), with subjects standing erect and without shoes. Body weight was recorded to the nearest 0.1 kg using professional dial scales (Healthometer, Bridgeview, IL, USA), with subjects wearing light clothing and no shoes. BMI was calculated using the standard formula: weight (kg)/height (m)<sup>2</sup>.

Waist circumference was measured midway between the lowest rib margin and iliac crest (Gibson, 1991) and recorded to the nearest 0.1 cm. Total body fat was estimated from the sum of four skinfold thickness measurements taken at the triceps, biceps, subscapular and suprailiac sites (with Holtain Tanner Whitehouse skinfold callipers; Holtain Ltd, Crosswell, Wales, UK) using the Durnin & Womersley (1974) equations. The physical characteristics of the subjects are summarized in Table 1.

**Table 1.** Physical characteristics of the nineteen subjects (Mean values, standard deviations and ranges)

	Mean	SD	Range
Age (years)	23.1	5.0	19–35
Height (m)	1.65	0.06	1.55–1.75
Body weight (kg)	69.1	15.7	51.5–104.2
BMI (kg/m <sup>2</sup> )	25.4	6.1	19.1–40.2
WC (cm)	76.5	9.8	63.9–94.0
Fat mass (% body weight)	29.7	5.8	20.7–39.3
Lean body mass (kg)	47.8	7.4	38.0–65.1

WC, waist circumference.

### Resting metabolic rate measurement

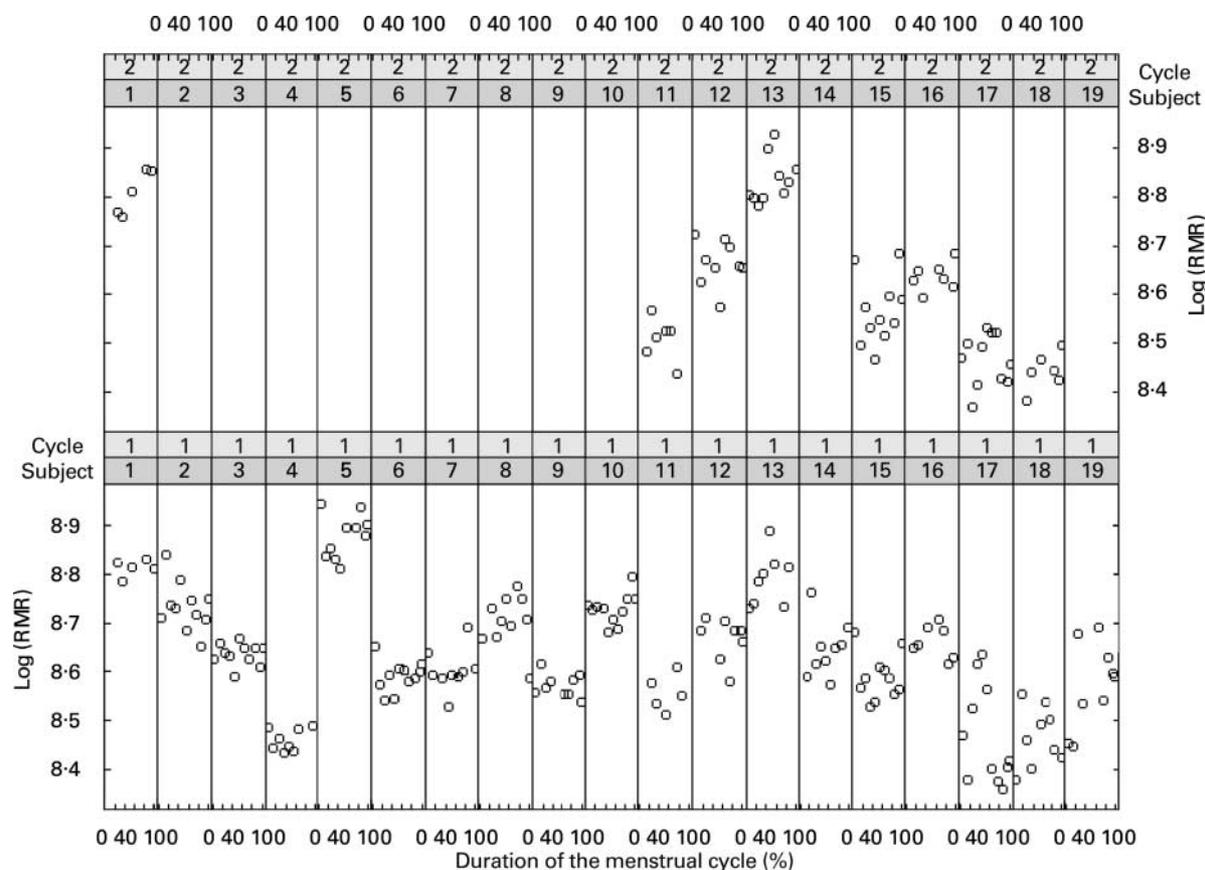
RMR was measured by indirect calorimetry using a ventilated hood system (Deltatrac, Datex-Ohmeda Instrumentarium Corp., Helsinki, Finland). The calorimeter was calibrated with a reference gas mixture (O<sub>2</sub>–CO<sub>2</sub>, 95:5, v/v) before each measurement session. Alcohol checks were performed every 3–6 months. All measurements were carried out in standardized conditions: early in the morning, with the subject at complete rest in a thermoneutral environment (24–26°C) and at least 12 h after the last meal. Subjects were asked to lie completely still during the measurements. After 10 min to allow for stabilization and for subjects to acclimatize to the canopy and instrument noise, respiratory gas exchange data were collected for 20 min and the average RMR calculated.

Subjects notified the investigator (H. J. L.) at the start of the menses; this was defined as day 0 of the menstrual cycle. Menstrual cycle phases were determined via self-reports of menstruation and cycle length. All anthropometric and RMR measurements were taken at least three times per week for the duration of one complete menstrual cycle in all subjects. In addition, measurements were taken for a second, consecutive menstrual cycle in eight of the nineteen subjects. As the length of the menstrual cycle varied between subjects, each menstrual cycle was normalized and expressed as a percentage of 100. The first day of the menstrual cycle was marked as 0%, 100% represented the day before the beginning of the next menses and ovulation roughly corresponded to 50% of the cycle. This allowed comparisons to be made between subjects. Technical error of measurement and coefficient of reliability ( $R$ ) were determined using formulae given by Ulijaszek & Kerr (1999). Measurement error values for body weight and RMR were 0.4 kg and 197 kJ respectively and 1.0 and 0.91 respectively ( $R$ ).

### Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 10.0.5, 1999; SPSS Inc., Chicago, IL, USA). Results are presented as mean values and standard deviations. Before statistical analysis, the normality of the data was tested using the Shapiro–Wilks statistic. When data were not normally distributed (BMI; body weight and lean body mass in the second menstrual cycle), a logarithmic transformation was applied to satisfy assumptions of normality; data were transformed back for presentation in tables and figures. Levels of inter- and intra-individual variation of body weight and RMR were assessed by determining the CV (%). Paired  $t$  tests were used to determine differences in mean body weight and RMR between menstrual cycles 1 and 2. Statistical significance was set at  $P < 0.05$ .

RMR data were transformed to log scale to remove the dependence of the variation on mean value (Fig. 1). Random-effects models (Pinheiro & Bates, 2000) with different random effects and different models of between- and within-subject variation were fitted to the data with the statistical package R (The R Project for Statistical Computing, 2002) using the nlme package. Each model



**Fig. 1.** Plot of log (resting metabolic rate (RMR)) through time. Each menstrual cycle is expressed as a percentage of 100. For details of subjects and procedures, see Table 1 and p. 812.

was fitted using the method of restricted maximum likelihood (ReML). The models were compared using likelihood ratio tests to determine the significant model components. The models fitted were: model 1 (a random effect for subject); model 2 (model 1+a random effect for session); model 3 (model 1+an exponential model of temporal correlation within each menstrual cycle); model 4 (model 3+subject-specific variance parameters); model 5 (model 4+a term specifying exponential decay of the variance through time); and model 6 (model 3+a term specifying exponential decay of the variance through time). Comparing models 1 and 2, the session random effect did not significantly improve the model fit ( $P=0.8611$ ) and so this component was omitted from subsequent models.

### Results

Mean menstrual cycle length was 30 (SD 4) (range 24–41) d. There were no significant differences in body weight for any subject during the duration of the study. Intra-individual variation in body weight ranged from 0.3 to 1.9% (Table 2).

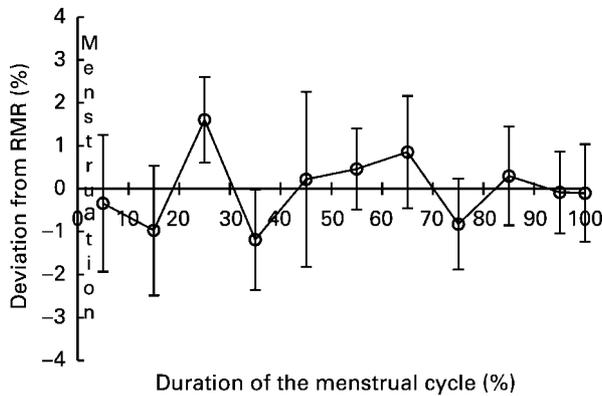
Mean RMR was 5686 (SD 674) kJ (1359 (SD 325) kcal)/d. Expressed per unit body weight, mean RMR was 84 (SD 12) kJ/kg per d. Inter-individual CV for RMR was 11.8%. Fig. 2 shows the variation in RMR for all subjects. Mean intra-individual variation in RMR expressed as CV was 4.6 (SD 2.2) (range 1.7–10.4)%. The intra-individual

variations in RMR and RMR expressed per unit body weight were similar ( $P=0.646$ ; Table 3). There was a high level of intra-individual variation in RMR during the menstrual cycle. The CV in ten subjects was at a level similar

**Table 2.** Intra-individual variation in body weight\* (Mean values, standard deviations and ranges)

Subject	Body weight (kg)			
	Mean	SD	Range	CV (%)
1	104.2	0.3	104.0–104.5	0.3
2	79.7	0.3	79.3–80.4	0.4
3	69.2	0.3	68.4–69.7	0.5
4	52.0	0.3	51.6–52.4	0.6
5	90.1	0.6	89.0–90.5	0.6
6	53.5	0.4	53.0–54.2	0.7
7	51.5	0.4	51.0–52.0	0.7
8	73.1	0.5	72.2–74.0	0.7
9	72.2	0.6	71.3–73.1	0.8
10	88.7	0.7	87.6–89.7	0.8
11	56.3	0.4	56.0–57.0	0.8
12	67.9	0.5	67.2–68.5	0.8
13	92.7	0.7	91.8–94.0	0.8
14	64.1	0.5	63.5–65.0	0.8
15	56.9	0.6	56.0–58.0	1.0
16	55.3	0.6	54.5–56.3	1.2
17	51.5	0.7	50.5–52.5	1.3
18	66.9	1.3	65.5–68.5	1.9
19	67.8	1.3	66.0–69.5	1.9

\* For details of subjects, see Table 1.



**Fig. 2.** Variation in resting metabolic rate (RMR) during the menstrual cycle. Each menstrual cycle is expressed as a percentage of 100 and the average variation at intervals of 10% determined. Ovulation roughly corresponds to 50%. For details of subjects and procedures, see Table 1 and p. 812. Values are the average deviation from the mean for nineteen subjects with their standard errors represented by vertical bars.

to that observed in men (2–4%) (Henry *et al.* 1989). The remaining subjects ( $n = 9$ ) had a much greater variation in their RMR (CV 5–10%). This indicates that there may be a significant variation in RMR during the menstrual cycle in some subjects.

Variation in RMR of representative subjects (two with a low CV (<4%) and two with a high CV (>5%)) is illustrated in Fig. 3. This figure illustrates the point that there is considerable biological variation in RMR during the menstrual cycle.

To assess whether there was a subject-specific component of variance, random-effects models were fitted to the data. The addition of a temporal correlation within

each menstrual cycle (model 2 compared with model 3) significantly improved the model fit ( $P=0.0025$ ). Fig. 4 shows the subject residuals from the model 3 fit and indicates that there may be a subject-specific level of variation. Comparing models 3 and 4, the addition of a subject-specific variance significantly improved the model fit ( $P=0.0001$ ). Comparing models 4 and 5, the addition of a term allowing a decay in variation through time did not significantly improve the fit ( $P=0.1505$ ). Finally, the subject-specific variance parameters were still significant in the presence of a possible decrease in variation through time (model 5 compared with model 6). This analysis suggests that within-cycle temporal correlation and subject-specific variation were significant factors in models for the data.

Data were collected during two consecutive menstrual cycles in eight subjects. Mean body weight was similar in cycles 1 and 2: 69.0 (SD 19.3) and 68.4 (SD 19.9) kg respectively ( $P=0.228$ ). Mean RMR was 5622 (SD 742) kJ/d and 85 (SD 14) kJ/kg per d in cycle 1 and 5576 (SD 851) kJ/d and 84 (SD 14) kJ/kg per d in cycle 2 ( $P=0.451$  and  $P=0.908$  respectively). Fig. 5 shows the variation in RMR during the menstrual cycles.

There was little difference in intra-individual variation in body weight and RMR between the two menstrual cycles (Table 4). At the group level, mean intra-individual CV in body weight was 1.0 (SD 0.5) % in cycle 1 and 0.9 (SD 0.2) % in cycle 2 ( $P=0.410$ ). Mean intra-individual CV in RMR was 5.0 (SD 2.6) and 4.6 (SD 1.2) % in cycles 1 and 2 respectively ( $P=0.680$ ).

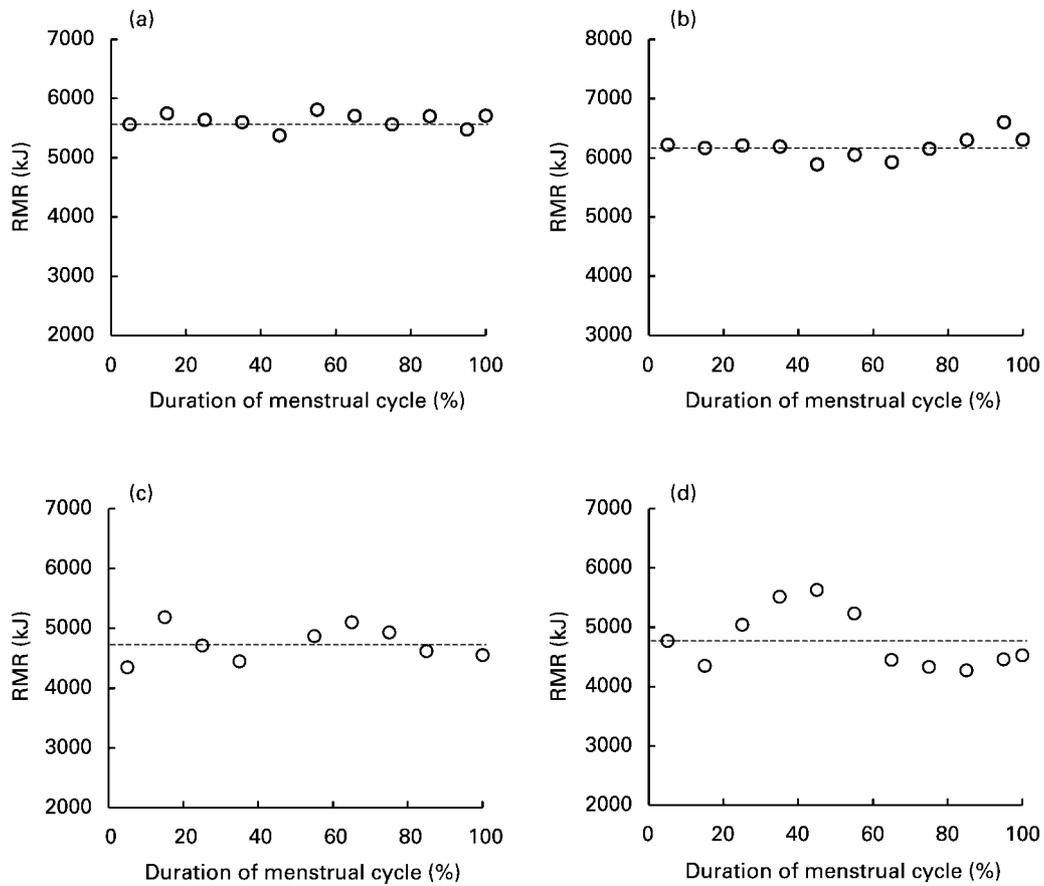
The pattern of RMR during each menstrual cycle of two representative subjects is shown in Fig. 6. This figure illustrates the point that there was no significant difference in the pattern of RMR between the two cycles.

**Table 3.** Intra-individual variation in resting metabolic rate (RMR)\*  
(Mean values, standard deviations and ranges)

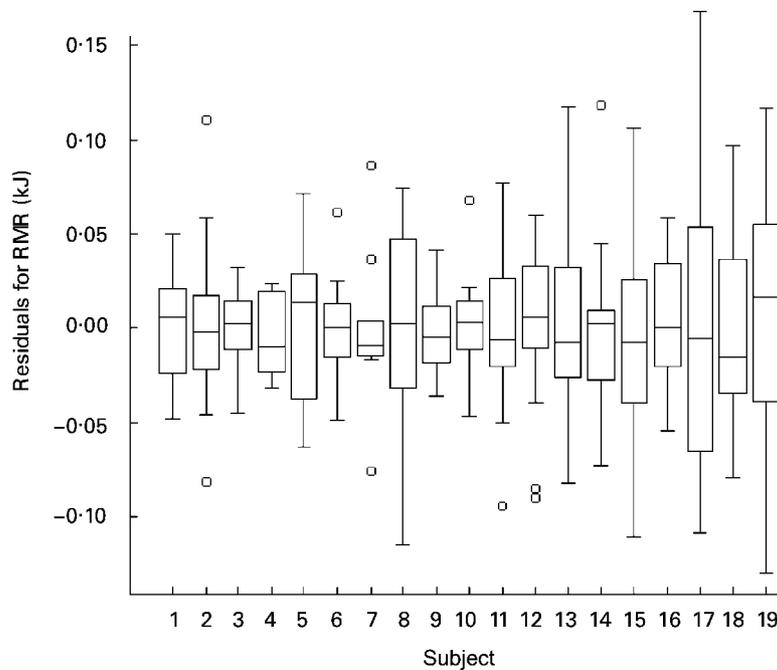
Subject†	RMR (kJ/d)				RMR (kJ/kg per d)			
	Mean	SD	Range	CV (%)	Mean	SD	Range	CV (%)
1	6718	116	6530–6830	1.7	64	1	63–66	1.7
3	5627	127	5377–5810	2.3	81	2	77–83	2.4
4	4720	107	4592–4853	2.3	91	2	89–93	1.9
9	5279	127	5097–5511	2.4	73	2	70–76	2.4
10	6182	194	5889–6600	3.1	70	2	67–74	2.8
6	5381	170	5127–5723	3.2	101	3	95–108	3.4
16	5776	193	5523–6046	3.3	105	3	101–109	3.1
11	5202	195	4977–5479	3.7	92	4	87–98	4.4
12	5807	246	5319–6054	4.2	86	3	79–88	3.7
7	5450	240	5050–5940	4.4	106	5	97–116	4.8
5	7185	323	6709–7670	4.5	80	4	75–85	4.4
15	5374	261	5050–5895	4.9	95	5	87–105	5.4
2	6210	322	5708–6914	5.2	78	4	71–87	5.4
8	6030	318	5363–6475	5.3	82	5	72–88	5.5
13	6567	362	6186–7243	5.5	71	4	66–78	5.6
14	5687	331	5280–6389	5.8	89	5	83–98	5.4
18	4752	290	4350–5188	6.1	71	4	66–78	5.4
19	5303	463	4650–5949	8.7	79	8	70–92	9.8
17	4781	496	4272–5630	10.4	93	10	82–109	10.5

\* For details of subjects and procedures, see Tables 1 and 2 and p. 812.

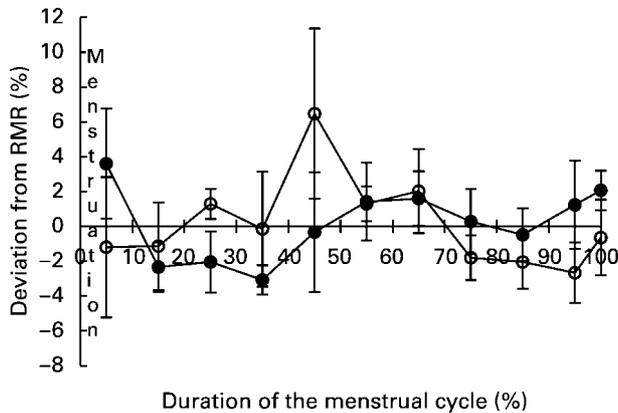
† Subjects listed in ascending order of CV.



**Fig. 3.** Resting metabolic rate (RMR) of representative subjects with a low or high CV (%). (a) Subject 3; (b) subject 10; (c) subject 18; (d) subject 17. - - -, Mean RMR. Each menstrual cycle is expressed as a percentage of 100. The first day of the menstrual cycle is marked as 0% and 100% represents the day before the beginning of the next menstrual period; ovulation roughly corresponds to 50% of the menstrual cycle. For details of subjects and procedures, see Tables 2–3 and p. 812.



**Fig. 4.** Box plots graph representing statistical residuals of resting metabolic rate (RMR) for each subject from the model 3 fit. For details of the model and procedures, see p. 812. Vertical bars above and below the box indicate the 90th and 10th percentiles; (○), outlying values.

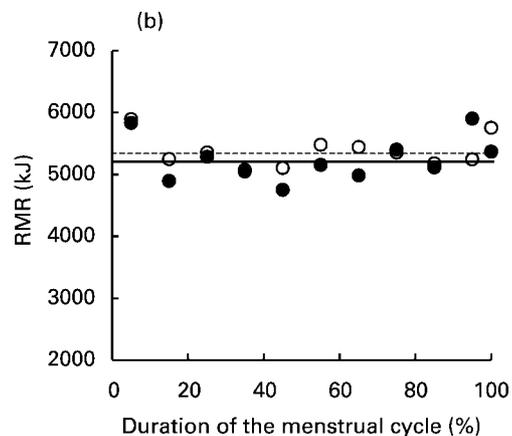
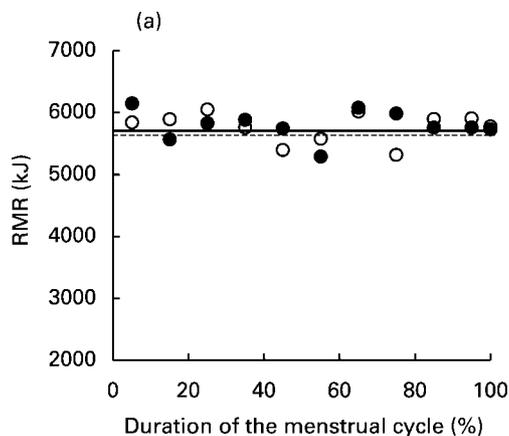


**Fig. 5.** Variation in resting metabolic rate (RMR) during menstrual cycles 1 (○) and 2 (●). Each menstrual cycle is expressed as a percentage of 100 and the average variation at intervals of 10% determined. Ovulation corresponds roughly to 50%. For details of subjects and procedures, see p. 812. Each value represents the average deviation from the mean for eight subjects with their standard errors represented by vertical bars.

**Table 4.** Intra-individual variation (%) in body weight and RMR for menstrual cycles 1 and 2 in eight subjects\* (Coefficients of variation)

Subject	Body weight		RMR	
	Cycle 1	Cycle 2	Cycle 1	Cycle 2
1	0.3	0.5	1.7	4.5
11	0.8	0.8	3.7	4.3
12	0.8	1.1	4.2	4.1
13	0.8	0.7	5.5	4.9
15	1.0	1.2	4.9	6.9
16	1.2	1.0	3.3	2.9
17	1.3	0.9	10.4	5.3
18	1.9	0.7	6.1	3.9

\* For details of subjects and procedures, see Tables 1 and 2 and p. 812.



**Fig. 6.** Resting metabolic rate (RMR) of subjects (a) 15 and (b) 17 during menstrual cycles 1 (○; ---, mean RMR) and 2 (●; —, mean RMR). Each menstrual cycle is expressed as a percentage of 100. The first day of the menstrual cycle is marked as 0% and 100% represents the day before the beginning of the next menstrual period; ovulation roughly corresponds to 50% of the menstrual cycle. For details of subjects and procedures, see p. 812.

## Discussion

The present study was an attempt to quantify the inter- and intra-individual variation in RMR during the menstrual cycle in naturally cycling women, and in particular to assess whether there was a subject-specific component of variance. This present study is of importance as RMR underpins the calculation of energy requirements of both individuals and populations; thus, a better understanding of the variability in RMR is essential in predicting energy requirements.

The biphasic pattern of RMR during the menstrual cycle (a fall in RMR with the onset of menstruation and a peak before the next menstrual period) observed in previous studies (Solomon *et al.* 1982; Curtis *et al.* 1996a) was not evident in our present study. However, considerable day-to-day variability of RMR was observed in some women. Some subjects did exhibit minor peaks in RMR during the late luteal phase or slight troughs in RMR during the early follicular phase, although differences in RMR during the follicular and luteal phases of the menstrual cycle were considered too small to be of any significance. Moreover, as ovulation was predicted from cycle length and not assessed biochemically, accurate determination of the luteal phase of the menstrual cycle could not be made.

Previous studies have suggested that the inter-individual variation in RMR in both men and women is at least 8% (Henry *et al.* 1989; Soares *et al.* 1989; Spurr *et al.* 1994). The findings from our present study substantiate this. In addition, our present study demonstrated that there are wide differences in the intra-individual variation in RMR in women and that this was the case even when accounting for a possible training effect. This is similar to findings from previous research (Solomon *et al.* 1982; Spurr *et al.* 1994; Curtis *et al.* 1996a).

In our present study, intra-individual variation in RMR in certain women was similar to that observed in men (Henry *et al.* 1989). However, intra-individual variation in RMR in nine subjects studied was greater, indicating

that there may be a significant variation in the menstrual cycle variation of each subject. For simplicity, two 'metabolic' type of women may be identified: those with low (CV 2–4%) and those with high (CV 5–10%) intra-individual variation in RMR.

It has been suggested that some of the intra-individual variation in RMR may be attributed to training effect or familiarization with the procedure involved in the measurement of RMR (Soares & Shetty, 1986). However, using the statistical models outlined previously, the findings from the present study indicate that there was a significant effect on RMR due to a subject-specific level of variability and this was evident even when the training effect was taken into account.

There are limited results available on between-cycle differences in RMR. Of the studies that have collected RMR data for 2 months or more, results have either been averaged (Solomon *et al.* 1982) or agreement between cycles has been analysed in one particular phase of the menstrual cycle only (Piers *et al.* 1995). Findings from the present study show little difference in intra-individual variation in RMR between the two menstrual cycles and this was observed at the group level.

Subjects in this current study were all naturally cycling non-pill users. It has been suggested that RMR in pill-users is not as variable as the RMR in normally ovulating women (Curtis *et al.* 1996*b*). This change in the variability of RMR may influence energy balance. Thus, due to the extensive use of oral contraceptive pills worldwide, their impact on RMR (and hence energy balance) needs to be investigated.

In conclusion, the findings from our present study show that RMR cannot be assumed to be 'stable' in all women. The implications of intra-individual variation in RMR during the menstrual cycle and its impact on energy balance and body weight regulation needs further research. A better understanding of the variation in RMR during the menstrual cycle may provide insights into the ability of certain women to maintain energy balance more effectively.

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