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Intraindividual Variation in the Basal Metabolic Rate of Women: Effect of the Menstrual Cycle

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ABSTRACT The validity of using the basal metabolic rate (BMR) to calculate an individual's energy requirements is based upon the assumption that the intraindividual variation in BMR is small. Early studies (pre-1940) on BMR in women had shown that the menstrual cycle may have a profound effect, contributing to high levels of intraindividual variation. To investigate this issue further, and to explore whether BMR is indeed a biological constant in women, sequential measurements of BMR were made in women over one menstrual cycle. Two independent studies were undertaken in which the BMR of 12 weight-stable women (not taking the contraceptive pill) was measured every day (excluding weekends) for a period of 5 weeks. The six women participating in the first study were measured using a Douglas bag, while the six subjects in the second study were measured with a Deltatrac (Datex, Helsinki). Nine of the 12 subjects demonstrated a peak in BMR during the late luteal phase of the menstrual cycle, while 8 of the 12 subjects exhibited a fall in BMR after the onset of menstruation. Group analysis of the results indicated that the BMR during the early follicular phase was significantly lower than the BMR during the late luteal phase (Wilcoxon's signed rank test: $P < 0.01$). The level of intraindividual variation was assessed by calculating the coefficient of variation (CV) for the measurement period. The CV in six of the women exhibited a level of variation comparable to men (2–4%). However, intraindividual variation in the BMR of the other six women was considerably higher (up to 12%). In these six women, therefore, BMR may not be considered a biological constant. All available data on sequential measurements of BMR in fertile women were collated from the literature for the first time, and statistically analyzed. BMR during the early follicular phase was found to be significantly lower ($P < 0.05$) than during the late luteal phase. Further work on the biological constancy of BMR in women and the impact of the menstrual cycle on BMR is required. This area is of particular importance given the fact that the energy requirements of both individuals and populations are now calculated using the BMR.

Basal metabolic rate (BMR), defined as the minimal activity of tissue cells under steady-state conditions (Schofield, 1985), constitutes a major proportion (up to 70%) of the total daily energy expenditure (Payne and Waterlow, 1971). The most recent FAO/WHO/UNU (1985) report on energy and protein requirements has recommended the use of energy expenditure rather than energy intake as the basis for determining energy requirements in humans. It is, therefore, of great importance that the BMR of males and females living under a wide range of environmental conditions are accurately assessed. Numerous factors are known to influence BMR in humans, including nutritional sta-

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tus, age, body composition, ethnic background, and gender (Benedict, 1938; Wilson, 1945; Miller and Blyth, 1953; Durnin, 1981; Henry and Rees, 1991; Poehlman, 1993). While an extensive literature exists on many of these factors, one of the least researched is the influence of gender, and in particular, the effect of the menstrual cycle.

Studies undertaken during the 1920s and 1930s suggest that the menstrual cycle may have a dramatic and consistent effect on the BMR (Hafkesbring and Collett, 1924; Benedict and Finn, 1928; Conklin and McClendon, 1930; Rubenstein, 1938). BMR was observed to drop with the onset of menstruation (the early follicular phase of the cycle) and reach a peak before the onset of the next menstrual period (the late luteal phase). Thus, a biphasic pattern in the BMR of fertile women was evident. However, the results of these studies appear to have been largely overlooked by many researchers and very few attempts have been made to further investigate this area.

The validity and use of BMR in calculating an individual's total energy requirements are based on the assumption that intraindividual variation in BMR is small. Indeed, repeated observations of BMR made on male subjects (Wishart, 1927; Benedict, 1935; Soares and Shetty, 1987; Henry et al., 1989) suggest that the coefficient of variation (CV) is approximately 2–4%. While this may be the pattern observed in males, little or no information exists on the intraindividual variation of the BMR in women. In fact, the "biological constancy" of BMR noted in males has been assumed to operate also in females.

This paper examines the impact of the menstrual cycle on the intraindividual variation in the BMR of 12 women. In addition, serial BMR data for women from the literature are collated and analyzed together for the first time. Whether BMR can be considered a biological constant in women is also discussed.

SUBJECTS AND METHODS

Two independent studies were undertaken separated by approximately one year. There were six subjects in each study recruited from the undergraduate and postgraduate population of Oxford Brookes University. Smokers, women with abnormal menstrual cycles, and those on the contraceptive pill were excluded. Table 1 summarizes the physical characteristics of the 12 subjects selected. All BMR measurements were carried out under standard conditions. These are: the subject must be rested, supine, in a fasted condition (usually 12–14 hours after a meal), and in a thermoneutral environment (24–26°C; McLean and Tobin, 1987). BMR was measured by either using a Douglas bag (Study 1) or the Deltatrac (Datex, Helsinki)-a ventilated hood system of indirect calorimetry (Study 2). For every subject in Study 1, two collections of 8 minutes were made with the Douglas bag and the average value taken as the BMR for that morning. All subjects were trained in the use of the Douglas bag, prior to commencement of the first study. BMR was calculated using the Weir formula (Weir, 1949), where the RQ assumed was 0.88.

Calibration of the oxygen analyzer (Servomex 570A, Taylor Instruments and Analytics Ltd.) and dry gas meter (Scientific and Research Instruments Ltd.) used in conjunction with the Douglas bag was carried out daily. The system was also regularly examined for leaks. Gas calibration (using a known gas mixture) and pressure calibration of the Deltatrac were performed daily. BMR measurements were recorded daily for each subject for a period of 5 weeks (excluding weekends). All measurements were completed by mid-morning. Body composition of the subjects was determined with skinfold measurements at the triceps, biceps, subscapular, and superiliac sites using a Holtain skinfold caliper according to the procedures outlined by Durnin and Womersley (1974).

Statistical methods and treatment of data

The mean BMR for the experimental period for each subject was calculated, and the daily deviation from this value as a percentage was graphed. Since the length of the menstrual cycle varied between subjects, each menstrual cycle was normalized and expressed as a total of 100%. 0% marks the first day of the menstrual period, 100% represents the day before the beginning of the next menstrual period, and ovulation roughly corresponds to 50%. This allowed comparisons to be made between subjects and enabled any trends to become visible. In addition, the average variation at intervals of 10% was determined for each subject. Data from all subjects were combined to produce a graph where the mean and the stan-

TABLE 1. Physical characteristics of the subjects in the two studies

Subject	Age (years)	Weight (kg)	Height (cm)	BMI (kg/m^2)	Fat (%)	Lean body mass (kg)
Study 1						
1	20	51	162	19.43	21	40.29
2	21	65.5	175.5	21.27	25	49.13
3	29	56.5	164	21.01	27	41.25
4	20	52	163	19.57	25	39
5	35	45	156	18.49	28	32.4
6	20	54	165	19.83	25	40.5
Mean ± SD	24.2 ± 6.4	54 ± 6.8*	164.3 ± 6.4	19.9 ± 1.04*	25.2 ± 2.4	40.4 ± 5.4
Study 2						
7	21	52	165	19.1	27	37.96
8	22	79	174	26.09	33	52.93
9	23	54	162	20.58	23	41.58
10	23	69	169	24.16	21	54.51
11	21	88	165	32.32	38	54.56
12	21	72	159	28.48	36	46.08
Mean ± SD	21.8 = 1.0	69.0 ± 14.0*	165.7 ± 5.3	25.1 ± 4.94*	29.7 ± 7.0	47.9 ± 7.2
Combined mean ± SD	22.5 ± 4.1	61.5 ± 13.1	165 ± 6.0	22.5 ± 5.5	27.4 ± 5.5	44.2 ± 7.2

Mean values with the same symbol are significantly different (Student's t-test): *($P < 0.05$).

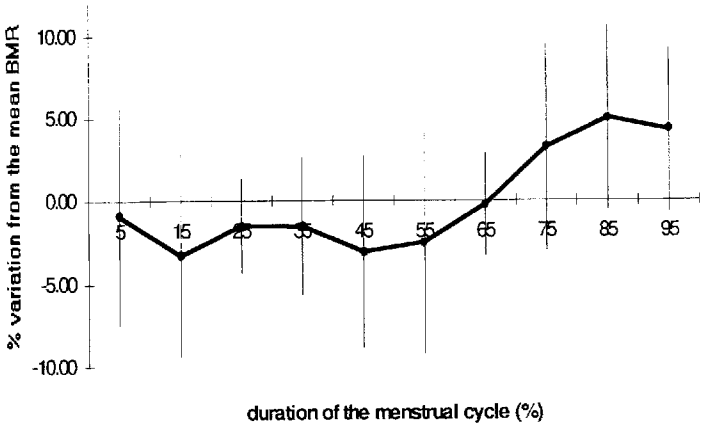

Fig. 1. Variation in BMR during the menstrual cycle—Results of 12 subjects measured in the present study. Each point represents the average deviation for 12 subjects from the mean ±1 standard deviation. BMR during the early follicular phase (taken as 15%) is significantly lower (Wilcoxon's signed rank test: $P < 0.01$) than BMR during the late luteal phase (taken as 85%).

dard deviation were calculated for each interval point (Fig. 1).

To expand the database available on sequential BMR measurements in women, literature values were collated from the 1920s onwards. Data were selected if repeated measurements were made in the same woman for at least one complete menstrual cycle and if the dates of the menstrual periods were provided. Where one woman was measured for more than one menstrual cycle, each month was considered separately. Due to the rigorous demands imposed by the experimental protocol on subjects, few studies sequentially measured BMR in women. By pooling all available data, including the results generated by the present study, 27 cycles from 23 subjects formed the basis of this analysis (Fig. 2).

The physical characteristics of subjects in the two studies were compared using the Student's t-test. However, the significance of

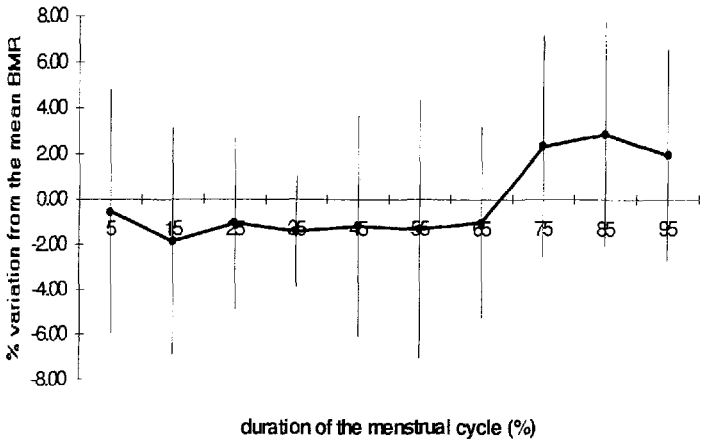

Fig. 2. Variation in BMR during the menstrual cycle—All available data. Each point represents the average deviation of 27 cycles from the mean ±1 standard deviation. BMR during the early follicular phase (taken as 15%) is significantly lower (Wilcoxon's signed rank test: $P < 0.05$) than BMR during the late luteal phase (taken as 85%). BMR during the mid-follicular (25%) and late follicular (35%) is also significantly lower ($P < 0.01$) than during the late luteal phase (85%).

TABLE 2. Intraindividual variation in BMR for subjects in the two studies[1]

Subject	BMR (KJ/d) Mean[2] ± SD	CV%	BMR (KJ/d) Minimum	Maximum
Study 1 (DB)				
1	4,604 ± 477	10.36	4,024	5,867
2	5,747 ± 577.5	10.05	5,001	6,889
3	4,905 ± 384.8	7.84	4,147	5,468
4	5,019 ± 602.1	12.0	3,981	5,668
5	5,233 ± 285.1	5.45	4,736	5,678
6	5,121 ± 290.5	5.67	4,610	5,642
Mean[3] ± SD	5,105 ± 436	8.56 ± 2.68**	4,417 ± 424*	5,869 ± 577
Study 2 (DT)				
7	4,746 ± 141.4	2.98	4,476	4,969
8	6,185 ± 306.3	4.95	5,708	6,711
9	5,367 ± 157.1	2.93	5,093	5,608
10	5,663 ± 179.1	3.16	5,409	6,068
11	6,179 ± 255.6	4.14	5,870	6,832
12	5,286 ± 139.9	2.65	5,074	5,511
Mean[3]	5,571 ± 197	3.45 ± 0.88**	5,272 ± 504*	5,950 ± 727

[1]CV% = coefficient of variation; DB = Douglas bag; DT = Deltatrac. Mean values with the same symbol are significantly different (Student *t*-test): *$P < 0.01$; ***$P < 0.001$.
[2]Mean BMR = mean of 25 measurements per subject.
[3]Mean = mean of BMR in six subjects.

any trends in both sets of data was tested using the Wilcoxon's signed rank test. This was carried out with the Unistat statistical package. Both individual and mean values are also quoted as appropriate.

RESULTS

BMR data for each of the 12 subjects, including the mean, maximum, and minimum BMR, are presented in Table 2. The mean BMR of the six subjects in both studies is similar, despite the notable difference ($P < 0.01$) in the minimum BMR measured. Nine of the 12 subjects exhibited a peak in their BMR during the late luteal phase, while 8 subjects had a trough in their BMR during the early follicular phase.

Figure 1 illustrates the variation in the BMR for all 12 subjects. BMR during the early follicular phase (taken as 15% of the

TABLE 3. Intraindividual variation in BMR of women: analysis of previous data

Investigator	Method	Subject[1]	CV(%)
Conklin and McClendon (1930)	Benedict-Roth apparatus	1	4.50
		2	3.73
		3	3.18
		4	4.39
		5	4.45
		6	3.63
		7	4.39
Benedict and Finn (1928)	Benedict spirometer	1 (A)	3.39
		1 (B)	3.06
Hafkesbring and Collett (1924)	Haldane apparatus	1 (A)	7.75
		1 (B)	7.3
		2 (A)	5.0
		2 (B)	5.0
		2 (C)	3.83

[1]A,B,C = cycle number in the same subject.

menstrual cycle) is significantly ($P < 0.01$) lower than BMR during the late luteal phase (taken as 85% of the cycle). When all the available BMR data (including that of the present study) are pooled, a similar cyclicity in BMR is observed (Fig. 2). The difference between the BMR during the early follicular and late luteal phases is statistically significant ($P < 0.05$), as is the difference between the BMR during the mid-follicular and late luteal phases ($P < 0.01$).

The within-subject variability of the BMR can be calculated by determining the CV. Previous work on the intraindividual variation of the BMR in male subjects reported a variability of 2–4% (Soares and Shetty, 1986; Henry et al., 1989). The CV of BMR data for the 12 subjects in this study are presented in Table 2 and the CV calculated from the results of previous studies in women are presented in Table 3. The level of intraindividual variation in the women in Study 1 is much higher ($P < 0.001$) than that observed of the women of Study 2. The level of within-subject variation of the women in Study 2 is comparable to that observed in men. Examination of the CV from previous results (Table 3) shows a high level of intraindividual variation in one study (Hafkesbring and Collett, 1924), but not in the others (Benedict and Finn, 1928; Conklin and McClendon, 1930).

DISCUSSION

The present study has attempted to quantify and establish the impact of the menstrual cycle on BMR, using daily sequential measurements. The findings confirm the biphasic pattern of BMR reported by the early studies (Snell et al., 1920; Rowe and Eakin, 1921; Hafkesbring and Collett, 1924; Boothby and Sandiford, 1924; Benedict and Finn, 1928; Rogers and Flemming, 1928; Conklin and McClendon, 1930; Sandiford et al., 1931; Wible, 1931; Rubenstein, 1937, 1938; Lockwood and Griffith, 1938; Maxwell and Wakeham, 1945). The present observations are also consistent with previous reports of a drop in BMR with the onset of menstruation and a peak in BMR before the next menstrual period.

Three of the four studies carried out since 1945 have just taken three or four point measurements per cycle rather than daily ones (Govorukhina, 1964; Bisdee et al., 1989a; Das and Jana, 1991). Nevertheless, they too had noted a similar biphasic pattern in BMR during the menstrual cycle. The fourth, and probably the most detailed study carried out since 1945, is that of Solomon et al. (1982). In that study, the BMR of six women was measured regularly over the course of 92 days while in a metabolic ward. The level of variation in the BMR exhibited by these subjects led Solomon and co-workers to question whether BMR could be considered a biological constant in women. More recently, the effect of the menstrual cycle on other components of energy expenditure, such as sleeping metabolic rate (SMR) and 24-hour energy expenditure, has been investigated (Webb, 1986; Bisdee et al., 1989a; Howe et al., 1991; Meijer et al., 1992). These studies have also revealed a biphasic pattern of either SMR or 24-hour energy expenditure, with a fall during the early follicular phase and a peak during the late luteal phase.

The results of the present study (Table 2) and previous studies (Table 3) show that there are wide differences in the intraindividual variation of the BMR in women (as measured by CV). Women measured using the Douglas bag in the present study have CVs much greater than those exhibited when using the Deltatrac. Other studies that used the Douglas bag to measure BMR in fertile women have also experienced similar levels of CV variation (8–12%; Solomon et al., 1982). While it could be inferred that the use of the Douglas bag itself may have contributed to the wider intraindividual variation, it should be pointed out that the trends in BMR during the cycle in all six

subjects were remarkably consistent. Furthermore, the training effect of this technique was taken into account at the beginning of the data collection period. A separate comparative study between the two techniques has been carried out in our laboratory (Reeves and Henry, 1995 unpublished data). BMR was measured in 12 subjects (6 males, 6 females) by both the Deltatrac and Douglas bags. The results were statistically analyzed using paired *t*-test. No significant difference ($P = 0.438$, and 0.574 for males and females, respectively) was found in BMR values obtained by either of the two techniques.

The distinct biphasic pattern of BMR during the menstrual cycle could not be demonstrated in every woman measured. It is not known what factors may contribute to this observation. However, variation in body composition and/or hormonal levels may exert an influence. Clearly this area needs further investigation.

The nature of the effect of the menstrual cycle on BMR means that even if the effect was pronounced, calculating the energy requirements of a population based upon a number of BMR data points from different subjects would not necessarily be problematic. Given the biphasic pattern of the BMR (generally lower in the follicular phase and higher during the luteal phase), the probability that all subjects were measured in their luteal phase or all in the follicular phase would be relatively low. It is likely that roughly one-half would be measured during the follicular phase and the other half measured during the luteal phase. Therefore, the overall average BMR would eventually "balance out." However, this would only be the case if the magnitude of any menstrual cycle effects experienced by women was roughly of a similar order.

Calculating the energy requirements for an individual woman based upon a single BMR measurement may, however, be problematic. If the menstrual cycle exerts a great effect on a woman's BMR, then her energy requirements may be over- or underestimated depending on what stage of the cycle was measured. The use of predictive equations may also pose problems. Table 4 shows a comparison between the actual BMR and the BMR as predicted by the Schofield (1985) equations (recommended by the WHO/FAO/UNU report) at different stages of the menstrual cycle of the 12 subjects in this study. A wide variation in the accuracy of these equations in predicting the BMR is evident during the course of the menstrual cycle. However, the difference between the measured mean BMR and predicted BMR was not statistically significant in either study.

A number of factors are known to influence the level of ovarian hormones (Rosetta, 1992; Ellison et al., 1993a,b; Cassidy et al., 1994). Therefore, it can be postulated that the magnitude of the response of the BMR to hormonal changes throughout the menstrual cycle may also be affected by the same elements. The levels of both estrogen and progesterone steadily decrease with increasing age after the mid 30s (Ellison et al., 1993b) and with poor nutritional status and insufficient food availability (Rosetta, 1992). High energy expenditure and heavy work loads can lead to a reduction in ovarian hormones and the incidence of amenorrhea and oligomenorrhea is particularly high among endurance athletes (Rosetta, 1992). Psychological stress and certain dietary practices (e.g., vegetarianism) have been associated with reduced ovarian hormone production (Cassidy et al., 1994).

In addition to environmental factors, genetic factors may influence the level of ovarian hormones produced. Ellison et al. (1993a) measured the levels of salivary progesterone of middle class women in Boston, Lese horticulturists of the Ituri Forest in Zaire, Tamang agro-pastoralists of central Nepal, and Quechua Indians of highland Bolivia. Considerable population variation was demonstrated, with the highest levels observed in the Boston women. Ellison et al. have remarked that the level of ovarian hormones observed in Western women may be at the extreme end of a broad spectrum, and that levels of ovarian hormones may not nearly be as high in women of other populations. Therefore, the patterns observed in previous studies and the present may be specific to women living in developed countries or leading a relatively affluent lifestyle.

Energy balance in women

Studies on the effect of the menstrual cycle and ovarian hormones on the patterns of food intake in women have shown that total energy intake is significantly higher during the late luteal phase of the menstrual cycle (Dalvit, 1981; Dalvit-McPhillips, 1983; Manocha et al., 1986; Lissner et al., 1988; Gong et al., 1989; Tarasuk and Beaton, 1991; Fong and Kretsch, 1993; Johnson et al., 1994;

TABLE 4. Comparison of measured and predicted BMR of subjects in the present study

Subject	Measured BMR (KJ/d) Mean[1]	Predicted BMR (KJ/d) (Schofield)	% Variation of BMR Early follicular	Mid-cycle	Late luteal
Study 1					
1	4,606	5,217	−18.55	−16.28	−7.62
2	5,067	6,108	−27.74	−15.21	−2.72
3	4,905	5,555	−24.14	−13.88	−6.28
4	5,019	5,278	−5.53	−22.75	4.05
5	5,233	4,848	10.04	2.5	13.84
6	5,121	5,401	−12.82	−3.34	3.10
Mean[2] ± SD	5,105 ± 381	5,401.2 ± 419			
Study 2					
7	4,746	5,282	−8.68	−11.61	−8.14
8	6,185	5,972	2.81	9.93	−2.55
9	5,367	5,370	−1.35	−0.75	3.45
10	5,663	6,333	−11.65	−10.3	−11.3
11	6,179	7,529	−15.65	−21.10	13.69
12	5,286	6,518	−18.35	−19.75	−18.72
Mean[2] ± SD	5,571 ± 558	6,167 ± 832			

[1]Mean of 25 measurements per subject.
[2]Mean of six subjects.

Kurzer et al., 1994). An increase in the intake and preference of certain macronutrients, namely carbohydrate, has also been noted. Ovulation has been linked to a decrease in food intake both in humans (Lyons et al., 1989) and in nonhuman primates (Rosenblatt et al., 1980), and it is believed that estrogen (which peaks during ovulation) may act as an appetite suppressant.

Energy balance may be summarized as: ± *Energy Balance = Energy Intake − Energy Expenditure.* The increase in energy intake during the late luteal phase corresponds to the increase observed in BMR (as well as SMR and 24-hour energy expenditure). An increase in BMR would require an increase in energy intake and the patterns observed may be a direct response to alterations in BMR. The peak in BMR (as well as other components of energy expenditure) observed in some women has been reported to coincide with the peak in secretion of progesterone (Fig. 3). It has been known for some time that progesterone has a thermogenic effect and is responsible for an increase in basal body temperature during the late luteal phase of the menstrual cycle (Barton and Wiesner, 1945). More recent studies have verified the thermogenic effect of progesterone and have demonstrated an upward shift in the core temperature threshold for sweating during the luteal phase (Haslag and Hertzman, 1965; Stephenson and Kolka, 1985; Kolka and Stephenson, 1989). The effect that progesterone has on the thermoregulation of women may be indirectly influencing BMR and other components of energy expenditure.

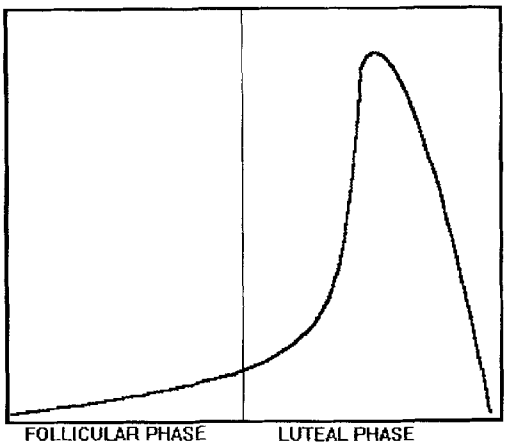

Fig. 3. Variation in progesterone secretion during the menstrual cycle. (From Carola et al., 1990, with permission of the publisher.)

Assuming that the pattern of energy intake is biphasic (Johnson et al., 1994; Kurzer et al., 1994), then it can be closely aligned with patterns of energy expenditure in fertile women (Fig. 4). The corresponding changes in energy expenditure and energy intake enable energy balance to be maintained over the course of the menstrual cycle. Wide (and unsynchronized) fluctuations in

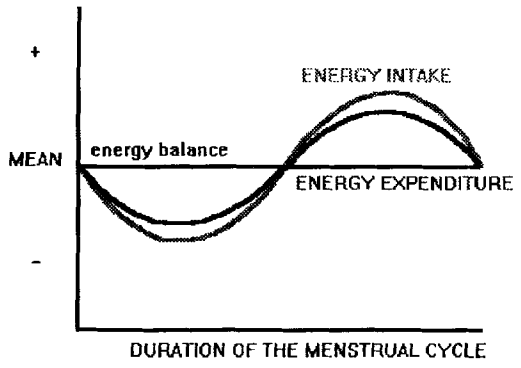

Fig. 4. Energy balance in women. A stylized relationship between energy intake and expenditure during the menstrual cycle.

its components, namely intake and expenditure, may make the certain individuals more susceptible to energy imbalance and to long-term weight gain. More women than men are affected by obesity (Garrow, 1974) and perhaps one of the reasons that this may be the case could be the more complex nature of energy balance in women. The role of the menstrual cycle and ovarian hormones in the etiology of obesity in some women, while speculative, may warrant further research.

In summary, the menstrual cycle appears to influence the constancy of BMR in a proportion of women, yet to be quantified. The impact of the menstrual cycle on BMR and the degree of intraindividual fluctuation do seem to vary considerably. It is clear that many factors must be considered if the BMR in women is to be accurately studied. It is recommended that future studies examine the levels of ovarian hormones and include subjects from non-Caucasian populations. In addition, energy balance may be a more complex issue in women, and further work on the influence of the menstrual cycle on energy regulation is vital.

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