



Menstrual Phase Response to Nocturnal Light

Arcady A. Putilov¹, Konstantin V. Danilenko², Alla Y. Protopopova³ and Daniel F. Kripke⁴

¹Institute for Medical and Biological Cybernetics, Siberian Branch, Russian Academy of Medical Sciences, Novosibirsk, and International Scientific Center ARKTIKA, Magadan, Russia; ²Institute of Internal Medicine, Siberian Branch, Russian Academy of Medical Sciences, Novosibirsk, Russia; ³Polyclinic Unit of the Central Clinical Hospital, Siberian Branch, Russian Academy of Sciences, Novosibirsk, Russia; ⁴Department of Psychiatry, University of California San-Diego, La Jolla, CA, USA

Abstract

The aims of the study were to test whether nocturnal white light can normalize menstrual cycles in oligomenorrheic women, and whether the phase of the menstrual cycle in which light is given is important for the shortening effect. Twenty-five women with long menstrual cycles (35.9–53.4 days on average) were treated for 1–3 cycles, each of which was preceded and followed by at least two untreated cycles. Treatments were 100 watt bedside lights administered for 5 consecutive nights. They centered at three different phases of the menstrual cycle: 6–7th, 14–17th or 23–25th days of the treated cycle (early, middle or late treatment, respectively). On average, the treatment cycle lengths were modestly, but significantly reduced compared to the duration of baseline cycles (more than 11%). The difference in the effects of the early, middle and late treatment was not significant. However, if middle or late treatments were administered in the latter half of the interval between the menstrual cycle onset and probable time of ovulation, reductions of the treated cycle length were substantial (more than 20%, resulting in cycles less than 33 days on average; $p < 0.001$). Other treatments produced only weak (up to 7%), if any, cycle reductions. Moreover, we found a strong correlation ($p < 0.001$) between the duration of baseline cycle and differential effect of middle treatment (compared to early or late treatment). Middle treatments reduced treated cycle duration to the normal range in the subjects with shorter mean baseline cycles (<42 days), while in the subjects with longer duration of baseline cycle the shortening effect was produced by late treatments ($p = 0.005$ and $p = 0.001$, respectively). The results support the suggestion that a bedside lamp used on nights prior to ovulation can cause reduction of long menstrual cycles.

Keywords: Menstrual cycle, oligomenorrhea, ovulation, light treatment, phase response.

Introduction

In 1967, Dewan suggested that the menstrual cycle may be synchronized by the phases of the moon, and that lunar synchronization of the menstrual cycle could be simulated by placing a 100 watt lamp at the foot of the bed from nights 14 to 17 after the start of menstruation (Dewan, 1967). Later, Dewan et al. (1978) published some experimental demonstrations that menstrual cycles in women with long and irregular cycle could be brought nearer to the lunar cycle of approximately 29.5 days by nocturnal exposure to artificial light. Nevertheless, for 20 years Dewan's results seemed to be virtually ignored by the scientific community.

Eventually, Dewan's studies were partly replicated in four controlled studies done in San Diego (Lin et al., 1990; Drennan et al., 1991; Rex et al., 1993, 1995). The first two replications (Lin et al., 1990; Drennan et al., 1991) showed that bedside lights on either nights 13–17 or nights 10–14 shortened cycles in women with long menstrual cycles. The menstrual cycle lengths were reduced from an average of 45.7 and 44.9 days at baseline to 33.1 and 33.2 days during the cycle treated on nights 13–17 and 10–14, respectively (Kripke, 1993). However, most women did not achieve a shortening of their cycles to 29–30 days, which would be expected if the effect simulated lunar synchronization. In the third and fourth replications (Rex et al., 1993, 1995), not only were the menstrual cycles shortened from baseline with white light treatments, but cycles were also shortened from baseline when women used <1 lux red light, irrespective of order of treatment (40.3 and 45.0 days for baseline, 32.7 and 33.8 days for white cycle, and 37.2 and 38.0 days for dim red cycles in the third and fourth study, respectively). It was suggested that the effects of very dim red light might be attributable to placebo effects or spontaneous remissions.

Some preliminary results obtained by Drennan et al. (unpublished) showed that subjects receiving 100-watt-bulb treatment appeared to ovulate 2.6 days earlier, had higher progesterone levels around the time of estimated ovulation, and were more likely to display probable ovulation. However, none of these differences reached statistical significance. Thus, the trend was for the 100 watt bulbs to strengthen ovulation process and to enhance the luteal endocrine response, as if correcting luteal phase insufficiency (Olive et al., 1990).

It may be hypothesized that, if any, only weak changes of the cycle length would be observed with nocturnal light administered during early preovulatory phase or after the presumed day of ovulation. However, to our knowledge, nobody has tested the effect of nocturnal light earlier than day 10 or later than day 17 after menstruation onset. In this study, we examined in oligomenorrhic women whether night lights at certain phases of the women's cycles differentially decrease or increase the duration of the cycle. Demonstration of a differential menstrual phase-response sensitivity would, of course, add further evidence that night lights actively alter menstrual cycle duration.

Methods

Subjects and treatment

Siberian women with a history of long menstrual cycles (longer than 33 days) were recruited through advertisements in mass media and at women's clinics. They had an interview with a physician to assure that they were free from any major medical disorders and that the majority of their cycles were lengthened. The confirmation of cycle lengthening was based on the analysis of calendars, and diagnostics of the causes of menstrual cycle disturbances were beyond the scope of the study. When women volunteered, they were informed that there is preliminary experimental evidence that nocturnal light treatment may reduce the duration of long menstrual cycles. However, there was no suggestion in the consent or instructions that the action of light had not yet been tested in the early or late portions of the cycle.

The analysis of the calendars showed that cycles of a normal length (27–33 days) appear as infrequent episodes of 2-yr histories of most oligomenorrheic women. Although in a selected subject, the normal cycles would occasionally happen, the longer cycles were at least twice more common. Only subjects reported at least one short cycle (<27 days) or at least two very long cycles (60–72 days) were excluded. The reason for exclusion of the latter subjects was that they might suffer from missed cycles. The former subjects were not included since the effect of night light on the length of their cycles would be masked by spontaneous shortening of the treated cycle.

Twenty nine women entered the study. However, four subjects were not included in the analysis. The 1st woman had too short, and the 2nd had too long pretreatment cycles, the 3rd women used light too late (on 30th to 34th nights after menstruation onset), and the 4th women interrupted light exposure for two nights (on 6th and 7th nights after onset of menstruation). The pretreated cycles of these women were 24, 102, 40 and 36 days, respectively. Their treated cycles were 41, 28, 46 and 34 days, respectively.

The remaining 25 women aged 25.3 ± 4.6 yr (mean \pm SD) participated in the study as paid subjects. To calculate their individual duration of baseline cycle, the cycles preceding the first treatment were averaged. A mean duration of their baseline menstrual cycle varied from 35.9 ± 5.5 to 53.4 ± 14.3 days. For comparison, in a general sample of 25 yr aged women, the 34-day interval between menstrual onsets falls on the upper bound of the central 90% of all intervals (see Treloar et al., 1967). Baseline cycles longer than 42 days were reported by 8 subjects. These longest cycles would be designed abnormal because they mostly fall above the central range including from 97.5% to 99% of intervals in women aged 20–25 and 35–40 yr, respectively (Treloar et al., 1967).

None of the selected women took the oral contraceptives on a regular basis. The last 3 cycles before the first light treatment were spontaneous (free of any medications). The first pretreated cycle lengths were within the range 27–72 days.

The treatment employed a bedside 100 watt incandescent lamp of similar type to that used by Lin et al. (1990) and Drennan et al. (1991). Each subject received treatment in her private setting (nobody had female roommates). The subjects were

instructed to turn on the bedside lamp 5–30 min before bedtime and to turn it off after wake-up. The lamps gave 240 photopic lux illumination at eye level at one m distance, which was the intended distance from the head.

The study was planned as a counter-balanced cross-over design. The women were randomly assigned to start an initial five-night treatment session during one of three ten-day intervals of the menstrual cycle (discussed as early, middle and late treatment, respectively). The centers of these treatments were timed at the 6–7th, 14–17th or 23–25th nights after the first bleeding day, respectively. The suggestion was that in the vast majority of subjects the lighting would not yet overlap 1) with the last several days prior to ovulation in the case of early treatment; 2) with the day of probable ovulation in the case of middle treatment; and 3) with the first menses day in the case of late treatment. The treated cycles were separated by at least two untreated cycles (discussed as posttreated and pretreated cycles).

Nine volunteers did not complete all 3 treatments because of change to another treatment ($n = 3$), normalization of the cycle ($n = 2$), pregnancy ($n = 1$) or poor cooperation ($n = 3$). Only one subject reported serious problems with sleep (she completed all three treatments, however).

Analysis of differential response to light

The primary prospective dependent measure was the absolute menstrual cycle length. The durations of pretreated, treated and posttreated cycles were obtained by averaging over treatments or subjects. Table 1 summarizes data on absolute cycle lengths in the entire sample ($n = 25$). Figure 1 illustrates data on absolute cycle lengths in the subsample of subjects who completed all 3 treatments ($n = 16$).

Retrospectively, in the light of the Drennan et al. data (see Introduction), we hypothesized that for some subjects with abnormally long cycles, a middle treatment could be too early to fall on the eve of probable ovulation, whereas a late treatment could fall on preovulatory phase of the cycle. Indeed, many reports suggest that long cycles usually appear due to a long preovulatory phase or, what is the same, due to late ovulation, and that variability of the postovulatory phase seems to be 1.5–2 times smaller than variability of preovulatory phase (see i.e., Potter et al., 1967).

To relate treatment timing to baseline cycle period, two scales for treatment times were introduced. By contrast with prospective classification relating treatment time to the beginning of the treated cycle, these two scales relate treatment time to the end of the mean baseline interval between menstruations. On the first scale every treatment time is expressed as a difference between a day at which a treatment was centered and mean baseline cycle duration (i.e., this is a number of days between treatment center and the last day of the mean baseline cycle). On the second scale (X-axis of Figs. 2–4), every treatment is expressed as a ratio between the day at which treatment was centered and mean baseline cycle duration without the last 14 days (i.e., this is a position of treatment relative to the proposed preovulatory interval of the baseline cycle). The second scale suggests the dividing of mean baseline cycle on individually variable preovulatory phase and fixed postovulatory phase (the latter phase generally tends to be on average 14 days long; i.e., Potter et

Table 1. Duration of menstrual cycles in the whole sample.*

Treatment timing (A)	early or early-phase		middle or middle-phase		late or late-phase	
	pre-treated	post-	pre-treated	post-	pre-treated	post-
Cycle length (B)						
1. Prospective design, n =	20	17	20	20	18	18
Mean, days	39.7	40.5	40.6	38.0	39.3	35.9 ^a
SD	8.7	9.6	8.3	11.9	8.9	7.4
1a. Baseline cycle <42 days, n =	12	11	14	14	13	13
Mean, days	38.6	36.3	40.0	31.6 ^b	38.2	37.5
SD	9.7	6.3	8.6	6.9	9.6	8.3
1b. Baseline cycle >42 days, n =	8	6	6	6	5	5
Mean, days	41.4	48.2	42.0	49.0	42.0	32.0 ^c
SD	7.4	10.3	9.3	12.8	7.0	2.0
2. Retrospective design, n =	23	20	21	21	14	14
Mean, days	40.4	41.3	40.1	33.0 ^d	38.6	37.2
SD	9.3	9.7	7.3	6.6	9.3	8.0

*In total, 25 subjects with mean baseline cycles of shorter (part 1a) or longer than 42 days (part 1b) completed 58 treatments classified either as early, middle and late treatments (part 1: prospective design) or as early-, middle- and late-phase treatments (part 2: retrospective design). Compared to mean baseline cycle duration (Student's paired t-test): ^at = 2.14, p = 0.047; ^bt = 3.41, p = 0.005; ^ct = 8.33, p = 0.001; ^dt = 4.89, p < 0.

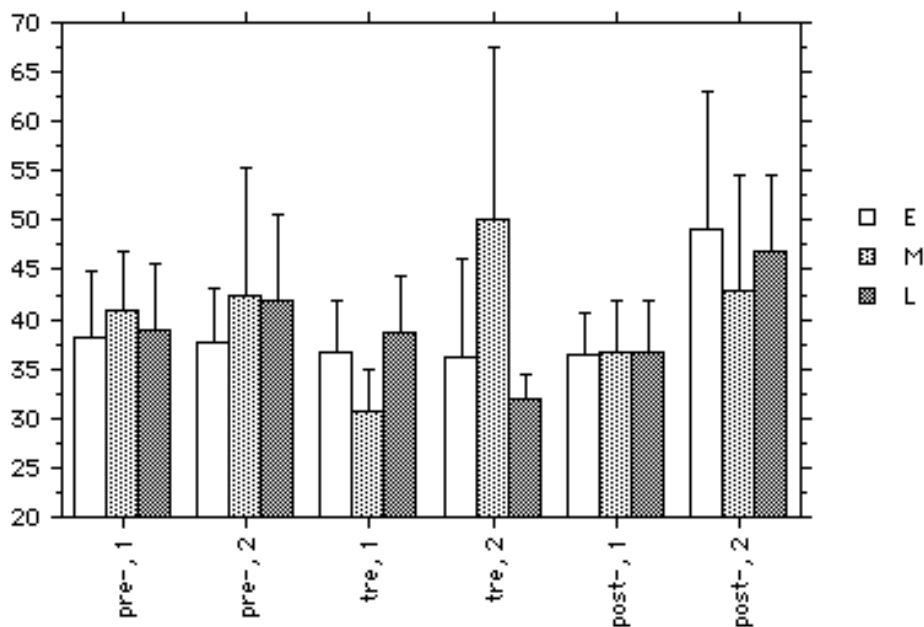


Figure 1. Absolute lengths of pretreated, treated and posttreated cycles in subsample.

Subjects with mean baseline cycle shorter (1, $n = 11$) or longer 42 days (2, $n = 5$) were treated three times (marked as early, middle- and late treatment).

al., 1967). The probable ovulation time is assigned to 1, and treatment centers are expressed as portions of the preovulatory phase interval, as shown in Figures 2–4 (X-axis).

Besides, the treatment responses shown in Figures 2–4 (Y-axis) were related to the durations of other menstrual cycles. A length of treated cycle was expressed either as percentage of mean baseline duration (Fig. 2) or as percentage of mean treated cycle duration (Fig. 3), or as a difference between middle treated cycle length and length of either early or late treated cycle (Fig. 4, upper and lower parts, respectively).

Special analyses were performed to examine the suggestion that greater responses would be expected for those treatments which more likely target the eve of probable ovulation. The following statistical approaches were applied for retrospective analyses of relationship between baseline cycle duration and cycle length response to middle or late treatments.

First, we examine the effect of abnormally long baseline cycle duration on the treatment response by dividing subjects into two subgroups, with mean baseline cycle of 35–42 and 42–54 day length. These subgroups included 17 and 8 subjects treated 39 and 19 times, respectively (Fig. 2). The cycle durations in the subgroups are shown in Table 1 (sample) and Figure 1 (subsample). The effects of light treatment upon menstrual cycle length were evaluated with two-tailed Student's paired *t*-tests (i.e., in

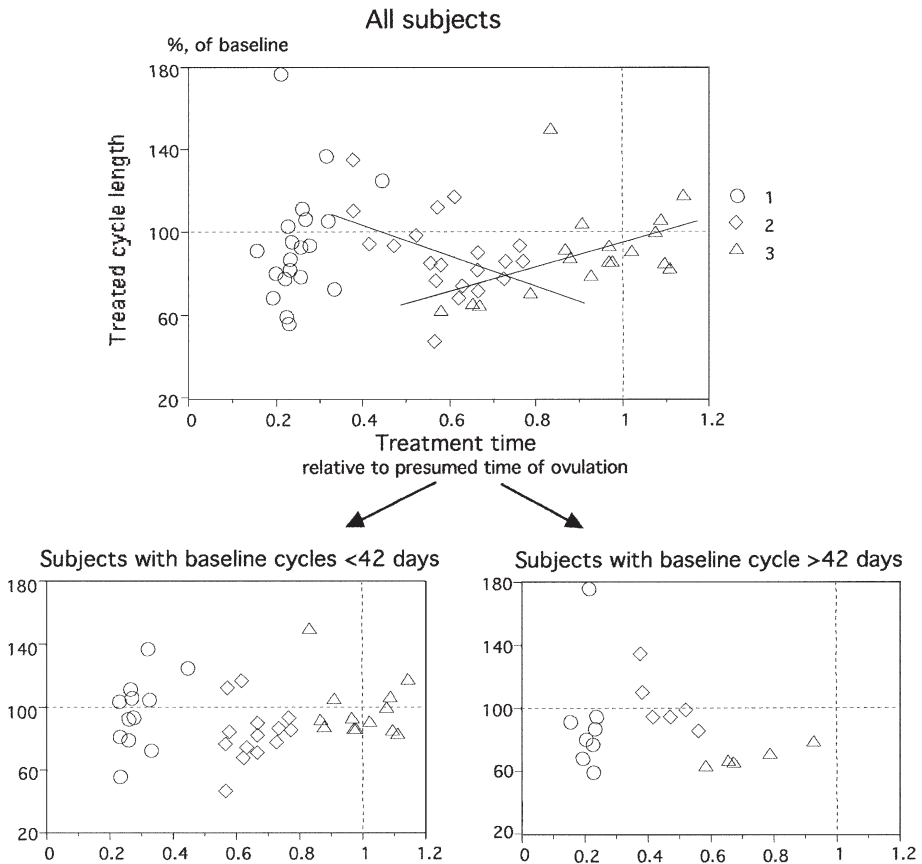


Figure 2. Relative treated cycle lengths (as percentage of mean baseline cycle length) in the whole sample ($n = 25$).

The symbols mark early (1, $n = 20$), middle (2, $n = 20$) and late treatments (3, $n = 18$) of the prospective design. The timing of treatment was expressed as ratio between a day on which treatment centered and mean baseline cycle length minus 14 days. Vertical dashed line marks the right limit for probable time of ovulation at baseline (1.00). Line regression lines are calculated separately for middle and late treatments. The lower graphs separate treatments for subgroups with shorter and longer mean duration of baseline cycle (< and >42 days, $n = 39$ and 19).

Table 1, the lengths of experimental cycles were compared with mean baseline cycle duration calculated by averaging lengths of the menstrual cycles preceding the first treatment). Besides, to reveal the effect of treatment timing on experimental cycle length in the subsample of subjects completing all three treatments, three-, two- and one-way rANOVAs were used with the factors subgroup (women with baseline cycles shorter and longer than 42 days), treatment timing (early, middle, and late) and treatment condition (sequence of treated and untreated — pre- and posttreatment —

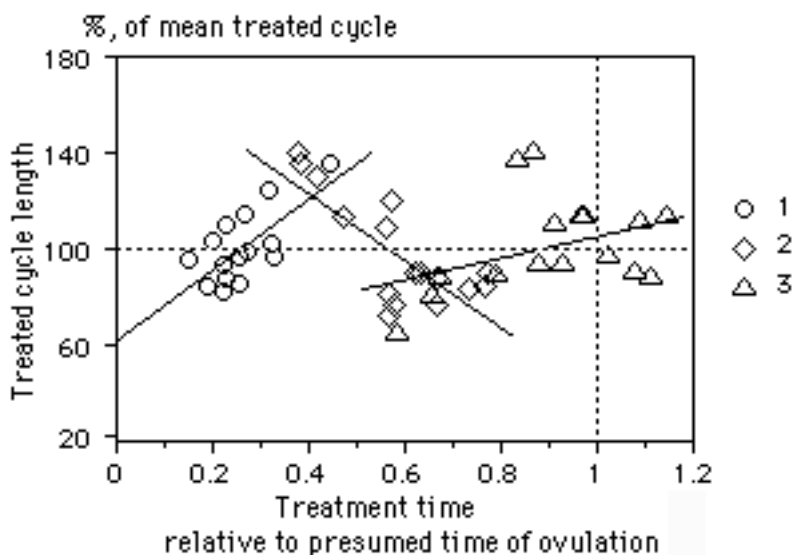


Figure 3. Relative treated cycle lengths (as percentage of mean treated cycle length) of early (1), middle (2) and late treatments (3) in the subsample ($n = 16$).

See also the note for Figure 2.

cycles). Huynh-Feldt's corrected p -values are reported in the text. Post hoc comparisons were then made with Fisher's PLSD test to evaluate significance of differences between experimental cycles.

Second, we calculated line coefficients of correlation between the effect of early, middle or late treatment and treatment phase (timed relative to baseline cycle duration). The line regressions in Figure 2 illustrate the patterns of correlation for treated cycle lengths measured as percentage of baseline duration. Since the subsample data allow us to examine the differential responses to early, middle and late treatment in a given subject, an additional correlation analysis was performed for these 16 subjects to check whether phase of treatment is important for cycle length response to light. The treatment phase was correlated with treated cycle length for early, middle and late treatments expressed as percentage of the mean treated cycle (Fig. 3) or as a difference between length of middle and length of another treated cycle — either early or late (Fig. 4). Unlike other retrospective analyses, the correlation analysis allows to avoid post hoc division of the sample or regrouping of treatments.

Third, the treatments planned prospectively as early, middle and late treatments depending on the days after start of menstruation were reclassified relative to probable time of ovulation (14 days before the end of mean baseline cycle). Figure 2 shows that the relative phase of treatment in our sample varied between 0.15 to 1.15. This treatment range was divided into three equal intervals: 0.15–0.45, 0.45–0.80 and 0.80–1.15. As can be seen in Figure 2, the border between first and second interval corresponds to the time of latest early treatment, and the border between second and

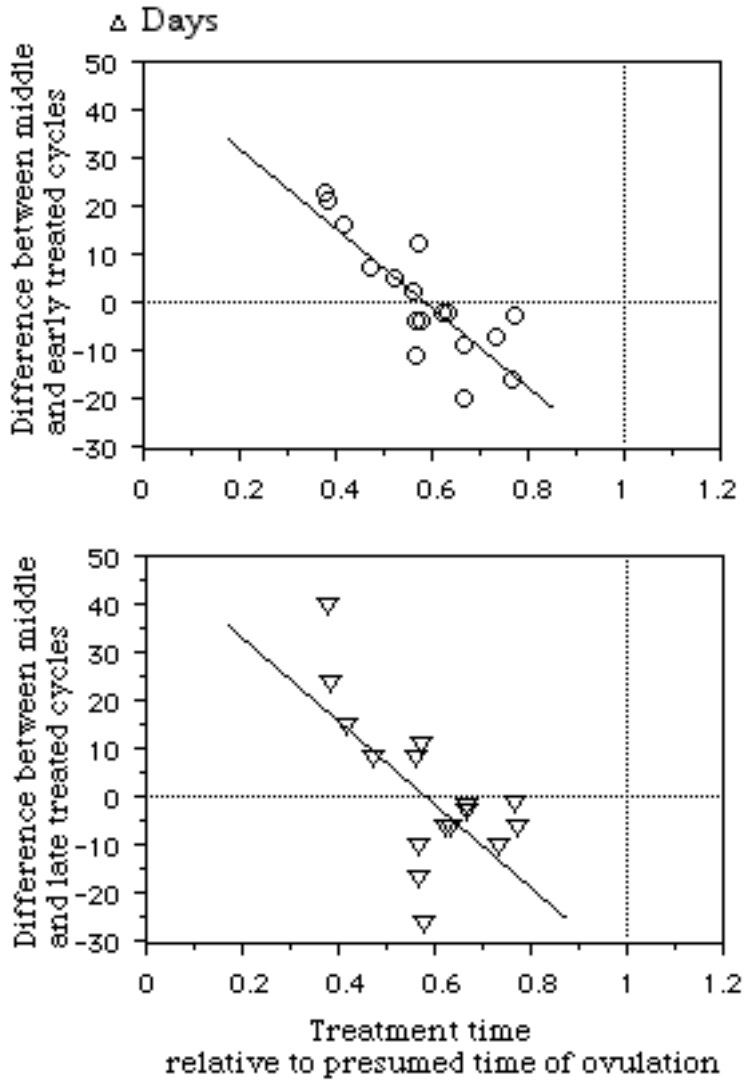


Figure 4. Difference between absolute lengths of middle cycle and other treated cycles — either early (upper graph) or late (lower graph) — in the subsample ($n = 16$).

See also the note for Figure 2.

third interval corresponds to the times of latest middle treatments. The treatments centered on the first, second and third intervals of the treatment range are discussed as early- middle- and late-phase treatments. Unlike other retrospective analyses, the regrouping of treatments allows us to estimate the mean duration of all those cycles ($n = 21$) that most probably were treated shortly before ovulation (Table 1).

Results

Prospectively grouped treatments

There was no difference between cycle lengths in the sample (Table 1) and subsample (Fig. 1). Table 1 show that neither treatment was able to reduce the treated cycle length in the sample to the 27–33-day range, and only one significant difference was found comparing baseline cycles with experimental cycles. Namely, late treated cycles were shorter than mean baseline cycles (Table 1), while reduction of middle treated cycles did not reach statistically significant level ($p = 0.053$). In the subsample, the lengths of treated cycles on average (36.6 ± 6.0 days, $n = 16$) were reduced compared to the mean baseline cycle length (41.2 ± 5.3 days; $t = 3.39$, $p = 0.004$), while the pretreated (39.8 ± 5.5 days) and posttreated cycles (39.6 ± 6.8 days) were not significantly reduced.

One-way rANOVA of treatment cycle by the prospective classifications of timing (early, middle, and late) did not reveal any significant effect of treatment timing, and two-way rANOVA did not yield significant interactions between treatment timing and treatment condition.

Thus, reductions of cycle length were observed only for treated cycles. The treatment effect was irrespective of the prospective timing and rather weak (i.e., the treated cycle lengths were still longer than 33 days). Besides, neither seasonal nor ordering effect on the cycle length were found when we compared the results obtained in four different seasons and in three different parts of the individual experimental protocol (i.e., for the 1st, 2nd and 3rd sequence of pretreated, treated and posttreated cycles).

Treatment effects in subgroups with shorter and longer baseline cycles

After retrospective division of the whole sample into two subgroups on the bases of their baseline cycle duration ($>$ or <42 days), the reduction of treated cycle length to the normal range was clear observed in both subgroups (Table 1 and Fig. 1). In women with the shorter cycles, the prospective design indicated extremely high efficacy of the middle treatments, while early and late treatments were less effective, if at all. By contrast, in the subgroup of women with longer cycles, early and middle treatments were not as effective as were late treatments.

Examination of the cycle lengths with paired Student's t -tests showed that in the subgroup of women with shorter cycles the middle treated cycles were significantly reduced compared to baseline, while in the subgroup of women with longer cycles, significant reduction compared to baseline were found for the late treated cycles (Table 1). This difference between the subgroups was confirmed by three-way rANOVA of subsample data (Fig. 1). The triple interaction between factors subgroup, treatment timing and treatment condition was found to be significant ($F_{4,55} = 4.26$, $p = 0.004$). One-way rAVOVAs of treated cycles yielded significant timing effects ($F_{2,20} = 3.95$, $p = 0.036$ and $F_{2,8} = 8.50$, $p = 0.018$ for subgroups with cycles shorter and longer than 42 days, respectively). The post hoc comparisons (Fisher's PLSD) gave $p = 0.054$ and $p = 0.014$ for the length of middle treated cycle compared to

lengths of early and late treated cycles in the former subgroup, respectively, whereas in the latter subgroup $p = 0.017$ and $p = 0.004$ were obtained for late treated cycle length compared to lengths of early and middle treated cycles, respectively.

The lower part of Figure 2 is designed to demonstrate that the time interval for middle treatments in the subjects with shortest cycles fully overlaps with the time interval for late treatments in the subjects with longest cycles, and the interval for early treatments in the former subjects mainly overlaps with the interval for middle treatments in the latter subjects.

Correlation patterns for early, middle and late treatments

When treatment responses and treatment timing were retrospectively related to mean baseline cycle duration, the expected patterns of correlation were found between the magnitude of cycle reduction and treatment phase expressed as a difference between central day of treatment and mean baseline cycle duration. The treatment responses to later middle treatments were bigger compared to the responses to earlier middle treatments. By contrast, the treatment responses to later late treatments were smaller compared to the responses to earlier late treatments. The coefficients of correlation were significant for both middle and late treatments ($r = -0.53$, $n = 20$, $p = 0.015$ and $r = 0.50$, $n = 18$, $p = 0.034$, respectively) and insignificant for the early treatments (0.32 , $n = 20$, $p = 0.171$).

Figures 2–4 illustrate that the earliest middle treatments centered on the first rather than second half of the interval from the first bleeding day to the probable day of ovulation, while the latest late treatments centered on the peri- and postovulatory rather than the preovulatory phase of the menstrual cycle. The line regressions for efficacy of the middle and late treatments in Figure 2 are crossing about 3/4 of the interval from the onset of the baseline cycle to the probable day of ovulation. The regression lines predict 20% reduction of the treated cycle length compared to the mean baseline cycle duration in this point. When the times of middle treatments were expressed as deviations from the crossing point, the positive correlation was obtained between the treatment response and treatment time ($r = 0.465$, $p = 0.039$).

These results were confirmed by the analysis of relationship between treatment phase and differential response to early, middle and late treatment in the subsample. Highly significant negative correlation ($r = -0.83$, $p < 0.001$) was obtained between relative duration of middle treated cycle (expressed as percentage of mean duration of treated cycle) and treatment phase (expressed as difference between a day at which treatment was centered and mean baseline cycle). By contrast, the correlations were found to be positive for relative durations of early and late treated cycles ($r = 0.59$, $p = 0.017$ and $r = 0.47$, $p = 0.063$). The highly significant correlations were also obtained between middle treatment phase and differences between middle treated cycle length and lengths of early and late treated cycle ($r = -0.86$, $p < 0.001$ and $r = -0.76$, $p < 0.001$, respectively).

Figures 3 and 4 illustrate the patterns of correlation for relative duration of middle treated cycle and differences between length of this cycle and lengths of other (early or late) treated cycles. Thus, correlation analysis of sample and subsample data

confirms the analysis of responses in women with shorter and longer cycles: the marked shortening effect was found for the treatments shortly before ovulation. Besides that, the correlation analysis of early treated cycle lengths suggest that there could be another interval for shortening response to nocturnal light, in the range of the earliest treatments (i.e., during or right after menses).

Retrospectively grouped treatments

In general, the results of correlation analysis and three-way rANOVA showed that the treatments require reclassification in accordance with their phase position relative to the presumed day of ovulation. The results presented in Table 1 (1a and 1b) and Figures 1, 3 and 4 suggest that the earliest middle treatments were administered too early, whereas the latest late treatments were administered too late to be considered as mid-cycle treatments.

In the subjects generating the longest baseline cycles, the timing of middle and late treatments shifted after reclassification in the range of early-phase and middle-phase treatments, respectively (Fig. 2). Of 16 subjects from the subsample (those who completed all three treatments) only 12 were treated in their late phase, while other 4 subjects were treated more than twice in early or middle phase (all these women had mean baseline cycle duration longer than 42 days).

Figures 2–4 show that the 1st treatment interval (0.15–0.45) corresponds to the first half of the preovulatory phase, and the treatments falling on this half of the phase would not yet be able to correct ovulation timing. The 2nd interval (0.45–0.80) more likely corresponds to the second half of the preovulatory phase, and the treatments within this interval would be more effective for strengthening ovulation compared to the earlier treatments. The 3rd interval (0.80–1.15) mostly corresponds to the periovulatory and early postovulatory phases, and the effects of treatment within this interval would be weaker compared to the effect of treatment falling in the previous interval. As illustrated in Figure 2, most treatments administered prior to the probable day of ovulation led to notable reductions of the cycle lengths. Tables 1 shows that, on average, the duration of cycles treated in the middle-phase reached the normal range.

After reclassification of treatments, only middle-phase treatment cycle was found to be significantly reduced, while the lengths of cycles treated in early or late phase were not significantly changed. The middle-phase-treated-cycle decreased compared to the duration of mean baseline cycle both in the whole sample (Table 1) and subsample (paired Student's *t*-test: $t = 3.88$, $n = 12$, $p = 0.003$). Moreover, this cycle decreased compared to lengths of pretreatment cycle and late-phase-treated-cycle ($t = 3.46$, $n = 21$, $p = 0.003$ and $t = 2.33$, $n = 12$, $p = 0.040$, respectively).

In sum, after a 5-night treatment the menstrual cycle was reduced more than 20% (compared to the baseline cycle) and reached the normal range (<34 days), only when the treatment was timed at the second part of the interval from the first bleeding day to the probable ovulation day (in the latter half of preovulatory phase.) Treatments at other menstrual phases had little or no benefit. Although the effect of the middle-phase treatment was highly significant ($p < 0.001$), the following (posttreated) cycle

was not much shorter than the baseline duration. Thus, the shortening effect of nocturnal light on the menstrual cycle length was not persistent.

Discussion

Effect of nocturnal light on cycle length

In agreement with the previous studies of Dewan (1967, 1969) and the San Diego group (Lin et al., 1990; Drennan et al., 1991; Rex et al., 1993, 1995), the results of our study suggest that night lights reduce the duration of menstrual cycles in women with long and irregular cycles. Because the 3-treatment design alternated treated and prospective untreated cycles, the significant difference between these cycles was less likely to be attributable to spontaneous remission, as had been suggested among possible explanations of the results obtained in the previous parallel designs (Rex et al., 1993, 1995).

Although our study design does not allow us to rule out the placebo effect, possible contribution of a placebo effect to the shortening action of light could not be of considerable size, because the general decrease in the cycle length was rather modest and insignificant when analyzed with the prospective design. The average duration of treated cycle was still longer than normal duration irrespective of the time interval after cycle onset at which the treatment falls.

Only when data were retrospectively regrouped (relating treatment timing to the baseline cycle duration), a more impressive result was observed. If a middle or late treatment centered on the mid-cycle phase (more than half way from the cycle onset to the presumed ovulation time), the menstrual cycle averaged normal in duration. By contrast, the duration of cycles falling on other phases was not markedly affected. If any shortening effect of other than mid-cycle treatments was noted, the treated cycle was still longer than normal and its duration was comparable with the durations of dim-red-light-treated cycles in the San Diego studies (see Introduction).

Possible effects of nocturnal light on ovulation

Most recently, the results of the fifth San Diego study were published (Rex et al., 1997). They did not replicate the earlier findings of shortening effect of light on menstrual cycle length. However, the detection of the ovulatory LH surge showed that the occurrence of ovulation was increased in the cycles observed during the first and, especially, the second treatment (61% and 79%, respectively), while only 48% women detected LH surge in their prospective cycle.

The discrepancy between this and other studies on response of cycle duration to light might be attributed, at least partly, to the selection bias. For example, in our study, those subjects who happen to have pretreated cycles in the normal range were not excluded, while in the Rex et al. investigation women with prospective cycles shorter than 35 days were dropped from the study. It is possible that the menstrual cycles in our subjects were more sensitive to light than the cycles of more strongly selected subjects.

Despite the absence of cycle shortening effect, the data of the fifth San Diego study suggest that a secretion of hormones mediating ovulation might be strengthened by light at nights 14–17 after start of the cycle. This result was replicated in a more recent Siberian study (Putilov, Danilenko, Protopopova et al., unpublished) in which the same kits for LH detection were used. It was found that the treatment timed on 3–9 nights prior to the presumed ovulation day significantly increased the detection of ovulation (more than 30% compared to baseline).

Our new study results were also similar to the results reported by Rex et al. (1997) in that we did not observe any sign of reduction of treatment cycle length. Such an effect, however, was not expected in our investigation, because most subjects from our new sample had cycles of variable, but, on average, normal duration. If the primary effect of nocturnal light consists of strengthening of ovulation process, the changes in duration and variability of period and phases of the cycle would be only the sequences of this effect.

Possible biological background of light action

The mechanisms by which light could affect menstrual periodicity are not clear. Dewan et al. (1978) suggested that light might induce ovulation via its suppressive action on melatonin. Indeed, in humans, night illumination as low as 5.5 lux of green light and <40 lux of white light was sufficient to suppress melatonin secretion (Brainard et al., 1997, 2000). Taking into account approx. 5% light transmission through the closed eyelids (Ando & Kripke, 1996) and cumulative effect over 5 full nights, we can suggest that the illuminance reaching the eyes might be sufficient for partial melatonin suppression.

Melatonin seems to be of importance for regulation of the secretion of gonadotropin releasing hormone, which, in turn, regulates pituitary secretion of the gonadotropins, the hormones controlling ovulation (Webley & Lenton, 1987; Woordouw et al., 1992). Both the levels and phase of the melatonin rhythm vary within the menstrual cycle (Dhami et al., 1989; Fernandez et al., 1990), and it may play a role in regulation of levels and timing of gonadotropins secretion during the follicular but not the luteal menstrual phase (Cagnacci et al., 1997). The women's cycle might be sensitive to light interventions only in a certain phase of the menstrual cycle, i.e., not long before ovulation, when light might strengthen the preovulation endocrine response by alternation of melatonin's levels and circadian phase.

In conclusion, our study gave further support from another continent to findings that night lights could be an active treatment for menstrual cycle disorders. Treatments administered not long before the time of probable ovulation caused shortening of menstrual cycles among oligomenorrhic women to normal, whereas the reduction were very modest (and of questionable validity) after other treatments (either in the early preovulatory phase or in peri- and postovulatory phases of the cycle). However, since evidence for an optimal menstrual-phase-of-treatment was only significant in retrospective grouping of the data, and not in the prospective grouping, the

finding merits replication based on the measurement of the time of ovulation and hormonal (i.e., melatonin) response to nocturnal light.

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