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ASSOCIATION BETWEEN PSYCHOLOGICAL STRESS AND MENSTRUAL CYCLE CHARACTERISTICS IN PERIMENOPAUSAL WOMEN

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In previous studies of the relationship between stress and menstrual cycles, stress has been found to be associated with longer cycles, to be associated with shorter cycles, and to have no association with cycle length. Some of the menstrual cycle changes that have been attributed to stress are similar to those experienced by women during perimenopause. In an effort to see whether an association between psychological stress and menstrual cycle characteristics can be detected in women approaching menopause, this study examines this relationship in perimenopausal women who are participants in the Tremin Research Program on Women's Health. The analyses used prospectively recorded bleeding data and retrospectively captured life-event data. A single-year cross-sectional analysis of data from 206 women shows no correlation between stress level, as measured by total number and severity of stressful life events, and cycle characteristics, including interval length, duration of bleed, and variability in both of these factors, nor are there significant differences in cycle characteristics between subgroups of women with different overall levels of stress. In analyzing stress levels and cycle characteristics across 2 years, however, women with marked increases in their level of stress ($n = 30$) are shown to have decreased length (−0.2 days/cycle) of menstrual cycle intervals and decreased duration of bleed (−0.1 day/cycle) compared with increases in these measures (+2.9 days/cycle for cycle interval; +0.3 days/cycle for duration of bleed) among women with no marked change in stress level ($n = 103$); *t*-tests indicate that these differences are significant ($p < .05$).

Introduction

Data from both animal (Kaplan et al. 1996) and human research (Fenster et al., 1999; Hatch, Figa-Talamanca & Salerno, 1999; Matteo, 1987) indicate that psychological stress is associated with altered menstrual function. However, most such studies exclude perimenopausal women, due to their irregular cycle characteristics; for this reason, it was not clear whether an association between stress and menstrual cycle characteristics could be detected in women approaching menopause. Although an association between stress and perimenstrual symptoms (such as mood swings, depression, fluid retention, etc.) has been described for women, including those over the age of 40 (Woods et al., 1997; Woods et al., 1998), the association between stress and measurable characteristics of the menstrual cycle is not clear. Therefore, the primary goal of this investigation was to describe the relationship, if any, between psychological stress and characteristics of the menstrual cycle in perimenopausal women.

Early studies documented the relationship between menstrual function and the severe stress experienced by women and girls during wartime in Europe; this type of extreme stress has long been associated with amenorrhea (Drew, 1961; Sydenham, 1946). In addition, research in nonhuman primates has consistently shown that social stressors (such as repeated change in housing conditions) can have substantial effects on menstrual cycles. For example, Kaplan and colleagues

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(1996) found that socially subordinate (and therefore stressed) female cynomolgus macaques are characterized by impaired ovarian function and low concentrations of circulating estrogen, in comparison with dominant females. However, in humans, the effects of less extreme stressors, such as those encountered in everyday life, are not as well documented.

A number of studies have examined the relationship between more common stressors (job strain, financial worries, daily hassles) and menstrual cycle characteristics, such as cycle length and quality of bleeding, as well as amenorrhea. The results of these studies are not always consistent with one another nor are they necessarily conclusive. High stress has been found to be associated with both longer menstrual cycles (Hatch et al., 1999; Matteo, 1987) and shorter than average menstrual cycles (Fenster et al., 1999), as well as with a higher incidence of anovulatory cycles (Hatch et al., 1999). Low stress was associated with a more regular pattern of cycling (Matteo, 1987). Other researchers (Clarvit, 1988; Nagata, Kato & Seki, 1986), however, found no significant association between perceived work-related stress and menstrual function. Pepitone-Arreola-Rockwell and colleagues (1981), for example, found that measures of job stress were not associated with symptoms of menstrual dysfunction, although they were associated with other nonmenstrual health symptoms.

Although a number of studies have assessed the relationship between stress and menstrual cycle characteristics or ovarian function in younger women, ages 18–40 (Harlow & Matanoski, 1991; Metcalf & Mackenzie, 1980; Tudiver, 1983), few studies have targeted perimenopausal women. One intriguing study (Ballinger, 1990) suggests that stress may play a major role in determining perimenopausal hormone concentrations. In that study, menopausal women reporting higher levels of negative affect had significantly lower levels of estrone and estradiol and significantly higher concentrations of cortisol, a primary hormone in the physiological response to stress.

The types of menstrual cycle disturbances associated with both stress and perimenopause are considered significant for a number of medical, economic, and social reasons. Abnormal bleeding may lead to significant blood loss. Unexplained alterations in bleeding may be symptomatic of an underlying pathology, such as endometrial cancer or uterine fibroids. Abnormal bleeding has long been considered indicative of the need for hysterectomy, though recent research (Mansfield & Voda, 1997; Voda, 1994) suggests that many such hysterectomies may be performed unnecessarily. Although anovulation and luteal insufficiency are by definition associated with infertility, their long-term health consequences are not known.

Understanding the factors associated with menstrual cyclicity is also important because women need to be able to distinguish normal, age-related changes from changes due to other influences. According to a National Ambulatory Care Survey, U.S. women aged 25–54 annually make 2.9 million office visits regarding menstrual disturbances; for women approaching menopause (35–44 years of age), the rate for visits concerning abnormal bleeding is 7.2 per 100 women (Harlow & Ephross, 1995). A more precise description of the relationship between stress and the menstrual cycle will enable women and their health care providers to make a more informed assessment of observed menstrual cycle changes and help them to distinguish between possibly incidental disturbances and underlying pathologies.

Menstrual cycle disturbances similar to those associated with stress are typically found in women approaching menopause; heavy bleeding, extremely short or extremely long cycles, greater variability in cycle length and flow rate, and a higher incidence of discomfort are commonly reported in perimenopausal women (Mansfield & Voda, 1997). Because these changes are presumed to be unavoidable in this group of women, most previous studies of stress and menstrual cycles excluded perimenopausal women; it is not known whether stress has a significant influence on cycle characteristics in this segment of the population.

One of the problems inherent in studying the psychosocial and health-related factors associated with changing menstrual cycles in perimenopausal women is the rigorous prospective data collection required to document menstrual cycle patterns and the psychosocial or health-related factors that may be related to reproductive function. The study reported here relies on prospectively reported menstrual bleeding data. We investigate the relationship between measures of stress, specifically the number and severity of stressful life events, and menstrual cycle characteristics, in a group of perimenopausal women, all of whom are participants in the Midlife Women's Health Survey and the Tremin Research Program on Women's Health, two longitudinal studies of women's reproductive health.

Methods

Sample

The study population was drawn from participants of the Tremin Research Program on Women's Health (Tremin), a predominantly white, well-educated group of women; 99.3% are white, 92.5% are college educated, and 81% are married (Mansfield & Voda, 1994). In 1990, a subgroup (n = 505) of these women, aged 35–55 and still menstruating, was invited to

Table 1. Percentage of respondents reporting in each category of stressful life events, 1992 sample only (n = 206)

Type of Stress	Did Not Occur or Not At All Stressful	A Bit Stressful	Stressful	Extremely Stressful	Number Missing
Own health	62.3	15	11.6	11.1	0
Other's health	60	14.2	13.2	12.7	2
Spouse death	98.5	0	1	.5	1
Other death	79.6	5.8	7.8	6.8	1
Moving	95.7	1	1	2.4	1
Family	69	4.4	9.2	17.5	1
New marriage	98.1	0	.5	1.5	1
Divorce	91.3	1.5	1.5	5.8	1
Job loss	68.5	4.9	14.1	12.6	1
New job	78.1	9.2	8.3	4.4	1
Child moving	71.2	15.1	7.3	6.3	2
Financial	77.2	9.7	9.2	3.9	1

participate in a special survey focusing on midlife and menopause (Mansfield & Voda, 1994).

Our first sample population was comprised of the 206 participants who responded to the 1992 surveys, were still premenopausal at that time, and were taking no form of exogenous hormones. The mean age for the sample was 48.2. (Premenopausal women who were taking exogenous hormones were excluded from the study because their menstrual cycle characteristics are presumed to reflect the activity of those hormones rather than endogenous hormones.) Data from this sample population were used for the single-year cross-sectional analysis.

A subset of these women (n = 159) who were still premenopausal and not taking hormones the following year also completed the 1993 survey; a t-test indicates that their mean age, 47.8, is not significantly different from that of the first sample population. They are the source of data for an analysis of the relationship between changes in stress measures from 1992 to 1993 and changes in menstrual cycle characteristics during the same time.

Measures

Women in the study prospectively completed daily menstrual calendar cards throughout their participation in the study and also completed annual health report forms at the end of each calendar year. The calendar cards, designed in 1934 by Alan Treloar at the inception of the Tremin Program, allowed women to circle their first and last days of each menses and draw a line through all the intermediate days of bleeding. The following menstrual cycle data were used: cycle interval (number of days between the first day of one menstrual period and the first day of the next), duration of bleed (number of days that a menstrual bleed lasts), and the variability, in this case standard deviation, of each of these measures; these measures are commonly employed in menstrual cycle research (Treloar et al., 1967; Whelan et al., 1994). Although the majority of participants have accrued several years of menstrual calendar records, the present analysis is restricted in its focus to 1992 and 1993 records, in part because a large number of women began using exogenous hormones during the subsequent years of the study.

Stress was measured using a modified version of the Holmes and Rahe Social Readjustment Rating Scale (Holmes & Rahe, 1967), which was part of the annual health report form. Our survey uses a 4-point Likert-type scale to allow women to assign a score to the perceived stressfulness of any event on the checklist, with "Not at all stressful" being the lowest point, and scored a 0, and "Extremely stressful" being the highest, and scored a 3. Scale items included health problems, death of spouse, moving, family problems, divorce, and financial problems (see Table 1). All items that received a score for stress were summed, resulting in a total stress score for each woman; the range of possible scores was 0 to 36.

For the cross-sectional study (n = 206), women whose total score was at least 13 were categorized as "high stress" (n = 38; average age = 48.4) and women whose total score was 2 or less were categorized as "low stress" (n = 38; average age = 48.8). These definitions reflect scores that are one standard deviation above or below the mean stress score. There were no significant age differences between these two groups or between either of these and the rest of the women (n = 130; average age = 48.0). Based on previous research showing that stress is related to menstrual cycle characteristics, we predicted that of the 206 perimenopausal women, those with high stress scores would exhibit one or more of the following characteristics: long average cycle intervals (≥34 days); short average cycle intervals (≤24 days); bleeding lasting 8 days or longer; cycle intervals that were significantly different from women with low stress scores; bleed duration that was significantly different from women with low stress scores; greater variability in length of cycle intervals and/or bleed duration (within the calendar year) than women with low stress

Table 2. Cycle characteristics for 1992 sample population ($n = 206$)

Variable	Mean	Standard Deviation	Minimum	Maximum
Age in years	48.2	.26	38	55
Average interval length in days	30.4	11.7	17.1	148
Average duration of bleed in days	5.8	1.5	2.4	10.3

scores. We also predicted that stress scores would be correlated with length of cycle intervals, duration of menstrual bleed, or variability (based on standard deviation) in either of those factors. The use of 34 and 24 days as reference points for long and short cycle intervals was based on previous work with a larger cohort of Tremin participants (Whelan et al., 1994).

In addition to studying stress levels in relation to menstrual cycles, we wanted to explore the possible importance of changes in stress levels in a 2-year data analysis. Data from 1992 and 1993 were used to determine whether changing levels of stress were related to menstrual cycle characteristics. For each of 159 women in this sample (mean age = 47.8), the changes in total stress score, in the average length of interval, and in the average duration of bleed were calculated. Women whose stress score increased by 4 or more points ($n = 30$; mean age = 47.5) were categorized as having "marked stress increase," and women whose score decreased by 6 or more points ($n = 26$; mean age = 48.3) were categorized as having "marked stress decrease." The remaining women ($n = 103$; mean age = 47.8) were described as having "no marked change in stress." These categories reflect scores that are beyond one standard deviation from the mean change in stress scores. There is no significant difference in mean age among these groups. Our prediction was that the change in stress scores would be related to corresponding changes in cycle interval length or duration of bleed.

Results

Our predictions about the effects of stressful life events on menstrual cycle characteristics were partially borne out by the data analysis. Although stress levels per se were not shown to be related to menstrual cycle characteristics, changing stress levels from 1 year to the next do appear to be related.

Single-year cross-sectional analysis

Table 2 presents the menstrual cycle characteristics for the sample of 206 women who completed the survey in 1992. The mean age of the sample is 48.2 years; with the average age of menopause at approximately 51 years, our sample is, on average, well into the menopausal transition.

In the single-year analysis ($n = 159$), no significant relationship was found between stress levels (as measured by total stress score) and menstrual cycle characteristics. Cycle intervals of high-stress women were somewhat longer than those of low-stress women (30.4 vs. 28.8 days), but this difference was not significant. The duration of menstrual bleeding in both groups was the same, with a mean of 5.8 days per menses. The average length of cycle intervals in the high-stress group was not unusually long or short, nor was bleed duration unusually long. The standard deviation of interval length for the high-stress group was, on average, greater than that of the low stress group (9.2 vs. 7.3 days), but this difference was not significant. Standard deviation of duration of bleed was likewise higher for the high-stress group, but not significantly so (1.8 vs. 1.4 days). No strong correlations were found between stress scores and the length of cycle intervals ($r = 0.09$), the variability of intervals ($r = 0.09$) duration of bleed ($r = 0.02$), and the variability of bleed duration ($r = 0.11$).

Two-year analysis

From 1992 to 1993, average stress scores in the 159 participants declined from 7.3 to 6.1, a significant decrease in a paired *t*-test ($p < .01$). At the same time, paired *t*-tests showed that cycle intervals increased significantly, from 28.7 to 30.8 days ($p < .01$), and duration of bleed increased slightly, but significantly, from 5.8 to 6.0 days ($p < .05$). There was no substantial correlation between change in stress scores and either length of cycle interval ($r = -0.10$) or duration of bleed ($r = 0.05$).

When the women with a marked increase in stress ($n = 30$) were compared (*t*-tests) with the women with no marked change in stress ($n = 103$), they proved to be significantly different from one another: for the women with a marked increase in stress, the mean interval length decreased by 0.2 days, while it increased by 2.9 days in the women with no marked change in stress score, a significant difference ($p < .05$) (see Figure 1); duration of bleed decreased by 0.1 days in women with marked increase in stress, while it increased by 0.3 days in women with no marked change in stress, also a significant difference ($p < .05$) (see Figure 2). There were no significant differences between the groups in terms of variability of either interval length or duration of bleed.

No significant differences in cycle characteristics were found between the women with marked decrease in stress and either of the other groups.

Discussion

Our results provide some evidence for a relationship between stress and menstrual cycles. The comparison

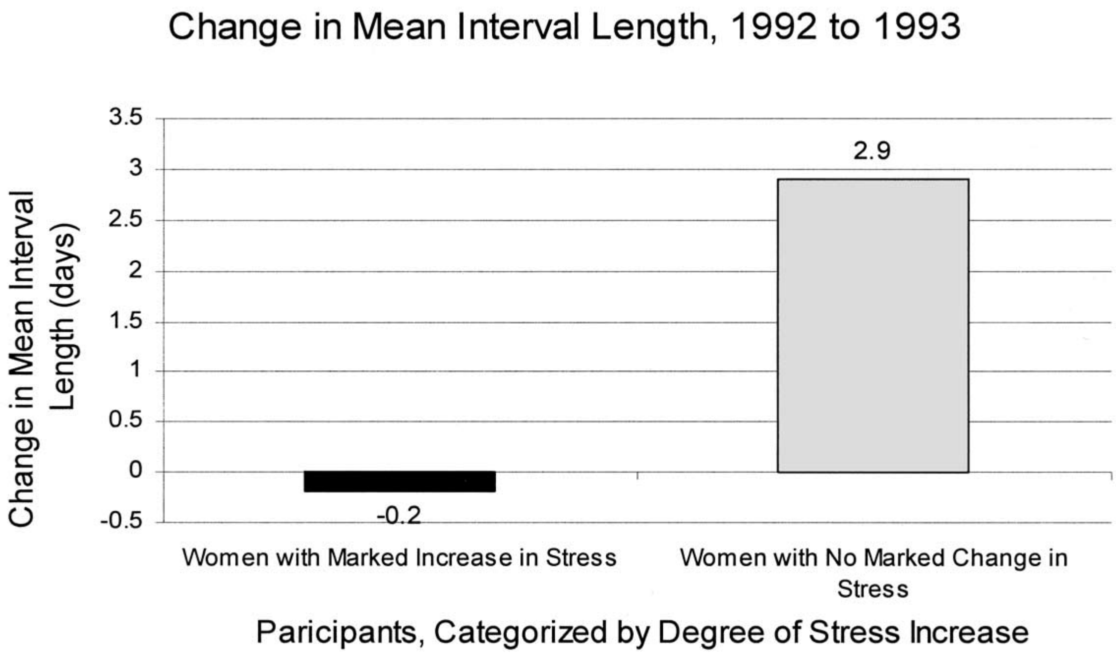

Figure 1. Changes in mean interval length from 1992 to 1993; t-test comparison ($p < .05$) of women with marked increase in stress ($n = 30$) to women with no marked change in stress ($n = 103$).

of 1992 and 1993 stress scores and cycle characteristics demonstrated that there were significant differences from one year to the next. While average stress scores declined, cycle intervals increased and duration of bleed decreased slightly. Given that the change in stress scores and change in cycle interval length were not strongly correlated, and that increasing length of cycle intervals is not unexpected during the later perimenopause, the relationship between the two factors appears to be weak, or at least unclear.

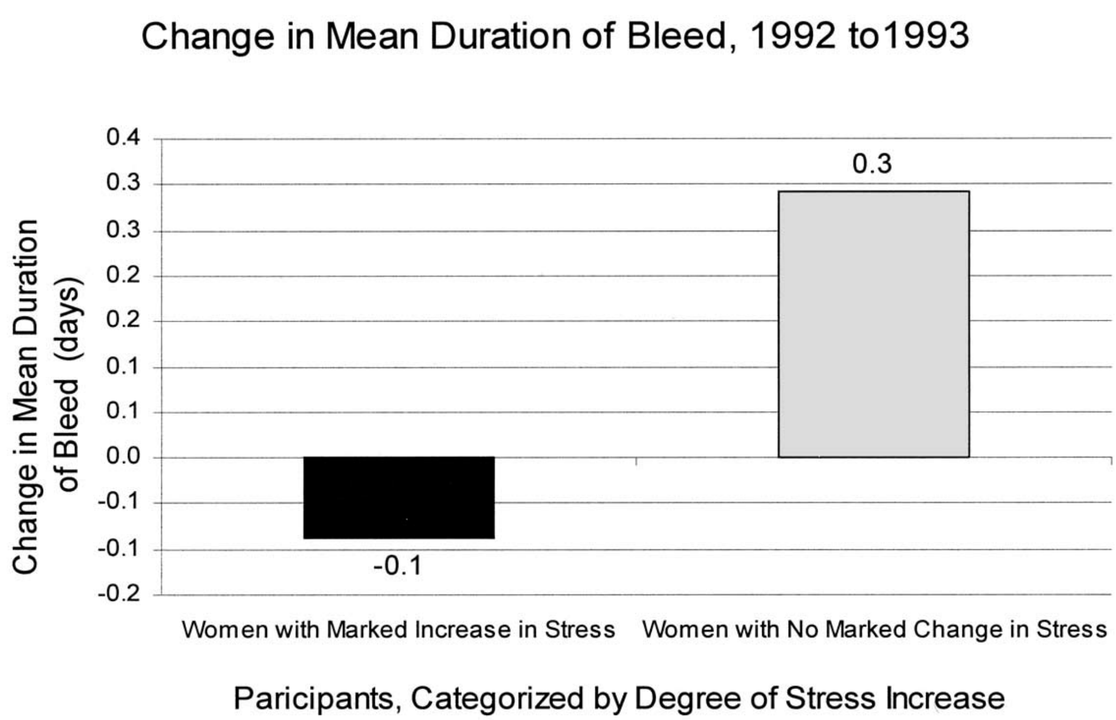

Figure 2. Change in mean duration of menstrual bleed from 1992 to 1993; t-test comparison ($p < .05$) of women with marked increase in stress ($n = 30$) to women with no marked change in stress ($n = 103$).

When women with marked changes (increase or decrease) in stress scores were compared to the women with no marked change, there was some indication that changing levels of stress, in particular markedly increasing stress levels, may be related to cycle characteristics. Perimenopausal women whose stress levels were relatively stable had longer cycles when they were a year older. Perimenopausal women with marked increases in stress levels had shorter-than-expected cycle intervals and duration of bleed. Changes in menstrual cycle characteristics in this group did not appear to be age-related, given that there was no significant difference in age across subgroups of women who differed on their self-reported stress levels.

Our findings are somewhat inconsistent, however, because when we look at stressful events in any 1 year, rather than change across years, we find no clear relationship between the occurrence of stressful life events and menstrual cycle characteristics. This result may be related to the type of data collected. Although the cycle data were recorded prospectively, the stressful life events data were retrospective, and no dates were associated with specific events. Therefore, it is possible that the stressful events did have an immediate impact on cycle characteristics, but that the effects were short-term and not large enough to alter the overall pattern of menstrual cycles across the year. It is also possible, of course, that the stressful events had no immediate impact and therefore no long-term impact on menstrual cycle characteristics. The fact that high-stress women and low-stress women do not differ significantly in the variability of their cycles supports this interpretation.

Several characteristics of the Tremin sample may have contributed to the modest relationship between stress and cycle characteristics that we observed. First, most of the previous work on stress and menstrual cycle characteristics was done in younger women. If the physiology of reproductive aging is the primary source of variation in cycle characteristics in perimenopausal women, environmental events might be expected to have little observable effect.

A second possibility is that the questionnaire that is part of the Tremin annual health report (a modified version of the Holmes and Rahe Social Readjustment Rating Scale) may not include the most important and salient stressors for the women in our sample. Although women who completed the survey were given the opportunity to enter additional stressful events, they very rarely did so. This suggests that the stressors we identified are among the most important challenges that women in our sample faced.

It is possible that age-related menstrual cycle changes themselves were a source of distress to these women and that this is the source of the relationship between changes in stress levels and cycle characteristics. However, few of the participants indicated that menopausal symptoms were a significant source of distress. Because stress measurements were retrospective and not linked to specific cycles, we cannot address the directionality of the relationship between change in stress levels and cycle characteristics. Furthermore, the instrument used in the present study was intended to estimate the frequency of stressor exposure as well as to allow for a personal appraisal of the severity of the stressors. Although this can be considered an improvement over studies that simply administer life events checklists, a more precise separation of distress measures from measures of event frequencies may have revealed stronger relationships.

The relative affluence and homogeneity of the Tremin sample may also have affected the results of this investigation. Only 13.1% of the respondents, for example, indicated that financial concerns were "stressful" or "extremely stressful." It could be argued that a more representative sample, with a wider range of socioeconomic status, might have resulted in a stronger relationship between stress and cycle characteristics.

Conclusions

The results of this investigation, like those of Nagata and colleagues (1986) and Clarvit (1988), suggest that, in the long term, stressful life events have little relationship to the length of menstrual cycle intervals and the duration of menstrual bleeding in perimenopausal women. Without data on the exact timing of stressful life events, however, these results are not conclusive. There is some indication that marked increases in the level of stress may be related to the length of cycle intervals and duration of menstrual bleeding in the short term. Future investigations should rely on prospective recording of stressful life events as well as prospectively recorded menstrual diaries.

It is not clear whether future investigations that include perimenopausal women will encounter the same sample size and attrition problems that this one did. If more women and younger women continue to rely on exogenous menopausal hormones (often to ameliorate symptoms of menopause that are not even occurring yet), fewer will remain eligible to participate over the course of an entire longitudinal study, making it even more difficult to execute the study design called for here. Although use of traditional combined hormone replacement therapy (conjugated equine estrogens plus medroxyprogesterone acetate) dramatically declined in the 18 months following the release of the Women's Health Initiative data, by the end of 2003, approximately 1.7 million women continued to use this form of exogenous hormones (Hersh, Stefanick, & Stafford, 2004); at the same time, there has been a small increase in the use of vaginally administered hormones, soy phytoestrogens, and other alternatives to full-dose hormone replacement therapy. Thus, the study of the "natural" menopausal transition and any relationship it may have to psychological stress may be even more difficult for future investigators.

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