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An ROC analysis of pain reactions in dysmenorrheic and nondysmenorrheic women

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Reactions to radiant heat stimuli were measured in dysmenorrheic and nondysmenorrheic women across a 4-week period. (Dysmenorrhea is a condition in which pain accompanies menstruation.) Receiver operating characteristic (ROC) curve parameters were computed for each of the phases of the menstrual cycle. When painful stimuli were used, a group × phase interaction was found in the analysis on the d'_e scores. Nondysmenorrheic women were found to vary cyclically in their ability to discriminate painful from nonpainful stimuli, whereas dysmenorrheic women showed consistent pain reactions throughout the whole cycle. Cyclic effects were not apparent in the analyses on the response criteria or in those on reactions to thermal stimuli. The results suggest that women who experience pain with menstruation differ from women who do not differ in their perception of pain across the menstrual cycle. The sensory differences between the groups of women were not characteristic of responses to thermal stimuli and were not accompanied by shifts in willingness to report pain. Biochemical differences between dysmenorrheic and nondysmenorrheic women are believed to be the cause of the differences in pain reactions across phase.

The present study uses modern psychophysics to compare reactions to radiant heat stimuli in dysmenorrheic and nondysmenorrheic women. Dysmenorrhea is a condition in which pain accompanies menstruation. It is a common gynecological disorder that affects approximately 52% of postpubescent women. When pain with menstruation occurs in the absence of pelvic abnormality, the term primary dysmenorrhea is applied. If, however, the painful menstruation occurs as a result of an organic pelvic disease, then the term secondary dysmenorrhea is used (Ylikorkala & Dawood, 1978). Women from the first group were the subjects in this study.

Pain reactions of women have always been of interest to pain researchers. Past studies have shown that, among women who menstruate normally, pain reactions vary in association with phase of the menstrual cycle (Goolkasian, 1980; Herren, 1933; Procacci, Zoppi, Maresca, & Romano, 1974; Tedford, Warren, & Flynn, 1977). Procacci et al. (1974) reported data from a series of investigations in which the radiant heat method was used to measure pain thresholds in both men and women. In women, pain thresholds were found to vary cyclically. Low threshold values obtained during ovulation were found to rise steadily and to reach a peak at menstruation. With women who took oral contraceptive pills, however, cyclic changes in pain thresholds were not apparent. Tedford et al. (1977) obtained similar effects with a shock aversion threshold. Cyclic effects were found in the pain reactions of women who menstruated, but such effects were not obtained in women who took oral contraceptives or in men. Goolkasian (1980) reported a receiver operating characteristic (ROC) analysis of pain responses to radiant heat stimuli. She showed that the cyclic changes in pain reactions experienced by women were due to an enhanced ability to discriminate painful stimuli during ovulation, and that the enhanced discrimination effect was apparent neither in the group of women who took oral contraceptives nor in men. These findings also showed that there were no group or phase differences in willingness to report pain.

The present study used a similar ROC curve analysis to study pain reactions of dysmenorrheic and nondysmenorrheic women across the four phases of the menstrual cycle. Women from these two groups have been reported to differ in their pain thresholds (Haman, 1944). However, the data are in the form of threshold changes, and it cannot be determined from such data whether dysmenorrheic women differed from other women in their ability to discriminate the presence of painful stimuli or differed merely in their willingness to report pain. The classical threshold has been reported to be a confounded measure of pain perception because it can be influenced by both sensory changes and changes in response bias (Chapman, 1974; Chapman, Murphy, & Butler, 1973; Clark, 1969; Clark & Mehl, 1971).

Clinicians and gynecologists who work with cases of dysmenorrhea sometimes propose the importance of non-sensory factors such as improper attitude or

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lack of proper preparation (Levitt & Lubin, 1967). Their hypotheses have marginal support in the literature. Paulson (1961) found significant correlations between the degree of premenstrual tension and such psychological variables as attitude and self-concept. Women who complained of dysmenorrhea were found to differ from other women on the Bell Adjustment Inventory (Rose, 1949), and, as children, dysmenorrheic women showed psychological maladjustment four times as often as did those in a control group (Witthower & Wilson, 1940). From clinical observations, then, it would be reasonable to predict that the threshold differences observed by Haman (1944) were due primarily to non-sensory attitudinal factors that increased the willingness to report pain of dysmenorrheic as compared with nondysmenorrheic women.

Recently, however, it has been demonstrated that there are biochemical differences between dysmenorrheic and nondysmenorrheic women. Concentrations of prostaglandins were found to be much higher in dysmenorrheic women during menstruation, and treatment with an antiprostaglandin compound has resulted in relief of menstrually related pain (Chan & Hill, 1978; Lundstrom & Green, 1978; Ylikorkala & Dawood, 1978).

Chan and Hill (1978) measured the menstrual prostaglandin activity by bioassay of a tampon. Prostaglandin activity was nearly twice as high in the dysmenorrheic subjects as in the control subjects. Lundstrom and Green (1978) measured plasma and endometrial specimens taken during menstruation. Concentrations of prostaglandins were found to be significantly higher in dysmenorrheic than in normal subjects. When oral contraceptives or prostaglandin synthetic inhibitors were used in the treatment of dysmenorrhea, a lower concentration of prostaglandins was found and subjects reported relief from pain. Ylikorkala and Dawood (1978), in reviewing the biochemical studies of dysmenorrhea, hypothesized that dysmenorrhea was due to an increase in endometrial prostaglandin production. Because prostaglandins have a direct effect on uterine contractions, their presence in high concentrations was believed to cause excessively strong "labor-like" contractions of the myometrium (the outer layer of muscle in the uterus), which resulted in dysmenorrheic pain.

The presence of this known biochemical difference between dysmenorrheic and nondysmenorrheic women offered sufficient reason to suspect that dysmenorrheic women might differ in their sensory reactions to the presence of painful stimuli. Haman's (1944) early findings may indicate an underlying sensory difference in the ability of women in these two groups to perceive pain.

In this study, cutaneous perceptions of radiant heat stimuli were observed in dysmenorrheic and nondysmenorrheic women for 12 sessions. The sessions were evenly distributed across menstrual, postmenstrual, ovulatory, and premenstrual phases of the menstrual cycle. The question of primary interest was whether the women in this study would display the same cyclic effects across phase as had been identified when women were observed without regard to the presence or absence of dysmenorrhea. The nondysmenorrheic women were expected to respond in the same manner as the women tested in the previous studies. However, if the enhanced levels of prostaglandins found in dysmenorrheic women affected the ability to sense pain, then it was expected that these women would respond to the painful radiant heat stimuli in a different manner from the nondysmenorrheic women. A group × menstrual phase interaction in the discrimination accuracy measure would indicate sensory differences, whereas the presence of an interaction effect in the analyses on the response criteria would indicate that the two groups of women differed in their willingness to report pain across phase.

Reactions to thermal stimuli were also included in the observations to control for effects that might be attributed to the nonpainful aspects of the stimuli. No phase or group effects were expected. Effects found at both thermal and painful stimulus levels would not be interpretable as a pain phenomenon.

Use of procedures derived from the theory of signal detection in pain investigations have been prevalent since the early 1970s, but this research has generated criticism. Some of the criticism justifiably highlighted weaknesses in the procedures that had been used by pain researchers (Hayes, Bennett, & Mayer, 1975; Grossberg & Grant, 1978; Lloyd & Appel, 1976; Rollman, 1977). Often, inappropriate measures were used, for example, d′ instead of the more general indexes that do not make as many assumptions about the data [d'_e, Δm, or the nonparametric measure P(A)]. In some investigations, an inadequate number of trials were used for a psychophysical measure. Subjects were not always allowed sufficient practice, and sometimes data were pooled from trials involving different stimulus intensities. Any one of these factors could have resulted in unreliable results with increased measurement error.

There are a few critics, however, who have raised serious objections regarding the appropriateness of the theory of signal detection in the study of pain (McBurney, 1975; McCreery & Bloedel, 1978; Rollman, 1977, 1979). Rollman (1977) argued that applying the theory of signal detection to pain research necessitates presenting subjects with two very discriminable stimulus categories—noise trials in which only blank stimuli are presented and signal trials in which very intense stimuli appear. Since these categories are so different, subjects respond with complete certainty, and, without some misses and false alarms,

it is difficult to compute measures of discrimination and response bias. Although this is a legitimate concern, there are ways of dealing with it. Since pain responses can be elicited with intermediate stimulus intensities, it is not necessary to use such intense stimulus values that errors will not be made in discriminating between signal and noise trials. In the present research, the stimulus categories were of sufficient intensity to evoke some discrimination errors. Also, in dealing with this problem, the use of a rating scale is preferred over the use of a binary response because, with a rating scale, the discrimination measure can be calculated from the whole ROC curve rather than from just one point on the curve, as is the case with a yes/no response. The d'_e and Δm measures are examples of recommended indexes. Also, when unfilled rating-scale categories are found, it is recommended that categories be summed to calculate the measures. Since the whole ROC curve is used in computing the measures, summing across categories is appropriate (McNicol, 1972).

The ROC analysis that was employed in this investigation was derived from the general model of the theory of signal detection as described by Green and Swets (1966). Differences in stimulus discriminability were measured with the d'_e score, and differences in willingness to report pain were indicated by beta scores that were calculated for each of the criterion positions in the rating scale.

METHOD

Apparatus

A dolorimeter was used to deliver various intensities of radiant heat to ink-blackened spots on the right forearm for 3 sec. The dolorimeter was constructed according to the design presented by Hardy, Wolff, and Goodell (1967). A Viewlex projector was modified to allow the light from a 300-W incandescent lamp to be focused by a condensing lens onto an ink-blackened spot on the right forearm. The size of the skin area affected was 2 cm in diameter. A tachistoscopic shutter was mounted on the outer casing of the projector to control the exposure duration, and the lamp intensity was controlled by a Variac that allowed the experimenter to vary the voltage to the lamp. The dolorimeter was plugged into an isolated transformer to prevent fluctuations in the power supply. To preserve the calibration of the instrument, the projector, shutter, and lens were mounted together with an armrest on a wooden frame.

Stimuli of two intensities (46.3 and 80.4 mW) were produced by delivering voltages of 60 and 70, respectively, to the projector lamp. A no-light control was used as a baseline. A black drape placed along one side of the dolorimeter prevented the subjects from viewing the apparatus and any changes in the light intensity that accompanied the changes in the Variac settings. The projector fan was in use at all times to mask auditory cues from the apparatus.

Subjects

Twelve dysmenorrheic and 12 nondysmenorrheic women were selected from among students who had volunteered at the University of North Carolina at Charlotte. A pretest questionnaire, which included a Menstrual Symptom Severity Scale (Chesney & Tasto, 1975), was used to place the women into the appropriate groups.

The Menstrual Symptom Severity Scale consisted of a list of 15 symptoms (e.g., cramps, nausea, dizziness). The subjects used a 5-point scale (which ranged from 1, symptom not present, to 5, very severe) to indicate the degree to which they had experienced a specific symptom during their last menstrual period. Each of the 15 items was weighted with a number from 1 to 5 according to the severity of the response, and the 15 item weights were summed into a score. The mean score for the 124 women who volunteered to fill out the pretest questionnaire was 29.2, with a standard deviation of 10.2. In selecting the subjects from the pool of available applicants, consideration was also taken of the response to an item that asked the women directly to rate the pain they experienced during menstruation.

Nondysmenorrheic women were selected from those women who reported only slight incidence of menstrually related symptoms. (The mean score on the Menstrual Symptom Severity Scale for this group was 19.8, with a standard deviation of 2.9). Dysmenorrheic women were selected from the women who reported a high incidence of menstrual symptoms and no history of an organic pelvic disorder. (These women obtained a mean score of 46.2, with a standard deviation of 8.4 on the Menstrual Symptom Severity Scale.) The subjects in both groups were selected randomly from those volunteers who had indicated that they were in good health, did not take oral contraceptives, drugs, or medicine, and had a regular 26-32-day cycle. The subjects were asked to refrain from alcohol and analgesic use in the 10-h period before each session. They were paid $48 for participation in a presession and in 12 experimental sessions held on consecutive Mondays, Wednesdays, and Fridays at the same time of day.

Procedure

During each session, the three stimulus intensities of radiant heat were presented randomly, and the subjects were instructed to assign each stimulus to one of the following response categories: (1) nothing, (2) warm, (3) hot, (4) faintly painful, (5) moderately painful, (6) strongly painful. To ensure adoption of stable response criteria across the 12 experimental sessions, the subjects were instructed in the use of the rating scale before each session and were given 20 practice trials to reacquaint themselves with the range of stimulus values. In each of the 30-min sessions, the subjects received 180 trials—60 at each of the intensity levels. For analysis, the data were blocked into four phases according to the subject's own menstrual cycle. Day 1 corresponded to the onset of menstruation, and all other days were aligned as follows: menstrual, Days 1-7; postmenstrual, Days 8-14; ovulatory, Days 15-21; premenstrual, Days 22-28. While participating in the experiment, the women were asked to record daily basal temperatures and the date of menstrual onset. These measures were used to block the data into menstrual phase. They were particularly useful in instances in which the length of the cycle varied from 26 to 32 days.

To control for possible session effects due to the repeated measurements, the beginning of the experiment was counterbalanced across menstrual phase. One-fourth of the subjects in each group began the experiment during each of the menstrual phases. To facilitate the assignment of a starting date for the experiment, the subjects had kept a record of dates of onset for 1 or 2 months prior to their experimental participation.

The data from each session were analyzed to compute the parameters that summarized the asymmetrical ROC curves. The measure of discrimination accuracy was d'_e computed from the point where the ROC curve crossed the negative diagonal. (The d'_e scores were computed by applying the formula $d'_e = 2\Delta m[s/(1+s)]$ to Δm and s values computed by the Dorfman and Alf (1969) computer program, where $\Delta m = a/b$ and $s = 1/b$). Beta values, which are indicative of the non-sensory factors that influence the response, were also calculated for each of the multiple criteria adopted by the subjects in using the six categories of the rating scale. (Beta values were computed by taking the ratio of the ordinate of the hit rate to the false-alarm rate at each of the five criterion settings. Fewer beta values were computed in some cases because subjects did not always use all

five categories of the rating scale.) Analyses were conducted on logarithmically transformed beta values. In calculating these measures, the responses to the no-light control were always used as the noise trials.

RESULTS

For each of the subjects, mean d'_e and beta scores were calculated across the sessions within each of the menstrual phases. Table 1 and Figure 1 present the data obtained under each of the experimental conditions. Use of the rating scale categories in response to stimuli of particular intensities can be determined from the beta scores. As expected, the lower intensity stimuli were rated as thermal. The subjects did not use the pain categories when responding to these stimuli. Pain ratings were made, however, in response to the higher intensity stimuli: Ratings of faintly and moderately painful were frequent, although a rating of strongly painful occurred rarely. For this reason, beta values were calculated for only four of the five response criteria.

Mean d'_e scores were treated with an analysis of variance with dysmenorrheic/nondysmenorrheic groups as a between-subjects variable and menstrual phase as a within-subjects variable. Responses to each of the intensity levels were analyzed separately.

The analyses on the discrimination measures showed that dysmenorrheic women and nondysmenorrheic women differed in their responses to painful stimuli across menstrual phase. Figure 1 displays the group × phase interaction [$F(3,66) = 2.95$, $p < .05$]. Although nondysmenorrheic women varied in their ability to discriminate painful from nonpainful stimuli in association with menstrual phase, the pain reactions of dysmenorrheic women were found to be stable across phase. There were no main effects of group ($F < 1$) or menstrual phase [$F(3,66) = 1.84$, $p < .15$].

A test for simple main effects of menstrual phase indicated that nondysmenorrheic women showed significant changes in d'_e scores across menstrual phase [$F(3,66) = 4.47$, $p < .01$], whereas the dysmenorrheic women did not ($F < 1$). Follow-up post hoc tests (LSD) showed that the phase effect found with the nondysmenorrheic women was due to a significant increase in pain discriminability during ovulation compared with the pre- and postmenstrual phases ($ps < .05$), but that there was no difference between discriminability in the ovulation and menstrual phases. Within each of the four menstrual phases, the groups did not differ.

The lower panel of Figure 1 presents the discrimination scores measured in response to a thermal level of radiant heat. It is apparent that the two groups of women did not differ in their discrimination of thermal stimuli across phase; also, there was no interaction of phase × group ($Fs < 1$). Although the figure indicates slightly higher scores for the dysmenorrheic women than for the other women, the group differences were not significant [$F(1,22) = 1.69$, $p < .20$].

Least square regressions were used in the analyses on the logarithmically transformed beta values be-

Table 1
Mean Beta (Logarithmically Transformed) Values for Each of the Experimental Conditions

Group	Menstrual Phase: M	Post-M	O	Pre-M
Thermal Stimulus Intensity				
Dysmenorrheic				
Warm	.37	.15	.17	.26
Hot	.91	.85	.67	.72
Nondysmenorrheic				
Warm	.18	.25	.17	.11
Hot	.91	.82	.85	.89
Painful Stimulus Intensity				
Dysmenorrheic				
Warm	−.06	−.21	−.19	−.13
Hot	.63	.51	.40	.40
Faint Pain	.86	.84	.71	.62
Moderate Pain	.91	.90	.87	.79
Nondysmenorrheic				
Warm	−.25	−.21	−.24	−.29
Hot	.72	.76	.71	.74
Faint Pain	.86	.82	.88	.89
Moderate Pain	1.05	.96	1.08	1.02

Note—M = menstrual; Post-M = postmenstrual; O = ovulatory; Pre-M = premenstrual.

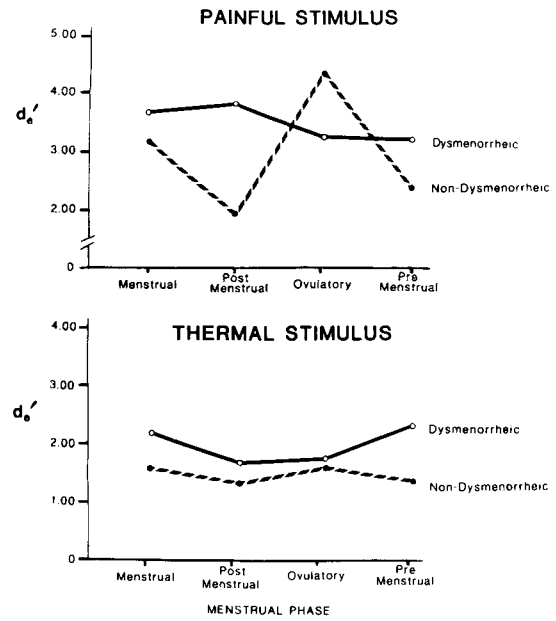

Figure 1. Mean sensitivity scores for the group × phase interaction. The upper panel represents the responses of the two groups of women to painful stimuli, and the lower panel displays the responses to the thermal stimuli.

cause there were missing cells. The subjects did not always use all of the categories of the rating scale. Separate analyses were made on each of the response criteria, and each analysis tested for the main effects and interaction of group and menstrual phase.

Dysmenorrheic women did not differ from nondysmenorrheic women in their tendency to rate painful stimuli as warm ($F < 1$), hot [$F(1,66) = 2.67$, $p < .11$], faintly painful ($F < 1$), or moderately painful [$F(1,30) = 1.30$, $p < .27$]. Menstrual phase did not influence willingness to rate painful stimuli as warm, hot, faintly painful, or moderately painful ($Fs < 1$). And there were no significant interactions in the analyses on the criteria for warm, hot, moderately painful ($Fs < 1$), or faintly painful [$F(3,52) = 1.51$, $p < .22$].

Similarly, the ratings in response to thermal stimuli did not show any group, menstrual phase, or interaction effects [$Fs < 1$, except for the following value, which was obtained for the menstrual phase effect in the analysis on the hot criteria: $F(3,60) = 2.08$, $p < .11$].

DISCUSSION

Women who experienced pain with menstruation differed from nondysmenorrheic women in their perception of painful radiant heat stimuli across menstrual phase. Nondysmenorrheic women experienced phase effects in pain discriminability, whereas dysmenorrheic women responded to painful stimuli in a consistent fashion across menstrual phase.

The results of the analysis on the responses to the thermal stimuli ruled out an explanation of the findings in terms of the thermal properties of the stimuli. Reactions to thermal stimuli did not show the same group × phase interaction that was found when painful stimuli were experienced. Also, since there were no group or phase differences in the willingness to report pain, the results cannot be attributed to response bias effects. The data clearly demonstrate a sensory effect on the pain phenomenon.

The changes in pain discriminability indicated by the group of nondysmenorrheic women across phase were consistent with previous studies that tested women's reactions to painful levels of radiant heat stimuli. In both the Goolkasian (1980) and the Procacci et al. (1974) studies, pain responses during the ovulatory phase indicated the most sensitivity. The findings differ, however, during the menstrual phase. Goolkasian found pain responses during menstruation to be consistent with responding during the pre- and postmenstrual phases, whereas Procacci et al. found that, during this phase, pain reactions indicated the lowest levels of sensitivity. It is not clear why the findings are not as consistent during the menstrual phase as they are during ovulation. The fact that the women under study in this investigation were limited to those who experienced menstruation with little or no pain might explain the lack of consistency in the findings during the menstrual phase. In the other studies, the presence or absence of dysmenorrhea was not taken into consideration.

The most likely explanation of the group differences in pain reactions across phase lies in the biochemical differences between the two groups of women tested in this study. Prostaglandin, in its effect as a powerful stimulator of uterine contractions, has been identified as an important factor in primary dysmenorrhea. That higher levels of prostaglandin are found in the menstrual fluid of dysmenorrheic women than in that of control women may explain why pain responses did not shift downward during the post- and premenstrual phases as they did with the nondysmenorrheic women. Whether prostaglandin operates directly or indirectly to produce these effects, however, is not clear at the present time. Ylikorkala and Dawood (1978) indicated that prostaglandin levels vary in concentration during the menstrual cycle. But since most of the empirical studies comparing dysmenorrheic and nondysmenorrheic women are restricted by technique to the menstrual phase, it is not known how the groups differ across menstrual phase in prostaglandin levels. These findings do point conclusively to the fact that women from these two groups show significant sensory differences in pain reactions across menstrual phase. Explanations of these behavioral findings, however, must await further biochemical investigations of the effect of prostaglandin on the menstrual cycle.

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