THE POSSIBLE RELATION OF THE MENSTRUAL CYCLE TO SUSCEPTIBILITY TO FEAR ACQUISITION

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Summary — Biological changes due to the menstrual cycle may account for the fact that fears are not equally distributed between the sexes. In a differential, classical conditioning paradigm, women in premenstrual phase of their menstrual cycles were compared with a control group of women at other points in their cycles except within seven days before menstruation. Electric shock and pictures of natural scenes were used as UCS and CS respectively. Premenstrual women showed an enhanced susceptibility to the acquisition of a conditioned skin conductance response and to delayed extinction, while control women did not. The possible role of an altered physiological state during the premenstrual phase in the acquisition of fear responses is discussed.

The sex distribution of anxiety disorders, particularly that of agoraphobia, is skewed. About 2/3 to 3/4 of the afflicted individuals are female (Emmelkamp, 1982; Schutz, 1981). Biological processes are often said to play a role here. More specifically, it has been argued that the hormonal changes inherent in the menstrual cycle and in the premenstrual phase in particular, predispose women to negative affect. While sociocultural factors may account, at least in part, for what has come to be called the "premenstrual syndrome" (PMS) (Ruble and Brooks-Gunn, 1979), a biological basis for PMS is also finding some support these days.

First, clinical observation suggests that in anxious female patients, symptoms increase premenstrually. For instance, in a recent study on the etiology of anxiety disorders (Breier, Charney and Heninger, 1986), it was found that 22 out of 43 normally menstruating patients suffering from agoraphobia or panic disorder experienced a worsening of anxiety complaints during the seven days prior to menstruation. Fourteen reported a remarkable increase in the number of panic attacks during this period.

Second, a good deal of research has been devoted to the relationship between hormonal changes during the menstrual cycle and vulnerability to a broad spectrum of emotional complaints and somatic symptoms. Most data, collected in retrospective self-report studies, demonstrate a wide range of negative mood changes that show a premenstrual peak (May, 1975; Wilcoxon, Schrader and Sherif, 1976). It should be noted that when prospective blind methods were used, no such dramatic effects could be demonstrated (Slade, 1984; Rubinov and Roy-Byrne, 1984; Halbreich and Endicott, 1985). However, there are some premenstrual somatic changes that are not under volitional control, such as water retention and pain threshold (Wilcoxon, Schrader and Sherif, 1976), changes in acid-base balance (Damas-Mora et al., 1980), heart rate changes (Kuczmerycz and Adams, 1986), low cortical alertness and high autonomic (electrodermal) reactivity (Asso, 1986).

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Finally, experimental indications that the premenstrual state is etiologically related to neurotic fears come from studies by Beech and colleagues. In their first study (Asso and Beech, 1975), 20 healthy women and 8 phobic women were subjected to a one-trial conditioning experiment, half of them premenstrually, the other half intermenstrually. The conditioning trial consisted of one pairing of the conditioned stimulus (CS), a blue light, with the unconditioned stimulus (UCS), a loud noise. The galvanic skin conductance response (SCR) to three CS presentations, before and after the UCS–CS pairing, were compared in order to provide a measurement of the conditioned response (CR). Both the phobic and the normal women showed an enhanced reaction premenstrually, this effect being even more pronounced for the phobic group. These findings were confirmed in a second study (Vila and Beech, 1977) on 16 phobic patients. A somewhat more complex design was used this time, consisting of a one-trial "acquisition phase" followed by two test trials and then two UCS–CS pairings followed by 10 extinction trials. The premenstrual women showed an increased susceptibility to the acquisition of SCR and possibly resistance to extinction.

To the best of our knowledge, only one attempt to replicate these experiments has been reported. The results of that study (Strauss, Schulteiss and Cohen, 1983) were however not in line with previous findings. Considering that these studies, together with the Vila and Beech study (1978), in which a defensive heart-rate pattern was found in premenstrual phobic women, can be very important in the understanding of the development of neurotic fears, the authors decided to conduct a replication experiment.

A number of methodological considerations were taken into account. To begin with, since there is ample evidence of increased sympathetic activity in anxiety states (Lader and Mathews, 1968; Deitz, 1982; Sartory, 1983), skin conductance seemed an appropriate choice as independent variable for the study of anxiety. Next, if the etiology of anxiety is associated with the menstrual cycle, it can be argued that in premenstrual women either the acquisition of classically conditioned SCR will be facilitated or there will be resistance to extinction of stimulus-bound SCR, or possibly both. Therefore, it was decided that a delayed conditioning paradigm be used to allow for the measurement of CR on every CS and that acquisition and extinction phases be distinguished to enable separate analyses of these phases. Since one-trial learning, as used in the Beech studies, may call for a rather intense UCS, another advantage of using a series of UCS–CS pairings is the use of a presumably less aversive UCS. To control for confounding factors, such as irrelevant features of the CS, a differential conditioning paradigm was used, in conformity with the studies by Öhman and co-workers (see: Öhman, Fredrikson and Hugdahl, 1978; Öhman, 1986). Olasov and Jackson (1987) pointed to the role of expectations on the relationship between negative mood changes and menstruation. To limit this influence, subjects were questioned about their menstrual cycles after the experiment. They received no information as to the CS–UCS contingency; they were only told that physiological reactions would be measured when looking at pictures of natural scenes.

It was hypothesized that women in their premenstrual phase of menstrual cycle would show an enhanced susceptibility to the acquisition of a conditioned skin conductance response and to delayed extinction, when compared with women at other points in their cycles.

METHOD

Subjects

The subjects were 31 female undergraduate students with no history of psychiatric complaints. Their mean age was 21.2 years, with a range from 18 to 28 years. The subjects were blind as to the purpose of the study and were
paid for their participation. During the experiment, they were seated in a comfortable chair in a dimly lit, sound-attenuated chamber. The recording apparatus was in an adjacent room.

**Apparatus and measurements**

SCR and skin conductance level (SCL) were recorded by means of the constant voltage method (0.5 volts) (Venables and Christie, 1973). Beckman Ag/AgCl electrodes (φ = 8 mm) were attached to the middle phalanx of the second and third fingers of the left hand. The recording apparatus allowed for maximum sensitivity of 0.05 μmho.

An electric stimulator with a maximum capacity of 40 mA delivered an electric current (d.c., 0.5 s) to each subject. Two shock electrodes were placed on the first finger of the subject’s left hand.

Slides were projected onto a white wall, 2.5 m in front of the subject. The size of each projected image, a picture of some natural scene, was approximately 80 × 120 cm. Projection lasted 8 s, UCS immediately followed projection offset.

Experimental procedure, inter-trial intervals, occurrence of the electric pulses, slide onset and offset, etc. were accomplished by means of a PDP-11 computer.

Since rate of conditioning is supposed to be linked to neuroticism, subjects filled out the “Amsterdamsse Biografische Vragenlijst” (Amsterdam Biographical Questionnaire) (Wilde, 1962), the Dutch equivalent of the Eysenck Personality Inventory (Eysenck and Eysenck, 1964), which measures neuroticism.

**Procedure and design**

The experimenter explained that electric shocks would occur at some time during the experiment. After the subjects had given their consent, the experimenter started the shock work-up procedure in which the shock level was gradually increased until the subject indicated that shock was “uncomfortable, but not painful”. Subjects were not told about the CS–UCS contingency. Each subject saw two slides, one of which (CS+) was followed by an electric shock (UCS) and the other (CS−) not. CS+ and CS− slides were randomly varied over subjects.

The experiment consisted of three phases. The first was a habituation procedure. It involved the presentation of 8 unreinforced trials (4 CS−-alone and 4 to-be CS+ -alone). An acquisition phase then followed in which 6 CS+–UCS pairings and 6 unreinforced CS− presentations occurred. To study the course of differential response during acquisition, a CS+–alone test-trial, that occurred halfway through the acquisition phase, was added. Finally, there was an extinction phase consisting of 10 unreinforced presentations of both slides. The order of presentation of the two slides was quasirandom; no more than two successive presentations of the same slide occurred.

**Analysis**

After the experimental procedure, subjects were questioned about their menstrual cycles. A period of five days prior to expected menstruation is usually considered premenstrual, but for caution reasons we extended it to seven. By this conservative estimate eight women fell into this group. The others (n = 23), at other points in their cycles except within seven days before menstruation, made up the control group.

Response to CS was defined as a maximal deflection occurring 0–4 s after CS-onset. Thus CR’s can be registrated independently from the occurrence of the UCS. SCR and SCL were measured in μmho and square-root transformed in order to normalize the distribution (Venables and Christie, 1973). Data were analysed as response magnitudes.

Using the t-statistic, group differences in mean shock level, resting SCL and neuroticism were examined. Separate three-factor analyses of variance with repeated measures were carried out for the three phases of the experiment. The first was a Group factor (premenstrual vs control group), the second a fac-
tor Stimulus (CS+ vs CS−) and the third a repeated measure factor Trials. The rejection level for all comparisons was set at p < 0.05 (Greenhouse–Geisser prob.).

RESULTS

The mean UCS level was the same for both groups, 9.3 mA (SD = 6.4) in premenstrual women and 8.9 mA (SD = 5.5) in the control group. These were moderate intensities, according to the criteria mentioned by Tursky (1973). There were also no significant differences in mean resting SCL (MPM = 4.26, SD = 4.46; MCTRL = 2.99, SD = 4.59) or in neuroticism scores (MPM = 55.1, SD = 15.1; MCTRL = 57.5, SD = 25.5).

SCR data are presented in Fig. 1. During habituation, the ANOVA revealed a significant Trials effect (F(3,87) = 4.92), indicating that habituation had occurred. No group differences were found.

Differences between groups emerged during acquisition and extinction. The significant Stimulus × Trials interaction (F(5,145) = 2.92) and the Trials factor (F(5,145) = 2.20) made it clear that the conditioning procedure had been effective; while responses to CS− trials showed a progressive decrease, the responses to CS+ increased. Post-hoc t-testing showed that this effect was due exclusively to differential responding in the premenstrual group (Fig. 1, middle panels). During the test trial, in the acquisition phase, more premenstrual women tended to react with a response (χ² = 2.57, 0.05 < p < 0.10) than did the control group and they tended to do so with a greater reaction (premenstrual = 0.600; control group = 0.280; 0.05 < p < 0.10) (Fig. 2).

Extinction is not complete as long as a reaction to CS+ is greater than it is to CS− slides. This is reflected in the significant Stimulus × Trials interaction (F(9,261) = 2.03). Post-hoc t-testing showed that this difference occurred only in the premenstrual group (Fig. 1, right panels). Another indication of the delayed extinction in the premenstrual group was the slight Group × Stimulus interaction (F(1,29) = 3.22; 0.05 < p < 0.10).

DISCUSSION

The data obtained are in line with those reported by Asso and Beech (1975) and Vila and Beech (1977) and they partly confirm our hypothesis. The acquisition of a classically conditioned skin conductance response was facilitated in premenstrual women as compared to women in all other phases of the menstrual cycle.

Though there was a significant difference between groups during extinction, this finding should be considered with some caution. Reactions to CS+ during acquisition did initially increase in the control group; however, reactions to CS− also followed the same course (Fig. 1). Therefore, one can hardly speak of acquisition of a conditioned response. This is in contrast to premenstrual women who showed an increased reaction to CS+ while the conditioned response to CS− decreased. The difference between the two groups during extinction can probably be explained by the simple fact that premenstrual women readily acquired a CR while the control group did not. Extinction in the premenstrual group did not occur immediately after the end of the acquisition phase, so that comparison of extinction between two groups is quite difficult and the question of delayed extinction remains as yet unresolved.

Differences emerge for the first time during acquisition. Why were premenstrual women readily conditioned to respond and the control group not? There were no striking differences that could account for this effect. The shock level was the same in both groups, so that the difference in reactions between the premenstrual and control groups cannot be explained by a difference in the intensity of the aversive stimulus. Neuroticism was also as high in the premenstrual women as in the control group. Thus, this particular psychological factor cannot have contributed to the facilitated conditionability of women in the premenstrual
Pre-menstrual women

Blocks of two trials

Control women

Blocks of two trials

Fig. 1. Mean SCR to reinforced (CS+) and unreinforced (CS-) stimuli as function blocks of 2 trials in premenstrual and control women.
phase. Both premenstrual women and the control group behaved the same during habituation. This means that women in the two groups did not differ in orientation reaction to the presentation of the slides. Another possibility could be the salience of the slides. However, slides were clearly recognizable pictures, with CS⁺ and CS⁻ equally balanced across groups. An important point to note is the intensity of the UCS. The UCS might have been not sufficiently aversive for strong conditioning to take place. As compared with the values reported by Tursky (1976) on the relationship between pain and electric shock, the intensities used are in between the “motivated” and “unmotivated upper threshold”. But we can only speculate about this effect, since in comparable studies (Öhman et al., 1978) no data about shock intensities have been reported.

To summarize, there is no psychological reason why women in this phase of menstrual cycle are more likely to form aversive associations. So the particular bodily state is probably what facilitates acquisition of fear and inhibits its extinction. These data add to the assumption that physiological state is a major determinant in the development of emotional disorders. The heightened susceptibility to phobic fears that returns each month, may be a reason for the high incidence of female phobic responses.

REFERENCES
MENSTRUAL CYCLE AND CONDITIONING


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