

THE INFLUENCE OF SHIFT WORK AND MENSTRUAL CYCLE PHASE ON
DEPRESSION AND OTHER SYMPTOMS REPORTED BY FEMALE NURSES

by

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The Influence of Shift Work and Menstrual Cycle Phase on

Depression and Other Symptoms Reported by Female Nurses

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ABSTRACT

The purpose of this study was to examine whether working night shifts has health consequences for female nurses and whether these consequences vary according to the phase of the menstrual cycle of the subjects. Both shift work and the premenstrual phase of the menstrual cycle have been found to produce a variety of symptoms, particularly depression, in women. The present study measured a series of symptoms with the Premenstrual Assessment Form, a questionnaire widely used for the assessment of premenstrual syndromes, and the Beck Depression Inventory on a sample of 26 female nurses. Repeated measures were taken weekly over a period of six weeks. The results show consistently higher endorsement of symptoms in a group of nurses who worked on rotating shifts compared with a group which worked only days. This effect was strongly related to the immediate consequences of working a night shift. There was an interactive effect between shift work and menstrual cycle which rendered women who work rotating shifts more vulnerable to depression premenstrually compared with the control group. This type of interaction was not found for the other symptoms examined. The results were discussed in terms of theoretical and practical implications.

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INTRODUCTION

While the awareness that we are influenced to some extent by environmental cycles, such as alternating day and night, tidal and lunar phases and seasonal changes, has been with humanity for a long time, we have only recently begun to understand the nature of this relationship. The systematic research accumulated over the last two decades has shown that practically all physiological parameters and many behavioral variables show some kind of rhythm (Webb, 1982; Aschoff & Wever, 1981). Many of these rhythms are not just passive responses to cyclic environmental conditions, but represent evolutionary adaptations that can anticipate environmental changes by means of a time-keeping biological mechanism (Aschoff, 1981a).

According to Monk (1982), the field had difficulties establishing itself initially because it challenged the widely accepted theories of static homeostasis in physiology and even now, disciplines such as medicine and psychology often do not take biological rhythms into account when giving out medication or conducting experiments. Possibly, the problem here lies in the interdisciplinary nature of the field and the difficulty of passing information across disciplinary boundaries. Nevertheless, the accumulated evidence indicates that there are specific daily, monthly, and even annual effects on many variables and that these

effects should be taken into account when doing research (Aschoff & Wever, 1981).

The application of biological rhythm research to psychology is very recent and has not yet permeated many areas of research. One of the first areas to be studied from the biorhythm perspective has been human performance. This type of research has primarily focused on the effect of night work on the job performance of shift workers (Colquhoun, 1981). To date, many other psychological, health, and physiological variables have been examined in shift workers and some of the findings from these studies now are ready to be applied to other areas of psychology.

The present study was stimulated by the need to continue to integrate biological rhythm research into psychological research. One area of research in psychology that seemed particularly connected with biological rhythms was the symptomatic changes that took place over the menstrual cycle in women. It was interesting to see that little research had been done on the relationship between menstrual changes and other types of biological rhythms. At the same time, a large proportion of research on the behavioral effects of biological rhythm manipulation (e.g., night work), had typically not included females in the studies. In the few cases where they had been included, controls for menstrual cycle phase had not been exerted. The aim of this study, then, became the examination of these

neglected areas in an attempt to clarify a part of the complex relationship between biological rhythmicity and behavior.

BIOLOGICAL RHYTHM RESEARCH

In order to describe this area of research it is necessary first to present some of the terms and definitions that have become part of the basic organization of the field. First of all, rhythms have typically been described in terms of sinusoidal curves that can succinctly display many of their temporal characteristics. The following are the basic terms used to describe these curves:

- Period: total time it takes for the repetition of a particular marker of behavior.
- Amplitude: half the difference between the peak value and the lowest value on the curve.
- Phase: the value of the variable at a particular point in time.
- Acrophase: time at which the measured variable has its maximum value.
- Mesor: the "center line" of the curve.
- Mean: the average value of the variable over the whole cycle.

(Rusak & Zucker, 1975).

About 30% of all biological rhythm research has concentrated on the detection of these rhythms and their description according to the parameters described above. Other studies have dealt with drug effects (18%), schedule effects (9%), and other theoretical or methodological

questions (Monk, 1982). Part of the task of defining a rhythm has been to demonstrate that the rhythm in question is not a passive response to an environmental cycle, but is produced by an internal clock mechanism. A way to do this has been to isolate subjects from environmental clues and then observe which rhythms continue to cycle on their own. Indeed, some observed rhythmicities appear to be entirely externally produced, and some authors have argued against the existence of internally controlled mechanisms. Brown, for example, has defended the hypothesis that all rhythms are externally produced. According to him, rhythms may appear to be internally originated because they persist under what is considered constant environmental conditions. However, normal laboratory constant conditions do not eliminate the influence of forces like geomagnetic fields that may very well be responsible for the rhythmicity. (Brown, 1976). With time, however, the evidence has come to support overwhelmingly the internal or "endogenous" origin of these rhythms. According to Moore-Ede, endogenicity of rhythms has been unquestionably supported, among other things, by the fact that they persist while on space capsules, are species specific, and can be genetically manipulated (Moore-Ede et al., 1982).

Endogenous rhythms are considered to be genetic adaptations to environmental periodicities (Pittendrigh, 1981a). Theoretically, this adaptation would have provided

an evolutionary advantage. An organism that can not only homeostatically respond to immediate changes but can also anticipate environmental changes relevant to food availability, safety from predators, mate finding, and climatic changes, can be best prepared to survive (Daan, 1981).

While the rhythms that we observe are not directly produced by the external environment, they are modified to some extent by environmental cycles. The endogenicity of a rhythm can be manifested only when we eliminate the influence of these external forces by placing the individual under constant environmental conditions. In these circumstances the rhythms are found to "free run", that is, they continue to cycle, but they do it with a periodicity that is slightly different from that of the removed environmental rhythm. This characteristic has given endogenous rhythms the denomination of "circa" (meaning, "near but not quite the same as") rhythms (Pittendrigh, 1981a). Of these "circa" rhythms, the daily or circadian ones have been most extensively studied, thus much of the information that follows is based on the properties of these circadian rhythms.

As we have seen, the rhythms that we observe under normal conditions are a composite of an internal periodicity and an external modifying or "entraining" influence. This entrainment changes the period of the rhythm in question and

fits it to the period of the environmental cycle. It also places the rhythms in phase with each other. Only some variables are capable of producing entrainment and these receive the denomination of "zeitgeber", German for "time giver". In the case of human beings, these zeitgebers are to a great extent time and social cues such as meal, sleep times, work hours, etc. Physical stimuli have been shown to also produce entrainment in humans, for example weak electric AC fields (Wever, 1986). Light, the major zeitgeber in animals, was until recently considered of lesser importance for human beings (Aschoff, 1980). However, recent research suggests that bright light, such as that found in most outdoors conditions, is indeed a very powerful zeitgeber for humans (Van Cauter, 1986).

Entrainment works by modifying the oscillator or clock mechanism inside the organism. The mechanism of entrainment has been extensively studied in animals, particularly for the zeitgebers light and food, and it basically consists of inducing phase shifts of up to two hours in one or the other direction (Mistlberger & Rusak, 1989). What has been found is that organisms respond differently to a zeitgeber input, depending on which phase of the examined cycle they are in. At some points of the curve the zeitgeber produces a maximal phase shift by phase delaying, at others by phase advancing. Yet, at other points there may be no response at all. The plotting of all these responses over the entire cycle

produces a "phase-response curve" (PRC) which is typical of each species, and even of individuals within a species (Moore-Ede, 1986). Because the typical free-running circadian period in humans is about 25 hours, and because normal zeitgebers can produce phase shifts of only up to two hours in either direction, we have a range of entrainment of 23 to 27 hours (Wever, 1986). Thus a zeitgeber with a period outside this range would not be able to entrain the circadian rhythms of an individual within a single cycle, even if the stimulus fell on the PRC zone where the response would be maximal. This is the problem we will encounter when we examine the consequences of shift work.

There are some added complications to the study of biorhythms. One of these arises from the fact that external influences can affect not only the oscillator, as in the case of entrainment, but can also influence a rhythm directly (Aschoff, 1980). This influence produces "masking" effects that alter the observable rhythm. This masking effect can even take place during "constant conditions" experiments because the subject's irregular routines of meals and bed times can modify the rhythms under study (Minors & Waterhouse, 1983). As a consequence, the underlying endogenous rhythm can be very difficult to isolate.

A second complication arises from the fact that some rhythms are strongly connected to the internal oscillator

while others are removed by several steps from this control. Furthermore, rhythms do not operate in isolation but influence each other in different ways. For example, the rhythm of deep body temperature, itself strongly dominated by the internal oscillator, can be externally modified by sleep since sleep onset decreases body temperature (Minors & Waterhouse, 1981). On the other hand, the structure of sleep is modified by the body temperature phase at which it takes place (Wever, 1982). Indeed, according to some authors, rhythms may not only act as masking influences on other rhythms, but may also become entraining internal zeitgebers themselves (Wever, 1986).

Under normal conditions, all the biorhythms of a particular organism have a constant phase relationship with each other and with the external environmental cycles. In this case it is said that they are internally and externally synchronized. As we have seen, when the individual is removed from his/her environment and placed in a situation of constant conditions, the rhythms free-run with a period of approximately 25 hours. This is a condition of internal synchronization and external desynchronization. However, after a prolonged period with constant conditions, the rhythms of some individuals become desynchronized from each other, that is, they start to free-run with different periods and a shifted phase relation to each other (Wever, 1986). Now these rhythms are said to be internally and

externally desynchronized.

According to Moore-Ede and Sulzman (1981), the fact that many individuals can maintain internal synchrony in the absence of strong environmental zeitgebers indicates that strong internal coupling mechanisms must exist. However, it is also true that under these conditions the internal coupling is more labile. About 24% of tested individuals desynchronize spontaneously in constant conditions and the proportion increases with age (Aschoff, 1981b). Furthermore, all subjects can be made to desynchronize when subjected to specific re-entrainment regimes. For example, under a 26 hr artificial zeitgeber, individuals can entrain their sleep-activity cycle, but their temperature rhythm continues to free-run with a near 25 hr period (Moore-Ede & Sulzman, 1981).

These findings are of particular interest because, together with the observation that different rhythms have a different rate of adaptation to a shift of the zeitgebers (Aschoff & Wever, 1981), they support the hypothesis that biorhythms are controlled by more than one central oscillator. The original interpretation of these findings defined two main oscillators, each driving their own rhythms (Wever, 1975). According to this position, one strong oscillator was thought to be responsible for the control of the rhythms of body temperature, urinary excretion of potassium, rapid eye movement (REM) sleep, and plasma

cortisol concentrations. Another, weaker, oscillator was thought to control the rest-activity cycle, urinary excretion of calcium, slow wave sleep, and plasma growth hormone concentration (Aschoff & Wever, 1981).

Recent research, however, has complicated the picture to some extent. While, as we shall see next, anatomical and physiological studies seem to support the existence of oscillatory capacity in different tissues, the question of how the system is coordinated remains unanswered (Menaker & Binkley, 1981). Some authors have added more organizing oscillators to the picture. For example, Moore-Ede and Sulzman (1981) hypothesize three main oscillator subsystems, one governing the rest-activity cycle, another the temperature cycle, and a third regulating the pituitary-adrenal axis. On the other hand, other authors have reanalyzed the evidence and found a plausible explanation with only one oscillator (Eastman, 1982), or have simply questioned the parsimony of the addition of more and more oscillators, suggesting instead that a central clock capable of multiple periodicities may explain the findings sufficiently (Folkard et al., 1985).

Evidence from anatomical and physiological studies suggests that we are dealing with a very complex system. To date, many body tissues, both inside and outside the central nervous system, have been found to have oscillatory properties. Adrenal gland, liver, kidney, pineal, and

suprachiasmatic nuclei (SCN) preparations all show persisting oscillations in vitro (Moore-Ede & Sulzman, 1981). While these oscillatory properties do not necessarily imply that all these tissues have the capacity to organize and coordinate the circadian system, they nevertheless indicate that many body systems have active rhythmic components.

According to Moore-Ede and Sulzman (1981), the circadian system is composed of many independent oscillators capable of entrainment to internal and/or external zeitgebers, and passive components which are responsible for immediate homeostatic responses. One example of this is the function of the kidney. The excretion of potassium appears to be controlled both by local oscillators which freerun in the absence of their entraining agent, cortisol, and by homeostatic passive responses mediated by aldosterone.

The next question, however, is whether there are centralized pacemaking structures which coordinate all these local oscillators and passive responders. To answer this question researchers have investigated specific areas of the central nervous system and, to date, the suprachiasmatic nucleus (SCN) has been found to be the best candidate. Support for its role as a pacemaker has come from experiments which have included lesions, electrophysiological recordings, electrical stimulation, and metabolic readings (Moore-Ede, 1986). The strongest

evidence, however, has been provided by studies in which animals lacking a SCN and showing no rhythmicity recovered their rhythms after an SCN transplant (Drucker-Colin et al., 1984).

A series of very detailed neuroanatomical studies has suggested that the SCN may be composed of two interconnected oscillators (the ventrolateral and the dorsomedial SCN), with the ventrolateral area receiving innervations from the two light-entraining pathways, the Retino-Thalamic-Tract (RHT) and the Geniculate-Hypothalamic-Tract (GHT) (Moore & Card, 1985). The nuclei would also receive input from other areas such as the hypothalamus and the midbrain, and relay their information to hypothalamic areas as well. All these characteristics, together with the additional information that there is great stability within the system, due to the large proportion of intrinsic connections within the nuclei, would give support to the role of this area as a central pacemaker.

The SCN may be a central pacemaker, but it may not be the only one. While it is possible that the SCN mediates the entrainment by light, entrainment by other zeitgebers, particularly feeding routines, appears to take place at some other site (Rosenwasser & Adler, 1985). Search for this pacemaker concentrated at first on the hypothalamic areas that have been associated with eating behavior. Initial results seemed promising, but later findings demonstrated

that ablation of these areas did not eliminate food anticipatory rhythms (Mistlberger & Rusak, 1989).

There is added complexity when we consider other physiological systems in relation to the SCN. According to Rosenwasser and Adler there are many influences that can modify the activity of the SCN. For example, the pineal gland and its hormone, melatonin, appear to have a feedback connection to the SCN via the hypothalamus; the raphe nuclei, implicated in circadian pituitary hormone secretion, has pathway links to the SCN, and the gonadal hormonal system has a feedback influence on the circadian system (Rosenwasser & Adler, 1985). In fact, gonadal hormones have been shown to modify the period of endogenous oscillations and thus exert an influence of the phase relationship between these oscillations and their entraining cycles (Aschoff & Wever, 1981; Moore-Ede & Sulzman, 1981).

In summary, anatomico-physiological studies indicate that the circadian system is composed of both passive and active elements, that oscillators exist both in the central nervous system and in other body tissues, and that there is possibly a central regulatory pacemaker, perhaps several, which have a coordinating function for the whole system. In turn, these central pacemakers can not only be entrained by environmental zeitgebers, but can be influenced by other central and hormonal systems as well.

The hormonal role is a particularly important one for

this study because the connection between the circadian system and the longer menstrual cycle is based on the role of these hormones. We have seen that hormones can have an influence on the oscillators or pacemakers. On the other hand, the circadian system is responsible for the rhythmic production of some hormones and, in some cases, uses hormones to transmit entraining information to different body systems (Moore-Ede & Sulzman, 1981). A more detailed review of this interrelationship will therefore be relevant for our section on the menstrual cycle later on.

First, however, we will have a closer look at the relationship between the circadian system and the consequences of shift work.

SHIFT WORK STUDIES

The consequences that the circadian system has for human behavior have been studied very extensively in regard to shift work. The interest in this area has been motivated by both theoretical and applied factors. On the one hand, shift work creates an ideal set-up for the study of how circadian rhythms respond to phase-shifting conditions. On the other hand, the increase in jobs demanding shift rotation has stimulated the study of the possible consequences that this disruption has on the workers. After two decades of intense study, it is well established now that shift work affects workers' behavior and that it produces undesirable health effects for some individuals (Colquhoun & Rutenfranz, 1980).

To understand why shift work can affect the worker's health, we have to examine how it affects the circadian system. The situation is similar to the situation we find in flights across several time zones: what we are dealing with is a shift of the entraining zeitgebers. The average person, with an endogenous period of 25 hrs and a range of entrainment of ± 2 hrs would take several days to readjust to a flight across 8 time zones. It is important to note that a change requiring a phase advance (as in eastward flights) forces one's internal clock to move towards "a shorter than 24-hour day". Because the entrainment to 24 hrs from 25 has

already used one of the two hours available in this direction, there is a possible phase advance of only one hour per day. In the other direction, however, a daily adjustment of three hours can take place. It is therefore generally easier to adjust to westward flights (Aschoff, 1980; Moore-Ede, 1986).

While adjustment to a new set of environmental zeitgebers takes place, the body is out of synchrony with the environmental cycle. Because different body rhythms adjust at different rates, as we shall see, these rhythms are out of phase with each other. The consequence of this state of affairs is what has been termed "jet lag", which produces symptoms such as disruption of sleep, feeling of malaise, gastrointestinal disturbances and decreased vigilance (Moore-Ede, 1986).

The symptoms described are similar to those found in night workers (Carpentier & Cazamian 1977). Adjustment to shift work requires a phase adjustment of at least 8 hours. The situation, however, is more complicated than in the case of time zone changes. With shift work not all the zeitgebers shift: changes in the sleep-activity cycle represents a change of only some zeitgebers, leaving the light-dark cycle and important social cues, such as meal times and activity schedules of other significant people, intact. Furthermore, the return to the normal schedule during weekends and days off counters any adaptation to

night work that may have taken place (Aschoff, 1980).

Even after prolonged periods on night shift, no circadian rhythm shows total reversal and different rhythms show different degrees of phase shift in response to a particular phase shift of the zeitgeber (Carpentier and Cazamian, 1977). Some rhythms are more persistent and adjust more slowly than others. This is due to the fact that they have a stronger endogenous component (Aschoff, 1980). A good example is the temperature rhythm. Under normal conditions this rhythm has a minimum at dawn, rises during the morning to peak at high afternoon and follows with a rapid fall after sleep onset. During night shift, rather than a total reversal of the curve following the rest-activity cycle change, we find that the curve flattens out, with a moderate fall during the night, a slight fall during the morning due to sleep, and a smaller rise in the afternoon (Van Loon, 1980).

A similar flattening of the curve is found in other resistant rhythms, such as those rhythms of urinary excretion of epinephrine and potassium, and of plasma cortisol (Folkard, Minors, & Waterhouse, 1985). Self-rated alertness and mood cycles also follow this pattern (Akerstedt, 1980a). More labile rhythms, however, can almost totally invert their pattern during night work. Good examples of this reversal are the rhythms of norepinephrine excretion (Akerstedt, 1980a), blood pressure, and, to a

lesser extent, heart rate (Sundberg et al., 1988). Given this anomalous situation, it is not surprising that night shift work can have adverse effects on the workers.

There is a copious literature dealing with symptoms found in shift workers. According to several large reviews of this literature, there is general agreement on the presence of certain symptoms, with gastrointestinal complaints, fatigue, and sleep difficulties being the most frequently cited. (Reinberg et al., 1983; Carpentier & Cazamian, 1977; Freser & Semmer, 1986). The symptoms studied generally fall under three main categories: sleep disturbances, somatic complaints, and mood problems.

In general, night workers complain of poor quality of sleep, difficulties remaining asleep, and generally shortened sleep (Akerstedt & Torsvall, 1980; Reinberg et al., 1983; Carpentier & Cazamian, 1977). This produces a state of sleep deprivation and fatigue which can result in reduced performance capacity (Akerstedt et al., 1987; Felton, 1975). As a consequence of this state of affairs, night workers tend to sleep more on days off to compensate for sleep loss (Tune, 1980).

The sleep disturbances experienced by night shift workers are a consequence of both the incomplete adaptation of the individual's rhythms to the new schedule and the environmental conditions under which they are trying to sleep. The first factor makes sleep more easily disrupted.

The second brings in variables such as environmental noises and light, which tend to disturb sleep.

The sleep period of a person who does night work takes place at a time when other circadian rhythms are preparing the body for action, not rest. Thus it is difficult to remain asleep (Carpentier & Cazamian, 1977). The tendency to wake up reaches a maximum at noon, when activating rhythms such as temperature and epinephrine have high values, and urine excretion is high thus adding the problem of a full bladder for the sleeping worker (Folkard, Minors, & Waterhouse, 1985). In addition, the pineal factor melatonin, which is important for sleep, is then at a low value (Akerstedt & Gillberg, 1982).

It has been found that sleep periods during which the temperature shows a steady increase, in contrast to the normal situation of progressive temperature decrease from the onset of sleep, are shorter. As well, sleep is reduced in cases where the temperature cycle has a low amplitude (Wever, 1982; Folkard, Minors, & Waterhouse, 1985). Both these conditions are met in the sleep of night workers. In addition, it has been found that the structure of sleep is affected by sleeping during the day. Both REM sleep and stage two sleep are shortened while slow wave sleep remains the same (Tune, 1980; Akerstedt & Gillberg, 1982).

Circadian disruption appears to be an important factor for the poor sleep of the shift worker. This is seen in

experiments which show that even under laboratory sound isolated conditions night workers sleep less well than day workers (Monk, 1989b). However, it has also been shown that several environmental factors affect the sleep of night workers in the home. Noise is an important variable since higher levels are found during the day, when the worker is trying to sleep (Knauth & Rutenfranz, 1980b). In addition, family and social demands interrupt this sleep: family duties such as child care, shopping, etc., still have to be met. As well, day sleep is not protected by general social customs, and so other people may, for example, phone in the middle of the worker's day sleep whereas they wouldn't think of calling someone in the middle of the night (Monk, 1989b).

In addition to sleep disturbances, a large group of somatic changes has been extensively studied in night shift workers. In a study of retrospective sick records of 370 male shift workers and 270 male day workers, Angersbach et al. (1980) found more gastrointestinal diseases, injuries related to accidents, and sickness-related work absenteeism in the group of night workers compared to the day workers. Many other studies in the work place have confirmed these results, particularly for gastrointestinal problems such as indigestion, constipation, and gastric ulcers (Reinberg et al., 1983; Carpentier & Cazamian, 1977, Koller et al., 1980). The results hold in experimental shift manipulation studies as well (Akerstedt & Torsvall, 1980). Furthermore,

night shift workers who go back to day work seem to experience a relief from the complaints they had under night work conditions (Akerstedt & Torsvall, 1978).

According to Carpentier and Cazamian (1977), digestive problems in night workers are connected to circadian rhythm desynchrony. This is due to the ingestion of food during the night shift, when the digestive system is in a state of deactivation. Furthermore, the presence of ulcers may indicate an abnormal function of digestive enzymes normally controlled by the hypothalamus and dependent on circadian rhythmicity. Finally, shift work is likely to increase life stressors due to the lack of synchrony between the worker's schedule and that of the rest of society, and this increased stress can also be responsible for digestive problems (Selye, 1982).

A third area of symptomatology found in night shift workers includes mood disturbances. According to Carpentier and Cazamian (1977), night shift workers experience 64% more nervous disorders than day workers. These disorders are particularly related to aggression and depression. Akerstedt & Torsvall (1980), in an experimental shift manipulation study, found complaints of depression, apathy, irritation and restlessness in subjects on the experimental shift group. Furthermore, these subjects had social difficulties (felt socially isolated). All these complaints disappeared or greatly improved when the subjects were returned to

normal day schedules. Reinberg et al. (1983), after a comprehensive review of the literature, also concluded that irritability and depression were common problems among shift workers. They also found that retired shift workers who had worked night shifts for many years presented more cases of depression than retired day workers. They suggested that this depression might be a lasting effect of working shifts. However, it could also be possible that the sample examined had more tendency for depression in the first place.

There is some evidence connecting depression to specific circadian changes. According to Reinberg et al. (1983), internal desynchronization of circadian rhythms is associated with major affective disorders. Endogenous depression has been related to a phase advance of the circadian rhythms by several authors (Goodwin, 1984). It also appears that subjects with a smaller circadian amplitude, also associated with night work conditions, tend to be more depressed (Wehr, 1982). Furthermore, studies of temporal isolation in which acute phase shifts were induced, produced a clear increase in sadness when compared with the base line (Monk, 1989a).

While the evidence supports a relationship between circadian changes and depression, it is also possible that social factors brought about by the shift schedule may be conducive to depression. Night workers do complain more than

day workers about not having enough time for leisure activities (Akerstedt & Torsvall, 1980). They are less likely to be members of organizations and have fewer friends (Folkard, Minors, & Waterhouse, 1985). Often the problem would seem to be due to the way that activities in society are normally scheduled to meet the requirements of people who work during the day. This fact may create a situation of social isolation for the night worker which may contribute to depression.

It appears then, that the sleep, somatic, and affective symptoms that we find in night shift workers are due in part to circadian changes and in part to environmental and social influences produced by the work schedule. In addition to these group differences, however, there are important individual differences that need to be considered.

It is well known that not all workers who work night shifts suffer from adverse symptoms. According to Folkard, Minors, and Waterhouse (1985), only 20 to 30% of shift workers are adversely affected by night work, 60% cope relatively well, and 10% positively enjoy it. However, it is hard to know what the adverse effects of night work can be in the general population because there is a certain degree of self-selection among shift workers. Often the workers who have the hardest time coping with shift work tend to find other jobs. In fact, according to Moore-Ede (1986), some early studies that showed no adverse effects for the

shift workers had failed to account for this self-selection effect.

A great body of research has concentrated on finding individual differences that may explain the observed differences in responses to night work. As we shall see next, many of the differences found appear to be related to specific characteristics of the circadian system of these individuals. Furthermore, other variables such as personality, age, and gender have been found to interact with shift work adaptation. More interestingly, there appears to be a relationship between these last three variables and the circadian type of the individual.

Among the circadian characteristics that appear to be related to better adaptation to shift work, amplitude of the circadian rhythms has been extensively studied. It has been found that the higher the amplitude of a rhythm, the greater its resistance to phase adjustment (Aschoff, 1980; Minors & Waterhouse, 1983). Because, as we have seen, it is impossible to completely adjust the circadian rhythms to the conditions of night work, it may actually be an advantage to have rhythms that are more resistant to change so that the worker remains synchronized to the stronger zeitgebers and thus avoids internal desynchronization. In fact, many studies have shown that a high amplitude of the body temperature rhythm is associated with a better tolerance for shift work. These individuals adjust their rhythms slowly

and only partially to a change of the zeitgeber (Reinberg et al., 1983; Reinberg, Vieux, et al., 1980; Reinberg, Andlauer, et al., 1980), and suffer from less desynchronization than subjects with a low amplitude rhythm (Reinberg et al., 1988).

Temperature rhythm amplitude has also been related to subjects' diurnal type. It is well established that some individuals tend to wake up spontaneously early in the morning and function better at this time, while others function better in the evening, tend to stay up later, and wake up later. The former is referred to in the literature as the morning type, the latter as the evening type (Horne & Ostberg, 1976). An interesting finding is that morning types tend to have a low-amplitude temperature rhythm while evening types have rhythms with a large amplitude (Reinberg et al., 1983).

It appears that morning types adjust less well to shift work than evening types do (Akerstedt, 1980b; Kerkhof, 1985; Folkard et al., 1979; Ostberg, 1980; Moog, 1987; Costa et al., 1989; Monk, 1989b). Compared to evening types, morning types give up shift work more frequently, have shorter sleep periods, have less REM sleep, and suffer greater desynchronization due to transmeridional flight (Kerkhoff, 1985). According to Breithaupt et al. (1980), morning types have more difficulties with shift work because their circadian rhythms are phase advanced compared with evening

types and, as a consequence, have more difficulty sleeping in the morning after night work. As a result, they are more sleep-deprived than evening types. However, the picture is probably more complicated than this, since, as we have seen, not only phase position but also amplitude and rhythm-resistance-to-zeitgeber influences are related to diurnal type. In fact, morning and evening types differ on many variables, such as catecholamine excretion, food intake, subjective alertness, and performance on some psychological tests (Colquhoun & Folkard, 1980; Patkai, 1971a).

Another level of complexity arises from studies showing that there is a relationship between diurnal type and some personality variables. Some authors have found that morning types tend to be more introverted and evening types more extroverted (Patkai, 1971b; Colquhoun, 1981). Colquhoun and Folkard (1980) studied the variables introversion, extroversion and neuroticism in relation to shift work and found that individuals classified as neurotic introverts using Eysenck's categories adapted poorly to shift work. These individuals also showed the greatest amount of desynchronization during transmeridian flights when compared to neurotic extroverts and non-neurotic individuals.

Neuroticism appears to interact both with introversion and morning-ness in terms of shift-adaptation capacity. Of all the possible combinations between the variables

neuroticism, introversion, extroversion, evening-ness, and morning-ness, the combination morning type neurotic introvert has the worst prognosis for adaptation to shift work, presenting more health complaints than any of the other groups (Nachreiner, 1980). On its own, neuroticism seems also to be related to a greater tendency to suffer spontaneous desynchronization in constant conditions (Colquhoun, 1981). Similar findings are supported by other studies as well (Kerkhof, 1985; Harma et al., 1988a).

Age is another important factor that is related to circadian characteristics and to adaptation to shift work. According to a review by Kerkhof (1985), temporal isolation studies show an increase in both internal and external desynchronization after a certain threshold age (between 35 and 45). As well, the amplitude of the rhythms diminishes and there is a tendency towards more "morning-ness". At the same time, it has been observed that adaptation to shift work is worse after the age of 40 (Akerstedt, 1980b). In some cases, workers who tolerated shift work well become intolerant after this age (Carpentier & Cazamian, 1977). Part of the problem is that sleep changes with age in a way that adds to the night worker's problems. Tune (1980), in a study of male workers, found that the sleep of night shift workers was subject to more disturbances after the age of 45.

Finally, another variable that may explain some individual differences and which is particularly relevant for this study is gender. Kerkhof recently conducted a comprehensive review of research in this area and concluded that the evidence is scant and inconsistent (Kerkhof, 1985). One of the problems has been that the majority of studies in the field have been conducted with male subjects only. However, as the number of women who work shifts increases, the question of how they are affected by this regimen becomes more relevant.

Some of the studies reviewed by Kerkhof showed differences in the circadian rhythms of females that may be relevant for shift work adaptation. With respect to the temperature rhythm, women seem to have a higher mean and a smaller amplitude than men. Wever (1984) conducted several studies in which he examined the free-running sleep-wake and temperature rhythms of women. It was found that when the rhythms were internally synchronized, the periods of the sleep-wake and temperature rhythms were shorter and the acrophases occurred earlier in females compared to males. At the same time, the fraction of the 24-hour period spent in sleep was longer in the females. However, during internal desynchronization, the rhythms changed in opposite directions. The sleep-wake cycle became even shorter in females but the temperature rhythm became more similar to the rhythm previously found in males. The sleep-wake cycle

thus appears to be responsible for the sex difference observed under normal conditions.

Overall, these findings indicate that females have a circadian pattern that tends more toward "morning-ness" (earlier acrophases and shorter periods) and produces more unstable rhythms (as found for individuals with smaller amplitudes). As we saw earlier, these characteristics have been associated with poor tolerance for shift work. Furthermore, the greater fraction of sleep found in females (Wever, 1984) may result in a greater impact by the sleep deprivation typically found in those who work nights.

Very rarely have the studies of shift work included both males and females in their samples. One of these rare studies of shift work done using both male and female subjects found that there was an overall similarity between males and females in terms of the kind of health disturbances which seem produced by shift work. Gastrointestinal complaints, sleep problems, irritability, tension and nervousness are reported with greater frequency both in male and female nurses on shift work schedules when compared with health care workers doing day work. However, the female nurses complained of fatigue more often than the male nurses did (Bosch and de Lange 1987).

Of the studies conducted with female subjects, the symptoms described are generally similar qualitatively to those found for male subjects in the literature, but it is

difficult to compare the intensity of the complaints. Again, greater fatigue and more sleep disorders have been found in women compared to men (Kerkhof, 1985). Other studies of female nurses have included additional variables that appear to interact with adaptation to shift work. For example, nurses on rotating shift schedules have been found to have more subjective health complaints compared to permanent night nurses (Verhaegen et al., 1987), and nurses with better physical fitness tolerate night shift work better (Harma et al., 1988b; Harma et al., 1988c). Marital status affects the adaptation of women to night work as well, with married female nurses presenting more psychological complaints than their single female coworkers (Bosch & de Lange, 1987).

Overall, we do not yet have a conclusive answer as to whether women are more severely affected by shift work than men. An added complication to the study of sex differences that is central to this study is the fact that, as we shall see in the next section, women experience circatrigintan rhythms related to the menstrual cycle and that these rhythms have some connection to the circadian system. For example, circadian phase shifts have been shown to affect the ovulatory cycle. Preston et al. (1974) found that ovulation was delayed during transmeridian flights. It is possible, as well, that menstrual cycle phase could affect the response to night work. Nevertheless, this factor has

typically not been examined in the studies of sex differences in circadian rhythms and shift work. Some of the contradictory results found in the literature and the greater variation observed in females (Kerkhof, 1985) may be related to this variable.

Some authors have suggested that the greater fatigue observed in female shift workers may be the result of an increased nocturnal deactivation during certain phases of the menstrual cycle (Carpentier & Cazamian, 1977). In fact, Lee (1988), in a careful study of the female temperature rhythm has found that the mesor was significantly higher and the amplitude significantly smaller during the second half of the menstrual cycle (luteal phase) compared to the first half (follicular phase). Higher premenstrual temperature, a widely reported result (Reinberg & Smolensky, 1974; Simpson & Halberg, 1974), has generally been associated with the thermogenic properties of progesterone, the hormone produced after ovulation. The sex difference found in the temperature mesor could be entirely related to this menstrual variation. The rhythm amplitude, however, remains lower in females compared to males throughout the whole cycle, but the difference is more extreme during the premenstrual phase of the females (Lee, 1988).

We have seen that a dampening of the temperature rhythm has been associated with poor adaptation to shift work. Since amplitude seems to be lower for women during the

luteal phase, it is possible that this factor would interact with shift work perhaps to produce more symptoms during this time. Typically, the premenstrual phase has been associated with symptoms similar to those found in poor shift work adaptation, thus, a connection seems likely. We will next review the area of research dealing with menstrual cycle physiological and behavioral changes.

MENSTRUAL CYCLE STUDIES

The female menstrual cycle has been a very widely studied rhythm due to its importance for human reproduction and the number of medical complaints related to it. It appears that in addition to the primary hormonal changes responsible for the cycle, there is a large number of secondary physiological and behavioral rhythms coupled to it. Some studies have concentrated on examining these primary and secondary rhythmic parameters over the whole cycle, but there is a large volume of recent studies that have centered on specific differences between the follicular and the luteal phases. This interest has arisen, as we shall see later, from the finding that some women appear to suffer from a series of medical and psychological symptoms of varied intensity during the premenstrual phase of their cycles.

The primary hormonal variations responsible for the ovulatory cycle show a reliable pattern. The concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) vary with a similar pattern, both increasing at mid-cycle. Estrogen production has a more complicated pattern, with a steady increase from the menstrual phase and a preovulatory maximum, followed by a rapid decrease and a new steady luteal increase followed by a final drop just before menstruation. The peak of LH that occurs at mid-cycle

is responsible for ovulation and takes place just after the peak of estrogen concentration. After ovulation progesterone production takes place, reaching a maximum at mid-luteal phase, falling rapidly just before menstruation, and remaining low throughout the rest of the cycle (Garling & Jo Roberts, 1980; Dyrenfurth et al., 1974).

While all ovulatory cycles in women are characterized by this same hormonal pattern, variations in cycle length are common, with average cycles between 25 and 30 days for women in their mid-twenties and thirties. Longer cycles are typical of very young women and women in their forties. This variation is mainly due to variability of the first part of the cycle. The postovulatory phase is less variable, lasting approximately 13 to 14 days. Anovulatory cycles, which do not show this hormonal pattern, are of longer duration, and again, are more frequent in women under 25 or over 40 (Presser, 1974).

Among the studies examining secondary rhythms associated with the menstrual cycle, contradictory results are frequently reported. Part of the problem has been methodological and part has been due to the existence of large individual differences in the normal population. Different studies have used different methods, some less precise than others, to determine the hormonal status of the individual cycle. In other cases, relevant confounding variables, such as cycle length, have not been considered

(Dennerstein & Burrows, 1979). For example, Dalton (1964) suggested that reaction time may be longer premenstrually after she observed test results with school girls. Other authors, however, found no evidence for this change (see review by Gamberale, 1985). Nevertheless, when cycle length is included as a variable, the picture changes. Engel and Hildebrand (1974) studied reaction time, heart rate and blood pressure, and found that all these variables peaked premenstrually in those with cycles of an average 28 days duration. In longer cycles, however, the acrophase advanced towards the follicular phase with the longest cycles showing, additionally, a second peak starting premenstrually again. This finding is particularly interesting because, as the authors concluded, it provides support for the existence of two different oscillator systems, one responsible for the main hormonal variations, the other for the secondary circatrigintan rhythms. It is then not surprising that we find wide inter-individual variations, depending on how these two systems are coupled to each other.

Reinberg and Smolensky (1974) conducted a meta-analysis of the menstrual cycle literature using the chronobiological statistical techniques of least squares spectral analysis and cosinor methods. About 60 parameters were found to have statistically significant circatrigintan variations. Of these, some neurological factors increased premenstrually, for example, reaction time, depression, irritability, and

sensitivity to pain. Other factors that peaked premenstrually were body weight, pulse rate, capillary permeability, oral temperature, and mammary volume, among many others. On the other hand, pulmonary variables, such as vital capacity, and gastrointestinal variables, such as parietal secretion and HCl concentration, peak before the ovulation takes place. Again, the studies show wide individual differences, and there is great variation among the studies in terms of methodology and design as well. However, the analysis allowed the authors to conclude that the patterns found were consistent with a premenstrual predisposition to certain correlates.

The literature available on premenstrual complaints has reported emotional changes that include increased tension, anxiety, depression, irritability, and hostility, and physical symptoms that include bloating, breast tenderness, weight increase, backache, headache, food cravings, and gastrointestinal problems. Fatigue and sleep problems have also been reported (Abplanalp, 1983; Logue & Moos, 1986). All these symptoms are consistent with the circatrigintan variations found by Reinberg and Smolensky (1974). A premenstrual psychological susceptibility to irritability and depression would explain the emotional changes. A change in water retention, as predicted by an increase in renin concentration and activity and high aldosterone levels, could be responsible for the weight increase, bloatedness,

and breast enlargement. Gastrointestinal problems could be a consequence of the changes in HCL and parietal secretion (Smolensky, 1980). Fatigue may be due to changes in pulmonary function and changes in the catabolic processes which rely more on anabolic processes premenstrually (Reinberg & Smolensky, 1974). Sleep problems may be influenced by any or a combination of these symptoms, or it may be due to a modulation of the circadian sleep-activity rhythm by the circatrigintan patterns.

Some authors have argued for the existence of a premenstrual syndrome (PMS) (Dalton, 1982), others for a series of premenstrual sub-syndromes (Endicott et al., 1986), yet others have argued against the existence of any syndrome at all (Ruble, 1977; Aubuchon & Calhoun, 1985). One of the problems is that some of the secondary menstrual changes are very subtle. For example, Henkin (1974) studied sensory changes for taste, smell, auditory signals, and tactile perception every two days for a period of six weeks in five women. The luteal phase of the menstrual cycle showed a decrease in detection acuity in each of the sensory modalities, but the changes remained well within normal range. Looking at auditory acuity more carefully, the authors argued that the changes could be caused by changes in sodium and potassium balance induced by progesterone which could alter the inner ear fluid balance. For some women, this could result in a serious problem, while for

others it would remain unnoticed. We are, then, talking about a certain predisposition, on the one hand, and individualized responses on the other.

Many of the studies that have found no premenstrual symptoms in women have used samples of normal, college aged women. Negative findings in these cases are not surprising since in fact, PMS as a medical or psychiatric category, is found primarily in a subgroup of women typically older than those found in a college sample. Prevalence estimates vary, ranging from 30% to 70% of women in the general population (Dalton, 1964). A more recent review estimated the prevalence of severe PMS at 2%-10%, while 40% of women may experience milder symptoms (Logue & Moos, 1986).

The problem does not end with the selection of the sample, however. The PMS literature has heavily relied on the use of retrospective questionnaires and has not controlled for subject bias. Youdale (1985) used a premenstrual symptom questionnaire both retrospectively and concurrently and found that while somatic symptoms were reported similarly in both cases, affective changes were over-reported in the retrospective measures compared to the concurrent ones. Similar findings have been obtained by other authors (Endicott & Halbreich, 1982) and raise the question of the degree to which results reported in the literature have been inflated by this retrospective bias.

Subject bias is an issue for all studies using

subjective questionnaires, especially if it is not possible to keep subjects naive as to the nature of the study. It is possible that once the purpose of the study has been guessed, variables such as social attributions, role expectancy, and compliance effects, would bias the answers (Abplanalp et al., 1980). For example, Aubuchon and Calhoun (1985) found that subjects who were informed of the purpose of the experiment reported more affective and somatic symptoms than subjects who were deceived with respect to the purpose of the study. Ruble (1977), in a very ingenious experiment, managed to get her subjects to believe that they were in their premenstrual phase and found that they consequently reported more symptoms, regardless of their true position in the cycle.

It is, therefore, possible that women have a negative attitude towards the premenstrual phase of the menstrual cycle and that this is reflected in how they answer on subjective measures. It is also possible, as some researchers have found, that women tend to attribute negative changes taking place premenstrually to health-cycle factors while the same changes would be attributed to work and personality factors intermenstrually (Bains & Slade, 1988). On the other hand, attitudes toward premenstrual changes can be a product of the experience with the symptoms suffered previously. For example, Woods (1985) examined factors such as stress, socialization and intensity of

somatic symptoms, and found that the latter had the strongest influence on negative premenstrual affective symptom reporting.

Bearing in mind these considerations, the large accumulated body of literature on PMS nonetheless provides enough support for the existence of a premenstrual syndrome to have it included as a tentative diagnostic category in the DSM-III-R (American Psychiatric Association, 1987). The symptoms that have received most attention from this perspective center on affective changes, particularly depression. This symptom, however, is particularly difficult to interpret due to several factors. First of all, it is one of the symptoms that can get differentially inflated in retrospective reports, as we saw earlier. Secondly, it may be tied to ongoing mental illness, or to personality factors.

Endicott and Halbreich (1982) found that women who suffered depression premenstrually tended to have depressive symptoms throughout the month and often had a history of affective illness. There is a higher probability that women with a history of mental illness will develop a premenstrual syndrome with affective symptoms (Endicott et al., 1985). As well, women with PMS have a higher risk for developing a mental illness later in their lives (Wetzel et al., 1975). Similar findings have been obtained by other authors as well, and while major depression has been most readily

associated with PMS, other mental disturbances, such as borderline personality disorder have been found to be correlated with it as well (Clare, 1983; Hurt et al., 1982,).

In spite of the relationship found between PMS, depression, and affective disorder, the depressive changes seen in PMS are not identical to those found in endogenous depression. On the one hand, premenstrual depression is not as severe and does not last as long as endogenous depression (Endicott et al., 1985). As well, some of the physiological changes found in endogenous depression, such as an abnormal cortisol response to suppression by dexamethasone, are not found during premenstrual depression (Haskett et al., 1984). However, the higher concentration of cortisol found in endogenous depression has been found in PMS as well, although there is no general agreement on this point. Some studies show a higher cortisol production in response to stress premenstrually, while others show no variation (Haskett et al., 1984; Collings et al., 1985; Abplanalp et al., 1977). Another factor typically associated with endogenous depression, insomnia with early morning awakening, is found in some PMS women while others show a pattern of hypersomnia more common in atypical depression (Patkai et al., 1974; Halbreich et al., 1983). These findings indicate that depression is a complex ailment and that premenstrual depression may include different subtypes

of the disorder in the same way that affective illness includes different types of depressive disorders.

A further complication is the fact that personality factors have been associated with PMS as well. On the one hand, some women seem to experience personality changes over the menstrual cycle. On the other, women with certain personality types are more likely to experience PMS. Mohan and Chopra (1986) found that scores on neuroticism, psychoticism, and anxiety all increased premenstrually while extroversion was not affected. Golub (1980) measured personality in women using an adjective checklist and found many significant correlations between personality variables and premenstrual mood changes. As well, women high in neuroticism have been found to experience PMS more frequently and the higher the neuroticism the higher the PMS affective changes reported (Van Der Ploeg, 1987).

Given all the findings described above, it is clear that the question of the aetiology of PMS could not be a simple one and that the finding of one single causal factor would be very unlikely. It is probably best to frame the question from the perspective of an "individual differences" model such as the one proposed by Sommer (1980). In this model, menstrual cycle events may or may not produce symptomatic problems in women, with the consequences mediated by individual differences in personality and coping factors, biochemical predispositions, stress level, current

health status, age, etc. In addition, a biological rhythm perspective could provide a good ordering framework for all these differences.

To date, no single factor has been found to account conclusively for the symptoms found in PMS. The first attempt was directed at the hormonal changes found during the menstrual cycle, but the results have been mixed. Katherine Dalton (1964, 1982) has argued on repeated occasions for the importance of low progesterone level as a causative factor in PMS and has defended the therapeutic properties of progesterone administration during the premenstruum. However, this conclusion has been questioned on the grounds that double-blind studies often do not show an advantage of progesterone over placebo administration (Parlee, 1982) and that the combination high progesterone and low estrogen may actually be associated with more depressive symptoms (Clare, 1985).

Klaiber et al. (1974) conducted an interesting study on plasma monoamine oxidase (MAO) activity, EEG, and behavior during the menstrual cycle. MAO is an enzyme responsible for the break down of monoamines in the brain. Low concentrations of these neurotransmitters, as well as high MAO activity have been associated with depression (Van Praag, 1978). Interestingly, Klaiber and co-workers found not only that MAO activity was significantly higher during the premenstrual phase in women, but also that this activity

could be slowed down by administration of estrogen. Furthermore, they studied the relationship between these two factors and central monoamine (adrenergic) activity by measuring EEG driving responses to photic stimulation (this is the ability of the EEG to couple its rhythm to the frequency of a flashing light placed in front of the closed eyes) which have been associated with central adrenergic function. Their results provided strong support for the association between low MAO activity, high central adrenergic function and the high estrogen level found during the follicular phase of the menstrual cycle. The opposite pattern was found premenstrually. In addition, they studied behavioral consequences of the central adrenergic function by examining the responses to the Frame and Rod Test for Perception of Verticality. Because increased central adrenergic activity has been associated with an enhanced sensory response, they hypothesized that poorer performance on the perceptual test would be found premenstrually. Their results confirmed this hypothesis, thus adding support to the association between premenstrual phase and low central adrenergic activity.

Other authors have found an association between estrogen production during the follicular phase and positive mood, and between progesterone production and negative mood during the luteal phase (Backstrom et al., 1983; Persky, 1974). Rossi (1980) found that the picture was a bit more

complicated. She studied psychological, physiological and social factors in relation to menstrual cycle mood changes and found that both positive and negative moods could be found in the follicular phase, and that these could be predicted to some extent from specific social and psychological influences. However, the luteal phase showed an increase in negative mood together with a decrease in positive mood, and that these changes could not be predicted well from psycho-social variables, thus leaving physiological variables as good explanatory candidates for these changes.

Aside from progesterone, estrogen and monoaminergic changes many other factors have been associated with menstrual changes. For example, aldosterone and renin have been associated with water retention (Janowsky & Raush, 1985), testosterone with irritability-aggression (Persky, 1974), and melatonin with hypersomnia (Clare, 1985). Despite all these correlations, however, it is important to note that when women with and without PMS are compared, no differences in their hormonal patterns are usually found (Backstrom et al., 1983, Clare, 1985). It could be that the circatrigintan hormonal changes could provide a susceptibility that only under given additional circumstances would produce disturbances. At this point, it is relevant to include in our review a broader discussion by integrating the biological rhythm perspective with the

menstrual cycle findings.

CIRCADIAN RHYTHMS AND MENSTRUAL CYCLE CHANGES

The menstrual cycle is related to other biological rhythms in a complex way. It has been observed that gonadotropins (LH and FSH) and the ovarian hormones are secreted with an ultradian or pulsatile rhythm (Yen et al., 1974) and that they also show circadian and circannual rhythms (Smolensky, 1980). These systems of rhythms are interconnected by feedback mechanisms that result in an interactive network that can be examined at the anatomical and physiological levels. As we saw earlier, the pituitary, responsible for the production of the gonadotropins which in turn stimulate the production of ovarian hormones, interacts with the Raphe nuclei. These nuclei are themselves connected to the SCN, the most likely central pacemaker, as discussed above. We also saw that gonadal hormones could modify the periodicity of endogenous rhythms. More specifically, animal studies have shown a two-way relationship: ovarian hormones seem to affect the circadian system, but changes in the circadian system also affect the production of ovarian hormones. For example, estrogen seems to have an effect on the circadian pattern of locomotor activity in rats, mice and hamsters, with estrogen increase resulting in a phase advance, a shortening of the period, and a higher mean activity rhythm (Wollnik & Turek, 1987; Moline & Albers, 1988; Cambell & Turek, 1981).

On the other hand, the production of estrogen seems to be controlled by an endogenous oscillator which is affected by the light-dark cycle. Support for this comes from studies which have shown that ovulation in rodents occurs at a fixed time of the day and that a phase advance of the light-dark cycle produces a phase shift of the timing of the ovulation (Turek et al, 1984). Furthermore, exposure to constant light leads to a disruption of the estrous cycle in the hamster and to a state of constant estrus in mice (Campbell & Turek, 1981).

The rhythmic control of the estrous cycle in animals appears to take place at the level of the secretion of gonadotropin. For example, lesions of the SCN in rats and hamsters prevent the surge of LH preceding ovulation (Turek et al., 1984). While estrogen has an important influence on the surge of LH, as demonstrated by studies with ovariectomized rodents treated with estrogen, it has been observed in ovariectomized hamsters that the LH surge can take place in the absence of estrogen as well (Turek et al., 1984).

Given this and other similar information, some authors have arrived at the conclusion that the SCN exerts some control over the production of ovarian hormones via the pituitary gonadotropins while at the same time, the ovarian hormones influence circadian rhythms via a feedback mechanism to the SCN. Because of the ability of gonadal

hormones to alter the period and phase of the circadian rhythms, some authors even suggest a role of these hormones in oscillator coupling (see review by Rosenwasser and Adler, 1986). In this way, variations in ovarian hormone concentrations throughout the menstrual cycle can be both connected to other centrally timed variables and also have specific effects on many other aspects of the hormonal and neural systems.

In this context, it would not be surprising to find a relationship between the alteration of circadian rhythms brought about by shift work and the monthly hormonal and behavioral variations brought about by the ovarian cycle. We saw earlier that shifts in the circadian system affected the time of ovulation in women (Preston, 1974). It has been observed that the surge of LH responsible for ovulation tends to happen in the morning in women, and that other events related to reproduction also show this tendency (e.g., births tend to occur more frequently in the early hours of the morning) (Smolensky, 1980). On the other hand, the menstrual cycle seems to have a modulating influence on the circadian variation of many parameters. We have seen how it tends to reduce the amplitude of the temperature and the rest-activity cycle premenstrually. Other cycles seem to be affected differently. For example, the cutaneous response to histamine, house dust, and other antigens shows a menstrual variation with higher premenstrual cutaneous

reactivity. At this phase of the cycle, the circadian amplitudes of these parameters are the largest and the acrophases occur later in the day. The opposite pattern is found at mid-cycle (Smolensky et al., 1974). These changes are the opposite of those found for the temperature and the rest-activity cycles. It is possible then, that the premenstrual period may induce desynchronization with different rhythms phase shifting in different directions.

This possibility for desynchronization we also saw to be greater under conditions of shift work, particularly for individuals with lower amplitude and earlier acrophases in their temperature rhythms ("morning types"). These characteristics were associated with more symptoms in these shift workers. As well, the menstrual cycle tends to produce symptoms in women at the time when lower temperature amplitudes and earlier acrophases are observed.

Interestingly, many of the symptoms experienced by shift workers and premenstrual women are similar. Fatigue, irritability, depression, sleep disturbances, social difficulties, and gastrointestinal problems are found in both groups. It is interesting to note that PMS seems to worsen in the mid-to late thirties (Dalton, 1964) and that shift workers experience more difficulties starting at this age as well (Kerkhof, 1985). As we saw earlier, these changes in shift work adaptation have been attributed to an increased tendency to more "morningness" with increasing

age. Perhaps we have a similar situation in the case of PMS.

Having a closer look at the symptom of depression, we have seen that there is solid support for the association of endogenous depression and a tendency to have circadian rhythms which are phase advanced (Goodwin 1984) and which are internally desynchronized (Reinberg et al., 1983). Some authors have suggested that the higher incidence of depression found in women could be related to the fact that women seem to have shorter circadian rhythms with earlier acrophases and smaller amplitudes (Wever, 1984). This, of course would be more prevalent premenstrually. On the other hand, as we saw earlier, individuals subjected to an experimental phase shift of their circadian rhythms showed an increase in sadness when compared to their previous baseline (Monk, 1989a). As well, the REM sleep pattern found in the sleep of night workers is similar to the pattern found in depression, with a shortened REM latency, longest first REM period, and progressive decrease of REM throughout the sleep period (Wever, 1982).

While the connection between depression, phase shifts, and circadian type is very compelling, many other influences could be important as well. As Reinberg et al. (1983) have pointed out, rhythm alterations do not by themselves produce a depressive illness. We have repeatedly seen how individual differences create a varied response to both shift work and

to menstrual cycle changes. A higher physiological or rhythmic vulnerability is moderated by different situational and personality variables which result in different coping capacity and different outcomes. For example, commitment to a particular job has been found to have an effect on the health consequences of shift work since committed workers tend to adapt their lives to the job in ways that minimize the impact on their health (Minors and Waterhouse 1983; Adams et al., 1986; Verhaegen et al., 1987). We have also seen how attitudes towards the menstrual cycle and attributional patterns influence how negatively women rate their symptoms.

While keeping in mind that many different influences come together to produce a specific symptom, it is at the same time not possible to attempt to measure every possible influence in one study. The present study has, then, selected only some variables that may be able to indicate whether the theoretical argument of a possible interaction between conditions of shift work and the menstrual cycle has some validity.

THE PRESENT STUDY

The purpose of this study was to examine the possibility that both shift-work and the premenstrual phase of the menstrual cycle combine their effects to render women more vulnerable to a series of symptoms. The independent variables used were type of permanent work schedule, with the grouping: nurses on night shift work and nurses on day work; and menstrual cycle phase, with the levels: "follicular phase" and "luteal phase". In addition, time of the work week was examined, with the levels: "beginning of work week" and "ending of work week".

The dependent variables were overall symptom ratings as measured by the Premenstrual Assessment Form (Halbreich et al., 1982), and some specific symptoms measured by PAF clinical scales and frequently endorsed by women filling out the questionnaire (Halbreich et al., 1982). These symptoms are impaired social functioning, fatigue and depression, all relevant for shift work and premenstrual syndrome studies. The scale "water retention", which includes items such as feeling of bloatedness, lowered urinary excretion, and increase weight, was also examined. This symptom has not been examined in shift-work studies, but it is the most frequently endorsed symptom in PMS. It also has been found to be intimately related to hormonal cycle changes (Janowsky et al., 1973). It was thought that a difference between the

groups on this symptom would give support to the hypothesis that shift-work may affect the physiological mechanisms underlying the menstrual cycle.

The other symptom examined, depression was considered in more detail because of the attention it has received in the literature and because of the complex network of neuropsychological implications that the presence of the symptoms would offer. The Beck Depression Inventory (Beck et al., 1961) was therefore added to the information obtained with the PAF.

Furthermore, an exploratory analysis was performed with the variable "menstrual cycle phase", comparing both groups of nurses in terms of their scores on the PAF during their menses, and again during their ovulatory time.

The following hypotheses were be examined:

- 1) Both women on regular day work schedules and shift workers will show an increase in overall symptoms during the luteal phase of their menstrual cycle. However, shift nurses will show more symptoms both during the follicular and luteal periods compared to the day nurses at the same menstrual phases. The same pattern will be found for the specific symptoms of "impaired social functioning", "fatigue", and "depression".
- 2) All the symptoms mentioned in hypothesis one will show an interaction effect, with the difference between nurses on shift work and nurses on day work being higher during the

luteal phase compared with the follicular phase.

3) All the symptoms mentioned in hypothesis one will be rated higher for the nurses on shift work at the ending of their work week compared to the beginning of their work week. The nurses on day work will not show this pattern and their symptoms will not change significantly over their work week.

4) The symptom "water retention" will increase for both groups of nurses during the luteal phase of the menstrual cycle. There will be no difference between the groups during the follicular phase, but the nurses on shift work will show more "water retention" than the nurses on day work during the luteal phase. The variable "time of the work week" will not affect this symptom.

METHOD

Subjects: Participants were recruited through an advertisement in a widely distributed nursing newsletter, notices in hospital wards, and word of mouth. A total of 30 female nurses from several hospitals, 15 working night shifts and 15 working only days, volunteered for the study. The subjects were selected for normal menstrual cycles and no use of oral contraceptives or hormonal medications. Two subjects, one from each group, were dropped from the study, one due to pregnancy, the other to a long period of holidays that would have come in the middle of her participation in the study. Later, another two subjects were dropped from the study, one because she started using oral contraceptives, the other because the timing of presentation of her questionnaires did not cover one of the menstrual periods under study.

The remaining 26 subjects completed all the measures. These subjects did not differ statistically in age and in length of their menstrual cycles (see Tables 11 and 12 in Appendix 1 for corresponding distributions and t-tests). Their ages ranged from 24 to 45, with most women clustering in mid-to-late thirties. The menstrual cycles were of approximately 28 days duration, with only one woman (in the control group) having a longer, i.e. 40 day, cycle.

It was almost impossible to find nurses who had never

worked on shift schedules at some time in their careers. Typically, newly trained nurses start doing shift work and eventually switch to a day-only job. Practically all the control subjects had worked shifts before but had not done so for at least a year before the study began.

Procedures: Ethical guidelines (University Ethics Review Committee, SFU) were followed throughout. All subjects completed an information sheet (see Appendix 2) and two questionnaires (see Appendices 3 and 4) concerned with symptoms experienced over the previous 48 hours. This was done both at the beginning and end of their work week for a period of six weeks. It was estimated that all women would have covered at least one complete menstrual cycle within this time frame, as was the case. It was requested that the questionnaires always be filled out during the same time of day, after the main sleep period. However, because of the differences in their schedules, the "clock" time of day was not consistent for all participants.

Approximately half the subjects in each group started with the questionnaires during the follicular phase of their menstrual cycle and the other half started during the luteal phase. Subjects were told of the importance of answering each questionnaire independently of how they had answered previously, in order to minimize any tendency on their part to be "consistent" rather than accurately reflect their

present condition.

The ovulation time for each menstrual cycle was estimated by counting back 14 days from day one of the menstrual flow (this method is widely used by menstrual cycle researchers, e. g., Presser, 1974). The luteal phase was defined as the last ten days before the menstrual flow began, the ovulation phase as the four days before the premenstrual phase, and the follicular phase as the period between the ovulation phase and the fifth day after the onset of menstruation.

Questionnaires were then selected for data analysis to ensure that both the follicular phase and the luteal phase had one measure each at the beginning and another at the end of the work week. In the cases where more than one measurement met this criterion, a further selection was done, with questionnaires representing the same week, and/or the same menstrual cycle chosen, as needed, from the remaining questionnaires. Another analysis was carried out with questionnaires filled out during the menstrual period (day one or two of the cycle) and during the ovulation phase (as defined above).

The work week was different for the day and the shift workers. Day workers had a regular Monday to Friday schedule. For this group of subjects the measurement taken at "the beginning of the work week" represented the symptoms experienced during the last 48 hours of the weekend. The

measurement taken at the "end of the work week" represented the last 48 hours of their work week. The shift nurses rotated shifts in a delaying fashion, changing from day shift to evening shift to night shift. The night shift consisted of three 12 hour nights and constituted the total work week for that particular seven day period, with the subjective "weekend" following the last night of work. Only the weeks which included a night shift were considered in the analysis. In this way, the measurement taken at "the beginning of the work week" represented the last 48 hours of the shift nurses' subjective weekend and the measurement taken "after the work week" represented the last 48 hours of the night shift period.

Measures: Each questionnaire package contained a Premenstrual Assessment Form (PAF) (Halbreich et al., 1982) (see Appendix 3) and a Beck Depression Inventory (Beck, 1974). The PAF has been widely used in menstrual cycle research. It contains 95 questions pertaining to behavioral, emotional and physical changes that are relevant in the assessment of the premenstrual syndrome. As we saw in the review section, many of these symptoms are also similar to the ones reported by night shift workers. The participants were asked to rate severity of their symptoms on a six-point scale with respect to how much they differed from their "normal" state. Halbreich et al. (1982) used this criterion

rather than absolute severity because it had been shown to produce better inter-individual discrimination.

The authors of the PAF questionnaire developed 18 summary scales based on item intercorrelation and alpha coefficients of internal consistency. Of these scales we chose the three which had at least one item from among the 12 most commonly endorsed by women in a study conducted by the authors of the questionnaire (Halbreich et al., 1982). The decision to use only three scales was based on the rationale that our sample was too small to examine a large number of variables meaningfully.

Halbreich et al., (1982) also developed typological categories for their questionnaire along criteria similar to those found in the Research Diagnostic Criteria of Spitzer et al. (1978). Of particular interest for this study were the typological categories "Major Depressive Syndrome", "Endogenous Depressive Features", and "Atypical Depressive Features". The diagnostic criteria for each of these typologies can be seen in Appendix 4.

The Beck Depression Inventory (Beck et al., 1961) has been widely used clinically to assess depression. It consists of 21 items covering several areas of behavior, including affective, cognitive, and physiological factors. It uses a four point scale of increasing severity from 0 to 3, giving a total sum of scores that can range from 0 to 63. A total score between 0 and 9 is categorized as not

depressed, between 10 and 15 as mildly depressed, between 16 and 23 as moderately depressed, and between 24 and 63 as severely depressed.

Data Analysis: A mixed design analyses of variance with one between subjects factor (shift nurses vs. day nurses) and two within subjects factors ("menstrual cycle phase" and "time of work week") were used for the overall PAF questionnaire scores and for the selected PAF summary scales. Differences in the "Major Depressive Syndrome" PAF category were analyzed using two Chi-square tests comparing shift nurses and day nurses at the follicular phase and also at the luteal phase. An assessment of whether a "Major Depressive Symptom" included "Endogenous" or "Atypical" features was also done. An exploratory t-test analysis was done to compare the PAF total scores obtained by the shift work nurses and the day work nurses during the first two days of their menstrual flow. Their ovulation phases were also compared in this way.

An analysis of variance was also conducted with the total scores obtained with the Beck Depression Inventory. As well, the severity scale of this questionnaire (see pp 61-62) was used to categorize the subjects into depressed and non-depressed groups. The resulting frequencies were analyzed using Chi-square tests.

RESULTS

PAF total scores.

The overall scores obtained on the PAF and the corresponding means and standard deviations can be seen in Table 1. The means are again displayed in Figure 1, together with the significance levels for the overall analysis of variance. As we can see, the bars representing the beginning and the ending of the work week for the control group are approximately equal, while there is more spread for the shift nurses. The between groups main effect is significant ($p < 0.009$), indicating that, overall, the nurses on shift work show more symptoms than the nurses on day work. The three-way interaction is not significant.

Averaging across "time of the work week", we find that the variable "menstrual cycle phase" has an effect on the nurses, significant with a probability $p < 0.003$. That is, nurses show more symptoms during the luteal phase of their menstrual cycle. However, the interaction is not significant, thus suggesting that there is no difference between the groups in terms of how they are affected by this variable at each level of the other factor.

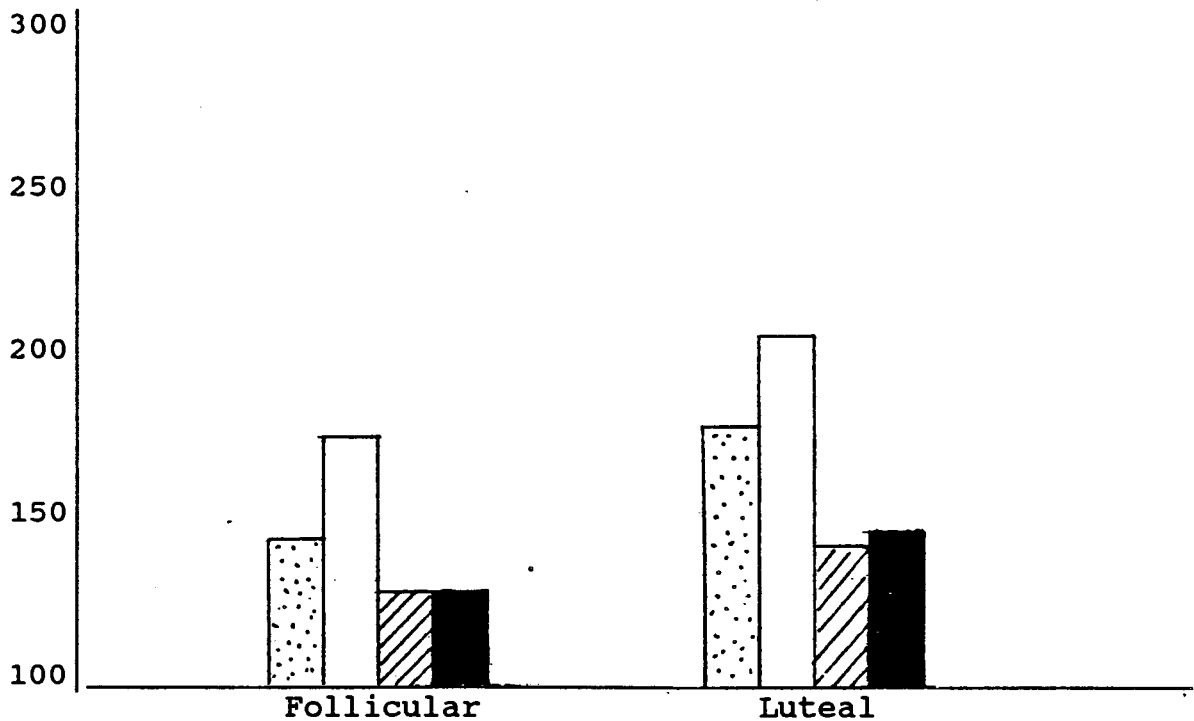
Table 1





Total PAF scores for nurses on shift work (subjects 1-13) and nurses on day work (subjects 14-26) during the follicular and luteal phases of their menstrual cycle.

Subject	Follicular		Luteal	
	Beginning work week	Ending work week	Beginning work week	Ending work week
1	185	186	121	155
2	108	111	120	99
3	128	155	145	214
4	146	244	307	274
5	118	135	141	200
6	119	118	168	147
7	140	138	148	189
8	137	300	186	313
9	212	219	206	217
10	98	157	97	159
11	184	168	252	182
12	134	146	211	219
13	148	167	204	276
Mean	142.85	172.62	177.39	203.39
SD	32.97	53.51	58.70	59.01
14	160	133	212	181
15	109	104	228	156
16	138	95	101	97
17	144	181	114	127
18	113	116	117	127
19	128	126	128	146
20	104	118	108	108
21	127	128	128	155
22	97	106	96	155
23	174	176	248	252
24	102	114	112	118
25	116	131	140	130
26	118	102	102	110
Mean	125.39	125.39	141.08	143.23
SD	23.19	26.34	52.26	40.39

Figure 1

Average scores obtained by nurses on shift work and nurses on day work on the PAF during the follicular and luteal phases of their menstrual cycle.



Nurses on shift work	Beginning of work week	
	Ending of work week	
Nurses on day work	Beginning of work week	
	Ending of work week	

Level of significance:

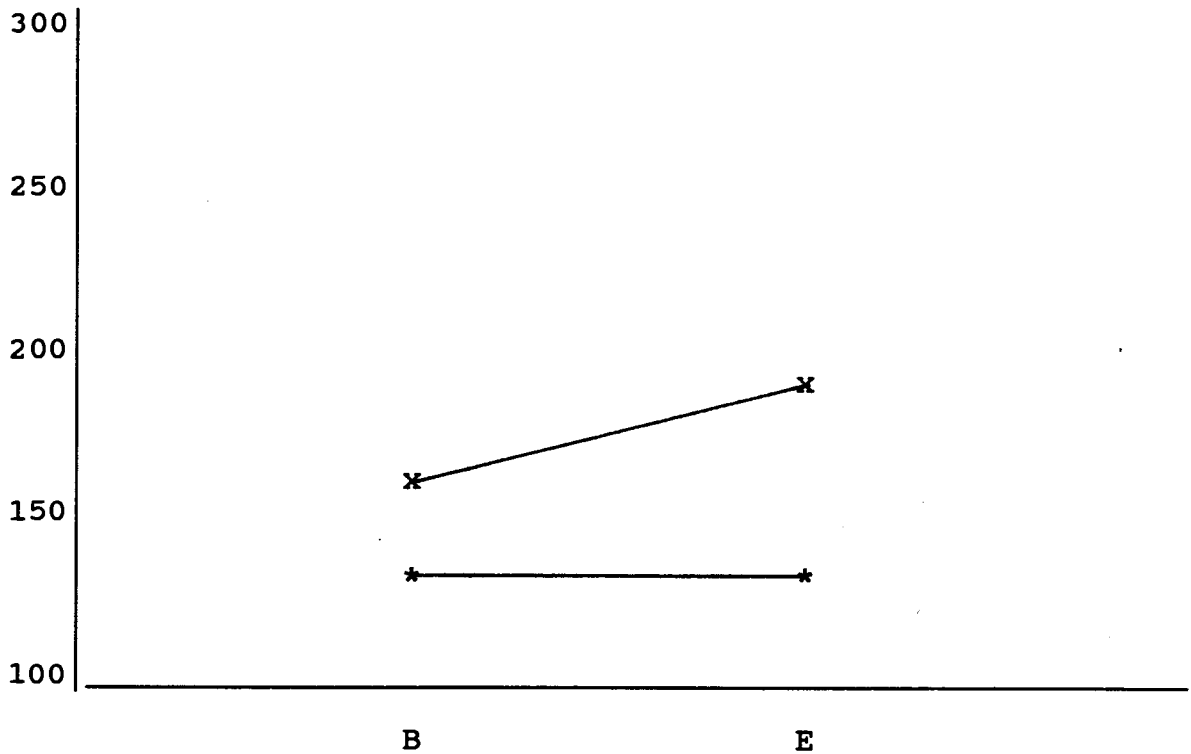
Between groups main effect: $F=8.16$, $df=1,24$, sig., $p < 0.009$
 Three-way interaction: $F=0.13$ $df=1,24$, n.s., $p < 0.724$

Figure 2 shows the PAF values averaged across "menstrual cycle phase". It can be seen that the variable "time of work week" has an effect on the nurses ($p < 0.046$). The interaction is very close to significance ($p < 0.063$), thus indicating that there is a trend suggesting that the groups may be affected differently by this variable. Our planned comparison for Hypothesis 3 was performed by two paired t-tests. It was found that the nurses on shift work had more symptoms at the end of their work week compared with the beginning of the week ($t=2.24$, $df=12$, $p < 0.05$). Symptoms, however did not increase for the day nurses between the beginning and the end of their work week.

The scores on the summary scale of the PAF "Impaired Social Functioning", together with the means and standard deviations, can be seen in Table 2. The analysis of variance shows a significant between groups main effect ($p < 0.011$) and a non-significant three-way interaction (see Figure 3). When we collapse cycle phase across "time of work week" we find that the variable has an effect on the nurses, with higher ratings found at the luteal phase of the menstrual cycle ($F=8.98$ $df=1,24$ $p < 0.006$). This effect is parallel in both groups, as indicated by the non-significant interaction ($F=2.72$ $df=1,24$ $p < 0.112$).

Figure 2

Average scores obtained on the PAF by nurses on shift work and nurses on day work at the beginning and the end of their work week, averaged across menstrual phase.



B=Beginning of work week, E=Ending of work week

Nurses on shift work x—x
Nurses on day work *—*

Level of significance

Time of work week: F=4.44 df=1,24 sig., p < 0.046
Interaction: F=3.80 df=1,24 n.s., p < 0.063

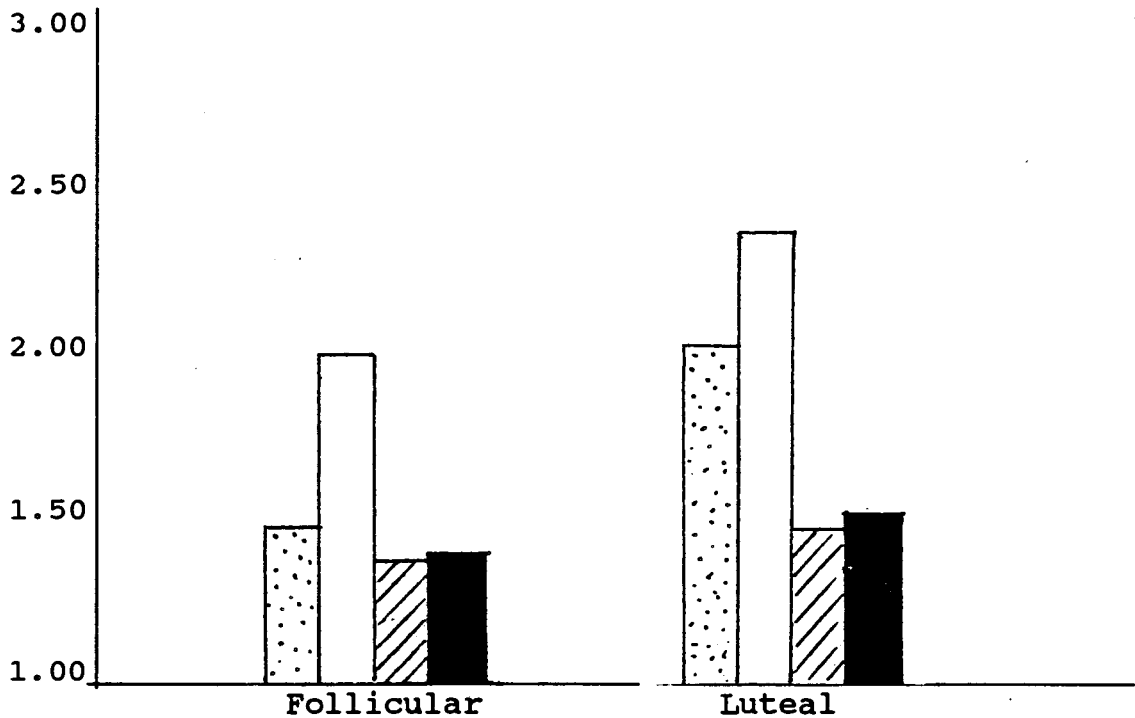
Table 2





PAF summary scale "Impaired Social Functioning" severity scores (range 1-6) for nurses on shift work (subjects 1-13) and nurses on day work (subjects 14-26) during the follicular and luteal phases of their menstrual cycle.

Subject	Follicular		Luteal	
	Beginning work week	Ending work week	Beginning work week	Ending work week
1	2.13	2.00	1.13	1.50
2	1.13	1.38	1.25	1.13
3	1.50	2.50	1.63	2.38
4	1.50	3.00	3.75	3.50
5	1.25	1.13	1.38	2.38
6	1.00	1.25	2.25	1.63
7	1.25	1.00	1.38	1.75
8	1.00	3.25	2.38	3.25
9	2.75	2.63	3.13	3.13
10	1.00	2.75	1.00	2.25
11	1.88	1.75	3.00	2.13
12	1.13	1.50	2.25	2.13
13	1.13	1.50	1.50	3.13
Mean	1.44	1.97	2.00	2.33
SD	0.53	0.77	0.87	0.74
14	1.13	1.38	1.75	1.13
15	1.13	1.00	2.25	1.50
16	1.63	1.00	1.00	1.00
17	1.00	2.38	1.00	1.00
18	1.38	1.13	1.13	1.38
19	1.25	1.00	1.13	1.63
20	1.25	1.13	1.13	1.13
21	1.25	1.75	1.75	1.75
22	1.00	1.13	1.00	1.50
23	2.37	2.00	2.87	3.25
24	1.00	1.00	1.00	1.00
25	1.63	1.50	1.75	2.13
26	1.25	1.00	1.00	1.00
Mean	1.33	1.34	1.44	1.49
SD	0.38	0.45	0.59	0.63

Figure 3

Average scores obtained by nurses on shift work and nurses on day work on the PAF summary scale "Impaired Social Functioning" during the follicular and luteal phases of their menstrual cycle.



Nurses on shift work	Beginning of work week	
	Ending of work week	
Nurses on day work	Beginning of work week	
	Ending of work week	

Level of significance

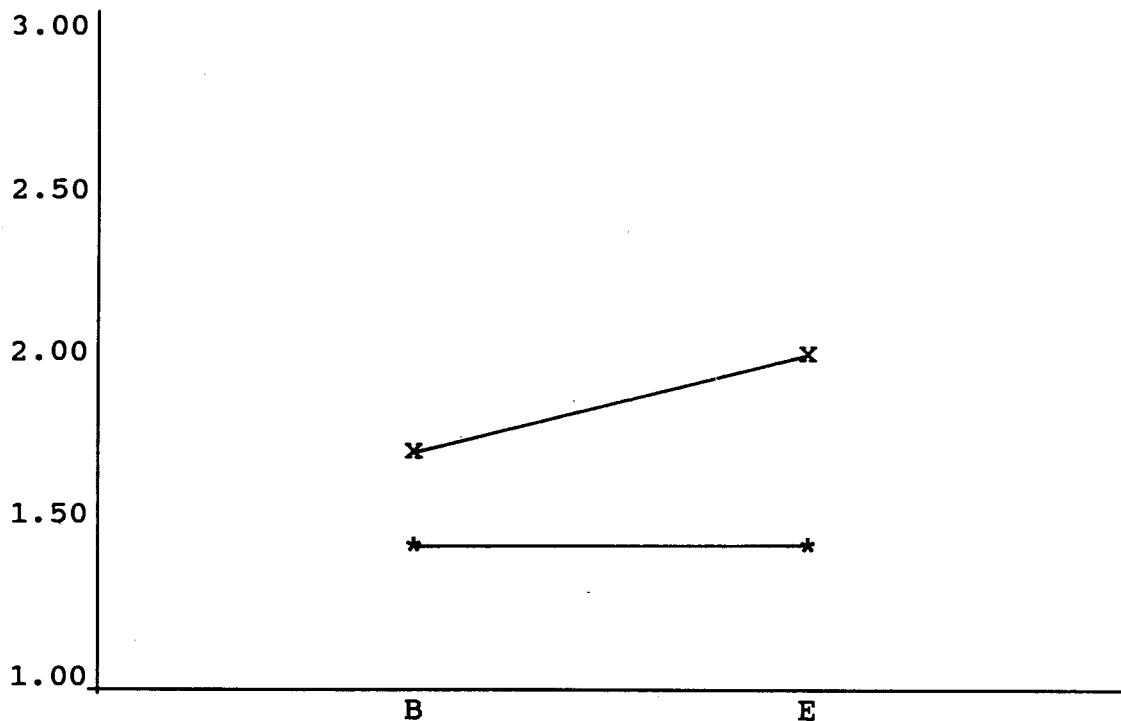
Between groups main effect: $F=7.67$, $df=1,24$, sig., $p < 0.011$
 Three-way interaction: $F=0.63$, $df=1,24$, n.s., $p < 0.435$

In figure 4 we can see that the variable "time of work week" shows an interaction effect ($p < 0.05$) and a main effect ($p < 0.026$). Our planned comparison for Hypothesis 3 was conducted by means of two paired t-tests. The results indicate that the nurses on shift work have a higher "Impaired Social Functioning" score at the end of their work week compared with the beginning of the work week ($t=2.44$, $df=12$, $p < 0.05$). Nurses on day work, on the other hand, do not show this difference.

Looking at the "Fatigue" scale (Table 3, Figure 5), we find that the analysis of variance supports an overall effect of the variables ($p < 0.000$) and shows a non-significant interaction. The effect of menstrual cycle phase averaged across "time of the work week" is significant, with both groups of subjects showing an increase in fatigue during the luteal phase of the menstrual cycle ($p < 0.007$). Again, the interaction is not significant; thus both groups vary in the same way. Figure 6 shows the effect of the time of the work week averaged across menstrual cycle phase. Here both the main effect and the interaction are significant. Our planned comparison for Hypothesis 3 was performed with two paired t-tests and it was found that the nurses on shift work have an increase in fatigue at the end of their work week compared with the beginning of the week ($t=3.44$, $df=12$, $p < 0.01$). The nurses on day work do not show this increase.

Figure 4

Average scores obtained on the PAF summary scale "Impaired Social Functioning" by nurses on shift work and nurses on day work at the beginning and the end of their work week, averaged across menstrual phase.



B=Beginning of work week, E=Ending of work week

Nurses on shift work x———x
Nurses on day work *———*

Level of significance

Time of work week: F=5.62 df=1,24 sig., p < 0.026
Interaction: F=4.27 df=1,24 sig., p < 0.050

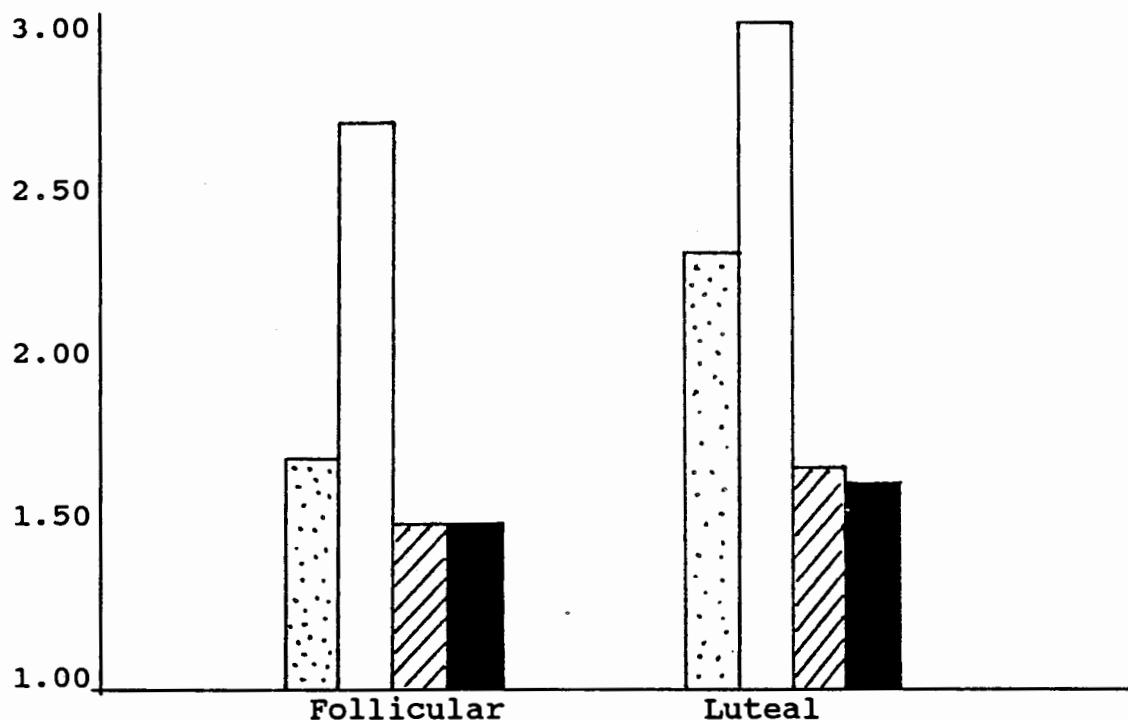
Table 3





PAF summary scale "Fatigue" severity scores (range 1-6) for nurses on shift work (subjects 1-13) and nurses on day work (subjects 14-26) during the follicular and luteal phases of their menstrual cycle.

Subject	Follicular		Luteal	
	Beginning work week	Ending work week	Beginning work week	Ending work week
1	2.00	2.75	1.25	3.25
2	1.00	1.25	1.50	1.50
3	2.00	2.75	2.75	3.50
4	1.25	4.00	4.25	4.00
5	1.00	2.25	1.50	2.50
6	1.25	1.50	1.25	2.00
7	2.00	2.25	2.50	3.00
8	1.50	4.00	2.25	5.00
9	2.75	3.25	2.75	2.75
10	1.00	2.00	1.00	2.50
11	2.75	2.25	3.25	2.75
12	1.75	2.50	3.00	3.50
13	1.75	2.00	2.50	2.75
Mean	1.69	2.52	2.30	3.00
SD	0.61	0.84	0.95	0.89
14	2.00	1.25	3.50	1.25
15	1.00	1.00	3.25	2.25
16	1.75	1.00	1.00	1.00
17	2.25	2.75	1.50	1.25
18	1.75	2.25	2.00	1.75
19	1.00	1.00	1.25	1.25
20	1.00	1.50	1.00	1.00
21	1.75	1.50	1.50	2.50
22	1.00	1.50	1.25	2.50
23	1.75	1.25	1.75	2.00
24	1.00	1.25	1.00	1.75
25	1.00	1.50	1.25	1.50
26	1.75	1.25	1.00	1.00
Mean	1.46	1.46	1.64	1.60
SD	0.47	0.51	0.83	0.53

Figure 5

Average scores obtained by nurses on shift work and nurses on day work on the PAF summary scale "Fatigue" during the follicular and luteal phases of their menstrual cycle.



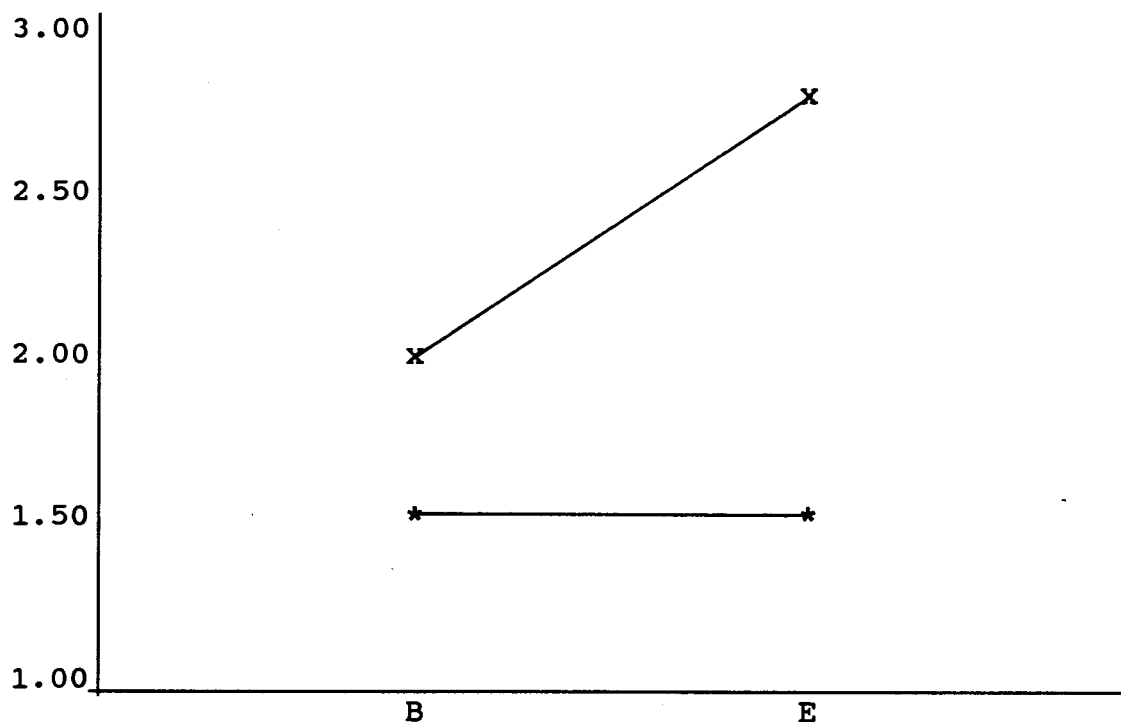
Nurses on shift work	Beginning of work week	
	Ending of work week	
Nurses on day work	Beginning of work week	
	Ending of work week	

Level of significance

Between groups main effect: $F=16.76, df=1,24, sig., p < 0.000$
 Three-way interaction: $F= 0.05, df=1,24, n.s., p < 0.830$

Figure 6

Average scores obtained on the PAF summary scale "Fatigue" by nurses on shift work and nurses on day work at the beginning and the end of their work week, averaged across menstrual phase.



B=Beginning of work week, E=Ending of work week

Nurses on shift work x——x
Nurses on day work *——*

Level of significance

Time of work week: F=7.89 df=1,24 sig., p < 0.010
Interaction: F=8.72 df=1,24 sig., p < 0.007

Table 4 shows the scores on the PAF "Water Retention " scale. Only the effect of menstrual cycle phase averaged across "time of the work week" was found significant ($F=12.70$ $df=1,24$ $p < 0.002$) with both groups of nurses showing higher water retention during the luteal phase of the cycle. The interaction was not significant ($F=1.33$ $df=1,24$ $p < 0.261$), and therefore, the two groups were influenced by the variable in the same way across the two levels studied.

Table 4

PAF summary scale "Water Retention" severity scores (range 1-6) for nurses on shift work (subjects 1-13) and nurses on day work (subjects 14-26) during the follicular and luteal phases of their menstrual cycle.

Subject	Follicular		Luteal	
	Beginning work week	Ending work week	Beginning work week	Ending work week
1	2.33	1.5	1.5	1.33
2	1	1	1	1
3	1	1.17	1.5	3.33
4	1.17	1	4.83	3.33
5	1	1.17	1.67	2.17
6	1	1	1.17	1
7	1	1	1.33	2.17
8	1.17	2	1.83	2.17
9	1.67	1.67	2.50	2.67
10	1	1	1.17	1
11	1.33	1.50	2.83	1.67
12	1	1.67	3.33	3.50
13	1.83	1.83	2.83	2.67
Mean	1.27	1.35	2.12	2.16
SD	0.42	0.31	1.11	0.91
14	2.50	1.50	5.17	3.50
15	1	1	3.50	2.67
16	1	1	1	1
17	1	1.50	1	1.33
18	1.17	1.50	1.50	1
19	1.17	1	1	1.83
20	1	1.17	1	1
21	1.17	1.50	1.50	1.67
22	1	1	1	3.17
23	1.50	1.17	1	1.33
24	1	1.50	1.17	1.33
25	1	1.33	1	1
26	1	1	1	1
Mean	1.19	1.24	1.60	1.68
SD	0.41	0.23	1.27	0.87

Table 5 shows the scores obtained for the Beck Depression Inventory together with the corresponding means and standard deviations. The means and the significance levels are displayed on Figure 7. The between groups main effect is significant ($p < 0.045$) thus indicating a differentiation of the two groups of subjects by the combined independent variables. The three-way interaction is not significant. Averaging across the "time of the work week" variable, we see that the variable "phase of the menstrual cycle" is significant ($F=9.28$ $df=1,24$ $p < 0.006$), while the interaction is not significant. Both groups therefore experience more depressive symptoms premenstrually, but they are not differentially affected across the two levels of the variable.

Figure 8 shows the Beck Depression Inventory scores averaged across menstrual cycle phase. The factor "time of work week" does not show an effect, but the interaction is significant ($p < 0.039$) thus indicating that there is a differential effect associated with this variable. However, when two paired t-tests were conducted to test Hypothesis 3, no differences in depression were found in either group between the beginning and end of their work week. A post-hoc t-test comparing the means of the two groups at the "end of the work week" showed significance ($t=2.61$, $df=24$ $p < 0.02$).

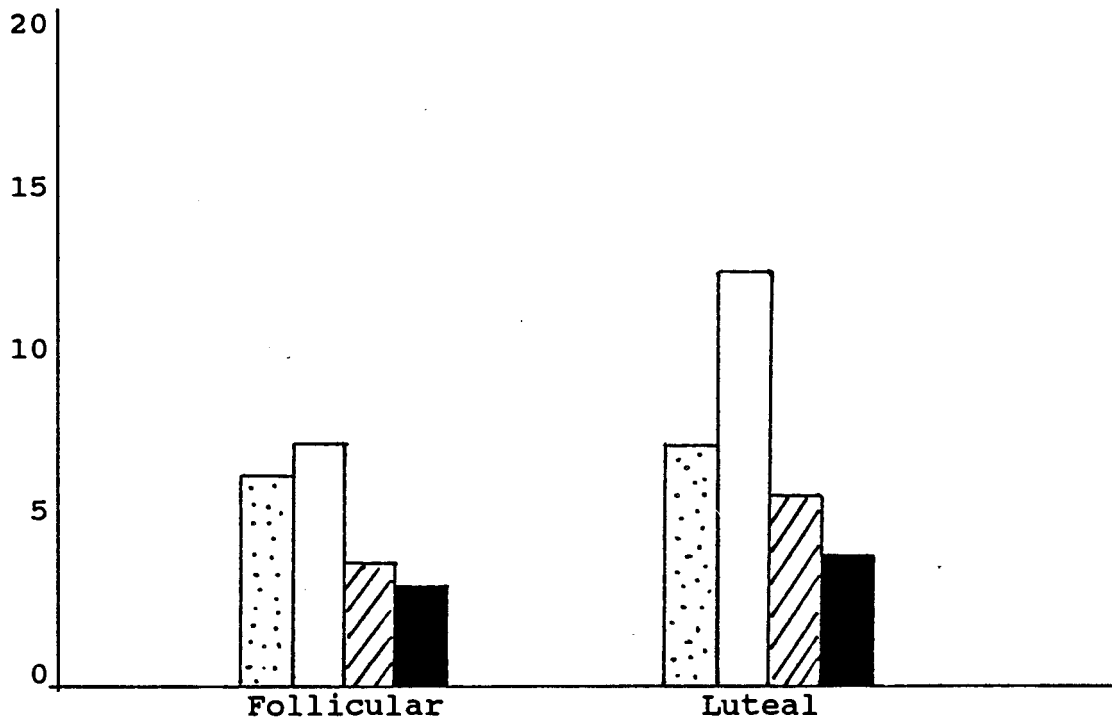
Table 5





Total Beck Depression Inventory scores for nurses on shift work (subjects 1-13) and nurses on day work (subjects 14-26) during the follicular and luteal phases of their menstrual cycle.

Subject	Follicular		Luteal	
	Beginning work week	Ending work week	Beginning work week	Ending work week
1	9	5	2	2
2	1	1	1	0
3	9	10	7	12
4	0	8	12	9
5	0	0	1	8
6	5	4	8	12
7	1	0	6	9
8	6	24	4	32
9	18	15	15	15
10	0	4	0	7
11	11	4	12	12
12	3	2	9	9
13	15	15	16	34
Mean	6.00	7.08	7.15	12.39
SD	6.03	7.17	5.44	10.01
14	0	0	0	2
15	0	0	13	6
16	14	0	0	0
17	1	11	20	1
18	2	1	1	4
19	0	0	1	0
20	0	3	2	2
21	2	1	5	9
22	0	0	0	0
23	18	15	20	14
24	2	2	5	6
25	3	1	3	0
26	1	1	2	2
Mean	3.31	2.69	5.54	3.54
SD	5.78	4.73	7.30	4.24

Figure 7

Average scores obtained by nurses on shift work and nurses on day work on the Beck Depression Inventory during the follicular and luteal phases of their menstrual cycle.



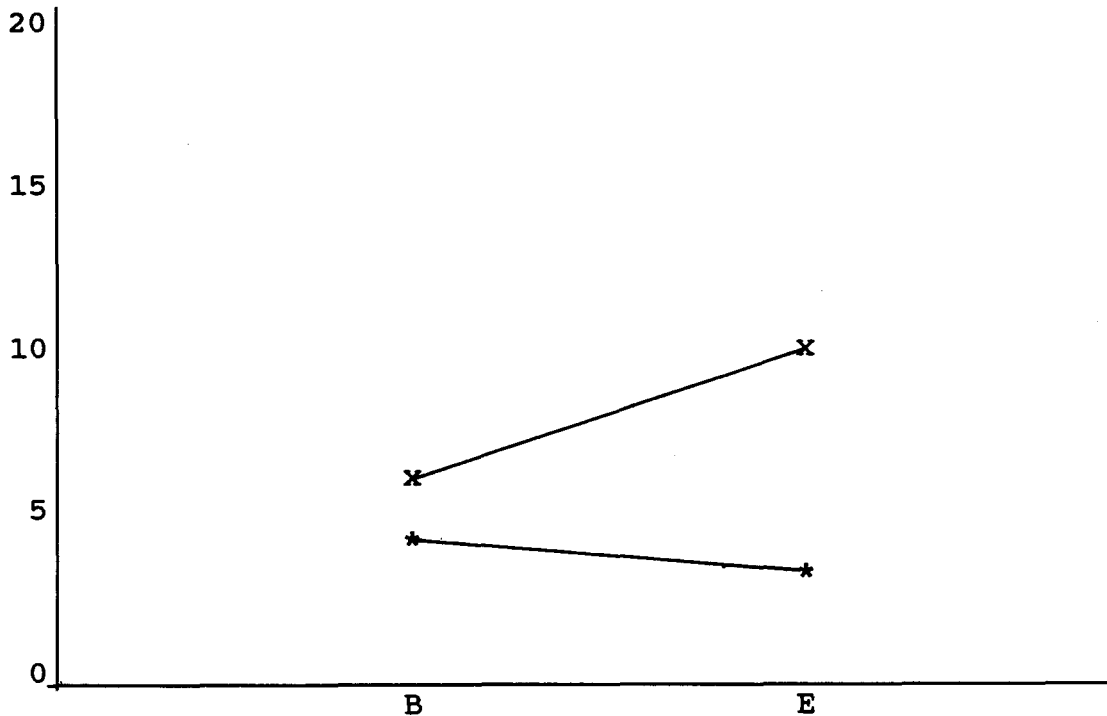
Nurses on shift work	Beginning of work week	
	Ending of work week	
Nurses on day work	Beginning of work week	
	Ending of work week	

Level of significance

Between groups main effect: $F=4.46$, $df=1,24$, sig., $p < 0.045$
 Three-way interaction: $F=2.92$, $df=1,24$, n.s., $p < 0.101$

Figure 8

Average scores obtained on the Beck Depression Inventory by nurses on shift work and nurses on day work at the beginning and the end of their work week, averaged across menstrual phase.



B=Beginning of work week, E=Ending of work week

Nurses on shift work x——x
Nurses on day work *——*

Level of significance

Time of work week: $F=0.81$ $df=1,24$ n.s., $p < 0.376$
Interaction: $F=4.75$ $df=1,24$ sig., $p < 0.039$

The frequencies obtained by applying the severity criteria to the Beck Depression Inventory scores can be seen in Table 6. There were only three reports of severe depression, all in the shift nurses after working a night shift, two of these occurring during the luteal phase and one during the follicular phase. Adding the depressed ratings from mild to severe and contrasting them with the non-depressed nurses we found that the groups only differed significantly at the end of the work week during the luteal phase of the menstrual cycle (see Chi-square tests in Table 7), with 6 shift nurses and one day nurse classified as depressed.

Two chi-square analyses were also conducted with the frequencies resulting from the application of the PAF typology for "Major Affective Syndrome" (see Table 8). During the follicular phase, at the "end of work week", four women from the shift work group met the criteria for "Major Affective Syndrome" while only two women from the day work group did. This difference was not significant. During the luteal phase, however, nine women from the shift work group compared with only one from the day work group met the criteria for depression, a result that was significant with a probability $p < 0.01$. The diagnosis "Endogenous Depressive Features" was examined and it was found that only one woman (from the control group) out of the total sample

met the criteria. This subject showed depression in all the phases of the month and work week examined. All the rest of the women diagnosed as having "Major Affective Syndrome" presented "Atypical Depressive Features" as well.

On an exploratory basis, overall scores on the PAF were obtained during the menses and the ovulation phase of the menstrual cycle. The results were analyzed separately by means of two t-tests (see Tables 9 and 10). The nurses on shift work experienced more symptoms during their menses than the nurses on day work ($p < 0.02$). However, in the ovulation phase there was no significant difference between the two groups.

Table 6

Beck Depression Inventory severity criteria as applied to the scores obtained by two groups of nurses at the follicular and luteal phases of their menstrual cycles: frequencies

	Follicular				Luteal			
	Beginning work week		Ending work week		Beginning work week		Ending work week	
	SN	DN	SN	DN	SN	DN	SN	DN
Not depressed	10	11	9	11	9	10	7	12
Mild	2	1	3	2	3	1	4	1
Moderate	1	1	0	0	1	2	2	0
Severe	0	0	1	0	0	0	2	0
Total depressed	3	2	4	2	4	3	6	1

SN = shift nurses DN = day nurses

Table 7

Beck Depression Inventory: depression criteria applied to two groups of nurses during the follicular and luteal phases of their menstrual cycle at the end of their work week. Chi-square analyses

	Follicular		Luteal	
	Shift nurses	Day nurses	Shift nurses	Day nurses
Depressed	4	2	6	1
Not depressed	9	11	7	12
	Chi-square=0.87 n.s. p < 0.50		Chi-square=4.89 sig. p < 0.05	

Table 8

A

"Major Affective Syndrome" diagnosis following PAF typological criteria in nurses on shift work and nurses on day work during the follicular and luteal phases of their menstrual cycle: frequencies

	Follicular				Luteal			
	Beginning work week		Ending work week		Beginning work week		Ending work week	
	SN	DN	SN	DN	SN	DN	SN	DN
Not depressed	10	13	9	11	9	11	4	12
Depressed	3	0	4	2	4	2	9	1

B

"Major Affective Syndrome" diagnosis following PAF typological criteria in nurses on shift work and nurses on day work during the follicular and luteal phases of their menstrual cycle: Chi-square analyses

	Follicular		Luteal	
	Shift nurses	Day nurses	Shift nurses	Day nurses
depressed	4	2	9	1
not dep.	9	11	4	12
	Chi-square=0.87 n.s. p < 0.50		Chi-square=10.4 sig. p < 0.01	

Table 9

Total PAF scores for nurses on shift work and nurses on day work during the first two days of the menstrual flow.

	Shift workers	Day workers
	172	153
	143	112
	172	143
	237	116
	228	116
	141	151
	229	102
	174	114
	104	270
	176	141
	260	137
	210	121
Mean	187.17	139.67

t=2.51 df=22 p < 0.02 two-tailed test

Table 10

Total PAF scores for nurses on shift work and nurses on day work during the ovulation phase of their menstrual flow.

	Shift workers	Day workers
	158	168
	103	121
	139	95
	141	128
	121	111
	110	126
	150	109
	164	241
	171	105
	206	122
	156	104
Mean	147.18	128.15

t=1.13 df=20 non-significant two-tailed test

DISCUSSION

The results obtained for the overall symptom ratings on the PAF, and the summary scales of "Impaired Social Functioning" and "Fatigue" all show the same general pattern. As was predicted in Hypothesis 1, both groups of nurses show an increase in overall symptoms, and specifically in impaired social functioning and fatigue, during the luteal phase of their menstrual cycle. Furthermore, the overall F-tests show that the two groups of nurses differ, with the nurses on shift work schedules showing more total symptoms, more impaired social functioning and more fatigue than the nurses on day work schedules. These results are basically in agreement with the literature. The symptoms "impaired social functioning" and "fatigue" have been widely reported in shift workers, particularly in women nurses, before (Bosch & de Lange, 1987; Folkard et al., 1985). They have also been reported in women during their premenstrual phase (Logue & Moos, 1986; Halbreich et al., 1982).

The next question was whether the higher symptom ratings found in the shift nurses were due primarily to a greater increase of premenstrual symptoms from the baseline (taken as follicular symptoms) in these nurses compared with the day nurses. Hypothesis 2, which addressed this question, was not supported by the data. None of the simple

interactions predicted for the PAF and for the two scales mentioned above was significant. It appears that working on rotating shifts does not have a differential effect on changes in the nurses' overall symptoms on the PAF, their impaired social functioning, or their fatigue ratings, over the two menstrual phases studied.

It is possible that the higher incidence of symptoms ratings found on shift work nurses in these scales are due mainly to the immediate effects that working a night shift may have on the nurses. The support found for Hypothesis 3 would indicate so. Nurses on shift work show a higher PAF total score, and more impaired social functioning and fatigue during their night shift (measurement at the "end of their work week") compared with their subjective "weekend" (measurement at the "beginning of their work week"). Nurses on day work, on the other hand, do not show changes in symptomatology between the weekend ("measurement at the "beginning of their work week") and the last two days of their work week (measurement at the "end of their work week"). As a consequence, the results obtained by the shift nurses on the follicular and luteal phases of the menstrual cycle, averaged over "time of the work week", would be inflated by this immediate effect of working a night shift.

A point to be made is that despite the significance of the results obtained with the PAF total score, taken as a group, these nurses present only minimal to moderate

changes. For example, the highest mean obtained by any group on the PAF total scores is 203.39 (shift work nurses during the luteal phase of the menstrual cycle, at the end of their work week: see Table 1). This mean value represents a severity score of about 2, or minimal disturbance (see PAF severity scale, Appendix 3).

This result is in agreement with much of the PMS literature which shows that samples of normal women present only small premenstrual changes compared with samples that have been clinically selected for their premenstrual difficulties (Logue and Moos, 1986). This would indicate that the nurses under study did not show a higher PMS rating than would normally be expected. However, this needs to be qualified on several grounds. First, the luteal period of 10 days chosen for this study is longer than the period normally chosen in PMS studies (usually six days or less). Symptoms are expected to increase as the time of the menstrual flow approaches (Dalton, 1982) and thus our results could be biased towards a lower rating of symptoms. The choice of a longer period was due to two factors. One factor is that menstrual changes of circadian patterns start soon after the ovulation, and not just on the few days before the menstrual flow. The other is a practical consideration: the smaller the period under consideration, the more difficult it is to find a scheduled night shift within it. Prolonging the testing period to assure this

scheduling would have been impractical.

Secondly, the validity of an "overall" PMS rating has been questioned by some authors who suggest instead an examination of varied "premenstrual syndromes". The point is that different women seem to develop different types of premenstrual syndromes and that severe impairment in one of them can be masked by an overall average rating (Halbreich & Endicott, 1982). For example, some women may show a "water retention syndrome" and no "depressive syndrome", while other women may show the opposite pattern. It is therefore important to look at the specific sub-syndromes before reaching conclusions.

In the present study we found that, compared with the overall PAF ratings and the impaired social functioning scale, the fatigue scale showed a group mean rating of higher severity (3 or "mild" compared with 2 or "minimal") for the shift nurses at the end of their work week during the luteal phase (see Table 3). However, the consequences that the symptoms would have for specific women could not be addressed without considering the issue of individual differences.

We saw in our literature review that only some women experience PMS and that only some workers respond negatively to shift work conditions. Data obtained with the PAF in other studies have shown large standard deviations (Halbreich et al., 1982), as is the case in the present

study. If we look at the range of severity for individual scales, and even individual items, we can appreciate the importance of this variation. For example, the scale "Impaired Social Functioning" shows ratings that vary from "absent" (or "1") to "moderate" (or "4") for the nurses on shift work, while the range is from "absent" to "minimal" (or "2") for the day nurses. In the case of the item "decreased energy" (item #2 in the PAF, Appendix 3), four shift work nurses rate it as "severe" (or "5"), while only one day nurse does so. We may conclude, then, that it is important to take into account the fact that some specific nurses, apparently more in the shift work group, can experience symptoms with enough severity to have ill consequences for their normal functioning.

Some of the same issues apply to the other two syndromes studied: "water retention" and depression. However, the pattern of the results here differs from those discussed above. The syndrome of "water retention" has been reported only in relation to the menstrual cycle of women, not to shift work. Furthermore, it is one of the most commonly reported symptoms in PMS (Garling and Jo Roberts, 1980). For these reasons, "water retention" is expected to vary not as a result of a particular night shift, but as a result of menstrual cycle changes. An interesting speculation arising from the physiological relationship between the circadian system and the hormones responsible

for changes in the menstrual cycle discussed earlier, is the possibility that repeated exposure to shift work may have an influence on the physiological mechanisms controlling the menstrual water retention changes. For this reason, this expectation was included as an exploratory hypothesis.

The results of the F-test support the first two hypotheses but, unfortunately for our speculative hypothesis, they do not support the last one. As expected, both groups of nurses showed an increase in water retention during the luteal phase of their cycles while the position in their work week had no influence on the symptom. However, the groups did not significantly differ from each other at any of the levels studied. While our hypothesis of a higher water retention in shift nurses compared to day nurses is not supported by the results, it is interesting to point out that the shift nurses have a greater luteal severity range varying from "absent" to "severe" while the range in the day nurses varies from "absent" to "moderate". It is still possible, if more highly speculative, that an effect of shift work on the menstrual physiological mechanisms controlling fluid excretion is taking place and that an increase in power by either increasing the sample size or by increasing the frequency of night shifts worked would tease out this effect.

The last symptom to discuss, depression, shows some interesting findings. Before we discuss these, however, it

is important to note that depression was not considered equivalent to the symptom "negative affect". This was so because depression is not clinically diagnosed in this way. Rather, the diagnosis is usually based on the presence or absence of certain groups of symptoms and includes an assessment of severity. Some of these symptoms relate to sleep patterns, eating habits, energy levels, mood, etc. Furthermore, different kinds of depression have been described and different measures tap more of one kind or another. Of the measures used in this study, the Beck Depression Inventory assesses mainly endogenous depression, while the PAF typologies are designed to diagnose premenstrual depression (usually less severe and of shorter duration than endogenous depression). The PAF is also designed to differentiate between specific kinds of depression, such as atypical and endogenous depression. (Appendix 4).

Going now to our results, we found that the total scores obtained with the Beck Depression Inventory gave some support to Hypothesis 1, with nurses on shift work showing overall higher ratings than the nurses on day work. As well, all the nurses presented higher ratings during the luteal phase of the menstrual cycle compared to the follicular phase. Hypothesis 2 was not supported by the data. The absence of an interaction effect when the results were averaged over the "time of the work week" indicated that the

two groups of nurses followed the same pattern of change from the follicular to the luteal phases of their cycles. Hypothesis 3 was supported by the data, thus indicating that the "time of the week" factor had a differential effect for the two groups, with nurses on shift work showing higher scores than day nurses when they are working a night shift, but not during their weekend.

The results with the total scores obtained with the Beck Depression Inventory could, however, be misleading. If we look at Table 5 we can see that there is only one mean that stands above the cut-off point for depression, "9". This is the value obtained by the shift nurses during the luteal period and during their night shift (12.39). Even this highest value, however, indicates only "minor" depression. The other approach followed, classifying the individual women in terms of absence or presence of depression and then examining the frequencies, was more productive and provided more information.

The results with the Beck Depression Inventory severity scale indicated that more shift nurses than day nurses suffered from depression at the luteal phase of the menstrual cycle, but only when it coincided with the tail end of the work week. This result partially supports Hypothesis 2. Shift work and the premenstrual phase of the menstrual cycle appear to combine and to produce an increase in depression. However, the influence that shift work may

have does not appear to be of a permanent nature. Rather, it is connected to the immediate effects that working a night shift has on the nurses.

The ratings obtained on the PAF typological categories follow this same pattern. The frequencies obtained show, again, partial support for Hypothesis 2, with more women on the shift work group showing a "Major Depressive Syndrome" during the luteal phase compared with the nurses doing day work. However, this difference is only present at the "end of the work week". Again, the immediate effects of working a night shift appear to combine with the premenstrual phase to produce depression in these women.

The results with the severity scale of the Beck Depression Inventory and the "Major Affective Syndrome" typology from the PAF parallel each other. The frequencies found were the same during the follicular phase at the "end of the work week" (Tables 7 and 8). At the luteal phase the PAF results showed a higher frequency of depression ($f=9$) than the Beck questionnaire ($f=6$) in the shift nurses. This difference can be readily explained. As we saw earlier, the Beck Depression Inventory does not assess "atypical" depression. However, all the depressed shift nurses presented "atypical" depressive features. The items that define this syndrome, hypersomnia (increased need for sleep) and hyperconsumption (measured as an increase in appetite and in cravings for specific sweet foods), are only taken

into account in the PAF typology. Because the shift nurses are more tired while they are working shifts, they would likely experience more hypersomnia. This factor seemed to add to the diagnosis of depression in the shift nurses. On the other hand, hyperconsumption also seemed to have an important contribution to the diagnoses. This factor has not been examined in shift work studies, but has been related to premenstrual syndrome (Halbreich et al., 1982).

Atypical depression has been frequently found in women during the luteal phase. Halbreich et al. (1982) found that 45% of their normative sample presented a "Major Depressive Syndrome" premenstrually and that 78% of these depressed women had atypical features. At the same time, they found no women who fitted the endogenous features category in their sample. In the present study 69% of the nurses on shift work presented the "Major Depressive Syndrome" while only 14% of the day nurses did. As we have seen, all the depressed women in the shift work group presented atypical features.

The difference between the normative sample and the group of day nurses may be explained in part by the different administration procedure used in the present study. While Halbreich and coworkers administered the questionnaire retrospectively, asking for a rating of the previous three months, the present study asked the nurses to answer in terms of how they had felt over the previous two days. As mentioned in the literature review, retrospective

measures tend to increase the reporting of depressive symptoms compared with concurrent measures (Endicott and Halbreich, 1982; Youdale, 1985). If this is the case, then the difference found between our sample of nurses doing shift work and the normative sample could actually have been greater had the normative sample used the same concurrent approach.

It is more difficult to compare the present results with other reports on depression in shift workers. The reason for this is that the studies vary enormously in how they have defined depression. In many instances, the criteria used were unclear or there may only have been a statement from the worker saying that he or she feels "depressed" (Monk, 1989a). Reinberg et al. (1983) focused their discussion of depression in shift work on typical endogenous features. Much of the theoretical discussion of a possible relationship between "morning-ness", maladaptation to shift work and depression has also been concerned mainly with endogenous features (Wever, 1984).

However, the atypical depression found during the premenstrual period has been found to be related to central monoaminergic depletion by some authors (Klaiber et al., 1974). To date, the most widely supported physiological theory of endogenous depression centers on central monoamine depletion as well (Van Praag, 1978). It is, then, possible that the shift schedule and the premenstrual physiological

changes combine at this level to produce a greater depressive effect. However, it is also possible that we are dealing with a reactive type of depression due to the added stressors of social disruption and fatigue caused by night work. At the luteal time, when the vulnerability to depression is higher, this would have a greater effect. Perhaps all these factors have contributing effects: shift work may interact with the premenstrual conditions both as a stressor and as a direct physiological modifier of certain hormonal and neurotransmitter systems. Future research is needed to clarify this point.

Focusing now on the results obtained at the other two phases of the menstrual cycle examined, it was found that the nurses on shift work had a higher number of symptoms on the PAF during their menses compared to the nurses on a day work schedule, and that the groups did not differ during the ovulation phase. Given the shortness of these two menstrual phases, it was impossible to compare the groups on the other variable, "time of the work week". The possible confounding here makes conclusions difficult. Tentatively, we may say that the overall increase in symptoms found on the shift nurses throughout this study might not necessarily be due to just a higher baseline throughout the month. It appears that there is a complex relationship between the changes induced by working shifts and the phases of the menstrual cycle. Some phases, like ovulation do not seem affected. On the

other hand, some specific symptoms, like fatigue seem more related to the immediate consequences of working a shift. Other symptoms, like depression, are differentially affected depending both on the phase of the menstrual cycle examined and the shift work rotation.

The symptoms experienced by some of these women can become severe, particularly when the night shift takes place during the luteal phase of their menstrual period. These women may benefit the most from the observation of specific behavioral measures geared to facilitate adaptation to shift work. For example, exercise has been found to help nurses on rotating shift schedules to reduce the severity of their symptoms (Harma et al., 1988b; Harma et al., 1988c). Changes in life style oriented to ameliorate the effect of night shifts by insuring regularity of meals and sleep periods have also been found helpful (Adams et al., 1986). On the other hand, it may be advisable that women who experience these severe symptoms try to avoid working night shifts when they are in the luteal phase of their menstrual cycle.

In conclusion, the results from this study show that there is a complex relationship between shift work health effects and menstrual cycle phase. The small sample used, as well as the self-selected nature of the sample, does not permit the wide generalization of the results. However, enough evidence is presented to suggest that menstrual cycle phase be considered an important variable in shift work

studies using female subjects. As well, studies of the menstrual cycle conducted with female nurses should take into account the potential interaction of the shift work schedule with the phase of the cycle under study.

Furthermore, given that some individual women appear to be severely affected by working a night shift during the luteal phase of their menstrual cycle, it seems desirable that more studies be conducted to investigate the individual characteristics that seem to render these women more vulnerable to these influences.

APPENDIX 1

Table 11

Age in study samples of nurses on shift work and day work

Shift work	Day work
36	40
29	41
38	27
35	41
31	37
34	37
24	38
37	30
34	35
38	38
36	32
34	45
35	42
Mean 33.91	36.75

t=1.81 p > .10 two-tailed test

Table 12

Menstrual cycle length in the study samples of nurses on shift work and day work

Shift work	Day work
27	26
29	24
26	23
28	29
28	26
30	25
28	40
31	30
27	31
28	26
23	28
29	33
29	25
Mean 27.92	28.42

t=.166 p > .20 two-tailed test

APPENDIX 2

BACKGROUND INFORMATION

Identification Number _____ Age _____ Date _____

Marital status: Single ___ Married ___ Separated/Divorced ___

Do you have children? ___ How many? ___ Are you pregnant? ___

1. Please indicate the date of the first day of your last menstrual flow. _____

2. Number of days of average menstrual cycle _____

3. Average duration of menstrual flow: _____

4. Are you currently using oral contraceptives? _____

5. Are you currently using any medication? _____
If you answered "yes" please indicate type of medication and reason taken: _____

6. Do you have or have had a serious medical problem? _____
Please, specify _____

7. Have you ever been hospitalized or received any other form of treatment for depression? _____
If you answered "yes" please specify when and what type of treatment received: _____

8. Has any member of your family been hospitalized or received any other form of treatment for depression? _____
If you answered "yes" please indicate your relationship to this person: _____

9. Have you ever worked night shifts? _____ If yes:
a) Give dates _____
b) If still working shifts, how often do you do a night shift? _____
how many nights in a shift? _____
how many hours per night? _____

10. Please give an estimate of your caffeine consumption per day _____
per week _____

11. Do you use sleeping pills? _____ How often? _____
What kind of pill? _____

APPENDIX 3

PAF SYMPTOMS QUESTIONNAIRE

Identification number_____

Date_____

Number of days since the beginning of the last menstrual flow_____

Beginning date of last night shift_____

End date of last night shift_____

INSTRUCTIONS FOR QUESTIONNAIRE

The following questions sample a great variety of symptoms which women may experience throughout the menstrual cycle. For your answer, please focus on the symptoms you have experienced during the past 48 hours only. It is very important that you do not let your answers to a previous questionnaire influence how you answer this one.

Please evaluate the severity of your symptoms and circle the corresponding number according to this scale:

- 1 Not applicable, not present at all.
- 2 Minimal symptom only slightly apparent to you.
- 3 Mild symptom definitely apparent to you.
- 4 Moderate symptom clearly apparent to you and others who know you well.
- 5 Severe symptom very apparent to you and others.
- 6 Extreme symptom of high severity.

QUESTIONNAIRE:

*On the average, how many hours did you sleep?_____

*How many times did you wake up during your sleep period?_____

*How long did it take you to fall asleep?_____

Symptoms Ratings:

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

1. Have rapid changes in mood (e.g. laughing, crying, angry, happy, etc.) all within the same day. _____ 1 2 3 4 5 6
2. Have decreased energy or tend to fatigue easily. _____ 1 2 3 4 5 6
3. Have decreased ability to coordinate fine movements, poor motor coordination or clumsiness. _____ 1 2 3 4 5 6
4. Feel anxious or more anxious. _____ 1 2 3 4 5 6
5. Sleep too much or have difficulty getting up in the morning or from naps. _____ 1 2 3 4 5 6
6. Have a feeling of malaise (i.e. general, non-specific bad feelings or vague sense of mental or physical ill-health). _____ 1 2 3 4 5 6
7. Feel jittery or restless. _____ 1 2 3 4 5 6
8. Have loss of appetite. _____ 1 2 3 4 5 6
9. Have pain, tenderness, enlargement, or swelling of breasts. _____ 1 2 3 4 5 6
10. Have headaches or migraines. _____ 1 2 3 4 5 6
11. Be more easily distracted. _____ 1 2 3 4 5 6
12. Tend to have accidents, fall, cut self, or break things unintentionally. _____ 1 2 3 4 5 6
13. Have nausea or vomiting. _____ 1 2 3 4 5 6
14. Show physical agitation (e.g. fidgeting, hand wringing, pacing, can't sit still). _____ 1 2 3 4 5 6
15. Have feelings of weakness. _____ 1 2 3 4 5 6
16. Feel that you just "can't cope" or are overwhelmed by ordinary demands. _____ 1 2 3 4 5 6
17. Feel insecure. _____ 1 2 3 4 5 6

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

18. Have "flare-ups" of allergy, breathing difficulties, stuffy feeling, or watery discharge from the nose. _____ 1 2 3 4 5 6
19. Feel depressed. _____ 1 2 3 4 5 6
20. Have periods of dizziness, faintness, vertigo (room spinning), ringing in the ears, numbness, tingling of skin, trembling, lightheadedness. _____ 1 2 3 4 5 6
21. Tend to "nag" or quarrel over unimportant issues. _____ 1 2 3 4 5 6
22. Think of what it would be like to do something to self, like crash the car, wish to go to sleep and not wake up, or have thoughts of death or suicide. _____ 1 2 3 4 5 6
23. Feel less desire to talk or move about (it takes an effort to do so). _____ 1 2 3 4 5 6
24. Become more forgetful. _____ 1 2 3 4 5 6
25. Feel dissatisfied with personal appearance. _____ 1 2 3 4 5 6
26. Become violent with people or things (e.g. deliberately break things, hit someone). _____ 1 2 3 4 5 6
27. Take naps during the day or have an overwhelming desire to do so. _____ 1 2 3 4 5 6
28. Feel sense of unreality, like in a dream. _____ 1 2 3 4 5 6
29. Feel pounding of heart or have rapid heart-beat. _____ 1 2 3 4 5 6
30. Get more enjoyment or excitement out of little things. _____ 1 2 3 4 5 6
31. Have difficulty concentrating. _____ 1 2 3 4 5 6
32. Feel confused. _____ 1 2 3 4 5 6

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

33. Have lowered judgement (i.e. realize judgement is less good than usual when looking back on decisions made at this time). _____ 1 2 3 4 5 6
34. Feel passive, want others to make decisions, to take charge, etc. _____ 1 2 3 4 5 6
35. Have an increased feeling of well being. _____ 1 2 3 4 5 6
36. Have a lack of self control. _____ 1 2 3 4 5 6
37. Tend to become more childlike. _____ 1 2 3 4 5 6
38. Tend to feel or be tearful, weep, or cry. _____ 1 2 3 4 5 6
39. Feel need to urinate more frequently or have an increased amount of urine. _____ 1 2 3 4 5 6
40. Become constipated. _____ 1 2 3 4 5 6
41. Tend to be self-indulgent in use of time, spending money, eating, etc. _____ 1 2 3 4 5 6
42. Have episodes of impulsive behavior. _____ 1 2 3 4 5 6
43. Tend to smoke more, drink more alcohol or use "drugs of abuse" (e.g. "pot", "speed"..) 1 2 3 4 5 6
44. Feel under stress. _____ 1 2 3 4 5 6
45. Pick at, bite or scratch skin, or bite fingernails. _____ 1 2 3 4 5 6
46. Have mood swings from high to low or low to high. _____ 1 2 3 4 5 6
47. Tend to become "hysterical" if something upsets you. _____ 1 2 3 4 5 6
48. Have guilt feelings. _____ 1 2 3 4 5 6
49. Feel "empty". _____ 1 2 3 4 5 6

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

50. Have outbursts of irritability or bad temper. _____ 1 2 3 4 5 6
51. Feel sad or blue. _____ 1 2 3 4 5 6
52. Have tired legs (weak, sore, tremble). _____ 1 2 3 4 5 6
53. Tend to have backaches, joint and muscle pains or stiffness. _____ 1 2 3 4 5 6
54. Family or friends know "she is in one of her moods today". _____ 1 2 3 4 5 6
55. Feel "at war" on awakening or have complaints or outbursts about old irritants. _____ 1 2 3 4 5 6
56. Act spiteful. _____ 1 2 3 4 5 6
57. Feel lonely. _____ 1 2 3 4 5 6
58. Urinate less frequently or in lesser amounts. _____ 1 2 3 4 5 6
59. Have weight gain. _____ 1 2 3 4 5 6
60. Tend to be intolerant or impatient or to lose the ability to respond to or understand the faults , needs, or errors of others. _____ 1 2 3 4 5 6
61. Tend to be overtalkative. _____ 1 2 3 4 5 6
62. Have relatively steady abdominal heaviness discomfort or pain. _____ 1 2 3 4 5 6
63. Have increased sexual activity or interest (fantasy, with self, with others). _____ 1 2 3 4 5 6
64. Have trouble sleeping. _____ 1 2 3 4 5 6
 Check, if wake early in morning and can't get back to sleep. _____
65. Have intermittent pain or cramps in the abdomen. _____ 1 2 3 4 5 6

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

66. Have a decrease in self-esteem (i.e. don't feel good about self or feel a failure).____ 1 2 3 4 5 6
67. Tend to blame others for problems (personal, at home, work, school, etc.)_____ 1 2 3 4 5 6
68. Have increase in activity, organization, efficiency, or involvement socially, at home or work. _____ 1 2 3 4 5 6
69. Tend to brood over unpleasant events. _____ 1 2 3 4 5 6
70. Have skin problems such as acne or pimples._ 1 2 3 4 5 6
71. Have edema, swelling, puffiness, or "water retention. _____ 1 2 3 4 5 6
72. Stay at home more. _____ 1 2 3 4 5 6
73. Have less sexual interest or activity (fantasy, self, others). _____ 1 2 3 4 5 6
74. Tend to avoid social activities. _____ 1 2 3 4 5 6
75. Feel bloated. _____ 1 2 3 4 5 6
76. Have lowered performance, output, efficiency or ease, in tasks at work, at home, or with hobbies, etc. _____ 1 2 3 4 5 6
77. Miss time at work because of changes from usual state. _____ 1 2 3 4 5 6
78. Want to be alone. _____ 1 2 3 4 5 6
79. Feel a lack of inspiration and creativity._ 1 2 3 4 5 6
80. Crave specific foods (sweets, bread, chocolate, pickles). _____ 1 2 3 4 5 6
81. Have an increase in appetite or tend to eat more. _____ 1 2 3 4 5 6
82. Feel worse in morning. _____ 1 2 3 4 5 6

1=Not present
 2=Minimal
 3=Mild
 4=Moderate
 5=Severe
 6=Extreme

83. Pay less attention to physical appearance. _ 1 2 3 4 5 6
84. Feel cold and/or more sensitive to temperature change. _____ 1 2 3 4 5 6
85. Have bursts of energy or feel more energetic. _____ 1 2 3 4 5 6
86. Become more sensitive to or intolerant of personal rejection of self or one's work. __ 1 2 3 4 5 6
87. Feel more affectionate. _____ 1 2 3 4 5 6
88. Tend to seek advice more often or about simple matters. _____ 1 2 3 4 5 6
89. Have pessimistic outlook. _____ 1 2 3 4 5 6
90. Drink more coffee, tea, or cold drinks with caffeine (cola, rootbeer, etc.) _____ 1 2 3 4 5 6
91. Feel pain or discomfort during intercourse. 1 2 3 4 5 6
92. Do less housework (cleaning, care of clothes, etc.) _____ 1 2 3 4 5 6
93. Spend less time at leisure activities (hobbies, TV, reading). _____ 1 2 3 4 5 6
94. Have "flare up" or appearance of cold sores, diarrhea, belching, spontaneous bruises, varicose veins, chest pain, hemorrhoids, numbing, tingling, epilepsy (fits), sensitivity of skin to sun. (specify _____). 1 2 3 4 5 6
95. Have an increase of eye problems or changes in vision (e.g. sty, redness, watering, mistiness, discomfort, sensitivity to light)(specify _____) 1 2 3 4 5 6

Please describe any unusual situation that you feel may have contributed to any marked changes indicated above (e.g. illness, medication, stressful or upsetting event).

APPENDIX 4

Criteria for PAF Major Depressive Syndrome

- A.
1. Depressed or low mood: one of the following five items must be rated as at least mild (rated 3 to 6): Feel depressed or Feel sad or blue or Feel lonely or Pessimistic outlook.
 - or 2. Loss of interest or pleasure: all of the following four items must be rated at least mild (rated 3 to 6): Less sexual interest and Avoid social activities and Want to be alone and Less leisure activities.
 - or 3. Irritable: one of the following two items must be rated as at least mild (rated 3 to 6): Outbursts of irritability or Feel "at war".
- B.
- If depressed: at least four of the following eight items, or item scales, must be rated as at least mild (rated 3 to 6): If irritable or loss of interest or pleasure only, at least five of the eight items must be rated as at least mild (rated 3 to 6):
1. Appetite change: Loss of appetite or Weight gain or Increased appetite.
 2. Sleep change: Hypersomnia or Trouble sleeping.
 3. Decreased energy.
 4. Psychomotor change: Physical agitation or Less desire to talk/move.
 5. Less interest: Less sexual interest or Avoid social activities or Want to be alone or Less leisure activities.
 6. Self-deprecation: Guilt feelings or Decrease in self-esteem.
 7. Concentration difficulties.
 8. Suicidal ideation.

Criteria for PAF Endogenous Depressive Features

- A. Meets criteria for major depressive syndrome.
- B. Loss of interest and pleasure defined as:
 - 1. More enjoyment/excitement (rated as absent, less than 2).
 - 2. Less sexual interest (rated as at least mild, i.e., 3 or more).
 - 3. Less leisure activities (rated as at least mild).
 - 4. Avoid social activities (rated as at least mild).
 - 5. Want to be alone (rated as at least mild).
- C. At least two of the following features rated as at least mild:
 - 1. Feel worse in morning.
 - 2. Guilt feelings.
 - 3. Trouble sleeping,
 - 4. Terminal insomnia.
 - 5. Physical agitation.
 - 6. Less desire to talk/move.
 - 7. Loss of appetite.
 - 8. Become constipated.
- D. No strong "atypical" features: None of the following rated as at least mild (rated 3 to 6).
 - 1. Hypersomnia.
 - 2. Crave specific foods.
 - 3. Increased appetite.

Criteria for PAF Atypical Depressive Features

- A. Meets criteria for major or minor depressive syndrome.
- B. At least two of the following four items rated as at least mild (rated 3 to 6):
 - 1. Hypersomnia.
 - 2. Feel sleepy.
 - 3. Crave specific foods.
 - 4. Increased appetite.

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