Paradoxical Sleep Deprivation Influences Sexual Behavior in Female Rats

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ABSTRACT ____

Introduction. Sleep disturbances are a frequent complaint in women and are often attributed to hormonal fluctuations during the menstrual cycle. Rodents have been used as models to examine the effects of sleep deprivation on hormonal and behavioral changes. Among the many comorbidities common to sleep disorders, sexual behavior remains the least well studied.

Aim. To determine whether paradoxical sleep deprivation (PSD) can affect sexual receptivity (male acceptance) and proceptivity (male solicitation) behaviors in female rats.

Methods. Female Wistar rats were subjected to PSD or were maintained as controls. After this period, the estrous cycle (proestrus, estrus, and diestrus) was determined, and all females were placed with a sexually experienced male. In order to investigate the role of hormones in sexual behavior, we included additional groups that were artificially induced to be sexually receptive via administration of a combination of estradiol and progesterone.

Main Outcome Measurements. Receptivity and proceptivity behaviors, as well as progesterone and corticosterone concentrations were monitored.

Results. Selective sleep loss caused a significant increase in proceptivity and receptivity behaviors in females exclusively during the proestrus phase. The rejection response was increased in PSD rats during the estrus and diestrus phases, as compared with PSD-receptive and proestrus females. PSD reduced progesterone levels during the proestrus phase relative to the respective control group during the same phase of the estrous cycle. The PSD-proestrus females that displayed the most robust sexual response exhibited greater concentrations of corticosterone than PSD-diestrus females, with an absence of sexual solicitation behaviors.

Conclusions. PSD produced a distinct response in the hormonal profile that was consistent with the phase of the estrous cycle. These results show that sleep loss can affect sexual motivation and might lead to important clinical implications, including alterations in female physiology and reproductive abnormalities. Andersen ML, Alvarenga TAF, Guindalini C, Perry JC, Silva A, Zager A, and Tufik S. Paradoxical sleep deprivation influences sexual behavior in female rats. J Sex Med 2009;6:2162–2172.

Key Words. Sleep; Sleep Deprivation; Sexual Behavior; Receptivity; Proceptivity; Progesterone; Cortisol; Corticosterone; Female Rats

Introduction

R ecently, Meston and Buss [1] published a comprehensive investigation regarding the

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reasons why people engage in sexual intercourse. Several evolution-based theories have suggested that men are motivated by a desire for sexual variety [2]. In contrast, women are more motivated by emotional reasons [3]. Several findings support the hypothesis that marked hormonal oscillations during the menstrual cycle function as key factors in the sexual motivational response of females (for a review, see Wallen and Zehr [4]). However, the extent to which hormones influence female sexual behavior depends on whether motivation is an important determinant of the sexual response [5].

In addition to sexual behavior, variations in hormonal concentrations during the menstrual or estrous cycle have been associated with changes in sleep patterns [6–8]. Indeed, sleep disturbances are a frequent complaint in women [9–12]. Sleep surveys have shown that women report considerably more sleep problems than men [9,12], along with a higher occurrence of insomnia [13,14]. Moreover, abnormal menstrual cycles have been associated with sleep difficulties [7,15], and premenstrual symptoms or secondary insomnia often occur at the onset of menses [16]. Certain women may live in a constant state of sleep restriction (e.g., shift workers), and this may have a dramatic impact on multiple physiological processes.

Sleep deprivation may modulate hormone release and sexual behavior through alterations in a hormonal-neurochemical mechanism. By investigating the effects of sleep deprivation in rats, Andersen and coworkers demonstrated the facilitatory effect of paradoxical sleep deprivation (PSD) on erection and ejaculation [17,18]. Additionally, PSD influences rodent hormone profiles, particularly by increasing progesterone and corticosterone in males [19] and by reducing estrogen in diestrus-phase females [20,21]. These findings suggest that the PSD model is a reliable tool for measuring physiological responses [22–24].

Both progesterone and estradiol influence the expression of female sexual behavior in rats (typically operationalized as lordosis [25,26]). Estrogen administered alone or in conjunction with progesterone to the ventral medial hypothalamus promotes lordosis in rats [27]. However, the proportion of rats displaying lordosis and its intensity are increased when progesterone is concurrently administered to the ventral tegmental area [28]. Progesterone also reduces rejection behavior [29,30]. Estrogen, in turn, induces a coordinated peripheral genital swelling and lubrication response, increasing clitoral and vaginal blood flow, among other effects [31].

Interestingly, the distinction between the ability to copulate and the desire to copulate has been reported to be based on female sexual initiation, as the latter is the only valid indicator of female sexual motivation [32]. Recently, Bullivant et al. [33] reported that women were more sexually active on days prior to and during the preovulatory surge. This pattern was evident only when women initiated sexual activity, indicating an increase in women's sexual motivation rather than improved attractiveness. Therefore, investigations of the potential hormonal mechanisms underlying sexual motivation in different contexts may provide important information regarding questions about sexual activity and the menstrual cycle.

Since most adults have experienced sleep deprivation at some stage of their lives, research using preclinical models can provide a framework to determine how sleep loss might affect female sexual behavior. We previously demonstrated that sleep deprivation disrupts the estrous cycle in rats by influencing hormonal profiles, and that stress (a factor that is associated with sleep loss) has a suppressive effect on the hypothalamic-pituitarygonadal axis. Accordingly, we hypothesized that female rats deprived of sleep would present a reduced sexual response because of the altered release of progesterone. To the best of our knowledge, this is the first study to investigate whether paradoxical sleep deprivation can affect receptivity (acceptance) and proceptivity (solicitation) behaviors in female rats. We also examined a possible hormonal basis for such behaviors in female rats exposed to PSD.

Methods

Subjects

Male and sexually inexperienced female Wistar rats (2.5 to 3 months of age) from the animal facility of the Institute of Pharmacology at the Universidade Federal de Sao Paulo were housed in standard polypropylene cages on a 12:12 hours light-dark cycle (lights on at 6:00 AM) at 22°C. Rat chow and water were provided ad libitum. The rodents used in this study were maintained and treated in accordance with National Institutes of Health guidelines. All animal procedures were approved by the university's Ethics Committee (CEP1503/07-434/05).

Determination of the Estrous Phase

The reproductive cycle of female rats is called the estrous cycle. It is characterized by the existence of the following distinct stages/phases: proestrus, estrus, metestrus (or diestrus I), and diestrus (or diestrus II). Ovulation occurs from the beginning of proestrus to the end of estrus. Vaginal smear cytology was used to determine the phase of the estrous cycle, and all samples were obtained Download English Version:

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