

Sleep, dreams, nightmares, and sex-related differences: a narrative review

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Abstract. – **OBJECTIVE:** The aim of this study was to review the available findings on sex-related differences for sleep disorders, dreams and nightmares.

MATERIALS AND METHODS: We explored the PubMed, EMBASE and Google Scholar electronic databases, with regards to the searching terms 'sleep', 'dreams', and 'nightmares' associated with 'sex' and/or 'gender'. Moreover, other supplementary terms for the searching strategy were 'chronobiology', and 'circadian rhythm'. Due to the relative paucity of studies including separate analysis by sex, and especially to their wide heterogeneity, we decided to proceed with a narrative review, highlighting the sex-related findings of each topic into apposite boxes.

RESULTS: On one hand, sleep disorders seem to be more frequent in women. On the other hand, sex-related differences exist for either dreams or nightmares. As for the former, differences make reference to dream content (men: physical aggression, women family themes), self-reported perspective (men dream in third person, women in first person), dream sharing (more frequent in women), lucid dreaming (women more realistic, men more controlled), and daydreaming (young men more frequently have sexual themes). Nightmares are more frequent in women too, and they are often associated with sleep disorders and even with psychiatric disorders, such as depression and/or anxiety. In women, a strong association has been shown between nightmares and evening circadian preference.

CONCLUSIONS: For many years, and for many reasons, laboratory experiments have been conducted mainly, if not exclusively, on male animals. Thus, a novel effort towards a new governance of scientific and research activities with a gender-specific perspective has been claimed

for all areas of medicine, and more research on sex-differences is strongly needed also on this topic.

Key Words:

Sleep, Sleep disorders, Dreams, Nightmares, Sex-related differences, Biological rhythms, Circadian rhythms, Chronotype.

Introduction

Sleep is not a uniform state of being, but it is characterized by cyclic alternations between rapid eye movement (REM) and non-REM (NREM) phases, with a periodicity of approximately 90-110 min¹. Moreover, sleep is a highly organized process, regulated by complex systems of neuronal networks and neurotransmitters, and is essential for every aspect of health and well-being². Sleep plays an important role in the regulation of central nervous system, as well as in either physiologic or emotional functions. Selected brain regions, activated during sleep and involved in the processing of emotional and reward-related information, are activated during sleep, and these nocturnal mechanisms promote adaptive cognitive and emotional responses in the waking state, including overnight performance improvement, creativity, and sexual functions³. Sleep also gives important contribution to brain resilience, intended as the capacity of adaptively overcoming stress and adversity while maintaining normal psychological and physical functioning⁴. If sleep is so important for the organism, it is evident that sleep deprivation, irregularly timed sleep, poor

quality sleep, and/or sleep disorders, may severely impact all physiological functions, and may expose to metabolic and cardiovascular disease risk, not only in adults⁵⁻⁹. A growing effort towards a novel governance of scientific and research activities, focused on gender-specific perspectives, has been recently claimed for all areas of medicine¹⁰. Moreover, an increasing amount of evidence is accumulating in the topic of gender-specific differences and the complex relationships between desynchronization of biological rhythms, individual circadian preference and health^{11,12}. We aimed to look for the available literature and explore the possible existence of findings on sex-related differences for sleep, dreams and nightmares,

by using the PubMed, EMBASE and Google Scholar electronic databases. The main searching terms were ‘sleep’, ‘dreams’, and ‘nightmares’ associated with ‘sex’ and/or ‘gender’. Moreover, the searching strategy was completed by other supplementary terms, such as ‘chronobiology’ and ‘circadian rhythm’. Due the relative paucity of studies, including separate analysis by sex, and their wide heterogeneity, we decided to proceed with a narrative review. For each main issue, a table briefly reported the main sex-related findings.

Sleep Disorders

The definition of ‘parasomnias’ includes a group of sleep disorders characterized by ab-

Table I. Sleep disorders and sex-related differences.

Issue	Findings
Menstrual cycle	Normal menstrual cycle and sleep: poor quality; disturbances especially during the premenstrual week ¹⁴ Severe premenstrual syndrome: disturbing dreams, sleepiness, ↓ alertness and concentration ¹⁴ Sleep disorders are associated with ↑ menstrual irregularity, subfertility/infertility, poor pregnancy and birth outcomes ¹⁵
Pregnancy	Sleep disturbances, usually increasing with the progress of pregnancy ¹⁴ Sleep architecture changes begin as early as the first trimester. Primigravid sleep structure never returns to pre-pregnancy levels after birth. Cesarean delivery frequency, early labor, labor length, depression, gestational hypertension, and gestational diabetes are influenced by sleep changes ¹⁶
Post-partum	Poor quality, daytime sleepiness ¹⁴
Perimenopause	Insomnia ¹⁴
Postmenopause Sleep disorders: prevalence Sleep disorders: risk of suicide	Sleep problems ¹⁷ High among college students: > 1/3 positive for insomnia, restless legs syndrome, periodic limb movement disorder; W: more insomnia and daytime impairment ¹⁸ More than 80% of college students classified with suicide risk meet cutoff criteria for sleep problems; 1/3 of students classified with sleep problems are also classified with suicide risk. Overall, after controlling for sex, the odds of being classified with suicide risk are 2.70 times ↑ for subjects with sleep problems ¹⁹
REM behavior disorders: prevalence REM behavior disorders: dream content	↑ in M aged > 50 years ¹³ W significantly younger than M, both for age of onset and age of diagnosis ¹⁸ No sex-related difference as for violent or frightening content W: less dream-enacting behaviors, especially in movement related dreams and falling out of bed ²⁰
Interpersonal violence and adverse childhood experiences	Sleep disorders may be secondary to interpersonal violence ²¹ , and adverse childhood experiences, e.g., family conflict or childhood sexual abuse, affecting > 50% of youth in the USA, and especially W ²²
Biological correlates	M: greater ↑ of sympathovagal balance during REM sleep than W ²³ Healthy, day-active young M, characterized by morning chronotype, have ↑ salivary cortisol levels in the first hour after awakening, independent of awakening time or sleep duration ²⁴

Abbreviations: M = Men; W = Women.

normal, unpleasant motor, verbal or behavioral events, occurring during sleep or wake to sleep transitions. The various stages of sleep cycle include the transition from wakefulness to NREM sleep and REM sleep, with the NREM mainly occurring in the first half of the night and typically categorized into stages I, II, III and IV. Parasomnias can be seen in both NREM and REM sleep states; the NREM stage is most often seen during the slow-wave sleep (SWS), but it can also be found in stage II as well¹³. Parasomnias are classified separately by the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) and International Classification of Sleep Disorders-3 (ICSD-3), and are more often seen in children, whereas lifetime prevalence in adults may range from 4% to 67%¹³. With respect to the official classification, parasomnias can be: a) NREM-related (confusional arousals, sleepwalking, sleep terrors, sleep-related eating disorder); b) REM-related (REM sleep behavior disorder, recurrent isolated sleep paralysis, nightmare disorder); and c) other forms (exploding head syndrome, sleep-related hallucinations, sleep enuresis, parasomnia due to medical or substance abuse, and unspecified¹³).

Dreams

Although dreaming has always been a fascinating mystery, it is somewhat difficult to provide an appropriate definition. According to the dictionary²⁵, a dream is: (1) a series of thoughts, images, or emotions occurring during sleep; (2) an experience of waking life having the characteristics of a dream: such as (a) a visionary creation of the imagination (daydream), (b) a state of mind marked by abstraction or release from reality (reverie), (c) an object seen in a dreamlike state (vision); (3) something notable for its beauty, excellence, or enjoyable quality. Moreover, scientific interpretation depends on the different perspective of each discipline involved, such as neuroscience, psychiatry, brain imaging, and so on. Thus, the first question ‘What is a dream?’ is immediately followed by ‘Why do we dream?’. Here, in brief, we report some of the proposed theories of dreaming, recently reviewed by Jacquelyn Flakerud²⁶.

Humans build up dream stories after they wake up, in a natural attempt to make sense of them²⁷. When brain and mind are completely free from any conventional control, such as during night hours, it becomes possible to find solutions that cannot be considered while awake, so that dream-

ing could be considered as an ideal moment for creativity and for mental performance. In fact, quoting John Steinbeck: “It is a common experience that a problem difficult at night is resolved in the morning after the committee of sleep has worked on it”²⁸. Another possible scenario hypothesizes that dreams play crucial adaptive function related to the regulation of emotion^{27,29}. Dreaming could allow to organize new material into the memory system, reducing emotional arousal, and helping to cope with further trauma or stressful events. Similarly, it is also hypothesized^{27,29} that dreams may serve as a precious training simulation field to threat fighting activity, so that the individual while dreaming learn how to solve possible threatening situations that could present during waketime. Sleep and dreams also play crucial role on the brain’s consolidation of working memories into long-term memories³⁰. Dreaming (and recalling dreams) stimulate memory processes at the same way as an amount of information is stored during wakefulness, and consolidation of information could be extremely useful for learning processes²⁷. It has been recently shown that REM theta activity is involved in memory processes during REM sleep, as well as during the waking state, and gamma activity seems to be related to emotional processes and dream recall, as well as to lucid dreams³¹. The changing nature of dreams across the sleep cycle could be favored by the increasing concentrations of cortisol over the course of the night’s sleep³².

Dream Content and Dream Recall

Dreaming is a universal experience, but significant inter-individual variability in dream recall frequency exists, and unpleasant thoughts are more prone to dream rebound than pleasant ones³³. Differences may depend on sex and socio-demographic variables. Women, and inhabitants of large cities, tend to report dreams more often than men and residents of small towns³⁴, and dream recall seems to exhibit the smallest effect size for children and the largest for adolescents³⁵. Moreover, the hormonal milieu may influence dream content. A study on 378 women who recalled the previous nights’ dreams (with 53% and 47% characterized by pleasant or unpleasant dream affect/content, respectively), showed that pleasant dream content was associated with the luteal phase³⁶. As for dream content, more often typical themes include falling, flying, failing an examination, being unable to find a restroom), and men more often report dreams about physical

aggression than women³⁷. In children and young adolescents, recurrent dreams most frequently deal with confrontations with monsters or animals, followed by physical aggressions, falling and being chased. In general, recurrent dreams are more likely to include negative content elements than positive ones³⁸, and by age of 11 years the presence of recurrent dreams may already reflect underlying emotional difficulties in boys, but not necessarily in girls³⁹.

Sharing Dreams

Dreaming is a private experience, but dream sharing is a common experience for most people. Usually, dreams are disclosed to partners, friends, and relatives, and dream sharing is often associated with enhancement of relational intimacy⁴⁰. In fact, revealing and telling a dream may act as a kind of fiction that can be explored by the dreamer together with other people, thus allowing an important emphatic effect⁴¹.

Lucid Dreaming

Lucid dreaming (LD) is defined as the awareness that one is dreaming, during the dream state. It has been proposed that the concept of LD also includes the possibility of controlling dream events, although such control is present only in a subset of events. LD has been claimed to represent well-being and has been proposed as a therapeutic agent for nightmares. During LD, in fact, subjects are aware that they are dreaming and may even control dream content. Thus, lucid dreamers might be able to transform nightmares into normal dreams, thereby assuring a restoring sleep⁴². Aviram and Soffer-Dudek⁴³, however, found that some aspects of LD could also be associated with psychopathological symptoms. Thus, the authors concluded that LD should not be considered as necessarily considered 'per se' a sign of well-being, but it can be positive or negative, depending on different features⁴³. Lucid dreaming has also been correlated with creativity, and some studies suggested a link between creativity and REM sleep. As for creativity, narcolepsy, a sleep disorder where subjects fall asleep directly into REM sleep, represents an interesting model for studies. In fact, subjects with narcolepsy obtained higher scores than controls on specific creative tests, in particular with reference to innovation, imagination, and research⁴⁴. These findings of higher creative potential in narcolepsy, give support for a role of REM sleep in creativity⁴⁴.

White Dreams & Non-Dreamers

We define the concept of White dreams (WD) as the feeling of having had a dream experience without being able to specify this experience any further. It is extremely frequent, since it makes up almost one third of all dream reports, and WD are typically interpreted as forgotten dreams⁴⁵. A certain number of subjects, who refer a complete lack of dreams, are considered as non-dreamers. However, studies with video-polysomnography showed that even non-recallers exhibited, several scenic and dreamlike behaviors and speeches, daily or almost nightly, which were also observed during REM sleep, suggesting that non-recallers produce dreams, but do not recall them⁴⁶.

Daydreaming

Characteristics of dreaming sleep are far stronger in stage I REM sleep than in any other state. Scholars⁴⁷ who performed studies by delaying the sleep onset and waking time of the subjects, showed that the major determinant of vivid visual imagery and enhanced cognitive activity during sleep was a pattern of subcortical and cortical activation, common to both the REM and NREM cycles, and the activated phase of the 24-h diurnal wake-sleep cycle. Similarly to the differences between nighttime REM and NREM dreams, daytime dreams may exhibit particular features. Studies on subjects with daytime naps, instructed to take note of both waking daydream and nap dream reports, and to give a rate for their bizarreness, sensory experience, and emotion intensity, showed that recall rates for REM and NREM naps were significantly higher than the typical recall rates for nighttime dreams. Compared with daydreams, NREM dreams had lower ratings for emotional intensity and sensory experience, while REM dreams had higher ratings for bizarreness and sensory experience⁴⁸.

Nightmares

Definition and Epidemiology

Nightmare is defined as an "extended, extremely dysphoric" dream that "usually involves efforts to avoid threats to survival, security, or physical integrity", and nightmare disorder is defined by the repeated occurrence of nightmares that cause clinically significant distress or impairment in social, occupational or other important areas of functioning, not attributable to physiological effects of drug abuse or medica-

Table II. Dreams and sex-related differences.

Issue	Findings
Dream content and dream recall	Boys more often dream of monsters and big animals; girls more often dream of humans and small animals as aggressors ⁴⁹ M: physical aggression ³⁷ M: the presence of violent dreams is not associated with testosterone levels ⁵⁰ W: ↑ number of family members, babies, children, and indoor settings ⁵¹ Normal dreams: recall is more prevalent for girls (age 13-16 years) ⁵² Disturbing dreams: recall is more prevalent for girls (age 13-16 years) than for boys, and ↑ over time for girls while it ↓ for boys. Anxiety is potential cause for the observed sex difference in disturbing dream prevalence ⁵² W: ↑both dreams recall frequency and time in bed ⁵³ Postpartum and pregnant W recall infant dreams and nightmares with equal prevalence, but anxiety is present especially in postpartum W. Postpartum W more often report dream-associated behaviors, with nightmares, post-awakening anxiety, confusion, and need to check on the infant ⁵⁴
Self-reported dream perspective	W more often dream exclusively in first person, and M exclusively in third person, but gender differences exist also in subjects dreaming in mixed perspective (a combination of first- and third person) ⁵⁵
Sharing dreams	W share their dreams more often than M ³⁴
Lucid dreaming	W: more realistic dreams, more logical thoughts and more dissociative experience during dreaming. M: more controlled dream events ⁵⁶
Daydreaming	W: ↑ levels of daydreaming and nightdreaming frequency, ↑ emotional reactions to daydreaming; ↑daydreams dealing with problem solving ⁵⁷ W: ↓ levels of daydreams of a sexual, bizarre-improbable, heroic and achievement-oriented nature ⁵⁷ Most sex differences persist over the life span, whereas sexual daydreams ↑ with increasing age level. Problem-solving daydreams are most likely for both sexes (except for M aged 17 to 29, who more frequently have sexual daydreams) ⁵⁷

Abbreviations: M = Men; W = Women.

tion, nor to coexisting mental and medical disorders^{58,59}. Nightmares usually occur during REM sleep^{52,60}, and are associated with symptoms of physical arousal, such as sweating and shortness of breath. The prevalent emotion is fear, although anger, shame and sadness may also occur either during the dreaming episode, upon awakening from the disturbing dream, or upon later recollection of the dream experience⁶¹. Although nightmares often lead to awakenings, waking up is not a necessary diagnostic criterion for nightmare disorder. As for their frequency, night disorder may be classified as mild (<one episode/week on average), moderate (one or more episodes/week, but less than nightly), and severe (nightly episodes). An acute episode has a duration of one month or less, a subacute episode a duration of at least one month but less than six months, while chronic nightmares endure for six months or longer⁵⁸. Prevalence of nightmares depend on age, ranging approximately from 10% to 50% in children aged <15 years, and 66% in adults¹³, and nightmares occur more frequently in women than in

men⁶²⁻⁶⁴. Frequent nightmares are associated with a wide range of mental complaints, such as sleep disruptions and insomnia, difficulties in sleep onset and maintenance, tiredness upon getting up, daytime sleepiness, lack of energy, difficulties in concentrating, mental distress, anxiety, depression, poor academic performance⁶¹. The impaired self-reported sleep quality could be explained by an increased autonomic response rather than altered sleep pattern. In fact, by analyzing heart rate (HR), heart rate variability (HRV), respiration cycle length, electroencephalographic (EEG) arousals, salivary cortisol values, and REM density during polysomnography in the course of a nightmare experience of participants, it has been shown⁶⁵ that autonomic activation was markedly increased compared to their own non-nightmare, even if with significant intraindividual differences. Despite these symptoms, however, nightmares are rarely reported to healthcare providers, since studies⁶⁶ showed that only 38% of participants reported discussing their nightmares with a healthcare professional, and 11% of participants

with significant nightmares reported having told a healthcare provider about that. This issue does not represent a secondary aspect, since the presence of recurrent nightmares increases the risk of suicidal behavior⁶⁷⁻⁷⁰.

Classification

Nightmares can be differentiated between (1) posttraumatic and (2) idiopathic. The former is either direct replications of a traumatic event, or contain trauma-related emotion or content, or refer to inappropriate family relationships^{71,72}. Post-traumatic nightmares lead to more severe arousal, more nocturnal awakenings, stronger aggression and more elevated helplessness than idiopathic nightmares do. Idiopathic nightmares may originate in early adverse experiences leading in later life to the expression of early memories and emotions in dream content, but they can also depict more imaginative stories, not necessarily reflecting a previous traumatic event^{61,73}.

Nightmare Themes

The most common themes include recall feelings of fear and threat, such as feeling lost or trapped, being chased or attacked, falling or drowning, suffering an injury, illness or death, loss of or damage to own house or property, and natural or man-made disasters. Anxiety and shame are also frequent themes, such as loose or malfunctions of phones or laptop, trouble with the car or any other vehicle, being unable to find a toilet, being naked or inappropriately dressed in public, failing or being unprepared for a test or exam. It has to be stressed that nightmares and bad dreams are different, since they represent separate entities, and are also characterized by different topics. Physical aggression is the most frequently reported theme in nightmares, whereas interpersonal conflicts predominated in bad dreams. Moreover, nightmares are rated as being substantially more emotionally intense than bad dreams. When compared to bad dreams, nightmares are more bizarre and contain substantially more aggressions, failures, and unfortunate endings⁷⁴. Being chased, physical aggression, including death/injury of close persons, are common findings also in childhood⁷⁵.

Biological Aspects

A dysfunctional, higher than normal, autonomic regulation has been reported in frequent nightmare subjects during REM sleep⁷⁶. Moreover, a markedly increased autonomic activation was

also demonstrated by ambulatory polysomnography in individuals with frequent nightmares⁷⁷. A higher amplitude of heartbeat-evoked potentials was observed in nightmare patients compared to healthy controls, but only during REM sleep, with no parallel difference in HRV or interbeat interval⁷⁸. On the other hand, a decreased hypothalamic-pituitary-adrenal (HPA) axis reactivity could be a trait-like feature of women with frequent nightmares. In fact, working women with frequent nightmares showed a blunted cortisol awakening response on a working day, compared to women who did not report nightmares⁷⁹. Nightmares and insomnia are hallmark symptoms of posttraumatic stress disorder (PTSD), since disturbed sleep increases the risk for PTSD. Although PTSD is not object of this review, the association with hormonal derangements is interesting. Veterans with PTSD, in fact, showed a significant increase of awakenings during sleep, that correlated positively with adrenocorticotrophic hormone (ACTH) levels and negatively with growth hormone (GH) secretion, whose plasma levels were reduced during the night. Thus, the activity of either HPA axis or the sympathetic nervous system seem to generate a negative loop: sleep fragmentation, nightmares, increased risk of PTSD⁸⁰.

Sleep, Autonomic Modulation, and Circadian Aspects of Cardiovascular Risk

The close relationship between sleep and autonomic modulation is known since the early 90's⁹⁰. Urinary free cortisol, epinephrine, and dihydroxyphenylacetic acid levels were significantly and positively correlated with the average values of percent REM sleep⁹¹, and studies with simultaneous analysis of sleep EEG activity, cortisol secretory rate, and HRV, revealed a close coupling of adrenocorticotrophic, autonomic, and EEG ultradian rhythms during sleep⁹². Studies based on HRV analysis, a widely investigated parameter regarding autonomic modulation, reported a higher parasympathetic tone during normal non-REM sleep and a sympathetic predominance during REM sleep. Moreover, there is also evidence of an association between HRV and dream intensity and emotionality. REM sleep dreams are longer, more vivid, bizarre, emotionally intense, and illogical than SWS dreams, while HRV has been associated with dream intensity and emotionality⁹³. Due to the higher cardiac parasympathetic modulation, lower levels of arterial blood pressure (BP) and HR have generally

Table III. Dreams and sex-related differences.

Issue	Findings
Frequency	W: significantly ↑ frequencies of all types of nightmares than M ^{81,82} W: more often reported nightmares than M in adolescents, young adults, and middle-aged adults, but not in children and older persons ⁸³
Association with sleep disorders	W (university students): ↑ risk of poor sleep quality, ↑ frequency of nightmares, ↑ propensity for nightmares, ↑ risk for a sleep disorder related to nightmares, worse sleep quality, ↑ frequency and propensity for suffering nightmares, compared with M ⁸⁴
Association with psychiatric disorders	W: strong association between report of nightmares and presence of depressive disorder, anxiety disorder, or both. Even after controlling results for effects of major psychiatric disorders, nightmares were significantly associated with being a W ⁸⁵
Mirror behavior	W: association of nightmares with voluntary and involuntary mirror behaviors (the propensity to imitate another person's emotions or actions) during wakefulness; M: association of nightmares with threat-related mirror behaviors during wakefulness ⁸⁶
Individual circadian preference (chronotype)	W: strong association between nightmares and eveningness. Definite evening-types display the most severe nightmares, independent of age and sleep duration. The nightmare/eveningness association appears at age 20-29 for definite evening-types, and at age 30-39, for moderate evening-types ⁸⁷
Biological correlates	Working W with frequent nightmares show a blunted cortisol awakening response on a working day, compared to those without nightmares ⁷⁹ After the menopause, the prevalence of spasmodic chest pain and irregular heartbeat ↑ with the number of nights a week disturbed by nightmares ⁸⁸ Elderly subjects with nightmares: no gender difference for irregular heartbeats (IH), whereas spasmodic chest pain (SCP) was significantly more frequent in M. IH significantly ↑ in association with increasing nightmares in both M and W. The percentages of M and W with both IH and SCP were 3- and 7-times higher among those who had nightmares very often than among those who very seldom or never had nightmares, respectively ⁸⁹

Abbreviations: M = Men; W = Women.

supported the concept that night is a protective timeframe for heart and cardiovascular system. However, a robust body of evidence revealed that the occurrence of cardiovascular events is not evenly distributed in time, but shows peculiar circadian temporal patterns, depending on the circadian variation of triggering mechanisms⁹⁴. Muller et al^{95,96} first reported an evident 24-hour distribution of acute myocardial infarction MI, characterized by a morning peak between 6 AM and noon⁹⁵⁻⁹⁷, and a similar pattern was also shown for the most important acute cardiovascular events⁹⁸⁻¹⁰⁰. Moreover, stress may exert major effects upon the circulatory system of coronary patients in multiple ways particularly in the morning, *via* a direct link between emotional stress and changes in HR, systolic and diastolic BP, cardiac output, blood viscosity and coagulation¹⁰¹. In addition to these 'diurnal' stressors, Somers et al¹⁰² revealed that, contrary to the other phases of sleep, the sympathetic-nerve activity

increased significantly during REM sleep, and BP and HR returned to levels similar, or even higher, to those recorded during wakefulness. This allowed to recognize that myocardial ischemia may also occur nighttime, with different mechanisms, either during NREM and REM sleep¹⁰³. Moreover, a series of nocturnal events driven by circadian rhythms, including cardiac responses to hypertrophic stimuli, activity and contractility of vascular smooth muscle activity, endothelial nitric oxide production, and capacity of monocytes to infiltrate atherosclerotic plaques, identified a 'perfect storm' scenario of higher cardiovascular risk¹⁰⁴. As for possible gender differences in the onset of acute cardiovascular events, a comprehensive review from our group on worldwide chronobiologic studies from 1996 to 2015 (n=64 studies, >650000 cases), showed that only less than one half of studies provided separate analysis by gender. However, these complete studies included 85% of total

cases, so that we can now assume that morning hours represent equally critical time for both men and women¹⁰⁵.

Desynchronization of Biological Rhythms, Shiftwork, Nursing, Sleep and Nightmares

It is widely known that shiftwork affects circadian alignment, and misalignment is associated with a series of diseases, including cardiovascular ones. A Swedish study¹⁰⁶ on more than 2000 cases with MI showed that, although overall risk was similarly associated with shiftwork both in men and women (OR 1.3 each), in the age group 45-55 the relative risk was much higher in women than in men (OR 3.0 and 1.6, respectively). Among shift workers, nurses are widely investigated. A study¹⁰⁷ on female nurses from the University of Alabama at Birmingham Hospital (USA), showed an evident phase desynchronization of core body temperature, peak cortisol, and dim light melatonin onset in individual night-shift subjects compared with dayshift subjects. Moreover, in a subset of subjects, a genome-wide microarray analysis of peripheral blood mononuclear cells revealed distinct gene expression patterns between nightshift and dayshift subjects¹⁰⁷. Shiftwork negatively affects also sleep quality and, as direct consequence, quality of life as well. Shao et al¹⁰⁸ on 435 female nurses found that more than one half of shift workers reported poor sleep, and the quality-of-life mean scores were significantly lower than those of the Taiwanese general female population. Quality of sleep represents crucial point for working performances of hospital nurses, and the risk of medication errors is independently associated with short resting time after night shift and poor quality of sleep (OR 3.165)¹⁰⁹. Self-perception of medication error has been associated with shiftwork, age, working experience, and chronotype also in a population sample of Italian in midwives¹¹⁰. Finally, poor sleep and nightmares are strictly coupled. The results of a large study¹¹¹ conducted on more than 2000 nurses (97% women), showed that nurses working two and three shift rotational schedules had more than 1.5-fold increased risk of nightmares, compared to nurses working daytime only. Women tend to report nightmares more often than men⁸², and a strong association between nightmares and eveningness has been shown for female subjects⁸⁷. A linear association between nightmare frequency and increasing eveningness exists, so that definite evening types display the

most severe nightmares⁸⁷. Individual circadian preference (chronotype) is shown to influence the neurophysiological substrate of emotional processing, as well the memory and affective processes of sleep and dreaming, and this could explain the diverse occurrence of nightmares for evening-type women.

Conclusions

For many years, laboratory experiments have been conducted mainly, if not exclusively, on male animals. Although many reasons were behind this choice, e.g., costs, biological complexity, menstrual cycles, pregnancy, we now are in possession of a huge amount of male-oriented medical knowledge. We need now to know more. As for the specific topic of this review, for example, sex differences in features of the sleep-wake cycle related to estrous phase that likely have been found in rats need to be further investigated¹¹². Moreover, female rats have been shown to be more resilient to the deleterious effects of REM deprivation¹¹³. Thus, research on sex-differences cannot be immune from the fascinating and mysterious world of dreaming, and that of circadian rhythms as well. Women represent ‘a world apart’. We all know, for example, that motor activity is inhibited during REM sleep. However, a study of the activity of the facial mimetic musculature during REM sleep showed that zygomaticus contractions were predictive of the experience of high positive emotions in women¹¹⁴. Thus, we have learned that women can smile even when dreaming.

Conflict of Interest

There are no financial or other conflicts of interest incurred by any of the authors due to the sources of funding, or utilized products, technology, or methods of our research and report of findings.

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Authors' Contribution

Conceptualization, R.C., A.D.G., F.F. and R.M.; Methodology, E.D.S., B.Z.; Literary analysis, A.D.G., E.D.S., B.Z.; Resources, R.C., R.M.; Writing – original draft preparation, R.C., A.D.G., B.Z., F.F. and R.M.; Writing – review and editing, R.C., A.D.G., M.A.R-B., P.J. L-S, F.F. and R.M.; Supervision, P.J. L-S, F.F. and R.M.; Project administration, B.Z.; Funding acquisition, R.M. All authors have read and agreed to the published version of the manuscript.

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