Gender differences in sleep disorders

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Purpose of review

To evaluate recent evidence regarding gender differences in sleep.

Recent findings

Women have better sleep quality compared with men, with longer sleep times, shorter sleep-onset latency and higher sleep efficiency. Despite this, women have more sleep-related complaints than men. The amount of slow-wave sleep decreases with age in men and women. Normal physiologic periods, including puberty, menstruation, pregnancy, and menopause, are associated with alterations in sleep patterns.

Gender differences in normal sleep may underlie the observed differences in risk of sleep disorders. Studies of insomnia support a female predominance, with increased divergence of prevalence between men and women with older age. Recent findings for the gender differences in obstructive sleep apnea have focused on differences in local neuromuscular reflexes and central ventilatory control. Restless legs syndrome has a slight female predominance, whereas rapid eye movement sleep behavior disorder and Kleine–Levin syndrome are more common in men.

Summary

Gender differences in sleep become apparent after the onset of puberty. Menstrual cycles, pregnancy, and menopause can alter sleep architecture. Gender-related differences in sleep disorders, such as obstructive sleep apnea, insomnia, and restless legs syndrome, include differences in prevalence, pathophysiology, clinical presentation, and response to therapy.

Keywords

gender, sleep, sleep disorders

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Abbreviations

NREM	nonrapid eye movement
OSA	obstructive sleep apnea
REM	rapid eye movement
RLS	restless legs syndrome
SWS	slow wave sleep

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Introduction

Sleep occupies one-third of our lifetime, and plays a major role in maintaining health. Gender-related differences in normal sleep may underlie the risk of developing sleep disorders. Previous reviews have been published on the topic of gender differences in sleep [1]. Our objective was to evaluate the recent evidence regarding gender differences in sleep and sleep disorders.

Gender differences in normal sleep

In order to understand the gender differences in sleep disorders, we must first address gender differences in 'normal sleep'. These include the stimulus for sleep onset, the duration of sleep, and sleep architecture.

What is 'normal sleep'?

Sleep is the 'reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment' [2]. Sleep is a heterogeneous state that includes rapid eye movement (REM) and nonrapid eye movement (NREM) sleep. REM is characterized by mixed-frequency electroencephalogram activity, muscle atonia, and eye movements, whereas NREM sleep is characterized by quiescent electroencephalogram synchrony with muscle activation potential. NREM sleep is further classified by depth of sleep, from Stage 1 to Stage 3–4 [slow wave sleep (SWS)].

The determinants of sleep onset are multifactorial, and include duration of prior wakefulness, time of day, genetics, environment, comorbid conditions and medication effects. The timing, duration and architecture of sleep changes in humans with age, as shown in Table 1. With older age, frequent arousals and advanced sleep phase contribute to decreased sleep efficiency, independent of the presence of sleep disorders.

Men and women sleep differently

Most research in gender differences in sleep has been conducted in adults. Among young adults, women have better sleep quality (shorter sleep onset latency, higher sleep efficiency) compared with men [3]. While healthy women appear to objectively have better quality sleep than men, women of all adult age groups report more sleep problems, including inadequate sleep time and insomnia [4,5•]. Additionally, men are more likely than women to function at their best during the day with less than seven hours of sleep (58% versus 43%) [6••]. This suggests that women are either more susceptible to clinical symptoms

Table 1 Normal sleep characteristics in humans across the age spectrum

Age group	Sleep onset	Sleep duration	Sleep architecture	Sleep cycling
Newborns	Via REM ('active') sleep	16 h – nonconsecutive. Usually four to five sleep periods per 24 h	'Active' and 'quiet' sleep represent immature forms of REM and NREM sleep	50–60 min
Childhood	Transitions from REM to NREM sleep	Circadian rhythm of sleep – majority of sleep during nocturnal hours. Single consolidated sleep period usually by age 5 years	Fully developed REM and NREM architecture achieved by age 6 months	60–90 min
Young adults	Via NREM sleep	7–8 h	Maximal amount of SWS Stage 1 NREM sleep : 2–5% Stage 2 NREM sleep : 45–55% Stage 3 NREM sleep : 3–8% Stage 4 NREM sleep : 10–15% REM : 20–25%	90–110 min SWS predominates in first one-third of night REM predominates in last one-third of night
Older adults	Via NREM sleep	Increased interindividual variability	Reduction in SWS. Increased number of arousals, decreased sleep efficiency	90–110 min REM predominates in last one-third of night

REM, rapid eye movement; NREM, nonrapid eye movement; SWS, slow wave sleep (Stages 3 and 4).

from inadequate sleep, or are more likely to report symptoms in general.

Subjective and objective sleep quality decline with age. REM sleep appears to be well preserved with age, while the amount of SWS declines. By visual staging methods, women appear to have less of a decline in SWS than men [7–9]. The use of electroencephalogram spectral analysis for sleep staging, however, does not support this gender difference in the amount of SWS [10,11]. Older women do have a higher rate of sleep complaints compared with age-matched men [12], but the reasons for this observed difference has not been elucidated to date.

Conditions that impact sleep

Gender differences in sleep and sleep disorders are exacerbated by distinct hormonal and physical changes in women that confer altered risk for sleep disturbances and sleep disorders.

Puberty

In prepubertal children, differences in sleep quality and sleep duration by gender have not been consistently shown. After puberty, hormonal fluctuations, environmental stresses (e.g. early school time), and onset of affective disorders (e.g. depression, anxiety) contribute to changes in sleep. Knutson [13] studied the association between sleep and pubertal development in cohort of adolescents aged 12–16 years. The author reported increased sleep problems (insomnia, daytime tiredness, and insufficient sleep) associated with pubertal development in girls, but not in boys [13]. The author did not find an association between height velocity (inches/year) and sleep duration in boys or girls in this study, suggesting that the hormonal changes, rather than the physical changes, associated with puberty may explain the changes in sleep.

Menstrual cycle

The menstrual cycle of young healthy women is characterized by fluctuations of hormone levels (e.g. gonadal steroids, pituitary hormones, melatonin, and cortisol) and temperature control. Clinical studies to examine the effect of the menstrual cycle phase on sleep have been limited by: small numbers of participants; high variance in the length of menstrual cycles within and between women; a lack of control for ovulatory timing, particularly in perimenopausal women and women with anovulatory cycles; differences in sleep at home (e.g. young children may interrupt sleep) versus in the sleep laboratory; time restrictions limiting the number of menstrual phases studied; and a lack of control for comorbid affective disorders that may affect sleep quality [14]. Nonetheless, there are data to suggest differences in objective sleep and subjective symptoms across the menstrual cycle. Survey studies have supported the finding that the luteal phase is associated with more sleep disruption, such as longer initial sleep latency, lower sleep efficiency, and poorer subjective sleep quality, compared with the follicular phase [15,16]. Other studies using overnight polysomnography, however, have failed to show objective differences in sleep architecture by menstrual phase [17,18].

The International Classification of Sleep Disorders (2nd edition) [19••] includes a diagnostic category for menstrual-related hypersomnia, which is described as recurrent 1-week episodes of hypersomnia that occur in association with the menstrual cycle, and usually resolves rapidly at the time of menses. Onset of this disorder generally occurs within a few months of menarche, and oral contraceptives are effective treatment.

Pregnancy

A review of the effects of pregnancy on respiration and sleep was recently published [20]. The physical changes of pregnancy, including abdominal distension, fetal movement, bladder distention, urinary frequency, backache and heartburn, may all result in reduced sleep efficiency and increased nocturnal awakenings. Insomnia and daytime sleepiness are common complaints during pregnancy. Polysomnography reveals reduced slow wave and REM stages of sleep, and increased total sleep time and wake after sleep onset, all of which progress during the course of the pregnancy. Sleep efficiency is also reduced, and remains poor up to 3 months post partum [21,22].

Hormonal changes with pregnancy, especially increased estrogen and progesterone, also affect sleep. Progesterone can stimulate the ventilatory drive, as well as have a strong sedating effect. Estrogen is related to changes of the upper airway, including mucosal edema, hyperemia, and mucus hypersecretion, all of which can increase upper airway resistance. Snoring is common during pregnancy, occurring in more than 14% of pregnant women by the third trimester, as compared with 4% of nonpregnant, age-matched controls [23]. Obstructive sleep apnea (OSA) has been described during pregnancy and is associated with pregnancy-induced hypertension and intrauterine growth retardation [24].

Restless legs syndrome (RLS) can contribute to sleep-onset insomnia, and can be associated with periodic limb movements, disrupting nocturnal sleep significantly. In one large study from Japan [25], the prevalence of RLS in pregnant women (who did not have RLS before pregnancy) ranged from 15% in the first trimester to 23% by the final trimester. This increased prevalence of RLS may reflect relative iron or folate deficiency during pregnancy [26].

Menopause

Menopause, the cessation of menstrual periods, is associated with a change in the hormonal environment in women. The perimenopausal period is associated with large fluctuations in hormone levels, with a decrease in circulating estradiol, inhibin, and testosterone, and an increase in follicular stimulating hormone and luteinizing hormone. These changes in hormones are associated with physical, physiologic, and psychologic changes that affect sleep.

The prevalence of insomnia increases following menopause, from 33–36% in premenopausal women to 44–61% postmenopause [14]. Reasons for this increase in insomnia include hot flashes, mood disturbances (e.g. depression and anxiety), and increase in primary sleep disorders (e.g. OSA and RLS) with age. Despite these symptoms, objective evidence of sleep from a large population-based polysomnographic study shows better sleep (longer total sleep times, increased SWS, and increased sleep efficiency) in postmenopausal compared with premenopausal women [27]. This points to a disconnection between subjective and objective qualities of sleep measured by polysomnography in older women.

Hormone replacement therapy may alleviate some of the sleep disturbances associated with menopause. Among postmenopausal women, the prevalence of obstructive sleep apnea in hormone replacement therapy users is approximately one-half that of nonusers [28]. Oral synthetic estrogens have been shown to objectively improve polysomnographic sleep parameters, whereas other studies of transdermal estrogen, oral conjugated estrogen with progestin and progesterones [29–31] show subjective sleep improvement without objective changes. Hormone replacement therapy is also highly effective in treating hot flashes and the accompanying discomfort [14].

Gender differences in sleep disorders

Gender differences have been observed in many sleep disorders, including insomnia, OSA, RLS, and others. Underlying reasons for gender differences in sleep disorders are attributed to differences in normal sleep, differences in clinical manifestations of disturbances of sleep, and differences in risk factors for sleep disorders.

Insomnia

Insomnia is the most common sleep complaint, with a lifetime prevalence of one-third of the general adult population. Johnson *et al.* [32] studied 1014 adolescents from a random sample of an urban health maintenance organization population, and found no difference in risk of insomnia in prepubertal girls compared with boys – but the onset of menses in girls conferred a 2.75-fold increased risk of insomnia. A recent meta-analysis found a higher risk of insomnia in women compared with men (risk ratio, 1.41; 95% confidence interval, 1.28–1.55) [5•]. In addition, this study suggested an increasingly divergent risk of insomnia in women compared with men with increasing age, with women over the age of 65 years having the highest risk of insomnia (risk ratio, 1.73; 95% confidence interval, 1.65–1.83).

The relationship between gender and insomnia may be related to the risk factors for insomnia. Anxiety and depression are affective disorders that are more common in women than men, and are associated with insomnia [33]. Whether the association between insomnia and depression is cause or effect is still in question – insomnia is used as a diagnostic criteria for affective disorders, but insomnia has also been shown to predate and predict a depressive episode [34]. Insomnia is also more common

in persons who are widowed, divorced, or separated, an association that is stronger in women than men [35]. Additionally, women are more likely to present with symptoms of insomnia for alternate primary sleep disorders, such as OSA, which contributes to misdiagnoses and delays in effective treatment.

Women are more likely to present to their physician with complaints related to sleep, and as a result are more likely to be prescribed hypnotics, such as benzodiazepines, sedating antidepressants, and antipsychotics, for the treatment of insomnia [36,37], despite a lack of evidence for efficacy and their side-effect profiles. Alcohol is more commonly used in men than women to self-treat insomnia [38], which is more likely to cause increases in subsequent daytime sleepiness.

Obstructive sleep apnea

OSA, defined as an apnea hypopnea index of at least five events per hour, is prevalent in 24% of men and 9% of women in the US adult population [39]. The inclusion of the diagnostic criteria of daytime hypersomnolence reduces the difference in prevalence between men and women (4% and 2%, respectively). Differences in the prevalence of OSA are attributed to differences in clinical presentation and differences in pathophysiology. A recent review of the current literature regarding gender differences in OSA has been published [40,41].

Clinical presentation of OSA

Typical symptoms associated with OSA include snoring, daytime sleepiness, and witnessed apneic events. Men usually present with typical symptoms of snoring or daytime sleepiness. Women, however, are more likely to present with atypical initial symptoms of insomnia or fatigue, or have concomitant clinical depression or hypothyroidism [42], all of which can cause diversion from the diagnosis of OSA. Witnessed apneic events are also less commonly reported for women than men.

The difference in the prevalence of OSA by gender is magnified in the clinic and hospital patient population. Reasons for this magnified difference include: atypical presentation of women with OSA making diagnosis and management of the sleep disorder less likely; the difference in prevalence of OSA by gender may be increased with higher severity of disease [43,44]; and women are less likely to come to the clinic accompanied by their bedpartner, whose complementary sleep history (of nocturnal snoring, witnessed apneas) may assist in the diagnosis of OSA.

Pathophysiology of OSA

The upper airway composition, including the soft palate and tongue volume [45] and pharyngeal length [46], has been shown to be larger in men than women. Nonetheless, the upper airway caliber is greater in men than in women in both normal [47] and OSA [48] patients during wakefulness, suggesting that characteristics other than upper airway anatomy are responsible for the predisposition to OSA. Obesity has been identified as a strong risk factor for OSA. Women are more likely to be obese (body mass index $\geq 30\,kg/m^2$) than men [49]. The distribution of total body fat, however, is probably more important than the overall body mass index. In men and women of similar body mass index and waist circumference, men have greater upper body obesity, as measured by smaller hip circumferences and greater subscapular skin fold thickness [50], which increases the resistive load of the upper airway.

Physiologic responses to upper airway collapse include local neuromuscular reflex activation and central ventilatory control. There is no conclusive evidence of gender differences in upper airway neuromuscular responses to inspiratory flow limitation or predisposition to local trauma caused by repetitive upper airway collapse. Central ventilatory control, however, does have gender differences. During sleep, women have a lower apnea threshold (level of arterial carbon dioxide below that at which an apnea is induced) compared with men [51]. Arousal from sleep induces greater ventilatory instability in men compared with women [52]. With inspiratory flow limitation during NREM sleep, women are also less likely to exhibit apneas [53] and hypoventilation [54] compared with men. The differences in responses to physical and chemical changes associated with OSA may therefore underlie the gender differences in prevalence and clinical presentation of the disorder.

Treatment of OSA

Conventional treatment of OSA [55–57] is via nasal continuous positive airway pressure. While nasal continuous positive airway pressure is effective in resolving upper airway obstruction, compliance to therapy is variable – from 46% to 89% depending on the definition of compliance. Gender differences in nasal continuous positive airway pressure compliance are not conclusive, with some studies showing higher compliance in men and others showing higher compliance in women.

Other modes of OSA therapy include weight loss, upper airway surgery, and oral appliances. While women with OSA have been shown to be generally more obese than their male counterparts, weight loss in patients with OSA has been shown to be a more effective treatment strategy in men compared with women [58]. Bariatric surgery has been shown to effectively decrease the apnea–hypopnea index. Men, however, are reported to have a higher risk of postoperative mortality than women [59], and therefore are generally not considered good candidates for this procedure. Upper airway surgeries have not been found to

be effective treatment options for OSA, and there is no evidence to suggest a difference in the results of this procedure by gender. Oral appliances relieve upper airway obstruction by mandibular advancement or tongue protrusion, both of which can potentially increase the posterior pharyngeal space. Oral appliances are most beneficial in mild to moderate OSA, which is more common in men, and in those with supine position-dependent OSA, which is again more common in men [60,61].

Restless legs syndrome

RLS is a sensory disorder that affects 10% of US adults [62•]. Prevalence studies of RLS indicate a slight female predominance for the disease [63,64]. This observation may be accurate and may result from gender differences in risk factors for developing RLS (e.g. iron deficiency, psychiatric disorders, medications for psychiatric disorders) or from selection biases inherent in prevalence studies. Studies of inheritance patterns of RLS are conflicted, showing either a higher female-to-female transmission predilection or no gender differentiation.

Prevalence studies for RLS may suggest a higher prevalence in women because the sleep disturbance caused by RLS may have more of an impact on women than men. As mentioned earlier, women are more prone to insomnia than men, and RLS may simply exacerbate this tendency for sleep disruption in women. Evidence that women have a lower threshold for pain [65] and will report increased distress of clinical pain [66] also suggests that women are more likely to present to their physician or participate in a research study to alleviate their symptoms of RLS.

Other sleep disorders

Sleep disorders of lesser prevalence have also been studied for gender differences. REM sleep behavior disorder is a parasomnia characterized by complex motor activity during REM sleep. While the overall prevalence of REM sleep behavior disorder is unknown, this disorder affects primarily men older than 50 years [67]. Narcolepsy is a sleep disorder that manifests with symptoms of excessive daytime sleepiness, cataplexy, hypnogogic hallucinations, and/or sleep paralysis, and has a slight male predominance [19••]. Kleine–Levin syndrome is a rare disorder of symptoms that include hypersomnia, hyperphagia, and hypersexuality. Arnulf *et al.* [68] reported a meta-analysis of all Kleine–Levin syndrome reports in

Table 2 International classification of sleep disorders and gender predominance

Insomnia	Sleep-related breathing disorders	Hypersomnia	Circadian rhythm sleep disorders	Parasomnias	Sleep-related movement disorders
Female predominant					
Adjustment insomnia		Menstrual-related hypersomnia		Nightmares	Restless legs syndrome
Psychophysiologic insomnia				Sleep-related dissociative disorders	
Idiopathic insomnia				Exploding head syndrome	
Insomnia due to mental disorder				Sleep-related hallucinations	
				Sleep-related eating disorders	
Male predominant					
	Central sleep apnea syndromes	Narcolepsy		Confusional arousals	Periodic limb movement disorder
	Obstructive sleep apnea syndromes	Kleine–Levin syndrome		Rapid eye movement sleep behavior disorders	Sleep-related leg cramps
	Idiopathic hypoventilation			Sleep terrors	
				Sleep paralysis	
No gender predominance					
Inadequate sleep hygiene	Congenital central alveolar hypoventilation	Idiopathic hypersomnia	Delayed sleep phase	Sleepwalking[a]	Sleep-related rhythmic movement disorder
Behavioral insomnia of childhood		Insufficient sleep syndrome	Advance sleep phase	Sleep enuresis[b]	Sleep-related bruxism
			Irregular sleep-wake	Sleep-related groaning	
			Free-running		

[a] Violent or injury associated with sleepwalking is more common in men.
[b] Sleep enuresis is more common in boys than girls; in older adults, sleep enuresis is more common in women than men.

the literature. They found a mean age onset of 15 years, with overall prevalence higher in males (68%) but a longer duration of disease in women (9 ± 8.7 versus 5.4 ± 5.6 years, $P = 0.01$).

Numerous other sleep disorders have been identified with potential gender differences in prevalence, symptoms, or predisposition. These are summarized in Table 2.

Conclusion

Gender differences in sleep quality and sleep efficiency have been established in healthy individuals. These differences are magnified in the presence of sleep disorders, such as insomnia and OSA, which further disrupt nocturnal sleep and subsequent daytime functioning. While gender differences in hormone milieu, body fat composition, and physical attributes contribute to differences in sleep disorder diagnosis and manifestation, it would clearly be an oversimplification to conclude that these are the only differences between men and women.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 467).

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