Published in final edited form as:

Sleep Med Clin. 2018 March ; 13(1): 1–11. doi:10.1016/j.jsmc.2017.09.001.

Sleep in Normal Aging

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SYNOPSIS

Along with many physiological alterations in normal aging, sleep patterns change with aging, independent of other factors such as medical comorbidity and medications. Age-related changes in sleep include advanced sleep timing, shortened nocturnal sleep duration, increased frequency of daytime naps, increased number of nocturnal awakenings and time spent awake during the night, decreased slow wave sleep, and other changes. Most of these changes appear to occur between young and middle adulthood, as sleep parameters remain largely unchanged among healthy older adults. In addition, the circadian system and sleep homeostatic mechanisms become less robust with normal aging. In addition, the amount and pattern of sleep-related hormone secretion change in normal aging. All these changes contribute to or correlate with age-related changes in sleep. However, healthy older adults are less likely to report sleep problems. Finally, the causes of sleep disturbances in older adults are multifactorial, which include medical and psychiatric conditions, primary sleep disorders, and changes in environment, social engagement, and lifestyle.

Keywords

Sleep architecture; Circadian rhythm; Sleep homeostasis; Hormone; Normal aging

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Disclosure Statement

N/A

INTRODUCTION

Sleep has received increasing attention within the context of geriatric research based on a growing body of evidence that links poor sleep with many adverse health outcomes, especially decline in cognition, in older adults. Along with many other physiological alterations in normal aging, sleep patterns change with aging, independent of many factors including medical comorbidity and medications.¹ Total sleep time, sleep efficiency, and deep sleep (slow wave sleep) decrease with aging; and number of nocturnal awakenings and time spent awake during the night increase with aging.² These age-related changes in sleep are associated not only with changes in the circadian and homeostatic processes, but also with some normal physiological and psychosocial changes in aging. This article describes age-related changes in sleep, circadian rhythms, and sleep-related hormones. We will focus on changes associated with normal aging rather than changes that accompany common pathological processes in older adults, which are discussed in detail in other chapters.

AGE-RELATED CHANGES IN SLEEP

There is no doubt that sleep changes as a function of age.³ Aging is associated with decreased ability to maintain sleep (increased number of awakenings and prolonged nocturnal awakenings), reduced nocturnal sleep duration, and decreased deep sleep (slow wave sleep).⁴ Here we discuss in detail age-related changes in sleep duration, sleep initiation, sleep efficiency, sleep maintenance, sleep stages, daytime sleep behaviors, and self-reported sleep quality. An important aspect of this discussion is to differentiate changes in sleep that occur from childhood to age 60 (or 65), versus those that occur after this point. Ohayon and colleagues comprehensively reviewed the normative sleep changes from childhood to old age using meta-analysis results from 65 studies (polysomnography or actigraphy) representing 3,577 healthy subjects aged between 5 and 102 years,² and this provides many of the insights discussed in this review. Older subjects (defined as age >60 years) in this analysis were more representative of older adults with excellent health and who were optimally aging, rather than the general older adult population.⁴

Sleep duration

The current literature supports that, in general, the total sleep time (TST) decreases with age (from pediatric to older adulthood). However, further age-associated decreases in TST have not been consistently observed after entering older age brackets. Campbell et al. 2007 conducted a laboratory study with 50 healthy adults aged between 19 and 81 years to evaluate the spontaneous sleep across the 24h day among young, middle-aged, and older adults. Compared with young adults (10.5 hours), middle-aged (9.1 hours) and older adults (8.1 hours) had significantly shorter average nighttime sleep duration.⁵ Data from 160 healthy adults (without sleep complaints) aged between 20 and 90 from the SIESTA database showed that TST decreased about 8 minutes per decade in males and 10 minutes per decade in females.⁶ Similarly, three meta-analysis reviews reported that age was linearly associated with decreased TST, with an approximately 10 – 12 minutes reduction per decade of age in the adult population.^{2,7,8} This association was stronger when comparing young adults with middle-aged or older adults, but vanished within older subjects who were 60

years and above. These findings indicate that TST plateaued after 60 years of age. Also, the association was stronger in women than men.²

Sleep initiation

People commonly assume that the ability to initiate sleep declines significantly with age. However, current evidence does not support this assumption but suggests that both sleep latency and the ability to fall back to sleep after nocturnal awakenings demonstrate minimal increases after age greater than 60 years. Results from two meta-analyses, for example, suggest that sleep latency does increase with age. However, the magnitude of change is very modest.^{2,8} In these studies, sleep latency holds constant from childhood to adolescence. The significant age-related increase in sleep latency was only found between very young adults and older adults. A mathematical modeling, which was conducted using data from seven laboratory sleep studies (258 subjects aged 17 to 91 years), suggested that sleep latency increased between late teens and twenties, remains constant from age 30 until approximate age 50 years, and then increased steadily after age 50 years.⁹ However, the amount or magnitude of changes were not reported. In addition, even though more frequent arousals were found in healthy older adults than young people, older adults maintained their ability to reinitiate sleep and fell back to sleep as rapidly as younger adults.^{3,10}

Sleep efficiency

Sleep efficiency remains largely unchanged from childhood to adolescence and significantly decreases with age in adulthood. Different from all other sleep parameters that hold steady after 60 years of age, sleep efficiency continues to decline very slowly with advancing age.²

Sleep maintenance

Aging from birth to older adulthood is associated with decreased ability to maintain sleep, which presents as the increased number of arousals (arousal index) and longer duration of wake after sleep onset (WASO), but also tends to plateau after age 60.^{2,8} In Ohayon and colleagues' meta-analysis, age-related change in WASO achieved the largest effect size among all sleep parameters, which yielded a steady 10 minutes increase of WASO per decade of age from 30 to 60 years. WASO remained mostly unchanged after age 60 years.²

Sleep stages

In general, deep sleep (slow wave sleep) decreases with age in the adult population. During nocturnal sleep, the proportion of non-rapid eye movement sleep (NREM) stage 1 and stage 2 increases with age, and the proportion of slow-wave sleep and REM sleep decreases with age^{2,11} (see Figure 1). These changes were not significant among healthy older adults aged above 60 years². Also, the association between age and decreased REM latency was minimal.² Floyd et. al.'s meta-analysis reported a linear decrease in the proportion of REM with a small rate of 0.6% per decade from age 19 until 75 years, then small increases were found in the proportion of REM between 75 and 85 years.⁷

There may be gender differences in age-related changes in sleep stages. Ohayon et al.'s meta-analysis suggested that the age effect on the percentage of stage 1 sleep was stronger in women, and women had less percentage of stage 2 sleep and a greater percentage of SWS

than age-matched men. The SIESTA study found that women had no change in SWS with age, in contrast to men who had a 1.7% decrease in SWS per decade of age. In addition, women had a smaller rate of increase in Stage 1 sleep, a greater rate of increase in stage 2 sleep, and a greater rate of decline in REM, in comparison with men.⁶ These results indicate that men may be more prone to age-related decline in SWS than women.

Daytime napping and daytime sleepiness

Daytime napping is a daily routine for many people across the lifespan. Results from epidemiology studies suggest that daytime napping is more prevalent in older adults than that seen in younger adults.^{12–15} Several studies have found that older adults nap more frequently than younger and middle-aged adults,^{14,16,17} this is also true when comparing healthy older adults with younger individuals.¹⁸ Within the older population, one study found that nap frequency increased with age.¹⁹ A recent study using 7664 people, aged 20–99 years, from a national representative sample of Japan, found that a higher proportion of older adults (27.4%) take frequent naps (≥ 4 days/week) than young (11.9%) and middle-aged (14.4%) adults.¹⁴ However, no clear evidence supports that nap duration is different between older adults and other adult populations.^{5,19} Campbell et al. 2007's laboratory study showed that nap durations were not different among the young, middle-aged, and older adults, but the number of daytime naps increased with age.⁵ Yoon and colleagues reported that older adults tended to nap at a different time than younger adults, where older adults were more likely to nap in the early evening, while younger adults were more likely to nap in the afternoon.^{18,20}

People choose to take a nap for many reasons, such as to compensate for nighttime sleep loss, to restore energy and reduce daytime sleepiness, or just to relax.²⁰ Cultural background also has a considerable influence on nap habits. For example, mid-day naps are a common practice of people from China, Mediterranean and several Latin-American countries.²¹ Older adults may nap more frequently due to both biological changes but also lifestyle changes that accompany aging. For example, older adults may spend less time on work, physical, and social activity, thus have more opportunities to nap than young and middle-aged adults during the day. Also, Foley and colleagues found that frequent napping was associated with excessive daytime sleepiness (EDS), depression, pain and nocturia in a U.S. nationally representative poll of older adults.²²

Epidemiological studies indicated that up to 20% of older adults reported EDS.^{23–26} EDS usually co-exists with multiple adverse health conditions, including cognitive impairment, cardiovascular events, and increased mortality risk.^{27,28} Certainly, EDS is not a part of normal aging, but may be a signal or symptom of certain diseases. An epidemiological study found a linear decline in the prevalence of EDS with age between 30 and 75 years. In addition, the prevalence of EDS dropped at a higher rate after the age of 75 years.²⁹ Daytime napping could be a practice to reduce daytime sleepiness,¹⁵ however, some older adults may experience daytime sleepiness but do not fall asleep during the day.²⁶

Self-reported sleep quality

People may expect that older adults complain more about their sleep than younger aged adults since most objectively measured sleep parameters decline with age. However, this may not be the case as there can be significant differences between objective and self-reported perceptions of sleep, and comorbidities can play a major role. For example, while some epidemiological studies found that up to 50% of older adults have self-reported poor sleep,^{30,31} a large proportion of these complaints are attributable to older adults' poor health status and disease burden.^{30,32} Evidence shows that older adults were less likely to self-report poor sleep than younger individuals, especially after controlling for comorbidities and health.³³ Vitiello and colleagues examined objectively measured sleep among 150 healthy older adults who reported no sleep problems and found that significant proportions of them (33% of women and 16% of men) had impaired objectively measured sleep.³⁰ Healthy older adults may be prone to perceive good sleep quality.³⁴ In addition, older adults may expect their sleep will be less consolidated as they age, and they may accept some noticeable sleep changes as a part of normal aging due to an adjustment of their perception of "acceptable" health with aging.^{33,35}

As described above, many sleep characteristics change with age in adulthood. For example, nocturnal sleep duration, sleep efficiency, slow wave sleep, and self-reported poor sleep decrease with age; while, number of awakenings, WASO, and daytime napping frequency increase with age. However, most of these changes stop at approximately 60 years of age. After that age, most sleep variables appear to remain largely unchanged within the older adult population.

AGE-RELATED CHANGES IN CIRCADIAN RHYTHMS

The circadian system regulates several human physiological functions, including body temperature, heart rate, blood pressure, release of certain hormones, bone remodeling, sleep-wake rhythm, and rest-activity pattern.³⁶ It is well documented in the literature that circadian rhythms become less robust with aging, which typically presents as an advance in circadian timing, a decrease in circadian amplitude, and a reduced ability to adjust to phase shifting (changes in the phase of circadian rhythms). The suprachiasmatic nucleus (SCN) is the central endogenous circadian pacemaker that regulates 24-hour circadian rhythms. The disruption of circadian rhythms with advancing age may be associated with a progressive decline in the function of the SCN.³⁷

Phase advance

The timing and structure of sleep are mainly regulated by the circadian system and homeostatic sleep regulation.³⁸ Older adults commonly experience an advance of sleep schedule to earlier hours. They tend to have sleepiness earlier in the evening and wake up earlier in the morning than desired.³⁶ This earlier sleep timing in older adults may be due to the age-related phase advance in their circadian rhythm. This phase advance is seen not only in the sleep-wake cycle, but also in the body temperature rhythm, and in the timing of secretion of melatonin and cortisol,³⁹⁻⁴¹ all of which are about one hour advanced in older people compared to young adults.⁴² Figure 2 compares circadian phase between older and

younger adults. However, Duffy and colleagues found that the phase advance in sleep timing was greater than phase advance in other circadian clocks, which suggested that a mechanism (e.g. sleep homeostasis) other than circadian phase advance alone may be involved in older adult's early sleep timing.⁴³

Reduced amplitude in circadian rhythms

Aging is associated with a reduction in the amplitude of several circadian rhythms in older adults, including core body temperature, melatonin, and cortisol secretion, activity, and sleep.^{44–47} The age-related reduction in circadian amplitude may be related to sleep disruption in older adults.⁴⁸ It was reported that, compared to young adults, older adults were more likely to wake up close to the timing when body temperature reached nadir.⁴⁹ This finding indicated that the biological clock (e.g., body temperature) in older adults might also regulate their awakening time, which may result in even earlier awakenings in older adults.^{36,49} Also, the reduced amplitude of daytime activity may result in daytime napping, which may further reduce the amplitude of the sleep-wake rhythm. Age-related decline in amplitude of melatonin secretion may also play a role in sleep problems in older adults.^{50,51} (as described below).

Decreased ability adjusting to phase-shifting

The ability to phase-shift decreases with aging.⁵² Older adults are subject to more difficulties in adjusting to phase shifts, such as shift work and jet lag.^{4,52} Monk and colleagues found that older adults needed more time to recover from phase-shifting, and experienced a longer period of sleep disruption and daytime disfunction.⁵³ The age-related loss of rhythmic function within the SCN may partially explain this impaired ability in phase shifting.⁵⁴

Changes in sleep homeostasis

Some research indicates that the earlier sleep timing and less consolidated sleep in older adults may be attributable to the interaction between the circadian system and homeostatic regulation, rather than simply resulting from an age-related phase advance in circadian rhythm.^{6,55} Sleep homeostasis regulates wake and sleep and generates sleep pressure as a function of time of being awake. Sleep pressure increases during waking and sleep deprivation, and decreases during sleep.⁵⁶ Sleep homeostasis declines with aging. The age-related decrease in TST and sleep efficiency may be partially due to the reduced homeostatic sleep pressure with aging.^{57–59} Also, this reduced homeostatic sleep pressure contributes to an increased number of nocturnal awakenings and reduced daytime sleepiness.^{58,59} For example, one study that forced desynchronized circadian cycles found that older adults had 2.7 times more nocturnal awakenings than young individuals at most circadian phases.¹⁰

SLEEP-RELATED HORMONES, AGING AND SLEEP

Age-related changes in neuroendocrine function are associated with alterations in sleep quality and sleep architecture with normal aging. We will briefly review changes of several sleep-related hormones with normal aging and their associations with sleep. Most studies in this area group older adults into a single age category as compared to young or middle-aged

adults, and limited data exists related to hormonal changes with advancing age within the older adult age group per se.

Growth hormone

Growth hormone (GH) secretion and slow wave sleep impact each other.^{60,61} GH secretion mainly pulses during nocturnal sleep (no matter whether the sleep is advanced, delayed, or fragmented) at about 1 hour after sleep onset and decreases at transient awakenings.⁶² On the other hand, the inhibition of growth hormone releasing hormone (GHRH) suppresses GH secretion, promotes corticotrophin releasing hormone, and reduces SWS.^{62,63} Further, there is an age-related decline in GH secretion.^{64,65} GH secretion reaches its peak during adolescence, rapidly declines in an exponential manner between young adulthood and middle age, and then declines slowly between middle to old age. This phenomenon is similar to the detected age-related decrease of SWS.⁶⁶ The decline in nocturnal GH with aging may have a direct or indirect impact on SWS, and may be partially responsible for the observed reduction of SWS in aging.

Cortisol

Cortisol secretion has a clear circadian pattern, which peaks shortly after the morning awakening, gradually declines throughout the day and reaches its nadir in the late evening, and then rises towards the morning peak.⁶⁶ Sleep, particularly SWS, inhibits cortisol secretion.^{67,68} The rise of cortisol secretion during sleep could lead to awakenings.^{68,69} The circadian rhythm of cortisol changes with aging, as manifested by a decreased circadian amplitude, an elevated nocturnal cortisol level, and likely a phase advanced rhythm.^{63,70,71} The elevated nocturnal cortisol level may contribute to decreased SWS and frequent awakenings during nocturnal sleep in older adults.⁷⁰

Prolactin

No clear evidence shows that the secretion of prolactin affects sleep. However, sleep has an influence on prolactin secretion.⁷⁰ Sleep onset is associated with an increased secretion of prolactin, regardless of day or night sleep.⁶⁶ Also, decreased SWS or fragmented sleep may be associated with a reduced elevation of prolactin during nocturnal sleep.⁶⁶ Studies show increased prolactin secretion during SWS or by enhancing SWS, and decreased prolactin secretion in prolonged awakening during the sleep period.^{72,73} Prolactin secretion during sleep may decrease with aging due to the lighter and more fragmented sleep in older adults. Studies suggest that nocturnal prolactin in healthy older adults was significantly lower than that in young adults.^{65,74}

Thyroid-stimulating hormone

Thyroid-stimulating hormone (TSH) secretion has a circadian pattern, which maintains a stable low level during the daytime, starts rising in the late afternoon, peaks around sleep onset, and then gradually declines through the night, and returns to its daytime level after morning awakenings.^{66,75} Studies have shown that SWS was associated with inhibited nocturnal TSH secretion, and awakenings were associated with increased nocturnal TSH secretion.^{76–78} The circadian release of TSH (with regards to acrophase and nadir) is

maintained with aging.⁷⁰ However, research suggests the overall 24-hour TSH secretion is decreased in older adults.⁷⁹

Melatonin

The 24-hour profile of plasma melatonin is primarily regulated by the light-dark cycle and the sleep-wake cycle.⁶⁶ Melatonin normally remains stable at a low level during the daytime, starts to increase progressively in the evening (2 hours before habitual bedtime) and remains elevated during the middle of the sleep period, and then drops gradually to its daytime level in the morning (8–9 am).⁶⁶ The onset of evening sleepiness correlates with the rise of evening melatonin secretion. Overall melatonin secretion decreases with aging, but daytime melatonin (which is already at a low basal level) may remain unchanged with aging. The elevation of nocturnal melatonin in older adults was significantly reduced when compared with young adults.^{50,80} Studies suggest that the age-related decline in melatonin secretion contributes to the increased sleep disruption in older adults.⁵⁰

Sex hormones

Changes in gonadotropins and sex steroids with aging are associated with sleep changes in older adults. In men, testosterone levels decrease progressively with aging after 30 years of age.^{81,82} Older men may also lose the diurnal testosterone pattern.⁸³ The decreased testosterone with aging may relate to the increased sleep fragmentation in older adults.⁷⁰ In women, estradiol levels decrease and follicle stimulating hormone levels increase significantly during the menopause transition and postmenopause. These changes in reproductive hormones have been associated with increased complaints of difficulty falling asleep and staying asleep.⁷⁰ Also, the decreased levels of endogenous estrogen and progesterone may have a negative impact on the upper airway, therefore, increasing the incidence of sleep disordered breathing (SDB) after menopause.⁸⁴

RISK FACTORS FOR SLEEP DISTURBANCES IN OLDER ADULTS

As reviewed above, most sleep parameters decline with age until the age of 60 years, but remain generally unchanged after 60 years of age. Also, older adults are less likely to complain of sleep problems and tend to accept some noticeable sleep alterations as normal changes with aging. The age-associated sleep changes discussed here are mostly relevant to older adults who have excellent health and are aging successfully. In the real world, medical comorbidities and psychiatric illness, primary sleep disorders, and changes in social engagement, lifestyle, and environment commonly accompany aging. These factors contribute to sleep disturbances in older adults. Indeed, up to 50–60% of older adults reported poor sleep quality.^{4,52} Therefore, sleep problems reported in older adults are usually multifactorial and are not necessarily explained by age alone.

Medical comorbidities and psychiatric illness

Approximately 67% of older adults have multiple comorbidities.⁸⁵ Osteoarthritis, cardiovascular disease, lung disease, gastroesophageal reflux, cancer, and diabetes are the most commonly reported medical comorbidities in older adults.^{4,86} About 90% of adults aged 65 and older take prescription drugs to treat their chronic medical conditions. More

than one-third of them routinely take over five medications.^{87,88} The discomfort and emotional distress from medical conditions contribute to an increased number of nocturnal awakenings and EDS in older adults. Also, chronic medical conditions are positively associated with the diagnosis or prevalence of sleep disorders, including insomnia, sleep apnea, and restless legs syndrome.⁸⁹ Of note, not only do these medical conditions cause sleep disturbances in older adults, but the sleep disturbances can also have a negative impact on medical illnesses and their associated symptoms. Evidence also shows that the multiple medications that older adults take can result in EDS, worsen primary sleep disorders, and contribute to comorbid insomnia.^{89,90}

Depression and anxiety, prevalent psychiatric problems among older adults, commonly coexist with insomnia in older adults. Epidemiological studies reported that more than 50% of older adults with depression have insomnia. Further, longitudinal studies have found that insomnia may increase the risk of depression in older adults. In addition, depression has been positively associated with EDS, and the diagnosis and severity of obstructive sleep apnea.⁹⁰

Primary sleep disorders

Several primary sleep disorders, which are common in older adults, contribute to poor sleep in older adults. These sleep disorders include insomnia, sleep-disordered breathing, periodic limb movements in sleep, restless legs syndrome, and REM sleep behavior disorder. Epidemiological studies found that the prevalence of these primary sleep disorders is considerably higher in older adults than that in younger adults.^{91,92} Medical and psychological comorbidities of aging contribute to the increased prevalence of insomnia symptoms (approximately 50%) in older adults. Interestingly, the prevalence of insomnia in older adults with excellent health is similar to that of younger adults.⁹³ The increase in SDB frequency in older adults may partially be due to an age-related reduction in pharyngeal muscle function and an increase in comorbidities in older adults.⁹⁴ The presentation of these primary sleep disorders contribute to poor sleep in older adults, in terms of difficulties in falling asleep, increased number of nocturnal awakenings, EDS, and complaints of non-restorative sleep.⁹¹

Social, lifestyle, and environmental factors

Many social and lifestyle change with aging contribute to sleep problems in older adults. Retired older adults have more flexible sleep schedules (which can be irregular), have more opportunity to nap during the day, are more sedentary, and are less involved in social activity than they used to be.^{95,96} These factors affect both sleep homeostasis and circadian regulation, thus contributing to sleep disturbances. In addition, the loss of loved ones can produce emotional distress and loneliness, which are known to contribute to sleep disturbance.⁴ Environmentally, many older adults, especially those who have multiple morbidities, lose independence in activities of daily living, and may move to new homes or long-term care facilities. This transition can be a major life event in later life and create several physical and psychological stressors. Sleep problems can rise or get worse during and after this transition. Finally, other environmental factors, such as temperature, noise, and light exposure, are also associated with sleep quality in older adults.^{97,98}

SUMMARY

Sleep changes with normal aging. In general, aging is associated with advanced sleep timing, decreased nocturnal sleep time and sleep efficiency, increased frequency of daytime naps, increased nocturnal awakenings, and decreased slow wave sleep. Most sleep parameters remain unchanged after 60 years of age in healthy older adults. Circadian system and sleep homeostasis become less robust with normal aging. The amount and pattern of sleep-related hormone secretion change in normal aging. All these changes contribute to or correlate with age-related changes in sleep. Poor sleep quality and sleep disturbances are not necessarily due to aging alone, even though sleep schedule, sleep quantity and sleep architecture change with age. Multiple factors that accompany the aging process, including medical and psychiatric conditions, and environmental, social and lifestyle changes, can contribute to sleep problems in older adults.

References

1. Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of psychosomatic research*. 2004; 56(5):497–502. [PubMed: 15172205]
2. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*. 2004; 27(7):1255–1273. [PubMed: 15586779]
3. Espiritu JR. Aging-related sleep changes. *Clin Geriatr Med*. 2008; 24(1):1–14, v. [PubMed: 18035227]
4. Vitiello MV. Sleep in normal aging. *Sleep Medicine Clinics*. 2006; 1(2):171–176.
5. Campbell SS, Murphy PJ. The nature of spontaneous sleep across adulthood. *J Sleep Res*. 2007; 16(1):24–32. [PubMed: 17309760]
6. Dorffner G, Vitr M, Anderer P. The effects of aging on sleep architecture in healthy subjects. *Adv Exp Med Biol*. 2015; 821:93–100. [PubMed: 25416113]
7. Floyd JA, Janisse JJ, Jenuwine ES, Ager JW. Changes in REM-sleep percentage over the adult lifespan. *SLEEP*. 2007; 30(7):829. [PubMed: 17682652]
8. Floyd JA, Medler SM, Ager JW, Janisse JJ. Age-related changes in initiation and maintenance of sleep: a meta-analysis. *Res Nurs Health*. 2000; 23(2):106–117. [PubMed: 10782869]
9. Floyd JA, Janisse JJ, Marshall Medler S, Ager JW. Nonlinear components of age-related change in sleep initiation. *Nurs Res*. 2000; 49(5):290–294. [PubMed: 11009124]
10. Klerman EB, Davis JB, Duffy JF, Dijk DJ, Kronauer RE. Older people awaken more frequently but fall back asleep at the same rate as younger people. *Sleep*. 2004; 27(4):793–798. [PubMed: 15283016]
11. Potari A, Ujma PP, Konrad BN, et al. Age-related changes in sleep EEG are attenuated in highly intelligent individuals. *Neuroimage*. 2016
12. Fang W, Li Z, Wu L, et al. Longer habitual afternoon napping is associated with a higher risk for impaired fasting plasma glucose and diabetes mellitus in older adults: results from the Dongfeng-Tongji cohort of retired workers. *Sleep medicine*. 2013; 14(10):950–954. [PubMed: 23831240]
13. Cao Z, Shen L, Wu J, et al. The effects of midday nap duration on the risk of hypertension in a middle-aged and older Chinese population: a preliminary evidence from the Tongji-Dongfeng Cohort Study, China. *Journal of hypertension*. 2014; 32(10):1993–1998. discussion 1998. [PubMed: 25023156]
14. Furihata R, Kaneita Y, Jike M, Ohida T, Uchiyama M. Napping and associated factors: a Japanese nationwide general population survey. *Sleep medicine*. 2016; 20:72–79. [PubMed: 27318229]
15. Milner CE, Cote KA. Benefits of napping in healthy adults: impact of nap length, time of day, age, and experience with napping. *J Sleep Res*. 2009; 18(2):272–281. [PubMed: 19645971]

16. Buysse DJ, Browman KE, Monk TH, Reynolds CF 3rd, Fasiczka AL, Kupfer DJ. Napping and 24-hour sleep/wake patterns in healthy elderly and young adults. *J Am Geriatr Soc.* 1992; 40(8):779–786. [PubMed: 1634721]
17. Ficca G, Axelsson J, Mollicone DJ, Muto V, Vitiello MV. Naps, cognition and performance. *Sleep Med Rev.* 2010; 14(4):249–258. [PubMed: 19962331]
18. Yoon IY, Kripke DF, Youngstedt SD, Elliott JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res.* 2003; 12(2):87–93. [PubMed: 12753345]
19. Beh HC. A survey of daytime napping in an elderly Australian population. *Australian Journal of Psychology.* 1994; 46(2):100–106.
20. Stong, KI, Ancoli-Israel, S. Napping in older adults. In: Avidan, AY., Alessi, C., editors. *Geriatric Sleep Medicine*. 1st. New York, NY: 2008. p. 227–240.
21. Naska A, Oikonomou E, Trichopoulou A, Psaltopoulou T, Trichopoulos D. Siesta in healthy adults and coronary mortality in the general population. *Arch Intern Med.* 2007; 167(3):296–301. [PubMed: 17296887]
22. Foley DJ, Vitiello MV, Bliwise DL, Ancoli-Israel S, Monjan AA, Walsh JK. Frequent napping is associated with excessive daytime sleepiness, depression, pain, and nocturia in older adults: findings from the National Sleep Foundation ‘2003 Sleep in America’ Poll. *Am J Geriatr Psychiatry.* 2007; 15(4):344–350. [PubMed: 17384317]
23. Chasens ER, Sereika SM, Weaver TE, Umlauf MG. Daytime sleepiness, exercise, and physical function in older adults. *J Sleep Res.* 2007; 16(1):60–65. [PubMed: 17309764]
24. Jaussent I, Bouyer J, Ancelin ML, et al. Excessive sleepiness is predictive of cognitive decline in the elderly. *Sleep.* 2012; 35(9):1201–1207. [PubMed: 22942498]
25. Empana JP, Dauvilliers Y, Dartigues JF, et al. Excessive daytime sleepiness is an independent risk indicator for cardiovascular mortality in community-dwelling elderly: the three city study. *Stroke* (00392499). 2009; 40(4):1219–1224.
26. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the Cardiovascular Health Study. *Sleep.* 1998; 21(1):27–36. [PubMed: 9485530]
27. Lopes JM, Dantas FG, Medeiros JL. Excessive daytime sleepiness in the elderly: association with cardiovascular risk, obesity and depression. *Revista brasileira de epidemiologia = Brazilian journal of epidemiology.* 2013; 16(4):872–879. [PubMed: 24896592]
28. Blachier M, Dauvilliers Y, Jaussent I, et al. Excessive daytime sleepiness and vascular events: the Three City Study. *Annals of neurology.* 2012; 71(5):661–667. [PubMed: 22271307]
29. Bixler E, Vgontzas A, Lin H-M, Calhoun S, Vela-Bueno A, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. *The Journal of Clinical Endocrinology & Metabolism.* 2005; 90(8):4510–4515. [PubMed: 15941867]
30. Vitiello MV, Larsen LH, Moe KE. Age-related sleep change: Gender and estrogen effects on the subjective-objective sleep quality relationships of healthy, noncomplaining older men and women. *J Psychosom Res.* 2004; 56(5):503–510. [PubMed: 15172206]
31. Luo J, Zhu G, Zhao Q, et al. Prevalence and risk factors of poor sleep quality among Chinese elderly in an urban community: results from the Shanghai aging study. *PloS one.* 2013; 8(11):e81261. [PubMed: 24282576]
32. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep.* 1999; 22(Suppl 2):S366–372. [PubMed: 10394609]
33. Gooneratne NS, Vitiello MV. Sleep in older adults: normative changes, sleep disorders, and treatment options. *Clinics in geriatric medicine.* 2014; 30(3):591–627. [PubMed: 25037297]
34. Gooneratne NS, Bellamy SL, Pack F, et al. Case-control study of subjective and objective differences in sleep patterns in older adults with insomnia symptoms. *J Sleep Res.* 2011; 20(3):434–444. [PubMed: 20887395]
35. Brouwer WB, van Exel NJ, Stolk EA. Acceptability of less than perfect health states. *Soc Sci Med.* 2005; 60(2):237–246. [PubMed: 15522481]

36. Wright, KP., Frey, DF. Age related changes in sleep and circadian physiology: from brain mechanisms to sleep behavior. In: Avidan, AY., Alessi, C., editors. *Geriatric Sleep Medicine*. 1st. New York, NY: 2008. p. 1-18.
37. Mattis J, Sehgal A. Circadian Rhythms, Sleep, and Disorders of Aging. *Trends in Endocrinology & Metabolism*. 2016; 27(4):192–203. [PubMed: 26947521]
38. Schmidt C, Peigneux P, Cajochen C. Age-related changes in sleep and circadian rhythms: impact on cognitive performance and underlying neuroanatomical networks. *Sleep and cognition in the elderly*. 2015:5.
39. Kripke DF, Elliott JA, Youngstedt SD, Rex KM. Circadian phase response curves to light in older and young women and men. *Journal of Circadian Rhythms*. 2007; 5(1):1. [PubMed: 17210086]
40. Kim SJ, Benloucif S, Reid KJ, et al. Phase-shifting response to light in older adults. *The Journal of physiology*. 2014; 592(1):189–202. [PubMed: 24144880]
41. Duffy JF, Zitting K-M, Chinoy ED. Aging and circadian rhythms. *Sleep medicine clinics*. 2015; 10(4):423–434. [PubMed: 26568120]
42. Tranah, GJ., Stone, KL., Ancoli-Israel, S. Circadian Rhythms in Older Adults. In: Kryger, MH.Roth, T., Dement, WC., editors. *Principles and Practice of Sleep Medicine*. 6th. Philadelphia: Elsevier; 2017. p. 1510-1515.
43. Duffy JF, Zeitzer JM, Rimmer DW, Klerman EB, Dijk DJ, Czeisler CA. Peak of circadian melatonin rhythm occurs later within the sleep of older subjects. *Am J Physiol Endocrinol Metab*. 2002; 282(2):E297–303. [PubMed: 11788360]
44. Czeisler CA, Dumont M, Duffy JF, et al. Association of sleep-wake habits in older people with changes in output of circadian pacemaker. *Lancet*. 1992; 340(8825):933–936. [PubMed: 1357348]
45. Huang YL, Liu RY, Wang QS, Van Someren EJ, Xu H, Zhou JN. Age-associated difference in circadian sleep-wake and rest-activity rhythms. *Physiol Behav*. 2002; 76(4–5):597–603. [PubMed: 12126998]
46. Dijk DJ, Duffy JF. Circadian regulation of human sleep and age-related changes in its timing, consolidation and EEG characteristics. *Ann Med*. 1999; 31(2):130–140. [PubMed: 10344586]
47. Carrier J, Monk TH, Buysse DJ, Kupfer DJ. Amplitude reduction of the circadian temperature and sleep rhythms in the elderly. *Chronobiol Int*. 1996; 13(5):373–386. [PubMed: 8957588]
48. Van Someren EJ. More than a marker: interaction between the circadian regulation of temperature and sleep, age-related changes, and treatment possibilities. *Chronobiol Int*. 2000; 17(3):313–354. [PubMed: 10841209]
49. Duffy JF, Dijk D-J, Klerman EB, Czeisler CA. Later endogenous circadian temperature nadir relative to an earlier wake time in older people. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 1998; 275(5):R1478–R1487.
50. Pandi-Perumal S, Zisapel N, Srinivasan V, Cardinali D. Melatonin and sleep in aging population. *Experimental gerontology*. 2005; 40(12):911–925. [PubMed: 16183237]
51. Kondratova AA, Kondratov RV. The circadian clock and pathology of the ageing brain. *Nature Reviews Neuroscience*. 2012; 13(5):325–335. [PubMed: 22395806]
52. Bliwise, DL., Scullin, MK. Normal aging. In: Kryger, MH.Roth, T., Dement, WC., editors. *Principles and Practice of Sleep Medicine*. 6th. Philadelphia: Elsevier; 2017. p. 25-38.
53. Monk TH, Buysse DJ, Carrier J, Kupfer DJ. Inducing jet-lag in older people: directional asymmetry. *Journal of Sleep Research*. 2000; 9(2):101–116. [PubMed: 10849237]
54. Farajnia S, Deboer T, Rohling JH, Meijer JH, Michel S. Aging of the suprachiasmatic clock. *The Neuroscientist*. 2014; 20(1):44–55. [PubMed: 23924666]
55. Dijk D-J, Duffy JF, Czeisler CA. Contribution of circadian physiology and sleep homeostasis to age-related changes in human sleep. *Chronobiology international*. 2000; 17(3):285–311. [PubMed: 10841208]
56. Taillard J, Philip P, Coste O, Sagaspe P, Bioulac B. The circadian and homeostatic modulation of sleep pressure during wakefulness differs between morning and evening chronotypes. *Journal of sleep research*. 2003; 12(4):275–282. [PubMed: 14633238]
57. Dijk DJ, Duffy JF, Riel E, Shanahan TL, Czeisler CA. Ageing and the circadian and homeostatic regulation of human sleep during forced desynchrony of rest, melatonin and temperature rhythms. *J Physiol*. 1999; 516(Pt 2):611–627. [PubMed: 10087357]

58. Carrier J, Land S, Buysse DJ, Kupfer DJ, Monk TH. The effects of age and gender on sleep EEG power spectral density in the middle years of life (ages 20–60 years old). *Psychophysiology*. 2001; 38(2):232–242. [PubMed: 11347869]
59. Dijk DJ, Groeger JA, Stanley N, Deacon S. Age-related reduction in daytime sleep propensity and nocturnal slow wave sleep. *Sleep*. 2010; 33(2):211–223. [PubMed: 20175405]
60. Gronfier C, Luthringer R, Follenius M, et al. A quantitative evaluation of the relationships between growth hormone secretion and delta wave electroencephalographic activity during normal sleep and after enrichment in delta waves. *Sleep*. 1996; 19(10):817–824. [PubMed: 9085491]
61. Holl RW, Hartman ML, Veldhuis JD, Taylor WM, Thorner MO. Thirty-second sampling of plasma growth hormone in man: correlation with sleep stages. *J Clin Endocrinol Metab*. 1991; 72(4):854–861. [PubMed: 2005213]
62. Van Cauter E, Caufriez A, Kerkhofs M, Van Onderbergen A, Thorner MO, Copinschi G. Sleep, awakenings, and insulin-like growth factor-I modulate the growth hormone (GH) secretory response to GH-releasing hormone. *J Clin Endocrinol Metab*. 1992; 74(6):1451–1459. [PubMed: 1592893]
63. Van Cauter E, Leproult R, Kupfer DJ. Effects of gender and age on the levels and circadian rhythmicity of plasma cortisol. *J Clin Endocrinol Metab*. 1996; 81(7):2468–2473. [PubMed: 8675562]
64. Van Cauter E, Leproult R, Plat L. Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA*. 2000; 284(7):861–868. [PubMed: 10938176]
65. van Coevorden A, Mockel J, Laurent E, et al. Neuroendocrine rhythms and sleep in aging men. *Am J Physiol*. 1991; 260(4 Pt 1):E651–661. [PubMed: 2018128]
66. Copinschi G, Caufriez A. Sleep and hormonal changes in aging. *Endocrinology and metabolism clinics of North America*. 2013; 42(2):371–389. [PubMed: 23702407]
67. Bierwolf C, Struve K, Marshall L, Born J, Fehm HL. Slow wave sleep drives inhibition of pituitary-adrenal secretion in humans. *J Neuroendocrinol*. 1997; 9(6):479–484. [PubMed: 9229358]
68. Caufriez A, Moreno-Reyes R, Leproult R, Vertongen F, Van Cauter E, Copinschi G. Immediate effects of an 8-h advance shift of the rest-activity cycle on 24-h profiles of cortisol. *Am J Physiol Endocrinol Metab*. 2002; 282(5):E1147–1153. [PubMed: 11934681]
69. Follenius M, Brandenberger G, Badesapt JJ, Libert JP, Ehrhart J. Nocturnal cortisol release in relation to sleep structure. *Sleep*. 1992; 15(1):21–27. [PubMed: 1557591]
70. Buckley, TM. Neuroendocrine and homeostatic changes in the elderly. In: Pandi-Perumal, SR, Monti, JM., Monjan, AA., editors. *Principles and Practice of Geriatric Sleep Medicine*. 1st. Cambridge University Press; 2010. p. 85–96.
71. Nater UM, Hoppmann CA, Scott SB. Diurnal profiles of salivary cortisol and alpha-amylase change across the adult lifespan: evidence from repeated daily life assessments. *Psychoneuroendocrinology*. 2013; 38(12):3167–3171. [PubMed: 24099860]
72. Spiegel K, Luthringer R, Follenius M, et al. Temporal relationship between prolactin secretion and slow-wave electroencephalic activity during sleep. *Sleep*. 1995; 18(7):543–548. [PubMed: 8552924]
73. Blyton DM, Sullivan CE, Edwards N. Lactation is associated with an increase in slow-wave sleep in women. *J Sleep Res*. 2002; 11(4):297–303. [PubMed: 12464097]
74. Greenspan SL, Klibanski A, Rowe JW, Elahi D. Age alters pulsatile prolactin release: influence of dopaminergic inhibition. *Am J Physiol*. 1990; 258(5 Pt 1):E799–804. [PubMed: 2333989]
75. Brabant G, Prank K, Ranft U, et al. Physiological regulation of circadian and pulsatile thyrotropin secretion in normal man and woman. *J Clin Endocrinol Metab*. 1990; 70(2):403–409. [PubMed: 2105332]
76. Goichot B, Brandenberger G, Saini J, Wittersheim G, Follenius M. Nocturnal plasma thyrotropin variations are related to slow-wave sleep. *J Sleep Res*. 1992; 1(3):186–190. [PubMed: 10607049]
77. Goichot B, Buguet A, Bogui P, et al. Twenty-four-hour profiles and sleep-related variations of cortisol, thyrotropin and plasma renin activity in healthy African melanoids. *Eur J Appl Physiol Occup Physiol*. 1995; 70(3):220–225. [PubMed: 7607196]

78. Hirschfeld U, Moreno-Reyes R, Akseki E, et al. Progressive elevation of plasma thyrotropin during adaptation to simulated jet lag: effects of treatment with bright light or zolpidem. *J Clin Endocrinol Metab.* 1996; 81(9):3270–3277. [PubMed: 8784082]
79. Van Coevorden A, Laurent E, Decoster C, et al. Decreased Basal and Stimulated Thyrotropin Secretion in Healthy Elderly Men*. *The Journal of Clinical Endocrinology & Metabolism.* 1989; 69(1):177–185. [PubMed: 2499589]
80. Zeitzer JM, Duffy JF, Lockley SW, Dijk DJ, Czeisler CA. Plasma melatonin rhythms in young and older humans during sleep, sleep deprivation, and wake. *Sleep.* 2007; 30(11):1437–1443. [PubMed: 18041478]
81. Shi Z, Araujo AB, Martin S, O'Loughlin P, Wittert GA. Longitudinal changes in testosterone over five years in community-dwelling men. *The Journal of Clinical Endocrinology & Metabolism.* 2013; 98(8):3289–3297. [PubMed: 23775354]
82. Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR, Baltimore Longitudinal Study of A. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. *Baltimore Longitudinal Study of Aging. J Clin Endocrinol Metab.* 2001; 86(2):724–731. [PubMed: 11158037]
83. Bremner WJ, Vitiello MV, Prinz PN. Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. *J Clin Endocrinol Metab.* 1983; 56(6):1278–1281. [PubMed: 6841562]
84. Lin CM, Davidson TM, Ancoli-Israel S. Gender differences in obstructive sleep apnea and treatment implications. *Sleep Med Rev.* 2008; 12(6):481–496. [PubMed: 18951050]
85. Salive ME. Multimorbidity in older adults. *Epidemiologic reviews.* 2013; mxs009.
86. Fillenbaum GG, Pieper CF, Cohen HJ, Cornoni-Huntley JC, Guralnik JM. Comorbidity of five chronic health conditions in elderly community residents: determinants and impact on mortality. *J Gerontol A Biol Sci Med Sci.* 2000; 55(2):M84–89. [PubMed: 10737690]
87. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *JAMA.* 2002; 287(3):337–344. [PubMed: 11790213]
88. Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivelä S-L, Isoaho R. Use of medications and polypharmacy are increasing among the elderly. *Journal of clinical epidemiology.* 2002; 55(8): 809–817. [PubMed: 12384196]
89. Barczy, SR. Sleep and medical comorbidities. In: Avidan, AY., Alessi, C., editors. *Geriatric Sleep Medicine.* 1st. New York, NY: 2008. p. 19-36.
90. Boockvar KS. Reducing sedative-hypnotic medication use in older adults with sleep problems. *Clinical Therapeutics.* 2016
91. Crowley K. Sleep and sleep disorders in older adults. *Neuropsychology review.* 2011; 21(1):41–53. [PubMed: 21225347]
92. Rissling, M., Ancoli-Israel, S. Sleep in Aging. In: Stickgold, R., Walker, MP., editors. *The Neuroscience of Sleep.* 2009. p. 78-84.
93. Ohayon MM. Prevalence of DSM-IV diagnostic criteria of insomnia: distinguishing insomnia related to mental disorders from sleep disorders. *Journal of psychiatric research.* 1997; 31(3):333–346. [PubMed: 9306291]
94. McMillan A, Morrell MJ. Sleep disordered breathing at the extremes of age: the elderly. *Breathe (Sheff).* 2016; 12(1):50–60. [PubMed: 27064674]
95. Li J, Yang B, Varrasse M, Li K. Sleep Among Long-Term Care Residents in China A Narrative Review of Literature. *Clinical Nursing Research.* 2016 1054773816673175.
96. Zantinge EM, van den Berg M, Smit HA, Picavet HSJ. Retirement and a healthy lifestyle: opportunity or pitfall? A narrative review of the literature. *The European Journal of Public Health.* 2014; 24(3):433–439. [PubMed: 24148557]
97. Li JA, Grandner M, Chang Y-P, Jungquist C, Porock D. Person-Centered Dementia Care and Sleep in Assisted Living Residents with Dementia: A Pilot Study. *Behavioral sleep medicine.* 2015:1–17. [PubMed: 26619760]
98. Hanford N, Figueiro M. Light therapy and Alzheimer's disease and related dementia: past, present, and future. *Journal of Alzheimer's Disease.* 2013; 33(4):913–922.

KEY POINTS

- Age-related changes in sleep include advanced sleep timing, shortened nocturnal sleep duration, increased frequency of daytime naps, increased number of nocturnal awakenings and time spent awake during the night, and decreased slow wave sleep.
- Most age-related changes in sleep are stable after 60 years of age among older adults with excellent health. Sleep remains largely unchanged among healthy older adults aged 60 years and older.
- Aging is associated with less robust circadian rhythms and sleep homeostasis, which contribute to sleep changes in aging.
- Age-related changes in neuroendocrine functions contribute to or correlate with alterations of sleep quality and architecture in normal aging.
- Multiple factors, including medical comorbidities and psychiatric illness, primary sleep disorders, and changes in social engagement, lifestyle, and environment contribute to sleep disturbances in older adults.

Figure 1. Age related changes in sleep architecture

Abbreviations: REM, rapid eye movement; SWS, slow wave sleep; WASO, wake after sleep onset

From Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*. 2004;27(7):1255–1273.

Figure 2. Circadian phase in older adults

Solid line represents older adults' body temperature and plasma melatonin circadian profile. Dashed line represents young adults' body temperature and plasma melatonin circadian profile. The bar across the top of panel A represents the clock time; The horizontal black bar denotes sleep/dark period; the horizontal white bar denotes wake/light period.

Panel A: when compared with clock time, the phase of both core body temperature and plasma melatonin is earlier in older adults (solid line) than it is in young adults (dashed line).

Panel B: when compared with their usual sleep-wake and dark-light timing (the phase of both core body temperature and plasma melatonin is later with respect to sleep/darkness in older adults (solid line) than it is in young adults (dashed line).

From Duffy JF, Zitting K-M, Chinoy ED. Aging and circadian rhythms. *Sleep medicine clinics*. 2015; 10(4):423-434.