14 Sleep Loss in Older Adults: Effects on Waking Performance and Sleep-Dependent Memory Consolidation with Healthy Aging and Insomnia

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Introduction

The effects of acute sleep deprivation on waking cognitive processes such as vigilant attention may be buffered in older adults, in comparison to younger adults, by normal changes in homeostatic and circadian regulation of sleep propensity [1]. These processes may confer a lesser need for total sleep in general, and slow wave sleep (SWS) in particular, in comparison to younger adults [1–3]. Although lowered sleep need may allow older adults a degree of cognitive protection against sleep loss, the sleep-wake regulatory systems in older adults are fragile and vulnerable to disruption. The risk of such disruption increases with aging not only due to a wide variety of medical conditions [4, 5], but also due to psychiatric disorders such as depression, anxiety disorders [6], and especially insomnia, the risk for which increases with aging [7]. Moreover, forms of memory consolidation that are dependent upon neural processes that occur during sleep may become degraded by normal declines in sleep duration and quality. Such changes may then be exacerbated by any further reduction in sleep quantity or quality when insomnia and anxiety are present in older individuals.

Changes in Sleep Quality and Architecture with Aging

Changes in sleep quality and polysomnographic (PSG) architecture as well as in the homeostatic and circadian control of sleep propensity accompany healthy aging (for reviews, see [4, 5, 8–12]. Studies using PSG (e.g., [13, 14]), actigraphy (e.g.,[15]) and subjective measures of sleep (e.g., [14]) reveal changes in sleep quality with aging that include decreased total sleep time (TST), increased wake time after sleep onset (WASO), and decreased sleep efficiency (for review, see ref. [8]). Nocturnal awakenings, especially in the early morning, increase in frequency and duration with aging [4, 5] and PSG studies show that older adults awaken more often from non-rapid eye movement sleep (NREM) vs. rapid eye movement sleep (REM) [16, 17].[1] This latter feature may render older adults more vulnerable to sleep inertia—reduced performance and alertness due to sleep-state carry over following awakening [18]. Studies comparing young-old to old-old individuals further suggest that deterioration of

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[1] Cited studies that differentiate REM and NREM or substages of NREM (e.g., slow wave sleep) or that report phasic features of sleep (e.g., sleep spindles) or EEG spectral power (e.g., slow wave activity) all employ PSG.

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sleep quality in aging becomes especially prominent with advanced age. For example, a combined PSG and diary study showed that "young-old" individuals (aged 60–74 years) showed few changes in sleep quality over 3 years of longitudinal monitoring, whereas "old-old" individuals (75–87 years) showed increasing WASO and sleep onset latency (SOL) over this same duration [19, 20].

Behavioral factors may further degrade sleep quality with aging. Most prominent of these behavioral factors is a changed frequency of daytime napping [21]. The frequency of diurnal naps increases markedly with aging and this increase continues from "young-old" into "old-old" age [22]. Changes in social patterns may also decrease natural light exposure [23] and reduce exposure to other naturally occurring time cues (zeitgebers) [12]. Circadian disruption may be further exacerbated by the normative circadian phase advance that accompanies healthy aging [12].

Sleep is additionally disrupted by medical conditions common in older adults such as arthritic pain, gastroesophageal reflux, nocturia, and polypharmacy [4, 5, 24]. Much greater disruption of sleep ensues with serious medical conditions such as obstructive sleep apnea (OSA) [25], heart failure [26], and neurodegenerative illnesses [27].

Reduced polysomnographically scored SWS as well as reduced Slow Wave Activity (SWA), defined as spectral power in the delta (0.5–4.5 Hz) frequency range, are the most prominent changes in sleep architecture that accompany healthy aging [2, 3, 28, 29]. Decreasing SWA reflects decline in both the amplitude and frequency of slow waves [2, 30, 31] and is also accompanied by reductions in the slow (<1 Hz) oscillation [28]. For example, in a carefully controlled study, Dijk et al. [3] demonstrated reduction in SWS in middle-aged (40–55 years) and older (66–83 years) adults compared to young (20–30 years) adults with the greatest change observed between the young and middle-aged groups. These age-related declines in SWA are most prominent in frontal brain regions [32]. Unlike in young adults for whom SWS is concentrated in the first one or two NREM-REM cycles of the night, SWS is distributed more evenly across the night in older adults [32, 33]. Carrier et al. [30] have shown that such changes relative to young adults are present at a mean age of 51 ± 4.6 years. They also showed that, by this age, slow waves are reduced in density and their morphology has changed such that the positive component of such waves has a reduced slope and increased duration. SWS declines less with aging in females vs. males [34] and older females better maintain the characteristic morphology of slow waves [30].

The total amount and percentage of REM sleep declines only slightly with aging [29, 35]. However, REM density, the number of rapid eye movements per unit time, is more prominently decreased [36]. With the decline in SWS and REM, lighter NREM sleep (N1 and N2) is increased proportionately. However, N2 sleep spindles are reduced in number, density, and amplitude [2, 37–42] as are the frequency and amplitude of N2 K-complexes [37, 43].

Experimental Sleep Loss and Cognition in Healthy Aging

Harrison and colleagues [44] have suggested that total sleep deprivation (TSD) in young adults may model the cognitive changes typical of normally rested, healthy older adults. However, paradoxically, waking performance is *less* disrupted in older vs. younger adults following TSD [45–49], reviewed in [1]. Moreover, performance of older adults is superior to young adults after sleep restriction [50, 51] and sleep fragmentation [52].

In an early study, the effects of 64 h TSD were compared between healthy young males (18–28 years) and older males (55–71 years) with and without insomnia [53]. Using a verbal memory and a reaction time (RT) test, individuals in these three groups were tested at bedtime, following three nocturnal awakenings by study staff, and upon morning awakening on baseline and recovery nights as well as at the corresponding times across 64 h (2 nights) of TSD [53]. Whereas performance on both the memory and RT task

deteriorated across 2 night's TSD in young males, it remained near baseline values in both the healthy and insomniac older males. In another study, during 26 h of constant routine conditions (continuous waking in a semi-recumbent position under dim light with regularly spaced caloric intake), performance on the psychomotor vigilance test (PVT) did not differ between young and older adults during the hours that they were normally awake. However, during hours that they were normally asleep, performance in older subjects was less impaired as indicated by both faster RTs and fewer lapses (RT > 500 ms) in performance [47]. Very similar results were seen in another study using TSD with a constant routine protocol in which a baseline slower RT on the PVT in older (mean 65 years) vs. younger (mean 25 years) adults disappeared during the hours normally occupied by sleep [48]. Similarly, in a sleep-laboratory study that employed repeated PVT testing over 40 h TSD, young males (mean 25.2 years) compared to older males (mean 66.4 years) displayed greater slowing of RT, more PVT lapses, and greater RT variability beginning after the 16 h of normal wake had elapsed [46]. This greater impact of TSD on young participants became highly pronounced by the time of the circadian nadir (the 24-h core temperature minimum occurring around 4 a.m.) and continued into the subsequent day. In a similar study, using a within-subject crossover design, young males (mean 22.5 years) showed a significant increase in number of lapses on a simple RT task following 24 h TSD compared to a night of normal sleep [49]. Older males (mean 58.2 years), on the other hand, showed no change in lapses with TSD. Along with a lesser performance deficit, older adults in some [46] but not all [49] studies report less subjective sleepiness during prolonged TSD. Older adults also display less increase, during TSD, in objective measures of sleepiness such as the multiple sleep latency test or MSLT [54].

These findings support earlier studies reporting less sleep deprivation-related decrement in older vs. younger individuals on a choice reaction time task [55] as well as on a vigilance task in old-old individuals (80 years) compared to young adults (20 years) [56]. In more ecologically realistic settings, cognitive resistance to sleep deprivation may buffer older-adult performance in some situations such as in a driving simulator [57] but not in others, such as maintaining postural control [58]. The latter effect of sleep deprivation has significant health and safety implications with regard to the risk of falling in older adults.

Older adults also show lesser cognitive sequela of sleep loss under conditions of partial sleep deprivation. For example, Bliese et al. [50] showed that 7 days of sleep restriction to 5 or 3 h time-in-bed (TIB) resulted in deterioration of PVT performance compared to performance following sufficient sleep (7 and 9 h TIB). Notably, however, this reduction in performance under partial sleep deprivation was negatively related to increasing age.

Similarly, although older adults are less able than younger adults to adapt their sleep schedules to shifted circadian phase [16, 59], they have been shown to display less subjective sleepiness as well as better-maintained vigilance performance during extended exposure to experimentally altered circadian phase [14, 60]. In one such study, older (mean 64 years) and younger (mean 24 years) adults underwent 18 days of a forced desynchrony protocol—an experimental procedure whereby circadian and homeostatic influences (see below) can be dissociated by imposing day–night schedules outside the range that can entrain the intrinsic human circadian clock—in this case consisting of 20-h days [60]. Across this extended disruption of circadian rhythmicity, unlike the younger adults, older adults showed neither an increase in subjective sleepiness nor an increase in RT on the PVT.

Changes in Circadian and Homeostatic Sleep Regulation with Aging

The Two-Process Model [61] postulates that sleep propensity results from the interaction of a homeostatic process (Process S) by which sleep propensity increases with increased duration of

prior waking and a circadian process (Process C) by which intrinsic drive to sleep or waking varies predictably across a 24-h period. The interaction of these two processes allows for a consolidated bout of nocturnal sleep in healthy adults [62]. Both homeostatic and circadian processes are believed to be damped in older adults [2, 3, 12] and changes in the homeostatic regulation of sleep may be of particular importance to the above-noted cognitive resistance to sleep deprivation with aging.

Circadian Changes in Sleep Patterns with Aging

The master circadian signal from the suprachiasmatic nucleus (SCN) of the anterior hypothalamus is believed to weaken with age [63, 64]. Biological changes in the human SCN with aging include decreases in cell number and neuroendocrine activity [12, 63]. These changes result in a decreased amplitude of circadian rhythms of both objective and subjective sleepiness [13] as well as of core body temperature, melatonin and cortisol, the amplitude of which may be 20–30 % lower in older compared to younger adults [11, 12, 63–66]. In older adults, the circadian rhythms of core body temperature, melatonin, and cortisol are phase advanced by approximately 1 h relative to younger adults [11, 12, 65, 67]. Nonetheless, the circadian period remains approximately 24.2 h across the lifespan [68].

The sensitivity of the SCN to photic entrainment appears also to diminish with age [64]. Nonetheless, bright light can reset the circadian clock in both young and older adults [69, 70]. The weakening of the circadian signal with aging may be exacerbated by behavioral and environmental factors such as increased time indoors away from natural light cues [71], degenerative changes in the eye [72], or reduced exposure to zeitgebers such as social stimuli [73] (see ref.[12] for a review). Older adults have more difficulty with sleep maintenance when attempting sleep at an unfavorable circadian phase as occurs with jet lag [16, 59]. Similarly, older adults may suffer greater sleep inertia because of their tendency both to awaken at an earlier circadian phase and to more frequently awaken from NREM relative to REM sleep in comparison to younger adults [18]. In addition to effects on cognition brought about by age-related effects on the circadian timing of sleep, age may also influence cognition-related circadian oscillators in the brain independently of the effects of such oscillators on sleep itself [64].

Homeostatic Changes in Sleep Patterns in Healthy Aging

The increase in SWS and SWA following sleep loss (discussed above) constitutes a sensitive measure of sleep homeostatic recovery [74]. Because of the increase in nocturnal awakenings and decrease in subjective and objective daytime sleepiness with aging, it has been suggested that concurrent reductions in SWS and SWA indicate a decrease in the degree to which sleep homeostatic pressure increases over prolonged wakefulness [1–3]. For example, in a large-scale study, Dijk et al. [3] used acoustic disruption of SWS in young, middle-aged, and older adults to examine age-related differences in homeostatic rebound of SWS. Compared to age-matched controls who were allowed undisturbed sleep, disruption of SWS produced a rebound of SWS as well as increased objective (MSLT) and subjective daytime sleepiness in all three age groups. This responsivity to curtailment of SWS in older adults indicated that their ability to homeostatically compensate for loss of SWS relative to their baseline remained intact. Dijk et al. [3] therefore concluded that the observed age-related baseline differences in SWS and SWA reflect a lesser buildup of homeostatic sleep pressure during normal waking rather than a putative inability to compensate for sleep loss that would lead to chronic sleep debt. As further evidence of lesser sleep need in aging, a smaller additional amount of TST was achieved by older compared to younger adults when an extended 16-h sleep opportunity was provided [75].

Nonetheless, other investigators have found differences in the way in which the sleep EEG

responds to sleep loss in older vs. younger adults. For example, following 40 h TSD under constant routine conditions, young adults (mean 25 years) showed a distinct frontal predominance of SWA during recovery sleep, whereas older adults (mean 65 years) had SWA more evenly distributed between frontal and posterior derivations as well as a slower decline in overall delta power across the remainder of recovery sleep [32]. However, as in Dijk et al. [3], a significant increase in SWS on the recovery vs. baseline night was present in both older and younger groups, a finding also replicated in middle-aged (40–60 years) adults [76]. Age differences in the response to the *lowering* of homeostatic sleep pressure using daytime naps have also been reported in some, but not all studies. For example, Campbell and Feinberg [77] report a nearly identical reduction in delta power relative to baseline following daytime naps in young (mean 22 years) and old (mean 71 years) adults. Similarly, Munch et al. (2007) showed that, following the lowering of sleep pressure using a constant routine procedure with extended naps, a reduction of delta power during the first sleep cycle occurred in both young (20–31 years) and older (57–74 years) adults. In contrast, however, in the young adults, this reduction persisted longer into recovery night sleep and showed a more posterior scalp-EEG topography. Nonetheless, there is a clear consensus that, despite such small differences, a functional homeostatic response to sleep and SWS loss persists into later adulthood [3, 32, 76, 78].

Recent findings suggest that the age-related increase in resistance to sleep deprivation-induced deficits in vigilance and subjective sleepiness may result from changes in adenosinergic systems underlying the buildup of homeostatic sleep pressure [1]. Desensitization of adenosine receptors with age is suggested by a positron emission tomography (PET) study showing reduced binding of an adenosine A1 receptor ligand in older vs. younger adults [79]. Vigilance in young adults who show high sensitivity to caffeine, a non-specific adenosine A1 and A2A receptor antagonist, is impacted more by sleep deprivation than in those with lower sensitivity, and such sensitivity is mediated by a polymorphism in the adenosine A2A receptor gene [1]. In both younger and older adults, sleep deprivation increased and caffeine decreased two indices of elevated homeostatic sleep pressure, namely, increased theta activity at frontal relative to posterior sites in the waking EEG and performance impairment on the psychomotor vigilance task (PVT). However, attenuated responses of these indices in older adults resembled more those of caffeine-insensitive vs. caffeine-sensitive young adults leading Landolt and colleagues (2012) to suggest possible reduction in adenosine A2A receptor function with aging.

Whereas in older adults vigilance and other forms of attention may suffer less from acute sleep loss compared to younger adults, normal changes in sleep quality and architecture may impact neural processes that take place during sleep itself. The best known of these processes is sleep-dependent memory consolidation [80, 81] and changes in this process with healthy aging are considered next.

Changes in Sleep-Dependent Cognition with Healthy Aging

Declarative memory recall is greater following an intersession interval containing sleep compared to when the intersession interval contains wake in young adults (e.g., [82]). Such facilitation has been demonstrated for intervals containing overnight sleep as well as daytime naps [83], thus ruling out circadian explanations for such effects. Offline changes in learning over sleep are thought to reflect consolidation of the memory, a process by which memory storage and retrieval become more efficient. Whereas memory consolidation takes place during both sleep and wake, a major component of consolidation takes place during sleep (e.g., [84], likely as a means to prevent consolidation processes from interfering with encoding of new material and vice versa [80]).

Studies using neural recordings in rat hippocampus suggest that sleep-dependent memory consolidation stems from neural replay. Wilson

and colleagues [85] recorded hippocampal place cell activity during active exploration and sleep. During exploration, place cells are active when the animal is in particular areas of an environment such that, collectively, place cells code a map of space. Interestingly, sequences of neural firing recorded during subsequent sleep mimicked patterns observed during waking exploration. Neuroimaging in humans suggests a similar neural process. Using PET imaging, Peigneux and colleagues [86] demonstrated hippocampal activation during learning that predicted subsequent reactivation during sleep. Moreover, the amount of hippocampal activity during sleep predicted performance improvements in the maze navigation task.

Given the drastic changes in sleep that occur with aging, one might expect sleep-dependent memory consolidation to be reduced in older adults. Indeed, performance changes over sleep relative to wake are reduced for procedural learning tasks even when participants are screened for sleep disorders, medication use, and other confounds. For instance, when young adults (mean 20.8 years) and older adults (mean 59 years) learned a ten-item sequence of finger movements, initial learning did not differ for the two groups [87]. When tested 12-h later, young adults demonstrated performance improvements of approximately 5 % if the interval contained wake and 18 % if the interval contained sleep. However, performance of older adults improved by only 2–5 % regardless of whether the interval contained wake or sleep. In other words, the performance benefits sleep exerted on this procedural task for young adults were absent in the older adult group. This result was subsequently replicated by the same group [88] and others [89, 90].

Likewise, Peters and colleagues [91] reported reduced sleep-related performance changes on a pursuit rotor learning task in a group of older adults (mean 69.8 years) relative to young adults (mean 20.1 years). Pursuit rotor learning requires participants to use a stylus to track a moving target. In this particular study, the target moved in a predictable fashion, thus the task requires learning of the stable movement pattern and prediction of the target's velocity, both forms of procedural learning. Performance improvements on this task 1 week later were associated with sleep spindles in NREM stage 2 in the young adults but not older adult participants.

While benefits to procedural learning from sleep are reduced or absent in older adults, (but see ref. [92]), declarative memory consolidation may be preserved. We directly contrasted overnight sleep changes in performance on a declarative word-pair learning task and a procedural motor sequence learning task in young (20–34 years), middle-aged (35–50 years), and older (51–70 years) adults [88]. While changes in motor sequence learning over sleep relative to wake were greater in the young adults (and nearly absent in middle-age and older adults), sleep's benefit on word-pair learning was spared. In fact, using a sleep benefit score which subtracts the change in performance over wake from changes over sleep (i.e., yielding a positive value indicating that the intersession interval with sleep was better than wake), we found no difference in sleep's benefit on word-pair learning across the three age groups. Likewise, older adults have been shown to have greater recall of personal events and standardized narratives (WMS-III Logic Memory stories) following sleep compared to wake [93], although the effect on memory for personal events was reduced relative to young adults. Differences in the amount of declarative memory consolidation achieved within the older adult group may be related to the quality of sleep. For instance, older women (61–74 years) with high spindle density had better performance on the Rey-Osterrieth Complex Figure Test, a measure of declarative memory, than women with low spindle density [94].

While it may be tempting to conclude that sleep-dependent consolidation is reduced for procedural but not declarative memories in older adults, the picture is not yet entirely clear. For instance, one recent study [95], using a similar word-pair learning task as [88], reported that older adults (mean 70.7 years) failed to consolidate declarative memory over sleep while the young adult group (mean 19.7 years) in this study showed a significant improvement. Notably, this improvement over sleep in young adults was

associated with the percent of TST spent in SWS. Notably, these older adults had significantly reduced SWS relative to the young adults. In fact, performance changes over sleep for older adults were on par with that of the younger adults who happened to have similar amounts of SWS [95]. This is consistent with a study by Backhaus and colleagues [96] who reported that middle-aged adults benefitted similarly from sleep on a declarative learning task when SWS time was equated.

Although healthy aging is, therefore, associated with a degree of preservation of sleep-dependent memory consolidation, further changes in sleep quality and architecture that accompany the increased risk of medical, neurological, and psychiatric illness with aging are likely to seriously impact this function of sleep in a large percentage of older adults. Indeed sleep-dependent memory consolidation has been shown to be diminished due to mild cognitive impairment [97, 98] and even more so with the onset of Alzheimer's disease [99]. Similarly, sleep disorders can impair sleep-dependent memory consolidation (for a review, see ref. [100]). For example, even the sleep fragmentation associated with mild OSA has been shown to diminish sleep-dependent memory consolidation in young to middle-aged (mean 30 years) adults [101] as has moderate OSA in middle-aged (mean 47 years) adults [102]. In the next sections, we examine associations of anxiety and insomnia—conditions that may affect a large percentage of otherwise healthy older adults—and consider whether resultant sleep disruption might also impact sleep-dependent memory consolidation.

Interactions of Anxiety and Insomnia in Aging

Incidence of sleep disorders greatly increases with advancing age [5, 103, 104]. Complaints of insomnia symptoms, including difficulty with sleep maintenance, early-morning awakening, and daytime fatigue and sleepiness, all become more prevalent with aging [5, 105, 106]. Indeed, aging itself constitutes the greatest independent risk factor for insomnia [7]. Difficulty sleeping is an increasing problem as aging advances [107] and may constitute the primary somatic complaint in old-old individuals [108].

An intriguing potential trigger for insomnia complaints in the elderly was suggested by Dijk et al. [3] who note that a normatively reduced sleep propensity might be interpreted as abnormal sleep loss by older individuals who believe that longer or more consolidated sleep is required for good health. Since maladaptive cognitions focused on sleep can themselves become initiating or perpetuating factors for chronic insomnia [109], misinterpretation of reduced sleep need as a health problem can lead to a positive feedback cycle that results in worsening symptoms of insomnia. For example, an individual may nap excessively during the day in the belief that it is necessary to compensate for shorter nocturnal sleep [110]. As such, they may unintentionally exacerbate sleep onset or maintenance problems by reducing homeostatic sleep pressure prior to their nocturnal sleep bout. Similarly, long-term use of hypnotic drugs can lead to a worsening rather than the intended improvement of sleep difficulties over time in older adults [111]. A common source of anxiety among older adults is concern regarding physical and, especially, mental decline particularly in the domain of memory. Such concerns during presleep rumination can exacerbate insomnia in much the same way as described above [110]. However, despite this potential for misattribution with regard to normal changes in sleep, self-reported poor sleep [112] and excessive daytime sleepiness [113, 114] have indeed both been found to be significantly associated with cognitive decline.

Anxiety disorders are highly comorbid with sleep disturbance in older adults [108, 110] with even subclinical levels of anxiety contributing significantly to sleep disturbance [115, 116]. Although overall prevalence of anxiety disorders is less in older compared to younger adults [6], they remain common in this population. Up to 10 % of older adults suffer from anxiety disorders [117] that can persist for many years [118]. Even in those of an advanced age (85–103 years), a 2.3 % prevalence of anxiety disorders has been reported [119]. Moreover, even greater numbers

of older adults report significant anxiety symptoms that do not fully meet diagnostic criteria for an anxiety disorder [110]. Poor sleep and anxiety have been found to constitute major risk factors for one another in older adults with the above-noted concerns about physical health and cognitive integrity being a major contributor to both conditions [110]. For example, in a large prospective study of adults in Norway that included older cohorts, persistent insomnia was shown to be a significant risk factor for later development of an anxiety disorder [120]. Thus, poor sleep may represent an independent risk factor for anxiety disorders in older adults, of the same order of magnitude as other risk factors such as severe stressors and neuroticism [121].

Large prospective epidemiological studies in older adults have clearly shown that sleep difficulties also constitute significant risk factors for both physical and cognitive decline. In a large cohort of non-frail men aged 67, poor sleep has been identified as a major risk factor for the onset of frailty (following the definitional criteria of Fried et al. [122]) at 3–4 year follow-up [123, 124]. Similar findings have been reported in a large sample of elderly women [125]. In the cognitive domain, a longitudinal study of 1,664 cognitively unimpaired older adults aged 65–95 showed that elevated Pittsburgh Sleep Quality Index (PSQI) scores and habitual sleep duration predicted Mini-Mental Statues Exam scores within the range of cognitive impairment at 12-month follow-up [126]. Similarly, sleep duration shorter than 6.5 h per night and excessive daytime sleepiness in older (median 75 years) adults at baseline were found to predict cognitive decline at 10-year follow-up [127]. Indicators of disrupted circadian rhythmicity such as delay in activity peak [128] and damped amplitude of circadian rhythms [129] have also been shown to predict cognitive decline. Therefore, buffering of the cognitive impact of sleep loss in older adults appears to be somewhat fragile and easily overcome by other factors that severely perturb sleep.

One such factor that is of great public health importance due to its ubiquity is insomnia, a disorder that, in turn, is clearly comorbid with and, in many cases the result of, subclinical anxiety and anxiety disorders [110, 115]. It is important to note that insomnia and sleep disturbances accompanying mood disorders may also have great impact on cognition in the elderly [130, 131] and mood disorders may bear a similar reciprocal etiological risk with insomnia as do anxiety disorders [110, 132].

Interaction of Sleep-Dependent Memory Consolidation with Insomnia

A small number of studies have begun to suggest that sleep-dependent memory consolidation can be impaired by insomnia. For example, middle-aged individuals (mean 41 years) with primary insomnia have been shown to have diminished consolidation of declarative memory (word pairs) relative to controls while, at the same time, showing preserved sleep-dependent consolidation of procedural (mirror-tracing) learning [133]. In contrast, in middle-aged (mean 46 years) subjects, those with primary insomnia who slept vs. those who remained awake failed to show greater percent improvement on the mirror-tracing task or enhanced retention of declarative learning on the visual verbal task (VVT) that were apparent in good-sleeping controls [134]. Both studies, however, demonstrate that primary insomnia can negatively impact sleep-dependent memory consolidation in otherwise healthy middle-aged adults. Similarly, psychiatric disorders that are associated with insomnia such as depression may impair sleep-dependent memory consolidation [135, 136] as may disorders such as schizophrenia that alter specific aspects of sleep such as sleep spindles [137–139].

Conclusions and Clinical Implications

In the future, it will be important to determine if sleep disruption associated with subclinical anxiety disorders and associated mild or situational insomnia can also impact the memory consolidation function of sleep in older adults. If this

proves to be the case, anxiety, insomnia, and cognitive impairment might constitute mutually reinforcing conditions that lead to increasing severity in symptoms of each. Hence, even cognitively intact older adults may find themselves experiencing daytime memory problems that lead to increased nocturnal rumination and, in turn increased sleep difficulties [3, 110]. Bearing in mind the actual epidemiological associations of sleep difficulties and neurodegenerative disease described above, sleep clinicians and mental health providers who treat older adults may benefit from considering such complex interactions of normal worry, memory, and sleep when advising and treating patients. In such patients, if more severe illnesses can be ruled out, cognitive-behavioral therapy for insomnia [140] may prove especially helpful and reduce the need for or the duration of treatment with hypnotic drugs.

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