CLINICAL REVIEW

Clinical effects of sleep fragmentation versus sleep deprivation

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Summary

Common symptoms associated with sleep fragmentation and sleep deprivation include increased objective sleepiness (as measured by the Multiple Sleep Latency Test); decreased psychomotor performance on a number of tasks including tasks involving short term memory, reaction time, or vigilance; and degraded mood. Differences in degree of sleepiness are more related to the degree of sleep loss or fragmentation rather than to the type of sleep disturbance. Both sleep fragmentation and sleep deprivation can exacerbate sleep pathology by increasing the length and pathophysiology of sleep apnea. The incidence of both fragmenting sleep disorders and chronic partial sleep deprivation is very high in our society, and clinicians must be able to recognize and treat Insufficient Sleep Syndrome even when present with other sleep disorders. © 2003 Published by Elsevier Science Ltd

INTRODUCTION

Sleep deprivation and sleep fragmentation are commonly found in both normal individuals and in patients with sleep disorders. Sleep disorders practitioners need to be able to identify patients who present with symptoms consistent with chronic partial sleep deprivation and distinguish them from patients who may actually have sleep apnea or other medical disorders producing excessive daytime sleepiness. This paper will first review the physiological and behavioral (clinical) findings in total and chronic partial sleep deprivation. The following section will compare and contrast those results with symptoms and findings secondary to sleep fragmentation. The paper will also examine the role of sleep loss and sleep fragmentation in various patient groups, discuss the medical risks associated with sleep deprivation and sleep fragmentation, and discuss means of identifying patients suffering from insufficient sleep syndrome as compared to other causes of hypersomnia. Knowledge of the clinical symptoms produced by sleep deprivation or sleep fragmentation in normal individuals helps to elucidate which symptoms are secondary to poor sleep and which symptoms are associated with the clinical pathology in patients with sleep disorders. Such differentiation can help to determine whether treatment should be directed toward improving sleep and/or alleviation of the medical complaint.

SLEEP DEPRIVATION

The present review of sleep deprivation will focus on aspects that are most relevant to sleep or other medical disorders and which have also been examined
in sleep fragmentation studies. A more complete recent review of sleep deprivation is available [1]. Total sleep deprivation is typically defined as the length of time since the end of the last sleep period. Partial sleep deprivation is typically defined both by the length of the partial sleep period and the chronicity of the shortened sleep schedule. Except in patients with clinical depression, the effects of partial and total sleep deprivation are qualitatively similar.

Sleep deprivation results will be divided into sections including (a) hormonal effects; (b) pulmonary effects; (c) behavioral effects and (d) alertness effects.

**Hormonal effects**

Several studies have examined various biochemical changes in humans during sleep loss. Thyroid activity is increased during sleep deprivation [2]. Changes in the adrenal or sex hormones have not been large. Significant changes in cortisol, adrenaline, catecholamine output, hematocrit, plasma glucose, creatinine or magnesium have usually not been found [1]. However, some recent studies have now shown that patterns of hormone secretion may change even though total amount of secretion does not. For example, Spath-Schwalbe et al. [3] found a different pattern of cortisol secretion during sleep deprivation, but total cortisol secretion during the night was the same whether Ss slept normally or were awake. Hormones such as noradrenaline, prolactin [4], and growth hormone, which also are dependent upon sleep for their circadian rhythmicity or appearance, lose their periodic pattern of excretion during sleep loss [5, 6].

**Pulmonary effects**

Total sleep deprivation produces small decreases in forced expiratory volume (FEV₁) and forced vital capacity (FVC) in patients with pulmonary disease [7]. In addition, two studies, one in healthy infants [8] and one in adults [9], have shown an increase apneic events and longer apneic events after sleep loss. All of these changes immediately reversed after recovery sleep.

**Behavioral effects**

Changes in mood such as increased sleepiness, fatigue, irritability, and decreased ability to think or concentrate are some of the earliest noted indicators of sleep loss. Some clinical symptoms of sleep deprivation are listed in Table 1.

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<th>Table 1 Clinical symptoms of sleep deprivation [1]</th>
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<tr>
<td>Longer reaction time</td>
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<td>Lapses in attention or concentration</td>
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<td>Lost information</td>
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<td>Errors of omission</td>
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<td>Poor short term memory</td>
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<td>Poor mood (increased fatigue, confusion, stress, and irritability)</td>
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<td>Reduced motivation</td>
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<td>Distractibility</td>
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<td>Sleepiness</td>
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<td>Poor performance:</td>
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<td>at circadian low points</td>
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<td>when sedentary</td>
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<td>on long, difficult, or externally paced tasks</td>
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<td>with no feedback</td>
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<td>in unchanging surround, particularly with</td>
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<td>reduced light or sound and</td>
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<td>low motivation, interest, or novelty</td>
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Psychomotor tasks most affected by sleep loss are those that are long, monotonous, without feedback, externally paced, newly learned, or have a short-term memory component. Typical laboratory tasks sensitive to sleep loss are vigilance and reaction time. One example of an applied task containing many of the elements sensitive to sleep loss is driving, and numerous studies have demonstrated decrements in driving ability related to sleep deprivation (see [10] for a recent review).

**Objective alertness effects**

The major objective measure of sleepiness (the Multiple Sleep Latency Test or MSLT) is also extremely sensitive to the effects of sleep deprivation. Sleep latency values are typically reduced by 60% or more after one night of total sleep deprivation [1, 11] (Fig. 1).

**PARTIAL SLEEP DEPRIVATION**

The effects of partial sleep deprivation are qualitatively similar to those seen after total sleep deprivation. However, those effects may seem more complex or variable based upon the frequency and degree of sleep loss. A great majority of studies have dealt with performance and objective alertness effects, and these will be emphasized in the current review.
Hormonal and pulmonary effects

The great majority of basic research on sleep deprivation in humans has examined changes after total sleep loss. Few studies have examined hormonal or pulmonary variables after partial sleep deprivation. One recent study [12] did look at metabolic and endocrine function after 4 h of sleep for 6 nights. Compared to baseline values, only cortisol was increased in the afternoon after each minute of sleep. For partial sleep deprivation, the solid part of the bar documents the percent reduction of MSLT after one night and the entire bar represents the total decrease in MSLT after 5, 5-hour [16] or 7, 6-h [81] nights of sleep.

Behavioral effects

Real world examples of total sleep deprivation are less common than examples of chronic partial sleep deprivation because some degree of chronic sleep loss is almost the norm in our society. In a study which screened large numbers of “normal” applicants for sleep research studies, 28% of the subjects reported sleeping 6.5 h or less each weekend [13, 14]. In a study which involved over 100 young adults screened for normal sleep habits, lack of shift work or sleep pathology, and infrequent naps, 32% were found to have daytime nap latency values of 5 min or less, and only 40% had nap latency values of greater than 10 min [13]. Data from a large study by Levine et al. [15] indicated that 17% of their sample of normal young adults had average MSLT values of 5 min or less and only 50% had average MSLT latencies of 10 min or greater. These data reflect significant partial sleep deprivation in normal adults. These data are also troubling from a clinical perspective, which views latencies of 5 min or less on the MSLT as pathological and latencies of less than 10 min as borderline pathological.

In a study where Ss were allowed 5 h of sleep for 7 consecutive nights [16], cumulative deficits were reported for both subjective and psychomotor performance measures starting after the first night. Over the course of the week, subjective sleepiness continued to increase and performance on a reaction time task continued to decrease in a linear fashion consistent with a slowly accumulating sleep debt. In a similar study, Carskadon and Dement [17] restricted sleep to 5 h per night for 7 consecutive nights. MSLT scores were significantly reduced after the second restriction night and continued a declining trend from baseline values of 17 min (after sleep satiation) to about 7 min after the last night of sleep reduction. Similar cumulative deficits are found after total sleep deprivation, but, of course, the deficits grow more rapidly after total sleep loss. Figure 1 provides MSLT change data after one night of total sleep loss in comparison with several nights of partial sleep deprivation. Comparing MSLT and findings on the subjective Profile of Mood States (POMS) Vigor subscale when given repeatedly across a period of total sleep deprivation [18] and across a period of repeated partial sleep deprivation allowing 5 h of sleep each night [16] gave the following results: after 5 nights of partial sleep deprivation, the MSLT was reduced to 26% of the baseline value [16]. This level was reached after 48 h of total sleep deprivation [18]. Subjective vigor was reduced to 46% of baseline after
7 nights of partial sleep deprivation but reached this level after 33 h of total sleep deprivation. The general conclusion available from this kind of data is that limiting sleep length to 5 h for five or more nights results in levels of alertness that are similar to those seen after periods of total sleep deprivation ranging from 33–48 h. Since participants had lost a total of about 12–20 h of sleep during partial sleep deprivation ranging from 5–7 days, their loss of function was only marginally less than in the total sleep deprivation study where the total sleep loss ranged from an acute loss of 8–16 h of sleep. The fact that sleepiness as measured by the MSLT seemed to accumulate more quickly than the decreases in subjective vigor can be interpreted as the development of habituation to some subjective mood changes during chronic partial sleep deprivation [16]. The practical implication of such a finding for clinicians is that patients suffering from chronic partial sleep deprivation may underestimate the degree of their sleepiness when giving a subjective report. Further, the high frequency of chronic partial sleep deprivation in our society predicts that many “normal” individuals would actually be classified as pathologically sleepy if routinely given MSLT evaluations. For example, in the Dinges et al. study cited above, the MSLT value on baseline was 11.6 min, and this had decreased to 3.0 min following 5 nights of 5 h of sleep. Using these values as predictors, MSLT values would also have been below 5 min after 4 nights of partial sleep loss.

Despite the high frequency of partial sleep deprivation and associated daytime sleepiness, less than 1% of patients seen in Sleep Disorders Centers are given a primary diagnosis of Insufficient Sleep Syndrome [19]. The implication is either that patients with insufficient sleep do not appear at sleep disorder centers or that Sleep Disorder Centers are insensitive to partial sleep deprivation as a common cause of excessive sleepiness. If Sleep Disorder Centers are insensitive to partial sleep deprivation as a common cause of excessive sleepiness, such individuals may inappropriately be diagnosed as having idiopathic hypersomnolence.

SLEEP FRAGMENTATION

There are at least 22 empirical studies of the effects of fragmented sleep in both animals and humans and a large number of other studies that have examined the relationship between sleep fragmentation variables and function in groups of patients with sleep disorders such as sleep apnea or periodic limb movements. The empirical studies have typically produced various degrees of sleep disturbance by using tones or other stimuli to briefly interrupt sleep at various periodicities. Outcome variables in these sleep fragmentation studies tend to be the same types of measures used in sleep deprivation experiments, and the studies will be reviewed in a similar framework.

Hormonal effects

Spath-Schwalbe [3] examined profiles of cortisol and ACTH during baseline and sleep fragmentation nights (fragmentation at a rate of once after each minute of sleep). They found that plasma cortisol increased significantly when the experimental sleep fragmentation began. However, this burst of secretion was inhibited after about 80 min and cortisol secretion dropped below baseline sleep levels before returning to normal. A similar but less pronounced effect was found for ACTH.

Patients with sleep apnea show decreased growth hormone and prolactin secretion at night [20, 21]. Although this decrease is probably secondary to sleep fragmentation and reverses after sleep is normalized, changes in these hormones have not been studied after simple sleep fragmentation.

Pulmonary effects

In an elegant series of animal studies, Phillipson’s group first demonstrated the impact of sleep fragmentation on increasing sleepiness in dogs and showed that the fragmentation procedure resulted in impaired arousal responses to hypercapnia and hypoxia during sleep [22]. More recently the group developed a model to allow normal sleep in dogs followed by a period of experimentally produced sleep apnea lasting up to 133 days followed by recovery and a period of experimental sleep fragmentation without apnea lasting up to 60 days [23]. The results of this remarkable study showed that both the sleep fragmentation procedure and the experimentally produced sleep apnea resulted in lengthening of the time to arousal in response to airway occlusion [24] and to greater tolerated oxygen desaturation, greater peak inspiratory pressure, and greater tolerated surges in blood pressure during airway occlusion. As a result, these authors concluded that simple sleep fragmentation is responsible not only for the sleepiness symptoms associated with sleep apnea but also that “the changes in the acute responses to airway occlusion resulting from OSA are primarily
the result of the associated sleep fragmentation” ([23] p. 1609).

**Behavioral and alertness effects**

In sleep fragmentation studies, it is common to find increased objective and subjective sleepiness and decreased psychomotor performance on days following disturbed sleep. Thirteen of 14 studies that measured objective sleepiness on the day after various sleep fragmentation paradigms found significant increases in sleepiness. Change in MSLT as a function of rate of sleep fragmentation is plotted in Figure 2 for a group of 8 studies (some with multiple conditions) which produced a consistent and identified rate of fragmentation for 1 night and measured MSLT as an outcome variable on the next day. As can be seen from the figure, sleepiness increased as the rate of fragmentation was increased (Pearson $r$ between rate of fragmentation and percent decrease across the studies was $r = 0.775, p < 0.01$). A best-fit logarithmic curve has been added to the data plot in the figure. Virtually every study that has measured mood change has found mood to be more negative after various schedules of sleep fragmentation. Mood and subjective report measures may be more impacted by a fragmentation paradigm which demands a conscious response from subjects, but changes in MSLT were similar regardless of the EEG or behavioral response as long as the rate of sleep fragmentation was the same [25]. It is common that individuals participating in a sleep fragmentation experiment will have many brief arousals during the night. This increase in arousals is normally accompanied by a significant increase in stage 1 sleep along with decreases in SWS and REM. Several sleep fragmentation studies have carefully controlled total sleep time to show that the effects of sleep fragmentation are not produced by partial sleep deprivation [26, 27]. Other studies have produced carefully controlled disturbance or have designed disturbance to have little or no impact on ongoing EEG as means of determining whether the effects of sleep fragmentation were specifically related to decreased sleep continuity as opposed to changes in sleep stage amounts (for example, the increase in stage 1 sleep mentioned earlier). One study [26] has shown significant increases in sleepiness as measured by the MSLT with no significant changes in any nocturnal sleep stage parameters. A second study has shown significant increases in sleepiness as measured by the MSLT and MWT [27] with the only sleep stage change being an 18% decrease in SWS. Two other studies have shown that small changes in SWS like the one in the Martin et al. [27] study do not have any additional impact above the effect of sleep fragmentation alone [28, 29]. Such studies provide evidence that it is the disturbance of sleep continuity rather than changes in sleep stages per se that produce the effects of sleep fragmentation.

**STUDIES COMPARING THE EFFECTS OF TOTAL SLEEP DEPRIVATION AND SLEEP FRAGMENTATION**

A few empirical studies have directly compared the impact of total sleep deprivation and sleep fragmentation within the same experiment [3, 11, 30, 31]. All four studies compared total sleep loss for one or two [11] nights with similar periods of sleep fragmentation. Sleep fragmentation was produced following each minute of sleep in three studies and at each onset of stage 2 in the fourth. In the Spath-Schwalbe study [3], profiles of cortisol and ACTH peaked shortly after the initiation of sleep deprivation or sleep fragmentation and then showed the same pattern of inhibition followed by a later peak in both conditions. This
pattern was different from the normal sleep condition. In the Levine et al. study [30], MSLT was reduced after both total sleep deprivation and 1-min sleep fragmentation, and these conditions did not differ statistically (the actual latencies were respectively 2.2 and 4.1 min). In the Bonnet study [11], performance deficits were significantly greater following total sleep deprivation than following 1-min sleep fragmentation on number of addition problems completed and simple reaction time. However, deficits were similar on vigilance hit rate (25% versus 25%) and on nap latency (2.2 versus 3.7 min). At least two studies have shown an increase in apnea/hypopnea events following sleep fragmentation [31, 32], and in one of these [31], a significant increase in both apnea/hypopnea and upper airway collapsibility was found after sleep fragmentation in comparison with a similar period of total sleep deprivation. This latter finding is the single instance where the effects of sleep fragmentation have been reported to be more extreme than a comparable period of total sleep loss.

These comparison studies are important because they establish direct links between the effects of sleep fragmentation and sleep deprivation. The demonstration of similar effects on hormones, respiratory parameters, psychomotor performance, and objective sleepiness provide strong concurrent evidence that the high frequency sleep fragmentation procedure is effectively the same as total sleep deprivation.

**CLINICAL EFFECTS OF SLEEP FRAGMENTATION: SLEEP APNEA AND PERIODIC LIMB MOVEMENTS**

Many clinical studies have examined the relationship between sleep fragmentation variables and daytime function. In an early study of the determinants of daytime sleepiness, Carskadon et al. [33] looked at many sleep-related variables but found that only measures of arousal and measures of sleep-related respiratory events correlated significantly with daytime sleepiness (with correlation values ranging from 0.41 to 0.49). In the years that followed, several studies attempted to differentiate the effects of sleep fragmentation from the effects of apnea-associated oxygen desaturation in producing the daytime sleepiness. For example, Colt et al. [34] treated sleep apnea patients with CPAP to reduce sleep fragmentation and daytime sleepiness before experimentally adding periods of oxygen desaturation while on CPAP to document that daytime sleepiness did not return from periods of oxygen reduction alone. Results from the many studies which have empirically produced fragmentation independent of apnea (and the study independently producing fragmentation and apnea in dogs) have been very clear in differentiating sleep fragmentation effects from desaturation effects [23]. Finally, patients with upper airway resistance syndrome are defined as having minimal oxygen desaturation and apnea but nonetheless suffering from significant daytime sleepiness. Despite the absence of clear apnea, these patients show periodic increases in airway resistance followed by arousal [35]. These several types of studies, in agreement with the empirical fragmentation studies, support the idea that it is the fragmentation rather than the oxygen desaturation in apnea patients that produces the sleepiness symptoms.

Guilleminault and others have noted that patients with sleep apnea and upper airway resistance may have respiratory events that are not followed by clear arousals. A recent examination of respiratory events not followed by scorable arousal compared to arousal events using spectral analysis of the EEG found that all of the respiratory events were followed by increases in alpha, beta, and theta and delta activity. However, those events that produced more alpha (i.e. visually scored arousals) resulted in a greater drop in pressure [35]. The results also imply that some EEG arousals may not be visually scorable. This might help explain why the correlations between visually scored arousals and measures of sleepiness in not always high. In fact, a number of other studies have questioned the low level of correlation between measures of sleep fragmentation and residual sleepiness. For example, several studies have employed a broad range of measures of sleep disturbance in an attempt to determine which physiological components of disturbance are most closely related to residual sleepiness. Martin et al. [36] found low but significant correlations between each of three arousal measures (1.5 s arousals, 1.5 s arousals plus EMG increase, and 3 s arousals) and MSLT. The correlations ranged from $\rho = -0.22$ to $-0.24$. The relationship with the Respiratory Disturbance Index (RDI) was marginally higher ($\rho = 0.30$), but the relationship with Rechtschaffen and Kales awakenings [37] was not significant ($\rho = -0.04$). In a conceptually similar study, Bennett et al. [38] looked at eight arousal measures including two “neural network” measures (two forms of digitized EEG changes), a measure based on pulse transit time, and a measure of movement based upon digital comparison of video
images. They also found that all of their momentary arousal measures were significantly correlated with their objective measure of daytime alertness but did not differ from each other (Rho ranged from −0.38 to −0.53). The traditional arousal scoring [39] was correlated with daytime alertness (Rho = −0.51), and the RDI relationship was similar (Rho = −0.41). All of these measures also remained significantly related with change in daytime alertness after the initiation of CPAP therapy. Other recent studies, including a very large study (n = 1,824) examining subjective sleepiness in relationship to RDI, have also shown significant relationships between this measure of sleep fragmentation and daytime sleepiness [40–42].

In summary, the relatively low correlation between arousal indices and daytime sleepiness may be secondary to lack of sensitivity of visual arousal scoring. Alternatively, however, the lack of agreement could be secondary to varying degrees of daytime sympathetic activation in apnea patients (see the “insomnia” section), or variable patterns or frequency of arousal in patients with positional apnea where position is not controlled on either sleep evaluation nights or preceding nights of sleep at home.

Several studies have examined the relationship between sleep fragmentation and cardiovascular variables. Davies et al. [43] found that brief arousals from sleep were associated with increases in blood pressure and that the degree of increase was about 75% of that seen during obstructive apnea. Two follow up studies showed that (1) the incidence of hypertension was higher in a group of snorers with fragmented sleep (but no apnea or hypopnea) than in a group of snorers without fragmented sleep [44] and (2) that, in a population-based study of individuals with an RDI of less than 1, a correlation of 0.54 (p = 0.005) was observed between blood pressure and a sleep fragmentation index [45]. Unfortunately, these studies did not control for the possible incidence of upper airway resistance syndrome. However, one single case study also has reported increases in blood pressure in conjunction with periodic limb movements [46]. Further research is needed to more firmly link sleep fragmentation directly with the hypertension.

A few studies have examined airway collapsibility and gas challenge responses in patients and normals. Gleadhill et al. [47] demonstrated that patients with obstructive apnea had a more easily collapsed upper airway than patients with obstructive hypopneas and patients who snored. Series et al. then demonstrated that sleep fragmentation by itself significantly increased collapsibility in the upper airway in normals to levels seen in some patients who snored [31]. In one study, sleep fragmentation was significantly related to a reduced vasodilation response to a hypercapnic challenge in the morning in a mixed group of normal and apnea patients [48], while in another study the hyperoxic hypercapnic ventilatory response was not altered after nights of fragmented sleep [32].

A final group of studies has examined sleep fragmentation variables in patients with periodic limb movements. An initial study split patients with periodic limb movements into groups based upon their primary complaint of either insomnia or excessive daytime sleepiness [49]. Measures of brief arousals were not reported in this study, but patients with excessive daytime sleepiness did have significantly increased shifts to stage 1 sleep and more (but shorter) awakenings. More recently, three studies have examined sleep fragmentation in sleepy patients with periodic limb movements with the hypothesis that medications that reduce the associated arousals should decrease arousals during sleep and improve daytime alertness. Doghramji et al. [50] found that short-term administration of triazolam at doses of 0.25 or 0.5 mg had no effect on the PLM index, but decreased total arousals significantly. Sleep latency on the MSLT was significantly longer following the final medication night. However, total sleep time was also increased by the medication. Two studies by Bonnet and Arand in a similar patient group also showed that triazolam increased total sleep at night and alertness during the day but showed no reduction in limb movements or arousals [51, 52]. However, a study in which triazolam was administered to patients with central sleep apnea showed a reduction in central apnea, a reduction in arousals, an increase in total sleep, and improvement in daytime psychomotor performance [53]. Together these studies provide evidence that reduction of arousals in patients with fragmenting sleep disorders can improve alertness and function on the day that follows.

SLEEP DEPRIVATION AND SLEEP FRAGMENTATION IN PATIENTS WITH INSOMNIA

A common complaint from patients with psychophysiologic insomnia is that they have reduced sleep at night and this leaves them tired the following day [54]. This implied chronic reduction in total sleep should leave these patients suffering from chronic partial sleep
deprivation. However, patients with chronic insomnia are not more sensitive to sleep deprivation than normal sleepers and do not have sleep rebounds, as normal sleepers would, after their typically poor sleep. The lack of recovery sleep after poor sleep implies (a) that primary insomnia patients do not have sufficient reduction in total sleep to produce recovery; (b) that primary insomnia patients are actually short sleepers who do not require additional sleep; or (c) that something partially blocks the sleep or recovery process. These hypotheses will be examined in the paragraphs that follow.

(a) Verifying the amount of sleep loss and the relationship of lost sleep to alertness and performance ability in patients with insomnia is difficult. Patients with insomnia typically underestimate the total amount of sleep that they obtain each night in comparison with polysomnographic findings. In fact, one subgroup of insomnia patients, currently given a diagnosis of Sleep State Misperception Insomnia, has normal total sleep time and sleep staging despite presenting with similar symptoms and complaints as insomnia patients who do have disturbed sleep. Because these patients cannot be separated from other insomnia patients based upon insomnia symptoms, the relevance of EEG sleep to the expression of the insomnia complaint can be questioned [55, 56].

In general, patients presenting with a complaint of insomnia do have increased time awake during their sleep period. However, the reduction in sleep time is usually not extreme. For example, the sleep requirement typical in studies of primary insomnia is sleep efficiency of 85% or less. This criterion means that patients evaluated frequently have a total sleep time of 6.5 h per night. Such total sleep times may not be short enough to produce measurable residual sleepiness or performance deficit.

(b) Patients with insomnia are typically differentiated from individuals with a characteristic short sleep pattern by their complaint of residual daytime dysphoria symptoms that they associate with their poor sleep. Individuals who have a decreased sleep requirement do not report residual effects associated with their reduced sleep. Therefore, patients with insomnia are typically differentiated from short sleepers by their daytime complaint.

(c) There is considerable evidence to support the hypothesis that the ability to fall asleep in patients with primary insomnia is inhibited by an overactive arousal system [57]. Studies have shown that patients with insomnia do respond to total sleep deprivation with increased sleepiness and rebounds in recovery sleep, as do normal sleepers [58, 59]. In a study involving experimental partial sleep deprivation (total sleep time reduced to 4.4 h for a week), insomnia patients also showed increased daytime sleepiness as measured by the MSLT [60]. However, the insomnia patients had longer MSLT latencies both prior to and after the partial sleep deprivation (15.6 and 11.1 min respectively) than would be expected in normal sleepers. A number of studies have reported that patients with insomnia have longer latencies on the MSLT in comparison to normal controls [61, 62]. Further, the correlation between total sleep at night and latency on the MSLT in these patients appears to be the opposite of what one might expect (i.e. the less sleep patients obtain at night, the longer their daytime nap latencies [61]). One could argue that these results reflect the fact that insomnia patients have an inherent “defect” in their ability to fall asleep and that the MSLT is just not valid for them. However, this “defect” is probably chronic heightened levels of physiological arousal. Similar increased MSLT latencies have been produced in normal sleepers by increasing their level of physiological arousal by having them take a 5-minute walk prior to the nap test [63]. Similar increased MSLT latencies have also been produced in normal sleepers by the administration of caffeine to produce physiological arousal [64]. In the latter study, chronic administration of caffeine also produced the other secondary symptoms of insomnia – poor EEG sleep, increased fatigue/decreased vigor, and personality change. The report of decreased vigor despite the chronic physiological arousal associated with caffeine provides evidence that the daytime dysphoria reported by patients with insomnia can be caused by physiological arousal and may not be a symptom of reduced or disturbed sleep as commonly assumed by patients.

It therefore seems most likely that many patients with primary insomnia have relatively small reductions in their total sleep time and that any residual sleepiness associated with this reduction is masked by the arousal system. Such data are important because increased central nervous system arousal may also make it more difficult to measure true sleep tendency in some depressed or anxious patients and in some sleep apnea patients, who may have considerable sympathetic arousal associated with their struggle to breathe (see [65] for a review of the impact of apnea upon sympathetic activity).

Sleep fragmentation is also reported as a problem in patients with insomnia. In older studies, it was not common to screen for or record respiration or anterior tibialis EMG in patients being evaluated for
insomnia. As a result, early reports of increased awakenings in insomnia patients may have come from sleep apnea or periodic limb movements as an underlying pathology. However, in more recent studies that have screened out patients with other sleep pathologies (see [66], for review), it appears that patients with primary insomnia do not have increased arousals or awakenings—they have longer awakenings to account for their decreased total sleep. Longer awakenings consistently demonstrate difficulty in ability to fall asleep (i.e. return to sleep after awakening) but not with the effects of sleep fragmentation, which reduces latencies to sleep onset.

Sleep fragmentation is much more common in patients who have truly fragmenting sleep disorders such as sleep apnea or periodic limb movements. As reviewed earlier, a number of studies have looked at the relationship between sleep fragmentation and daytime function in these clinical groups. Other groups of patients, such as those with rheumatoid arthritis or chronic pain may also report fragmented sleep and daytime symptoms. However, even patients with rheumatoid arthritis, for example, have not been shown to have significantly increased arousals compared to control groups in polygraphic studies [67].

In summary, patients with insomnia report chronically reduced sleep. However, in most patients, the lost sleep is less than subjectively reported, and the patients do not display significant daytime sleepiness even after as many as seven nights with total sleep reduced to less than 4.5 h per night [60]. Evidence suggests that the arousal system modulates ability to fall asleep (see Bonnet [1] for a review of arousal effects) as well as producing insomnia symptoms. Changes in level of arousal certainly could also modulate response to both sleep loss and sleep fragmentation.

DIFFERENTIATING MSLT RESULTS IN PATIENTS WITH SLEEP DISORDERS VERSUS SLEEP DEPRIVATION

Patients presenting in Sleep Disorder Centers who suffer from fragmenting sleep disorders can almost universally be identified by frequent EEG arousals in their polysomnograms. However, patients presenting in Sleep Disorders Centers who suffer from chronic partial sleep deprivation may not always be easily identified without a careful history of sleep habits balanced with information about individual sleep requirement. Partial sleep deprivation, for example, reduction of sleep time to 4 h for one night, results in a 50% reduction in REM with no change in SWS [68]. Significant changes in sleep were not found in an 8-h recovery sleep, but increased REM was found in ad lib recovery sleep [68] and in a 10-h recovery sleep [17]. In a separate condition, Carskadon [17] found that 80% of her normal young adult subjects had a REM onset in a daytime nap given after 7 nights of sleep restricted to 5 h per night. The implications of such findings for clinicians can be confusing. Normal individuals who are partially sleep deprived may not show obvious increases in SWS or REM in an 8-h nocturnal recording but may still have decreased sleep latency on the MSLT, REM pressure, and REM sleep onsets during the day that follows. For this reason, some patients suffering from only chronic partial sleep deprivation could be inappropriately given a diagnosis of narcolepsy. Also, recovery sleep after sleep deprivation is significantly different in older individuals, and chronic partial sleep deprivation studies have not been done in this group. For example, older individuals have reduced SWS and are therefore less likely to have large SWS rebounds after total sleep loss. As a result, older sleepers are more prone to have REM rebound, including REM onset sleep during recovery from total sleep deprivation [69]. Again, the increased propensity for REM onset after sleep loss may make it difficult to differentiate older patients who have been sleep deprived from older patients with narcolepsy. Additional studies of recovery from partial sleep deprivation in these groups are necessary to improve the ability to make these diagnoses.

SLEEP DEPRIVATION OR FRAGMENTATION AND MEDICAL RISK

It is well known that sleep fragmentation and sleep deprivation are sedating. Several recent studies have examined the comparative risks between alcohol use, sleep deprivation, and sleep fragmentation. Dawson and Reid [70] calculated increasing decrements on a hand/eye coordination task after increasing doses of alcohol and sleep deprivation. They found that performance with blood alcohol content 0.10% was equivalent to performance at 8am after staying awake all night. Williamson compared performance on a range of tasks including vigilance and response speed during sleep deprivation and after alcohol at
blood alcohol concentrations of 0.05 and 0.1% [71]. Performance ability on all tasks declined as sleep deprivation increased and as alcohol level increased. Performance at the 0.1% alcohol level was similar to that seen after 18–20 h of sleep deprivation (about 4 am during the first night of total sleep loss). These results were replicated for simulated driving – tracking, tracking variability and speed variability were similar after 21 h of wakefulness to those measures with a blood alcohol concentration of 0.08% [72]. Another study has replicated these findings (similar decrements after either total sleep deprivation for 1 night or 5 h of sleep for 7 nights as compared to a BAC of 0.08%) for increase in reaction time and number of cones hit in an actual driving course [73]. In another study, performance in patients suffering from sleep fragmentation (sleep apnea patients with an apnea index of 29) had psychomotor performance at about same level as normal controls who had blood alcohol levels of 0.08% [74]. Several studies have documented the increased risk of driving accidents for patients with untreated sleep apnea. Other studies have shown that the sedating effects of sleep deprivation plus alcohol use are additive – performance with the combination of these factors was worse than either of the individual factors alone [75, 76].

Both sedating medications and sleep deprivation (or sleep fragmentation) increase the number and length of apneas in patients with sleep apnea and produce apnea in patients who snore [9, 77]. Patients with sleep apnea are at increased risk from both their compromised upper airway and their chronic sleep fragmentation when they use sedating medications, are subjected to general anesthesia, or are in any situation that produces sedation or removes sources of exogenous stimulation. It is common practice in medicine to carefully identify and label sedating medications to reduce the risk that these medications will potentiate the effect of other sedating medications or debilitating medical conditions such as pulmonary disease. However, similar risks are also associated with sleep deprivation and sleep fragmentation and need to be considered as interacting factors with all medications and medical conditions sensitive to sedation.

**APPROACHES TO TREATMENT OF FRAGMENTATION AND DEPRIVATION**

The sleep system is homeostatically biased to reduce or eliminate the impact of both sleep deprivation or sleep fragmentation. An immediate outcome of both sleep deprivation and sleep fragmentation is increased subjective sleepiness, that under most circumstances, increases the likelihood of recovery sleep. Individuals in experimental sleep fragmentation paradigms rapidly habituate to non-meaningful disturbance as a means of preserving sleep continuity. Individuals experiencing sleep fragmentation or sleep deprivation increasingly attempt to obtain non-disturbed sleep by falling asleep more rapidly as their sleep is increasingly denied or disturbed. They also display significantly increased thresholds to arousal [78], as a sleep restoration protective mechanism, when sleep is allowed. For these reasons, the treatment for sleep fragmentation involves only the removal of the disturbing stimulus (e.g. provision of an unobstructed airway). Unfortunately, treatment for sleep deprivation, especially chronic partial sleep deprivation, requires significant education and public awareness because the “disturbing stimulus” in this case is often the desire to remain awake and active. The several studies that have shown similar loss of function between sleep deprivation and alcohol use offer insight. First, it is important to understand that the effects of even a few hours of sleep deprivation are both real and clinically significant. The fact that driving performance is as bad during the first night of sleep deprivation as that seen in adults who were legally intoxicated means that our attitude toward seemingly trivial amounts of sleep deprivation needs to shift in the same manner as our attitude toward alcohol has shifted in recent years. No one would think of suggesting that a drunk driver should “tough it out” for a few more hours while driving. Similar requests should not be made of sleep-deprived employees in hospitals or factories. Sleep deprivation must be seen as producing risks similar to alcohol, and societal attitudes must shift to reflect the risk. For example, New Jersey recently made it a crime to drive under the influence of sleep loss.

Almost all empirical studies of sleep deprivation or sleep fragmentation choose normal young adults as subjects. Part of the selection process includes the requirement that participants typically spend 7–9 h in bed each night. As such, current knowledge may not be relevant for individuals who require more or less sleep. There are numerous reports of individuals who are true short sleepers but there is a general feeling among researchers that many individuals who report usual short sleep times are more likely to be chronically partially sleep deprived. However, it is unknown how many short sleepers actually have a decreased sleep requirement versus the impression that they can get by
with less sleep. Conversely, some individuals may display compromised alertness despite having more than 8 h of sleep at night. Understanding and differentiating these groups is essential because it will allow us to know if anyone can be exempted from findings based upon individuals spending about 8 h in bed.

If we drink alcohol and have a car accident, culpability is easily established. If we have a car accident driving home after a night shift, how does one assign blame, and where does it belong? Determining industrial, medical, and personal responsibility for such accidents is difficult and evolving [79]. Much work remains to be done to educate sleep practitioners, other physicians, and the public to the consequences of partial sleep loss. A first step is for each of us to recognize and limit partial sleep loss in our own lives.

**CONCLUSION**

Awareness of the consequences of both sleep deprivation and sleep fragmentation has grown significantly in the past few years. Increased funding from the NIH and the National Transportation Safety Board has followed this awareness. One crucially missing component in the identification of sleepiness in applied settings is the “sleepalizer” (a simple rapid test of alertness which can be easily administered and scored in the field like the breathalyzer test used for alcohol). The standard test (MSLT), which involves attaching electrodes and waiting for sleep onset, is much too cumbersome as are other similar EEG measures. Psychomotor performance measures tend to be highly variable based upon age and experience factors. Other research must refine our definition of sleep “need”. It is the common belief that each individual has a unique sleep need that changes across the life span. However, no research has examined the genetics or development of sleep need in humans.

As mentioned earlier, differentiation of patients suffering from chronic partial sleep deprivation and patients suffering from idiopathic hypersomnia may be difficult. Both groups of patients may display similar sleep at night and reduced latency on the MSLT. Few empirical studies have looked at recovery sleep or MSLT after various periods of partial sleep deprivation or as a function of age. A closer examination of clearly identified hypersomnia patients in direct comparison with sleep-deprived normals might clarify diagnostic differences.

A large number of papers (see [80] for review) have consistently reported that patients who are depressed frequently show significant clinical improvement after sleep deprivation. However, this improvement in mood is typically reversed when patients go to sleep. There are few studies that have examined sleep deprivation under the same conditions in parallel groups of depressed patients and normal controls to document the predicted interactions in mood change. One explanation for improvement in mood following sleep deprivation is that the sedating effect of sleep deprivation balances some of the agitation or arousal common in clinical depression and therefore helps to normalize mood. However, significant research must be done to understand the conflicting response to total sleep deprivation in depressed patients.

**Practice Points**

Total sleep deprivation, partial sleep deprivation and sleep fragmentation all have a significant impact on sleepiness and psychomotor performance — they differ in degree rather than in dimensions.

Polysomnograms can identify most types of sleep fragmentation, but clinical identification of chronic partial sleep deprivation (as opposed to idiopathic hypersomnia) can be difficult.

Always consider a differential diagnosis of insufficient sleep syndrome in any patient suffering from excessive sleepiness even if another source of sleepiness such as sleep apnea is identified.

**Research Agenda**

1. Development of a simple rapid test of alertness that can be easily administered and scored in the field.
2. Improved identification of the sleepiness effects of chronic partial sleep deprivation and identification of polygraphic or other markers indicating chronic partial sleep deprivation in various age groups to improve the diagnosis of Insufficient Sleep Syndrome.
3. Differentiation of the effects of sleep deprivation in patients with depression as compared to other groups.
4. Identification of objective indicators of sleep “need” and determination if underlying sleep need varies as significantly as subjectively described sleep habits.
REFERENCES


* The most important references are denoted by an asterisk.


