Consequences of Insomnia
Michael H. Bonnet, PhD a,b,c,*, Donna L. Arand, PhD a,c

The diagnosis of psychophysiologic or primary insomnia historically has required a patient report of both poor sleep and “decreased functioning during wakefulness” [1]. The requirement for decreased function as a defining factor may be related to the idea that insomnia produces reduced sleep time at night and that this chronic reduction in sleep is the same as chronic partial sleep deprivation in normal individuals. This article reviews studies that have examined the consequences of insomnia as related to findings that suggest that primary insomnia is more closely associated with inappropriate arousal.

Chronic reduction in sleep time resulting from difficulty initially falling asleep, from awakenings during the night, or from awakening early in the morning without being able to return to sleep serves as the current basis for identification of insomnia. One means of understanding problems that become apparent in patients who have insomnia is to determine the extent to which reduction in sleep in normal individuals produces similar changes. Chronic reduction of sleep has been examined in numerous studies including total sleep deprivation in normal sleepers [2] and in patients who have insomnia [3], chronic partial sleep deprivation in normal sleepers [4], sleep reduction in patients who have insomnia, [5] and in a specific yoked-control design where normal sleepers were awakened or aroused in a pattern mimicking the sleep of a patient who has insomnia [6]. Sleep-restriction and sleep-deprivation designs in normal sleepers consistently have shown that sleep loss produces changes in mood, particularly increased sleepiness and fatigue with decreased alertness, and in a broad range of psychomotor performance variables including vigilance, reaction time, and memory [2]. Sleep deprivation in normal sleepers also results in increased objective sleepiness as measured by the Multiple Sleep Latency Test (MSLT) and increased sleep time when sleep is allowed. Specific evidence for similar changes in patients who have

This work was supported by the Dayton Department of Veterans Affairs Medical Center, Wright State University School of Medicine, and the Sleep-Wake Disorders Research Institute.

a Wright State University School of Medicine, 4100 W 3rd Street, Dayton, OH 45428, USA
b Sleep Center at the Department of Veterans Affairs Medical Center, 4100 West Third Street, Dayton, OH 45428, USA
c Kettering Medical Center Sleep Disorders Center, Wallace Kettering Neuroscience Institute, 4545 Southern Boulevard, Kettering, OH 45459, USA
* Corresponding author. Dayton Department of Veterans Affairs Medical Center, 4100 West Third Street, Dayton, OH 45428.
E-mail address: bonnetmichael@yahoo.com (M.H. Bonnet).
insomnia will be examined in the categories of psychomotor performance, subjective reports, quality of life, and objective measures of sleep and sleepiness.

**Psychomotor performance**

At least 15 studies have compared performance on various psychomotor tasks in patients who have primary insomnia and normal controls, and review of studies that took place before 2000 has been published [7]. These studies have examined more than 30 different performance measures. To summarize the data, findings were sorted into seven broad test categories. Results tallied by reports of significant decrements in performance in patients, are plotted in Fig. 1. An examination of significant test results within categories showed that about as many significant results as would be expected by chance were seen for the mathematics, vigilance, hand/eye coordination, and reasoning tasks. For the memory tests, about 20% of the reported findings reached statistical significance. Six studies reporting number of words recalled in an immediate memory task were reviewed, and data from the three of those that included means plus SD in comparable patient and control groups were combined to calculate a power statistic. In those studies [8–10], the mean numbers of words recalled by normal sleepers and by patients who had insomnia were 11.1 and 8 words, respectively (combined SD of 2.94 with 89 and 166 subjects [Ss]), giving a power of 1.04. Effect sizes (ES) for other types of memory measures were lower (in the range of 0.28), however. Simple reaction time (five studies reporting) was examined from the many reaction-time measures. Of studies reporting mean and SD [11,12], reaction times from normal sleepers and patients who had insomnia were 290 and 364 milliseconds, respectively (combined SD of 256 with 56 Ss in both groups), giving a power of 0.288. Both studies that examined balance reported statistically significant decreases in patients who had insomnia, and ES from the one study with data to sufficient to calculate ES was 3.1 [13]. To determine if these results might depend on definition of insomnia, test results also were examined from studies that required a diagnosis of insomnia based upon sleep electroencephalographic (EEG) criteria. EEG criteria reduced the total number of studies and tests in the sample, but the pattern of results was similar to that presented in Fig. 1.

When these psychomotor performance results from patients who had insomnia are compared with typical findings from sleep-deprived normal sleepers, there are clear differences. Patients who have insomnia show no differences in the vigilance and mathematics domains and only mild effects on reaction time. This finding suggests a major difference in response in insomnia and sleep deprivation and suggests that the performance differences identified might be related to a variable other than sleep loss.

**Subjective reports**

Dysphoria is reported commonly by patients who have insomnia. A number of studies have assessed various mood components in these patients. The most commonly reported mood dimensions have been subjective fatigue and sleepiness. In a review of studies before 2000 [7], it was reported that 7 of 12 studies using the Stanford Sleepiness Scale in patients who had insomnia found significantly greater sleepiness in patients than in controls. Fatigue has also been measured with several scales including the Profile of Mood States (POMS) and the Fatigue Severity Scale. Significant increases in fatigue have been reported in patients who have insomnia in four [14–17] of seven studies [8,18,19].

![Fig. 1](image.png) The total number of psychomotor tests reported in controlled studies of patients who have insomnia (black bars) compared with the number of statistically significant test results (striped bar) by test category.
Objective measures of sleepiness and sleep

One obvious difference between patients who have insomnia and sleep-deprived normal sleepers is what is called “recovery.” When normal sleepers are allowed to sleep after sleep deprivation, the universal response is a decrease in sleep latency and an increase in sleep time. Patients who have insomnia rarely seem to obtain such a recovery or to demonstrate sleep-stage rebounds during their sleep despite continuing reports of reduced and ineffective sleep. These incongruous sleep-rebound findings extend to results with the MSLT. If patients who have insomnia suffer from sleep deprivation, it would be expected that they would fall asleep rapidly on the MSLT. In fact, none of 12 studies that have performed the MSLT in patients who have insomnia and controls has found a significant decrease in MSLT in the patients compared with the controls. Six studies actually have shown a significant increase in MSLT in patients who have insomnia as compared with controls (see the later section on physiologic measures). Such a significant finding, the opposite of the predicted response in patients who have insomnia compared with normal sleepers, has led to an examination of other underlying variables as major precipitants in insomnia complaints.

Comparisons of patients who have insomnia and normal sleepers using sleep-deprivation protocols

Several studies have subjected patients who have insomnia to total sleep deprivation and have reported that these patients do, in fact, become sleepier, fall asleep more quickly on the MSLT, and have increased total sleep time when allowed to sleep after 1 or more nights of total sleep deprivation [3, 25, 26]. Studies, however, have not shown an interaction that would indicate that patients who have insomnia are more sensitive to sleep deprivation, as might be expected if they had been exposed to chronic partial sleep deprivation before the acute sleep loss. Also, when allowed recovery sleep after 64 hours of total sleep deprivation, patients who have insomnia returned to their previous poor sleep pattern during recovery sleep nights [3].

One study [6] has used a yoke-control design to mimic the arousals, awakenings, and wake time of patients who have insomnia in a group of normal sleepers for 1 week to determine the extent to which the disturbed sleep of patients who have insomnia is responsible for their reported symptoms. The data suggested that an insomnia sleep pattern imposed on normal sleepers was consistent with mild sleep loss; that is, after 1 week, normal sleepers with such disturbed sleep (resulting in about 5.8 hours of sleep per night) had a significant decrease in their MSLT (latency to stage 2 declined from 15.8 to 10.9 minutes) and decreased vigor and alertness without significant declines in performance. Inability to document a decline in psychomotor
performance secondary to the mild sleep disturbance in this study replicates the earlier reported spotty record of objective performance decline actually found in patients who have insomnia. The general conclusion of the study was that poor sleep per se is not the major cause of many of the symptoms reported by patients who have insomnia. For example, the MSLT was significantly decreased in normal sleepers who experienced the sleep pattern of a patient who has insomnia, whereas the MSLT of the patients who have insomnia was significantly increased [6].

A follow-up study sought to determine if especially poor sleep in patients who have insomnia would exacerbate insomnia symptoms [5]. In that study, patients who had primary insomnia were chosen based on their complaint of insomnia and documented EEG poor sleep. Patients then had their total nocturnal sleep reduced by an additional 2 hours (from the usual 6.5 hours to about 4.4 hours total) by the imposition of additional wake time during the night for 1 week. The remarkable conclusion of this study was that the patients did not rate their sleep quality as significantly worse after additional sleep reduction. The patients did become sleepier during the day, as indexed by the MSLT, which decreased from 15.6 to 11.1 minutes (latency to stage 1) after 1 week of sleeping 4.4 hours per night. Their level of sleepiness after 1 week, as indexed by the MSLT, would be considered in the normal range for the MSLT, however [27]. By comparison, in a study in which normal sleepers were allowed 5 hours of sleep per night for 1 week, the MSLT decreased to 3.0 minutes after the first 5 nights [28]. The implication is that patients who have insomnia do become sleepier when their total sleep time is artificially decreased, but their level of alertness may still be elevated compared with normal individuals with similar amounts of sleep reduction. Similarly, large performance deficits were found secondary to the chronic sleep reduction in normal sleepers [28], but no difference in performance was found when sleep was chronically reduced to 4.4 hours in the patients who have insomnia, despite their chronic sleep problem. The patients who have insomnia also showed only a nonsignificant increase in their total sleep (ie, no significant increase in short-wave sleep or rapid eye movement) on their recovery night, and this finding again suggests a more muted response to sleep restriction.

Taken together, these studies indicate that reduced or disturbed sleep by itself cannot account for symptoms reported by patients who have insomnia and conversely that the consequences of insomnia are not directly related to simple sleep loss. Such findings suggest that problems reported by patients, including poor sleep, are secondary to a different pathologic process.

### Arousal as a model for insomnia and consequences

Patients who have insomnia frequently indicate that they have difficulty relaxing so they can fall asleep. There is historic disagreement about whether such difficulty is a learned behavior or is associated with a physiologic abnormality. It has been relatively easy to test the extent to which insomnia is secondary to pure physiologic arousal by producing arousal and measuring the consequences. Physiologic arousal paradigms that are conventionally used to produce insomnia include stress associated with sleeping in an unusual place (usually the first night in a sleep laboratory), arousal associated with trying to fall asleep when bedtimes have been advanced 3 to 6 hours from normal, and sleep after the administration of stimulants.

As an example, one study sought to model insomnia by administering caffeine, 400 mg three times per day for 1 week [29]. It is well known that caffeine administration near habitual bedtime can produce poor sleep. The purpose of this study, however, was to determine the extent to which chronic caffeine use could produce both physiologic arousal and the full spectrum of complaints commonly made by patients who have insomnia. The study reported that caffeine administration was associated with physiologic arousal as indexed by whole-body metabolic rate and sleep disturbance as indexed by both EEG and subjective measures. There was some habituation in both metabolic and sleep measures across the week. The most important findings were

1. Latency on the MSLT was increased, as seen in patients who have insomnia, despite poor sleep at night, and this significant increase was found throughout caffeine administration.
2. Few changes, positive or negative, were found in psychomotor performance variables across the week.
3. POMS results showed a significant increase in vigor on the first day of caffeine administration followed by a significant decrease in vigor (both values compared with baseline) on the final day of caffeine administration.
4. A significant increase was found on the anxiety (PT) scale of the Minnesota Multiphasic Personality Inventory on the final day of caffeine administration as compared with baseline.

These findings suggested that the immediate arousal produced by the caffeine was not
maintained subjectively (decreasing vigor) despite continuing arousal measured by the MSLT and perhaps beginning to appear in a more general personality measure. This spectrum of mild sleep disturbance with subjective dysphoria despite elevated MSLT and negative trends in personality measures matches the spectrum of symptoms reported by patients who have primary insomnia and suggests that chronic physiologic arousal could produce both the objective and mood changes reported by these patients. A number of studies have reported physiologic differences in patients who have primary insomnia.

**Physiology in insomnia**

Several studies have found significantly increased physiologic activation in patients who have primary insomnia. At least 11 physiologic measures have been shown to differ in patients who have insomnia compared with controls. The common measures, along with number of studies employing the test, significant results, and ES estimate are presented in **Fig. 2**. Patients who have insomnia were found to have significantly elevated heart rate in five of six studies [30–35]. Cortisol was significantly increased in four of five studies [30,36–39]. Body temperature was significantly elevated in patients who had insomnia compared with controls in two of five studies [8,30,33,40,41]. Increased beta EEG activity was noted in five of six studies of patients who had insomnia compared with normal sleepers [42–47]. A number of additional significant physiologic changes, including increased 24-hour whole body metabolic rate [19,48] and brain metabolic rate [49]; increased heart rate variability suggestive of increased sympathetic and decreased parasympathetic activity [32]; increased corticotropin [36] and norepinephrine [30,50]; decreased melatonin [39,51]; decreased natural killer cell activity [50]; increased frontalis and mentalis electromyographic activity [52]; and increased basal skin resistance [33], have been reported in patients who have insomnia as compared with normal sleepers. Finally, two of four studies from the same laboratory [53–56] have reported significantly decreased pupil size (indicative of lower arousal) in insomnia groups compared with normal sleepers. Neither of the two studies reporting decreased pupil size was done with patients whose insomnia was objectively verified, however, and the one pupil-size study that was done with patients who had objectively verified insomnia found a numerically larger pupil size in the patients who had insomnia [54].

ES, as indicated in **Fig. 2**, have been moderately large for these physiologic variables. For example, ES for significant differences in heart rate found in waking and in matched sleep stages ranged from 0.875 to 1.05 [32], whereas ES for a significant low-power heart rate variable (sympathetic nervous system analogue) ranged from 0.38 to 0.81 during waking and matched sleep stages. ES from hormone studies have been large (range, 0.68–3.0) [36,38,50]. ES in studies of EEG beta have averaged 0.88 [44,46] and are similar to those reported for metabolic rate [19,48].

A number of studies have examined the ability of patients who have insomnia to fall asleep during daytime nap opportunities (usually in the MSLT). These studies are of particular interest because, if patients suffer mainly from reduced sleep at night, their daytime nap latencies should be significantly reduced [6]. If, however, patients suffer primarily from physiologic hyperarousal, their daytime nap latencies should be increased. Twelve studies were identified in which daytime nap latency was compared between patients who had insomnia and patients who had normal sleep.

**Fig. 2.** The total number of physiologic measures reported in controlled studies of patients who have insomnia (black bars) compared with the number of statistically significant test results (striped bar) by type of measure. MSLT, Multiple Sleep Latency Test.
study controls [8,10,18,19,41,54,57–62]. Sleep latency was not significantly reduced in patients who had insomnia as compared with controls in any study. Sleep latency was significantly increased in patients who had insomnia as compared with controls in 6 of the 12 studies. Insomnia was defined based upon EEG rather than on subjective report findings in 6 of the 12 studies. In four of these six studies sleep latency was significantly increased in patients who had insomnia as compared with controls. Four of these studies reported mean and SD data for the groups [10,19,57,58]. When the data for these four studies were combined, the average sleep latency for patients who had insomnia (N = 108) was 16.1 (± 4.4) minutes and for controls (N = 83) was 13.6 (± 4.8) minutes. This difference was statistically significant (t189 = 3.698; \( P < .001 \)). The power, calculated based upon these group data, was ES = 0.55.

Another means of evaluating the strength of these physiologic findings is to compare them with the strength of EEG sleep findings in studies in which the selection of patients who had insomnia was based on subjective criteria rather than on EEG findings. Nine studies with subjective selection criteria and objective sleep data were evaluated [8,9,12,18,41,54,59,61,63]. Of the nine studies, only three reported either a significant increase in EEG sleep latency or a significant decrease in EEG sleep efficiency in patients who had insomnia compared with controls. EEG sleep latency averaged across studies was 22.5 minutes (± 27) in patients who had insomnia (N = 394) versus 17.3 (± 13) minutes in controls (N = 228). Sleep efficiency averaged across studies was 81.8 (± 11.1) in patients who had insomnia (N = 394) versus 86.6 (± 7.4) in controls (N = 228). Both of these differences were statistically significant (\( P < .01 \)); ES were 0.24 for sleep latency and 0.49 for sleep efficiency.

These data suggest that numerous physiologic measures can differentiate patients who have primary insomnia from controls. Consistent activation, occasionally noted as extending throughout the 24 hours, suggests that patients who have primary insomnia may have a more general problem with arousal and that the reported poor sleep may be their easiest descriptor of the underlying arousal problem.

**Implications**

Patients who have chronic insomnia frequently complain of dysphoric mood, and such subjective complaints have a significant negative impact upon physical and emotional indicators of quality of life that are at least as extreme as those reported by other groups of patients who have chronic illness. Despite complaints of poor performance in a number of dimensions, significant decreases in psychomotor performance, with the possible exception of balance and perhaps memory, have not been seen at levels greater than would be expected by chance. This gap (reported versus objectively observed decrement in performance) is similar to the degree of sleep disturbance, which also is reported as much greater subjectively than is measured by objective EEG recordings. The lack of psychomotor performance decrements and research modeling of insomnia [6] suggest that patients’ subjective complaints are not secondary to simple sleep deprivation. The documentation of consistent physiologic changes in patients who have insomnia in numerous studies does suggest an important physiologic basis for the disorder and the subjective complaints [29].

The spectrum of physiologic changes reported in patients who have chronic primary insomnia is consistent with sympathetic nervous system activation. Chronic physiologic arousal can produce poor sleep, elevated MSLT, dysphoria, and anxiety [29]. In addition, chronic physiologic arousal may predispose patients to increased risk for depression [64], hypertension [65], alcohol abuse [66–68], and cardiac disorders [69–71] over time. Such a view suggests, however, that many current treatment studies (acute effects of therapy on EEG parameters or subjective sleep parameters) may not address the underlying disorder or ameliorate long-term risks.

**References**


Bonnet MH. Recovery of performance during sleep following sleep deprivation in older


