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Insomnia with Short Sleep Duration: Nosological, Diagnostic, and Treatment Implications

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Abstract

The diagnosis of insomnia is based solely on subjective complaints. This has contributed to the low reliability and validity of the current nosology of insomnia as well as to its lack of firm association with clinically relevant outcomes such as cardiometabolic and neurocognitive morbidity. We review evidence that insomnia with objective short sleep duration is associated with physiological hyperarousal, higher risk for hypertension, diabetes, neurocognitive impairment, and mortality as well as with a persistent course. It also appears that objective short sleep duration in poor sleepers is a biological marker of genetic predisposition to chronic insomnia. In contrast, insomnia with objective normal sleep duration is associated with cognitive-emotional and cortical arousal and sleep misperception but not with signs of physiological hyperarousal or medical complications. Thus, short sleep duration in insomnia may be a reliable marker of the biological severity and medical impact of the disorder. We propose that (a) objective measures of sleep be included in the diagnosis of insomnia and its subtypes, (b) objective measures of sleep obtained in the home environment of the patient would become part of the routine assessment and diagnosis of insomnia in a clinician's office setting, and (c) insomnia with short sleep duration may respond better to biological treatments, whereas insomnia with normal sleep duration may respond primarily to psychological therapies.

Keywords

Insomnia; short sleep duration; cardiometabolic; neurocognitive; physiological hyperarousal; morbidity; mortality

1. Nosology of Insomnia

The prevalence of insomnia in the general population ranges between 8-40%, depending on the definition used. While 20-30% of the general population has poor sleep (i.e., insomnia symptoms of difficulty initiating or maintaining sleep, early morning awakening, or non-restorative sleep at any given time), another 8-10% of the population suffers from chronic insomnia.¹⁻³ Insomnia is a major public health problem as it is associated with impaired occupational performance, increased absenteeism at work, higher health care costs, and worse quality of life.⁴⁻⁵ However, the connection of insomnia with cardiometabolic risk and cognitive impairment has not been examined until very recently. This has led some

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clinicians to view insomnia and its associated mental and physical health complaints as obsessions of otherwise healthy individuals.

The diagnostic nosology of insomnia has traditionally faced the dilemma of lumping vs. splitting insomnia subtypes. The former view is represented in the Diagnostic and Statistical Manual of Mental Disorders (DSM) that reflects the predominant view of the American Psychiatric Association, while the latter is represented in the International Classification of Sleep Disorders (ICSD) reflecting the predominant view of the sleep specialists in North America. In 1987, sleep disorders were included for the first time in the 3rd revised edition of the DSM (DSM-III-R) and overall diagnostic criteria for “insomnia disorders” were included based on the subjective complaints of difficulty initiating or maintaining sleep or of non-restorative sleep, occurring at least 3 times a week for at least 1 month, and associated daytime functioning complaints. The DSM-III-R⁶ allowed the diagnoses of “insomnia related to another mental disorder” or “to a known organic factor”, “primary insomnia”, and “dysomnia NOS” (see Table 1). The DSM-IV-TR eliminated the definition of “insomnia disorders” and included the diagnoses of “primary insomnia”, “dysomnia NOS”, insomnia “related to another mental disorder”, “due to a general medical condition”, and “substance-induced”.⁷ The DSM-5 is expected to be published in May 2013 and the diagnoses of “primary insomnia”, “sleep disorder related to another mental disorder”, and “sleep disorder due to a general medical condition” will most probably be eliminated in favor of “insomnia disorder” with concurrent specification of clinically comorbid mental and/or physical conditions so that no causal attributions between insomnia and the physical/mental condition are made and the independent clinical attention of insomnia is warranted.⁸ The DSM-5 is expected to incorporate the use of self-reported severity measures with the aim of identifying sub-threshold sleep disturbances in patients at risk for developing a full-fledged “insomnia disorder” and who may be candidates for preventive interventions.⁸ Also, it is expected an extension of the duration criterion from 1 month to 3 months. However, no objective measures of the biological severity of the disorder are expected to be included in the forthcoming DSM-5.

The ICSD (1990), and its revised form ICSD-R (1997), also defined insomnia based on subjective sleep and daytime functioning complaints but, in contrast, attempted to identify subtypes based on “intrinsic” factors such as etiology (i.e., “psychophysiological”), age of onset (i.e., “idiopathic insomnia”), degree of discrepancy between objective sleep findings and subjective perception of sleep (i.e., “sleep state misperception”) or “extrinsic” environmental factors such as “inadequate sleep hygiene”, “food-allergy” or “altitude insomnia” (see Table 1). However, these subtypes, even when refined in the ICSD-2,⁹ have not proven to be clinically useful and their reliability is at best modest.¹⁰⁻¹² For example, although the ICSD-2 diagnosis of “psychophysiological insomnia” is based solely on the subjective reports of the patient, it is presumed to be associated with physiological hyperarousal and polysomnographic (PSG) disturbances. The diagnostic subtype of “idiopathic insomnia” has produced very little research since it was first proposed¹³ and it appears that the proposed differences between “psychophysiological” and “idiopathic insomniacs”¹⁴ are not large enough to determine a true differential treatment approach, e.g., medication vs. psychotherapy. Finally, the subtype of “paradoxical insomnia” is estimated to represent as little as 5% of all insomnia sufferers according to the ICSD;⁹ however, recent epidemiological studies have shown that insomnia sufferers with clinically significant sleep misperception represent about 50% of all insomnia sufferers.¹⁵ Consequently, large multicenter studies have shown that the current insomnia diagnoses available have low diagnostic reliability and validity.¹⁰⁻¹² Finally, although PSG features are suggested, but not required, for virtually all ICSD subtypes, their usefulness in terms of differential diagnosis or severity assessment have not been demonstrated and are not currently used in clinical practice.

The sleep laboratory is essential for the evaluation of patients with sleep-disordered breathing (SDB), the diagnosis of narcolepsy, and the differential diagnosis of idiopathic vs. psychogenic hypersomnia.^{16,17} In addition, sleep laboratory measurements provide valuable objective information on the initial effectiveness, continued efficacy or tolerance, and potential withdrawal effects of a hypnotic drug. With the disorder of insomnia, the usefulness of the sleep laboratory has been at best controversial. As mentioned above, the ICSD-2 includes PSG findings as diagnostic criteria, although not required, for virtually all diagnoses.⁹ The validity and clinical utility of sleep lab testing for diagnosing insomnia has been evaluated in large studies^{11,18,19} and it has been concluded that (a) PSG is not useful in the evaluation of insomnia except to confirm or exclude other sleep pathologies when there is reasonable evidence from clinical history (e.g., SDB or periodic limb movements)^{4,20-22} and (b) sleep integrity measures, such as latency to sleep onset, total sleep time, number of arousals and awakenings, and sleep efficiency, are not useful in the diagnosis or differential diagnosis including subtyping of insomnia.^{4,11,18-23} The current consensus is, therefore, that PSG is not recommended for routine, differential diagnosis, or severity assessment of insomnia in clinical practice.²²

However, we are going to present and discuss evidence, accumulated in the recent years, that objective measures of sleep (1) are useful in predicting the biological severity of insomnia (i.e., cardiometabolic morbidity and mortality as well as cognitive impairment) and (2) should be included in the new nosology of insomnia given their clinical utility for severity assessment and choice of treatment based on relevant clinical outcomes.

2. Pathophysiology of Insomnia

In the last two decades, several models have been proposed to understand the etiology and pathophysiology of insomnia.²⁴⁻³⁰ Most of these models have emphasized the importance of the joint effect of stress and psychological factors in the pathogenesis of insomnia. Kales and Kales early stated that “stressful events . . . when mediated by certain predisposing emotional factors and inadequate coping mechanisms, are indeed closely related to the onset of long-term sleep difficulty”.²⁴ The characteristic psychological profile of insomnia sufferers, consisting of cognitive-emotional hyperarousal (i.e., obsessive, anxious, ruminative, and dysthymic personality traits) and emotion-oriented coping strategies,^{24,31,32} is thought to be present pre-morbidly and play a key role in the etiology of the disorder.^{24,33-36} The 3-P model by Spielman et al²⁵ specified each of the predisposing, precipitating, and perpetuating factors involved in the etiopathogenesis of insomnia and provided with a framework for therapies targeting the cognitive-behavioral factors that perpetuate insomnia after the resolution of the original stressor.

Stress has been associated with the activation of the hypothalamic-pituitary-adrenal (HPA) and the sympatho-adrenal-medullary axes, whereas corticotropin-releasing hormone (CRH) and cortisol (products of the hypothalamus and adrenals, respectively), and catecholamines (products of the sympathetic system) are known to cause arousal and sleeplessness to humans and animals. On the other hand, sleep and particularly deep sleep has an inhibitory effect on the stress system including its main two components, the HPA axis and the sympathetic system. Given that insomnia is associated with precipitating stressful life events³⁷ and cognitive-emotional arousal,²⁴ it was only natural for researchers to explore the association of this disorder with the stress system. Several studies have shown increased HPA axis, sympathetic, and central activation in insomnia sufferers, including increased cortisol and catecholamine secretion, heart rate and impaired heart rate variability, and 24-hour whole body and brain metabolic rate. While the majority of early studies reported no difference between subjectively defined “poor sleepers” and controls in the levels of 24-h cortisol and 17-hydroxysteroid excretion,³⁸⁻⁴⁰ later studies found that 24-h urinary free

cortisol, norepinephrine, and catecholamine metabolites levels were either increased in insomnia sufferers with objective sleep disturbances as compared to controls or were correlated with PSG indices of sleep disturbance in insomnia patients.⁴¹⁻⁴⁷ Only two recent studies have not replicated these findings. However, in one of these studies the objective sleep of insomnia sufferers was very similar to that of controls,⁴⁸ while in the other study⁴⁹ cortisol levels and other indices of physiological arousal were increased but not to a statistically significant level due to lack of power and controls not being carefully selected.⁵⁰ Finally, of interest is a study that demonstrated that middle-aged healthy individuals are more vulnerable to the sleep disturbing effects of CRH, which may explain physiologically the increased prevalence of insomnia in older subjects.⁵¹

Furthermore, although two early studies found small differences between subjectively defined good and poor sleepers in heart rate measures,^{38,52} two more recent studies that included insomnia patients who also met objective criteria for sleep disturbances have found significant changes in nocturnal heart rate and heart rate variability.^{53,54} Two studies have shown that overall oxygen consumption (VO₂), a measure of whole-body metabolic rate, is constantly elevated in insomnia patients with PSG documented sleep disturbance as compared to controls, whereas VO₂ is increased in sleep misperception insomnia sufferers but to a lesser degree compared to insomnia patients with PSG documented sleep disturbance.^{55,56} In a group of insomnia patients with PSG verified sleep disturbance, a significantly increased pupil size, indicative of sympathetic system activation, was observed,⁵⁷ whereas two other studies, in which insomnia diagnosis was based only on subjective measures, showed opposite results, i.e. decreased pupil size.^{58,59}

Although insomnia sufferers typically complain that they are fatigued and sleepy during the day, and one would expect that during the Multiple Sleep Latency Test (MSLT) they would demonstrate short sleep latencies, they have either similar or increased daytime sleep latencies when compared to controls.⁵⁹⁻⁶² Importantly, several studies have shown that, within insomnia sufferers, those with shorter objective sleep duration show longer sleep latencies in the MSLT^{61,63-65} and are more alert in vigilance tests.^{55,56,63} This is in contrast to normal individuals who after modest short-term sleep loss experience significantly reduced sleep latencies on the MSLT and decreased alertness in vigilance tests, i.e., physiological sleepiness.^{66,67} Thus, long latencies in the MSLT may represent a reliable marker of physiological hyperarousal in insomnia patients.

Finally, evidence about the presence of central nervous system hyperarousal in insomnia comes from studies using human subjects using neuroimaging,^{68,69} and spectral,⁷⁰⁻⁷⁵ arousal,^{76,77} and event-related^{78,79} electroencephalography analyses, and from studies on the neural circuitry of stress-induced insomnia in rats.⁸⁰ Increased cortical arousal during sleep is present to a variable degree in all insomnia sufferers⁷⁰⁻⁷⁵ and may explain why they perceive their sleep as wake and as non-restorative.^{15,28,81,82}

Collectively, these findings suggest that 1) the activity of the stress system is directly proportional to the degree of objective nighttime sleep disturbance or daytime increased vigilance in insomnia sufferers, 2) physiological hyperarousal, i.e. hyperactivity of both limbs of the stress system, is primarily present in insomnia patients with objective short sleep duration, while cognitive-emotional and cortical arousal is present to a variable degree in all insomnia sufferers, 3) objective short sleep duration appears to be a marker of the physiological hyperarousal in insomnia and not a measure of cumulative chronic sleep loss, and 4) objective sleep measures, i.e., short sleep duration (PSG) or increased daytime sleep latencies (MSLT), can provide a reliable index of the biological severity and medical impact of the disorder.⁸³

3. Insomnia and Cardiometabolic Morbidity

Many studies have established that insomnia is highly comorbid with psychiatric disorders and is a risk factor for the development of depression, anxiety, and suicide.⁴ However, in contrast to SDB, chronic insomnia has not been linked firmly with significant medical morbidity, such as cardiovascular disease. Several questionnaire-based studies have shown a significant relationship between difficulty falling asleep or poor sleep with cardiometabolic outcomes such as hypertension⁸⁴⁻⁸⁶ and diabetes.⁸⁷⁻⁹⁰ For example, in a prospective study from Japan,⁸⁵ persistent (>4 years) complaints of difficulty initiating or maintaining sleep were associated with an increased risk of hypertension (OR = 1.96). In another prospective study, difficulty falling asleep (HR = 1.4) and difficulty staying asleep (HR = 1.3) were associated with acute myocardial infarction.⁸⁶ Furthermore, other studies have shown that sleep disturbances or complaints are associated with increased incidence of type 2 diabetes.⁸⁷⁻⁹⁰ However, these studies showed relatively small effect sizes and did not include a PSG evaluation so as to control for SDB or other sleep pathology. The findings of these early studies were dismissed as artifacts or flawed by many clinicians and researchers alike.^{91,92} In fact, at least one report showed a reduced mortality rate for those individuals complaining of sleep difficulties after 6 years of follow-up.⁹³

Given the well-established association of hypercortisolemia with significant medical morbidity, (i.e., hypertension, diabetes, metabolic syndrome, osteoporosis, and others) and the findings that hypercortisolemia is primarily associated with insomnia with objective short sleep duration,⁴¹⁻⁴⁷ we hypothesized that this type of insomnia is associated with significant cardiometabolic morbidity and mortality. A series of recent epidemiological studies from the Penn State Adult Cohort,^{94,95} that used in-lab PSG, have shown that insomnia with objective short sleep duration is associated with a high risk of hypertension,⁹⁶ diabetes,⁹⁷ and mortality.⁹⁸ For example, compared to normal sleepers who slept 6h per night, the highest odds of hypertension or diabetes was in insomnia sufferers who slept 5h (OR = 5.1 and OR = 2.95, respectively) and the second highest in insomnia sufferers who slept 5-6 h (OR = 3.5 and OR = 2.07, respectively), while insomnia sufferers who slept 6h were not at significantly increased risk of hypertension or diabetes (OR = 1.3 and OR = 1.1, respectively). Recent longitudinal data from the same cohort has shown that insomnia sufferers who slept < 6h were at a significantly higher risk of incident hypertension (OR = 3.75),⁹⁹ suggesting that it is insomnia that causes hypertension and not vice versa. Furthermore, other longitudinal research showed that mortality risk in men was significantly increased in insomnia sufferers who slept < 6 h compared to normal sleepers (OR = 4.00), and that there was a marginally significant trend toward higher mortality from insomnia with short sleep duration in men with diabetes or hypertension (OR = 7.17) than in those without these comorbid conditions (OR = 1.45). Thus, the impact of insomnia with short sleep duration was much stronger in those with diabetes and hypertension at baseline versus those who were healthy.⁹⁸ In women, mortality was not associated with insomnia with short sleep duration, a finding that might be related to the fact that women were followed-up for a shorter time period and that a smaller number were deceased at the time of follow-up compared to men (5% vs. 21%, respectively).

Consistent with the findings of these population-based studies, other recent studies have shown that nighttime systolic blood pressure is higher and day-to-night systolic blood pressure dipping is reduced in insomnia sufferers and that the magnitude of beta EEG activity correlates with their systolic blood pressure dipping.¹⁰⁰ Also, impaired heart rate variability,¹⁰¹ lower cardiac pre-ejection period,¹⁰² and poorer indices of glucose metabolism¹⁰³ are primarily present in insomnia sufferers with objective short sleep duration. Cumulatively, these data indicate that objective short sleep duration may predict the biological severity of chronic insomnia.

4. Insomnia and Cognitive Impairment

Insomnia is associated with complaints of difficulty concentrating, memory problems, and inattention. However, studies using objective neuropsychological testing have produced inconsistent findings. This has led some researchers to question the existence of true cognitive impairments in insomnia¹⁰⁴ and attribute daytime complaints to excessive attention to the expected consequences of poor sleep.²⁹

A recent meta-analysis has shown that individuals with insomnia exhibit performance impairments of small to moderate magnitude in several cognitive functions, including working memory, episodic memory, and some aspects of executive functioning.¹⁰⁵ However, an important factor that has not been examined in meta-analytic research of the neurocognitive literature is the degree of objective sleep disturbance shown by the insomnia sufferers across studies. For example, most of the studies included in meta-analyses have shown that cognitive performance is impaired in insomnia sufferers with objective sleep disturbances^{60,106-110} or that it correlates with objective markers of sleep disturbance in insomnia sufferers,¹¹⁰⁻¹¹⁶ whereas those studies in which performance was not significantly impaired established insomnia diagnoses using solely subjective criteria.^{56,113,117-119} The role of objective sleep measures in the association of insomnia with cognitive impairment has been addressed in a recent study from the Penn State Adult Cohort.¹²⁰ This study showed that insomnia sufferers, based solely on a subjective complaint, did not differ significantly from controls on either PSG variables or neurocognitive performance. However, significant interactions between insomnia and objective short sleep duration (i.e., < 6h) on specific neurocognitive tests were found. Specifically, insomnia sufferers with objective short sleep duration showed poorer neuropsychological performance on tests of processing speed, set-switching attention, and number of short-term visual memory errors and omissions compared to control groups with normal or short sleep duration. In contrast, insomnia sufferers with normal sleep duration group showed no significant deficits when compared to controls. Based on these findings, it seems that insomnia with objective short sleep duration is associated with deficits in set-switching attention, a key component of the “executive control of attention”.¹²⁰ Importantly, the presence of a group of good sleepers with short sleep duration allowed to demonstrate that deficits in executive functions were associated with underlying physiological hyperarousal, a characteristic of chronic insomnia, rather than to short sleep per se.¹²⁰ Cumulatively, the data from these studies indicate that objective short sleep duration may predict the biological severity of chronic insomnia, including its effect on cognitive functions.

Brain functions such as set-switching attention, working memory, and interference control have been linked to the activation of the prefrontal and anterior cingulate cortices. Tasks of set-switching attention also require the ability to retain both sets so they are ready to be recalled and, in fact, neuroimaging studies show that set-switching attention and working memory cooperate in the same areas of the prefrontal cortex.^{121,122} Together, these findings suggest that insomnia with objective short sleep duration, via hypercortisolemia, may affect brain structures and associated cognitive functions.¹²³⁻¹²⁶ Furthermore, insomnia with objective short sleep duration may be a premorbid risk factor for amnesic and non-amnesic mild cognitive impairment (MCI), an area open to future studies.

5. Natural History of Insomnia

As mentioned in the introduction, about 20% of the general population has poor sleep (i.e., insomnia symptoms at any given time) and about another 10% has chronic insomnia. Natural history studies have shown that chronic insomnia is a highly persistent condition, whereas the course of poor sleep is more variable and has a higher remission

rate.^{33,35,36,127,128} This suggests that insomnia is a disorder while poor sleep is a symptom of underlying mental and physical health problems.^{35,36,128} Furthermore, objective short sleep duration has been shown to be a risk factor for poor sleep evolving into the more severe form of chronic insomnia³⁶ as well as of chronic insomnia becoming persistent.¹²⁸ These latter findings suggest that objective short sleep duration may be a biologic marker of genetic predisposition to chronic insomnia³⁶ and of the severity and chronicity of the disorder.¹²⁸

6. Clinical Implications

The evidence presented in this paper has led us to suggest two phenotypes of chronic insomnia that are different in terms of etiology, pathophysiology, biological severity, natural course, psychological characteristics, and possibly, treatment response. The **first phenotype** is primarily associated with physiological hyperarousal (i.e., short sleep duration and activation of both limbs of the stress system), significant medical sequelae (e.g., hypertension, diabetes, cognitive impairment, increased mortality), and a persistent course. The **second phenotype** is associated with cognitive-emotional and cortical arousal, but not with physiological hyperarousal (i.e., normal sleep duration and normal activity of the stress system) or significant medical sequelae, and is more likely to remit over time. Furthermore, the first phenotype is associated with a psychological profile typical of medical outpatients, whereas the second phenotype is associated with sleep misperception, anxious-ruminative traits, and poor coping resources.⁸³ Table 2 summarizes the findings of key studies, while Figure 1 depicts a heuristic model of the underlying pathophysiological mechanisms and clinical characteristics of the two insomnia phenotypes.

Our proposed model for the two insomnia phenotypes has several implications in terms of nosology, diagnostic procedures and specificity of treatment for chronic insomnia. As we have stated earlier, previously proposed subtypes of insomnia have been associated with low diagnostic reliability and have not been associated with clinically relevant outcomes. In addition, the current diagnostic procedures used in insomnia are subjective tools such as clinical interviews, questionnaires, and specific scales. The data reviewed here suggest that objective measures of sleep can be useful in detecting the most severe form of insomnia in terms of its importance on the patient's health. Thus, we propose the inclusion of objective sleep duration as a criterion in future diagnostic manuals for insomnia in order to differentiate these two clearly different and clinically relevant subtypes of insomnia.

Further, our data suggest that objective measures of sleep, in addition to a thorough clinical evaluation, should become part of the standard diagnostic procedures for insomnia.⁸³ Although our studies have focused on the utility of sleep duration, other studies suggest that other variables of sleep efficiency and continuity or of physiological hyperarousal (i.e., MSLT) may also serve as markers of the biological severity of the disorder.^{36,42,106,110,112,129,130} However, a potential disadvantage of biomarkers such as stage 1, SWS, or MSLT is that they require a full PSG study or daytime laboratory assessment, whereas sleep duration perhaps could be obtained with simpler methods, e.g., actigraphy. In this regard, several studies suggest the potential usefulness of actigraphy to assess sleep patterns for a period of days or weeks in the "habitual home environment", to characterize the severity of the insomnia disorder.^{21,131,132} A similar amount of home sleep monitoring with PSG would be difficult and impractical for clinical venues. However, several problems associated with the use of actigraphy, such as lack of an industry standard for the sleep algorithms used in different actigraphic devices and the propensity to over-or underestimate sleep time, make its current use limited. Future studies using cost-effective methods should examine whether night-to-night variability in sleep duration may be a

stronger predictor of cardiometabolic and neurocognitive morbidity compared to average sleep duration.

Finally, our findings may affect the way we treat both chronic insomnia and poor sleep. The insomnia phenotype with short sleep duration may respond better to treatments that primarily aim at decreasing physiological hyperarousal and increasing sleep duration, such as medication or other biological treatments.⁴⁶ Previous studies have shown that sedative antidepressants such as trazodone or doxepin, used at low dosages, down-regulate the activity of the HPA axis, decrease cortisol levels, and increase sleep duration.^{46,133,134} We should note that biological treatments should be part of a multidimensional approach that combines behavioral changes, i.e., sleep hygiene, and psychological interventions, i.e., cognitive-behavioral therapy (CBT), when indicated from the clinical evaluation. The second phenotype, i.e., insomnia with normal sleep duration, is not likely associated with physiological hyperarousal and hypnotics or sedative antidepressants may not be warranted. This phenotype may respond better to treatments that primarily aim at decreasing cognitive-emotional arousal, changing sleep-related beliefs and behaviors, and altering sleep misperception, such as CBT.^{135,136} In fact, given that insomnia with normal sleep duration is associated with poor coping resources and anxious-ruminative traits that extend beyond sleep-related preoccupation, other psychotherapeutic techniques such as behavioral experiments or emotion regulation techniques may be indicated. Of course use of psychotherapeutic medication may be indicated based on the presence of comorbid psychiatric conditions, i.e., anxiety or depressive disorders. The differential treatment response of these two phenotypes should be tested in future placebo-controlled clinical trials.

In the prevention of insomnia, treatment strategies for persistent poor sleep should focus on treating the underlying physical health conditions (e.g., cardiovascular disorders, ulcer, or allergy/asthma) as well as the associated psychological distress with, for example, CBT. Given that poor sleepers with shorter objective sleep duration and a family history of sleep problems are at greater risk of developing chronic insomnia,³⁶ their appropriate detection with objective sleep measures is warranted and treatment should focus on decreasing physiological hyperarousal and lengthening sleep duration.

Summary

In this article we present evidence that the degree of objective sleep disturbance in insomnia is directly proportional to the activity of both limbs of the stress system and other indices of physiological hyperarousal. Evidence suggests that insomnia with objective short sleep duration is associated with a significant risk of cardiometabolic morbidity and mortality and cognitive impairment. In contrast, insomnia with normal sleep duration is associated with cognitive-emotional and cortical arousal and sleep misperception but not with signs of physiological hyperarousal or cardiometabolic or neurocognitive morbidity. We propose that objective measures of sleep duration may become part of the routine evaluation and diagnosis of chronic insomnia in an office setting. Also we propose that these insomnia phenotypes may respond differentially to treatment, i.e., insomnia with short sleep duration may respond better to biological treatments, whereas insomnia with normal sleep duration may respond better to psychological treatment alone.

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Key Points

- The nosology of insomnia is associated with unsatisfactory reliability and validity, whereas current clinical practice guidelines do not recommend the use of objective sleep measures in the diagnosis, evaluation, and treatment of insomnia.
- Recent evidence shows that objective measures of sleep are useful in predicting the biological severity of insomnia, i.e., activation of both limbs of the stress system, cardiometabolic morbidity and mortality as well as cognitive impairment.
- We propose two phenotypes of insomnia, based on objective sleep duration, that differ in terms of physiological hyperarousal, medical morbidity, psychological profiles, and natural course.
- Objective sleep measures, i.e., sleep duration, should be included in the diagnostic criteria for subtyping insomnia.
- Objective measures of sleep duration obtained with cost-effective and simpler methods than polysomnography may become part of the routine diagnosis and treatment of chronic insomnia in an office setting.
- These two phenotypes may respond differentially to treatment, i.e., insomnia with short sleep duration may respond better to biological treatments, whereas insomnia with normal sleep duration may respond primarily to psychological treatments.

Figure 1. Heuristic model of the underlying pathophysiological mechanisms and clinical characteristics of the two insomnia phenotypes based on objective sleep duration
The common characteristics of the two phenotypes are presented in the overlapping area, while their unique characteristics are presented in the areas of each phenotype that do not overlap.⁸³

Table 1

Insomnia diagnoses across DSM and ICSD most recent versions

DSM-III-R (1987)	DSM-IV-TR (2000)	ICSD-R (1997)	ICSD-2 (2005)
Dysomnias Insomnia Disorders Insomnia related to Another Mental Disorder (nonorganic) Insomnia related to a Known Organic Factor Primary Insomnia Dysomnia Not Otherwise Specified	Primary Sleep Disorders Dysomnias Primary Insomnia Dysomnia Not Otherwise Specified Sleep Disorder related to Another Mental Disorder Insomnia related to Another Mental Disorder Sleep Disorder Due to a General Medical Condition Insomnia type Substance-Induced Sleep Disorder Insomnia type	Dysomnias Intrinsic Sleep Disorders Psychophysiological Insomnia Sleep State Misperception Idiopathic Insomnia Intrinsic Sleep Disorder Not Otherwise Specified Extrinsic Sleep Disorders Inadequate Sleep Hygiene Environmental Sleep Disorder Altitude Insomnia Adjustment Sleep Disorder Limit-setting Sleep Disorder Sleep-onset Association Disorder Food Allergy Insomnia Hypnotic-Dependent Sleep Disorder Stimulant-Dependent Sleep Disorder Alcohol-Dependent Sleep Disorder Toxin-Induced Sleep Disorder Extrinsic Sleep Disorder Not Otherwise Specified Sleep Disorders Associated with Other Disorders Associated with Mental Disorders Associated with Neurologic Disorders Associated with Other Medical Disorders	Insomnias Adjustment Insomnia Psychophysiological Insomnia Paradoxical Insomnia Idiopathic Insomnia Insomnia Due to Mental Disorder Inadequate Sleep Hygiene Behavioral Insomnia of Childhood Insomnia Due to Drug or Substance Insomnia Due to Medical Condition Insomnia Not Due to Substance or Known Physiological Conditions, Unspecified Physiological (Organic) Insomnia, Unspecified

Table 2

Association of insomnia with short sleep duration with physiological hyperarousal, cardiometabolic morbidity, neurocognitive impairment, and a persistent course

	Controls	Insomnia with Normal Sleep Duration	Insomnia with Short Sleep Duration
Physiological Hyperarousal			
Cortisol levels (20:00-8:00h), nmol/L ⁴³	189.8	172.0	302.0 *
Cortisol AUC (Evening 4 h), µg/ml ⁴⁴	15.6		24.3 *
Cortisol AUC (19:00-9:00h), µg/dl ⁴⁸	253.7	214.4	
Heart rate variability (LHF ratio wake), power ⁵⁴	0.8		1.2 *
Heart rate variability (SDNN wake), ms ¹⁰¹	63.5	64.1	50.5 *
Whole body metabolic rate (VO ₂), % increased ^{55,56}	---	6 *	9 *
MSLT, minutes ^{55,56}	9.5	10.2	13.3 *
Cardiometabolic Morbidity			
Hypertension, OR ⁹⁶	1.0	1.1	5.1 *
Incident Hypertension, OR ⁹⁹	1.0	0.9	3.8 *
Diabetes, OR ⁹⁷	1.0	1.1	2.9 *
Mortality in Men, OR ⁹⁸	1.0	0.7	4.0 *
Mortality in Men w/ hypertension/diabetes, OR ⁹⁸	1.0	0.6	7.2 *
Neurocognitive Impairment			
SDMT, # correct ¹²⁰	50.6	52.4	46.3 *
TMT-B, seconds ¹²⁰	75.2	68.0	87.8 *
TMT B-A, seconds ¹²⁰	43.6	36.0	54.6 *
SAT, error rate ¹³⁰	2.5	3.2	4.5 *
BVRT, # omissions ¹²⁰	0.4	0.4	0.7 *
Short-term memory, words ^{55,56}	7.5	7.2	5.7 *
Sleep Misperception			
Subjective sleep time, hours ¹⁵	6.5	5.6 *	5.0 *
Objective sleep time, hours ¹⁵	6.6	6.6	4.7 *
Subjective – objective sleep time, hours ¹⁵	-0.1	-1.0 *	0.3
Psychological Profile			
MMPI-2 Psychasthenia, score ¹⁵	49.1	54.5 *	51.8
MMPI-2 Anxiety, score ¹⁵	48.2	53.8 *	49.4
MMPI-2 Ego Strength, score ¹⁵	48.7	44.4 *	47.8
STAI Trait Anxiety, score ¹³⁷	30.7	37.0 *	34.9
DBAS Effects, score ¹³⁷	33.2	44.6 *	41.5
DBAS Needs, score ¹³⁷	37.2	46.3 *	38.3
Natural History			

	Controls	Insomnia with Normal Sleep Duration	Insomnia with Short Sleep Duration
Persistence vs. Full remission, OR ¹²⁸	1.0	0.2	4.9 [*]

* Value significantly higher or lower as compared to controls; AUC = Area Under the Curve; BVRT = Benton Visual Retention Test; DBAS = Dysfunctional Beliefs and Attitudes about Sleep; MMPI-2 Minnesota Multiphasic Personality Inventory-2; MSLT = Multiple Sleep Latency Test; OR = odds ratio; SAT = Switching Attention Task; SDMT = Symbol Digit Modalities Test; STAI = State-Trait Anxiety Inventory; TMT-B = Trail Making Test part B; TMT B-A = Trail Making Test part B – part A