Chapter 82

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Etiology and Pathophysiology of Insomnia

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Chapter Highlights

p0010

- Since the 1990s there has been a proliferation of theoretical perspectives on the etiology of insomnia that now includes nine human models. The central concepts for the nine models include the following:
  - u0015 Stress-diathesis
  - u0020 Stimulus dyscontrol and classical conditioning
  - u0025 The interaction of basal arousal and sleep requirement
  - u0030 Sleep extension and the mismatch between sleep opportunity and ability
  - u0035 Altered sensory and information processing and an attenuation of the normal mesograde amnesia of sleep
  - u0040 Appraisal as a determinant of the patient's perception of disease
  - u0045 The concept of "the inhibition of sleep-related dearousal" (vs. hyperarousal)
  - u0050 The role of attention, intention, and effort
  - u0055 The etiologic importance of daytime deficits, selective attending to sleep-related threats, and safety behaviors
  - u0060 Chronic insomnia as a hybrid state that occurs in association with local neuronal wakefulness during non–rapid eye movement and rapid eye movement sleep

p0070 Until the late 1990s there were only two models regarding the etiology and pathophysiology of insomnia. The relative lack of theoretical perspectives was due to at least three factors. First, the widespread conceptualization of insomnia as owing directly to hyperarousal (levels of physiologic or central nervous system arousal that are sufficiently high as to directly prohibit sleep) may have made it appear that further explanation was not necessary. Second, the long-time characterization of insomnia as a symptom carried with it the clear implication that insomnia was not itself worth modeling as a disorder or disease state. Third, for those inclined toward theory, the acceptance of the behavioral models (i.e., the three-factor model [3P] and the stimulus control model[1,2]) and the treatments that were derived from them might have had the untoward effect of discouraging the development of alternative or elaborative models. Since the 1990s there has been a proliferation of theoretical perspectives on the etiology and pathophysiology of insomnia that includes both human and animal models. In this chapter, nine of the human models are described and critiqued. The models presented span from the classical behavioral perspectives, to the traditionally cognitively focused frameworks, to the more modern cognitive information–processing perspectives, to an interaction paradigm that takes into account basal arousal and sleep requirement, to the neurocognitive and neurobiologic models that essentially frame insomnia, from a functional and neurophysiologic point of view, as a hybrid state (part wake and part non–rapid eye movement [NREM] sleep).

DEFINITION OF INSOMNIA

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p0075 The *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition (DSM-5)[3] and *International Classification of Sleep Disorders,* third edition (ICSD3[4]) define *insomnia disorder* as difficulty initiating or maintaining sleep on three or more nights per week for at least 3 months. This definition further stipulates that the diagnosis of insomnia must take into account sleep opportunity, level of daytime impairment and distress, whether symptom presentation (in the case of children and elders) varies with caregiver presence, and the possibility that the insomnia is not better explained by (or does not occur exclusively during the course of) other sleep disorders or medical or psychiatric illnesses.

p0080 This definition is different from the DSM-IV-TR and the ICSD2 in several important ways. First, the diagnostic terms primary insomnia and secondary insomnia have been replaced to reflect the change that insomnia is now viewed as a disorder, regardless of whether it is comorbid with other disorders. Second, although quantitative values are not given for insomnia severity (i.e., that sleep latencies or wake after sleep onset durations must be greater than some minimum duration to be of clinical significance), insomnia frequency and chronicity are explicitly stated. The frequency criterion is new, and the

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chronicity criterion has been changed from 1 month to 3 months. Third, nonrestorative sleep has been removed as a diagnostic criterion for insomnia. Finally, both the DSM-5 and the ICSD3 allow for the identification of insomnia types (different modes of clinical presentation including initial, middle, and late insomnia), but only the ICSD3 specifies insomnia subtypes, including idiopathic, psychophysiologic, and paradoxical insomnia.

s0015 ## MODELS OF INSOMNIA

p0085 Nine models of insomnia are critically reviewed in this chapter. Each of the models described and critiqued presents a view of how insomnia develops, becomes chronic, or comes to be self-perpetuating. Basic and experimental models are not reviewed in this chapter. Information about these may be found in the prior edition of this text (fifth edition). The review is organized chronologically. Following the explication of each of the nine models, a discussion is provided regarding the issues that have not been well integrated into existing models, including how dysregulation of normal sleep-wake regulatory processes may contribute to the development, incidence, or severity of chronic insomnia and why it may be that chronic insomnia occurs disproportionately in women and older adults. The final section of the chapter provides an integrative or transtheoretical perspective represented by a parallel process model that attempts to illustrate how all of the models contribute something unique to our understanding of the etiology of insomnia.

s0020 ### Stimulus Control Model (1972)

s0025 #### *Basic Description*

p0090 Stimulus control, as originally described by Bootzin in 1972,[2,5] is based on the behavioral principle that one stimulus may elicit a variety of responses, depending on the conditioning history. A simple conditioning history, wherein a stimulus is always paired with a single behavior, yields a high probability that the stimulus will yield only one response. A complex conditioning history, wherein a stimulus is paired with a variety of behaviors, yields a low probability that the stimulus will elicit only one response. In individuals with insomnia, the normal cues associated with sleep (e.g., bed, bedroom, bedtime) are frequently paired with behaviors other than sleep. For instance, in an effort to cope with insomnia, the patient may spend a large amount of time in the bed and bedroom awake and engaging in behaviors other than sleep. These coping behaviors appear to the patient to be both reasonable (i.e., staying in bed at least permits the patients to get "rest") and reasonably successful (i.e., engaging in alternative behaviors in the bedroom sometimes appears to result in cessation of the insomnia). These practices, however, set the stage for stimulus dyscontrol, that is, reduced probability that sleep-related stimuli will elicit the desired response of sleepiness and sleep. Figure 82-1 provides a schematic representation of stimulus control and stimulus dyscontrol.

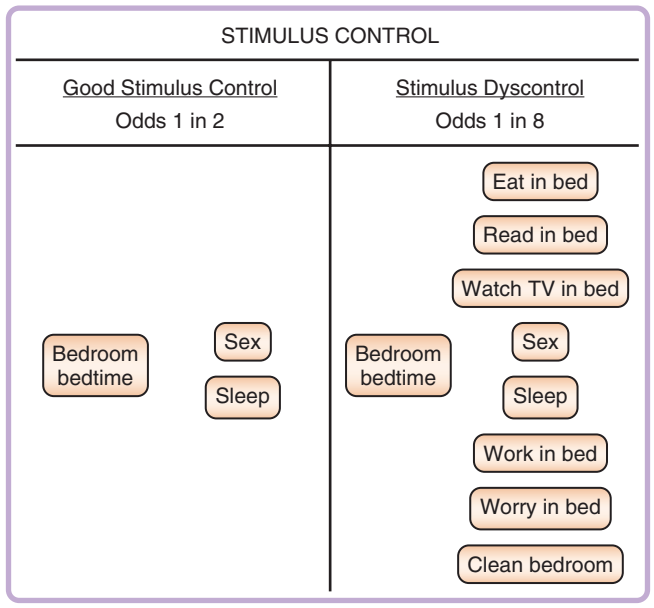

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Figure 82-1 The Stimulus Control Model. The schematic represents the instrumental conditioning perspective on stimulus control. In the *left frame* (good stimulus control) the bedroom is tightly coupled with sleep and sex where, given the orthogonality and equal probability of events, the probability of association of bedroom to sleep is 1 in 2. In the right frame (stimulus dyscontrol) the bedroom is no longer a strong associate of sleep and sex where, given the orthogonality and equal probability of events, the probability of association of bedroom to sleep is 1 in 8. The treatment implication of stimulus dyscontrol is that the voluntary elimination (hence instrumental conditioning) of the nonsleep associates except for sex should make it more likely that sleep will occur in the bedroom.

s0030 #### *Strengths and Limitations*

p0095 The treatment derived from stimulus control theory is one of the most widely used behavioral treatments, and its efficacy has been well established.[6-10] The success of the therapy, however, is not sufficient evidence to say that stimulus dyscontrol is responsible for predisposition to, precipitation of, or perpetuation of insomnia.* In fact, one investigation found that the reverse of stimulus control instructions also improved sleep continuity.[11] Another limitation of the stimulus control perspective is that it focuses on instrumental conditioning. That is, there are behaviors that reduce or enhance the probability of the occurrence of sleep. The original model does not explicitly delineate how classical or Pavlovian conditioning may also be an operational factor. Specifically, the regular pairing of the physiology of wakefulness with sleep-related stimuli may lead to sleep-related stimuli becoming conditioned stimuli for wakefulness. This latter possibility, although not part of the classical stimulus control perspective, is clearly consistent with it. p0100

s0035 #### *Implications for Current and Future Research and Therapeutics*

p0105 Given the efficacy of stimulus control therapy, it would be useful to determine how much of the treatment outcomes with cognitive behavior therapy for insomnia (CBT-I) result from the manipulation of this factor. One way to assess the relative importance of stimulus control would be as part of a dismantling study. This alone would not, however, confirm the importance of stimulus dyscontrol as a perpetuating factor. Perhaps what is needed is a dismantling study for stimulus

*The conceptual frame for causality in terms of "predisposition, precipitation, and perpetuation" was first articulated by Spielman as part of the three-factor model. It is used in this context for its general explanatory value.

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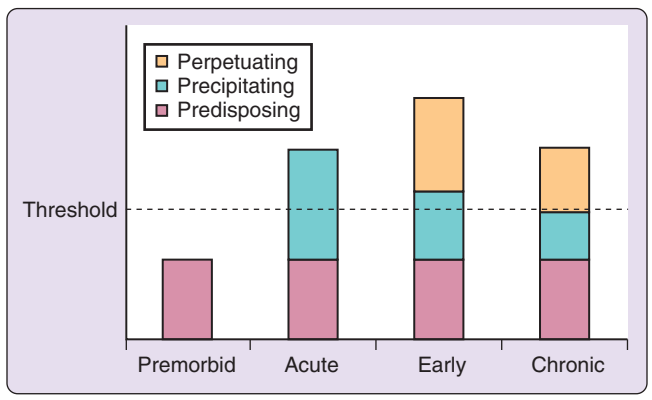
control itself, given that the treatment contains not only the instruction to limit activities in the bedroom to sleep and sex but also instructions to go to bed only when sleepy, leave the bedroom when awake, get up at the same time every morning irrespective of how much sleep is obtained, and not nap during the day. Any of these components, alone or in combination, may account for the efficacy of stimulus control and may do so through mechanisms other than stimulus dyscontrol, such as sleep homeostasis dysregulation. This is particularly true for the prescription to get up at the same time every morning irrespective of how much sleep is obtained. When patients are compliant with this instruction, it prevents the deleterious effects of excessive time in bed (see Spielman's three-factor model discussed next) and may ensure that sleep loss will prime for better sleep on subsequent nights.[12] In a related vein, the instruction to leave the bedroom when awake may serve as a means of ensuring that patients are fully awake (vs. micro-sleeping) and thus may also improve sleep through sleep homeostatic or circadian processes.

s0040 **Three-Factor Model (1987)**

s0045 ***Basic Description***

p0110 This model, alternatively referred to as the Spielman model, 3P model, or behavioral model, delineates how insomnia occurs acutely and how acute insomnia becomes both chronic and self-perpetuating[1] (Figure 82-2). The model is based on the interaction of three factors. The first two factors (predisposing and precipitating factors) represent a stress-diathesis conceptualization of how insomnia comes to be expressed. The third factor (perpetuating factor) represents how behavioral considerations modulate chronicity. Predisposing factors extend across the entire biopsychosocial spectrum. Biologic factors include, for example, the genetic predisposition for insomnia or related etiologic factors, increased basal metabolic rate, hyperreactivity, and fundamental alterations to the neurotransmitter systems associated with sleep and wakefulness. Psychological factors include worry or the tendency to be excessively ruminative. Social factors, although rarely a focus at the theoretical level, include factors such as the bed partner keeping an incompatible sleep schedule or social pressures to sleep according to a nonpreferred sleep schedule (e.g., child rearing). Precipitating factors are acute occurrences that trigger sleep continuity disturbance.[†] The primary "triggers" are thought related to life stress events, including medical and psychiatric illness. Perpetuating factors refer to the behaviors adopted by the individual that are intended to compensate for or cope with sleeplessness, but that actually reinforce the sleep problem. Perpetuating factors include the practice of nonsleep behaviors in the bedroom, staying in bed while awake, and spending excessive amounts of time in bed. Stimulus control speaks to the first two of these (as reviewed earlier). The classic version of the three-factor model focuses primarily on the last of these. Excessive time in bed (or sleep extension) may involve going to bed early, getting out of bed late, and napping as ways of coping with insomnia. Such compensatory behaviors are enacted to increase the opportunity to get more sleep and are likely to be highly self-reinforcing because they allow lost sleep to be "recovered" and the daytime effects of lost sleep to be ameliorated. Extension of sleep opportunity can lead to a mismatch between sleep opportunity and sleep ability.[1,13] The greater the mismatch, the more likely the individual will spend prolonged periods of time awake during the given sleep period, regardless of what factors predisposed to or precipitated the insomnia.



f0015 **Figure 82-2 The 3P Model.** This schematic represents the classic 1987 rendition of the 3P model. There are two more recent representations in Figure 82-3. The reader is encouraged to compare the three versions of the model.

p0120 The three-factor model and its graphic representations have periodically been updated by Spielman.[14] As shown in Figure 82-3, one version of the model represents the speed of onset and offset of events in the development of insomnia, and a 4P representation takes into account Pavlovian (classical) conditioning as a perpetuating factor. Classical conditioning refers to the reliable elicitation of specific physiologic responses by what were once neutral stimuli. In the context of insomnia, classical conditioning refers to the elicitation of arousal or wakefulness in response to what were once sleep-related stimuli. This phenomenon corresponds to the common patient report that "it's as if I just walk into the bedroom and I am suddenly wide awake … it's like some switch got flipped from sleepy to wide-awake."

Strengths and Limitations s0050

p0125 The three-factor model is conceptually appealing and comports well both with clinical experience and with the two-process model of sleep-wake regulation.[15] The model has good face validity for both patients and clinicians, and the therapy derived from the model (sleep restriction) is efficacious. This said, there have been very few studies evaluating sleep restriction therapy as a monotherapy[16] and no studies evaluating the relative efficacy of sleep restriction therapy as a component of CBT-I (i.e., no dismantling studies). It is therefore difficult to assess the extent to which treatment efficacy supports the model. Further, even if studies could show that sleep restriction therapy accounted for most clinical gains with CBT-I, formal validation of the model would still require a natural history study showing that the transition from acute to chronic insomnia is largely mediated by sleep extension.

p0130 Another limitation of the original model is the implication that the predisposition for insomnia varies across individuals

[†]Sleep continuity is meant to denote the class of variables that include sleep latency, number of awakenings, wake after sleep onset, total sleep time, and sleep efficiency (i.e., sleep architecture vs. sleep continuity).

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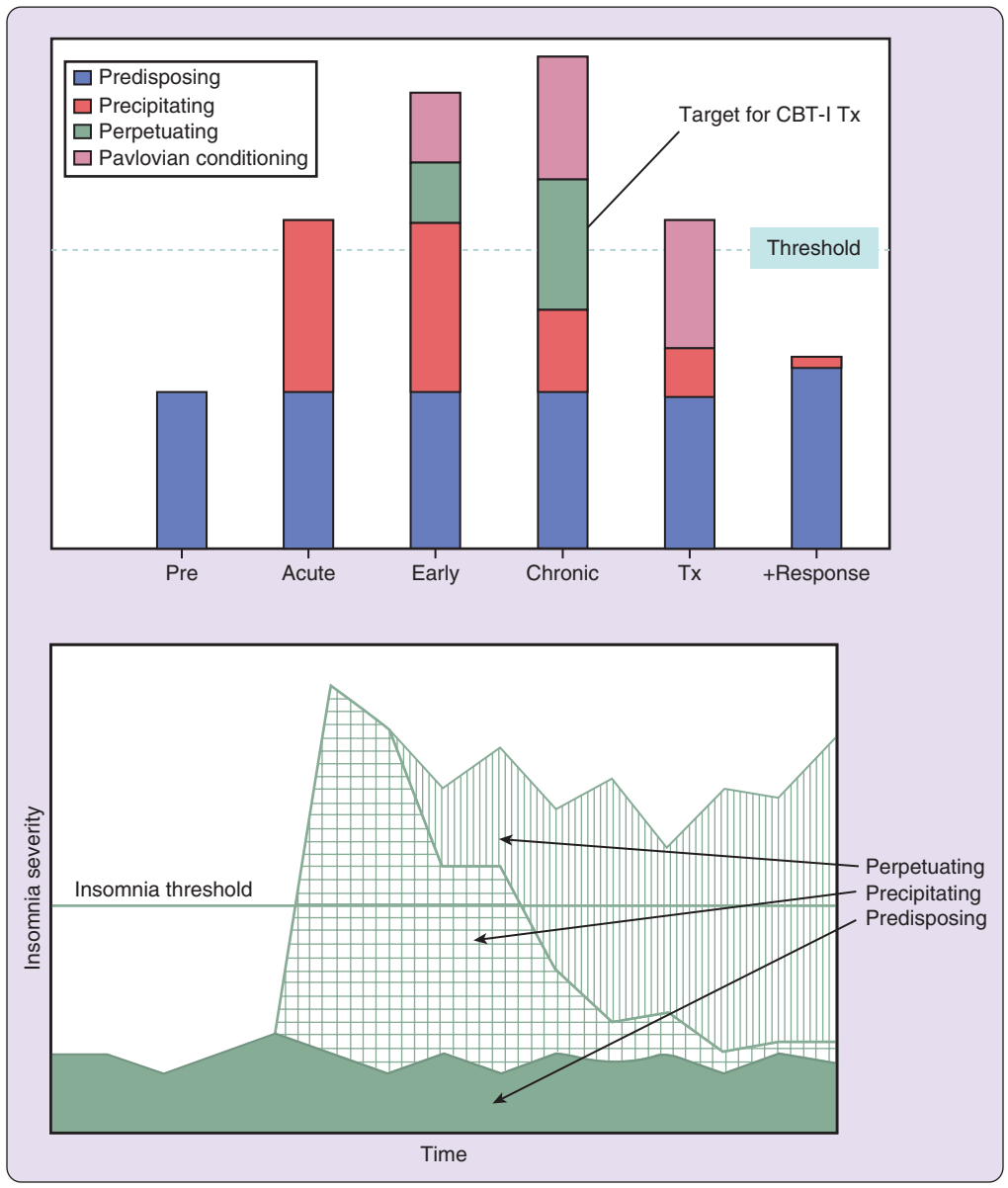

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Figure 82-3 The Dynamic 3P and the 4P Models. The dynamic 3P model has the added value (compared with the original model) of illustrating the temporal course of each of the factors. The 4P model has the added value of explicitly incorporating Pavlovian conditioning and how this factor affects the clinical course of insomnia and response to treatment (Tx). CBT-I, Cognitive behavior therapy for insomnia.

but is a trait factor within the individual. With respect to between-subjects variability, presumably this means that some individuals are not prone to insomnia, some are marginally at risk, and still others are at high risk. Although it stands to reason that the vulnerability for insomnia exists on a continuum, it is also plausible that *all individuals* are at risk for insomnia (acute insomnia) and that this may be so to the extent that insomnia represents an adaptive response to stress (i.e., a real or perceived threat, as part of the flight-fight response, triggers a systemic response that overrides the normal homeostatic and circadian imperatives for sleep). Although some predispositions may be indeed be "hard-wired," some predispositions vary over the life span (e.g., new sleep environments or partners, pregnancy or child rearing, altered hormonal status, aging effects, prior insomnia experience). The newer rendition of the Spielman model explicitly allows predisposing factors to vary with time.[14]

Implications for Current and Future Research and Therapeutics s0055

Despite its heuristic and practical value, most tenets of the three-factor model have not been empirically tested. Several avenues for research are possible. Predisposition to insomnia could be, and has recently been, evaluated using molecular and behavioral genetic approaches.[17-20] As a complement to this approach, medical anthropologic studies could be used to assess vulnerability to insomnia at the cultural level (e.g., industrial vs. nonindustrial societies). The precipitation of insomnia, while evaluated with stress induction studies in good sleepers,[21] has not been studied prospectively to p0135

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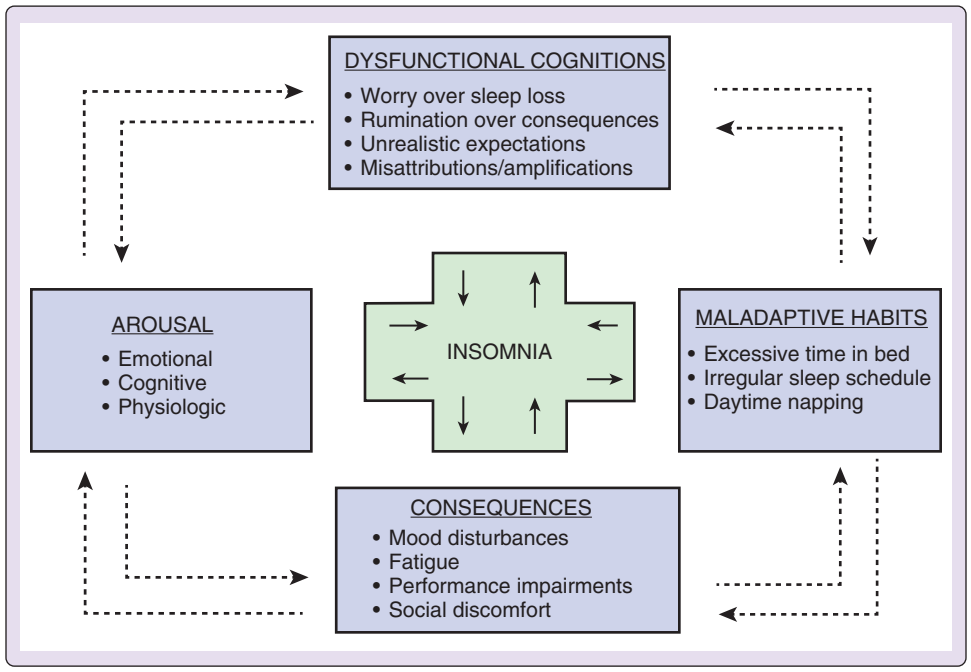

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Figure 82-4 The Microanalytic Model. As noted in text, this is primarily a state model that focuses on how insomnia may be self-perpetuating. Note that arousal is arrayed as occurring within three domains: emotional, cognitive, and physiologic.

determine what events reliably trigger acute insomnia. Finally, as noted earlier, natural history studies (with high temporal resolution) are now assessing whether the putative perpetuating factor of sleep extension does indeed mediate the transition from acute to chronic insomnia.

p0140 The three-factor model has served as the conceptual basis for one treatment modality in particular: sleep restriction. This therapy, although believed by many to be the single most potent component of CBT-I, was developed to target one particular perpetuating factor, sleep extension. In multicomponent CBT-I, other treatment components may address other perpetuating factors (e.g., stimulus control addresses the engagement of nonsleep behaviors in the bedroom and the tendency to remain in bed when awake; cognitive therapy addresses the problem of catastrophic or dysfunctional thinking about insomnia; sleep hygiene addresses the misuse of counterfatigue measures). The three-factor model may also help to identify alternative treatment targets for insomnia. For instance, this model could help guide the development or adaptation of existing therapies to target predisposing factors. Such treatments could be used to increase treatment response, diminish the risk for recurrence (as an adjuvant to traditional CBT-I), or prophylactically to prevent first episodes of insomnia.

s0060 ## Microanalytic Model (1993)

s0065 ### *Basic Description*

p0145 Morin put forward the microanalytic model in his seminal book, *Insomnia: Psychological Assessment and Management*[22] (Figure 82-4). This model suggests that four bidirectional factors account for the perpetuation of insomnia over time (i.e., how it is that insomnia is self-perpetuating through arousal, dysfunctional cognitions, consequences, and maladaptive habits.) Arousal is conceptualized in terms of emotional, cognitive, and physiologic components. Dysfunctional cognitions are construed in terms of worry, rumination, and unrealistic expectations about sleep and sleep loss. Consequences refer to the negative psychosocial outcomes that occur with insomnia. Maladaptive habits refer to behaviors such as excessive time in bed, irregular sleep-wake schedules, and napping, each of which presumably occurs in relation to the effort to recover lost sleep. Central to this model is the concept that each occurrence of insomnia has consequences, including increased arousal, and results in the engagement of cognitions and behaviors that prolong the index episode or increase the likelihood of additional occurrences of insomnia.

Strengths and Limitations s0070

p0150 Major strengths of the microanalytic model are that it posits that insomnia is a self-reinforcing phenomenon that will continue unabated without an adaptive response on the part of the individual or the provision of treatment; construes arousal along multiple dimensions; incorporates the central behavioral concept of excessive time in bed (i.e., the behavioral maladaptation of sleep extension); and implies that adaptive responses or treatment can target any of the four contributory factors. This model, however, is not an etiologic model; that is, it does not delineate how the first episode of acute or chronic insomnia occurs.

Implications for Current and Future Research and Therapeutics s0075

p0155 The delineation of the four contributory factors provides a conceptual basis for the assessment of the relative contribution of each to the occurrence and severity of chronic insomnia. To our knowledge, no such study has been conducted on this topic. The clear therapeutic implication of the model is that treatment of insomnia may benefit from adopting a

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multicomponent approach. This is appropriate given that the model was introduced as part of a treatment manual (the first of its kind) that delineated a multicomponent treatment approach to insomnia. Given the centrality of dysfunctional cognitions to the model, the form of CBT-I standardized by Morin and colleagues[22] has a cognitive component that is dedicated to the assessment and treatment of dysfunctional beliefs and attitudes about sleep.[23] To date, there is evidence that dysfunctional beliefs and attitudes about sleep vary with treatment outcome with CBT-I[24]; whether monotherapy with this component of CBT-I is effective is not known.

s0080 **Neurocognitive Model (1997)**

s0085 ***Basic Description***

p0160 The neurocognitive model (Figure 82-5) is based on and is an extension of the 3P and 4P models[25] (see Figure 82-3). The central tenets of neurocognitive model include (1) a pluralistic perspective of hyperarousal (cortical, cognitive, and somatic arousal); (2) the specification that cortical arousal (as opposed to cognitive or somatic arousal) is central to the etiology and pathophysiology of insomnia; (3) the proposition that cortical arousal, in the context of chronic insomnia, occurs as a result of classical conditioning and is permissive of cognitive processes that do not occur with normal sleep; (4) the proposition that sleep initiation and maintenance problems do not occur because of hyperarousal but because of increased sensory and information processing at sleep onset and during NREM sleep; and (5) the suggestion that sleep state misperception derives from increased sensory and information processing during NREM sleep or the attenuation of the normal mesograde amnesia of sleep.

p0165 As with the 3P and 4P behavioral models of insomnia, the neurocognitive model posits that acute insomnia occurs in association with predisposing and precipitating factors and that chronic insomnia occurs in association with perpetuating factors. Like the 3P model, chronic insomnia is perpetuated by the instrumental conditioning that occurs with sleep extension. Like the 4P model, the neurocognitive model posits that classical conditioning also serves as a perpetuating factor for chronic insomnia; that is, the repeated pairing of sleep-related stimuli with insomnia-related wakefulness (arousal) ultimately causes sleep-related stimuli to elicit (or maintain) higher than usual levels of cortical arousal at around sleep onset or during the sleep period. This form of arousal is, in the context of chronic insomnia, thought to be independent of somatic arousal; the biological substrate for, and precipitant of, cognitive arousal; and the form of arousal that directly contributes to sleep continuity disturbance and sleep state misperception. In the case of sleep continuity disturbance and sleep state misperception, cortical arousal is not necessarily antithetical to sleep but exerts its deleterious effects through enhanced sensory processing, enhanced information processing, and long-term memory formation.

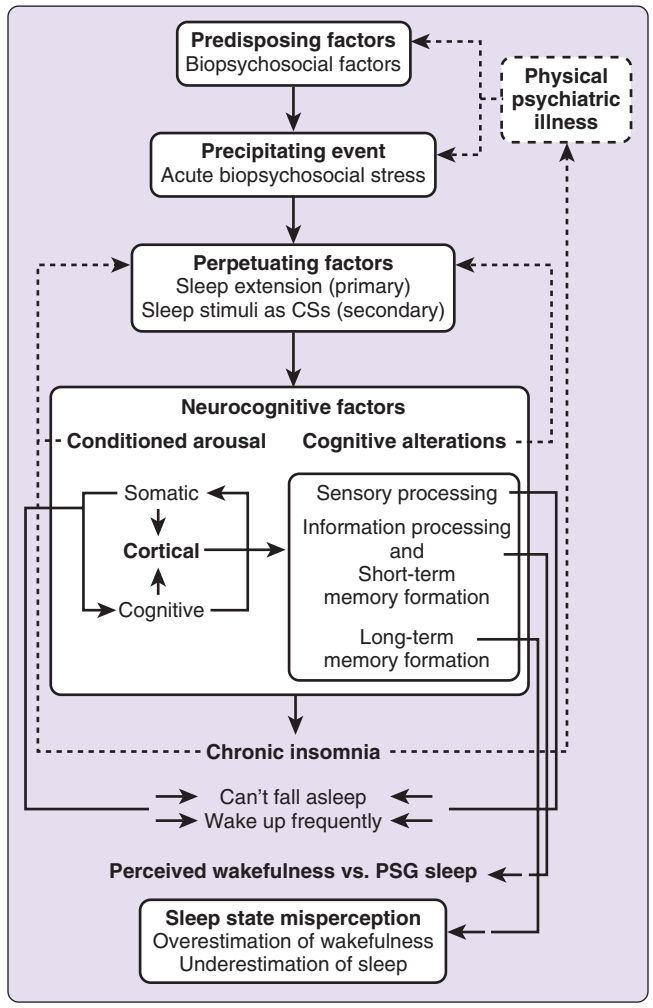

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Figure 82-5 The Neurocognitive Model. The schematic is different from prior publications of the neurocognitive model in several ways: (1) *Dotted lines* are provided to highlight feedback loops (*solid lines* represent feed-forward loops). (2) The examples provided for perpetuating factors have been changed. The primary factor is designated as "sleep extension" (previously denoted as increased time in bed and staying awake in bed). The secondary factor is designated as "sleep stimuli as CSs." This is meant to represent when "sleep stimuli" become conditioned stimuli for wakefulness (arousal). The section of the diagram denoted "neurocognitive factors" may well correspond to the "persistence of wakefulness" (when such events occur before sleep onset proper) and the "failure to inhibit wakefulness" (when such events occur during NREM sleep). The latter may correspond to what is characterized by Cano and Saper as a "hybrid state" (not entirely sleep or wakefulness) and may be accounted for by "local neuronal wakefulness" as posited by Buysse and colleagues. PSG, Polysomonography.

u0065 *Enhanced sensory processing* (detection of endogenous or exogenous stimuli and, potentially, the emission of startle or orienting responses) around sleep onset and during NREM sleep is thought to directly interfere with sleep initiation or maintenance.

u0070 *Enhanced information processing* (detection of and discrimination between stimuli and the formation of a short-term memory of the stimulating events) during NREM sleep is thought to blur the perceptual distinction between sleep and wakefulness and thus contribute to sleep state misperception.

u0075 *Enhanced long-term memory* (detection of and discrimination between stimuli and recollection of the stimulating event hours after its occurrence) around sleep onset and during NREM sleep is thought to interfere with the subjective experience of sleep initiation and duration and thus contribute to the discrepancies between subjectively and objectively assessed sleep continuity.

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p0185 Finally, conditioned cortical arousal is hypothesized to be self-reinforcing and thus, like sleep extension, serves to perpetuate insomnia in the absence of the original precipitants. That is, each time sleep-related stimuli (i.e., the specifics of the sleep environment) elicit cortical arousal, this reinforces the potential of sleep-related stimuli to serve as conditioned stimuli for enhanced sensory and information processing or long-term memory formation.

s0090 ***Strengths and Limitations***

p0190 In general, the major strengths of the neurocognitive model are that it allows for a pluralistic perspective on the concept of arousal; does not require that hyperarousal be so intense as to directly interfere with sleep initiation and maintenance; delineates a mechanism beyond that of instrumental conditioning (i.e., classical conditioning as a perpetuating factor); specifies how chronic insomnia "takes on a life of its own" (i.e., is self-reinforcing); and is based on hypotheses that are falsifiable.

p0195 To date, the evidence for the model derives from observations about patients with insomnia compared with good sleepers exhibiting increased cortical or central nervous system arousal using such measures as quantitative electroencephalography[26-30] and positron emission tomography[31-32]; increased sensory or information processing using such measures as evoked response potentials[33-35]; an attenuation of the normal mesograde amnesia of sleep using such measures as implicit and explicit memory tests for semantic stimuli presented during sleep[36]; and an association between sleep state misperception and objective measures of cortical arousal or evoked response potential abnormalities.[37-39]

p0200 The primary limitations of the neurocognitive model are that it does not adequately account for the transition from good sleep to acute insomnia, the importance of circadian and homeostatic influences on sleep, which brain regions or circuits are abnormally activated around sleep onset and during NREM sleep, the likely possibility that abnormal activation may also occur in subcortical regions, and the neurobiologic mechanisms by which insomnia may occur as a hybrid state. Some speculations regarding the functional anatomic substrate of the neurocognitive model have subsequently been published.[40]

s0095 ***Implications for Current and Future Research and Therapeutics***

p0205 Many of the model's central tenets require further empiric validation. For instance, natural history studies are needed to determine whether the transition from acute insomnia to chronic insomnia is accounted for by sleep extension, and laboratory studies are needed to determine whether neurocognitive processes (sensory and information processing and long-term memory formation) are altered before and during the sleep period in patients with chronic insomnia. Further, it must be shown that altered cognitive processing has clear neurobiologic substrates (e.g., altered metabolic activity in specific brain regions or the occurrence of local neuronal wakefulness) and functional consequences (sleep continuity disturbance and sleep state misperception). In short, novel experimental paradigms need to be developed to test the model's core hypotheses.

p0210 The neurocognitive model may provide some insight into the potential mechanisms of action of existing therapies and also some guidance regarding potential targets for new treatments. In the case of existing therapies, pharmacotherapy might be effective to the extent that the various compounds block sensory and information processing or promote amnesia for episodic memories formed during the sleep period. This idea, first espoused by Mendelson,[41-47] seems probable given the effects of benzodiazepines and benzodiazepine receptor agonists on arousal thresholds and memory formation. Sleep restriction therapy might also work through these mechanisms to the extent that this treatment modality serves to deepen sleep, which may augment the endogenous form of sleep-related mesograde amnesia. Potential avenues for new medical treatments include the assessment of compounds that have greater than normal amnestic potential for their efficacy as hypnotics, provided that such effects can be limited to the desired sleep period. Given that this is not possible, potent amnestics may be used experimentally to determine the extent to which amnesia for events occurring during the sleep period influences morning recall about sleep continuity and sleep quality. Alternatively, it may be possible to use stimulants during the day (e.g., modafinil) to promote wake extension and thereby their potential to diminish nocturnal cortical arousal through increased sleep pressure. The latter has been attempted with modafinil alone and in combination with CBT-I. Potential avenues for behavioral treatment include protocols that use more intensive forms of sleep restriction to promote counterconditioning, such as intensive sleep retraining therapy.[48]

Two-Factor Model (1997) s0100

Basic Description s0105

p0215 Bonnet and Arand propose a two-factor model to account for the incidence of insomnia and hypersomnia[49] (Figure 82-6). As described by the authors,

p0220 > *… each individual has his own sleep requirement determined by his sleep system and each individual has a basal level of arousal determined by his arousal system. Sleep deprivation will eventually override the arousal system, but the arousal system can also mask the sleep system. By thinking of these systems as relatively independent, one can dichotomize their effects. (p. 99)*

p0225 High basal arousal and a short sleep requirement are posited to account for idiopathic or psychophysiologic insomnia. Psychophysiologic insomnia occurs when the individual attempts to sleep when sleep is not required and the concurrent high level of basal arousal prohibits the obtention of "optional" sleep. Idiopathic insomnia likely represents the same scenario but as a life-long problem. High basal arousal and a long sleep requirement are posited to account for sleep state misperception (paradoxical insomnia). Presumably, sleep state misperception occurs when individuals sleep "because they can" but the concurrent high level of basal arousal results in shallow sleep, which may be perceived as wakefulness.

Strengths and Limitations s0110

p0230 The major strengths of this model are that it has a corresponding program of research that empirically assesses and experimentally models the hyperarousal and sleep continuity disturbance that occurs with insomnia; allows for the distinction between primary insomnia (psychophysiologic insomnia), idiopathic insomnia, and sleep state misperception insomnia

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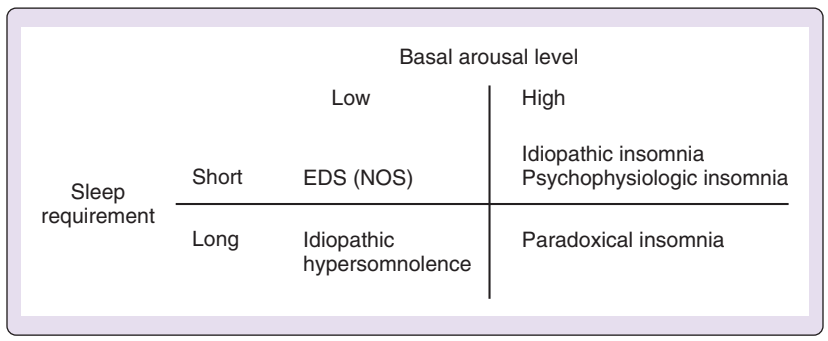

Figure 82-6 The Two-Factor Model. This schematic illustrates how high and low basal arousal and long and short sleep requirement interact to produce six forms of sleep continuity disturbance. EDS, Excessive daytime sleepiness; NOS, not otherwise specified.

(paradoxical insomnia); and takes into account sleep requirement as a moderator of hyperarousal. Programmatic research on this model has included measures of heart rate variability and Vo_2 measures of metabolic rate and experimental studies based on a "yoked insomnia" protocol and a high-dose caffeine paradigm.[50-53] The former provides evidence that patients with primary insomnia do indeed exhibit increased basal metabolic arousal compared with normal controls and patients with sleep state misperception (paradoxical insomnia). The latter provides evidence that many of the symptoms of insomnia can be produced experimentally (i.e., induced hyperarousal or sleep continuity disturbance).

p0235 The weaknesses of the model are that it does not directly provide a perspective on the etiology of insomnia (i.e., how basal arousal comes to be or continues to be elevated or how basal arousal varies with time); the concept of sleep requirement appears to combine the concepts of sleep need and sleep ability into a single factor and does not account for the related concept of sleep opportunity (how much sleep individuals attempt to obtain).

s0115 ***Implications for Current and Future Research and Therapeutics***

p0240 The work related to the definition and measure of arousal has been, and will continue to be, an essential goal for insomnia research. Moving forward, it will be important to determine what type of arousal (e.g., cognitive arousal vs. general metabolic rate vs. global cortical arousal vs. local activation within the central nervous system) and what level of arousal (how much activation) are required to prohibit sleep initiation or maintenance. Further, the delineation of sleep requirement as a potential moderator of insomnia type or subtype will need to be specifically defined, operationalized, and further studied.

p0245 The therapeutic implications of the model are clear: arousal and sleep requirement are potential targets for interventions. Currently, basal arousal is targeted pharmacologically with benzodiazepines, benzodiazepine receptor agonists (putatively altering central nervous system arousal through gamma-aminobutyric acid modulation), melatonin agonists (presumably affecting propensity for wakefulness), histamine antagonism (depotentiation of wakefulness), and most recently, with orexin antagonism (depotentiation of wakefulness). Although many directions for research and new therapeutics are possible, one possible direction would be to evaluate the soporific potential of compounds administered at time of bed that attenuate arousal in the periphery (e.g., heart rate) as opposed to within the central nervous system.

p0250 Basal arousal is targeted with cognitive behavioral treatments through sleep restriction (diminishes arousal by mild sleep deprivation) and relaxation training. Stimulus control may also serve to diminish basal arousal to the extent that leaving the bedroom and engaging in a nonsleep behavior prevents microsleeps and increases the time awake during the night. This may, in turn, result in mild sleep deprivation and thereby diminish arousal. Newer approaches include the anxiolytic potential of the practice of mindfulness. Currently, there are no therapies that address (modulate) sleep requirement, although CBT-I clearly involves a reset with respect to sleep opportunity and sleep ability.

Sleep Interfering-Interpreting Process Model (2000)

s0120

Basic Description

s0125

p0255 Lundh and Broman propose a two component etiologic model[54] (Figure 82-7). One of the components is identified as sleep interfering and is responsible for arousal and sleep continuity disturbance. The other is identified as sleep interpreting and is responsible for the individual's appraisal of the emergent insomnia (i.e., whether the insomnia is viewed or reported as a problem). The sleep interfering component is represented at two levels of causality.

p0260 The first level (distal causation) represents several factors that may lead to or be permissive of hyperarousal. These factors include arousability, stimulus arousal associations, behavioral and cognitive coping strategies, and interpersonal relations. Stimulus arousal associations and behavioral and cognitive strategies are also articulated in other insomnia models, but arousability and interpersonal relations are more novel constructs. Arousability, the magnitude of the individual's tendency to react to and recover from elicited arousal, appears to constitute a predisposing factor for insomnia. Interpersonal relations refer to the potential of social conflict to increase arousal and predispose the individual to insomnia. The second level (proximal causation) is arousal itself, conceptualized in terms of emotional, cognitive, and physiologic activation. These forms of arousal (alone or in combination) are posited to interfere with sleep initiation and maintenance. Finally, the sleep interpreting component is also represented at two levels of causality. The first level includes attributions, perfectionism, and beliefs about sleep and daytime functioning. These factors feed forward and determine the individual's

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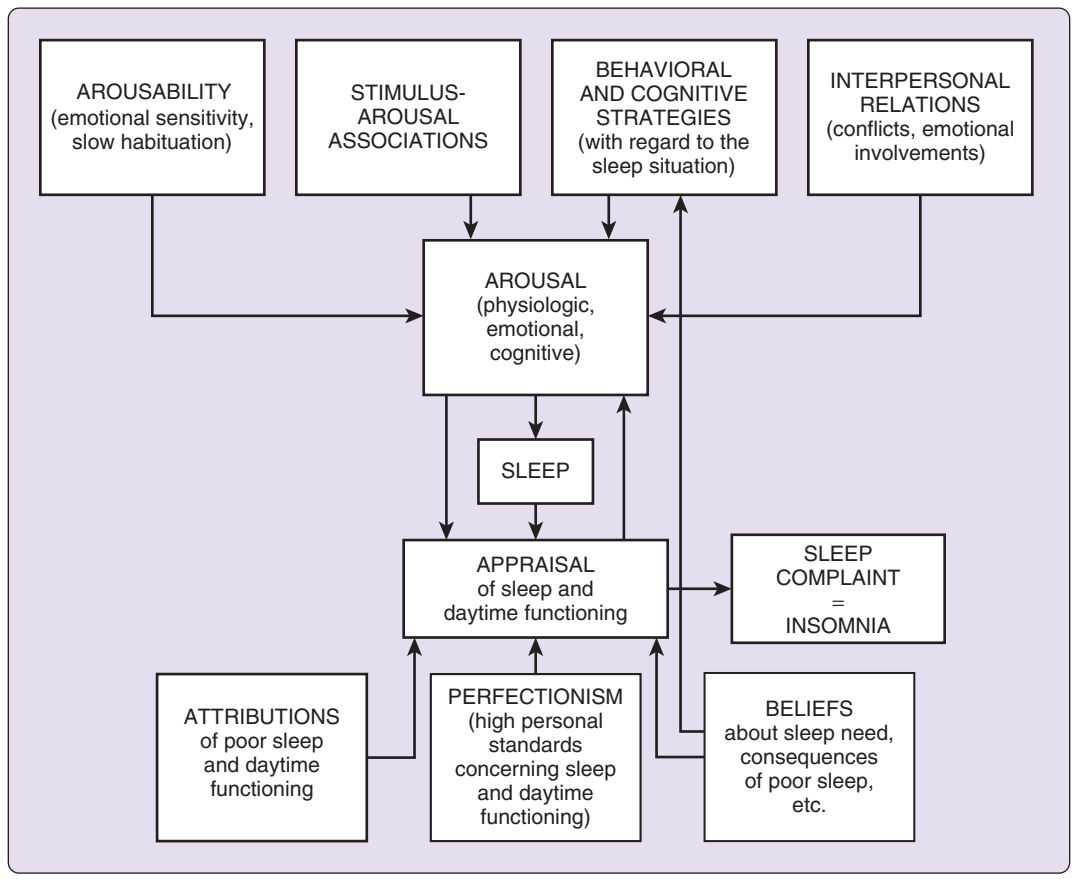

f0040

Figure 82-7 Sleep Interfering-Interpreting Process Model. This schematic represents the components of the two factors (sleep interference and sleep interpretation) and how they lead to the physiologic, emotional, and cognitive arousals that impinge on sleep.

appraisal (second level) of whether the insomnia is viewed or reported as a problem.

s0130 ***Strengths and Limitations***

p0265 The major strengths of the model are that it takes into account the importance of individual factors (arousability and appraisal) and interpersonal relationships as primary triggers for emotional, cognitive, and physiologic arousal. The identification of individual factors appears to be unique to the Lundh and Broman model and is critical because it may explain why, given similar levels of life stress, some develop acute or chronic insomnia, and some do not and why when sleep continuity disturbance occurs, some view the emergent insomnia as a problem whereas others do not. The major limitations of the model are that it does not account for the difference between acute and chronic insomnia and that it assumes that increased arousal necessarily results in sleep continuity disturbance.

s0135 ***Implications for Current and Future Research and Therapeutics***

p0270 If appraisal and interpretation moderate insomnia severity, these factors may constitute targets for intervention. Morin and colleagues, as part of their formulation of CBT-I, single out at least one aspect of appraisal for assessment and treatment: dysfunctional beliefs and attitudes about sleep.[23] More recently, two additional approaches have been developed to address appraisal and interpretation: behavioral experiments[55] and mindfulness training.[56] Both are likely to influence patients' tolerance of or response to the experience of insomnia or the consequences of insomnia. Empiric studies can evaluate the extent to which each of these approaches produces different outcomes or additive effects when combined with behavioral or pharmacologic interventions.

Psychobiologic Inhibition Model (2002) s0140

Basic Description s0145

p0275 The psychobiologic inhibition (PI) model posits that good sleep is ensured by automaticity and plasticity[57,58] (Figure 82-8). Automaticity refers to the involuntary nature of sleep initiation and sleep maintenance, governed by processed such as homeostatic and circadian regulation.[15] Plasticity refers to the ability of the system to accommodate real-world circumstances. Under normal circumstances, sleep occurs passively (without attention, intention, or effort). Within the context of normal sleep, stressful life events precipitate both physiologic and psychological arousal, which can result in inhibition of sleep-related dearousal and the occurrence of selective attending to the life stressors and insomnia symptoms. In acute insomnia, physiologic and psychological arousal interfere with the normal homeostatic and circadian regulation of sleep. Acute insomnia may, in turn, resolve or be perpetuated based on whether the stressor resolves or the individual attends to the insomnia symptoms that occur with the acute insomnia.

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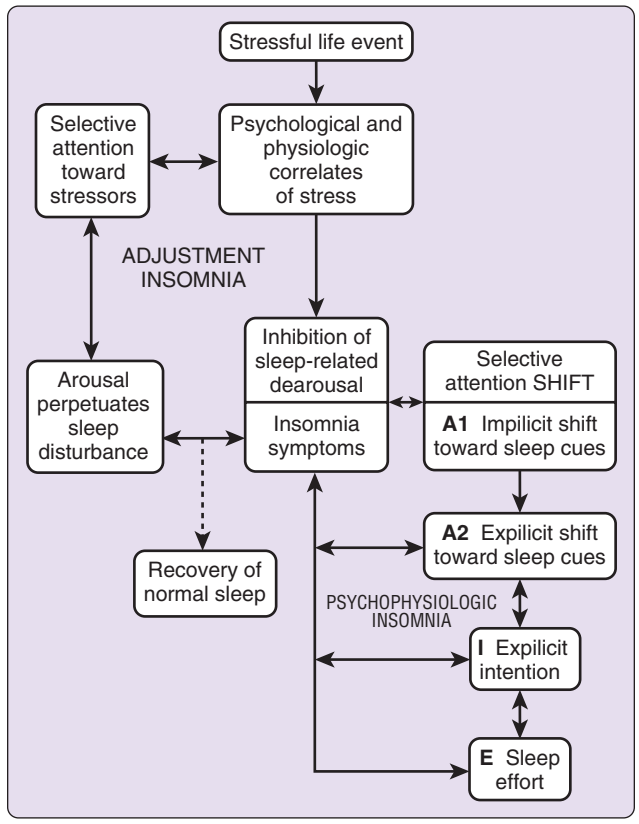

f0045 **Figure 82-8** The Psychobiologic Inhibition Model. The psychobiologic inhibition model focuses on how insomnia may be perpetuated by (1) the inhibition of sleep-related dearousal and (2) increased sleep-related attention, intention, and effort.

The shift of attention from the life stressor, implicitly or explicitly, to the insomnia symptoms is posited to be the first of three critical events that transition acute insomnia to a form of sleep disturbance that is self-perpetuating. Collectively, the three events (attention, intention, and effort) are referred to as the A-I-E pathway. When individuals are unable to sleep, their attention is drawn to an otherwise automatic process. The very process of attending, in turn, prevents perceptual disengagement and behavioral unresponsiveness (sleep).[59] Because a primary function of attention is to promote action in response to perceived need, an intentional (purposive) process is initiated that acts to further inhibit the normal downregulation of arousal. Finally, the intention to fall asleep triggers sleep effort, and this effort, like enhanced attention and intention, serves only to further inhibit sleep-related dearousal. Ultimately, in chronic insomnia, the inhibition of sleep-related dearousal reflects ongoing or elicited sleep-related attention, intention, and effort.

s0150 ***Strengths and Limitations***

p0280 Major strengths of the PI model are that it differentiates between acute and chronic insomnia and clearly delineates the mechanisms that are thought to mediate the transition between acute and chronic insomnia. Not only are these mediating variables clearly specified, there is also substantial support for attention bias or selective attention as operational in both in mental illness and insomnia.[60-72] Several studies have assessed the descriptive and predictive utility of the PI model. For instance, sleep-related mental preoccupation appears to be associated with the transition from acute to persistent insomnia in cancer patients.[66] Further, attention bias has been observed in individuals with psychophysiologic insomnia compared with good sleepers and subjects with delayed sleep phase syndrome,[68,69] and sleep-related attentional bias is also associated with self-reported sleep quality and sleepiness.[71] Finally, individuals with psychophysiologic insomnia exhibit effortful preoccupation with sleep.[73]

Another strength of the PI model is that it allows for objective measurement of cognitive processes in insomnia. Insomnia patients commonly complain of mental events interfering with sleep, such as intrusive thoughts, racing thoughts, worry, and inability to disengage from environmental "noise" or bodily sensations. The identification of such mental events relies on self-report. The constructs of the PI model can be operationally defined and tested with objective measures like the computerized emotional Stroop task, the induced-change blindness task, and the dot probe task. p0285

Finally, the PI model poses the novel hypothesis that inhibition of sleep-related dearousal rather than hyperarousal may be responsible for acute and chronic insomnia. In acute insomnia the inhibition of dearousal is engaged by the psychologic and physiologic correlates of stress. In chronic insomnia, the engagement of sleep-related attention, intention, and effort further inhibit dearousal. This shift from hyperarousal as the primary explanatory variable for chronic insomnia to inhibition of sleep-related dearousal represents a potential paradigm shift with regard to the etiology of insomnia. p0290

One limitation of the PI model and the A-I-E pathway is the need for further validation, particularly the intention and effort components. Some conceptual limitations are also present. First, the model focuses on cognitive factors and does account for behavioral mediators or moderators such as sleep extension and stimulus dyscontrol. These factors could be considered forms of sleep effort and thus be accounted for implicitly within the model. This said, explicit inclusion of sleep extension and stimulus dyscontrol would allow the PI model to be more comprehensive and integrative. Second, sleep-related attentional bias tends to be conceptualized as a perpetuating factor, but this factor may also serve as a vulnerability factor for acute or recurrent insomnia.[74] Third, the conceptualization of sleep-related dearousal needs to be explicated in a way that specifically delineates how it is similar to, and different from, the more traditional concept of hyperarousal[75] and the potentially related and alternative concept of the failure to inhibit wakefulness. p0295

s0155 ***Implications for Current and Future Therapeutics and Research***

The PI model may help to explain the efficacy of many existing elements of CBT-I and potentially of medical therapies as well. Any behavioral or cognitive intervention that potentiates sleep-related dearousal or promotes the disengagement of attention, intention, and effort should help to restore normal sleep. For example, sleep restriction may help to reinstate sleep automaticity by increasing homeostatic pressure and overcoming the effects of increased attention, intention, or effort. Similarly, stimulus control may strengthen adaptive and automatic bed-sleep dearousal associations. Finally, p0300

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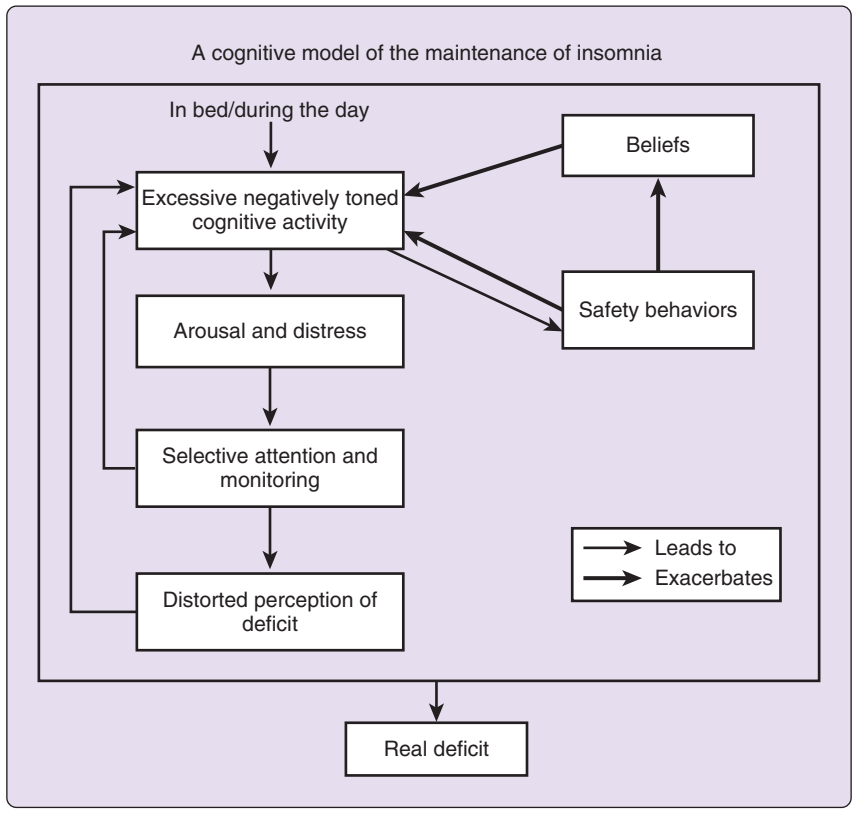

f0050

Figure 82-9 The Cognitive Model. The cognitive model was originally rendered as a state model that focuses on how insomnia may be perpetuated by (1) selective attention to sleep-related threats and the daytime consequences of insomnia and (2) the engagement of safety behaviors.

relaxation, distraction, and imagery methods may reduce worry about sleep, and paradoxical intention methods may entirely refocus the A-I-E pathway away from sleep preoccupation. The PI model suggests that the mechanisms for existing pharmacotherapies may reside in their capacity to promote relaxation, inhibit exteroception, and reduce sleep-related attention, intention, and effort. Clearly these are features of traditional sedatives (e.g., barbiturates, benzodiazepines, and benzodiazepine receptor agonist therapies). Finally, the model may point to the development of new approaches. For instance, the PI model supports the rationale for sensory gating training and mindfulness therapies. From the pharmacologic point of view, the PI model suggests that it may be productive to antagonize wake-promoting or wake-consolidating systems, for instance, through the modulation of orexin or a histamine.

s0160 ## Cognitive Model (2002)

s0165 ### *Basic Description*

p0305 Harvey's cognitive model adopts a framework that has been applied to anxiety disorders and uses the concepts of selective attention, monitoring, and detection of threat described previously[76] (Figure 82-9). The model posits that in chronic insomnia, sleep-related worry, selective attention and monitoring, and the detection of sleep-related threats perpetuate a level of physiologic arousal that continuously interferes with sleep initiation or sleep maintenance. The transition from acute to chronic occurs when individuals perceive that they have a sleep problem and engage in sleep-related worry, which in turn, prompts them to selectively attend to sleep-related threats and the daytime consequences of insomnia. Enhanced monitoring inevitably results in the increased detection of sleep-related threats and daytime effects of insomnia and the engagement of safety behaviors. Sleep-related worry includes thoughts and ruminations about sleep timing, duration, and quality and the functional and health consequences of sleeplessness. Selective attention to sleep-related threats, including both internal events, such as experiences of alertness or sleepiness, pain or discomfort, and the passage of time, and external events, such as environmental stimuli (e.g., light, sound, temperature) and the passage of time. The detection of sleep-related threats is coupled with the belief that internal sensations or environmental stimuli are interfering with sleep initiation or maintenance. The individual may also detect adverse outcomes during the day (e.g., being late to, missing, or performing badly at work) and attribute them to sleep loss or poor sleep quality. Finally, the engagement of safety behaviors includes both compensatory behaviors (e.g., extending sleep opportunity) and avoidance behaviors (e.g., cancelling social activities) that are intended to mitigate poor sleep and its effects.

Strengths and Limitations s0170

Major strengths of the cognitive model include an explicit p0310 focus on the etiologic relevance of the daytime consequences of insomnia, identification of specific factors that perpetuate insomnia (sleep-related worry), and identification of specific mechanisms for how sleep-related worry is perpetuated over

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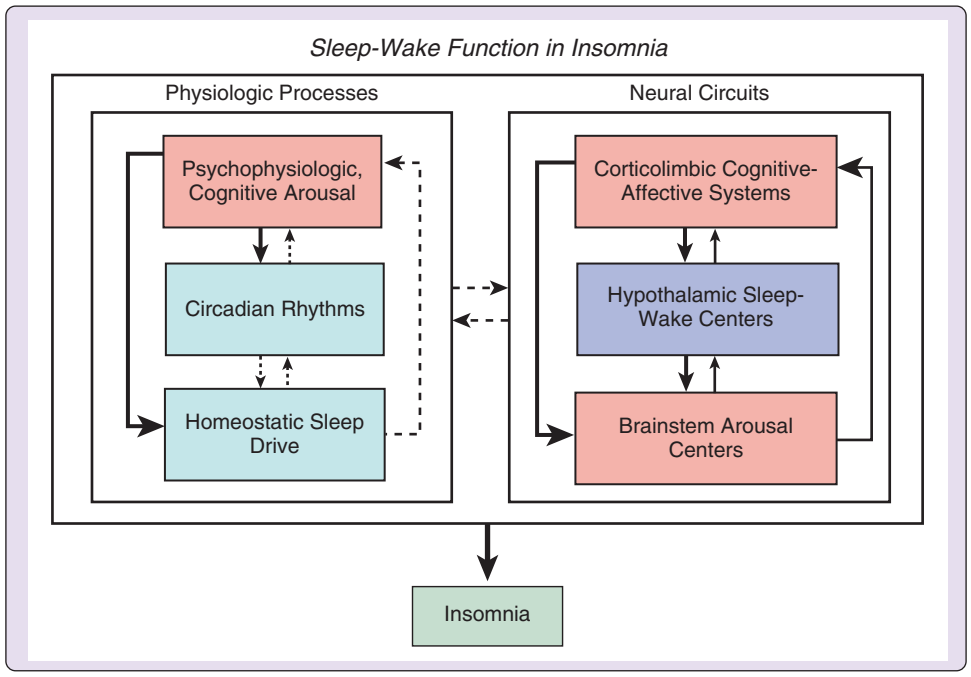

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Figure 82-10 The Neurobiologic Model. The neurobiologic model is primarily a state model that focuses on how insomnia may be a hybrid state that has as its neurobiologic substrate "local neuronal wakefulness" during NREM sleep.

time through selective attention and detection of sleep-related threats and consequences. Multiple studies have been conducted on several of the central tenets of the model, including experimental assessments of the relative roles of worry, selective attention, and safety behaviors. For example, experimental manipulations designed to increase worry among good sleepers increase sleep-onset insomnia,[77,78] and experimental manipulations designed to decrease worry in insomnia patients shortened sleep-onset insomnia.[79,80] A range of methodologies, including daily diaries, interviews, questionnaires, and experimental manipulations of monitoring,[81-85] support the prediction that attention to internal and external sleep-related threat is higher among individuals with insomnia relative to good sleepers and contributes to the vicious cycle of insomnia. In addition, one study provided evidence for the predicted association between monitoring and increased negative thoughts and use of safety behaviors at night and during the day. Furthermore, safety behaviors among patients with insomnia have been documented.[86] In addition, one study supported the predicted relationship between unhelpful beliefs about sleep and use of safety behaviors. Specifically, unhelpful beliefs about sleep predicted the use of daily safety behaviors.[86]

s0175 ***Implications for Current and Future Research and Therapeutics***

p0315 The cognitive model and related empiric work challenge the predominant behavioral perspective on insomnia. The model reasserts the relevance and centrality of cognition as an etiologic factor for insomnia and in so doing suggests that cognitive approaches, long deemphasized in favor of sleep restriction and stimulus control therapies, may deserve further study and clinical use. Several approaches to the management of sleep-related worry have been evaluated, including disputation of dysfunctional beliefs, decatastrophization exercises, mindfulness training to evoke moment-to-moment, nonjudgmental awareness, and behavioral experiments to invalidate worry-related thoughts and beliefs. Dismantling studies could be useful for evaluating the efficacy of cognitive versus behavioral approaches. To date, one such study[87] has been attempted that concluded that, "full CBT is the treatment of choice. Both BT and CT are effective, with a more rapid effect for BT and a delayed action for CT. These different trajectories of changes provide unique insights into the process of behavior change via behavioral versus cognitive routes" (p. 670). Beyond this, the emphasis on centrality of cognition may also provide an insight into the common use of antipsychotics in the management of chronic and severe or treatment-resistant insomnia. Although such treatments may or may not directly alter dysfunctional beliefs, catastrophization, sleep-related worry, or selective attention and monitoring, it remains possible that the sedating effects of these agents (and benzodiazepines and benzodiazepine receptor agonists as well) alter cognition in a manner that contributes to their efficacy.

Neurobiologic Model (2011) s0180

Basic Description s0185

The neurobiologic (NB) model of insomnia primarily focuses p0320 on the changes in brain activity and function that may account for insomnia (Figure 82-10). Specifically, Buysse and colleagues[88] posit that insomnia is "a disorder of sleep–wake regulation characterized by persistent wake-like activity in neural structures during NREM sleep, resulting in simultaneous and regionally specific waking and sleeping neuronal activity patterns" (p. 133). Wakelike levels of activity during cortically defined sleep (NREM sleep) are specified as occurring in the prefrontal and parietal cortices, the paralimbic

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cortex, the thalamus, and the hypothalamic-brainstem arousal centers. Localized activation within these regions (local wakefulness) during what is otherwise more globally sleep can be expected to be associated with "persistent awareness of the environment" (p. 133). Put differently, coactivation of this sort may directly result in an altered or attenuated capacity to initiate and maintain sleep (hypothalamic-brainstem) but also in abnormal levels of sensory and information processing (thalamus and parietal cortex), emotional processing (paralimbic cortex), and formation of perceptual representations that are evaluated for their appropriateness for action or nonaction (prefrontal cortex) during polysomnographically defined sleep.

s0190 ***Strengths and Limitations***

p0325 The NB model attempts to be an integrative model that proposes a more specific mechanism for insomnia than provided by the general concept of hyperarousal or the inhibition of "sleep-on" systems. This model defines insomnia as a hybrid state (part sleep and part wakefulness) that occurs with local neuronal variations in sleep depth and may help to explain clinical features of insomnia. The model is informed by the neurocognitive model (described previously), the neuronal transition probability model,[89] the two-process model of normal sleep-wake regulation,[15] and recent findings within neuroscience regarding both the sleep switch[90] and the phenomenon of local neuronal sleep.[91] Further, the NB model echoes the concept of status dissociatus as propounded by Mahowald and Scheck,[92] which suggests that hybrid states of consciousness (coactivations of wake, NREM, and rapid eye movement [REM] sleep) may occur in a variety of the sleep disorders, including narcolepsy, REM sleep behavior disorder, and confusional arousals. The concept of insomnia as a hybrid state was first suggested by Cano and Saper in conceptualizing findings from their rodent model of insomnia.[93]

p0330 The proposal that insomnia represents an aberrant state of persistent awareness that occurs as a result of local neuronal wakefulness adds to the existing literature in two ways. First, the model is explicit about what other models only imply: insomnia is, in part, a disorder of persistent wakefulness that may occur globally (objective insomnia) or more locally (subjective insomnia [i.e., sleep state misperception]). Second, the application of the concept of local sleep provides a mechanistic explanation for the proposition that insomnia entails aberrant levels of sensory and information processing or memory formation during the sleep onset period or during sleep. The NB model provides a framework for understanding the phenomena of shallow sleep or sleep state misperception and the paradox that small objective treatment gains are regularly paralleled by larger subjective effects. With respect to paradoxical treatment gains, small treatment-related changes in the polysomnogram may be associated with larger subjective improvements given reduced local waking neural activity in critical regions or circuits, such as the default mode network or the thalamocortical system.

p0335 The primary limitation of the NB model is that it is not an etiologic model. It does not focus on how good sleep transitions to insomnia nor on how acute insomnia transitions to the chronic form of the disorder. Like Morin's microanalytic model, the NB model adopts a state perspective. Future elaborations of this model could address how local wakefulness develops and how the functional and physiologic abnormalities that occur with this phenomenon map onto the symptoms of insomnia (difficulties initiating and maintaining sleep).

s0195 ***Implications for Current and Future Research and Therapeutics***

p0340 Future investigations of the NB model are likely to rely heavily on neuroimaging studies before and during sleep to document regional and circuit-level brain dysregulation in patents with insomnia. Extending such paradigms cross-sectionally and longitudinally could address the transition between acute and chronic insomnia. The therapeutic implications of the NB model are varied and include the exploration of whether present medical and cognitive behavioral approaches minimize or eliminate neuronal local wakefulness. CBT-I may accomplish this by increasing homeostatic pressure for sleep and medical treatment with benzodiazepines, and benzodiazepine receptor agonists may do this through modulation of central nervous system gamma-aminobutyric acid activity. Techniques to increase regional brain activity during wakefulness or to decrease such activity during sleep, such as transcranial magnetic stimulation, may also warrant further study.

LIMITATIONS OF THE EXISTING MODELS

s0200

p0345 In aggregate, the models presented in this chapter help to explain many of the clinical features and treatment effects commonly observed in chronic insomnia. However, several important aspects of insomnia are not well accounted for.

Most Models Do Not Explicitly Take into Account the Role of Classical Conditioning

s0205

p0350 Most of the etiologic models do not explicitly address the issue of classical or Pavlovian conditioning, focusing instead on the instrumental side of behavioral processes, that is, on the behaviors that maintain insomnia. Being awake in bed may directly elicit arousal responses or wakefulness through classical conditioning, and such conditioning may contribute to the self-perpetuating nature of insomnia. Classical conditioning as a perpetuating factor can help to explain two reliable findings from the treatment outcome literature. First, CBT-I produces about a 50% reduction in symptoms during the acute treatment phase,[94] which is less than might be expected if only instrumental behavioral factors were responsible for chronic insomnia (see Figure 82-3). Second, patients treated with CBT-I continue to improve over follow-up periods as long as 12 months.[95,96] If only instrumental factors were responsible for chronic insomnia, no additional improvements would be expected beyond the acute treatment phase. From a classical conditioning perspective, successful treatment with CBT-I in the short term may result in counterconditioning over the longer term: Repeated pairing of sleep-related cues with sleep over time may extinguish conditioned arousal.

Most Models Do Not Take into Account Normal Sleep-Wake Sleep Regulation

s0210

p0355 Although most of the human models of insomnia are compatible with Borbély's two-process model, only the NB and PI models explicitly embrace this perspective on sleep-wake

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regulation and how these abnormalities within these systems may serve to predispose, precipitate, or perpetuate insomnia. This is unfortunate because it leaves out the likely possibility that at some point abnormalities within these arenas (process S and process C) contribute to the etiology of insomnia. For example, from the 3P point of view, sleep expansion by retiring to bed earlier likely leads to dysregulation of sleep homeostasis and possibly to a phase advance. Retiring to bed earlier in the evening (while keeping rise time constant or delaying this as well) not only creates a potential mismatch between sleep opportunity and ability but also likely diminishes the homeostatic prime for good sleep continuity and normal sleep architecture and may promote shallow sleep if not local wakefulness. Phase-advancing the sleep period (and the resultant alterations to light exposure and melatonin secretion) may prompt a fundamental shift in all the physiologic parameters that have circadian or ultradian rhythms.

Most Models Do Not Explicitly Differentiate between Acute and Chronic Insomnia

s0215

p0360 All of the models presented directly or indirectly address how acute insomnia transitions to chronic insomnia or how chronic insomnia is maintained over time. Significantly less attention is paid to what precipitates acute episodes of insomnia, whether acute insomnia is a distinct entity from chronic insomnia, and what may characterize the differences between acute and chronic forms of the disorder.

p0365 Within the current nosologies (e.g., the DSM-5[3] and ICSD3[4]), acute and chronic insomnia are defined temporally, with a threshold of 3 months. Individuals who meet all criteria for chronic insomnia except duration are diagnosed with acute insomnia (adjustment insomnia, short-term insomnia disorder, or transient insomnia). It is unclear, however, whether other clinical or physiologic factors distinguish acute and chronic insomnia, such as precipitating and perpetuating factors, symptoms, and polysomnographic features. On a more basic level, it is not clear whether acute insomnia should even be considered a pathologic state. It could be argued that acute insomnia is a normative adaptive phenomenon, part of the fight-or-flight response to threat that overrides the normal homeostatic and circadian imperatives for sleep. Put differently, "it may be the case that we live with insomnia today, because at some point in our evolutionary history insomnia allowed us to live."[97]

Most Models Do Not Account for Gender and Age Differences with Respect to Chronic Insomnia

s0220

p0370 Women experience insomnia at a rate nearly double that of men,[98-99] and older adults report chronic insomnia at a rate that is approximately three times that of general population,[100] but the reasons for these differences are not well-defined. Although none of the models presented here explicitly address sex or age discrepancies, several of them provide a framework for doing so. For example, within the 3P framework, specific predisposing factors for women may include physiologic and psychosocial concomitants of menstrual cycles, childbirth, and menopause,[101-105] and predisposing factors in older adults may include chronic medical and psychiatric conditions, other sleep disorders, medication effects, and age-related changes in sleep behaviors and physiology (e.g., advanced time to bed, weakened homeostatic sleep drive). Precipitating factors specific to women may again include physiologic and psychosocial aspects of reproductive function, as well as a host of more general interpersonal and social factors; precipitating factors in older adults include acute illnesses, new medications, and psychosocial stressors such as retirement, bereavement, and loss of independence. Finally, although many perpetuating factors may be common across sex and age, worry, rumination, and anxiety are more often exhibited by women,[106,107] which may help explain why acute insomnia occurs with about equal prevalence in men and women[108] but chronic insomnia appears more often in women. Older adults may be particularly vulnerable to increased time in bed as a perpetuating factor.

Most Models Do Not Account for the Types and Subtypes of Insomnia

s0225

p0375 Most of the models reviewed in this chapter do not account for different clinical presentations such as initial insomnia, middle or late insomnia, or a combination of these symptoms. The models also do not consistently address other phenomena, such as varying degrees of subjective-objective sleep discrepancy or varying age of onset. Finally, most models do not account for differences in clinical presentation that are characterized as idiopathic, psychophysiologic, or paradoxical insomnia. More research is needed to determine whether these states differ with respect to etiology, pathophysiology, or their responsiveness to treatment.

Most Models Posit that Insomnia Occurs in Association with Elevated Arousal or Hyperarousal

s0230

p0380 At present, no theoretical distinctions have been made (or studies conducted) showing that the hyperarousal of acute insomnia is the same as or different from the hyperarousal that is present with subchronic and chronic insomnia. In the absence of data, it seems reasonable to hypothesize that the arousal (at least somatic hyperarousal) that occurs with the hypothalamic-pituitary axis–related fight-or-flight response far exceeds the arousal that occurs with chronic insomnia. If this is the case, then it follows that the persistent inability to initiate or maintain sleep occurs, in part, as a result of other factors. The NC model focuses on functional changes with respect to perceptual disengagement. The PI focuses on a weakening of the sleep system in terms of the inhibition of sleep-related dearousal. The NB model focuses on the persistent wakelike activity in neural structures during NREM sleep. Taken together, along with basic findings from the Cano-Saper rodent model,[93] this suggests not only that chronic insomnia may be maintained by unique factors but also that chronic insomnia may well be a hybrid state in which there is either a persistence of wakefulness (at sleep onset) or a failure to inhibit wakefulness (following nocturnal awakenings). Moving forward such concepts should be evaluated for how they differ from and interact with the concepts of basal arousal and hyperarousal. Further, these concepts should serve to spur the development of novel interventions.

CONCLUSION

s0235

p0385 Each of the models presented in this chapter provides a unique perspective, and for the most part, none are mutually exclusive. In recognition of this, we provide in Figure 82-11 an integrative perspective, parallel process model. This model

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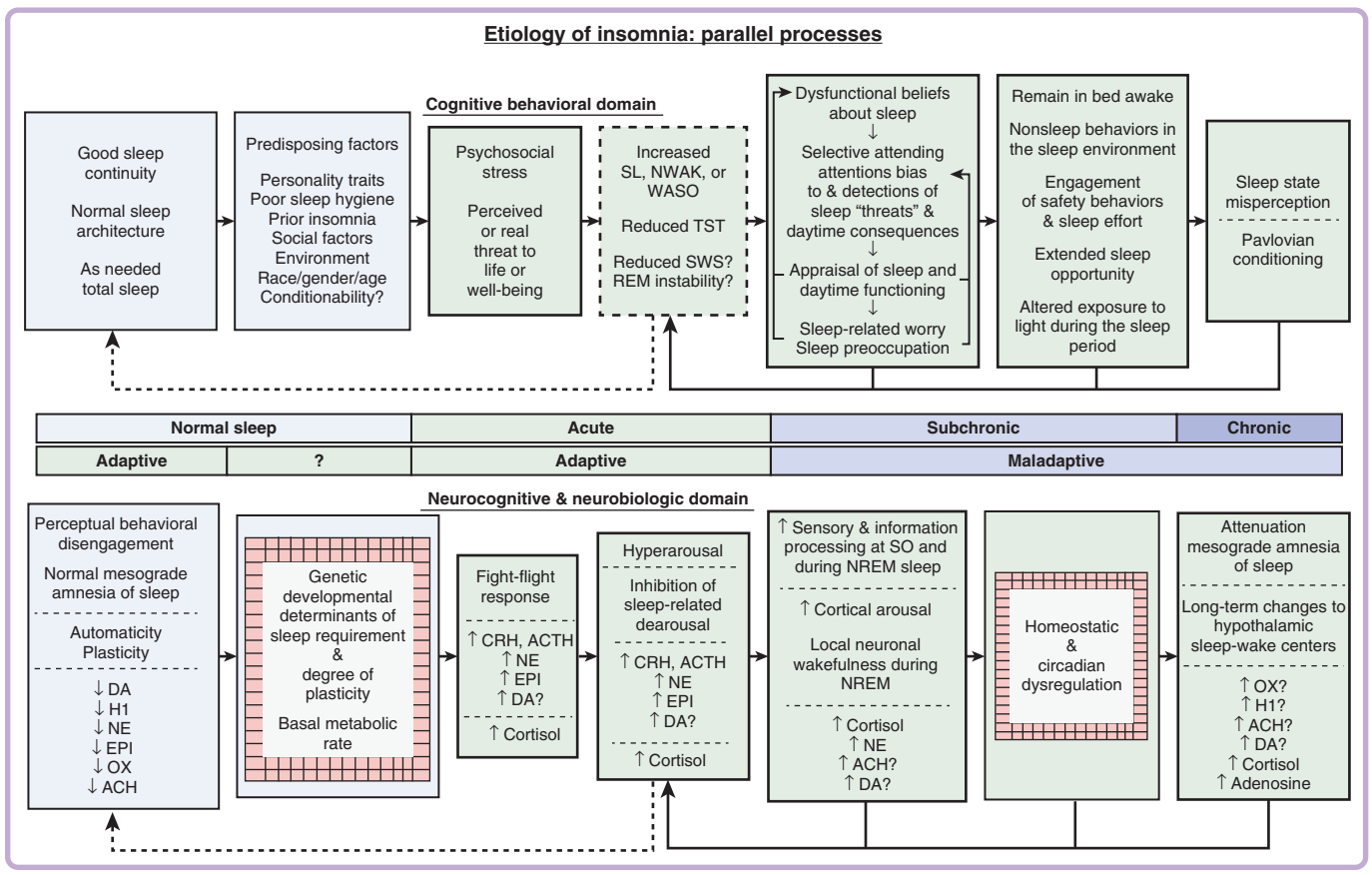

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Figure 82-11 The Parallel Process Model. The parallel process model is provided to illustrate how (1) all of the identified factors may be contributory and (2) the cognitive and behavioral domains may be viewed as parallel processes to the neurocognitive and neurobiologic domains. ACH, Acetylcholine; ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; DA, dopamine; EPI, epinephrine; H1, histamine-1 receptor antagonist; NE; norepinephrine; NWAK, number of awakenings; OX, orexin; SL, sleep latency; SO, sleep onset; TST, total sleep time; WASO, wake after sleep onset.

is intended to represent each of the core components from the nine models within one framework, the perspective that the cognitive-behavioral and the neurocognitive-neurobiologic domains represent two sides of the same phenomena, and the possibility that acute insomnia is adaptive. In framing the various factors in this manner we hope to stimulate new ideas for both research and possible interventions.

b0010 **CLINICAL PEARL**

p0390 Although many consider theory to be largely an academic enterprise, the models presented in this chapter provide a framework for understanding how insomnia becomes chronic, why the disorder presents as it does, and how or why different treatments may work. Such frameworks, although inevitably imperfect and incomplete, help in the conceptualization of both individual cases and the directions for future research.

s0240 ## SUMMARY

p0395 Since the 1990s there has been a proliferation of theoretical perspectives on the etiology of insomnia that now includes nine human models. Each is summarized, reviewed for its strengths and weaknesses, and evaluated for its potential to generate new research and therapeutics. Following the summaries, limitations of the present models are considered and an integrative perspective provided.

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REVIEW QUESTIONS

p0405 1. Classical conditioning is a central component of which model on the etiology and pathophysiology of insomnia?
o0085 A. Stimulus control model
o0090 B. 3P behavioral model
o0095 C. 4P behavioral model
o0100 D. Neurobiologic model
o0105 2. It is widely believed that insomnia occurs in association with hyperarousal. An alternative point of view is that insomnia results from which of the following?
o0110 A. Increased cortical arousal at and around sleep onset
o0115 B. Inhibition of sleep-related dearousal
o0120 C. Dysregulation of the sleep homeostat
o0125 D. All of the above.
3. All but which one of the following represent major perspectives on the etiology of insomnia? o0130
A. Sleep interfering-interpreting process model (Lundh and Broman) o0135
B. Neurocognitive model (Perlis et al.) o0140
C. Microanalytic model (Morin et al.) o0145
D. Psychobiologic inhibition model (Espie et al.) o0150
4. Only one of the etiologic models provides a dedicated focus on the importance of the daytime sequelae of insomnia. Which of the following models has this component? o0155
A. Cognitive model (Harvey) o0160
B. Neurocognitive model (Perlis et al.) o0165
C. Microanalytic model (Morin et al.) o0170
D. Two-factor model (Bonnet and Arand) o0175

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ANSWERS

p0510 1. **C.** Although it is widely held that classical conditioning is a relevant consideration for the stimulus control and behavioral 3P models, the 4P model explicitly embraces this process as one of the factors responsible for chronic insomnia.

o0185 2. **D.** All of the considerations listed constitute central concepts within the models reviewed in this chapter.

o0190 3. **C.** The microanalytic model focuses on how insomnia is self-perpetuating.

o0195 4. **A.** Harvey explicitly addresses the importance of the daytime consequences of insomnia as a perpetuating factor.

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