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REVIEW ARTICLE

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The Natural History of Insomnia: What We Know, Don't Know, and Need to Know

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To date, studies of the natural history of insomnia have focused on the prevalence, incidence, and persistence of chronic insomnia. While these studies have provided seminal information about the epidemiology of insomnia, no studies to date, have been conducted in a manner to 1) allow for a close resolution of the "transitions" from good sleep to acute insomnia, from acute insomnia to the recovery of good sleep, or from acute insomnia to chronic insomnia and/or 2) allow for a comprehensive assessment of the factors that have been theorized to mediate or moderate these transitions.[1-4] The present paper provides a review of these issues and sets forth a research agenda.

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Key Words Insomnia, Natural history, Etiology.

What We Know and Don't Know (Empirical Findings)

Over the last several decades the prevalence and incidence of insomnia has been described in great detail. These data, while essential to document the magnitude of this health problem, infrequently provide information related to the incidence of new-onset insomnia and even less frequently provide information on the incidence of spontaneous remission and relapse. Of the groundbreaking studies that document these phenomena, none have provided information about the factors that mediate/moderate the transitions between good sleep to acute insomnia and from acute insomnia to either recovery or chronic insomnia. In this review, what is known about the natural history of insomnia (in terms of prevalence, incidence, and clinical course) will be reviewed. In addition, the leading theoretical perspectives on insomnia will be reviewed (with an eye towards identifying the factors that may mediate/moderate the above noted transitions) and a research agenda provided.

Prevalence

The prevalence of insomnia has been examined in several dozen studies. These studies were comprehensively reviewed by Ohayon[5] in 2002. One of the most important findings from this literature was that the prevalence varied considerably depending on how insomnia was defined (Fig. 1). Many studies used one or more questions pertaining to symptoms of insomnia, asking respondents to indicate whether they had trouble falling asleep, staying asleep, or with early morning awakenings. When no frequency/severity/chronicity criteria were specified, prevalence rates ranged from 30% to 48% of respondents. When frequency considerations were taken into account, as well as the complaint of daytime consequences, then the prevalence rates were reduced to between 6% and 18%. The latter definitions, while not taking into account severity or chronicity, do approximate the level of detail required for formal diagnosis using current nosologies[6,7] and thus likely represent the prevalence of insomnia as a disorder in the population at large. While it is important to estimate point prevalence (to define how

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widespread a disorder or disease is), such data do not address several related issues: 1) what is the relative prevalence of acute and chronic insomnia; 2) how frequently do acute episodes of insomnia occur within the individual; 3) how many episodes of acute insomnia occur, on average, before the insomnia condition becomes chronic; and 4) what factors mediate/moderate the transition from acute to chronic insomnia.

To our knowledge, only one study has specifically assessed lifetime prevalence. Breslau et al.[8] used the Diagnostic Interview Schedule to assess lifetime prevalence of DSM-III-R diagnoses in a sample of 21-30 year-olds. The lifetime prevalence of insomnia, defined as ≥ 2 weeks of trouble falling or staying asleep, was 24.6%. In an older sample, the lifetime prevalence would likely be substantially higher if for no other reason than increased opportunity to experience insomnia, not to mention the cumulative effects of aging and illness. Perhaps a more reasonable estimate can be drawn from a recent study on the long-term course of insomnia reported by Buysse et al.[9] In this 20-year prospective study 591 adults completed six separate interviews over the course of two decades. Sleep questions from each interview were used to determine both the occurrence of insomnia symptoms as well as a insomnia diagnosis using a proxy definition. Approximately 70% in this cohort reported insomnia symptoms during at least one interview, indicating a very high 20-year prevalence. These data, while suggestive, do not allow for a determination of 1) the lifetime prevalence of acute and chronic insomnia; 2) how frequently acute insomnia occurs within the individual over the lifespan; 3) the factors mediate/moderate the transition from acute to chronic insomnia.

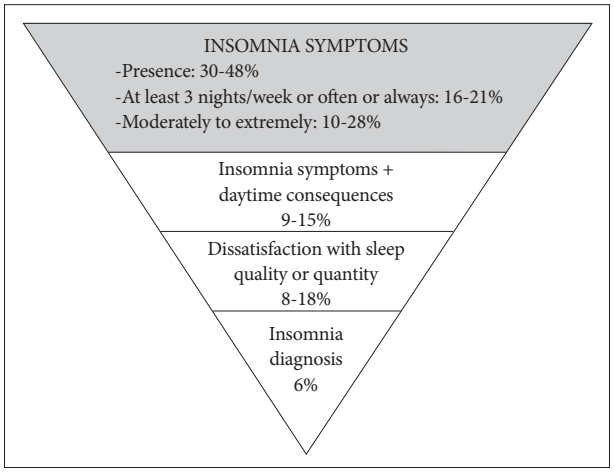

Fig. 1. Insomnia symptoms pyramid.

Incidence of Insomnia

Surprisingly, there are eleven studies that provide data regarding rates of new-onset insomnia (variously defined) in individuals who were initially assessed as good sleepers.[8,10,11-19] This is surprising because such data are, more often than not, contained within investigations that have as primary end points, the assessment of prevalence. Thus, the incidence data may not be featured in the titles and/or abstracts of such reports. Follow-up periods for the 11 studies ranged from 1 to 12 years. The average per-year incidence rate across studies was 5% with a range of 1% to 15% (Fig. 2). The lowest rate was found in a sample consisting only of men.[15]

The highest rates were found in a sample of people with chronic medical conditions,[13] and in a sample taken from general practitioner offices.[16] These findings are not surprising given that medical illness, especially those involving physical pain, can act as a precipitant of acute insomnia. In the studies that examined predictors of new-onset insomnia, risk factors included female gender, depression, poor health, and low physical activity.[11,12,14] It should be noted that, contrary to what one might imagine, studies of older adult samples did not find higher incidence rates than younger samples.[12,14] As with prevalence studies, insomnia definitions affected study results. For example, Katz and McHorney.[13] in a study of individuals with chronic medical and psychiatric conditions, computed separate incidence rates for 'severe' and 'mild' insomnia, a distinction not made in other

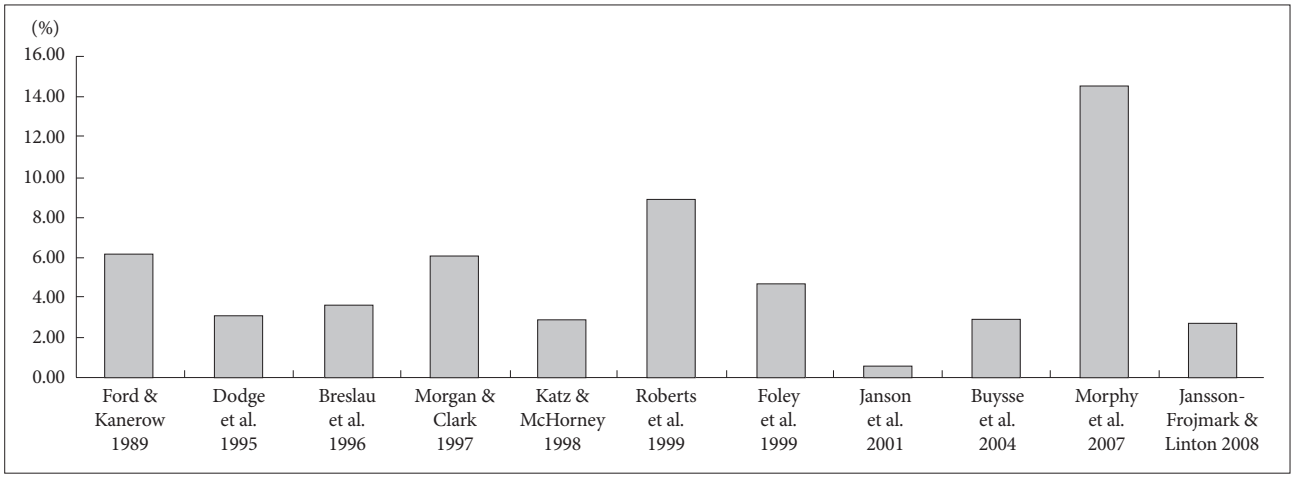

Fig. 2. One year incedence rate of insomnia.

studies, and found widely disparate incident rates of 3% and 21%, respectively. This finding, while underlining the importance of how insomnia is defined, is nevertheless consistent with what one might expect, which is that a broader definition of insomnia will yield higher incidence rates. To date, no studies have yet determined: 1) the incidence rate for insomnia using quantitative criteria (along with traditional diagnostic criteria) or narrow sampling intervals (1-3 month repeated assessments), and 2) the relevance of factors that have been hypothesized to increase risk for new onset acute and chronic insomnia.

Persistence of Insomnia Over Time

A total of 25 studies of insomnia have been conducted that included a longitudinal component assessing chronicity.[8-11,13-32] The majority were epidemiological studies that included samples of both good and poor sleepers. Follow-up periods ranged from 4 months to 20 years. The findings from these studies, which in part constituted the source data for the Ohayon meta-analysis,[5] are represented in Fig. 3. The mean rate of persistence (insomnia at baseline and at follow-up) was 54.8% with a range of 13% to 88%. The highest rates were in longitudinal follow-ups of patients from sleep clinics[27,31] and are hence less representative of the overall population because their samples consisted of solely treatment-seeking individuals. Persistence rates were higher when only individuals with severe insomnia were examined.[13] As with incidence, greater persistence was associated with chronic medical and psychiatric conditions.[14,32] One study explored several variables, based on constructs related to the etiology of insomnia, and found greater persistence to be associated with greater reported somatic arousal and more highly endorsed dysfunctional beliefs and attitudes about sleep.[32] Interestingly, longer follow-up periods were not associated with lower rates of persistence (i.e., it seems to follow that the longer follow-up period, the greater the opportunity for recovery-and this was not the case).

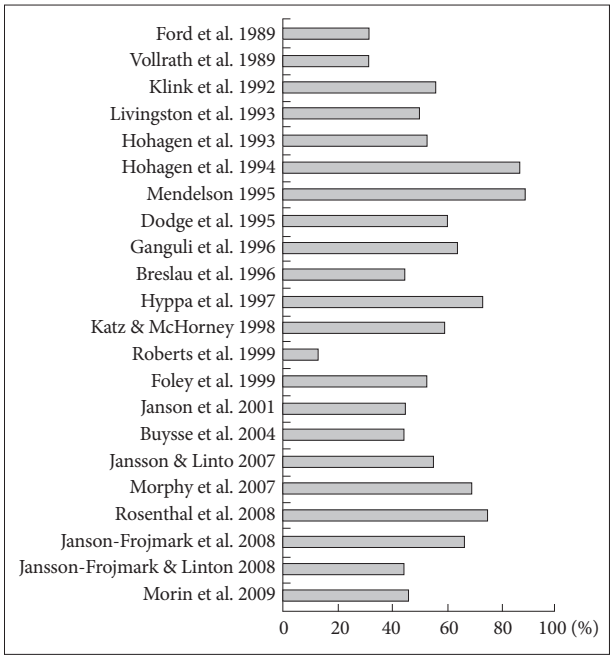

Fig. 3. Persistence of insomnia.

To date, the most comprehensive natural history of insomnia study has been undertaken by Morin et al.[21] They conducted a longitudinal study of 388 adults with insomnia in which there were annual assessments each year for three years. One of the many strengths of this study is that subjects were operationally defined as good sleepers or having insomnia based on current research diagnostic criteria, rather than relying on non-standard assessments and definitions of insomnia. One of the seminal findings of this study (to date) is that insomnia was shown to persist over time, with 74% of subjects reporting insomnia for at least one year. Even in those who experienced remission of symptoms at one assessment, 27% eventually had a relapse. Greater severity of insomnia at baseline was associated with higher rates of persistence over time, as one might expect.

The data from these studies suggest that once insomnia persists for some unknown time period, remission is unlikely. The fundamental question that remains to be empirically determined regarding the persistence of insomnia is: "How persistent must the insomnia be before it is truly self-perpetuating and chronic".

Synopsis of Empirical Findings

The combination of the studies summarized above suggest that insomnia is highly prevalent (with rates up to 48%), occurs with an annual incidence rate of approximately 5%, and tends to be unremitting for 55% of affected individuals. One of the major limitations of the longitudinal studies thus far is that they provide only a snapshot of the course of insomnia that is low in resolution, with most assessments occurring with a frequency of once per year. A finer grained analysis is needed in order to resolve phenomena that are conceptualized as occurring within shorter time frames. For example, it's not possible to characterize the transition from acute to chronic insomnia with assessments once per year; this transition is thought to occur in time frames from one to three months.[6,7,33] These time frames, it should be noted, have more to do with traditional conceptualizations of what constitutes chronic than an empirical assessment of how severe and how persistent insomnia needs to be before it is improbable that it will spontaneously resolve (i.e. exist in a chronic form). As important, the current studies only provide descriptive, numerical analyses regarding prevalence, incidence, and persistence. They do not provide information regarding the process of how insomnia develops over time. For example, while it may be the case that 45% of subjects with acute insomnia experience remission or recovery, very little is known about what differentiates these individuals from those who develop chronic insomnia. In order to accomplish this, lo-

ngitudinal studies would need to be deployed that have a high sampling resolutions (e.g., once every 1-12 weeks) and that directly measure the factors that have been posited to account for how insomnia becomes chronic. Below the leading theoretical perspectives on insomnia (Human Models) will be reviewed with an eye towards identifying the factors that may mediate/moderate the transitions from 1) good sleep to acute insomnia, 2) acute insomnia to the recovery of good sleep, and 3) acute insomnia to chronic insomnia.

What We Know (Models of Insomnia)

Up until the mid-1990s there were very few theories regarding the etiology and pathophysiology of insomnia and only two gained widespread acceptance and served as platforms for treatment: the Stimulus Control Model[34,35] and the 3 Factor Model.[1,36] In more recent years, there has been a focus on how neurophysiologic and cognitive processes may contribute to the incidence, severity and chronicity of insomnia. These perspectives (Neurocognitive, Morin, Harvey and Psychobiological Inhibition Models) are briefly reviewed below.

Stimulus Control Perspective (1972)

Stimulus control, which is based on principles of instrumental conditioning, was originally applied to the problem of insomnia by Bootzin and Nicassio.[37] The general principle is that one stimulus may elicit a variety of responses, depending on the conditioning history. When a stimulus is always paired with a single behavior there is a high probability that the stimulus will yield only one response. In a more complex conditioning history, a stimulus is paired with a variety of behaviors and this leads to a low probability that the stimulus will yield only one response. In individuals with insomnia, it is frequently the case that large amounts of time are spent in the bedroom and/or the bed itself engaging in non-sleep related behaviors (reading, watching TV, working, spending time on the internet, worrying, etc.). From the patient point of view, engagement in these behaviors is justified because 1) leaving the bedroom would make it more likely that the bout of wakefulness would be prolonged and 2) staying in bed is restful and thus is somewhat recuperative. From the conditioning point of view, the increase in the number of non-sleep behaviors in the bed and bedroom leads to stimulus dyscontrol: the reduced probability that sleep-related stimuli will occur in association with sleepiness and sleep. Stimulus dyscontrol can therefore be conceptualized as a problem that grows out of a normal process: instrumental conditioning. Further, the problem consists of two components: 1) time spent engaged in non-sleep activities in the bed and bedroom and 2) time spent in bed "awake" (i.e., wakefulness is a non-sleep activity). The latter, while not an explicit focus of the stimulus control perspective, is also thought to be problem that grows out of a normal process: classical conditioning. In this instance, the repeated pairing of bed and bedroom with the physiologic/neurobiologic state of wakefulness makes it likely that these stimuli may become conditioned stimuli, not for sleepiness and sleep (as is normally the case), but for wakefulness itself. Interestingly, patients often allude to this state of affairs when they report being sleepy while watching TV in the living room only to become inexplicably alert and awake upon crossing the threshold into the bedroom.

Most would agree that the stimulus control perspective is compelling. Further, the important role of stimulus dyscontrol as a perpetuating factor for insomnia is supported by the finding that Stimulus Control Therapy (which involves reestablishing a one-to-one correspondence between sleep-related stimuli and sleep by eliminating non-sleep activities in the bed and bedroom) is highly efficacious.[38,39] This said, the efficacy of the therapy (while important clinically) is not proof positive that stimulus dyscontrol is, in part or large measure, pathogenic. To date, no prospective study has been undertaken to shown that the transition from acute insomnia to chronic insomnia is associated with an increased occurrence of (or time spent in) non-sleep related behaviors in the bed and bedroom. Further, there has been no direct demonstration that the bed/bedroom acts as a conditioned stimulus for wakefulness, increased alertness, or "hyperarousal" (in e.g., chronic but not acute insomnia), although there is one self report study that supports this concept.[40]

The Three Factor Model (1987)

This model (also referred to as the Spielman model, the Behavioral model, or the "Three P model") is essentially a stress-diathesis model with an additional component that delineates how acute insomnia becomes chronic.[1] In brief, this model posits that insomnia occurs acutely in relation to both trait (predisposing factors) and life stress (precipitating factors) considerations. Chronic insomnia occurs as a result of maladaptive coping behaviors (perpetuating factors). Predisposing factors include: trait hyperarousal; personality characteristics such as the tendency to worry or ruminate; and social factors, such as incompatible sleep schedules between bed partners and social pressures to sleep according to a non-preferred sleep schedule (e.g., child rearing). Precipitating factors are acute occurrences that trigger sleep continuity disturbance. The primary "triggers" are thought to be related to life stress events (e.g., perceived or real threat) and medical and psychiatric illness. Perpetuating factors refer to the behaviors adopted by the individual, which are intended to compensate for sleep loss. In the original conceptualization of the behavioral model, Spielman focused on the role of sleep extension. Extending sleep opportunity refers to the tendency of patients to compensate for sleep loss by napping and/or going to bed earlier (advance of time to bed) and/or by getting out of bed later (delay of time out of bed). Such changes are enacted in order to "recover what has been lost"

and thus 1) appears to the patient to be a reasonable strategy for coping with insomnia and 2) is reinforcing to the extent that additional sleep diminishes insomnia related symptoms (fatigue, concentration and memory problems, malaise, etc.). The consequence of sleep extension, however, is the dysregulation of sleep homeostasis. That is, the reduction in the amount of time spent continuously awake can be expected to result in reduced "sleep pressure" and that this in turn serves to perpetuate insomnia in the relative, or complete, absence of the original precipitants.

There is no doubt that the Spielman model is powerful and persuasive. It has high face validity, is based on a well established concept (stress-diathesis), and its "third factor" (sleep extension) is firmly grounded on behavioral principles (instrumental conditioning) and is clearly consistent with the two-process model of sleep wake regulation (i.e., de-priming the sleep homeostat* while keeping sleep opportunity constant, will necessarily result in sleep continuity disturbance). Further, the important role of sleep extension is supported by the findings 1) of low sleep efficiency in patients with insomnia and 2) that Sleep Restriction Therapy, which involves limiting time spent in bed both at night and during the day, is highly efficacious. These lines of evidence are not, once again, "proof positive" of the importance of sleep extension as a primary perpetuating factor for insomnia. To date no prospective study has shown that patients with acute insomnia who develop chronic insomnia do indeed compensate for sleep loss with sleep extension and that this differentiates them from both good sleepers and subjects who recover from acute insomnia. Moreover, there is no evidence that one form of the three possible forms of sleep extension (advancing time to bed, delaying time out of bed, or napping) is more damaging than the other two and/or that the various forms sleep extension when combined have additive or multiplicative effects with respect to insomnia morbidity.

The Neurocognitive Model (1997)

The Neurocognitive model[37,41] is based on, and is an extension of, the Spielman model.[42] The central tenets of the model include

1) A pluralistic perspective of "hyperarousal". That is hyperarousal may exist within several domains (alone or in combination) including the cortical, cognitive and somatic domains.

2) The specification that cortical arousal is central to the etiology and pathophysiology of insomnia (as opposed to cognitive or somatic arousal).

3) The proposition that cortical arousal, in the context of chronic insomnia, occurs as a result of classical conditioning and is permissive of processes that do not occur with normal sleep (i.e., increased sensory and information processing at sleep onset and during NREM sleep).

4) The proposition that sleep initiation and maintenance problems do not occur because of "hyperarousal" per se, but because of increased sensory and information processing (i.e., the increased likelihood of detecting internal or external events and experiencing startle and/or orienting responses to such events).

5) The suggestion that sleep state misperception derives from an attenuation of the normal mesograde amnesia of sleep (i.e., the recollection of events that occur during the sleep period serves to blur the phenomenologic distinction between sleep and wakefulness).

6) The hypothesis that conditioned cortical arousal is self reinforcing. That is, if sleep related stimuli (X) elicit cortical arousal (Y), and the occurrence of Y reinforces the association of X and Y, then pairing is self-reinforcing. This is particularly important in that this virtually guarantees that the insomnia will 1) in the absence of its original precipitants, continue unabated, and 2) not be subject to extinction as it usually occurs with classical conditioning.

The Neurocognitive model is supported by a series of small scale studies that show: 1) patients with chronic insomnia (as compared to good sleepers) exhibit increased CNS activation, as assessed with quantitative EEG and imaging studies[43-46]; 2) that the regions identified as activated via imaging are associated sensory processing, information processing, and/or long term memory formation[46,47]; 3) patients with chronic insomnia (as compared to good sleepers) exhibit increased sensory and information process (and also a lack of inhibition of these processes) at around sleep onset and during NREM sleep, as assessed with Evoked Response Potential methodology[43-45]; and 4) patients with chronic insomnia (as compared to good sleepers) exhibit increased long term memory for acoustic stimuli presented at around sleep onset and during NREM sleep.[48] To date no prospective study has shown that patients with acute insomnia who develop chronic insomnia do indeed exhibit alterations in sensory processing, information processing, and/or long term memory formation and that this differentiates them from subjects who recover from acute insomnia.

Cognitive Models

The cognitive perspective has been, in principle, around since time immemorial and is essentially the proposition that worry has a central etiologic role in the precipitation and perpetuation of insomnia.[49] With respect to the precipitation of insomnia, the concept is that sleep is characterized by, initiated by, and maintained by, the absence of cognitive processes. Therefore, any event or disease process that gives rise to intrusive thoughts, rumination, or perseveration (regardless of the content of the thoughts themselves) should prohibit the initiation and/or maintenance of sleep. Consistent with this view, are the

*The term "Sleep Homeostat" is used for its heuristic value, at present no structure has been identified as the "master controller of sleep homeostasis (i.e., a structure that is akin to the SCN).

results from a variety of studies that show that patients with chronic insomnia exhibit higher scores on instruments measuring factors related to worry[50,51] and that patients with insomnia engage in more sleep-related worry during the pre-sleep period.[52,53] Moreover, there is one study, although cross-sectional, that does show differences in worry between normal sleepers, people with acute insomnia and people with chronic insomnia.[54] What has not been demonstrated is that intrusive thoughts, rumination, or perseveration (in and of themselves) mediate the transition from good sleep to acute insomnia.

With respect to the perpetuation of insomnia, the role of worry was not formally explicated until Morin[55] suggested that dysfunctional beliefs about sleep (specifically this type of worry) may serve to perpetuate insomnia. This point of view is buttressed by several studies which show that patients with insomnia endorse sleep related dysfunctional beliefs to a greater extent than good sleepers, and that treatment of insomnia is associated with a reduction in these beliefs.[56] While most would agree that dysfunctional beliefs play an important role in the perpetuation of chronic insomnia, the empirical findings to date are limited. A strong "proof of concept" is required, one where it is shown that patients with acute insomnia who develop chronic insomnia do indeed exhibit more dysfunctional beliefs and that this differentiates them from subjects who recover from acute insomnia.

More recently, the cognitive perspective has been greatly elaborated to include an information processing perspective. That is, insomnia not only occurs in association with worry but with a fundamental alteration in the way that individuals perceive, remember, and respond to events related to the experience of insomnia. This paradigmatic shift was nearly simultaneously initiated by the group at Oxford University led by Dr. Allison Harvey (now at UC Berkeley) and the group from the University of Glasgow led by Dr. Colin Espie.

According to the Harvey[2] model (2002), acute insomnia occurs in association with life stress, sub-chronic insomnia occurs with worry about sleeplessness, and chronic insomnia is maintained by selective attention, distorted perceptions of daytime deficits, and counterproductive safety behaviors. Selective attention refers to the development of an attentional set where the individual regularly monitors the internal (e.g., mental alertness or body sensations) and external (e.g., the bedroom clock or noise) environments for sleep-related threats. This change in attentional set is thought to be automatic and the increased effort to detect sleep related 'threats' is presumed to result in increased detection of sleep-related threats. Detection of sleep-related threats increases both cognitive and physiologic arousal and reinforces monitoring behavior and is therefore self-perpetuating. In addition to the sleep-related alterations in attentional processes, Harvey also points to increased attention to the daytime consequences of insomnia (e.g., increased fatigue, irritability and dysphoric mood, gastrointestinal distress, loss of perceived attractiveness, and memory and concentration problems). Individuals with insomnia are concerned about the consequences of sleeplessness and are thought to selectively attend to daytime problems and attribute these problems exclusively to poor sleep. As with monitoring for "sleep-related threats", monitoring for daytime deficits also increases the chance of detecting both the occasional relevant symptom and/or random symptoms. Unlike the monitoring that occurs at night (which directly interferes with sleep initiation and maintenance), the detection of daytime consequences prompts the engagement of safety behaviors. This term, which is borrowed from the anxiety disorders literature, refers to the engagement of compensatory behaviors which are thought to mitigate the social or personal costs of sleeplessness. For example, if one is particularly irritable owing to sleep loss, one might avoid social interactions and thereby the occurrence of adverse events. From the patient point of view, this may seem a reasonable strategy and a successful one. From the cognitive point of view, the need for "avoidance" is never actually put to the test. The consequence of the strategy is that safety behaviors become self reinforcing and thus ensures that the insomnia always has daytime effects (and this contributes to illness chronicity, if not severity). It should be noted that the behavioral phenomenon of sleep extension could easily be considered one kind of safety behavioral (i.e., a behavioral adaptation to perceived sleeplessness). To our knowledge, Harvey and colleagues do not specify that this is the case.

This important conceptualization is supported by a variety of empirical studies conducted by the Oxford/Berkeley group wherein they have shown that patients with insomnia do indeed appear to excessively monitor their sleep environment,[57] selectively attend to sleep related stimuli,[58,59] and engage in daytime safety behaviors.[60] Whether the cognitive and behavioral factors delineated by this perspective represent primary perpetuating factors for chronic insomnia, versus predisposing factors, remains to be demonstrated. Although there is evidence that children who are 'at risk' of developing insomnia demonstrate an attention bias to sleep-related cues.[61] Further, the primacy of these factors with respect to the natural history of insomnia have yet to evaluated. That is, whether these factors distinguish between patients with acute and chronic insomnia, and at what point do these factors come into play across the illness trajectory relative to other factors (e.g., instrumental and classical conditioning, cortical activation, etc.).

The Espie cognitive model (2002/2006)[3,62] differs from that of Harvey in that it proposes that insomnia occurs in association with 1) the inhibition of sleep related de-arousal (failure to inhibit wakefulness) and 2) attention to the phenomenon of sleep (as opposed to sleep related threats), the intention to "get sleep", and effort to "achieve sleep". The model, variably referred to as the "Psychobiological Inhibition Model and/or the A-I-E Model (for attention-intention-effort), posits that acute insom-

nia occurs because of an alteration in the neurobiologic mechanisms that normally inhibit wakefulness. While the authors do not explicitly address the issue, the alteration may be viewed as inherently pathological or as systemic part of the "flight-fight" response (which depending on the context may or may not be adaptive). The failure to inhibit wakefulness is, in turn, thought to result in two cognitive phenomena. First, when individuals are unable to sleep, attention is drawn to what is otherwise an automatic process. Increased attention prevents the perceptual and behavioral disengagement necessary for sleep onset to occur. Second, attentional focus produces an intention to sleep, where sleep becomes a purposeful goal; one which cannot be attained simply by virtue of the occurrence of attention and intention. Third, effort is expended in achieving "what is intended" and the individual "tries" to fall asleep. This effort, like enhanced attention and intention, serves only to extend wakefulness. Support for the Psychobiological Inhibition Model is provided by eight studies where the findings reliably indicate

- Sleep-related mental preoccupation may be associated with the transition from acute to chronic insomnia[52,63,64]
- That subjects with psychophysiological insomnia exhibit heightened levels of attention bias (as compared to good sleepers and individuals with Delayed Sleep Phase Syndrome subjects)[65,66]
- Attention bias to sleep-related stimuli detected in patients with psychophysiological insomnia may be driven by 'threat'[66-69]
- That there are positive linear relationships between sleep-related attentional bias and self reported sleep quality and sleepiness[65]
- That subjects with psychophysiological insomnia exhibit "effortful preoccupation with sleep"[70]

Both the Harvey and Espie models provide formidable conceptualizations of the role of cognitive processes in the development of chronic insomnia. The models are similar owing to a common focus on attentional processes. A distinction of the Harvey model is that it is more articulate with respect to the consequences of selective attention being the engagement of 'safety behaviors'. It is also much more elaborative when it comes to diurnal effects of insomnia and how selective attention and safety behaviors in that context serve to make insomnia self-perpetuating. A distinction of the Espie model is that it is more articulate with respect to how the attentional bias comes to be and how it leads to sleep effort, with the latter proposed as a primary precipitating and perpetuating factor. Finally, the Espie model provides for a paradigmatic shift in how the pathophysiology of insomnia is conceptualized. The central etiologic agent is not hyperarousal, it is the failure to inhibit wakefulness.[71] The conceptual distinction may ultimately lead to the proposition that acute insomnia occurs in relation stress induced hyperarousal but that chronic insomnia occurs simply as sustained wakefulness (despite the proper circadian phase for sleep and "normal" homeostatic pressure for sleep).

From a natural history point of view, the two models suggest a clear sequence of events in the transition from good sleep to acute insomnia to chronic insomnia: 1) There is a real or perceived stressor; 2) with a resolution (partial or total) of the stressor there is a attentional shift toward sleeplessness itself and/or toward factors that are thought to interfere with the ability to initiate or maintain sleep; and 3) behavioral changes are enacted to "get more sleep" and/or to fend off the consequences of sleep loss. To date, the sequence as whole has not been evaluated in a longitudinal study (from good sleep to chronic insomnia). Cross sectional studies have provided support for the models to the extent that patients with chronic insomnia exhibit more of these signs than good sleepers, subjects with acute insomnia, or subjects with forms of insomnia that are presumably more biologically based (e.g., delayed sleep phase syndrome). Longitudinal studies with limited sampling and large temporal windows (i.e., two point sampling where the assessments are separated by months) have provided support for the models to the extent that patients with acute insomnia show fewer of the aforementioned phenomena than then when the insomnia is chronic.

What We Need to Know (Towards a Natural History of Insomnia)

One definition for the natural history of a disease is that it "…refers to a description of the uninterrupted progression of the disease in an individual from the moment of exposure to the causal agents until recovery or death".[72] As such, a true understanding of the natural history of insomnia requires 1) agreement about what insomnia is and 2) detailed investigation at the time the insomnia is first developing with a temporal resolution that allows for the detection of behavioral and cognitive changes that over days to weeks. Accordingly, what is needed is a large scale, multi-year, prospective study to evaluate the putative "causal agents" delineated in the above models and how they vary in time, are sequenced, and predict clinical course and illness severity. More specifically, the following issues need to be addressed.

1) The distinction between acute and chronic insomnia needs to be formulated on the basis of data such that an empirically determination is made regarding how frequent the insomnia has to be and/or how persistent the insomnia has to be before it may be considered likely to become chronic (i.e., how much time must pass before it is unlikely that the patient will exhibit a spontaneous remission or recovery).[73] For a comprehensive review of this issue, please see Ellis et al.[74]

2) The assessment and diagnosis of insomnia needs to take into account illness severity (e.g., Sleep Latency of 0-5 minutes = excessively sleepiness, 5-15 minutes = normal, 15-30 = mild insomnia, 30-45 = moderate insomnia, 45-90 minutes = se-

vere, > 90 minutes is suggestive of Paradoxical Insomnia). Such scaling could be done based on historical precedence but would like be more useful if these determinations were made empirically. An ideal approach to this determination would be to both account for population norms [what number has the best fit (sensitivity and specificity) to the occurrence of complaint][73] and how illnesses severity maps onto functional consequences. Put differently, 1) how long does sleep latency or wake after sleep onset need to be considered by the individual as problematic (based on epidemiologic assessment strategies that take into account at least age and sex) and 2) how severe do sleep initiation and maintenance problems need to be to correspond to interpersonal, performance, and/or health deficits. As, or more important, illness severity needs to be tracked over time to directly test the association between chronicity and severity (i.e., is it the case that with time sleep initiation and/or maintenance problems become worse, less severe, or simply stable).

3) While the DSM V will provide quantitative cutoffs for illness frequency and chronicity, it may be argued that these cutoffs should also be re-evaluated using empirical strategies like those specified above. Further, the frequency of insomnia (nights per week) also needs to be tracked over time to directly test this association.

4) The factors that have been hypothesized to predispose, precipitate, and perpetuate insomnia (and to mediate/moderate the transitions from good sleep to acute insomnia, from acute insomnia to the recovery of good sleep, or from acute insomnia to chronic insomnia) need to be directly assessed from within a large scale natural history study (longitudinal study) that has a sufficient "sampling rate" to detect when transitions occur and sufficient power to assess the predictive utility of, alone and in combination, multiple mediators and moderators. Ideal candidates are suggested in Table 1.

Concluding Remarks

In 2005 NIH State of the Science Conference report[75] stated that "the paucity of literature describing the natural course of insomnia underscores the need for large-scale longitudinal studies…". To date there has only been one published study by the Laval group that responded to NIH's call for additional research. The data from this study have been informative and are likely to continue to yield important findings in the future. This said, the Laval study needs to be followed up with an investigation that has enhanced temporal resolution (ideally daily assessments over months to years) and uses instruments that allow one to assess the constructs of interest (ideally dedicated and validated measures). Such a study will 1) allow for an as-

Table 1. Factors to track

Predispositional factors	Precipitational factors	Perpetuational factors
Good sleep to acute insomnia	Good sleep to acute insomnia	Acute to chronic insomnia
Biological domain	Biological domain	Biological domain
Sleep need, ability, & plasticity	New onset medical illness[4]	Chronic medical illness[4]
Metabolic rate cumulative	New onset psychiatric illness[4]	Chronic psychiatric illness[4]
Medical burden cumulative	Acute injury[4]	Conditioned CNS activation[5]
Psychiatric burden	Psychological domain	Altered sensory processing[6]
Psychological domain	Emergent life stress events	Psychological domain
Personality factors (N.E.O)[1]	Cumulative stress	Poor stimulus control[7]
Stress reactivity	Social domain	Bedroom as CS for insomnia[8]
Current stress	Change in safety of sleep environs	Sleep extension[9]
Life stress events[2]	Change in co-sleeping conditions	Altered information processing[10]
Coping style and ability	Change in sleep schedule	Attention bias[11]
Social domain		Selective attention & monitoring[12]
Safety of sleep environs		Attenuation of normal sleep MA[13]
Co-sleeping[3]		Engagement of safety behaviors[14]
New parenthood		Engagement of sleep effort[15]
		Social domain
		Change in safety of sleep environs
		Change in co-sleeping conditions
		Change in sleep schedule

[1]Neuroticism, introversion/extroversion, openness, etc. [2]Positive or negative events. [3]Coherence of preferred sleep phases between partners. [4]Illness or injury may precipitate (and/or perpetuate) sleep initiation or maintenance problems via pain and/or discomfort... or thru the alteration of sleep need and/or ability. [5,6,10,13]Neurocognitive model. [7,8]Stimulus Control model. [9]Spielman-3P model. [11,15]Psychobiological Inhibition Model, A-I-E Model. [12,14]Harvey model.
MA: Mesograde amnesia, CS: conditioned stimulus.

sessment of the relative importance of the putative causal factors and 2) position the field to develop not only better therapies but also preventive strategies.

Conflicts of Interest

The authors have no financial conflicts of interest.

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