Alternative and complimentary methods in the treatment of sleep disorders and/or insomnia.

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ABSTRACT

OBJECTIVE: Insomnia is defined as the subjective experience of insufficient sleep or of sleep that is not refreshing. People troubled by insomnia often report difficulty falling asleep, frequent nightmare awakenings or excessive arousal in the morning . Over the course of a year, over one-half of the United States will have difficulty falling asleep. About 20-30% of the population experiences insomnia on a regular basis. Many use over-the-counter sedative medications to combat insomnia, while others seek stronger drugs. Each year up to 10 million people in the United States receive prescriptions for drugs to help them to go to sleep, the side effects of which are well known but the ramifications of sleepless nights make many choose the lesser of two evils. The objective of this literature review is to present a narrative review regarding the efficacy of alternate and complimentary methods to hypnotic and narcotic prescription based drug use in the treatment of sleep disorders and/or insomnia.

METHOD: A PubMed search was conducted including randomized, controlled trials and/or meta analyses in which the main objective of the study was the treatment of insomnia either with traditional or non-traditional therapies.

DISCUSSION: This literature review outlines the current available research on the biology of sleep as it relates to traditional and alternative approaches to treatment for insomnia. There were no randomized clinical trials specific to chiropractic and insomnia. The studies for herbal supplementation by and large had low methodological scores. Research on the biology and function of sleep are also highlighted in an effort to better illustrate the necessity of clinical understanding of sleep related disorders. Author algorithms for the assessment and management of insomnia in primary care are also presented.

CONCLUSION: Current literature is less favorable for the use of herbal supplementation in the treatment of insomnia, however cognitive behavioral therapies (as an adjunct to better sleep hygiene practices) and acupuncture seem to have positive evidence to support preliminary conclusions though more research is needed.

INTRODUCTION:

"Sleep is a behavioral state that is a natural part of every individual's life. We spend about one-third of our lives asleep. Nonetheless, people generally know little about the importance of this essential activity. Sleep is not just something to fill time when a person is inactive. Sleep is a required activity, not an option. Even though the precise functions of sleep remain a mystery, sleep is important for normal motor and cognitive function. We all recognize and feel the need to sleep. After sleeping, we recognize changes that have occurred, as we feel rested and more alert. Sleep actually appears to be required for survival. Rats deprived of sleep will die within two to three weeks, a time frame similar to death due to starvation."[1]

It is not normal for a person to be sleepy at times when he or she expects to be awake. Problem sleepiness may be associated with difficulty concentrating, memory lapses, loss of energy, fatigue, lethargy, and emotional instability.[2] The prevalence of problem sleepiness is high and has serious consequences, such as drowsy driving or workplace accidents and errors.[2-4] Lifestyle factors and undiagnosed or untreated sleep disorders can cause problem sleepiness. Lifestyle factors include not getting enough sleep, having an irregular sleep schedule, and using alcohol or certain medications.[3] Of the more than 70 known sleep disorders, the most common are obstructive sleep apnea, insomnia, narcolepsy, and restless legs syndrome.[1,3,6] Large numbers of individuals suffering from these sleep disorders are unaware of—and have not been diagnosed or treated for—their disorder.[3]

Insomnia can mean different things depending on the clinical picture presented by the subject. Insomnia can be a complaint (related to sleep quantity or quality), a symptom (part of a sleep disorder or of a mental or organic disorder) or a diagnosed sleep disorder (primary or secondary), indicating the need for a differential diagnosis process.[3] Some epidemiological studies have attempted to define these distinctions. The DSM-IV describes the essential features of insomnia disorder as follows: a predominant complaint of insomnia that lasts for at least one month and that causes significant distress or daytime impairments in social, occupational or other sectors of daily life.[5]

The prevalence of insomnia increases with age, and is more common in women than in men. Lower socioeconomic status, divorce, widowhood, separation, recent life stressors, depression, and substance abuse increase the risk of insomnia. Insomnia has also been independently associated with worse health-related quality of life in outpatients at family medicine, internal medicine, endocrinology, cardiology, and psychiatry clinics. Women are twice as likely to suffer from insomnia than men, due to bodily changes (eg, pregnancy, menopause), or perhaps as some of the social factors (eg, unemployed or divorced) may be more common in women.[3,5]

Normal sleep architecture refers to a characteristic pattern of sleep and consists of two major stages, nonrapid eye movement (NREM; comprises 75%–80% of total sleep) and rapid eye movement (REM). Normal adult sleep begins with NREM and alternates between NREM and

REM every 90 minutes. Normal sleep latency is approximately 10–20 min and total sleep time (TST) averages 6–9 hours. NREM sleep is characterized by relatively quiescent brain activity, decreased metabolic rate, and slow-wave sleep, which are theorized to be necessary for physiologic restoration. Sleep is greatest when very young and least when old.[1; 43]

Concerning sleep quality, 25.3% of the general population were dissatisfied with their sleep, 29.9% reported insomnia symptoms and 9.5% met criteria for an insomnia syndrome.[3] While few insomnia sufferers seek professional consultations, many individuals initiate self-help treatments, particularly when daytime impairments such as fatigue become more noticeable.[4-6]

Insomnia is associated with increased psychological symptomatology and perceived stress, higher predisposition to arousal and higher impairment of health quality. Insomnia has a close association with depression and anxiety.[5;34]

Chronic insomnia affects approximately 9% to 12% of the population as defined by the DSM-IV criteria.[3,4-6] Hypnotic drugs are generally prescribed to patients with insomnia. The frequency with which sleep medication is prescribed vary widely. Prescription rates of anxiolytic, hypnotic and sedative medications increased sharply over the last half decade, and zolpidem (generic for the popular drug, Ambien) is increasingly prescribed for insomnia for the general population. Gender differences in prescription rates reflect the higher prevalence of anxiety and sleep disorders in women.[6-7] Some sources say that the frequent use of these drugs in elderly people warrants further exploration because of the concomitant increased risks of mortality and morbidity.[3;8]

A meta-analysis of studies on sedative hypnotics (which typically include benzodiazepines) has shown that these drugs caused a number of side effects when used repeatedly for as little as a few weeks. Side effects included habituation, physical and psychological dependency, daytime psychomotor and cognitive impairment, daytime drowsiness or anxiety, iatrogenic sleep disturbance (involving suppression of slow-wave sleep and rapid eye movement (REM) sleep) and rebound insomnia upon the abrupt discontinuation of sedative hypnotic therapy. (See also discussion below related to study by Zavesicka et al).[39]

In addition, the use of non-pharmacological interventions has been increasing in the general population. According to a nationwide government survey, approximately 38% of U.S. adults aged 18 years and over and approximately 12% of children use some form of complementary or alternative medicine (CAM). CAM is a group of diverse medical and health care systems, practices and products that is not generally considered part of conventional medicine. Complementary medicine is used together with conventional medicine, while alternative medicine is used in place of conventional medicine. Integrative medicine combines conventional and CAM treatments for which there is evidence of safety and effectiveness.[1]

BIOLOGY OF SLEEP (SLEEP ARCHITECTURE)

Sleep is a very important process and is characterized by a stereotypical posture, little movement, and a decrease in response to stimuli. These characteristics might also describe coma, but in sleep, unlike in coma, the characteristics are reversed each morning. Because creatures are not eating or mating and are also very vulnerable to attack by predators during sleep, sleep must have a very important function to make it worthwhile.[1;9]

Sleep is also a very insistent drive. Whereas a person can voluntarily stop eating until he or she dies, the human body cannot force itself to stay awake indefinitely. In fact, there are situations when falling asleep might mean death (while driving a car, for example), yet the desire to sleep is so insistent that body will still succumb to it.[9]

Sleep Stages: Sleep architecture describes the structure and pattern of sleep and encompasses several variables.[1;9;39] Sleep quotas refer to the amount of time spent in REM and NREM sleep**.** Sleep is divided into two main stages: REM sleep (which stands for "rapid eye movement"), and non-REM (NREM) sleep. These stages are characterized by changes measured on instruments such as the electroencephalograph (EEG), which measures changes in electrical signals in the brain; electrooculogram (EOG), which measures eye movements; and the electromyogram (EMG), which measures muscle movements. In humans, REM and NREM sleep alternate in ninety-minute cycles approximately three to six times per night. During the first part of the sleep cycle, REM sleep takes approximately ten minutes of each cycle, but REM sleep periods become longer and closer together as the course of sleep progresses (see figure 1).

Non-REM sleep is divided into four stages. As one progresses from stage one to stage four, sleep gets deeper and EEG waves become taller and slower; stages three and four are often grouped together and called slow wave sleep (SWS). During SWS, muscle movements and eye movements are diminished in comparison to wakefulness, and the EEG is more synchronized, indicating that large portions of brain tissue are firing together.[9]

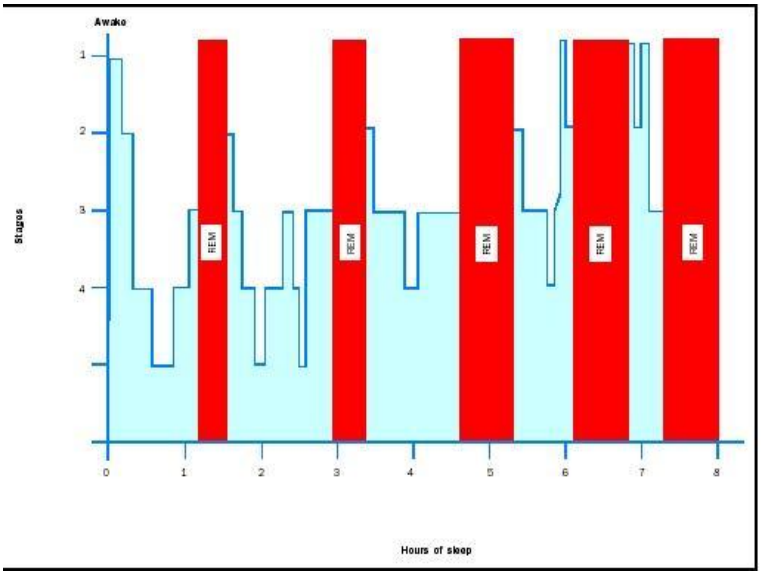

Figure 1. Stages of sleep (Images Courtesy of Wikipedia.org)

REM sleep is characterized by a desynchronized EEG, a lack of thermoregulation, loss of tone in the skeletal muscle, erections of the penis or clitoris, rapid eye movements, and dreams. As seen by the desynchronized EEG, which is similar to the brain patterns seen during wakefulness, the brain is very active during REM sleep. However, one part of the brain that does shut off during REM sleep is the part of the hypothalamus that is responsible for temperature regulation. During REM sleep, the body does not thermoregulate and therefore does not shiver or sweat.[9]

Skeletal muscles are also less active during REM sleep and thus lose muscle tone. This loss enables the muscles to relax during REM sleep. It also prevents people from acting out their dreams (sleep walking occurs during NREM sleep, when muscle tone is maintained but diminished). Not all muscles lose their tone during REM sleep. The diaphragm, necessary for breathing, continues to contract. Muscles are also active in the eyes: although the lids are closed, the eyes dart back and forth during REM sleep, which gives REM its name.[9-10]

During REM sleep the penis and clitoris often become erect, but this is not necessarily related to dream content. Although REM sleep is associated with dreams, dreams actually occur during all stages of sleep. The dreams that occur during REM sleep have characteristics different from those dreams in NREM sleep. REM dreams are longer, more emotional, and more visual than NREM dreams, and they usually do not follow the events of the day as closely as NREM dreams.[1;9-10]

Neurological Control: A common misconception is that the brain shuts down during sleep.[9] In truth, parts of the brain may be even more active during NREM or REM sleep than during wakefulness. The level of consciousness depends upon the activity of the reticular activating system, a network of neurons in the brainstem that send projections throughout the thalamus, hypothalamus, and cerebral cortex. Certain areas of the brain have been found to be responsible for causing different sleep stages. Whereas NREM sleep is controlled by the basal forebrain (the anterior hypothalamus and adjacent forebrain areas), REM sleep is mostly controlled by an area in the brainstem called the pons.[9-10]

Biological clock: An internal biological clock regulates the timing for sleep in humans. The activity of this clock makes us sleepy at night and awake during the day. Our clock cycles with an approximately 24-hour period and is called a circadian clock (from the Latin roots *circa* = about and *diem* = day). In humans, this clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus in the brain (see Figure 2). The SCN is actually a very small structure consisting of a pair of pinhead-size regions, each containing only about 10,000 neurons out of the brain's estimated 100 billion neurons.[9]

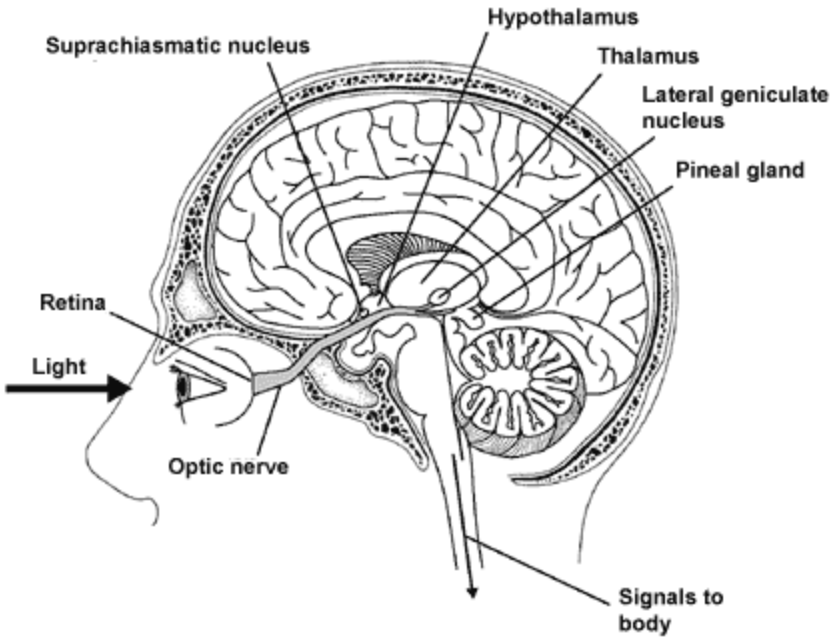

Figure 2. The biological clock is located within the suprachiasmatic nucleus in the brain[8-9] (Image courtesy of Wikipedia.org)[39]

Biological clocks are genetically programmed physiological systems that allow organisms to live in harmony with natural rhythms, such as day/night cycles and the changing of seasons. The most important function of a biological clock is to regulate overt biological rhythms like the sleep/wake cycle. The biological clock is also involved in controlling seasonal reproductive cycles in some animals through its ability to track information about the changing lengths of daylight and darkness during a year.[10]

Biological rhythms are of two general types. Exogenous rhythms are directly produced by an external influence, such as an environmental cue. They are not generated internally by the organism itself, and if the environmental cues are removed, the rhythm ceases. Endogenous rhythms, by contrast, are driven by an internal, self-sustaining biological clock rather than by anything external to the organism. Biological rhythms, such as oscillations in core body temperature, are endogenous. They are maintained even if environmental cues are removed.

Because the circadian clock in most humans has a natural day length of just over 24 hours, the clock must be entrained, or reset, to match the day length of the environmental photoperiod (that is, the light/dark, or day/night, cycle).

Because the circadian clock in most humans has a natural day length of just over 24 hours, the clock must be entrained, or reset, to match the day length of the environmental photoperiod (that is, the light/dark, or day/night, cycle).[11] The cue that synchronizes the internal biological clock to the environmental cycle is light. Photoreceptors in the retina transmit light-dependent signals to the SCN.[9-10] Interestingly, our usual visual system receptors, the rods and cones, are apparently not required for this photoreception. Special types of retinal ganglion cells are photoreceptive, project directly to the SCN, and appear to have all the properties required to provide the light

signals for synchronizing the biological clock. At the SCN, the signal interacts with several genes that serve as "pacemakers."[9]

Another interesting rhythm that is controlled by the biological clock is the cycle of body temperature, which is lowest in the biological night and rises in the biological daytime. This fluctuation persists even in the absence of sleep. Activity during the day and sleep during the night reinforce this cycle of changes in body temperature.[10]

The release of melatonin, a hormone produced by the pineal gland, is controlled by the circadian clock in the SCN. Its levels rise during the night and decline at dawn in both nocturnal and diurnal species.[11] Melatonin has been called the hormone of darkness because of this pattern. The SCN controls the timing of melatonin release; melatonin then feeds back on the SCN to regulate its activity. In mammals, for example, most of the brain receptors for melatonin are located in the SCN.[9] Research has demonstrated that administering melatonin can produce shifts in circadian rhythms in a number of species including rats, sheep, lizards, birds, and humans. These effects are most clearly evident when melatonin is given in the absence of light input. Thus, for example, giving melatonin to blind people can help set their biological clocks. Melatonin is available as an over-the-counter nutritional supplement.[10] Although claims are made that the supplement promotes sleep, the evidence for this is inconclusive. Potential side effects of long-term administration of melatonin remain unknown, and its unsupervised use by the general public is discouraged.

In addition to synchronizing these daily rhythms, biological clocks can affect rhythms that are longer than 24 hours, especially seasonal rhythms. Some vertebrates have reproductive systems that are sensitive to day length. These animals can sense changes in day length by the amount of melatonin secreted. The short days and long nights of winter turn off the reproductive systems of hamsters, while in sheep the opposite occurs. The high levels of melatonin that inhibit reproduction in hamsters stimulate the reproductive systems of sheep, so they breed in winter and give birth in the spring.

Biological clocks exist in a wide range of organisms, from cyanobacteria (blue-green algae) to humans.[9] Clocks enable organisms to adapt to their surroundings. Although scientists currently believe that clocks arose through independent evolution and may use different clock proteins, they all share several regulatory characteristics. In particular, they are maintained by a biochemical process known as a negative feedback loop. This feedback loop often involves cues from the environment which directly impacts biological processes in the brain.[9-11] Jet lag is a common example of the disruption of the clock which results from the inability of our circadian clock to make an immediate adjustment to the changes in light cues that come from a rapid change in time zone.[12-15]

One negative consequence of our circadian cycle afflicts travelers who rapidly cross multiple time zones. Jet lag produces a number of unwanted effects including excessive sleepiness, poor sleep, loss of concentration, poor motor control, slowed reflexes, nausea, and irritability.[12] Jet lag results from the inability of our circadian clock to make an immediate adjustment to the changes in light cues that an individual experiences when rapidly crossing time zones. After such travel, the body is in conflict. The biological clock carries the rhythm entrained by the original time

zone, even though the clock is out of step with the cues in the new time zone. This conflict between external and internal clocks and signals is called desynchronization, and it affects more than just the sleep/wake cycle. All the rhythms are out of sync, and they take a number of days to re-entrain to the new time zone. Eastward travel generally causes more severe jet lag than westward travel, because traveling east requires that we shorten our day and adjust to time cues occurring earlier than our clock is used to.[13]

In general, the human circadian clock appears better able to adjust to a longer day than a shorter day. For example, it is easier for most people to adjust to the end of daylight savings time in the fall when we have one 25-hour day than to the start of daylight savings time in the spring, when we have a 23-hour day. Similarly, traveling from the West Coast of the United States to the East Coast produces a loss of three hours—a 21-hour day. Thus, travelers may find it difficult to sleep because of the three-hour difference between external cues and their internal clock. Likewise, travelers may find it difficult to awaken in the morning. We may try to go to sleep and wake up at our usual local times of, say, 11 p.m. and 7 a.m., but to our brain's biological clock, the times are 8 p.m. and 4 a.m.[11-13] Other circadian rhythm problems include:

- *Monday morning blues.* By staying up and sleeping in an hour or more later than usual on the weekends, we provide our biological clock different cues that push it toward a later nighttime phase. By keeping a late sleep schedule both weekend nights, our internal clock becomes two hours or more behind our usual weekday schedule. When the alarm rings at 6:30 a.m. on Monday, our body's internal clock is now set for 4:30 a.m. or earlier.[12-15]
- *Seasonal affective disorder (SAD).* A change of seasons in autumn brings on both a loss of daylight savings time (fall back one hour) and a shortening of the daytime. As winter progresses, the day length becomes even shorter. During this season of short days and long nights, some individuals develop symptoms similar to jet lag but more severe. These symptoms include decreased appetite, loss of concentration and focus, lack of energy, feelings of depression and despair, and excessive sleepiness. Too little bright light reaching the biological clock in the SCN appears to bring on this recognized form of depression in susceptible individuals. Consequently, treatment often involves using light therapy. [13]
- *Shift work.* Unlike some animals, humans are active during daylight hours. This pattern is called diurnal activity. Animals that are awake and active at night (for example, hamsters) have what is known as nocturnal activity. For humans and other diurnally active animals, light signals the time to awake, and sleep occurs during the dark. Modern society, however, requires that services and businesses be available 24 hours a day, so some individuals must work the night shift. These individuals no longer have synchrony between their internal clocks and external daylight and darkness signals, and they may experience mental and physical difficulties similar to jet lag and SAD.[13;15]

Functions of Sleep: Animal studies have demonstrated that sleep is essential for survival. Consider studies that have been performed with laboratory rats. While these animals will normally live for two to three years, rats deprived of REM sleep survive an average of only five months. Hamsters deprived of all sleep survive only about three weeks.[15] In humans, extreme sleep deprivation can cause an apparent state of paranoia and hallucinations in otherwise healthy individuals.[12] However, despite identifying several physiological changes that occur in the brain

and body during sleep, scientists still do not fully understand the functions of sleep.[9] Many hypotheses have been advanced to explain the role of this necessary and natural behavior. The following examples highlight several of these theories:

*Hypothesis: Restoration and recovery of body systems***.** This theory recognizes the need of an organism to replenish its energy stores and generally repair itself after a period of energy consumption and breakdown (wakefulness). The brain remains active during sleep, and the low metabolic rate characteristic of sleep is thought to be conducive to biosynthetic reactions. There is little, if any, evidence that more repair occurs during sleep than during rest or relaxed wakefulness. In fact, whole-body protein synthesis decreases during sleep, which is consistent with sleep being a period of overnight fasting.

Hypothesis: Energy conservation. This theory states that we sleep to conserve energy and is based on the fact that the metabolic rate is lower during sleep. The theory predicts that total sleep time and NREM sleep time will be proportional to the amount of energy expended during wakefulness. Support for this theory is derived from several lines of evidence. For example, NREM and REM sleep states are found only in endothermic animals (that is, those that expend energy to maintain body temperature). Species with greater total sleep times generally have higher core body temperatures and higher metabolic rates. Consider also that NREM sleep time and total sleep time decrease in humans, with age, as do body and brain metabolism. In addition, infectious diseases tend to make us feel sleepy. This may be because molecules called cytokines, which regulate the function of the immune system, are powerful sleep inducers. It may be that sleep allows the body to conserve energy and other resources, which the immune system may then use to fight the infection.

Hypothesis: Memory consolidation. The idea here is that sleeping reinforces learning and memory, while at the same time, helping us to forget or to clear stores of unneeded memories. During the course of a day we are inundated with experiences, some of which should be remembered while others need not be. Perhaps sleep aids in rearranging all of the experiences and thoughts from the day so that those that are important are stored and those that are not are discarded. A recent study of songbirds suggests that sleep may play an important role in learning. Young birds listened to the songs of adult birds and began to practice and refine their own songs. The scientists were able to monitor the firing of individual brain cells involved with singing. They found that if sleeping birds listened to a recording of their own song, their neurons would later fire in a pattern nearly identical to that of song production though no sound was produced. The researchers speculate that the birds dream of singing; they relay and rehearse their songs and strengthen the nerve patterns required for song production. Sleep appears to be important for human learning as well. People who get plenty of deep NREM sleep in the first half of the night and REM sleep in the second half improve their ability to perform spatial tasks. This suggests that the full night's sleep plays a role in learning—not just one kind of sleep or the other.

Hypothesis: Protection from predation. Inactivity during sleep may minimize exposure to predators. At the same time, however, sleep decreases sensitivity to external stimuli and may, as a consequence, increase vulnerability to predation.

Hypothesis: Brain development. This proposed function of sleep is related to REM sleep, which occurs for prolonged periods during fetal and infant development. This sleep state may be involved in the formation of brain synapses.

Hypothesis: Discharge of emotions. Perhaps dreaming during REM sleep provides a safe discharge of emotions. As protection to ourselves and to a bed partner, the muscular paralysis that occurs during REM sleep does not allow us to act out what we are dreaming. Additionally, activity in brain regions that control emotions, decision making, and social interactions is reduced during sleep. Perhaps this provides relief from the stresses that occur during wakefulness and helps maintain optimal performance when awake.

Unfortunately, each of these hypotheses suffers from flaws. Most fail because they cannot offer a mechanism for why sleep is more valuable than simply resting while remaining awake. In others, the shortcomings are more subtle. Although humans spend approximately one-third of their lives asleep, no one knows for sure what the function of sleep is. It is known that sleep is necessary for life. Constant sleep deprivation in rats leads to death. Studies suggest that constant deprivation of REM sleep alone causes metabolic changes in rats that can also lead to death.

There are a number of theories on the function of sleep. Sleep may help the body recover from an active day and give it the chance to restore substances that are lost during the day. However, since simply resting the body without sleep does not fulfill the same function as sleep, it is thought that there is more to sleep than resting.

Sleep may have developed evolutionarily as an adaptive mechanism to keep animals out of harm's way, preventing them from wandering around in the dark, vulnerable to accidents and attack by predators, during a time when food foraging may be less efficient. It is interesting to note that small animals with safe hiding places and large predators sleep a lot, whereas large prey sleep less often, suggesting sleep may be related to an animal's relative safety, although the evidence for this is far from clear. The question remains, however, why the complex process of sleep would have evolved to merely keep animals out of danger.

It is known that REM sleep is a necessary stage of sleep; however, the function of REM sleep is also unclear. Temporary REM sleep deprivation can lead people to become bad-tempered and uneasy. If REM deprivation continues, and the subject is then allowed to sleep undisturbed, he or she experiences "REM rebound," which means that REM sleep occurs more frequently and lasts longer than normal. There is evidence that REM sleep is necessary for learning and memory. Furthermore, theorists are proposing that REM sleep may be important in the development of the brain.

FACTORS AFFECTING SLEEP

Insomnia and other sleep disorders are caused by: medical, neurological, pain, and psychiatric disorders. In addition, medications and environmental factors can cause insomnia.[1,3-6] Finally, conversely, sleep disorders can worsen medical conditions. This section provides an overview of these interactions.

General medical disorders: Causes of insomnia include sleep disordered breathing, congestive heart failure, diabetes mellitus, thyroid disorders, chronic obstructive pulmonary disease (COPD), gastroesophageal reflux, cardiovascular disease, and renal disease. Problems such as frequent nocturnal awakenings in patients with congestive heart failure may be related to orthopnea or paroxysmal nocturnal dyspnea, or may reflect undiagnosed sleep breathing problems such as obstructive sleep apnea (OSA) or Cheyne–Stokes Breathing. Patients with COPD have decreased total sleep times and REM sleep. Shortness of breath, nocturnal cough, and wheezing worsen sleep. This leads to fatigue and sleep deprivation, which undermine the work of breathing and impair gas exchange. Airflow obstruction tends to worsen in the early morning hours in patients with COPD and asthma and may be related to REM effect on the diaphragm.[3]

Endocrine disorders: Endocrine disorders have also been associated with sleep disruption. Studies suggest that patients with diabetes mellitus have decreased total sleep times and impaired sleep quality secondary to nocturia and neuropathic pain. There is accumulating evidence that poor sleep impairs glucose metabolic control. Inadequate quality or quantity of sleep is shown to be a risk factor for developing type 2 diabetes in large prospective studies, and predicted increased levels of HbA1c in type 2 diabetics.[3]

Neurological disorders: Since the brain and its various systems are critical in regulating sleep and wakefulness, patients with neurologic disorders have an increased risk of developing sleep disorders. Patients with dementia, other neurodegenerative disorders (eg, Parkinson's), epilepsy, and traumatic brain injury (TBI) have a higher prevalence of sleep disturbance and sleep disorders. Post-stroke patients can develop insomnia or hypersomnia, which is a reduction in sleep latency, increased sleep, or excessive daytime sleepiness. Brain-injured patients are also susceptible to sleep problems, with incidences as high as 72.7% in the hospital (mostly sleep initiation and maintenance) and 51.9% in the community (mostly excessive somnolence); many with circadian rhythm sleep disorders.[3]

Pain: Between 50% and 70% of patients with chronic pain complain of impaired sleep. Sleep disruption is so common in fibromyalgia (75%) that it is considered to be a key diagnostic symptom. In burn patients, pain was associated with increased intermittent awakenings, prolonged periods of wake time, poor pain tolerance, and complaints of higher pain intensity the following day. Pain increases cortical arousals and awakening, and sleep deprivation increases pain sensitivity and vulnerability to pain by inhibiting opioid protein synthesis and/or reducing opioid receptor affinity.[3;5]

Women's health: Women have a higher rate of insomnia than men, nearly 2:1 in one survey. Psychosocial risk factors may be higher in women and they also contest with significant changes during pregnancy. Peri- and post-menopausal changes (eg, nocturia, hot flashes) affect many women, though ageing associated with such change may account for differences compared to pre-menopausal women.[3;5;8]

Psychiatric disorders: Sleep problems are so common in psychiatric conditions that insomnia is listed as a symptom for mood (eg, manic or depressive), anxiety, and substance abuse disorders. Sleep disturbance in patients with undiagnosed psychiatric disorders may alert primary care

providers to these problems. In a survey of 200 general medical patients in a hospital, 112 (56.5%) complained of insomnia and 100 (50%) met criteria for at least one psychiatric disorder – only 1.5% of those were charted – with depression most common at 35%. The results showed that patients with insomnia had 3.6 times higher risk of having depression than those without insomnia.[3;5]

An outpatient survey noted that chronic insomnia patients were 40 times more likely to have depression and six times more likely to have an anxiety disorder compared to those without insomnia. Longitudinal studies link prior insomnia with 2- to 5-times increased risk of mood and anxiety disorders and suicide.[5]

An estimated 65% with major depression have difficulty falling asleep, frequent awakenings, or early morning awakenings. Three patterns of sleep architecture abnormalities have been observed in patients with major depression: 1) sleep continuity disturbances characterized by prolonged sleep-onset, increased wake time during sleep, increased early morning wake time, and decreased total sleep time; 2) decreased proportion and length of SWS; and 3) REM sleep abnormalities such as reduced time to REM sleep, prolonged first REM sleep period, and increased REM sleep percentage.[5]

Medications affecting sleep: Sedatives and opioids may help with sleep onset, but actually impair sleep architecture. Hypnotic agents with a significant anticholinergic component, such as diphenhydramine, are particularly prone to decrease cognitive performance and may precipitate frank delirium. Hypnotics are often prescribed and mainly work for initial insomnia, but can sometimes worsen sleep. Similarly, benzodiazepines can be problematic, particularly in older patients by causing motor impairment and increasing risk for delirium. Other common offenders are anti-hypertensives, antihistamines, corticosteroids, antiepileptics, beta antagonists (particularly lipophilic ones like propranolol and timolol) decrease REM sleep and increase nightmares and insomnia, anabolic steroids and bronchodilator therapy.[4;6;17]

Environmental Factors: Many hospitals have difficulty adhering to the World Health Organization's recommendation of keeping noise level to ≤35 dB in hospital rooms, particularly intensive care units (ICUs), daytime peaks up to 150–200 dB and nighttime peaks >80 dB. By comparison, a running vacuum cleaner is about 80 dB. It follows, then, that residences, hotels and apartments have varying dB levels, often affecting sleep. Irregular sleep schedules, parenting young children and nighttime bathroom trips are common for many.[11;13]

Circadian rhythm sleep disorders are disorders that are related to the timing of sleep within the 24-hour day. They include time-zone change syndrome (ie, jet lag), shift work sleep disorder, irregular sleep-wake pattern, delayed or advanced sleep phase syndromes, and non-24-hour sleep-wake disorder. Some of these disorders are influenced by an individual's control (eg, shift work or time zone change) or secondary to disorders of neurological mechanisms (eg, irregular sleep-wake pattern and advanced sleep phase syndrome).[12-15]

TREATMENT OF INSOMNIA

Traditional Pharmaceutical Approach: Traditional allopathic medication options include the benzodiazepine $GABA_A$ receptor agonists (BzRAs), nonbenzodiazepine $GABA_A$ receptor agonists (non-BzRAs), melatonin-receptor agonists, antidepressants (ADs), atypical antipsychotics (APs) and other medications. The latter three groups are not FDA-approved for insomnia, but are commonly used. Suggestions for medication selection are based on the diagnosis, the evidence base and strength and weaknesses of the medications.[4]

The FDA has approved three classes of medications for the treatment of insomnia: BzRAs, non-BzRAs and melatonin-receptor agonists. The number of comparison studies is limited, but the available data reveal that: 1) zolpidem (Ambien) may be better than temazepam (Restoril) in terms of sleep latency and quality; and 2) zaleplon (Sonata) may lead to a shorter sleep latency than zolpidem (Ambien), but the latter has longer sleep duration.[2-5]

BzRAs include estazolam, flurazepam, quazepam, temazepam, and triazolam. Though BzRAs decrease sleep latency and increase total sleep time, they also have adverse side effects such as anterograde amnesia, daytime sedation, cognitive impairment, poor motor coordination, dependence, tolerance, and rebound insomnia. Due to these side effects, BzRAs should be limited to generally healthy, young (eg, <45 years old) patients with initial insomnia and who are expected to have brief medication trials. BzRAs should be avoided in patients with a history of substance abuse, elderly patients, and others with a particularly high risk for falls or delirium (eg, traumatic brain injuries, strokes, multiple new medications).

Non-BzRAs seem to have a superior side effect profile when compared to BzRAs. Non-BzRAs include eszopiclone (Lunesta), zaleplon (Sonata), zolpidem (Ambien), and zolpidem extended-release. They have less next-day sedation, psychomotor dysfunction, or tolerance/withdrawal; less REM rebound; and lower abuse potential than BzRAs. Studies have included short-term effects for insomnia, short-term effect in comorbid medical and psychiatric disorders (eszopiclone) and long-term effects (eszopiclone; zolpidem extended-release). The sole melatonin-receptor agonist, ramelteon (Rozerem), also reduces time to fall asleep without next-day psychomotor and memory effects. Ramelteon is believed to target receptors melatonin 1 and 2 receptors located in the brain's suprachiasmatic nucleus to stabilize circadian rhythms and stabilize the sleep-wake cycle.[4]

Limited data exist on the efficacy of non-FDA approved medications such as ADs and APs for insomnia. Sedating antidepressants that may be useful for some hospitalized patients, include trazodone (Desyrel) and mirtazapine (Remeron). Trazodone and mirtazepine are used most noticeably, though the former is associated with priapism in approximately 1:10,000 males. They may be an acceptable short-term alternative to BzRAs, but data are limited on them and recommended duration of use is unclear. Short-term studies have shown that low-dose trazodone (50 mg) is less efficacious than zolpidem. Mirtazapine, which promotes both sleep and appetite, may be particularly helpful for patients with cancer, AIDS and other conditions in which the trio of poor sleep, anorexia, and depression are common.[4] Although sedating, tricyclic antidepressants (TCAs) are not recommended to such patients because they increase the risk of

cardiac conduction abnormalities, reduce the seizure threshold, and have significant anticholinergic effects.[5]

Antipsychotics are not routinely used first-line for the treatment of insomnia, except in patients who are in the midst of acute manic or psychotic episodes. They typically increase sleep continuity and do not affect sleep architecture much. Sedating APs include risperidone (Risperdal; 0.5–2 mg HS), olanzapine (Zyprexa; 2.5–10 mg HS), quetiapine (Seroquel 12.5–300 mg HS); ziprasidone (Geodon) and aripiprazole (Abilify) are not usually sedating. Delirious patients or elderly patients with dementia who have nightly episodes of confusion, agitation, and cognitive decline ("sun-downing") may benefit from a low dose of a sedating AP to promote sleep and to prevent or treat these episodes. Common side effects include sedation, weight gain and metabolic changes (glucose, cholesterol, lipids). Rare, but important side effects, include neuroleptic malignant syndrome (a triad of mental status changes, increased muscle tone and autonomic hyperactivity), tardive dyskinesia, and akithisia (restlessness or inability to sit still). The administration of antihistamines, barbiturates, chloral hydrate, and alternative/herbal therapies has been discouraged in recent years, since the benefits rarely outweigh the risks associated with their use. In the US, antihistamines such as diphenhydramine are the most commonly used over the counter agent for chronic insomnia. However, anticholinergic action of antihistamines may lead to orthostatic hypotension, and induce delirium in vulnerable patients, especially the elderly, and should be avoided if possible.[4]

In a study by Hoque et al. they report a literature review on the unexpected clinical effects of zolpidem (Ambien) use. They cite a number of case reports involving sleepwalking and involuntary eating and other parasomnia behaviors of patients while under the influence of zolpidem (typically 10 mg). Most occurrences were within one hour of oral administration of the drug. Ample case studies have documented similar events but authors have failed to categorize events as examples of parasomnia in large part because the patients are so lucid when participating in activities. In one case (Cohen et al.) reported a who was previously minimally conscious following cardiac arrest resulting in a post-anoxic encephalopathy within a minimally conscious state was given 10 mg was actually more aroused and could toss a football with caregivers while on zolpidem. This point goes to the complex CNS mechanisms with which the drugs acts on the CNS sedating some aspects while awaking others. Others have been reported to have abruptly awoken from what witnesses call a "deep sleep" only to arise in the middle of the night to prepare lavish meals with little or no memory. These events ceased with discontinued use of the drug. With the use of zolpidem increasing, the authors noted that "hotels across the United Kingdom reported an increase in the number of hotel guests found sleepwalking." Though the evidence is circumstantial, the authors note that the general incidence of sleep walking is less than 10% if the general population. The substantial rise in hypnotic use and increased incidence of sleep walking now seen at large could be related secondary to zolpidem use. While direct causal relationships are merely circumstantial, there is ample evidence based on numerous case reports that suggest the use of zolpidem should be used with caution since many of these strange side effects cease when the use of the drug ceases.[7]

One possible explanation for the zolpidem-induced nocturnal events is that after an arousal from sleep into wakefulness, nocturnal activity (i.e. walking, eating, and driving) occurred and was subsequently not recalled after returning to sleep because of the sedation-mediated amnestic

properties of the drug. Hoque et al. subscribe to this theory in the patients they studied who exhibited similar parasomnia events. They do cite unexpected benefits like that of the semi-unconscious patient who reportedly threw a football with his caregivers as noteworthy. These include improvements in post-stroke Broca's aphasia, blepharospams, quadriparesis of central pontine myelinolysis, catatonia of schizoaffective disorder and patients with Parkinson's disease. In these cases, patients displayed increased arousal and cognitive function opposed to those using the medication for sedative qualities. This however, provides a substantial paradox in the increased use by the general public for the treatment of insomnia.[1;4-5]

HERBAL SUPPLEMENTATION

The lack of standardization and quality control for dietary/herbal supplements is an area of concern. Under the Dietary Supplement and Education Act of 1994, these products are not required to undergo testing for safety and efficacy. Also, since there is a lack of standardization within the herbal industry, it is difficult to assess whether retail products actually contain the ingredients as advertised. In particular, one investigation conducted by a consumer group in 2004, found that four out of five valerian products tested had no detectable valerian content, another four only had half the amount listed, and one was contaminated with cadmium.[17] Additionally, herbal supplements may interact with prescription medications.[17-25] This is a particular concern among the elderly who typically take multiple prescription medications.[20]

In the US, there is a growing interest in the use of CAM interventions for sleep. The NIH defines CAM as "a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine--that is, medicine as practiced by holders of MD (medical doctor) or DO (doctor of osteopathy) degrees and their allied health professionals." In CAM, *complementary* medicine is used *together with* conventional medicine, and *alternative* medicine is used *in place of* conventional medicine." In the United States, 36% of adults are using some form of CAM. When megavitamin therapy and prayer specifically for health reasons are included in the definition of CAM, that number rises to 62%. Overall, Americans spend about $5 billion out-of-pocket on herbal products, with sleeping problems accounting for about 2% of natural product use.[1]

The following reviews the available evidence for the use of valerian, melatonin and hop extracts (h. lupulus) as common CAM therapy in the treatment of insomnia.

Valerian: Valerian (*Valeriana officinalis*) is a perennial plant native to Europe and Asia and naturalized in North America. Preparations of valerian marketed as dietary supplements are made from its roots, rhizomes (underground stems), and stolons (horizontal stems). There is no scientific agreement as to the active constituents of valerian, and its activity may result from interactions among multiple constituents rather than any one compound or class of compounds. Valerian has been used as a medicinal herb since at least the time of ancient Greece and Rome. Its therapeutic uses were described by Hippocrates, and, in the 2nd century, Galen prescribed valerian for insomnia. It was listed as an anxiolytic and hypnotic in the US National Formulary until the 1940s, when more potent pharmacologic agents became available.[18]

There is currently no uniform agreement on the mechanism of valerian's pharmacological activity. One proposal suggests GABA agonistic activity.[16] Other more recent studies have found possible effect on adenosine and 5HT-5a receptors. 5HT-5a receptors are expressed in the suprachiasmic nucleus, the intergeniculate leaflet, the dorsal raphe nucleus and the medial raphe nucleus, which are involved in the body's circadian (24-hour) timekeeping system.[19] Heiligenstein and Guenther state that valerian root contains two substances known to have sedative effects, namely valepotriates and sequiterpenes. Still the mechanism of action for these substances are unknown. Though they site several small studies in which the findings were participants reported "improved sleep" though their review is fair scant with regards to details.[36]

According to Salter and Brownie, in total nine studies (six of which were randomized, double blind, placebo controlled trials) that assessed the efficacy of valerian alone, and three studies (two of which were randomized, double blind, placebo controlled trials) that assessed the efficacy of primary insomnia found "that subjects reported improvement in at least one sleep parameter, often sleep latency and sleep quality." Valerian singularly or in combination with hops "may be suitable as a trial in patients wanting an alternative to current treatment," but better studies are needed before physicians can confidently promote their use.[37]

Improvement in sleep latency (i.e., how long it takes to fall asleep after going to bed) and sleep duration with valerian compared to placebo was noted in several other studies as well.[19-24] A pilot study by Schulz et al. utilizing polysomnography (the gold standard method for sleep assessment) on 14 elderly female poor sleepers found, after eight days of valerian, significant increases in slow wave sleep (i.e., deep sleep) and decreases in stage 1 sleep (i.e., the lightest stage of sleep) compared to placebo, suggesting valerian improved overall sleep quality. Another study by Vorbach et al. monitored 128 individuals (across age groups) with sleep difficulty who received valerian or placebo for 28 days, following treatment response with questionnaires. Valerian resulted in improvement in sleep quality, less difficulty falling asleep, and fewer nighttime awakenings. Overall, significant differences were noted more frequently in studies with more prolonged administration and in individuals with prior sleep complaints. Two randomized double blind comparative studies have been performed comparing valerian to oxazepam for insomnia. Both utilized sleep questionnaires and followed patients for either four or six weeks. No significant differences were noted between the two treatments, as they were comparable in improved sleep parameters.[21]

One study investigated the usefulness of valerian in patients discontinuing benzodiazepine use. Nineteen non-elderly chronic benzodiazepine users were followed with polysomnography and questionnaires. There was a 14-day tapering period, followed by a 2-day washout, then 15 days of valerian or placebo. Both groups showed increased slow wave sleep and decreased stage 1–2 sleep, which were thought to show physiological recovery after washout. The valerian patients had decreased wake time after sleep onset (WASO) compared with placebo, which appeared to correlate with reports of improved sleep compared to placebo.[24]

Still additional research needs to be conducted before any reliable conclusions can be made about the efficacy of valerian root as well as they appropriate clinical dose to give. Historically, Valerian has been consumed in the form of a tea, (1.5 to 3 grams root steeped for 5 to 10 minutes in 150 milliliters boiling water); however, this formulation has not been studied for insomnia.

Studies of insomnia have included a broad range of doses (400–900mg) taken 30–60 minutes before bedtime as an aqueous solution or in tablet form. While no consensus exists on precise dosing, a 600mg dose one hour before bedtime has been most widely studied.[23]

Melatonin: Melatonin (N-acetyl-5-methoxytryptamine) is a naturally occurring neurohormone primarily produced by the pineal gland. Its secretion is timed by the oscillation of the endogenous circadian pacemaker. Since its discovery in 1958 there have been descriptions of its use as a hypnotic. It has been proposed that melatonin acts on receptors of the suprachiasmatic nucleus (SCN), causing adjustments in the timing of the circadian pacemaker, and possibly attenuating a daytime alerting process emanating from the SCN.[8-11;14;25]

Melatonin uses is popular with the geriatric population. A variety of theories are postulated for this including its popularity in the 1960s. A systematic review of treatment of elderly insomnia patients with melatonin was performed by Rikkert. Six double blind randomized crossover trials were evaluated, with measurements in these studies done with polysomnography or wrist actigraphy. In five of six studies, melatonin improved either sleep latency (time to fall sleep) or sleep efficiency (time asleep out of the total time in bed) compared to placebo. One study found even more striking improvements in patients who were prior benzodiazepine users. The review did note that there did not appear to be a simple causal relationship between low melatonin levels (measured in urine, serum or saliva) and insomnia in the elderly. No changes were noted in subjective sleep improvement, and slow wave sleep (i.e., deep sleep) was not increased. The studies reviewed all had small sample sizes, ranging from 10 to 26 participants.[26]

A more recent study with elderly subjects was done by Zhdanova. In a double blind, placebo-controlled study, patients were monitored with polysomnography and given three different doses of melatonin with washout periods in-between. At all doses, sleep efficiency in the middle and latter third of the night was improved. No other differences were noted on other objective parameters. Percentage of slow wave sleep was unchanged. As in the other studies, no correlation was seen between serum melatonin levels resulting from exogenous melatonin administration and sleep quality.[27] Singer et al. studied the efficacy of melatonin on insomnia in Alzheimer's patients. This was a randomized, placebo controlled trial of 157 patients, who were treated for a 2-month period. No significant differences in objective sleep measures were noted.[28] In 2005, Brzezinski et al. performed a meta-analysis of the effects of exogenous melatonin on sleep across age groups. This meta-analysis only included trials that were randomized, double-blind, placebo controlled and used objective measures of sleep evaluation (actigraphy or polysomnography). Overall, the authors concluded that melatonin caused statistically significant decreases in sleep onset latency, increases in sleep efficiency, and increases in total sleep duration; however, only changes in sleep efficiency and duration were clinically significant. Sleep architecture was not significantly affected, and no next-day "hang over" effects were noted with melatonin, as may occur with some benzodiazepines used to treat insomnia.[29]

Administration of melatonin requires consideration of the natural activity of the hormone. Melatonin can have both sleep inducing and chronobiologic (i.e., circadian rhythm) effects.[30] Studies have typically tried to capitalize on the sleep-inducing effects with administration at or near the desired bedtime. To capitalize on the chronobiologic effects, timing of administration must be linked to biological markers of the circadian clock. Clock timing is typically determined

in a laboratory setting in which natural melatonin levels and/or body temperature rhythms are measured. Natural melatonin levels typically peak several hours after habitual sleep onset time. To shift the timing of sleep earlier, melatonin should be given before natural melatonin levels peak, and to shift the timing of sleep later, melatonin should be given after natural melatonin levels peak. In the nursing home setting, one typically wishes to shift sleep to a later time (to improve evening alertness and reduce early morning awakenings). Melatonin should then be given in the early morning. Melatonin has not been studied in this way in the nursing home. While early studies of melatonin used super-physiologic doses (5–10mg), more recent studies have found that very low doses (0.1–0.25mg) are generally more effective, perhaps because these doses more closely mimic physiological melatonin levels.[31]

Although not an herbal supplement, one recently-approved prescription sleep aide acts on melatonin receptors MT1 and MT2. A double-blind, placebo controlled crossover study was done by Zelman et al. in 2005, using Beta-Methyl-6-Chloromelatonin (ramelteon), a melatonin receptor agonist that does not cause hyopothermia, as high doses of melatonin occasionally can. This choice was designed to eliminate hypothermia as a possible mediator of melatonin's soporific effect. The study included 40 patients who used three different doses of the melatonin agonist with washout periods between dose changes. Sleep latency was significantly reduced with an escalating dose effect. Other objective sleep parameters including sleep efficiency, sleep architecture, and total sleep were not significantly changed. There were no significant differences in serious side effects across groups.[32]

In a large study (n=829) of the effects of ramelteon on subjective sleep quality among older adults with chronic insomnia, Roth et al. found that 4 or 8 mg of ramelteon led to improved sleep latency (i.e., participants fell asleep more quickly) compared to placebo. They also found no evidence of negative consequences with discontinuation of the agent after 5 weeks.[47] Ramelteon (Rozerem™) was recently approved by the FDA for use as a sleep aide. The adult dose is typically 8mg, taken at bedtime for sleep onset insomnia. The effectiveness and safety of this agent has not been fully evaluated in the frail elderly, however, and additional research is needed.[33;39]

Hops (Humulus Lupulus Extract): Cornu, Remontet, et al conducted a randomized controlled study of 101 patients found no statistical significance in the efficacy of humulus lupulus extract as compared to the placebo group, though both groups improved in sleep quality according the Lees Sleep Evaluation Questionnaire (LSEQ). The study product is a dietary supplement composed of natural components. It contained a specific ratio of polyunsaturated fatty acids (PUFA, linolenic and linoleic acids), in association with Humulus lupulus extract. PUFA were claimed to favor melatonin synthesis (see also above). The short half-life of melatonin requires the administration of high doses to balance its quick metabolism. Humulus lupulus extract is purported to decrease the hepatic metabolism of drugs which are metabolised by the CYP1A2, a cytochrome that also allows melatonin transformation into its main metabolite: 6 sulfatoxymelatonin (aMT6s). This combined action could increase melatonin bioavailability and is likely to reset the endogenous biological clock. According to this study however, Humulus lupulus extract did not improve the quality or the duration of sleep as compared to the olive oil placebo capsules. Furthermore, no significant change of melatonin or aMT6S urinary excretion

was observed, suggesting that the dietary supplement had no effect on the melatonin metabolism.[35]

OTHER CAM THERAPIES

Acupuncture: Acupuncture represents a potentially unique and different avenue for insomnia intervention because of its direct effects on the autonomic nervous system. It has been shown to influence some known indicators of autonomic activities, such as blood pressure, pupil size, skin conductance, thermography recorded skin temperature, microneurography recorded muscle sympathetic nerve activities, heart rate and/or pulse rate, and heart rate variability.

How acupuncture produces changes in autonomic activities remains uncertain. Traditional acupuncture requires elicitation of the Deqi ("Da Chee," literally translated "getting the energy") sensation, achieved by twisting and thrusting the needle after its insertion into an acupuncture point. It is experienced as local soreness and heaviness as well as radiating paresthesia, a sensation that can also be obtained in strong muscle contractions. Because of such practice in traditional acupuncture, Andersson and Lundeberg hypothesized acupuncture in producing effects via sympathetic regulation in the same way as other forms of sensory stimulation or strong muscle contractions. Their theory has been instrumental in understanding the pain relief effects of acupuncture needling, as well as exercise, massage, or transcutaneous electrical nerve stimulator (TENS) treatments.

In their systemic review, Cao et al noted the preliminary evidence supports the conclusion that acupuncture appears to be effective in the treatment of insomnia, particularly in conjunction with other therapies, namely CBT. The clinical success observed after acupuncture treatments in our patients included sleep improvements some of the research they studied such as prolonged sleep duration and increased sleep efficiency, anxiety symptom improvement, headache improvement/resolution, functional improvement, and/or less medication intake. Because this was a preliminary clinical case series, objective measurements of sleep outcome were not widely used, nor were measurements of autonomic activities included. Thus, the interpretation of these results remains clinical rather than mechanistic. They further cite the need for further, larger more rigorous trials to guide clinical practice.

Huang et al present more support for the autonomic role of the CNS in treating insomnia through autonomic activation. They state that besides generalized effects via sensory stimulation, acupuncture seems to also produce some specific effects on the autonomic nervous system, supported by experimental and clinical data, though most studies are quite small when it comes to direct application of sleep disorders. Though Huang et al state the following points which account for different effects on the autonomic nervous system, such as facilitation of parasympathetic and suppression of sympathetic activities (PC-4 Ximen, GV-14 Dazhui – PC-6 Neiguan, EX-HN1 Sishencong, BL-15 Xinshu), significant increase of parasympathetic activity without effects on sympathetic activity (auricular Lung), coactivation of both parasympathetic and sympathetic activities (LI-11 Quchi), or increase of segmental sympathetic vasomotor activity with central sympathetic inhibition (LI-4 Hegu, ST-36 Zusanli).

Huang et al does reiterate that introduction of acupuncture into sleep medicine must "await well-designed randomized clinical trials showing unequivocal evidence of improvement with subjective as well as objective outcome measures, with close attention paid to the control of nonspecific effects of acupuncture using careful sham design." Nonetheless they offer three case studies which represent a diverse sample of patients with chronic insomnia. They based their acupuncture points on common and frequently used points used for their sedating qualities (specific points omitted by this author but mirrored in prior studies). The three patients were reported to have improved sleep including prolonged sleep duration and increased sleep efficiency, decreased anxiety about sleep, headache improvement/resolution, functional improvement and/or decrease in prescribed sleep medication intake. Despite this success, the authors note that objective sleep outcome assessments were not widely used nor were measurements of autonomic activities included. Thus, the interpretation remains clinical rather mechanistic.

Additional evidence in support of acupuncture in the treatment of insomnia was made in Yeung et al. which evaluated the efficacy of electroacupuncture as additional treatment for residual insomnia associated with major depressive disorder (MDD). Their study included about one hundred individuals whose primary complaint was insomnia and who met the DSM-IV criteria for MDD. Compared to the placebo group, electroacupuncture and minimal acupuncture for a short term period of time (less than four weeks) resulted in greater improvement in subjective and measure in as early as week one and continued to as long as four weeks after treatment. Though no statistical significance was observed between electroacupuncture and needle acupuncture.

Cognitive Behavior Therapy: Mind-body interventions use a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms. Some techniques that were considered CAM in the past have become part of the mainstream [for example, patient support groups and cognitive behavior therapy (CBT)]. Other mind-body techniques are still considered CAM, including meditation, prayer, mental healing and therapies that use creative outlets such as art, music or dance.

It is hypothesized that mind-body interventions reduce sympathetic nervous system activity and increase parasympathetic nervous system activity, thereby restoring homeostasis in the balance of sympathetic/parasympathetic function. Mind–body techniques, including the relaxation response and cognitive restructuring, have been shown to be effective for the treatment of chronic insomnia. Mind-body interventions involving cognitive restructuring in the treatment of sleep maintenance in older adults with insomnia were more effective in the long term as compared to pharmacotherapy. The effects of pharmacotherapy were essentially limited to the period during which patients were taking the drug.

Use of a mind-body intervention can be combined with pharmacotherapy in the treatment of insomnia. Studies examining the relative advantages of CBT and pharmacotherapy have found that improvements may be achieved more quickly with drug treatment; however, improvements are more sustained with CBT. Combining

modes of treatment is not necessarily superior to monotherapy because long-term effects can vary between patients. Deciding which treatment to initiate first, or whether to run treatments concurrently, depends on factors such as the nature of the insomnia, treatment history, comorbid conditions, acceptability of treatment to the patient and treatment cost or availability.

For example in their study on discontinuing the use of hypnotics Zavesicka et al. found application of CBT was **"the best way to avoid the chronic use of hypnotics."** They cited that many patients suffering from chronic insomnia participate in long-term daily use of hypnotics. Those who are inadequately treated have a tendency to increase their daily dose in an effort to combat their continuing insomnia. Such patients are clearly at risk for hypnotics abuse and dependence. However they do note that, discontinuation of hypnotic administration is not always possible, because both the patient and the therapist may be concerned about worsening insomnia. There is a fear that abrupt withdrawal of hypnotics could result in worse therapeutic outcomes. However, practical experience with discontinuation of hypnotics does not justify this concern. There are reports on long-term outcomes of discontinuing hypnotics, particularly benzodiazepines.

In the Zavesicka et al study, they studied two subgroups of patients, with and without a history of hypnotic abuse. They found in hypnotics-abusing patients a relative increase in sleep stage 3, sleep stage 4, and REM sleep could be demonstrated in comparison with the hypnotic non-abusing subgroup. Both subgroups of patients were then treated with CBT while the long-term hypnotic regimen was gradually discontinued. Afterwards, the therapeutic outcomes were evaluated, using the differences between pre- and post-treatment sleep variables as indicators. Sleep was significantly improved in both subgroups after CBT. The only exception was the proportion of sleep stages 1 and 2, in which statistical significance could not be confirmed. As a next step, the possible effects of discontinuing hypnotics were investigated. Statistical analysis revealed an additional improvement of sleep efficiency and WASO in the abusing group after therapy.

AUTHOR RECOMMENDATIONS:

First and foremost, gaining an initial sense of acute versus chronic complaints will help guide the nature, depth, and breadth of a focused interview about insomnia and its differential. Acute insomnia may last from a single night to several weeks (stress, changes in schedule and time zone changes) may not require treatment. Mild insomnia often can be prevented or cured by practicing good sleep habits (see author recommendations and discussion on sleep hygiene below). If the insomnia interferes with daily function because the patient is sleepy and tired, more investigation may be required, and sleeping pills may be indicated short- and long-term. Treatment for chronic insomnia includes first treating any underlying conditions or health problems that are causing the insomnia. Sleep habits, behavioral approaches and medications may be helpful.

Specific questions in the history to determine the exact *nature of the complaint* include:

- Do you have problems falling asleep or staying asleep?
- Do you frequently awaken, and is that associated with anything (eg, pain)?
- Do you awaken tired or unrefreshed despite many hours of sleep?

It is important to know the patient's usual sleep habits and behaviors – and for acute insomnia, recent changes – are associated with sleep hygiene.

- What time do you go to bed and get up?
- Is the insomnia related to any new habits lately (eg, travelling) or adjustments in day-night changes (eg, new shift at work)?
- What activities do you normally have throughout the day?
- Have there been any recent changes in your routine or health?
- When going to sleep, how anxious are you or how mentally aroused are you?

The simplest method to ascertain the patient's routine is to have him/her describe a typical day. Patients' routines may be severely disrupted during illness or stress. Staying in bed for prolonged periods and sleeping during the day can impair nighttime sleep.

Chronic insomnia may require a personal or family history of over-the-counter medication, substance disorders, primary sleep disorders (eg, restless leg syndrome) or symptoms of common sleep problems.

- Do you snore when you sleep? If so, how often? Do family members complain that you snore very loudly? Does drinking alcohol before sleep worsen the snoring?
- Has anyone noticed that you appear to "stop breathing" while asleep?
- Have you recently increased or decreased the amount of alcohol you drink? By how much, and over what period of time?
- Do you use cocaine, methamphetamine, "speed," or other substances?
- Do you smoke? If so, when?

Patients may have underlying sleep and psychiatric disorders that they are unaware of, insufficiently diagnosed or simply forgotten when feeling ill. For example, insomnia is often a comorbidity other pathological problems and mere presence of it may be dismissed. Snoring may be dismissed as insignificant or "normal" especially in male patients. Additional medical and psychiatric history should be obtained for anxiety, depression, substance and psychotic disorders. Alcohol and drug use can have profound effects on sleep, with the former normally suppressing REM sleep.

On more difficult patients, the provider can consider the following:

- 24-hour assessment of activities

- Diary logging daily activities and sleep patterns by the patient over 7–30 days
- Collateral information

This author recommends sleep hygiene as preliminary trial of care. Sleep hygiene can be defined as the controlling of "all behavioural and environmental factors that precede sleep and may interfere with sleep." It is the practice of following guidelines in an attempt to ensure more restful, effective sleep which can promote daytime alertness and help treat or avoid certain kinds of sleep disorders. Trouble sleeping and daytime sleepiness can be indications of poor sleep hygiene. The International Classification of Sleep Disorders-Revised (ICSD-R) states on page 74: "The importance of assessing the contribution of inadequate sleep hygiene in maintaining a preexisting sleep disturbance cannot be overemphasized." In the ICSD-R, the diagnosis inadequate sleep hygiene is classified as an extrinsic sleep disorder, code 307.41-1.

Doctors and clinicians who advise sleep hygiene for patients and families have lists of suggestions which may include advice about timing of sleep and food intake in relationship to it, exercise, sleeping environment, etc. Which items are suggested for which patients are selected by the clinician, depending on knowledge of the individual situation; the counseling is presented as a form of patient education. Re-education involves a combination of advice about homeostatic, adaptive and circadian aspects of sleep control, how to avoid sleep deprivation, and how to respond to unwanted awakenings from sleep if these occur. As the second edition of the ICSD (ICSD2, 2005) points out, the "sleep disruptive effects of poor sleep hygiene are often obvious to others, but the patients show little insight into this fact."

The most important sleep hygiene measure is to maintain a regular sleep and wake pattern seven days a week. It is also important to spend an appropriate amount of time in bed, not too little, or too excessive. This may vary by individual; for example, if someone has a problem with daytime sleepiness, they should spend a minimum of eight hours in bed, if they have difficulty sleeping at night, they should limit themselves to 7 hours in bed in order to keep the sleep pattern consolidated. In addition, good sleep hygiene practices include:

- Avoid napping during the day; it can disturb the normal pattern of sleep and wakefulness.
- Avoid stimulants such as caffeine, nicotine, and alcohol too close to bedtime. While alcohol is well known to speed the onset of sleep, it disrupts sleep in the second half as the body begins to metabolize the alcohol, causing arousal.
- Exercise can promote good sleep. Vigorous exercise should be taken in the morning or late afternoon. A relaxing exercise, like yoga, can be done before bed to help initiate a restful night's sleep.
- Food can be disruptive right before sleep; stay away from large meals close to bedtime. Also dietary changes can cause sleep problems, if someone is

struggling with a sleep problem, it's not a good time to start experimenting with spicy dishes. And, remember, chocolate has caffeine.

- Ensure adequate exposure to natural light. This is particularly important for older people who may not venture outside as frequently as children and adults. Light exposure helps maintain a healthy sleep-wake cycle.
- Establish a regular relaxing bedtime routine. Try to avoid emotionally upsetting conversations and activities before trying to go to sleep. Don't dwell on, or bring your problems to bed.
- Associate your bed with sleep. It's not a good idea to use your bed to watch TV, listen to the radio, or read.
- Make sure that the sleep environment is pleasant and relaxing. The bed should be comfortable, the room should not be too hot or cold, or too bright.

As discussed above, a number of randomized clinical trials have been done with CBT, showing great promise in primary and secondary insomnias, with as few as 1–4 sessions having short- and long-term effect. CBT was highly effective with or without sedative-hypnotic cessation. This coupled with good exercise of sleep hygiene has been shown to produce the greatest changes in total sleep time, REM sleep and sleep efficiency.

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