

The Effect of Sleep on Chronic Pain

Enhancing sleep can lead to less pain and better outcomes

The importance of sleep to a person’s overall well-being is long supported by research and is well documented. A positive outlook, alert mind and energetic body are all recognized signs of adequate sleep – just as persistent yawning, anxiety, curt temperament and lethargy can demonstrate lack of sleep.

Most of us encounter periods of poor sleep from time to time. Social obligations, entertainment, household/job responsibilities and the many activities of daily living, can impede one’s ability to obtain the recommended seven to nine hours of nightly rest. The existence of aches and musculoskeletal pain are other factors that may make it difficult to fall or stay asleep throughout the night. As such, chronic pain resulting from a workplace injury is often associated with sleep disturbances.

These disturbances can lead to a total loss of sleep time or fractured sleep, which prevents the body’s completion of a sleep cycle, thus what little sleep is attained is not restorative. Although occasional bouts of insomnia can be frustrating and disruptive, they are relatively harmless to one’s overall sense of well-being. Chronic sleep loss, however is a more serious concern due to its influence on metabolism, mood and memory, as well as cardiovascular health and immune function.

Chronic sleep loss can also impair our ability to cope with pain and eventually lead to a state of decreased stamina. The lack of energy makes it difficult to be active, and the lack of exercise can exacerbate pain. The outcome is a vicious cycle in which a lack of sleep worsens pain, which in turn makes it more difficult to sleep.

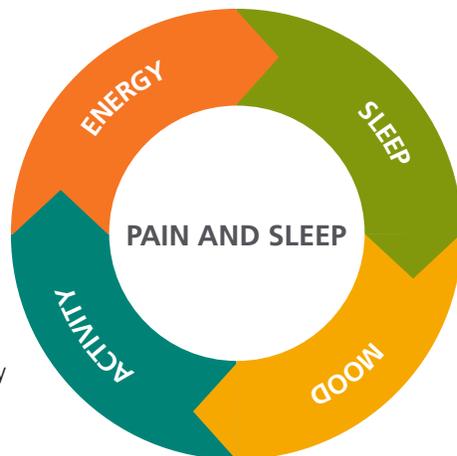
Figure 1. The sleep-pain cycle

ENERGY

Coping with pain decreases energy. Lack of energy makes it hard to be active and stay in shape.

ACTIVITY

Pain and lack of energy make it hard to be active. Lack of exercise worsens pain.



SLEEP

Pain and anxiety make it hard to sleep. Lack of sleep worsens pain and decreases energy.

MOOD

Chronic pain can lead to depression, anger and anxiety. These feelings make coping with pain more difficult.

Breaking the sleep-pain cycle is critical to advancing recovery, particularly when the underlying cause of chronic pain is workplace injury.

This paper offers an overview of the process of sleep, sleep disturbances and insomnia. Additionally, it outlines treatment options and therapeutic recommendations focused on achieving better outcomes by advancing recovery and ultimately returning to function.

Sleep is defined as a state in which there is total or partial unconsciousness and our senses and motor activities are suspended.¹

Understanding sleep

To understand the interaction of chronic pain and sleep it is necessary to understand sleep itself. Sleep is defined as *a state in which there is total or partial unconsciousness and our senses and motor activities are suspended*.¹ The average human spends one third of his or her life asleep.^{1,2,3} Sleep is required for a number of important physiological functions related to growth and development, as well as for the overall health of the immune, nervous, skeletal and muscular systems.² For optimal body function, general guidance calls for adults to pursue seven to nine hours of sleep per night; however, just as no two people are alike, studies show that neither are sleep requirements. In fact, the amount of sleep a person requires varies depending on his or her age and physiological growth demands.

Sleep is divided into two categories, non-rapid eye movement (NREM) and rapid eye movement (REM). NREM and REM sleep make up a single sleep cycle. A person should experience several sleep cycles during a traditional eight hour sleep period, with the first cycle usually lasting 70-100 minutes, the second cycle lasting 90-120 minutes, and subsequent cycles averaging 90 minutes in duration.

NREM

Between 70-80 percent of total sleep time is spent in NREM. It is split into three distinct stages based upon brain activity and physiology. During NREM sleep, the heart rate slows, breathing rate slows, blood pressure drops, there is limited muscle movement and the activity in the brain changes from wakefulness to slow-wave sleep.

Figure 2. The three stages of NREM sleep

Stage 1 NREM Sleep	Stage 2 NREM Sleep	Stage 3 NREM Sleep
<p>The transition period between wakefulness and sleep. It represents roughly 2-5% of the total sleep cycle and usually lasts one to seven minutes. During this stage, a person will experience slow eye movements and involuntary twitching. Sleep can easily be interrupted by noise and those awakened from this stage, do not believe they were asleep.</p>	<p>The transition into deeper sleep and memory consolidation. This stage represents 45-55% of the total sleep cycle. The initial cycle lasts 10 to 25 minutes and then lengthens with each successive cycle. A person will have no eye movement and it will be very difficult to awaken an individual from this stage of sleep. It is during this stage that declarative memories (memories regarding facts and knowledge) are believed to be consolidated. Dreaming in this stage rarely occurs.</p>	<p>The final stage of NREM and represents the transition into deep sleep and slow-wave (delta-wave) brain activity. This stage encompasses roughly 13-23% of the total sleep cycle and usually lasts 20 to 40 minutes. At this stage, there are no eye or body movements and a person awakened from this stage is disoriented. Stage 3 sleep is critical and encompasses the restorative period of sleep when the body performs vital repairs and regeneration of tissues.</p>

REM

Known as the “dream” stage, REM sleep is the most important stage for memory consolidation. REM sleep represents roughly 20-25 percent of the total sleep cycle, with the initial cycle lasting as little as one to five minutes and then lengthening with each successive cycle. During REM there is a complete loss of muscle tone and reflexes, which is believed to prevent people from “acting out” their dreams. A person in REM sleep will characteristically show bursts of rapid eye movement, as well as an increase in heart rate, blood pressure and respiratory rate.

Brain activity is increased during REM and is believed to be important in long-term memory formation. This stage also embodies the vivid dreams or nightmares that people may experience during sleep, with approximately 80 percent of dream recall occurring after awakening from REM sleep.

Sleep regulation

A system known as the circadian rhythm regulates a person’s “biological” or “24-hour” clock. This clock creates the daily routines, physiological patterns and behaviors. It controls a number of functions, including the sleep-wake cycle, physical activity, food consumption, body temperature, heart rate, muscle tone and hormone secretion. The circadian rhythm is self-registered and is synchronized with cycles of light and dark, as well as the seasons.

Insomnia

Insomnia is defined as *a difficulty in initiating or maintaining sleep, or waking up unrefreshed*. An estimated 5-15 percent of the U.S. population suffers from insomnia, which results in daytime impairment, such as fatigue, distress, irritability and/or poor concentration. Insomnia is generally considered either “acute” or “chronic.” Acute insomnia is generally characterized as lasting four weeks or less, whereas chronic insomnia persists for more than one month.

Insomnia can also be broken down based on causation, differentiated as either being “primary” or “secondary.” Primary insomnia is defined as *sleeplessness not attributable to a medical, psychiatric or environmental cause*. Rarely diagnosed and considered a diagnosis of exclusion, people suffering from primary insomnia must meet the following criteria:

- Difficulty initiating or maintaining sleep or suffering from non-restorative sleep, for at least one month
- Sleep disturbance or associated daytime fatigue causing clinically-significant distress or impairment in social, occupational or other important areas of functioning
- Sleep disturbances does not occur exclusively during the course of narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder or a parasomnia
- Sleep disturbance does not occur exclusively during the course of another mental disorder, such as a major depressive disorder
- Sleep disturbances does not occur as a result of pharmacologic or alcohol dependence or any other medical condition, such as pain

An estimated 5-15% of the U.S. population suffers from insomnia.

Secondary insomnia is defined as *sleeplessness that occurs as a result of a medical, psychiatric or psychological process*. It is the most common form of insomnia, representing an estimated 80 percent of all cases and is caused by numerous factors, including:

- Situational influences or activities such as daytime napping, jet lag, stress or shift work
- Medical conditions, such as depression, pain, sleep apnea or gastroesophageal reflux disease
- Medication usage, such as alcohol, nicotine, caffeine or pseudoephedrine
- Natural product usage, such as St. John's Wort, green tea or ginseng

Understanding the distinction between primary and secondary insomnia is key to addressing the origin of the sleep disorder. The majority of people have an identifiable cause to their insomnia, and when the underlying condition is adequately treated, their insomnia will dissipate.

Diagnosing insomnia

There are a number of diagnostic tools that are used to diagnose insomnia and pinpoint its root causes; they are outlined in the table below.

Test	Description	Measures/Parameters	Clinical Value
Sleep Diary	Log of sleep habits and patterns used to make clinical assessment of sleep, usually over two weeks	Start and stop times of sleep, medications and time take, mood before and after sleep, meal times, activities before sleep, stress before sleep, issues encountered initiating or maintaining sleep and overall quality of sleep	A sleep diary can be important to help pinpoint if a particular activity (or series of activities) is causing the insomnia and facilitate alteration of behavior(s)
Pittsburgh Sleep Quality Index	Self-rated questionnaire that assesses sleep quality and disturbances over one month	Sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction	Used in the office to determine how the person perceives his or her sleep, quality of sleep and function
Epworth Sleepiness Scale	Questionnaire used to determine level of daytime sleepiness	A score of 10 or more is considered sleepy (indicative of lacking adequate sleep) whereas a score of 18 or more is very sleepy	Another test that can be used to determine how the person perceives his or her sleep quality
Polysomnography	Sleep study that monitors a person as he or she sleeps or tries to sleep	Lung air flow, breathing rates, blood oxygen levels, body position, brain waves (EEG), eye movement, heart rate	Generally used to diagnose respiratory associated insomnia, such as sleep apnea. Beneficial in determining whether insomnia's root cause is apnea or something else
Actigraphy	Assesses sleep-wake patterns over time	Assesses real-time daytime sleepiness	Beginning to replace polysomnography in diagnosing certain conditions

While the accepted standard for diagnosis of insomnia is an extensive physician-based interview and clinical evaluation, in practice most instances of insomnia are diagnosed based on the person's self-reported complaints.

Once a diagnosis of insomnia is confirmed, any contribution of underlying medical conditions should also be assessed. In the case of insomnia related to chronic pain, adequate treatment of pain and any pain-related psychological issues, such as anxiety, depression or stress should be optimized because often appropriate treatment of the underlying medical condition alleviates insomnia and enables the person to obtain adequate sleep. However, if the underlying condition is already being treated optimally and insomnia persists, non-pharmacological interventions should be incorporated prior to, during and after any pharmacological intervention.

Treating insomnia

Non-pharmacologic treatment

Non-pharmacologic interventions for insomnia due to chronic pain should be incorporated prior to, during and after any pharmacological intervention.

Among the most widely used and accepted non-pharmacologic therapies are stimulus control, behavioral intervention, sleep hygiene and relaxation therapy; while other options include sleep restriction, imagery training, paradoxical intention and biofeedback therapy.

- **Stimulus control:** Therapy consists of a set of instructions designed to re-associate the bedroom with sleep and to curtail behaviors that are incompatible with sleep. Examples of instructions given to the person (and for which adherence is expected) include "lie down to sleep only when sleepy," and "get out of bed when unable to sleep and go to another room until tired enough to sleep." The goal of the therapy is to reestablish a consistent sleep-wake schedule.
- **Relaxation training:** Involves teaching a person progressive muscle relaxation techniques consisting of tensing and relaxing different muscle groups throughout the body. It has been found to be especially helpful for people experiencing chronic pain.

Relaxation training is fairly straightforward to learn and teach, reasonably accessible online, and considered a standard of therapy with evidence supporting its use and efficacy.

- **Sleep hygiene:** Similar to stimulus control therapy, sleep hygiene provides information regarding appropriate sleep behavior and practices. Examples of commonly presented information include avoiding caffeine and nicotine, avoiding exercising four hours before bedtime and avoiding large evening meals.

This particular form of therapy is simple to incorporate and requires little to no intervention. Growing evidence supporting the efficacy of good sleep hygiene exists.

- **Cognitive behavioral therapy:** Aimed at modifying faulty beliefs and attitudes about sleep, insomnia and next day consequences, this therapy generally involves a psychiatric or psychological intervention to assist in modifying a person's sleep-related beliefs and emotions. The goals of therapy include addressing thoughts such as "I can't sleep without medication," "I have a chemical imbalance," "if I can't sleep I should stay in bed and rest," and "my life will be ruined if I can't sleep."

People with chronic pain often benefit from a combination of sleep hygiene therapy, stimulus control, relaxation techniques and cognitive behavioral therapy interventions.

Pharmacological treatment

The neurochemistry of sleep is complex and multiple pathways exist in the brain that affect how we sleep. Each medication class affects sleep in a different manner and at different stages of the sleep cycle. Our Pharmacological Treatment Options document at the end of this paper lists several treatments and their general advantages and disadvantages.

People with chronic pain may benefit from the short-term use of a pharmacologic sleep aid *in conjunction* with non-pharmacological therapy. Long-term or ongoing pharmacological treatment, however, is not recommended.

Pharmacological side effects

Although medications can provide assistance with sleep, they can also alter the normal sleep cycle and may produce adverse events and/or dependence. Common side effects include daytime drowsiness, dizziness, hallucinations and behavioral changes such as agitation and bizarre or complex behaviors, such as sleepwalking and sleep driving.

Recommendations

The application of a multi-faceted therapeutic approach combined with the requisite effort by the person experiencing insomnia can break the sleep-pain cycle. The key is to ensure that the therapy regimen accurately addresses and treats the underlying condition. In cases of insomnia caused by chronic pain, the pain must be as controlled as effectively possible.

With adequate sleep being so important to a person's wellbeing and their ability to recover from an injury, identifying and treating the underlying cause of insomnia using a multi-faceted approach is essential. In cases of insomnia caused by chronic pain, this means the pain must be controlled as effectively as possible in order to break the sleep-pain cycle, advance recovery and ultimately achieve a better outcome.

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Non-Benzodiazepines

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Eszopiclone (Lunesta®)	Sleep maintenance insomnia	Adults: 1mg immediately before bedtime, maximum dose 3mg Older adults: Difficulty falling asleep - 1mg immediately before bedtime, maximum dose 2mg Difficulty staying asleep - 2mg immediately before bedtime, maximum dose 2mg	↑ NREM sleep ↓ Sleep latency (NREM Stage 1) ↑ NREM Stage 3	↑ time to achieve REM sleep, interferes with normal sleep architecture Abnormal dreams, concentration problems	Risk of next-morning impairment higher if Ambien, Edluar and Zolpimist are taken with < 7-8 hours of sleep remaining; or if Intermezzo is taken with < 4 hours of bedtime remaining; risk also increases with higher doses or concurrent use with other sedating medications. Intermezzo should not be used with other sleep aides or zolpidem products. Lunesta, Sonata and all zolpidem products NOT RECOMMENDED for use in older adults.
Zolpidem ER (Ambien® CR)	Sleep maintenance & sleep onset insomnia	Males: 6.25-12.5mg Females: 6.25mg Older adults: 6.25mg	↓ Sleep latency (NREM Stage 1) ↑ NREM Stage 1 and 2 (only Zolpidem)	Parasomnias such as sleep-walking, sleep-eating, sleep-driving	
Zolpidem (Ambien®)	Sleep onset insomnia	Males: 5-10mg, maximum dose 10mg daily Females: 5mg, maximum dose 10mg daily Older adults: 5mg	No effect on NREM Stage 3, REM	Daytime drowsiness, fatigue	
Zolpidem oral spray (Zolpimist®)	Sleep onset insomnia	Males: 5-10mg Females: 5mg, up to 10mg if needed Older adults: 5mg			
Zolpidem sublingual tablet (Edluar®)	Sleep onset insomnia	Males: 5-10mg Females: 5mg, up to 10mg if needed Older adults: 5mg			
Zolpidem sublingual tablet (Intermezzo®)	Middle-of-the-night awakening due to insomnia	Males: 3.5mg, lower dose to 1.75mg if taking other CNS depressants Females: 1.75mg Older adults: 1.75mg			
Zaleplon (Sonata®)	Sleep onset insomnia	Adults: 10mg at bedtime (range: 5-20mg) Older adults: 5mg at bedtime, maximum dose 10mg daily			

Benzodiazepines

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Estazolam (ProSom®)	Sleep maintenance insomnia	Adults: 1mg at bedtime, maximum dose patient dependent Older adults: 0.5-1mg at bedtime*	↓ Sleep latency (NREM Stage 1) ↓ Awakenings and duration	↓ NREM Stage 3, REM Patient often feels sleep was not restorative Anterograde amnesia	Due to reduced NREM Stage 3 sleep, side effects frequently include patients feeling unrefreshed from sleep and having memory problems. Benzodiazepine hypnotics are NOT RECOMMENDED for use in the older adults.
Flurazepam (Dalmane®)	Sleep maintenance insomnia	Adults: 15-30mg at bedtime, maximum dose patient dependent Older adults: 15mg at bedtime; avoid use if possible*	↑ Total time spent asleep	Daytime drowsiness	
Quazepam (Doral®)	Sleep maintenance insomnia	Adults: 15mg at bedtime, maximum dose patient dependent Older adults: 7.5mg at bedtime*			
Temazepam (Restoril®)	Sleep maintenance insomnia	Adults: 15-30mg at bedtime, maximum dose patient dependent Older adults: 7.5mg at bedtime*			
Triazolam (Halcion®)	Sleep onset insomnia	Adults: 0.25mg at bedtime, 0.125mg for low body weight, maximum dose 0.5mg daily Older adults: 0.125mg at bedtime, maximum dose 0.25mg daily*			

Sleep Latency Insomnia: Amount of time it takes to fall asleep after the lights have been turned off.

Sleep Maintenance Insomnia: Difficulty staying asleep or waking too early and struggling to get back to sleep.

Sleep Onset Insomnia: Transition from wake to sleep.

Older Adult: 60 years of age or older.

Melatonin-Receptor Agonist

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Ramelteon (Rozerem™)	Sleep onset insomnia	Adults and older adults: one 8mg table within 30 minutes of bedtime	Tries to help regulate the sleep-wake cycle ↓ Sleep latency by 15-20 minutes	Minimal gain in sleep latency High cost	Not recommended for long-term use despite being approved for such.

Over-The-Counter (OTC) Products

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Diphenhydramine (Benadryl®)	Decrease sleep-latency	Adults and older adults: oral, 50mg at bedtime	↓ Sleep latency	Daytime drowsiness Rebound insomnia Low effectiveness, 2-3 days maximum	Poor evidence of efficacy, not recommended for long-term use or in the older adults
Doxylamine (Unisom®)	Decrease sleep-latency	Adults and older adults: one tablet 30 minutes before bedtime			

Antidepressants

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Trazodone (Desyre®)	Insomnia due to depression (off-label)	Adults: 50-150mg Older adults: 25mg at bedtime, to a maximum of 100mg at bedtime	↑ Total time spent asleep No abuse potential; useful with concurrent depression	Impairment of short-term memory, verbal learning or motor skills No effect on sleep cycle	Off-label use for insomnia (due to sedative side effects) Limited efficacy data
Amitriptyline (Elavil®)	Insomnia due to depression (off-label)	Adults: 10-50mg Older adults: Not recommended	Useful with concurrent depression or neuropathic pain	Strong anticholinergic and sedative side effects No effect on sleep cycle	Off-label use for insomnia (due to sedative side effects) NOT RECOMMENDED for use in older adults
Doxepin (Silenor®)	Sleep maintenance insomnia	Adults: 6mg Older adults: 3mg, dosing > 6mg/day not recommended	↑ Total time spent asleep No rebound insomnia	Sleep-driving activities, anticholinergic side effects	Not to be taken within 3 hours of a meal due to delayed absorption and potentials for next day drowsiness Long-term safety and efficacy not established

Orexin Receptor Antagonist

Medication	Use	Recommended Dosing	Advantages	Disadvantages	Important Considerations
Suvorexant (Belsomra®)	Sleep onset and/or sleep maintenance insomnia	Adults and older adults: 10mg within 30 minutes of bedtime, up to 20mg	↓ Awakenings	Daytime drowsiness, sleep-driving activities, sleep paralysis, hallucinations	Contraindicated for use in those with narcolepsy Long-term safety and efficacy not established

Sleep Latency Insomnia: Amount of time it takes to fall asleep after the lights have been turned off.

Sleep Maintenance Insomnia: Difficulty staying asleep or waking too early and struggling to get back to sleep.

Sleep Onset Insomnia: Transition from wake to sleep.

Older Adult: 60 years of age or older.