

# Understanding and Managing the Interaction between Sleep and Pain: An Update for the Dentist

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## A b s t r a c t

*Pain is a symptom well known to disrupt numerous aspects of normal physical and psychological life, including work, social activities and sleep. In daily practice, general dentists and specialists are frequently confronted with issues concerning pain, as their patients seek management that integrates oral health with overall well-being. An example of a dental condition involving pain is temporomandibular disorder, which is one of the most common sources of chronic orofacial pain and which shares similarities with back pain in terms of intensity, persistence and psychosocial impact. The objective of this paper is to inform and aid the general dentist and the specialist concerned with the sleep quality of patients with orofacial pain.*

**MeSH Key Words:** facial pain/complications; sleep/physiology; temporomandibular joint disorders/physiopathology

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This article has been peer reviewed.

**P**ain disrupts numerous aspects of physical and psychological life, including sleep, and dental problems, such as temporomandibular disorder, are often sources of chronic pain that can alter sleep patterns. The objective of this paper is to inform and aid the general dentist and the specialist concerned with the sleep quality of patients with orofacial pain.

### Pain

Pain creates behavioural states that allow the conscious individual to react to noxious threats. It is characterized by the integration of sensory (e.g., intensity), emotional (e.g., unpleasant) and motivational (e.g., running for survival) experiences.<sup>1</sup> The behavioural and cognitive aspects of pain perception are complex; clinicians need to understand this complexity when treating patients who complain of pain. For example, when a clinician asks a patient about pain relief, the patient is invited to compare what he or she is currently feeling with feelings that prompted a prior visit. In addition, a person's memory of

chronic pain is known to increase the intensity of current reported pain, which can complicate a clinician's understanding of the signs and symptoms of pain.<sup>2</sup>

Diffuse musculoskeletal pain is often associated with complaints of poor sleep and fatigue.<sup>3-6</sup> Brain imaging studies have revealed that "emotional" brain areas (e.g., the cingulate cortex, the prefrontal cortex and the hypothalamus) have a direct role in pain perception and that subjects reporting the most severe pain may have fewer binding sites for brain opioids (e.g., brain morphine, known as endorphin).<sup>6,7</sup> These observations could account for some of the high variability in measured pain perception and efficacy of analgesics. Moreover, in recent years, the placebo effect has been rediscovered as a powerful factor influencing pain behaviour, pain reporting and use of medication.<sup>8,9</sup>

Pain is reported by approximately 15% of the general population and by over 50% of older people. With aging, pain perception either remains relatively constant or decreases.<sup>10,11</sup> Interestingly, even though older patients use more medications (because of an increased prevalence of

various diseases and disorders), in general they are better able to cope with the effect of pain on their quality of life than middle-aged adults.<sup>12,13</sup> This could be because older patients accept and understand pain as an unpleasant companion of age, whereas younger patients may feel that pain threatens their capacity for life and productivity.

If a conscious person interprets a potentially harmful sensory input as painful, he or she reacts accordingly to protect bodily integrity and physiological homeostasis. In the absence of consciousness (e.g., under general anesthesia or hypnosis and, to a certain degree, during sleep), the brain retains the ability to detect painful input, thereby maintaining some protective reactivity.<sup>14</sup> The processing of pain from the periphery toward the brain, in particular toward the cortex, involves a complex sequence of events. First, specific receptors (e.g., free nerve endings) are activated; then, relay neurons in the spinal cord and thalamus change their firing patterns, and finally, information about the noxious stimulant reaches the sensory motor and emotional brain areas. The autonomic nervous system is also activated when pain is perceived: the heart rate increases, respiration is faster, and sudation is frequently present. A rise in cyclooxygenase 2, commonly recognized in the periphery, has also been observed recently in the spinal cord and brain neurons, which suggests that analgesic medications (e.g., rofecoxib and celecoxib) do not act exclusively in the periphery.<sup>15,16</sup> More recently, a third cyclooxygenase has been found in the heart and brain, which supports a role for the analgesic acetaminophen.<sup>17</sup>

Pain can be either acute and transient or chronic and persistent (more than 1 to 6 months, depending on the condition). Acute pain is common after dental surgery and endodontic treatments. Chronic pain, which can last for years, often affects quality of life and may persist long after an injury has apparently healed. Chronic pain is frequently associated with permanent modifications of central nervous system processes, such as chemical overexpression due to gene induction; lack of enzymatic chemical degradation (e.g., of inflammatory or pain mediators); nerve overactivity associated with aberrant connections (e.g., nerves or cells in the spinal cord that normally respond only to touch now respond to painful stimuli); a damaged dental nerve that sprouts and makes unusual connections to bone, mucosa, periodontal ligament, blood vessels and other tissues.<sup>15,16</sup>

## Sleep

Sleep is a regular process within the 24-hour cycle; humans typically have approximately 16 hours of wakefulness and 8 hours of sleep. Each night's sleep is divided into 2 main types of sleep periods: non-rapid eye movement (REM) periods (which have a sequence of light sleep [stages 1 and 2 non-REM] and deep sleep [stages 3 and 4 non-REM, responsible for restorative function]) and REM periods

(also named paradoxical sleep, characterized by muscle atonia and paralysis). Humans dream during various sleep stages, but the dreams of REM sleep are, in general, more vivid, creative and fantastical. The dreams of patients with chronic pain encompass pain experiences from several body sites, including the head and neck regions.<sup>18,19</sup> Patients with chronic pain can be encouraged to keep a journal of their dreams (with instruction about avoiding overinterpretation), which may improve their understanding of the causes (e.g., a traumatic event) and consequences (e.g., mood alteration, familial roles, avoidance of social activities) of the pain.

Sleep is a behavioural and physiological state that is generally resistant to nonmeaningful external stimuli.<sup>20</sup> In the general population, the proportion of people reporting insomnia (either a long delay in sleep onset or no return to sleep if awakened) increases from 20% among people 15 to 24 years of age to 36% after the age of 75. Anxiety is an important factor in insomnia and poor sleep,<sup>21,22</sup> and patients with chronic pain are at high risk of insomnia.<sup>22-24</sup>

In most (50% to 90%) patients with acute pain, the occurrence of pain generally precedes complaints of poor sleep.<sup>22,24</sup> However, studies of patients with burn pain or chronic pain have indicated bidirectional influences: a night of poor sleep may be followed by greater pain the next day, and a day with high pain levels is often followed by a night of poor sleep.<sup>25,26</sup>

In general, the percentage of time spent in each sleep stage is not markedly different between patients with chronic pain and control subjects. However, in patients with chronic pain and other poor sleepers, sleep is often more fragmented than that of "normal" healthy adults (i.e., the overall sleep period is broken down into several brief periods of sleep). This fragmented sleep is characterized by subtle changes, including frequent micro-arousals (3 to 10 seconds long, involving transient brain, heart and muscle activations), awakenings (activations lasting longer than 10 to 15 seconds, with possible consciousness), shifts in sleep stage (e.g., from a deeper to a lighter sleep stage) or body movements (or some combination of these characteristics). These subtle changes may occur in clusters, repeating every 20 to 40 seconds, accompanied by rapid alpha cortical waves (known as alpha wave intrusions) and increases in heart rate and muscle tone. These changes are collectively termed cyclic alternating pattern (CAP), and when CAP occurs too frequently, it can lead to poor sleep.<sup>27,28</sup> Interestingly, a recent report indicates that patients with fibromyalgia do not display the reduction in heart rate that is usually observed during the deeper restorative sleep stages (i.e., stages 3 and 4 of non-REM sleep).<sup>29</sup> Thus, if the brain is overactive during sleep (i.e., an excessive frequency of CAP), with heart rate remaining at daytime levels, sleep could be nonrefreshing. This might

account for complaints of poor sleep, daytime fatigue, lack of concentration, memory dysfunction and increased risk of motor vehicle crashes and workplace accidents.<sup>30–33</sup> These findings might also explain the interrelationship between poor sleep and other manifestations of pain, including fatigue and irritability. These observations merit consideration when planning both basic research and clinical assessments of pain management strategies.

The pain perceived during an unconscious or unresponsive state, such as sleep or general anesthesia, is termed nociception.<sup>34</sup> During sleep, nociception remains active to protect bodily integrity. In light sleep (stages 1 and 2 non-REM) and in REM sleep, the body can react rapidly to meaningful external stimuli (e.g., the sound of a telephone, an alarm or a crying baby).<sup>35,36</sup> However, in deep sleep (stages 3 and 4 non-REM), this responsiveness is partially suppressed to protect sleep continuity. To better understand how the brain processes sensory pain information, the authors used young, healthy subjects in a laboratory setting to compare intramuscular injection of noxious hypertonic saline solutions with injection of non-noxious solutions and vibrotactile stimulation during sleep. Patients experiencing pain were not included in these studies since it would have been difficult to isolate sleep fragmentation variables from the influence of medications, mood alteration, poor sleep and other factors. The results revealed that experimental pain stimulations triggered awakenings and shifts in sleep stage over all sleep stages, including the usually less responsive deep sleep and REM sleep.<sup>37</sup> This novel finding suggests that management strategies should focus on all sleep stages to maintain the best sleep quality. Additional studies are now underway to determine whether these responses explain the poor sleep, fatigue (e.g., low restorative effect) and lower cognitive function reported by patients with chronic pain.<sup>38</sup>

### Clinical Guidelines

The assessment and treatment of sleep problems among patients with chronic pain can be approached in 4 steps (see below and **Table 1**). Management of pain and sleep may include the use of behavioural strategies with or without medications that improve sleep by reducing microarousal or CAP activation and thereby decrease persistent autonomic–cardiac activation (e.g., strategies that improve the parasympathetic drive during deep sleep). Because a higher quality of life is important for all patients, it is considered necessary to prevent the effects of sleepiness on important cognitive functions (e.g., memory and driving). This paper does not address the use of oral splint appliances and physical therapy in the management of orofacial pain; reviews of these subjects can be found elsewhere.<sup>39,40</sup>

### Step 1: Evaluation for Primary Sleep Disorder

Before pharmacological approaches are considered, it is important to obtain a complete history of the patient's sleep habits and to determine if he or she has a primary sleep disorder (e.g., a disorder that affects breathing, such as snoring or apnea, periodic limb movement syndrome, sleep bruxism or insomnia). For this, a screening questionnaire<sup>41</sup> can be invaluable. If a primary sleep disorder is suspected, the patient needs to consult the family physician for possible referral to a sleep centre.

### Steps 2 and 3: Sleep Hygiene and Behavioural and Cognitive Strategies

If a primary sleep disorder is not suspected, the patient's sleep hygiene is then reviewed. This review includes questions about the sleep environment, such as whether a baby sleeps in the same bedroom, whether the bedroom is also used as an office (with or without a computer) and the level of outside traffic noise. For optimal sleep, the bedroom should be a quiet "oasis," not an area for work and negotiation. The patient should be asked whether he or she has a regular daily schedule (i.e., a regular 24-hour sleep–wake cycle on both weekdays and weekends). Furthermore, lifestyle issues should be assessed, including evening habits (e.g., caffeine intake, smoking, alcohol consumption or intense exercise late in the evening); such habits are to be discouraged, since this time should be reserved for relaxing before sleep.

Several well-defined behavioural and relaxation methods are available for stress management in relation to the interaction of sleep and pain.<sup>42–44</sup> These techniques include progressive muscle relaxation (sequential relaxation of major muscle groups), meditation, imagery training and hypnosis. Although relaxation techniques differ in philosophical approach, they share 2 main components: repetition of a specific activity, such as words, sounds, prayers, phrases, body sensations or muscular activity; and a passive attitude toward intruding thoughts, which should result in a return of focus. These techniques are intended to induce a common set of physiological changes, such as decreased metabolic activity, heart rate and muscle tone.

Relaxation methods require training motivation and daily practice, but the patient can anticipate long-term effects if compliant. Professional guidance from a psychologist or a physical therapist is often necessary during the initial stages of treatment to help patients master the selected technique.

Meditation techniques do not involve suggestion; rather, the individual is trained to passively attend to a bodily process, a word or a stimulus. The goal of "mindful meditation" is the development of nonjudgemental awareness of bodily sensations and mental activities occurring in the present moment.

**Table 1 Essential sleep management issues to be addressed in patients with orofacial pain**

Step of assessment and treatment	Comments
Step 1 Evaluation for primary sleep disorder	Examples: insomnia, sleep-disordered breathing, primary snoring, daytime fatigue or sleepiness Consult physician if necessary
Step 2 Review of sleep hygiene	Evaluate: <ul style="list-style-type: none"> <li>• Sleep environment (e.g., bedroom dark, cool and quiet)</li> <li>• Wake-sleep cycle (e.g., consistent bedtime and morning awakening)</li> <li>• Lifestyle habits (e.g., intense exercise, smoking or alcohol intake at night)</li> </ul>
Step 3 <sup>a</sup> Behavioural and cognitive strategies	Examples: establish regular routines for evening relaxation, avoid intense or troubling evening discussions
Step 4 <sup>a,b</sup> Pharmacological interventions <sup>c</sup>	<p><b>Short-term therapy</b> Analgesic, either alone or combined with a muscle relaxant, administered in the evening:</p> <ul style="list-style-type: none"> <li>• ibuprofen (Advil, Motrin), acetylsalicylic acid (ASA; Aspirin) or acetaminophen (Tylenol)</li> <li>• acetaminophen with chlorzoxazone (Tylenol Aches and Strains)</li> <li>• methocarbamol with either acetaminophen (Robaxacet) or ASA (Robaxisal)</li> </ul> <hr/> <p><b>Mild condition</b> <i>Muscle relaxant or sedative (in early evening, to reduce morning dizziness)</i></p> <ul style="list-style-type: none"> <li>• low-dose cyclobenzaprine (Flexeril, half or full 10-mg tablet)</li> <li>• clonazepam (Rivotril 0.5 mg short term because of risk dependence)</li> <li>• analgesics such as acetaminophen, ibuprofen or ASA can be taken with cyclobenzaprine and clonazepam if the pain is too great</li> </ul> <hr/> <p><i>Sleep facilitator</i></p> <ul style="list-style-type: none"> <li>• triazolam (Halcion 0.125 to 0.250 mg)</li> <li>• temazepam (Restoril 10 to 20 mg)</li> <li>• zopiclone (Imovane 5 to 7.5 mg)</li> <li>• zolpidem (Ambien 5 to 10 mg): not currently available in Canada</li> <li>• zaleplon (Starnoc, 10 to 20 mg)<sup>d</sup> — very short acting, useful for middle of the night or late-night wakefulness or insomnia</li> </ul> <hr/> <p><b>More severe or persistent cases (physician consultation recommended)</b></p> <ul style="list-style-type: none"> <li>• low-dose amitriptyline (Elavil 5 to 50 mg, in increasing doses if required) in the evening</li> <li>• trazodone (Desyrel 150 mg)</li> <li>• nefazodone (Serzone)</li> <li>• gabapentin (Neurontin), codeine (Codeine Contin) + morphine (MS Contin)</li> </ul> <hr/> <p>Others:</p> <ul style="list-style-type: none"> <li>• valerian</li> <li>• lavender</li> <li>• glucosamine sulphate</li> <li>• kava</li> </ul>

<sup>a</sup>For steps 3 and 4, combined strategies could be considered but only on a case-by-case basis.

<sup>b</sup>Patients should be forewarned of potential side effects associated with the medications listed; these may include daytime sleepiness and dizziness. Patients should avoid driving in the morning and they should use caution in operating any potentially hazardous tool.

<sup>c</sup>Brand names are included only as examples and not to promote any one product. The manufacturers are as follows: Advil, Whitehall-Robins; Motrin, McNeil Consumer Healthcare; Aspirin, Bayer Consumer; Tylenol and Tylenol Aches and Strains, McNeil Consumer Healthcare; Robaxacet and Robaxisal, Whitehall-Robins; Flexeril, Alza; Rivotril, Roche; Halcion, Pharmacia; Restoril, Novartis Pharmaceuticals; Imovane, Aventis Pharma; Ambien, Sanofi-Synthelabo Inc.; Starnoc, Servier; Elavil, Merck Frosst; Desyrel, Bristol; Serzone, Bristol-Myers Squibb; Neurontin, Pfizer; Codeine Contin and MS Contin, Purdue Pharma.

<sup>d</sup>Ideal for patients with sleep apnea.

Medical hypnotic techniques induce a state of selective attention in which the subject isolates himself or herself from his or her thoughts. It is often combined with enhanced imagery. Patients may also learn autohypnosis, a relaxation technique in which thinking is directed toward pleasant images. People vary widely in their “hypnotic susceptibility” and “suggestibility,” although the reasons for these differences are not clearly understood.

### *Stimulus Control and Sleep Hygiene*

Improvement of sleep quality through changes in sleep hygiene proves beneficial for many patients. For example,

the patient may be instructed to go to bed only when sleepy, to get out of bed when unable to sleep, to rise at the same time every morning and to take only brief naps during the day (20 to 30 minutes or less before 3 p.m. is thought to not significantly alter nighttime sleep). Patients should avoid caffeinated beverages after dinner and smoking around bedtime and upon nighttime waking, and should either reduce or avoid alcohol consumption in the evening. Patients should also avoid intense exercise before bedtime and should minimize bedroom noise, light and extreme temperatures.<sup>45</sup>

### Cognitive Strategies

Cognitive-behavioural therapy attempts to reorient patterns of negative thoughts and dysfunctional attitudes toward a focus on healthy adaptive thoughts, emotions and actions. Patients must be reminded to keep expectations realistic and to avoid blaming insomnia for all of life's difficulties. In addition, patients should avoid catastrophic attitudes (exaggerated negative orientation toward experiences) after a poor night's sleep.<sup>46</sup>

### Step 4: Pharmacological Interventions

If poor sleep persists during or after institution of steps 1 to 3, the dentist, in consultation with a physician, may consider pharmacotherapy.

### Pharmacological Strategies for Short-Term and Mild Conditions

Among the pharmacological agents available, analgesics alone or in combination with a mild muscle relaxant, administered in the evening, can be tried (see Table 1). A low dose of cyclobenzaprine or clonazepam, taken in the evening, either alone or with an analgesic (e.g., acetaminophen or ibuprofen), may promote muscle relaxation, reduce pain and produce light sedation. Sleep facilitators, such as zaleplon, triazolam, temazepam and zopiclone, may also prove helpful for short periods, but they are not recommended in very young or older patients. In the presence of sleep-disordered breathing (e.g., sleep apnea), zaleplon or zopiclone is preferred. For refractory cases, physicians may prescribe low-dose amitriptyline (with slowly increasing doses), trazodone or nefazodone before sleep. These medications may have the secondary effect of improving mood and altering the experience of pain. Gabapentin, codeine and morphine are sometimes used for severe pain, but these drugs are known to interfere with sleep quality. Caution is advised in prescribing selective serotonin reuptake inhibitors such as fluoxetine, sertraline, and paroxetine, since these medications can trigger or aggravate movement during sleep, including periodic limb movement and sleep bruxism. The use of cardioactive medications for pain management (e.g., propranolol) is associated with increased risk of sleep apnea and nightmares.<sup>47</sup>

### "Natural" and Herbal Products

Herbal medicines are widely used in the treatment of pain and to aid sleep, but most lack evidence to support these uses. Examples include St. John's wort (for depression), valerian (for sedation and sleep),<sup>48,49</sup> lavender (for sleep),<sup>49,50</sup> kava (for anxiety and sleep),<sup>51</sup> glucosamine sulfate (for arthritis)<sup>52,53</sup> and even cannabis. Nonetheless, given their growing popularity, dentists should ask patients whether they are using any of these products before contemplating the prescription of a more conventional medication that might have an additive sedative action or

that might cause an adverse drug interaction.<sup>48</sup> Most natural medicines have the potential to produce interaction effects with conventional medications.

### Conclusions

Dentists play an important role in relieving orofacial pain and are front-line managers of temporary sleep disturbances associated with pain.<sup>41</sup> Given the increasing popularity of herbal and other alternative medicines, the risks of adverse interactions with more conventional medications need to be assessed for each patient. Three Web sites are suggested as sources of additional information: Saskatoon Health Region ([www.sdh.sk.ca](http://www.sdh.sk.ca)), National Center for Complementary and Alternative Medicine ([www.nccam.nih.gov](http://www.nccam.nih.gov)) and Réseau Proteus ([www.reseauproteus.net/1001solutions](http://www.reseauproteus.net/1001solutions)). ♦

*Acknowledgments:* The authors' research is supported by the Canadian Institutes of Health Research and the Quebec Health Research Fund (FRSQ). This paper was presented in part at the "Sleep in older person" symposium held at the Faculty of Medicine, University of Toronto, March 2002, and at the Canadian Pain Society meeting held in Winnipeg, May 2002.

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The authors have no declared financial interests in any company manufacturing the types of products mentioned in this article.

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