Sleep disturbances in chronic pain : neurobiology, assessment, and treatment in physical therapist practice

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Abstract

Among people with chronic pain, insomnia is highly prevalent, closely related to the mechanism of central sensitization, characterized by low-grade neuroinflammation, commonly associated with stress or anxiety, and often does not respond effectively to drug treatments. This review article applies the current understanding of insomnia to clinical practice, including assessment and conservative treatment of insomnia in people with chronic pain. Cognitive behavioural therapy for insomnia (CBT-I) can be efficacious in improvements of sleep initiation, sleep maintenance, perceived sleep quality and pain interference with daily functioning in people with chronic pain. A recent systematic review concluded that with additional training, physical therapist-led cognitive-behavioral interventions are efficacious for low back pain, allowing their implementation within the field. CBT-I, as provided to people with chronic pain, typically includes psycho-education, sleep restriction measures, stimulus control instructions, sleep hygiene, and cognitive therapy.

Introduction

Conservative and pharmacological strategies for chronic pain management offer at best modest effect sizes in reducing pain and related disabilities[1-3], urging the need for an improved care. A comprehensive approach to chronic pain management should also address pain interfering conditions such as comorbid insomnia, a seldom addressed topic in physical therapy literature. Indeed, sleep is increasingly recognized as a plausible therapeutic target for a range of chronic conditions, including chronic pain[4,5]. If left untreated, insomnia can represent a barrier for an effective chronic pain management[6]. Chronic pain is **described** as debilitating pain of at least 3 months duration, and **is targeted here at persisting** musculoskeletal pain.

In the absence of other intrinsic sleep disorders and inadequate opportunity or circumstances for sleep (e.g. shift work), insomnia in adults is defined as > 30 minutes sleep latency and/or minutes awake after sleep onset for > 3 days / week for > 3 months[5-7]. Insomnia is highly prevalent among people with chronic pain, with 53% to 90% of chronic pain patients suffering from a clinically significant degree of insomnia[8-11]. People suffering from chronic back pain are 18 times more likely to experience clinically defined insomnia compared to those without chronic back pain[10].

Insomnia is closely related to pain severity in people with chronic (low back) pain[10]. People with whiplash associated disorders present with insomnia complaints such as difficulties initiating sleep and difficulties maintaining sleep, which are related to their cognitive

disturbances like reduced information processing speed[12]. Insomnia is usually considered a consequence of chronic pain, but research findings show that sleep disturbances may have a bidirectional relation with chronic pain[6,9,**13**].

Insomnia may act as both a precipitating and perpetuating factor[5]. Population-based longitudinal studies showed that sleep impairments predict the onset and exacerbations of chronic pain[13]. Based on the available literature it was concluded that sleep impairments predict chronic pain more strongly than pain predicts sleep impairments[13]. Insomnia is independently associated with the perceived impact of pain on daily functioning and life satisfaction in people with chronic spinal pain[5]. Lastly, people with chronic pain spontaneously engage in more physical activity following a better night of sleep[14] (figure 1). The latter suggests that improving nighttime sleep may be a novel avenue for promoting greater daytime physical activity in people with chronic pain[14].

- Insert Figure 1 here -

Despite the growing body of scientific literature pointing towards the high prevalence of insomnia in individuals with chronic pain, many pain treatment programs nowadays propose little other than sedative pain and/or hypnotic neuropharmacological drugs for the treatment of comorbid insomnia[10]. These drugs include anticonvulsants, non-benzodiazepines, benzodiazepines or tricyclic antidepressants. This is problematic for 2 reasons. First, the efficacy and safety of drug treatment for insomnia in people with chronic pain has not been established. Furthermore, the usage of hypnotic medications is associated with a number of side-effects including sedation, daytime drowsiness, dizziness, lightheadedness, cognitive and

psychomotor impairments[15,16]. Pharmacological strategies directed at nociceptive mechanisms do not yield improvements in sleep in people with chronic pain[17-20]. Moreover, many trials in people presenting with headaches or musculoskeletal pain found that medication may both disturb sleep and even increase pain[21]. Finally, reliance on pharmacological treatments for insomnia often opposes patients' preferences for non-pharmacological alternatives[22].

Consequently, there is an urge to inform physical therapists about the close interaction between insomnia and the chronic pain experience. With the following we aim to update the reader with the current understanding of the neurobiology behind the interaction between insomnia and chronic pain, therewith clearing the path for a conservative approach to the management of insomnia in people with chronic pain within a physical therapy setting. Henceforth, clinical guidelines for the assessment and treatment of insomnia in people with chronic pain within a physical therapy setting will be provided. **These recommendations for assessment and treatment of insomnia are based on the available scientific evidence and the authors' clinical expertise.**

How sleep can influence chronic pain: neuroinflammation, central sensitization and beyond

Sleep and central sensitization: a bidirectional interaction

Central sensitization implies increased neuronal response to stimuli in the central nervous system (i.e. central hyperexcitability) and reduced pain modulation [23-25]. Although the

concept of central sensitization originates primarily from laboratory, the awareness is growing that it should be part of our clinical reasoning in daily practice [26-28]. There is a close interaction between central sensitization and sleep disturbances in people with chronic pain. A single night of total sleep deprivation has been shown to induce generalized hyperalgesia and increase state anxiety in healthy people[29,30]. Likewise, sleep curtailment impairs endogenous nociceptive-inhibitory function and increases spontaneous pain in healthy people[31]. These findings suggest that sleep disturbances might not only perpetuate central nervous system hyperexcitability in people with chronic pain, but may also serve as an aetiological factor. This may in turn ensue a vicious cycle: poor sleep lowers pain thresholds[6,31], which then contributes to hyperalgesia[31] and subsequent increased incidence and/or severity of insomnia[6].

The link between central sensitization and insomnia is underscored by various research findings. People with knee osteoarthritis have more central sensitization when they suffer from comorbid insomnia[32]. The same study revealed that people with osteoarthritis who have reduced sleep efficiency and higher catastrophizing show more signs of central sensitization[32]. Likewise, in a large sample of 961 people with chronic pain, pain-related sleep interference was significantly associated with pain hypersensitivity **as measured by quantitative sensory testing**, but not with spinal nociceptive hypersensitivity **as typically assessed by means of the electromyography response to an electrical stimulus (nociceptive withdrawal reflex**)[33]. Pain hypersensitivity was assessed using pain threshold to electrical stimulation. Moreover, the magnitude of pain-related interference with sleep was associated with increased risk of pain hypersensitivity in people with chronic pain[33]. The authors concluded that improving sleep and sleep quality may be important for the management of pain hypersensitivity, potentially

leading to pain reduction[33]. In people with temporomandibular joint disorder, insomnia is associated with hyperalgesia at a nonorofacial site, suggesting that insomnia may be linked with central sensitization[34].

The role of the dopaminergic, serotonergic and opioidergic systems in explaining insomnia in chronic pain

The link between **insomnia** and central sensitization might imply overlapping mechanisms in the central nervous system, for instance mesolimbic dopaminergic pathways playing a cardinal role in both sleep regulation and endogenous analgesia[35]. Hence, decreased dopamine availability may explain both sleep disturbances and dysfunctional endogenous analgesia in people with chronic pain. Serotoninergic pathways are also implicated in shared modulatory mechanisms of pain and sleep regulations. Serotonin is critical for top-down orchestration of endogenous analgesia[36] as well as of circadian rhythm control[37]. Serotoninergic dysfunction can result in altered patterns of circadian behavior or even contribute to a disruption of sleep-wake homeostasis[37] along with dysfunctional endogenous analgesia[38]. While it is unlikely that either one of the two mentioned neurotransmitters are the sole factors underlying the links between pain and **insomnia**, both seem to play major roles in explaining sleep disturbances in people with chronic pain. Essentially, a possible dysfunction in either dopaminergic or serotonergic systems fits within the view that central sensitization is exacerbated or even initiated by sleep disturbances. Preclinical studies support this view by revealing that selective MT2 melatonin receptor partial agonists hold analgesic properties through modulation of ON/OFF cells of brainstem descending antinociceptive systems in neuropathic pain models[39,40].

Opioidergic signalling is also implicated in shared modulatory mechanisms of pain and sleep regulations. Opioids are known to influence sleep-wake regulation at least in part mediated by central opioid input to the ventrolateral preoptic nucleus, a key cell group for producing behavioral sleep[41]. Morphine decreases the total amount of deep sleep and rapid eye movement sleep in humans through inhibiting the firing rate of sleep-promoting neurons in the ventrolateral preoptic area[42].

Poor sleep results in a low-grade central nervous system inflammation

In addition, our current understanding of sleep-related neuro-immunology provides potential links between sleep impairments and pain. While healthy sleep facilitates immune functions, impaired sleep quality or quantity can result in low-grade inflammatory responses[43-45]. This low-grade inflammatory response as a consequence of sleep deprivation includes increased levels of interleukin 6, prostaglandin E2[44,45] and nitric oxide[46] possibly mediated by cerebral microglia[46]. Allegedly, even low levels of inflammatory cytokines are known to potentially affect brain function[47]. These cytokines interfere with central nervous system-mediated fatigue[48] and correlate with observations of increased sensitivity to painful stimuli following sleep restriction[30,44,49]. Taken together, sleep deprivation conveys a glia-mediated low-grade inflammatory response leading towards increased sensitivity to pain as observable in people with chronic pain[50]. The nature of neuro-immunologic links between sleep and pain may be important for the inclusion of pain neuroscience education in people with chronic pain (i.e. empower patients to invest time in **cognitive behavioural therapy for insomnia**).

*The role of stress in explaining **insomnia** in people with chronic pain*

Stress and sleep are consistently interconnected, as evidenced in numerous studies reporting strong associations between anxiety levels and insomnia severity[51,52], for instance in people with chronic low back pain[10]. Daily life stress (e.g., worries about the next morning's workload) can negatively impact sleep[53]. Similarly, major stressful life events and/or traumatic events such as natural disasters, combat or a traffic accident can result in sleep architecture alterations reflecting poor sleep[53]. Increased night-time arousal and decreased sleep efficiency are among the most sensitive sleep variables in response to stressors[53].

In addition, health anxiety has also been described as a significant predictor of insomnia severity[10]. Health anxiety refers to a specific type of anxiety characterized by excessive concerns about one's health (e.g., a preoccupation with fears of having a serious disease, despite of medical reassurance). It may contribute to aggravate or even trigger insomnia by inducing hypervigilance and arousal by activation of a cascade of cognitive and behavioral processes such as selective attention to threats and negative appraisal[10]. Likewise, depression accounts in part for the variance in sleep quality among people with chronic pain[54,55].

The previous paragraphs document how stress can impair sleep, but sleep itself can be a stressor. Individuals with insomnia often show high levels of apprehension about bedtime and performance anxiety in an attempt to control the process of sleep onset; and even engage in catastrophic thinking about potential consequences of poor sleep[56]. The latter may in turn result in a marked decrease of coping abilities with every day life's stressors. For these

reasons, it comes as no surprise that sleep management is mostly included as a part of stress management programs and vice versa. In a successful trial of cognitive behavioral treatment for **insomnia** in people with chronic pain, improvers not only showed a significant increase in perceived sleep efficiency but also a decrease in self-reported levels of distress[57], suggesting that effective coping with stress is a key factor for sleep improvements.

In the preceding parts it was explained how insomnia is of significance to people with chronic pain, with special emphasis on the neurobiology of these interactions. In what follows our current understanding of insomnia in people with chronic pain is applied to clinical practice (including assessment and **cognitive behavioural therapy for insomnia**).

Applying science to practice I: Assessment of insomnia in people with chronic pain in clinical practice

Depending on the education received, physical therapists may not be trained to screen for insomnia, **and patients are not referred to physical therapists for insomnia either. Yet physical therapists are** advised to briefly question people with chronic pain about sleep latency and minutes aware after sleep. This can allow them to estimate whether the patient complies with the definition of insomnia (i.e. > 30 minutes sleep latency and/or minutes awake after sleep onset for > 3 days / week for > 3 months[5-7]). **It is advised to determine from the patient if the insomnia began before or after the pain condition and consider how the pain condition is influencing their insomnia symptoms. In addition,** the Insomnia Severity Index generates reliable and valid data to quantify the subjective harshness of insomnia[58]. A cut-off

level of 14 (i.e., range 0-14 versus 15-28) has been proposed for the clinical significance of chronic insomnia in patients presenting with chronic back pain[10], and >10 was recommended as the cut-off in a community sample[59]. In case of suspected insomnia the physical therapists should refer the patient to a sleep physician who can use polysomnography to ascertain whether or not underlying primary sleep disorders are present[6,60]. Such primary sleep disorders include sleep-related breathing or movement disorders, circadian sleep-wake disorders, etc. **The polysomnography is not used to diagnose insomnia but to rule-out other sleep disorders.**

In case of diagnosed insomnia disorder, physical therapists should then explore whether insomnia is co-existing with the chronic pain experience. This is achieved by ascertaining that insomnia is reported by the patient to originate after, and/or aggravated by the current pain condition[6], or presents in the absence of pain. If this is the case and the physical therapist is planning to provide **cognitive behavioural therapy for insomnia**, a thorough questioning of the patient's sleep habits and difficulties is required. Such an interview may include the items listed in Table 1. **That table 1 not only comprises of items to be included for questioning of the patient's sleep habits and difficulties, it also entails a guide on how to interpret the obtained information as well as treatment implications.**

- Insert table 1 here -

Whether the patient has been or is currently a substance abuser is not only important because of its potentially negative impact on biological functions of sleep, but also because past or current substance abusers' dopaminergic circuits may be altered as a consequence of

repeated activations associated with consumption[35]. In addition to sleep history taking, therapists may consider using self-reported tools for the assessment of sleep parameters. Such self-reported tools include sleep diaries, questionnaires like the Insomnia Severity Index, the Pittsburgh Sleep Quality Index and/or the Epworth sleepiness scale[61,62].

Applying science to practice II: Conservative treatment of insomnia in people with chronic pain

Cognitive behavioural therapy (CBT) is effective for the treatment of chronic pain[2,63-65]. **CBT is a psychosocial intervention that aims at changing unhelpful thoughts, beliefs and attitudes in order to improve their coping skills, self-regulation and healthy behaviour. CBT is widely used for the treatment of chronic pain and depression.** A systematic review concluded with high quality evidence that with additional training, physical therapist-led cognitive-behavioural interventions are effective for low back pain[66]. Cognitive behavioural therapy for insomnia (CBT-I) is a specific form of CBT for a specific condition, one that is a candidate to be considered for Psychologically Informed Practice delivered by physical therapists[67].

Available evidence for conservative sleep treatment in people with chronic pain

A meta-analysis of available studies examining the effects of non-pharmacological treatments of insomnia for cancer and non-cancer related chronic pain conditions showed that addressing sleep resulted in large immediate improvements in sleep quality, relatively small reductions in pain and fatigue and moderate decrease of depression symptoms[4]. The improvements in sleep quality and fatigue were maintained after a 1 year follow-up[4].

CBT-I is the recommended evidence-based treatment for chronic primary insomnia[60]. The advantage over sedative drugs or classical hypnotics mainly lies in the sustainability of treatment effects and a lower risk for side-effects[60]. Based on the available treatment studies in people with chronic pain, a similar picture arises. The first report of a treatment trials targeted at sleep for people with chronic pain dates back to 2010[5,68]. CBT-I results in improvements in various sleep parameters (e.g. self-reported sleep onset latency, wake time after sleep onset, sleep efficiency, sleep quality, etc.), sleep and pain interference with daily functioning in people with chronic pain[5,68,69]. Improvements were maintained at 3-month follow-up[68]. The clinical relevance of the treatment effects was emphasized by the large difference between group responders (78% in the CBT-I-group versus 22% in the control group) and patients considered as remitted (42% versus 11%)[5]. The effect sizes for sleep parameters and pain interference varied from moderate to large, but small for pain intensity[5].

Should CBT only target sleep, or should it target both pain and sleep? The results from 2 smaller pilot studies are in support of the latter: combining CBT for pain with CBT-I was feasible and produced significant improvements in sleep, disability from pain, pain interference, depression and fatigue[6,70]. Importantly, the combined intervention appeared to have a strong advantage over CBT for pain alone and modest advantage over CBT-I alone in reducing insomnia severity in people with chronic pain[6]. The gains in insomnia severity and pain interference were maintained at 1- and 6-months follow-up[70].

Taken together, recently accumulated knowledge in the field has progressed and contributed to increase our understanding about the interplay between sleep and pain. It has been shown that CBT-I is efficacious for the improvement of sleep duration, maintenance of sleep, perceived sleep quality [60] and pain interference in daily functioning[5] in people with chronic pain. Additionally, there is relatively little available evidence about the optimal care-path for sleep related problems in the context of chronic pain[11]. There is a need for an improved reporting of procedural information allowing clinicians to replicate study findings in daily routine[66]. To these extents, the subsequent question is: what should be the exact content of such a CBT-I in people with chronic pain?

An introduction to CBT-I for people with chronic pain and insomnia

CBT-I includes sleep and bedtime restriction, stimulus control instructions, psycho-education for sleep and promoting good sleep habits (or sleep hygiene), teaching relaxation skills, and cognitive therapy[5,68,71]. Each of these main tenants of CBT-I are introduced and described in table 2 **(to be used together with table 1 to allow an individually-tailored CBT-I)**. For more details and a comprehensive guide for clinicians, the readers are referred to an available manual[72]. **Clinicians who wish to provide CBT-I can benefit from additional training and are advised to attend and educational course.**

- insert table 2 here -

Addressing poor sleep routine by scheduling a new sleep pattern[11] and poor sleep efficiency (e.g., 8 hours in bed and only 4 hours of sleep)[11] can be done by providing classical bedtime restriction approaches[5,11]. In case of impaired sleep efficiency and inappropriate sleep

routines, this includes sticking to the same getting up time (or advancing the latter) as usual, but getting into bed at a later time when sufficiently sleepy, in order to reduce the amount of time spent in bed and increase homeostatic sleep pressure at sleep onset. In case that sleep efficiency increases to 85% or more, the upward titration is initiated by adding 15 minutes to the prescribed time in bed[5]. While people with insomnia knowingly often have lower levels of sleep pressure and increased levels of wake drives (respectively sleep onset or maintenance difficulties and hypervigilance[73]), interventions on sleep and bedtime restrictions therewith aim at improving sleep homeostasis that occurs with the expansion of sleep opportunity, not only in response to sleep loss but also as a means of managing pain[5].

Sleep hygiene should be improved alongside with improved stimulus control in order to re-establish an enhanced and optimal associations between bedroom and sleep, allowing for sleep to solely occur in association with the bedroom and related controlled parameters (complete darkness, stable and sufficiently low room temperature, lowest levels of sensory stimuli, etc.)[5]. Cognitive therapy entails changing negative thoughts about sleep. It includes "decatastrophization" to address the perception of dire consequences of sleep loss[5]. It is essential for clinicians to acknowledge that the barriers for achieving adequate sleep can present with substantial inter-individual variabilities[11]. Such interventions are not limited to a specific discipline but available for any caregiver willing to learn more about the role of sleep and how to improve it. Regarding administration modalities, conservative sleep treatment are effective when delivered face-to-face[4,5] or through internet[74,75].

Other interventions not directly targeting sleep may have a positive effect on sleep quality and quantity. For instance, stress management[76] and exercise therapy[76-79] improve sleep in patients following cancer treatment.

Conclusion

Insomnia among individuals with chronic pain is highly prevalent and closely related to mechanisms of central sensitization. It is characterized by low-grade neuroinflammation, associated with stress/anxiety, and does not respond effectively to pharmacological treatment. CBT-I is effective for improvements of sleep initiation, efficiency and maintenance, perceived sleep quality and pain interference in daily activities in people with chronic pain. In addition, there is relatively little evidence about optimal administration procedures (timing, simultaneous priming or hierarchy) for the treatment of sleep disorders in contexts of chronic pain. A recent systematic review concluded with high quality evidence that with additional training, physical therapist-led cognitive-behavioral interventions are effective for low back pain, allowing implementation within the field. CBT-I typically includes sleep (or bedtime) restriction recommendations, stimulus control instructions, psycho-education regarding sleep and sleep hygiene, and cognitive therapy. CBT-I may not be a stand-alone treatment for people with chronic pain and comorbid insomnia, but may preferentially be combined with other effective treatment interventions, such as exercise therapy and cognitive behavioural therapy for pain.

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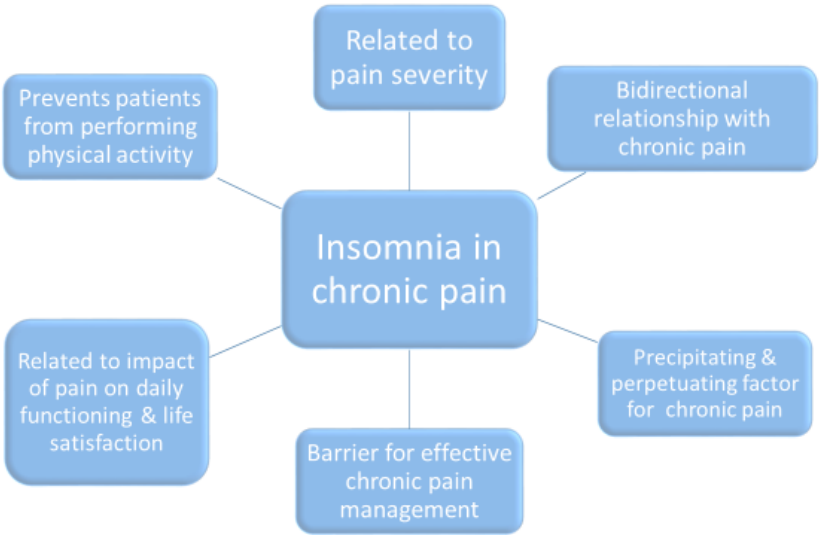

Figure 1. The clinical importance of insomnia in people with chronic pain[5,6,8-11,14].

Item	Explanation	Mode of assessment	Sample questions	Interpretation	Treatment implications
(Non-)restorative sleep	Recuperative sleep or not; whether the patient feels refreshed at final awakening.	Questioning/ PSQI#.	Do you feel refreshed when you wake up?	Ideally, good sleep should be refreshing. Non-restorative sleep can be a symptom of a disordered sleep.	In case of recurrent sensations of non-restorative sleep or unrefreshing morning arousals, further inquiring about sleep is indicated.
Time-in-bed[5]	Amount of time spent in bed	Questioning/ sleep diary / PSQI#/ actigraphy.	How much time do you spent in bed over the course of 24h?	Interpretation should take into account time spent in and out of bed, as well as time awake in bed (i.e. sleep efficiency).	Treatment implications rely on the interpretation of various sleep items taken together – the amount of time spent in bed at night alone has no treatment implication per se.
Time-out-of-ded[5]	Amount of time spent (awake or asleep) out of bed at night.	Questioning/ sleep diary / actigraphy.	How much time do you spent out of bed during the night?	If the patient spends more than half an hour out of bed at night, further questioning about what they do when being out of bed is required. In general, this may be related to poor sleep quality.	Unless the time spent out of bed is part of stimulus control instructions (table 2), efforts should be made to limit time-out-of-bed during nighttime. Activities during the time-out-of-bed should be relaxing and not physically or emotionally stimulating. Activities done at night when spending time-out-of-bed should aim at not further interfering with sleep.
Sleep latency[5]	Time from 'lights off' to sleep onset.	Questioning/ sleep diary / PSQI#/ actigraphy.	How long does it take for you to fall asleep?	Sleep latency should ideally not be longer than 30 minutes.	If sleep latency appears to be recurrently longer than 30 minutes, treatment should aim at decreasing sleep latency. This can be done for instance by delaying bedtime (i.e. increasing sleep pressure), improved preparation, reducing the level of stimulating activities or food (energy) intake, or using relaxation techniques in the hour before getting to bed.
Wake after sleep onset[5]	Time spent awake in bed, after sleep onset.	Questioning/ sleep diary / actigraphy.	How much time do you spent awake in bed after falling asleep?	If the patient spends more than half an hour awake in bed after sleep onset, this should be addressed.	This can be reduced by applying bedtime restriction/sleep compression. In case of lying awake more than half an hour, advise to get out of the bedroom and do something relaxing until feeling sleepy again. Apply motivational interviewing to induce behavioral change.
Early Morning Awakening[5]	Time awake prior to planned wake time.	Questioning / sleep diary / actigraphy.	Do you wake up prior to your planned wake up time?	The time awake in bed prior to getting out of bed should be as short as possible. Preferentially one gets out of bed as soon as possible after final arousal.	In case the patient stays in bed awake after final arousal, the patient is advised to get out of bed as soon as possible to prevent wake inertia and daytime fatigue. Apply motivational techniques to impart behavioral change.
Number of awakenings[5]	The number of conscious arousal experienced per night.	Questioning / sleep diary / actigraphy.	Do you wake up during the night, and if so how many times?	On average, the patient should not consciously wake up more than 2 times during the allotted sleep period. Waking up once per night (bathroom visits), may however not be a clinically relevant issue.	Various parts of CBT-i (table 2) can decrease the number of arousals. In case recurrent awakenings (>2) and/or lasting more than half an hour in total, please do so as explained above under 'wake after sleep onset'.
Sleep efficiency[5,11]	(total sleep time / total time in bed) X 100 in percent	Calculation.		Sleep efficiency should ideally be above 90% and is acceptable from 85% considering adequate sleep duration.	In case of lowered sleep efficiency, bedtime restriction (table 2) may be required. Aim at finding a compromise with respect to a realistic estimation of quantitative sleep needs.
Sleep hygiene	Recommended behavioral practices intended to promote improved sleep quality	Questioning.	Do you monitor time while being awake in bed? Do you consume stimulant beverages prior to bedtime? Do you intensively exercise close to bedtime? What do you eat before going to bed?	Stimulants (i.e. caffeine, nicotine, …) close to bedtime may impair sleep onset and/or maintenance. Small amount of aerobic exercise could improve sleep quality; however avoid intense workouts close to bedtime. Food with high caloric load and/or impacting absorption processes in the digestive tract can induce sleep disruption.	Sleep hygiene (table 2) instructions are needed to explain that clock monitoring in bed, food and beverage consumption and intense exercise before bedtime may disrupt sleep initiation and maintenance. Apply motivational interviewing to impart a behavioral change.

Napping	Whether the patient sleeps or lays down with the intention to sleep; at what time, how long and how often.	Questioning / sleep diary / actigraphy.	Do you sleep during the day or evening, and if so how long and how often?	In insomnia, napping is not recommended in general. It may be acceptable if the nap is ≤20 minutes ('power nap') and has appropriated timing with respect to circadian rhythms (i.e. not later than 15.30h). Otherwise, naps can lower sleep pressure or disrupt nighttime's sleep. Naps also include falling asleep before bedtime while watching TV for instance.	Sleep hygiene (table 2) instructions are needed to explain that daytime sleeping may disrupt circadian rhythms or lower sleep pressure at bedtime. Patients should avoid daytime sleeping beyond the duration of a power nap in any case.
Sleep environment	Physical bedroom characteristics like darkness, temperature, noise/quietness, humidity, etc.	Questioning.	Is your bedroom sufficiently dark (i.e. even after sunrise)? What's the temperature in your bedroom? Is it sufficiently quiet in your bedroom?	Ambient light may interfere with sleep quality and/or continuity. Bedroom temperature should ideally be between 16 and 19 degrees Celsius and should be isolated from noise disturbances.	Sleep hygiene (table 2) instructions are needed to explain and improve sleep environment.
Perceived sleep quality[11]	Subjective sleep quality.	Questioning / sleep diary / PSQI#/ rating.	How well do you sleep?	In case the patient perceives sleep quality as satisfying, further inquiry may not be compulsory. If not, sleep quality can be used to monitor therapeutic response.	When sleep quality does not improve over time, it may be indicative for patients and therapists that treatment response to CBT-i does not evolve as intended.
Beliefs and attitudes with respect to the nature/etiology of the sleep problem	Patients' erroneous causal attributions with respect to insomnia.	Questioning/ DBAS*.	What do you think causes your sleep problem?	Assess whether their sleep beliefs are adaptive or prevent a behavioral change.	In case of maladaptive sleep beliefs, general sleep education as explained in table 2 is indicated.
Beliefs and attitudes regarding the evolution of the sleep problem	Whether the patient expects improvement or not.	Questioning/ DBAS*.	Do you think that your sleep can improve?	Assess whether beliefs and attitudes regarding the evolution of insomnia are adaptive or prevent a behavioral change.	Maladaptive beliefs and attitudes regarding the evolution of the sleep problem require addressing during general sleep education (table 2).
Identification of (life) stressors[35]	Whether the patient has experienced life stressors and is currently struggling to cope with certain (daily) stressors.	Questioning.	Are you struggling to deal with daily stressors, and if so, which ones?	Interpret the obtained information to assess whether or not stress is an issue to the patient. If stress is an issue, assess whether stress influences sleep or not.	If stress has a negative impact on the patient's sleep, relaxation training/stress management should be included in the CBT-i treatment (table 2).
Sleep medication	Whether the patient uses any hypnotic or sedative drug (including any synthetic or herbal treatments).	Questioning / reviewing medical record.	Are you using any drug treatment for your sleep? If so, do you consider them useful? Would you like to pursue them?	Solely administrating sleep medication is not recommended for treating chronic insomnia, but may show some temporarily benefit or an improved therapeutic response (bimodal therapy).	The patients' perception of sleep medications may interfere with counseling and CBT-i. If patients desire discontinuation of drug treatment, systematic withdrawal may be initiated. If not, treatment may be substantiated by CBT-I anyhow and withdrawal may be postponed (i.e. when the patient is improving; showing increased self-efficacy in regaining sleep efficiency and sleep quality). In any case, therapists may discuss the treatment plan with the prescriber to prevent contradictory messages.
Substance abuse[35]	Past or present substance abuse.	Questioning / reviewing medical record.	Are you currently using, or have been using any substances or drugs (including nicotine)?	Substances may have negative impact on biological functions of sleep. Past or current substance abuse may interfere with adrenergic, cholinergic and/or dopaminergic pathways.	Use motivational interview techniques to promote behavioral change.

#PSQI: Pittsburgh Sleep Quality Index ; *DBAS: Dysfunctional Beliefs and Attitudes about Sleep; CBT-i: cognitive behavioral therapy for insomnia.

Table 1. Items to be included for questioning of the patient's sleep habits and difficulties, combined with a guide on how to interpret the obtained information as well as treatment implications.

Component	Description / content
General sleep education[6,60]	Explaining the importance of sleep, the behavioral neuroscience behind sleep, including the role of melatonin and its role in initiating / sustaining deep sleep, the role of daylight and the influence of regular sleeping hours etc.
Sleep restriction therapy[5,6,60]	The manipulation of homeostatic sleep drive to consolidate sleep via sleep restriction[60]: initially limiting the amount of time spent in bed to an amount equal to their average sleep time for a week[6]. Once sleep becomes more efficient, total sleep time is incrementally increased on a week-to-week basis and the sleep window adjusted in time[6]. In broader sense, sleep restriction therapy also included the alteration of circadian regularity and alignment[60], i.e. imposing regular wake-up time in an attempt to synchronize "strong" (fairly unresponsive to light) and "weak" (depending on bright light exposure) endogenous clocks by modulating behavior.
Stimulus controls instructions[5,6,60]	The application of operant and classical conditioning principles via stimulus control instructions[60]: - Restrict bedroom behaviors to sleep and sex[6]; - Limit the amount of time spend awake in bed or in the bedroom[6]; - Promote counter-conditioning by insuring that bed and bedroom environment are tightly coupled with sleepiness and sleep[6].
Sleep hygiene instructions[5,6,60,71]	The replacement of sleep-interfering behaviors with sleep-promoting behaviors through sleep hygiene education and behavior change councelling[60].
(Sleep specific) cognitive therapy[5,6,60]	To modify maladaptive sleep-related cognitions[60].
Relaxation training / stress management[6,60]	Learning patients to cope better with stress, including relaxation skills training (e.g., deep breathing[60], guided imagery[60]).
Patient's self-monitoring of daily sleeping patterns[60]	Daily self-monitoring of time in bed, sleep onset latency, wake after sleep onset, and total sleep time[60].

Table 2. **Components of cognitive behavioral therapy for insomnia in** people with chronic pain and comorbid insomnia.