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Sleep Disorders in Rehabiliation Patients

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Introduction

Sleep disturbances in rehabilitation patients have not yet been the object of much attention. Studies are only emerging to document different types of sleep disorders in the context of acquired injuries or progressive conditions. A variety of physiological, psychological or environmental factors may affect sleep habits, sleep organization, and sleep quality for individuals undergoing rehabilitation. Although difficulties with sleep are often regarded as secondary problems, or are hoped to resolve spontaneously with the recovery of other problems, it is becoming increasingly obvious that sleep disorders can hinder the rehabilitation process and affect global outcomes for patients. For example, it has been shown that the presence of sleep-wake cycle disturbances is related to prolonged stays in the hospital or in the rehabilitation center (Makley et al. 2008). Given the efforts and costs of rehabilitation, it is imperative to consider sleep disorders as possible deterrents to the whole process, and to allocate appropriate scientific and clinical attention and resources to the field.

In this review, we will first provide a very general overview of normal sleep, followed by a brief description of sleep disorders more commonly seen in rehabilitation. We will then describe specific factors related to the rehabilitation process which may influence the quality, quantity or organization of sleep. This section will be followed by a literature review of the prevalence of specific sleep disorders (i.e. sleep apnea, insomnia) in different rehabilitation populations (e.g. stroke, traumatic brain injury, spinal cord injury, chronic pain) with reference to studies evaluating treatment options in these specific populations. We conclude this article with recommendations regarding the evaluation and treatment of sleep disorders in the rehabilitation context.

Overview of normal sleep

As necessary as light, food and water, the role of sleep is nonetheless still not completely understood. It is a state composed of diverse and complex processes orchestrated by different cerebral systems. Adaptive theories suggest that sleep serves as a protective mechanism to keep the organism out of danger during periods of inactivity. Recuperative theories, however, put forward a "maintenance" role for sleep through which organic tissues and psychic functions are restored. Sleep may also play important parts in energy conservation, regulation of body temperature, and immunity.

Sleep, just like many other biological (e.g., body temperature, growth hormone secretion) and behavioral functions (e.g., eating, working), is regulated by circadian rhythms. Internal biological clocks located in the hypothalamus control the alternation between different states by interacting closely with time cues in environment, also called *zeitgebers*. For sleeping functions, the most important of these environmental cues is the light-dark cycle, but other extrinsic cues include social interactions, work schedules, and meal times. Daily variations in core body temperature, which are also controlled by circadian factors, are closely tied to sleep-wake patterns. At its lowest point in the early hours of the day (e.g., 3:00 to 5:00 AM), body temperature starts to increase near the time of awakening and peaks in the evening. Alertness is at its maximum during the ascending slope of the body temperature curve. In contrast, sleepiness and sleep occur as temperature decreases. In the absence of time cues or any constraint, individuals tend to choose a bedtime that is closely linked to a decrease in body temperature, while awakening occurs shortly after it begins to rise again. Homeostatic factors are also at play in sleep. For instance, the time to fall asleep is inversely related to the duration of the previous period of wakefulness. With prolonged sleep deprivation, there is an increasing drive to sleep. Upon recovery, there is a rebound effect producing a shorter sleep latency, increased total sleep time, and a larger proportion of deep sleep.

Using a technique called polysomnography – which combines the measurement of brain activity, eye movements , and muscle tone– two types of sleep can be distinguished: non-rapid-eye-movement (NREM) and rapid-eye-movement (REM) sleep. Different brain activity patterns detected during NREM sleep can be subdivided into four distinct sleep stages: stages 1, 2, 3, and 4. From a state of drowsiness, the individual first enters stage 1, a light sleep, then progresses sequentially through deeper stages (stages 2, 3 and 4 of NREM sleep). Of short duration (about 5 minutes), stage 1 is a transitional phase between wakefulness and more definite sleep. Stage 2 generally lasts 10 to 15 minutes. For most people, stage 2 corresponds to the phenomenological experience of falling asleep. Stages 3 and 4 are considered the deepest stages of sleep and together last between 20 to 40 minutes in the first sleep cycle. They are often referred to as "delta," or "slow-wave sleep" because of the presence of slow waves of high amplitude called delta waves. After reaching stage 4, the EEG pattern reverses through stage 3, stage 2, and finally gives place to the first REM sleep episode. These NREM/REM cycles are repeated four to five times during the night according to an organized sequence with slow-wave sleep being more prominent in the first third of the night whereas REM sleep is more prominent in the last part of the night or early morning hours. Adults with normal sleep patterns spend approximately 25% of their sleep time in REM sleep and 75% in NREM sleep. NREM Stage 1 represents about 5%, Stage 2 about 45 to 60%, Stages 3-4 between 5 and 20%, and REM sleep represents 15 to 35% of total sleep time.

In REM sleep, brain activity is very similar to that observed in stage 1. Unlike initial stage 1 sleep, however, the eyes move rapidly under the eye-lids and there is a simultaneous loss of core muscle tone in the rest of the body. This stage is often called "paradoxical sleep" because the body is essentially paralyzed, apart from occasional muscle twitches, but the activity in the brain and in the autonomic system are at a level similar to that seen during wakefulness. This is also the stage when the most vivid dreams occur. Evidence from sleep deprivation studies suggests that NREM sleep, particularly Stages 3-4 sleep, is important for the restoration of physical

energy, while REM sleep is presumed to have a role in the consolidation of newly acquired memories and emotional processing.

Overview of Sleep Disorders

Sleep can be abnormal in a number of ways, affecting either nighttime sleep episodes, daytime alertness or functioning and/or the timing of the sleep-wake cycle. To appreciate the complexity of the area of disordered sleep, one can simply browse through the International Classification of Sleep Disorders, 2nd edition (American Academy of Sleep Medicine 2005) which lists these different categories of sleep disorders:

- Insomnia (e.g., psychophysiological insomnia; insomnia comorbid to a medical illness).
- Sleep related breathing disorders (e.g. obstructive sleep apnea, central sleep apnea)
- Hypersomnias of central origin (e.g. narcolepsy, hypersomnia due to medical condition)
- Circadian rhythm sleep disorders (e.g. delayed or advance sleep-phase syndrome)
- Parasomnias (e.g. sleepwalking, sleep terrors, nightmares, bruxism)
- Sleep related movement disorders (e.g. periodic limb movement disorder, restless legs syndrome)
- Isolated symptoms and normal variants
- Other sleep disorders

The most common sleep disorders encountered in the rehabilitation context include insomnia, hypersomnia (or excessive daytime sleepiness), sleep apnea, narcolepsy, and circadian rhythm sleep disorders, and will be presented briefly in the present text.

Insomnia

Insomnia is an extremely common health complaint in medical practice and may be due to a variety of factors including primary medical conditions, intrinsic factors (somatized tension, worrying), or other sleep disorders (e.g. periodic leg movements). It is generally defined as a difficulty initiating (falling asleep) or maintaining sleep (staying asleep). Insomnia is associated with significant functional daytime problems, reduced quality of life, and increased health-related complaints (Ohayon 2002, Simon and VonKorff 1997).

Certain criteria are routinely used to define an insomnia syndrome. In research, most studies use a combination of criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV (American Psychiatric Association 2000), the International Classification of Sleep Disorders (ICSD-2) and/or the International Classification of Diseases (ICD-10). An insomnia syndrome is generally defined by the following criteria:

- The person has a dissatisfaction with sleep quantity or quality;
- The person has difficulties initiating and/or maintaining sleep, characterized by a sleep-onset latency and/or wake time after sleep onset greater than 30 minutes, as well as a sleep efficiency (ratio of total sleep time to time spent in bed) lower than 85%;
- The sleep difficulties occur at least 3 nights a week;
- The sleep disturbance causes significant distress or impairment in social, occupational or other areas of daytime functioning attributed to the sleep difficulties.

Insomnia is considered situational if it lasts less than one month, subacute if it lasts between 1 and 6 months, and chronic when it has been present for more than 6 months. It should be noted that because of individual differences in sleep needs, total sleep time is not a good marker of insomnia when considered alone.

Hypersomnia

Hypersomnia is characterized by prolonged nighttime sleep and/or excessive daytime sleepiness. The main feature of sleepiness is the inability to maintain a desired level of alertness or wakefulness during the day (American Academy of Sleep Medicine 2005). Individuals having excessive sleepiness have trouble staying awake and alert not only when doing a quiet activity but also at unusual, even inappropriate times such as at work, while driving or during a conversation.

Excessive daytime sleepiness is often confused with fatigue. While the presence of sleepiness is often associated with fatigue, a sensation of fatigue is not necessarily accompanied by sleepiness or sleep propensity. Fatigue is a subjective state that can be defined as weariness, weakness, or depleted energy but is quite difficult to measure objectively. Sleepiness refers to sensations of physiological drowsiness, sleep propensity, or reduced alertness (Pigeon et al. 2003) and can be objectified with proper standardized techniques such as daytime polysomnography (PSG) recordings in a sleep laboratory (see Polysomnography section below).

The most common causes of prolonged nighttime sleep and excessive daytime sleepiness are chronic sleep deprivation, the presence of underlying sleep disorders (e.g., sleep apnea and other sleep related breathing disorders, narcolepsy), neurological disorders (e.g., epilepsy, stroke, traumatic brain injury, multiple sclerosis, dementia) psychopathology (e.g., major depression, dysthymia, substance addiction disorders), and the utilization of some types of medication (e.g., antipsychotics, antidepressants, benzodiazepines, muscle relaxants) (Billiard 2003, Black et al. 2005, Happe 2003, Krahn 2005, Pagel 2005). Sleep apnea and narcolepsy, two sleep disorders that have been documented in rehabilitation populations and that are among the most common causes of sleepiness, will be delineated below.

Sleep Apnea

Sleep apnea is part of a broad category of sleep disorders (i.e., sleep related breathing disorders; AASM, 2005) and is characterized by altered respiratory function during sleep. In individuals with sleep apnea, pauses in breathing are associated with arousal, blood oxygen desaturation or both. A high proportion of the population experiences apneas or breathing pauses during the night. However, to be considered abnormal or pathological, the number of respiratory events has to be equal or greater than five per hours, in such case meeting criteria for a sleep apnea syndrome. The diagnosis of sleep apnea has to be confirmed by overnight PSG recordings in the sleep laboratory. Most apnea sufferers are not aware of their condition until it is recognized by others witnessing interrupted breathing episodes or daytime consequences. Sleep apnea can be either obstructive (i.e., episodes of complete (apnea) or partial (hypopnea) upper airway obstruction occurring during sleep) or central (i.e., absence of ventilatory effort due to impaired brain's respiratory control). The most common form by far is obstructive sleep apnea, for which obesity, older age and male gender are documented risk factors. Untreated sleep apnea is

associated with several negative consequences such as loud snoring, restless sleep, daytime sleepiness and increased risk of cardiovascular diseases, stroke in particular.

Narcolepsy

Narcolepsy is a rare sleep disorder characterized by a tetrad of classic symptoms, which are (from the most to the least prevalent): excessive daytime sleepiness, cataplexy (i.e., episodic loss of muscle function, often triggered by an emotional reaction), sleep paralysis (i.e., transitory inability to talk or move when waking) and hypnagogic hallucinations (i.e., vivid dreamlike experiences taking place while falling asleep, dozing or awakening). Overnight and daytime polysomnographic recordings are required for the diagnosis of narcolepsy. Although the majority of narcolepsy cases are idiopathic, the disorder can be secondary to various conditions.

Circadian Rhythm Sleep Disorders

Circadian rhythm sleep disorders are characterized by a mismatch between the individual's sleep-wake rhythm and the 24-hour environment. In other words, people having such disorders have trouble following habitual or desired schedules. In addition to the sleep-wake cycle, circadian rhythms of body temperature and secretion of melatonin, a hormone implicated in the regulation of circadian rhythms, are often disturbed. Some individuals may display delayed sleep phase disorder, characterized by consistently delayed sleep-wake episodes relative to conventional times (i.e., bedtime and arising time usually more than two hours later than normative values). The opposite pattern is called advanced sleep phase disorder. Finally, the variant called irregular sleep-wake rhythm disorder consists in high day-to-day variability in sleep onset and offset (Ayalon et al. 2007).

Sleep in rehabilitation: specific factors affecting sleep

Lesions to brain systems regulating sleep

Sleep is a complex process involving the interaction of several cerebral regions. Certain structures have key-roles in sleep regulation, particularly the brain stem, the thalamus and the anterior basal brain regions (Bear et al. 1996, Espinar-Sierra 1997, Mahowald 2000). Any condition leading to brain cell damage or neurotransmitter dysfunction is thus susceptible to influence the functioning of cerebral structures or interconnections between structures responsible for regulating sleep-wake processes or including breathing during sleep.

Medications

Different medications prescribed during rehabilitation can alter the quality, quantity, and organization of sleep as well as influence daytime levels of fatigue or sleepiness. In fact, medications prescribed for sleep, pain, seizures, muscle relaxation or management of stress, anxiety or depressive symptoms can interact with sleep processes, for example by increasing or decreasing the amount of time spent in REM and NREM sleep stages. The timing of medication intake can also negatively influence sleep quality and should thus be monitored carefully.

In a rehabilitation hospital, Freter and Becker (1999) studied the use of sleeping pills by elderly patients with mainly orthopedic and neurological diagnoses. They found that although 40% of their sample had a prescription for "as needed" use of either a variety of benzodiazepines or

chloral hydrate to help them sleep better, the use of these agents did not seem related to improved nighttime sleep quality as rated by night nurses, nor was it associated with improved ratings of daytime alertness or restfulness, either from treating professionals (occupational therapists or physiotherapists) or even from the patients themselves. The authors thus questioned the usefulness of hypnotic prescription in this population, especially since the use of hypnotics has been linked to daytime drowsiness, confusion and falls. (Freter and Becker, 1999)

Pain

Diverse medical conditions producing pain (e.g., low back pain, arthritis, cancer) are known to cause sleep disturbances, which may be a particularly relevant issue in rehabilitation as many patients suffer from various types of pain. Creating increased physiological arousal, pain can affect patients' ability to fall asleep, to stay asleep or to return to sleep after an awakening. Research has shown that pain can cause frequent periods of wakefulness during NREM sleep, a phenomenon referred to as alpha-delta sleep and related to a subjective perception of poor sleep quality (Moldofsky, 1989). In turn, sleep deprivation has been shown to decrease the pain threshold, thus worsening pain sensations (Kundermann et al. 2004, Roehrs et al. 2006).

Environmental factors

Factors inherent to the hospital or rehabilitation environment may, in themselves, contribute to produce sleep disturbances in some patients. For example, patients treated in intensive care units have been shown to have very disturbed sleep–sometimes even lacking deep or REM sleep– because of factors such as frequent interventions, pain, anxiety, noise and lights (Friese 2008, Friese et al. 2007, Gabor et al. 2001). During inpatient hospital or rehabilitation stays, similar factors, as well as additional ones such as co-habitation with other patients and the imposed schedules (e.g. early bedtime) may affect sleep-wake routines and contribute to sleep difficulties. Furthermore, when patients leave the facility in either re-integrate their home or start living in a new setting, they again must adjust to changes in the environment and their life habits.

Lifestyle factors

Several lifestyle factors such as diet, alcohol or drug use, exercise, and sleep schedules have impacts on sleep patterns and may be at play in producing sleep disturbances during rehabilitation. For example, heavy meals eaten late in the evening can disrupt sleep and substances such as caffeine, nicotine, and alcohol can alter sleep quality depending on the time, quantity and frequency of consumption. Obesity is linked to sleep disordered breathing. Physical exercise can either promote or interfere with sleep, depending on its timing, intensity, and regularity, as well as the physical fitness of an individual.

Sleep habits

Patients who are hospitalized or need to live in a rehabilitation center may be temporarily deprived of cues normally associated with their normal sleep patterns. This change in itself may lead to alterations in sleep habits and problems with sleep. Indeed, for many people, sleep is associated with rather fixed bedtime rituals and for the most part regular sleep-wake patterns. There is thus an important psychological conditioning phenomenon whereby cues such as bedtime rituals, and the bedroom environment become associated with sleep and sleepiness. For persons who have sleep disturbances, however, these cues may have become associated with

negative emotions and thoughts related to anxiety, frustration or fear of not sleeping well. Poor sleepers tend to adopt sleep habits such as increasing the time they spend in bed (in an effort to get more sleep), nap during the day, or have irregular sleep-wake schedules. These strategies may in fact result in even more fragmented and restless sleep. Naps, particularly those taken late in the day, can have a detrimental effect on the quality of nighttime sleep, for example by delaying sleep onset or affecting the proportion of deep sleep. In patients with neurological conditions provoking intense and chronic fatigue such as stroke, traumatic brain injury or multiple sclerosis, nap-taking habits have not yet been investigated fully yet these habits may actually contribute to sleep problems. In a study of fatigue up to 8 years after mild to severe traumatic brain injury (TBI), it was found that TBI survivors took on average six naps per week (Ouellet and Morin 2006).

Recently, Alessi and colleagues studied the association between sleep-wake patterns and functional recovery in a cohort of 245 elderly patients treated in inpatient post-acute rehabilitation settings for a variety of problems, the majority of which were orthopedic injuries (Alessi et al. 2008). This team found that more daytime sleep was associated with less functional recovery in elderly patients, and this relationship persisted up to 3 months post-discharge even when other potential predictors of functional recovery were controlled for in the analyses. Night-time sleep, however, was not found to be related to functional outcome, but was nonetheless found to be disturbed in a high proportion of patients. One of the hypotheses put forward to explain this relationship is that daytime sleep may decrease motivation or efforts put into therapy. This study revealed the unique contribution of sleep-wake problems on functional recovery and points to potential intervention targets.

Psychosocial stressors

Sleep is very sensitive to stress and emotional distress. Major life events (e.g., divorce, death of a family member) and more minor but daily stressors (e.g., difficulties with interpersonal relationships difficulties, work-related stress) can affect sleep patterns in otherwise healthy individuals by heightening arousal before falling asleep and during nocturnal awakenings. Although sleep usually returns to normal once the acute stressful situation has resolved, insomnia symptoms may become chronic due to a variety of perpetuating factors including maladaptive habits, thoughts, and attitudes about sleep (Morin 1993). In the early phases after an injury or an illness, patients may experience high levels of stress, anxiety and feelings of hopelessness or loneliness, particularly during acute hospitalization or rehabilitation stays. In the later phases of rehabilitation, most patients are particularly likely to experience psychosocial stressors such as major emotional adjustments to newly acquired cognitive and physical limitations, inability to return to work, inability to resume previous social roles, problems with interpersonal relationships, and litigation over compensation. Because of these stressors, patients may experience heightened emotional or cognitive activity at bedtime because they can be tense, may worry or ruminate, factors which are all linked to difficulty falling asleep. Sleep problems can thus appear in every phase of rehabilitation, from the acute phase after an injury or event, during rehabilitation, upon returning home, upon trying to resume previous occupations and roles, and many years after the injury or event when coping with permanent limitations.

Comorbid psychopathology

When a person cannot cope effectively with important or repeated stressors, psychopathology may develop for example in the form of major depression or anxiety disorders. Sleep problems are often a hallmark of psychopathology: sleep disturbances such as insomnia or hypersomnia are known to be intimately linked to psychological problems such as depression or anxiety disorders. Epidemiological surveys in the general population indicate that the relationship between psychopathology and sleep disturbances may go both ways. For example, insomnia has been found to be both a consequence and a potential cause of depression. Unfortunately, depressive and anxiety symptoms are very common in rehabilitation populations. Recent studies have found prevalence rates of major depression following TBI varying between 17% and 42% (Dikmen et al. 2004, Hibbard et al. 2004, Jorge et al. 2004, Kreutzer et al. 2001). Jorge and colleagues (Jorge et al. 1993, Jorge et al. 2004) found that approximately 60% to 75% of the TBI patients who developed major depression also suffered from an anxiety disorder. In trauma survivors without brain injury, anxiety and depression affect proportions of individuals varying from 7 to 17% at three to six months post-injury (Mason et al. 2002, Mayou et al. 2001, O'Donnell et al. 2004, Shepherd et al. 1990), 6 to 19% at one-year (Mayou et al. 2001, O'Donnell et al. 2004), and from 11% to 30% beyond two years (Andersson et al. 1997, Piccinelli et al. 1999). In stroke patients, depression and anxiety was found to be present in 18 to 27% of patients (Appelros and Viitanen 2004, Barker-Collo 2007, Beekman et al. 1998, Masel, Scheibel et al. 2001).

Sleep disorders and treatments documented in specific rehabilitation populations

Stroke

Obstructive Sleep Apnea

There is a clear relationship between sleep disordered breathing, such as obstructive sleep apnea (OSA), and stroke although it remains unclear whether OSA is a consequence of stroke or if it acts as a potential cause of stroke. Complex processes involving neural, hemodynamic, metabolic, and inflammatory mechanisms may all be triggered by abnormal respiratory events and lead to stroke. Conversely, stroke may also exacerbate sleep disordered breathing (Bassetti et al. 2006, Wessendorf et al. 2000).

Compared to matched controls, snoring has been found to be significantly more common in persons who have suffered a stroke, affecting approximately half (47.4%) of patients. OSA has been found to be present in as many as 60% of stroke patients in the post-acute period (Disler et al. 2002). Arzt and colleagues (2005) report data indicating that sleep-disordered breathing precedes stroke and may thus play an important role in its development (Arzt et al. 2005).

Excessive daytime sleepiness due to OSA has major impacts on patient’s capacity to engage in their rehabilitation efforts. In fact, research has shown that the recovery and functional outcome of stroke survivors is compromised when they suffer from sleep-disordered breathing (Cherkassky et al. 2003, Dyken et al. 1996, Kaneko et al. 2003), such data underscoring the importance of detecting and treating sleep disorders in this population.

The typical treatment for sleep apnea is the use of a mask-like device called nasal continuous positive airway pressure (nCPAP). Although research on the efficacy nCPAP in stroke patients is scarce, there is some indication that it may be used with this population despite hemiplegia, hemiparesis, cognitive deficits and impaired overall functional independence (Disler et al. 2002, Wessendorf et al. 2001). Disler and colleagues (2002) suggest that treating OSA following stroke may help prevent secondary stroke.

Insomnia

The literature on insomnia in stroke patients is very limited despite the fact that insomnia complaints (e.g. difficulties falling or staying asleep) are present in 57 to 68% of persons with stroke (Leppavuori fet al. 2002, Palomaki et al. 2003). Using the diagnostic criteria of the DSM-IV, one study indicated that 37.5% of a sample of stroke patients fulfilled the diagnostic criteria of insomnia (Leppavuori et al. 2002). The etiology of stroke-related insomnia has not been explored, although it may be postulated that different factors may be at play, such as neurological damage (i.e. to sleep-regulating neurological systems), environmental factors, and psychological stressors (e.g. stress, anxiety and depression related to rehabilitation challenges). Documented effective treatments of insomnia following stroke include the pharmacological agents lorazepam, zopiclone (Li Pi Shan and Ashworth 2004) and mianserin (Palomaki et al. 2003). One small study using intradermal acupuncture (Kim et al. 2004) suggested some benefits. There are no existing studies of behavioral treatments for insomnia in this population.

Traumatic brain injury (TBI)

Insomnia

Insomnia is the most common sleep disorder observed following TBI. Although its etiology remains unclear in this population, it has been suggested that structural damage to sleep-related structures such as the brain-stem or the reticular formation may lead to changes in sleep architecture or sleep quality (Mahowald 2000). Furthermore, changes in intracranial pressure, hormonal or neuropeptide or neurotransmitters have also been suggested as factors responsible for sleep changes following TBI (Baumann et al. 2005, Frieboes et al. 1999, Mahowald 2000). Psychological factors have been proposed to be important actors in the development of insomnia following TBI (Ouellet and Morin 2007, Ouellet et al. 2004) given the various stressors faced by these patients and the high prevalence of mood and anxiety disorders following TBI. Pain, and particularly headaches, may also be a causative factor in post-TBI insomnia. Indeed Beetar and colleagues (1996) showed a significant interaction between sleep and pain complaints. Patients experiencing pain, which represented 59% of their sample, reported approximately twice as much sleep complaints compared to those who did not report pain, with sleep maintenance complaints (problems staying asleep) being the most common problem (Beetar et al. 1996).

During the acute period after the accident about 70% of patients have significant disturbances of their nighttime sleep as noted by staff members (Burke 2004, Makley et al. 2008). In the post-acute period, heterogeneous studies report insomnia symptoms in 30 to 70% up to many years post-injury (see Ouellet et al. 2004 for a review). Fichtenberg et al. found a 30% prevalence rate of insomnia as defined with the operational criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in patients on average 4 months post-injury (Fichtenberg et al.

2002). Using a combination of the criteria of the DSM-IV and the International Classification of Diseases (ICD-10). Ouellet et al. (2006) found 29.4% of a sample of 452 patients to suffer from clinically significant insomnia on average 8 years post-injury (Ouellet et al. 2006). Of these, 60% were not receiving any treatment for their sleep disturbances. Medications usually prescribed for insomnia in the general population or for other medical conditions have not been studied specifically in the context of TBI although but it has been recommended to avoid benzodiazepines in these patients because of potential adverse effects (altered psychomotor activity and cognition, influence on sleep architecture and potential for abuse). The newer non-benzodiazepine sleep medications are more recommended (e.g. zolpidem, zaleplon, zopiclone and eszopiclone). These are now routinely used to treat insomnia and have fewer withdrawal effects, a lower risk for tolerance and less impacts on daytime cognitive function (Flanagan et al. 2007, Goldstein 1995). Recently, Ouellet and colleagues have published preliminary data indicating that cognitive behavior therapy (therapy aimed at changing maladaptive habits, thoughts and attitudes towards sleep) is effective to treat insomnia in TBI patients (Ouellet and Morin 2004, 2007) with results durable for at least three months after treatment has ended. This type of therapy can serve either as an adjunct or an alternative to sleep medication.

Excessive daytime sleepiness

Subjective feelings of excessive daytime sleepiness (EDS) are reported by 14-55% of TBI patients (Baumann et al. 2007, Castriotta et al. 2007, Clinchot et al. 1998; Cohen et al. 1992, Parcell et al. 2006, Perlis et al. 1997, Verma et al. 2007, Watson et al. 2007) but are sometimes difficult to differentiate from post-TBI fatigue which is widespread. Certain sleep laboratory tests (the Multiple Sleep Latency Test or the Maintenance of Wakefulness Test) can measure objectively whether individuals have problems of EDS. Recent investigations reported prevalence rates of objective EDS between 11% and 53% (Baumann et al. 2007, Castriotta et al. 2007, Guilleminault et al. 2000, Verma et al. 2007). Modafinil has been investigated as a potential medication to treat daytime fatigue and sleepiness following TBI with very limited success (Jha et al., 2008).

Sleep apnea

Sleep disordered breathing, and mainly obstructive sleep apnea has been found to affect 30 to 40% of TBI patients who complain of daytime sleepiness (Guilleminault et al. 1983, Guilleminault et al.,\ 2000, Verma et al. 2007). There are not yet any published studies on the efficacy of nCPAP for sleep disordered breathing in the TBI populations.

Narcolepsy

There have been at least 22 published case reports of posttraumatic narcolepsy confirmed by polysomnographic tests (Ebrahim et al. 2005). Recent studies indicate that, similarly to patients suffering from narcolepsy, patients having sustained TBI have decreased levels of hypocretin, a hypothalamic neuropeptide involved in sleep-wake regulation (Baumann et al. 2005; Baumann et al. 2007). More research is needed to study this link. One case of a 27 year old patient with post-TBI narcolepsy successfully treated with methylphenidate was reported but more research is needed on this and other potential agents such as Modafinil (Francisco and Ivanhoe 1996).

Circadian rhythm sleep disorders

There have been a few reports of individuals developing circadian rhythm sleep disorders after TBI, most presenting a delayed sleep phase disorder (Ayalon et al. 2007, Boivin et al. 2004, Nagtegaal et al. 1997, Patten and Lauderdale 1992, Quinto et al. 2000).

Spinal Cord Injury (SCI)

Sleep Apnea

Very high proportions of obstructive sleep apnea (OSA) have been noted in patients with SCI, with rates oscillating between 15 and 62% according to different studies (Berlowitz et al. 2005, Burns et al. 2000, Klefbeck et al. 1998, Stockhammer et al. 2002). Few studies have examined the specificities of treatment of OSA in SCI patients. Due to limitations such as impaired hand function, nasal congestion or weakness of the expiratory muscle, Burns and colleagues hypothesized that long-term acceptance and daily use of CPAP would be compromised in persons with SCI. However, in a sample of 40 patients, they found that CPAP was tried by 80% of patients and 63% of these continued to use it regularly, an adherence rate resembling that of persons suffering from OSA without SCI. Common side effects (nasal congestion, mask discomfort, claustrophobia) leading to discontinued use of CPAP were similar to those noted in the general population (Burns et al. 2005).

Insomnia

Fichtenberg and colleagues (2002) included 25 individuals with SCI as part of a comparison group in a study of insomnia complaints after TBI. They were surprised to find significantly higher mean Pittsburgh Sleep Quality Index scores in the SCI group compared to the TBI group with 72% reporting poor sleep quality and 56% having a score indicative of the presence of insomnia. Scheer et al., (2006) found that persons with cervical SCI had significantly lower sleep efficiency compared to control participants with thoracic SCI. The latter's sleep efficiency was comparable to healthy control participants. These authors suggest that the interruption of the secretion of melatonin during nighttime may be a potential mechanism to explain reduced sleep efficiency in cervical SCI patients (Scheer et al. 2006). Given the seemingly very high prevalence of insomnia following SCI, more research is warranted to explore this area.

Musculoskeletal injuries and Chronic Pain Conditions

Although pain is known to interfere with sleep quality, poor sleep may also worsen pain felt by persons with musculoskeletal conditions. Experimental studies have shown that sleep deprivation may decrease the pain threshold (Kundermann et al. 2004, Smith et al. 2004). Marty et al., (2008) found that 49.5% of Chronic Low Back Pain patients complained of poor sleep compared with 10.4% of controls (Marty et al. 2008). Marin et al., (2006) also found a very large proportion of patients referred to a tertiary physical medicine and rehabilitation clinic for chronic low back pain to suffer from sleep disturbances. They documented a 55% increase in the proportion of patients reporting light or restless sleep after the onset of chronic pain. A positive relationship between the intensity of pain and the severity of sleep disturbance was also found in these patients (Marin et al. 2006). Fichtenberg and colleagues (2002) reported that 56% of patients having sustained muksculoskeletal injuries had a Pittsburgh Sleep Quality Index in the insomnia range. Although medications remain the most common treatment option offered to

patients with medical illnesses suffering from insomnia, Currie and colleagues demonstrated that cognitive-behavioral therapy is as effective in this population (Currie et al. 2000).

Multiple Sclerosis

Research on sleep problems in MS is very scarce. Recently, Bamer and colleagues (2008) conducted a cross-sectional survey of sleep problems in a sample of 1063 persons with multiple sclerosis. They found that 51.5% of the sample suffered from moderate or severe sleep problems with women being more at risk than men (Bamer et al. 2008).

Recommendations for the evaluation and treatment of sleep disorders in rehabilitation

Evaluation

Clinical interviews

The evaluation of sleep disturbances in rehabilitation patients has to be comprehensive, taking into account all potential contributing factors. First, a detailed interview with the patient, ideally complemented by information obtained from significant others, is essential to document the subjective complaint. Clinicians should investigate both premorbid sleep patterns and quality (i.e. before the accident or the onset of the disorder) and present sleep, with questions on the nature, severity, duration and evolution of sleep disturbances, on the person's typical sleep-wake cycle, as well as on daytime functioning such as levels of alertness. In addition, clinicians must have a clear portrait of the medications taken, of interactions between medications, and of the presence of other problems which may contribute to the sleep disorder. This is especially important with rehabilitation patients because of the high occurrence of comorbidity, and associated poly-pharmacy (use of several medications simultaneously) within this population. Fatigue should also be carefully evaluated and differentiated from sleep disturbances such as sleepiness. Moreover, a thorough assessment should cover the presence of psychiatric symptoms or disorders (e.g., depression, anxiety, substance abuse), medical illnesses, and pain which are all extremely prevalent in rehabilitation patients. Physical and neurological examination, blood sample) can also be helpful to document other factors (Morin and Edinger, 1997).

Self-report questionnaires

Although essential, the information gained from interviewing the patient and collaterals should be validated or complemented with more systematic data obtained from subjective, behavioral or physiological assessment tools. There is a wide variety of self-reported questionnaires evaluating various aspects of sleep. The following are among the most commonly used and potentially helpful in the rehabilitation population:

- *Pittsburgh Sleep Quality Index*, which evaluates several features of sleep quality, including utilization of sleep-promoting medication and the presence of daytime dysfunction;
- *Insomnia Severity Index*, which assesses insomnia severity;
- *Epworth Sleepiness Scale,* which evaluates the probability of falling asleep in eight situations

- *Morningness-Eveningness Questionnaire*, which can be used to determine preferences in circadian rhythms.

Although they can provide useful information, results from these questionnaires have to be corroborated from other sources. This is especially true with patients suffering from cognitive deficits such as impaired learning and memory functions and reduced self-awareness, as these can alter their responses.

Sleep diary

A simple sleep diary can be used to monitor sleep-wake patterns and factors which may affect sleep. Patients are typically asked to record bedtime and arising times, estimate how long they took to fall asleep (sleep-onset latency), as well as the number and duration of awakenings. They can also use the diary to document the use of medications , alcohol, caffeine and other substances. A period of at least two consecutive weeks of completed sleep diaries is recommended to get a good overview of sleep patterns and inter-night variability.

Polysomnography (PSG)

A laboratory study of sleep using polysomnography may be necessary to identify sleep disorders in certain patients. Polysomnography includes electroencephalographic (EEG; brain activity) , electrooculographic (EOG; eye movements) and electromyographic (EMG; muscle movements) measures. PSG yields comprehensive information on the continuity of sleep (sleep latency, time awake after sleep onset, sleep time, sleep efficiency) and on the architecture of sleep (proportion of time spent in each sleep stage or awake). Additional measures may be included to detect other sleep disorders such as periodic limb movements or disorders of breathing during sleep (for example oxygen saturation or muscle activity in the legs).

PSG can be also used during the day to evaluate daytime sleepiness and screen for disorders associated with such symptoms. The Multiple Sleep Latency Test (MSLT) consists in the daytime PSG recording of 4 to 5 20-minute nap opportunities evaluated at 2-hours intervals. The Maintenance of Wakefulness Test is another objective test of sleepiness where the nap opportunities last 40 minutes as opposed to 20 in the MSLT, and the instruction given to participants specifies to try to stay awake, as opposed to trying to fall asleep as quickly as possible in the MSLT. In these two tests, patients who fall asleep rapidly (e.g. within 5 minutes) and exhibit REM periods during the naps may be considered as having problems with excessive daytime sleepiness (e.g., narcolepsy).

Disadvantages of PSG techniques include their large costs and limited availability. Because of the laboratory environment and devices which can be cumbersome, PSG measures may also not be adequately representative of the patient's typical sleep patterns at home. Ambulatory PSG devices have been developed to measure sleep at home with their own advantages and disadvantages.

Actigraphy

An actigraph is a small watch-like device that records motor activity continuously for several days. The data from the actigraph allows the estimation of sleep-wake parameters based on the

presence or absence of motor activity and represents a lower-cost alternative to obtain objective measures of sleep-wake patterns.

Treatment recommendations

As seen in the previous literature review, there are very few studies documenting the efficacy of different treatments for sleep disorders specifically in rehabilitation patients. For some conditions (e.g. TBI, Multiple Sclerosis), sleep is just starting to emerge as an important issue to consider during rehabilitation. Most clinicians thus probably rely on evidence obtained in non-rehabilitation patients and use the hypnotic medications, behavioral interventions, and technical devices (for example nCPAP) which are presently known to have the best effects and least side effects. Research is very much needed, however, to make sure these treatments are as safe and efficacious in rehabilitation patients who have particular characteristics such as motor limitations, cognitive deficits, and increased risk for seizures or perhaps cardiovascular events in some cases.

The side-effects usually associated with different treatment options should be the object of specific study within particular rehabilitation population. In the case of medications for insomnia, for example, appropriate caution should be given to potential daytime effects which could exacerbate cognitive deficits in certain patients (e.g. stroke, TBI) or alter levels of alertness in patients who are already prone to daytime sleepiness. One side-effect of cognitive-behavioral therapy for insomnia may be temporary exacerbation of feelings of fatigue during the initial weeks of treatment. Patients should be informed and monitored closely if they already suffer from fatigue related to stroke or a brain injury.

Another issue which needs more attention in the rehabilitation context is that of treatment adherence. Wearing a device such as nCPAP, taking medications regularly and respecting guidelines related to their use (e.g. avoid alcohol), or following a regular sleep routine may be difficult for some rehabilitation patients due to factors as diverse as pain, hemiplegia, memory problems or impulsivity. There is a need for clinicians and researchers to identify the specific barriers to the effective treatment of sleep disorders in different rehabilitation populations.

Conclusion

Sleep is a complex experience which is still not fully understood. As our knowledge about different sleep disorders is consolidating, still much progress is needed to evaluate and control for risk factors and to pinpoint effective treatment options. In the field of rehabilitation, sleep is probably one of the aspects of functioning which may be least taken into account by professionals and by patients themselves because of the high predominance of physical, cognitive and functional impairments or limitations which need rapid and massive attention. From this review, it becomes clear that several factors related to the rehabilitation context have detrimental effects on sleep and make patients more at risk of developing sleep disorders. We know that insomnia, sleep apnea (and other sleep related breathing disorders) are the most common sleep disorders in these populations. It is also well known that sleep disorders can have detrimental effects on other areas of patients' lives, consequently decreasing their quality of life and compromising their full recovery potential. Researchers and clinicians are becoming increasingly aware of these facts, and studies are beginning to emerge in specific fields of rehabilitation (e.g., stroke, TBI). There is a pressing need to conduct more research to understand

the etiology, evolution and treatment options of the various sleep disorders affecting different rehabilitation populations. We hope this review will have increased the knowledge and awareness of patients, health professionals, researchers and decision-makers to the importance of sleep during the rehabilitation process.

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