The Treatment of Sleep Disorders in Acute Patient Populations Following a Traumatic Brain Injury: Exploring the Potential Benefits of Non-Pharmacological Treatments

Katie O’Brien

Traumatic brain injury (TBI) is a major cause of inpatient rehabilitation hospital admission in both military and civilian populations. Over 50% of people who have sustained a TBI present with symptoms of a sleep disorder. A variety of conditions have been noted related to sleep disturbance, including obstructive sleep apnea, periodic leg movement syndrome, insomnia and hypersomnia. Consolidated and efficient sleep is imperative for neurorehabilitation; therefore, disordered sleep should be corrected to maximise recovery. The standard treatment for disordered sleep is pharmacological intervention, and whilst this may be effective, research suggests that many medications prescribed for sleep disorders could impede neuronal repair, which may consequently slow recovery. Benzodiazepines and non-benzodiazepine hypnotics are commonly prescribed, but evidence suggests that melatonin agonists may be more suitable in this particular population. There is a growing body of literature to suggest that light therapy may be a viable non-pharmacological treatment of disordered sleep. In particular, blue light therapy has promising theoretical and evidentiary potential for treatment of sleep disorders in TBI patients. Combining the implementation of effective pharmacological and non-pharmacological treatment options has the potential to be the most effective solution for these disorders.

Keywords: sleep, brain injury, light therapy, blue light, traumatic brain injury.

Katie O’Brien: School of Biosciences and Medicine, Faculty of Health and Medical Sciences, University of Surrey. Sleep and Performance Research Center, Washington State University, Spokane, WA, USA. Email: ko00054@surrey.ac.uk

Copyright © 2017 Katie O’Brien; licensee SURJ. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercialShareAlike 4.0 International Licence.

ISSN: 2058-5551 (Online)
Introduction

There are a number of classifications for a brain injury, with a primary categorisation of traumatic or non-traumatic. A traumatic brain injury (TBI) is due to an external mechanical force causing a structural or functional abnormality within the brain. A non-traumatic brain injury (non-TBI) includes a variety of brain pathologies acquired after birth, rather than a congenital or genetic source, which would be classified as a defect. The non-TBI diagnosis includes stroke, meningitis, anoxia due to a cardiac event and brain tumours.

Traumatic brain injuries are highly prevalent in the US, being a leading cause of disability and death. It is estimated that 1.7 million people sustain a TBI annually, of which 52,000 die (Faul et al., 2010). This figure accounts for 30% of deaths caused by an injury.

A TBI can result in a variety of physical and cognitive deficits. A common, yet largely overlooked problem to arise after a TBI is the development of a sleep disorder. Over 50% of patients who have sustained a TBI are diagnosed with a sleep disorder in the weeks or months following a brain injury (Mathias et al., 2012). The limited research on sleep disorders in patients with acute TBI indicates that such disorders are common, with 68% of acute TBI patients displaying disrupted night time sleep (Makley et al., 2008).

The correction of abnormal sleep in acute care is imperative for the recovery of the patient. Not only does fatigue discourage participation in rehabilitation activities, but poor sleep quality inhibits the neural plasticity that is vital for neurorehabilitation and improvement of functional outcomes (Elbaz et al., 2017; Pekna et al., 2012). Moreover, lack of sleep induces a pro-inflammatory state in the brain, increasing the secretion of interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α) (Krueger, 2008). These cytokines may inhibit recovery by exacerbating inflammation in the brain that has arisen from the injury, thereby inhibiting recovery. Disrupted sleep may also impede therapeutic rehabilitation outcomes: one study demonstrated that TBI patients with a sleep-wake cycle disturbance had a mean length of stay in an inpatient rehabilitation facility of 22 days, whereas the mean length of stay for those without a sleep-wake cycle disturbance was only nine days (Makley, 2008).

Therefore, it is imperative to explore potential treatment options for disordered sleep in this patient population. Doing so would increase the likelihood of successful recovery and improve long-term functional outcomes. The objective of this review is to explore current literature regarding available
and potential treatment options for acute TBI patients with sleep disorders, with a particular focus on non-pharmaceutical methods. The data in this review will primarily focus on a US population.

**Disordered Sleep in Acute TBI Populations**

The majority of available literature addresses the prevalence of disordered sleep in populations who are several months post-TBI (Baumann *et al.*, 2007; Castriotta and Murthy, 2011; Mathias and Alvaro, 2012). Nonetheless, there is clear evidence of sleep-wake cycle disruption in acute TBI patients. The most accurate way to assess an individual’s sleep is through polysomnography (PSG), which records a subject’s brain waves during sleep, as well as other factors such as blood oxygen levels and heart rate. There is little PSG data available regarding patients with acute brain injuries, possibly due to the fact PSG requires access to a person’s scalp, which may not be possible with an acute head injury. However, one study (Wiseman-Hakes *et al.*, 2015) with acute TBI patients showed that, despite having a relatively normal sleep architecture, patients had fragmented sleep with low efficiency, indicative of poor sleep quality. These findings are supported by studies which use actigraphy, a wrist activity-based measure of sleep and wake times. One particular study (Makley *et al.*, 2008) determined that 68% of the acute TBI patients had fragmented sleep. Another study conducted by the same group determined that 78% of patients had severely reduced mean sleep efficiency (Makley *et al.*, 2009). Mean sleep efficiency is calculated from the ratio of inactivity to activity during normal sleeping hours. Normal sleep efficiency ranges from 85–95%; however, those 78% of subjects had a sleep efficiency of ≤65%. Furthermore, in a study with severe TBI patients (Nakase-Richardson *et al.*, 2013), 84% of patients had a sleep-wake disturbance upon admission to a rehabilitation facility.

While there is consensus that sleep-wake disturbances are prevalent in TBI patients, the types of sleep complaints are widely varied. Insomnia is the most commonly reported disturbance, with up to 50% of TBI patients presenting with this symptom (Ouellet *et al.*, 2015). Insomnia has also been noted in individuals whose TBI occurred as a result of a physical attack or warfare, suggesting that in some instances the sleep disorder may be of a psychological nature, rather than physiological. In these cases, the sleep-wake disturbance tends to arise after the patient is discharged from an acute care setting, as opposed to immediately after the injury.

Excessive daytime sleepiness is also commonly reported in TBI populations, with literature estimating its prevalence at 25–54% (Masel *et al.*, 2001; Verma *et al.*, 2007). This has been demonstrated through both subjective and objective measures, including the Epworth Sleepiness Scale (ESS) and the Multiple Sleep Latency Test (MSLT).
Circadian rhythm sleep disorders have also been noted in TBI patients. One such example is delayed sleep phase syndrome (DSPS), a circadian rhythm disorder in which sleep time is typically delayed by two or more hours later than a conventional bedtime (Sack et al., 2007). Another study in mild TBI patients noted DSPS, as well as a prevalence of irregular sleep-wake pattern (Ayalon et al., 2007); the sleep of these patients was fragmented throughout the day and night (Sack et al., 2007). One study found that fragmentation of sleep-wake cycles worsens as the severity of the sustained injury increases (Duclos et al., 2014). Perhaps most notably, TBI patients who were discharged from inpatient rehabilitation with less functional deficits experienced a more rapid resolution of their disordered sleep than those discharged with a higher level of disability.

These statistics demonstrate the range of sleep disorders diagnosed in TBI patients, all of which can significantly impact quality of life long after recovery from the primary brain injuries. This supports the need to investigate effective treatments for sleep disorders in TBI patients. In order to develop effective treatments, we need to ascertain why sleep disorders are so prevalent in this population.

**Physiology of Sleep-Wake Cycles**

In order to understand the sleep-wake disruptions in TBI patients, it is necessary to be aware of the underlying physiology. Whilst there are many biological processes regulating sleep, two key regulators of the sleep-wake cycle are the homeostatic sleep process and the circadian process (Borbély, 1982). Sleep-wake homeostasis is the physiological sleep drive, a process involving the accumulation of sleep-promoting neurotransmitters during a waking period. The circadian pacemaker originates in the suprachiasmatic nucleus (SCN) located in the anterior hypothalamus of the brain and regulates the timing of many biological processes that have a daily rhythm, such as sleep.

There are a number of physiological processes that are synchronised with the sleep-wake cycle. For example, core body temperature declines during sleep and cortisol levels are low during sleep but rise gradually in the early hours, peaking in the morning (Duffy et al., 2009). Melatonin is also a key circadian hormone, peaking nocturnally. Melatonin is produced by the pineal gland, which receives sympathetic input from the SCN. Unlike cortisol and core body temperature, which are controlled by endogenous processes, melatonin levels are greatly influenced by exogenous sources of light (Zeitzer et al., 2007). Light does not entrain the circadian system through the cone and rod photoreceptors in the eye, but rather through a distinct set of ganglion cells that project from the inner retinal layer through the retinohypothalamic tract to the SCN. Melatonin production
can be suppressed by light exposure, and more significantly, light exposure has been shown to phase shift the sleep-wake cycle (Czeisler et al., 2007; Shanahan et al., 1997). This suggests a relationship between physiological levels of melatonin and time of sleep onset, making melatonin an important hormone to investigate in relation to sleep disturbances.

**Sleep-Wake Pathophysiology in Patients with an Acquired Brain Injury**

The high prevalence of sleep disorders in those who have sustained a brain injury is likely due to a number of contributing factors. A possible cause of sleep disruption is a lesion on the brain, which may interrupt the communication between the SCN and its projections, such as the pineal gland. This interruption disrupts endocrine rhythms, and evidence suggests it also disrupts sleep-wake cycles due to altered melatonin levels. For example, research shows that individuals who have sustained a TBI had 42% less melatonin production in the evening than healthy individuals (Grima et al., 2016). Moreover, it has been noted that patients with spinal cord injuries resulting in tetraplegia (partial or total paralysis of the torso, arms and legs), demonstrated no melatonin rhythmicity, suggesting an interruption of sympathetic innervation of the pineal gland (Zeitzer et al., 2000).

Hypocretin-1 is a neurotransmitter that promotes wakefulness. 95% of patients who have sustained an acute TBI have been shown to have decreased levels of Hypocretin-1 in their cerebral spinal fluid (CSF) acutely following their injury (Baumann et al., 2005). Six months after the TBI, 15% of patients had sustained low CSF concentrations of Hypocretin-1. A chronic reduction in CSF Hypocretin-1 may have long-term effects on sleep as 72% of these patients with low Hypocretin-1 demonstrated symptoms of a sleep-wake disorder. This may be due to hypothalamic damage, as the hypothalamus is the primary area for secretion of Hypocretin-1 (Baumann et al., 2007).

It is also possible that the hospital environment is perpetuating disorders of sleep. Sleep consolidation is extremely difficult in a hospital environment; patients are likely to be woken multiple times in the night due to vital sign monitoring (Yoder et al., 2013), noise or being generally uncomfortable. This may lead to sleep deprivation and further skewing of patient sleep/wake times.

**Treatment of sleep disorders in TBI**

**Pharmaceutical Interventions**
Patients admitted to an acute care facility for treatment of a TBI are typically prescribed a variety of medications. There is currently little literature published that supports the efficacy of commonly prescribed sleep drugs in acute TBI patients. Most evidence is from the literature on healthy populations. In a study of 2,130 inpatients, 72% were prescribed narcotic analgesics, 67% antidepressants, 47% anticonvulsants, 33% anti-anxiolytics, 25% stimulants, 25% anti-parkinson agents and 18% miscellaneous psychotropics (Hammond et al., 2015). Due to the lack of evidentiary support in acute TBI populations, the United States Food and Drug Administration (FDA) have not approved any drugs specifically for the treatment of TBI and its associated sleep deficits. Essentially, all prescriptions in this population are off-label uses of the drugs. Whilst recovery of sleep is important, some sleep medications may actually worsen the cognitive and functional deficits of a brain injury, impeding recovery (Bhatnagar et al., 2016).

As previously mentioned, healthy sleep is essential for TBI rehabilitation. Sleep may be vital for maintenance of neurotransmitters, neuronal activation and neurogenesis (Holcomb et al., 2016). For example, in a rat model with induced cerebral ischaemia (Zunzunegui et al., 2011), sleep deprivation appeared to significantly reduce neural cell proliferation involved in healing, and caused a significant reduction in recovery of motor skills compared to non-sleep deprived rats. Further, while many medications are effective, they are not without considerable side effect profiles. One study found that 68% of TBI patients in an inpatient facility were prescribed benzodiazepines (Mysiw et al., 2006), an alarming statistic considering the growing literature discouraging the use of benzodiazepines in TBI populations (Flanagan et al., 2007; Rao et al., 2002; Schallert et al., 1986). Benzodiazepines have been documented to impede neuronal recovery, decrease coordination and impair memory (Larson et al., 2010).

More recently, non-benzodiazepine-hypnotics (Z-Drugs) such as Zolpidem have been prescribed to TBI patients for treatment of insomnia (Larson et al., 2010). Drugs in this class have fewer side effects and long-term consequences than benzodiazepines due to their shorter half-life, which makes them a more suitable choice in this patient population. Although cognitive impairment does not appear to occur in healthy populations taking Z-Drugs, it has been noted in elderly populations who are prescribed this class of drug (Scharf et al., 1994). One of the few studies to investigate the long-term use of Z-Drugs in TBI patients found that TBI patients with insomnia who took hypnotics had an increased risk of dementia compared to those who did not (Chiu et al., 2015). This is not an isolated piece of literature; previous studies have found this link in non-TBI populations with insomnia who were prescribed sedative-hypnotics (Gallacher et al., 2012) with a greater than two-fold increase in dementia risk (Chen et al., 2012).
Melatonin agonists are a more promising drug class. As previously mentioned, melatonin is a hormone produced by the pineal gland, with high plasma levels increasing the pressure for sleep. In both the US and the UK, melatonin has been classified as a dietary supplement and not a drug. In the US it is available without prescription. Its use in the UK is more complex: it has been banned from general sale as it has medicinal effects, but there is no license to sell it as a medicine, even though it is prescribed by a doctor. A synthetic melatonin agonist, Ramelteon, has been produced and is subject to regulation unlike its naturally-occurring counterpart. Ramelteon reduces the time it takes to fall asleep, while increasing total sleep time and quality of sleep (Kuriyama et al., 2014).

Unlike the benzodiazepines and Z-drugs, melatonin agonists only come with a very mild side-effect profile. Melatonin agonists do not have significant effects on other neurotransmitters, which is potentially why there are limited cognitive and psychomotor effects. These factors make it a more suitable option in a TBI population. A small study in TBI patients supported this (Lequerica et al., 2015), with patients showing significantly improved sleep characteristics and an improvement in neuropsychological test results. Unlike benzodiazepines, melatonin is also well-tolerated long-term (Pandi-Perumal et al., 2011; Uchiyama et al., 2011), making it more suitable in this patient population.

Modafinil has been investigated as a treatment for daytime fatigue, which is extremely common among TBI patients. In a small study with TBI patients recruited from a surgical intensive care unit, Modafinil was found to significantly improve excessive daytime sleepiness, but not post-traumatic fatigue (Kaiser et al., 2010). However, the study only had 20 participants: 10 received Modafinil and 10 received a placebo. The sample size may not have been sufficient, and a larger-scale study may be necessary to validate these findings. These findings are contrary to a larger study involving 53 TBI patients one year post-injury, which did not find any significant improvement in excessive daytime sleepiness between the Modafinil treatment and the placebo (Jha et al., 2008). Further research is needed to conclusively determine the efficacy of Modafinil in the treatment of daytime fatigue in TBI populations.

The current medications prescribed to treat sleep disorders in TBI patients carry the risk of impeding neuronal recovery, and display a potential risk regarding long-term neurological health. It is important that further research is conducted to identify treatments which carry the risk of reasonable and minimal side effects, and receive regulatory board approval for use in this population. Such treatments could lead to improved functional outcomes and reduced risk of developing other neurological diseases. The only treatment options for sleep disorders in this
population should not be off-label. With further research, drugs such as melatonin agonists have the potential to be a solution.

Taking into consideration the side effect profiles for a number of commonly prescribed sleep-inducing medications, an exploration of alternative options could be valuable. A non-pharmacological approach is a potential avenue of research to consider.

**Non-Pharmaceutical Interventions**

**Sleep Hygiene**

Basic sleep hygiene in the preliminary stages of sleep disturbances can be undertaken to improve insomnia. This approach is utilised in healthy populations, particularly those with shift work who are unable to sleep at the same time every day (Bajraktarov *et al.*, 2011). It is also recommended for hospital inpatients (Thaxton *et al.*, 2002) and, therefore, could be translated into the acute TBI patients. Improving sleep hygiene involves steps such as limiting caffeine and nicotine consumption, and reducing distractions in the sleeping environment. Chronotherapy can also be implemented for those with delayed sleep phase syndrome: it is the process of moving the person’s bed time and wake time earlier or later slowly over time, until the individual is on a normal sleep schedule (Bootzin *et al.*, 1992).

Sleep hygiene is key for improving the sleep-wake pattern in non-TBI populations. However, due to the nature of an inpatient acute care facility it may be difficult to ensure the necessary regime is followed in acute TBI populations. Regular nursing throughout the night limits consolidated sleep, and the hospital ward environment is disruptive and uncomfortable (e.g. IV lines and wires from ambulatory monitoring devices).

**Cognitive Behavioral Therapy**

Cognitive Behavioural Therapy (CBT) - a widely used psychosocial intervention for the treatment of mental disorders - helps the patient change how they perceive certain aspects of their life and the emotions attached to them (Ouellet *et al.*, 2007). CBT aids patients in identifying possible psychological reasons for poor sleep, and has been shown to successfully improve sleep quality (Maercker *et al.*, 2006). Post Traumatic Stress Disorder (PTSD) is a psychological disorder that includes symptoms such as intense fear, insomnia and nightmares. PTSD is commonly diagnosed as a result of warfare and car accidents (Maercker *et al.*, 2006; U.S. Department of Veterans Affairs, 2015), both of which are leading causes of TBI. Therefore, CBT may be particularly useful
in treating sleep disorders in TBI patients whose sleep disorder is a result of PTSD. It has also been proven to be effective in TBI populations directly. When implemented in TBI patients in an outpatient rehabilitation facility (Ouellet et al., 2007), CBT combined with good sleep hygiene and fatigue management led to 73% of the study population experiencing significant increase in total sleep time and increased sleep efficiency.

Whilst CBT has shown promise in TBI populations, its implementation into acute care may not be feasible. For example, patients may not be able to fully engage in CBT for weeks after their accident due to cognitive deficits, and by this point the patient could have already developed a sleep disorder. Further, patient daily schedules are typically full due to varying degrees and types of treatment, so the remaining time available for CBT may be limited.

**Bright Light Therapy**

As mentioned previously, bright light is capable of entraining circadian rhythms through activation of specialised ganglion cells in the retina. Current commercial light therapy devices such as the Litebook® ADVANTAGE are marketed as treatments for Seasonal Affective Disorder, with evidence supporting this usage (Rosenthal et al., 1984). Light therapy has also been investigated for treating depression (Perera et al., 2016) and symptoms of dementia (Hanford et al., 2013), as well as circadian rhythm disorders (Gooley, 2008).

Light therapy treatment must be administered at specific times of the day for it to be effective and produce the desired change in the sleep-wake cycle. The regular endogenous melatonin rhythm has highest concentrations at night when it is dark (Zeitzer, 2007). As light therapy suppresses melatonin production, it should be administered either prior to bed or shortly after waking, depending on the desired result. If a patient falls asleep too early in the day they may benefit from light treatment prior to their normal sleep time. This would delay their sleep time to a more appropriate one, due to a delay in dim light melatonin onset (DLMO), which is the most accurate marker for assessing the circadian pacemaker (Pandi-Perumal et al., 2007). In contrast, administering light early in the morning upon waking leads to an advancement in DLMO and a delay in the sleep-wake cycle. This treatment would be utilised in patients who go to sleep later than is desired (Hilaire et al., 2012). It is important to note that just 50–130 lux is capable of producing a half-maximal response in melatonin suppression, evoking a phase shift of 1.5 hours after 6.5 hours of exposure to bright light (Zeitzer et al., 2000). This is just 1% of the 10,000 lux illuminance typically used in bright light therapy such as the Litebook® ADVANTAGE.
Research to date has demonstrated the efficacy of bright light; however, it may not be the most suitable option in a brain-injured population. The typical dosage of bright light, of 10,000 lux may be aversive and agitating, heightened by the fact that a brain injury may increase sensitivity to light (Kapoor et al., 2002).

**Blue Light Therapy**

Blue light therapy is similar to bright light therapy, but it uses only the blue wavelengths of visible light rather than the whole spectrum. The ganglions that project to the SCN from the retina to suppress melatonin contain the photopigment melanopsin. Melanopsin is most sensitive to light of a wavelength of 450–500 nm, which corresponds to visible blue light (Thapan et al., 2001). Exposure to light of 460 nm (blue light) has been shown to suppress melatonin production, and in one particular study in healthy individuals caused a phase delay of melatonin rhythm of 2.58 hours when exposed for 6.5 hours (Lockley et al., 2003). This was compared with light of a wavelength of 555 nm (blue-green light), which produced a phase delay of 1.27 hours when also administered for 6.5 hours. Subjects in the blue light group also had significant plasma melatonin suppression of 65–96%. Thus, blue light could be a more targeted treatment than bright light therapy, and is more effective at suppressing melatonin production and consequently shifting sleep-wake cycles. This suggests that blue light does not need to be administered for as long as bright light to produce a similar phase delay. Therefore, blue light would be particularly useful in a rehabilitation setting where there are time constraints.

Blue light may prove to be superior to bright light when treating sleep-wake disorders in TBI patients because the intensity of the light is much lower than white light. Brain injured patients can be easily agitated, and intense light may exacerbate this symptom (Kapoor, 2002). Blue light devices generally do not surpass 200 lux (e.g. Phillips GoLite HF3429) in comparison to competing bright light devices (e.g. Litebook® ADVANTAGE), which emit up to 10,000 lux. The phase shift occurs at a much lower illuminance, making blue light superior in this particular population.

Blue light therapy has been investigated for efficacy in a range of sleep-disordered populations, including the elderly (Van Someren, 2000), those with dementia (Figueiro et al., 2015) and those with Delayed Sleep Phase Syndrome (Cole et al., 2002). All three studies concluded that blue light therapy lead to an improvement in sleep quality and schedule, and also mood and cognitive behavior in dementia populations. However, blue light therapy with TBI patients is a relatively new avenue of research, reflected by the small amount of literature available.
Most existing studies using blue light in TBI populations administer the light treatment several months after the injury. In one particular study (Sinclair et al., 2013), 30 post-acute TBI patients were enrolled. Subjects were randomised into three light conditions: blue light (n=10), yellow light (n=10) and no light intervention (n=10). After two weeks of 45-minute daily light exposure, patients completed a series of questionnaires and a psychomotor vigilance test (PVT), which is a simple serial reaction time test. Slower reaction times reflect worsening vigilant attention, which is associated with sleep loss and fatigue (Lim et al., 2008). The results indicated that those in the blue light treatment group showed a significant reduction in fatigue and daytime sleepiness compared to the control and yellow light groups. Yellow light produced a slight reduction in fatigue and daytime sleepiness compared with the control, but the effect size was much smaller than from blue light, based on a number of metrics.

Blue light therapy is, therefore, an important avenue of research to pursue. Light has the ability to alter melatonin levels without medication, directly influencing the circadian-driven process of the sleep-wake cycle. This is incredibly important because, whilst other non-pharmaceutical methods have shown promise, they may not have the direct physiological impact that light has. Medication has the advantage of producing direct physiological effects, but it is accompanied by a greater potential for side effects. The less agitating properties and shorter use times of blue light in comparison to bright light make it the more advantageous option to pursue in the future for patients receiving acute inpatient care following a TBI.

Problems with Data Collection and Study Design

A barrier to treating sleep disorders in the acute TBI populations is the identification of patients with sleep problems. Patients with acute brain injuries often have difficulty with their cognitive ability and may not be able to process information in the same way that healthy sleep-disturbed populations can. Therefore, they may not be able to communicate what they are experiencing, such as difficulty falling asleep. Additionally, this population may have difficulty in accurately understanding and completing questionnaires to aid in identifying these symptoms, such as the Karolinska Sleepiness Scale and the Fatigue Severity Scale. This is because these are subjective measures; the patient must be able to understand how they are feeling to accurately answer them. Answers to these questionnaires may also be inconsistent as the patient may be more lucid one day compared to another. This could be a real problem considering that subjective responses from healthy, lucid sleep-restricted populations may not reflect objective levels of fatigue. The possibility of this occurring has been demonstrated in a chronic sleep restriction study. It showed that while the number of PVT lapses increased, subjective fatigue scores remained relatively consistent (Van
Dongen et al., 2003), which suggests that the subjects were not aware of how mentally fatigued they were. This raises the question of whether or not subjective sleep measures are reliable enough to detect sleep disorders in this population. Future studies may want to ensure that objective sleep measures such as actigraphy and/or polysomnography supplement the subjective questionnaires.

Moreover, sleep disorder prevalence figures in TBI patients appeared to range drastically from 23% to 70% (Castriotta et al., 2011). This is due to the selection criteria differing between studies. For example, one particular study recruited participants because they were referred to a sleep lab with suspected sleep disorders, showing evidence of bias in sample selection (Holcomb et al., 2016). Such a bias in sample selection would cause disordered sleep prevalence to be much higher than from a randomised study of post-acute populations. The discrepancies in data are also likely to result from the variation in assessment tools. Some studies rely solely on subjective sleep measures such as questionnaires (Nakase-Richardson et al., 2013), whereas others use both objective and subjective sleep measures (Makley, 2008), which would theoretically be more accurate. Additionally, there are a large number of variables within TBI populations, including the type of injury, prescribed medication, patient age and gender. To account for this, sample sizes need to be large. However, many of these studies have very small sample sizes, with some having as little as ten patients (Parcell et al., 2008). Additionally, participants in acute TBI studies are often withdrawn from participation due to being readmitted to an intensive care unit (Hammond et al., 2015; Makley, 2009). This demonstrates that recruitment for these studies is difficult, which is a reasonable explanation for small sample sizes.

Conclusions

Whilst it is clear that disrupted sleep is prominent among brain injured populations, in acute care there are more pressing conditions for which treatment is focused. The majority of TBI patients are admitted with life-threatening injuries, at risk of acquiring long-term cognitive and functional deficits. In these instances, the medical care is targeted towards more urgent matters such as controlling cerebral hemorrhage, monitoring intracranial pressure or extensive physical and cognitive rehabilitation to improve long-term functional outcomes. However, this approach needs to be reconsidered; more evidence is accumulating which links poor sleep to impedance of neuronal recovery. This prompts the need to view sleep disturbances as an important symptom that requires correction to aid in optimal rehabilitation of a TBI.
Many common treatments for sleep disorders in TBI patients lack conclusive evidentiary support and may potentially be detrimental to neurorehabilitation. Evidence to date suggests that melatonin agonists are a potential pharmacological treatment option. They do not appear to alter the action of neurotransmitters in the brain, which is possibly why they have a mild side effect profile. Moreover, evidence also suggests that blue light therapy is an effective method of synchronising the biological clock with minimal to no side effects.

This raises the question of whether future treatment regimens should combine pharmacological and non-pharmacological options in order to more efficiently treat disordered sleep in acute TBI patients, whilst minimising side effects. The future direction of this research should be larger scale studies, both for determining the prevalence of sleep disorders in acute TBI populations and the efficacy of pharmacological and non-pharmacological treatments, such as blue light therapy.

**Acknowledgements**

I would like to thank Dr. Kimberly Honn, Ph.D. and Ms. Amy Sparrow, M.S. of the Sleep and Performance Research Center, Washington State University, for reviewing drafts of my article prior to submission.
References


U.S. Department of Veterans Affairs. (2015) How Common is PTSD? - PTSD: National Center for PTSD. Available at: http://www ptsd va gov/public/ PTSD overview/basics/how common is-


